COVER PAGE

Title of Proposal: The Human Brain Project - Framework Partnership Agreement (HBP-FPA)

P No.	Name of Partner Organisation	Short Name	Country
1	École Polytechnique Fédérale de Lausanne	EPFL	CH
2	Aalto-korkeakoulusäätiö	AALTO	FI
3	Academisch Ziekenhuis Leiden - Leids Universitair Medisch Centrum	LUMC	NL
4	Athens University of Economics and Business	AUEB	GR
5	Barcelona Supercomputing Center - Centro Nacional de Supercomputacion	BSC	ES
6	Bauhaus University Weimar	BAUW	DE
7	Bergische Universität Wuppertal	BUW	DE
8	Bloomfield Science Museum Jerusalem	BSMJ	IL
9	Cardiff University	CF	GB
10	Centre National de la Recherche Scientifique	CNRS	FR
11	Commissariat a l'énergie atomique et aux énergies alternatives	CEA	FR
12	Consiglio Nazionale delle Ricerche	CNR	IT
13	Consorzio Interuniversitario Cineca	CINECA	IT
14	Danmarks Tekniske Universitet	DTU	DK
15	Debreceni Egyetem	UoD	HU
16	De Montfort University	DMU	GB
17	École Normale Supérieure	ENS	FR
18	Eidgenössische Technische Hochschule Zürich	ETHZ	CH
19	Fonden Teknologirådet	FT	DK
20	Forschungszentrum Jülich GmbH	JUELICH	DE
21	Fortiss Gmbh	FORTISS	DE
22	Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V.	FG	DE
23	Fundacao D. Anna Sommer Champalimaud E Dr. Carlos Montez Champalimaud	FCHAMP	PT
24	Heinrich Heine Universität Düsseldorf	UDUS	DE
25	Helsingin yliopisto	UH	FI
26	HITS gGmbH	HITS	DE
27	Hospices Cantonaux, Centre Hospitalier Universitaire Vaudois	CHUV	CH
28	Imperial College of Science, Technology and Medicine	ICL	GB
29	Institut de Cerveau et de la Moelle Épinière	ICM	FR
30	Institute of Experimental Medicine, Hungarian Academy of Sciences	IEM HAS	HU
31	Institute of Science and Technology Austria	IST	AT
32	Institut Jozef Stefan	JSI	SI
33	Institut National de Recherche en Informatique et en Automatique	INRIA	FR
34	Institut Pasteur	IP	FR
35	Johann Wolfgang Goethe Universität Frankfurt am Main	UFRA	DE
36	Karlsruher Institut für Technologie	KIT	DE
37	Karolinska Institutet	KI	SE
38	King's College London	KCL	GB
39	Kungliga Tekniska Hoegskolan	KTH	SE
40	Laboratorio Europeo di Spettroscopie Non Lineari	LENS	IT
41	Linneuniversitetet	LNU	SE
42	Medizinische Universität Innsbruck	MUI	AT
43	Ethniko Kai Kapodistriako Panepistimio Athinon	UoA	GR

44	Norges miljø- og biovitenskapelige universitet	NMBU	NO
45	Österreichische Studiengesellschaft für Kybernetik	OFAI	AT
46	Rheinisch-Westfälische Technische Hochschule Aachen	RWTH	DE
47	Ruprecht-Karls-Universität Heidelberg	UHEI	DE
48	Sabancı Üniversitesi	SU	TR
49	Scuola Superiore di Studi Universitari e di Perfezionamento Sant'Anna	SSSA	IT
50	Centrum voor Wiskunde en Informatica	CWI	NL
51	Stichting Katholieke Universiteit	SKU	NL
52	Stiftung FZI Forschungszentrum Informatik am Karlsruher Institut für Technologie	FZI	DE
53	Technical University of Crete	TUC	GR
54	Technische Universität Dresden	TUD	DE
55	Technische Universität Graz	TUGRAZ	AT
56	Technische Universität München	TUM	DE
57	Tel Aviv University	TAU	IL
58	(blank)		
59	The Chancellor, Masters and Scholars of the University of Oxford	UOXF	GB
60	The Hebrew University of Jerusalem	HUJI	IL
61	The University Court of the University of Aberdeen	UABER	GB
62	University of Edinburgh	UEDIN	GB
63	University of Manchester	UMAN	GB
64	Universidad Autonoma de Madrid	UAM	ES
65	Universidad de Castilla - La Mancha	UCLM	ES
66	Universidad de Granada	UGR	ES
67	Universidade Do Minho	UMIHNO	PT
68	Universidad Politécnica de Madrid	UPM	ES
69	Universidad Rey Juan Carlos	URJC	ES
70	Universita degli Studi di Pavia	UNIPV	IT
71	Universität Bern	UBERN	CH
72	Universität Bielefeld	UNIBI	DE
73	Universitätsklinikum Aachen	UKAACHEN	DE
74	Universitätsklinikum Hamburg-Eppendorf	UKE	DE
75	Universität Zürich	UZH	CH
76	Universitat de Barcelona	UB	ES
77	Universitat Pompeu Fabra	UPF	ES
78	Université d'Aix Marseille	AMU	FR
79	Université Victor Segalen Bordeaux II	UBO	FR
80	Universiteit Antwerpen	UA	BE
81	Universitetet i Oslo	UiO	NO
82	University College London	UCL	GB
83	Uppsala Universitet	UU	SE
84	Weizmann Institute of Science	WEIZMANN	IL
85	Technische Universität Darmstadt	TUDA	DE
86	Université de Genève	UNIGE	CH
87	Consorci Institut d'Investigacions Biomediques August Pi i Sunyer	IDIBAPS	ES
88	Fundacio Institut de Bioenginyeria de Catalunya	IBEC	ES
89	Deutsches Zentrum fuer Neurodegenerative Erkrankungen EV	DZNE	DE
90	Humboldt-Universitaet zu Berlin	UBER	DE

91	Istituto Nazionale di Fisica Nucleare	INFN	IT
92	Istituto Superiore di Sanità	ISS	IT
93	Koninklijke Nederlandse Akademie van Wetenschappen - Knaw	KNAW	NL
94	Medical Research Council	MRC	GB
95	Universita Degli Studi Di Milano	UMIL	IT
96	Université de Liege	ULG	BE
97	Universiteit van Amsterdam	UvA	NL
98	University of Glasgow	UGLA	GB
99	University of Hamburg	UHAM	DE
100	University of Sheffield	USFD	GB
101	University of the West of England, Bristol	UWE	GB
102	University of Surrey	SURREY	GB
103	TTY-Saatio	TUT	FI
104	University of Leeds	ULEEDS	UK
105	Université Pierre et Marie Curie - Paris 6	UPMC	FR
106	University of Sussex	UoS	UK
107	Middlesex University Higher Education Corporation	MU	GB
108	Université Lyon 1 Claude Bernard	UCBL	FR
109	Politecnico di Torino	POLITO	IT
110	Universiteit Gent	UGENT	BE
111	Katholieke Universiteit Leuven	KUL	BE
112	Universitaet Basel	UNIBAS	CH
113	Stichting VU-VUmc	VU	NL
114	Institut Suisse de Bioinformatiquefondation ISB	SIB	CH
115	European Brain Research Institute Rita Levi-Montalcini Fondazione*EBRI	EBRI	IT
116	Scuola Normale Superiore	SNS	IT
117	Universiteit Maastricht	UM	NL

Table 1: List of Partners in HBP Core Project at start of the FPA

Table of Contents

2.1 Excellence 9
2.1.0 Background and Context 9
2.1.1 Concept and Objectives 9
2.2 Impact 24
2.2.1 Expected Impact 24
2.2.2 Measures to maximise impact 29
2.3 Implementation 51
2.3.1 Work Plan 51
2.3.2 Management structures and procedures 77
2.3.3 Planned use of resources 110
2.4 Consortium 121
2.4.1 Consortium as a whole 121
2.4.2 Capacity of participants and links to third parties 127
2.5 Responsible Research and Innovation 128
2.5.1 Ethics Issues and Related Measures 128
2.5.2 Coverage of EC Ethics Requirements 143
Appendix 1: Overview of the Flagship Objectives and Strategic Research Roadmap .. 149
A1.1 Concept and Strategy 149
A1.2 Flagship Objectives (FOs) 151

A1.3. Research Roadmap 152
A1.4 Subproject 1: Mouse Brain Organisation 154
A1.4.1 SP1: General Objectives 154
A1.4.2 SP1: State of the Art 156
A1.4.3 SP1: Advances over State of the Art 157
A1.4.4 SP1: Operational Objectives 158
A1.4.5 SP1: Main Objectives / Deliverables per SGA 159
A1.4.6 SP1: Collaborations with other National, European and International Initiatives 160
A1.4.7 SP1: Impact and Innovation Potential 160
A1.5 Subproject 2: Human Brain Organisation 161
A1.5.1 SP2: General Objectives 161
A1.5.2 SP2: State of the Art 162
A1.5.3 SP2: Advances over State of the Art 163
A1.5.4 SP2: Operational Objectives 164
A1.5.5 SP2: Main Objectives / Deliverables per SGA 166
A1.5.6 SP2: Collaborations with other National, European and International Initiatives 166
A1.5.7 SP2: Impact and Innovation Potential 167
A1.6 Subproject 3: Systems and Cognitive Neuroscience 167
A1.6.1 SP3: General Objectives 168
A1.6.2 SP3: State of the Art and Advances over the State of the Art 168
A1.6.3 SP3: Operational Objectives 171
A1.6.4 SP3: Main Objectives / Deliverables per SGA 174
A1.6.5 SP3: Collaborations with other National, European and international Initiatives 174
A1.6.6 SP3: Impact and Innovation Potential 174
A1.7 Subproject 4: Theoretical Neuroscience 175
A1.7.1 SP4: General Objectives 176
A1.7.2 SP4: State of the Art 176
A1.7.3 SP4: Advances over the State of the Art 176
A1.7.4 SP4: Operational Objectives 177
A1.7.5 SP4: Main Objectives / Deliverables per SGA 177
A1.7.6 SP4: Impact and Innovation Potential 178
A1.8 Subproject 5: Neuroinformatics Platform 178
A1.8.1 SP5: General Objectives 178
A1.8.2 SP5: State of the Art 178
A1.8.3 SP5: Advances Beyond the State of the Art 179
A1.8.4 SP5: Operational Objectives 179
A1.8.5 SP5: Main Objectives / Deliverables per SGA 181
A1.8.6 SP5: Collaborations with other National, European and International Initiatives 182
A1.8.7 SP5: Impact and Innovation Potential 182
A1.9 Subproject 6: Brain Simulation Platform 182
A1.9.1 SP6: General Objectives 182
A1.9.2 SP6: State of the Art 183
A1.9.3 SP6: Advances over the State of the Art 184
A1.9.4 SP6: Operational Objectives 184
A1.9.5 SP6: Main Objectives / Deliverables per SGA 186
A1.9.6 SP6: Collaborations with other National, European and International Initiatives 187
A1.9.7 SP6: Impact and Innovation Potential 187
A1.10 Subproject 7: High-Performance Analytics & Computing Platform 188
A1.10.1 SP7: General Objectives 188
A1.10.2 SP7: State of the Art 189
A1.10.3 SP7: Advances over State of the Art 190
A1.10.4 SP7: Operational Objectives 191
A1.10.5 SP7: Main Objectives / Deliverables per SGA 192
A1.10.6 SP7: Collaborations with other National, European and International Initiatives 193
A1.10.7 Impact and Innovation Potential 193
A1.11 Subproject 8: Medical informatics Platform 194
A1.11.1 SP8: General Objectives 194
A1.11.2 SP8: State of the Art 194
A1.11.3 SP8: Advances over State of the Art 195
A1.11.4 SP8: Operational Objectives 195

A1.11.5 SP8: Main Objectives / Deliverables per SGA 196
A1.11.6 SP8: Collaborations with other National, European and International Initiatives.... 197
A1.11.7 SP8: Impact and Innovation Potential 197
A1.12 Subproject 9: Neuromorphic Computing Platform 198
A1.12.1 SP9: General Objectives 198
A1.12.2 SP9: State of the Art 199
A1.12.3 SP9: Advances over State of the Art 200
A1.12.4 SP9: Operational Objectives and Related Actions 201
A1.12.5 SP9: Main Objectives / Deliverables, per SGA 203
A1.12.6 SP9: Collaboration with other National, European and International Initiatives..... 204
A1.12.7 SP9: Impact and Innovation Potential 204
A1.13 Subproject 10: Neurorobotics Platform 204
A1.13.1 SP10: General Objectives 204
A1.13.2 SP10: State of the Art 205
A1.13.3 SP10: Advances over the State of the Art 206
A1.13.4 SP10: Operational Objectives 206
A1.13.5 SP10: Main Objectives / Deliverables per SGA 208
A1.13.6 SP10: Collaborations with National, Regional, European and International Projects and Initiatives 209
A1.13.7 SP10: Impact and Innovation 209
A1.14 Subproject 12: Ethics and Society 210
A1.14.1 SP12: General and Operational Objectives 210
A1.14.2 SP12: State of the Art 210
A1.14.3 SP12: Advances over State of the Art 212
A1.14.4 SP12: Operational Objectives and Related Actions 213
A1.14.5 SP12: Main Objectives & Deliverables per SGA 214
A1.14.6 SP12: Collaborations with other National, European and International Initiatives .. 214
A1.14.7 SP12: Impact and Innovation Potential 215
A1.15 Integration of Core and Partnering Projects 215

Appendix 2: Partnering with the Human Brain Project Flagship 217
A2.1 An Introduction to HBP Partnering Projects 217
A2.2 Current HBP priorities for Partnering Projects 218
A.2.3 What are Partnering Projects and Associated Members? 218
A2.3.1 Partnering Projects 218
A2.3.2 Associated Members 218
A2.4 What are the eligibility requirements for becoming PPs and AMs? 219
A2.5 What are the selection criteria and procedures of PPs/AMs? 219
A2.6 What are the nomination, application and selection procedures for Partnering Projects? 219
A2.6.1 Application procedures 220
A2.6.2 Selection Procedure 220
A2.7 How will Partnering Projects and Associated Members be integrated into the Flagship? 221
A2.8 Potential Research Areas for Partnering Projects 222
A2.8.1 SP1: Mouse Brain Organisation 222
A2.8.2 SP2: Human Brain Organisation 223
A2.8.3 SP3: Systems and Cognitive Neuroscience 223
A2.8.4 SP4: Theoretical Neuroscience 224
A2.8.5 SP5: Neuroinformatics Platform 224
A2.8.6 SP6: Brain Simulation Platform 224
A2.8.7 SP7: High-Performance Analytics & Computing Platform 225
A2.8.8 SP8: Medical Informatics Platform 225
A2.8.9 SP9: Neuromorphic Computing Platform 226
A2.8.10 SP10: Neurorobotics Platform 226
A2.8.11 SP11: Central Services 226
A2.8.12 SP12: Ethics and Society 226

Appendix 3: White Paper "Transforming the Human Brain Project Platforms into a Community-Driven Infrastructure for Brain Research 228
A3.1 Preamble 228
A3.2 Background and Significance 228

A3.3 The Need for a Neuroscience-Driven Research Infrastructure 229
A3.4 Structuring HBP Information Technology 230
A3.5 Roadmap for HBP Research Infrastructure 232
A3.5.1 Base Infrastructure 233
A3.5.2 Software Infrastructure 235
A3.6 Project Management Structure 237
A3.8 Next steps (work in progress) 238
A3.9 References 238
A3.10 Attachments 239
A3.10.1 URIS WG Decision Proposal Passed by the HBP BoD on 28 April 2015 239
A3.10.2 Technology Readiness Levels taken from [5] 239
Appendix 4: Community Engagement 241
Appendix 5: HBP Core Project Partner Details 243
Appendix 6: Consortium Partners' HBP Third Parties 353
Appendix 7: Critical Infrastructure for the HBP 366
Appendix 8: Risk Detection & Mitigation 370
Appendix 9: Glossary 371
Appendix 9: References 378

List of Figures

Figure 1: HBP Flagship Components 11
Figure 2: HBP Activity Clusters: Scientific Research, Software Development & Infrastructure Operations . 14
Figure 3: The Innovation Team 44
Figure 4: The HBP Legal Entity Phase Governance Structure 82
Figure 5: The HBP Interim Phase Governance Structure 90
Figure 6: Software, Service or Data Development lifecycle 94
Figure 7: Mapping to Technology Readiness Levels 96
Figure 8: Data deliveries from data projects 97
Figure 9: Graphical overview of the current content of the HBP Ethics Map 139
Figure 10: Relationship between the operational objectives of SP10 Neurorobotics Platform 207
Figure 11: Relationship between the ICT infrastructure "Platforms" developed in the HBP. 231
Figure 12: Timeline of the base infrastructure for the HBP 235
Figure 13: Structure of the different service components in the Research Infrastructure. 236
Figure 14: Community Engagement "Funnel" 241
Figure 15: Project Lifecycle Framework problem detection strategies 370
Figure 16: Project Lifecycle Framework mitigation strategies 370

List of Tables

Table 1: List of Partners in HBP Core Project at start of the FPA 3
Table 2: Structure of the different service components in the Research Infrastructure. 19
Table 3: Timeframe for Implementation of HBP Innovation Support Activities 47
Table 4: Main Objectives / Deliverables per SGA for SP1: Mouse Brain Organisation 54
Table 5: Main Objectives / Deliverables per SGA for SP2: Human Brain Organisation 57
Table 6: Main Objectives / Deliverables per SGA* for SP3: Systems and Cognitive Neuroscience 61
Table 7: Main Objectives / Deliverables per SGA for SP4: Theoretical Neuroscience 62
Table 8: Main Objectives / Deliverables per SGA for SP5: Neuroinformatics 65
Table 9: Main Objectives / Deliverables per SGA for SP6: Brain Simulation Platform 67
Table 10: Main Objectives / Deliverables per SGA for SP7: High-Performance Analytics & Computing Platform 69
Table 11: Main Objectives / Deliverables per SGA for SP8: Medical Informatics Platform 71
Table 12: Main Objectives / Deliverables per SGA for SP9: Neuromorphic Computing Platform (NM) 73
Table 13: Main Objectives / Deliverables per SGA for SP10: Neurorobotics Platform 75
Table 14: Main Objectives / Deliverables per SGA for SP11: Central Services 76
Table 15: Main Objectives / Deliverables per SGA for SP12: Ethics and Society 77
Table 16: Technology Readiness Levels (TRLs) 93
Table 17: Data Accessibility Criteria 98
Table 18: HBP Key Performance Indicators (KPIs) 101
Table 19: Risks and Contingency Plans 108
Table 20: Human, major equipment and research facility resources available by Partners. 117
Table 21: Estimated additional financial resources available to Partners in the Consortium at national, European and international levels. 120
Table 22: Partners' expertise and experience for implementing the Work Plan. 124
Table 23: Number of beneficiaries in each Subproject, by country 124
Table 24: Overview of the HBP Ethics Map 138
Table 25: HBP's EU Research Ethics Questionnaire 142
Table 26: HBP FPA - Ethics Issues and Requirement Descriptions 148
Table 27: Main Objectives / Deliverables per SGA for SP1: Mouse Brain Organisation 160
Table 28: Main Objectives / Deliverables per SGA for SP2: Human Brain Organisation 166
Table 29: Main Objectives / Deliverables per SGA* for SP3: Systems and Cognitive Neuroscience 174
Table 30: Main Objectives / Deliverables per SGA for SP4: Theoretical Neuroscience 177
Table 31: Main Objectives / Deliverables per SGA for SP5: Neuroinformatics 182
Table 32: Main Objectives / Deliverables per SGA for SP6: Brain Simulation Platform 187
Table 33: Main Objectives / Deliverables per SGA for SP7: High-Performance Analytics & Computing Platform 193
Table 34: Main Objectives / Deliverables per SGA for SP8: Medical Informatics Platform 197

Table 35: Development roadmap for Physical Model Neuromorphic Computing Systems (PM-NCS)..... 201
Table 36: Development Roadmap for Many Core Neuromorphic Computing Systems (MC-MCS)..... 201
Table 37: Main Objectives / Deliverables per SGA for SP9: Neuromorphic Computing Platform (NM) 203
Table 38: Main Objectives / Deliverables per SGA for SP10: Neurorobotics Platform..... 209
Table 39: Main Objectives / Deliverables per SGA for SP12: Ethics & Society 214
Table 40: Benefits of Participating in the HBP as a Partnering Project 222
Table 41: Overview of the HBP Timeline, RI Development and Adoption Cycle. 233
Table 42: HBP Core Project Partners' Third Parties 365
Table 43: HBP Core Project Partners' Key Infrastructure Contributions 369

Part B (Narrative) of Annex 1 to the Human Brain Project's Framework Partnership Agreement

2.1 Excellence

2.1.0 Background and Context

The EC Staff Working Document on FET Flagships (September 2014) states that: "In October 2013, after a preparatory period of three years, the Commission launched through its FET scheme two FET Flagships, Graphene and the Human Brain Project (HBP). Each of them is implemented initially as an FP7 project preparing the ground for what will be a new kind of partnership. In complement to these two projects, the Commission has also launched a coordination action bringing together Member States (MS) to jointly define and implement activities and finance projects in support of the Flagships. These two Flagships are the result of a Communication adopted in April 2009, in which the Commission stressed the need for Europe to address grand scientific challenges through sufficiently long-term multi-disciplinary research initiatives, termed FET Flagships." The implementation modalities for the FET Flagships are set out in the same EC Staff Working Document.

As the EC Work Programme states: "The objective is to establish, for each of the FET Flagships, a stable and structured partnership between the EC and the institutions and organisations who commit themselves to establish, maintain and implement the strategic research roadmap of the flagship. These partnerships will be set up through a Framework Partnership Agreement (FPA) which will cover the full initiative in order to enable completion of the research roadmap within the context of the agreement."

This document is the narrative part of the Action Plan for the HBP FPA.

As the HBP does not yet have its own legal entity, agreements should be subject to the involved Partners' approval in accordance with their institutional rules, unless otherwise agreed.

2.1.1 Concept and Objectives

2.1.1.1 Concept

Understanding the human brain is one of the greatest challenges facing 21st century science. If we can rise to it, we can gain profound insights into what makes us human, build revolutionary computing technologies and develop new treatments for brain disorders. Today, for the first time, modern ICT has brought these goals within reach.

The HBP will put in place a **cutting-edge ICT-based scientific research infrastructure**, that will permit scientific and industrial researchers to advance our knowledge in the fields of neuroscience, computing and brain-related medicine.

Neuroscience is generating exponentially growing volumes of data and knowledge on specific aspects of the healthy and diseased brain, of different ages and genders, and belonging to a broad range of species. However, we still do not have effective strategies to experimentally map the brain across all its levels and functions, and to link such information across the different spatial and temporal scales. Modern supercomputing and data analytics technologies make it possible — for the first time — to integrate these data in detailed reconstructions and simulations. These new methods allow researchers not only to analyse big data, reflecting brain organization with unprecedented detail, but also to predict missing data and principles, and enable measurements and experimental manipulation that would be ethically or technically impossible in animals or humans. New

in silico neuroscience has the potential to reveal the detailed mechanisms leading from genes to cells and circuits, and ultimately to cognition and behaviour – the biology that makes us human.

Computing can be similarly transformed. The human brain performs information processing tasks that are inaccessible to the most powerful of today's computers - all while consuming no more power than a light bulb. Understanding how the brain "computes" reliably with unreliable elements, and how different elements of the brain communicate, can provide the key to a completely new category of hardware (Neuromorphic Computing Systems) and to a paradigm shift for computing as a whole. What is more, neuroscience will be a driver for more powerful and highly interactive computing systems as well as innovative visualization technologies. The economic and industrial impact is potentially enormous.

Medicine is experiencing a data explosion driven by advances in genetics and imaging. But again, we lack effective strategies to integrate the data, while safeguarding the privacy of patient data. New database and data mining technologies offer a solution, making it possible to federate and analyse the data accumulating in hospital archives, without moving it to central storage, allowing researchers to identify the biological changes associated with disease ("biological signatures of disease") and opening possibilities for early diagnosis and personalised medicine. In the longer term, the data will make it possible to modify models of the healthy brain to simulate disease. Disease simulation will provide researchers with a powerful new tool to probe the causes of neurological and psychiatric disease, and to screen putative treatments. Disease and drug simulation has the potential to accelerate medical research, reducing the huge economic and social burden of brain disease.

The goal of the Human Brain Project is to translate these prospects into reality, building a scientific research infrastructure to catalyse a global collaborative effort to integrate neuroscience data from around the world, to understand the human brain and its diseases, and ultimately to emulate its computational capabilities.

2.1.1.2 HBP Flagship Components

The HBP Flagship brings together a number of different elements:

- The Funders: the European Commission, Member and Associated States, and other countries
- The Project Partners: the Partners and their institutional organisations participating in the HBP Core Project (see Appendix 5: HBP Core Project Partner Details) and the HBP Partnering Projects (see Appendix 2: Partnering with the Human Brain Project Flagship). They bring the knowledge and skills, as well as the data and computational infrastructural support that the HBP needs.
- The HBP Legal Entity (see section 2.3.2.4).
- The Activities: The HBP builds the Research Infrastructure and performs related Scientific Research

How these elements fit together and who does what is shown in the figure below.

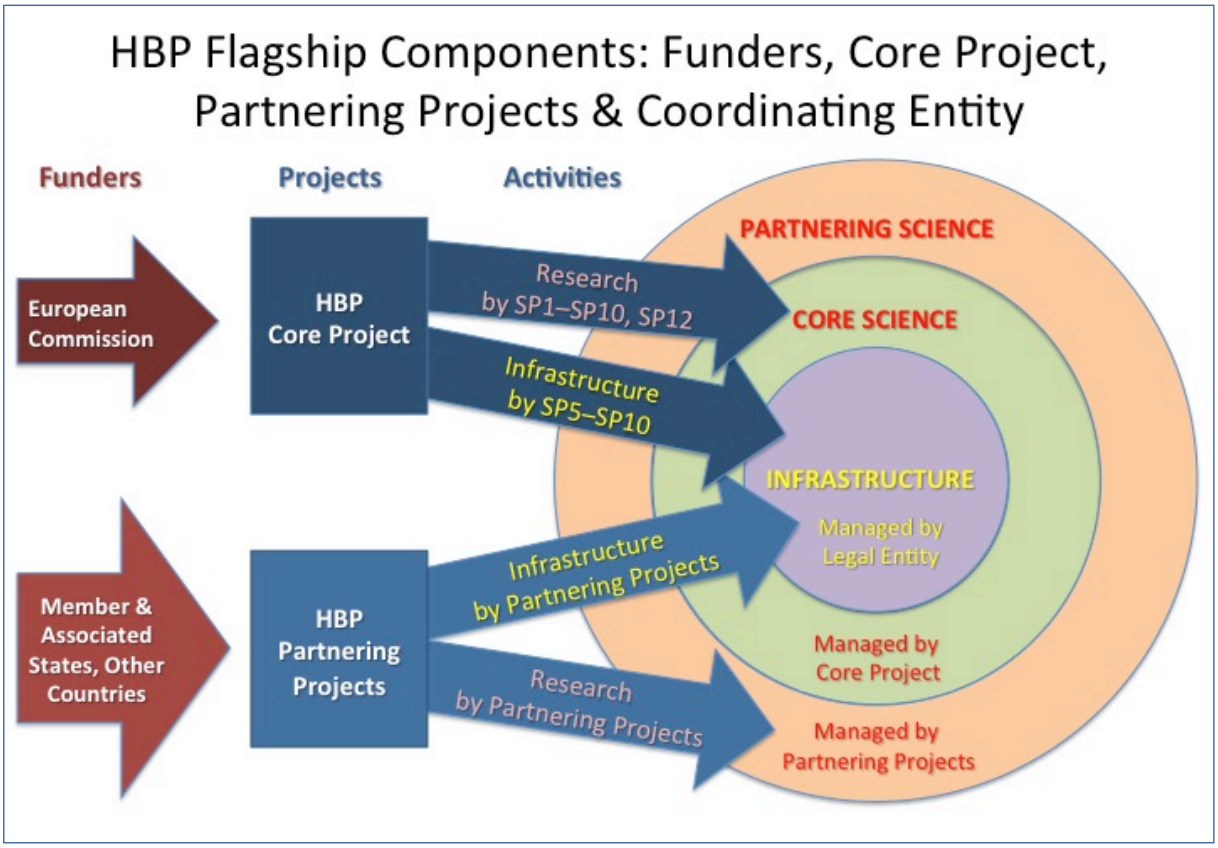

Figure 1: HBP Flagship Components

2.1.1.3 The Core Project and the Partnering Projects

After the current Ramp-Up Phase of the HBP, the HBP's goals will be pursued through a Core Project (CP), and Partnering Projects (PPs), which together constitute the HBP Flagship Initiative. The Core Project and the Partnering Projects are equally essential to achieving the strategic goals of the Flagship Initiative.

- The Core Project, funded by the FET Flagship Programme, will build and operate an integrated research infrastructure, comprising six ICT Platforms. These will enable the scientific community to perform radically new kinds of research in neuroscience, computing and medicine. The CP will be articulated in several (probably three) phases, each regulated by a Specific Grant Agreement between the Partners and the European Commission.
- The Partnering Projects, funded from regional, national, European, international and other sources (e.g., private industry, donors), will develop new ideas, approaches and technologies proposed by independent research groups. PPs will perform research that uses the HBP research infrastructure to address previously intractable issues in neuroscience and that adds novel capabilities to its Platforms; develop novel computing technologies and applications; and improve understanding, diagnosis and treatment of brain disorders. In close collaboration with the Funders, the HBP Core Project partners will select PPs through clear, fair and transparent processes, ensuring maximal scientific excellence and fit with the HBP, working in close coordination with funding agencies and other organisations supporting the projects.

2.1.1.3.1 *Why some objectives are in the FPA and others outside (Core & Partnering Projects)*

The Core Project (CP) will be responsible for executing a detailed plan of tightly coordinated research and development, critical to building and operating the HBP Research Infrastructure and for the overall governance and coordination of the Flagship Initiative. In addition to research, addressing fundamental challenges in neuroscience, computing and medicine, the responsibilities of the CP include scientific coordination, communication and dissemination, education, promotion of innovation and industry collaboration, citizen engagement, and other activities to promote and enforce the Consortium's policy of Responsible Research Innovation.

Criteria for participation in the Core Project:

- Research and development critical for building and operating the HBP Research Infrastructure.
- Research and development that is unique and unlikely to receive funding from other sources (e.g., generation, aggregation, curation, and integration of data into models as a community resource, tool building, developing and operating the Research Infrastructure as a service to the scientific community).
- Research and development whose primary goal is to translate cutting-edge science into novel technologies and services for the scientific community.
- Research that requires tight integration with work by other researchers and teams across multiple disciplines.

Partnering Projects (PPs) will develop new ideas, approaches and technologies, proposed by independent research groups. Partnering Projects will add novel capabilities to the Platforms and use the Platforms to address questions far beyond the capabilities of any individual laboratory. The PPs will also bring the funds needed to operate and maintain the Research Infrastructure.

Criteria for participation in the Partnering Projects:

- Research that provides capabilities to the Platforms, beyond those developed by the Core Project, and which can further open it up to the broader scientific community.
- Scientifically excellent research that can only be performed using the HBP Platforms.
- Research that has won or is likely to win funding through the competitive selection processes, operated by regional, national, European, International and other sources of funding.
- Research whose primary goal is to achieve breakthroughs in specific areas of neuroscience, computing or medicine.
- Supporting the operation of the Research Infrastructure.

The actions prospectively assigned to the PPs in the Research Roadmap are set out in Appendix 2: Partnering with the Human Brain Project Flagship.

2.1.1.4 Flagship Objectives

The HBP Flagship aims to achieve the following objectives, through the Core Project and/or the Partnering Projects.

FO1 - Create and operate a European scientific research infrastructure for brain research, cognitive neuroscience, and other brain-inspired sciences: Develop and operate six specialised Platforms dedicated respectively to Neuroinformatics, Brain

Simulation, High-Performance Analytics and Computing, Medical Informatics, Neuromorphic Computing, Neurorobotics, and a Collaboratory (formerly Unified Portal) providing a collaborative, transdisciplinary environment and community services that enable industry and academic researchers to co-develop and share methods, tools and data, and to work together to address novel research questions. Leverage investment in platform development to catalyse a phase shift in neuroscience, computing, and medical research. Establish synergistic collaborations with national, European and international initiatives contributing to the Strategic Flagship Objectives.

FO2 – Gather, organise and disseminate data describing the brain and its diseases: Generate targeted data sets that can act as anchor points for future data generation and for high fidelity reconstructions of the brain. Targeted data sets for mouse will make it possible to develop the integration and algorithmic reconstruction processes required for high-fidelity reconstruction of the mouse brain across all levels of biological organisation, from genes to cognition. Parallel data sets for humans will enable the application of technologies developed in animals to mapping the human brain, facilitate translation of knowledge about the mouse brain to the human brain and constrain human brain models. The availability of these data sets will expose critical gaps in our current knowledge, catalysing collaboration with large-scale brain mapping initiatives around the world. Detailed data on brain structure, at different levels of biological organisation, will provide a vital tool for functional studies mapping the links from genes to cognition and behaviour. Human specific data, e.g., with respect to genetic patterns, cognitive processes and behaviour, brain architecture and inter-subject variability, will be collected on all levels of brain organisation, not only to further constrain such models, but also to understand better the biological basis of what makes us Human. Develop ICT tools to federate and cluster anonymised patient data. The new tools will make it possible to identify patterns of alteration across different levels of biological organisation, suggesting new diagnostic indicators and drug targets, facilitating the selection of subjects for clinical trials, providing the data required for disease modelling and simulation, and facilitating the translation of knowledge about the brain from the laboratory to the clinic.

FO3 - Simulate the brain: Develop ICT tools that would enable HBP Researchers as well as the broader neuroscience community to generate high-fidelity digital reconstructions and simulations of the mouse brain, and ultimately the human brain. Bottom-up and top-down reconstructions and simulations of the brain provide a radically new approach to neuroscience, helping to fill gaps in the experimental data, connecting different levels of biological organisation, and enabling *in silico* experiments impossible in the laboratory. Such experiments can provide fundamental new insights into the biological mechanisms underlying cognition and behaviour, make it possible to test hypotheses of disease causation, and provide a valuable new tool for drug development.

FO4 - Build multi-scale scaffold theory and models for the brain: Develop multi-scale scaffold theory and models of the brain that merge theory-based, top-down and data-driven, bottom-up approaches. Theory and models developed in the HBP will provide a framework for understanding learning, memory, attention and goal-oriented behaviour, the way function emerges from structure; and the level of biological detail required for mechanistic explanations of these functions. Simplification strategies and computing principles resulting from this work will make it possible to model specific brain functions, both in neuromorphic and digital computing systems.

FO5 - Develop brain-inspired computing, data analytics and robotics: Develop ICT tools supporting the re-implementation of bottom-up and top-down models of the brain in neuromorphic computing and neurorobotic systems. HBP Neuromorphic Computing Systems will use brain-like principles of computing and architectures to achieve high-energy efficiency and fault tolerance, together with learning and cognitive capabilities comparable to those of biological organisms. Neurorobotic systems will use them as

controllers, enabling a new category of closed loop experiment that dissects how different levels of brain organisation contribute to cognition and behaviour. Develop hardware architectures and software systems for visually interactive, multi-scale supercomputing and big data analytics, moving towards the exascale. The new systems will make extreme-scale computing accessible to neuroscientists and clinicians, supporting the requirements of brain simulation and of high throughput, big data analytics, and enabling a broad range of other data-intensive applications.

FO6 – Ensure that the HBP's work is undertaken responsibly and that it benefits society. Promote engagement with industry to translate HBP research results into technologies, products and services benefitting European citizens and European industry. Expected HBP results in brain-inspired computing and medicine have the potential to give European industry a leading position in key areas of the 21st century economy. Implement a programme of multi-disciplinary education by using innovative online education approaches that focus on the convergence of ICT, biology and medicine. This programme should prepare a new generation of researchers capable of working across different fields, including neuroscience, medicine and computing. Implement a strategy of Responsible Research Innovation, monitoring science and technological results as they emerge, analysing their social and philosophical implications, and raising awareness of these issues among researchers and citizens, involving them in a far-reaching conversation about future directions of research.

2.1.1.5 Research Roadmap and Action Plan

The present document is the Action Plan for the CP. The Research Roadmap for the whole HBP Flagship Initiative, comprising both the CP and the PPs, is described in Appendix 1: Overview of the Flagship Objectives and Strategic Research Roadmap and Appendix 2: Partnering with the Human Brain Project Flagship.

2.1.1.6 Actions foreseen under this FPA to achieve the objectives

2.1.1.6.1 The Activity Clusters

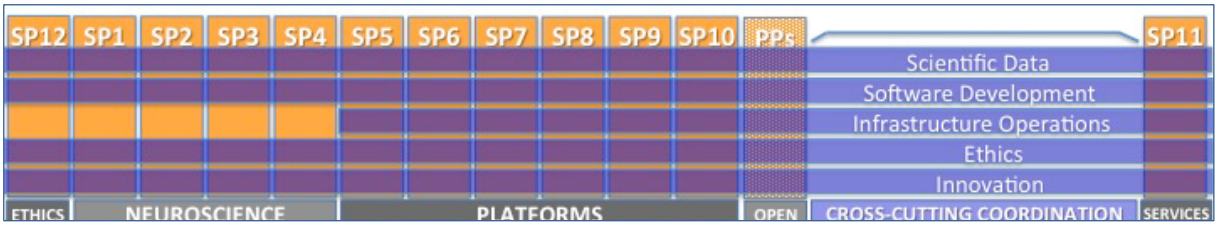

Figure 2: HBP Activity Clusters: Scientific Research, Software Development & Infrastructure Operations

Under the FPA, the HBP CP will be divided into 12 Subprojects (SPs), working in close cooperation and linked by many cross-cutting activities. While all SPs (except SP 11 – Central Services) undertake scientific research and contribute to building the HBP ITC research infrastructure, some are more biased towards scientific research (the "Neuroscience" SPs), while others place a heavier emphasis on the infrastructure side (the "Platform" SPs).

However, for operational coordination of cross-cutting work which affects more than one SP, the 11 scientific Subprojects (SPs 1-10 and 12) can be subdivided into 3 groups or clusters: the Scientific Research Cluster, the Software Development Cluster and the Infrastructure Operations Cluster. The Clusters are focused on the following types of activity:

Scientific Research: Production of scientific data, knowledge, models and simulations (all SPs).

Software Development: Creation and refinement of software tools (mainly SPs 5-10, but SPs 1-4 also contribute through the co-design process – see Section 2.1.1.7).

Infrastructure: Development, operation and maintenance of the production hardware and operation and maintenance of the production software that together comprise the research infrastructure (SPs 5-10).

The Clusters reflect the fact that, while each Subproject is focused on its own scientific area, there are some distinct types of activities which are performed in multiple Subprojects. These activities require similar skills, share similar concerns and are subject to similar requirements. The addition of the activity-based Cluster structure on top of the discipline-based Subprojects allows a cross-cutting management structure that brings together similar activities across multiple Subprojects. The HBP faces a particular challenge in the area of software development, where it needs to make software developed within a particular neuroscience lab accessible and robust enough for large-scale use by a wide range of researchers from different institutions.

The Clusters not only play an important role in coordinating the HBP (see section 2.3.2.10), but they also underline the increased importance attached to the Project's role as a provider of European scientific research infrastructure.

2.1.1.6.2 Central Services

SP11 (Central Services) provides the support services needed to coordinate and manage a project as large and as complex as the HBP.

Descriptions of the HBP SPs can be found in Section 2.3.1 and in Appendix 1: Overview of the Flagship Objectives and Strategic Research Roadmap.

2.1.1.7 Using Co-Design to shape the HBP Research Infrastructure

The organisation of science into Subprojects, co-design projects and cross-cutting initiatives reflects the dynamic and inter-disciplinary nature of the HBP. The partnership will implement appropriate organisational groupings to meet evolving needs driven by progress in science, research, development and translation. Co-design projects are an important instrument for harnessing the HBP ICT Platforms to constitute a community-driven Research Infrastructure for neuroscience computing and medicine. Close interaction with the broader scientific community will be sought, as this is considered key for the RI's success.

At the start of the FPA Phase, development of the RI capability will be driven by five co-design projects in the areas of:

1) **Development of the Whole Mouse Brain Model and the related Mouse Brain Atlas:** This project will result in a simplified model simulation of the whole mouse brain, initially using the NEST code and implemented on a supercomputer. It will reflect major principles of the cortical organisation and include subcortical structures. Initially, individual neurons will be represented as simplified "point neurons", while more complex neuronal models will be used later on. Both short- and long-range connections will be modelled. The model will employ whole-brain quantitative data; for example, regarding cell type and synaptic distributions, and long-range projections. The source for this data will be the Multilevel Mouse Brain Atlas being developed in SP5 in conjunction with SP1 and 6. It will contain the required background data for the simulations, in terms of genetic, molecular, cellular, synaptic and connectivity data, as well as microcircuit information and relevant aspects of behaviour. The model will be

verified against empirical data such as whole-brain early gene expression mapping, *in vivo* functional cortical maps and fMRI data. Further validation will be provided by closed-loop neurorobotic experiments, especially for the motor-rehabilitation task. Functional connectivity data will also be provided by selective stimulation maps from optogenetics. All cellular and network data, including corresponding models and simulations results, will be openly available to the community. Principal Subprojects: SP1, SP3, SP4, SP6, SP7, SP9, SP10.

2) **Mouse-Based Cellular Cortical and Subcortical Microcircuit Models:** Cellular network models of cortical and subcortical structures, such as the neocortex, the hippocampus, basal ganglia and the cerebellum, will be developed, using the NEURON simulation platform as a tool to integrate and cross-validate the available morphological and physiological data, and to simulate numerically the microcircuit on supercomputers in order to gain insights into its emerging dynamics and computational capabilities. This model will employ detailed empirical, quantitative data from cellular anatomy (cell types and dendritic, axonal and synaptic structures), physiology (firing patterns of various cell types and synaptic dynamics) and cellular genome data. It will be verified against physiological data measured at the level of the corresponding microcircuit. All cellular and network data, including corresponding models and simulations results, will be openly available to the community. This work will enhance and further constrain the whole brain model developed in co-design project 1) above and co-design project 4) below, on visuo-motor integration. Principal Subprojects: SP1, SP3, SP4, SP5, SP6, SP7.

3) **Multi-Level Human Brain Atlas:** The aim is to develop a prototype of a Human Brain Atlas in collaboration with SP5 and SP7. The atlas will be constituted by several widely accepted template spaces, a set of nonlinear spatial voxel-to-voxel mappings between them and a collection of high-quality 3D image datasets, as well as 3D parcellations generated in SP2, representing structure, connectivity and function. To achieve this goal, novel image alignment methods that bridge scales, modalities and inter-individual variability will be developed. Another aim is to generate novel label propagation methods that will make SP2's contribution relevant to mining image data in SP8 (Medical Informatics). This would also allow the wider scientific community to project atlas data onto their own scans via the Collaboratory. To allow for continuous enrichment of the atlas, mature image-processing and big data analytics tools will be implemented as efficient HPC production workflows in collaboration with SP7. These workflows will provide anatomically consistent 3D volumes, as well as quantitative data anchored in their respective atlases. Principal Subprojects: SP2, SP3, SP5, SP6, SP7, SP8.

4) **Visuo-Motor Integration:** The aim of this project is to develop multi-modal, top-down models of sensory-motor integration based on experimental studies (e.g., employing ultra-high field MR imaging in the human brain and physiological recordings and ultra-high field MR imaging in brains of experimental animals) and to match those models with bottom-up simulations prepared in collaboration with SP6 and SP7. Empirically validated computational architectures of, for example, the visual cortex provided by SP1, SP2, SP3 and SP4, will be directly compared with the architecture of other sensory modalities, with a focus on the somatosensory and auditory systems. These generic architectures will be integrated to develop algorithms for multi-modal guidance of robotic motor control with feed-forward (visual and auditory) and feedback (somatosensory) loops, in collaboration with SP10. Principal Subprojects: SP1, SP2, SP3, SP4, SP6, SP7, SP9, SP10.

5) **Plasticity, Learning and Development: Modelling The Dynamic Brain.** The aim is to address the dynamic properties of neural networks: in particular features involved in plasticity, learning, and development. This is the way that nature configures large

neural systems, and the hypothesis is that in the long term this will prove to be the best way to configure large models to perform generic computational algorithms. At the end of SGA1, we will be required to demonstrate our platforms and show their capabilities. For convincing demonstrations of all simulation platforms (HPC, and NM-PM and NM-MC), we will need our neural networks to be trained to perform "interesting" tasks that can take advantage of machines of the scale we will be able to provide. In principle, we can use plasticity and learning to train a network, but this will require us to simulate periods of time of the order of days, and thus we will need to use simplified models (PyNN/NEST) to achieve this. We then need a way to translate the trained network back into a more detailed model (NEURON). An alternative approach to construct networks is to use primitive functional units expressed as simple neural networks. This would also allow us to construct simple models of things such as visual cortex and striatum for testing purposes. Finally implementable model description(s) of computational architectures are created from theoretical models. Principal Subprojects: SP1, SP2, SP4, SP6, SP7, SP9, SP10.

The aim of these projects is to pursue some of the most challenging problems that cannot be addressed with traditional approaches in neuroscience, but that can be solved with advanced technologies developed in the RI. The projects will give focus and allow prioritisation of the capability development in the RI. Whereas the first two focus on mouse brain research, the last two address the human brain in more detail. Moreover, co-design projects 1 and 3 are whole-brain approaches, while 2 and 4 are starting to analyse specific functional systems in more detail, and at a higher level of granularity. Such characterisation is not exclusive, but rather illustrates a certain focus of research collaboration.

Most of the resources for the co-design projects will be drawn from existing work within the HBP that was started in the Ramp-Up Phase, plus the projects added through the Expression of Interest Call in 2015, which will contribute to the fourth co-design project. Scientists who aim to produce new scientific results while building a productive infrastructure will lead the co-design projects. They will lead teams consisting of additional scientists, as well as infrastructure developers.

The RI will have a Base Infrastructure that includes all HBP compute and data storage systems; networks with all associated services; a part of the offerings as infrastructure-as-a-service; as well as all enabling services, such as resource management and schedulers and programming environment, plus scientific libraries that are generic to many domains. This base infrastructure will be installed and operated in a federated manner at the major data centres in Germany, Italy, Spain and Switzerland that were involved in the Ramp-Up Phase of the HBP, as well as at prospective centres in France and the United Kingdom.

The second major component of the RI will be a Software Infrastructure that consists of applications (Apps) with Web GUIs for certain services; services that will include Software-as-a-Service and Platform-as-a-Service offerings; as well as more generic Web services, Source control (git), continuous integration, databases, configuration and deployment services.

Details of the infrastructure roadmap, and how base and software infrastructure development will be organized are discussed in Appendix 3: White Paper "Transforming the Human Brain Project Platforms into a Community-Driven Infrastructure for Brain Research". The co-design projects will, by and large, prioritize the software and base infrastructure that needs to be developed. The co-design projects will be complemented by other elements, notably high-level support teams that run the services, as well as a user program with resource-allocation based on expert peer review.

A key change in the FPA will be the creation of separate structures to manage Research and Infrastructure activities. This type of separation is standard practice in successful user

facilities of other science domains. It is necessary to assure fair access to the RI to both internal and external researchers, and is the only way a credible user programme can be developed. Building, operating and improving the RI will require a new organization for the HBP that clearly distinguishes between RI development and operation, on the one hand, and internal and external research, on the other.

These organisational changes will be implemented at the very beginning of SGA1. Resources permitting, within the same timeframe, a plan for the RI should also be completed and peer reviewed. This should include:

- A road map
- Construction plans with a detailed work breakdown structure
- A data management plan
- Principles for software development
- An operational plan with support and user programmes
- An overall business plan that identifies the funding sources for a sustained long-term development and operation of the RI.

The co-design research infrastructure will be created in distinct phases:

- Ramp-Up Phase: development of prototypes
- SGA1: infrastructure construction
- SGA2: infrastructure operation

RI construction will begin at the start of SGA1 and the infrastructure should be operational at the start of SGA2. As is common with ICT-based infrastructures in other domains, the development of the HBP RI will continue in SGA2 and SGA3. It will thus be essential that community involvement in the governance and strategic planning of the RI be strengthened during SGA1. This will be accomplished by involving important researchers from outside the HBP who will represent external user communities in strategic planning activities of the new governance structure.

The plan for the evolution of the HBP governance structure for the FPA period can be found in Section 2.3.2, but it is important to emphasise that a progressive separation of the project's research activities and its infrastructure operations is envisaged. Currently, the infrastructure elements are embedded in individual SPs along with research activities. To guide the creation of the infrastructure in SGA1, the infrastructure elements within any given SP will be grouped into dedicated infrastructure WPs. Coordination between these infrastructure WPs will be assured by cross-SP groups. This will permit a cross-cutting, project-wide view of different aspects of infrastructure, such as software development or user experience, which nevertheless have a presence in multiple SPs under the current structure. In SGA2, it is envisaged that the infrastructure WPs will be detached from their parent science & infrastructure SPs and regrouped in purely infrastructure SPs, and the infrastructure board will be formalised. Research input into further infrastructure development will continue to be assured via co-design projects. However, the infrastructure board will also be paying attention to the operational infrastructure's robustness, ease-of-use, etc.

2.1.1.7.1 Background to HBP's Co-Designed Research Infrastructure Goal

The HBP's emphasis on using Co-Design to shape a robust Research Infrastructure (for more on this, see Section 2.1.1.7) within the Project is, in part at least, a response to feedback received from the European Commission and its external reviewers via their review of the HBP FPA Proposal submitted in June 2014 and the more complete 1st periodic review of the

HBP in January 2015, and also from the Mediation Process initiated by the HBP Board as part of its response to the critical Open Letter that appeared mid-2014.

As a result, the HBP has explicitly adopted the goal of turning the six HBP ICT Platforms into robust, durable research infrastructure that will endure after the EC-funded HBP ends. This infrastructure is intended to attract ICT, medical and neuroscience researchers to advance European science and technology broadly by sharing knowledge and working in a more collaborative way. In contrast, the research actually undertaken within the HBP Core Project is limited to what is needed to get a scientifically useful research infrastructure up and running. An infrastructure of this sort, to advance cutting-edge scientific research cannot be created by scientists alone, nor by technologists alone, but only by both working together, in a cross-cutting co-design approach. While the HBP is designed to create an ICT-based research infrastructure, its focus is provided by neuroscience; systems and cognitive neuroscience is an integral part of the Core Project, and its contribution will evolve as research progresses.

Most HBP Scientific Subprojects currently contain a mix of infrastructure and research activities. The Platform Cluster (SPs 5-10) has more emphasis on infrastructure, the Neuroscience Cluster (SPs 1-4) more on research. The infrastructure side can be broadly divided into base infrastructure (high-performance computers and data analytics, plus networks) and software infrastructure. The services provided by the HBP infrastructure are discussed in detail in Appendix 3: White Paper "Transforming the Human Brain Project Platforms into a Community-Driven Infrastructure for Brain Research, but can be summarised as follows:

Gateway	Collaboratory			
Software as a Service	Neuroinformatics	Brain Simulations	Neurorobotics	Medical Informatics
Data as a Service	Neuroinformatics		Medical Informatics	
Platform as a Service	HPC platform (e.g. interactive supercomputing)		Neuromorphic computing platform	
Infrastructure as a Service	Compute & data infrastructure services (including HPC)		Neuromorphic compute services	
Base infrastructure (compute, storage, & network)	Public data centers in France, Germany, Italy, Spain, Switzerland and the UK; IT infrastructure at Hospitals; Neuromorphic computing systems			

Table 2: Structure of the different service components in the Research Infrastructure.

For a research infrastructure that will serve the scientific community, robustness is essential. Infrastructure performance will be measured against pre-defined levels of performance for individual components and services. Quality metrics will be developed in SGA1 to assess the actual state and capabilities of the infrastructure, *vis-à-vis* what is planned. Risk management measures will also be refined in SGA1 to identify and mitigate risks to the key services. Research performance will be measured through peer-reviewed scientific publications. The science and technology monitoring function of the Ramp-Up Phase will be replaced under the FPA by a range of cross-cutting coordination committees (see 2.3.2.10). For example, the Scientific Data Committee will be responsible for ensuring that data and knowledge generated in one SP correspond to the needs of platform developers in another, while the Software Development Committee will ensure that software developed within the project is adequately defined and tested.

2.1.1.7.2 Community Engagement

Engaging with external research communities is essential for all research infrastructures. This typically takes place on four different levels:

1) The broad scientific community (more specifically, neuroscience, computing and medicine) has to be involved in the definition of the infrastructure roadmap and the capabilities that are to be developed and made available. Research infrastructure projects must demonstrate community support as part of their mission requirement. The present infrastructure project emerged out of a FET Flagship Project as a standalone scientific effort. Extensive efforts were undertaken during the Ramp-Up Phase to gather feedback from the community about the needs. However, based on recommendations of the European Commission and a mid-term Review, the community must be more directly involved in defining the requirements of the infrastructure with the HBP is building.
2) The scientific community is involved in the construction of the infrastructure through co-design projects, as discussed above.
3) Every research infrastructure operates a user programme; the HBP will be no exception. This programme will have an outreach component - though workshops, training programs, etc. - and direct engagement with scientists who are of strategic interest to the infrastructure.
4) Finally, the research infrastructure will maintain high-level support teams that provide support to users whose research proposals have been approved by a rigorous selection process. These teams typically include domain scientists who have become expert users of the infrastructure though their involvement in co-design projects. The high-level support teams are funded by the research infrastructure and collaborate with the external users. Their mission is to help the external user projects to succeed.

Since much of the user-facing infrastructure of the HBP is software that is developed on an open-source basis, there will be many opportunities to engage users at different levels, targeting developers who may be potential contributors to the software infrastructure. This will be accomplished with an approach that turns domain science users into contributors and in some cases even into developers of the software infrastructure.

This user engagement must be coordinated with the overall communications efforts of the project. A model for community engagement and coordination is presented in Appendix 4: Community Engagement. This model will be harmonized with the specific needs of established co-design activities, user programmes and software service support efforts in following SGAs.

2.1.1.8 Gender Balance in the HBP

2.1.1.8.1 Gender Balance in HBP Recruitment and Management

Gender balance is one of a number of items that fall under the global heading of Responsible Research and Innovation (RRI). Gender balance is addressed in this section and other RRI topics are covered in a separate RRI section (see 2.5). Research in the Human Brain Project includes work in a broad range of disciplines, from molecular and cellular biology to mathematics, medicine, computer engineering, robotics and even philosophy. These disciplines are characterised by widely differing rates of female participation, often with large variations between countries. Nonetheless two tendencies stand out. First, in all major disciplinary areas, except engineering, manufacturing and construction, at least 40% of new PhDs. in the EU-27 countries are female (EC data for 2006). Second, in these same countries, the proportion of women decreases with each successive level from students to researchers to professors.

A recent EU study found that in 2010 just 32% of scientists and engineers in the EU-27 were women. Only in three countries — Iceland (50%), Bulgaria (50%), and Poland (53%) — did the proportion of female scientists and engineers reach 50% or higher. The same study showed a worrying drop in women's share of higher ranking positions: "from 35% of female PhD graduates, the proportion of women drops to 32% in grade C academic staff, 23% in grade B and just 11% in grade A" [1]

This inequality is "largely due to employer policies and/or strategies" [2]. Many studies on female professional careers show, in fact, that activities designed to promote the advancement of women have no lasting effect without major changes in management and organisational structures [3] [4, 5], [1],[6].

In view of these findings, and of the high profile of FET Flagships in European research, the HBP will play a pioneering role in achieving a well-balanced share of male and female scientists at all hierarchic levels within the Project, in particular among Subproject and Work Package leaders and in the Project's governing bodies.

Since the original Project proposal was submitted, the HBP has modified its leadership structure to include more women. As a result, the proportion of women at Board level has increased from 15% at the beginning of the Ramp-Up Phase to 20% today.

The HBP aims to increase the proportion of female researchers at different levels within the Project (PhD students, post docs, Work Package (WP) Leaders, Subproject (SP) Leaders, senior management positions) and for different Project activities (Core Project, Partnering Projects, research grants and studentships, management). In the case of senior researchers, the goal is to increase the proportion of female Subproject and Work Package leaders.

In adapting its governance structures for the Operational Phase, the HBP has introduced requirements to ensure female participation in key governance bodies. In addition, the Management SP will have a Task focused on gender balance. Further actions to promote equal opportunities include the following:

Management Culture: HBP senior management will follow a systematic top-down approach, defining a comprehensive mission statement on gender equality and organising a workshop to sensitise SP/WP/Task-Leaders to gender and diversity issues.

Reconciling Professional and Family Life: Women and men pursuing a scientific career face immense pressures due to short-term contracts, high mobility and long working hours. To alleviate these pressures, the HBP Partners will support flexibility in working hours and places of work, facilitating part-time work and time-sharing for both genders. Additionally, the HBP PIs will cooperate with their institutions dual career centres, where they exist, and make their best effort to ensure their staff have adequate access to advice on child-care (family services), extensions of their contracts to accommodate parenthood, and training in self-management and work-life balance. Regular information about HBP Actions and success stories in this area will be distributed via the Project's internal newsletter.

The HBP Partners will promote the personal development of staff members, support equal opportunities and help members of staff to reconcile their professional and family lives.

In addition to the above activities, the HBP will work with external organisations with a proven track record in promoting the role of women in science and business (e.g., the independent non-profit European Academy for Women in Politics and Business).

2.1.1.8.2 Gender Balance in HBP Research

As pointed out in a recent European Commission publication,

> *"Sex and gender can influence all stages of research or development processes, from strategic considerations for establishing priorities and building theory to more*

routine tasks of formulating questions, designing methodologies, and interpreting data" [7].

For instance, many experiments in behavioural neuroscience avoid problems related to the oestrogen cycle by using only male rodents, but the results obtained may only apply to males. Similarly, drugs affecting the brain can act differently in males and females due to differences in brain microstructure and in the hormonal and biochemical environment. Failure to consider these and other gender differences in experimental subjects can lead to unreliable results. It is thus imperative that researchers in basic and clinical include subjects of both genders in their studies and take gender into account in their analyses.

HBP research will pay special attention to sex and gender in SP2: Human Brain Organisation and SP8: Medical Informatics Platform.

SP2 Human Brain Organisation

Sex and gender differences in brain architecture and cognition represent a fundamental issue in neuroscience, with sex differences making a significant contribution to inter-subject variability, in particular on the systemic level. The relationship of these differences to cognitive function and behaviour is a research question that needs to be formulated in different ways, according to the level of brain organisation under consideration and the methods used in the research.

SP2 will not stratify all its data for gender. For example, the multi-modal brain atlas will sometimes refer to individual brains (which are either male or female); in other cases it will use results by averaging hundreds of MR data sets for human brains. In this way, inter-subject variability will be considered as a facet of human brain organisation, in the same way as age and handedness. The atlas is flexible enough to be extended if specific scientific questions require other templates in the future. All SP2 experiments will record metadata on inter-subject variability, including sex. All single cell experiments on human brain tissue from neurosurgery will test for dependence on patient gender and age. Given the small number of subjects studies (N=12), we do not expect to find significant sex differences All morphometric data from *post mortem* studies will be tested for sex differences to identify sources of variation in the structure and function. Since sample sizes will be small, we expect that few if any differences will be statistically significant. Finally, we will adapt and apply methods developed by HBP Partners in their previous research. These methods have already demonstrated the existence of significant sex differences in the Broca region [8], the motor cortex [9], the extrastriate visual cortex [10], and other systems.

SP8 Medical Informatics Platform

SP8 will work with SP6 to build models of brain diseases. To be useful, the models need to be accurate, represent the whole human population, and explain important sources of inter-individual differences. In this context, sex and gender will be included in the analyses. Variables corresponding to sex and gender are used in two different circumstances.

First, they are included in the models as a covariate. Global covariates (e.g., sex, total-intracranial volume, head size) make it possible to measure the significance of the biological variables (e.g., local grey-matter volume) over and above the global effects captured by the covariates.

Second, gender and sex will also be considered as variables of interest. It is important to consider sex and gender not *per se*, but their interactions with the different biomarkers of the diseases. Epidemiological studies show that there are large gender imbalances in the prevalence of many neurological and psychiatric diseases. For example, diagnoses of Mild Cognitive Impairment are more frequent for males, while diagnoses of Alzheimer's disease

are more frequent in the female population. Gender differences remain largely unexplained at the biological level. Including gender and sex will help us to determine different risk factors and discover different pathways. The same reasoning applies to the variable “age”.

2.2 Impact

2.2.1Expected Impact

2.2.1.1 Impact through delivery of the HBP Research Infrastructure

The HBP Research Infrastructure will facilitate neuroscience research, inside and outside the HBP, by creating and maintaining multi-level atlases of the mouse and human brain and related atlasing tools, and by making them available to European and other researchers, who will also help to fill it with data. It will make it possible, for the first time, for many academic researchers to use reconstructions and simulations of the brain in their research. The HBP RI will be a major public data resource that will strengthen Europe's position as leader in international neuroscience research.

The HBP RI will also provide neuroscientists and neurologists with unprecedented access to sub-exascale and exascale supercomputing capabilities, including large volumes of neuroscience and anonymised patient data, creating new opportunities for basic and applied research. Tools and methods supporting this strategy will also have a substantial impact on future medical research, facilitating the development of personalised treatments. Better understanding, diagnosis and treatment of brain disease will reduce costs for national health services and insurance companies, and help to reduce the suffering of patients and their families.

In terms of future computing, the HBP RI will offer academic researchers and technology developers the possibility to experiment with state-of-the-art neuromorphic devices and systems. It will make it possible, for the first time, for researchers to design and perform behavioural and cognitive experiments using virtual robots connected to HBP brain simulations and inhabiting virtual experimental set-ups. The services offered by the HBP RI will facilitate the emergence of a rich ecosystem of academic and industrial researchers, exploring, and ultimately commercialising, completely novel applications.

2.2.1.2 Scientific Impact

IMP1.1: The data collected in SP1 will make a vital contribution to the Multi-level Atlas of the Mouse Brain, created in SP5.

IMP1.2: The data collected in SP1 will enable the use of gene expression data to predict features of the brain that have not been measured experimentally, drastically reducing the number of experiments necessary to build high fidelity reconstructions of the brain.

IMP1.3: The data collected in SP1 will provide the initial scaffolding and validation tests for high-fidelity reconstructions and simulations of the mouse brain, to be filled in with data from the HBP's European and International collaborations and with predictions from reconstructions.

IMP1.4: Comparative assessment of the data collected in SP1 and SP2 will identify principles allowing the use of mouse data to predict features of the human brain for which experimental data are not available.

IMP2.1: Research in SP2 will contribute empirical data, methods/tools and new concepts; it will validate predicted features, and identify and obtain the characteristics of brain organisation that are unique for the human brain.

IMP2.2: The data collected in SP2 will make a vital contribution to co-design projects, and to the Multi-level Atlas of the Human Brain, set up in SP5, in particular.

IMP2.3: The data collected in SP2 will provide the initial scaffolding and validation tests for high fidelity reconstructions and simulations of the human brain, to be filled in with data from the HBP's European and International collaborations and with predictions from reconstructions.

IMP2.4: SP2 will drive the development of tools for big data analytics.

IMP3.1: SP3 will deliver novel data, behavioural tests, neuroscientific analyses, software tools, computational models, and new mechanistic insights in cognitive functions in "Systems and Cognitive Neuroscience", as studied in both mice and humans, and in combination with model simulations and real-world artifacts.

IMP3.2: SP3 will link the newly gained knowledge on brain mechanisms underlying cognition to the other HBP Subprojects, and thus show how the knowledge can be used and applied in Neuroscience Research (SPs1-4), in the Platform infrastructures (SPs5-10) and similarly in the co-design projects (Whole mouse brain model; Microcircuit models; Human brain atlas, Visuomotor integration and Plasticity).

IMP3.3: SP3 will make use of facilities and knowledge generated in other SPs to test theoretical predictions experimentally, and generate further data to improve simulations and Platform infrastructure. It will thus act as a testbed both for theoretical models and practical research infrastructure, such as neuromorphic technology. As such it will also exert a cross-linking function across HBP subprojects, binding together different disciplines and advancing cognitive and systems neuroscience in terms of experiment, theory and modelling.

IMP 3.4: Develop macro- and mesoscopic scale parallel-distributed simulations, matching experimental results produced by a range of observational and perturbational techniques, at the abstraction level of spiking neuron networks, and thereby benchmarking severalHBP platforms.

IMP 3.5: Experimental and computational characterization of cortico-thalamic and cortico-hippocampal systems at the transition between wakefulness-like complex patterns and sleep-like slow-wave activity and in relation to episodic memory, recognition, and conscious vs. unconscious brain states. Use this reference system to understand pathological alterations of brain dynamics and cognitive brain function.

IMP 3.6: To test how light-regulated molecular systems may emulate transitions between sleep-like and wake-like dynamics, and affect perceptual and memory operations in the brain, by the combination of opto-pharmacological stimulation and electrophysiological/optical recordings at the slice and intact brain level.

IMP4.1: SP4 will generate new theoretical insights into issues of key importance to neuroscience. These include the link between different levels of biological organisation in the brain, the dynamics of single neurons, plasticity mechanisms and their impact, network dynamics and the mechanisms underlying specific cognitive functions.

IMP4.2: SP4 will implement theoretical insights in high-level operational models, suitable for implementation in neuromorphic computing.

IMP5.1: SP5 will facilitate neuroscience research, inside and outside the HBP, by creating and maintaining multi-level atlases of the mouse and human brain and related atlasing tools, and by making them available to European and international researchers through the HBP Neuroinformatics Platform.

IMP5.2: By creating a major public data resource, SP5 will strengthen Europe's position as leader in international neuroscience research.

IMP6.1: SP6 will establish high-fidelity reconstructions and simulations of the brain as an essential tool for integrating and curating multi-level experimental data.

IMP6.2: SP6 will establish in silico experimentation as a powerful method for addressing scientific questions that cannot be addressed experimentally.

IMP6.3: SP6 will establish brain simulation as an effective technique for understanding the cascades of biological events implicated in psychiatric and neurological diseases.

IMP6.4: SP6 will make it possible for a broad community of academic researchers to use reconstructions and simulations of the brain in their research.

IMP6.5: SP6 will generate fundamental new insights into the basic computational mechanisms underlying human and animal cognition and behaviour.

IMP6.6: Simplified reconstructions of the brain, generated by SP6, will serve as the basis for novel neuromorphic computing systems and devices.

IMP6.7: SP6 will establish European scientific leadership in high-fidelity reconstructions and simulations of the brain and their technological and clinical applications.

IMP7.1: SP7 will provide neuroscientists and developers with extreme-scale supercomputing and data analytics systems, reaching exascale capabilities.

IMP7.2: SP7 will establish completely new technologies for remote interactive simulation, visualisation and analytics in high-performance computing. The new technologies will facilitate the adoption of simulation-based research methods in neuroscience, the other life sciences and many other domains.

IMP7.3: SP7 will operate a Europe-wide, dedicated highest-speed network for data exchange and global data access, based on the PRACE network as part of the HBP Research Infrastructure. With fixed routing and encryption, the HBP/PRACE network will guarantee the security of highly sensitive data.

IMP7.4: SP7 will pioneer the use of low-power neuromorphic technologies in High-Performance Computing.

IMP8.1: SP8 will establish novel techniques and practices for the extraction of clinically valuable information from large volumes of patient data, exploiting the competitive advantage offered by European National Health Systems, and establishing European leadership in a broad field of medical research. The techniques established by the Subproject will have a major impact on medical research outside the HBP.

IMP8.2: SP8 will offer researchers unprecedented access to large volumes of anonymised patient data, creating new opportunities for basic and applied research. The federation and querying methods at the core of the Platform will make it possible to leave personally sensitive data in the systems and formats where they were originally stored, without moving them to a central system. Tools and methods supporting this strategy will have a substantial impact on future medical research.

IMP8.3: SP8 will contribute to establishing objective, biologically grounded classifications of neurological and psychiatric disease. Compared to current symptom and syndrome-based methods of diagnosis, this will represent a major step forward.

IMP8.4: "Biological signatures of disease", identified in SP8, will provide the data required for high fidelity reconstructions and simulations of disease and possible treatments. Simulations will provide a novel tool for understanding the causes of brain disease, and simulating the effects of drug candidates and other treatments.

IMP9.1: SP9 will establish designs and technologies for large-scale neuromorphic devices and systems with novel learning capabilities, low energy consumption and high reliability.

IMP9.2: SP9 will offer academic researchers and technology developers the possibility to experiment with and test state-of-the-art neuromorphic devices and systems.

IMP10.1: SP10 will establish neurorobotics as a valid technique for exploring the causal relationships between the multi-level structure of the brain, cognition and behaviour

IMP10.2: SP10 will make it possible, for the first time, for researchers to design and perform behavioural and cognitive experiments using virtual robots connected to HBP brain simulations and inhabiting virtual experimental set-ups.

IMP10.3: Research performed in SP10 will contribute to creating a new multi-level understanding of the relationships between brain structure, cognition and behaviour.

IMP10.4: SP10 will create the first prototype applications exploiting the novel cognitive and behavioural capabilities of physical robots with neuromorphic controllers.

IMP12.1: SP12's Foresight Lab will inform the debate on the social and economic implications of HBP research in neuroscience, medicine and computing, helping to allay groundless fears, while identifying areas of genuine concern

IMP12.2: SP12 will have an important impact on the emerging academic debate around the conceptual and ethical implications of recent neuroscience research, in particular of brain simulation.

2.2.1.3 Social and Economic Impact

IMP3.7: By linking work on genetic mouse models of disease with human neuroimaging, SP3 will contribute to the impact of HBP on clinical neurosciences, in collaboration with SP8.

IMP 3.8: Perturbing the cerebral cortex of brain-injured patients reveals sleep-like changes of brain responses that correlate with loss/recovery of function. Computer simulations of sleeping and awake brains similarly perturbed will afford crucial insight at the bedside.

IMP 3.9: Light-regulated molecular systems that control both local and global transitions between wake and sleep states, and perception and memory operations, will facilitate the development of novel treatments for brain-injured patients, consciousness/sleep and learning and mental retardation disorders and help reduce their social and economic burden.

IMP 3.10: The capability to simulate the effect of non-invasive/reversible perturbations will open the path to the creation of dedicated bedside high-performance computing applications.

IMP6.8: The research conducted in SP6 will make it possible to create brain simulation services available through the HBP RI for commercial researchers in neuroscience, computing, medicine, and pharmacology, improving European competitiveness in those areas.

IMP6.9: Tools for brain reconstruction and simulation have the potential to generate licensing revenues from commercial users in the pharmaceutical and computing industries.

IMP6.10: Models of specific diseases have the potential to generate licensing revenues from users in clinical and pharmacological research.

IMP6.11: Simplified brain models have the potential to generate licensing revenues from technology developers wishing to develop their own Neuromorphic Computing Systems.

IMP7.4: New technologies for remote interactive simulation, visualisation and analytics, generated by SP7 and made available through the HBP RI, have the potential to generate significant licensing revenue and generate increased industrial development in those sectors in Europe.

IMP7.5: Novel HPC hardware based on low-power neuromorphic technologies also has the potential to generate licensing revenue.

IMP8.5: Biologically grounded classifications of brain disorders established by SP8 will allow more effective diagnosis and treatment of psychiatric and neurological disease, and more effective selection of participants in clinical trials.

IMP8.6: Disease and drug simulations will facilitate the development of drug and other treatments.

IMP8.7: The data and tools made available by the Medical Informatics Platform will facilitate the development of personalised treatments.

IMP8.8: Better understanding, diagnosis and treatment of brain disease will reduce costs for National Health Services and insurance companies and reduce the burden on patients and their families.

IMP8.9: SP8 will enable commercial services allowing clinicians and pharmaceutical researchers to query and analyse anonymised patient data, using the HBP RI.

IMP8.10: SP8 will enable commercial services allowing clinicians and pharmaceutical researchers to simulate brain diseases and candidate treatments.

IMP8.11: SP8 will enable commercial services for personalised medicine via the HBP RI (diagnosis, prognosis, selection of optimal treatment).

IMP9.3: The technologies and systems developed in SP9 have the potential to revolutionise computing technology, enabling a very broad range of completely novel applications.

IMP9.4: The services offered by the Neuromorphic Computing Platform will facilitate the emergence of a rich ecosystem of academic and industrial researchers, exploring, and ultimately commercialising, completely novel applications.

IMP9.5: SP9 will establish European leadership in an area of research of vital importance to the European computing industry and to applications developers.

IMP9.6: SP9 has the potential to develop commercial services made available through the HBP RI, offering industry researchers and technology developers the possibility to experiment with and test applications based on state-of-the-art neuromorphic devices and systems, potentially improving European competitiveness in these fields.

IMP9.7: Neuromorphic designs and technologies developed in SP9 have the potential to generate licensing revenues from industry and applications developers.

IMP9.8: Neuromorphic technologies developed in SP have the potential to generate commercially valuable applications for manufacturing, transport, health care, and consumer electronics.

IMP10.5: Physical robots with neuromorphic controllers will have functional capabilities (e.g., learning, effective handling of multimodal real-time input) not present in current robotic technologies. These capabilities will have a major impact over a broad range of domains from manufacturing to transport, healthcare, and the home.

IMP10.6: The Neurorobotics Platform, made accessible through the HBP RI, will enable the HBP to realise commercial services offering industrial researchers the possibility to experiment with state-of-the-art neurorobotics setups.

IMP10.7: HBP neurorobotic technology has the potential to generate significant licensing revenues.

IMP10.8: Applications developed based on neurorobotic technology have the potential to generate significant licensing revenues.

IMP12.3: SP12 will build public awareness of the economic and social potential of HBP research and encourage public participation in priority setting and decision-making. Public acceptance of and participation in the Project is a pre-condition for effective commercial exploitation of Project results.

2.2.2 Measures to maximise impact

2.2.2.1 Actions for stability, structure, continuity and coherence for the realisation of the Flagship as a whole

2.2.2.1.1 Stable Governance and Management

The HBP FPA will allow for a formalised commitment of the partners of the Flagship, provide for a stable and structured environment for the benefit of the realisation of the Flagship and overall continuity and coherency in the execution of the Flagship. Robust and effective governance and management structures are an important part of the HBP FPA and critical for the long-term success of the HBP. For more on the evolution of HBP governance and management structures, see Section 2.3.2.

Key elements in the FPA governance structure that should contribute to the stability, continuity and coherence of the Flagship are the move to Legal Entity and a three-tier governance structure, separating scientific direction (by the Science and Infrastructure Board – see 2.3.2.5.5 from executive direction (by the Directorate – see 2.3.2.5.3), from overall supervision and confirmation of resource allocation (by the Stakeholder Board – see 2.3.2.5.1), and also from supervisory auditing and control (via the Audit Committee – see 2.3.2.7). At the same time, a change process has been initiated in the coordination of the HBP, to make it dependent on a group of major Stakeholders, rather than just one Partner (as in the Ramp-Up Phase). This process will put the management into a Legal Entity (see 2.3.2.4) with its own legal identity, allowing it to sign agreements on behalf of the Project. It will also have its own independent sources of funding, to equip it to maintain and operate the Research Infrastructure being created by the HBP, and to allow this to continue functioning after the end of the Project.

2.2.2.1.2 A Stable Model for Maintaining and Revising the Research Roadmap and the Membership of the FPA

Science and technology evolve and progress. This implies that the HBP Flagship's Research Roadmap (including the CP's Action Plan) must evolve over time; for example, shifting emphasis from less promising areas to ones showing greater potential, and adapting to bring in new skills and competencies. In practical terms, this will often take the form of new Partners joining the Consortium. The evolution of the Consortium and its work will be guided by an external Scientific Advisory Board (SAB – see section 2.3.2.5.7).

At the same time, some Partners would have to leave the HBP when their contribution has been completed or if they have not been able to deliver what was expected of them.

During the course of a Specific Grant Agreement (SGA), a detailed Work Plan for the following SGA will be drawn up and approved by the whole Consortium. This will involve identifying work that will cease in the future SGA, new work that will need to start, and on-going work that is being performed unsatisfactorily by Partners that will need to be replaced. The internal approval process will make it clear which Partners will be asked to leave the Consortium at the end of the current SGA. A Call for Expression of Interest process involving external experts will be used as a transparent mechanism for inviting new Partners/groups of Partners to apply to join the CP. This process is described in more detail in Section 2.4.1.2.

2.2.2.1.3 A Stable Set of Relationships with the European Commission, the Member States, other Stakeholders and the General Public

The HBP has stable long-term relationships with the European Commission, the Member States, industry, and other stakeholder organisations, as well as with regional, national, European and International initiatives in relevant areas of research and development.

At the institutional level, the exchange of information with the Member States and the European Commission will be coordinated initially through the Flagship Governance Forum and then through the Stakeholder Board (see 2.3.2.5.1), once the HBP Legal Entity (see 2.3.2.4) is created.

At the implementation level, the HBP's Project Coordination Office (PCO – see 2.3.2.5.6) is working to build long-term relationships with the European Commission, National Funding Agencies, large-scale European and international programmes, and the Consortium Partners. The next phase of the Project will see a strengthening and expansion of this role.

The Project will engage the scientific community through normal channels of scientific communication (publications in scientific journals, participation in conferences and workshops), through the community engagement programme (see section 2.1.1.7.2) but also through new channels that exploit the potential of the HBP Platforms and of "dissemination systems" created within the Project.

The Initiative will also initiate a broad range of activities to engage students and the general public. These include an Education Programme (see 2.2.2.3.6) addressing PhD students and post-docs in the CP, the PPs and outside the HBP Flagship Initiative (see section on HBP Education Programme), as well as public engagement activities organised by the HBP Responsible Research and Innovation activities (see section 2.2.2.3.3).

2.2.2.2 Actions for enabling complementarities, synergies, and an enhanced overall outcome of regional, national, European and international research programmes)

2.2.2.2.1 Objectives

Since the CP will focus on the development of technologies allowing for the integration of data from multiple sources, the success of the Action Plan will depend on the HBP's success in building collaboration with organisations and initiatives outside the HBP. It is these organisations that will contribute the majority of the data and knowledge the Project uses. Screening and selecting potential collaboration Partners will be the responsibility of the HBP Science & Infrastructure Board (see section 2.3.2.5.5). Implementation of collaborations will be the responsibility of the Subprojects concerned. The Research Roadmap (see A1.3. Research Roadmap) specifies areas of research and potential Partners with which the Projects have already identified possibilities for collaboration. Details of the collaborations planned by individual Subprojects are found in the relevant sections of Appendix 1: Overview of the Flagship Objectives and Strategic Research Roadmap.

The HBP will Identify and establish collaborations with national, European and transnational, international and global initiatives in relevant areas of research and development, avoiding duplication of effort and building momentum behind the global effort to understand the brain and its diseases.

Such collaborations will help to maximise use of the HBP Platforms and HBP know-how by organisations that are not signatories of the FPA. The HBP will also promote translational research that transforms HBP research results into products and services that are valuable to European society and that strengthen the competitive position of European industry. Collaboration with other initiatives will help the parties concerned to make the best possible use of the data, know-how, tools and infrastructures they have created, contributing to the development of standards, resources and infrastructures of general benefit to the scientific community. Collaboration will make it easier for the parties to contribute to the formulation of national and European research priorities, to national and European policymaking, and to regulatory decision-making in areas relevant to the Project (e.g., data protection, research ethics etc.).

2.2.2.2.2 Implementation

Building and maintaining relationships with other national, European, international and global research initiatives and with relevant funding sources is the responsibility of the HBP's Project Coordination Office (PCO – see 2.3.2.5.6) and its relations team, which is already in operation, and will continue its activities for the whole duration of the CP.

The current HBP Description of Work identifies a non-exhaustive list of eight European initiatives (BIOMEDBRIDGES, CERN, ELIXIR, ESFRI, FLAG-ERA, ICON, IMI, PRACE) and eight International initiatives with which the HBP is attempting to build relationships. The PCO has already held meetings with seven of these organisations (CERN, PRACE, FLAG-ERA, IMI, INCF, Allen Institute, US BRAIN Initiative) and has established a close working collaboration with the FLAG-ERA. Contact with the others will be established before the end of the Ramp-Up Phase. The PCO is currently working to identify other organisations with which the HBP should build relationships. This activity will continue for the whole duration of the HBP Flagship Initiative.

Collaborations with outside initiatives may be regulated by formal collaboration agreements or memoranda of understanding negotiated by the Directorate (in consultation/approval of the authorized representatives of HBP Partners). Collaborations

will take different forms according to the nature and objectives of the organisations concerned.

Promotion of Synergies and Efficiency in Research: The HBP will establish formal collaboration agreements or memoranda of understanding with other large national, European, international and global research agreements. The joint activities foreseen in these agreements may include exchanges of information and staff; joint workshops and conferences; sharing of data, tools and infrastructure; and joint research projects.

Promotion of PPs and use of the HBP RI: The HBP will work with national funding agencies and European funding programmes outside FET to encourage proposals for PPs that facilitate the development of the HBP RI, or that use the RI to perform research contributing to the HBP's Strategic Goals. Planned promotional activities include: HBP participation in coordination meetings (such as those currently organised by FLAG-ERA), exchanges of information about relevant national and European funding programmes, HBP contributions to the formulation of work programmes in relevant areas of research, and HBP participation in workshops, info days and other activities. PPs that pass the HBP selection process will be integrated in the HBP Flagship Initiative and will benefit from full access to the HBP RI (once related IP issues and other legal aspects have been resolved) and know-how and will have full access to HBP training and education activities.

Standards Development: The HBP will work with other research initiatives to develop standards of general benefit to the research community. These may include standard protocols, ontologies and file formats for experimental data and metadata, and standardised approaches to informed consent for human volunteers. The Resource Description and Access (RDA) standard could be a starting point for such activities.

2.2.2.2.3 Measurement of Success

The success of the HBP's efforts to collaborate with other initiatives will be measured in terms of:

- The number of formal collaboration agreements or MoUs in place.
- The number of collaboration agreements or MoUs that are active.
- The number of proposals for Partnering Projects and the geographical and disciplinary diversity of the proposals.
- The number of participants in other initiatives who are active users of the HBP Platforms.
- The number of other initiatives that are actively sharing data, know-how and tools with the HBP.
- Presence, number and impact of collaborative joint publications, meetings, workshops, conferences, etc., which result from these collaborations.

2.2.2.3 Communication, dissemination and exploitation of results

2.2.2.3.1 Communications and Dissemination Strategy

Purpose

The purpose of the communications team in the Project Coordination Office (PCO – see 2.3.2.5.6) is to support the Human Brain Project (HBP) in achieving its objectives and to promote the Project as an innovative European Commission Flagship initiative that will have a significant impact on society.

The HBP's communications will focus on science dissemination, sharing successes, building engagement for the usage of the infrastructure, and promoting the Project's objectives and achievements.

Outreach events, information sessions and workshops will target both HBP Partners and the scientific community, as well as industry, and national, European and transnational brain initiatives. These events will provide interactive mechanisms for a wide range of stakeholders to discuss the Project, provide feedback and express their needs. They will also be able to start using the HBP RI, and the Project leaders will share findings and opportunities for innovation.

Audiences

The HBP has a broad range of audiences and stakeholders, both inside, and outside the HBP. These have various interests and motivations regarding the Project, which need to be taken into account when determining the right messages, channels and tools for each audience.

Key external audiences include:

- The neuroscience community and potential users of the HBP Research Infrastructure
- National, regional, European and international research institutions, initiatives and infrastructures
- Member states
- Funding agencies
- International organisations, Intergovernmental Organisations
- Academics
- Civil society, Non-Governmental Organisations and interest groups
- Industry
- Media
- The public at large

Key internal audiences include:

- Opinion leaders and decision makers of the Consortium (e.g SP Leaders, Board members)
- Subprojects (SPs)
- The Consortium at large
- The European Commission and its affiliate groups
- Flag-ERA

Objectives & Strategy

Improve internal communication and engagement

We will first focus on building a sense of team spirit and excitement for belonging to the HBP, across the Consortium, through regular communication and information to ensure that all HBP Partners are kept informed of what is going on in the project and of the actual state of progress of the whole Project. Content areas will include science progress reports and updates, as well as decisions taken at board level, ongoing work, changes in organisations/management – e.g. interactions with the Member States, Partnering Projects, Open Calls, SGAs, project reviews, and information about what is going on in the

other SPs. Key messages, talking points and Q&As for Managers on key topics and issues will be provided on a regular basis to help leaders play their role as communicators with their staff. We will also include bottom-up communications working with the communications coordinators who are not only responsible for disseminating message from the centre to the sub-projects but also to pass critical information in the opposite direction, helping project management to be aware of issues and opportunities on the ground.

Improve external communication and interactions with the media

We intend to work proactively with the media, focusing on promoting science stories. A full-time media manager will be hired as part of the communications team in the Project Coordination Office; media requests for scientific topics will be directed to experts. In addition, a spokesperson with a good understanding of the Project's management, politics and high-level scientific aspects will be nominated. We will address misleading information through more positive messages. These will clarify and illustrate what the HBP is, why it is necessary, how it will reach its objectives, and the potential impact of the HBP on research, science and society. We will develop an issues management strategy and provide management teams/Partner Institutions with regular updates and talking points to handle media locally if/as appropriate. This will ensure that a consistent message is given, and that the Consortium speaks with one voice.

Strengthen relationships with the community

We will increase the number of open forums and events throughout member states and beyond via established conferences. These include among others the Brain Forum, the Society for Neuroscience (SFN), the Forum of Neuroscience, and the American Association for the Advancement of Science (AAAS) and the Horizon 2020 ICT events. We will increase the number of open forums and events throughout member states and beyond via established conferences. We will also collaborate with Partner Institutions that support relationship building. These forums will provide information explaining what the HBP is, why it exists, and how it will impact a wide range of stakeholders. These points will be communicated in a transparent way, to further people's understanding of HBP. A toolkit will be developed to ensure that each forum is managed and executed similarly. This will maximise consistency, interaction and Project clarity. In addition, online systems such as blogs will provide transparent environments for scientific communities to discuss the Project.

Engage potential users

We will support all activities intended to recruit Platform users, and we will reinforce the concept of the HBP as a European Research Infrastructure. The Project will be advanced as a major portal for national and international scientific thought on the brain. Engagement strategies will focus on getting users to interact with all aspects of the HBP.

Build public support

In addition to open forums, more content highlighting the HBP's science stories will be developed. This content will be suitable for media consumption, and will illustrate the positive and realistic impact of the Project. To maximise the public understanding and reach of HBP research, science centres and museums will be used to engage the public with educational, dynamic and interactive exhibition content.

Empower the Consortium to communicate consistent and realistic messages

We aim to empower the Consortium by providing consistent and realistic messages and talking points on key topics and issues. This will help increase Partner visibility and amplify the HBP's reputation. It will also give the Consortium responsibility for communications

and dissemination, and maximise their reporting activities. Integration with SP activities will be established by creating a communications representative in each SP. This representative will talk about the SP's scientific developments, and will collaborate with the communications team regarding information and actions. This will ensure the SPs are well represented in both internal and external communications. It will also ensure that each SP's "client" base can be used for the benefit of the Project for external communications and outreach activities, and will reinforce Partner Institutions' roles in communicating directly with researchers. Scientists are responsible for promoting their work, always referencing the HBP, and for providing regular input for their research areas. Young scientists will be encouraged to contribute, e.g. by using social media.

"Ambassadors' kits" will be developed, including positioning statements, key messages, and talking points on key topics and issues. These will allow for internal and external communication as appropriate. An intranet (the "Comms Hub") has also been planned. This will function as a repository for communication content that Consortium members can use in their dissemination efforts.

Collaborate with the ethics and society group (SP12) for public engagement

The communications team in the Project Coordination Office will work closely with SP12 (Ethics and Society) in support of the latter's public engagement activities. For more details on these, see section 2.2.2.3.3).

Measuring and evaluating HBP communication activities

Evaluation of the HBP communication activities will be qualitative and quantitative, and both internally and externally focused. It will be based on regularly gathered data and facts, as well as on feedback from interactions with key stakeholders. Corrective actions and adjustments regarding content, tools and channels will be proposed, and integrated into the communications strategy.

Internal communications assessment measures will include: regular meetings with key stakeholders/groups for feedback and progress reports, and interviews.

External communications assessment measures may include: feedback from target groups, value added media monitoring service for evaluating message pick-up and positive vs. negative coverage, web traffic analysis to establish the "so what?" analysis of hit rates and unsolicited mails to the website email accounts, e.g. change in rates, peaks, match to events/news; analysis of social media, including pick-up, key messages, links/follows, and twitter tweet rates; conference/meeting attendance, and feedback forms.

Channels

At a high-level, a combination of face-to-face and written channels will be used to reach target audiences with the right messages.

Reaching the public may require a combination of open forums, media outlets and science museums. The weighting of these channels will shift and evolve based on resources and message effectiveness over time.

Scientific communities will need more direct contact with HBP scientists through conferences and workshops, as well as publications in scientific journals.

Communication with the media will involve HBP scientists, Project spokespeople and the Consortium's network of Partner Institution media departments at local, regional, national and international levels.

Specific channel strategies include media dissemination and monitoring, social media, the public website, communications team online portal, the HBP newsletter and magazine, and science centres and museums.

Media dissemination and monitoring

The HBP plans to use a journalist database to disseminate HBP news to targeted journalists, and a news monitoring service to monitor relevant global news. The journalist database will provide validated contact information, support for targeted press release distribution, journalists' tweet tracking and topic/specialist segmentation. The news monitoring service will monitor global news, so we can validate and post relevant news to the HBP website, and to social networking environments.

Social media

The HBP's social media presence will be emphasised to encourage conversations among the Public, scientists, government personnel, and industry. The HBP aims to develop content specifically for the social networking environment and maintain an on-going, two-way dialogue with targeted audiences via Twitter, Facebook, Instagram, Google+, and other emerging systems. YouTube will be used to host videos describing the HBP and its SPs. A professional network for HBP personnel and researchers outside the HBP will be constructed using LinkedIn and similar online environments.

Public website

The HBP will develop and update its website to clearly inform the public about what HBP is, why it exists, its on-going activities, and its various impacts on society. The website is intended to be a portal and an authoritative information resource for the HBP and other brain research around the world. It will provide access to information about the HBP, its research, its Partners, and opportunities to get involved. A calendar will allow HBP Partners to provide information about their meetings, conferences and special events.

Communications online team portal

The HBP intends to disseminate its communication and identity materials (visual guidelines, presentations, images and videos, facts and figures) to its Partners through a communication intranet portal hosted within the HBP website. In addition, the portal will provide Partners with a way to exchange material and request graphic design and other services, along with a blog to discuss communications and dissemination ideas.

HBP eNewsletter and digital magazine

A digital news magazine is planned to disseminate information about Partners' activities and other relevant news to internal and external audiences, stakeholders and decision makers. The content, which will include general information regarding global brain research, will also be used for the website. A printed version should be produced for conferences. In addition, an eNewsletter should be periodically distributed to HBP Consortium members. This would keep them informed of the latest scientific publications, news and events.

Science centres and museums

There are approximately 3,000 science centres and museums around the world, most of which participate in national, regional and global public education associations. The HBP will reach out to these organisations though a privately funded science centre and museum programme designed to make the public aware of HBP research and its scientific, social and economic impact.

If sufficient additional funds can be found, the HBP will work with its partners to produce scalable exhibitions targeting families, educational institutions, and the rest of the general public. Content will be periodically updated to make the public aware of the Project's latest achievements.

The exhibitions will be rich in 2D and 3D content that is highly interactive and educational. A particularly important goal is to engage the public in a conversation about the ethical and social impacts of HBP's research.

An HBP Science Centre Advisory Group will provide input on strategic direction. This will help guide the development of a global strategy to co-create and distribute HBP research, through interactive and educational exhibition content. The programme will be supported through additional fundraising activities. Pending available funds, the HBP Science Centres & Museums Programme aims to be established in some 20 museums in 15 Member States and in an additional 12 museums outside of Europe during the operational phase of the Project.

Measuring and evaluating HBP communication activities

Evaluation of the HBP communication activities will be qualitative and quantitative, and both internally and externally focused. It will be based on regularly gathered data and facts, as well as on feedback from interactions with key stakeholders. Corrective actions and adjustments regarding content, tools and channels will be proposed as needed, and integrated into the communications strategy. We will make sure our monitoring activities are as simple and cost-effective as possible.

Internal communications assessment measures will include: regular meetings and interviews with key stakeholders/groups for feedback.

External communications assessment measures may include: feedback from target groups, value added media monitoring service for evaluating message pick-up and positive vs. negative coverage, web traffic analysis to establish the "so what?" analysis of hit rates and unsolicited mails to the website email accounts, e.g. change in rates, peaks, match to events/news; analysis of social media, including pick-up, key messages, links/follows, and twitter tweet rates; conference/meeting attendance, and feedback forms.

2.2.2.3.2 Dissemination to the Scientific Community

The ICT Platforms

The HBP's most important channel for communicating with the scientific community will be the HBP Research Infrastructure that will be accessible via the HBP Collaboratory. During the period covered by the FPA, the HBP will operate its RI on a continuous basis, providing access as a service to the Partnering Projects and the broader scientific community, and offering all necessary documentation, training and technical support. Quality of service will be defined in Service Level Descriptions (SLDs). Institutions and commercial companies wishing to guarantee access to a Platform for their researchers will also be able to do so, in return for a fee.

Data and Software

The RI will provide access to data and tools generated by the Project. Software for academic use will be released under a variety of open source licenses.

The Consortium will report on International Standards on which it works and on its contributions to open source projects. In both cases, the Consortium will ensure that its reports are as open, complete and auditable as possible, and that they are in accordance with the applicable FET-flagship reporting guidelines that may be in force at the time.

Access to Neuromorphic Hardware ("Dissemination Systems")

The HBP has already created a small number of low-cost USB-based neuromorphic computing systems and made them available to students, researchers and developers. The Project will continue with this policy in the future, making the systems available without

payment or for a nominal fee. The HBP will use these systems to leverage community talent and enthusiasm, funding awards and competitions for novel applications.

Publications and Conferences

Scientific publications: The HBP publishes its methods and results in international journals and at leading international conferences. As much as possible, papers will be published in Open Access Journals and/or deposited on pre-print. In addition to publications in journals, the Project will fund the publishing of a series of monographs dedicated to different aspects of the Project (neuroscience, brain simulation, medical informatics, neuromorphic computing, neurotechnologies, neurorobotics and ethics).

Conferences: The HBP organises a series of annual conferences (two during the CP-CSA) dedicated to themes relevant to the Project. Each includes speakers from outside the HBP.

The World Wide Web and other online media: The HBP website is being updated to include sections for scientists and technologists in specific disciplines. Other online channels for scientific audiences include science blogs, Facebook pages, as well as live streaming and videos of events and lectures. Plans for the use of new media will be regularly updated as technology evolves.

Links with the neuroscience community: In addition to the co-design and user engagement activities, the European Institute for Theoretical neuroscience (EITN) will have a fundamental in creating further interactions with the relevant scientific communities. Its mission is to be an open place to foster theoretical neuroscience activities that are related to the HBP, and to build strong interactions with the theoretical neuroscience community in order to bring new ideas and theories to the Project. The EITN will organise numerous workshops for communities outside the HBP to interact with the Project's theoretical neuroscience and modelling activities. The EITN will also be open to hosting more general workshops organised by HBP members, where the entire Project can interact with the community.

2.2.2.3.3 Ethics and Society programme (SP12)

In addition to the HBP's overall dissemination strategy, the HBP Ethics and Society programme (SP12) will conduct a major public engagement programme based on "Citizen Conventions", in close collaboration with the PCO's communications team. These events, held each second year, will use a range of public participation methods fitting the specific purpose of each consultation. These methods will include: interview meetings, citizen hearings, citizen summits and consensus conferences. Other methods include Focus Groups, Scenario Workshops and Future Labs. However, a single Convention could examine the social, economic, health, environment, consequences and benefits of a specific science or technology result coming from an HBP research group.

2.2.2.3.4 Potential of Consortium to Exploit Results

Potential for Exploitation

The HBP will open new horizons for brain research and stimulate brain-inspired innovation with the potential to generate social and economic benefits for Europe and enhance the competitiveness of European industry.

The HBP will generate novel results in the areas of Future Neuroscience, Future Medicine and Future Computing. Results with exploitation potential are detailed in Section 2.2.1and include diverse research results, as well as the HBP Research Infrastructure (the HBP's six ICT Platforms).

The HBP understands innovation as an activity that promotes the subsequent exploitation of the Project's results in four different ways: 1) facilitating further research, 2) creating

or marketing products or processes, 3) providing services or 4) using the results in standardisation and any activity that fosters an innovation culture within the project. The channels used for exploitation will include technology transfer, new ventures and the public domain. Appropriate IP protection will be sought, based on asset assessment by the relevant Technology Transfer Offices (TTOs) of the HBP Partner organisations, which are responsible for the exploitation of the research results.

The Project's innovation activities will be linked closely with the development phases of the HBP Research Infrastructure, and an Innovation Member will be appointed to the Directorate (DIR – see 2.3.2.5.3).

HBP Innovation Objectives

The HBP aims to:

- Use the HBP Research Infrastructure and research results to strengthen European competitiveness and to create value for society.
- Become a marketplace for European research and industrial applications that bring together knowledge, technologies and services that contribute to understanding the brain.
- Advance the development of European commercial services, technologies and applications based on HBP fundamental research, by facilitating relations with appropriate industries.
- Build skills, competencies and professional innovation management capacity within the Project, and help Partner organisations to develop the capacity to exploit HBP research results and exploit the HBP Research Infrastructure.
- Develop a comprehensive Technology Map for Europe that would facilitate collaboration between the HBP and industry.

HBP Innovation Principles

The HBP has developed a set of principles to guide activities and decision-making regarding innovation:

Focus on bottom-up innovation

HBP innovation starts at the SP and WP levels, where results are generated and relations with potential industrial partners could be developed into research collaborations or collaborations to translate scientific results into innovation opportunities.

Strategic coordination and support by the HBP Legal Entity

The HBP Legal Entity is the natural contact point for external parties seeking to work with the Flagship. The Legal Entity will help to coordinate and support innovation activities across the Project, maximizing synergies in collaborations with industry, maintaining a Project-wide overview of innovation via the Technology Map and a consolidated "innovation road map", and also fostering a culture of innovation and entrepreneurship throughout the Project, including raising Partners' awareness of the importance of IPRs.

Maintain a Technology Map

The Technology Map of HBP results with innovation potential (IP, software, inventions, discoveries, prototypes, etc.) that emerge from the SPs. The Technology Map will provide the HBP Partner organisations with a comprehensive registry of HBP technologies and serve as an information resource for European industry. The first technology map will become available during SGA1.

Collaborate with industry

The HBP will develop and maintain active collaborations with industry, including industry associations, at all levels within the Project. These will help to promote knowledge exchange, through research collaborations and technology transfer.

Standardisation

The HBP will use existing standards, where available and appropriate, to ensure interoperability, quality assurance and collaboration with other networks. Where appropriate standards do not exist and are needed, in areas such as data representation formats and vocabularies for describing and annotating neuroscience data, the HBP will develop and apply its own software and data standards.

Build on HBP Consortium capacities and networks for exploitation

The HBP will collaborate with the Technology Transfer Offices (TTOs) of the HBP Partner organisations through their participation in the HBP Innovation and Technology Transfer Committee (ITTC). This body will help to facilitate the exploitation of the HBP research results. The TTOs will be responsible for exploiting the technologies through the following channels:

- Knowledge/technology transfer to industry: Attention will be paid to the necessary instruments and agreements (such as patents and licenses). Particular attention will be given to high-tech SMEs that may drive early exploitation of the research results.
- Transferring research results to stakeholders in the public domain: building and providing end users with open access to software, tools, data, models, etc., to optimise coordination, independent validation, and exploitation by academic and commercial end users.
- New ventures: facilitating collaborations with industry, start-ups/spin-offs, ventures, based on HBP results, and exploring the possibilities of building innovation hubs.

The HBP will also explore relations with other networks, including European programmes, initiatives and industry-driven initiatives that can support the exploitation of research results.

Build and retain user communities, including industry

- The HBP Legal Entity's ability to "exploit" the infrastructure beyond the ten-year life span of the HBP Project depends on the Flagship's success in attracting and retaining diverse communities of users from academic research and industry.
- The exploitation plan for the HBP Research Infrastructure (business model) will be developed by the HBP Legal Entity in consultation with other entities in the Project looking at end user requirements and interests, such as those of the pharmaceutical industry. The exploitation plan will become available and will be regularly maintained in all the subsequent SGAs.

HBP Approach to Innovation

The HBP's approach to innovation has three main elements:

1) Supporting exploitation of the research results in cooperation with the HBP Partner organisations.
2) Driving exploitation of the HBP Research Infrastructure (the six ICT Platforms).
3) Seeding innovation through training and industry partnerships.

The HBP Consortium will retain its focus on research and not engage in pure commercial development. Technologies with a potential industrial application will be transferred to industry for development and commercialization, possibly via new ventures or with contractual arrangements governing the transfer of IP.

Exploitation of Research Results

Some of the HBP research results are likely to have commercial value as stand-alone products (e.g. neuromorphic computing hardware) or could become the basis of future services (e.g. data analysis tools).

The HBP Legal Entity will work with the TTOs of its Partner organisations to identify the best channels for these results to be given appropriate IP protection and transferred to stakeholders via suitable licencing mechanisms, with the capacity and need to use new solutions, or become the basis of new ventures. The TTOs are ultimately responsible for the exploitation of the research results and the transfer of technologies to industry.

Other results (scientific knowledge, tools) will create the greatest value for society in the public domain, such as the brain models and disease signatures.

The HBP Research Infrastructure (RI)

The HBP RI will be made available to European research and industry in the Operational Phase of the Project to be exploited for academic research and commercial purposes.

The RI will provide a supportive environment for new discoveries, new technologies and new ventures:

- New discoveries: the RI will be an ecosystem of information, data, technologies and research communities on the brain, facilitating easy access to resources to support new discoveries leading to public benefit.
- New technologies: The research undertaken on the platforms will lead to the identification of potential new approaches and technologies and provide industries with mechanisms to survey, test and market new and emerging technologies (e.g. software and tools) with large groups of users and to survey users.
- New ventures: the Platforms will provide a core Research Infrastructure to users. Third parties will be able to add optional commercial services to the core Research Infrastructure such as storage and analysis tools that could be used on a pay-per-use basis. New technologies developed as part of the Platform development process or by using the Platforms could inspire the setting up of new ventures including new services, in areas such as elastic computing.

Seeding innovation through training, incentives and industry collaborations

The HBP will promote innovation and entrepreneurship through a range of activities designed to motivate and empower HBP researchers and incentivize innovation. These activities include:

- Training in Entrepreneurship through the HBP Education Programme (see 2.2.2.3.6) and by encouraging HBP researchers to participate in training at their institutions.
- IPR awareness training, which will be provided by the IPR helpdesk through webinars and face-to-face training during the HBP schools.
- Recognition of young scientists making outstanding and innovative contributions within the HBP. Young scientists (PhDs and Postdocs) will be invited to submit recent work to the Scientific Advisory Board (SAB – see 2.3.2.5.7). Three winners will be selected annually and receive a certificate of scientific and innovation excellence. Criteria will

be developed for the selection of the winners. The certificates will be presented at the HBP Summit.

Through the ITTC, the HBP will build a link between the labs participating in the HBP and the TTOs, which can provide guidance and support on IPRs, negotiating licensing agreements with industry, and support in creating spin-offs and start-ups.

Interactions with industry at the SP level will provide a basis for identifying research and technology collaboration opportunities and for knowledge exchange.

Innovation Management Framework

The innovation management framework of the HBP reflects the above approach, and includes distributed activities integrated in the SPs and within the HBP Legal Entity (see 2.3.2.4).

The main objective of the innovation management framework is to help the Flagship to document, assess and govern results, and maximize opportunities for innovation, including beneficial collaborations, ultimately supporting HBP achieve its innovation goals.

The HBP intellectual property policy and a structure for "seeding innovation" provide a framework for innovation including driving the exploitation of results.

HBP Intellectual Property Policy

The HBP recognises that intellectual property protection is key to providing incentives for developing content for the platforms and translating research results into public benefit.

Access rights to HBP intellectual property for HBP Partners are defined in the Consortium Agreement. As the HBP evolves into a European Research Infrastructure and the HBP Legal Entity is established, separate rules may be need to govern access to and use of the HBP Research Infrastructure.

A key component of the policy is to ensure that the HBP Legal Entity is granted long-term irrevocable rights to any intellectual property critical for the operation of the Platforms, to ensure the long-term sustainability and viability of the Platforms.

Core elements of the policy include prompt assessment of the exploitation potential of any result, proper protection of inventions and other assets suitable for commercial exploitation, speedy identification of most suitable channel for exploitation so that benefits can be generated for society (e.g. transfer to stakeholders, new venture, public domain), and speedy exploitation to generate the greatest value for Europe and society.

Together with the ITTC, the HBP Legal Entity will develop an IP policy, including tools for intellectual asset assessment, for dispute resolution and guidelines for the exceptional situations when software may be other than open source.

Innovation Tools

The Flagship will develop and use several tools to plan, manage and drive innovation. These tools are likely to develop and change with time and new tools may have to be added.

Innovation Roadmap

The SPs will collaborate to develop innovation road maps for each of the key areas of the project – future medicine, future computing and future neuroscience. The HBP Legal Entity will facilitate cross-SP discussions and will consolidate these innovation roadmaps into a single roadmap for the Project.

The roadmaps will be reviewed and adjusted every two years, based on input from industry regarding factors such as market pull and technology push. Annual feedback from the EC

reviews will also help to update the roadmaps. The roadmaps will consider the progress of the research and identify cooperation opportunities with potential industrial partners and other groups. The roadmaps will also consider the positioning of European companies, especially SMEs.

Technology Map

Technology and IP developments within the HBP will be systematically tracked to ensure that innovative ideas are identified early, and can be tracked and communicated as they mature. Ideas identified in this way will be captured in the HBP Technology Map. The Technology Map will be maintained and managed by the HBP Innovation Team and the Scientific and Technical Coordinators within Project Coordination Office in the HBP Legal Entity, working in collaboration with ITTC.

HBP innovation hubs

Innovation hubs might be structures created at Member State level to facilitate the interaction between HBP knowledge production and the local industrial landscape. Specifically, they are designed to make available information about maturing HBP technology that is relevant to these industries. The innovation hubs will ideally be created as cooperative venture between industry and the local members of the HBP Consortium, represented by, for example, state innovation agencies or relevant TTOs. The first examples are emerging in the HBP Consortium today.

The Legal Entity will support the creation of innovation hubs by facilitating exchanges of good practice in setting up such hubs and in the use of available local, national and EU instruments. Public events will be used to highlight emerging HBP technologies with innovation potential and opportunities for commercialization and technology transfer through partnerships with industry. They will also facilitate the exchange of good practice. The Innovation Coordinators in each SP will be available to support the formation of innovation hubs and will form the first point of contact for the local hubs with the HBP innovation ecosystem. The Legal Entity will make available the results of their work (surveys, Technology Map, Technology Readiness Level assessments etc.) to the hubs.

Financing of hubs: ideally through public-private partnerships or local associations receiving seed funding from state agencies and industry membership contributions.

HBP Infrastructure Exploitation plan (business model and plan)

The HBP Legal Entity will oversee the development of an Exploitation Plan (business model) for the HBP Research Infrastructure that will consider the costs of operating the infrastructure, the needs and interests and “ability to pay” of the different communities of users, and the mechanisms for operating commercial services alongside open access ones.

2.2.2.3.5 Leadership for Innovation

The HBP foresees three groups dedicated to leading HBP’s efforts on innovation: the ITTC, the Innovation Team within the Legal Entity and the Innovation Coordinators within the SPs. Focused external expertise will be sought as needed from specific stakeholder groups, notably European industry, the neuroscience research community, European programmes on innovation, and venture capital funds.

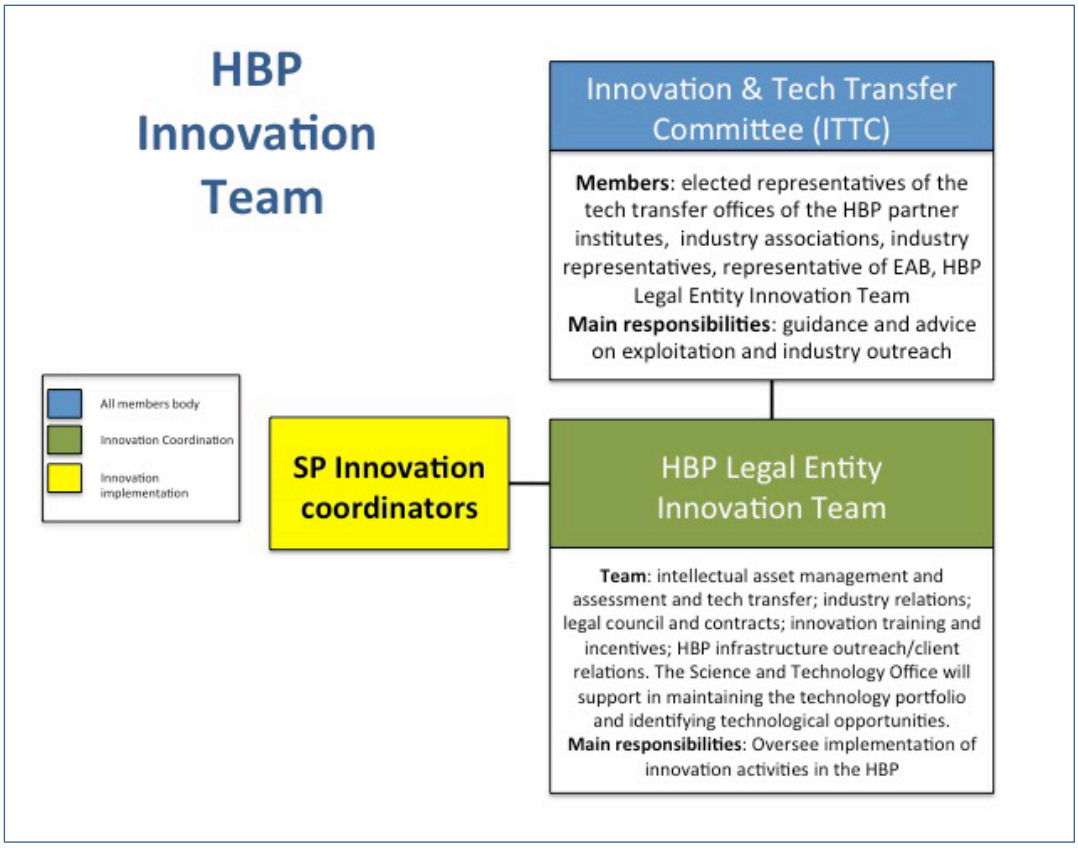

Figure 3: The Innovation Team

The Innovation and Technology Transfer Committee (ITTC)

The HBP Partner organisations own the research results generated by the HBP, making them an essential part of HBP's innovation leadership. The ITTC is an elected advisory body consisting of 10 representatives of the Technology Transfer Offices (TTOs) of the HBP Core Consortium, representatives of relevant industries and industry associations in the HBP's focus areas of future neuroscience, future medicine, future computing, plus the HBP innovation team and a representative of the HBP Ethics Advisory Board.

The ITTC serves an important coordinating and advisory role to the HBP. For example, the ITTC might facilitate exploitation of research results by helping the Innovation Team to organizing events with industry, or by identifying opportunities for Partnering Projects – perhaps including SMEs - to access regional structural funds for innovation.

The HBP innovation team in the Project Coordination Office

The HBP innovation team consists of a group in the HBP Legal Entity and Innovation Coordinators in the HBP Subprojects, eventually led by an Innovation Director. It is responsible for carrying out specific actions to support the HBP's overall innovation policy. This team will be built up over the Operational Phase.

Innovation Coordination: The HBP innovation team within the Project Coordination Office (PCO) serves as the main focal point on innovation issues. The innovation team, headed by the Innovation Coordinator, maintains "the big picture" on innovation across the Project and manages its innovation ecosystem, ensuring synergies and coordinating relations with external stakeholders such as industry. Key roles in the team include intellectual asset management and assessment and technology transfer; industry relations; legal counsel and contracts; innovation training and incentives; HBP infrastructure outreach/client relations.

The Scientific and Technological Coordinators in the PCO will help maintain the Technology Map and identify technological opportunities.

HBP Subproject Innovation Rapporteurs: The Innovation Rapporteurs in each SP will receive training in innovation management, including scouting for technological opportunities, intellectual asset assessment and IPRs. They will be Subproject Managers, PhDs or Postdocs who have an interest in innovation and entrepreneurship, over and above their regular work. They will play a critical role in identifying exploitable results, encouraging their Subprojects to build relations with their TTOs regarding intellectual asset assessment and technology transfer opportunities, and with potential users of HBP results in industry and the broader research community.

The innovation team within the HBP Legal Entity will be responsible for ensuring these tasks are introduced as the Project evolves to prevent possible lost opportunities.

The Innovation Rapporteurs, together with the Innovation Coordinator, form the Innovation Coordination Committee, which is one of a number of cross-cutting committees which bring the different SPs together to focus on a specific issue (see Section 2.3.2.10)

Interaction between the Innovation actors

The Innovation Team within the Legal Entity will fulfil its principal role as focal point on innovation issues by having regular bilateral interactions with:

- The TTOs of HBP Partner Organisations, which are ultimately responsible for exploiting their HBP results.
- The Innovation Coordinators within the SPs, who will link with the TTOs in their own parent institutions.
- The ITTC.
- Innovation Hubs (as and when appropriate).

The role of the Innovation Team within the Legal Entity is high level and strategic, focusing on building and maintaining momentum for innovation within the project and coordinating among the innovation actors within the project and with outside stakeholders, while the HBP Subproject Innovation Coordinators and the HBP Partner Organisations' roles will be more hands-on, focusing on developing relations with European industry and exploitation. The ITTC meetings will serve as an important junction point to bring together all these HBP innovation actors.

Implementation

Innovation support activities will be built up gradually throughout the operational phase (FPA), also to reflect the evolution of the HBP Flagship into a European Research Infrastructure.

SGA	Governance	Infrastructure	Innovation Support	Specific Activities
SGA1	Setting up the Legal Entity	In development	Innovation coordinators	Training and start industry outreach at SP level to explore R&D collaborations
			Technology Map	Develop mapping tool Initiate mapping
			ITTC	Set up Advice and guidance on exploitation and industry outreach Collaboration with relevant industry associates established

			Industry	Industry workshops – future computing, neuroscience, medicine
			Exploitation plan for the infrastructure	Development of the plan – cost model, services, training needs
			Road maps	Develop first road maps for future neuroscience, computing and medicine
			Innovation incentive scheme	Entrepreneur training Researcher recognition award at HBP Summits
			Innovation hubs	Develop concept for innovation hubs
SGA2	Legal entity set up	Operational	Innovation coordinators	Engagement and further outreach to relevant industries
			Technology Map	Continue mapping Use as communications tool for disseminating info to industries/TTOs and supporting industry outreach
			Industry	Active engagement with industry through SP innovation coordinators outreach activities
			Road Maps	Communicate widely about the road maps, use road maps as tool for industry engagement
			Infrastructure exploitation plan	Plan being implemented
			Innovation incentive scheme	Entrepreneurship and IPR training Researcher recognition
			Innovation hubs	HBP conference on innovation hubs – exchanging good practice among the HBP partner countries on innovation hub development linked with HBP technologies
SGA3	Legal entity firmly operational	Operational	Innovation coordinators	Active engagement with industries through knowledge transfer and brokering research collaborations
			Technology Map	Communications tool for disseminating info to industries/TTOs
			Industry	Active engagement with industry through SP innovation coordinators outreach activities Use of the platforms
			ITTC	Monitoring technologies

				and exploitation opportunities, with innovation coordinators Support industry outreach and technology transfer activities
			Road maps	Communicate widely about the road maps, use road maps as tool for industry engagement
			Infrastructure exploitation	Plan being implemented including active collaboration with industry
			Innovation hubs	Further exchange of good practice among the HBP partner countries on innovation hub development linked with HBP technologies and examples from within the HBP shared

Table 3: Timeframe for Implementation of HBP Innovation Support Activities

The Subprojects with the greatest innovation potential will be prioritised in the first Specific Grant Agreement period (2016-2018), receiving more advanced training in innovation management. All SPs will have access to training in IPR awareness and all SPs will be expected to contribute to the innovation road map. The ultimate goal will be for all SPs to benefit and participate.

2.2.2.3.6 Contributions to Education and Training

HBP Education Programme

Future progress in neuroscience and medicine will be increasingly dependent on ICT. Leadership of these fields will be assumed by scientists who have an understanding of computer science, and how it can be harnessed to help advance their own disciplines. However, people with such multi-disciplinary education are still rare, and this scarcity is a constraint for the HBP and more generally for European growth. The HBP therefore includes an Education Programme (EP) as one of the key features of the Flagship Action Plan, which educates hundreds of researchers from various disciplines within Europe and beyond, and helps train a new generation of skilful researchers in academia and industry. The Education Programme is also a contribution to encouraging Responsible Research and Innovation (see Section 2.5 below).

The Education Programme aims to:

- Attract new talent and secure the knowledge, competencies and skills needed within the Project in all its dimensions: science and technology, innovation, dissemination of knowledge, responsible research and innovation, etc.
- Provide young HBP scientists specialised in neuroscience, medicine or ICT with an appropriate introductory education in the other disciplines they will need to participate in multi-disciplinary research inside and outside the project.
- Offer them complementary education in research ethics, the societal impact of research, intellectual property rights (IPRs), and the translation and exploitation of research results, and

- Make the same multi-disciplinary and complementary education available to the broader scientific community and general public.

The transition of HBP education activities from Relations to Knowledge Management reflects the expansion of the Project's activities within the scientific community and the public domain. The HBP's science education activities will become increasingly synergistic with the Project's general dissemination and outreach efforts throughout Europe and the world.

Syllabi

The new EP academic curriculum comprises five separate syllabi. It includes detailed user material, mandatory lectures and workshops on innovation (including responsible innovation) for all PhD candidates participating in HBP-related research, as well as similar training for more senior researchers. Formal examinations and a multi-university certification process are planned. Enrolment of new HBP Students will be based on online testing of performance on the HBP ICT Platforms. Teaching will be based on innovative forms of online education, in which webinars are complemented by face-to-face workshops. The syllabi are being developed and taught by senior scientists leading or working in HBP Subprojects. The commitment of the Syllabus leaders and associated teachers will be supported by a limited financial contribution from the EP budget. The syllabi will introduce young scientists to disciplines outside the speciality in which they have been trained, prepare them to use the HBP ICT platforms and stimulate their entrepreneurial skills. By helping them acquire new competencies and skills, they will be better placed to turn Flagship results into useful innovations. Syllabus teaching materials will be made available via an EP website, accessible through the Collaboratory, that will direct students towards further reading material.

Student Community

The HBP EP will support a Student Community, guide young scientists through the many new avenues of multidisciplinary R&D, provide infrastructure to facilitate interaction between young scientists and create the conditions for fostering and bringing together research talent across the HBP and Europe. Privileged access to HBP data, knowledge and resources will be provided. An annual school will link young scientists inside and outside the HBP, providing a forum for learning and sharing insights into cutting-edge research issues within a specific HBP discipline. The Student Community will give young HBP scientists a voice in HBP decision-making via a seat for a student representative on the Education Programme Committee. The HBP EP will also provide special support and encouragement for young female scientists.

Student Conference, Prizes and Credits

An annual student conference will be associated with the HBP Annual Summit. The Education Programme Office (part of the PCO, see section 2.3.2.5.6) will therefore establish a student committee that will be actively involved in designing the programme for the conference. This student conference will be an important opportunity for students to collaborate with and present their research to each other, either via talks or poster presentations. Students may invite senior scientists to give highlight talks about HBP research areas. A prize will be awarded during the HBP Summit to the student with the best PhD thesis in the HBP Education Programme. The Education Programme Office will launch a call for applications for the student prize via the Education Website one year before the Summit, and close it six months before the Summit. This will allow the Education Programme Committee to review all applications and select the best PhD thesis. As the award will be given to PhD students who have completed their studies, the first prize will be awarded in year four or five of the Operational Phase.

The HBP Curriculum and respective Syllabi would be more attractive to students if they could receive academic credits for taking these courses. However, the HBP does not yet have a legal status that permits the Education Programme to request ECTS credits. The Education Programme Office is working to find a solution to this issue. One possible solution is to found an HBP graduate school that is attached to the HBP's future Legal Entity or NFP Foundation. Another possible solution is to approach each individual HBP Partner about the training offered via the HBP Curriculum, so that students can transfer the Syllabus teaching into their PhD programme. To prepare for accreditation, the requirements, quality standards and templates for EP training materials have been aligned with the standards for quality assurance in European higher education.

2.2.2.3.7 Knowledge Management (apart from IPR)

Publications

The HBP strongly supports European policy on Open Access. To meet the requirements of the policy, all HBP scientific publications will be deposited in an HBP-managed searchable repository, accessible via the Collaboratory (Green Open Access). After they have been deposited in this repository, it will then be possible to link them to data/analysis/models/simulations registered with the Neuroinformatics Platform. Doing so will greatly increase the ability of researchers to understand the relationship between new data/analysis/models/simulations and results portrayed in publications, and also to the data/analysis/models/simulations that are their basis.

HBP researchers will also be encouraged to deposit their publications in other well-known repositories, giving the publications the broadest possible audience, and in particular with the European OpenAIRE repository.

HBP scientists will be free to choose the journals where they publish their research. Partners will be expected to include funds for publication fees in their research budgets.

Data

The CP and the PPs will use and generate petabytes of data. Broad categories of data include:

- Mouse Brain Data for the HBP Mouse Brain Atlas.
- Human Brain Data for the HBP Human Brain Atlas.
- Models from research in theoretical neuroscience.
- Brain atlases and the Knowledgebase (a wiki of information about the brain) made available through the Neuroinformatics Platform.
- Brain simulation data used and models from data-driven reconstructions generated by the Brain Simulation Platform.
- High-performance computing data generated by the High-performance analytics & Computing Platform.
- Clinical data made accessible through the Medical Informatics Platform.
- Data used and generated by the Neuromorphic Computing Platform.
- Data used and generated by the Neurorobotics Platform.
- Data used and generated in Systems and Cognitive Neuroscience.
- Data used and generated during exploration of novel applications.
- Ethical documentation generated by the Ethics and Society Programme.

- Software and technical documentation for the Platforms.
- Administrative documentation.

The HBP has already created a Data Management Plan (Deliverable D13.3.2) that defines general principles for managing the data generated by the Project and applies these principles to the different categories of data described above. The plan, which will be continuously updated over the lifetime of the Project, is based on the template defined by the Horizon 2020 programme, and defines specific provisions for data sharing, backup, archiving and preservation for each data set.

The HBP strongly supports European policy on Open Data, and will define its policies for data access in line with the requirements of the policy. In principle, the Project will follow a dual licensing policy. Academic users will access project data, software, and documentation free of charge. Commercial users may be required to pay a fee. In line with European policy, the Project reserves the right to restrict access to specific data sets, where this is necessary for reasons of security, to allow protection of Intellectual Property, or to protect the privacy of human volunteers. Any such restrictions will be made explicit in the Data Identification Cards, annexed to the Project's Data Management Plan.

Access to medical data will be possible via the Medical Informatics Platform, while non-medical data, analysis results, models and simulations will be accessible via the Neuroinformatics Platform. Both Platforms will be accessible via a GUI and an API-based web service.

2.3 Implementation

2.3.1 Work Plan

The Core Project Objectives will be implemented through 12 Subprojects (SPs), organised into Work Packages, implementing the specific Actions described below. The principal aim of the HBP is to build a cutting-edge scientific research infrastructure that will help to advance neuroscience, and brain-related aspects of computing and medicine. Subprojects differ between each other in their balance between research and ICT. In the first four Subprojects, neuroscience predominates. Research also takes place in Subprojects 5 to 10, but ICT infrastructure work assumes a much larger role.

The primary role of SPs 5-10 is to create the ICT Platforms that constitute the HBP Research Infrastructure. SP5 provides structured access to brain data and knowledge, not just for HBP participants, but also for the broader scientific community. SP6 provides advanced brain modelling and simulation facilities. SP7 adapts and harnesses high-performance data analytics and computing to serve the HBP's specific research areas. SP9 creates ICT systems inspired by the organisation and functioning of the human brain. SP10 creates robot bodies, environments and brain interfaces to test and apply brain simulations. Subproject 11 provides support services, while Subproject 12 addresses ethics and society.

The overarching aim of SPs 1-4 is to advance our understanding of the structural and functional organization of the human brain, from the level of genetic and molecular architecture (including genes, single cell transcriptomes, data on epigenetics, genetic regulatory networks, proteome composition and organisation, distribution of transporters, ion channels, transmitter receptors, cells and their microcircuits, cytoarchitecture and fibre tracts to complex cognitive systems), up to the higher aggregate level of systems mechanisms regulating brain states and cognitive functions. **Since not all of the available research techniques can be applied to the human brain, data derived from mouse and, if necessary, other animal brains will be included for comparison and extrapolation.**

Empirical research will enable the formulation of multi-scale theories and predictive neuroinformatics by modelling and simulation to identify organizational principles of spatial and temporal brain architecture. Addressing the multi-scale organization of the human brain as a complex system is only possible through integration of top-down modelling and bottom-up simulations.

Progress in neuroscience will be significantly advanced by SP1-4s' iterative contributions to the co-design of the HBP's ICT platforms being constructed by SPs 5-10. SPs 1-4 represent the Platforms' first users, piloting the widening of the Platforms to meet the needs of the broader scientific community. This includes developing methods and techniques to characterise brain development and inter-subject variability, as well as tools for big data management and HBP Brain Atlases.

2.3.1.1 Subproject 1: Mouse Brain Organisation

SP1 is an HBP Neuroscience SP.

The objective of SP1 is to generate neuroscientific concepts, knowledge, experimental data sets and tools, which will be used to build models for the simulation of the brain. These models will be integrated, for example, into neuromorphic systems (SP9) or neurorobotics controllers (SP10) in order to create cost-effective, energy-efficient, high-performance systems. Empirical data will also be obtained, when it is hardly or not possible to get it in the human brain, due to technical or ethical reasons (e.g., high-resolution, whole brain synaptic maps, single cell transcriptomes, mapping &

characterization of long-range projection neurons). SP1 will study also mutations, which have been identified in SP2 in the human brain in cohort studies and analyse transgenic animals as disease models in collaboration with SP8 and SP3 (e.g. slow-wave activities in murine transgenic models of neurological disorders). The empirical data obtained in SP1 are synergistic with physiological, connectomics and other data obtained in SP3.

SP1 will investigate differences between the mouse brain and those of other species, and the human brain in particular (in conjunction with SP2) to allow filling in the gaps in our knowledge of the structural organisation of the human brain.

An important role for SP1 is to provide data and knowledge to support activities undertaken by other SPs. Various mechanisms will be used to help inform SP1 about user requirements, including:

- Via SP5 and its rodent atlas WPs, where there are specific Tasks WPs aiming to coordinate atlas activities with external partners.
- Co-design projects (including different components such as community building); in particular CDP1 (development of the whole mouse brain model and related atlas) and CDP2 (Mouse-based cellular cortical and subcortical microcircuit models)
- Open calls
- Other ways, including conferences, meetings, workshops, publication, internet, etc.)

The framework of SP1 will supplement existing activities of the Allen Brain Institute (e.g., with respect to proteomic and metabolomics data. It will take advantage of the existing Allen Mouse Brain Atlas with its comprehensive data on gene expression patterns, transcriptomics, neuronal morphology & physiology and other data sets. A collaboration between the Allen Brain Institute and the HBP has been established to make sure that there is a continuous exchange of research plans, to achieve maximal synergy.

Its Operational Objectives are detailed below. For more on the rationale behind the objectives chosen by SP1, please see Appendix 1: A1.4.1.

Subcellular and molecular level

- Define molecular components including epigenomes, transcriptomes, proteomes and metabolomes, and generate HBP Atlases at different physical scales (e.g. single molecules, subcellular assemblies, cell-types, brain regions) and temporal scales (e.g. molecular dynamics and activity-dependent processes). Regions of interest to be agreed with SP2 and SP3.
- Define subcellular molecular anatomy in synapses, neurons, glia and neuro-glia-vasculature system.
- Identify genetic and molecular networks involved in neuromodulation, plasticity and other critical brain processes. (SP1 genetic work will link to and support SP2 & SP8 genetic work, including that focused on brain diseases such as autism.)
- Study mutations identified in SP2 and analyse transgenic animals in agreement with SP2, 3 and 8
- Align subcellular and molecular datasets with the cellular and whole-brain scale anatomical techniques and datasets, and transfer it to the mouse brain atlas (together with SP5).
- Coordinate design with SP6's modelling and simulation objectives; SP5's atlases and databases; SP4's multiscale theory and SP2's human brain datasets.

Cellular and whole-brain

- Define cellular morphologies of cell-types including neurons, glia and vascular cells.
- Map the distribution of contacts between cell types, in particular synapses.
- Generate projectomes and connectomes at microcircuit, meso-circuit (brain regions) and macro-circuit (whole-brain) scales.
- Characterise cell type distribution and vasculature structure
- Coordinate design with SP6's modelling and simulation objectives; SP5's atlases and databases; SP4's multiscale theory and SP2's human brain datasets.

Integration of multilevel data to brain function

- Obtain, integrate and analyse physiological, behavioural and other functional datasets with the molecular and subcellular, as well as cellular and whole brain datasets, to allow multi-scale synthesis, addressing important unresolved questions in Theoretical Neuroscience (SP4) and contributing to the Neuroinformatics (SP5), Brain Simulation (SP6) and Neurorobotics (SP10) Platforms.
- Obtain and integrate datasets from mice carrying genetic mutations, variations, pharmacological treatments and other manipulations/perturbations of biological and medical relevance (coordinated with disease studies by SP8).
- Co-design and integrate studies with cross-SP collaborative projects (e.g. biologically relevant molecular simulations of synapses - SP4, 5, 6 and 7, - and systems and cognitive neuroscience work undertaken by SP3.
- Work with community partners and international programmes to integrate novel datasets and identify standardised and scalable approaches.
- The datasets that SP1 is committed to produce will be shared with HBP modellers to fulfil the needs of future users. The modellers will tell SP1 which datasets they are interested in using, what data are missing, and what data they would like to generate.

SP1: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Maps of the vasculature of the whole mouse brain. Whole-brain maps of different cellular types based on gene expression. Microcircuitry analysis, proteins and receptor distributions, fibers architecture in a specific large area brain region. Maps of cellular distributions, long-range axonal projections, and synaptic proteins; reconstructed morphologies of major neuron types. Whole-brain activation maps related to selected behaviors. Spatial organization principles in brain activation. Functional maps of cortical activity during learning of the motor task after stroke during learning in the robotic platform.
SGA2	M55-78	Single-cell transcriptome classification of cell-types; reconstructed morphologies of neurons and glia; data for neuron-glial ratios, excitatory-inhibitory ratios; neuron-glia-vascular structural relationships, projections between brain regions, projections of single neurons, synaptic connectivity between identified neurons, whole brain density and distributions of excitatory and inhibitory synapses, ultrastructure properties of neurons and glia, whole-brain cell-specific projection maps. Extend microcircuitry analysis, synapses and receptor distributions to further large area selected brain regions. Refine whole-

		brain distribution maps of cellular types by accounting also to cell shape. Spatio-temporal cell-specific organization principles in brain activation. Functional maps of rehabilitation-assisted plasticity. Functional maps of cortical activity during learning of the motor task in the robotic platform at cellular resolution. Atlasing of activation and functional maps with fMRI maps.
SGA3	M79-M102	Incorporation of data from Partnering Projects and external collaborations; refocused experimental mapping guided by reconstruction; initial integrated multi-level map of the mouse brain.
SGA4	M103-	Fully integrated multi-level map of the mouse brain including data from the Core Project, Partnering Projects and collaborations

Table 4: Main Objectives / Deliverables per SGA for SP1: Mouse Brain Organisation

2.3.1.2 Subproject 2: Human Brain Organisation

SP2 is an HBP Neuroscience SP.

The objective of SP2 is to generate neuroscientific concepts, knowledge, data sets and tools contributing to a better understanding of the multi-level and multi-scale organisation of the human brain. Such results will be used to constrain and validate a first reconstruction and simulation of the human brain. Human brain functional and structural segregation, its inter-subject variability and genetic factors represent central elements of SP2, and contribute to the multimodal HBP-atlas (developed and populated in conjunction with SP5), reaching from the molecular, through the cellular, up to the systems level. SP2 will study differences between the human brain and those of other species, and the mouse brain in particular (in conjunction with SP1). This will make it possible to use transformed versions of data for mouse genes, transcripts, proteins, neuron morphologies, etc. to fill in gaps in our knowledge of the structural organisation of the human brain. Considering the sheer size and complexity of the human brain, this research requires the development and application of big data analytics, which will be done in conjunction with SP7. By bringing in a broad range of expertise in human brain research, SP2 will actively contribute to co-design projects for developing the infrastructure of the HBP, in particular to “Human Brain Atlas”, and “Visuo-motor control”. Synergy will be achieved by collaboration with SP3; e.g., linking cytoarchitectonic maps and receptorarchitectonic data obtained in SP2 with laminar resolution 7T data and dopamine release data in SP3, and align movie and retinotopic data from SP3 with cytoarchitectonic maps, functional segregation data and connectomics data of SP2, to name only a few examples of many.

An important role for SP2 is to provide data and knowledge to support activities undertaken by other SPs. Various mechanisms will be used to help inform SP2 about user requirements, including:

- Via SP5 and its two atlas WPs (5.2.5, 5.3.6), where there are specific Tasks in rodent and human brain WPs aiming to coordinate atlas activities with external partners.
- Co-design projects (including different components such as community building); in particular (but not exclusively) CDP3 (Multi-level human brain atlas) and CDP4 (visuo-motor integration)
- Open calls
- Other ways, including conferences, meetings, workshops, publication, internet, etc.)

SP2’s Operational Objectives are:

Human neurogenomics:

- Provide genetic factors involved in the maintenance and inter-individual variability of structural, functional, and cognitive brain phenotypes using genome-wide **imaging genomics** approaches. Imaging genomics has the potential to identify previously unknown biological pathways and mechanisms influencing the organisation of the human brain. This information will feed the Brain Simulation Platform (SP6) and Medical Informatics Platform (SP8).
- Identify **mutations in genes** involved in brain diseases (such as autism) by genetic analysis of large patient cohorts. There is a strong link to SP1, where the identified mutations will be studied functionally in mice. The identified mutations will also provide valuable input for the Brain Simulation Platform (SP6) and Medical Informatics Platform (SP8).
- Create a **fundamental set of biological information**, **including genomics, transcriptomics and methylomics data,** for a limited number of single cells (agreed with SP1) and brain regions (in conjunction with SPs 1 & 3) linking to the Brain Simulation Platform (SP6) and Medical Informatics Platform (SP8), and contributing to the HBP Brain Atlas (SP5). This project will use methodological experience acquired in mice by SP1 during a pilot phase.

Morphology and molecular architecture:

- Provide quantitative estimates of cytoarchitectonic organization at the level of cortical layers and sublayers, as a microstructural reference for the Human Brain Atlas (SP5) and Brain Simulation Platform (SP6).
- Provide multilevel, quantitative maps of cell and subcellular distributions and morphologies in selected regions of the human brain including mouse–human brain comparison, as well as functional data as a microstructural reference for the Human Brain Atlas (SP5) and the Brain Simulation Platform (SP6).
- Provide maps of quantitative receptor distributions in selected regions of human brain including mouse – human brain comparison, and correlation with functional characteristics of layers and areas as a microstructural reference for the HBP Human Brain Atlas (SP5) and the Brain Simulation Platform (SP6).
- Provide maps of bundles (e.g. U-fibres) and long distance fibre tracts, as well as quantitative measures of their microstructure as an anatomical reference for the Human Brain Atlas (SP5).
- Provide quantitative morphological data for selected fibre tracts and intracortical fibre architecture in the human brain, using polarised light imaging and electron microscopy for the Neuroinformatics Platform (SP5) and Brain Simulation Platform (SP6).

Brain function, segregation, computational architecture and variability:

- Provide a cytoarchitectonic, probabilistic map of the whole human brain, as a microstructural reference for the Human Brain Atlas (SP5).
- Provide parcellations of white matter into fibre bundles and cortical fibre architecture for the Human Brain Atlas (SP5).
- Provide maps of the functional segregation of the human brain using fMRI, provide models of bottom-up and top-down processing (with SP4) and provide a first cognitive ontology of brain territories to SP5.

- Map features coded in columns of the higher visual and auditory cortex and provide models for processing top-down and bottom-up information (with SP4) for validation in SP9.
- Provide models and data on the role of the six cortical layers arising from the architecture of neurons and their connections.
- Provide a first mechanistic model of how neural activity is related to brain regions in collaboration with SP4 and SP6.
- Provide information on the relationship between the variability of neurobiological features and inter-individual differences in behavioural phenotypes.

Methods, Big data analytics & Co-design:

- Link SP2's datasets and parcellations to the accepted template spaces to make the data useful for scientists and other SPs, by developing novel image alignment methods that bridge scales, modalities, and inter-individual variability.
- Develop novel label propagation methods that make SP2 relevant to mining image data to SP8's Medical Informatics Platform, as well as to the wider scientific community who would like to project high-resolution atlas data onto their own scans through the Collaboratory.
- Develop methods and high-performance computing production workflows, in conjunction with SP7, to reconstruct large image datasets, and to extract and analyse quantitative data including big data analytics for processing data in the TeraByte to PetaByte range.
- Ensure the transition of the methods, models and quantitative data into practical tools accessible through the Collaboratory, by designing use cases, defining requirements, implementing software interfaces, and testing.
- Generate a library of synthetic datasets, providing a broad spectrum of modelled fibre arrangements simulating brain tissue.
- Push forward agreements or MoUs, in consultation with authorized representatives of involved HBP Partners, and subject to such HBP Partners' institutional regulations, between SPs 2, 5 and 7, about tools and formats to exchange large datasets.

SP2: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Protocols established for *post mortem* connectomics and multi-level architecture; subjects recruited and ethical approval received for *in vivo* connectomics and functional neuroimaging; initial datasets generated for neuronal and glial cell compositions and genetic architecture; initial data uploaded to Human Brain Atlas on the Neuroinformatics Platform.
SGA2	M55-78	Initial multi-level targeted mapping of the human brain; datasets generated for synapses, channels, neuronal network and behaviour, as well as neuronal and glial cell morphologies obtained and uploaded to Human Brain Atlas on the Neuroinformatics Platform; transcriptome and epigenetics data connected to cell morphology and connectomics; neuro-vascular relationships; updated cortex parcellation.
SGA3	M79-M102	Initial multi-level map of the human brain incorporating data from

		Core Project, Partnering Projects and collaborations; predictive reconstructions and refocused experimental mapping; synaptic properties; neuron and glial morphologies; whole brain cognitive and genetic maps, initial integrated atlas.
SGA4	M103-	Draft multi-level map of the human brain including brain regions, cellular distributions, cell-types, connectivity between and within brain regions, connectivity between local neurons, cellular protein and receptor distribution and their gene expression, synaptic proteins; comprehensive models of human specific mental processes established and their relationship to structural, genetic and epigenetics described; concepts of multi-level brain organisation.

Table 5: Main Objectives / Deliverables per SGA for SP2: Human Brain Organisation

2.3.1.3 Subproject 3: Systems and Cognitive Neuroscience

SP3 is an HBP Neuroscience Subproject and will form the Systems and Neuroscience component of the HBP Core Project under the FPA. It comprises four scientific Work Packages, with teams of 3 to 5 partners. The research themes cut across and link the existing HBP Subprojects, and proposed activities aim to develop ground-breaking scientific knowledge, concepts and models that bring the field closer to the solution of concrete and important problems in cognitive and systems neuroscience in an interdisciplinary research approach. Proposed activities also aim to demonstrate their potential to shape the evolving HBP ICT Platforms (SPs 5-10), thus showcasing the value that these Platforms can add for the neuroscience community.

The selected Projects are expected to play an exemplary role within HBP: they would constitute the first examples of actual use of the HBP ICT Platforms and of their integration into the HBP Neuroscience Subprojects. Activities aim to generate highly innovative scientific knowledge, concepts and models that cut across multiple other SPs, contribute as such to the five co-design projects, and thus bind together various disciplines, techniques, and infrastructures. Examples of SP3 crosscutting targets are included in the operational objectives below. These can be parsed into four distinct work packages, each with a set of objectives. It should be emphasized that, also within SP3, cross-connections between the projects will be established. For instance, work on slow-wave activity can be combined with memory retrieval during sleep, and also connects to work on consciousness. Also work on multisensory object recognition will be linked to multisensory episodic memory. Within each project, data from multiple scales and multiple methods are combined for the investigation of the respective cognitive domain including recognition, memory, sleep and consciousness, and motor behaviour.

Multi-scale organization of slow-wave activity in thalamocortical systems

- Slow-wave activity changes during sleep/anaesthesia-wake transition. Investigate the evolution of slow-wave activity and its multi-scale organization when brain state changes. Infer properties of awake resting states from the multi-scale organization of slow-wave activity, matching experimental evidence with large-scale models of the cortico-thalamic system. Cooperation planned with: SP1, SP2, SP4, SP6 and SP7.
- Slow-waves and complexity: from microscale to bedside. Characterize through a perturbational approach the multi-scale organization (functional differentiation, integration and complexity) of the brain across different states, and understand how the latter is affected by the intrinsic modular bistability underlying slow-wave activity. Cooperation planned with: SP2, SP4, SP6, SP7 and SP8.

- Slow-wave activity in murine transgenic models of neurological disease. From the differences in the spontaneous and perturbed slow-wave activity, infer which are the pathological features of the cortico-thalamic system in neurological disease models and the related mechanistic interpretation of each dysfunction. Cooperation planned with: SP1, SP4, SP6, SP7 and SP8.
- Modulation of slow-wave activity with opto-pharmacology. Development of a toolbox of light-regulated drugs targeting excitatory and inhibitory neuronal receptors. Implement a spatiotemporally selective illumination of brain regions to manipulate slow-wave activity with light. Cooperation planned with: SP1, SP4, SP5 and SP6.
- Slow-wave simulation platforms. Develop parallel simulations of slow-wave activity and its changes in a model of the cortico-thalamic system, using inter-areal connection atlases and a layered grid of columns for each area, as a spiking neuronal network distributed over several thousands of MPI processes. Cooperation planned with: SP1, SP2, SP5, SP6 and SP7.

Context-sensitive multisensory object recognition

- Develop a deep learning network that will eventually incorporate realistic spiking neural networks using the NEST simulator (SP6/SP7), and test alternative models with biologically plausible learning rules based on feedback and neuromodulatory effects. Progressively refine and validate features and connections in these brain models with high-resolution columnar-level and layer-precise fMRI (collaboration with SP2).
- Generate brain imaging data sets hyper-aligned across individual subjects providing high-resolution activation profiles in response to large data sets of visual images. By occluding visual stimuli in one quarter of the visual field, we will extract contextual cortical feedback signals in the occluded region. Representational similarity analysis of cortical feedback will reveal common properties of contextual cortical feedback across subjects and computational models.
- Investigate context-dependent nonlinearity of image formation when one object is occluded by another object and both representations are kept separately in the brain. Occlusion data will be used to investigate neural representations of front and occluded objects separately in brains and computational models.
- Broaden the understanding of basic mechanisms that integrate feedback for context-sensitive amplification. Conduct behavioural animal studies describing the perceptual and circuit level effects of the activation and inactivation of long-range feedback to somatosensory cortex while imaging effects of feedback from cortical and subcortical areas on large-scale populations in a cortical column.
- Record in rodents dendritic feedback mechanisms for the integration of feedback and use this as model constraints. Neuronal ensembles coding for newly learned objects will be extracted using two-photon microscopy and tissue-cleared cortex. Investigate model constraints for invariant object recognition in rodents at single cell and at network level.
- Acquire structural and functional data of cataract reversal individuals to gain insights about plasticity and development of visual feature representation in primary and specialized visual cortex. Investigate differences in plasticity and development (substrate, regulation) during sensitive phases (e.g. critical periods) and in adulthood (perceptual learning) in rodents and human cataract patients. Investigate interactions between critical periods of V1 and higher visual areas.

Episodic memory as multisensory reconstruction:

- Identify multi-scale mechanisms for episodic memory comprising multiple sensory modalities, more specifically of pattern completion and multisensory memory reinstatement in the human brain by measuring hippocampal-cortical interactions at laminar resolution with 7T. To relate activity of hippocampal subfields during pattern completion to memory representations decoded at the level of hippocampal input and output regions. We will couple subfield activity during formation and retrieval of rewarding events to dopamine release (measured by fMRI-PET). This work links to SP2, SP4, SP5, and SP8.
- Identify multi-scale mechanisms that determine the balance between visuospatial pattern separation (creation of new memory representations) and pattern completion (retrieval of old representations). In addition we will determine the role entorhinal grid cells play in these two processes. This work links to SP1, SP4, SP5 and SP6.
- Identify multi-scale mechanisms underpinning multisensory episodic memory by multi-area ensemble recordings and optogenetic interventions. This will allow us to investigate how multisensory events, set in space and time, are encoded and reconstructed in sensory-hippocampal networks during episodic memory operations. This work links to SP1, SP4, SP5, SP6, SP9 and SP10.
- Develop a systems-level computational model of multisensory memory function in rodents and humans that subserves the core functions of compression, pattern completion and separation, and multisensory integration, thereby supporting both memory for past events and prediction of future experience. The new model will instantiate constraints identified by newly acquired data and detailed models of relevant brain substrates. This work links to SP1, SP2, SP4, SP6, SP7 and SP9.
- Build and test embodied (robotic) implementations of the episodic memory systems developed as above that address the challenges of (i) multisensory simultaneous localization and mapping in a rodent-like robot equipped with biomimetic vibrissal and visual senses, and (ii) human-like episodic memory for a humanoid robot that can facilitate situational awareness in tasks requiring robot-human interaction. This work links to SP4, SP9 and SP10.

Neural and computational mechanisms of consciousness

- Test ideas about principles and mechanisms for cortical integration and differentiation, by using mouse experiments and multilevel simulations, including studies of: (1) neuromodulation of brain connectivity (synaptic, somato-dendritic and axonal signalling) and their effects on states of consciousness, arousal, attention; (2) functional roles and effects of oscillations and resonance; (3) functional roles of specific ion channels and receptors in cortex and thalamus, and their effects on states of consciousness, arousal, attention; (4) testing of methods for assessing consciousness by mouse experiments and multilevel simulations; (5) developing, in rodents, novel measures of corticothalamic connectivity, using electrocorticography (ECoG) from implanted electrode arrays, and cell-imaging-based measures. This work links to SP1, SP4, SP5, SP6 and SP9.
- Refine, test, and compare established methods, and develop novel methods, for assessing consciousness, functional brain connectivity and differentiation, by sleep and anaesthesia experiments in humans; and directly compare these with leading methods based on transcranial magnetic stimulation combined with electroencephalography (TMS/EEG) and event-related potentials (ERP) . Apply TMS to different cortical areas to test the roles of the different areas. Develop, in humans, novel imaging-based measures (using fMRI or PET imaging following TMS or transcranial direct current stimulation (tDCS) in humans) of cortico-thalamic connectivity, integration and

differentiation. Further development of clinically useful methods to assess brain state, connectivity and consciousness, including novel "PCI-like" (PCI, perturbational complexity index) indices of network integration and complexity based on sensory stimulation instead of TMS.This work links to SP2, SP4, SP5, SP8, SP11 and SP12.

- Study the effects of cortical lesions on PCI and ERP to test whether structural lesions may drive the rest of the brain into a state of low-complexity and/or sensory disconnection: (1) in brain injured conscious patients, identify cases in which local lesions may affect ERPs and PCI differentially; and (2) evaluate whether specific cortical lesions may lead to changes in ERPs and complexity in distant parts of the brain. This work links to SP2, SP4, SP5, SP8, SP11 and SP12.
- Use large-scale models of the thalamocortical system to simulate (1) conditions where sensory inputs are gated by lesions in thalamus or (2) primary cortices, (3) conditions in which bistable dynamics are gradually induced in neural elements. This work links to SP1, SP2, SP4, SP5, SP6, SP8 and SP9.
- Test different methods for assessing consciousness (1) during transient anaesthesia of one hemisphere (Wada test), and (2) in callosotomy (split brain) in humans, in order to begin testing leading theories of consciousness. This work links to, e.g., SP2, SP4, SP5, SP8, SP11 and SP12.

SP3 methodological and technological operational objectives

- To develop and validate novel cognitive and behavioural paradigms and setups which can be combined with research into the neural mechanisms underlying the cognitive processes under study
- To develop and validate novel software to quantify and analyse behavioural, neurophysiological and computational results obtained in the cognitive studies
- To test predictions made from theoretical and simulation work, done in other SPs and CDPs, against experimental results obtained in SP3 projects
- To establish databases on neural mechanisms underlying mouse as well as human cognition and behaviour, and linking them to databases in SP1, SP2 and Medical Informatics (SP8)
- To apply simulation software, and robotics as well as neuromorphic hardware, to investigate the cognitive and systems functions raised above, and to validate and further enhance these platforms through feedback.

SP3: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Building experimental setups, methods, data analysis tools and simulations of behavioural-cognitive processes and brain states. Validate experimental protocols and acquire initial datasets. Establish key collaborations with other SPs to enable, e.g., large-scale simulations, high-performance computing, theoretical analyses, neuromorphic and robotic implementations. Show examples of how cognitive functions and brain states can be measured and compared between animal, human and computational systems.
SGA2	M55-78	Upscale neuroscientific data, acquire full datasets, and integrate data gathered by different methods, to provide multiscale descriptions of neural substrates of behavioural and cognitive processes. Develop comprehensive, multiscale models, simulations and robotic

		implementations of different cognitive functions such as learning, memory, multisensory integration and perception, object recognition and conscious state changes. Evaluate novel measures, in rodents, humans and simulations, to quantify the complexity and dynamics of these processes.
SGA3	M79-M102	Define key areas where models and experiments need to be improved, and where predictions from theory and modelling should be tested further. Perform these tests by new experiments and simulations, adding newly developed tools for perturbing and manipulating nodes of brain systems to infer causal roles of neural substrates, and applying newly developed tools from other SPs and CDPs. Apply key results to areas of related brain disorders (e.g. Alzheimer's dementia, loss of consciousness, impaired perception).
SGA4	M103-	Formulate full systems-wide computational models of cognitive processes under scrutiny, with inventory of brain structures and functions involved and backed by multiscale simulations. Achieve well-behaved robotic and neuromorphic implementation of these processes.

Table 6: Main Objectives / Deliverables per SGA* for SP3: Systems and Cognitive Neuroscience

*Timings for attainment of these objectives are approximate and need to be confirmed by the partners undertaking the work.

2.3.1.4 Subproject 4: Theoretical Neuroscience

SP4 is an HBP Neuroscience SP. Its Operational Objectives are:

- Develop a multi-scale theory of the brain, creating a synthesis between top-down and data-driven bottom-up approaches.
- Unify theories of learning, memory, attention and goal-oriented behavior, gaining insights into the way function emerges from structure, and identifying the data and computing principles required to model specific brain functions in neuromorphic computing systems.
- Identify bridges linking the multiple temporal and spatial scales implicated in brain activity and in the signals captured by imaging and other technologies.
- Understand complex cognitive functions such as spatial navigation, recursion, and symbolic processing.
- Continue operating the European Institute for Theoretical Neuroscience (EITN), which was set up during the Ramp-Up Phase, to serve as an incubator of ideas, where independent neuroscientists following different approaches can work together to understand the fundamental computational principles underlying brain function and to work towards a unifying theory.

These objectives will be pursued throughout the whole duration of the Project. SP4 will have with strong links to the neuroscience SPs (SP1, SP2 and SP3), and Platforms (providing models and coding principles). In particular, SP4 models will be conceived in a form compatible with the Neuromorphic Computing Platform. They will also be made publically available.

SP4: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Set of models from cellular to network levels, and different brain areas, using different modelling approaches (detailed models, simplified models and population models)
SGA2	M55-78	Comparative assessment of brain data and different modelling approaches (analytical models, large-scale network models, neuromorphic computing systems, neurorobotics experiments) Progressively reduced models of both human and mouse neurons
SGA3	M79-M102	Set of theory-driven models of cognitive processes at the level of neurons and synapses, which are implementable by software simulation and neuromorphic hardware.
SGA4	M103-	Multi-scale theory of brain structure and function that creates a synthesis between top-down and data-driven bottom-up approaches. Applications to unify theories of learning, memory, attention and goal-oriented behaviour, as well as the genesis of brain pathologies.

Table 7: Main Objectives / Deliverables per SGA for SP4: Theoretical Neuroscience

2.3.1.5 Subproject 5 Neuroinformatics Platform

SP5 is an HBP Platform SP. The objectives of SP5 are to provide a Platform for large-scale federated data mining, search and integration, while engaging the community in both using and contributing to the Platform in the course of their scientific and clinical activities.

Brain atlases for rodents and humans

Ensuring that large and diverse datasets, organized across the different levels of the brain and within standard spatial coordinate systems, will allow search and correlative analysis within and across data modalities.

- Identify, curate and integrate multilevel human data from the neuroscience community, as well as SP2 and SP3.
- Identify, curate and integrate multilevel rodent data from the neuroscience community, as well as SP1.
- Engage the community to contribute atlases and additional multi-level data from other species, as well as atlas tools.

Tools for integrating brain data

The necessary tools to register, anchor, align and integrate diverse multilevel data will be built and provided through the web portal, web services or downloadable applications. Packages for establishing data repositories with standard data services, including metadata indexing, search, and data-type specific services, will be provided.

Big data analytics and prediction

Providing the core capability of large-scale data analysis for diverse neuroscience datasets will allow the extraction of key parameters and features necessary for modelling. In

addition, through large-scale feature extraction, clustering and prediction, SP5 will enable prediction of missing data values to help constrain the model building process.

- Provide a data analysis engine for extracting, analysing and classifying features from distributed datasets
- Use data and text mining to analyse data and literature to predict the cellular, synaptic and connectomic properties required to build whole brain scaffold models in SP6
- Populate the multilevel atlases with predicted brain properties:
  - Data-mined and predicted cell composition, distribution and properties
  - Data-mined and predicted synapse composition, distribution and properties
  - Data-mined and predicted connectivity

Knowledge management

Knowledge management is a key objective of SP5 ensuring that the ontologies are maintained keeping the latest concepts up-to-date and pointing to the latest supporting data, models and literature.

- Engage community in contributing, curating, refining and linking to ontologies
- Maintain and organise ontologies
- Develop data-driven ontologies

Interaction with the INCF and other organisations

The goals of HBP and the International Neuroinformatics Coordinating Facility (INCF) are complementary. The HBP currently interacts closely with the INCF, and collaborates in many areas; one example is the development of ontologies at different levels of organisation. This will be continued and further strengthened. This area is critical for SP5 for the development of both the human and rodent atlases. There is, and will continue to be, a close interaction with the Allen Brain Institute, which will utilise the atlas structure developed within HBP.

Develop, maintain and operate the Neuroinformatics Platform

The Neuroinformatics Platform will need to be reliable with a robust operational deployment including continuous build, testing and monitoring. Core services of the Neuroinformatics Platform will have to be sufficiently reliable for, potentially, many thousands of users worldwide.

Data Accessibility and Quality

The data required for the atlases will be of different organisational levels and of widely different types, such as genetics, molecular, electrophysiological, connectivity, behaviour and cognition. It will also contain models/simulations of different types from the subcellular to the systems level. The data obtained by SPs 1, 2 and 3 will be entered into the human and rodent atlases, and although important, this will represent a small part of the data required. The majority of the data used will instead be data sets from the literature. In addition, we will interact with other data providers like the Allen Institute. The community will also be encouraged to deposit their data sets. As indicated above, the data will be curated.

Community engagement

A key objective for the Neuroinformatics Platform is to ensure that the Platform is highly useful to the broader community of neuroscientists; both as an important source of information for the entire community, and also in terms of enabling researchers to add new data to the different atlases. This requires both enabling key community use cases, but also developing the incentives and rewards to motivate continued use and active contribution to the platform. Workshops and other types of training and education will be necessary to engage students, postdocs and other researchers.

SP5: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Establish standard software for federated active data repositories with a focus on European data producing sites. Launch strategic data repositories in key member states. Integrate key data sets from SP1, literature and community data repositories. Curate key datasets and ontologies required for atlases and brain modelling. Integrate Allen Institute datasets containing whole brain gene expression, single cell morphologies, electrophysiology, transcriptome and mesoscale brain connectivity. Provide initial data mining infrastructure for extraction of key modelling parameters of whole rodent brain model. Use predictive neuroscience approaches to predict additional parameters and constraints for whole rodent brain model. Establish initial human atlas and human brain atlas analytics capabilities.
SGA2	M55-78	Extend federated data repository network to include key strategic sites worldwide, including US, Japan, China and Australia. Integrate whole rodent brain projectome data and single cell transcriptome data sets with prediction of whole brain structural and functional properties. Develop continuous integration of datasets from remote repositories, automated feature extraction and initial data-driven ontologies. Develop additional curation workflows and tools to support new datatypes. Enhance datamining infrastructure to support new machine vision classifiers for additional datatypes and features. Release enhanced rodent brain atlases with deep analytics capabilities targeted to modelling extended cellular, synaptic and connectomic properties. Establish additional strategic data curation centers. Integrate vascular and glial data and predictions. Release multilevel human brain atlas with structural and functional data and layers of predicted cellular, synaptic and connectomic properties. Establish initial brain disease atlases for the human brain.
SGA3	M79-M102	Establish federated data mining workflows with increased computational resources and active data repositories. Release enhanced data curation tools and atlas building tools for complex disease/disorder atlases (e.g. traumatic brain injury, epilepsy, etc). Establish workflows to integrate large disease study datasets into human brain atlases. Develop data analysis approaches to further develop data-driven ontologies. Release multilevel human brain atlas including data for whole brain structure, brain region parcellations, nuclei, layers/modules, vasculature, cellular distributions, single cell transcriptome-based cell types, morphologies, electrical behaviour, protein and gene expression, synaptic density and type, neuron and glial morphologies, axonal projections between and within brain regions, synaptic connectivity between neurons, functional cognitive

		maps and initial predicted structural and functional properties.
SGA4	M103-	Deliver data management tools for the analysis, mining and tracking of data in globally distributed repositories. Establish continuous integration of data from strategic active data repositories. Develop additional data curation centers for rodent, human and cross-species datasets and atlases. Establish automated data-driven ontology workflows. Release human brain atlases integrating multilevel multiomic datasets ranging from gene expression to whole brain cognitive and behavioural maps. Establish key cross-species predictive neuroscience workflows to enable cellular level prediction of morphological, electrophysiological, synaptic and connectomic properties of the human brain. Establish tools to explore relationships between genetics and epigenetics, structure, cognition and behaviour. Release multilevel disease human brain atlases.

Table 8: Main Objectives / Deliverables per SGA for SP5: Neuroinformatics

2.3.1.6 Subproject 6: Brain Simulation Platform

SP6 is an HBP Platform SP. Its operational objectives are:

Subcellular and molecular level models and simulations

- Use Molecular Dynamics (MD)-based methods to estimate thermodynamic and kinetic parameters, required for subcellular modelling.
- Build and simulate molecular-level models of neurons, synapses, glia and the Neuro-Glia-Vasculature system.
- Develop multi-scale (atomistic and coarse-grained) models and simulations of the molecular interactions involved in neuromodulation, plasticity and other critical brain processes (notably, protein-protein and protein-drug interactions).
- Integrate these models in single neuron models.
- Encourage and participate in community modelling efforts contributing to SP6's General Objectives.

Cellular and whole-brain modelling

- Build scaffold models of target areas of the mouse brain (such as cerebellum, hippocampus, basal ganglia and somatosensory cortex) and of the whole mouse brain.
- Encourage and participate in community efforts extending and validating existing HBP scaffold models and building models of brain areas not addressed within the core project.
- Work with the community to build models and simulations of the human at the subcellular, cellular, micro (column/module/nucleus), meso (region), and macro (whole brain) levels.
- Collaborate with the community to design and perform *in silico* studies (e.g. in *in silico* electrophysiology, using brain models developed within the SP.
- Work with SP1-4, SP8-10 to develop simplified versions of high-fidelity brain models and participate in cognitive, behavioural and clinical research.

Reconstruction and simulation tools

- Work with SP5 to develop tools allowing automated incorporation of data from the Neuroinformatics platform in reconstructions and simulations.
- Work with the MD and other relevant communities to develop highly integrated, high-throughput, multi-scale simulation tools for the calculation of kinetic constants, drug affinities and for understanding molecular events in neuronal cascades.
- Develop tools for subcellular level reconstructions and simulations, which integrate estimated parameters from MD simulations, and which are suitable for integration in single neuron models.
- Work with experimental neuroscientists and model builders to develop algorithms and workflows for the multi-level (molecular, sub-cellular and cellular level) reconstruction and simulation of neurons, synapses, the Neuro-glia-vasculature system, microcircuits, meso-circuits (brain regions), and macro-circuits (the whole brain).
- Implement theoretical insights from SP4 in algorithms for synaptic plasticity, re-wiring, axon remodelling and neuromodulation.
- Develop algorithms and workflows for the simplification of high fidelity brain models.
- Develop algorithms and workflows for the systematic validation of brain models and their components, allowing comparisons between different models and modelling approaches.
- Translated these algorithms and workflows first into software tools and workflows suitable for use by members of the outside community.
- Advance and maintain existing simulators for molecular dynamics, reaction-diffusion dynamics, cellular-level simulation and point neuron network simulation, to take account of SP6 and SP4 developments and requirements.
- Work with SP7 to optimize these simulators for use with HBP High-Performance Computing Resources.
- Work with SP8 and SP10 to develop models and simulations of brain disease, based on data collected by the Medical Informatics Platform.
- Work with community partners to develop standards for representing, and sharing brain models.
- Develop tools allowing comparison of brain models against results obtained with commonly used experimental techniques (LFP, EEG, Calcium Imaging etc.).
- Make these tools available to the community as Open Source Software (OSS), accessible via the HBP Brain Simulation Platform.

Brain Simulation Platform

- Design, implement and operate the HBP Brain Simulation Platform, facilitating collaboration between HBP researchers and community researchers.
- Integrate the platform in the HBP Collaboratory.
- Work with community users to develop Apps providing a user-friendly graphics interface to tools and models developed within the project and to design APIs providing programmatic access.
- Provide documentation, training and support for users of the Platform; integrate with the HBP Collaboratory.

Community outreach

- Participate in and facilitate community modelling efforts extending HBP scaffold models or addressing areas of the brain/species not directly addressed within the Core Project.
- Participate in and facilitate community efforts to standardize model and data representations and to facilitate comparisons between different models and modelling approaches.
- Participate in and facilitate projects using *in silico* reconstructions and simulations to address unresolved issues in theoretical and experimental neuroscience.

SP6: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Scaffold models of molecular-level principal neurons, cellular-level reconstructions of selected cortical and sub-cortical regions; network-level models of the whole mouse brain; simplified models exported for implementation in neuromorphic computing systems. Initial version of Brain Simulation Platform incorporating algorithms and workflows for reconstruction and simulation of subcellular, cellular, microcircuit, and meso-circuit (brain region/system) levels; tools and protocols for *in silico* experimentation and model validation.
SGA2	M55-78	Scaffold cellular level models of the mouse brain; reconstruction of molecular level neurons, synapses and glia; scaffold models of human neurons algorithms and workflows for reconstructions and simulations of the whole mouse brain; tools and protocols for interactive *in silico* experimentation and model validation; first publications on *in silico* neuroscience experiments in Partnering Projects.
SGA3	M79-M102	Algorithms and workflows for multi-level reconstruction and simulation of the mouse brain; first draft multi-level reconstruction and simulation of the mouse brain; first draft reconstruction of the human brain at the cellular level; predictive reconstruction of reactants and reaction kinetics, protein-protein interactions, ion channels, and receptors involved in the action of drugs; first publications of *in silico* neuroscience cognition and behaviour experiments in Partnering Projects.
SGA4	M103-	Algorithms and workflows for predictive multi-level reconstruction and simulation of the mouse brain; first draft multi-level reconstruction and simulation of the human brain; *in silico* validation experiments for human brain models; *in silico* neuroscience, cognition and behaviour experiments; first publications of *in silico* neuroscience, cognition and behaviour experiments in Partnering Projects.

Table 9: Main Objectives / Deliverables per SGA for SP6: Brain Simulation Platform

2.3.1.7 Subproject 7: High-Performance Analytics & Computing Platform

SP7 is an HBP Platform SP. Its Operational Objectives are to:

- Design, implement and operate a federated High-Performance Analytics and Computing Platform consisting of the central HBP supercomputer, satellite HPC and data facilities, Cloud storage and high-fidelity visualisation capabilities, evolving towards exascale performance and data management capabilities.
- Extend these capabilities and the capacity of the High-Performance Analytics and Computing Platform by inviting further European HPC and Data Centres to join and complement the current ones.
- Establish co-design processes with the user community on the one hand, and with the vendors of HPC technology on the other hand, to tailor the High-Performance Analytics and Computing Platform to the needs of neuroscience and drive the development of future HPC systems.
- Design, implement and deploy novel software capabilities, algorithms and numerical methods for brain simulations and big data analytics to allow for an efficient use of the HPC capabilities and for multi-scale simulations.
- Develop programming models, middleware, libraries, algorithms and data stores to exploit data locality and avoid data movement on supercomputing systems.
- Develop middleware, software and functionality for large-scale visual data analysis and large-scale, interactive and immersive visualisation environments for neuroscience.
- Design, implement and deploy big data analytics methods, algorithms, libraries and tools, including data mining, machine learning and workflow support, in particular for the processing of large-scale multidimensional image data sets.
- Develop middleware, libraries, APIs and scheduler software for dynamic resource management enabling applications to dynamically change their use of resources and for *in situ*, co-scheduled execution of analysis and visualisations on heterogeneous hardware.
- Develop tools, models, description languages, and simulation frameworks to model software performance on different machine architectures.
- Deploy the software components in production level quality by using state-of-the-art software development techniques, such as agile methodology, continuous integration and continuous deployment.
- Create documentation, training and appropriate support structures, helping users apply for access to Platform resources, adapt and optimise their codes for supercomputers, and make efficient use of the infrastructure and services provided by the High-Performance Analytics and Computing Platform.
- Reach out to the user community by dissemination, training and support, as well as by collecting their requirements and feedback, up to the level of active collaboration in the form of co-design projects.

SP7: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
Ramp-Up	M01-30	Prototype version of High-Performance Analytics & Computing Platform, based on existing supercomputers at Jülich, CSCS, BSC and Cineca; Cloud storage at KIT; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services

SGA1	M31-54	Operational version of pan-European High-Performance Analytics & Computing Platform, based on supercomputers at Jülich, CSCS, BSC, Cineca and further hosting sites in other countries; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT and interoperable with public Cloud providers
SGA2	M55-78	High-Performance Analytics & Computing Platform including pre-exascale, data-centric HBP supercomputer at Jülich with up to 50 PFlops and basic hardware and software support for interactive supercomputing (large memory capacity, dynamic resource management, visualisation and steering capabilities tightly coupled to simulations, visual analysis algorithms for basic multi-level post-processing); supercomputers at CSCS, BSC, Cineca and other hosting sites; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT, interoperable with public Cloud providers; joint operation with Neuromorphic Computing systems
SGA3	M79-M102	Continued operation of High-Performance Analytics & Computing Platform including pre-exascale, data-centric HBP supercomputer with advanced hardware and software support for interactive supercomputing (advanced in-situ visualisation methods for multi-scale and steerable simulations, supported by session management and annotation); supercomputers at CSCS, BSC, Cineca and other hosting sites; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT, interoperable with public Cloud providers; joint operation with Neuromorphic Computing systems
SGA4	M103-	High-Performance Analytics & Computing Platform including exascale, data-centric HBP supercomputer supporting full multi-scale visualisation and analysis of brain models up to the size of the whole human brain; supercomputers at CSCS, BSC, Cineca and other hosting sites; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT, interoperable with public Cloud providers; joint operation with Neuromorphic Computing systems

Table 10: Main Objectives / Deliverables per SGA for SP7: High-Performance Analytics & Computing Platform

2.3.1.8 Subproject 8: Medical Informatics Platform

SP8 is an HBP Platform SP. Its Operational Objectives are to:

- Design, implement and operate a federated clinical infrastructure comprising tools for harmonizing heterogeneous clinical databases, data anonymisation, ontology-based query interfaces, federated search and distributed analysis of clinical data.

- Establish agreements or MoUs, in consultation with authorized representatives of involved HBP Partners, for access to hospital data, centralized large-scale clinical research databases and biobanks. Provide documentation, training and support to the users.
- Develop generic tools for data curation, quality control and provenance. Develop, implement and deploy tools to extract brain morphology, genomic, proteomic behavioural and cognitive features from clinical and research databases.
- Develop, implement and deploy mathematical methods for predicting multi-level features of diseases; develop tools for identification of homogeneous disease using the Biological signatures; construct unified models of brain diseases.
- Contribute data, novel disease classification for disease simulation and *in silico* experimentation.

SP8: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	First version of Medical Informatics Platform; scale-out implementation of data management platform for distributed infrastructures; access for academic researchers, epidemiologists and clinicians; federation nodes in 5 R&D hospital partners for in-situ querying of anonymised data; web-based services for neuro-epidemiological studies, interactive analysis and exploration of the biological signatures of Alzheimer's disease; initial publications demonstrating the value of the Platform. Once adequate functionality has been achieved, the plan is to transfer the hospital software bundle developed in academia to industry for its industrialisation, commercialisation and wider deployment (industry standard software, accreditation for clinical use by the European Medicines Agency, installation and service contracting, updating software apps, etc.). Further development of functionality in SGA2 and 3 will depend on research and clinical community needs, success in defining disease signatures and other developments. Such development work may be carried out jointly by research teams and industrial partners (see SGA2-SGA4 below).
SGA2	M55-78	Development will include refined tools for analysing medical data at Federation level, enriched user-interaction functionalities, real-time automated data workflows; foundations for distributed mining of medical data; tools for identification of homogeneous, disease-related biological constructs. Only the parts of such work that still have a clear research component and which are essential for the HBP RI will be carried out as part of the Core Project. Essential ones from the computer science viewpoint is implementation of efficient continuous real-time integration of globally distributed medical data and ontologies, and distributed system-level result caching and workflow optimization strategies. Outputs and metrics will include publications that demonstrate the value of the platform and first disease signatures.
SGA3	M79-M102	Predicting further developments is difficult but likely elements include: extension of the federation with hospital nodes world-wide; graph-based mathematical models for interactive analysis; tools for large-scale mining of medical data, using complex features;

		sophisticated disease models with variables from *in silico* experimentation; tools for identification of homogeneous disease-related biological constructs; external validation of disease models using post-hoc clinical phenotyping; interactions with brain simulation results and tuning of brain disease signatures. Only the parts of such work that still have a clear research component and which are essential for the HBP RI will be carried out as part of the Core Project. Examples of essential ones include: efficient distributed querying support of complex user-defined functions, tight integration to user logs, declarative specification of complex data mining workflows, and automated matching and mapping between medical and research datasets.
SGA4	M103-	As the federation is further extended, accompanying developments could include: graph-based mathematical models and support for graph-based ad-hoc medical query processing; automated mapping, integration and addition to existing workflows of new data sources; tools for large-scale mining of medical data; predictive and prescriptive disease models; disease simulation, with a generative model of disease comorbidities and resilience; unified model of brain diseases, generating a biologically grounded classification of brain disorders; evaluations and cross-analyses using brain simulation; medical guidelines based on disease models, with extension of Platform use into personalised medicine and patient selection for clinical trials.

Table 11: Main Objectives / Deliverables per SGA for SP8: Medical Informatics Platform

2.3.1.9 Subproject 9: Neuromorphic Computing Platform

SP9 is an HBP Platform SP. Its Operational Objectives are to:

Operate, use and maintain the large-scale Platform installations

This is initially the most important objective as it makes existing and unique neuromorphic facilities available to non-expert users. The use cases are basic neuroscience research and applications in cognitive computing outside neuroscience. For the first use case, cross-Platform cooperation within the HBP is carried out with:

- SP3: Cognitive architectures in closed-loop experiments with special emphasis on plasticity, learning and development.
- SP4: Implementation and testing of theoretical models of neural computation with special emphasis on bridging spatial and temporal scales.
- SP6: Transferring reduced complexity circuits to the Neuromorphic Computing Platform.
- SP7: Using the High Performance Computing Platform to process circuit mapping, executable system specifications and data analysis.
- SP10: Using the virtual robotic environment for closed-loop experiments.

Training for external neuroscience users is provided through education and training events. Support for experiments is provided as part of the Platform Work Plan.

Cognitive computing applications outside neuroscience that use the Neuromorphic Computing Platform are expected to be carried out by collaborations outside the HBP.

These will involve academic research groups from machine learning (e.g. deep learning) and industry as external Platform users.

Build, operate and distribute reduced size portable systems as subsets of large systems

Reduced size systems are available today, and are used by a broad community inside and outside the HBP. The SpiNNaker boards are used in robotics as real-time systems, as they can interface to electronic sensors and actuators. The most important application of reduced size systems throughout the FPA will be in education and training. In the HBP this is carried out via cross-SP cooperation with SP11, in particular the education section. The systems will be used as follows:

- To introduce new HBP students and scientists to neuromorphic computing during HBP Schools, summits and similar events.
- Outside the HBP, small systems will be used at summer schools, and will be given to academic groups for evaluation and research. The use in undergraduate and graduate teaching will be essential to broaden the user base in the future.

Next generation chips (see next objective) will also be used for next generation reduced size systems throughout the FPA.

Developing the next generation neuromorphic chips for large-scale and reduced size systems

This is the first genuine HBP work in neuromorphic chip development as both existing hardware systems have been developed in previous projects (SpiNNaker and FACETS / BrainScaleS). The development work is carried out in cross-SP collaboration, and with two SPs in particular:

- SP1: Building structured models of neurons based on experimental data from neuroscience.
- SP4: Preparing next generation systems for implementing new developments in theoretical neuroscience. These focus on plasticity, learning and development, stochastic computing, and reduced complexity neuron models.

The expected funding of SP9 for this objective is focused on chip design, prototyping and prototype testing. The required funding for actual system construction is provided for information (see Tables 24 & 25).

Providing software access to neuromorphic computing

This is a prerequisite for the use of all neuromorphic systems (large, small, next phase) in the HBP. This work is carried out in close collaboration with all other Platforms, and with the Collaboratory group.

SP9: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
Ramp-Up	M01-30	NM-PM-1: With 4 million neurons and 1 billion synapses, x10,000 acceleration NM-MC-1: With 100 million neurons and 100 billion synapses
SGA1-4	M31-	NM-PM-1: Small-scale systems available for training & development NM-MC-1: Small-scale systems available for training & development

SGA1	M31-54	NM-PM-2: Feature set described in Roadmap table to get ready for NM-PM2 NM-MC-1: increasing scale, performance and on-line accessibility, with real-time closed-loop virtual robotics environment from SP10. NM-MC-2: Architecture model, and test silicon where appropriate
SGA2	M55-78	NM-PM-3: Feature set described in Roadmap table to get ready for NM-PM3 NM-PM-2: Construction starts (subject to availability of about ~EUR 3.8 million construction funding) NM-MC-1: continuing evolution of on-line access in response to user feedback. NM-MC-2: Silicon samples tested and evaluated (subject to availability of NRE funds ~EUR 2 million)
SGA3	M79-M102	NM-PM-2: Operational (subject to construction starting in SGA2) NM-PM-3: Construction starts (subject to availability of ~EUR 11 million construction funding) NM-MC-1: Continuing evolution of on-line access in response to user feedback NM-MC-2: Large-scale system build to single rack scale (subject to availability of ~EUR 3 million build funds)
SGA4	M103-	NM-PM-3: Operational (subject to construction starting in SGA3) NM-MC-1: Continuing evolution of on-line access in response to user feedback NM-MC-2: Large-scale system available on-line (subject to availability of ~EUR 6 million build funds)

Table 12: Main Objectives / Deliverables per SGA for SP9: Neuromorphic Computing Platform (NM)

2.3.1.10 Subproject 10: Neurorobotics Platform

SP10 is an HBP Platform SP. Its Operational Objectives are:

In silico models of behaviour, cognition and motor control

- Develop and perform pilot *in silico* experiments that drive the development of the Neurorobotics Platform (NRP).
- Work with SP1-SP6 to integrate brain models with models of spinal cord, sensory, motor and vestibular systems and to close the sensory-motor loop of CNS, PNS and body.
- Work with SP1-SP6 and community to reconstruct sensory motor maps needed for basic motor control.
- Work with SP1-SP6 and community scientists to reconstruct basic drives, value- and motivation systems for autonomy.

In silico models of bodies, robots and environments

- Develop and maintain community accessible libraries of bodies, robots, environments and their parts.
- Develop scaffold models of bodies and muscoloskeletal system for use in the Neurorobotics Platform.
- Identify strategically important robot and body models and integrate them into the NRP community libraries for use in the Neurorobotics Platform.
- Develop benchmarks and validation tools for *in silico* neurorobotics.
- Co-design will be used to refine the accuracy and resolution of robots and environments.

Future robotics technology

- Develop and explore closed-loop neurorobotics systems using neuromorphic hardware (SP9).
- Translate virtual robots and brain-derived controllers to physical prototypes.
- Transfer controllers to modular robots and state-of-the-art embedded systems.

Simulation and visualisation tools for neurorobotics

- Develop tools to plan, run and analyse *in silico* experiments with neurorobotics systems, enabling life-like neurorobotics experiments with robots in sensory rich environments and users in the loop.
- Develop innovative tools for immersive high-fidelity rendering and real-time user interaction.
- Develop simulation tools for robots and sensory-rich environments (World Simulation Engine).
- Develop tools to interoperate simulated and physical robots.
- Incorporate physical robots, starting in SGA1, with user requirements integrated *via* co-design.

Neurorobotics Platform

- Design, implement and operate the HBP Neurorobotics Platform, facilitating collaboration between HBP researchers and community researchers.
- Integrate the HBP Neurorobotics Platform in the HBP Collaboratory.
- Work with community users to develop Apps providing a user-friendly graphics interface to tools and models developed within the project and to design APIs providing programmatic access.
- Provide documentation, training and support for users of the Platform.

Community outreach

- Participate in and facilitate community modelling efforts extending HBP scaffold models or addressing areas of the brain/species not directly addressed within the Core Project.
- Participate in and facilitate community efforts to standardize model and data representations and to facilitate comparisons between different models and modelling approaches.

- Participate in and facilitate projects using *in silico* reconstructions and simulations to address unresolved issues in theoretical and experimental neuroscience.

SP10: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Initial version of Neurorobotics Platform; capabilities to design virtual robots, environments and experiments and to link them to existing brain simulations; pilot experiments using Platform capabilities.
SGA2	M55-78	Enhanced user access and control; enhancements to simulated robots, environments and experiments; closed-loop support for simplified brain models; first published experiments using Platform capabilities; pilot experiments using high-level simulations with in-built plasticity; pilot experiments using cellular level reconstructions of the mouse brain; links to Brain Simulation, High-performance analytics & Computing and Neuromorphic Computing Platforms; first simulated robots and devices, environments and experimental conditions. Value of platform for users demonstrated in co-design pilot projects.
SGA3	M79-M102	Closed-loop support for *in-silico* mouse experiments; first published behavioural experiments using brain reconstructions with plasticity and cellular level reconstructions of the mouse brain; comprehensive library of simulated robots and devices, environments and experimental conditions for customisation.
SGA4	M103-	Closed-loop support for human brain models; pilot studies in human behaviour and cognition; finalised services for customisation of robots and devices, environments and experimental conditions. The types of models to be built will be defined closer to the date.

Table 13: Main Objectives / Deliverables per SGA for SP10: Neurorobotics Platform

2.3.1.11 Subproject 11: Central Services

SP11's Operational Objectives are:

- Provide the Project and its Legal Entity with strong project management, support services and a robust and transparent governance system.
- Coordinate and manage the project, including these aspects:
  - Reporting, helping scientists to write deliverables, consortium management, performance and risk management.
  - Communication & dissemination.
  - Political environment of the Project.
  - Science & technology.
  - Innovation and technology transfer.
- Support decision-making of Governing Bodies.
- Ensure transparency and accountability.
- Maintain quality and performance standards.

- Provide support services for the rest of the project:
  - Web-based management and collaboration tools.
  - Communications.
  - Industry Relations.
- Develop and manage an Education Programme (see 2.2.2.3.6)

SP11: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Submit proposal for and secure EC agreement on SGA2
SGA2	M55-78	Submit proposal for and secure EC agreement on SGA3
SGA3	M79-M102	Submit proposal for and secure EC agreement on SGA4
SGA4	M103-	Launch HBP as durable European Research Infrastructure

Table 14: Main Objectives / Deliverables per SGA for SP11: Central Services

2.3.1.12 Subproject 12: Ethics and Society

SP12 (Ethics and Society) is the hub of responsible research and innovation (RRI) in the HBP. It undertakes foresight research on social, ethical, legal and cultural implications of HBP research, explores conceptual and philosophical issues and challenges raised by HBP research, builds awareness and capacity for social and ethical reflection among HBP researchers, engages HBP researchers with external stakeholders and the general public, and supports the robust management of ethical issues of the HBP as a whole. SP12 will collect and develop good practice in RRI.

Its approach overall has four interlinked components: anticipation (of future implications, based on research); reflection (activities to enhance ethical and social awareness and reflection among HBP researchers; engagement (engaging, disseminating and debating HBP research with stakeholders and the general public); action (ensuring the results of these activities help shape the direction of the HBP itself in ethically robust ways that serve the public interest).

Three concrete overall objectives of SP12 to which all SPs will be relating to are:

- Privacy and data protection
- Ethics of simulation
- Mind and Brain disorders

RRI issues facing the HBP and the project's approach to managing them are examined in depth in Section 2.5.

SP12's Operational Objectives are:

Foresight Analyses and Researcher Awareness

- Undertaking foresight studies on key aspects of the HBP
- Working with scientists and other members of the HBP to reflect on ethical, social and regulatory issues

Neuroethics and Philosophical Analyses

- Exploring the role of contexts and cultural imprinting in understanding the brain's functional architectures
- Investigating philosophical and ethical challenges of modelling cognitive processes in silica

Public Engagement & Communication

- Undertaking citizen dialogue and consultation
- Engagement between HBP scientists and external stakeholders in "Stakeholder Forums" on issues of possible controversy

Ethics Management

- Developing Principles and Implementation of Ethics Management including Standard Operating Procedures and mapping ethical issues of the HBP
- Ethics Compliance Management
- Supporting relevant groups such as the Ethics Advisory Board and Ethics Rapporteur Programme.

SP12: Main Objectives & Deliverables per SGA

SP12 deliverables consist of reports on activities, detailing the main outcomes and results achieved by SP12 work packages, and "opinions" reports formulating SP12 observations and recommendations about ethical and social issues arising during the course of HBP. SP12 will deliver one report of each type per year.

SGA	Deliverable	Due date
SGA-1	SP12 first "opinions" report	End of SGA-1 Y1
	SP12 second "opinions" report	End of SGA-1 Y2
	SP12 first activities report	End of SGA-1 Y1
	SP12 second activities report	End of SGA-1 Y1
SGA-2	SP12 first "opinions" report	End of SGA-2 Y1
	SP12 second "opinions" report	End of SGA-2 Y2
	SP12 first activities report	End of SGA-2 Y1
	SP12 second activities report	End of SGA-2 Y1
SGA-3	SP12 first "opinions" report	End of SGA-3 Y1
	SP12 second "opinions" report	End of SGA-3 Y2
	SP12 first activities report	End of SGA-3 Y1
	SP12 second activities report	End of SGA-3 Y1
SGA-4	SP12 first "opinions" report	End of SGA-4 Y1
	SP12 second "opinions" report	End of SGA-4 Y2
	SP12 first activities report	End of SGA-4 Y1
	SP12 second activities report	End of SGA-4 Y1

Table 15: Main Objectives / Deliverables per SGA for SP12: Ethics and Society

2.3.2 Management structures and procedures

2.3.2.1 The FET Flagships Governance Framework

2.3.2.1.1 Framework Partnership Board (FPB)

A Framework Partnership Board (FPB) will link the Commission and the EU- funded HBP Core Project. The FPB provides the mechanisms to discuss the commitments of the participating organisations and the Commission to the Flagship. It will mainly contribute to maintaining relations of mutual co-operation and regular and transparent exchange of information between the CP consortium and the Commission on the planning, implementation and follow-up of the Flagship activities funded by the Commission and on any other matter of common interest. Representatives of the PPs who participate in the management framework of the CP will also be invited to attend the FPBs.

Examples of subjects that FPB meetings will be addressing include: planning and implementation of the Flagship and execution of its activities as defined in the Flagship Action Plan; identifying new relevant H2020 work programme activities; discussing the collaboration framework, selection and integration of PPs within the CP; international collaboration aspects, etc.

2.3.2.1.2 Board of Funders

The Board of Funders brings together representatives from the participating countries and the Commission with the purpose of programming of activities in support of the Flagships.

The role of this Board is essential for defining and planning the financial support to the Flagships for their whole duration. The Board Members will discuss the overall progress of the Flagships and will exchange information on European, national and regional activities in the areas of the Flagships. They will address the orientation and funding possibilities of their respective programmes and their synchronisation with the aim to maximise synergies and help Flagships meet their objectives. They may also focus on the selection and integration mechanisms of PPs within the Flagships. Representatives of the CP and PP Consortia will be invited to participate to the Board meetings, as appropriate.

The Board will help to promote an environment that stimulates innovation by linking the S&T developments to innovation policies at national and European level.

The Board is to be co-chaired by the Commission and the participating countries, which need to be represented at the right policy level where decisions about national programmes and budgets are planned.

2.3.2.1.3 Flagship Governance Forum (FGF)

The Flagship Governance Forum (FGF) links the Commission, the participating countries and representatives from the CP and PP consortia. The FGF has the form of a non-binding discussion forum which aims at achieving an efficient inter-working and synchronisation of the main stakeholders involved in the implementation of the Flagships and their respective activities. The FGF contributes to the development of a common European effort around the Flagships. It supports their further development, stimulates synergies between the CPs, PPs and related activities funded at regional, national, transnational or European level and promotes their innovation potential. Examples of subjects that FGF meetings may be addressing include:

- Overall progress of the Flagships and their positioning with regards to the advancement of research in related S&T areas and to relevant international initiatives;
- Hosting discussions (in the form of open forums) that are related to scientific, governance, or other aspects of relevance to the Flagships. Such discussions will be open to all, whether or not they are part of the Flagships.

- Education and training activities, international cooperation aspects, etc.

The FGF will cover both the Graphene and the HBP Flagships, and may meet in different configurations according to the agenda topics under discussion.

The stakeholders will nominate their representatives at the appropriate level for best representing themselves in the FGF. The FGF is to be co-chaired by the Commission and the participating countries.

2.3.2.2 HBP Governance: Underlying Factors and Principles

The HBP has evolved considerably since the Project was accepted by the European Commission (EC) in 2012. Originally conceived as a straightforward EC-funded, single-consortium research project under FP7 rules, albeit on a larger scale than usual and with a longer timeframe, it has evolved into a broader, more complex Flagship Initiative, with an EC-funded Core Project (equivalent to the original consortium) plus Member State-funded Partnering Projects. Whatever the future evolution of the HBP, it will remain a science-driven project.

In addition, the goal of the HBP is now shifting more explicitly in the direction of building an enduring European scientific infrastructure. Given that EU infrastructure projects are funded and managed rather differently from research projects, this shift has had a profound influence on the new HBP governance arrangements outlined here. The HBP governance should also ensure a clear "separation of powers" (see next section below), to implement the principle that the people who decide the allocation of money within the Project should not be the ones who are responsible for spending it. Finally, the HBP should ensure that its governance structure is transparent and simple, fairly represents Partner organizations, funders and other stakeholders, and provides adequate accountability to all these parties, as well as including appropriate mechanisms for resolving conflicts.

In addressing the governance imperatives outlined above, the HBP also had to take into account the fact that EC-funded projects operate under different rules and expectations from those funded by Member States. Because of the complexity of this challenge, the HBP formed an external advisory Governance Working Group (GWG), comprising the heads of various large EU or Member State research infrastructure bodies, such as the CEA (France), CERN, EMBL, ESA, ESRF, ESFRI, Helmholtz (Germany) and NHS (UK). The GWG unequivocally advised the HBP to adopt a single governance structure, built around a European infrastructure model, such as the European Research Infrastructure Consortium (ERIC) framework.

Described below is the HBP's new governance structure. Central to this is the creation of a Legal Entity, to assume the role of Coordinator for the HBP and assure the continuity of the HBP as a major European scientific research infrastructure. The description starts with the arrangements envisaged once the HBP Legal Entity is operational. However, the Legal Entity cannot be created overnight. Therefore, an Interim Phase is also envisaged, while the Legal Entity is being created, but other key governance changes can be made. During this time, the supreme body of the HBP will remain the General Assembly (GA), until it can be replaced by the Stakeholder Board (SB). The Interim Phase will commence as soon as the FPA has been signed and the Legal Entity Phase should start as soon as possible, but at the latest one year after the FPA has been signed. The transfer of overall authority, from the GA to the SB, will take place during the Interim Phase.

2.3.2.3 Separation of Powers: the roles of the main governance bodies

In the HBP governance structure, the principle of "separation of powers" (or system of "checks and balances") is achieved by allocating specific responsibilities to different

bodies. The checks and balances are achieved, not within any single body, but in the interaction between the different bodies. This is best exemplified in the process for agreeing the scientific action plan and related budget for each Specific Grant Agreement (SGA) in the period covered by the FPA:

The Science and Infrastructure Board (SIB) is composed of the SP Leaders, who are proposed by the Task and Work Package Leaders in each SP and co-opted in the SIB. The SIB proposes the work plan and related budget estimates for the different activities within a given SGA to the Directorate.

The Directorate, which is led by a Director-General (DG) and includes – amongst others - the Chair and Vice-Chairs of the Science and Infrastructure Board (SIB), executes on behalf of the SB and prepares the decisions for the SB. In particular, the Directorate will review the work plan and budget for achievability and compatibility with the long-term HBP objectives, as set out in the FPA. In the event of disparities or incompatible budget estimates, the Directorate will consult with the SIB and the HBP's external advisory bodies, and then recommend possible solutions to the General Assembly (GA) - or Stakeholder Board (SB)- for a final decision. In all cases, final approval for the work plan and budget, plus any other major decisions, has to be given by the GA / SB, thereby providing the necessary "separation of powers".

The SB represents the owners of the HBP that are organized in a Legal Entity. The SB decides on strategy, budgets, and all senior appointments in the project. Until the SB is established, the GA will remain the supreme decision-making body of the HBP.

In brief, the General Assembly (later the Stakeholder Board) fulfils the Supervisory Board function identified by the mediator, while SIB provides the scientific leadership and the Directorate the executive leadership.

No single HBP Partner organisation should have its employees chairing more than one of the three main governance bodies of the HBP (SIB, DIR and SB).

2.3.2.4 The HBP Legal Entity

In the Ramp-Up Phase, the role of HBP Coordinator was fulfilled by the École Polytechnique Fédérale de Lausanne (EPFL). In the future, this role will be taken on by an HBP Legal Entity, which should provide a more suitable organisational basis for managing an enduring European scientific research infrastructure and avoid giving a disproportionate project management role to a single participating institution.

The Legal Entity will be headed by the Director General (see 2.3.2.5.3), backed by the Executive Director (see 2.3.2.5.3). Its principle staff component will be the Project Coordination Office. These personnel will be employees of the Legal Entity.

Once it has become operational, the responsibilities of the Legal Entity might include:

- Ensuring the establishment, operation and improvement of the HBP Research Infrastructure.
- Helping the key decision-making and executive bodies of the HBP (the Stakeholder Board, the Science and Infrastructure Board, and the Directorate) to run the HBP.
- Supporting the HBP's key external advisory bodies: the Scientific Advisory Board, the Ethics Advisory Board, the Innovation and Technology Transfer Committee, the National Infrastructure Representatives Board and the Audit Committee.
- Receiving EC funds on behalf of the HBP Core Project and distributing it appropriately to individual Partners, in accordance with the agreed action plan and EC project rules.
- Coordinating the HBP Core Project's reporting to the EC.

- Ensuring adherence to contractual agreements signed with the EC, notably Specific Grant Agreements, and with other external parties.
- Concluding collective agreements or MoUs with other research initiatives on behalf of the HBP.
- Concluding commercial agreements with companies to promote downstream applications of HBP technology and discoveries.
- Managing the HBP's openness-related activities, such as calls and user access to the infrastructure.
- Fundraising and sponsorship management.
- Running training programmes for Research Infrastructure users.
- Facilitating student and employee mobility between members of the Legal Entity and helping to educate the next generation of researchers in ICT-based neuroscience and brain medicine.

The transition to the Legal Entity and associated governance arrangements should be completed as soon as possible, but not later than one year after signature of the FPA. It should be operational shortly afterwards.

The Legal Entity will formally take over the Coordinator role from the EPFL. It will exercise this role through the Director General.

2.3.2.4.1 Stakeholder Board to replace General Assembly

Another key change required for the long-term governance solution is the move from a General Assembly, in which each of more than 80 Partner institutions spread across some 20 countries has its own voting representative to a Stakeholder Board, in which all the participating institutions in one country share a single representative. This development will not only make for a more manageable governance structure, but it will also pave the way for transforming the HBP into a Legal Entity which can become an enduring Member State-owned European Scientific Research Infrastructure when EC funding ends in 2023. It will take time to negotiate its terms of reference. While this change is being prepared, Member States' interests in the HBP will be assured through the Funders Board and/or other mechanisms foreseen in the EC Staff Working Document.

2.3.2.4.2 Interim governance changes

An interim governance structure will be implemented in the period from the signature of the FPA to the moment that the Stakeholder Board and the Legal Entity become operational. In this period, the role of supreme decision-making body will continue to be fulfilled by the General Assembly (GA), until it can be replaced by the Stakeholder Board (SB). However, a key difference in the functioning of the GA in the interim phase will be that each Partner represented in the GA will have one, equal vote instead of the arrangement in the Ramp-Up Phase where voting rights were in proportion to a Partner institution's share of EU funding. The SP Leaders (i.e. the Science and Infrastructure Board) will be confirmed by the GA / SB. The SIB Chair and two SIB Vice-Chairs will be elected by the SIB and confirmed by the GA / SB.

The Directorate will be headed by a Director General (DG), who should be a prominent scientist and experienced manager of large-scale scientific undertakings. The Chair and Vice-Chairs of the SIB will represent the SIB on the Directorate, to help ensure a close working relationship between the two bodies.

Persons filling HBP leadership positions, including the DG and all Members of HBP governance bodies (SB, DIR and SIB), must make a full declaration of their interests to the

SB and satisfy the SB that any possible conflicts are identified and addressed. In the interim period, until the SB is established, the Coordinator will employ the DG.

The Steering Committee of the Stakeholder Board (SCSB, see Section 2.3.2.5.2 below) will be created as soon as the FPA is signed. It will lead the Interim Phase, working in close collaboration with the GA. In particular, it will define the status and internal functioning of the Stakeholder Board and, later on, the Legal Entity.

2.3.2.5 The Legal Entity Phase Governance Structure

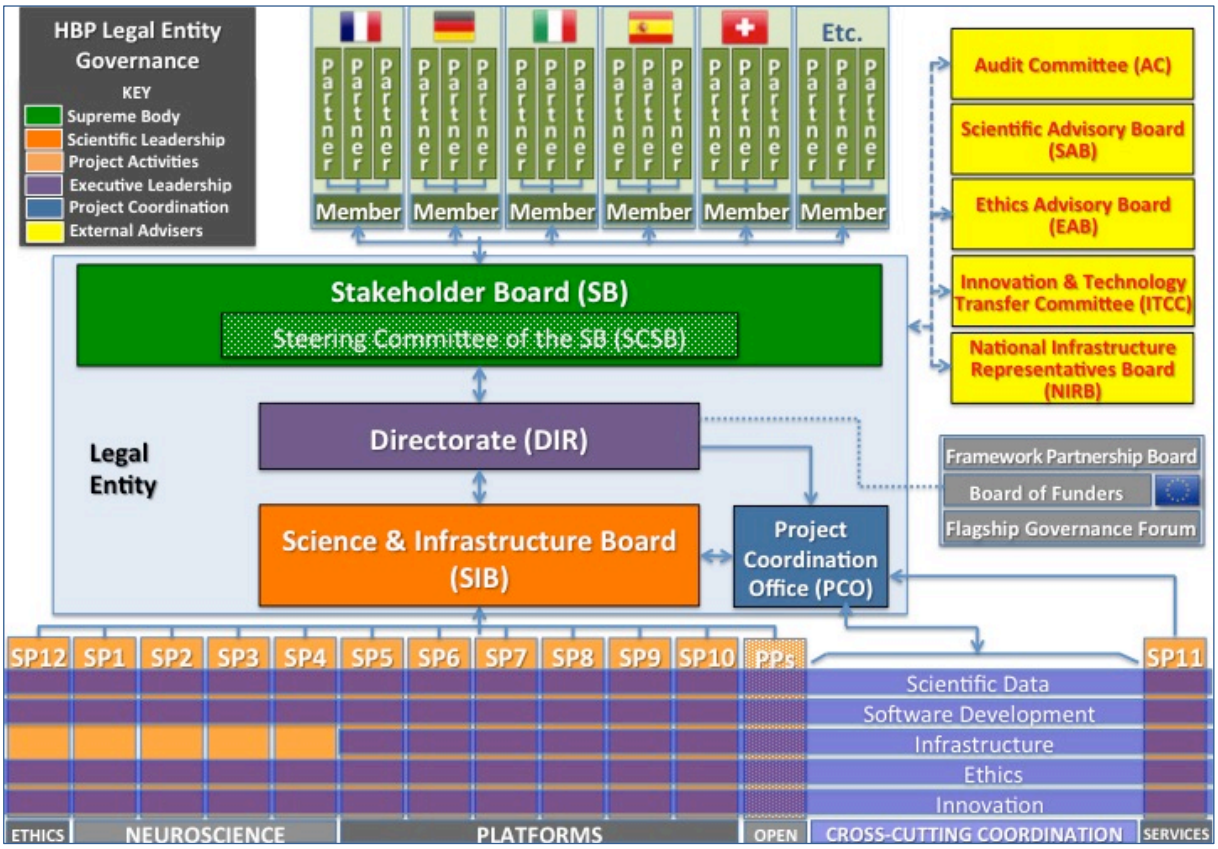

Figure 4: The HBP Legal Entity Phase Governance Structure

2.3.2.5.1 The Stakeholder Board (SB)

The SB exercises ultimate authority over HBP. It is the assembly of members and replaces the General Assembly. It:

- Approves or rejects the Legal Entity annual budget and work plan, its statutes and implementing rules and procedures.
- Approves or rejects proposals for amendments of the statutes and implementing rules.
- Can terminate the Legal Entity.
- Approves changes to the membership of the Legal Entity. Can terminate membership of individual members.
- Can adjust the composition of the Legal Entity, adding or removing members, individuals and/or Partner institutions as it sees fit.
- Appoints (after consultation with the SIB), suspends or dismisses the Director General.
- Confirms, suspends or dismisses the Chair and/or Vice-Chairs of the SIB.

- Confirms the Members of the SIB.
- Makes decisions related to the amount or method for calculating member contributions.
- Decides the HBP action plan and related budget proposed by the SIB and prepared by the Directorate.
- Elects an SB Chair. The terms are linked to the SGA phases. Re-election is possible.
- Approves or rejects the annual report of the Legal Entity.
- Each SB member is responsible for communicating HBP-related information to the individual institutions that it represents.
- The SB may modify the mandate of the Steering Committee of the SB and appoint or dismiss its members (see section 2.3.2.5.2).

Composition:

Composition: One representative per Member of the Legal Entity. Each representative has one vote of equal weight. Decisions are taken by simple majority. The Members will be one participating organisation per participating country that is part of the HBP Core Project Consortium. Where there is more than one participating organisation in a country, the participating organisations in that country will select one of their number to represent their interests on the SB. Representatives on the Stakeholder Board should have a scientific background commensurate with understanding the aims and work of the HBP.

The terms of reference of the SB (level and qualifications of representatives, number of meetings, interactions with the Directorate, etc.) will be specified in a separate document, prepared by the Steering Committee of the SB and approved by the SB.

2.3.2.5.2 The Steering Committee of the Stakeholder Board (SCSB)

The Steering Committee of the SB is a group of representatives of core member countries which make major financial contributions to the HBP. Its responsibilities include:

- Guiding the setting up of the Legal Entity.
- Drafting the initial terms of reference of the SB.
- Establishing the terms for recruiting, appointing and dismissing members of the DIR, including the DG.

The mandate of the SCSB may be revised by the SB once it is fully established.

Composition: One representative from each of five to seven national Member organisations. The Chair of the SB should be a member of the SCSB.

2.3.2.5.3 The Directorate (DIR)

The Directorate (DIR) is the executive body and is headed by the Director General (DG). The DIR will normally take decisions by consensus.

The Directorate:

- Is responsible for ensuring that the HBP and the Legal Entity fulfil their obligations to the stakeholders and other contractual partners, as set out in the FPA, individual SGAs or other collective agreements.
- Takes proposals decided on by the SIB, including the SGA action plans and budgets, and consults with the appropriate HBP advisory boards, prior to submitting them to the Stakeholder Board (SB) for its decision.

- Ensures that the SB's decisions are implemented appropriately.
- Ensures that the scientific and infrastructure work plans and related budgets proposed by the Science and Infrastructure Board (SIB), with the assistance of the Project Coordination Office, are achievable with the resources available and that are appropriate for achieving the HBP goals set in the FPA and successive SGAs, and that the corresponding work plans are implemented appropriately.
- Manages the Legal Entity, including its finances, material and human resources.
- In conjunction with the SIB, presents an annual project activity and progress report to the SB, covering the scientific, operational and financial activities of the HBP.
- Approves or rejects (with reasons) recommendations from the SIB and PCO for new contractual agreements and amendments to existing agreements (FPA, SGAs, Consortium Agreement), plus changes to the Membership of the Core Project Consortium, and submits them to the SB for decision.
- Adopts all audit reports and implements requested measures.

Composition:

- Director-General (DG):
  - The Directorate will be headed by the Director General (DG), who should be a prominent scientist and experienced manager of large-scale scientific undertakings. Persons who have been involved with the HBP during the Ramp-up Phase can be considered for the DG position only if any potential conflicts of interest are resolved to the satisfaction of the SB. In the interim period, until the Legal Entity is established, the Coordinator will fulfil the DG role.
  - At least 50% position, funded by the project.
  - Personifies the HBP Legal Entity/Coordinator role and signs contracts on behalf of HBP (once the Legal Entity has been established).
  - Appoints and dismisses PCO staff.
  - 4 year term, renewable.
- Chair of the SIB / Scientific Research Director (SRD)
- Vice-Chair of the SIB / Software Development Director (SDD)
- Vice-Chair of the SIB / Infrastructure Operations Director (IOD)
- Innovation Director (nominated by the ITTC, approved by the SB, may not be a member of the SIB)
- Ethics Director (Nominated by the EAB, approved by the SB, may not be a member of the SIB)
- Partnering Project Director (nominated by the representatives of the PPs, approved by the SB)
- Executive Director (appointed by the Director General)

2.3.2.5.4 Scientific Leadership: the Scientific Research Director (SRD), the Software Development Director (SDD) and the Infrastructure Director (ISD)

SIB Chair / Scientific Research Director (SRD)

The Scientific Research Director (SRD) is the overall scientific leader of the HBP, Chair of the Science and Infrastructure Board (SIB – see Section 2.3.2.5.5), and an *ex officio* member of the Directorate (DIR – see section 2.3.2.5.3). The SRD also chairs the Scientific Data Coordination Committee. The SRD is elected by the SIB from amongst the leaders of all SPs, approved by the DG and confirmed by the SB.

SIB Vice-Chair / Software Development Director

The Software Development Director (SDD) coordinates the HBP's software development activities, is a Vice-Chair of the SIB, and an *ex officio* member of the DIR. The SDD also chairs the Software Development Coordination Committee. The SDD will normally be the leader of one of the Platform Subprojects (SPs 5-10). The SDD is elected by the SIB, approved by the DG and confirmed by the SB. The ISD is elected by the SIB, approved by the DG and confirmed by the SB.

SIB Vice-Chair / Infrastructure Director (ISD)

The Infrastructure Director (ISD) leads the HBP's infrastructure operations and is a Vice-Chair of the SIB and an *ex officio* member of the DIR. The ISD also chairs the Infrastructure Operations Coordination Committee. The ISD must be the leader of a Platform SP.

Their responsibilities are as follows:

- To chair the SIB and be responsible for the effective operation of that body.
- Ensure the coherence of Work Plans and related budgets proposed by the SIB.
- Ensure close cooperation between the SIB and the DIR, in pursuit of the HBP's common objectives.
- Brief the SB and DIR on project progress and any issues encountered, at intervals determined by the SB.
- Bring proposals from the SIB to the DIR.
- Communicate to the SIB requests from the DIR.
- Represent the interests of the SIB in the DIR.
- Represent the interests of the DIR in the SIB.
- Lead the cross-cutting activities related to their title, via the coordination committee of the same name (Scientific Data, Software Development or Infrastructure). These committees formalise current practice by bringing together representatives of each of the relevant SPs. In this role, each Director is assisted by the corresponding Coordinator in the PCO.

The Chair and Vice-Chairs of the SIB will normally be elected by the SIB members for the duration of one SGA, and may be re-elected for subsequent SGAs.

The SIB may oblige the Chair and Vice-Chairs to relinquish day-to-day leadership of their SPs to their Deputies.

To help achieve separation of powers and reflect the diversity of the HBP, the DG, the SIB Chair and SIB Vice-Chairs should each come from different institutions. This principle may be overridden with the express approval of the SB.

2.3.2.5.5 The Science and Infrastructure Board (SIB)

The SIB is central to the HBP Core Project. It provides the scientific leadership of the HBP. It decides the scientific content of the project and is responsible for proposing and implementing the scientific and infrastructure Work Plan agreed for each SGA. It:

- Proposes the Work Plan and related budget allocation to each SP for each SGA for SB approval, via the DIR.
- Proposes adjustments to the membership of the Core Project Consortium for each SGA, based on the SB-approved Action Plan for that SGA, coupled with a review of Partner performance during the previous SGA.
- Is responsible for proposing changes to the work plan to take account of scientific and technological advances inside and outside the Project.
- Is responsible for ensuring that the Scientific SPs achieve the objectives set out in the relevant SGA.
- Is responsible for identifying and implementing corrective actions when SPs fail to provide sufficient corrective action themselves.
- Can request or impose changes by an SP in case of underperformance, following the procedure for correcting underperformance.
- Reviews and approves scientific Partnering Projects requesting to join the HBP Flagship Initiative. The SIB is responsible for ensuring that the Partnering Projects (PPs) contribute to the Strategic Flagship Objectives.
- The SIB is responsible for the HBP Collaboratory.

Composition: The SIB will initially comprise the Subproject (SP) Leader of each scientific SP (SPs 1-10 & 12) in the HBP Core Project, plus one representative from the Partnering Projects (PPs). The composition of the SIB may be altered in the Interim Phase.

Selection: The SIB is a collegiate body which provides scientific leadership for the HBP. It is constituted by co-opting the SP Leaders. Each SP's Leader and Deputy Leader is elected by the Work Package and Task Leaders in that SP, and proposed to the SIB.

2.3.2.5.6 Project Coordination Office (PCO)

The PCO, headed by the Executive Director, manages and coordinates the Core Project and acts as the intermediary between the HBP Legal Entity and the European Commission. It:

- Maintains the Consortium Plan (budget) and administers the EU contribution.
- Helps the SIB to compile SGA Action Plans and related budgets, prior to review by the DIR and decision by the SB.
- Coordinates the planning, writing and timely submission of SGA proposals and amendments to the European Commission.
- Monitors and supports the implementation of the Action Plan by the SPs. Identifies emerging problems, signals them to the SIB and DIR and requests or takes corrective action, as appropriate.
- Monitors the functionality and operation of the HBP Research Infrastructure. Is responsible to the DIR for ensuring the availability and functionality of the HBP Research Infrastructure. Coordinates common infrastructure procurement and technology choices.
- Monitors and facilitates the integration of Partnering Projects (PPs) in the HBP.

- Provides coordinators to support key cross-cutting committees (Scientific Data, Software Development, Infrastructure, Ethics and Innovation). These committees formalise existing practice, bringing together representatives of each of the relevant Subprojects.
- Provides central services and support across the Core Project.
- Coordinates standards development within the HBP and with external standardization groups.
- Collects, reviews and submits Reports and other Deliverables to the DIR and European Commission.

2.3.2.5.7 Scientific Advisory Board (SAB)

The SAB is a high-level body that advises on the scientific direction of the whole Flagship. It reports to the Legal Entity.

Composition: Scientists at the top of disciplines of current and future interest to the HBP, but no participation or interest in the HBP. Members are nominated through a process determined by the GA / SB and then are appointed and dismissed by the GA / SB. The SAB will be initially appointed by the GA, upon signature of the FPA. When the Legal Entity becomes operational and the SB takes over from the GA as the HBP's supreme decision-making body, the SB will have the opportunity to review composition of the SAB.

2.3.2.5.8 Ethics Advisory Board (EAB)

The EAB advises the SIB and DIR on specific ethical, regulatory, social and philosophical issues raised by HBP research. It reports to the Legal Entity.

Composition: Unpaid experts chosen for their knowledge in a specific area relevant to the HBP. Membership of the EAB is adjusted to ensure expertise, geographical and gender balance. Members are nominated by the DG, appointed and dismissed by the SB.

2.3.2.5.9 Innovation and Technology Transfer Committee (ITTC)

The ITTC is responsible for helping HBP to implement a commercial and downstream activity related to the infrastructures or other outputs from the HBP. It reports to the Legal Entity.

Composition: Technology Transfer Officers from Partner institutions. Nominated by the Partner concerned, confirmed and dismissed by the SB.

2.3.2.5.10 National Infrastructure Representatives Board (NIRB)

Supports and advises the SIB, the DIR and the SB in the establishment and operation of the HBP infrastructure, ensuring consistency, coherence and stability of infrastructure services, supporting the coordination of procedures, tools and practices, making proposals to improve the quality and efficiency of the services. The Vice Chair of the SIB / Infrastructure Operations Director is an *ex officio* member of the NIRB.

Composition: Representatives of the national infrastructure facilities involved in the HBP infrastructure and the SIB Vice Chair / Infrastructure Operations Director (who may not chair the NIRB).

2.3.2.6 Dispute Resolution Mechanism

If a person working within the project has an issue with the leadership, management or another person working on the project, they may raise this issue with the external

Ombudsman, appointed by the DG and confirmed by the SB. The Ombudsman is responsible for investigating the issue and referring it to the DG and/or SB for resolution, as needed.

2.3.2.7 Audit Committee

Where external quality control of an HBP Deliverable is required, impartial investigation of alleged underperformance by an element within the HBP, oversight of HBP financial matters or prevention of deviation from work plan and expected underperformance, the General Assembly or Stakeholder Board may order the creation of an audit committee to investigate, report and make appropriate recommendations for corrective action, should this be required. Due to the variable nature of the mission, individual audit committees may vary in size, composition and duration of activity.

The project-oriented audit committee described above will be separate and quite distinct from any internal audit division that the Legal Entity may be obliged to create under the laws regulating the setting up of companies and non-profit organisation in the country in which it is established.

2.3.2.8 Other Organisational Requirements

The Legal Entity may be obliged to reflect other organisational requirements, depending on the form of association adopted (e.g. association or foundation) and the laws of the country in which it is established.

2.3.2.9 Proposed Procedure for addressing underperformance

1) The PCO monitors implementation of HBP work plan.
2) The PCO identifies problems to the DIR.
3) The PCO formally requests remedies from the SP concerned. A formal request includes a standard time limit on proposal for corrective action from the SP. Possible outcomes:
   a) The SP responds with sufficient corrective action within the standard time limit.
   b) The DIR grants an explicit extension for the delivery of corrective action.
   c) The DIR decides for formal escalation to the SIB.
4) In the case of c) above, the DIR requests remedies from the SIB. A formal request includes a standard time limit on proposal for corrective action from the SIB. This can include proposing changing a Task, a WP or an SP or change the Partners and/or leaders involved. Possible outcomes:
   a) The SIB responds with sufficient corrective action within the standard time limit
   b) The DIR grants an explicit extension for the delivery of corrective action
   c) The DIR decides for escalation to the GA/SB.
5) In the case of c) above, the DIR can propose to the GA/SB to change a Task, a WP or an SP or change the Partners and/or leaders involved.

2.3.2.10 Cross-Cutting Coordination Committees

To ensure the smooth running of HBP's scientific research and infrastructure, there is a need for permanent and/or ad-hoc committees, which undertake particular coordination responsibilities.

This arrangement formalises current practice, whereby specialists in these areas from each Subproject concerned network with counterparts in SP11 to coordinate a particular cross-cutting subject. The representatives in the Subprojects for a particular cross-cutting activity will be known as “Rapporteurs” and the SP11 managers responsible for such activities will be known as “Coordinators”. The cross-cutting coordination committees for Data, Software and Infrastructure will each be chaired by a Chair or Vice-Chair of the SIB. In addition, there are separate coordination committees for innovation and ethics.

The following committees, appointed by the SIB, are envisaged:

2.3.2.10.1 The Scientific Data Coordination Committee

The role of this Committee is to ensure that the scientific data and outputs of one Subproject are compatible with the needs of the remainder of the Project. This Committee is chaired by the SIB Chair / Scientific Research Director (SRD). He or she is supported in this role by the Scientific Data Coordinator, who is a member of the Project Coordination Office. The members of the Committee are Scientific Data Rapporteurs – at least one from each Subproject.

The Scientific Data Coordination Committee will play an important role in setting standards for HBP scientific data and ensuring compliance with such standards. Its mission includes ensuring that data needed to meet the Project’s scientific objectives are clearly understood by data-producing SPs and data-producing third parties. It must also ensure that the data that is delivered satisfies quality criteria for immediate use and long-term accessibility. The Project Lifecycle Framework describes how data projects are developed to ensure quality for immediate use. See also the Data Accessibility Criteria, for more details on metadata criteria to address long-term accessibility considerations.

2.3.2.10.2 The Software Development Coordination Committee

The role of this Committee is to ensure that the software developed by one Subproject is compatible with the needs of the remainder of the Project and of external users. This Committee is chaired by the SIB Vice-Chair / Software Development Director (SDD). He or she is supported in this role by the Software Development Coordinator, who is a member of the Project Coordination Office. The members of the Committee are Software Development Rapporteurs – at least one from each Subproject.

The Software Development Coordination Committee is charged with ensuring the coordination and quality of the software and services produced within the Project and which underpin the capabilities of the HBP’s six ICT Platforms. The Committee will oversee the development and application of appropriate software standards. It will also ensure that SPs implement thorough testing regimes, which include exposure to typical users, to ensure the appropriateness and reliability of production software before its general release.

2.3.2.10.3 The Infrastructure Coordination Committee

The role of this Committee is to ensure that the Scientific Research Infrastructure developed and made available to the scientific and other communities by the HBP meets the required standards of functionality and availability. This Committee is chaired by the SIB Vice-Chair / Infrastructure Director. He or she is supported in this role by the Infrastructure Coordinator, who is a member of the Project Coordination Office. The members of the Committee are Infrastructure Rapporteurs – at least one from each Platform Subproject. This Committee should also liaise closely with and seek the advice of the Infrastructure Coordination Committee, comprising representatives of the national infrastructure facilities involved in the HBP.

2.3.2.10.4 Ethics Coordination Committee

The Ethics Coordination Committee comprises the Ethics Rapporteurs in each Subproject and the Ethics Manager. It may seek guidance from the Ethics Director on the Directorate (see Section 2.3.2.5.3 above), the Ethics Advisory Board (see Section 2.3.2.5.8) or Subproject 12 – Ethics and Society.

2.3.2.10.5 Innovation Coordination Committee

The Innovation Coordination Committee comprises the Innovation Rapporteurs in each Subproject and the Innovation Coordinator in the Project Coordination Office. It may seek guidance from the Innovation Director on the Directorate (see Section 2.3.2.5.3) and the Innovation and Technology Transfer Committee (ITTC).

2.3.2.11 Core Project Governance for the Interim Phase

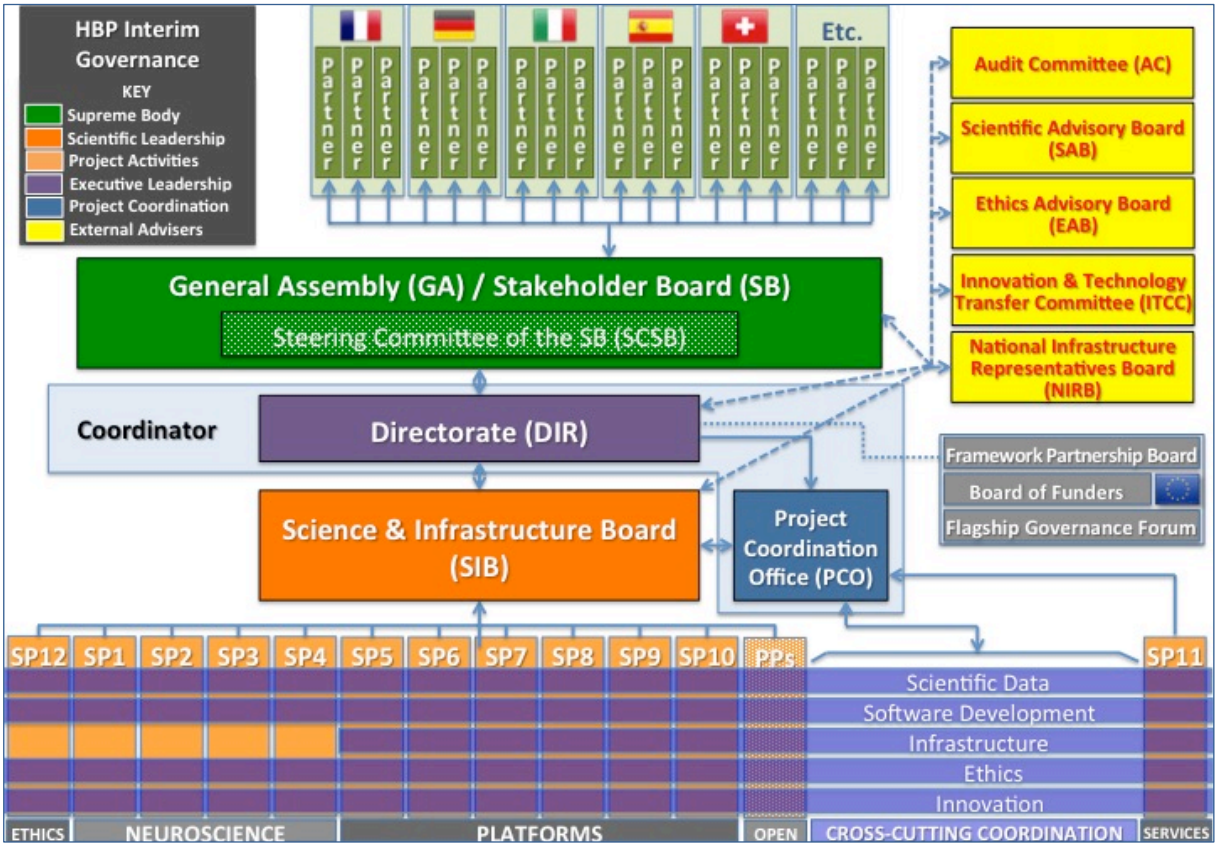

Figure 5: The HBP Interim Phase Governance Structure

2.3.2.12 Coordination, monitoring, quality assurance and risk management

The FPA brings with it a stronger emphasis on the research infrastructure being created by the HBP. An infrastructure that is placed at the disposal of the broader scientific community imposes more stringent demands in terms of the reliability and ease-of-use of its tools than one which is the preserve of a smaller circle of user-developers who have been intimately involved in the creation of the tools and may therefore have a more tolerant attitude towards minor defects.

However, the richness and value of the research infrastructure is proportional to its ability to adapt and to incorporate new ideas, generated both within the HBP and in the broader scientific community. This presents an additional challenge for the HBP, that of assuring

the quality and robustness of infrastructure features which are "co-designed", either in collaboration with HBP Core Project and Partnering Project scientists, or with ones from outside the HBP Flagship Initiative.

These challenges are explicitly recognised in the HBP's White Paper on User Recruitment and Infrastructure Strategy (URIS), which can be found in Appendix 3: White Paper "Transforming the Human Brain Project Platforms into a Community-Driven Infrastructure for Brain Research". This is a living document that will evolve as the HBP refines and develops its thinking about the most appropriate way to ensure a reliable yet flexible research infrastructure.

The HBP's FPA framework also attaches increased importance to the role of the SP Leaders in the reporting and monitoring process, requiring them to submit their own written evaluation of progress within their SP, as part of the regular semester and periodic reporting. To help the SP Leader, each SP will also deploy an SP Manager.

2.3.2.12.1 Degree of HBP involvement will vary across the infrastructure

As described in Appendix 3: White Paper "Transforming the Human Brain Project Platforms into a Community-Driven Infrastructure for Brain Research", not all infrastructure services will need to be managed with the same level of discipline. Reducing the investment in robustness for less-critical services is an essential part of cost-effective development and maintenance. To clarify the prioritization of parts of the Service-Oriented Architecture (SOA), there will be an adoption of a tiered classification of services and Foundation software delivered by the various SPs. The tiers are described as "HBP-Managed", "HBP-Coordinated", and "Community-Coordinated".

The HBP-Managed infrastructure tier:

This will adhere to strict standards with centrally managed Service Level Agreements (SLAs) that guarantee high availability. A combination of essential Software and Base Infrastructure, federated over multiple sites, will have to be committed to HBP needs to achieve the necessary service availability. A support plan will be documented and will have resources committed to its implementation. A sustainable roadmap for both Base Infrastructure and Software Infrastructure will form the core of the HBP RI. An external evaluation panel that is not involved in the implementation will assess Technology Readiness Levels (TRL).

The HBP-Coordinated infrastructure tier:

Here, components are provided and owned by individual Partners (Partner institutions and conglomerates, or HBP Subprojects). Adherence to the HBP standards is optional and SLAs will have negotiated availability. HBP Coordinated services will be deployed on a mix of HBP managed and non-HBP managed Base Infrastructure. All Apps and Services are monitored for health and availability by the HBP Managed services. The provider/owners manage support and provide the intended service(s) with a view to encouraging user adoption of their respective infrastructure components. The provider/owners are responsible for assessing TRLs.

Community-Coordinated infrastructure tier:

Its software components are provided and managed by third parties not involved in the HBP. Apps and services may be monitored, and the third parties decide on SLAs and Support levels.

2.3.2.12.2 Scientific and Technical Coordination Framework

The coordination of scientific, software and infrastructure activities in the Human Brain Project will be based on a hybrid model of best practices, drawn from existing

infrastructure projects with lean management principles that have proven effective in many technical domains. This hybrid model is driven by the need for a management framework which addresses key concerns about oversight, while also enabling scientists and engineers involved in implementation of the Project to function with minimal management overhead, while facilitating synergistic interactions with collaborators across the HBP and broader scientific community.

Software/Infrastructure framework goals:

- Clarify ownership of implementations and their respective outcomes.
- Align inputs and outputs of SGA activities with HBP strategic objectives.
- Detect problems during implementation.
- Resolve detected problems.
- Provide clear feedback to improve outcomes.
- Delineate clear Quality targets, based on Technology Readiness Levels (TRLs).
- Provide incentives for adoption of standards.
- Align of HBP Research Infrastructure (RI) development with user needs.
- Maximize TRL values ≥6 (see TRL definitions below) for outputs in a given SGA. Rollover development of TRL <6 outputs from SGA-X to SGA-X+1 should be the exception, not the norm.

2.3.2.12.3 Technology Readiness Level (TRL) Definitions

The TRLs set out below correspond to the standard European Commission TRLs. The properties required of an infrastructure component at each TRL are also defined. The TRLs are intended to be applied, not only to systems delivered as RI, but also to the systems producing key datasets as well.

Technology Readiness Level	Expected Properties
TRL 1 Project Initiation	• Project owner identified • Project principles and high-level objectives defined • Use case definitions (includes target users and activities)
TRL 2 Conceptualization	• Analytic study of the problem space • Identify key functions which must be validated in Component Implementation • Formulate validation criteria for critical components • Formulate validation criteria of complete prototype system • Prototype Epic planning
TRL 3 PoC Implementation	• Implementations of key functions • Validation of critical concepts • Identification of additional validation criteria for TRL4
TRL 4 Prototype Component	• Validation of prototype components in Lab • PoC has become prototype components • System technology selection has been made • Load testing of components under key load criteria • Identification of additional validation criteria for TRL5
TRL 5 Prototype Integration	• Validation of integrated system in a real-world environment • Tested in restricted environment with a small number of real users • Data formats specified • Identification of additional validation criteria for TRL6

TRL 6 Prototype-to-Real-world Integration	• Validation of integrated system in a real-world environment • Load testing of integrated system under expected load • Tested in a real-world environment with a small number of real users • Initial System documentation • Initial User documentation • System monitoring points specified (for services) • Identification of additional validation criteria for TRL7
TRL 7 Operational Integration	• Validation of integrated system in a real-world environment • Tested in a real-world environment with a small number of real users (canary testing for SoA) • System monitoring implemented (for services) • No expected data format or API changes (for services or software components) • Load testing of integrated system under expected load • SLA monitored (for services)
TRL 8 Deployment	• Validation of integrated system in a real-world environment • Tested in a real-world environment with a small number of real users • SLA enforced (for services)
TRL 9 Production	• Validation of integrated system in a real-world environment • Tested in a real-world environment with a target number of real users

Table 16: Technology Readiness Levels (TRLs)

2.3.2.12.4 Project Lifecycle Framework

With the infrastructure terminology and TRLs set out, it is possible to describe how the coordination process works.

The Project Lifecycle Framework is key to the coordination of implementation within a given SGA. It defines a set of outputs, which will be used to identify problems during implementation and mitigate risks associated with the inevitable implementation challenges. It also describes how specific types of Key Performance Indicator (KPI) will be used at various points in the lifecycle to identify potential problems.

The Framework will be applied to all software, service or data-producing activities within a given SGA. It is a generic method that will be applied to all Platforms, and will be monitored by the Scientific and Technical Coordinators. In some cases, it will be adapted to better suit certain activities. These adaptations will be written into the Project Implementation Proposal (PIP), described on the next page.

There are two major types of lifecycle that can be employed: Agile and Co-design. The relevant Project Implementation Team will choose which type of lifecycle to use. The most important factor in determining the type is the expected length of the development cycle. Co-design closely involves target users, ensuring alignment of projects with longer development cycles. The Agile variant allows looser coupling of the development team and target users. Agile variants should be used for short development cycles, so that re-alignment with target users can happen on regular cycle boundaries.

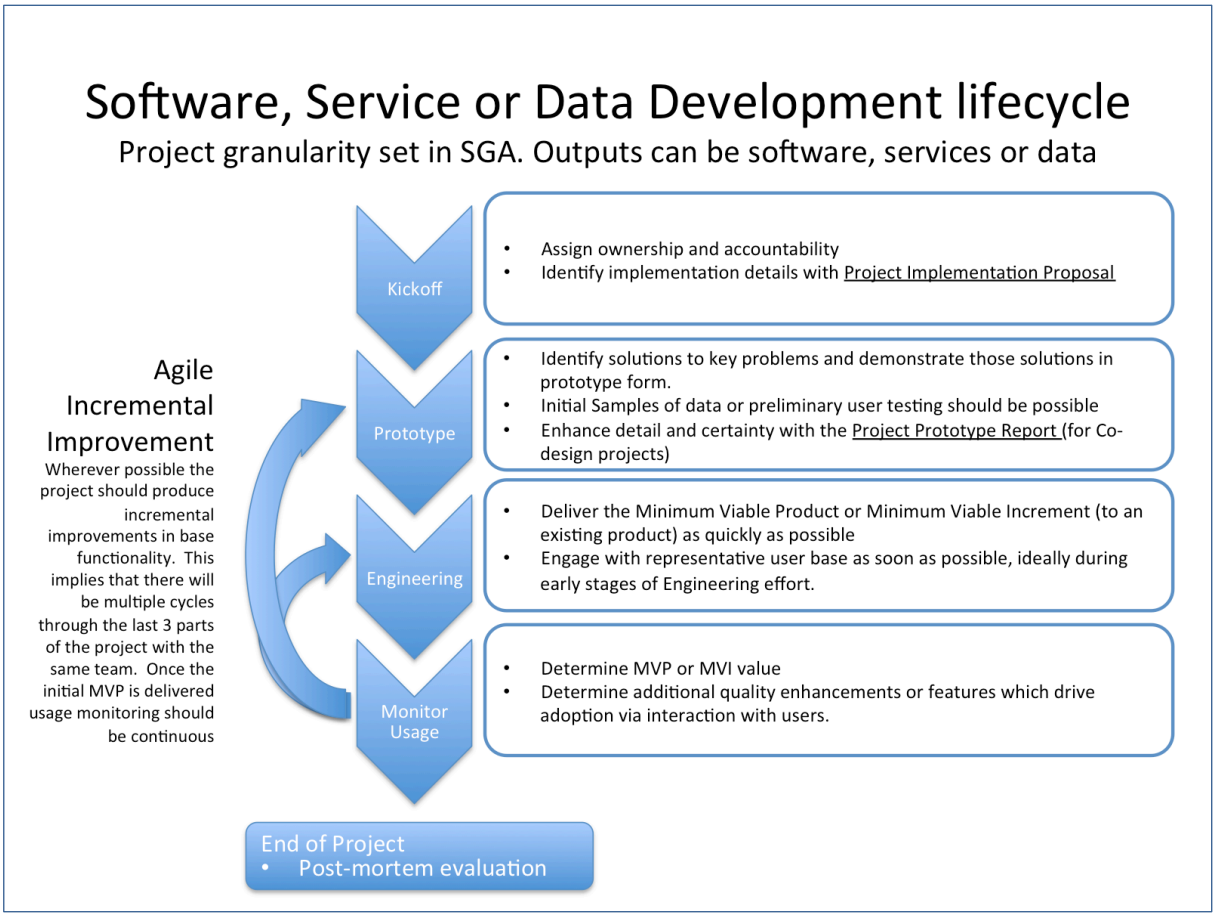

Figure 6: Software, Service or Data Development lifecycle

The Agile Project Lifecycle Framework requires:

1) A Project Implementation Proposal (PIP)
2) A mechanism for tracking agile activity metrics. The specific mechanism will be described in the SGA, but will likely be a variant of a burndown chart.
3) Post-mortem evaluation

The Co-Design Project Lifecycle Framework requires:

1) A Project Implementation Proposal (PIP)
2) A Project Prototype Report
3) Milestone reports for milestones in the PIP
4) Post-mortem evaluation

Project Implementation Proposal (PIP)

The PIP is a critical output of the Project Lifecycle Framework intended to:

- Take a high-level proposal for an activity from the SGA and make it a more concrete, detailed implementation plan.
- Be prepared by the Implementation team
- Mark the point at which the Implementation Team takes over responsibility for the specific activity or project.
- Describe the following:

- Clear project objectives:

  Define planned outputs: software components, data and target TRLs for the project completion

  The software components, data and target TRLs shouldn't be considered fixed until the prototype phase is complete.

- Determine which Project Lifecycle Framework model will be used:

  Agile development - multiple passes through the Project lifecycle, ≤1 month cycles for prototype to monitor phases.

  Co-design – 3 month or longer projects with a single pass through the Project lifecycle. Need to provide detailed milestones in this case.

- Target user group and engagement model:

  Co-design – for longer development cycles.

  Agile customer engagement – for short development cycles.

  Both – for short development cycles.

  Will define adoption targets.

  Will define engagement channels for project outputs. Includes first 3 months' Epic planning (if using Agile model).

  Team profile – role definitions not assigned people, will include co-design team for projects using the co-design engagement model.

Project prototype report

For Co-design projects, a prototype phase will be used to ensure feasibility of longer-term developments (which are inherently riskier):

- Prepared by the Implementation team.
- Describes the outcome of the prototype.
- Clearly describes changes to the PIP and planned activities based on insight gained during the prototype activity.

Post-mortem evaluation

For teams involved in development activities, projects will neither be their first nor their last. In an attempt to increase team capacities, the Project Implementation Team will perform a *post mortem* review after completion of their project (probably at the end of each SGA period). This will formalise the reflection process that will be necessary to continually improve on the performance of Partners who stay with the HBP as the Project moves from SGA to SGA.

Mapping to TRLs

Mapping to Technology readiness Levels will be used to show the relationship between the Project Lifecycle Framework and the Technology Readiness Levels. This will graphically represent the expected activity and outputs throughout a given project.

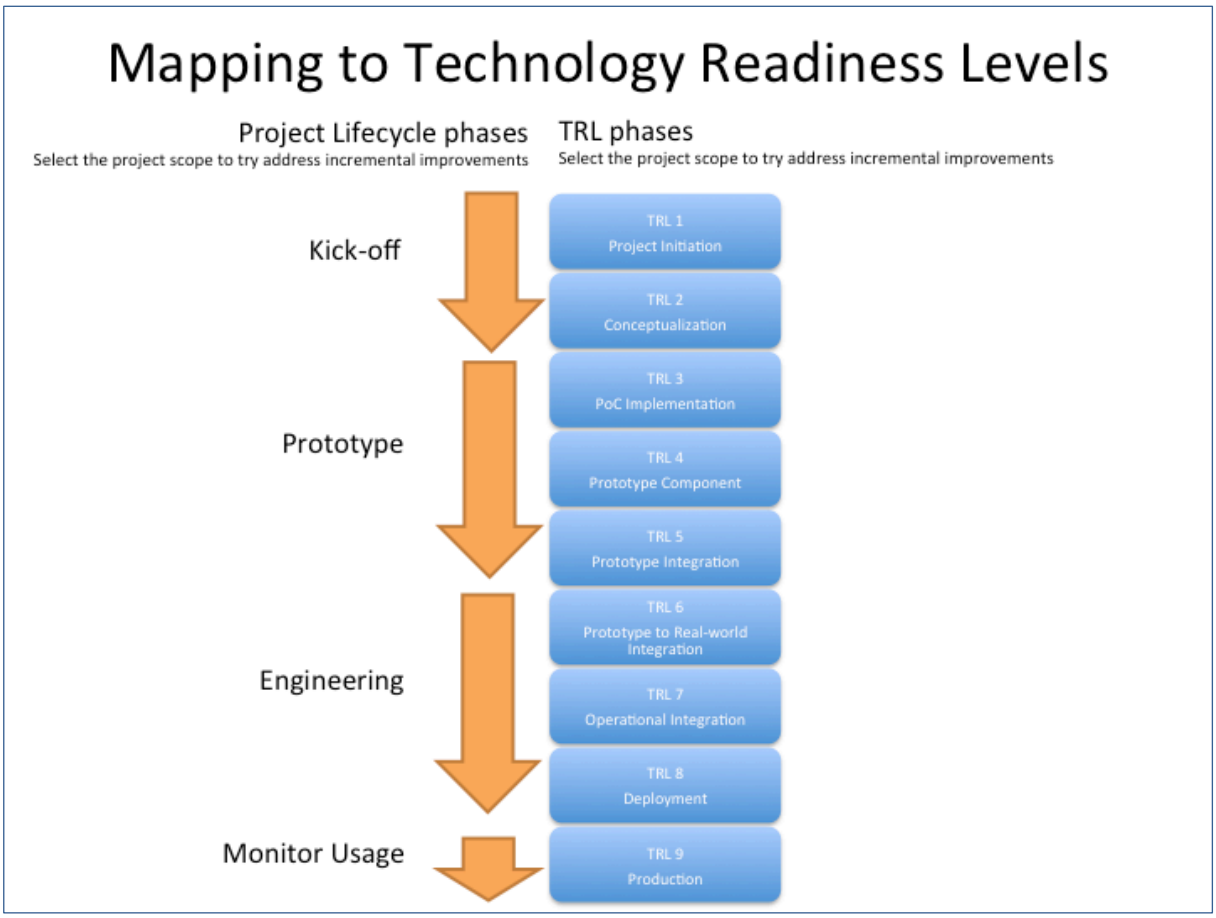

Figure 7: Mapping to Technology Readiness Levels

Data generation is a critical part of the HBP strategy. These data will be produced by low, medium and high-volume pipelines. The pipelines themselves have a Technology Readiness Level based on their data outputs and the validation of those outputs with criteria set by the intended consumer. This relationship between the data outputs and the TRL is outlined in the figure below.

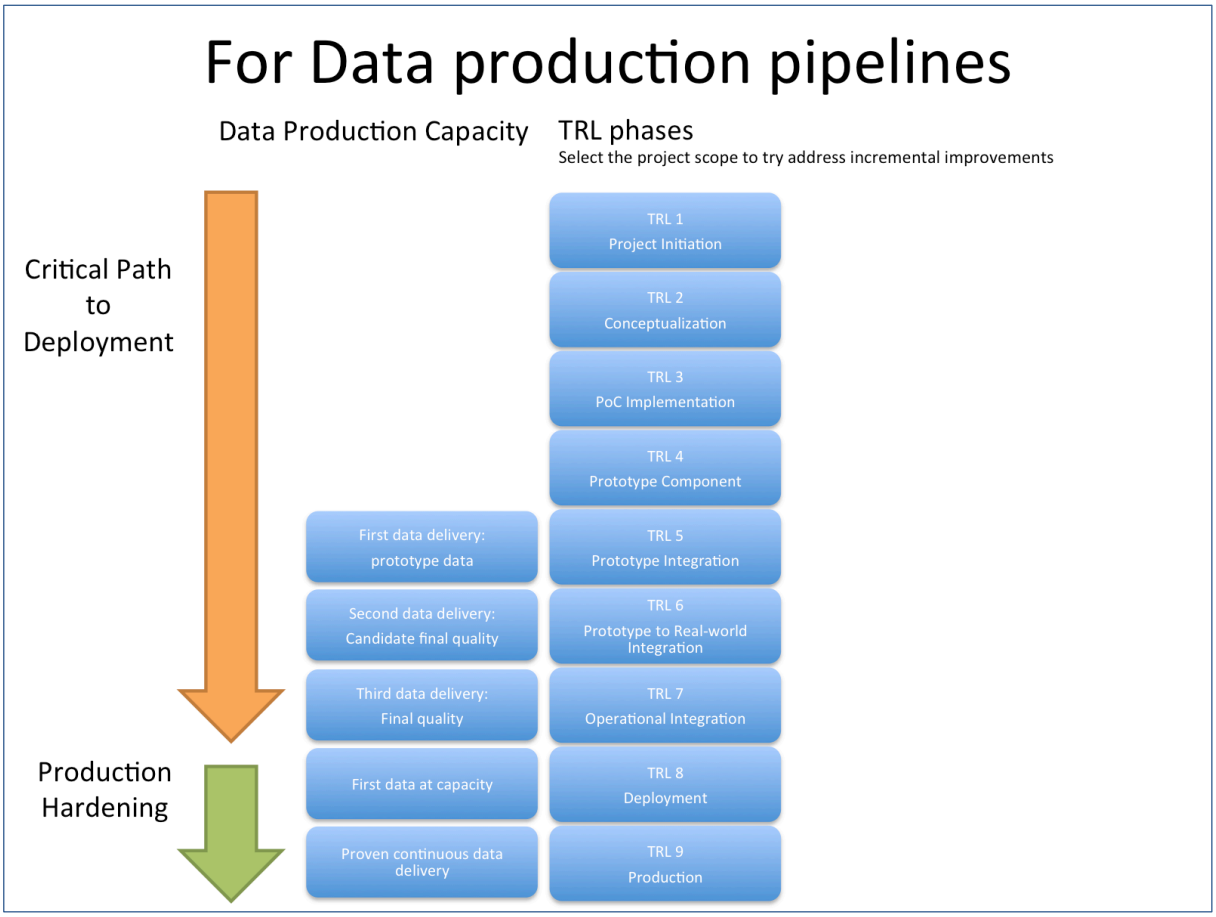

Figure 8: Data deliveries from data projects

If a data project is not required to produce high-volume data, it can reasonably target a TRL5 for its data generation systems unless its data-generation systems are also intended to be delivered as RI.

2.3.2.12.5 Data Accessibility and Quality

Data gathering takes place in two different phases. The exploratory, or set-up, phase is where researchers determine the possible protocol to generate a certain type of data. They will follow the Project Lifecycle Framework to ensure that there is alignment between the producer and the quality needs of the consumer. Early parts of the Project Lifecycle will establish the quality criteria for a given data project, along with data analyses to ensure that outputs achieve unambiguous quality metrics.

Quality metrics such as these will never be total. The data-driven modelling approaches will provide a critical element of cross validation. This will reinforce the principles of integrating data into models as early as possible, and data generation activity should be paired with an immediate HBP consumer wherever possible. Where there is no immediate consumer, the data project will be scrutinised carefully to determine whether the data is sufficiently strategic to warrant the effort of generating it.

Once a data standard has been agreed by the producer and the consumer, the data producer will then apply this to all data produced during the later (engineering) phases of the project lifecycle. In these phases, the protocol applied to generate the data is not altered, to guarantee consistent data generation.

The Data Accessibility Criteria (DAC) are a set of annotation/processing criteria which will be applied to data deliveries to determine their readiness for general availability. Ideally,

all data will possess as many DACs as possible, as these criteria provide critical metadata to ensure that data can be found and interpreted by later researchers, who might not have access to the operational knowledge of the original data production team.

These criteria will also guide metadata production for data produced by Partnering Projects and other data-generating partnerships that the HBP has or may have during the lifetime of the FPA, and beyond.

Data Accessibility Criteria	Stages
DAC - Provenance	1) Data Generation Provenance is accessible in text format. 2) Data Generation Provenance uses ontological terms for protocol, methods, experimenter roles, and entity classifications. 3) Data Generation Provenance is stored in a well-defined data provenance model (e.g. W3C prov, HBP core)
DAC – Spatial Anchoring	1) Location of Data, or a source sample, is available. 2) Location of Data, or a source Sample, can be linked to spatial ontology. 3) Data, or it's source Sample, can be aligned to a standard reference space. (e.g. ABA, MNI, Collins)
DAC - Accessibility	1) Data is saved in a proprietary format, which is accessible via a software vendor. 2) Data is saved in an open format, which can be accessed via a publicly available file reader/service.

Table 17: Data Accessibility Criteria

2.3.2.12.6 KPIs and Related Methodologies to assess Progress and Achievements

The Project Lifecycle is intended to maximise the ability of the project to produce work of the highest technical and scientific quality. This in turn will maximise the ability of the project to deliver progress towards the HBP Core Project Objectives.

The framework for monitoring progress and impact within the HBP is built around the line management and governance structure, complemented by supporting specialists within the HBP Management. Experience gained in the Ramp-Up Phase has led to some significant changes in line management, governance and specialist support under the FPA. This led directly to the creation of the Technical and Scientific Coordinator positions described above.

The progress monitoring system is centred on the Project Milestones and Deliverables, plus the semester and periodic reporting, performed at HBP, SP, WP and Task level. However, critical issues are monitored with much greater frequency through regular board and management videoconferences. In addition to the Milestones and Deliverables, the HBP uses a number of other Key Performance Indicators (KPIs), to measure both the project's progress and its impact on the scientific community, on industry and on the general public. These KPIs will allow the HBP leadership to identify areas where progress or impact are unsatisfactory and to implement timely corrective actions. The Progress and impact metrics will be reviewed and modified as necessary over the lifetime of the HBP. The principal KPIs used by the HBP are summarised below.

Flagship Objective	Key Performance Indicator (KPI)	Alignment with HBP Flagship Objectives (FOs)
Project Performance	% of Deliverables achieved in period due	FO1; FO2; FO3; FO4; FO5; FO6
Project Performance	% of Milestones achieved in period due	FO1; FO2; FO3; FO4; FO5; FO6
Scientific Excellence	Number of research agreements & MoUs	FO1; FO2; FO3; FO4; FO6
Scientific Excellence	Number of agreements & MoUs with data providers	FO1; FO2; FO3; FO4; FO6
Scientific Excellence	Number of scientific publications in peer reviewed magazines	FO1; FO2; FO3; FO4
Scientific Excellence	Number of data features curated and validated	FO1; FO2; FO3; FO4
Scientific Excellence	Number of validations in the data mining algorithms library	FO1; FO2; FO3; FO4
Scientific Excellence	Number of validations in the disease models library	FO1; FO2; FO3; FO4
Scientific Excellence	Number of citations	FO1; FO2; FO3; FO4
Scientific Excellence	Number of awards to HBP researchers	FO1; FO2; FO3; FO4; FO5; FO6
Scientific Excellence	Number of invited talks at conferences	FO1; FO2; FO3; FO4; FO5; FO6
Technological Excellence*	Number of Platform users (measure by number of users having an account)	FO1; FO5; FO6
Technological Excellence*	Number of active Platform users (users who logged on at least once in last month)	FO1; FO5; FO6
Technological Excellence*	Number of software component releases	FO1; FO5; FO6
Technological Excellence*	Number of software components open sourced	FO1; FO5; FO6
Technological Excellence*	Number of patents granted	FO1; FO5; FO6
Technological Excellence*	Number of commercial licenses executed	FO1; FO5; FO6
Technological Excellence*	Size of user uploads	FO1; FO5; FO6
Technological Excellence*	Number of public Knowledgegraph entries created	FO1; FO5; FO6
Technological Excellence*	Number of searches executed	FO1; FO5; FO6
Technological Excellence*	Number of jobs run	FO1; FO5; FO6
Technological Excellence*	Number of Virtual Machines used	FO1; FO5; FO6
Technological Excellence*	Project storage allocated --+	FO1; FO5; FO6
Technological Excellence*	Project storage consumed	FO1; FO5; FO6
Technological Excellence*	Number of cores available (federation construction)	FO1; FO5; FO6
Technological Excellence*	Core-hours consumed	FO1; FO5; FO6
Cross-cutting SP collaborations	Number of scientific publications co-authored by PIs from multiple SPs in peer reviewed magazines	FO1; FO2; FO3; FO4; FO6
Cross-cutting SP collaborations	Number of joint grant applications featuring contributors from different SPs	FO1; FO2; FO3; FO4; FO6

Flagship Objective	Key Performance Indicator (KPI)	Alignment with HBP Flagship Objectives (FOs)
Cross-cutting SP collaborations	Number of software components released which rely on components delivered by another SP	FO1; FO5; FO6
Cross-cutting SP collaborations	Number of platform components released which rely on components delivered by another SP	FO1; FO5; FO6
Societal impact	Number of PhDs & postdocs hired by the project	FO1; FO2; FO3; FO4; FO5; FO6
Societal impact	Number of PhDs graduated	FO1; FO2; FO3; FO4; FO5; FO6
Societal impact	Number of HBP post-docs taking jobs in industry	FO6
Education Programme	Number of Courses organised by the HBP Education Programme	FO6
Education Programme	Number of academic attendees at Courses organized by the HBP Education Programme	FO6
Education Programme	Number of Schools organized by the HBP Education Programme	FO6
Education Programme	Number of academic attendees at Schools organized by the HBP Education Programme	FO6
Industry engagement	Number of industrial contacts reported at international events	FO6
Industry engagement	Number of face to face meetings with companies	FO6
Industry engagement	Number of Industry attendees at the Courses organised by the HBP Education Programme	FO6
Industry engagement	Number of Industry attendees at the Schools organised by the HBP Education Programme	FO6
Industry engagement	Number of industry/HBP academic collaborations	FO6
Industry engagement	Number of spinoffs established	FO6
Community engagement	Number of applicants in Competitive Call (FLAG-ERA or for Core)	FO1
Community engagement	Number of Associated Members/Partnering Projects joining the HBP	FO1
Community engagement	Number of platform components with Partnering Project contributions	FO1
Community engagement	Articles with joint Core and Partnering Projects authorship	FO1
Gender balance	Change in % of female PhDs & post-Docs recruited	FO6
Gender balance	Change in % of female PhDs graduated	FO6
Gender balance	Change in % of female PhDs taking jobs in Industry	FO6
Gender balance	% of female attendees at Courses organised by the HBP Education Programme	FO6
Gender balance	% of female attendees at Schools organised by the HBP Education Programme	FO6
Dissemination	Number of HBP mentions in public media	FO6

Flagship Objective	Key Performance Indicator (KPI)	Alignment with HBP Flagship Objectives (FOs)
Dissemination	Number of HBP-organised conferences	FO6
Dissemination	Number of press releases	FO6
Responsible Research & Innovation	% of research activities requiring local IRB approval with no documentation copied to the Ethics Manager	FO6
Responsible Research & Innovation	Number of non-EU research ethical review requests submitted to Ethics Advisory Board.	FO6
Responsible Research & Innovation	% of non-EU research ethical review requests submitted to Ethics Advisory Committee and are refused.	FO6

Table 18: HBP Key Performance Indicators (KPIs)

* Technological Excellence measured on HBP Managed and HBP Coordinated infrastructure only

2.3.2.12.7 Risk analysis and management

Research projects, especially large-scale ones like the HBP Flagship, face a number of scientific, technological, financial, managerial, political and societal risks. A well-planned monitoring and management process is key to analysing and mitigating these risks. An overview of identified risks and contingency plans is provided in the figures below, where the estimated probabilities are given as High, Medium or Low. The impact is also measured as High, Medium or Low.

To monitor risks, we will build a risk management plan based on the following points:

- A Risk Register listing critical risks, complemented by a Watch List for non-critical risks.
- Contingency plans for each risk, identifying specific actions to be taken.
- A Risk Owner: each risk is assigned to an owner, who is responsible for detection and reporting, related contingency plans and for monitoring contingency plan implementation if the risk event occurs. The Risk Owner will be a member of the Subproject management or a member of the Management Subproject and will be assigned in a given SGA in accordance with the governance structure in place during that SGA.
- Qualitative and Quantitative analysis tools, including probability impact matrix, decision tree and sensitivity analysis.

2.3.2.12.8 Roles and Responsibilities in HBP Risk Management

The Risk Coordinator in the Management Subproject is responsible for coordinating the development and implementation of the HBP risk management framework. He/she works with the Scientific and Technical Coordinators (see above), whose performance management role, and overview of project-wide scientific and technological issues makes them valuable adjuncts in risk management. The Risk Coordinator also interfaces with the Risk Owners, who will be distributed across the Subprojects, according to the nature of the risk concerned. Collectively, the Risk Coordinator, the Scientific and Technical Coordinators and the Risk Owners form the Risk Management Group, which is a Project wide network of people with risk management responsibilities.

The Risk Coordinator and the Risk Management Group will periodically review and revise the risk register. This will ensure that we have an updated view of risks as they evolve, helping us to (re)assign management responsibilities appropriately, to update our contingency plans and to act if any discrepancies are observed.

The Risk Coordinator will communicate an updated analysis of HBP risk exposure to the Project's governing bodies on a regular basis, along with recommendations for any corrective action that might be felt appropriate. The Risk Coordinator must ensure that the minutes of each governance body's meetings confirms that the body concerned has received the risk exposure analysis and is aware of the contents.

The Risk Category identifies the general approach that can be taken with a given risk in the registry. The categories are as follows:

- Implementation: internal project implementation strategies should be largely governed by the risk detection and mitigation strategies described in the Project Lifecycle Framework. These are described in more detail in the following subsection.
- Organizational: higher-level strategic risks. Can be detected with high-level KPIs. In most cases, mitigation of these risks will require larger strategic organizational action.
- External: these risks are the result of external factors and can't be detected with KPIs. Mitigation strategies might also require broader strategic organizational action.

Implementation of risk detection and mitigation measures via the Project Lifecycle Framework can be found in Appendix 8: Risk Detection & Mitigation.

Scientific & Technological Risks

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
Risk of delay in cell-type transcriptomics.	SP1 - SP10	Medium	Medium	Implementation	Other organisations (e.g. Allen Brain Institute, Wellcome Trust's Sanger Institute) are working intensively in this area. Risk that no group will produce key data over Project lifetime is low. New predictive informatics strategies help to minimise the amount of data required to predict complete cell-type transcriptomes.	This risk will be cleared when the Project generates enough transcriptomic data to accurately predict neuron morphologies and electrophysiology. The quantity of data required is not known. This risk will only be cleared in the Operational Phase.
Failure to create sufficient data, due to technical/organisational problems.	SP1 - SP10	Medium	Medium	Implementation	If the volumes of data generated during the Ramp-Up Phase are below target, the Project will rely on lower fidelity reconstructions until the necessary data becomes available.	This risk will fall as volume of available data increases, allowing construction of progressively more accurate models. It will only be cleared in the Operational Phase.
Delays in software development	SP5 - SP10	High	Medium	Implementation	Platforms have mitigated this risk by adopting a modular, incremental development process. Software architecture also minimizes dependencies between components. This reduces risk that a single technical problem or delay will compromise the overall development schedule. See Project Lifecycle for detection and mitigation details.	The risk for specific versions of the Platform will be cleared with the releases planned in M30, M60, M90 and M120. However, the general risk of delay will persist for the whole duration of the Project.
Insufficient financial resources for effective operation of the ICT Platforms	SP5 - SP10	Medium	Medium	Organizational	If necessary, the Project will seek funds from outside the Project for running and operating the ICT Platforms.	For specific SGA cycles the risk will be cleared when the Project demonstrates it can operate the ICT Platforms for a satisfactory number of users. However, funding risks will persist for the whole duration of the Project.
Lack of community uptake of ICT Platform services	SP5 - SP10	High	Medium	Implementation	The Project is already investing significant resources to recruit and engage potential users. If uptake is low, it will most probably be because the tools are not tailored to Use Cases that the users care most about. See Project Lifecycle for detection and mitigation details.	The risk will only be cleared one or two years into the operational phase when the ICT Platforms have been open to the community for sufficient time to become well-known.
Delays in deployment of required supercomputing power	SP5 - SP10	High	Medium	Implementation	Discussions with possible Partners have begun. If deployment of large supercomputing resources is delayed, the Project will use the resources already available.	The risk for multi-petaflop capabilities will be cleared with the installation of a multi-petaflop machine at Jülich, planned for late 2018. The risk with respect to exascale capabilities will only be cleared towards the end of the Project.
Delays in generation of data required for modelling	SP5 - SP10	Medium	Medium	Implementation/ Organizational	If data volumes are insufficient, Project can build lower fidelity reconstructions until the data becomes available. Project could reallocate	This risk will fall gradually as the volume of available data increases, allowing the construction of progressively more accurate models. The risk

					additional financial resources to SP1 and SP2, and/or to bring in new research groups.	will only be completely cleared towards the end of the Project.
Failure of predictive neuroscience strategy	SP6	Low	High	Implementation	The Project is already exploring multiple predictive neuroscience methods. This strategy reduces dependency on any specific method.	The first high-fidelity reconstructions of the mouse brain, planned for M60 will demonstrate the general validity of the Project's approach and reduce risk. However, the sparse data available for the human brain poses additional issues. This risk will completely cleared only at the end of the Project.
Technical & scientific problems in the digital reconstruction of brain components, regions and whole brains.	SP6	High	Medium	Implementation	SP6 adopts a modular, incremental reconstruction process in which many activities are carried out in parallel. This minimises the risk that a single technical problem or delay will compromise the overall schedule.	The first high-fidelity reconstructions of the mouse brain, planned for M60, will demonstrate the general validity of the Project's approach and reduce risk. However, the human brain poses additional issues. This risk will only be cleared at the end of the Project.
Failure to recruit hospitals and other data sources	SP8	Low	High	Implementation	If recruitment does not reach the targets set by the work plan, the Medical Informatics Platform will extend its recruitment effort to organizations and countries not included in its original plan. As targets are very conservative, it is highly unlikely that this will be necessary.	The Project has goal of recruiting five hospitals by the end of the Ramp-Up Phase. Achieving this would be strong evidence that it can also achieve its longer-term goals. The risk will only be completely ended when SP7 is regularly recruiting new data sources from many different countries. We expect that this will be fully achieved only towards the end of the Project.
Changes in regulations for data protection, limiting the use of anonymised data for research	SP8	High	High	External	Informed consent procedures would be amended to obtain explicit consent from patients entering the system, allowing the use of the data.	This risk will last for the whole duration of the Project.
Novel rule-based clustering algorithms fail to generate unique biological signatures of disease	SP8	High	Medium	Implementation	The project has used the Ramp Up Phase Competitive Call to diversify its portfolio of candidate algorithms, improving its chances of success. Following the Project Lifecycle, kick-off and prototype activities should address key scientific issues. See Project Lifecycle for detection and mitigation details.	This risk can be considered cleared with the delivery of efficient algorithms and their incorporation into the Medical Informatics Platform, planned for Month 30.
Delays in neuromorphic computing hardware	SP9	Medium	Medium	Implementation	Experiments are routinely planned using software simulations of neuromorphic computing hardware. This strategy minimises the	The risk for specific versions of the Platform will be cleared with the Platform releases planned in M30, M60, M90 and M120. The general risk of delay in

development					consequences of delays in hardware development. See Project Lifecycle for detection and mitigation details.	hardware development will persist for the whole duration of the Project.
Delay in production of simplified or theory-driven brain models	SP9	Medium	Medium	Implementation	SP9 will obtain brain models both from SP4 (theory-driven models) and SP6 (simplified models derived from high-fidelity reconstructions). The use of two alternative sources significantly reduces risk. In addition there will be multiple simplification strategies which will employed. See Project Lifecycle for detection and mitigation details.	This risk will reduce gradually over the duration of the Project, as more and better models become availability. However models of the whole human brain will only be available at the end of the Project. Therefore, some risk will persist for the whole duration.
Lack of interest in using Neuroinformatics, Brain Simulation and Neurorobotics platforms by European neuroscientists	SP5, SP6 & SP10	Low	High	External	The Project will receive early indications if European neuroscientists do not show enough interest in Platforms. The project could revise its strategy, if necessary investing new expertise and resources in its promotional efforts. See Project Lifecycle for detection and mitigation details.	This risk will only be cleared in the operational phase, when the Platforms begin to be used by a substantial number of neuroscientists.
Lack of interest in using Brain Simulation and Medical Informatics Platforms from European medical researchers and pharmaceutical industry	SP6 & SP8	Low	High	Implementation	The Project will receive early indications if the pharmaceutical industry does not show enough interest in the Platforms. The project would therefore revise its strategy, if necessary investing new expertise and resources in its promotional efforts. See Project Lifecycle for detection and mitigation details.	This risk will only be cleared in the operational phase, when the Platforms begin to be used by a substantial number of pharmaceutical and medical researchers.
Lack of interest in the use of the Neuromorphic Computing Platform from potential applications developers.	SP9	Low	High	Implementation	Project will seek early indications if the target industries do not show enough interest in Platforms. Project could revise its strategy, if necessary investing new expertise and resources in its promotional efforts. See Project Lifecycle for detection and mitigation details.	This risk will only be cleared in the operational phase, when the Platforms begin to be used by a substantial number of technology researchers and industrial developers.

Management Risks

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
Lack of support from countries that do not currently make	All SPs	High	High	External	The ERP Office will dedicate a major effort to building dialogue with National Funding Agencies from countries that do not yet contribute to the	This risk should be cleared by time the HBP presents its proposal for the Operational Phase.

a major contribution to the HBP.					HBP or whose contribution is not yet proportional to their standing in the European science.	
Difficulties in creating an independent legal entity.	All SPs	Low	High	Implementation	HBP is developing an independent legal entity and the governance model that will operate this entity.	This risk will end at the creation of the legal entity.
Management of internal and external stakeholders	SP11	Medium	Medium	Implementation	HBP will inform the internal and external stakeholders via a communication strategy to address stakeholders expectations provide key information such as: Opportunities to collaborate in the different phases. Participation or exclusion of the next phase Announcement of Calls for Expression of Interest Information on how to collaborate with the Project	This risk will last for the whole duration of the Project.
Difficulties in recruiting young scientists to the Education Programme (especially young scientists who are not employed by HBP partners)	SP11	Low	Medium	Implementation	HBP Partners will recruit many PhD students for HBP research, who will be automatically enrolled in the HBP Education Programme. There is no risk that the programme will fail. Recruitment of external students will be more difficult but is expected to grow during the Project.	This risk will decrease with every successful school/workshop organised by the HBP Education Programme. The end of the Ramp-Up phase should effectively clear the risk.

Financial Risks

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
Unwillingness of National Funding agencies to provide indirect forms of support for the Project	All SPs	Medium	Medium		The Project will receive early indications if funding agencies do not show enough interest in the Project and its extension into the operational phase. The Project would revise its strategy, if necessary investing new expertise and resources in its promotional efforts.	This risk should be cleared when the results of the calls for Partnering Projects will be known.
Major exchange rate fluctuations or price inflation (break-up of the Eurozone)	All SPs	Medium	High	External	Professional financial management can provide some risk protection. Funds will be held by the Coordinator in a Euro account to hedge against FOREX risks. However, this will not protect against major events, such as Eurozone breakup that might require contract renegotiation.	This risk will be present for the whole duration of the Project.
Unforeseen cost	All SPs	Medium	High	Implementation	This is a risk in large projects. HBP infrastructure	This risk will be present for the whole duration of

overruns in major infrastructure (CAPEX or operating costs)					investments usually come from National Funding Agencies, which would use their standard methods to monitor and manage cost overruns, so reducing risk of serious problems.	the Project.
Uncertainties over the status of the Flagships in H2020	All SPs	Medium	High	External	The Project will work with the Commission, with National Representatives and with members of the European Parliament to ensure that there is no diluting of the Flagship concept and that all parties commit to plans for H2020 as early as feasible.	This risk will be cleared as soon as the relevant budgets are approved and the Commission makes a detailed announcement of its plans.

Political & Societal Risks

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
Public opposition to HBP research practices (in particular, animal experimentation) possibly leading to the introduction of new legal restrictions	All SPs	Medium	High	External	The project's Ethics and Society programme (SP12) will play a major mitigating role through dialogue with animal rights groups and other concerned citizens. In operational terms, the Project could compensate for a loss of non-human primate data (only relevant in the Operational Phase) by using data from sources outside the project. The same is not true, however, for rodent data. The project's scientists and their institutions work with the relevant national regulatory bodies on matters of compliance. New regulations that could adversely affect the HBP's research would be known in advance. The HBP would adjust its research strategies accordingly.	This risk will be present for the whole duration of the HBP, and will grow as the Project gains visibility.
Reputation of the project	All SPs	Medium	High	External	The project will ensure to be transparent and open with the scientific community and the public in general. Rapid and effective response to sudden or unexpected events can enhance the reputation. The project will put in place a communication strategy on how it deploys in the media and social media networks to inform and educate about the scientific and technological aspects of the project.	This risk will last for the whole duration of the Project.
Potential military use of future HBP results	SP1 – SP10	Medium	High	External	Nearly all ICT (including consumer devices and systems) has potential military applications. Ethically, this is insufficient ground to halt the development and	This risk will be present for the whole duration of the HBP, and will grow as the Project gains visibility.

					commercialisation of new technology. However, it is more than sufficient grounds to try and identify these applications in advance, to make the public aware of potential abuses and to debate the way new technologies should be regulated. The Citizen Conventions and other forms of public awareness building organised by the HBP Ethics and Society Programme will contribute to this goal.	

Table 19: Risks and Contingency Plans

2.3.2.12.9 Contingency/mitigation plans for delays in exascale computing

Lack of financial resources/partnerships for the deployment and operation of pre-exascale and exascale supercomputing infrastructures with appropriate compute and memory capabilities

- Probability: high; Impact: moderate.
- Risk: Deploying and operating the planned HBP hardware infrastructure will require financial resources beyond those available in the budget. This creates the risk that the Project will not be able to access and provide the supercomputing capabilities it requires to build the envisioned European Research Infrastructure.
- Impact: Failure to deploy the planned pre-exascale supercomputer would limit the granularity and accuracy of the mouse brain simulations that the HBP infrastructure should support (planned for M60) and limit community efforts towards simulating models at the scale of the full the human brain. Failure to deploy the exascale supercomputer would limit the accuracy and granularity of human brain models.
- Contingency plans: SP7 is working with national and European Partners to allow joint deployment and operation of expensive data-centric supercomputing capabilities. In the event of delays the HBP will continue to use existing supercomputing resources.
- End of risk: This risk will be cleared with the introduction of the Jülich pre-exascale machine, currently planned for M60, and with the deployment of the exascale machine (M120).

Delays in manufacturer deployment of exascale computing and memory technology

- Probability: moderate; Impact: moderate.
- Risk: The development of future supercomputers with exascale computing performance and sufficiently large memory capacity poses severe technical challenges. These issues could delay the commercial availability of such systems beyond the timeframe of the HBP. However, the last three years have already seen major progress. The risk of major delays thus appears to be falling.
- Impact: The pre-exascale HBP supercomputer planned by Jülich (see above) should provide sufficient resources to enable cellular-level simulations of the whole mouse brain (planned for M60). The main impact of delays would thus be on reconstructions of the human brain. The HBP's multi-scale computing strategy allows the users to make optimal use of available computing resources. Delays in the deployment of exascale capabilities would not block progress towards the simulation of human brain models in general, but would constrain the granularity of simulations and limit the level of detail attainable.
- Contingency plans: In the event of delays, the HBP will continue to use the Jülich pre-exascale machine and the additional machines deployed by the other HPC Partners.
- End of risk: This risk will be cleared with the deployment of exascale computing capabilities, expected only in M120.

2.3.3 Planned use of resources

2.3.3.1 Estimated costs

The overall cost of the HBP Flagship Initiative over its planned ten-year lifespan is estimated at around EUR 1 019 million. The Initiative will be separated into three components: the Core Project (CP), the Partnering Projects (PP) and other EU-funded, Flagship-related projects, such as FLAG-ERA and other Coordination and Support Actions (CSA).

The Initiative will be implemented in five phases, based on the different phases and Specific Grant Agreements (SGAs) of the CP.

- Ramp-Up Phase: October 2013 to September 2016, EU contribution of EUR 54 million
- SGA1: April 2016 to March 2018, planned EU contribution of EUR 89 million
- SGA2: April 2018 to March 2020, planned EU contribution of EUR 88 million
- SGA3: April 2020 to March 2022
- SGA4: April 2022 to September 2023.

2.3.3.2 Funding sources

It is estimated that the EUR 1 019 million HBP budget will be funded from three sources:

- European Commission: EUR 500 million
- National, public and private organisations: EUR 500 million
- Core Project Ramp-Up Phase Partners: EUR 19 million.

The EUR 19 million contributed by the Ramp-Up Phase Partners comes from the difference between the total costs and the EU contribution in the FP7-funded phase of the HBP. To reach the ambitious goal of leveraging EUR 500 million for the Partnering Projects, the Project Coordination Office (PCO), along with the Science and Infrastructure Board (SIB), will communicate the Partnering Projects concept and topics to potential funding organisations. Further details of this process can be seen in Appendix 2: Partnering with the Human Brain Project Flagship.

2.3.3.2.1 Education Programme funding

Education Programme (see 2.2.2.3.6) management resources will be centralised at MUI (P43), except for the Female Coaching and Mentoring Programme, and the coordination of the MSCA-applications. While the management of these two tasks will be supported by the Education Programme Office budget, the assigned resources will be distributed to the respective task leaders. Limited funding will be assigned to syllabus leaders as seed money for coordinating teaching activities. Coordinating, managing and implementing the Education Programme requires basic funding from the Project's core budget. Additional funding for the Education Programme may come from Partnering Projects, such as the Marie Skłodowska-Curie actions. Furthermore, the Education Programme Office will work to exploit the possibilities offered by the European Institute of Innovation & Technology.

The Education Programme Office and the Education Programme Committee have made plans to exploit Horizon 2020 programmes, which meet the requirements and objectives of education and training for HBP Early Stage Researchers (ESR) and Experienced Researchers (ER), as defined by the Marie Sklodowska-Curie programme. The initial focus will be on Marie Sklodowska-Curie actions of the Initial Training Networks (ITN) type, such as European

Training Networks (ETN), European Joint Doctorates (EJD), European Industrial Doctorates (EID), and fellowships. One ITN with 10 Partners, among them 6 HBP Beneficiaries and 4 industrial companies, was submitted in January 2015. Several more are at a preliminary planning stage.

An estimated total funding of EUR 15.5 million for the four ETNs in the next phase of HBP is planned. It is estimated that six further ETNs could be created in the last two Phases of the Project for a total value of EUR 23 million. Finally, the total budget of ER fellowships could be around EUR 4 million. This brings the potential budget for Education Programme-related Partnering Projects to a total of EUR 43 million.

The HBP Education Programme Office will provide incentives to HBP Partners for collaborating with the Office and enabling proper coordination and monitoring of grant applications. Incentives will include guidance and advice for structuring the networks and proposals according to the Horizon 2020 Work Programme and the objectives of the HBP. These coordinating actions will avoid duplication, overlaps or redundancies of proposals from different HBP Partners and consortia.

In addition, the Education Programme Office will provide limited funds for meetings and other measures to foster the formation of consortia. ITN ESRs will have the added value of enrolment in the HBP Education Programme curriculum. The Education Programme Office will coordinate and foster multi-disciplinary activities between HBP-related ITNs.

2.3.3.3 Resources made available by Partners

In addition to the budgets described above, each Partner in the HBP Core Project has provided a list of resources currently or planned to be made available to the HBP for the period 2014-2023. The amounts presented there are estimates. At the time of the writing, the estimated value of the resources made available as in kind contribution by Partners amounts to EUR 493 million. The most important is Major equipment and Research Facility with EUR 315 million or 63% of the total resources made available. The partners contributing the most to this category are JUELICH with EUR 81 million (HPC, visualisation and characterization resources), EPFL with EUR 109 million (mainly for HPC and animal experimentation resources), FG with EUR 50 million (Clean room facilities), and CINECA with EUR 26 million (HPC resources). Many Partners will provide personnel to the project without claiming their cost. The value of personnel made available in this way amounts to EUR 182 million. The personnel provided by the Partners will produce around 2,500 person-years of effort at an average cost of EUR 75,000 per person-year. For personnel, the largest contributors are EPFL with EUR 98.5 million, JUELICH with EUR 31.4 million and UPM with EUR 7.5 million.

P No	Partner	Human resources (PMs)	Estimated value (EUR millions)	Major equipment / Research facility	Estimated value (EUR millions)
P1	EPFL	14000	98.5	CoMan, a compliant humanoid robot. Upper limb exoskeleton. Hand prostheses. VICON motion analysis system and systems for EMG recordings. Equipment for animal experiments. Overground robotic support systems for rats and mice. Light sheet microscope. Neuroscientific data. Advanced animal experimentation platform, Blue Brain Project computing and storage infrastructure. HBP Development Supercomputer. Such	109

				availability of EPFL equipment or research facilities is subject to legal restrictions (if any).	
P2	AALTO				
P3	LUMC				
P4	AUEB	50	0.3	Computing cluster	0.1
P5	BSC	400	1.5	1.1 petaflop Mare Nostrum Supercomputer facility	0.9
P6	BAUW			Projection-based multi-user virtual reality display systems	1.0
P7	BUW	32	0.2		
P8	BSMJ				
P9	CF				
P10	CNRS	300	4.4	Computational clusters. National (and potentially European) HPC resources	0.9
P11	CEA		2	2 clinical systems.	1.6
P12	CNR	300	1.5	Computing lab space and logistics.	0.3
P13	CINECA	3000	3	Big Data HPC cluster system.	26
P14	DTU	50	0.4	Modular robotic prototypes. Equipment, components, consultancy, modular system production	2.4
P15	UoD	50	0.2	High fidelity light microscopes. Complete fixed-slice apparatus. EM facility, Confocal microscope, in vivo neurophysiology laboratory, animal house.	0.5
P16	DMU	70	0.1		
P17	ENS				
P18	ETHZ				
P19	FT				
P20	JUELICH	3100	31.4	JUQUEEN Blue Gene/Q Supercomputer, Pre-Exascale HBP Supercomputer, Exascale HBP Supercomputer.	81
P21	FORTISS			Baxter robot.	0.1
P22	FG			Operation of two state-of-the-art clean room facilities.	50
P23	FCHAMP				
P24	UDUS	100	0.5	Lightcycle PCR, Tissuescope.	1.7
P25	UH				
P26	HITS		0.3	Computing cluster.	0.8
P27	CHUV	100	0.7		1.3
P28	ICL			iCub 2.0, with skin sensors, and iKart mobile base, RethinkRobotics Baxter humanoid, with electric grippers, 2 NAO v4 Humanoids.	0.4
P29	ICM				
P30	IEM HAS	50	0.3	2 in vitro electrophysiology setups. Animal facility and gene technology	0.1

				unit.	
P31	IST			SP5 confocal microscope. Ultima 4 two photon – confocal – uncaging system.	0.6
P32	JSI	100	0.5	Computing cluster with 1024 cores.	0.1
P33	INRIA				
P34	IP				
P35	UFRA	200	0.1		
P36	KIT				
P37	KI	600	3.5	Two-photon confocal microscope, patch clamp setups.	0.2
P38	KCL				
P39	KTH	500	5.7		
P40	LENS	500	1.6	Laser scanning two-photon microscope. Random access two-photon microscopy. Light-sheet microscope. Animal surgery facility. Patch clamp system. Animal housing facility, Biochemical laboratory, Electron microscopy centre.	1.6
P41	LNU				0.6
P42	MUI		0.5	Service Centre Research MUI.	0.1
P43	UoA			EXAREME: Platform for distributed data-flow processing on cluster and cloud infrastructures. AITION Knowledge Discovery Framework	1.2
P44	NMBU	200	2		
P45	OFAI	20	0.2		
P46	RWTH	200	0.1	Cave for immersive visualization. High-resolution display.	0.6
P47	UHEI			Heidelberg University + Helmholtz Association, Normalverfahren, Collaborative Research Centres	2.9
P48	SU			IC Test and Measurement Laboratory High Speed IC and Board Test Equipments. Board design and fabrication, system assembly (including in clean room) and testing.	0.5
P49	SSSA	100	0.3		
P50	CWI				
P51	SKU	100	0.1	Computing or storage infrastructures.	0.1
P52	FZI	200	2.2	FZI Living Lab Service Robotics. IT Infrastructure of FZI. Computing and storage resources.	0.2
P53	TUC				
P54	TUD	200	1.3	IT Infrastructure for integrated circuit design, Software Licences from Europractice Program.	0.3
P55	TUGRAZ			Various computing clusters.	0.5
P56	TUM	100	0.7	Various trackers and displays. Head-mounted displays. Haptic output devices.	0.3

P57	TAU	100	0.1		
P58	(blank)				
P59	UOXF	12	0.1	Fluidigm C1, CGAT Code Collection, Genserv Mouse Layers Database, Computing Cluster and Storage	0.2
P60	HUJI	700	0.9	Computer cluster. Lab space.	1
P61	UABER	60	0.5		
P62	UEDIN			Medical Research Council	1.4
P63	UMAN			The SpiNNaker machine – NM-MC-1.	3.6
P64	UAM				
P65	UCLM	130	0.3	Transmission Electron Microscope Jeol-1010. Zeiss LSM710 Confocal Laser Scanning Microscope System. Photomicroscope Leica DM 2500.	0.2
P66	UGR		0.2	1 robotic arm.	0.1
P67	UMIHNO		0.7	Laser Microdissection MMI Olympus Microscope, Confocal Microscope Olympus Fluoview 1000, PhenoWorld Multidimensional Behavioral Analysis System, Microbrightfield Bioscience Stereology Microscope,	1.1
P68	UPM	1000	7.6	Transmission Electron Microscope Jeol 1011. Confocal Microscope LSM 710. Dual-Beam Electron Microscope (NEON 40EsB). Intercellular Inyection System. Image Analysis, Animal Facilities. Large Computing infrastructure. Large Visualization Infrastructure. Robotics Laboratory.	3.8
P69	URJC			Lab space	0.2
P70	UNIPV	300	1	Computing clusters. 4 patch clamp systems. 1 VSD imaging systems. 1 MEA in vivo system. MR 3T scanner Siemens Skyra. MagStim TMS and BCI system. 2 patch-clamp laboratories. 1 MEA in vivo laboratory. 2 cellular imaging laboratories. 1 neurocomputing laboratory. 1 molecular biology laboratory. MRI laboratory. TMS/BCI laboratory.	1.6
P71	UBERN		0.1		
P72	UNIBI	100	0.8	Measuring station. FPGA-Cluster.	1
P73	UKAACHEN		0.5	Imaging Facility. 3 Tesla Siemens Prima.	0.3
P74	UKE			2 labs for high-density (128 channel) EEG recordings, BCI lab with two 64-channel Biosemi EEGamplifiers, MEG lab with a 275-channel CTF whole-head system, Setup for intraoperative microelectrode recordings, Robot lab with Robotino robots, multi-core workstation computers for real-time control, Data analysis cluster with 35 nodes, parallel computing facilities, and 50TB data storage.	0.8

P75	UZH				
P76	UB				
P77	UPF				
P78	AMU	30	0.4	INS houses a high-performance computing cluster dedicated to neural modelling.	0.1
P79	UBO				
P80	UA				
P81	UIO	250	2.5	Slide scanners. Serial 2-foton, microscopes. Small animal PET, and experimental computing setup. Laboratories for animal experiments and tissue processing/histology. Computing and storage infrastructure.	1.5
P82	UCL			Multiphoton and confocal microscopes. Lasers. Electrophysiology rigs.	1.3
P83	UU		0.3	Lab space	0.2
P84	WEIZMANN				
P85	TUDA				
P86	UNIGE	40	0.3	NeuGRID.	4.3
P87	IDIBAPS				
P88	IBEC	57	0.07	Fully equipped cell culture room for cell lines and primary cultures; three electrophysiology set-ups fully equipped with fluorescence microscopes and photostimulation lamps; fluorescence microscope that includes advanced features; additional equipment used for chemical synthesis and characterisation; automated system for observation and tracking	0.56
P89	DZNE			MR-PET, access to 7Tesla, Memory Clinic of the DZNE Magdeburg)	Cannot be estmated
P90	UBER		0.25	Three *in vitro* dendritic patch recording set-ups, two *in vivo* patch recording set-ups, three *in vivo* recording set-ups, and Neurocure Center for Excellence, which brings together a vital vector core, joint and shared spinning disc confocal facilities, and 2-photon imaging facilities, with lab's own resources for imaging calcium signals *in vitro* and *in vivo* in dendrites	1.95
P91	INFN	90	0.49	Existing experimental computing set-up and subsequent upgrades (1-4)	0.46
P92	ISS	136	0.64	HPC server and HPC co-processing board	0.02
P93	KNAW	30	0.19	Two photon microscopes, behavioural set-up, two slice patch clamp electrophysiology set-ups, Two *in*	0.35

				vivo electrophysiology/imaging set-ups, transgenic and conventional mouse facilities, monkey facility, molecular biology laboratory, IT	
P94	MRC				
P95	UMIL	86	0.42	Navigated Brain Stimulation System (NBS), TMS compatible EEG amplifier, air-cooled NBS, other UMIL contribution (overheads not withheld)	0.97
P96	ULG			3T research dedicated MRI CRCyclotron, 3T clinical MRI University Hospital, high-density EEG-TMS, medical transportation, overnight stay, clinical/electrophysiological and imaging assessments performed in post-coma patients	
P97	UvA		1.0	Microscopes, 2-photon imaging systems, patch clamp systems, computer cluster, *in vivo* ensemble recording systems and *in vivo* optogenetic equipment, behavioural training equipment, all facilities and lab space required for ensemble recordings, behavioural set-ups, animal housing, histology, surgery, biotechniques, including viral transfections, and neural data analysis, engineering support required for producing microdrives for ensemble recordings, behavioural set-ups, animal caretaker, animal welfare officer, support for histology, biotechniques and neural data analysis, opto-electric silicon probes, viral particles, amplifiers, animals, lab supplies, electrodes, genotyping, transgenic breeding, and general support for running lab costs	
P98	UGLA		0.04	3T fMRI, 7T fMRI, 7T fMRI building, computational storage, and research costs	0.14 (excluding 7T fMRI and building, which are in progress - figures to be update in completion of the facility)
P99	UHAM			Three EEG labs, access to MRI scanner, IT infrastructure, six behavioural testing rooms	
P100	USFD	2	0.01	iCub humanoid robot and real-time computing cluster	0.23
P101	UWE			Bristol Robotics Laboratory	~30.0
P102	SURREY			Three high-performance simulation servers	0.02
P103	TUT	15	0.13	Computing infrastructure	0.1
P104	ULEEDS				

P105	UPMC	38.6	0.15		
P106	UoS			UoS HPC equipment is available for supporting computational work	0.01
P107	MU				
P108	UCBL				
P109	POLITO				
P110	UGENT	156			
P111	KUL	96	0.2	3T scanner and technical infrastructure (animal housing, ICT, software and set-ups)	5.3
P112	UNIBAS		0.8		
P113	VU			Research and technical infrastructure	5.0
P114	SIB			Cluster of compute nodes	0.15
P115	EBRI	59	0.20		
P116	SNS	69	0.43		
P117	UM				
Total		**28168.6**	**185.42**		**355.86**

Table 20: Human, major equipment and research facility resources available by Partners.

2.3.3.3.1 Financial resources

Apart from the resources available by the Partners described in the above table, additional financial resources identified by Partners include grants received by Partners for HBP-related activities and grants that the partners expect to apply for and receive in the future. It is difficult or even impossible for funding agencies, governments and other sources to make financial commitments beyond their normal planning horizon. Furthermore, the experience of the HBP shows that funding agencies and other sources are more willing to commit to the funding of HBP activities once they are certain that EC funding will also be available. Nevertheless, current estimated financial resources expected to be available for HBP have already reached EUR 463 million. Of this sum, EUR 344 million from national funding sources, EUR 104 million from European funding sources, and EUR 15 million from international funding organizations.

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P1	EPFL		190	2.5	0.8
P2	AALTO				
P3	LUMC		2	0.2	
P4	AUEB		0.2		
P5	BSC		1.4		
P6	BAUW				
P7	BUW				
P8	BSMJ				
P9	CF		32	4	3
P10	CNRS		1		
P11	CEA				

P12	CNR		4		0.2
P13	CINECA		3		
P14	DTU		0.8		
P15	UoD		0.4		
P16	DMU			0.1	
P17	ENS				
P18	ETHZ		2	0.4	
P19	FT				
P20	JUELICH		36	25	1.2
P21	FORTISS				
P22	FG				
P23	FCHAMP				
P24	UDUS		1.4		0.7
P25	UH				
P26	HITS				
P27	CHUV				0.4
P28	ICL		1.5	1.8	
P29	ICM		0.5	1.2	0.8
P30	IEM HAS		0.2		
P31	IST			0.1	
P32	JSI		0.3	0.1	
P33	INRIA		2		
P34	IP				
P35	UFRA		1.4		
P36	KIT				
P37	KI		1.5	0.4	2.7
P38	KCL				
P39	KTH		5	1	
P40	LENS		1.9	1	
P41	LNU				
P42	MUI			43	
P43	UoA			0.5	
P44	NMBU		2	1.1	
P45	OFAI		0.4		
P46	RWTH		0.8		
P47	UHEI		26		
P48	SU		2		
P49	SSSA				
P50	CWI				
P51	SKU		0.2		
P52	FZI				

P53	TUC				
P54	TUD			1.3	
P55	TUGRAZ		0.1	0.1	
P56	TUM		0.5	0.8	
P57	TAU			0.1	0.1
P58	(blank)				
P59	UOXF		0.5	0.7	
P60	HUJI		1.5		3.7
P61	UABER		0.1		
P62	UEDIN				
P63	UMAN		3.5	2.5	
P64	UAM		0.1		0.1
P65	UCLM		0.2	2.2	
P66	UGR		0.1		
P67	UMIHNO		2.8	1.2	
P68	UPM		4	5.6	0.2
P69	URJC		0.2	0.1	
P70	UNIPV		2	1	
P71	UBERN		0.1		
P72	UNIBI		0.5		
P73	UKAACHEN		0.5		
P74	UKE		0.9		
P75	UZH				
P76	UB	1.2	0.3	4.1	
P77	UPF			1.8	
P78	AMU		0.5		
P79	UBO				
P80	UA				
P81	UIO		4.4		
P82	UCL		1.5		
P83	UU				
P84	WEIZMANN			1.6	
P85	TUDA				
P86	UNIGE			0.2	0.3
P87	IDIBAPS				
P88	IBEC	0.04	0.31	0.34	
P89	DZNE		1.9		
P90	UBER		0.42	1.01	
P91	INFN				
P92	ISS				
P93	KNAW		0.06	0.14	

P94	MRC			1.5	
P95	UMIL				
P96	ULG				
P97	UvA	0.83	0.73	0.25	
P98	UGLA			1.5	
P99	UHAM	0.26	4.07		2.81
P100	USFD			0.6	
P101	UWE		6.0		
P102	SURREY				
P103	TUT	0.8	0.99		
P104	ULEEDS				
P105	UPMC				
P106	UoS			0.05	
P107	MU				
P108	UCBL		1.43		
P109	POLITO				
P110	UGENT	0.4			
P111	KUL	5.8	0.9		
P112	UNIBAS				
P113	VU				
P114	SIB		0.1		
P115	EBRI				
P116	SNS				
P117	UM				
Total		**9.33**	**361.11**	**111.09**	**17.01**

Table 21: Estimated additional financial resources available to Partners in the Consortium at national, European and international levels.

2.4 Consortium

2.4.1 Consortium as a whole

2.4.1.1 Expertise and experience for implementing the Work Plan

The FPA consortium comprises 86 organisations in 19 countries. The majority of partners are universities, public/non-profit private research organisations or non-profit organisations. At the moment, there are no SMEs or large enterprises in the FPA Consortium. These organizations will participate in the Flagship Initiative primarily through the Partnering Projects.

The Partners provide the knowledge and competencies necessary to cover the Project's three main areas of research, namely neuroscience, computing, and medicine. Within each discipline, different groups provide complementary expertise. In neuroscience, the Project has a large number of groups working in mouse and human neuroscience; this knowledge is complemented by a similar number of groups working on theoretical modelling. The Project brings together different kinds of complementary knowledge, from leading groups in high-performance computing to experts in massive data management, neuromorphic computing (where the Project covers the complementary "physical model" and "multicore" approaches) and neurorobotics. Competences in brain simulation overlap with competencies in basic and theoretical neuroscience, and in high-performance computing. These overlaps enhance the integration of the Consortium. In medical informatics, the HBP brings together groups actively engaged in the analysis of imaging data with more technical groups working in the areas of distributed querying, and advanced data analysis. Brain simulation groups aim to integrate these two very different kinds of knowledge in unifying models.

Finally, the HBP has brought together a strong team in Ethics and Society, including sociologists, philosophers, and historians, practicing neuroscientists and researchers with practical experience in medical ethics.

The table below shows the expertise and experience of the partners in relation to the S&T objectives and the non-scientific aspects of the HBP roadmap.

P No.	Acronym	Country	SP-1 Mouse Brain Organisation	SP-2 Human Brain Organisation	SP-3 Systems and Cognitive Neuroscience (*)	SP-4 Theoretical Neuroscience	SP-5 Neuroinformatics Platform	SP-6 Brain Simulation Platform	SP-7 High Performance Computing Platform	SP-8 Medical Informatics Platform	SP-9 Neuromorphic Computing Platform	SP-10 Neurorobotics Platform	SP-12 Ethics & Society	SP-11Central Services	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
1	EPFL	CH	X			X	X	X	X	X	X	X		X	X	X	X
2	AALTO	FI										X					
3	LUMC	NL								X							
4	AUEB	GR								X							
5	BSC	ES							X								
6	BAUW	DE										X					
7	BUW	DE							X								
8	BSMJ	IL													X		
9	CF	UK								X							
10	CNRS	FR				X		X			X						
11	CEA	FR		X			X										
12	CNR	IT						X									
13	CINECA	IT							X								

P No.	Acronym	Country	SP-1 Mouse Brain Organisation	SP-2 Human Brain Organisation	SP-3 Systems and Cognitive Neuroscience (*)	SP-4 Theoretical Neuroscience	SP-5 Neuroinformatics Platform	SP-6 Brain Simulation Platform	SP-7 High Performance Computing Platform	SP-8 Medical Informatics Platform	SP-9 Neuromorphic Computing Platform	SP-10 Neurorobotics Platform	SP-12 Ethics & Society	SP-11Central Services	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
14	DTU	DK										X					
15	UoD	HU	X														
16	DMU	UK											X				
17	ENS	FR						X									
18	ETHZ	CH							X								
19	FT	DK											X				
20	JUELICH	DE		X		X	X	X	X		X						
21	FORTISS	DE										X					
22	FG	DE							X		X						
23	FCHAMP	PT		X													
24	UDUS	DE		X													
25	UH	FI										X					
26	HITS	DE						X									
27	CHUV	CH								X							
28	ICL	UK								X							
29	ICM	FR								X							
30	IEM HAS	HU	X					X									
31	IST	AT	X														
32	JSI	SI								X							
33	INRIA	FR		X		X											
34	IP	FR		X									X				
35	UFRA	DE							X								
36	KIT	DE							X								
37	KI	SE	X				X	X					X				
38	KCL	UK											X				
39	KTH	SE				X		X			X						
40	LENS	IT	X	X													
41	LNU	SE											X			X	
42	MUI	AT														X	
43	UoA	GR								X							
44	NMBU	NO				X		X	X								
45	OFAI	AT										X					
46	RWTH	DE							X								
47	UHEI	DE					X				X			X			X
48	SU	TR									X						
49	SSSA	IT										X					
50	CWI	NL					X										
51	SKU	NL					X										
52	FZI	DE										X					
53	TUC	GR					X										
54	TUD	DE									X						
55	TUGRAZ	AT									X						
56	TUM	DE										X					X
57	TAU	IL								X				X		X	
58	(blank)																
59	UOXF	GB										X					

P No.	Acronym	Country	SP-1 Mouse Brain Organisation	SP-2 Human Brain Organisation	SP-3 Systems and Cognitive Neuroscience (*)	SP-4 Theoretical Neuroscience	SP-5 Neuroinformatics Platform	SP-6 Brain Simulation Platform	SP-7 High Performance Computing Platform	SP-8 Medical Informatics Platform	SP-9 Neuromorphic Computing Platform	SP-10 Neurorobotics Platform	SP-12 Ethics & Society	SP-11Central Services	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
60	HUJI	IL				X		X									
61	UABER	UK						X									
62	UEDIN	UK	X														
63	UMAN	UK									X					X	
64	UAM	ES	X														
65	UCLM	ES	X														
66	UGR	ES										X					
67	UMINHO	PT										X					
68	UPM	ES	X				X	X	X								
69	URJC	ES	X						X								
70	UNIPV	IT	X					X									
71	UBERN	CH				X											
72	UNIBI	DE									X						
73	UKAACHEN	DE								X							
74	UKE	DE										X					
75	UZH	CH	X														
76	UB	ES										X					
77	UPF	ES				X											
78	AMU	FR				X											
79	UBO	FR								X							
80	UA	BE				X											
81	UIO	NO			X		X										
82	UCL	UK		X	X	X		X		X							
83	UU	SE								X			X				
84	WEIZMANN	IL				X											
85	TUDA	DE							X								
86	UNIGE	CH								X							
87	IDIBAPS	ES			X												
88	IBEC	ES			X												
89	DZNE	DE			X												
90	UBER	DE			X												
91	INFN	IT			X												
92	ISS	IT			X												
93	KNAW	NL		X	X												
94	MRC	UK			X												
95	IMIL	IT			X												
96	ULG	BE			X												
97	UvA	NL			X												
98	UGLA	UK			X												
99	UHAM	DE			X												
100	USFD	UK			X												
101	UWE	UK			X												
102	SURREY	UK				X											
103	TUT	FI				X											
104	ULEEDS	UK				X											
105	UPMC	FR				X											
106	UoS	UK									X						

P No.	Acronym	Country	SP-1 Mouse Brain Organisation	SP-2 Human Brain Organisation	SP-3 Systems and Cognitive Neuroscience (*)	SP-4 Theoretical Neuroscience	SP-5 Neuroinformatics Platform	SP-6 Brain Simulation Platform	SP-7 High Performance Computing Platform	SP-8 Medical Informatics Platform	SP-9 Neuromorphic Computing Platform	SP-10 Neurorobotics Platform	SP-12 Ethics & Society	SP-11Central Services	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
107	MU	UK									X						
108	UCBL	FR		X													
109	POLITO	IT									X						
110	UGENT	BE										X					
111	KUL	BE		X													
112	UNIBAS	CH		X													
113	VU	NL	X	X													
114	SIB	CH	X														
115	EBRI	IT	X														
116	SNS	IT	X														
117	UM	NL		X													

Table 22: Partners' expertise and experience for implementing the Work Plan.

Table 23 below provides a breakdown of the partners by country and their distribution across Subprojects. A complete list of the Partners can be found in the table at the beginning of this document. Further details on these partners such as their role in the Research Roadmap and the resources they bring to the Project, can be found in Appendix 5: HBP Core Project Partner Details.

Considered as a whole, the team appears to have an extremely good balance, which will be further enhanced through the Partnering Projects.

	SP1	SP2	SP3	SP4	SP5	SP6	SP7	SP8	SP9	SP10	SP11	SP12	TOTAL
Austria	1								1	1	1		4
Belgium		1	1	1						1			4
Denmark										1		1	2
Finland				1						2			3
France		4		4	1	2		2	1			1	15
Germany		2	3	1	2	2	7	1	5	5	2		30
Greece					1			2					3
Hungary	2					1							3
Israel				1				1			2		4
Italy	4	1	3	1		3	1		1	1			15
Netherlands	1	3	2		2			1					9
Norway			1	1	1	1	1						5
Portugal		1								1			2
Slovenia								1					1
Spain	4		2	1	1	1	3			2			14
Sweden	1			1	1	2		1	1		1	3	11
Switzerland	4	1		2	1	1	2	3	1	1	1		19
Turkey									1				1
United Kingdom	1	1	5	3		2		3	3	1	1	3	23
TOTAL	18	14	17	17	10	15	14	15	14	16	8	8	

Table 23: Number of beneficiaries in each Subproject, by country

2.4.1.1.1 International Involvement in the HBP

The idea of strengthening international collaboration in science has always been central to the HBP. The Operational Phase of the HBP will be shaped by the FPA, which is a new and untried European Commission instrument. It has therefore been agreed that international partners (based outside Europe) will not be included in the FPA at this stage. However, HBP policy on openness and flexibility (see section 2.4.1.2) provides that new Partners may be admitted to the Core Project each time a new Specific Grant Agreement is formulated and there is no reason why these should not include international partners. International entities are also eligible to propose HBP Partnering Projects and will take part in the international collaborations envisaged by the HBP. The HBP is currently working with other large Brain Initiatives in Australia, China, Japan and the USA, to create a Global Network of Brain Initiatives. The HBP is also discussing cooperation in disease classification and intellectual property with WHO and WIPO.

2.4.1.2 Openness and flexibility/evolution of the Consortium

The HBP will be structured to facilitate integration of new ideas and Partners, both in the Core Project and in Partnering Projects (PPs). Organisations based in countries other than European Union Member States and H2020 Associated Countries may participate in the HBP (see 2.4.1.2.3).

2.4.1.2.1 The Core Project

This FPA document sets out the framework for the HBP's Operational Phase, which will be subdivided into three or four successive Specific Grant Agreements (SGAs). The FPA lists the Partners that are expected to participate in the Core Project during the first Specific Grant Agreement (SGA). However, it is clearly understood that the list of Partners comprising the Core Project Consortium will need to evolve as the Project progresses.

Approximately 18 months before the start of a new SGA, the HBP's Science and Infrastructure Board (see 2.3.2.5.5), aided by the Project Coordination Office (see 2.3.2.5.6), will prepare the CP scientific Work Plan for the new SGA (the work to be undertaken in the forthcoming period). This will then be reviewed by the Directorate (DIR) and then approved by the General Assembly (GA) or Stakeholder Board (SB). In performing this exercise, the SIB and PCO will take into account the overall strategic goals as set out in the FPA, the HBP's progress to date, the past performance of individual Partners, plus external developments. The SIB and PCO will also look at feedback from the European Commission and its external reviewers, especially to identify activities in the current SGA that may need reinforcing in the next one. In this process, the SIB will be able to seek the advice and counsel of the Scientific Advisory Board (see 2.3.2.5.7), as well as the Ethics Advisory Board (see 2.3.2.5.8)

The CP Work Plan for the new SGA will identify current activities that will continue from the current SGA, and new activities, not undertaken currently, that will start only when the new SGA starts. Where there is no Partner in the current Consortium able to undertake the new activities, the SIB's roadmap will recommend recruiting new Partners to fill the gap. The new roadmap will also identify current activities that will cease for scientific reasons in the new SGA. Current Partners with no activities in the new SGA will leave the Consortium when the current SGA finishes.

At the same time, individual researchers and Partners which have not performed satisfactorily in the previous SGA will be identified, and may be asked to leave the Consortium. In the normal course of its work, the PCO will monitor achievement of milestones, deliverables and formal reporting, and issue warnings to underperformers. When the planning for the future SGA begins, the PCO will make a formal recommendation to the SIB for the exclusion of underperforming researchers and/or Partners who have not

responded to warnings. If the work undertaken by such a researcher or Partner is deemed scientifically necessary for the next SGA, the SIB will recommend in the draft CP Work Plan to engage a new researcher or Partner to take on this work. It can be seen that the proportion of the total budget for the new SGA that is reserved for new researchers or Partners via EoI calls will vary from one SGA to another, according to need.

The CP Work Plan for the next SGA, including identification of underperforming researchers and Partners that need to leave the Consortium, will then be submitted for approval by the Directorate (see 2.3.2.5.2) and then the General Assembly (see 2.3.2.4.1) for endorsement by the whole Consortium. (NOTE: When the planned Legal Entity (see 2.3.2.4) becomes active, a Stakeholder Board (see 2.3.2.5.1) will replace the GA as supreme authority.) This internal process should make clear to all current Partners how the Consortium composition will change in the new SGA. Once the CP Work Plan is approved by the GA/SB, an Expression of Interest (EoI) call process will be initiated to identify and select such new researchers and/or Partners as might be needed. However, the requirement for evaluation via a call might be modified in the case of new researchers or Partners from outside the EU, especially if they have their own independent funding. The selection of new researchers and/or Partners will be done by a combination of internal and external reviewers. The EoI call must be completed and new researchers and/or Partners identified before the SGA proposal can be sent to the Commission and the intended composition of the Consortium for the next SGA can be made public. Each EoI Call will involve the publication of a list of all the new pieces of work to be undertaken in the new SGA, for which new Partners are sought. The call will also specify the required format and content of proposals to undertake the advertised work. Universities, companies and other entities with the requisite skills and knowledge will be invited to respond with formal proposals to undertake a specific piece of work.

These proposals will be evaluated by external and internal reviewers in a formal review process. This will score proposals on a range of criteria, including scientific and technological excellence, impact, implementation and compatibility with the rest of the Core Project. Other criteria may be considered. The reviewers will then submit their recommendations to the SIB and DIR for validation. To maintain the breadth and diversity of the Consortium, current HBP researchers and/or Partners are strongly discouraged from putting forward proposals for the EoI Calls for new researchers and/or Partners.

To ensure transparency, the results of each evaluation will be made available to the Commission and the Consortium, including the scores attributed under each criterion, as well as a short written commentary by the leader of the relevant Subproject on the reasons for the acceptance or rejection of the proposal. In addition, the results and the identities of the reviewers will be made public after the Call is complete.

2.4.1.2.2 Partnering Projects (PPs)

The main mechanism through which independent academic and industry researchers can become Partners in the HBP Flagship Initiative will be through the Partnering Projects. This openness is key to the Flagship's ability to remain agile and at the cutting edge of science. Furthermore, PPs will enable the Flagship to involve the best research available anywhere in Europe.

The HBP will cooperate with European funding and coordinating instruments, large-scale initiatives in related fields, such as Art. 171 and 185 initiatives, and engage with industry to ensure a wide reach into the European innovation systems as well as alignment with available national and European support mechanisms. New projects will be evaluated and selected in a regular cycle.

More details on the selection, evaluation and integration of the PPs can be found in Appendix 2: Partnering with the Human Brain Project Flagship.

Relations between PPs and the HBP will be regulated by Partnering Project Agreements (PPA). Partnering Project Agreements (PPAs) should include access to the Research Infrastructure (once related IP issues and other legal matters have been resolved), plus access to online discussions, meetings, knowledge, and education facilities, as well as principles and guidelines for cooperation, such as Open Access, commitment to exploit IP, etc.

2.4.1.2.3 Third Country Participants

Organisations based in third countries – ones other than European Union Member States and H2020 Associated Countries - may participate in the HBP, once the HBP Legal Entity (see 2.3.2.4) has been established. For such an organisation to participate, the country concerned will need to join the Legal Entity via a suitable national organisation, in the same way as participating EU Member States and H2020 Associated Countries.

2.4.1.2.4 Support for Activities Elsewhere in the Flagship

The main beneficiaries of support for activities outside the FPA will be the Partnering Projects, which together with the CP constitute the HBP Flagship Initiative. An important pillar will be the HBP's relationships with national funding agencies and member/associated state governments, through instruments like FLAG-ERA and its successors, which will contribute to the initial set-up and funding of PPs. A well-defined and organised integration process (see Appendix 2: Partnering with the Human Brain Project Flagship) will facilitate seamless scientific integration with the relevant SPs.

PPs will also receive communications support, including visibility on HBPs website and digital media, as well as access to information and marketing materials.

The HBP Education Programme (see 2.2.2.3.6) and participation in workshops, conferences, and web-based exchanges are open to all Flagship partners, supporting a productive exchange of knowledge within the FS. As the Flagship grows, an internal exchange programme and conference travel grants may be set up.

PPs will also have access to HBPs international network, and will be actively integrated in scientific workshops, conferences, and other networking activities.

It is intended that IP generated in PPs will be integrated in HBP databases and innovation support mechanisms, like the HBP innovation hubs, and should be available to all Flagship partners.

The HBP Communications and Dissemination Programme will give visibility to research by the Partnering Projects. An especially important role will be played by the Museums Programme, which will have a worldwide reach.

Non-research partners (education, dissemination, international organisations, etc.) will receive tailor-made access to HBPs support functions as part of their engagement with the Flagship.

2.4.2 Capacity of participants and links to third parties

2.4.2.1 Participants

See Appendix 5: HBP Core Project Partner Details

2.4.2.2 Third parties involved

See Appendix 6: Consortium Partners' HBP Third Parties

2.5 Responsible Research and Innovation

2.5.1Ethics Issues and Related Measures

2.5.1.1 Objectives

The HBP aims to achieve a unified understanding of the human brain, to design a new generation of computing technologies using brain-like circuitry and computing principles, and to develop a radically new approach to the classification, diagnosis and treatment of brain disease. Within this setting the HBP pursues a policy of Responsible Research and Innovation (RRI), which it implements through specific bodies and procedures for ethics governance, through the Project's Ethics and Society (SP12) and through ethics-related activities within individual SPs.

The objective of these efforts is to integrate principles of RRI throughout the Project. The core of the RRI activities in SP12 is focused on the AREA acronym, which stands for Anticipate (WP12.1, Foresight), Reflect (WP12.2, Conceptual and Philosophical research and Researcher Awareness in WP 12.1), Engage (WP12.3) and Act (via Ethics Management in WP12.4 and various engagement activities in the other WPs).

This aligns with the majority of the RRI activities as proposed by the EC: People and Civil Society Engagement (WP12.3), Ethics Compliance (WP12.4) and Governance (WP12.4). Other aspects of RRI are reported by SP11, the Project Coordination Office (see section 2.3.2.5.6). To achieve this, SP12 will:

1) Ensure that the HBP complies with European and national ethical requirements, including the specific requirements of the H2020 programme.
2) Encourage HBP scientists to reflect on the ethical implications of their work and to use those reflections to inform their decisions.
3) Ensure that society at large (stakeholders, general public) is involved 'upstream' in the processes of research and innovation
4) Help to align emerging technologies with key social challenges.

2.5.1.2 Guiding Principles of Ethics Management

HBP implementation of RRI entails, but is not limited to, effective ethics management to ensure compliance with all local, national, European and International laws, regulations and guidelines. In relation to ethics management, it will act in conformity with the following guiding principles:

1) The HBP will do everything in its power to ensure that all research performed within the Project conforms to relevant European and national legislation and to Horizon 2020 rules.
2) The HBP will establish best practice concerning ethics and RRI on the basis of existing legislation and the H2020 programme. The HBP has established an independent Ethics Advisory Board (EAB – see 2.3.2.5.8) that can advise on all research in the HBP to ensure compliance with local, national and international regulations.
3) An Ethics Manager has been appointed to ensure that the principles of RRI are respected and implemented throughout the HBP. Where appropriate, the EAB may request advice and guidance from the Ethics Manager or Subproject 12.
4) The legal and professional responsibility for ensuring compliance with ethical and legal principles and regulations will lie with the research organizations and research groups

actually undertaking the research, respecting the principle of subsidiarity. The EAB will not duplicate the work of organisations and procedures for vetting and approving research activities, already established by European, national or local legislation, and will, as a general rule defer to the decisions and interpretations of such organisms.

5) The EAB can provide ethical advice regarding the ethical review of research whose conformity with relevant legislation and Horizon 2020 rules is not guaranteed by existing bodies and procedures. This includes research involving use of data, samples or resources generated outside the Project or carried out in non-EU countries, data sharing agreements and MoUs with third parties contributing data to HBP Platforms (e.g. data sources for the Medical Informatics and Neuroinformatics Platforms), using data provided by the Platforms, or proposals for Partnering Projects. The final responsibility for gaining ethics approval remains with the HBP Partner leading the research.

2.5.1.3 Ethical Governance Bodies

2.5.1.3.1 Background

Since its launch in October 2013, the HBP has worked to establish an effective model of ethics governance. Drawing on the experience of the Ramp Up Phase, and evaluations by ethical and technical reviewers, a revised model of ethics governance has been developed for the Operational Phase. This model, which is set out below, aims to achieve more effective integration and management of different ethics-related activities carried on within the Project. The plans define governance structures and procedures that will be reviewed regularly, but are expected to remain valid for the whole duration of the FPA. Additional organizational and scientific details (e.g. adjustments to management structures and procedures, ethical authorizations for specific experiments, choice of technologies to implement specific ethical requirements) will be specified in each SGA.

2.5.1.3.2 Overview of HBP Ethics Governance Bodies

- The SP12 Steering Committee (SP12 SC) coordinates the work of SP12 and its integration with the work of other SPs.
- The Ethics Manager, supported by the SP12 SC, is responsible for ensuring that the HBP conforms to the principles of RRI, with the support of a new EAB, which will subsume the functions of the previous Ethics, Legal and Social Affairs Committee (ELSA) and the Research Ethics Committee (REC).
- The Ethics Director who is responsible for ethical questions in the Directorate.
- The EAB can provide advice on all ethical issues.
- Decision making: The Ethics Manager helps the SIB and DIR to take decisions that ensure that RRI principles are adhered to.
- Coordination, monitoring, reporting and documentation of HBP actions on ethics-related issues is the responsibility of the Ethics Manager who is a member of the SP12 SC and is a non-voting member of the HBP Science and Infrastructure Board (SIB).
- Partners are individually responsible for ensuring that their research complies with relevant European Union, national and local law, and thus for requesting approval from the relevant Institutional Review Boards, and respecting their decisions.
- Decision making with respect to these requests and enforcement of these decisions is the responsibility of competent authorities, such as local or national research ethics committees.

- The flow of information between the Ethics Manager, the EAB, the SIB and the SP12 SC and individual Subprojects and the implementation of RRI within the Subprojects will be facilitated by Ethics Rapporteurs embedded in the HBP Subprojects (minimum of one per Subproject).
- Administrative and logistical support for ethics management is provided by a special Task in the Ethics Management Work Package (WP12.4)
- Research and Engagement to underpin RRI within the HBP is undertaken by the four main Work Packages of SP12

These bodies and activities are described in greater detail below, together with their Standard Operating Procedures.

2.5.1.3.3 Ethics Director

The Ethics Director is a member of the Director, where he or she is responsible for ethical questions. The post holder is nominated by the EAB and approved by SB. She or he may not be a member of the SIB, nor a member of SP12. However, he or he will work closely with SP12, in particular the Steering Committee and the Ethics Management WP.

2.5.1.3.4 Ethics Advisory Board

The Ethics Advisory Board is an independent body that advises the HBP Legal Entity (including the Science and Infrastructure Board, the Directorate and the Stakeholders Board) on specific ethical, regulatory, social and philosophical issues raised by research that is being undertaken or planned under the auspices of the Human Brain Project.

The advisory status of an EAB recommendation implies that individual researchers, investigators, laboratories and institutions will retain their legal responsibilities under the terms of local, national and international regulations, as well as professional obligations in place from time to time.

The EAB will advise on its own initiative, as well as upon requests made by researchers or other members of the HBP, about specific ethical, regulatory, and social issues arising from their research undertaken within the HBP or by collaborators.

Regular members who comprise the EAB are unpaid experts, who have been chosen for their knowledge in a specific area relevant to the HBP. Membership of the EAB is determined by competence, geographical and gender balance.

The EAB reports to the Legal Entity (via Ethics Manager, directly where required). Details of the EAB are described in a separate standard operating procedure (SOP).

2.5.1.3.5 Ethics Rapporteurs

To facilitate the interaction between the EAB and the Ethics Management Work Package in SP12, each SP will appoint at least one Ethics Rapporteur, who will be responsible for liaising with WP 12.4 and the EAB on ethics-related issues within that Subproject. More specifically, the Rapporteur will coordinate the preparation of any ethical documentation required by the EAB, coordinate SP requests for advice or support from EAB or SP12 and respond to queries by EAB and SP12.4 concerning the documentation provided. The Ethics Rapporteurs and the Ethics Manager together form the Ethics Coordination Committee, one of a number of cross-cutting committees (see Section 2.3.2.10).

2.5.1.3.6 Local Research Ethics Committees

Local Research Ethics Committees or comparable competent authorities (also referred to as Institutional Review Boards or IRBs) will be responsible for ethical decision-making relating to research within in a specific EU country, where existing legislation specifies procedures

for approval of the research. The researchers concerned must communicate the relevant documentation to WP12.4, before beginning their research, or, if the research is already in progress, within one month of the approval of the relevant SGA. WP12.4 will maintain an Ethics Compliance Registry, documenting HBP-related ethics requests and approvals, accessible to the EC and EC ethics reviewers. A summary of non-confidential information contained in the registry will be published on the HBP public website.

2.5.1.3.7 Administrative and Logistics Support for Ethics Governance Bodies

HBP ethics governance bodies will receive administrative and logistics support from WP 12.4. The responsibilities of WP12.4 will include coordination of the recruitment of new members of the EAB, assisting EAB Chairs in their duties (preparation of agendas and minutes, etc.), ensuring that all Project Partners provide required ethical documentation, performing preliminary checks of the documentation provided, managing the Registries that the Project will make available to the EC and its ethical reviewers, managing the PORE (the Point Of Registration of incoming requests to the committees), and HBP reporting requirements with respect to the EC and its ethical reviewers. In addition to these duties, WP12.4 will be responsible for maintaining the content of section(s) of the HBP public website dedicated to ethical issues.

2.5.1.3.8 SP12 Steering Committee

The day-to-day running of SP12 will be the responsibility of the SP12 Steering Committee (SP12 SC). The committee will consist of the leaders of each WP in SP12. The SP12 SC will be assisted by a small secretariat and chaired by the SP12 leader. The SP12 SC will hold video meetings at least monthly and face-to-face meetings at least once every six months.

The SP12 SC will be responsible for:

- Coordination, monitoring and documentation of RRI activities.
- Completing the ethics sections of Periodic Progress Reports and six-month progress reports, and responding to requests for RRIs-related documentation from EC officials and reviewers
- Facilitation of collaboration of SP12 work packages with one another, with other HBP Subprojects, with stakeholders and with members of the public to ensure the implementation of the principles of RRI in the HBP.
- Coordination of RRI-related events and communications in close liaison with the HBP communications team.

The SP Coordinator (WP12.5) will support the SP12 SC, create agendas and oversee execution of decisions.

2.5.1.3.9 Ethics Management

A new WP on Ethics Management (WP 12.4) will be created to coordinate to oversee and execute all activities related to the management of ethical and social issues in the HBP. This covers all research ethics questions, but goes beyond this in translating research findings and recommendations into SOPs and integrating these into the HBP. The leader of the Ethics Management WP will be the Ethics Manager.

The Ethics Manager ensures that ethical issues are managed to highest standards within the HBP. Ethics (management) is one of the six components of RRI, according to the EC view of the term. The Ethics Manager ensures that the HBP takes a leading role in defining best practice in dealing with ethics in brain simulation and big data in health-care more generally.

To achieve this, she or he:

- Represents ethics management issues on the HBP Science and Infrastructure Board.
- Interfaces with the European Commission:
  - Prepares responses to EC ethics reviews.
  - Provides required ethical information to the EC.
  - Leads HBP interactions with ethics audits.
- Works with HBP general management to ensure that RRI management and SOPs are appropriately integrated in HBP management structures.
  - Oversees the development of SOPs in collaboration with the EAB, SP12, the management of the HBP overall and other bodies where required.
- Works with all scientific SPs and ensures that RRI management issues are addressed appropriately
  - Prioritises ethical issues raised by the Point of Registration (PORE) in collaboration with SP12 SC and EAB.
  - Monitors compliance and analyses regular reports with ethics-related SOPs in all SPs.
  - Oversees the Ethics Rapporteur programme.
  - Contributes to the Education Programme (see 2.2.2.3.6) to ensure it covers HBP ethics management.
- Leads the ethics management team
  - Develops and oversees ethics management processes.
  - Ensures that relevant information (if not confidential) is publicly available.
  - Updates the HBP Ethical Issues Map.
- Represents ethics management in the data governance committee
- Establishes links with related initiatives using big data in health-related research such as ELIXIR, BBMRI, EuroGentest and ECRIN to identify good practice.

2.5.1.3.10 Ombudsman

The Ombudsman is an individual who is independent from the HBP and serves as the recipient of confidential information about the HBP that may require further investigation and action (i.e. facilitation of whistleblowing). The Ombudsman has the right to access all information and members of the HBP, and is bound by a non-disclosure agreement. The Ombudsman has the right to attend and speak at all governance bodies of the HBP, including the right to add items to agendas. The Ombudsman can raise PORE issues and thereby involve SP12 and the EAB in investigations and recommendations. The Ombudsman is appointed by the DG on the recommendation of the EAB.

2.5.1.4 Standard Operating Procedures (SOPs)

In order to ensure consistent treatment of ethical and social issues, the Ethics Management WP will develop SOPs that provide clear guidance in particular situations. SP 12 will create both internal and external SOPs. Internal SOPs specify the roles and workings of the SP, whereas external SOPs govern the behaviour of scientists and other Project members across the HBP. The process for developing SOPs is as follows:

1) The need for an SOP has to be agreed by the SP 12 SC.

2) The SP12 SC gives the task of creating the SOP to a designated individual or body (typically the Ethics Manager).
3) The first draft of the SOP is circulated within SP12, the EAB and affected SPs for discussion and comment.
4) The SOP is revised by the author(s) in light of feedback received.
5) SP12 SC adopts the SOP or requests further changes.
6) The SOP is forwarded to the SB for general adoption.
7) Once adopted, the SOP is implemented in collaboration with the relevant SPs.
8) If necessary, the SOP should be revised.
9) SOPs that are no longer needed required should be terminated.

In the following sections, key SOPs required by the HBP are identified. These will be developed in more detail, made publicly available and be integrated into the HBP Education Programme (see 2.2.2.3.6).

The EAB and the SP12 SC will operate according to the SOPs outlined below. These SOPs will be fully developed and reviewed regularly by Task T12.4.2 (SOPs), in accordance with the principles outlined above.

2.5.1.4.1 Mandatory Documentation of Request for Ethics Approval to Local IRB

Any Partner undertaking an HBP research activity which requires approval by a local IRB must provide full documentation of requests for approval and IRB decisions to the HBP compliance management team. If the original documentation is not in English, an English translation must also be provided. If the EAB or its secretariat determines that the documentation submitted is not sufficient or if additional information is requested by EC reviewers, it is empowered to require the submission of additional documentation and, if necessary, to request the suspension of the research and related payments.

The Ethics Management WP will check that SPs, Work Packages and Tasks provide all the required ethical documentation. Documentation will be stored in a repository open to the EU and its ethical review bodies.

2.5.1.4.2 Mandatory Ethical Review of Specific Areas of HBP Activity

The HBP has identified the following areas of HBP activity where existing review boards and procedures cannot ensure compliance with European law and H2020 rules:

- Research involving use of data, samples or resources generated outside the Project or carried out in non-EU countries,
- Data sharing agreements and MoUs with third parties contributing data to HBP Platforms or using data provided by the Platforms
- Work in areas of research not legally subject to approval by Institutional Review Boards
- Proposals for Partnering Projects, insofar these do not undergo regular national / local ethics review.

All these activities are subject to mandatory ethical review by local IRBs, for which HBP PIs are responsible. Ethical reviews will consider compliance with the requirements of European Union law, and H2020 policies and will use procedures similar those applied by the EC in vetting research proposals under H2020. Approvals will need to be given by competent local or national authorities. The Ethics Management WP will review and log approval. Where appropriate, Partners may be required to submit additional documentation in support of their request. The Ethics Management WP or EAB is empowered to propose amendments to

proposals, which, in its opinion, do not comply with European law and H2020 policy, or which do not provide adequate documentation to evaluate their compliance.

HBP ethical reviews will be designed to minimize the administrative burden on researchers. Specifically, in cases where researchers in non-EU countries have already requested approval from a local IRB, the initial HBP vetting will be based on the documentation submitted at that time, or (in cases in which the documentation is not in English) on an English language summary of the documentation. If the Ethics Management WP or EAB determines that the documentation submitted is not sufficient to evaluate the research, it is empowered to require the submission of additional documentation.

Projects requiring ethical approval will forward the appropriate documentation to the Ethics Management WP. Documentation must be provided in English. If the original documentation is not in English, a certified English translation must also be provided. The secretariat will check that the documentation is complete and sufficient to allow evaluation. If necessary, it will request additional information. The secretariat will also check that Work Packages expected to provide ethical documentation have done so. Documentation will be stored in a repository open to the EU and its ethical review bodies.

2.5.1.5 Ethical issues within the HBP

2.5.1.5.1 The HBP Ethics Map

As a large, multidisciplinary project, the HBP can raise a large number of ethical, social and regulatory questions. Some of these are subject to European or national legislation, guidance by the EU or other regulatory funding bodies, or social and cultural views.

In order to track these issues, prioritise them and find ways of appropriately addressing them, SP12 works with all other SPs to ensure responsibilities are clarified and realised. These issues are collected on the HBP Ethics Map, with a view to creating discussion and finding solutions. This map is a high-level overview of ethical issues, that links to the compliance registry where some, but not all, of the issues are processed. It is informed by the PORE process, and populated by the Ethics Management WP under the supervision of the SP12 Steering Committee.

The HBP Ethics Map consists of a list of issues that are linked to more detailed documents providing background and log developments. This HBP Ethics Map is, by its nature, a dynamic document that will change over time.

The current structure of this HBP Ethics Map contains a short name for the ethical issues in question, the classification of the issue according to the H2020 ethics self assessment guide, an indication of which SP is affected, who is responsible for addressing it, an indication of the status of the issue, and the immediate next steps to take.

The full map is to be hosted online, and will contain a link to one document per issue. This will serve as a log of activities, discussions and agreements on actions. It will also be linked to other related documents, notably the Ethics Compliance Registry and, where appropriate, to specific SOPs or other documents that can support addressing the issue. This structure of the Map will be reviewed in light of further developments, and may be subject to change.

2.5.1.5.2 Data-related considerations

Re-use of Clinical Data

The HBP Medical Informatics Platform (SP8) will federate large volumes of anonymised data (genetic data, imaging data, and other clinical data) originally generated for clinical purposes, and make it available to the research community. Procedures for anonymisation

are described in detail later in this section, under the heading "De-identification (anonymisation) of data". De-identification and anonymity are ensured to the highest possible standards by a combination of technical architecture and procedural safeguards, overseen by mechanisms of audit and data governance. Partnering Projects and other users will mine these data for biological signatures of disease, which, if found, could provide important insights into disease mechanisms, contributing to the development of new diagnostic tools and new treatments. The Project will encourage community efforts to use MIP data and tools for studies of a broad range of brain disorders. Below we discuss the implications of this approach.

Compliance with European and National Data Protection Law

At the time of writing, data protection in EU Member States is regulated by EU Directive 95/46/EC and by derived national legislation. Negotiations for a new Data Protection Regulation are now at an advanced stage. Given, however, the draft Regulation has yet to be finalised, the discussion here will be limited to existing law.

For the purposes of data protection law, health-related data pertaining to a data subject is personal data, which can only be gathered legally under strict conditions, for a legitimate purpose. In particular, Recital 33 of the Data Protection Directive provides that "data should not be processed unless the data subject gives his explicit consent" [1] However, Recital 26 states that "the principles of protection shall not apply to data rendered anonymous in such a way that the data subject is no longer identifiable".

Architectural Considerations

In the architecture adopted by the MIP, all data referring to human volunteers is held in local data repositories managed by the individual hospitals that contribute data to the Project. There is no central repository and no transfer of raw data outside the hospital perimeter. Thus, the raw data are protected by the same technical infrastructure and technical measures and receives the same legal protection provided to all patient data. This implies that any attempt to re-identify patient data would constitute a criminal offence. Access to raw data is restricted to authorised personnel. Access is protected by passwords, and additional physical protection measures (e.g. use of smart cards), in line with the policies adopted by individual hospitals. Servers are protected using the same measures used to protect other hospital information systems containing patient data.

De-identification (anonymisation) of Data

Given the recitals of the Data Protection Directive, the applicability of data protection legislation depends on whether or not the data accessed via stored in the MIP can be treated as anonymous data.

De-identification or anonymisation of data is the process whereby personal data is processed with the aim of preventing identification of the data subject. Several anonymisation techniques may be envisaged. No prescriptive standard is defined in EU legislation. Relevant standards and regulations include ISO 29100:2011, and the US HIPAA regulation.

In its Opinion 05/2014 on anonymisation techniques, the EU "Data Protection Working Party" examined the robustness of a broad range of anonymisation techniques. The Working Party concluded that,

"anonymisation techniques can provide privacy guarantees and may be used to generate efficient anonymisation processes, but only if their application is engineered appropriately (…) The optimal solution should be decided on a case-by-case basis, possibly by using a

combination of different techniques, while taking into account the practical recommendations developed in this Opinion."

In the light of these recommendations, SP8 has adopted a strategy of "defence in depth" which combines different technical and organisational measures. In line with the findings of the Working Group, SP8 recognises that anonymity and anonymisation are lively fields of research and will update its protection measures as the field progresses.

Local HBP data repositories contain only anonymised data. Thus, even an HBP user with system administrator rights cannot access individual patient records. The data repositories are populated using a pipeline that extracts data from hospital medical records, and applies filters to remove information that could allow the identification of a patient. The procedure includes removal of identifiers and pseudo-identifiers that could allow the re-identification of patients, as specified by the US HIPAA regulation. It also provides for addition of noise to some kinds of clinical data to prevent identification of patients. In particular, brain imaging data is "defaced" (i.e. image parameters are altered to prevent reconstruction of a patient's face).

No End-user Access to Raw Data

The HBP MIP will provide hospitals with the software to post-process the raw data contained in local data repositories and extract features of interest (grey and white-matter volumes, as revealed by medical imaging). The post-processing software is controlled and run by the hospitals. End-users of the MIP will be able to query the feature data but not the raw data. De-identified raw data (e.g. imaging data) will be conserved in local repositories for use by HBP researchers involved in the development of new feature extraction algorithms. Access to the data will be restricted to researchers authorized by individual hospital data controllers.

k-anonymity

The MIP will use the technique of k-anonymity. It will provide end-users with descriptive statistics for particular features (or correlations among them) in a set of records matching a query, only when the number of records in the set is greater than a threshold-value. If only one, or a small number of records, satisfies a query, the MIP will not respond to the query. Work is in progress to extend this approach to genetic data. The software will include filters that block suspicious queries.

Audit Trail

With the protective measures in place it would be virtually impossible for an attacker to infer data about an individual patient. Nonetheless, the Medical Informatics System will maintain an audit trail, recording the origin, time, date and content of individual queries and the records used to generate the response. Analysis of these data could in principle detect suspicious activity.

Software

Software implemented in the MIP, the development of which has been funded by the HBP, will be released under an open-source license such as BSD. The same code will be available for privacy impact audits (see below). To extract data in primary hospital information systems, and remove HIPAA identifiers, the HBP will use existing software available on each hospital site, or software provided, configured and maintained by an appropriate Subcontractor with expertise in medical informatics, and a track record in research initiatives in managing, securing and mining large data sets.. The software will meet HIPAA standards and additional HBP requirements, and will allow system administrators to define access rights precisely. The software will run on servers managed by hospital staff. The subcontracting company will have no access to patient data.

#	Issue Name	H2020 Category	SP	Responsible	Status	Action	Target date
1	Animal experimentation	Animals	SP1	PI	Approval secured	Apply ethics compliance SOP	Review annually
2	Animal data sharing with China	Third countries	SP1	HBP contact (PI)	Approval secured	PI to check whether Chinese approval is valid in EU	Beginning of SGA1
3	Transcriptome sequencing from human tissue	Human cells/tissues	SP1	PI	Approval secured	Apply ethics compliance SOP	Review annually
4	Imaging research on human volunteers	Humans	SP2	PI	Approval secured	Apply ethics compliance SOP	Review annually
5	Experiments on human tissue from brain banks and local hospitals	Human brain	SP2	PI	Approval secured	Apply ethics compliance SOP	Review annually
6	Longitudinal data collection	Personal data	SP2	PI	Approval secured	PI to clarify whether longitudinal data can be anonymous	Beginning of SGA1
7	Imaging research on non-human primates	Animals	SP2	PI	Approval secured	By vote of local ethics committees	Review annually
8	Experiments on brains of non-human primates	Animals	SP2	PI	Approval secured	By vote of local ethics committees	Review annually
9	Data protection in clinical research	Personal data	SP3	PI	Approval secured	PI to clarify data protection aspect	Review in the course of integration of new SP3 partners
10	Non human primate experiments	Animals	SP3	PI	Approval secured	PI to clarify use of human data and term "genetic programming"	Review in the course of integration of new SP3 partners
11	Data protection of visitors names	Personal data	SP4	PI	Open	PI to clarify data protection of visitors to EITN	Beginning of SGA1
12	Data sharing with China/Australia	Third countries	SP5	PI	Open	HBP to develop data sharing agreements and MoUs	Beginning of SGA1
13	Data set processing	Other	SP5	HBP	Open	Data protection principles for the HBP to be developed and implemented	Beginning of SGA1
14	Missing specifications for unified portal	Misuse	SP6	HBP	Open	Specification for portal containing data protection measures to be developed	Beginning of SGA1
15	Incomplete consideration of ethical issues of technical infrastructure	Other	SP6	HBP	Open	Development of a holistic and coherent assessment of the ICT platforms, their interactivity and the data sources and standards	During SGA1
16	Dual use of brain simulation platform	Dual use	SP6	HBP	Open	Explore dual use issues of simulation platform	During SGA1
17	Data protection and HPCP	Personal data	SP7	PI	Open	Data protection principles for the HBP to be developed and implemented in HPCP	Beginning of SGA1
18	Dual use of HPCP	Dual use	SP7	HBP	Open	Explore dual use issues of HPCP	During SGA1
19	Misuse of HPCP	Misuse	SP7	HBP	Open	Explore misuse issues of HPCP	During SGA1

20	Consent to use hospital clinical data	Humans	SP8	PI	Open	Develop and implement consent policy for MIP	Beginning of SGA1
21	Secondary use of hospital clinical data	Personal data	SP8	PI	Open	Develop and implement consent policy for MIP	Beginning of SGA1
22	Implications of personalised medicine	Other	SP8	HBP	Open	Explore possible implications of personal medicine	During SGA1
23	Dual use of neuromorphic computing	Dual use	SP9	HBP	Open	Explore dual use issues of neuromorphic computing	During SGA1
24	Dual use of neurorobotics	Dual use	SP10	HBP	Open	Explore dual use issues of neuro-robotics	During SGA1
25	Implications of soft robotics	Other	SP10	HBP	Open	Explore dual implications of soft robots	During SGA1
26	Incomplete CIRCABC repository	Other	SP12	SP12, EM	SOP being developed	Develop and implement ethics management principles and SOPs	Beginning of SGA1
27	Quality assured ethics management	Other	SP12	SP12, EM	SOP being developed	Develop and implement ethics management principles and SOPs	Beginning of SGA1
28	Quality assurance of technical development	Other	HBP	SP13	Open	QA policy to be developed and implemented	During SGA1
29	Research integrity / malpractice	Other	HBP	SP12, EM / SP13	Open	HBP research integrity policy to be developed	Beginning of SGA1
30	Implications for industry and employment	Other	HBP	HBP	Open	Explore implications for industry and employment	During SGA1
31	Ethics of HBP communications	Other	SP13	SP13	Open		During SGA1

Table 24: Overview of the HBP Ethics Map

The figure below shows a graphical representation of the issues. This is to provide an overview of issues that are currently in the Map, and allow for them to be clustered. The figure was developed by locating the issues along two axes. The x-axis represents the question of whether the issue relates to the process of doing research, or to the outcome of this research. The y-axis relates to whether the issue is explicitly regulated, or whether there is flexibility in how it is addressed. All issues were distributed along these two axes, which led to the development of clearly identifiable clusters of issues. These are expressed by the larger shapes. The names of the clusters indicate their content, which overlaps with the H2020 categories to some degree.

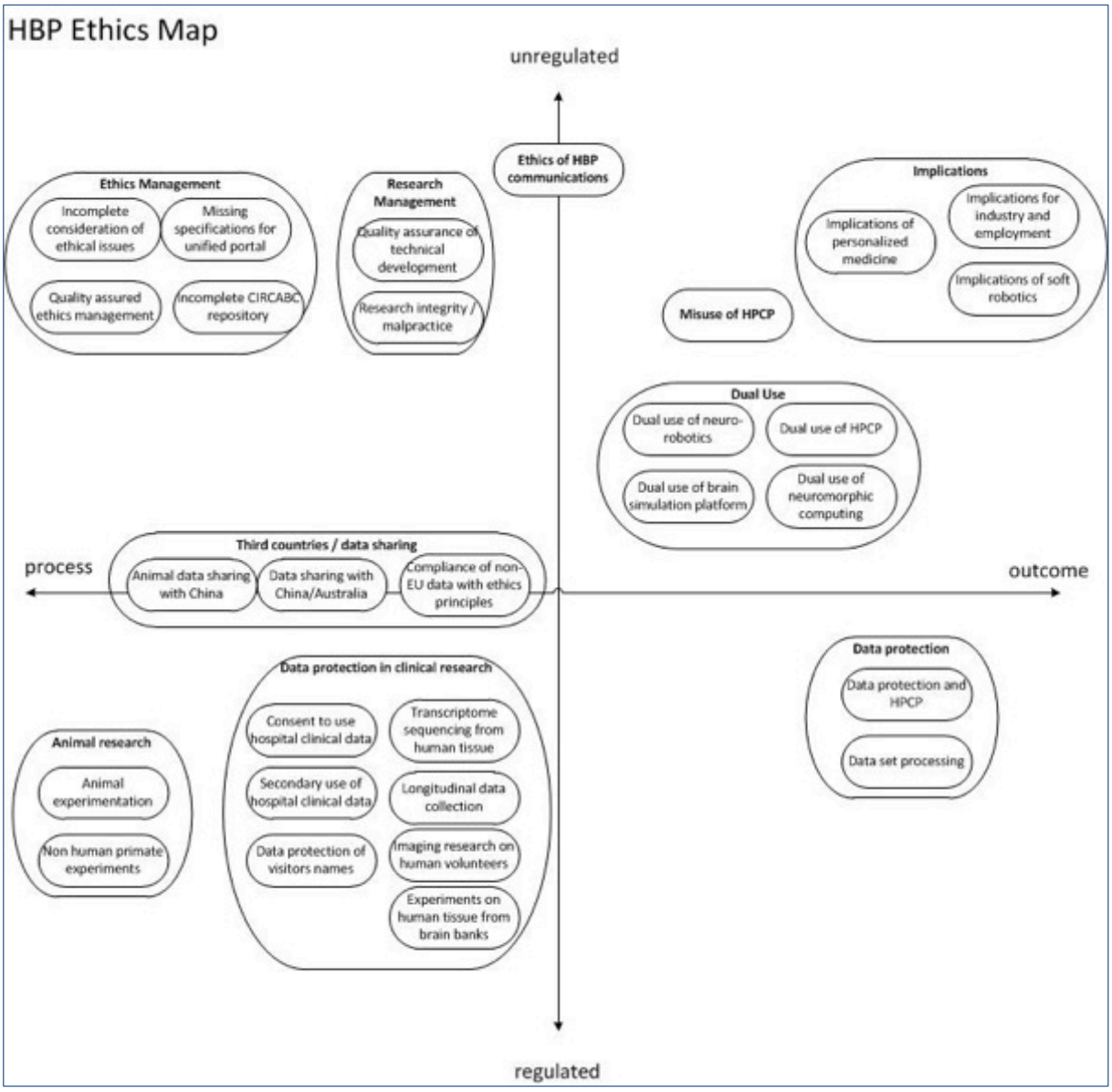

Figure 9: Graphical overview of the current content of the HBP Ethics Map

The purpose of this figure is to give a better insight into the highlighted issues. The clusters may serve to set priorities for SP12 and the HBP as a whole. The figure may also help to identify related issues that should be addressed in similar ways. Just as the HBP Ethics Map will evolve, its graphical representation will change over time.

2.5.1.5.3 HBP's EU Research Ethics Questionnaire

HUMAN EMBRYOS/FOETUSES	
Does your research involve Human Embryonic Stem Cells (hESCs)?	☐Yes ☒No
Will they be directly derived from embryos within this Project?	☐Yes ☒No
Are they previously established cells lines?	☐Yes ☒No
Does your research involve the use of human embryos?	☐Yes ☒No
Does your research involve the use of human foetal tissues / cells?	☐Yes ☒No
HUMANS	
Does your research involve human participants?	☒Yes ☐No
Are they volunteers for experiments in social or human sciences research?	☐Yes ☒No
Are they persons unable to give informed consent?	☒Yes ☐No
Are they vulnerable individuals or groups?	☐Yes ☒No
Are they children/minors?	☒Yes ☐No
Are they patients?	☒Yes ☐No
Are they healthy volunteers for medical studies?	☒Yes ☐No
Does your research involve physical interventions on the study participants?	☒Yes ☐No
Does it involve invasive techniques?	☐Yes ☒No
Does it involve collection of biological samples?	☒Yes ☐No
If your research involves processing of genetic information, please also complete the section "Protection of personal data" [Box 4].	
HUMAN CELLS / TISSUES	
Does your research involve human cells or tissues? If your research involves human embryos/foetuses, please also complete the section "Human Embryos/Foetuses" [Box 1].	☒Yes ☐No
Are they available commercially?	☐Yes ☒No
Are they obtained within this Project?	☒Yes ☐No
Are they obtained within another Project?	☒Yes ☐No
Are they deposited in a biobank?	☒Yes ☐No
PROTECTION OF PERSONAL DATA	
Does your research involve personal data collection and/or processing?	☒Yes ☐No
Does it involve the collection and/or processing of sensitive personal data (e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?	☒Yes ☐No
Does it involve processing of genetic information?	☒Yes ☐No
Does it involve tracking or observation of participants?	☒Yes ☐No
Does your research involve further processing of previously collected personal data (secondary use)?	☒Yes ☐No
ANIMALS	
Does your research involve animals?	☒Yes ☐No
Are they vertebrates?	☒Yes ☐No
Are they non-human primates?	☒Yes ☐No
Are they genetically modified?	☒Yes ☐No
Are they cloned farm animals?	☐Yes ☒No

Are they endangered species?	☐Yes ☒No
Please indicate the species involved (Maximum number of characters 1000) Mouse, Rat, Macaque	
NON-EU COUNTRIES	
Does your research involve non-EU countries?	☒Yes ☐No
Currently: Argentina, Australia, Canada, China, Israel, Japan, Norway, Switzerland, Turkey, USA.	
Do you plan to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples, etc.)?	☐Yes ☒No
Do you plan to import any material - including personal data - from non-EU countries into the EU? If you consider importing data, please also complete the section "Protection of Personal Data" [Box 4].	☒Yes ☐No
Specify material and countries involved (Maximum number of characters allowed: 1000) Data (e.g. cell morphologies, results from experiments) from all countries listed above. The data will not as a rule include personal data. Data from non-partner institutions will be covered by data sharing agreements, which will be subject to ethical vetting as described in the main document.	
Do you plan to export any material - including personal data -from the EU to non-EU countries? If you consider exporting data, please also complete the section "Protection of Personal Data" [Box 4].	☒Yes ☐No
Specify material and countries involved (Maximum number of characters allowed: 1000) The HBP Platforms will be accessible to users outside the EU. Use of data will be subject to data use agreements, which will be subject to ethical vetting as described in the main document.	
If your research involves low and/or lower middle income countries, are benefits-sharing measures foreseen?	☐Yes ☒No
Could the situation in the country put the individuals taking part in the research at risk?	☐Yes ☒No

ENVIRONMENT PROTECTION vi - Directive 2001/18/EC vii - Directive 2009/41/EC viii - Regulation EC No 1946/2003 ix Directive 2008/56/EC x - Council Directive 92/43/EEC xi - Council Directive 79/409/EEC xii - Council Regulation EC No 338/97	
Does your research involve the use of elements that may cause harm to the environment, to animals or plants?	☐Yes ☒No
Does your research deal with endangered fauna and/or flora and/or protected areas?	☐Yes ☒No
Does your research involve the use of elements that may cause harm to	☐Yes ☒No

humans, including research staff?	
DUAL USE	
Does your research have the potential for military applications?	☒Yes ☐No
MISUSE	
Does your research have the potential for malevolent/criminal/terrorist abuse?	☒Yes ☐No
OTHER ETHICS ISSUES	
Are there any other ethics issues that should be taken into consideration? Please specify	☒Yes ☐No
Maximum number of characters 1000 Issues of mission creep - see main text of document for discussion.	

Table 25: HBP's EU Research Ethics Questionnaire

Details on how individual ethical issues are treated, e.g. those arising from the Research Ethics Questionnaire, Ethics Review or the Ethics Compliance processes are available from the Ethics Manager and will, where appropriate, be made publicly available as SOPs, EAB Opinions or in a similar form, via the HBP website.

2.5.2 Coverage of EC Ethics Requirements

Ethics requirements according to the H2020 regulations reflected in the H2020 self assessment process (Ref: http://ec.europa.eu/research/participants/portal/doc/call/h2020/h2020-msca-if-2015/1645175-h2020_-_guidance_ethics_self_assess_en.pdf)

will be fully adhered to. The Ethics Management processes outlined above will ensure that these issues are monitored and, where required, followed up. The table below gives a brief overview that indicates the principles to be applied, as well as actions to be implemented.

Ethics Issue Category	*Ethics Requirement Description*	*Actions / Plans by HBP*
ANIMALS	Detailed approach to be provided in DoA of relevant SGAs	HBP animal experimentation will follow the principle of the "Three Rs": replacement, reduction and refinement, according to Directive 63 / 2010 and its implementation in Member States. General principles are provided below, instantiation to specific cases and related implementation aspects will be detailed in relevant SGAs proposals. **Replacement:** All proposed experiments involving animals will use only laboratory animals bred specifically for research. In the investigations of complex brain structures and dynamics that the HBP requires, there is currently no alternative to the use of animals. However, experimental approaches can be improved enormously by close interaction between experimental and computational approaches. This is reflected in the present proposal, where some Partners already use brain modelling and simulation as their principal research tool. Validated predictive methods have the potential to reduce the number of animal experiments needed for future brain research. **Reduction:** Reduction of the use of animals and of potential suffering will be achieved through an appropriate choice of experimental techniques. The majority of mouse and rat experiments will be carried out either under terminal anaesthesia or using isolated tissue prepared at euthanasia. According to the UK Home Office Guidance Notes (2002) to the Animals (Scientific Procedures) Act 1986 (A(SP)A), the severity of these experimental protocols therefore falls in the category "Unclassified" (of low severity). Where *in-vivo* experiments are necessary, pain and suffering will be avoided by non-recovery protocols; wherever possible, experiments will be conducted under terminal anaesthesia. Experiments to study behaviour in awake animals will be performed following recovery from minimally invasive surgery under full surgical anaesthesia and involving no more than mild pain. No pathological states will be induced and no pharmacological testing will be performed. No painful or psychologically distressing protocols will be used. Measures will be taken to maximise the chances of obtaining useful data from each individual animal (e.g., sterile surgery conditions, healthy animals). State-of-the-art electrophysiological and imaging methods make it possible to obtain comprehensive detailed data from a single animal. In particular, optogenetics and multi-electrode, multi-site, electrophysiological recording methods enable researchers to collect data about neuronal activity in many cells simultaneously. In vivo imaging methods for repeated monitoring of neural

		networks in the same animal (longitudinally) and for data collection in awake, behaving animals also help to maximise the information gathered from individual animals. For behavioural experiments, extensive training of limited numbers of animals will assure collection of high-quality meaningful data. Given low inter-individual variability, firm conclusions can usually be reached from small numbers of animals. Animal numbers will be further reduced by conducting small-scale pilot experiments before proceeding to experiments using larger numbers of animals, where necessary. Finally, as indicated above, computational modelling will reduce the number of animals needed for experiments by maximising the data that can be extracted from individual data sets. **Refinement (animal welfare):** Animals will be obtained from animal housing facilities that are dedicated to institutional research and whose work practice has been scrutinised and authorised by an official homologation review led by local veterinary services, as mandated by applicable law. HBP research teams will ensure that animal houses offer the best possible conditions. Laboratory staff are trained in the handling of laboratory animals, health is monitored daily, and all participant laboratories have veterinary assistance. Trained personnel with official authorisations for animal experimentation perform all surgical operations under anaesthesia and analgesia (as approved by ethical committees). Experimental procedures for behavioural experiments are being steadily improved and refined to optimise the well being of experimental animals – a prerequisite for collecting high-quality data.
OTHER ETHICS ISSUES	Ethics management and governance including responsibilities and interaction with vertical SPs and with the Central Services SP, to be further elaborated	Ethics management is covered by a separate WP in SP12 in the FPA. This includes the earlier governance activities but also includes explicit attention to the development of standard operating procedures, compliance management, management of the point of registration, ethics rapporteurs and Ethics Advisory Board. SOPs on the EAB, compliance management and ethics rapporteurs have been approved by the BoD in September 2015 and are already in force in the ramp-up phase.
	Retrofitting the ethics research results into the rest of HBP to be clarified	The insights produced by the research WPs of SP12 are put in practice in the HBP. The crucial transmission mechanism is the Ethics Management WP (12.4). This contains several mechanism that will strengthen the mutual exchange between SP12 and the scientific and technical SPs. Key among these are: The Ethics Rapporteur programme which will ensure an on-going dialogue between the technical experts from the SPs and SP12. The PORE programme that will be the mechanism whereby SP1-10 experts can raise concerns and bring them to the attention of SP12 The Compliance Management task which will not only collect data on ethics approvals but work with the SPs in developing action plans that will be linked to clear deliverables and timelines whose execution will be monitored by the Ethics Management team.
	Monitoring of application of	This monitoring of appropriate ethics standards is the remit the Compliance Management task. The principle

	appropriate ethics standards and guidelines to be organised, including when the R&D is carried out outside the Core Project.	is that adherence to ethics standards and the collection of ethics approvals is the role of the local PI. However, Compliance Management will ensure that all ethics approval exist and are valid for the duration of the project and make copies of such approvals available to ethics reviewers. The monitoring of these standards will cover core and partnering projects.
HUMANS	Possible involvement of children or minors in the Core Project to be further justified	Involvement of children and minors requires specific justifications. Such justification along with details on recruitment and selection are a precondition of receiving ethics permission via local IRBs. No study will commence without such local IRB approval. The HBP ethics compliance procedures will ensure that relevant ethics permissions are collected and made available to reviewers.
	Approach for the use of post-mortem samples to be clarified	This information is part of the ethics approval documentation to be provided by the local PIs in order to gain ethics approval. Studies will only be permitted to commence once local IRB approval is provided.
	An incidental findings policy is to be defined for the relevant research	Incidental findings policies are typically part of ethics approval documentation. Where incidental findings are not covered in existing ethics protocols and approvals they will be made available. This will be detailed in the context of each relevant SGA.
DUAL USE	SP12 to include a scheme for assessing potential dual-use risks during the Flagship duration.	"Dual use" refers to research and development for civilian applications that could be used for military applications (for example, research using neural implants to control prosthetic limbs that could also be used to control drones or military robots). No technologies developed in the HBP are designed with dual use in mind and HBP research aims exclusively at civilian applications. According to the H2020 ethics self-assessment guidance, dual use issues can be identified when products are in need of export licences or if the result of research can change current standards in military ethics (e.g. autonomous robots). These issues may arise with regards to neuromorphic computing or neurorobotics. The Ethics Compliance Task of Ethics Management will work with the relevant SPs to monitor regularly the possible evolution of the situation and ensure that no HBP work raises dual use problems.
MISUSE	SP12 to include a scheme for assessing potential misuse risks during the Flagship duration.	In ethical discussions, "misuse" refers to malevolent or criminal use of research results or products. As in the case of dual use, the special status of HBP technologies as tools, makes it difficult or impossible to predict all possible forms of abuse.
NON-EU COUNTRIES	Monitoring application of appropriate ethics standards and guidelines to cover also the included R&D carried out outside EU	The initial responsibility for checking that third country research processes and data conform with EU ethics requirements rests with the PI who leads the research or wishes to import data. This is the case where data is imported and processed in the HBP. The ethical status of data (e.g. consent status and usage permission) will be included in the meta-data to ensure that data is used appropriately. If HBP research is undertaken in non-EU countries, then the normal HBP Ethics Compliance processes apply

		and the local PI will have to submit the IRB approvals which will be scrutinised by the Compliance Management team and made available to EU ethics reviewers. In some cases, HBP researchers will want to make use of data gathered independently of the HBP. Such data may be ethically relevant (e.g. animal or human data). In such cases, a check will have to be performed to determine if the data collection followed EU ethical guidelines. This will be done as part of the process leading to signature of the data use agreements which are a precondition for the use of data in the HBP. It will be the responsibility of the local PI to ensure that data use agreements are signed. These will be collected by the Ethics Compliance process.
	Approvals and related material in a non-EU language to be complemented with English summary translations	This requirement for English translations is embedded in the Ethics Compliance SOP and has been adopted by the Board of Directors.
PROTECTION OF PERSONAL DATA	Data protection, anonymisation and security to be further elaborated.	***Pseudonymity*** The policy of some hospitals requires that patients should be able to request details of the purposes for which their data have been used. This may make it necessary to maintain a table linking patient codes and identifiers. Such a table would be held by local hospital data controllers and would not be accessible to HBP staff or to users of the MIP. Given that researchers using the MIP will not have access to data for individual patients, they would not be able to use the code to trace individual patients. Nonetheless, hospitals with this policy (a subset of the hospitals contributing to the MIP) would not be able to consider the data as anonymous for the purposes of data protection law. Discussions are in progress with hospital administrations to find a suitable solution before the MIP comes on line. ***Organisational Measures and Legal Responsibility*** For the purposes of data protection legislation, the data controllers of individual hospitals are responsible for anonymised patient data held in their own hospital repositories. The data controller for the overall MIP and for metadata and provenance files will be the partner responsible for the MIP. The MIP is evaluating additional procedural safeguards, regarded as best practice for large databanks of medical data (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2744675/). An initial set of safeguards will be in place before the MIP comes online in Project Month 30. They will include the creation of a Data Governance Committee responsible for ensuring that the acquisition of data by the MIP and the use of the data by users of the MIP comply with relevant law, regulation and professional standards. The committee will include representatives of different stakeholders including data providers, members of local IRBs and patient groups, etc. ***Data Protection Impact Assessment***

		The anonymisation techniques used in SP8 will be subjected to periodic data protection impact assessment by an independent third party. The first assessment will take-place before the end of the Ramp-Up Phase. ***Technical Measures to Enforce Anonymisation*** Metadata associated with clinical records stored in local hospital data repositories will routinely include details of the hospital archive from which the data was taken, the form of consent, the location of consent documents, measures to de-identify the data, and relevant data use agreements/MoUs and plans (see below). The HBP provenance tracking system will make it possible to analyse these data and to retroactively exclude data that does not meet emerging ethical standards. ***Requests for Ethical Approval*** No clinical data will be made available through the MIP without the approval of the hospitals or other organisations holding the data. These organisations will be responsible for requesting ethical approval (where required) from the relevant Institutional Review Boards. Staff from SP12 and staff from the MIP will assist hospitals in formulating their applications and in providing any information IRBs may require. The goal of the Project is that all necessary applications for ethical approval should be completed not later than the end of Month 24, and that all requests should be approved not later than Month 30. As the pool of hospitals grows, all new hospitals joining the HBP will have to undergo the same ethics approval process. The SP8 data protection officer / data governance officer will ensure compliance with these principles. NOTE: Additional data-related topics are covered in section 2.5.1.5.2
PROTECTION OF PERSONAL DATA	Potential risks of commercial exploitation of patients' data initially provided for research only to be clarified.	This will be clarified in the context of the commercialisation of medical outputs of the project.
OTHER ETHICS ISSUES	A mechanism (Ombudsperson scheme or other Point of Registration and related SOP) to be available internally and externally to allow R&D PIs and other stakeholders to raise additional ethics concerns	The Ombudsman is described in section 2.5.1.3.9 of this FPA. The Point of Registration constitutes a separate task of the Ethics Management WP and is fully functional and available under www.HBP-PORE.eu.
OTHER ETHICS ISSUES	HBP governance to ensure high level management support for the ethical dimensions of HBP and to make clear to all partners, in CP or	The creation of the role of the Ethics Manager and the development of the Ethics Management WP within SP12 has provided the focal point where the various ethics management activities come together. Furthermore, this FPA document defines the role of an Ethics Director (section 2.5.1.3.10) who will be elected by the EAB and who will be a member of the Directorate, thus ensuring the presence of ethics on all

	PPs, that ethical and legal compliance is of high priority for the long term sustainability of the initiative.	key HBP decisions.
OTHER ETHICS ISSUES	FPA Action Plan to include a general inventory (Map) of the types of ethical issues to be addressed (in relation to the H2020 ethics framework) and the corresponding approaches foreseen (research, EAB, local/national approvals); this Map will then support the monitoring. More detailed descriptions to be provided in the Description of Actions of the successive SGAs	The Ethics Map was developed and is maintained by the Ethics Management WP. It is a living document that contains key issues raised by internal and external stakeholders and links to specific action plans that allow addressing these issues. The current version of the Ethics Map is included in section 2.5.1.5.1 of this FPA document. The Ethics Map provides the general overview of the ethical and social issues. It is linked to the Ethics Registry which is the document where the Ethics Compliance team collects all IRB approvals and other relevant documents that indicate how particular issues are addressed. The actual documents, such as research protocols or IRB approval documents are held on a secure server and linked to the ethics registry.
OTHER ETHICS ISSUES	EAB to provide opinion on the final version of the FPA Action Plan (and, later, on the (and, later, on the SGA proposals submitted).	The EAB was involved in the development of the FPA and provided input to the Board on how to deal with ethical issues in the HBP. Minutes of the EAB meetings in Paris (June 2015) and Madrid (September 2015) demonstrate that the EAB discussed the FPA, in particular the ethics section and questions of future governance.

Table 26: HBP FPA - Ethics Issues and Requirement Descriptions

Appendix 1: Overview of the Flagship Objectives and Strategic Research Roadmap

A1.1 Concept and Strategy

Every year, the world spends more than EUR 7 billion on brain research, producing rapidly growing volumes of data and knowledge. To date, however, the scientific, social and economic returns have, to a certain extent, been disappointing. Neuroscience is still far from achieving a unified understanding of the multi-level mechanisms that give rise to cognition and behaviour. Our steadily improving understanding of the brain has yet to give rise to new computing technologies. Most importantly of all, brain research has had too little impact on the way we understand, diagnose and treat brain disorders – diseases that already cost the European economy more than EUR 800 billion per year [11, 12]. This is a burden expected to grow with the aging of European population. To make progress, there are three critical challenges to overcome.

The first challenge is in neuroscience. Despite decades of effort, we still do not fully understand the brains of very simple animals, let alone the human brain, with its approximately 100 billion neurons and 100 trillion synapses. Modern experimental research produces massive volumes of data, but has only generated a tiny fraction of the data that would be needed to create a complete map of the brain. To achieve a unified understanding of the brain, we need is a new strategy that makes it possible to integrate the data coming from research, and to fill in the huge gaps where data are not available. This strategy obviously includes tools to handle massive amounts of data, to analyse them and to exchange the results with other researchers.

The second challenge is in computing. Current computing technologies cannot match the brain's reliability, fault-tolerance, energy, or ability to process complex data streams in real-time and to learn without explicit programming. Some of the hardware needed to build brain-like devices and systems is on the horizon. But to use this hardware effectively, we have to understand the basic computational principles and circuit designs that give the brain its capabilities, and build the tools to translate this understanding into practical technology.

The third challenge is in medicine. Today there are few disorders of the brain whose causes are fully understood, and few effective treatments. The high risks associated with the development of CNS drugs have led many pharmaceutical companies to cut back on their research. Effective diagnosis and treatment of neurological and psychiatric diseases require a shift away from symptom and syndrome-based classifications of disease toward objective, biologically grounded classifications. As a first step, we need to identify the biological changes associated with disease at different levels of brain organisation: the “biological signatures” of disease. Ultimately, we have to understand the causal mechanisms that give rise to these changes and their effects.

Until recently these challenges were intractable. The HBP Flagship Initiative proposes a new strategy that exploits the possibilities opened up by modern ICT. A community-driven Research Infrastructure (RI) for brain research, including cognitive and systems neuroscience, as well as brain-inspired sciences such as future computing, will be built from the HBP information and communications technology (ICT) Platforms. Close interaction with the global neuroscience community will be key to its success — from defining the RI’s strategic goals, to measuring how well it performs. Building the RI will require a new organisation for the HBP that clearly distinguishes RI development and operations from internal and external research projects. As an overarching goal, we will try to link closely external and internal neuro-research, so that a world-leading RI in neuroinformatics, data-

driven brain modelling, brain simulations, neurorobotics, and medical informatics can emerge. The RI will bring together, and build on, advanced concepts of data-centric, high-performance and neuromorphic computing. The Project is developing six ICT Platforms, covering Neuroinformatics, Brain Simulation, High-Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics. Early versions of the Platforms, accessible via a single Collaboratory, will open for community use at the end of the Ramp-Up Phase. The Platforms will be regularly updated at 30-month intervals, and are likely to include novel tools and technologies proposed and contributed by Partnering Projects.

The HBP Platforms will enable members of the community to perform research and collaborate on a very broad range of topics in neuroscience, computing and medicine. It is this research, enabled by the Platform that will enable the Project to achieve its Strategic Objectives. The Research Roadmap identifies many possible themes but is deliberately formulated in such a way as to be open to new ideas and contributions.

In neuroscience, this new infrastructure will allow the use of state-of-the-art supercomputers to build high-fidelity brain models, for reconstructing the brain from sparse experimental data, exploiting interdependencies in the data to predictively fill in gaps where no data is available and steadily improving the accuracy of the reconstructions as more data become available. In the first five years of the HBP, the Project will reconstruct and simulate the mouse brain. It will examine whether and in how far they can be extrapolated to human brain models. In parallel, it will start to produce first draft reconstructions and simulations of the human brain – starting from a very coarse level, and providing more and more details. Simulations will be linked to virtual robots interacting with a virtual environment, creating a closed loop. *In silico* simulation experiments using these systems will make it possible to dissect the basic biological mechanisms underlying cognition and behaviour.

In computing, this will allow the building of machinery and methods to translate high-fidelity reconstructions into simplified models of the brain, and to implement these models in neuromorphic and neurorobotic devices and systems. The Project will explore potential applications for industry, transport, health-care, the home, high-performance computing etc. Much of the work performed in the Project also requires new developments in high-performance computing (new architectures, new methods for interactive visualisation, new techniques of multi-scale simulation). The potential applications go far beyond brain simulation.

In medicine, this will allow the federation of hospital archives and other sources of anonymised clinical data, and building the analytical tools to extract “biological signatures of disease” from very large volumes of heterogeneous data (genetics, blood chemistry, structural data from imaging, EEG, clinical signs, treatment response, etc.) and mapping the similarities and differences between different disorders. This work will allow more effective diagnosis and treatment of patients, better identification of potential drug targets, and better selection of participants for clinical trials. Ultimately, the Project will develop the capability to simulate brain disorders, reconfiguring reconstructions of the healthy brain to reflect biological signatures of disease. Disease simulation will make it possible to investigate the causal mechanisms responsible for disease and to screen potential treatments, accelerating the drug development process.

The HBP’s approaches to neuroscience, computing and medicine require technological know-how and infrastructure that are currently available only to very few research groups. One of the first goals of the HBP Core Project is thus to make these capabilities available to members of the relevant scientific communities. To achieve this, the Project is developing six ICT Platforms dedicated respectively to Neuroinformatics, Brain Simulation, High-Performance Computing, Medical Informatics, Neuromorphic Computing and Neurorobotics. The first versions of the Platforms, accessible via a single Collaboratory, will open for community use in Month 30. The Platforms will be regularly updated at 30-month intervals,

and are likely to include novel tools and technologies proposed and contributed by Partnering Projects.

The HBP Platforms will enable members of the community to perform research and collaborate on a very broad range of topics in neuroscience, computing and medicine. It is this research, enabled by the Platform that will enable the Project to achieve its Strategic Objectives. The Research Roadmap identifies many possible themes but is deliberately formulated in such a way as to be open to new ideas and contributions.

In sum, the HBP Flagship Initiative will drive a completely new mode of organising collaborative, transdisciplinary research, of accelerating basic science, and of translating results from basic research into products and services that benefit the European economy and European citizens.

A1.2 Flagship Objectives (FOs)

The HBP Flagship aims to achieve the following objectives, through the Core Project and/or the Partnering Projects.

FO1 - Create and operate a European scientific research infrastructure for brain research, cognitive neuroscience, and other brain inspired sciences: Develop and operate six specialised Platforms dedicated respectively to Neuroinformatics, Brain Simulation, High-Performance Analytics and Computing, Medical Informatics, Neuromorphic Computing, Neurorobotics, and a Collaboratory (formerly Unified Portal) providing a collaborative, transdisciplinary environment and community services that enable industry and academic researchers to co-develop and share methods, tools and data, and to work together to address novel research questions. Leverage investment in platform development to catalyse a phase shift in neuroscience, computing, and medical research. Establish synergistic collaborations with national, European and international initiatives contributing to the Strategic Flagship Objectives.

FO2 - Gather, organise and disseminate data describing the brain and its diseases: Generate targeted data sets that can act as anchor points for future data generation and for high fidelity reconstructions of the brain. Targeted data sets for mouse will make it possible to develop the integration and algorithmic reconstruction processes required for high-fidelity reconstruction of the mouse brain across all levels of biological organisation, from genes to cognition. Parallel data sets for humans will enable the application of technologies developed in animals to mapping the human brain, facilitate translation of knowledge about the mouse brain to the human brain and constrain human brain models. The availability of these data sets will expose critical gaps in our current knowledge, catalysing collaboration with large-scale brain mapping initiatives around the world. Detailed data on brain structure, at different levels of biological organisation, will provide a vital tool for functional studies mapping the links from genes to cognition and behaviour. Human specific data, e.g., with respect to genetic patterns, cognitive processes and behaviour, brain architecture and inter-subject variability, will be collected on all levels of brain organisation, not only to further constrain such models, but also to understand better the biological basis of what makes us Human. Develop ICT tools to federate and cluster anonymised patient data. The new tools will make it possible to identify patterns of alteration across different levels of biological organisation, suggesting new diagnostic indicators and drug targets, facilitating the selection of subjects for clinical trials, providing the data required for disease modelling and simulation, and facilitating the translation of knowledge about the brain from the laboratory to the clinic.

FO3 - Simulate the brain: Develop ICT tools that would enable HBP Researchers as well as the broader neuroscience community to generate high-fidelity digital reconstructions and simulations of the mouse brain, and ultimately the human brain. Bottom-up and top-down reconstructions and simulations of the brain provide a radically new approach to

neuroscience, helping to fill gaps in the experimental data, connecting different levels of biological organisation, and enabling *in silico* experiments impossible in the laboratory. Such experiments can provide fundamental new insights into the biological mechanisms underlying cognition and behaviour, make it possible to test hypotheses of disease causation, and provide a valuable new tool for drug development.

FO4 - Build multi-scale scaffold theory and models for the brain: Develop multi-scale scaffold theory and models of the brain that merge theory-based, top-down and data-driven, bottom-up approaches. Theory and models developed in the HBP will provide a framework for understanding learning, memory, attention and goal-oriented behaviour, the way function emerges from structure; and the level of biological detail required for mechanistic explanations of these functions. Simplification strategies and computing principles resulting from this work will make it possible to model specific brain functions, both in neuromorphic and digital computing systems.

FO5 - Develop brain-inspired computing, data analytics and robotics: Develop ICT tools supporting the re-implementation of bottom-up and top-down models of the brain in neuromorphic computing and neurorobotic systems. HBP Neuromorphic Computing Systems will use brain-like principles of computing and architectures to achieve high-energy efficiency and fault tolerance, together with learning and cognitive capabilities comparable to those of biological organisms. Neurorobotic systems will use them as controllers, enabling a new category of closed loop experiment that dissects how different levels of brain organisation contribute to cognition and behaviour. Develop hardware architectures and software systems for visually interactive, multi-scale supercomputing and big data analytics, moving towards the exascale. The new systems will make extreme-scale computing accessible to neuroscientists and clinicians, supporting the requirements of brain simulation and of high throughput, big data analytics, and enabling a broad range of other data-intensive applications.

FO6 – Ensure that the HBP's work is undertaken responsibly and that it benefits society. Promote engagement with industry to translate HBP research results into technologies, products and services benefitting European citizens and European industry. Expected HBP results in brain-inspired computing and medicine have the potential to give European industry a leading position in key areas of the 21st century economy. Implement a programme of multi-disciplinary education by using innovative online education approaches that focus on the convergence of ICT, biology and medicine. This programme should prepare a new generation of researchers capable of working across different fields, including neuroscience, medicine and computing. Implement a strategy of Responsible Research Innovation, monitoring science and technological results as they emerge, analysing their social and philosophical implications, and raising awareness of these issues among researchers and citizens, involving them in a far-reaching conversation about future directions of research.

A1.3. Research Roadmap

The Research Roadmap defines the research that the HBP Flagship Initiative will perform over the duration of the Project. Some of the planned Actions contribute directly to the FOs – as when the Project produces an important new scientific insight, a new computing technology, or a new clinical application of its results. Others contribute indirectly, for instance by contributing data, knowledge, models, methods, algorithms and tools, or by enabling the Project to follow a policy of Responsible Research Innovation.

The research and development performed by the Project can be roughly divided into two categories: research contributing to the Project's scientific and technical capabilities (made available to the scientific community through the HBP Platforms) and research driving the

development of such platforms by its intrinsic needs, co-developing them and using their capabilities.

The demands placed by modern brain research on ICT are increasing rapidly. A comprehensive understanding of human brain organisation requires us to consider the multi-level organisation of the brain, including different aspects of brain organisation (e.g. genes, molecules, cells and cell connections), and also the different spatial (nanometers to centimetres) and temporal (milliseconds to years) scales, each spanning several orders of magnitude. The brain is a highly complex organ – successfully addressing such a complex organ requires highly specialised tools to handle and analyse the data, and a research infrastructure, which goes far beyond the capacities and capabilities of individual labs.

Neuroscience areas with a particular need for high-performance research infrastructures include:

- Electrophysiological (e.g. multi-unit recordings) and cellular-resolution imaging studies, in particular in behaving animals; this includes the challenges of comprehensive and reliable meta data, as well as questions of data handling, storage and visualisation.
- Analyses of ultra-high resolution brain models at cellular and subcellular scales.
- Simulation of brain regions or whole brain simulations, with high spatial and/or temporal resolution.
- Neuroimaging studies in large cohorts with thousands of subjects in combination with genetic data.
- Analyses of decentralised data from hospital patients with special requirements in terms of safety and security, requiring special methods of data access and analysis.

Particular challenges arise from the ultra-high dimensionality and time-series characteristics of most of these data, and from the demands of high-throughput analysis and interactive visualisation.

Such research is addressed in the HBP's first four neuroscience Subprojects. The objective of SP1, Mouse Brain Organisation, is to generate neuroscientific concepts, knowledge, data sets and tools, contributing to a better understanding of the multi-level and multi-scale organisation of the mouse brain. SP1's results will be used to constrain and validate reconstructions and simulations of the mouse brain. The objective of SP2, Human Brain Organisation, is structured along similar lines. In addition, human brain functional and structural segregation, its inter-subject variability, and genetic factors represent central elements of SP2, and contribute to SP5's multimodal HBP Atlas.

SP3, Systems and Cognitive Neuroscience, will form a matrix-like structure in the Project. Its cross-cutting activities will address challenging problems of systems and cognitive neuroscience, relying on and driving the development in the Platform SPs.

The overall objective of SP4 is to establish solid theoretical foundations for modelling the brain across different levels of biological organisation, and to investigate models for key aspects or functions in conjunction with other SPs. For example, these include simplified models of neurons, including non-linear dendritic computations, models of different brain signals, and models of synaptic plasticity, learning and memory.

Part of the empirical and theoretical neuro-research in all SPs is the development of new methods, tools and research environments. The HBP Consortium is developing a detailed strategy, and plans to effectively integrate and align the work in the Neuroscience Cluster (SPs 1 to 4) with that of the Platform Cluster (SPs 5-10). Additionally, an SP1-4 Working Group has been set up, which closely interacts closely with the SP5-10 Working Group looking at User Recruitment and Infrastructure Strategy. The neuroscience SPs will:

- Act through co-developing the Platforms that are being developed by SPs 5—10, where, in an iterative way, neuroscience contributes to the Platforms through a co-design process.
- Attract first users, and introduce the Platforms to both the neuroscientific community and broader scientific world, with the goal of providing an easy-to-use neuroinformatics infrastructure for day-to-day challenges in data acquisition, analysis, visualisation and storage.
- Perform empirical modelling and simulation-based research to support the formulation of multi-scale theories of brain architecture.
- Link this research with clinical data (SP8's Medical Informatics Platform).
- Analyse and, wherever possible, realise, in collaboration with the Platforms, real-world applications (e.g. robotics, neuromorphic computing, software, atlases).
- Co-design methods, tools and techniques to characterise development, inter-species and inter-subject variability.

All stages of the Project are designed to make meaningful contributions to the FOs. Success will be measured, not just in terms of its final results, but also in terms of intermediate outputs. Major Milestones are planned for Month 30 (the end of the Ramp-Up Phase), Month 60, Month 90 and Month 120. More detailed Milestones will be fixed in successive SGAs (for the Core Project) and in Descriptions of Work or equivalent documentation (for Partnering Projects). Other outputs (especially from the Partnering Projects) will be defined over the duration of the Project.

The Research Roadmap groups planned Actions into the 11 research Subprojects. Below, the Roadmap defines each Subproject's general and operational objectives, going on to describe the relevant state of the art, planned advances beyond the state of the art, planned Actions, output targets and Milestones, risks and contingency plans, and potential impacts.

A1.4 Subproject 1: Mouse Brain Organisation

SP1 is an HBP Neuroscience SP.

A1.4.1 SP1: General Objectives

SP1 will perform targeted mapping of the adult mouse brain structure and function, generating data required to constrain and validate high-fidelity reconstructions and modelling. Specifically, the Core Project will generate systematic, standardised structural and functional data for key levels of biological organisation (e.g. the genome, the transcriptome, the proteome, cells, synapses, and connectomics, as well as key data on physiology and behaviour). The Partnering Projects will generate complementary data sets documenting brain function and links from structure to cognition and behaviour. These data are unlikely to come from other research in progress or planned.

Current techniques make it possible to obtain data for every level of biological organisation of the mouse brain. No other species can provide similar coverage. Mouse data will thus make a vital contribution to the HBP's reconstruction and validation processes. Comparison with human datasets will facilitate translation to the human brain, which has many features not present in mouse. The data generated will contribute to the Mouse Brain Atlas generated in SP5, and to the high-fidelity reconstructions of the mouse brain generated by SP6. Ultimately, it will contribute to high-fidelity reconstructions of the human brain. Functional data, on the other side, will provide the basis for brain models in SP4 and validate simulations done in SP6. To maximise compatibility with on going work, SP1 will focus on the adult mouse and will use the same strain of mouse used by the Allen Institute.

In general, we propose using eight-week (56-day) old male C57BL/6j mice as the standard laboratory animal. Some tasks will involve analysis of data from the whole brain (for example brain vasculature, protein synaptic maps, etc.), while other tasks will involve one or a few major brain regions, depending on the level of analysis required. For example, realistically only one brain region can be examined for detailed electron microscopy analysis or detailed protein synaptic maps of molecular or anatomically-identified neurons. In the latter case, the choice would be the hippocampus proper in some laboratories and the hind limb region of the primary somatosensory cortex in others, depending on their expertise and tasks. If it were possible to examine an additional area, we would propose the primary visual cortex (V1).

The rationale is as follows:

- Eight-week (56-day) old male C57BL/6j mice: These mice are used at the Allen Institute (and in many other laboratories) and we are going to collaborate with, and use a lot of data from, this laboratory. In addition, at this age, most neuroanatomical and physiological characteristics can be considered stable ("adult"), as all neurodevelopmental sequences terminate a few days earlier.
- Hippocampus proper: Since different neuronal cell types are precisely organised into layers, it is an excellent model system for studying neurophysiology and behaviour processes related to memory and learning.
- Hindlimb region of the primary somatosensory cortex (S1HL): In contrast to the widely examined barrel cortex, the S1HL shows principles of cortical organisation that are common to several other cortical areas in various species, including humans. In addition, the Blue Brain team has already generated an enormous amount of information on the columnar organisation in the S1HL of the rat, and on relationships between morphological features of neurons and their physiological and neurochemical characteristics, giving rise to sophisticated models of simulation of columns. Thus, the analysis of strategic data from the mouse S1HL would be a perfect complement to the Blue Brain and other initiatives already underway, to try to find out what are the basic principles of the columnar organisation that are conserved throughout evolution in different species. This would be an ideal proof of concept for the development of Predictive Neuroinformatics.
- Primary visual cortex (V1). This is the best studied area in the brain, and the mouse visual system is one of the main subjects of research at the Allen Institute.

The BXD family of strains are a well defined and well known resource for multiscalar data integration and computational and genetic modeling (PMID: 15043220, 15114364, 15474587, 15711545, 25215496, 22939713, 26140590, and see References below). We and our colleagues in the HBP have assembled a massive phenome of brain morphometry (including structural MRI and stereology) and brain gene expression data for more than 10 brains regions and over 50 strains that are being used to systematically explore genome-to-phenome relations (see www.genenetwork.org).

How do these data coordinate with those obtained in SP2 and SP3? Human molecular, neuroanatomical, and behavioural variation (normal and clinical) can be mechanistically studied using the rapidly growing BXD data sets being generated by dozens of groups in Europe and world-wide (e.g. at the EPFL and ETH, see PMID 22832527, 22506031, 20582282). For example, in a recent Nature paper (PMID 25607358), Hibar and colleagues demonstrated that variants in the *KTN1* gene in humans are associated with volumetric differences in the putamen—a key brain region involve in movement control and cognition. A matched analysis of *KTN1* expression in the striatum of BXDs showed that variation is also linked to significant variation in volume, providing both validation of the GWAS results and a novel animal model to study functional effects by experimentation.

A1.4.2 SP1: State of the Art

Current neuroscience research comprises many disciplines and communities, each focusing on a specific level of biological organisation and on the brain regions, species and methods best adapted to its specific goals. Progress is rapid at all levels. However, our current knowledge has many gaps. At the molecular level, we lack a complete description of the genes expressed in single neurons or the way proteins are targeted in neurons. At the cellular anatomy and connectivity levels, we still do not have complete data for a single species. Even in *C. elegans* – the only animal whose neuronal circuitry has been completely deciphered – essential information such as data on neural morphologies is still missing. At the physiological level, we do not have a clear, quantitatively accurate picture of physiological response in different types of synapse, cell and circuit. Data on long-range connections between different brain regions is also sparse. Above all, we still do not have a clear picture of the brain as an integrated system. Without a systematic programme of research in a single species, it will be extremely difficult to understand the relationships between different levels of brain organisation; e.g., how a variant in a specific gene affects the architecture of an animal's neural circuitry and its subsequent behaviour. The vertebrate species for which we have the most data and the best techniques of data generation is mouse.

Although an enormous amount of work remains to be done, new technologies are making it easier to generate data on the mouse brain, and to relate them to data for humans. At the molecular level, we already have a large volume of quantitative data on DNA sequences and modifications, [13] RNA [14] and proteins [15] [16]. The last three years have seen the release of the first molecular-level atlas of the mouse [15] and human brain transcriptomes [17]. In principle, these atlases, combined with RNA and protein profiles for different cell and synapse types, could make it possible to estimate the numbers of different types of cells in different brain regions and to relate the data for the two species. The Human Brain Project will fully exploit these possibilities.

Specific references that provide examples of the mouse-human/human-mouse translational relevance that is germane to SP1-SP2-SP3 linkages include:

- Chesler EJ, Lu L, Shou S, Qu Y, Gu J, Wang J, Hsu HC, Mountz JD, Baldwin N, Langston MA, Threadgill DW, Manly KF, Williams RW (2005) Complex trait analysis of gene expression uncovers polygenic and pleiotropic networks that modulate nervous system function. **Nature Genetics** *37*: 233–242
- Badea A, Johnson GA, Williams RW (2009) Genetic dissection of the mouse CNS using magnetic resonance microscopy. **Current Opinion in Neurology** *22*: 379–386 (PMC2734144)
- Hibar DP, Stein JL,.Rosen GD, Lu L, Hager R, Williams RW,..Thompson PM, Medland SE (2015) Common genetic variants influence human subcortical brain structure. **Nature** *520*:224-229
- Ashbrook DG, Williams RW, Lu L, Hager R (2015) A cross-species genetic analysis identifies gene for mouse anxiety and human bipolar disorder. **Frontiers in Behavioral Neuroscience** 9:171
- Ye R, Carneiro A, Giao H, Airey DC, Zhang B, Lu L, Williams RW, Blakely RD (2014) Quantitative trait loci mapping and gene network analysis implicate protocadherin-15 as a determinant of brain serotonin transporter expression. **Genes, Brain & Behavior** *13:* 247–260
- Overall RW, Williams RW, Heimel JA (2015) Collaborative mining of public data resources in neuroinformatics. **Frontiers in Neuroscience** 9: 90

- Mulligan MK, Williams RW (2015) Systems genetics of behavior: a prelude. **Current Opinion in Behavioral Sciences** *2*:108–115

At higher levels of organisation, breakthroughs in scalable methods — particularly in optogenetics [18] and MRI — are paving the way for comprehensive studies comparable to work being done in molecular biology and proteomics. In particular, there has been considerable progress in connectomics. Molecular tracer methods now make it possible to trace connections between different types of cells and their synapses. Clearing Methods [Chung *et al.*, Nature 2013] and high throughput imaging via serial two photon sectioning [Ragan *el al*. Nath Meth. 2012] allow to reconstruct entire mouse brain with high resolution on hours to days. These methods make it possible to measure thousands of animals and compare the data with data from behavioural studies.

A1.4.3 SP1: Advances over State of the Art

Work in SP1 has the potential to produce the most complete multi-level map of a vertebrate brain ever produced - spanning all levels of biological organisation from molecules to large-scale brain architecture.

At the molecular level, SP1 will generate profiles of the molecular components of individual cells (neurons and glia) with an emphasis on the genome (DNA and epigenome), the transcriptome (RNA), the proteome (proteins), and the metabolome (metabolites). This will be the first time these data are collected.

SP1 will go on to characterise the dendritic, axonal and synaptic architecture of neurons at the molecular scale, identifying hierarchies of organisation and regulation, including transcriptional and RNA regulatory networks, protein complexes and organelles. Equivalent information will be collected for different types of brain cells in different regions of the brain. These molecular maps will provide vital information for the reconstruction and simulation of the healthy brain, and for the exploration and simulation of hundreds of brain diseases.

Molecular maps will be integrated with the cellular scale maps. This second series of maps will catalogue and profile the synapses, axonal projections and dendritic morphologies that characterise different cell types. Combining the molecular and morphological maps will make it possible to systematically assign cells to different cell types.

Molecular and cellular levels will be integrated with maps of cell type distributions in the brain and of the short and long-range connections within and between brain regions and nuclei to create the first multi-level map of the whole mouse brain. The map will enable the first high-fidelity reconstructions and simulations of the whole mouse brain.

From the functional point of view, maps of neural activation on the whole brain are available nowadays with a resolution limited to standard detection techniques such as FMRI and relying on indirect information. In this respect, SP1 will produce these sorts of activation maps on whole brain with single cell resolution by detecting phenomena such as immediate early gene (IEG) expression. These maps are complementary to fMRI data or other *in vivo* functional analysis in the sense that they have high spatial resolution (single cells) across the entire brain but have coarse temporal resolution (few hours) and are limited to a single map per subject. The quantification and spatial arrangement of cells activated as a result of selected behaviours will provide insights into the principles which orchestrate brain activity on a large spatial scale and into inter-subject variability. The activity maps will be further refined by classifying activated neurons according to gene expression and shape. Integration between IEG expression maps and other functional data, such as fMRI scans and electrophysiology, will be crucial for building realistic simulations (SP6) and theoretical models (SP4) of spatio-temporal brain activity and will take advantage of the Neuroinformatics Platform (SP5). Furthermore, these maps will be monitored in

conjunction with behaviour and cognition experiments, also in relation to cross cutting activities.

Finally, SP1 contributes to translational research by investigating the remapping of cortical activity triggered by robot-assisted rehabilitation. A "mesoscope" will image the activity of large-scale cortical networks thus dissecting the computational roles of neuronal populations within meso-circuits and their relevance for animal behaviour. A strong link with the Neurorobotics Platform (SP10) will allow the running of parallel experiments using simulated robotic platforms and environments linked to simplified versions of HBP brain models. Experimental measurement of kinetics and functionality will be strengthened by data-driven predictive reconstruction of the system and simulation of brain models performed in collaboration with SP5 and SP6. Functional maps of cortical activity during learning of a motor task and during rehabilitation in the robotic platform will allow building more sophisticated theoretical models of motor control in SP4. Theoretical models developed in SP4 will, in turn, help in extracting general principles of neural computation from the generated maps of functionality that can guide the implementation of Neuromorphic Computing Systems in SP9.

A1.4.4 SP1: Operational Objectives

The objective of SP1 is to generate neuroscientific concepts, knowledge, experimental data sets and tools, which will be used to build models for the simulation of the brain. These models will be integrated, for example, into neuromorphic systems (SP9) or neurorobotics controllers (SP10) in order to create cost-effective, energy-efficient, high-performance systems. Empirical data will also be obtained, when it is hardly or not possible to get it in the human brain, due to technical or ethical reasons (e.g., high-resolution, whole brain synaptic maps, single cell transcriptomes, mapping & characterization of long-range projection neurons). SP1 will study also mutations, which have been identified in SP2 in the human brain in cohort studies and analyse transgenic animals as disease models in collaboration with SP8 and SP3 (e.g. slow-wave activities in murine transgenic models of neurological disorders). The empirical data obtained in SP1 are synergistic with physiological, connectomics and other data obtained in SP3.

SP1 will investigate differences between the mouse brain and those of other species, and the human brain in particular (in conjunction with SP2) to allow filling in the gaps in our knowledge of the structural organisation of the human brain.

An important role for SP1 is to provide data and knowledge to support activities undertaken by other SPs. Various mechanisms will be used to help inform SP1 about user requirements, including:

- Via SP5 and its rodent atlas WPs, where there are specific Tasks WPs aiming to coordinate atlas activities with external partners.
- Co-design projects (including different components such as community building); in particular CDP1 (development of the whole mouse brain model and related atlas) and CDP2 (Mouse-based cellular cortical and subcortical microcircuit models)
- Open calls
- Other ways, including conferences, meetings, workshops, publication, internet, etc.)

The framework of SP1 will supplement existing activities of the Allen Brain Institute (e.g., with respect to proteomic and metabolomics data. It will take advantage of the existing Allen Mouse Brain Atlas with its comprehensive data on gene expression patterns, transcriptomics, neuronal morphology & physiology and other data sets. A collaboration between the Allen Brain Institute and the HBP has been established to make sure that there is a continuous exchange of research plans, to achieve maximal synergy.

Its Operational Objectives are detailed below. For more on the rationale behind the objectives chosen by SP1, please see A1.4.1 SP1: General Objectives.

Subcellular and molecular level

- Define molecular components including epigenomes, transcriptomes, proteomes and metabolomes, and generate HBP Atlases at different physical scales (e.g. single molecules, subcellular assemblies, cell-types, brain regions) and temporal scales (e.g. molecular dynamics and activity-dependent processes). Regions of interest to be agreed with SP2 and SP3.
- Define subcellular molecular anatomy in synapses, neurons, glia and neuro-glia-vasculature system.
- Identify genetic and molecular networks involved in neuromodulation, plasticity and other critical brain processes. (SP1 genetic work will link to and support SP2 & SP8 genetic work, including that focused on brain diseases such as autism.)
- Study mutations identified in SP2 and analyse transgenic animals in agreement with SP2, 3 and 8
- Align subcellular and molecular datasets with the cellular and whole-brain scale anatomical techniques and datasets, and transfer it to the mouse brain atlas (together with SP5).
- Coordinate design with SP6's modelling and simulation objectives; SP5's atlases and databases; SP4's multiscale theory and SP2's human brain datasets.
- Define cellular morphologies of cell-types including neurons, glia and vascular cells.
- Map the distribution of contacts between cell types, in particular synapses.
- Generate projectomes and connectomes at microcircuit, meso-circuit (brain regions) and macro-circuit (whole-brain) scales.
- Characterise cell type distribution and vasculature structure.

Integration of multilevel data to brain function

- Obtain, integrate and analyse physiological, behavioural and other functional datasets with the molecular and subcellular, as well as cellular and whole brain datasets, to allow multi-scale synthesis, addressing important unresolved questions in Theoretical Neuroscience (SP4) and contributing to the Neuroinformatics (SP5), Brain Simulation (SP6) and Neurorobotics (SP10) Platforms.
- Obtain and integrate datasets from mice carrying genetic mutations, variations, pharmacological treatments and other manipulations/perturbations of biological and medical relevance (coordinated with disease studies by SP8).
- Co-design and integrate studies with cross-SP collaborative projects (e.g. biologically relevant molecular simulations of synapses - SP4, 5, 6 and 7 - and studies of synaptic plasticity and cognition by SP3.
- Work with community partners and international programmes to integrate novel datasets and identify standardised and scalable approaches.
- The datasets that SP1 is committed to produce will be shared with HBP modellers to fulfil the needs of future users. The modellers will tell SP1 which datasets they are interested in using, what data are missing, and what data they would like to generate.

A1.4.5 SP1: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Maps of the vasculature of the whole mouse brain. Whole-brain maps of different cellular types based on gene expression. Microcircuitry analysis, proteins and receptor distributions, fibers architecture in a specific large area brain region. Maps of cellular distributions, long-range axonal projections, and synaptic proteins; reconstructed morphologies of major neuron types. Whole-brain activation maps related to selected behaviors. Spatial organization principles in brain activation. Functional maps of cortical activity during learning of the motor task after stroke during learning in the robotic platform.
SGA2	M55-78	Single-cell transcriptome classification of cell-types; reconstructed morphologies of neurons and glia; data for neuron-glial ratios, excitatory-inhibitory ratios; neuron-glia-vascular structural relationships, projections between brain regions, projections of single neurons, synaptic connectivity between identified neurons, whole brain density and distributions of excitatory and inhibitory synapses, ultrastructure properties of neurons and glia, whole-brain cell-specific projection maps. Extend microcircuitry analysis, synapses and receptor distributions to further large area selected brain regions. Refine whole-brain distribution maps of cellular types by accounting also to cell shape. Spatio-temporal cell-specific organization principles in brain activation. Functional maps of rehabilitation-assisted plasticity. Functional maps of cortical activity during learning of the motor task in the robotic platform at cellular resolution. Atlasing of activation and functional maps with fMRI maps.
SGA3	M79-M102	Incorporation of data from Partnering Projects and external collaborations; refocused experimental mapping guided by reconstruction; initial integrated multi-level map of the mouse brain.
SGA4	M103-	Fully integrated multi-level map of the mouse brain including data from the Core Project, Partnering Projects and collaborations

Table 27: Main Objectives / Deliverables per SGA for SP1: Mouse Brain Organisation

A1.4.6 SP1: Collaborations with other National, European and International Initiatives

The HBP will work closely with existing and future initiatives that generate structural and functional data about the mouse brain or comparable data for other species (non-human primates, simpler animals, etc.). Other collaborations will focus on comparisons between the mouse brain and the brains of other species, on studies of genotype/phenotype relationships, and on the adaptation of techniques used in mouse for application to humans. Especially important will be collaboration with the Allen Brain Institute and with the US BRAIN Initiative. The Project may also develop collaborations with initiatives addressing related themes, such as prenatal alterations in gene expression and postnatal environmental influences, brain development, aging, and inter-individual variations.

A1.4.7 SP1: Impact and Innovation Potential

Scientific impact

IMP1.1: The data generated in SP1 will make a vital contribution to the Mouse Brain Atlas, created in SP5.

IMP1.2: The data generated in SP1 will enable the use of gene expression data to predict features of the brain that have not been measured experimentally, drastically reducing the number of experiments necessary to build high-fidelity reconstructions.

IMP1.3: The data generated in SP1 will provide the initial scaffolding and validation tests for high-fidelity reconstructions and simulations of the mouse brain, to be filled in with data from the HBP's European and International collaborations and with predictions from reconstructions.

IMP1.4: Comparative assessment of the data generated in SP1 and SP2 will identify principles allowing the use of mouse data to predict features of the human brain for which experimental data are not available.

Social impact and Innovation Potential

The social impact of SP1 and its contribution to innovation will be indirect, through its contribution to other Subprojects.

A1.5 Subproject 2: Human Brain Organisation

SP2 is an HBP Neuroscience SP.

A1.5.1 SP2: General Objectives

The objective of SP2 is to generate neuroscientific concepts, knowledge, data sets and tools contributing to a better understanding of the multi-level and multi-scale organisation of the human brain. Such results will be used to constrain and validate a first reconstruction and simulation of the human brain. Human brain functional and structural segregation, its inter-subject variability and genetic factors represent central elements of SP2, and contribute to the multimodal HBP Atlas (developed and populated in conjunction with SP5), reaching from the molecular, through the cellular, up to the systems level. SP2 will study differences between the human brain and those of other species, and the mouse brain in particular (in conjunction with SP1). This will make it possible to use transformed versions of data for mouse genes, transcripts, proteins, neuron morphologies, etc. to fill in gaps in our knowledge of the structural organisation of the human brain. Considering the sheer size and complexity of the human brain, this research requires the development and application of big data analytics, which will be done in conjunction with SP7. By bringing in a broad range of expertise in human brain research, SP2 will actively contribute to co-design projects for developing the infrastructure of the HBP, in particular the Human Brain Atlas, and Visuo-motor control.

Synergy will be achieved by collaboration with SP3; e.g., linking cytoarchitectonic maps and receptorarchitectonic data obtained in SP2 with laminar resolution 7T data and dopamine release data in SP3, and align movie and retinotopic data from SP3 with cytoarchitectonic maps, functional segregation data and connectomics data of SP2, to name only a few examples of many.

An important role for SP2 is to provide data and knowledge to support activities undertaken by other SPs. Various mechanisms will be used to help inform SP2 about user requirements, including:

- Via SP5 and its two atlas WPs (5.2.5, 5.3.6), where there are specific Tasks in rodent and human brain WPs aiming to coordinate atlas activities with external partners.

- Co-design projects (including different components such as community building); in particular (but not exclusively) CDP3 (Multi-level human brain atlas) and CDP4 (visuo-motor integration)
- Open calls
- Other ways, including conferences, meetings, workshops, publication, internet, etc.)

A1.5.2 SP2: State of the Art

Genetics and gene sequencing. Genetics is the method of choice for understanding genome-to-phenome linkage at the molecular, cellular and behavioural levels. Two genetic strategies have proven particularly valuable. The first compares phenotypes produced by point mutations against controls; the second examines small populations of individuals and assesses the role of endogenous genetic variation (natural polymorphisms).

Combined with massive "-omic" data sets, such as ENCODE [20] and the recently released atlas of the adult human brain transcriptome [21], these approaches make it possible to build and test complex systems models where every trait, at every level and scale, can be linked to specific gene loci and regulatory sequences [16]. Despite the limitations of mouse models for predicting complex behaviour and cognition in humans, comparative studies of mice and humans can provide valuable information about putative mechanisms. Functions amenable to this approach include attentional processing, visual and auditory memory, as well as cognitive flexibility and response inhibition. These methods provide a valuable tool for studies of normal human genetic variation.

Human mutations as a major cause of brain disease. Studies have identified over two hundred single gene mutations affecting human postsynaptic proteins and over a hundred and thirty brain diseases in which they are believed to play a role. Regulatory sequences may also play an important role [20]. Studies of individuals with these mutations can provide useful insights into the way variation in specific proteins contributes to differences in cognitive, behavioural and emotional phenotypes, while simultaneously providing valuable information on mechanisms of disease causation. Large cohort studies of patients and healthy subjects provide a powerful basis on which to perform such investigations. Studies of affected individuals, who display no overt signs of disease, are particularly interesting.

Molecular systems biology. Molecular systems biology uses mathematical and computational methods to understand the molecular basis of information processing in the brain. For example, multi-scalar analysis of genomic variation data and quantitative phenotype data make it possible to map patterns of gene and protein expression to specific neuronal and synapse types. Massive, well-structured molecular data sets for key brain cell and synapse types make it possible to build rich quantitative models of synapses, cells, neuronal ensembles and brain areas, and to link these models to precisely matched anatomical, functional, and behavioural datasets, a precondition for predictive modelling.

Cataloguing cell types using transcriptomic data. Large-scale mapping of gene expression patterns in the mouse brain [23] [24] has confirmed that morphologically distinct cells express different combinations of the same genes. The Allen Institute is now conducting similar studies on human brain tissue [25]. Combined with data from single cell transcriptomics – not yet available but on the horizon – these data will make it possible to predict cell types composition of different regions of the brain. In principle, the data could also enable prediction of the proteins present in different types of cells.

Cataloguing synapse types using proteomic data. Proteomics studies of human synapses have demonstrated that human synapses contain over a thousand different proteins [26]. Certain patterns of synaptic protein are typical of specific cell types and brain regions [27]. Array Tomography, a new technique, makes it possible to map synapse diversity at the single synapse level [28]. Recently developed optogenetic methods for labelling synaptic

proteins allow rapid, highly efficient mapping of individual synapse types, characterisation of the synapses present in different regions of the brain, and identification of their role in neuronal information processing.

Living human neurons from stem cells. It is now possible to study living human neurons derived from human-induced Pluripotent Stem Cells (iPSCs) [29]. The combination of iPSCs with developmental neurobiology makes it possible to model human cortical function in a dish [30] and to generate human neurons carrying specific disease mutations [31].

In vivo **imaging and optical imaging at microscopical level.** Structural and functional imaging of the living human brain provide a valuable supplement to high-resolution data from *post mortem* studies [26]. Maps of the density and distribution of the main types of neurons in *post mortem* brains can link functional imaging data to underlying brain anatomy [27]. Recent *in vivo* imaging techniques, particularly diffusion and resting state imaging, have made it possible to map large-scale patterns of structural connectivity [28] [29] [30]. Polarised Light Imaging (PLI), detecting the myelin surrounding axons, makes it possible to link DTI data to the microscopic level and to verify data from *in vivo* experiments [31] [152](Caspers *et al.*). Furthermore, PLI also provides the link to microcircuits obtained, for example, via a combination of clarity methods with serial two-photon microscopy and/or light sheet imaging [153] (Silvestri *et al.*). Intra- and subcortical connection profiles for individual areas are likely to provide new insights into the structure and function of the brain. For the human brain, PLI is one of the few methods that can bridge the gap between macroscopic organisation and more detailed knowledge about long and short fibre tracts. Given that most current information on human brain connectivity is extrapolated from animal and developmental studies, this is a crucial step. Another imaging technique involves neuronal recordings from healthy neocortical and hippocampal tissue that has been surgically resected to gain access to deep epileptic foci or tumours. This method provides 3D neuronal reconstructions in conjunction with functional connectivity, synaptic and neuronal physiology data. Finally, functional neuroimaging makes it possible to localise regions specific to sensory, motor or cognitive effects of interest. A key topic for research is between-subject variability, which has thus far hampered the creation of functional atlases of the brain.

Microscopical brain models provide useful information about the distribution of different types of cells, fibres and transmitter receptors different regions of the brain [32]. Receptors play a key role in neurotransmission and are highly relevant for understanding neurological and psychiatric diseases and the effect of drugs. So far, however, most of this work has been based on static interaction representations that do not capture the full dynamics of the nervous system at the molecular level. This will require models that exploit HBP high-performance computing capabilities to describe the time evolution of molecular species. There is evidence that many diseases (e.g., epilepsy, schizophrenia, major depression) depend on equilibrium among multiple receptors. Modelling and simulation provide an essential tool for understanding these complex mechanisms.

Brain models require precise data on the cellular organisation of different brain areas (e.g., cortical layers and columns) and their intrinsic connectivity at micro- and meso-scales including neuron type-specific connections and neuronal population-specific connections such as clustered connections. Unravelling the intrinsic wiring rules of identified human cortical areas will pave the road to high fidelity large-scale modelling and simulation, e.g. based on the NEST code. Recent studies have combined post mortem studies of laminar cell distributions with in vivo diffusion techniques to measure the distribution of cell and fibre diameters, opening the road to *in vivo* studies of human cytoarchitecture and connectivity.

A1.5.3 SP2: Advances over State of the Art

Techniques introduced by SP2 will make it possible to generate new data sets of critical importance for reconstruction of the human brain.

Multiplying the diffusion MRI acquisition time on a 7T magnet with a powerful gradient system over 5 to 10 sessions will make it possible to perform imaging protocols with varying water diffusion time, and thus to estimate the distributions of axon diameters in each fibre bundle. These distributions will be used to count the number of axons in each bundle — a key parameter for simulation. Data will be validated against PLI data from *post mortem* specimens. The same dMRI acquisition protocol may make it possible to distinguish boundaries cortical architectural *in vivo,* and to link them to the functional maps.

PLI will provide information about connectivity of the human brain that is far beyond existing knowledge, offering excellent spatial resolution at the micrometre scale and allowing the identification of currently unknown fibre tracts. This will have important implications both for basic research and for clinical applications (e.g., studies of diseases such as stroke, multiple sclerosis, and schizophrenia, that are characterised by changes in connectivity).

Microstructural models of the whole human brain on the cellular scale will enable data on different levels of brain organisation to be integrated. The model will serve as a reference brain with ultra-high resolution, and as a source of morphometric data.

By collaborating with the Netherlands Brain Bank Amsterdam (http://www.brainbank.nl), it will be possible to record and label neurons from *post mortem* specimens. This work will yield 3D morphological reconstructions of neurons from different areas of the brain together with single cell-type transcriptome (SCT) data. These data are critically important for reconstructions of the brain.

SP2 will also perform a systematic analysis of the receptor architecture of transmitter systems, providing a "gold standard" for *in vivo* receptor PET studies of normal subjects and patients. The results will make it possible to identify hierarchies of areas, and thus to develop a theoretical model of cortical organisation. Such a model is a prerequisite for the analysis and integration of top-down and bottom-up processes.

A1.5.4 SP2: Operational Objectives

SP2's Operational Objectives are to:

Human neurogenomics:

- Provide genetic factors involved in the maintenance and inter-individual variability of structural, functional, and cognitive brain phenotypes using genome-wide **imaging genomics** approaches. Imaging genomics has the potential to identify previously unknown biological pathways and mechanisms influencing the organisation of the human brain. This information will feed the Brain Simulation Platform (SP6) and Medical Informatics Platform (SP8).
- Identify **mutations in genes** involved in brain diseases (such as autism) by genetic analysis of large patient cohorts. There is a strong link to SP1, where the identified mutations will be studied functionally in mice. The identified mutations will also provide valuable input for the Brain Simulation Platform (SP6) and Medical Informatics Platform (SP8).
- Create a **fundamental set of biological information**, **including genomics, transcriptomics and methylomics data,** for a limited number of single cells (agreed with SP1) and brain regions (in conjunction with SPs 1 & 3) linking to the Brain Simulation Platform (SP6) and Medical Informatics Platform (SP8), and contributing to the HBP Brain Atlas (SP5). This project will use methodological experience acquired in mice by SP1 during a pilot phase.

Morphology and molecular architecture:

- Provide quantitative estimates of cytoarchitectonic organization at the level of cortical layers and sublayers, as a microstructural reference for the Human Brain Atlas (SP5) and Brain Simulation Platform (SP6).
- Provide multilevel, quantitative maps of cell and subcellular distributions and morphologies in selected regions of the human brain including mouse–human brain comparison, as well as functional data as a microstructural reference for the Human Brain Atlas (SP5) and the Brain Simulation Platform (SP6).
- Provide maps of quantitative receptor distributions in selected regions of human brain including mouse – human brain comparison, and correlation with functional characteristics of layers and areas as a microstructural reference for the HBP Human Brain Atlas (SP5) and the Brain Simulation Platform (SP6).
- Provide maps of bundles (e.g. U-fibres) and long distance fibre tracts, as well as quantitative measures of their microstructure as an anatomical reference for the Human Brain Atlas (SP5).
- Provide quantitative morphological data for selected fibre tracts and intracortical fibre architecture in the human brain, using polarised light imaging and electron microscopy for the Neuroinformatics Platform (SP5) and Brain Simulation Platform (SP6).

Brain function, segregation, computational architecture and variability:

- Provide a cytoarchitectonic, probabilistic map of the whole human brain, as a microstructural reference for the Human Brain Atlas (SP5).
- Provide parcellations of white matter into fibre bundles and cortical fibre architecture for the Human Brain Atlas (SP5).
- Provide maps of the functional segregation of the human brain using fMRI, provide models of bottom-up and top-down processing (with SP4) and provide a first cognitive ontology of brain territories to SP5.
- Map features coded in columns of the higher visual and auditory cortex and provide models for processing top-down and bottom-up information (with SP4) for validation in SP9.
- Provide models and data on the role of the six cortical layers arising from the architecture of neurons and their connections.
- Provide a first mechanistic model of how neural activity is related to brain regions in collaboration with SP4 and SP6.
- Provide information on the relationship between the variability of neurobiological features and inter-individual differences in behavioural phenotypes.

Methods, Big data analytics & Co-design:

- Link SP2's datasets and parcellations to the accepted template spaces to make the data useful for scientists and other SPs, by developing novel image alignment methods that bridge scales, modalities, and inter-individual variability.
- Develop novel label propagation methods that make SP2 relevant to mining image data to SP8's Medical Informatics Platform, as well as to the wider scientific community who would like to project high-resolution atlas data onto their own scans through the Collaboratory.

- Develop methods and high-performance computing production workflows, in conjunction with SP7, to reconstruct large image datasets, and to extract and analyse quantitative data including big data analytics for processing data in the TeraByte to PetaByte range.
- Ensure the transition of the methods, models and quantitative data into practical tools accessible through the Collaboratory, by designing use cases, defining requirements, implementing software interfaces, and testing.
- Generate a library of synthetic datasets, providing a broad spectrum of modelled fibre arrangements simulating brain tissue.
- Push forward agreements/MoUs, in consultation with authorized representatives of involved HBP Partners, between SPs 2, 5 and 7 upon tools and formats to exchange large datasets.

A1.5.5 SP2: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Protocols established for *post mortem* connectomics and multi-level architecture; subjects recruited and ethical approval received for *in vivo* connectomics and functional neuroimaging; initial datasets generated for neuronal and glial cell compositions and genetic architecture; initial data uploaded to Human Brain Atlas on the Neuroinformatics Platform.
SGA2	M55-78	Initial multi-level targeted mapping of the human brain; datasets generated for synapses, channels, neuronal network and behaviour, as well as neuronal and glial cell morphologies obtained and uploaded to Human Brain Atlas on the Neuroinformatics Platform; transcriptome and epigenetics data connected to cell morphology and connectomics; neuro-vascular relationships; updated cortex parcellation.
SGA3	M79-M102	Initial multi-level map of the human brain incorporating data from Core Project, Partnering Projects and collaborations; predictive reconstructions and refocused experimental mapping; synaptic properties; neuron and glial morphologies; whole brain cognitive and genetic maps, initial integrated atlas.
SGA4	M103-	Draft multi-level map of the human brain including brain regions, cellular distributions, cell-types, connectivity between and within brain regions, connectivity between local neurons, cellular protein and receptor distribution and their gene expression, synaptic proteins; comprehensive models of human specific mental processes established and their relationship to structural, genetic and epigenetics described; concepts of multi-level brain organisation.

Table 28: Main Objectives / Deliverables per SGA for SP2: Human Brain Organisation

A1.5.6 SP2: Collaborations with other National, European and International Initiatives

The HBP will work closely with existing and future initiatives that generate structural and functional data about the human brain or comparable data for other species (non-human primates and other animals). Some collaborations will focus on comparisons between the human brain and the brains of other species, and on genotype/phenotype relationships.

Especially important will be collaboration with the Allen Brain Institute, the US BRAIN Initiative and the US Connectome Project The Project may also develop collaborations with initiatives addressing related themes. Examples include the role of the prenatal alterations in gene expression and postnatal environmental influences, brain development, aging, and inter-individual variations.

A1.5.7 SP2: Impact and Innovation Potential

Scientific impact

IMP2.1: Research in SP2 will contribute empirical data, methods/tools and new concepts; it will validate predicted features, and identify and obtain those characteristics of brain organization, which are unique for the human brain.

IMP2.2: The data collected in SP2 will make a vital contribution to co-design projects, and to the Multi-level Atlas of the Human Brain, set-up in SP5, in particular.

IMP2.3: The data collected in SP2 will provide the initial scaffolding and validation tests for high fidelity reconstructions and simulations of the human brain, to be filled in with data from the HBP's European and International collaborations and with predictions from reconstructions.

IMP2.4: SP2 will drive the development of tools for big data analytics.

Social Impact and Innovation Potential

The social impact of SP2 and its contribution to innovation will be indirect, through its contribution to other Subprojects.

A1.6 Subproject 3: Systems and Cognitive Neuroscience

SP3 is an HBP Neuroscience Subproject and will form the Systems and Neuroscience component of the HBP Core Project under the FPA. It comprises four scientific Work Packages, with teams of 3 to 5 partners. The research themes cut across and link the existing HBP Subprojects, and proposed activities aim to develop ground-breaking scientific knowledge, concepts and models that bring the field closer to the solution of concrete and important problems in cognitive and systems neuroscience in an interdisciplinary research approach. Proposed activities also aim to demonstrate their potential to shape the evolving HBP ICT Platforms (SPs 5-10), thus showcasing the value that these Platforms can add for the neuroscience community.

The selected Projects are expected to play an exemplary role within HBP: they would constitute the first examples of actual use of the HBP ICT Platforms and of their integration into the HBP Neuroscience Subprojects. Activities aim to generate highly innovative scientific knowledge, concepts and models that cut across multiple other SPs, contribute as such to the five co-design projects, and thus bind together various disciplines, techniques, and infrastructures. Examples of SP3 crosscutting targets are included in the operational objectives below. These can be parsed into four distinct work packages, each with a set of objectives. It should be emphasized that, also within SP3, cross-connections between the projects will be established. For instance, work on slow-wave activity can be combined with memory retrieval during sleep, and also connects to work on consciousness. Also work on multisensory object recognition will be linked to multisensory episodic memory. Within each project, data from multiple scales and multiple methods are combined for the investigation of the respective cognitive domain including recognition, memory, sleep and consciousness, and motor behaviour.

A1.6.1 SP3: General Objectives

SP3 research addresses ambitious systems and cognitive neuroscience questions and cuts across other HBP Subprojects. As was outlined in the EoI Call, activities are based on the latest scientific knowledge, and include innovative concepts and models that bring the field closer to the solution of a concrete and important problem in systems and cognitive neuroscience in an interdisciplinary research approach. In addition, they help to shape the evolving HBP ICT platforms (SPs 5-10), and show the value that these platforms can add to the neuroscience community. SP3 research activities aim to:

- Bridge from basic anatomy and physiology to mapping, cognition, as well as theory and modelling. This work will link activities from the different neuroscience Subprojects, and strengthen efforts to acquire new, strategic data, tools, and scientific concepts. Research work includes disease models (e.g., transgenic animals) related to cognitive functions, which also links it to the platforms (SP8).
- Provide the capacity to interact with (use and/or feed) the HBP ICT Platforms, including specification of data and/or tools, which are accessible to the scientific community through the Platforms. It includes, for example, to provide empirical data to the HBP atlas (SP5), to support modelling by providing new data from experiments in human and mouse brain (SP4), to supplement simulation by integrating top down and bottom up models based on studies in experimental animals (SP4 and SP6). The projects have the potential for real-world applications (e.g. in software, atlas, robotics, neuromorphic computing and drug design).

To achieve these goals, the new systems and cognitive projects cover two or more spatial and/or temporal scales, because to bridge the scales is one of the crucial questions in addressing the multi-level organization of the brain.

SP3 aims are realized in different fields of cognitive and systems neuroscience – initially, they target the way in which the brain represents invariant objects, and investigate the foundations of sleep and wakefulness, episodic memory and consciousness (see below). It is expected that the scope of fields will be enlarged as the HBP advances, to include new partners from the science community, and to maintain flexibility of scientific focus in a dynamic research field.

A1.6.2 SP3: State of the Art and Advances over the State of the Art

Wave Scaling Experiments and Simulations

How can disparate multiscale phenomena like those underlying sleep and wakefulness emerge from the same cortico-thalamic system? How do these processes vary across pathological and normal brains? WaveScalES will deal with these long-standing issues exploiting the synergy between experimental observations/manipulations, theoretical models and predictions produced by HPC simulations. Relying on the universality of the default dynamical mode (slow-oscillations) observable in both humans and rodents during deep sleep and anesthesia, we will aim at further characterizing the underlying machinery at different scales looking at its changes when: i) wakefulness is naturally approached; ii) an exogenous perturbation or a photomanipulation is administered; iii) normal and pathological brains are compared. We will leverage on the available HBP atlases and HPC tools to model large-scale spiking neuron networks and we will contribute to the development and refinement of several HBP platforms with our own experimental data, models and simulation tools. We expect our studies to be facilitated by the set of already available HBP platforms and by the participation to an integrated research community.

Context-sensitive Multisensory Object Recognition

Understanding how the human brain achieves invariant and context-sensitive representations of objects from multi-sensory (visual, auditory, and somatosensory) stimulation is a question of fundamental importance in cognitive neuroscience. Furthermore, context-sensitive representations of perceived objects serve as building blocks for more complex cognitive processes such as category formation, reasoning and language. There has been impressive progress over the last years in creating neurobiologically inspired multi-layer ("deep") models of invariant object recognition (e.g. Fukushima, Riesenhuber, DiCarlo). The object recognition performance of the most recent approaches, convolutional deep learning networks, even matches that of humans (LeCun *et al* 2015; Szegedy, 2013).

These feedforward networks are inspired by the brain. However, many of their particular design decisions are based on engineering considerations and are not necessarily desirable when modelling brain function (LeCun *et al* 2015; Kriegeskorte, in press). For example, while deep learning networks are inspiring for building brain simulations, we know still little about the real features used in mid-level and higher areas of the visual auditory and somatosensory cortical systems. Moreover, we know little about the functions of cortical and sub-cortical feedback. Deep learning networks are feedforward networks while real brains receive feedback from approximately 66% of cortical areas (Markov *et al* 2013; Larkum, 2013), including direct reciprocal connections from neighbouring areas, remote areas and subcortical areas (i.e. unspecific thalamus). Feedforward connections and feedback connections do not simply excite or inhibit but can also amplify or dis-amplify (Phillips *et al* 2015; Phillips, submitted; Roelfsema, 2006).

Episodic memory as multisensory reconstruction

Episodic memory defines who we are, and its loss is one of the cruellest consequences of dementia. Episodic memory records our personal, daily-life experiences, which are characterized by a rich set of multisensory features, ordered in a spatiotemporal context. We need to understand how the human brain combines multisensory information from higher sensory areas to compose episodic scenes that can be encoded in memory, and how low-dimensional cues can result in the recall of high-dimensional memories that we can re-experience so vividly. To achieve key advances on this topic, we will conduct a coordinated series of experiments to identify the precise neuronal mechanisms behind episodic memory, to validate them by implementing them in computational models and robotic systems, and begin to test how they fail in old age and dementia.

David Marr's well-established but unproven (1971) computational framework suggests that the hippocampus binds together the multimodal features of an event so that they can be retrieved via pattern completion, leading to their reinstatement in neocortex. We aim to identify the specific neural mechanisms behind pattern completion and reinstatement of multisensory information. Research in humans will combine novel behavioural experiments with functional and molecular brain imaging (fMRI at 7T and simultaneous PET-fMRI) to investigate the role of distributed brain activity, inter-regional interactions and neuromodulation in pattern completion and multisensory reinstatement. At connected but finer scales, experiments in rodent models will reveal the detailed neuronal mechanisms underlying pattern completion in hippocampus and the representation of multisensory information across multiple cortical areas, using multi-electrode, virtual reality and optogenetic techniques. These data will be integrated in a computational model using multimodal attractor dynamics to explain the neural basis of human episodic memory and to extract the core principles for implementing episodic memory in artificial devices. The computational model will be tested using two types of robot functioning in real-world tasks, including a mobile visual-tactile rodent-like robot, and a humanoid (iCub) engaged in human-robot interaction. Our long-term vision is to develop a comprehensive, empirically buttressed computational model of how the brain synthesizes and recalls multisensory

episodes, a key aspect of human cognition, and how these processes break down in old age and dementia, one of the key clinical challenges of our time.

Experimental and computational exploration of consciousness mechanisms and methods in mice and humans

Insight into the nature of consciousness is central to understanding the human brain, and is widely regarded as one of the deepest unsolved problems in science. It has been called “the ultimate intellectual challenge of this new millennium” and “the major unsolved problem in biology”, with wide-ranging theoretical and clinical implications. The subjective nature of consciousness has strongly impeded its scientific investigation and is causing severe clinical and ethical problems regarding patients with disorders of consciousness (DOC) following brain injury. Also during surgical anaesthesia, reliable methods for assessing consciousness are needed, since patients occasionally regain consciousness without this being detected (1-2 cases per 1,000 operations). Recently however, novel methods and theoretical advances have yielded remarkable results, and opened up the field for scientific and clinical progress.

Although a generally accepted theoretical framework for consciousness is still lacking, some leading theories are widely recognized as highly promising and supported by considerable experimental evidence. The Global Neuronal Workspace (GNW) theory states that conscious perception depends on “ignition” of a fronto-parietal workspace that globally broadcasts information. The integrated information theory (IIT) starts from phenomenology and claims that the neural substrate of human consciousness is a cortical system that is both integrated (behaves as a single entity) and differentiated (has a large repertoire of available activity patterns). Both theories have recently received remarkable, albeit indirect experimental support, but this field is at an early stage, relevant experimental data are still limited, and the theories need further testing and development.

Why does consciousness fade during dreamless (NREM) sleep, although the brain remains active? Using transcranial magnetic stimulation (TMS) combined with electroencephalography (EEG), Massimini *at al* found that NREM sleep is characterized by non-propagating, rapidly extinguished responses to TMS, in contrast to wakefulness, when TMS evokes complex sequences of waves spreading widely across cortical areas. In rapid eye movement (REM) sleep, when consciousness is often regained during dreaming, TMS again triggers more widespread and differentiated patterns, supporting the idea that the loss of consciousness during NREM sleep reflects a breakdown in cortical effective connectivity.

Also during general anaesthesia, TMS-evoked EEG responses were more local and of shorter duration than in awake subjects. This was seen both with the benzodiazepine midazolam and propofol-induced anaesthesia suggesting that a breakdown of cortical effective connectivity may be a common feature of loss of consciousness. However, there are apparent discrepancies, e.g. regarding the roles of gamma activity and synchrony. Disorders of consciousness (DOC) following brain injury include “vegetative” state/unresponsive wakefulness syndrome (VS/UWS) and minimally conscious state (MCS). At present, diagnostic precision of DOC depends on validated behavioural assessment scales and repeated evaluations. However, reported misdiagnosis rates of DOC have been as high as 37-43%, often failing to detect consciousness. Even when standardized scales based on overt behaviour are used, diagnostic uncertainty remains high due to confounding factors such as fatigue, aphasia, motor deficits, fluctuations of responsivity or vigilance, etc. Bekinschtein, *et al* and Boly, Laureys, *et al* developed elegant auditory event-related potential (ERP) paradigms and identified possible markers of consciousness, including the ”global P3b”, a late, positive ERP component peaking at around 300 ms (P300), evoked by improbable events. Rosanova and Gosseries *et al* showed that TMS/hdEEG can be used reliably to track recovery of consciousness in severely brain injured, non-communicating VS/UWS patients, by directly measuring brain connectivity while by-passing subcortical pathways, and without requiring active subject participation. In VS/UWS, TMS evoked only simple, local EEG responses, indicating breakdown of effective connectivity, whereas conscious subjects

showed more complex, propagating activations, and recovery of consciousness was paralleled by clear changes in effective connectivity. Moreover, the perturbational complexity index (PCI), a measure that estimates both the information content and integration of brain activations, has been able to successfully differentiate between conscious and unconsciousness states within and across subjects and conditions. Thus, TMS/hdEEG or ERP responses may offer effective ways to detect and track recovery of consciousness in DOC patients., requiring further studies of how anaesthetics induce unconsciousness.

A1.6.3 SP3: Operational Objectives

SP3's Operational Objectives are:

Multi-scale organization of slow-wave activity in thalamocortical systems

- Slow-wave activity changes during sleep/anaesthesia-wake transition. Investigate the evolution of slow-wave activity and its multi-scale organization when brain state changes. Infer properties of awake resting states from the multi-scale organization of slow-wave activity, matching experimental evidence with large-scale models of the cortico-thalamic system. Cooperation planned with: SP1, SP2, SP4, SP6 and SP7.
- Slow-waves and complexity: from microscale to bedside. Characterize through a perturbational approach the multi-scale organization (functional differentiation, integration and complexity) of the brain across different states, and understand how the latter is affected by the intrinsic modular bistability underlying slow-wave activity. Cooperation planned with: SP2, SP4, SP6, SP7 and SP8.
- Slow-wave activity in murine transgenic models of neurological disease. From the differences in the spontaneous and perturbed slow-wave activity, infer which are the pathological features of the cortico-thalamic system in neurological disease models and the related mechanistic interpretation of each dysfunction. Cooperation planned with: SP1, SP4, SP6, SP7 and SP8.
- Modulation of slow-wave activity with opto-pharmacology. Development of a toolbox of light-regulated drugs targeting excitatory and inhibitory neuronal receptors. Implement a spatiotemporally selective illumination of brain regions to manipulate slow-wave activity with light. Cooperation planned with: SP1, SP4, SP5 and SP6.
- Slow-wave simulation platforms. Develop parallel simulations of slow-wave activity and its changes in a model of the cortico-thalamic system, using inter-areal connection atlases and a layered grid of columns for each area, as a spiking neuronal network distributed over several thousands of MPI processes. Cooperation planned with: SP1, SP2, SP5, SP6 and SP7.

Context-sensitive multisensory object recognition

- Develop a deep learning network that will eventually incorporate realistic spiking neural networks using the NEST simulator (SP6/SP7), and test alternative models with biologically plausible learning rules based on feedback and neuromodulatory effects. Progressively refine and validate features and connections in these brain models with high-resolution columnar-level and layer-precise fMRI (collaboration with SP2).
- Generate brain imaging data sets hyper-aligned across individual subjects providing high-resolution activation profiles in response to large data sets of visual images. By occluding visual stimuli in one quarter of the visual field, we will extract contextual cortical feedback signals in the occluded region. Representational similarity analysis of cortical feedback will reveal common properties of contextual cortical feedback across subjects and computational models.

- Investigate context-dependent nonlinearity of image formation when one object is occluded by another object and both representations are kept separately in the brain. Occlusion data will be used to investigate neural representations of front and occluded objects separately in brains and computational models.
- Broaden the understanding of basic mechanisms that integrate feedback for context-sensitive amplification. Conduct behavioural animal studies describing the perceptual and circuit level effects of the activation and inactivation of long-range feedback to somatosensory cortex while imaging effects of feedback from cortical and subcortical areas on large-scale populations in a cortical column.
- Record in rodents dendritic feedback mechanisms for the integration of feedback and use this as model constraints. Neuronal ensembles coding for newly learned objects will be extracted using two-photon microscopy and tissue-cleared cortex. Investigate model constraints for invariant object recognition in rodents at single cell and at network level.
- Acquire structural and functional data of cataract reversal individuals to gain insights about plasticity and development of visual feature representation in primary and specialized visual cortex. Investigate differences in plasticity and development (substrate, regulation) during sensitive phases (e.g. critical periods) and in adulthood (perceptual learning) in rodents and human cataract patients. Investigate interactions between critical periods of V1 and higher visual areas.

Episodic memory as multisensory reconstruction:

- Identify multi-scale mechanisms for episodic memory comprising multiple sensory modalities, more specifically of pattern completion and multisensory memory reinstatement in the human brain by measuring hippocampal-cortical interactions at laminar resolution with 7T. To relate activity of hippocampal subfields during pattern completion to memory representations decoded at the level of hippocampal input and output regions. We will couple subfield activity during formation and retrieval of rewarding events to dopamine release (measured by fMRI-PET). This work links to SP2, SP4, SP5, and SP8.
- Identify multi-scale mechanisms that determine the balance between visuospatial pattern separation (creation of new memory representations) and pattern completion (retrieval of old representations). In addition we will determine the role entorhinal grid cells play in these two processes. This work links to SP1, SP4, SP5 and SP6.
- Identify multi-scale mechanisms underpinning multisensory episodic memory by multi-area ensemble recordings and optogenetic interventions. This will allow us to investigate how multisensory events, set in space and time, are encoded and reconstructed in sensory-hippocampal networks during episodic memory operations. This work links to SP1, SP4, SP5, SP6, SP9 and SP10.
- Develop a systems-level computational model of multisensory memory function in rodents and humans that subserves the core functions of compression, pattern completion and separation, and multisensory integration, thereby supporting both memory for past events and prediction of future experience. The new model will instantiate constraints identified by newly acquired data and detailed models of relevant brain substrates. This work links to SP1, SP2, SP4, SP6, SP7 and SP9.
- Build and test embodied (robotic) implementations of the episodic memory systems developed as above that address the challenges of (i) multisensory simultaneous localization and mapping in a rodent-like robot equipped with biomimetic vibrissal and visual senses, and (ii) human-like episodic memory for a humanoid robot that can facilitate situational awareness in tasks requiring robot-human interaction. This work links to SP4, SP9 and SP10.

Neural and computational mechanisms of consciousness

- Test ideas about principles and mechanisms for cortical integration and differentiation, by using mouse experiments and multilevel simulations, including studies of: (1) neuromodulation of brain connectivity (synaptic, somato-dendritic and axonal signalling) and their effects on states of consciousness, arousal, attention; (2) functional roles and effects of oscillations and resonance; (3) functional roles of specific ion channels and receptors in cortex and thalamus, and their effects on states of consciousness, arousal, attention; (4) testing of methods for assessing consciousness by mouse experiments and multilevel simulations; (5) developing, in rodents, novel measures of corticothalamic connectivity, using electrocorticography (ECoG) from implanted electrode arrays, and cell-imaging-based measures. This work links to SP1, SP4, SP5, SP6 and SP9.
- Refine, test, and compare established methods, and develop novel methods, for assessing consciousness, functional brain connectivity and differentiation, by sleep and anaesthesia experiments in humans; and directly compare these with leading methods based on transcranial magnetic stimulation combined with electroencephalography (TMS/EEG) and event-related potentials (ERP) . Apply TMS to different cortical areas to test the roles of the different areas. Develop, in humans, novel imaging-based measures (using fMRI or PET imaging following TMS or transcranial direct current stimulation (tDCS) in humans) of cortico-thalamic connectivity, integration and differentiation. Further development of clinically useful methods to assess brain state, connectivity and consciousness, including novel "PCI-like" (PCI, perturbational complexity index) indices of network integration and complexity based on sensory stimulation instead of TMS.This work links to SP2, SP4, SP5, SP8, SP11 and SP12.
- Study the effects of cortical lesions on PCI and ERP to test whether structural lesions may drive the rest of the brain into a state of low-complexity and/or sensory disconnection: (1) in brain injured conscious patients, identify cases in which local lesions may affect ERPs and PCI differentially; and (2) evaluate whether specific cortical lesions may lead to changes in ERPs and complexity in distant parts of the brain. This work links to SP2, SP4, SP5, SP8, SP11 and SP12.
- Use large-scale models of the thalamocortical system to simulate (1) conditions where sensory inputs are gated by lesions in thalamus or (2) primary cortices, (3) conditions in which bistable dynamics are gradually induced in neural elements. This work links to SP1, SP2, SP4, SP5, SP6, SP8 and SP9.
- Test different methods for assessing consciousness (1) during transient anaesthesia of one hemisphere (Wada test), and (2) in callosotomy (split brain) in humans, in order to begin testing leading theories of consciousness. This work links to, e.g., SP2, SP4, SP5, SP8, SP11 and SP12.

In addition to these cross-cutting project-specific goals, SP3 has the following methodological and technological operational objectives:

- To develop and validate novel cognitive and behavioural paradigms and setups which can be combined with research into the neural mechanisms underlying the cognitive processes under study
- To develop and validate novel software to quantify and analyse behavioural, neurophysiological and computational results obtained in the cognitive studies
- To test predictions made from theoretical and simulation work, done in other SPs and CDPs, against experimental results obtained in SP3 projects
- To establish databases on neural mechanisms underlying mouse as well as human cognition and behaviour, and linking them to databases in SP1, SP2 and Medical Informatics (SP8)

- To apply simulation software, and robotics as well as neuromorphic hardware, to investigate the cognitive and systems functions raised above, and to validate and further enhance these platforms through feedback.

A1.6.4 SP3: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Building experimental setups, methods, data analysis tools and simulations of behavioural-cognitive processes and brain states. Validate experimental protocols and acquire initial datasets. Establish key collaborations with other SPs to enable, e.g., large-scale simulations, high-performance computing, theoretical analyses, neuromorphic and robotic implementations. Show examples of how cognitive functions and brain states can be measured and compared between animal, human and computational systems.
SGA2	M55-78	Upscale neuroscientific data, acquire full datasets, and integrate data gathered by different methods, to provide multiscale descriptions of neural substrates of behavioural and cognitive processes. Develop comprehensive, multiscale models, simulations and robotic implementations of different cognitive functions such as learning, memory, multisensory integration and perception, object recognition and conscious state changes. Evaluate novel measures, in rodents, humans and simulations, to quantify the complexity and dynamics of these processes.
SGA3	M79-M102	Define key areas where models and experiments need to be improved, and where predictions from theory and modelling should be tested further. Perform these tests by new experiments and simulations, adding newly developed tools for perturbing and manipulating nodes of brain systems to infer causal roles of neural substrates, and applying newly developed tools from other SPs and CDPs. Apply key results to areas of related brain disorders (e.g. Alzheimer's dementia, loss of consciousness, impaired perception).
SGA4	M103-	Formulate full systems-wide computational models of cognitive processes under scrutiny, with inventory of brain structures and functions involved and backed by multiscale simulations. Achieve well-behaved robotic and neuromorphic implementation of these processes.

Table 29: Main Objectives / Deliverables per SGA* for SP3: Systems and Cognitive Neuroscience

*Timings for attainment of these objectives are approximate and need to be confirmed by the partners undertaking the work.

A1.6.5 SP3: Collaborations with other National, European and international Initiatives

The new SP3 has the potential to interact with a wide range of projects, in the EU and elsewhere in the world.

A1.6.6 SP3: Impact and Innovation Potential

Scientific Impact

IMP3.1: SP3 will deliver novel data, behavioural tests, neuroscientific analyses, software tools, computational models, and new mechanistic insights in cognitive functions in "Systems and Cognitive Neuroscience", as studied in both mice and humans, and in combination with model simulations and real-world artefacts.

IMP3.2: SP3 will link the newly gained knowledge on brain mechanisms underlying cognition to the other HBP Subprojects, and thus show how the knowledge can be used and applied in Neuroscience Research (SP1–4), in the Platform infrastructures (SP5–10) and similarly in the co-design projects (Whole mouse brain model; Microcircuit models; Human brain atlas, Visuomotor integration and Plasticity).

IMP3.3: SP3 will make use of facilities and knowledge generated in other SPs to test theoretical predictions experimentally, and generate further data to improve simulations and Platform infrastructure. It will thus act as a testbed both for theoretical models and practical research infrastructure, such as neuromorphic technology. As such it will also exert a cross-linking function across HBP subprojects, binding together different disciplines and advancing cognitive and systems neuroscience in terms of experiment, theory and modelling.

IMP 3.4: Develop macro- and mesoscopic scale parallel-distributed simulations, matching experimental results produced by a range of observational and perturbational techniques, at the abstraction level of spiking neuron networks, and thereby benchmarking several HBP platforms.

IMP 3.5: Experimental and computational characterization of cortico-thalamic and cortico-hippocampal systems at the transition between wakefulness-like complex patterns and sleep-like slow-wave activity and in relation to episodic memory, recognition, and conscious vs. unconscious brain states. Use this reference system to understand pathological alterations of brain dynamics and cognitive brain function.

IMP 3.6: To test how light-regulated molecular systems may emulate transitions between sleep-like and wake-like dynamics, and affect perceptual and memory operations in the brain, by the combination of opto-pharmacological stimulation and electrophysiological/optical recordings at the slice and intact brain level.

Social and Economic Impact

IMP3.7: By linking work on genetic mouse models of disease with human neuroimaging, SP3 will contribute to the impact of HBP on clinical neurosciences, in collaboration with SP8.

IMP 3.8: Perturbing the cerebral cortex of brain-injured patients reveals sleep-like changes of brain responses that correlate with loss/recovery of function. Computer simulations of sleeping and awake brains similarly perturbed will afford crucial insight at the bedside.

IMP 3.9: Light-regulated molecular systems that control both local and global transitions between wake and sleep states, and perception and memory operations, will facilitate the development of novel treatments for brain-injured patients, consciousness/sleep and learning and mental retardation disorders and help reduce their social and economic burden.

IMP 3.10: The capability to simulate the effect of non-invasive/reversible perturbations will open the path to the creation of dedicated bedside high-performance computing applications.

A1.7 Subproject 4: Theoretical Neuroscience

SP4 is an HBP Neuroscience SP.

A1.7.1 SP4: General Objectives

The overall objective of SP4 is to provide solid theoretical and mathematical foundations for work performed in the other SPs.

The Core Project of SP4 has five goals. The first is to enable horizontal collaboration among researchers from different SPs to develop strategies and algorithms for the comparative assessment of brain data and data from different model approaches. The second goal is to develop theoretically grounded methods to bridge between different brain scales, and generate performing simplified models of brain cells, circuits up to entire brain areas. The third goal is to integrate top-down models with advanced learning algorithms that replicate the learning and cognitive behaviour observed in non-human animals and ultimately in humans. The fourth goal is to produce models of complex cognitive functions such as spatial navigation, recursion, and symbolic processing. The final goal is to operate the European Institute for Theoretical Neuroscience, set up in the Ramp-Up Phase. The Institute provides a forum where independent neuroscientists following different approaches can work together to understand the fundamental computational principles underlying brain function and to work towards a unifying theory. This work will be implemented through Partnering Projects and in collaborations with other regional, national, European and International Initiatives.

A1.7.2 SP4: State of the Art

Understood as mathematical modelling, theoretical neuroscience has a history of at least a hundred years. In general, theoreticians have focused on models addressing specific levels of brain organisation, for instance, the relation of Hebbian learning to cortical development [33], the recall of associative memories [34], the link of temporal codes and Spike Timing-Dependent Plasticity [35] and the dynamics of neuronal networks with balanced excitation and inhibition [36] [37]. In most cases, the output has consisted of “toy models”, amenable to mathematical analysis and to simulation on small personal computers. What is not clear is how to connect the insights from these models, or how to ground them in detailed biophysical observations.

These are key themes in the work of the theoretical neuroscientists who have contributed to the preparation of the HBP proposal. For example, W. Gerstner has shown how to extract parameters for simple neuron models directly from experimental data, and from detailed biophysical models [38] [39]. M. Tsodyks, W. Gerstner, N. Brunel, A. Destexhe, and W. Senn have produced models of synaptic plasticity suitable for integration in models of large-scale neuronal circuitry [40] [41] [42] [43]; W. Gerstner, D. Wierstra, and W. Maass have explored models in which plasticity is modulated by a reward signal [23] [24] [44], a basic requirement for so-called reinforcement learning. N. Brunel has produced models of population dynamics using networks of randomly connected simple neurons [37] an approach exploited by G. Deco to construct models of decision-making [45]. A. Destexhe [46] [47] has investigated the integrative properties of neurons and networks, while W. Maass has studied their underlying computational principles [25] [22].

A1.7.3 SP4: Advances over the State of the Art

SP4 aims to develop a multi-scale theory of the brain, creating a synthesis between top-down and data-driven bottom-up approaches. A second goal is to unify theories of learning, memory, attention and goal-oriented behaviour, gaining insights into the way function emerges from structure, and identifying the data and computing principles required to model specific brain functions in neuromorphic computing systems. The third goal is to identify bridges linking the multiple temporal and spatial scales implicated in brain activity and in the signals captured by imaging and other technologies. A fourth goal is to understand complex functions such as spatial navigation, recursion, and symbolic processing. A key advance will be the development of models, suitable for implementation

in neuromorphic and neurorobotic systems and in large-scale, top-down simulations of the brain.

A1.7.4 SP4: Operational Objectives

SP4's operational objectives are to:

- Develop a multi-scale theory of the brain, creating a synthesis between top-down and data-driven bottom-up approaches.
- Unify theories of learning, memory, attention and goal-oriented behavior, gaining insights into the way function emerges from structure, and identifying the data and computing principles required to model specific brain functions in neuromorphic computing systems.
- Identify bridges linking the multiple temporal and spatial scales implicated in brain activity and in the signals captured by imaging and other technologies.
- Understand complex cognitive functions such as spatial navigation, recursion, and symbolic processing.
- Continue operating the European Institute for Theoretical Neuroscience (EITN), which was set up during the Ramp-Up Phase, to serve as an incubator of ideas, where independent neuroscientists following different approaches can work together to understand the fundamental computational principles underlying brain function and to work towards a unifying theory.

These objectives will be pursued throughout the whole duration of the Project. SP4 will have strong links to the neuroscience SPs (SP1, SP2 and SP3), and the Platforms (providing models and coding principles). In particular, SP4 models will be conceived in a form compatible with the Neuromorphic Computing Platform. They will also be made available publicly.

A1.7.5 SP4: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Set of models from cellular to network levels, and different brain areas, using different modelling approaches (detailed models, simplified models and population models)
SGA2	M55-78	Comparative assessment of brain data and different modelling approaches (analytical models, large-scale network models, neuromorphic computing systems, neurorobotics experiments) Progressively reduced models of both human and mouse neurons
SGA3	M79-M102	Set of theory-driven models of cognitive processes at the level of neurons and synapses, which are implementable by software simulation and neuromorphic hardware.
SGA4	M103-	Multi-scale theory of brain structure and function that creates a synthesis between top-down and data-driven bottom-up approaches. Applications to unify theories of learning, memory, attention and goal-oriented behaviour, as well as the genesis of brain pathologies.

Table 30: Main Objectives / Deliverables per SGA for SP4: Theoretical Neuroscience

A1.7.6 SP4: Impact and Innovation Potential

Scientific Impact

IMP4.1: SP4 will generate new theoretical insights into the link between different levels of biological organisation in the brain, the dynamics of single neurons, plasticity mechanisms and their impact, network dynamics and the mechanisms underlying specific cognitive functions.

IMP4.2: SP4 will implement theoretical insights in high-level operational models, suitable for implementation in neuromorphic computing.

Social Impact and Innovation Potential

The social impact of SP4 and its contribution to innovation will be indirect, through its contribution to other Subprojects.

European Institute of Theoretical Neuroscience (EITN) outreach

The EITN has developed tools to communicate with the neuroscience community and is constantly adapting its communication actions to reach a wider audience. In parallel, the EITN website is evolving to meet the needs of EITN partners and the public.

Workshop, conference and visitor programmes, as well as EITN partners' activities, are currently promoted in various ways, including the EITN and the HBP Newsletters, and the EITN twitter account. Results and outcomes of these different events will be made available via the EITN website.

A1.8 Subproject 5: Neuroinformatics Platform

SP5 is an HBP Platform SP.

A1.8.1 SP5: General Objectives

SP5 has two objectives. The first is to build and operate a Neuroinformatics Platform that makes it easier for neuroscientists to organise and access the massive volumes of heterogeneous data, knowledge and tools produced by the international neuroscience community. The first version will be released at the end of the Ramp-Up Phase, providing a single source of curated, high-quality data for the HBP's brain modelling effort and for the wider international neuroscience community. The second objective is to develop multi-level atlases of the mouse brain and the human brain and integrate them into the Platform.

SP5's work in the Core Project will coordinate tool development (e.g., viewers for specific classes of data), promote the population of the mouse and human Brain Atlases, and operate the Platform for the benefit of the community. A key goal will be to provide users with effective training, mentoring, documentation, helplines, etc. Partnering Projects will contribute additional tools and data, as described below. SP5 will collaborate closely with other organisations and initiatives with similar objectives, in particular, the INCF [26] and the Allen Institute's Brain Atlas projects (http://www.brain-map.org).

A1.8.2 SP5: State of the Art

World neuroscience research generates an enormous amount of data. However, there is no plan for organising and sharing this data, much of which is lost due to inadequate data preservation [48], or is available is often in non-standard formats.

The first attempts to provide easy access to high quality, well-curated data in standard formats date back to 1989, when the Institute of Medicine at the US National Academy of Sciences received funding to examine how information technology could create the tools

needed to handle the growing volume and diversity of neuroscientific data. The study report, published in 1991 [27] enabled NIMH, to create its own Human Brain Project, an effort that lasted until 2004. The work produced many important neuroscience databases. However, it never created a standard interface for accessing the data and provided no specific tools for relating and integrating the data.

Soon after the NIMH project ended, the OECD launched the International Neuroinformatics Coordinating Facility (INCF) [49]. Since 2005, the INCF has driven international efforts to develop neuroscience ontologies, Brain Atlases, model descriptions and data sharing, and has played an important role in coordinating international neuroscience research and setting up standards. Other initiatives such as the US-based Neuroscience Information Framework (NIF) [29], and the Biomedical Informatics Research Network (BIRN) [50] are collaborating with INCF.

Another important initiative was the foundation of The Allen Brain Institute, which, since 2003, has become a world leader in industrial-scale data acquisition for neuroscience. The Institute has recently developed a Brain Atlases including the recently published Allen Mouse Brain Connectivity Atlas [51]. This work contributes directly to the HBP brain reconstruction process.

A1.8.3 SP5: Advances Beyond the State of the Art

The Neuroinformatics Platform and the Brain Atlases developed in SP5 will allow neuroscientists to collaboratively curate, analyse, share, and publish large-scale neuroscience data. SP5 is collaborating with INCF, the Allen Institute and other international partners to develop a global data registry and knowledge base where data, models and literature are registered and annotated with high-level metadata, allowing their use in multi-level Brain Atlases. This represents a major step forward.

Brain Atlases will be constructed by curating data, depositing them in the data registry and linking them to established atlas ontologies and coordinates for rodent and human brains. Central to the goal of curating the data analysis will be the development of tools for large-scale data analysis and data mining. The atlases and related tools will be an important tool for neuroscientists working on predictive and computational models.

A1.8.4 SP5: Operational Objectives

The objectives of SP5 are to provide a Platform for large-scale federated data mining, search and integration, while engaging the community in both using and contributing to the Platform in the course of their scientific and clinical activities.

Brain atlases for rodents and humans

Ensuring that large and diverse datasets, organized across the different levels of the brain and within standard spatial coordinate systems, will allow search and correlative analysis within and across data modalities.

- Identify, curate and integrate multilevel human data from the neuroscience community, as well as SP2 and SP3.
- Identify, curate and integrate multilevel rodent data from the neuroscience community, as well as SP1.
- Engage the community to contribute atlases and additional multi-level data from other species, as well as atlas tools.

Tools for integrating brain data

The necessary tools to register, anchor, align and integrate diverse multilevel data will be built and provided through the web portal, web services or downloadable applications.

Packages for establishing data repositories with standard data services, including metadata indexing, search, and data-type specific services, will be provided.

Big data analytics and prediction

Providing the core capability of large-scale data analysis for diverse neuroscience datasets will allow the extraction of key parameters and features necessary for modelling. In addition, through large-scale feature extraction, clustering and prediction, SP5 will enable prediction of missing data values to help constrain the model building process.

- Provide a data analysis engine for extracting, analysing and classifying features from distributed datasets
- Use data and text mining to analyse data and literature to predict the cellular, synaptic and connectomic properties required to build whole brain scaffold models in SP6
- Populate the multilevel atlases with predicted brain properties:
  - Data-mined and predicted cell composition, distribution and properties
  - Data-mined and predicted synapse composition, distribution and properties
  - Data-mined and predicted connectivity

Knowledge management

Knowledge management is a key objective of SP5 ensuring that the ontologies are maintained keeping the latest concepts up-to-date and pointing to the latest supporting data, models and literature.

- Engage community in contributing, curating, refining and linking to ontologies
- Maintain and organize ontologies
- Develop data-driven ontologies

Interaction with the INCF and other organisations

The goals of HBP and the International Neuroinformatics Coordinating Facility (INCF) are complementary. The HBP currently interacts closely with the INCF, and collaborates in many areas; one example is the development of ontologies at different levels of organisation. This will be continued and further strengthened. This area is critical for SP5 for the development of both the human and rodent atlases. There is, and will continue to be, a close interaction with the Allen Brain Institute, which will utilise the atlas structure developed within HBP.

Develop, maintain and operate the Neuroinformatics Platform

The Neuroinformatics Platform will need to be reliable with a robust operational deployment including continuous build, testing and monitoring. Core services of the Neuroinformatics Platform will have to be sufficiently reliable for, potentially, many thousands of users worldwide.

Data Accessibility and Quality

The data required for the atlases will be of different organisational levels and of widely different types, such as genetics, molecular, electrophysiological, connectivity, behaviour and cognition. It will also contain models/simulations of different types from the subcellular to the systems level. The data obtained by SPs 1, 2 and 3 will be entered into the human and rodent atlases, and although important, this will represent a small part of the data required. The majority of the data used will instead be data sets from the literature. In addition, we will interact with other data providers like the Allen Institute. The community

will also be encouraged to deposit their data sets. As indicated above, the data will be curated.

Community engagement

A key objective for the Neuroinformatics Platform is to ensure that the Platform is highly useful to the broader community of neuroscientists; both as an important source of information for the entire community, and also in terms of enabling researchers to add new data to the different atlases. This requires both enabling key community use cases, but also developing the incentives and rewards to motivate continued use and active contribution to the platform. Workshops and other types of training and education will be necessary to engage students, postdocs and other researchers.

A1.8.5 SP5: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Establish standard software for federated active data repositories with a focus on European data producing sites. Launch strategic data repositories in key member states. Integrate key data sets from SP1, literature and community data repositories. Curate key datasets and ontologies required for atlases and brain modelling. Integrate Allen Institute datasets containing whole brain gene expression, single cell morphologies, electrophysiology, transcriptome and mesoscale brain connectivity. Provide initial data mining infrastructure for extraction of key modelling parameters of whole rodent brain model. Use predictive neuroscience approaches to predict additional parameters and constraints for whole rodent brain model. Establish initial human atlas and human brain atlas analytics capabilities.
SGA2	M55-78	Extend federated data repository network to include key strategic sites worldwide, including US, Japan, China and Australia. Integrate whole rodent brain projectome data and single cell transcriptome data sets with prediction of whole brain structural and functional properties. Develop continuous integration of datasets from remote repositories, automated feature extraction and initial data-driven ontologies. Develop additional curation workflows and tools to support new datatypes. Enhance datamining infrastructure to support new machine vision classifiers for additional datatypes and features. Release enhanced rodent brain atlases with deep analytics capabilities targeted to modelling extended cellular, synaptic and connectomic properties. Establish additional strategic data curation centers. Integrate vascular and glial data and predictions. Release multilevel human brain atlas with structural and functional data and layers of predicted cellular, synaptic and connectomic properties. Establish initial brain disease atlases for the human brain.
SGA3	M79-M102	Establish federated data mining workflows with increased computational resources and active data repositories. Release enhanced data curation tools and atlas building tools for complex disease/disorder atlases (e.g. traumatic brain injury, epilepsy, etc). Establish workflows to integrate large disease study datasets into human brain atlases. Develop data analysis approaches to further develop data-driven ontologies. Release multilevel human brain atlas including data for whole brain structure, brain region parcellations, nuclei, layers/modules, vasculature, cellular distributions, single cell transcriptome-based cell types, morphologies, electrical behaviour,

		protein and gene expression, synaptic density and type, neuron and glial morphologies, axonal projections between and within brain regions, synaptic connectivity between neurons, functional cognitive maps and initial predicted structural and functional properties.
SGA4	M103-	Deliver data management tools for the analysis, mining and tracking of data in globally distributed repositories. Establish continuous integration of data from strategic active data repositories. Develop additional data curation centers for rodent, human and cross-species datasets and atlases. Establish automated data-driven ontology workflows. Release human brain atlases integrating multilevel multiomic datasets ranging from gene expression to whole brain cognitive and behavioural maps. Establish key cross-species predictive neuroscience workflows to enable cellular level prediction of morphological, electrophysiological, synaptic and connectomic properties of the human brain. Establish tools to explore relationships between genetics and epigenetics, structure, cognition and behaviour. Release multilevel disease human brain atlases.

Table 31: Main Objectives / Deliverables per SGA for SP5: Neuroinformatics

A1.8.6 SP5: Collaborations with other National, European and International Initiatives

SP5 will collaborate with other existing and future initiatives to develop global policies and standards for data, ontologies, nomenclature, data preservation and data sharing. Particularly important will be collaboration with the International Neuroinformatics Coordinating Facility (INCF). Other planned collaborations include the Allen Brain Institute, Seattle Washington, USA; the US BRAIN initiative funded by NIH, NSF and DARPA; the Visible Brainwide Networks Project of the Britton Chance Center for Biomedical Photonics in Wuhan China; the Australian Research Center of Excellence for Integrative Brain Function, led by Monash University; the Kavli Foundation Neurodata without borders initiatives; and the CENTER-TBI, International Traumatic Brain Injury Study.

A1.8.7 SP5: Impact and Innovation Potential

Scientific Impact

IMP4.1: SP5 will facilitate neuroscience research, inside and outside the HBP, by creating and maintaining multi-level atlases of the mouse and human brain and related atlasing tools, and by making them available through the HBP Neuroinformatics Platform.

IMP4.2: By creating a major public data resource, SP5 will strengthen Europe's position as leader in international neuroscience research.

Social Impact and Innovation Potential

The social impact of SP5 and its contribution to innovation will be indirect, through its contribution to other Subprojects.

A1.9 Subproject 6: Brain Simulation Platform

SP6 is an HBP Platform SP.

A1.9.1 SP6: General Objectives

SP6 has three objectives. The first is to establish a generic strategy to reconstruct and simulate the multi-level organisation of the brain for different brain areas and species. The second is to use this strategy to build high-fidelity reconstructions, first of the mouse brain and ultimately of the human brain. The third is to support community-driven reconstructions and simulations and to support comparisons between models based on different tools and approaches.

As the Project proceeds, the Core Project will integrate the tools and workflows it develops in a Brain Simulation Platform, which it will operate as a community resource. The platform will provide tools and services for the collaborative reconstruction and simulation of the brain, models of different brain areas and whole brains (including models developed outside the HBP), and tools for *in silico* experimentation, supporting comparisons between different models and approaches.

In the first five years of the Project, the Core Project will develop and validate its tools and strategy in mouse — the species for which most data are available. The result will be a scaffold model of the cellular-level organization of the mouse brain. In the following five years, SP6 will produce a scaffold model of the human brain. This work will involve the integration of sparse data from the human brain with data inferred from non-human primates, mouse, and simpler animals. Partnering Projects will enrich the Platform with new capabilities (e.g. new algorithms and workflows, new techniques of data analysis and visualisation, new tools for comparing models, models of brain areas and of levels of organization not addressed within the Core Project).

Users of the Platform will be able to perform novel *in silico* experiments (e.g., experiments in virtual electrophysiology, experiments investigating the multi-level mechanisms leading from genes to behaviour, disease simulation, drug simulations). A key goal is to collaborate with SP1-SP4, SP9 and SP10 to develop simplified versions of high fidelity brain models, for cognitive, behavioural and clinical studies, and to participate in research using these models.

A1.9.2 SP6: State of the Art

Early models of the brain explained brain functions, such as learning and memory, in terms of the behaviour of neurons and neuron populations, thus giving rise to the fields of Artificial Neural Networks and Machine Learning [52]. In parallel, other researchers developed mechanistic models. In particular, Hodgkin and Huxley's seminal model of the generation of neuronal action potentials [53] and Rall's application of cable theory to signal propagation in dendrites [54] made it possible to build models of the brain from its basic components. Other models cast light on the dynamics of large networks of excitatory and inhibitory neurons. In the 1980s, Roger Traub [55] [56] used an IBM 3090 mainframe computer to simulate 10,000 neurons, each with about twenty compartments. Since then, rapid improvements in supercomputer performance have made it possible to simulate ever-larger models. In 2007, Djurfeldt et al. reported a large-scale simulation of a columnar cortex with 10^7 detailed multi-compartment neurons and 10^{10} synaptic connections [57]. In the same year, Morrison reported the simulation of a network with 10^9 synapses and spike-timing dependent plasticity (STDP) [58]. In 2009, the Modha group at the IBM Almaden Research Centre reported the simulation of a network, with roughly the same numbers of neurons and synapses as the brain of a cat (10^9 neurons and 10^{13} synapses) [59] [60]. In 2012 Potjans and Diesmann [61] carried out a simulation of a cubic millimetre of cortex using single compartment model neurons that accounted for 8 neuronal populations. This simulation was full-scale in the sense that all local synapses were represented. Recently, Jülich and RIKEN reported the simulation of a generic random network of single compartment neurons with synaptic plasticity and a total of 1.73 10^9 billion nerve cells connected by 1.04 10^{13} synapses orchestrating about a petabyte of main memory [62].

In parallel with this work on very large-scale networks, other groups have developed general-purpose simulators allowing simulation of the brain at different levels of biological detail. For example, NEURON [63] makes it possible to simulate morphologically complex neurons and networks of neurons. STEPS [64] MCELL [65] and Brownian Dynamics simulations bridge the gap between NEURON's compartment electrical model and the molecular-scale processes of diffusion in complex fluid environments and reaction mechanisms such as ligand binding to receptors. To date, however, there have been relatively few attempts to integrate models and simulations across multiple levels of biological organisation. This is one of the aims of EPFL's Blue Brain Project [66], which has developed software and workflows [67] [68] to reconstruct the neural microcircuit of juvenile rat, from detailed anatomical and electrophysiological data. This work continues in the HBP.

A1.9.3 SP6: Advances over the State of the Art

SP6 is developing a generic strategy to reconstruct and simulate the multi-level organisation of the brain. Top-down models have been established for several decades. SP6 offers a complementary, bottom-up approach that makes it possible, for the first time, to achieve a mechanistic understanding of brain function.

With current technology, there is no practical way to measure every aspect of the brain experimentally, and it is extremely unlikely that this will become possible at any time in the foreseeable future. SP6 offers a novel solution to this seemingly intractable problem, leveraging interdependencies within and between levels, thereby avoiding the need to measure everything. This implies a change in the criteria for what to measure. Classical neuroscience assesses data according to the light it throws on specific hypotheses. In contrast, the HBP prioritises data that are constrained by, and that constrain other data. Implemented in multi-constraint algorithms, these interdependencies make it possible to reconstruct the brain from sparse datasets, and to predict the data points needed to fill gaps in our knowledge.

The strategy proposed by the HBP is generic. In principle, it can be used to reconstruct and simulate the whole brain or any part of the brain of any healthy or diseased animal, of any species or gender, at any age. *In silico* experiments based on high-fidelity reconstructions and simulations will allow researchers to perform experiments that would not be possible in the laboratory. Examples include experiments to dissect the role of different levels of biological organisation in cognition and behaviour, and simulations of brain disorders to test hypotheses of disease causation, candidate treatments and their mechanisms of action. The HBP Brain Simulation Platform will give researchers the tools to perform such experiments. This is an enormous step beyond the current state of the art, and represents a phase-shift for neuroscience.

SP6 will develop a novel multi-scale simulation approach that makes it possible to link scales from molecules to brain activity, and to run simulations in which different regions of the brain are simulated at different levels of detail, at different points during the simulation. This will require major advances in supercomputer simulation technology enabling dynamic coupling of different simulation engines, and the use of advanced techniques in data management and load balancing.

A1.9.4 SP6: Operational Objectives

SP6's operational objectives are to:

Subcellular and molecular level models and simulations

- Use Molecular Dynamics (MD)-based methods to estimate thermodynamic and kinetic parameters, required for subcellular modelling.

- Build and simulate molecular-level models of neurons, synapses, glia and the Neuro-Glia-Vasculature system.
- Develop multi-scale (atomistic and coarse-grained) models and simulations of the molecular interactions involved in neuromodulation, plasticity and other critical brain processes (notably, protein-protein and protein-drug interactions).
- Integrate these models in single neuron models.
- Encourage and participate in community modelling efforts contributing to SP6's General Objectives.

Cellular and whole-brain modelling

- Build scaffold models of target areas of the mouse brain (such as cerebellum, hippocampus, basal ganglia and somatosensory cortex) and of the whole mouse brain.
- Encourage and participate in community efforts extending and validating existing HBP scaffold models and building models of brain areas not addressed within the core project.
- Work with the community to build models and simulations of the human at the subcellular, cellular, micro (column/module/nucleus), meso (region), and macro (whole brain) levels.
- Collaborate with the community to design and perform *in silico* studies (e.g. in *in silico* electrophysiology, using brain models developed within the SP.
- Work with SP1-4, SP8-10 to develop simplified versions of high-fidelity brain models and participate in cognitive, behavioural and clinical research.

Reconstruction and simulation tools

- Work with SP5 to develop tools allowing automated incorporation of data from the Neuroinformatics platform in reconstructions and simulations.
- Work with the MD and other relevant communities to develop highly integrated, high-throughput, multi-scale simulation tools for the calculation of kinetic constants, drug affinities and for understanding molecular events in neuronal cascades.
- Develop tools for subcellular level reconstructions and simulations, which integrate estimated parameters from MD simulations, and which are suitable for integration in single neuron models.
- Work with experimental neuroscientists and model builders to develop algorithms and workflows for the multi-level (molecular, sub-cellular and cellular level) reconstruction and simulation of neurons, synapses, the Neuro-glia-vasculature system, microcircuits, meso-circuits (brain regions), and macro-circuits (the whole brain).
- Implement theoretical insights from SP4 in algorithms for synaptic plasticity, re-wiring, axon remodelling and neuromodulation.
- Develop algorithms and workflows for the simplification of high fidelity brain models.
- Develop algorithms and workflows for the systematic validation of brain models and their components, allowing comparisons between different models and modelling approaches.
- Translated these algorithms and workflows first into software tools and workflows suitable for use by members of the outside community.

- Advance and maintain existing simulators for molecular dynamics, reaction-diffusion dynamics, cellular-level simulation and point neuron network simulation, to take account of SP6 and SP4 developments and requirements.
- Work with SP7 to optimize these simulators for use with HBP High-Performance Computing Resources.
- Work with SP8 and SP10 to develop models and simulations of brain disease, based on data collected by the Medical Informatics Platform.
- Work with community partners to develop standards for representing, and sharing brain models.
- Develop tools allowing comparison of brain models against results obtained with commonly used experimental techniques (LFP, EEG, Calcium Imaging etc.).
- Make these tools available to the community as Open Source Software (OSS), accessible via the HBP Brain Simulation Platform.

Brain Simulation Platform

- Design, implement and operate the HBP Brain Simulation Platform, facilitating collaboration between HBP researchers and community researchers.
- Integrate the platform in the HBP Collaboratory.
- Work with community users to develop Apps providing a user-friendly graphics interface to tools and models developed within the project and to design APIs providing programmatic access.
- Provide documentation, training and support for users of the Platform; integrate with the HBP Collaboratory.

Community outreach

- Participate in and facilitate community modelling efforts extending HBP scaffold models or addressing areas of the brain/species not directly addressed within the *Core Project*.
- Participate in and facilitate community efforts to standardize model and data representations and to facilitate comparisons between different models and modelling approaches.
- Participate in and facilitate projects using *in silico* reconstructions and simulations to address unresolved issues in theoretical and experimental neuroscience.

A1.9.5 SP6: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Scaffold models of molecular-level principal neurons, cellular-level reconstructions of selected cortical and sub-cortical regions; network-level models of the whole mouse brain; simplified models exported for implementation in neuromorphic computing systems. Initial version of Brain Simulation Platform incorporating algorithms and workflows for reconstruction and simulation of subcellular, cellular, microcircuit, and meso-circuit (brain region/system) levels; tools and protocols for *in silico* experimentation and model validation.
SGA2	M55-78	Scaffold cellular level models of the mouse brain; reconstruction of molecular level neurons, synapses and glia; scaffold models of human neurons algorithms and workflows for reconstructions and simulations

		of the whole mouse brain; tools and protocols for interactive *in silico* experimentation and model validation; first publications on *in silico* neuroscience experiments in Partnering Projects.
SGA3	M79-M102	Algorithms and workflows for multi-level reconstruction and simulation of the mouse brain; first draft multi-level reconstruction and simulation of the mouse brain; first draft reconstruction of the human brain at the cellular level; predictive reconstruction of reactants and reaction kinetics, protein-protein interactions, ion channels, and receptors involved in the action of drugs; first publications of *in silico* neuroscience cognition and behaviour experiments in Partnering Projects.
SGA4	M103-	Algorithms and workflows for predictive multi-level reconstruction and simulation of the mouse brain; first draft multi-level reconstruction and simulation of the human brain; *in silico* validation experiments for human brain models; *in silico* neuroscience, cognition and behaviour experiments; first publications of *in silico* neuroscience, cognition and behaviour experiments in Partnering Projects.

Table 32: Main Objectives / Deliverables per SGA for SP6: Brain Simulation Platform

A1.9.6 SP6: Collaborations with other National, European and International Initiatives

SP6 will collaborate with other existing and future initiatives to jointly develop large-scale brain models. Particularly important will be collaboration with the Allen Brain Institute, Seattle Washington, USA on models of the visual and motor systems of the mouse ultimately leading to models of visuomotor behaviour in mouse. Collaboration with CENTER-TBI will provide data on specific traumatic brain injury lesions and multi-level data including electrophysiology, imaging and cognitive measures that could be used to build models of brain injury.

A1.9.7 SP6: Impact and Innovation Potential

Scientific Impact

IMP6.1: SP6 will establish high-fidelity reconstructions and simulations of the brain as an essential tool for integrating and curating multi-level experimental data.

IMP6.2: SP6 will establish in silico experimentation as a powerful method for addressing scientific questions that are difficult or impossible to address experimentally.

IMP6.3: SP6 will establish brain simulation as an effective technique for understanding the cascades of biological events implicated in brain disorders.

IMP6.4: The Brain Simulation Platform will make it easier for academic researchers to use reconstructions and simulations of the brain in their research.

IMP6.5: SP6 will generate fundamental new insights into the basic computational mechanisms underlying human and animal cognition and behaviour.

IMP6.6: Simplified reconstructions of the brain will serve as the basis for novel neuromorphic computing systems and devices.

IMP6.7: SP6 will establish European scientific leadership in high-fidelity reconstructions and simulations of the brain and their technological and clinical applications.

Social and Economic Impact

The social and economic impact of SP6 will be indirect, through the Subproject's contribution to the development of new services for disease and drug simulation in SP6 and new neuromorphic and neurorobotic technologies in SP9 and SP10.

Innovation Potential

IMP6.8: The research conducted in SP6 will make it possible to create brain simulation services for commercial researchers in neuroscience, computing, medicine, and pharmacology.

IMP6.9: Tools for brain reconstruction and simulation have the potential to generate licensing revenues from commercial users in the pharmaceutical and computing industries.

IMP6.10: Models of specific diseases have the potential to generate licensing revenues from users in clinical and pharmacological research.

IMP6.11: Simplified brain models have the potential to generate licensing revenues from technology developers wishing to develop their own Neuromorphic Computing Systems.

A1.10 Subproject 7: High-Performance Analytics & Computing Platform

SP7 is an HBP Platform SP.

A1.10.1 SP7: General Objectives

The goal of SP7 is to provide the high-performance analytics and computing capabilities, systems and middleware necessary for the analysis of massive neuroscience data sets and the simulation of large multi-scale brain models. The data analytics and computing infrastructure, which SP7 will build in a co-design process with the users, will form the basis of the HBP's community-driven research infrastructure for brain research.

The first objective of the Core Project is to design and operate the HBP High-Performance Analytics & Computing Platform. This Platform will be federated, consisting of a central HBP supercomputer complemented by initially three satellite facilities dedicated to software development, molecular dynamics simulations, and massive data analytics. The first version of the Platform will be operational at the end of the Ramp-Up Phase. Over the duration of the Project, it will gradually evolve toward exascale performance and data management capabilities, complementing the capabilities provided by the Partnership for Advanced Computing in Europe (PRACE) and others. The hardware capabilities required will be based on innovative, energy efficient technologies including multi and many-core processors, and possibly neuromorphic acceleration. The system will include hierarchical memory and I/O sub-systems with multi-petabytes of capacity and data rates of many terabits per second, as well as hardware-integrated optical communication technologies with the lowest possible latencies, possibly complemented by brain-inspired communication sub-systems.

The second objective is to design, implement and deploy the novel software capabilities and algorithms required for brain simulation and big data analytics on HPC systems. These include enhancements to existing simulator software, allowing it to make efficient use of HBP hardware capabilities; novel capabilities for multi-scale simulation (simulations in which different areas of the brain are simulated at different levels of detail); and novel capabilities for interactive visualisation of brain reconstructions and simulations.

The Partnering Projects will extend the Platform with new HPC technologies and architectures and will study ways of integrating neuromorphic technologies in HPC systems.

A1.10.2 SP7: State of the Art

Since the introduction of the first supercomputers in the 1960/70s, trends in computer performance and memory have followed "Moore's Law", doubling the number of transistors on a computer chip approximately every eighteen months. According to the International Technology Roadmap for Semiconductors (ITRS) [69] this trend will continue for several processor generations to come.

Since the introduction of the Cray-1 in 1976, improvements in supercomputer performance have outstripped Moore's Law, increasing by roughly a thousand fold every ten years - an improvement primarily due to ever increasing numbers of processors. Achieving exaflop performance by 2020 – a thousand-fold increase with respect to 2010 – will require further massive increases – a goal that poses severe technical challenges [70] [71]. For environmental and business reasons, vendors have set themselves the task of containing energy consumption to a maximum of 20 megawatts per exaflop/s, driving processor design in the direction of power-efficient many-core CPUs, similar to today's GPUs but with greater autonomy. Issues of resilience combined with memory and I/O constraints present additional obstacles, including problems with end-to-end data integrity. With present technology, it is unlikely that memory capacity and bandwidth will keep up with the expected increase in compute performance.

International supercomputer vendors are making intense efforts to solve these problems [72] [73]. IBM is exploring the use of storage-class memory technologies, as in its highly innovative BGAS project. Cray focuses on the exploitation of parallelism, at all levels. In Europe, CRESTA [74], coordinated by the University of Edinburgh, is working with Cray and others to explore potential applications of exascale computing and to develop appropriate system software. DEEP [75], led by Forschungszentrum Jülich, aims to achieve very high scalability using many-core X86 technology from Intel and the very low latency EXTOLL network. DEEP-ER [76] will extend the Cluster-Booster architecture of the DEEP project with a highly scalable I/O system and implement an efficient mechanism to recover application tasks that fail due to hardware errors. Mont-Blanc [77], led by BSC, is working with Bull to study energy efficiency using ARM embedded system cores.

Since the work of Gerstein and Mandelbrot in the 1960s [98], brain simulation has always used the latest computing hardware. This tendency continues as teams in the USA, Europe, and Japan work to increase the power of simulation technology. In the USA, many of these efforts are coordinated by the DARPA SyNAPSE programme [78]. In Japan, efforts to simulate the whole brain are funded by the MEXT "Next Generation Supercomputer" project [79]. In 2013, a German-Japanese team led by researchers from Forschungszentrum Jülich succeeded in simulating a neuronal network consisting of 1.73 billion nerve cells connected by 10.4 trillion synapses using the simulation software NEST on the Japanese K supercomputer [62]. However, even this very large network represents only 1% of the neurons in the human brain.

Most of the brain simulation projects just described focus on models with large numbers of neurons and synapses but with relatively little or no detail at lower levels of biological organisation. By contrast, EPFL's on-going Blue Brain Project (BBP) [80], builds and simulates biologically realistic models. The BBP team has produced a parallel version of the NEURON code, running on an IBM Blue Gene/P supercomputer with a peak performance of 56 Teraflops. The project has demonstrated that this capability is sufficient to run cellular-level models with up to one million detailed, multi-compartment neurons. A simple extrapolation suggests that after optimisation, a large system such as the 6 Petaflop Blue Gene/Q supercomputer at the Jülich Supercomputing Centre would provide enough computing power and memory to simulate up to five hundred million neurons. Cellular-level simulations of the 100 billion neurons of the human brain will require compute power at the exascale (10^{18} flops, 100 Petabytes of memory).

A unique requirement of the HBP is that supercomputers should act as flexible interactive scientific instruments, enabling *in silico* experiments on virtual brains by providing researchers with visual feedback and allowing them to "steer" simulations while they are underway. The fundamental idea behind interactive supercomputing was outlined by McCormick et al. in their landmark report on scientific visualisation as early as 1987 [81] They state that: "Scientists (sic.) not only want to analyze (sic.) data that results from super-computations; they also want to interpret what is happening to the data during super-computations."

Johnson re-iterated this point in his 2006 article on top challenges for scientific visualisation research where he included the design and implementation of "integrated problem solving environments" as one major challenge [82]. Despite these early, specific requirements, only limited progress has been made in this direction until recently. Two popular visualisation systems, Paraview and VisIt, now include libraries that enable the integration of visualisation capabilities into running simulations [83] [84], either to perform *in situ* visualisation and analysis or to present simulation results to the user at runtime. These capabilities may ultimately lead to the realisation of interactive steering capabilities.

A1.10.3 SP7: Advances over State of the Art

The "Interactive Supercomputing" capabilities envisaged by the HBP require changes to HPC hardware architecture, run-time systems and resource management, as well as novel techniques of visualisation, analysis, and steering. The HBP supercomputer must allow large amounts of data to be held within the system, support dynamic management of all relevant system resources, and provide *in-situ* visualisation and data analysis. In addition, new techniques of numerical computing are needed to achieve the necessary effectiveness.

Dynamic resource management. Complex workflows including interactive visualisation and data analysis require dynamic management of relevant system resources (including memory). The HBP will develop mechanisms to support scenarios in which users launch long lasting simulations that may request further simulations at different scales to provide parameters at different points during the simulation process. The mechanisms provided will allow users to launch analytics computational workflows and visualisation pipelines at any point during a long simulation. Each of the components will constitute a different application run within the context of a "session". Each job will consist of potentially multiple MPI processes, each potentially multi-threaded. The relative computational demands of the different jobs (components of the multi-scale simulation, visualisation and analysis) are likely to change with time.

Interactive visualisation, analysis and steering. Steering of simulations requires novel forms of interactivity that today's HPC environments do not usually provide. A key priority is to reduce data movement. To achieve this, the HBP will develop software capabilities to filter and visualise data *in situ*. This includes streaming data primitives that extract and efficiently compress the current state of the simulation before it is shipped to the user for (immersive) visualisation in real time. Further improvements in performance will be achieved by developing highly scalable, parallel visualisation and rendering algorithms as well as by extracting only an approximate state of the simulation.

Data-intensive supercomputing. Simulations of detailed biophysical and multi-scale brain models require large overall memory capacity and memory bandwidth. For economic reasons, it is likely that this memory will be realised as a hierarchy of different technologies. This requires explicit management of the data distribution and flow that takes account of these novel memory technologies. Data-locality aware programming models and compute offloading will provide means to perform computation across different levels in the memory hierarchy in a way that is transparent to applications.

New techniques of numerical computing. Real time demands in steering and accuracy demands in simulation can only be met with substantial progress in numerical methods.

Optimal complexity will be achieved by developing new multi-level algorithms for all different scales of human brain modelling. The new numerical methods will respect the design of the simulation software developed by the neuroscientific simulation community, as well as the architecture of current and upcoming supercomputers. Further, communication-avoidance will be integrated, resulting in highly efficient massively parallel numerical algorithms tailored for the specific needs of brain simulation.

Big data analytics. The rapid development of ultrahigh resolution imaging technologies with high-throughput automation allows neuroscientists to acquire massive amounts of multidimensional image data that offer unprecedented insight into the micro- and nanostructure of the brain. These massive datasets become useful only through automatic quantitative and morphological analysis, and results being linked to known spatial spaces or ontologies. As lab hardware and conventional image processing methods will fail to do so, the HBP will establish scientific big data analytics methods and production workflows for storing, processing, analyzing and transferring large neuroscientific image datasets on HPC infrastructures. These workflows demand new aspects to be considered in HPC, especially highly scalable machine learning algorithms, increased memory and I/O requirements, GPU programming, data-dependent provisioning, in-situ visual inspection, and technologies for convenient exchange of algorithms between centres hosting such datasets.

A1.10.4 SP7: Operational Objectives

SP7's operational objectives are to:

- Design, implement and operate a federated High-Performance Analytics and Computing Platform consisting of the central HBP supercomputer, satellite HPC and data facilities, Cloud storage and high-fidelity visualisation capabilities, evolving towards exascale performance and data management capabilities.
- Extend these capabilities and the capacity of the High-Performance Analytics and Computing Platform by inviting further European HPC and Data Centres to join and complement the current ones.
- Establish co-design processes with the user community on the one hand, and with the vendors of HPC technology on the other hand, to tailor the High-Performance Analytics and Computing Platform to the needs of neuroscience and drive the development of future HPC systems.
- Design, implement and deploy novel software capabilities, algorithms and numerical methods for brain simulations and big data analytics to allow for an efficient use of the HPC capabilities and for multi-scale simulations.
- Develop programming models, middleware, libraries, algorithms and data stores to exploit data locality and avoid data movement on supercomputing systems.
- Develop middleware, software and functionality for large-scale visual data analysis and large-scale, interactive and immersive visualisation environments for neuroscience.
- Design, implement and deploy big data analytics methods, algorithms, libraries and tools, including data mining, machine learning and workflow support, in particular for the processing of large-scale multidimensional image data sets.
- Develop middleware, libraries, APIs and scheduler software for dynamic resource management enabling applications to dynamically change their use of resources and for *in situ*, co-scheduled execution of analysis and visualisations on heterogeneous hardware.
- Develop tools, models, description languages, and simulation frameworks to model software performance on different machine architectures.

- Deploy the software components in production level quality by using state-of-the-art software development techniques, such as agile methodology, continuous integration and continuous deployment.
- Create documentation, training and appropriate support structures, helping users apply for access to Platform resources, adapt and optimise their codes for supercomputers, and make efficient use of the infrastructure and services provided by the High-Performance Analytics and Computing Platform.
- Reach out to the user community by dissemination, training and support, as well as by collecting their requirements and feedback, up to the level of active collaboration in the form of co-design projects.

A1.10.5 SP7: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
Ramp-Up	M01-30	Prototype version of High-Performance Analytics & Computing Platform, based on existing supercomputers at Jülich, CSCS, BSC and Cineca; Cloud storage at KIT; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services.
SGA1	M31-54	Operational version of pan-European High-Performance Analytics & Computing Platform, based on supercomputers at Jülich, CSCS, BSC, Cineca and further hosting sites in other countries; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT and interoperable with public Cloud providers.
SGA2	M55-78	High-Performance Analytics & Computing Platform including pre-exascale, data-centric HBP supercomputer at Jülich with up to 50 PFlops and basic hardware and software support for interactive supercomputing (large memory capacity, dynamic resource management, visualisation and steering capabilities tightly coupled to simulations, visual analysis algorithms for basic multi-level post-processing); supercomputers at CSCS, BSC, Cineca and other hosting sites; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT, interoperable with public Cloud providers; joint operation with Neuromorphic Computing systems.
SGA3	M79-M102	Continued operation of High-Performance Analytics & Computing Platform including pre-exascale, data-centric HBP supercomputer with advanced hardware and software support for interactive supercomputing (advanced in-situ visualisation methods for multi-scale and steerable simulations, supported by session management and annotation); supercomputers at CSCS, BSC, Cineca and other hosting sites; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT, interoperable with public Cloud providers; joint

		operation with Neuromorphic Computing systems
SGA4	M103-	High-Performance Analytics & Computing Platform including exascale, data-centric HBP supercomputer supporting full multi-scale visualisation and analysis of brain models up to the size of the whole human brain; supercomputers at CSCS, BSC, Cineca and other hosting sites; high-fidelity visualisation systems at RWTH and EPFL; high speed network connection; web-enabled platform components integrated into the Collaboratory; federated data services, including Cloud services at KIT, interoperable with public Cloud providers; joint operation with Neuromorphic Computing systems

Table 33: Main Objectives / Deliverables per SGA for SP7: High-Performance Analytics & Computing Platform

A1.10.6 SP7: Collaborations with other National, European and International Initiatives

SP7 will work closely with industry and with existing and future research projects and relevant research communities engaged in the development of high-performance computing technologies and related software. Possible themes for collaboration include next generation compilers and runtime systems, debugging and virtualisation techniques for supercomputing, and fault tolerance.

A1.10.7 Impact and Innovation Potential

Scientific Impact

IMP7.1: The High-Performance Analytics & Computing Platform will provide neuroscientists and developers with extreme-scale supercomputing and data analytics systems, reaching exascale capabilities.

IMP7.2: SP7 will establish completely new technologies for remote interactive simulation, visualisation and analytics in high-performance computing. The new technologies will facilitate the adoption of simulation-based research methods in neuroscience, the other life sciences and many other domains.

IMP7.3: SP7 will operate a Europe-wide, dedicated highest-speed network for data exchange and global data access, based on the PRACE network as part of the HBP Research Infrastructure. With fixed routing and encryption, the HBP/PRACE network will guarantee the security of highly sensitive data.

IMP7.4: SP7 will pioneer the use of low-power neuromorphic technologies in High-Performance Computing.

Social and Economic Impact

The social and economic impact of SP7 will be indirect through the services it provides to brain simulation (SP6), neuromorphic computing (SP9), neurorobotics (SP10) and any potential co-design projects that engage the base infrastructure.

Innovation Potential

IMP7.4: New technologies for remote interactive simulation, visualisation and analytics generated by SP7 have the potential to generate significant licensing revenue.

IMP7.5: Novel HPC hardware based on low-power neuromorphic technologies also have the potential to generate licensing revenue.

A1.11 Subproject 8: Medical informatics Platform

SP8 is an HBP Platform SP.

A1.11.1 SP8: General Objectives

The general objective of SP8 is to achieve a multi-level understanding of the similarities and differences among brain diseases, and to use this knowledge to improve the classification, diagnosis and treatment of these diseases.

The Core Project will design and operate a Medical Informatics Platform that federates clinical data stored in hospitals and research archives (clinical records, imaging data, genetic data and other data from laboratory tests), makes them available to researchers, and provides the tools to analyse the data and identify "biological signatures of disease". The Platform will include tools to anonymise, search, query, analyse and mine patient data while simultaneously providing technical guarantees that researchers cannot link the data to individual patients except under strict medical control and legal supervision. It will use these tools and methods to identify Biological Signatures of diseases and to produce a draft map of the similarities and differences among diseases. Partnering Projects will use them to identify additional "biological signatures of disease" and, on this basis, to develop a new, comprehensive classification of brain diseases, new biologically based diagnostics and new tools for personalised medicine.

A1.11.2 SP8: State of the Art

Traditional epidemiology and drug development rely on a univariate model in which a single outcome is linked to a small set of risk factors (epidemiology) or the modulation of a single drug target (drug development). This model fails to take account of the complexity of biological systems, in which multiple redundancies can stabilise the functioning of the system even when a particular pathway is blocked [64]. This is particularly true of the brain, whose intrinsic plasticity gives it the ability to adapt to major changes in the external environment and even to significant internal damage. This means that most psychiatric and neurological diseases cannot be identified through a simple biomarker and cannot be treated by modulating a single drug target.

The HBP Medical Informatics Platform is based on the premise that the best way of identifying more complex disease signatures and exploring new treatment options is to explore very large volumes of multivariate patient data, using methods from bioinformatics. Under the impulse of the Human Genome Project, bioinformatics has already developed extremely effective tools for exploring and annotating genetic data. To date, however, there has been relatively little work on other classes of clinical data.

The need for large volumes of data poses technical, cultural and organisational issues. On the technical side, it has long been recognised that that the needs of researchers seeking to store, query and manipulate scientific data are profoundly different from the commercial needs that have driven the development of relational database technology [85] [86]. In the case of medical informatics, these issues are especially acute, leaving many gaps between the requirements of research and the capabilities of the technology. Despite intensive research, this requirements gap has yet to be adequately filled.

A crucial issue is how to provide scientists with quick access to raw medical data, such as data from imaging [87]. Loading these large datasets into a database is a time consuming process, particularly when it is not known what parts of it will actually be used. The development such functionality will require extensive research on how to execute queries on different raw data formats [88].

On the organisational side, sharing of data is less common among clinical scientists than in other scientific communities. According to Visscher *et al*. [89] the reasons include the need

for standardisation, the time required to transfer data to repositories, the need to protect clinical confidentiality, the perceived risk of jeopardising publications, and difficulties in assessing the accuracy of results. All these problems are soluble in principle, and have already been solved by other scientific communities.

Imaging presents an illustration of the challenges and potential solutions. European hospitals and research establishments generate an enormous number of brain images, most of which are only viewed once before being archived on hospital or laboratory servers. Several attempts to exploit such data are already in progress. Preliminary international data generation initiatives, such as the ADNI database [90] have demonstrated practicability and value for money, The ENIGMA Consortium (http://enigma.loni.ucla.edu), has recently brought together 125 institutions in a very large brain imaging study, analysing brain images and genome-wide scan data from 21,151 subjects. As a result of these and similar studies, grant-awarding institutions such as the NIH and Wellcome Trust require that studies they fund make their databases available on the Internet, facilitating data sharing. Switzerland, among other countries, already allows hospital data mining by health economists and insurance companies. Pilot studies by the HBP Partners are profiting from this situation to mine anonymised patient data generated by pharmaceutical firms, including data from failed clinical trials.

A1.11.3 SP8: Advances over State of the Art

Federating hospital data requires systems with scalable storage, high availability, and effective mechanisms to protect patient data when they are queried over the network. The traditional approach is to copy the data into a distributed store, which ensures high availability through redundancy. However, this strategy does not provide security for patient data, which is no longer stored at the hospital. To preserve hospital ownership and control, the HBP will develop a federated query engine that leaves patient data in its original location and format. Compared to traditional schemes in which data are moved to accommodate the needs of the query engine, this a fundamental change.

To protect patient data, the HBP will introduce novel methods of anonymisation that can precisely quantify and control the amount of information disclosed, and techniques to ensure that it is impossible to infer personal information about patients from query results.

An important goal for the HBP is to characterise complete disease pathways, from the molecular level, up to observable disorders of cognition and behaviour, and to identify unique combinations of biological and clinical signals associated with specific pathways. To pursue this goal, SP8 will use continuous dynamic data mining to identify biological signatures of disease—constellations of biological, anatomical, physiological and clinical variables that define homogeneous populations. The data mining will be based on state of the art machine learning algorithms. The HBP will extend current methods to take into account the specificity of clinical data, high dimensionality, high heterogeneity and high noise due to missing values. However, the more data becomes available, the greater will be the discriminatory power of the analysis. As new hospitals are recruited and hospitals already in the network contribute data from new patients, the resulting data will be incorporated into this dynamic, continuous, background process. The result will be a constantly optimised constellation of disease signatures defining a new biologically based disease nosology. Disease signatures will make it possible to derive causal models of diseases and treatments. Inferences based on these models and further interaction with brain simulation results will enable major advances in the diagnosis, classification, understand and treatment of brain diseases, preparing the way for new techniques of personalised medicine.

A1.11.4 SP8: Operational Objectives

SP8's operational objectives are to:

- Design, implement and operate a federated clinical infrastructure comprising tools for harmonizing heterogeneous clinical databases, data anonymization, ontology-based query interfaces, federated search and distributed analysis of clinical data.
- Establish agreements/MoUs, in consultation with authorized representatives of involved HBP Partners, for access to hospital data, centralized large-scale clinical research databases and biobanks. Provide documentation, training and support to the users.
- Develop generic tools for data curation, quality control and provenance. Develop, implement and deploy tools to extract brain morphology, genomic, proteomic behavioural and cognitive features from clinical and research databases.
- Develop, implement and deploy mathematical methods for predicting multi-level features of diseases; develop tools for identification of homogeneous disease using the Biological signatures; construct unified models of brain diseases.
- Contribute data, novel disease classification for disease simulation and *in silico* experimentation.

A1.11.5 SP8: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	First version of Medical Informatics Platform; scale-out implementation of data management platform for distributed infrastructures; access for academic researchers, epidemiologists and clinicians; federation nodes in 5 R&D hospital partners for in-situ querying of anonymised data; web-based services for neuro-epidemiological studies, interactive analysis and exploration of the biological signatures of Alzheimer's disease; initial publications demonstrating the value of the Platform. Once adequate functionality has been achieved, the plan is to transfer the hospital software bundle developed in academia to industry for its industrialisation, commercialisation and wider deployment (industry standard software, accreditation for clinical use by the European Medicines Agency, installation and service contracting, updating software apps, etc.). Further development of functionality in SGA2 and 3 will depend on research and clinical community needs, success in defining disease signatures and other developments. Such development work may be carried out jointly by research teams and industrial partners (see SGA2-SGA4 below).
SGA2	M55-78	Development will include refined tools for analysing medical data at Federation level, enriched user-interaction functionalities, real-time automated data workflows; foundations for distributed mining of medical data; tools for identification of homogeneous, disease-related biological constructs. Only the parts of such work that still have a clear research component and which are essential for the HBP RI will be carried out as part of the Core Project. Essential ones from the computer science viewpoint is implementation of efficient continuous real-time integration of globally distributed medical data and ontologies, and distributed system-level result caching and workflow optimization strategies. Outputs and metrics will include publications that demonstrate the value of the platform and first disease signatures.
SGA3	M79-M102	Predicting further developments is difficult but likely elements

		include: extension of the federation with hospital nodes world-wide; graph-based mathematical models for interactive analysis; tools for large-scale mining of medical data, using complex features; sophisticated disease models with variables from *in silico* experimentation; tools for identification of homogeneous disease-related biological constructs; external validation of disease models using post-hoc clinical phenotyping; interactions with brain simulation results and tuning of brain disease signatures. Only the parts of such work that still have a clear research component and which are essential for the HBP RI will be carried out as part of the Core Project. Examples of essential ones include: efficient distributed querying support of complex user-defined functions, tight integration to user logs, declarative specification of complex data mining workflows, and automated matching and mapping between medical and research datasets.
SGA4	M103-	As the federation is further extended, accompanying developments could include: graph-based mathematical models and support for graph-based ad-hoc medical query processing; automated mapping, integration and addition to existing workflows of new data sources; tools for large-scale mining of medical data; predictive and prescriptive disease models; disease simulation, with a generative model of disease comorbidities and resilience; unified model of brain diseases, generating a biologically grounded classification of brain disorders; evaluations and cross-analyses using brain simulation; medical guidelines based on disease models, with extension of Platform use into personalised medicine and patient selection for clinical trials.

Table 34: Main Objectives / Deliverables per SGA for SP8: Medical Informatics Platform

A1.11.6 SP8: Collaborations with other National, European and International Initiatives

SP8 will collaborate closely with industry, international organisations and research consortia. Possible themes include data sharing and related technologies and standards, exploitation of data from large longitudinal and cross-sectional databases, and epidemiological applications of the Medical Informatics Platform (e.g., compilations of statistics showing associations between disease prevalence and geographical, social and economic data, and development of a Mental Health Index allowing comparisons between different countries and different geographical regions).

A1.11.7 SP8: Impact and Innovation Potential

2.5.2.1.1 Scientific Impact

IMP8.1: SP7 will establish novel techniques and practices for the extraction of clinically valuable information from large volumes of patient data, exploiting the competitive advantage offered by European National Health Systems, and establishing European leadership in a broad field of medical research. The techniques established by the Subproject will have a major impact on medical research outside the HBP.

IMP8.2: The Medical Informatics Platform will offer researchers unprecedented access to large volumes of anonymised patient data, creating new opportunities for basic and applied research. The federation and querying methods at the core of the Platform will make it possible to leave personally sensitive data in the systems and formats where they were

originally stored, without moving them to a central system. Tools and methods supporting this strategy will have a substantial impact on future medical research.

IMP8.3: SP8 will contribute to establishing objective, biologically grounded classifications of neurological and psychiatric disease. This represents a major step forward, compared to current symptom and syndrome-based methods of diagnosis.

IMP8.4: "Biological signatures of disease", identified in SP8, will provide the data required for high-fidelity reconstructions and simulations of disease and possible treatments. Simulations will provide a novel tool for understanding the causes of brain disease, and simulating the effects of drug candidates and other treatments.

2.5.2.1.2 Social Impact

IMP8.5: Biologically grounded classifications of brain disorders established by SP8 will allow more effective diagnosis and treatment of brain disorders, and more effective selection of participants for clinical trials.

IMP8.6: Disease and drug simulations will facilitate the development of drug and other treatments.

IMP8.7: The data and tools made available by the Medical Informatics Platform will facilitate the development of personalised treatments.

IMP8.8: Better understanding, diagnosis and treatment of brain disease will reduce costs for National Health Services and insurance companies and reduce the burden on patients and their families.

2.5.2.1.3 Innovation Potential

IMP8.9: SP8 will enable commercial services allowing clinicians and pharmaceutical researchers to query and analyse anonymised patient data.

IMP8.10: SP8 will enable commercial services allowing clinicians and pharmaceutical researchers to simulate brain diseases and candidate treatments.

IMP8.11: SP8 will enable commercial services for personalised medicine (diagnosis, prognosis, selection of optimal treatment).

A1.12 Subproject 9: Neuromorphic Computing Platform

SP9 is an HBP Platform SP.

A1.12.1 SP9: General Objectives

The overall goal of SP9 is to establish Neuromorphic Computing as a new paradigm of computing, complementary to current designs, and to explore potential applications in neuroscience and machine learning. To achieve this goal, SP9 will design, implement and operate a Neuromorphic Computing Platform that allows non-expert neuroscientists and engineers to perform experiments with highly configurable Neuromorphic Computing Systems (NCS) implementing simplified versions of brain models developed on the Brain Simulation Platform as well as generic circuit models based on theoretical approaches. The Platform will also provide software simulations for circuit verification of NCS and software support for configuring, running and analysing experiments. The first version of the Platform, accessible to researchers inside and outside the HBP Flagship Initiative, will be released to the community at the end of the Ramp-Up Phase.

The Neuromorphic Computing Systems developed by SP9 are hardware devices incorporating the developing state-of-the-art electronic component and circuit technologies as well as knowledge arising from other areas of HBP research (experimental and cognitive

neuroscience, theory, brain modelling). The Platform will allow researchers to use two distinct categories of NCS: (1) Physical (analogue or mixed-signal) emulations of brain models (NM-PM), running in time-accelerated mode, and (2) Digital Multicore systems implementing numerical models running (NM-MC), as well as hybrid systems, integrating NCS with conventional computing technologies.

NCS will be tightly integrated with the High Performance Computing Platform, which will provide essential services for mapping and routing circuits to neuromorphic substrates, benchmarking and simulation-based verification of hardware specifications.

The distinguishing feature of the HBP's strategy for neuromorphic computing is that neural architectures will be derived from detailed multi-level brain models, developed on the Brain Simulation Platform. The HBP will systematically study the relationship between different features of the models and their computational performance, identifying and implementing strategies to reduce complexity while preserving functionality.

The Core Project will design, implement and deploy the planned Neuromorphic Computing Systems (up to three versions of the NM-PM system, two versions of the NM-MC system, depending on availability of construction budget) and integrate them in the Neuromorphic Computing Platform, which it will open to the community at the end of the Ramp-Up Phase.

The Partnering Projects will explore novel applications of the technology. Potential application areas include pattern detection in spatio-temporal data streams, finding causal relations in big data, data mining, temporal sequence learning, and approximate computing. Other themes for investigation in the Partnering Projects include new hardware devices incorporating Neuromorphic Technology, new device technologies (resistive memories, magnetic memories, organic devices, distributed powering, etc.) and hybrid HPC-neuromorphic computing systems for accelerated, energy efficient brain simulations.

A1.12.2 SP9: State of the Art

The primary technological challenges for traditional computing are energy consumption, software complexity and component reliability. One strategy to address these challenges is to use neuromorphic technologies inspired by the architecture of the brain. Some approaches have focused on physical emulation of brain circuits. These approaches have the potential to exploit the characteristics of inherently noisy and unreliable micro- or nanoscale components with feature sizes approaching the atomic structure of matter, and with an energy cost per neural operation six orders of magnitude lower than that of equivalent brain models running on conventional supercomputers. Other approaches use massively parallel many-core architectures that simulate neural models on digital processors. In both strategies, communications among model neurons use clockless, inherently asynchronous "spiking neural networks"– a "brain-like" feature that offers major savings in energy consumption. Other advantages include support for plasticity and learning and (in the case physical emulation) the ability to run at speeds from 1,000 to 10,000 times faster than biological real time. This capability allows model systems to emulate real world learning processes and physical dynamics lasting weeks, months and even years.

The main scientific challenge for neuromorphic computing is the choice of the computational paradigm to be implemented on the electronic substrate. This requires basic research into the way the brain stores and processes information, the way it accommodates and even exploits the variability of its components, and the role of stochastic neuronal behaviour.

Neuromorphic computing with modern microelectronics was pioneered by the group of Carver Mead [91] at Caltech, the first to integrate inspired electronic sensors with analogue circuits and to introduce an address-event-based asynchronous, continuous time communications protocol. Today, many groups follow the Mead approach, notably the Institute for Neuroinformatics at ETH Zürich (Switzerland) [92].

The Mead work focuses on the demonstration of basic high-level computational principles. IBM's SyNAPSE (Systems of Neuromorphic Adaptive Plastic Scalable Electronics) project, by contrast, aims to reproduce large systems that abstract away from the biological details of the brain. Proponents argue that the inherent scalability of this approach allows them to build systems that match the computing efficiency, size and power consumption of the brain and its ability to operate without programming [78].

The European FACETS project has pioneered a different approach that combines local analogue computation in neurons and synapses with binary, asynchronous, continuous time spike communication [93] [94] [95]. FACETS systems can incorporate $50*10^6$ plastic synapses on a single 8-inch silicon wafer. In the near future, advances in CMOS feature size, connection technologies and packaging will make it possible to build multi-wafer systems with 10^{13} plastic synapses operating at acceleration factors of 10,000 compared to biological real-time. The FACETS group has also pioneered a network description language (PyNN) that provides Platform independent access to software simulators and neuromorphic systems [96]. BrainScaleS – a follow-up project – was pioneering the use of the technology to replicate behaviour and learning over periods of up to a year while simultaneously emulating the millisecond-scale dynamics of the system.

Another strategy is to implement brain models in classical many-core architectures. This is the approach adopted by the UK SpiNNaker group [97] [98]. The group, which has a strong grounding in the ARM architecture, has recently completed the integration of a SpiNNaker chip into an operational system and is now running experiments. Each chip has eighteen cores and a shared local 128M byte RAM, and allows real-time simulation of networks implementing complex, non-linear neuron models. A single chip can simulate 16,000 neurons with eight million plastic synapses running in real time with an energy budget of 1W.

A1.12.3 SP9: Advances over State of the Art

The Neuromorphic Computing Platform developments will be based on functional, large-scale architectures and proven device technologies. The most important goal is to provide the best possible neuromorphic processing performance in term of possible system size and accessibility with the goal to study and understand the circuit architectures and their use for information processing. The development of the concepts, including the necessary test-chips requires a funding of 4 Mio€/year for both system approaches. This includes costs for hardware, software and personnel. Producing the 2 large scale phase-2 systems planned for construction start in M100 and completion in M120 of HBP, will require in addition 11 Mio€ for the hardware of each system types (PM and MC). The total of 22 M€ for phase-2 production cost is currently not accounted for in the project planning. In addition an intermediate update of the NM-PM1 system is possible with a construction start in month 60 for 3.8 Mio € construction cost.

Planned advances beyond the state of the art include the following.

1) **Moving to advanced process nodes.** The test chips from advanced process nodes being designed for both systems will be used as basic components for the next generation systems.
2) **Integrating recent neurobiological knowledge.** As the Project proceeds, SP9 will integrate more structured, multi-compartment neuron models. Future systems will make it possible to model plasticity, supervised and unsupervised learning, and developmental processes and a far more flexible and user controllable way than this is done with the current systems.
3) **Integrating next generation chips into next generation systems.** The technologies and time planning are described in the roadmaps below. Key novel features for new versions are indicated in **bold**

Note: The realisation of these system development roadmaps requires the availability of EUR 4 million for the NM-Computing Platform (NM-PM, NM-MC, software, computational principles, development, maintenance and platform services work).

System Version	Unit Numbers / HW cost	Neuroscience Features	Technologies	Infrastructure	System construction costs
NM-PM-1 Ramp-up phase	20 Wafers 4M Neurons 0.9B Synapses	AdEx Point Neurons Up to 14336 syn. inputs 4-bit synapses STP, STDP x1000-x10.000 acc.	180nm CMOS 20 cm Wafers Wafer-on-PCB	5+2 Rack Architecture FPGA digital links 3 TFlop local cluster	(Has been constructed in ramp up phase. Development by BrainScaleS project)
NM-PM-2 (upgrade possibility to the ramp-up system, construction start possible in month 60)	20 Wafers 4M Neurons 1B Synapses	Adex Point Neurons Up to 16000 syn. inputs **6-bit synapses** STP, STDP **Plasticity Processor** x1.000-x10.000 acc.	**65nm CMOS** 20 cm Wafers Wafer-on-PCB	NM-PM-1 compatible FPGA digital links 3 TFlop local cluster	System construction cost (in addition to the capability development cost) 3.8 Mio Euro
NM-PM-3 Option a (*) construction start possible in month 100	**50 Wafers** 50M Neurons 13B Synapses	**Structured Neurons** Up to 16000 syn. inputs 6-bit synapses STP, STDP Plasticity Processor x1.000-x10.000 acc.	65nm CMOS **30 cm Wafers** Wafer-on-PCB **FPGA-less**	**Torus Architecture** **On-wafer digital links** 100TFlop local cluster	System construction cost (in addition to the capability development cost) 11 Mio Euro
NM-PM-3 Option b (*) construction start possible in month 100	**500 Wafers** 500M Neurons 130B Synapses	Structured Neurons Up to 16000 syn. inputs 6-bit synapses STP, STDP Plasticity Processor x1.000-x10.000 acc.	65nm CMOS 30 cm Wafers **Wafer-in-PCB** FPGA-less PCB embedding	Torus Architecture On-wafer digital links 100TFlop local cluster	

Table 35: Development roadmap for Physical Model Neuromorphic Computing Systems (PM-NCS)

(*) The choice between options a and b will depend on the result of technology R+D on wafer-PCB embedding

System Version	Unit Numbers	Neuroscience Features	Technologies	Infrastructure	System construction costs
NM-MC-1 Ramp-up phase M30 Deliverable	600 Boards 100M Neurons 100B Synapses	Any Point Neuron 1000 16-32 bit fixed or plastic synapses per neuron. Real time.	130nm CMOS co-packaged 1Gb DDR2 DRAM	Rack Architecture Chip and FPGA digital links Small cluster for routing/job queuing	(Has been constructed in ramp up phase. Construction and development by SpiNNaker project)
NM-MC-2 construction start possible in month 100	**360 Boards** 1B Neurons 10,000B Synapses	**Multi-compartment Neurons** 10,000 16-32 bit fixed or plastic synapses per neuron. Real-time.	**28nm CMOS: interposer with 4 die and 32Gb HMC DRAM in 2cm x 2cm bga package**	Rack Architecture Chip and FPGA digital links Small cluster for routing/job queuing	System construction cost (in addition to the capability development cost) 11 Mio Euro

Table 36: Development Roadmap for Many Core Neuromorphic Computing Systems (MC-MCS)

A1.12.4 SP9: Operational Objectives and Related Actions

SP9's Operational Objectives are to:

Operate, use and maintain the large-scale Platform installation

This is initially the most important objective as it makes existing and unique neuromorphic facilities available to non-expert users. The use cases are basic neuroscience research and applications in cognitive computing outside neuroscience. For the first use case, cross-Platform cooperation within the HBP is carried out with:

- SP3: Cognitive architectures in closed-loop experiments with special emphasis on plasticity, learning and development.
- SP4: Implementation and testing of theoretical models of neural computation with special emphasis on bridging spatial and temporal scales.
- SP6: Transferring reduced complexity circuits to the Neuromorphic Computing Platform.
- SP7: Using the High Performance Computing Platform to process circuit mapping, executable system specifications and data analysis.
- SP10: Using the virtual robotic environment for closed-loop experiments.

Training for external neuroscience users is provided through education and training events. Support for experiments is provided as part of the Platform Work Plan.

Cognitive computing applications outside neuroscience that use the Neuromorphic Computing Platform are expected to be carried out by collaborations outside the HBP. These will involve academic research groups from machine learning (e.g. deep learning) and industry as external Platform users.

Build, operate and distribute reduced size portable systems as subsets of large systems

Reduced size systems are available today, and are used by a broad community inside and outside the HBP. The SpiNNaker boards are used in robotics as real-time systems, as they can interface to electronic sensors and actuators. The most important application of reduced size systems throughout the FPA will be in education and training. In the HBP this is carried out via cross-SP cooperation with SP11, in particular the education section. The systems will be used as follows:

- To introduce new HBP students and scientists to neuromorphic computing during HBP Schools, summits and similar events.
- Outside the HBP, small systems will be used at summer schools, and will be given to academic groups for evaluation and research. The use in undergraduate and graduate teaching will be essential to broaden the user base in the future.

Next generation chips (see next objective) will also be used for next generation reduced size systems throughout the FPA.

Developing the next generation neuromorphic chips for large-scale and reduced size systems

This is the first genuine HBP work in neuromorphic chip development as both existing hardware systems have been developed in previous projects (SpiNNaker and FACETS / BrainScaleS). The development work is carried out in cross-SP collaboration, and with two SPs in particular:

- SP1: Building structured models of neurons based on experimental data from neuroscience.
- SP4: Preparing next generation systems for implementing new developments in theoretical neuroscience. These focus on plasticity, learning and development, stochastic computing, and reduced complexity neuron models.

The expected funding of SP9 for this objective is focused on chip design, prototyping and prototype testing. The required funding for actual system construction is provided for information (see Tables 24 and 25).

Providing software access to neuromorphic computing

This is a prerequisite for the use of all neuromorphic systems (large, small, next phase) in the HBP. This work is carried out in close collaboration with all other Platforms, and with the Collaboratory group.

A1.12.5 SP9: Main Objectives / Deliverables, per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
Ramp-Up	M01-30	NM-PM-1: With 4 million neurons and 1 billion synapses, x10,000 acceleration NM-MC-1: With 100 million neurons and 100 billion synapses
SGA1-4	M31-	NM-PM-1: Small-scale systems available for training & development NM-MC-1: Small-scale systems available for training & development
SGA1	M31-54	NM-PM-2: Feature set described in Roadmap table to get ready for NM-PM2 NM-MC-1: increasing scale, performance and on-line accessibility, with real-time closed-loop virtual robotics environment from SP10. NM-MC-2: Architecture model, and test silicon where appropriate
SGA2	M55-78	NM-PM-3: Feature set described in Roadmap table to get ready for NM-PM3 NM-PM-2: Construction starts (subject to availability of about ~EUR 3.8 million construction funding) NM-MC-1: continuing evolution of on-line access in response to user feedback. NM-MC-2: Silicon samples tested and evaluated (subject to availability of NRE funds ~EUR 2 million)
SGA3	M79-M102	NM-PM-2: Operational (subject to construction starting in SGA2) NM-PM-3: Construction starts (subject to availability of ~EUR 11 million construction funding) NM-MC-1: Continuing evolution of on-line access in response to user feedback NM-MC-2: Large-scale system build to single rack scale (subject to availability of ~EUR 3 million build funds)
SGA4	M103-	NM-PM-3: Operational (subject to construction starting in SGA3) NM-MC-1: Continuing evolution of on-line access in response to user feedback NM-MC-2: Large-scale system available on-line (subject to availability of ~EUR 6 million build funds)

Table 37: Main Objectives / Deliverables per SGA for SP9: Neuromorphic Computing Platform (NM)

A1.12.6 SP9: Collaboration with other National, European and International Initiatives

SP9 plans to engage in joint technology development with major European players including Fraunhofer FhG (Germany), CEA-Leti (France), and IMEC (Belgium). Possible themes for joint projects include new devices, connection technologies, and software tools. The European electronics design and manufacturing industry will play a key role in the development and construction of neuromorphic systems. SP9 plans to develop national technology nodes for a neuromorphic applications, with a focus on robotics, automotive, manufacturing and telecommunication systems. The planned Global Network of Brain Initiatives will enable SP9 to exchange information with other international initiatives. Plans for collaboration include bi-annual EU-US workshops on neuromorphic computing, and joint workshops to develop a global strategy for future development.

A1.12.7 SP9: Impact and Innovation Potential

Scientific Impact

IMP9.1: SP9 will establish designs and technologies for large-scale neuromorphic devices and systems with novel learning capabilities, low energy consumption and high reliability.

IMP9.2: The Neuromorphic Computing Platform will offer academic researchers and technology developers the possibility to experiment with and test state-of-the-art neuromorphic devices and systems.

Social and Economic Impact

IMP8.3: The technologies and systems developed in SP9 have the potential to revolutionise computing technology, enabling a very broad range of completely novel applications.

IMP8.4: The services offered by the Neuromorphic Computing Platform will facilitate the emergence of a rich ecosystem of academic and industrial researchers, exploring and ultimately commercialising novel applications.

IMP8.5: SP9 will establish European leadership in an area of research of vital importance to the European computing industry and to applications developers.

Innovation Potential

IMP8.6: SP9 has the potential to develop commercial services offering researchers and technology developers the possibility to experiment with and test applications based on state-of-the-art neuromorphic devices and systems.

IMP8.7: Neuromorphic designs and technologies developed in SP9 have the potential to generate licensing revenues from industry and applications developers.

IMP8.8: Neuromorphic technologies developed in SP9 have the potential to generate commercially valuable applications for manufacturing, transport, healthcare, and consumer electronics.

A1.13 Subproject 10: Neurorobotics Platform

SP10 is an HBP Platform SP.

A1.13.1 SP10: General Objectives

The overall objective of SP10 is to provide tools allowing researchers to test the cognitive and behavioural capabilities of the brain models developed in SP6, and the neuromorphic implementations of these models from SP9. Even with the high-performance computers of

the HBP, it will initially not be possible to simulate HBP brain models in real time. Thus, SP10 will initially rely on simulated robots and simulated environments. The Neurorobotics Platform will provide researchers with access to detailed brain models on the Brain Simulation Platform running slower than real time, and to emulated models on the Neuromorphic Computing Platform running at or faster than real time. It will also allow them to use mixed models in which some areas of the brain are represented in full biological detail, while others are represented by phenomenological models. The tools provided by the Platform will allow researchers to operate robots remotely, to repeat experiments as often as they need, and to visualise the behaviour of the robots as if they were running in real time.

The Core Project will design and implement the tools, incorporating them in the HBP Neurorobotics Platform. The first version of the Neurorobotics Platform will be released at the end of the Ramp-Up Phase. The Platform allows researchers to design simulated robot bodies, connect these bodies to brain models, embed the bodies in rich simulated environments, and calibrate the brain models to match the specific characteristics of the robot's sensors and "muscles". The resulting set-ups will allow researchers to replicate classical animal and human experiments *in silico,* and ultimately to perform experiments that would not be possible in the lab. During the Operational Phase, the Platform will also provide access to physical robots controlled by brain-models that can be executed in real time, on analogue or digital neuromorphic hardware provided by the Neuromorphic Computing Subproject. Partnering Projects will enhance the methods and technologies used in the Platform and explore their applications, both in neuroscience research (*in silico* behavioural experiments) and for potentially valuable commercial applications. Partnering Projects may also extend the Platform to enable experiments involving multiple neurorobotic systems and their interactions.

A1.13.2 SP10: State of the Art

Neurorobotics can be defined as the science and technology of robots which are controlled by a simulated nervous system that reflects, at some level, the architecture and dynamics of the brain [99]. Such robots can are situated in a real-world environment, sense environmental cues, and act upon their environment. Robots with these properties make it possible to study brain models in closed-loop experiments.

Probably the first researcher to develop a robot that fulfilled these criteria was Thomas Ross, who in 1933 devised a mobile robot with a small electromechanical brain, which could navigate through a maze in real time [100]. Today, there are two main strands in neurorobotic research, the first focusing on biologically inspired robots, the second on brain-inspired control architectures.

Historically, biologically inspired robots have mainly come from academic research. However, recent advances in humanoid and four-legged robots have lead to a renewed interest in applications for the military (BigDog, BostonDynamics.com), aeronautics (NASA Robonaut2), and entertainment (Honda ASIMO, Sony AIBO). Biologically inspired robots are adaptable and can display rich perceptual and behavioural capabilities. In contrast to industrial robots, they often use compliant materials, which make their mechanics intrinsically flexible. Researchers have also developed a large number of robots, three of the most advanced are iCub (a humanoid robot "child") [101], Kojiro (a humanoid robot with about 100 "muscles" [102] and ECCE (a humanoid upper torso that attempts to replicate the inner structure and mechanisms of the human body [103]. Brain-inspired control architectures are robotic control systems, which at some level reflect properties of animal nervous systems. In general, they are tailor made for a specific set of tasks, often using a combination of Artificial Neural Networks, Computer Vision/Audition, Machine Learning algorithms, and recently Spiking Neural Networks [104] [105] [106] [107]. A typical experiment might involve the emulation of a rat as it navigates through a maze. In this

case, the control architecture for the simulated rat could comprise sensory areas, a hippocampus, and a motor area to generate movements.

A1.13.3 SP10: Advances over the State of the Art

SP10 will deviate radically from traditional brain-inspired control architectures. Rather than designing specific neural control architectures for each experiment, HBP neurorobots will be controlled by generic brain models provided by the Brain Simulation Platform that are additionally constrained by behavioural and cognitive data from experiments with closed sensory motor loops. To design a robot for use in an experiment, researchers will connect models of sensors (vision, audition, touch, balance) and actuators to a brain model, calibrate the robot brain so that it can process the relevant signals, and translate the model's neural activity into control signals for the robot. Researchers will then use classical techniques (lesion studies, manipulations of neurons, etc.) to identify the control architecture for specific tasks. This approach allows researchers to monitor and control all states and parameters of the experiment (brain, body, and environment) – something technically impossible to achieve in the laboratory. Since there is a clear trend in general robotics towards the use of modular building blocks and since the NRP control structures can also be assembled from building blocks, the defining theme for SP10 is "Building modular brains for modular bodies".

In terms of the development tool chain, the NRP aims to build an open source software solution. Software modules will be derived from established tools with a strong developer community and from software already developed in the Blue Brain Project. Developers from the robotics and open source communities are encouraged to take part in this continuous effort. The current understanding of neurorobotics is largely bound to the idea that the environment in which the robot interacts must be the real world, but the gap between simulation and reality is decreasing. A well-designed simulation environment would make it possible to perform studies much faster than would ever be possible with physical robots, which need to be designed, built, programmed, and re-designed, etc. in a never-ending cycle.

So, while current neurorobotics research focuses on physical robots, SP10 will focus on virtual robots and environments. Simulation experiments using virtual robots and environments will allow researchers to perform completely novel *in silico* experiments investigating the link between brain circuitry and high-level cognitive and behavioural functions. Use cases might include: rapid prototyping of cognitive and robotics experiments, simulated human robots in the real visual and auditory environment for psychology and autism research, and a combination of virtual and physical robots. Insights gained from this work will facilitate the development of new types of robot controller.

A1.13.4 SP10: Operational Objectives

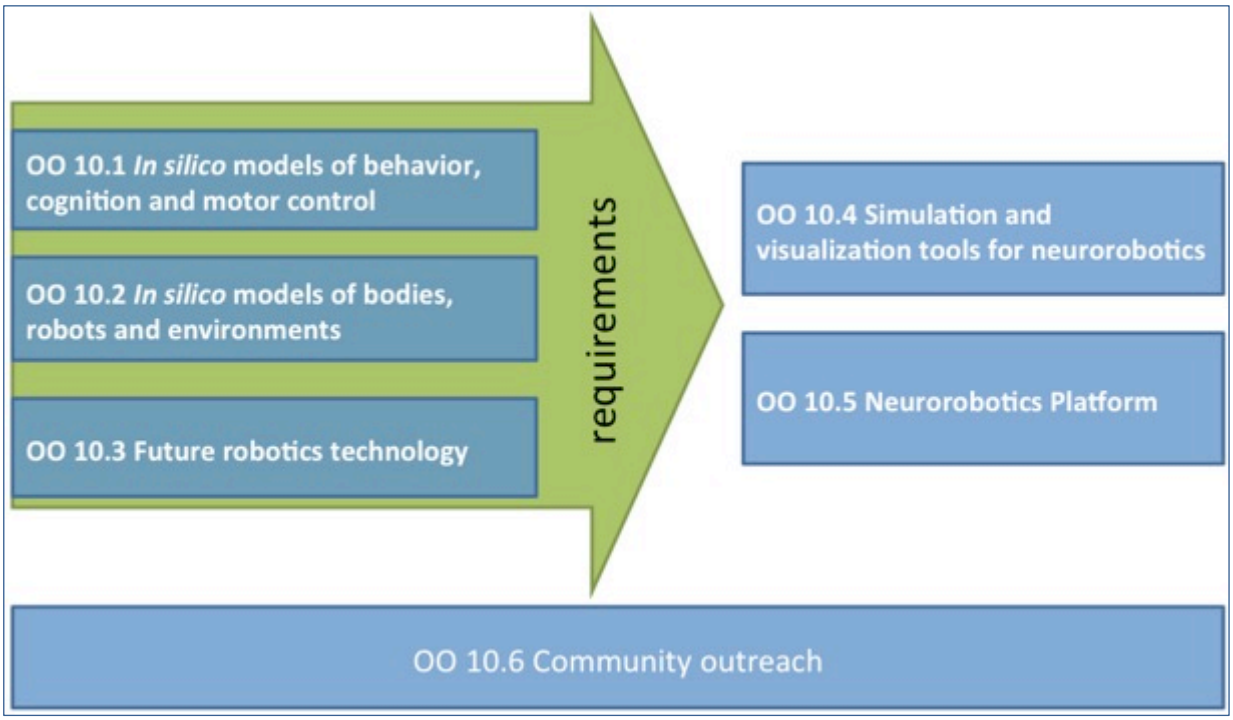

Figure 10: Relationship between the operational objectives of SP10 Neurorobotics Platform

SP10s operational objectives are to:

OO 10.1: In silico models of behaviour, cognition and motor control

- Develop and perform pilot *in silico* experiments that drive the development of the Neurorobotics Platform (NRP).
- Work with SP1-SP6 to integrate brain models with models of spinal cord, sensory, motor and vestibular systems and to close the sensory-motor loop of CNS, PNS and body.
- Work with SP1-SP6 and community to reconstruct sensory motor maps needed for basic motor control.
- Work with SP1-SP6 and community scientists to reconstruct basic drives, value- and motivation systems for autonomy.

OO 10.2: In silico models of bodies, robots and environments

- Develop and maintain community accessible libraries of bodies, robots, environments and their parts.
- Develop scaffold models of bodies and muscoloskeletal system for use in the Neurorobotics Platform.
- Identify strategically important robot and body models and integrate them into the NRP community libraries for use in the Neurorobotics Platform.
- Develop benchmarks and validation tools for *in silico* neurorobotics.

SO 10.3: Future robotics technology

- Develop and explore closed-loop neurorobotics systems using neuromorphic hardware (SP9).
- Translate virtual robots and brain-derived controllers to physical prototypes.

- Transfer controllers to modular robots and state-of-the-art embedded systems.

OO 10.4: Simulation and visualization tools for neurorobotics

- Develop tools to plan, run and analyze *in silico* experiments with neurorobotics systems, enabling life-like neurorobotics experiments with robots in sensory rich environments and users in the loop.
- Develop innovative tools for immersive high-fidelity rendering and real-time user interaction.
- Develop simulation tools for robots and sensory rich environments (World Simulation Engine).
- Develop tools to interoperate simulated and physical robots

OO 10.5: Neurorobotics Platform

- Design, implement and operate the HBP Neurorobotics Platform, facilitating collaboration between HBP researchers and community researchers.
- Integrate the HBP Neurorobotics Platform in the HBP Collaboratory.
- Work with community users to develop Apps providing a user-friendly graphics interface to tools and models developed within the project and to design APIs providing programmatic access.
- Provide documentation, training and support for users of the Platform; integrate with the HBP Unified Portal.

OO 10.6 Community outreach

- Participate in and facilitate community modelling efforts extending HBP scaffold models or addressing areas of the brain/species not directly addressed within the *Core Project*
- Participate in and facilitate community efforts to standardize model and data representations and to facilitate comparisons between different models and modelling approaches
- Participate in and facilitate projects using *in silico* reconstructions and simulations to address unresolved issues in theoretical and experimental neuroscience.

A1.13.5 SP10: Main Objectives / Deliverables per SGA

Phase	Months	Main Objective(s) / Deliverable(s)
SGA1	M31-54	Initial version of Neurorobotics Platform; capabilities to design virtual robots, environments and experiments and to link them to existing brain simulations; pilot experiments using Platform capabilities.
SGA2	M55-78	Enhanced user access and control; enhancements to simulated robots, environments and experiments; closed-loop support for simplified brain models; first published experiments using Platform capabilities; pilot experiments using high-level simulations with in-built plasticity; pilot experiments using cellular level reconstructions of the mouse brain; links to Brain Simulation, High-performance analytics & Computing and Neuromorphic Computing Platforms; first simulated robots and devices, environments and experimental conditions. Value of platform for users demonstrated in co-design pilot projects.

SGA3	M79-M102	Closed-loop support for *in-silico* mouse experiments; first published behavioural experiments using brain reconstructions with plasticity and cellular level reconstructions of the mouse brain; comprehensive library of simulated robots and devices, environments and experimental conditions for customisation.
SGA4	M103-	Closed-loop support for human brain models; pilot studies in human behaviour and cognition; finalised services for customisation of robots and devices, environments and experimental conditions. The types of models to be built will be defined closer to the date.

Table 38: Main Objectives / Deliverables per SGA for SP10: Neurorobotics Platform

A1.13.6 SP10: Collaborations with National, Regional, European and International Projects and Initiatives

SP10 will collaborate with academic and industry researchers on a broad range of themes including basic robotic technologies, user interface/simulator technology, and possible medical applications. Collaboration with industry will focus on the translation of virtual models into physical robots, the commercialisation of simulation, visualisation and robotics technologies and specialised neuro-controllers. SP10 will also work closely with open source organisations that are building tools of strategic importance for the Subproject. These include the Open Robotics Foundation, the Blender Foundation, and the Open Dynamics Engine (ODE).

A1.13.7 SP10: Impact and Innovation

Scientific Impact

IMP10.1: SP10 will establish neurorobotics as a reliable technique for exploring the causal relationships between the multi-level structure of the brain, cognition and behaviour.

IMP10.2: The HBP Neurorobotics Platform will make it possible, for the first time, for researchers to design and perform behavioural and cognitive experiments using robots connected to HBP brain simulations and inhabiting virtual or physical experimental set-ups.

IMP10.3: Research in SP10 will contribute to creating a new multi-level understanding of the relationships between brain structure, cognition and behaviour.

IMP10.4: SP10 will create the first prototype applications exploiting the novel cognitive and behavioural capabilities of physical robots with neuromorphic controllers.

Social and Economic Impact

IMP10.5: Physical robots with neuromorphic controllers will have functional capabilities (e.g., learning, effective handling of multimodal real-time input) not present in current robotic technologies. These capabilities will have a major impact over a broad range of domains from manufacturing to transport, healthcare, and the home.

Innovation Potential

IMP10.6: The Neurorobotics Platform will enable the HBP to realise commercial services allowing industry to experiment with state-of-the-art neurorobotics setups.

IMP10.7: HBP neurorobotic technology has the potential to generate significant licensing revenues.

IMP10.8: Applications developed based on neurorobotic technology have the potential to generate significant licensing revenues.

A1.14 Subproject 12: Ethics and Society

A1.14.1 SP12: General and Operational Objectives

The overall objective of SP12 is to assist the HBP in pursuing a policy of Responsible Research and Innovation (RRI). SP12 will monitor science and technological results as they emerge, analyse their social and philosophical implications, and work to involve researchers decision-makers, and the general public in a far-reaching conversation about future directions of research. SP12's strategy involves: anticipation, through the work of the Foresight Laboratory, which will produce scenarios of potential developments and their implications and feed them back to HBP researchers; reflection to encourage ethical reflection among researchers of the HBP to increase their capacity to consider the social and ethical implications of their work; engagement involving public dialogues with stakeholders and citizens; and action (feeding the results back to the HBP leadership).

A central aim is to identify potential ethical and social concerns at an early stage and to address them in an open and transparent manner, providing HBP scientists with opportunities to gauge public reaction to their work, and to hone their research objectives and processes accordingly.

The Core Project will manage a major Ethics and Society Programme, which will explore the Project's social, ethical and philosophical implications, promote engagement with decision-makers and the general public, work to raise social and ethical awareness among Project participants, and ensure that the Project is governed in a way that ensures full compliance with relevant legal and ethical norms. The programme will draw on the methods developed during empirical investigations of emerging technologies in genomics, neuroscience, synthetic biology, nanotechnology and information and communication technologies [108]. It will also draw on the biomedical tradition of engaging with ethical issues through the application of formal principles [109] – now usually implemented through ethical review processes. Partnering Projects will encourage research and outreach beyond the scope of the Core Project, offering new perspectives and new approaches, and involving new target populations.

A1.14.2 SP12: State of the Art

Forecasting innovation and its social and economic impact. HBP research entails high expectations of social and economic benefits. However, the impact of basic research results on society often depends not so much on the research itself as on developments in apparently unconnected areas of science and technology or on social, political and legal factors external to science [110] [111] [112].

Current approaches to forecasting development pathways use one of two strategies. The first studies the views, attitudes and strategies of key stakeholders with methods from the empirical social sciences [113] [114]. The second, which has reached its highest stage of development in the UK (http://www.bis.gov.uk/foresight), uses systematic foresight techniques such as modelling, horizon scanning and scenario planning. The goals of these exercises are, on the one hand, to identify new developments and assess their potential impact over the short, medium and longer term; on the other to assess key ethical concerns such as privacy, autonomy, transparency, the appropriate balance of risks and benefits, responsibility and accountability, equity and justice [115]. Foresight exercises play a central role in responsible innovation as they enable 'anticipatory' action to shape the pathways of development in desired ways and to assess and manage risks in a timely manner.

Conceptual and philosophical issues. Since the 1960s, scientific and technical advances [116] have made it ever easier to anatomise the brain at the molecular, cellular and circuit levels, encouraging claims that neuroscience is close to identifying the physical basis of mind. Such claims have major implications not only for medicine but also for policies and

practices dealing with normal and abnormal human conduct, and for conceptions of personhood. The significance and consequences of these developments are strongly debated, with some authors arguing that we now know enough to understand the neural bases of human selfhood and higher mental functions [117] [118], while for others, the neuroreductionist model attributes capacities to brains that can only properly be attributed to persons [119] [120]. Some have suggested that progress in neuroscience will lead to radical improvements in our ability to treat psychiatric disease [121] [122]; others are more doubtful [123] [124]. Although functional imaging has been crucial in the development of new conceptualisations of human mental states, many leading researchers remain highly critical [125].

Meanwhile, studies of the neural basis of higher brain functions have fed scientific and semi-popular debates about ideas of personhood [126] [127] [128] and free will [129] [130] [131] while studies combining psychophysics and brain imaging (e.g., [132] have encouraged philosophers to readdress the eternal mystery of conscious awareness. The capabilities developed by the HBP will provide new material for these debates.

The public, dialogue and engagement. Attempts to achieve public dialogue and engagement during the development of new technologies [133] [134] have used a range of methods and approaches [135] including consensus conferences, citizen juries, stakeholder workshops, deliberative polling, focus groups and various forms of public dialogue. The motivations for such exercises [111] [136] [137] are sometimes normative – citizens affected by research have a right to participate in crucial decision-making – sometimes instrumental. Many authors have argued, for instance, that dialogue can reduce conflict, help to build trust and smooth the introduction of innovative technology. The strongest conclusion from these debates is that not even the best prepared exercises can comprehensively represent the positions of all parts of society or resolve the issue of which groups or opinions should have most weight in a particular decision. It is important, therefore, that such exercises respect scientists' legitimate desire to inform the public about their research, while avoiding self-conscious attempts to steer public opinion in a particular direction. Experience from other areas of emerging technology research shows that this requires a sensitive approach [138]. Public engagement exercises are successful only if participants are convinced that they can genuinely influence the course of events [139].

Methods such as consensus conferences, scenario workshops and citizen's hearings have developed and spread since the late 1980s, allowing for technology assessment institutions to act as 'knowledge brokers' among science, society and policymakers [140]. One motivation for using participatory methods concerns normativity in science-based policy advice. Expert methods to support decision-making, often overlook or simplify complex contextual factors such as policy trends and societal values [141] [142]. The "laws of progress" built into scientific forecasting methods presuppose a linear societal development and cannot embrace the complexity of factors influencing a society over time [143]. To gain relevance, objective scientific knowledge must be "contaminated" by normative evaluations, incorporating the complexity at stake [144]. The import of norms into science must happen in a transparent and socially responsible way. Including citizens in the evaluation of societal development means that scientific advice is supplemented by the tacit knowledge of those affected by political decisions [134]. This tacit knowledge often reveals blind angles in science-based scenarios and administrative thinking. Today, inclusion of citizens' perspectives is often seen as necessary for maintaining the legitimacy of science in society and science-based policy [145].

Researcher awareness. Ethical issues cannot be reduced to algorithms or prescriptions; moral statements and positions always require higher-level ethical reflection and justification. From an ethical point of view, this reflection will come not just from external "ethical experts", but also from researchers and their leaders. This kind of general reflexivity is currently not the norm and is likely to meet resistance. It is nevertheless a key component of Responsible Research and Innovation [146]. Studies suggest that the best way

to achieve it is to raise researcher awareness in governance structures [147]—a technique already applied in other areas of cutting-edge technical research, notably nanotechnology (http://www.nanocode.eu) [148] and synthetic biology..

Governance and regulation. Today's science regulatory environment is a result of past research that provoked a vigorous social and governmental response [149].One example is animal research, in which the response took the form of The Council of Europe's Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (ETS 123) (1985), and the EU Directive for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes [150] – documents that have set European standards for the laboratory use of mice and other vertebrates. Another more recent example is synthetic biology. In this case, the reaction came only after a private institution had created the first self-replicating bacterial cell from a completely synthetic genome [108].

Modern governance of innovation in biotechnology involves a variety of actors, including research organisations, national and supranational regulators, governmental or quasi-governmental organisations, professional bodies, publishers of science journals, and representatives of the mass media and public opinion. As Gottweis [151] noted for the case of transnational research on embryonic stem cells, decision-making takes place "… at the fuzzy intersection between science, society, and politics". This is complicated, in the case of international projects, by the need to take account of different national jurisdictions.

There are many research initiatives in a number of countries exploring the problems and strategies for data protection in an era experiencing an unprecedented explosion of networked personal data and of other online sensitive data that is potentially insecure. Most accept that absolute security, confidentiality and secrecy cannot be assured by technological means, however advanced, and that, in the case of medical data, informed consent, while necessary, is highly limited as it is impossible to fully inform data subjects of all potential current and future uses of their data. Hence most researchers and experts suggest that the best approach is multifaceted and multi-layered, involving consent, technological protections and robust procedures for data governance. The Foresight Lab, in conjunction with the Ethics Manager and the EAB, will continue to review the emerging legal and regulatory regimes in Europe and to evaluate the potential implications of the diverse data governance regimes currently in use or proposed to identify best practice for the HBP.

A1.14.3 SP12: Advances over State of the Art

Foresight as anticipatory knowledge and capacity building. The HBP Foresight Lab is testing new approaches for integrating responsible research and innovation with emerging biotechnologies. The Foresight Lab will begin a multi-institutional process of capacity building, both within the HBP and with relevant constituencies outside. It will consider questions of institutions, research and innovation systems, business and investment strategies and their implications, public values (including those of consumers and patients), and challenges for governance. The Foresight Lab will use an iterative process in which the views and priorities of different communities interact with one another in an expanding dialogue, and feed back into the direction, management, and priorities of HBP researchers. This represents a significant advance beyond the current state of the art.

Conceptual and philosophical issues. SP12 applies neuroscientific and medical analysis to the philosophical analysis of core concepts such as the mind-brain relationship, consciousness, self-awareness, human identity and simulation, enhancing the explanatory power of these concepts. This approach is already producing results of strong theoretical, societal and clinical relevance; one example is an assessment of the role of simulation as a scientific method in neuroscience and of the way simulation can increase our understanding of residual conscious function in patients with disorders of consciousness. Conceptual and

philosophical analyses will help the HBP to interpret the results of neuroscientific experiments and models. They will also draw attention to the implications, e.g., changes in our understanding of human identity, self-hood, personhood, and the relationship between mind and body.

Public, dialogue and engagement. The HBP will adapt its stakeholder and citizen involvement activities to specific issues that arise during the Project. Rather than having stakeholders debate HBP from afar, SP12 will facilitate direct interaction between citizens and HBP researchers. The results will be concrete enough to directly impact the work of the Project.

Researcher Awareness. Researcher awareness and reflection is recognised as a key component in all responsible innovation activities. SP12 will tailor methodologies proposed in contemporary discussions of Responsible Research and Innovation (RRI), to the needs of the HBP. Increased awareness of RRI will facilitate communication related to individual and collaborative research interests, and will contribute significantly to the HBP's success.

A1.14.4 SP12: Operational Objectives and Related Actions

SP12 is the hub of responsible research and innovation (RRI) in the HBP. It undertakes foresight research on social, ethical, legal and cultural implications of HBP research, explores conceptual and philosophical issues and challenges raised by HBP research, builds awareness and capacity for social and ethical reflection among HBP researchers, engages HBP researchers with external stakeholders and the general public, and supports the robust management of ethical issues of the HBP as a whole. SP12 will collect and develop good practice in RRI.

Its approach overall has four interlinked components: anticipation (of future implications, based on research); reflection (activities to enhance ethical and social awareness and reflection among HBP researchers; engagement (engaging, disseminating and debating HBP research with stakeholders and the general public); action (ensuring the results of these activities help shape the direction of the HBP itself in ethically robust ways that serve the public interest).

Three concrete overall objectives of SP12 to which all SPs will be relating to are:

- Privacy and data protection
- Ethics of simulation
- Mind and Brain disorders

Key activities of SP12 will be:

Foresight Analyses and Researcher Awareness

- Undertaking foresight studies on key aspects of the HBP
- Working with scientists and other members of the HBP to reflect on ethical, social and regulatory issues

Neuroethics and Philosophical Analyses

- Exploring the role of contexts and cultural imprinting in understanding the brain's functional architectures
- Investigating philosophical and ethical challenges of modelling cognitive processes in silica

Public Engagement & Communication

- Undertaking citizen dialogue and consultation

- Engagement between HBP scientists and external stakeholders in "Stakeholder Forums" on issues of possible controversy

Ethics Management

- Developing Principles and Implementation of Ethics Management including Standard Operating Procedures and mapping ethical issues of the HBP
- Ethics Compliance Management
- Supporting relevant groups such as the Ethics Advisory Board and Ethics Rapporteur Programme.
- Details of the various activities of SP12 have been provided to the EC and the reviewers via the response to the January 2015 Ethics Review. Section 2.5.2 of this document contains further details of the work to be undertaken in SP12 and the substantive ethical and social issues to be addressed.

A1.14.5 SP12: Main Objectives & Deliverables per SGA

SP12 deliverables consist of reports on activities, detailing the main outcomes and results achieved by SP12 work packages, and "opinions" reports formulating SP12 observations and recommendations about ethical and social issues arising during the course of HBP. SP12 will deliver one report of each type per year.

SGA	Deliverable	Due date
SGA-1	SP12 first "opinions" report	End of SGA-1 Y1
	SP12 second "opinions" report	End of SGA-1 Y2
	SP12 first activities report	End of SGA-1 Y1
	SP12 second activities report	End of SGA-1 Y2
SGA-2	SP12 first "opinions" report	End of SGA-2 Y1
	SP12 second "opinions" report	End of SGA-2 Y2
	SP12 first activities report	End of SGA-2 Y1
	SP12 second activities report	End of SGA-2 Y2
SGA-3	SP12 first "opinions" report	End of SGA-3 Y1
	SP12 second "opinions" report	End of SGA-3 Y2
	SP12 first activities report	End of SGA-3 Y1
	SP12 second activities report	End of SGA-3 Y2
SGA-4	SP12 first "opinions" report	End of SGA-4 Y1
	SP12 second "opinions" report	End of SGA-4 Y2
	SP12 first activities report	End of SGA-4 Y1
	SP12 second activities report	End of SGA-4 Y2

Table 39: Main Objectives / Deliverables per SGA for SP12: Ethics & Society

A1.14.6 SP12: Collaborations with other National, European and International Initiatives

SP12 is already in contact with groups studying ethical and social issues, on behalf of other large brain initiatives, in particular the US BRAIN initiative and is working to expand these contacts.

A1.14.7 SP12: Impact and Innovation Potential

Scientific Impact

IMP12.1: SP12's Foresight Lab will inform the debate on the social and economic implications of HBP research helping to allay groundless fears, while identifying areas of genuine concern.

IMP12.2: SP12 will have an important impact on the emerging academic debate around the conceptual and ethical implications of recent neuroscience research, in particular of brain simulation.

Social and Economic Impact

IMP12.3: SP12 will build public awareness of the economic and social potential of HBP research and encourage public participation in priority setting and decision-making. Public acceptance of and participation in the Project is a pre-condition for effective commercial exploitation of Project results.

Innovation Potential

IMP12.4: SP12 will contribute to the Project's innovation potential indirectly, by making the public aware of the potential of new computing technologies and new approaches to the diagnosis and treatment of brain disease.

A1.15 Integration of Core and Partnering Projects

Integrating Partnering Projects is of central importance for the HBP, enabling the HBP to take on board the latest advances in science and technology as the Core Project moves forward, and keeping the project open to Partners across Europe for the entire duration of the Project.

The key idea underlying Partnering Projects is mutual benefit: Partnering Projects should benefit from the Platforms and the other capabilities made available by the HBP; the HBP should benefit from the novel know-how, technologies and ideas brought in by the Partnering Projects.

In many cases, Partnering Projects will be projects that have already been evaluated and already have funding from national funding agencies or other sources. In these cases, the funding agency or the project itself will request that the HBP gives the project the status of a Partnering Project, and integrate its work in the HBP subprojects.

The HBP will also work with FLAG-ERA and successor projects, national research funding agencies (NRFOs) and JTCs, to develop Calls for Proposals and other mechanisms to generate new project proposals, directly targeting Actions listed in the HBP Research Roadmap.

Finally, the HBP will provide support to research institutions in the Member States and the Associated Countries who wish to develop independent proposals for submission to national, EU, national or other potential sources of funding.

Relevant Core Project SP Leaders, a CP Principal Investigator and the HBP PCO will examine proposals and assess the benefits new Partnering Projects would offer the HBP, and the HBP's ability to provide them with the capabilities they require. Where necessary, the relevant SP Leaders, with the help of the HBP PCO, and the Partnering Projects will negotiate adjustments to ensure the maximum mutual benefit. At the end of this process, the SP Leaders and the HBP PCO will formulate a recommendation to the SIB, which will be formally responsible for the approval of new Partnering Projects. However, the SIB may

delegate this responsibility to a smaller committee of the SIB to facilitate the approval procedure.

The HBP will make a concerted effort to give as much support as possible to Partnering Projects and to give them the maximum possible support. Planned measures include the nomination of an HBP call/project integration manager; support for FLAG-ERA and similar initiatives generating transnational calls, communication to NFROs, prospective project consortia and researchers; promotion of PPs to other relevant European initiatives such as IMI, to pan-European R&D consortia such as EUREKA, and to programmes such as Eurostars; promotion of PPs to HBP SP Leaders; and measures to give visibility to new and existing PPs

Once Partnering Projects have been approved, HBP Central Services will ensure their smooth integration into the HBP. Key steps include the signature of Memoranda of Understanding, administrative integration (assignment of access rights on HBP systems subject to legal vetting, EMDESK integration, legal, data security, etc.); information to the EC Project Officer, the SIB, the Directorate, and the management team in the PP; a public announcement on the HBP Portal; information to relevant WP and Task Leaders; implementation of a plan for the integration of the PP in the HBP; showcasing of PPs through the Annual HBP Summit and through other dissemination channels. Partnering Projects that are highly successful in a particular phase of the HBP may be invited to become members of the CP in the next phase.

For more information on Partnering Projects, see Appendix 2: Partnering with the Human Brain Project Flagship.

Appendix 2: Partnering with the Human Brain Project Flagship

This document is largely complete, but cannot yet be considered final, requiring clarification of the agreements to be concluded between the HBP and other parties. It will be regularly updated as experience is acquired on the selection and integration of Partnering Projects in the Flagship.

Contents

A2.1 An Introduction to HBP Partnering Projects

A2.2 Current HBP priorities for Partnering Projects

A.2.3 What are Partnering Projects (PPs) and Associated Members (AMs)?

A2.4 What are the eligibility requirements for becoming PPs and AMs?

A2.5 What are the selection criteria and procedures of PPs/AMs?

A2.6 What are the integration mechanisms of selected PPs in the HBP Flagship?

A2.7 What are the benefits of AMs in the HBP Flagship?

A2.1 An Introduction to HBP Partnering Projects

The Human Brain Project (HBP) Flagship[2] was launched in October 2013 as a 10 year-long initiative with a 1 billion Euro budget. It will develop a number of ICT Platforms for neuroscience, medicine and computing that will catalyse collaborative effort to better understand the brain and its diseases and emulate its computational capabilities. The platforms will provide neuroscientists with open data access and data analysis capabilities to brain research data from all over the world.

As a means of achieving its goals and expected impact on the European economy and society, there is a need for HBP to leverage available resources in Europe and build a scientific and technological research community that extends beyond the HBP Core Project (CP) Consortium.

The concept of a Partnering Project (PP) was introduced in the Flagship model, to define the principles by which additional relevant research activities can be integrated into the HBP Flagship initiative. The aim is to provide flexible and efficient mechanisms to perform research and innovation activities that will be in line with the overall Flagship objectives and be of mutual benefit to the research roadmap. In the Flagship model, the CP is funded by the European Commission (EC) under Horizon 2020 and its budget corresponds to half of the budget of the whole initiative. The other half would come mainly from the Member States and possibly the private sector, through the financing of Partnering Projects at regional, national or transnational level and also through in-kind contributions to the Flagship[3]. For a comprehensive presentation of the Flagship model, including the concepts of Core Project and Partnering Projects, please see http://ec.europa.eu/information_society/newsroom/cf/dae/document.cfm?action=display&doc_id=8204. PPs and their partners, who become Associated Members (AMs) of the

[2] https://www.humanbrainproject.eu/

[3] Such in-kind contributions, from organisations in the Core and Partnering Projects, include access to research infrastructures, experimental facilities and use of technical equipment, extra personnel, etc.

Flagship, bring new knowledge, new competencies, new ideas and new resources to the HBP Flagship. PPs and AMs are an integral part of the Flagship and contribute to its overall scientific and technological (S&T) agenda by performing research and innovation activities in cooperation with the CP Consortium. By becoming part of the HBP Flagship, PPs/AMs may have access to and contribute to the Flagship's Research Infrastructure (once related IP issues and other legal matters have been resolved) and engage with the CP Partners in future planning and research road mapping activities of the Flagship.

A2.2 Current HBP priorities for Partnering Projects

In its initial phase, HBP aims to build up large user communities of its ICT platforms, i.e., by teaming up with end-user partners. HBP also seeks partnerships with large projects generating neuroscience data to be integrated in the HBP ICT platforms and be largely shared and used by neuroscientists. Moreover, strategic partnerships with large-scale initiatives in neuroscience, medicine, and computing will be important for consensus building and the strategic development of the ICT platforms and, more broadly, the HBP research roadmap.

A.2.3 What are Partnering Projects and Associated Members?

A2.3.1 Partnering Projects

A Partnering Project (PP) is a research or innovation activity whose objectives are relevant to the HBP Flagship's research roadmap.

PPs contribute to the implementation of the HBP research roadmap by performing research, innovation and networking activities of mutual interest in cooperation with members of the HBP CP, including:

- Research that adds novel capabilities to the ICT platforms;
- Research that uses the ICT platforms to address previously intractable issues in neuroscience;
- Develop novel computing and robotics technologies and applications;
- Improve understanding, diagnosis and treatment of brain disorders;
- Use the ICT platforms to innovate in any field profiting from technology and tools developed by the CP.

These PPs:

- May involve one or more entities (e.g., public or private organisations, etc.), i.e., they may be multi-partner collaborative projects or single-partner projects;
- Are funded by regional, national or European public research funding bodies or other sources (e.g., private industry, donors, etc.), for example, the Joint Transnational Call (JTC) by the FLAG-ERA ERANET, or the follow-up action under H2020;
- Are selected by the HBP;
- Can include partners that are already members of the CP Consortium.

A2.3.2 Associated Members

Members of a PP become Associated Members (AMs) of the Flagship. AMs can apply as far as they come with an own, publicly or privately funded, research project (the candidate PP), contributing to the HBP Flagship's S&T roadmap and objectives.

An overview of such benefits is provided in a table at the end of the Annex.

PPs facilitate the achievement of the S&T targets of the Flagship and promote the alignment and information flow between the CP and related national and regional activities. They help create synergies between the CP and activities receiving funding at regional, national or transnational level. This openness is key to the Flagship's abilities to remain agile and at the cutting edge of S&T developments.

All the procedures described in this document apply to all kinds of PPs.

A2.4 What are the eligibility requirements for becoming PPs and AMs?

There are two eligibility requirements for becoming candidate PPs:

- The projects and their partners have already their own funding or can demonstrate that they will soon have it.
- The projects significantly contribute to the Flagship's strategic research roadmap.

A2.5 What are the selection criteria and procedures of PPs/AMs?

Candidate PPs are selected based on their level of complementarity and added expertise with respect to the existing competencies and future needs of the HBP Flagship.

The specific selection criteria are:

- Relevance of the scientific and technological objectives to the HBP Flagship work plan and roadmap;
- Complementarity and added value in terms of scientific, technological or innovation expertise and know-how;
- Potential contribution to the HBP ICT platforms;
- Potential for spreading excellence and widening participation across Europe or internationally;
- Ease of integration of the proposed activities within the HBP Flagship;
- Respecting ethics guidelines, dual use declaration and non-military application requirement.

A2.6 What are the nomination, application and selection procedures for Partnering Projects?

Candidate PPs may be identified by:

- The HBP CP members
- The European Commission (EC)
- The national and regional funding agencies
- Their own initiative.

Members of a candidate PP are advised to contact the HBP Flagship Project Coordination Office prior to the submission of the formal application. The HBP Flagship Project Coordination Office is the main contact point for obtaining information about the application and association process. The contact email is relations@humanbrainproject.eu.

Candidate PPs that have been nominated by the EC, national bodies or the CP partners should submit an application as described below. Spontaneous applications from projects or (public or private) organisations interested in associating with the HBP Flagship are also accepted and should follow the same procedures. A Partnering Project Leader (typically the PP's scientific coordinator) is responsible for the preparation and submission of the application.

A2.6.1 Application procedures

Applications for becoming a PP and AM are submitted to the HBP Project Coordination Office. Applications are accepted on a continuous basis and there is no submission deadline.

Each application shall consist of maximum four A4 pages comprising:

1) Title, source of funding (EC, National, Regional, other), duration and total amount of funding of the existing project;
   In case of a nomination by an EU, or national/Regional funding agency, the name of the responsible project officer should be included;
2) The name and contact information of the Partnering Project Leader or Coordinator; The name and contact information of the Partnering Project Ethics Rapporteur;
3) The motivation for joining the Flagship as a PP;
4) A description of how the research conducted by the applicants in their project aligns and complements the activities of the CP, and a description of how the applicants will facilitate alignment and information flow with the CP;
5) The Subproject(s) where the applicants would like to see their activities integrated;
6) A list of the entities that wish to be associated with the Flagship, with names of Principal Investigators;

Applications can be shorter than 4 pages, provided they contain all the information requested above, and that the information is sufficient for the appropriate HBP governing body to take a decision.

A2.6.2 Selection Procedure

Applications are reviewed by CP representatives, typically the relevant Subproject Leader(s) or deputy Leader(s) and another Principal Investigator, working in a related area of research, as well as the HBP PCO. They provide a recommendation to the HBP Science & Infrastructure Board (SIB - see 2.3.2.5.5) on whether the project should become a PP with a short explanation. In case of nominations by the EC or national funding agencies, the relevant programme manager may also be consulted. Based on the recommendations, the HBP Science & Infrastructure Board makes the final decision and appoints the PP and its AMs. The SIB may delegate this approval responsibility to a smaller committee of the SIB.

Applicants will be informed of the decision by the Project Coordination Office in writing or by electronic mail. The new PP and AMs will formally join the HBP upon signature of a Memoranda of Understanding. Additional agreements may need to be signed between AMs and relevant HBP Core Project Partners. Once the HBP Legal Entity is established, agreements may need to be signed with such HBP Legal Entity.

If the application is not approved, the applicants will receive a note explaining such decision.

At least once per year, the Project Coordination Office will inform the Member States and the EC of the applications received and the results of the evaluation.

Partnering Projects selected from a Joint Transnational Call on HBP

All those projects that are successful from a FLAG-ERA Joint Transnational Call (JTC) on HBP (under FP7 or Horizon 2020) are natural candidates to become PPs of the HBP Flagship. These projects have provided the information for the association with HBP when they submitted their proposal to the JTC. Their potential to become PPs was checked by the evaluators of the JTC through an explicit evaluation criterion. Therefore, successful JTC projects are expected to become PPs of HBP. The information they submitted to the JTC for the association with HBP is then sent to the HBP Project Coordination Office for final consideration by the HBP CP Consortium. The feedback of the Flagship is communicated shortly. HBP may raise objection to such association in few, very well justified cases.

A2.7 How will Partnering Projects and Associated Members be integrated into the Flagship?

Until the creation of the HBP Legal Entity, when a PP has been approved by the Science & Infrastructure Board, the AMs are expected to sign Memoranda of Understanding (outlining a set of principles that will govern the interaction between the HBP Core Project and the Partnering Project), as well as Confidentiality terms and Conditions. Depending on the evolution of the HBP, the new Consortium Agreement, and the Legal Entity, AMs may need to adhere to further terms and conditions, or enter into agreements as appropriate.

If appropriate, agreements may also be established between AMs and Core Project partners. Such agreements will have to take into consideration the rights of CP partners, as well as the relevant grant agreements or existing Consortium agreements. AMs may be requested to sign additional confidentiality undertaking before participating in a particular project activity.

Once approved, the PPs and their AMs are encouraged to actively engage in cooperation with the relevant partners of the HBP CP Consortium. This may include, but is not limited to:

- Research collaborations in areas of mutual interest and in accordance with the Specific Grant Agreements supporting the respective projects;
- Exchange of information, data and material in accordance in particular with confidentiality and intellectual property agreements in place;
- Networking and training activities;
- Identification of future opportunities for collaboration;
- Engaging in road mapping and planning activities.

Possible general benefits of Partnering Projects and their Associated Members (may be subject to agreements):

- Access to and ability to contribute to the Research Infrastructure (once related IP issues have been resolved).
- Visibility due to involvement in the HBP Flagship
- Contributing to the effort of addressing one of the grand challenges of the 21st century
- Insight on HBP methodologies, research roadmaps, and discoveries
- Access to HBP communication tools and dissemination activities
- Direct exchange of insights and ideas with the broad HBP Consortium through access to a strong and large European and international network

- Participation in HBP workshops, conferences, meetings, and annual summit
- Contribution to the evolution of the research roadmap of the Flagship (parts not covered by the CP)
- Possibility to influence research topics called by Member States, e.g. transnational calls

Benefits of being an Associated Member may be summarized as follows:

Benefits	Non-Member	Associated Member	Core Project Partner
Participation in open activities	Yes	Yes	Yes
Publications listed on HBP web page	No	Yes	Yes
Job listings published on HBP web page	No	Yes	Yes
Coverage of activities of the Partnering Project by Flagship Science Writer/Communications Officer	No	Yes	Yes
Included in the Flagship mailing list	No	Yes	Yes
Direct invitation to industrial workshops (priority access)	No	Yes	Yes
Direct invitation to Flagship conferences and schools (priority access)	No	Yes	Yes
Inclusion of results from the Partnering Project in Deliverable Reports to the EU	No	Yes[4]	Yes
Attendance at HBP Summit	No	Yes	Yes
Participation in confidential S&T activities	No	Yes	Yes
Attendance at Core Project meetings	No	Yes	Yes
Access rights to foreground and background	No	No[5]	Yes
Direct funding from the core project	No	No	Yes

Table 40: Benefits of Participating in the HBP as a Partnering Project

A2.8 Potential Research Areas for Partnering Projects

A2.8.1 SP1: Mouse Brain Organisation

Physiological Data: collect targeted physiological data going beyond the data sets collected in the Core Project; candidate data sets include data on whole brain dynamics neuroendocrinology and neuroimmunology, metabolism and energetics, microcircuit dynamics and information processing, the physiology of neurons and synapses, receptor and channel biophysics, and gene expression.

From Genes to Cognition: Perform experimental and informatics studies on the link between genes and cognition and the impact of normal genetic variations and mutations; develop links to human brain disease signatures established in SP8 and to human work in SP2.

Functional Architectures of Cognition: Collect data on functional architectures of cognition in mouse; possible themes include multi-modal perception and action, motivation,

[4] Inclusion of published results by permission only. Work not funded by the CP will be clearly identified.

[5] Unless otherwise agreed in an agreement.

reward and decision making, synaptic plasticity, learning, memory and goal-oriented behaviour, representations of space time and quality in planning and navigation, and the architecture of gene-behaviour-environment interactions.

Comparative studies: Perform research comparing structural and physiological data in mouse, humans and other animals (joint work with SP2).

For more details on SP1, see A1.4 Subproject 1: Mouse Brain Organisation.

A2.8.2 SP2: Human Brain Organisation

Physiological Data: Collect targeted physiological data going beyond the data sets collected in the Core Project; possible data sets data on whole brain dynamics, neuroendocrinology and neuroimmunology, metabolism and energetics, microcircuit dynamics and information processing, the physiology of neurons and synapses, receptor and channel biophysics, and gene expression, as well as pharmacology.

From Genes to Cognition: Perform experimental and informatics studies on the link between genes and cognition and the impact of normal genetic variations and mutations; develop links to human brain disease signatures established in SP8 and to human-related work in SP1.

Functional Architectures of Cognition: Collect data on functional architectures of cognition in humans; possible themes include multi-modal perception and action; motivation, reward and decision making; synaptic plasticity, learning, memory and goal-oriented behaviour; representations of space time and quality in planning and navigation; the architecture of gene-behaviour-environment interactions. Study their dynamics and plasticity, e.g. with respect to pharmacological intervention.

Comparative studies: perform research comparing structural and physiological data in mouse, humans, non-human primates, and other animals (joint work package with SP1).

Neuron-glia vasculature system: Perform experimental and informatics studies on the link between neurons, glia and vasculature at different levels of brain organization including the cellular, microscopical level and the level of large cognitive systems.

Development and aging: Perform neuroimaging, physiological and other studies to examine the dynamics of brain organization throughout the whole lifespan for answering basic neuroscience questions.

A2.8.3 SP3: Systems and Cognitive Neuroscience

SP3 forms the Systems and Neuroscience component of the HBP Core Project under the FPA. It comprises four scientific Work Packages, each of which will contains no more than five Tasks. The scientific focus of these WPs will not be on the following research themes:

- Invariant object recognition
- Interaction between multisensory perception action and episodic memory (encoding and retrieval)
- Multi-scale organization of slow-waves and related features of brain state dynamics
- Neural mechanisms of consciousness.

Technically, Partnering Projects will be able to interface with SP3 in the following areas:

- Pharmacological modulation of cortical circuits and cognition
- Ensemble (multi-neuron) recordings and 2-photon imaging in relation to behaviour and cognition

- Electrocorticography and local field potential analysis
- Interventional techniques in humans and mice, such as transcranial magnetic stimulation (TMS) and optogenetics
- Genetic manipulations in relation to behaviour and cognition
- Computational modelling of cognitive processes
- Neuromorphic computing and robots performing cognitive tasks.

For more details on suggested research themes for SP3, see section A1.6 Subproject 3: Systems and Cognitive Neuroscience.

A2.8.4 SP4: Theoretical Neuroscience

Model Development: Develop theory-driven models of brain function suitable for implementation on the Brain Simulation, Neuromorphic Computing or Neurorobotics Platforms; use the Platforms for *in silico* experiments validating and refining the models; possible themes include but will not be restricted to perception-action, surprise, novelty, multi-sensory integration, decision making, goal-oriented behaviour, reward, wakefulness, sleep, dreams and the wake-sleep cycle, learning and memory, working memory, declarative memory, skills and habits, symbols and language (development in conjunction with SP9 and SP10).

Novel brain-inspired concepts for information processing: develop HPC architectures inspired by theoretical and experimental insights into the structure and function of the brain (joint work package with WP7 and WP8).

Disease modelling: develop theory-driven models of disease from the biological signatures of disease and the disease classifications identified by researchers using the Medical Informatics Platform (joint work package with SP6 and SP8).

A2.8.5 SP5: Neuroinformatics Platform

Methods and tools: develop methods and tools expanding the functionality of the Neuroinformatics Platform and integrate them into the Platform; possible tools include tools and methods for the analysis of large volumes of structural brain data (e.g., image stacks) and for the analysis of large volumes of functional data.

Sensory organs, the spinal cord and the peripheral nervous system: expand the mouse and the Human Brain Atlases to accommodate data on sensory organs, the spinal cord and the peripheral nervous system in mouse and in humans; generate initial data sets to populate the expanded atlases.

Atlases for other species: create multi-level atlases for the brains of species not covered by the HBP Mouse Brain and Human Brain Atlases on the Neuroinformatics Platform; integrate the atlases with the HBP Mouse Brain and Human Brain atlases, enabling cross-species comparisons.

A2.8.6 SP6: Brain Simulation Platform

Tools, methods and workflows: develop tools, methods and workflows expanding the functional capabilities of the Brain Simulation Platform; possible topics include new techniques for multi-scale simulation, new simulation engines and enhancements to existing engines, new tools for data analysis and visualisation, and virtual instruments (in silico molecular imaging, large-scale synaptic imaging, whole-brain in silico electrical recording, in silico optogenetics, virtual MRI, DTI, and PET).

Brain reconstruction: develop high-fidelity reconstructions of specific regions of the mouse or human brain, or of specific levels of biological organisation not fully covered by HBP

models; create high-fidelity reconstructions of the brains of species not covered by the HBP; create data-driven models of sensory organs or the spinal cord.

***In silico* neuroscience:** use the Brain Simulation Platform (where necessary, in combination with the Neuromorphic Computing or Neurorobotics Platforms) for in silico experiments in basic neuroscience, cognition and behaviour.

Disease and drug simulation: use biological signatures of disease from the Medical Informatics Platform and simulation capabilities from the Brain Simulation Platform to gain new clinical insight; possible themes include mechanisms of disease causation, mechanisms of action of known therapeutic agents, and screening of drug candidates (joint work package with SP8).

Other Applications of Brain Simulation: Develop other applications of brain simulation of commercial and/or clinical value; examples include fast prototyping of new experimental methods; fast prototyping of neuroprosthetic devices, etc.

A2.8.7 SP7: High-Performance Analytics & Computing Platform

Technologies and architectures: develop supercomputing technologies and architectures meeting the specific requirements of brain simulation and expanding the capabilities of the High-Performance Analytics & Computing Platform; possible themes for research include novel solutions for multi-scale simulation, novel solutions for resiliency, fault tolerance and self repair; new hardware/software solutions for memory and I/O hierarchies, new interconnect architectures; joint work with WP6.9 for HW/SW co-design.

Software, algorithms and numerical methods: develop software, algorithms and numerical methods that meet the specific requirements of brain simulation and expand the capabilities of the High-Performance Analytics & Computing Platform; joint work with WP 6.8 for HW/SW co-design

Hybrid HPC-neuromorphic architectures: develop conceptual designs for hybrid HPC-neuromorphic computing systems for energy efficient, accelerated simulations in neuroscience; demonstrate feasibility using the Neuromorphic Computing Platform and the HBP Platform; possible architectures include hybrid systems linked across networks, on-board hybrids, on-chip hybrids (Neuromorphic cores) (joint work package with SP9).

Novel brain-inspired concepts for information processing: develop HPC concepts inspired by theoretical and experimental insights into the structure and function of the brain (joint work package with SP4 and SP6).

A2.8.8 SP8: Medical Informatics Platform

Clinical studies: use the data and analysis tools provided by the Platforms to gain new insights into the diagnosis, and classification of brain disorders and to identify potential targets for treatment; studies may include cluster analysis of data from retrospective studies, analysis of changes in disease signatures at different stages in disease progression, re-analysis of data from clinical trials and epidemiological studies (e.g. measure impact of common genetic and/or environmental risk factors)

Disease and drug simulation: use data from the Medical Informatics Platform and simulation capabilities from the Brain Simulation Platform to gain new clinical insights; possible themes for research mechanisms of disease causation, mechanisms of action of known therapeutic agents, and screening of drug candidates (development in conjunction with SP6).

Services for personalised medicine: use the capabilities of the Medical Informatics Platform to develop and trial new services for personalised medicine: personalised diagnosis and quantitative prognosis, personalised treatment, etc.

Methods and tools: develop and integrate new tools and methods contributing to the capabilities of the Medical Informatics Platform; possible tools and methods include integrated machine learning, data mining, and data intensive analysis for the identification of clusters in large volume of data.

A2.8.9 SP9: Neuromorphic Computing Platform

Applications for neuromorphic computing: use the NM-PM and NM-MC systems to demonstrate applications of Neuromorphic Computing Systems; potential application areas include pattern detection in spatio-temporal data streams, finding causal relations in big data, data mining, temporal sequence learning, approximate computing; feed back the results for further development and feature upgrades of the Neuromorphic Platform systems.

Portable hardware systems for neuromorphic computing: use the NM-PM and NM-MC systems to derive specialised and resource efficient neuromorphic circuit architectures for custom, special purpose low-power, compact, low-cost hardware implementations as neuromorphic cores or complete stand-alone systems; application areas include robotics, automotive, manufacturing, telecommunication.

Devices for neuromorphic computing: develop and evaluate new device technologies for neuromorphic computing; simulate, construct and evaluate small- scale demonstrator systems; evaluate integration into the HBP Neuromorphic Platform systems; possible themes for development work include resistive memories, magnetic memories, organic devices, 3D Integration, and distributed powering.

Hybrid HPC-neuromorphic architectures: develop conceptual designs for hybrid HPC-neuromorphic computing systems for energy efficient, accelerated simulations in neuroscience; demonstrate feasibility using the Neuromorphic Computing Platform and the HBP Platform; possible architectures include hybrid systems linked across networks, on-board hybrids, and on-chip hybrids with Neuromorphic cores.

A2.8.10 SP10: Neurorobotics Platform

Software, tools and technologies: develop software, tools and technologies that expand the capabilities of the Neurorobotics Platform; possible themes include the high-performance, high-fidelity simulation technologies for robots and their environments.

Embodied neurorobotics: perform research on the physics and function of bodies (bones, muscles, tissue), sensors (vision, audition, touch, balance) and peripheral nervous system (spinal cord) and integrate the results into the Neurorobotics Platform.

Social neurorobotics: expand the Neurorobotics Platform to enable experiments involving interactions among multiple neurorobotic systems.

Neurorobotics as a tool for in silico neuroscience: use neurorobotic systems to perform in silico experiments investigating fundamental issues in basic neuroscience, cognition and behaviour.

Applications: use the Neurorobotics Platform to develop applications of commercial or clinical value; possible applications include applications in manufacturing and mechanical engineering, personalised neuro-prosthetics and neuro-muscular controllers, robots for healthcare, robotic vehicles, and robots for domestic applications.

A2.8.11 SP11: Central Services

No Partnering Projects are anticipated in this SP.

A2.8.12 SP12: Ethics and Society

Ethical, conceptual and philosophical issues: perform research on ethical, conceptual and philosophical issues, going beyond the research already planned within the Core Project.

Public outreach: organise outreach activities to promote public debate and participation on issues related to HBP research.

Appendix 3: White Paper "Transforming the Human Brain Project Platforms into a Community-Driven Infrastructure for Brain Research

A3.1 Preamble

In the following White Paper, we discuss how the Human Brain Project's Platforms will be transformed into a community-driven infrastructure for brain research.

The white paper proposes how part of the research agenda of the HBP is transformed into a research infrastructure. Because of time constraints the development starts within the project, but in the mid- to long term, external users will help drive the HBP research infrastructure as well.

A3.2 Background and Significance

In this White Paper, we discuss how a community-driven research infrastructure (RI) for brain research, including cognitive and systems neuroscience, as well as ~~other~~ brain-inspired sciences such as future computing will be built from the Human Brain Project (HBP) information technology (IT) Platforms. Close interaction with the global neuroscience community will be key to its success — from defining the RI's strategic goals, to measuring how well it performs. Building the RI will require a new organisation for the HBP that clearly distinguishes RI development and operations from internal and external research projects. As an overarching goal, we will try to closely link external and internal neuro-research, so that a world-leading RI in neuroinformatics, data-driven brain modelling, brain simulations, neurorobotics, and medical informatics can emerge. The RI will bring together, and build on, advanced concepts of data-centric, high-performance and neuromorphic computing. As with comparable RI projects in other domains, such as the European Organisation for Nuclear Research (CERN) for high-energy physics, the technological developments within the RI promise to advance the state-of-the-art in information and communications technologies (ICT). The HBP realises that engagement with user communities is an integral part of responsible research and innovation, which is a requirement of the European Commission but also an important component of ensuring public and political acceptance of any large scale publicly funded project. RI development will incorporate principles of RRI as defined by the EC.

The need to reshape the HBP's IT Platforms into a user-centric RI emerged from the recommendations of the Technical Review Report in January 2015 [1]. The HBP will have to follow a rigorous path to accommodate these recommendations, which, we believe, will also allow the Project to fulfil the commitments made by the Board of Directors (BoD – predecessor of the SIB) when it accepted the recommendations of the Mediation Report [2]. A working group (WG) was formed to develop the user recruitment and infrastructure strategy (URIS). A first URIS WG report was discussed at the HBP BoD Meeting on 27—28 April in Madrid. At this meeting, the BoD decided to develop "a decentralised, federated research infrastructure with established rules in science [for] dissemination [of results] (through peer reviewed journals) and quality control (through expert peer review)", where the infrastructure will be "developed based on a coherent roadmap [that will be] annexed to the [Framework Partnership Agreement] FPA". The full decision proposal that was agreed upon by the BoD can be found in the Appendix.

The HBP's infrastructure development brings together the best practices from RI construction and operations in science, and modern IT software development methodology. Technology development beyond simple prototypes for proof of principles will be driven by

co-design projects. These will be led by scientists who aim to produce new science results, while building a productive infrastructure. With these projects, we intend to pursue some of the most challenging problems that cannot be addressed with traditional approaches in neuroscience, but that can possibly be solved with advanced technologies being developed in the RI. Co-design projects will be chosen from both internal and external research projects, via a transparent process. Similarly, access to the RI for internal and external users, once operational, will require a process based on expert peer review. Dissemination of results will be based on peer-reviewed publications, providing the basis for success metrics. Most of the technology developed for the HBP RI is software that requires elastic compute and data storage resources, with relatively short lifecycles compared to RI in other science domains. Thus, a software development methodology that can accommodate evolving requirements (even late in the development phase) needs to be applied, and should frequently deliver releases. This can be accomplished by combining the AGILE approach to software development with the principles of co-design, and the success metrics based on established rules of scientific dissemination.

The mission needs for an RI in neuroscience will be discussed in the next section. Section three provides a brief description of the current HBP ICT Platforms, and how they can be structured to produce the present RI. Section four presents a roadmap for the base infrastructure, the overall timeline for construction and operations, and describes how this timeline maps onto the HBP's current plans. The project management structure for the construction phase and the organisational structure will be discussed in sections five and six respectively. Finally, we discuss the next steps in section seven.

A3.3 The Need for a Neuroscience-Driven Research Infrastructure

The ICT demands of modern brain research are increasing rapidly. A comprehensive understanding of human brain organisation requires us to consider the multi-level organisation of the brain, including different aspects of brain organisation (e.g. genes, molecules, cells, cell connections), and also the different spatial (from nanometers to centimetres) and temporal (from milliseconds to years) scales, each spanning several orders of magnitude. The brain is a highly complex organ — it has roughly 100 billion neurons, with about 10,000 synapses per neuron, and a similar number of glial cells. Successfully addressing such a complex organ requires highly specialised tools to handle and analyse the data, and a research infrastructure, which goes far beyond the capacities and capabilities of single labs.

Neuroscience areas with a particular need for high-level research infrastructures include:

- Electrophysiological (e.g. multi-unit recordings) and cellular-resolution imaging studies, in particular in behaving animals; this includes the challenges of comprehensive and reliable meta data, as well as questions of data handling, storage and visualisation.
- Analyses of ultra-high resolution brain models at cellular and subcellular scales.
- Simulation of brain regions or whole brain simulations, with high spatial and/or temporal resolution.
- Neuroimaging studies in large cohorts with thousands of subjects in combination with genetic data.
- Analyses of decentralised data from hospital patients with special requirements in terms of safety and security, requiring special methods of data access and analysis.

Particular challenges arise from the ultra-high dimensionality and time-series character of most of these data, and from the demands of high-throughput analysis and interactive visualisation.

Such research is addressed in the HBP's first four neuroscience Subprojects (SPs). The objective of SP1, Mouse Brain Organisation, is to generate neuroscientific concepts, knowledge, data sets and tools, contributing to a better understanding of the multi-level and multi-scale organisation of the mouse brain. The SP's results will be used to constrain and validate reconstructions and simulations of the mouse brain. The objective of SP2, Human Brain Organisation, is structured along the same lines. In addition, human brain functional and structural segregation, its inter-subject variability, and genetic factors represent central elements of SP2, and contribute to the multimodal HBP atlas.

The new SP3, Systems and Cognitive Neuroscience, will form a matrix-like structure in the Project. Its crosscutting activities will address challenging problems of systems and cognitive neuroscience, relying on and driving the development in the Platform SPs.

The overall objective of SP4 is to establish solid theoretical foundations for modelling the brain across different levels of biological organisation, and to investigate models for key aspects or functions in conjunction with other SPs. For example, these include simplified models of neurons, including non-linear dendritic computations, models of different brain signals, and models of synaptic plasticity, learning and memory.

Part of the empirical and theoretical neuro-research in all SPs is the development of new methods, tools and research environments. In accordance with the Technical Review Report [1], the HBP Consortium is developing a detailed strategy, and plans to effectively integrate and align the work in neuroscience SPs 1 to 4 with the Platform developments. Additionally, an SP1 to SP4 Working Group has been set up, and closely interacts with URIS. The neuroscience SPs will:

- Act through co-developing the Platforms that are presently in SPs 5—10, where, in an iterative way, neuroscience contributes to the Platforms in the form of a co-design process.
- Attract first users, and introduce the Platforms to both the neuroscientific and broader science community, with the goal of providing an easy-to-use neuroinformatics infrastructure for day-to-day challenges in data acquisition, analysis, visualisation and storage.
- Perform empirical modelling and simulation-based research to support the formulation of multi-scale theories of brain architecture.
- Link this research with clinical data (Medical Informatics Platform).
- Analyse and, wherever possible, realise, in collaboration with the Platforms, real-world applications (e.g. robotics, neuromorphic computing, software, atlases).
- Co-design methods, tools and techniques to characterise development, inter-species and inter-subject variability.

A3.4 Structuring HBP Information Technology

Figure 1 depicts the relationships between different parts of the HBP RI, wherever possible using the nomenclature of the "Platforms" developed in SPs 5—10 during the Project's Ramp-Up Phase. The figure clearly shows that the SP 5—10 "Platforms" are not equivalent from an infrastructure point of view, which is why quotation marks are used for "Platforms" in the context of the Ramp-Up Phase. In some cases, the "Platforms" will have to be generalised in order to make for a functioning IT infrastructure.

The base infrastructure consists of compute and data storage, as well as neuromorphic computing systems. Much of SP7's High Performance Computing (HPC) focus during the first half of the Ramp-Up Phase was to federate the supercomputing systems in four centres: Jülich Supercomputing Centre (JSC) in Jülich, Germany; the Swiss National Supercomputing

Centre (CSCS) in Lugano, Switzerland; *Consorzio Interuniversitario del Nord Est italiano per il Calcolo Automatico* (CINECA) in Bologna, Italy; and Barcelona Supercomputing Centre (BSC) in Barcelona, Spain. A second SP7 effort, that will be important for future phases of the HBP, is the pre-commercial procurement (PCP) by which SP7, under the lead of JSC, is developing the HBP's future production supercomputer. The focus in the first part of the Ramp-Up Phase was on HPC, which may be the most cost intensive part of the infrastructure. A functioning ICT based RI for the HBP will, however, require more general compute and data storage services. The participating centres and medical institutions will contribute in providing such services. In addition, interfaces with public clouds will have to be considered.

Two alternative approaches to brain-inspired neuromorphic computing are currently being implemented as custom hardware systems of the neuromorphic computing base infrastructure. These are a many-core architecture based on programmable ARM cores, operating as a real-time simulation system, and a physical model architecture based on custom mixed-signal CMOS circuits, operating as time-compressed models of brain circuits to study learning and development. These systems are physically located in Manchester (UK) and Heidelberg (Germany).

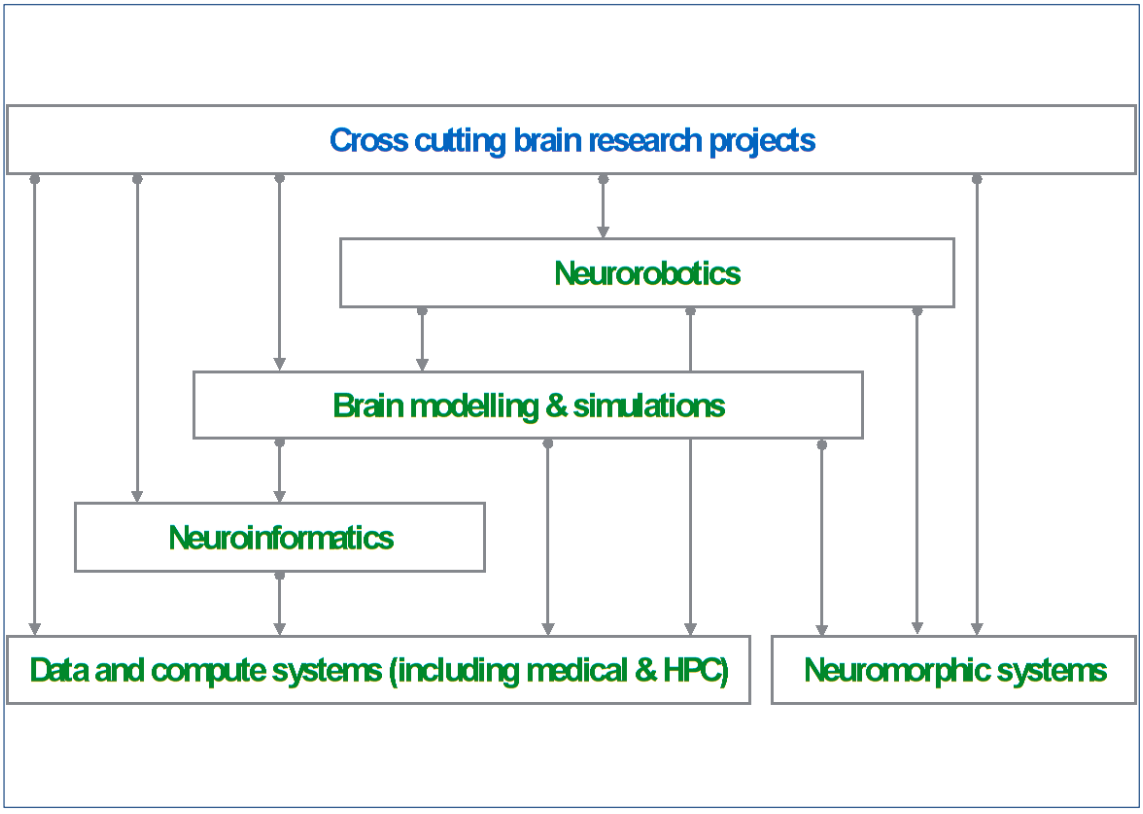

Figure 11: Relationship between the ICT infrastructure "Platforms" developed in the HBP.

(NOTE: Arrows indicate most important dependencies on lower infrastructure levels.)

The remaining HBP "Platforms", with the possible exception of SP8, will develop software systems that make use of the base infrastructure. For instance, the Neuroinformatics "Platform" developed in SP5 provides software tools that rely on storage and compute services running on public clouds, similar to data centres participating in the HBP. The services provided by the Neuroinformatics "Platform" are probably the most basic services that will be used by almost all HBP research projects, as well as by external users. In addition, brain simulations developed in SP6 are one of the hallmarks of the HBP. Since they will provide tools for data driven modelling, they need to rely on data services provided by

Neuroinformatics, and make significant use of the supercomputing systems. Certain brain simulations will be ported to the Spinnaker system in Manchester (SP9). The SP10 Neurorobotics Platform develops simulation tools that will run on both HPC systems provided by the participating SP7 centres, and SP9's Neuromorphic systems. It will make extensive use of the brain simulation software tools developed in SP6.

The tools developed in SP8 for the Medical Informatics Platform (MIP) will mostly rely on hospital IT infrastructures. The MIP will install small compute systems at the hospitals, which will serve as entry points for distributed queries of the hospital data systems.

A3.5 Roadmap for HBP Research Infrastructure

A high-level summary of the HBP timeline through 2020 is given in Table 1. We show the first three phases:

1. The Ramp-Up Phase that is currently running and produces prototypes,
2. Specific Grant Agreement (SGA) 1, which will be generally considered as the infrastructure construction phase,
3. SGA2 when the infrastructure will be in operation.

From a maturity point of view, prototypes demonstrate the technology validated in a lab, and in important cases, even in relevant environments. The technology has to go though a product development cycle. This is in order for it to reach the maturity and qualification level for deployment in a research infrastructure that supports non-expert users in operations. From a technology adoption [3] point of view, prototypes are created and used by innovators. Scientists who help build the infrastructure through co-design projects are early adopters, and those who will use it can be considered the early majority.

Since the technology life cycle in ICT can be short — typically 3—5 years — a corresponding IT-based RI will have to continually innovate. Therefore, co-design projects will continue to exist, and the construction of new base infrastructure and software tools will persist, even during the operational phase. This situation is common at computing facilities. Science users will always be early adopters or the early majority [3]. The "late majority" in the typical technology adoption curve does not exist in scientific IT-based infrastructure. This has implications, as product development has to be amortized over short periods and a limited customer base. Technology transfer into a more commercial setting should thus be considered in parallel. This approach works rather well for other IT-based RI, and has, for instance, led to sustainable developments in HPC and data analytics.

	HBP Project Phase		
	Ramp-Up	SGA1	SGA2
Timeframe	Oct 2013 – Sep 2016	Apr 2016 – Mar 2018	Apr 2018 - Mar 2020
RI phase	Prototyping	Implementation	Scale out & Operations
Technology Readiness	Technology Demonstration	System/Subsystem Development	Operations
Adoption Cycle	Innovators	Early adopters	Early majority
User Types	Internal co-design	Internal and external co-design	General user and co-design

Table 41: Overview of the HBP Timeline, RI Development and Adoption Cycle.

We distinguish base infrastructure from software infrastructure. The former includes all compute and data storage systems; networks with all associated services; Infrastructure-as-a-Service offering; as well as all enabling services such as resource management and schedulers, programming environment, as well as scientific libraries that are generic to many domains. The base infrastructure will also include neuromorphic compute systems and services as well as physical robotics facilities.

The software infrastructure on the other hand will consist of applications (Apps) with Web GUIs for certain services; services that will include Software-as-a-Service and Platform-as-a-Service offerings; as well as more generic Web services, SSH, Source control (git), Continuous integration, databases, configuration and deployment services. Some of the software infrastructure may be moved into the base infrastructure as time progresses and other scientific domains that use the same data centres adopt associated services.

A3.5.1 Base Infrastructure

Presently, the most visible foundation of the HBP base infrastructure roadmap is the pre-exascale productions system. This is anticipated to be installed at JSC, with operations picking up in late 2018 (note that the European Commission will partially fund this system, based on a competitive process). The PCP running in SP7 is fully dedicated to this development and the federation of the supercomputing services at the other three HBP centres, with JSC being the highest priority. However, the roadmap will have to be extended in order to make the base infrastructure viable for the HBP. It should consist of the following (see also Figure 2):

- Federated data services by the end of the Ramp-Up Phase: the participating data centres will have to extend their portfolio to include data services that can be inter-federated between all sites. These services will be storage centric, but sufficient compute resources will have to be made available to support adequate data analysis capabilities. A process similar to the peer-reviewed compute allocations that are already in place at the supercomputing facilities, and within PRACE, will have to be developed for data services. This is in order to guarantee transparent and fair access to these services, and the quality of the data and science it supports.
- Public cloud services: interoperability with public cloud providers will have to be developed during SGA1. This will be necessary for all data services, in order to support a straightforward path of commercialisation. Similarly, the majority of architectures and

technologies developed for the HBP should be integrated into vendors' roadmaps, to provide opportunities for commercial systems to develop.

- Extend federated data centre to other countries by SGA1: the HBP is a pan-European project, and should include hosting Partners in more than four countries. As a minimum, the project should add hosting sites in France and the United Kingdom in the timeframe of SGA1. Discussions with GENCI, the French national Tier-0/1 supercomputing organisation, and the HBP Partner EPCC, Edinburgh, have been started by SP7.
- Development system: the Blue Brain Project (BBP) presently operates the HBP development system at CSCS. Since this architecture has no resemblance to the future production system at JSC, a new development platform will be created at CSCS. This will be done in two phases: (1) during the remainder to the Ramp-Up Phase, the CSCS HPC infrastructure will serve as a second HBP development system, and data driven modelling and simulations developed in SP6 will also be adapted to this platform; (2) in Q4 2016, BBP will invest in a follow-up development system at CSCS. This will be available to the co-design projects during SGA1 and beyond.
- PCP and development of pre-exascale supercomputer: during the Ramp-Up Phase, JSC, as lead procurer, runs a PCP in close collaboration with the four HBP supercomputing centres, as well as other HBP partners. This PCP aims to enhance the pre-exascale roadmaps of relevant supercomputer solution providers, in the areas of dense memory integration, visualisation and dynamic resource management. The goal is to have solutions for pre-exascale systems, suited to the needs of the HBP RI and its users, available in 2017—18. The PCP is planned to finish in October 2016, and vendors who had been awarded a contract for Phase III of the PCP are expected to deliver a pilot system demonstrating the readiness of the technology six months before the end of the PCP.
- Production pre-exascale supercomputer: in late 2018, i.e. the first year of SGA2, the production system, so far anticipated to be at JSC (subject to competitive funding), will pick up operations. All simulation software will have to be migrated from the development systems to this platform ahead of time.
- Access to neuromorphic computing systems: prototype systems, including a software workflow for non-expert access to the neuromorphic computing systems, are currently to be brought into operation in the Ramp-Up Phase. In SGA1, the systems will be maintained and further developed into a research infrastructure, with 24/7 availability and secure remote access.
- Operation of Neuromorphic Computing systems: access for a broad user base from neuroscience, machine learning and cognitive computing will commence in SGA2. Further development of this research infrastructure will be driven from two sides: neuroscience with special emphasis on studying time-dependent processes in brain circuits, and data analytics to transfer principles of brain computing to applications outside neuroscience. The user base will comprise both scientists and industrial users
- Joint operation of HPC and Neuromorphic Computing systems: during SGA1, network capabilities, and storage and compute systems at the HPC facilities, will have to be extended to accommodate the conventional computing requirements of the Neuromorphic Compute platform. Joint operation includes executable system specifications, place and route algorithms, data analysis, and visualisations. This will need to accommodate the developing workflows of the Neuromorphic Computing research systems during SGA2.
- Medical informatics data systems: the MIP will federate data systems at hospitals and public data centres. This will allow straightforward, scalable access to medical information, without breaching patient anonymity. The MIP will also provide data mining

infrastructure to support the development of algorithms, which will define disease signatures.

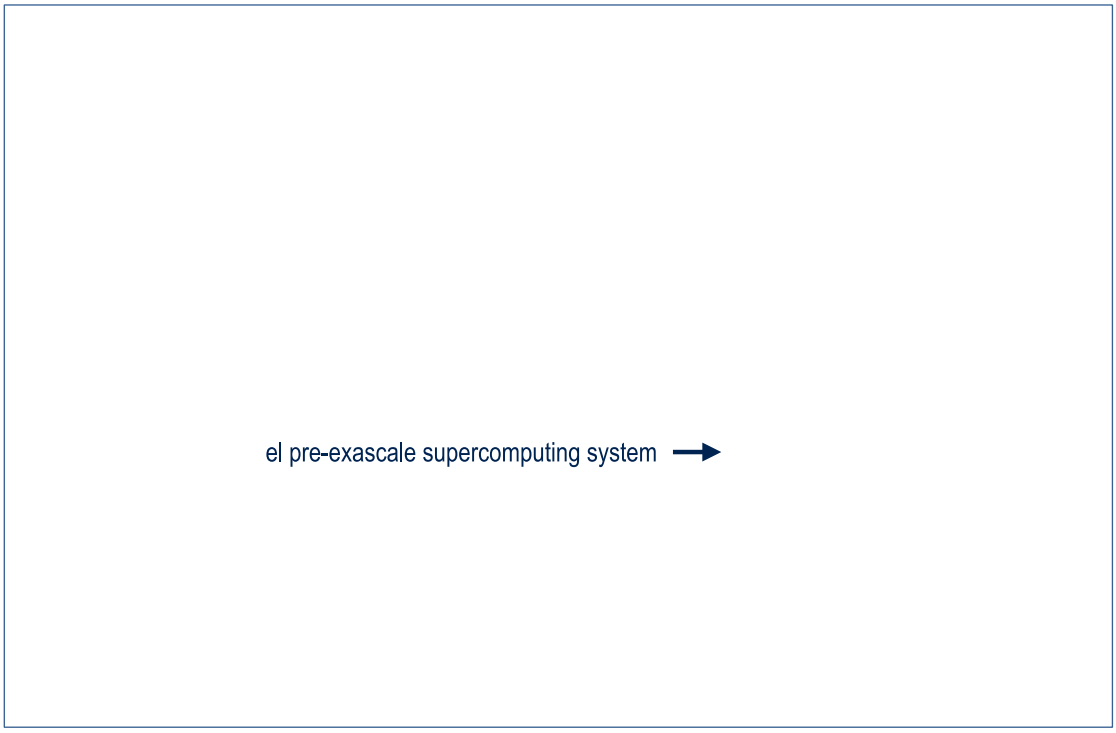

Figure 12: Timeline of the base infrastructure for the HBP

A3.5.2 Software Infrastructure

All software development work for Neuroinformatics (SP5), Brain Simulations (SP6), Medical Informatics (SP8) and Neurorobotics (SP10) during the remainder of the Ramp-Up Phase and SGA1 will be aligned with this base infrastructure roadmap, and the latter will have to be continually adapted to evolving user needs. The same will apply to the development of Collaboratory software, a gateway by which the RI can be accessed by users. Furthermore, in all these areas, new tools will have to be developed in order to meet user needs, which, during the construction phase, will be devised, in part, from co-design projects. Two to three such projects will be started from within the HBP during the second stage of the Ramp-Up Phase. Several more will be derived from crosscutting projects that are being sought in an open call. These externally led projects will begin to run during SGA1.

The software infrastructure portion of the HBP RI will require significant organizational changes to transition to a robust, scalable and agile Service-Oriented Architecture (SOA). Part of this change will require explicit publication of software components by the HBP tasks. The components will be organized into the hierarchy depicted in Figure 3.

Gateway	Collaboratory			
Software as a Service	Neuroinformatics	Brain Simulations	Neurorobotics	Medical Informatics
Data as a Service	Neuroinformatics		Medical Informatics	
Platform as a Service	HPC platform (e.g. interactive supercomputing)		Neuromorphic computing platform	
Infrastructure as a Service	Compute & data infrastructure services (including HPC)		Neuromorphic compute services	
Base infrastructure (compute, storage, & network)	Public data centers in France, Germany, Italy, Spain, Switzerland and the UK; IT infrastructure at Hospitals; Neuromorphic computing systems			

Figure 13: Structure of the different service components in the Research Infrastructure.

(NOTE: Service quality will have to allow users to access any service level in the hierarchy.)

Not all software components will need to be managed with the same level of discipline. Reducing the investment in robustness for less critical services is an essential part of cost-effective development and maintenance. To clarify the prioritization of parts of the SOA, there will be an adoption of a tiered classification of services and Foundation software delivered by the various SPs. The tiers are described as HBP Managed, HBP Coordinated, and Community Coordinated.

The HBP Managed infrastructure tier will adhere to strict standards with centrally managed Service Level Agreements (SLA) that guarantee high availability. A combination of essential Software and Base Infrastructure that is federated over multiple sites will have to be committed, to achieve the necessary service availability. A support plan will be documented and will have resources committed. A sustainable roadmap for both Base Infrastructure and Software Infrastructure forms the core of the HBP RI. An external evaluation panel that is not involved in the implementation will assess technology Readiness Levels (TRL).

HBP Coordinated components of infrastructure are provided for and owned by individual partners (partner institutions and conglomerates, or subprojects). Adherence to the HBP standards is optional and SLA will have negotiated availability. HBP Coordinated services will be deployed on a mix of HBP Managed and non-HBP managed base infrastructure. All Apps and Services are monitored for health and availability by the HBP Managed services. The respective partners are managing support and providing the service prioritized to encourage adoption for their respective infrastructure components. The partners are responsible for assessing TRLs.

Community Coordinated software infrastructure is provided for and managed by a Third Party not involved in the HBP. Apps and services may be monitored, and the Third Party decides on SLA and Support levels.

Furthermore, the components delivered by the RI will need to address the following high-level principles. Each service requires clear resource allocation, quality metrics, monitoring and support appropriate to its target service level. For any services that are critical to the operation of the overall infrastructure, a risk assessment and mitigation plan will be essential.

Service descriptions: each HBP Managed and HBP Federated service will be documented to describe its intended purpose and specific capabilities. The interfaces (user interfaces, APIs, etc.) that are provided will also be documented. The standards adopted by the service should be clearly specified and referenced. The agreed level of service, including the

supported number of concurrent users, will be documented. Finally, the authentication method, required by each service should be part of the service description.

Quality metrics: in order to adequately assess the state and capabilities of the HBP infrastructure, quality metrics to characterise individual services during a given period will have to be clearly defined. The maturity of a service is critical, and it is important to differentiate between an early prototype, the development phase, and the delivery of services, in order to assess capability levels. The reliability and availability of the service is essential for judging the extent to which it can be depended upon. Monitoring can play an important part of evaluating quality.

Monitoring: monitoring an infrastructure's services is an essential part of ensuring the infrastructure as a whole is operational, and that key services are, and remain, available. In order to ensure effective monitoring, each service should provide the appropriate hooks for monitoring dashboards, and metering software to provide usage accounting.

Support: defining clear support levels for each service will be essential for developing the adoption and trust of the community.

Resource allocation: the allocation of resources needs to be based both on a clear cost model, and a transparent allocation process that is based on expert peer review. The latter may be an institutionalised process with external peer review and transparent allocation panels for projects with clearly defined resource requirements in a given time period. Resources for long-term access and developer's discretion will be subject to the RI peer review. The cost model needs to satisfy the accounting from both the service provider and user perspective.

Risk assessment: the HBP infrastructure is as robust and valuable as its component services. The integrity of the infrastructure can be shattered if essential core services break or are not reliable. Thus, the risk of losing any key services should be addressed, and plans defined to mitigate their loss or outage.

Licensing: Opensource licensing should be employed wherever possible to catalyse strong community involvement. Opensource licensed software should be developed on a public community software forge under an HBP compatible Opensouce license. Much of the research software community is moving to Opensource by default. There are numerous successful business models under this approach and the HBP leadership may consider moving by default to Opensource licenses in some future SGA.

A3.6 Project Management Structure

Compared to a pure research project, developing an RI will require an entirely different approach to project management. This is because the success metrics of the two kinds of projects are fundamentally different. In research, new scientific insight is the immediate goal. Results are communicated in peer-reviewed journals, where their success is measured by an impact factor that may be normalised for a particular science domain. There is no immediate expectation that research projects produce tools that can be used by others, although they may arise as by-products.

In contrast, mature tools or instruments that deliver new capabilities to other scientists (i.e. users), are the primary goal of a RI project. Success will ultimately be measured by the research impact of future users. This is a long-term metric that will not be useful during construction and initial operation, and different, short-term metrics must be developed to assess progress and measure success during construction and early usage. In RI projects, expert peer review is used to establish the quality of a roadmap, and a baseline against which the improved capabilities can be measured. This allows the definition of the planned scope, schedule and cost, as well as a value system in which progress can be monitored during construction.

While research projects are usually managed bottom-up, and often organised as rather loose collections of subprojects, RI construction projects require a hierarchical work breakdown that is derived from the roadmap. Each level (or node) in the hierarchy is itself a project with an owner, project manager, and a team. Progress is continually reported at every level of the hierarchy, and compared to the projected readiness of the RI at any given stage of construction. In this way, progress in the RI construction can be continually monitored, and it is possible to detect, at an early stage, the parts of the project that are in danger of falling behind schedule. If the deviation between projected and earned value is greater than an agreed tolerance, or if an important Deliverable is approaching, tiger teams containing the necessary expertise will support the troubled parts to get the construction back on track.

Given the diversity of the services anticipated to be delivered by the HBP's RI, it will be important to differentiate the baseline for different levels in the service hierarchy given in Figure 3. The desired quality of a service at a higher level will define the required scope of a service or capability at a lower level. The cost and affordability of capabilities or services at the lower levels will determine the quality of services at a higher level. Finding an optimum value that can be achieved for a fixed cost will require some degree of global optimisation of the work plan. This is again different from the pure research project, where resources are spread more equally between subprojects.

Finally, since the HBP is building a community driven RI, it is essential to have some form of representation from the neuroscience community concerning the development of the baseline and value metrics. Furthermore, since disruptive technologies are common in ICT, it is important for the community representation to be forward-looking. A mechanism will have to be put in place to discover and manage "innovator's dilemma" [4] situations.

A3.8 Next steps (work in progress)

To summarise, the following concrete steps have to be taken swiftly:

1) The BoD / SIB has to agree on a roadmap, and funding has to be identified for the necessary base infrastructure.
2) Separate the internal research from infrastructure development and construction, assign TRL for end of Ramp-Up Phase and commit to TRL at end of SGA1.
3) Identify science drivers, and implement through co-design projects — internal co-design projects should be identified immediately; external co-design projects will be selected though open calls, the first of which has just been published.
4) Align Ramp-Up Phase and SGA1 Work Packages with a new organisational structure that will be further refined in the process; develop a change management plan.
5) Prioritise work in SGA1 according to the roadmap; define a baseline and earned value metrics system.
6) Develop an implementation plan (including management plan and WBS) for the roadmap that will be part of the SGA1 proposal.
7) Implement with discipline and monitor earned value.

A3.9 References

[1] A copy of the review report can be downloaded from https://www.humanbrainproject.eu/-/hbp-technical-review-report-now-available.

[2] A link to the mediation report can be found at https://www.humanbrainproject.eu/-/the-hbp-mediation-report-delivered-today.

[3] We use the terminology from the technology adoption lifecycle that distinguishes "innovators" from "early adopters" and "early majority". See: http://en.wikipedia.org/wiki/Technology_adoption_lifecycle.

[4] "The Innovator's Dilemma" by Clayton M. Christensen, Harvard Business Review Press (1997)

[5] We use the definitions given in Annex G of the "HORIZON 2020 — WORK PROGRAMME 2014—2015"; they are reproduced in this Appendix (see below).

A3.10 Attachments

A3.10.1 URIS WG Decision Proposal Passed by the HBP BoD on 28 April 2015

1) The HBP develops a decentralised, federated research infrastructure, with established rules in science of dissemination (through peer reviewed journals) and quality control (through expert peer review).
2) Collaboration software (Collaboratory) will be deployed to facilitate user access to the infrastructure and to support user interactions. The infrastructure is developed based on a coherent roadmap annexed to the FPA.
3) The support and services for the base infrastructures of High Performance Computing and Neuromorphic Computing will be developed independently. They will define common requirements like network specifications and data storage.
4) The HBP will implement a horizontal organisation for system integration. This will include project management, and will implement a uniform project structure across all HBP Subprojects. Depending on their maturity, all HBP Platforms will transition into a research infrastructure organised in a unified work-breakdown structure, the units of which will have a well-defined owner, manager, and team.
5) HBP uses co-design projects to take technology from proof-of-principle to supported infrastructure. Owners of co-design projects are scientists with teams consisting of technology developers and scientists.
6) Based on the HBP Infrastructure Development Roadmap, the HBP will work out a funding model for the infrastructure with the EC (parts that cannot be financed in the HBP Core Project), and an engagement model and timeline for HBP-relevant existing or developing European infrastructures.

A3.10.2 Technology Readiness Levels taken from [5]

Where a topic description refers to a TRL, the following definitions apply, unless otherwise specified:

- TRL 1 — basic principles observed
- TRL 2 — technology concept formulated
- TRL 3 — experimental proof of concept
- TRL 4 — technology validated in Lab
- TRL 5 — technology validated in relevant environment (industrially relevant environment in the case of key enabling technologies)
- TRL 6 — technology demonstrated in relevant environment (industrially relevant environment in case of key enabling technologies)

- TRL 7 – system prototype demonstration in operational environment
- TRL 8 – system complete and qualified
- TRL 9 – actual system proven in operational environment (competitive manufacturing in the case of key enabling technologies; or in space).

Appendix 4: Community Engagement

The HBP is a global research effort, in which collaboration is essential to achieving the Project's strategic and operational objectives. To ensure collaboration, the HBP must have a proven and accessible Community Engagement framework.

The HBP's Community Engagement Framework is based on the concept of an engagement funnel. The funnel concept is well developed in the professional communications sector, and provides critical focus for targeted engagement activities. The figure below shows examples of activities that are appropriate for achieving the Project's engagement objectives when interacting with particular users, who are grouped by role.

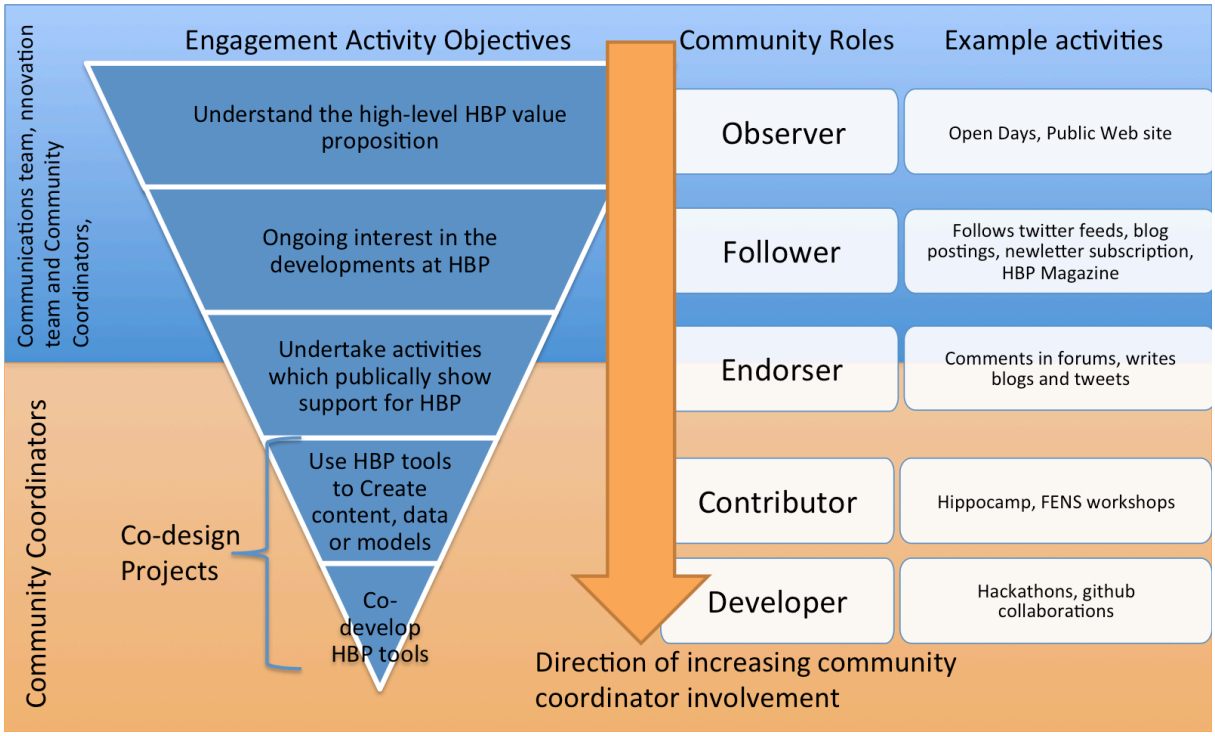

Figure 14: Community Engagement "Funnel"

There are three main principles at work in the funnel. To summarise:

1) Objectives are level specific, and coupled to the channels employed at that level. For example, Contributors do not need to be convinced of the HBP value proposition, and probably will not be convinced further by activities targeting Observers.
2) An unwritten objective of all levels is to transition people in each level to deeper levels of engagement. Activities targeting Observers should try to convert Observers into Followers, Followers into Endorsers, and so on.
3) There are fewer people in the community roles in the deeper levels of the funnel. This means that Community coordinators can expect to be more hands-on with Contributors and Developers than Communications and Innovation teams will be at higher levels of the funnel.

The framework assigns three HBP roles: Communications Team Member, Innovation Team Member and Community Coordinator.

Communication Team Members and Innovation Team Members are expected to be specialists in corporate communication and networking, where the skills and channels are broadly similar to any large communication effort. In the early stages of the funnel, the professional communications activities dominate. As engagement develops, the Innovation and Communications teams should transition the engagement activities to the Community

Coordinators. The Community Coordinators will be scientific and engineering specialists in the HBP Subprojects tasked with engagement activities, mostly at the Contributor and Developer levels. This approach is intended to address the challenges communications specialists will face in engaging productively in the increasingly domain-specific activities found deeper in the funnel.

One advantage of this approach is that the engagement framework and the HBP roles can be largely maintained for Industry engagement, with a small adjustment to the objectives at the different levels of the funnel. This ensures that Communication, Innovation and Coordinator team members can maintain a consistent dialogue and approach in their engagement activities.

This framework also provides an engagement model for Subprojects to follow when building self-sustaining open source communities around particular software capabilities. Where those self-sustaining communities can be built (it is clear that not all of the HBP's software outputs can self-sustain), the HBP will limit the long-term cost of software maintenance, while providing low-cost access to global experts in scientific software development.

Finally, and perhaps most importantly, this framework is designed to support one of the key mechanisms for shaping and maintaining a Research Infrastructure that produces innovative science: the Co-design projects described in the section 2.1.1.7. Co-design activities take place at the deepest levels of the funnel, and their continued progress and outputs serve as a key driver for the success of the Project.

Appendix 5: HBP Core Project Partner Details

P1) EPFL, *École Polytechnique Fédérale de Lausanne*, Switzerland (SPs1, 4—11)

Blue Brain Project (BBP)

Launched in 2005, and directed by Prof Henry MARKRAM, the Blue Brain Project (BBP) is the first comprehensive attempt to use detailed modelling and simulation as tools to systematically integrate data about the brain. The mission of the BBP is to spearhead simulation-based neuroscience research using supercomputers and Big Data technologies as a strategy to integrate fragmented knowledge and scientific data, first for the rodent brain and ultimately for the human brain. The BBP is divided into three divisions: the Computing Division led by Prof. Felix SCHÜRMANN, the In silico Neuroscience Division led by Prof. Henry MARKRAM, and the Neuroinformatics section Division led by Prof. Sean HILL.

The key to the BBP's strategy is to develop the field of Predictive Neuroinformatics, aimed at accelerating data integration by using fundamental generalising principles of the brain's structural and functional organisation, thus filling huge gaps in knowledge. Prof. Markram also runs a state-of-the-art multi-patchclamp and molecular and cell biology experimental lab to validate these principles, the state of the model and the results from the simulations. The BBP has developed a novel suite of software and workflows that form a coherent platform for collaborative brain simulation. The BBP has published a series of more than 60 neuroscientific, theoretical, modelling and computer science papers on data integration, automated modelling and the use of supercomputers for brain simulation, visualisation and analysis. These include a first draft reconstruction of neocortical microcircuitry in rat somatosensory cortex, recently published in the journal Cell and a paper in Frontiers in Neural Circuits showing how the connectome can be informatically and algorithmically derived by following biological rules. Other publications include a paper in PLoS Computational Biology, presenting a data-driven strategy to automatically build electrical models of neurons and a J. Physiology paper showing how in silico synapses match biological synapses and how intrinsic morphological diversity enables robustness and invariance of synaptic pathways. The BBP facility hosts an extensive programme of in silico experimentation and is evolving into a true community asset. The BBP has been declared one of Switzerland's three National Research Projects, and is composed of more than 60 scientists and engineers. The BBP is a major contributor of matching funds and in-kind support for the HBP.

Key Personnel

Henry MARKRAM (male) is full professor, founder and director of the Blue Brain Project, founder of the Brain Mind Institute (EPFL), and founder of the Human Brain Project.

Felix SCHUERMANN (male) is adjunct professor, co-director of the Blue Brain Project, and head of the Blue Brain Project Computing Division.

Sean HILL (male) is adjunct professor, co-director of the Blue Brain Project, and head of the Blue Brain Project Neuroinformatics Division.

Eilif MULLER (male) is a senior researcher and section manager for the Simulation Section of the Blue Brain Project.

Marc-Oliver GEWALTIG (male) is a senior researcher and section manager for the Neurorobotics Section of the Blue Brain Project and is Co-Leader of the Neurorobotics Subproject in HBP.

Fabien DELALONDRE (male) is a senior researcher and section manager for the High Performance Computing Section of the Blue Brain Project.

Jean-Denis COURCOL (male) is a senior engineer and section manager for the Platform Development Section of the Blue Brain Project.

Katrien VAN LOOK (female) is a scientific project coordinator in the Blue Brain Project

Catherine ZWAHLEN (female) is section manager for the Neuroinformatics Section of the Blue Brain Project.

Key Expertise

- Data driven cellular level circuit reconstruction and validation
- Data driven subcellular level reconstruction and validation
- Internet accessible Neuroinformatics infrastructure development
- Internet accessible simulation infrastructure development
- Cellular level simulator development
- Subcellular level simulator development
- Data-driven cell morphology synthesis (neurons and astrocytes)
- Data driven neuron electrophysiology modelling
- Brain model simulation and visualisation
- Coarse-grained particle-based simulations of complex fluids and nanoparticles
- Biophysical theory and modelling
- Connecting simulation techniques across multiple length and time scales
- Scientific software development in Python and C++, and Object-Orientated programming
- Large-scale simulation technology (network level)
- Theoretical neuroscience, network dynamics, stochastic processes, unsupervised and reinforcement learning
- Closed-loop simulations
- Reconstruction of neocortical and hippocampal anatomy and physiology *in silico*
- Modelling and analysis workflows for reproducible *in silico* experimentation
- Data-driven modelling of the physiology, plasticity and life-cycle of synapses
- Theory and simulation of structure-function-plasticity relationships *in silico*
- Data integration
- Data analysis and data mining
- Application performance analysis, characterisation, optimisation and modelling
- Highly scalable numerical and computational methods and implementations
- Adaptive multi-scale, verification and validation methods
- High performance and memory intensive supercomputing
- Evaluation of cutting edge and emerging computer architectures including GPU, Intel Xeon/MIC, Power and ARM
- High performance computing (HPC), Cluster & Cloud System Configuration & management
- Authentication, authorisation and access control

- IT security and networking
- Interactive Scientific Visualisation
- Rendering algorithms for very large data sets
- Software engineering including Q&A, continuous integration and deployment
- SCRUM software development
- Brain function and activities
- Brain health
- Brain diseases
- Cognitive functions

Human Brain Project Coordination Office (HBP PCO)

The HBP PCO unit at EPFL, formerly known as the HBP unit, was created in 2013 to handle the coordination and management activities of the Ramp-Up Phase HBP Core Project under FP7. Gearing up for the next Phase of HBP, it is now a team of more than 20 project managers, administrative managers, communications specialists, writers, editors, jurists, assistants, engineers and scientists. Coming from diverse backgrounds, such as the industry, NGOs, governmental agencies, and the academia (four have PhDs in different scientific disciplines, including neuroscience), the PCO team is versatile and shares a common passion and dedication for supporting, facilitating and enabling HBP, leveraging value creation across the Project. In the transition leading to its transfer from EPFL to the new HBP Legal Entity that will coordinate the Core Project in the future, the PCO will Plan and create the HBP Legal Entity, support the Directorate, the Stakeholder Board and other governing bodies, coordinate the Core Project for the Ramp- Up Phase and SGA1, and build and operate the HBP infrastructure.

Key Personnel

Philippe GILLET (male) is the Chairman of the Board of Directors of HBP and Vice-President for Academic Affairs at EPFL.

Christoph EBELL (male) is the Executive Director of HBP, Leader of SP11 (Central Services), and head of the HBP PCO unit at EPFL.

Christian FAUTEUX (male) is Deputy Executive Director of HBP, Deputy Leader of SP11, and Head of Project Coordination for HBP.

Kathleen ELSIG (female) is responsible for Partnerships for HBP.

Jeffrey MULLER (male) is the Technology Coordinator of HBP.

Martin TELEFONT (male) is the Science Coordinator of HBP.

Guy WILLIS (male) is Head of Editorial Services for HBP.

Key Expertise

- Project management in general
- Governance
- Administrative performance and risk management
- Administrative management
- Public administration and diplomacy
- EU-funded projects and programmes

- Copy-editing
- Technical writing
- Communications
- Public affairs
- Meetings and events organisation
- External relations
- Partnership building
- IP/Tech transfer/Innovation management
- Neuroscience
- IT and Web services
- IT project management
- Software engineering including QA, continuous integration and deployment
- Agile software development
- Data integration
- Internet accessible infrastructure development

Data-Intensive Applications and Systems

Profile

The Data-Intensive Applications and Systems (DIAS) Laboratory focuses on database systems and applications, and is headed by Anastasia AILAMAKI. Researchers in the Laboratory adapt data management technology to computer architecture trends, by designing data manipulation techniques that make optimal use of the underlying hardware and I/O devices. DIAS research enables new scientific discoveries by automating physical database design for complex datasets, and revolutionising access methods for specialised data structures and scientific models. DIAS laboratory results are regularly featured in top database conferences and journals, such as ACM SIGMOD and VLDB.

Key Personnel

Anastasia AILAMAKI (female) is a Professor of Computer Sciences at EPFL.

Key Expertise

- Database systems
- Scientific data management
- Hardware-aware algorithms and data structures
- Spatial Indexing
- Adaptive query processing
- Solid-state storage.

Laboratory of Computational Neuroscience

Profile

The Laboratory of Computational Neuroscience at EPFL focuses on theoretical and computational neuroscience, with a special emphasis on synaptic plasticity, and learning in

networks of spiking neurons. The Laboratory is headed by Professor Wulfram GERSTNER, and is affiliated with the school of Computer and Communications Sciences and the school of Life Sciences. The staff of around fifteen lab members includes ten PhD students, three postdoctoral fellows, students working on semester and master projects, and a part-time administrative assistant. The Lab is equipped with state-of-the art computers, and receives generous basic funding from the Swiss Federal Government. The Lab has on-going collaborations with experimental neuroscientists at EPFL, and with other theory groups in Switzerland.

Key Personnel

Wulfram GERSTNER (male) is the Director of the Laboratory of Computational Neuroscience at EPFL. He also has a joint appointment at the School of Life Sciences, and the School of Computer and Communications Sciences.

Key Expertise

- Simplified models of spiking neurons
- Models of synaptic plasticity and learning rules
- Mean-field analysis of activity in model networks.

Microelectronics Systems Laboratory

Profile

The Microelectronic Systems Laboratory (LSM) at EPFL operates as part of the Institute of Electrical Engineering (IEL). Its main areas of research include the design and implementation of high-performance digital and mixed-signal VLSI circuits, language-based modelling and validation of SoC components, neuromorphic/bio-inspired system architectures, and integration of new technologies for complex system design. The teaching objective of LSM is to offer comprehensive undergraduate and graduate education programmes in digital/mixed-signal IC design and VLSI system design to our Electrical Engineering and Microengineering (Microtechnique) students. Lab facilities include a state-of-the-art EDA environment for VLSI design, and test and measurement labs for detailed chip-level and system-level characterisation.

Key Personnel

Yusuf LEBLEBICI (male) is a Chair Professor at EPFL, and Director of the Microelectronic Systems Laboratory.

Key Expertise

- Digital chip design
- FPGA design
- System design, integration and testing
- New technologies
- Low level access to hardware
- Training, education and community building
- Innovation, Industry relations, IPR
- Computational theory
- Cellular neuroscience

- Network neuroscience.

Biorobotics Laboratory

Profile

The Biorobotics Laboratory (BIOROB) has worked extensively on neuromechanical models of animal locomotion, and dynamical system control for articulated robots and exoskeletons. It has developed several numerical models of animal motor control, including models of central pattern generators and motor primitives. The Lab is a pioneer in using robots as tools for testing hypotheses concerning the organisation of motor circuits, and of spinal cord circuits in particular. It has developed and/or worked with a large variety of robots, ranging from from lamprey-like, salamander-like, and cat-like robots, to humanoid robots.

Key Personnel

Auke IJSPEERT (male) is the Director of the Biorobotics Laboratory (BIOROB) and Associate Professor in the School of Engineering at EPFL.

Key Expertise

- Neuromechanical models for locomotion
- Dynamical systems
- Amphibious Robotics
- Humanoid Robotics.

Translational Neural Engineering Laboratory

Profile

The mission of the Translational Neural Engineering Laboratory (TNE) is to develop neurotechnologies that restore sensorimotor function in people affected by different kinds of disabilities. The Lab aims to achieve this by translating neuroscience findings into clinical practice. We are currently working on neuro-controlled bidirectional prostheses, implantable neuroprostheses to restore locomotion, and wearable robotics for assistance and rehabilitation.

Key Personnel

Silvestro MICERA (male) is the Director of the TNE Lab, and Associate Professor at the EPFL School of Engineering and the Centre for Neuroprosthetics.

Key Expertise

- Implantable neuroprostheses
- Rehabilitation robotics
- Wearable devices
- Neuro-controlled artificial limbs
- Reaching, grasping and locomotion
- Functional electrical stimulation.

International Paraplegic Foundation Chair in Spinal Cord Repair (G-Lab)

Profile

The mission of the International Paraplegic Foundation Chair in Spinal Cord Repair (G-Lab) is to design innovative interventions to restore sensorimotor functions after neurological disorders. We aim to translate our findings into effective clinical applications, to improve the quality of life for people with neuromotor impairments. To achieve this goal, we are developing neuroprosthetic systems, robotic interfaces and advanced neurorehabilitation procedures, which we combine with neuroregenerative interventions. Using genetically modified mice, optogenetics and novel viral tools, we also aim to uncover the neural mechanisms underlying the control of locomotion in intact animals, and the processes that re-establish motor functions following neuromotor disorders.

Key Personnel

Grégoire COURTINE (male) holds the International Paraplegic Foundation Chair in Spinal Cord Repair. He is also Associate Professor at the School of Life Sciences, the Brain Mind Institute and the Centre for Neuroprosthetics at EPFL.

Key Expertise

- Neurorehabilitation
- Neuroregeneration
- Neuroprosthetics
- Locomotion
- Spinal cord injury.

Laboratory of Psychophysics

Profile

The Laboratory of Psychophysics (LPSY) is one of the most prominent psychophysics laboratories, and uses TMS, EEG, and mathematical modelling to study visual information processing in humans. Key topics of research include feature integration, contextual modulation, time courses of information processing, perceptual learning and mathematical modelling. Clinical studies at the Lab have investigated deficits of visual information processing in schizophrenic patients.

Key Personnel

Michael HERZOG (male) is a Professor of Psychophysics at the EPFL Brain Mind Institute (BMI).

Key Expertise

- Psychophysics
- Visual perception.

Computer Vision Laboratory

Profile

Headed by Pascal FUA, the research activities of the Computer Vision Laboratory (CVLab) focus on shape and motion recovery from images. These include the modelling of neural structures from Electron and Light Micrographs, fast object detection, and real-time reconstruction of deformable 3D surfaces. The CVLab also provides undergraduate and

graduate teaching, and performs technology transfer for start-up and established companies. Its current staff includes one professor, one senior scientist, six post-doctoral fellows and twelve doctoral students. It is funded by the Swiss Federal Institute of Technology, the National Swiss Research Foundation, the Federal Office for Education and Science, and by several European Union projects, including a senior European Research Council grant.

Key Personnel

Pascal FUA (male) is a Professor at the School of Computer and Communication Science.

Key Expertise

- Segmentation of organelles in EM imagery
- Delineation of neuronal structures in LM imagery
- Registration of EM and LM images.

Laboratory of Computational Chemistry and Biochemistry (LCBC)

The LCBC research interests are concentrated on ab initio MD methods based on density functional theory (Car-Parrinello simulations) and their application, adaption and extension to systems of chemical and/or biological interest, this includes the following research topics:

- Development of Hybrid QM/MM Methods for Combined Quantum/Classical Car-Parrinello Simulations.
- Development of Long-Time Scale Techniques for Ab initio MD Simulations.
- In situ Simulations of Chemical Reactions and Photoactive systems in Gas Phase and in Solution.
- Ab initio Simulations of Biological Systems.

Key Personnel

Ursula ROETHLISBERGER (female) is an Associate Professor of Computational Chemistry and Biochemistry. She is also Director of the Section of Chemistry and Chemical Engineering of the Faculty of Basic Sciences at the EPFL.

Key Expertise

- Simulations of chemical and biological systems
- Ab initio MD methods
- Density functional theory

P2) AALTO, *Aalto-Korkeakoulusäätiö*, Finland (SP10)

Department of Electrical Engineering and Automation

Profile

The Department of Electrical Engineering and Automation began operating on 1 January 2014. It represents the merger of three departments: Automation and Systems Technology, Electronics and Electrical Engineering. All three departments have significant shared research interests, and have worked with common industrial partners. The new department is an ecosystem where scientists and engineers from different fields interact, and work together by crossing traditional boundaries to solve the most challenging scientific and

technological problems. They also provide an excellent education, and produce greater wellbeing for society in general. Our interdisciplinary team, which combines expertise from microsystems, electrical engineering and automation, will expand scientific and technological knowledge. Our mission is to contribute to society through innovations, education and research at the highest international level. The total size of the staff is 180, including 16 tenured professors.

Key Personnel

Ville KYRKI (male) is an Associate Professor at EEA and Head of the Intelligent Robotics group. He is also the founder and current chair of the IEEE Finland Robotics & Automation Chapter.

Key Expertise

- Intelligent robotic systems
- Robotic vision
- Feature extraction
- Tracking
- Visual serving
- Tactile sensing
- Robotic grasping
- Sensor fusion
- Planning under uncertainty
- Machine learning.

P3) LUMC, *Academisch Ziekenhuis Leiden - Leids Universitair Medisch Centrum*, The Netherlands (SP8)

Division of Image Processing (LKEB, www.lkeb.nl)

Profile

The Leiden University Medical Centre (LUMC) has a top international position in research, characterised by an interaction between fundamental research and patient care. The Division of Image Processing (LKEB, ww.lkeb.nl) is a computer science research group within the Department of Radiology. It has a strong track record in developing and publishing innovative biomedical image and data analysis algorithms, and transferring these to industry under strict software quality standards (e.g. companies such as Medis, GE, Toshiba, Agfa, Terumo, Lightlab, Volcano and Boston Scientific). In addition, we have experience with open-source code distribution, as evidenced by the LKEB-co-developed elastix platform for non-rigid image registration (>25000 downloads). This way of working has resulted in several widely used clinical software packages, some of which have been recognised as *de-facto* standard in the field, and a strong publication track record. LKEB's collaboration with the Pattern Recognition and Bioinformatics group at DELFT, which is part of the team researching mining in the Allen Brain Atlas, gives access to state-of-the-art pattern analysis and bioinformatics expertise. In addition, its position within the LUMC connects LKEB to state-of-the-art neuroscience research.

All Principle Investigators (PIs) in this project have either a primary or secondary appointment at LUMC. Boudewijn LELIEVELDT and Marcel REINDERS combine their complementary expertise in medical image analysis and bioinformatics, which are essential

for the project to be successful. They jointly lead the research team that focuses on mining the rich information in the Allen Brain Atlas data. Arn VAN DER MAATEN is a specialist in high-dimensional data analysis and information visualisation. He has developed the state-of-the-art t-SNE, and is regularly invited as a guest speaker by data analytics companies such as Facebook, who routinely use t-SNE in their data analysis processes. VAN DEN MAAGDENBERG and his group are recognised world experts in migraine research. His research activities involve the collection and analysis of patient and mouse material, with various genetic (i.e. at DNA, RNA and protein level), electrophysiological and imaging approaches. His multidisciplinary data is ideally suited for an interactive analysis, as proposed in the current application. Willeke VAN ROON is an expert with over 15 years' experience in Huntington disease research. She was extensively involved in the Brain Bank in Auckland, New Zealand, and has performed many immunohistochemical studies of Huntington disease brain tissue. At the LUMC, she combines this expertise with state-of-the-art, next generation sequencing technology, to further unravel the pathogenic mechanisms behind this devastating disease. She also develops new potential therapies. This diverse expertise, from the anatomy of the human brain down to the regulatory mechanisms of gene transcription, makes her an ideal partner to validate the linking of t-SNE mappings with GENESPACE clusterings.

Key Personnel

- Boudewijn LELIEVELDT (male) is full professor of Biomedical Imaging at the LUMC Department of Radiology, where he heads the Division of Image Processing (LKEB). He is also part of the Pattern Recognition and Bioinformatics group, in the faculty of Electrical Engineering, Mathematics and Computer Science at the Delft University of Technology.

Key Expertise

- Image analysis
- Linking imaging and genetic data
- Mining the Allen Brain database
- Bioinformatics
- Machine learning and Pattern Recognition.

Specific keywords

- Non-linear similarity embeddings (t-SNE)
- Acceleration of tSNE to tackle big-data analysis in life science and clinical research.
- Applications of tSNE in spatially-resolved -omics data
- Integration of similarity embeddings into distributed mining framework
- Domain expertise on Migraine and Huntington's disease.

P4) AUEB, Athens University of Economics and Business, Greece (SP8)

Information Systems and Database Laboratory (ISDL) at AUEB Athens

Profile

The Information Systems and Database Laboratory started work in 1994. The laboratory has developed extensive research and engineering activity in its area of expertise, and has

successfully led and participated in numerous national and international projects, including Marie Curie actions, FET projects and STREP and Integrated Projects. It currently hosts more than ten PhD students and postdoctoral fellows, and supports the Graduate Program in Information Systems. The Laboratory includes five main activity areas: Distributed Information Management and Exploration, Data Mining from Databases and the World Wide Web, Information Security And Critical Infrastructure Protection, Knowledge Management and Organisational Memory, and Software Engineering. The Distributed Information Management and Exploration (DIME) is led by Professor Vasilis VASSALOS, and deals with theoretical and technical aspects of large scale information management, such as distributed query processing and optimisation, data integration, semi-structured data processing, in particular XML documents, query optimisation, peer-to-peer systems, development of Web information Systems, digital libraries, and large scale data analytics.

Key Personnel

- Vasilis VASSALOS (male) is an Associate Professor in the Department of Informatics at the Athens University of Economics and Business.

Key Expertise

- Data and knowledge integration
- Theory and database systems
- Big Data analytics
- Natural language processing
- Knowledge discovery
- Knowledge representation and reasoning
- Ontologies and ontology-based data access
- Distributed computing
- Information technologies
- Management of semi constructed data
- XML query processing
- Network-centric information systems and peer to peer systems
- Semantic access and interconnection of information systems
- Semantic interoperability
- Sensor networks and data streams.

P5) BSC, Barcelona Supercomputing Centre - *Centro Nacional de Supercomputación*, Spain (SP7)

Barcelona Supercomputing Centre (Computer Science and Operations Departments)

Profile

The Barcelona Supercomputing Centre (*Centro Nacional de Supercomputación*, BSC-CNS), was established in 2005, and serves as Spain's national supercomputing facility. The Centre hosts and operates MareNostrum, the most powerful supercomputer in Spain. Currently headed by Mateo VALERO, the BSC is a consortium that includes the Spanish Ministry of Economy and Competitiveness, the Department of Economy and Knowledge of Catalonia and the *Universitat Politècnica de Catalunya* (UPC). BSC-CNS's mission is to develop and manage

cutting-edge information technology tools for scientific research. To further these goals, the BSC-CNS has brought together a group of over 250 Spanish researchers, and more than 100 international researchers. In 2011, the Centre won recognition as a "Severo Ochoa Centre of Excellence" for its major contributions in the area of computing and applications.

Key Personnel

- Jesus LABARTA (male) is full Professor in the UPC Computer Architecture department and Director of the BSC Computer Sciences research department.
- Sergi Girona (male) is Operations Director at BSC and he is responsible for MareNostrum operations and coordination of the Spanish Supercomputing Network. He is also member of the Board of Directors of PRACE.

Key Expertise

- High Performance Computing
- Distributed computing (cluster, cloud)
- Parallel programming models
- Performance analysis of parallel and distributed applications
- Dynamic resource scheduling
- Resource management
- Data management (NoSQL DB)
- HPC system management
- Computing infrastructure
- Cutting-edge supercomputers
- Highly scalable computational methods and implementations
- Emerging computer architectures
- Hybrid multi-core systems with GPUs.

P6) BAUW, Bauhaus University, Germany (SP10)

Virtual Reality and Visualisation Research Group

Profile

The Virtual Reality and Visualisation Research Group carries out research and development (R&D) in stereoscopic display technology, 3D human-computer interaction, information visualisation, scientific visualisation and real-time rendering. We developed and operate the only projection-based stereoscopic display that provides six users with individual, perspectively-correct 3D images and, for the first time, enables effective teamwork when visualising complex 3D models. Recent work on immersive group-to-group telepresence allows distributed groups of users to meet in shared virtual 3D worlds, and explore them together. Our innovative user interfaces are designed and evaluated for complex two- and three-dimensional tasks in collocated and distributed virtual reality environments. We also develop the rendering and visualisation infrastructure for the real-time display of large multivariate image, volume and time-dependent data sets, which occur in medicine and other fields. The VR group has received various awards for its work over the past few years. See (www.uni-weimar.de/medien/vr).

Key Personnel

Bernd FROEHLICH (male) is a full Professor of Computer Science at Bauhaus University. He is also chair of the Virtual Reality and Visualisation Research Group.

Key Expertise

- Multi-user virtual reality
- 3D user interfaces
- Visualisation
- Rendering algorithms for very large datasets
- Information visualisation.

P7) BUW, *Bergische Universität Wuppertal*, Germany (SP7)

Institute of Mathematical Modelling, Analysis and Computational Mathematics (IMACM): Applied Computer Science Group

Profile

The Institute of Mathematical Modelling, Analysis and Computational Mathematics (IMACM) exploits the expertise of mathematical groups at the *Bergische Universität Wuppertal* to solve real-life problems in the natural and social sciences, economics and engineering. The Applied Computer Science Group focuses on efficient numerical algorithms for computer simulation in the sciences, and in particular on numerical linear algebra, algebraic multi-level methods and the numerical solution of PDEs, and of systems of ODEs on highly parallel super-computers. Key application fields include theoretical physics (quantum chromodynamics) and particle simulation. The Group currently consists of three professors, two permanent scientific staff, two postdoctoral fellows and around ten PhD students, financed by the University, and by projects funded by DFG, the German Science Foundation. The group has strong ties with the Jülich Supercomputing Centre.

Key Personnel

- Andreas FROMMER (male) is a Professor of Applied Computer Science in the Mathematics and Science Department.

Key Expertise

- Numerical solvers for ODEs
- Further development of NEST
- Network simulation
- Linear system solvers on parallel machines
- Eigensolvers on parallel machines
- Multigrid methods and adaptivity
- Methods for linear system with special structure
- Particle simulation methods.

P8) BSMJ, Bloomfield Science Museum Jerusalem, Israel (SP11)

Bloomfield Science Museum Jerusalem

Profile

The Bloomfield Science Museum Jerusalem is one of Israel's leading informal cultural and educational institutions. The museum's goals are to increase the general public's interest in science and technology, to present science and technology as an integral part of human culture, and to develop dialogue between scientists and society. The museum promotes public engagement with science, using exhibitions of cutting-edge research, and innovative technologies and debates to promote the exchange of ideas. Planned activities include launching a Science Café, and a series of film screenings ("science and movies"). The BSMJ operates under the auspices of The Hebrew University of Jerusalem. The museum is very active in the European Network of Science Centres and Museums (ECSITE), the Association of Science and Technology Centres (ASTC), and the European Science Events Association (EUSEA). BSMJ has participated in several EU SiS projects under FP6 and FP7, and is currently coordinating the ENGINEER project.

Key Personnel

Maya HALEVY (female) is the Director of the Bloomfield Science Museum in Jerusalem. She has initiated and participated in several Israeli-Palestinian Science Museum programmes – part of the people-to-people philosophy that encourages cooperation in science education.

Key Expertise

- Science museums and science centers and multi-level cooperation
- Multi-national co-design and co-development of content of exhibitions and programs, as coordinators and as partners
- Operate living labs in the museum
- Development of teams and processes for interactive exhibitions and museum environment
- Professional team and physical infrastructure for building interactive environment.
- Making cutting edge research accessible through exhibitions and engaging scientists with the general public through social platforms.
- Operation of a science museums as a hub for very diverse population - from different communities and ages

P9) CF, Cardiff University, United Kingdom (SP8)

MRC Centre for Neuropsychiatric Genetics and Genomics (MRC CNGG), Division of Psychological Medicine and Clinical Neurosciences

Profile

The MRC Centre for Neuropsychiatric Genetics and Genomics (MRC CNGG) focuses on common psychiatric and neurodegenerative disorders. The Centre brings together strong gene discovery programmes, which are supported by MRC, the Wellcome Trust, the EU, and other major funders. It is organised into three broad disease themes: Psychosis and Mood Disorders (schizophrenia (SZ), bipolar disorder (BD), puerperal psychosis, depression), Developmental Disorders (ADHD, childhood depression, carriers of structural chromosomal rearrangements), and Neurodegenerative Disorders (Alzheimer's disease (AD), Parkinson's Disease (PD), fronto-temporal dementia (FTD), Huntington's disease (HD)). This work is complemented and enhanced by four crosscutting themes: Biostatistics and Bioinformatics, Neuroimaging, Cellular and Animal Models, and the National Centre for Mental Health. The

work of the CNGG involves genetics and genomics, including large-scale GWAS and NGS studies. Data analysis and storage is supported by a dedicated Biostatistics and Bioinformatics Unit. It also includes work on genomic epidemiology, brain imaging (MRI, fMRI, MEG, EEG), iPSC and animal models of disease mutations, and other forms of genetic risk.

Key Personnel

Andrew Pocklington (male) is Senior Lecturer in Bioinformatics at the Medical Research Council's Centre for Neuropsychiatric Genetics and Genomics at Cardiff University.

Key Expertise

- Genetics
- Genomics
- Functional genomics
- Bioinformatics
- Biostatistics
- Clinical psychiatry
- Clinical neurology
- Rodent models
- Cellular models (including iPSC)
- Brain imaging
- Cognitive phenotyping
- Schizophrenia
- Bipolar disorder
- ADHD
- PD
- AD
- HD.

P10) CNRS, *Centre National de la Recherche Scientifique*, France (SPs 4, 6, and 9)

CNRS FRE3693 Unité de Neuroscience, Information et Complexité

Profile

The *Unité de Neuroscience, Information et Complexité* (CNRS-UNIC, Gif sur Yvette) was created in 2000, as a multidisciplinary research unit combining experimental and theoretical neuroscience. This Unit has played a leading role in the biology coordination of FET integrated projects (Facets) and in the Marie Curie training network (FACETS-ITN). UNIC, directed by Yves FRÉGNAC, is currently a major integrative and computational neuroscience partner in the FP7 integrated project BrainScaleS, one of the foundations of the Human Brain Project. The research, led by the seven multidisciplinary, interactive teams composing UNIC, focuses on:

1) Multi-scale acquisition of *in vitro* and *in vivo* electrophysiological and network imaging data, related to information processing and multi-sensory integration in cortical-like structures in different species (electric fish, mouse, rat, ferret and cat).
2) Theoretical modelling of thalamic and neocortical dynamics.
3) The creation of tools for large-scale, data-driven neural network simulation.

This highly integrated interdisciplinary work has led to significant advances in generic concepts for brain theory, and strategic data for computational neuroscience and neuromorphic hardware developers.

Key Personnel

Alain DESTEXHE (male) is a physicist and Research Director (DR1) at CNRS. He is the Head of the computational neuroscience group at UNIC.

Andrew P. DAVISON (male) is a senior research scientist (CR1) at CNRS-UNIC, where he leads the Neuroinformatics group.

Irina KOPYSOVA (female) is a Computer Science Engineer (IE1) at CNRS-UNIC.

Key Expertise

- Modelling of the local field potential and of the surface EEG
- Modelling of neuronal magnetic fields
- Design of simplified neuron models at several levels e.g. morphology and dynamics
- HW system simulation ("ESS")
- Meta-languages (PyNN)
- Analysis tools for experiment results
- Model adaptation to hardware
- Integration with HPC
- Collaboratory integration
- Platform operation and user support
- Training, education and community building
- Benchmarking
- Network neuroscience
- System and computational neuroscience.

Université Lyon I / CNRS UMR 5086 Bioinformatics: Structures and Interactions group, Institute of Biology and Chemistry of Proteins

Profile

The Bioinformatics: Structures and Interactions group (CNRS-IBCP, Lyon), directed by Richard LAVERY, is one of ten that form the *Institut de Biologie et Chimie des Protéines* (IBCP), an institute centred on molecular microbiology and structural biochemistry. Our research involves molecular modelling, molecular simulation and structural bioinformatics. We use these to analyse and to predict the structure, dynamics and functional interactions of biomacromolecules. To this end, we use existing computational methods and databases, but we also develop new methods applicable to biomacromolecules. Our work within the HBP involves refining and applying coarse-grain models to predict the structure and stability of protein assemblies, notably those involved in intra-neuronal signalling cascades. To

achieve this goal, we exploit existing sequence and structural information, combined with new high-throughput simulation methods that are applicable to a wide variety of multi-protein complexes.

Key Personnel

Richard LAVERY (male) is the Head of the Bioinformatics group at the Institute of Biology and Chemistry of Proteins, Lyon, CNRS UMR 5086 / University of Lyon.

Key Expertise

- Molecular modelling and simulation
- Molecular graphics
- Structural bioinformatics
- Conformational analysis
- All-atom molecular simulations
- Development of coarse-grain models
- Coarse-grain molecular simulations
- Molecular docking
- Protein dynamics
- Predicting protein-protein interactions.

P11) CEA, *Commissariat à l'Énergie Atomique et aux Énergies Alternatives*, France (SP2, SP5)

Laboratoire de Neuroimagerie Assistée par Ordinateur

The *Laboratoire de Neuroimagerie Assistée par Ordinateur* (LNAO) is a group led by Jean-François MANGIN at NeuroSpin. It is involved in algorithmic research in neuroimaging. The group's aims include the study of the dynamics and variability of the cortical folding process, and the organisation of MRI-defined white matter bundles. The group's strategy relies on building bottom-up representations of individual data, to be matched to graph-based models of human brain architecture. The resulting computer vision tools have been used to create brain atlases of cortical folds and brain fibre bundles, to infer biomarkers of psychiatric syndromes and to study brain plasticity.

Key Personnel

Jean-François MANGIN (male) is the Head of the NeuroSpin LNAO group, and the Director of CATI, a French national platform for multicentre neuroimaging studies.

Key Expertise

- Neuroimaging
- Image analysis
- Neuroanatomy
- Neuroinformatics
- Connectivity.

Nuclear Magnetic Resonance Imaging and Spectroscopy Unit

The NeuroSpin centre's Nuclear Magnetic Resonance Imaging and Spectroscopy Unit (UNIRS), led by Cyril POUPON, is in charge of driving research and methodological developments in the field of Magnetic Resonance (MR) physics, including MR imaging and Spectroscopy. This is focused on the use of a unique ultra-high field MR platform (three clinical systems at 3T, 7T and 11.7T whole-body (90 cm), three preclinical systems at 7T, 11.7T and 17T small-bore (26 cm) horizontal magnet) to push the limits of spatial, temporal and spectral resolutions of brain imaging.

Key Personnel

Cyril POUPON (male) is the Head of LRMN and co-Principal Investigator for the multi-scale architecture research and Magnetic resonance imaging at ultra high field programmes.

Key Expertise

- Neuroimaging
- MR physics
- Diffusion imaging
- Tractography
- Microstructure mapping
- Connectivity

P12) CNR, *Consiglio Nazionale Delle Ricerche*, Italy (SP6)

National Research Council, Institute of Biophysics, Laboratory of Computational Neuroscience

Profile

The Italian National Research Council (CNR) is a public organisation; its duty is to carry out, promote, transfer and improve research activities in the main sectors of knowledge growth, and their applications for the scientific, technological, economic and social development of the country. CNR Institutes are distributed all over Italy. The Institute of Biophysics is based in Genoa, and has four separate research divisions located in Milan, Pisa, Palermo, and Trento. The Laboratory of Computational Neuroscience (Palermo division) has a very active group of researchers, and several on-going international collaborations with leading laboratories. It focuses on modelling realistic implementations of brain structures at different levels, ranging from neurons to large-scale networks, synaptic transmission, signal integration processes, plasticity mechanisms, and ion channels. The aim is to study their role in modulating neuronal excitability, firing behaviours, and the emergence of pathologies and dysfunctions.

Key Personnel

Michele MIGLIORE (male) is a senior research scientist at the Italian National Research Council's Institute of Biophysics.

Key Expertise

- Synaptic transmission and plasticity models
- Cellular level modelling and simulation
- Large-scale simulations of realistic networks

- Methods for complexity reduction of neurons
- Modelling higher brain functions
- Modelling brain dysfunctions and diseases.

National Institute of Optics (INO)

Profile

The current National Institute of Optics (INO) has been working for over ninety years in the field of Optics, understood in its broadest meaning, and has updated its fields of activity in line with the huge innovations that have characterised this area over the last century. Nowadays, its activities are: pure and applied research, technological transfer, consulting for public institutions and businesses. These are accompanied by metrology measurements and testing services (again for public institutions and businesses), and training activities.

Key Personnel

Dr. Leonardo SACCONI (male) is a CNR permanent researcher at INO.

Key Expertise

- Pure and applied research
- Technological transfer
- Consulting services
- Metrology measurements and testing

P13) CINECA, *Consorzio Interuniversitario Cineca*, Italy (SP7)

Consorzio Interuniversitario CINECA

Profile

Founded in 1969, Cineca is a non-profit consortium of 70 Italian universities, the National Institute of Oceanography and Experimental Geophysics (OGS), the National Research Council (CNR), and the Ministry of Education, University and Research (MIUR). Cineca is the Italian national supercomputing centre. It has an HPC & Data Analytics environment equipped with cutting-edge technology and highly-qualified personnel. It cooperates with researchers in the use of the HPC infrastructure, in both academic and industrial fields. Cineca's mission is to enable researchers to use HPC systems in a profitable way, exploiting the newest technological advances in HPC and Data Analytics. Cineca represents Italy in the Partnership for Advanced Computing in Europe (PRACE), and is one of the four PRACE Tier-0 Hosting Centres. Cineca plays an active role in many national and EC-funded projects concerning HPC Infrastructures and R&D. In 2017—18, the Cineca HPC infrastructure Roadmap plans to host a system in the range of 50 PFlops, integrated with an enhanced fast storage data facility in the order of 50 PBytes. This will be able to manage Big Data analytics and visualisation activity related to data produced by the HBP.

Key Personnel

- Giovanni ERBACCI (male) is responsible for the Division for the Academic and EU HPC Projects in CINECA's Supercomputing Application and Innovation Department.

Key Expertise

- Supercomputing infrastructure

- High performance computing
- Hybrid multi-core systems with GPUs and Intel MIC
- Emerging and energy efficient computing architectures
- Data facilities infrastructures
- Highly scalable computational methods and implementations
- New programming models and methodologies
- Analysis and enabling of advanced computational applications
- Algorithms for brain images
- Computational materials science
- Management of large volumes of data
- Pre and post processing of data
- Scientific visualisation
- Remote visualisation and in-situ visualisation
- Analytics frameworks (Apache Hadoop, Apache Spark, etc.)
- Big Data analytics
- Machine learning, data mining, predictive modelling and text mining
- Cloud Computing technology
- High-performance bioinformatics and epigenomic services.

P14) DTU, *Danmarks Tekniske Universitet*, Denmark (SP10)

The Centre for Playware

Profile

The Centre for Playware at DTU focuses on modular robotic hardware development, constructionist methods for developing robotic applications, and on the robot morphology-control relationship. The Centre uses its extensive experience in biologically inspired robotics and modern artificial intelligence to develop user-guided approaches based on behaviour-based robotics, evolutionary robotics, multi-agent systems, and neural network control for modular robotic systems. The underlying hypothesis is based on a modular robotics concept, which makes robotic devices applicable in a wide range of areas, and which allows users to generate knowledge with hands-on development of artefact morphology. The Centre collaborates with large companies such as LEGO, and uses insight into modern artificial intelligence, interaction design and modular robotics to create novel intelligent artefacts with a seamless interface for end-users in rehabilitation, therapy, care of children and the elderly, sport, music, education, and home entertainment.

Key Personnel

- Henrik HAUTOP LUND (male) is Head of the Centre for Playware at the Technical University of Denmark (DTU Electro).

Key Expertise

- Modular robotics
- Biomimetic robotics

- Self-reconfigurable robots
- Embodied artificial intelligence
- Adaptive and self-organising control
- Locomotion
- Playful interaction
- Robots for rehabilitation
- Distributed control strategies
- Scalable robots
- Fault-tolerant robots.

P15) UoD, *Debreceni Egyetem*, Hungary (SP1)

Laboratory for Cortical Systems Neuroscience

Profile

The Laboratory for Cortical Systems Neuroscience (LCSN) is a multidisciplinary research laboratory, which focuses on the organisation of the cerebral cortex at micro- and mesocircuitry levels. The group's main aim is the investigation of input-output relationships of neuronal cell types in the cerebral cortex, and their role in visual contour integration processes. To achieve this, *in vivo* functional imaging (intrinsic signal optical imaging), single and multi-unit electrophysiology, and a host of anatomical labelling techniques have been used. We determine the anatomical correlates of functional properties, and estimate the impact on wiring and communication of the cortical network. Our recent work concerns the anatomical mapping of human cortical tissue for intrinsic cortical architecture, and its correlate with connectivity clustering rules. The group is well equipped with the necessary experimental devices, and benefits from the university's core research facilities. It has strong ties with the groups at CNRS and EPFL.

Key Personnel

Zoltan KISVARDAY (male) is Head of the research group at the Laboratory for Cortical Systems Neuroscience.

Key Expertise

- Experimental animals and human brain
- Visual cortical areas
- *In vivo* electrophysiology of single units
- *In vivo* intra- and extracellular labelling
- *In vivo* functional mapping (intrinsic and VSD optical imaging)
- Three-dimensional neuron reconstruction
- Electron microscopy.

P16) DMU, De Montfort University, United Kingdom (SP12)

Centre for Computing and Social Responsibility (CCSR)

Profile

The Centre for Computing and Social Responsibility (CCSR), a research centre located in DMU's School of Computing in the Faculty of Technology, is the largest research centre of its kind in the UK, and one of few in Europe and the world. It includes twelve full-time academics, of which three are professors. The CCSR has undertaken funded research for a range of stakeholders, including private organisations, professional bodies, NGOs, the UK government and the European Union. As one of the leading research centres in the field of information technology ethics, the CCSR set up, and runs, the ETHICOMP conference series. Since 2008, members of the CCSR have led successful research funding bids, leading to a research income for the group of more than EUR 2 million. Taking an interdisciplinary approach, the CCSR has gained an impressive reputation as a key player in the international research network for the ethical and social implications of ICT. With a growing demand from both the public and government to deliver acceptable ICT, its mission is to undertake research and provide teaching, consultancy and advice to individuals, communities, organisations and governments at local, national and international levels on the actual and potential impacts of computing and related technologies on society and its citizens.

Key Personnel

Bernd Carsten STAHL (male) is a Professor of Critical Research in Technology, and Director of the Centre for Computing and Social Responsibility.

Key Expertise

- Computer ethics
- Responsible research and innovation, in particular in ICT
- Ethics of technology
- Technology assessment.

P17) ENS, *École Normale Supérieure*, France (SP6)

Cell Biology of the Synapse Group

Profile

The goal of the Cell Biology of Synapse Group is to understand the basic mechanisms regulating synaptic function in normal and pathological situations. Since 2001, the Group has combined methods from cell biology and physics to study the movement of receptors in real time. In 2003, in collaboration with Maxime DAHAN, it developed new video microscopy techniques using nano-semiconductor particles, also known as quantum dots. The new approach made it possible to directly visualise the movement of receptors, in and out of synapses. This single particle tracking (SPT) method has made it possible to characterise the diffusive properties of receptors in sub-membrane domains, and has validated the mechanism of diffusion capture for the stabilisation of receptors at central synapses. The Group is composed of five permanent researchers, six postdoctoral fellows, six PhD students, and three engineers and technicians.

Key Personnel

Antoine TRILLER (male) is the Director of the *Institut de Biologie de l'École Normale Supérieure* (IBENS).

Key Expertise

- Biology of the synapse
- Super-resolutive microscopy
- Modelling of dendrites
- Molecular Imaging and receptor diffusion
- Modelling diffusion process
- Modelling synaptic strength
- Excitation-inhibition interaction.

P18) ETHZ, *Eidgenössische Technische Hochschule Zürich*, Switzerland (SP7)

Swiss National Supercomputing Centre at ETH Zurich

Profile

Founded in 1991, the Swiss National Supercomputing Centre (CSCS) partners with Swiss universities and research institutions on all issues related to high performance computing. Headed by Thomas SCHULTHESS, CSCS provides scientists with the computing infrastructure and expertise they need, from cutting-edge supercomputers, to a full range of services delivered by an international fifty-person team. CSCS is an autonomous unit of the Swiss Federal Institute of Technology in Zurich (ETH Zurich) and is located in Lugano, in the Italian-speaking region of Switzerland. CSCS also caters for users from business and industry, and works with the world's leading computing centres and hardware manufacturers to guide and develop the state-of-the-art.

Key Personnel

Thomas C. SCHULTHESS (male) is the Director of CSCS, and leads the Swiss initiative for High-Performance Computing and Networking.

Key Expertise

- Computing infrastructure
- High performance computing
- Cutting-edge supercomputers
- Highly scalable computational methods and implementations
- Emerging computer architectures
- Hybrid multi-core systems with GPUs
- Computational materials science
- Large ensemble simulations
- Computational methods and algorithms for quantum simulations
- Quantum cluster methods
- Interacting electron systems models
- 3D algorithms for cellular radio propagation
- Modelling signals

- Visualisation algorithms
- Visualisation and supercomputing
- Interactive visualisation and analysis of running supercomputing applications
- Communication middleware
- Data sharing
- HPC system management, scientific computing, grid computing and distributed systems.

P19) FT, *Fonden Teknologirådet*, Denmark (SP12)

Danish Board of Technology (DBT)

Profile

The Danish Board of Technology Foundation (DBT) is the parliamentary technology assessment institution of Denmark. It is an independent, non-profit, common good, corporative foundation SME, committed to technology assessment and parliamentary advisory activities on science, technology and innovation foresight. The DBT is an expert in political deliberation and advice, and interactive methodologies involving trans-disciplinary research, stakeholder involvement, citizen participation and public communication. The DBT is at the forefront of praxis, particularly in the domain of stakeholder and citizen consultation, which is connected to policy analysis. The DBT's method includes scenario workshops, future labs, future search conferences, voting conferences, expert and citizen hearings, crowdsourcing, and multi-Site citizen participation processes. The DBT has historically emphasised the importance of citizen participation in technological development, administrative planning, and political decision-making. In its 30 years of methodological development, it has built a world-class skillset for the facilitation of trans-disciplinary dialogue and solution-orientated research.

Key Personnel

Lars KLÜVER (male) is the Director of the Danish Board of Technology Foundation.

Key Expertise

- Citizen participation and engagement
- Multi-stakeholder and trans-disciplinary dialogue and deliberation processes
- Science, technology and innovation policy advice
- Technology assessment and foresight
- Processes of responsible research and innovation.

P20) JUELICH, *Forschungszentrum Jülich GmbH*, Germany (SPs 2, 4, 5, 6, 7 and 9)

Institute of Neuroscience and Medicine — Structural and Functional Organisation of the Human Brain

Profile

The Institute of Neuroscience and Medicine — Structural and Functional Organisation of the Human Brain (INM-1), headed by Katrin AMUNTS, is developing a 3D model of the human brain, which considers cortical architecture, connectivity, genetics and function – known as

the JuBrain. To reach this goal, researchers collaborate closely with the Jülich Supercomputing Centre and the Virtual Reality Group at RWTH Aachen University. The Institute is currently developing a multimodal Human Brain Atlas that integrates data on cellular and molecular architecture, connectivity, and brain function. It hosts fully equipped labs for histological processing and receptor autoradiography of entire human brains. INM-1 has developed state-of-the-art and unique post mortem brain characterisation methods for quantitative cyto and receptor architecture, 3D-reconstruction, atlasing and visualisation. During the last few years, methods of high performance computing and Big Data analytics have been integrated in the portfolio. The Institute has approximately 90 researchers, technicians and doctoral students. Current collaborations include an NIH project with UCLA, a GIF project with the University of Tel Aviv, and projects with the Department of Psychology, at Stanford University, and the Ahmanson Brain Imaging and Neurology Centre, UCLA.

Key Personnel

- Katrin AMUNTS (female) is Professor for Brain Research at the *Heinrich-Heine Universität Düsseldorf*, Director of the C. and O. Vogt Institute for Brain Research, and Director of the Institute of Neuroscience and Medicine (INM-1). She is also member of the German Ethics Council.
- Karl ZILLES (male) has a joint JARA-Senior-Professorship at the Research Centre Jülich and the Department of Psychiatry, Psychotherapy and Psychosomatics at RWTH Aachen University. He is Fellow of the German National Academy of Sciences Leopoldina, and Fellow of the North-Rhine Westphalia Academy of Science and Arts. He is Editor-in-Chief of *Brain Structure and Function*, and Chair of the International Organisation of Human Brain Mapping.
- Sven CICHON (male) is Research Group Leader of "Genomic Imaging" at INM-1 in JUELICH. He is also Director of the Division of Medical Genetics at the University Hospital Basel, and Head of the Human Genomics Research Group at the University of Basel Department of Biomedicine.
- Markus AXER (male) is the Head of the "Fibre Architecture" group at the Institute of Neuroscience and Medicine (INM-1).
- Timo DICKSCHEID (male) is the Group Leader of "Big Data Analytics" at Jülich.
- Markus Diesmann (male) is Research Group Leader of the “Computational Neurophysics” group in the Computational and Systems Neuroscience (INM-6) & Theoretical Neuroscience (IAS-6) at Forschungszentrum Jülich.
- Simon B. Eickhoff (male) is Professor for cognitive neuroscience at the Heinrich-Heine University in Duesseldorf and deputy Director of the Institute of Neuroscience and Medicine in Jülich, where he leads the Brain Network Modelling group.

Key Expertise

- High- and ultrahigh resolution 3D Human Brain Models
- Human brain atlasing
- Standard reference space
- Integration of structural, physiological and functional imaging data
- Cortical architecture
- Fibre architecture
- Cyto- and receptorarchitectonic data acquisition and analysis of entire human brains

- 3D Polarised Light Imaging
- Integrated models of structure, function, and connectivity
- Genomic imaging
- 3D image reconstruction and segmentation
- Big Data Analytics and High Performance Computing for Image Analysis
- Fibre architecture in post mortem rodent, monkey, and human brains
- Polarised Light Microscopy (3D-Polarised Light Imaging, 3D-PLI)
- Image processing: 3D reconstruction, registration, segmentation, stitching
- Automated workflow development and supercomputing
- Visualisation
- Multimodal and multiscale image processing and analysis
- Large-scale data processing on HPC infrastructures.

Institute of Neuroscience and Medicine — Molecular Organisation of the Brain

The Institute of Neuroscience and Medicine — Molecular Organisation of the Brain (INM-2) investigates organisational principles of the brain from the molecular level to that of small neuronal networks. The different research groups want to gain insight into the distribution and function of neurotransmitters, the structural properties of synapses, and the connectivity of small neuronal microcircuits. Based on these key structures of neuronal information processing, we want to understand principles of sensory, motor, cognitive, and emotional performances of the brain, and to be able to predict (patho)physiological processes and the underlying morphological changes. Within INM-2, Dirk FELDMEYER's laboratory focuses on structural, functional and developmental characteristics of neuronal connectivity in the neocortex, and aspects of neuronal modulation in the neocortex of normal animals and models related to neurological/psychiatric diseases.

Key Personnel

Dirk FELDMEYER (male) is a Professor at RWTH Aachen University. He is also the Head of the "Function of Neuronal Microcircuits" group in the Institute of Neuroscience and Medicine (INM-2), and of the "Function of Cortical Microcircuits" group in the Department of Psychiatry, Psychotherapy and Psychosomatics at RWTH Aachen University.

Joachim Lübke (male) is Research Group Leader of the "Structure of Synapses" group in the Institute of Neuroscience and Medicine (INM-2) at Forschungszentrum Jülich.

Key Expertise

- Functional and structural characterisation of excitatory and inhibitory neurons in the neocortex
- Functional and structural analysis of identified neuronal microcircuits in the neocortex
- Developmental processes involved in sculpturing neocortical neuronal networks
- Neuromodulation of synaptic transmission in the neocortex
- Pathological changes in neuronal networks in animal models of neurological and psychiatric diseases.

Institute of Neuroscience and Medicine — Computational and Systems Neuroscience, and Institute for Advanced Simulation — Theoretical Neuroscience

Profile

The Institute of Neuroscience and Medicine — Computational and Systems Neuroscience (INM-6) and the Institute for Advanced Simulation — Theoretical Neuroscience (IAS-6) specialise in integrating experimental data on the structure and dynamics of the brain into mathematical models, and in overcoming bottlenecks in simulation technology and workflows. The Statistical Neuroscience group, led by Sonja GRÜN, focuses on the development and application of methods to analyse multi-channel activity data in close contact to experimental groups. One focus is the connection between neural data recorded on different temporal and spatial scales, and on the structure of correlations of spiking activity. The Computational Neurophysics group, headed by Markus DIESMANN, focuses on bottom-up approaches to integrating physiological and anatomical data into models. It focuses in particular on model development, theory of neuronal networks, and correlation dynamics. This also requires the development of simulation technology for neural networks. The Functional Neural Circuits group, led by Abigail MORRISON, investigates mechanisms underlying neural computation through the development of models on the level of networks of spiking neurons. It applies a predominantly top-down approach, to discover functional constraints on structure, plasticity and dynamics, particularly with respect to learning and memory. The secondary focus is on simulation technology for high-performance computers. Moritz HELIAS' Theory of Multi-scale Neuronal Networks group focuses on investigating mechanisms that shape the correlated and oscillatory activity in neuronal networks, with structured connectivity on several spatial scales. This requires the development of quantitative theoretical descriptions, adapted from statistical physics, combined with direct simulations of neuronal networks at cellular resolution. The INM-6/IAS-6 puts special emphasis on the selection and promotion of top rank PhD candidates in neuroscience, and has developed standard operating procedures to identify ideal candidates. On top of a research centre-wide PhD program and doctoral studies at local universities, PhD candidates at INM-6/IAS-6 follow a dedicated in-house PhD program, including PhD plan proposal meetings, PhD plan meetings, regular one-to-one meetings with supervisors, lectures, tutorials, and specific training on crucial scientific skills.

Key Personnel

- Sonja GRÜN (female) is the Vice Director of INM-6, where she heads the Group on Statistical Neuroscience. She is also full professor for Theoretical Systems Neurobiology at RWTH Aachen University.
- Markus DIESMANN (male) is Professor of Computational Neuroscience at RWTH Aachen University, and is the Director of the Institute of Neuroscience and Medicine (INM-6), Computational and Systems Neuroscience, and the Institute for Advanced Simulation (IAS-6), Theoretical Neuroscience, at *Forschungszentrum Jülich*.

Key Expertise

- Statistical analysis of (massively) parallel neuronal data
- Development of methods and tools for the analysis of network interactions
- Development of tools for reproducibility in neuroscience
- Electrophysiological and behavioural data of awake animals
- Experiment design for awake animals
- Simulation technology for large-scale neuronal networks
- Hybrid parallelisation of neuronal networks simulation codes

- Profiling and performance analysis of network simulation codes
- Theory of spiking neuronal networks
- Functional neuronal network models
- Scientific software development
- Extensive experience with mentoring programs
- Career development planning
- Supervision and promotion of young scientists

Simulation — Computational Biomedicine

Profile

The Computational Biomedicine Lab (INM-9/IAS-5) uses a range of computational molecular biology approaches. Its aim is to dissect structural and energetic aspects of cellular pathways that relate to perception and deranged cascades of events in molecular medicine and neurobiology. Most of the work is conducted in collaboration with experimental labs.

Key Personnel

Paolo CARLONI (male) is the Director of the Computational Biomedicine lab (IAS-5), and the Director of the Computational Biomedicine section (INM-9) at the Institute of Neuroscience and Medicine at *Forschungszentrum Jülich*.

Key Expertise

- Molecular simulations
- Hybrid QM/MM calculations
- Coarse-Grain simulations
- Structural Bioinformatics
- High performance computing.

Jülich Supercomputing Centre

Profile

As a European leader in high performance computing, the Jülich Supercomputing Centre (JSC) has long-standing expertise in operating supercomputers of the highest performance. In cooperation with industry partners, the JSC co-designs innovative high performance computing technology, meeting the challenges of the next supercomputer generation. Led by Thomas LIPPERT, the JSC plays an active role in various national and EC-funded R&D and infrastructure projects in high performance computing, networking, and distributed/Grid computing. In particular, it has been pivotal in the creation of PRACE, the European supercomputing research infrastructure.

Key Personnel

- Thomas LIPPERT (male) is the Director of the Jülich Supercomputing Centre. He is also the Executing Director of the John von Neumann Institute for Computing of the Helmholtz Association (NIC) and the Director of the Jülich Aachen Research Alliance, section HPC (JARA-HPC).

Key Expertise

- High Performance Computing

- Cutting-edge supercomputers
- Data storage including end-to-end data integrity
- High speed network and communications
- HPC system management
- Data and compute system integration
- Data management, transfer, and sharing
- Grid computing, distributed system s and infrastructure federa
- Authentication, authorisation, and access control
- IT Security
- HPC architecture (co-)design with industry partners
- Future HPC architectures and technologies
- HPC on massively parallel processing devices (GPU, Xeon Phi)
- Computational science
- Highly scalable computational methods and implementations
- High-level community-specific user support through Simulation Labs
- Optimisation and tuning of parallel programs (instrumentation, measurement, analysis, visualisation, and modelling of parallel program performance)
- Development and maintenance of middleware and tools for HPC
- Visualisation and supercomputing
- Management of national and European R&D and infrastructure projects.

P21) FORTISS, *Fortiss GmbH*, Germany (SP10)

Fortiss GmbH

Profile

Fortiss is a Technical University of Munich (TUM) affiliated institute (*An-Institut*) for research and technology transfer. As such, it is a fully-fledged academic research institute, while also enjoying the independence granted by its legal form as a not-for-profit LLC (*gemeinnützige Gesellschaft mit beschränkter Haftung - gGmbH*). The shareholding partnership has been divided between Freistaat Bayern (the Free State of Bavaria) and the *Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V*. The Free State of Bavaria owns 66%, *Fraunhofer* owns 33%. Fortiss' mission is to facilitate research and technology transfer in software-intensive systems and services, thereby triggering future-ready innovation.

Key Personnel

Patrick VAN DER SMAGT (male) is a Professor of Biomimetic Robotics and Machine Learning at TUM.

Key Expertise

- Probabilistic machine learning
- Deep neural networks and recurrent neural networks

- Biomimetic robotics, wearable robotics
- Tactile sensing
- Computational neuroscience.

P22) FG, *Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V.*, Germany (SP7, SP9)

Fraunhofer Institute für Zuverlässigkeit und Mikrointegration (IZM)

Profile

FHG-IZM is a world leader in microelectronics and microsystem packaging. It offers advanced packaging concepts, such as packaging material science and characterisation, package design and simulation, high density interconnect and wafer level packaging, chip and board interconnection technologies, 3D packaging, and vertical chip integration. The Department Wafer Level System Integration (WLSI) develops wafer level system integration technologies, including wafer level packaging (WLP), chip size packaging (CSP), thin film technology, and 3D integration using through silicon vias (TSVs). It operates two state-of-the-art clean room facilities, and cooperates with manufacturers, material suppliers and end users to create cutting-edge wafer level packaging solutions. Its FHG-IZM is a world leader in microelectronics and microsystem packaging, offering advanced packaging concepts such as packaging material science and characterisation, package design and simulation, high density interconnect and wafer level packaging, chip and board interconnection technologies, 3D-packaging and vertical chip integration. The WLSI Department Wafer Level System Integration (WLSI) develops wafer level system integration technologies, including wafer level packaging (WLP), chip size packaging (CSP), thin film technology and 3D integration using through silicon vias (TSVs). It operates two state-of-the-art clean room facilities and cooperates with manufacturers, material suppliers and end users to create cutting-edge wafer level packaging solutions. Its technology branches develop, prototype and produce MCM-D, wafer-level CSP with redistribution layer (RDL), 3D integration and wafer-level bumping.

Key Personnel

Oswin EHRMANN (male) is the Head of the Department Wafer Level System Integration (WLSI) at the Fraunhofer IZM in Berlin.

Key Expertise

- System design, integration and testing
- New technologies.

Fraunhofer Institute for Algorithms and Scientific Computing (SCAI)

Profile

The Fraunhofer Institute for Algorithms and Scientific Computing (SCAI) is directed by Michael GRIEBEL. It conducts research in the field of computer simulations for product and process development, and is a prominent corporate partner in the industrial and scientific sectors. SCAI designs and optimises industrial applications, implements custom solutions for production and logistics, and offers calculations on high performance computers. SCAI services combine industrial engineering with state-of-the-art methods from applied mathematics, computer science and information technology. The Institute excels in coupling simulation with efficient numerical tools, and in developing scientific visualisation software.

Key Personnel

- Michael GRIEBEL (male) is a Professor of Scientific Computing and Numerical Simulation at the University of Bonn, Director of the Institute for Numerical Simulation at University of Bonn, and also Director of the Fraunhofer Institute for Algorithms and Scientific Computing SCAI.

Key Expertise

- Scientific computing
- Numerical simulation
- Computational science
- Multiscale modelling
- Multilevel methods
- Hierarchical methods
- High performance computing
- Molecular dynamics simulation
- Molecular modelling
- Ion migration simulation
- Non-linear Poisson-Nernst-Planck solver
- High dimensional numerical methods
- Sparse grids
- Optimisation
- Uncertainty quantification
- Parameter estimation
- Model order reduction.

P23) FCHAMP, *Fundaçao D. Anna Sommer Champalimaud E Dr Carlos Montez Champalimaud*, Portugal (SP2)

The Champalimaud Foundation

Profile

The Champalimaud Foundation (CF), based in Lisbon, Portugal, is an international organisation. It aims to stimulate new theoretical and practical methodologies by using the experience of both research scientists and medical practitioners. The Foundation supports individual researchers and research teams working at the cutting edge of biomedical science. By supporting these active research programmes, The Champalimaud Foundation intends to stimulate further clinical research, particularly in the non-profit sector. By doing so, the Foundation aspires to make a significant contribution to reducing the global burden of illness and disease. The Champalimaud Neuroscience Programme (CNP) was created in 2007, via a collaborative agreement between the Champalimaud Foundation and the Calouste Gulbenkian Foundation. It is a basic-research team, with the broad aim of understanding brain function through integrative biological approaches. CNP laboratories apply advanced molecular, physiological and imaging techniques to clarify the function of neural circuits and systems in animal models. These include drosophila, mouse, rat and

zebrafish. The CNP is based at the Champalimaud Centre for the Unknown (CCU). The CCU is a multidisciplinary centre for neuroscience, translational cancer research and clinical practice. The Centre contains state-of-the-art facilities for basic and clinical research, which have cutting edge technological tools and equipment. The CNP also organises the International Neuroscience Doctoral Programme. In this programme, students are provided with a broad educational background through both formal classes and hands-on experience. They cover basic topics of contemporary neuroscience, such as cellular and synaptic physiology, sensation and action, and cognitive neuroscience. We emphasise quantitative approaches, and students also receive background courses in mathematics and programming.

Key Personnel

Rui Costa (male) is Principal Investigator and Director of Champalimaud Foundation Research. He is the President of the American-Portuguese Biomedical Research Fund and Vice-President of the Portuguese Society for Neuroscience.

Key Expertise

- Imaging techniques
- Neural circuits and systems in animal models
- Cellular and synaptic physiology
- Cognitive neuroscience

P24) UDUS, *Heinrich Heine Universität Düsseldorf*, Germany (SP2)

The C. and O. Vogt Institute for Brain Research

The C. and O. Vogt Institute of Brain Research is one of Germany's major centres of neuroscience, and has a long and prominent history in brain mapping. Brodmann's cytoarchitectonic maps and Vogt's myeloarchitectonic maps of the cerebral cortex from the beginning of the 20th century have formed the basis for the Institute's recent activities in modern structural and functional neuroimaging. Today, the Institute houses not only the 200 000 histological brain sections collected by the Vogts, but also other unique collections, including brains of humans, great apes, non-human primates and other mammals. The JuBrain atlas, a cytoarchitectonic, probabilistic atlas of brain areas, is based on this collection. It has been developed in partnership with Forschungszentrum Jülich. Under the leadership of Karl ZILLES, the Institute has been developed into a modern institute for brain research. It has established modern quantitative tools of analysis and 3D mapping of human brains. The lab has a staff of four postdoctoral fellows, four technicians, and four doctoral students. It is also fully equipped for histology, autoradiography, *in situ* hybridisation and image analysis, and has access to an animal house and a 3T MR scanner.

Key Personnel

Katrin AMUNTS is a Professor for Brain Research at the Heinrich-Heine University Düsseldorf, Director of the C. and O. Vogt Institute for Brain Research, and Director of the Institute of Neuroscience and Medicine (INM-1), *Forschungszentrum Jülich*. She is also member of the German Ethics Council.

Key Expertise

- High- and ultrahigh resolution 3D Human Brain Models
- Human brain atlasing
- Integration of structural, physiological and functional imaging data

- Cortical architecture
- Fibre architecture
- Cyto- and receptorarchitectonic data acquisition and analysis of entire human brains
- 3D Polarised Light Imaging
- Integrated models of structure, function, and connectivity
- Genomic imaging
- 3D Image reconstruction and segmentation
- Big Data Analytics and High Performance Computing for Image Analysis
- Fibre architecture in post mortem rodent, monkey, and human brains
- Polarised Light Microscopy (3D-Polarized Light Imaging, 3D-PLI)
- Image processing: 3D reconstruction, registration, segmentation, stitching
- Automated workflow development and supercomputing
- Visualisation
- Multimodal and multi-scale image processing and analysis
- Large-scale data processing on HPC infrastructures.

The Institute of Clinical Neuroscience and Medical Psychology

The Institute of Clinical Neuroscience and Medical Psychology is dedicated to the integrated understanding of physiological and pathological brain organisation. The Institute investigates brain structure, function and connectivity in a multimodal fashion, using MRI and electrophysiological approaches. Once we understand normal brain networks and their inter-individual variability, changes in patients with Parkinson's disease, depression or schizophrenia, for example, are then investigated to clarify dysfunctional processes and their relation to clinical symptoms.

Key Personnel

Simon B. EICKHOFF (male) is a Professor for cognitive neuroscience at the Heinrich-Heine University in Düsseldorf, and deputy Director of the Institute of Neuroscience and Medicine in Jülich, where he leads the Brain Network Modelling group.

Key Expertise

- Multi-modal integration of neuroimaging data and the analysis of structure-function relationships in the human brain.
- Mapping regional differentiation in the human brain based on functional neuroanatomy.
- Microscopic mapping of the human brain by establishing structure-function relationships, and behavioural associations of histological areas in health and disease.
- Investigation of brain structure, function and connectivity in a multi-modal framework, including inter-individual variability in various aspects of macroscopic human brain organization related to behavioural phenotypes in health and disease.

P25) UH, *Helsingin yliopisto*, Finland (SP10)

The Neuroscience Centre (NC) is one of the University of Helsinki's independent multi-disciplinary research institutes. Its research includes molecular neuroscience, *in vitro*/*vivo* electrophysiology and *in vivo* imaging of awake animals, human genetics and human brain

imaging. The NC has at its disposal equipment for concurrent magneto- and electroencephalography, functional and anatomical magnetic resonance imaging, multi-site transcranial magnetic stimulation, and server resources for data management.

Matias Palva's Group

Profile

Matias PALVA's Group (MPG) performs non-invasive brain imaging, such as magnetoencephalography (MEG) and magnetic stimulation experiments with healthy subjects and select patient groups, and invasive stereo-electroencephalography (SEEG) recordings through collaboration projects. MPG has significantly advanced MEG and SEEG data-analysis and informatics methods. The overarching aim of MPG is to identify the systems-level neuronal mechanisms that causally underly human behaviour and mental states, and the fluctuations therein. MPG is also developing first-person computer games for measuring goal-oriented human behaviours and decisions in a complex, dynamic, and ecologically valid environment.

Key Personnel

J. Matias PALVA (male) is a group Leader at Helsinki University of Technology's Neuroscience Centre.

Key Expertise

- Non-invasive and intra-cranial eletrophysiological recordings and stimulation
- Neuroinformatics and data-analysis method development
- Systems-level mechanisms underlying the regulation of scattered neuronal processing into perception, cognition, and action
- Video games for brain research.

Satu Palva's Group

Profile

Satu PALVA's Group (SPG) laboratory investigates the system-level neuronal mechanisms underlying perception, attention, and memory, as well as the mechanisms that lead to short- and long-term variability in these functions' behavioural performance. SPG uses magneto- and electroencephalography (MEG/EEG) to non-invasively record neuronal activity during cognitive tasks. It employs Neuroinformatics-oriented data-driven analysis approaches to identify the local and large-scale cortical networks of neuronal interactions that beget momentary task performance. It uses rhythmic transcranial magnetic stimulation (rTMS) to entrain or disengage these MEG/EEG targeted cortical processes.

Key Personnel

Satu PALVA (female) is a group Leader at the Neuroscience Centre, University of Helsinki.

Key Expertise

- MEG/EEG recordings
- Rhythmic transcranial magnetic stimulation
- System-level neuronal mechanisms
- Short- and long-term variability of cognitive functions.

P26) HITS, *HITS gGmbH*, Germany (SP6)

Molecular and Cellular Modelling group

Profile

HITS is a private, non-profit research institute that carries out multidisciplinary research in the computational sciences. The Molecular and Cellular Modelling group focuses on the development and application of computer-aided methods to predict and simulate protein interactions, using approaches based on the 3D structure of macromolecules. The group uses a broad spectrum of techniques, ranging from interactive, web-based visualisation tools, to molecular and Brownian dynamics simulations. Led by Rebecca WADE, the group currently includes around twelve researchers with expertise in computational structural biology, molecular modelling and simulation and bioinformatics.

Key Personnel

Rebecca WADE (female) is the Leader of the Molecular and Cellular Modelling group at HITS. She has also holds a Professorship in Computational Structural Biology at the University of Heidelberg.

Key Expertise

- Molecular Modelling
- Molecular simulations
- Systems biology
- Structure-based drug design
- Brownian dynamics simulation
- Molecular dynamics simulation
- Molecular electrostatics
- Structural bio informatics
- Protein dynamics
- Molecular recognition.

P27) CHUV, *Hospices Cantonaux*, *Centre Hospitalier Universitaire Vaudois*, Switzerland (SP8)

Laboratoire de recherche en neuroimagerie

Profile

The *Laboratoire de recherche en neuroimagerie* (LREN) consists of a cross-disciplinary team of basic and clinical neuroscientists, with an interest in the role of human brain structure and function in neurological disorders and healthy aging. The LREN develops and applies neuroimaging analysis methods to study brain plasticity, brain repair mechanisms, and the pathological processes that underlie neurodegenerative diseases. Ultimately, the goal is to translate basic research findings into clinical applications for early disease detection and prediction of clinical outcomes. Headed by Bogdan DRAGANSKI, the lab is part of the Department of Clinical Neurosciences (DNC) at CHUV. This allows close collaboration with clinicians, and access to neuroimaging tools including 3T MRI, 7T MRI, and EEG. On-going collaborations with the *Centre Leenaards de la Mémoire* (part of CHUV-DNC) and the CHUV hospital data warehouse provide access to large, well-characterised, cohorts of patients

with neurodegenerative disorders. Within HBP, the LREN is responsible for setting up the Medical Informatics Platform, under the leadership of Richard FRACKOWIAK and Ferath KHERIF. The platform will federate hospital and other clinical data on all brain diseases and across multiple levels of biology.

Key Personnel

Bogdan DRAGANSKI (male) is Consultant Neurologist at the Department of Clinical Neurosciences, CHUV, and Director of the neuroimaging laboratory LREN.

Ferath Kherif (male) is a Senior Lecturer at the University of Lausanne and Deputy Director at the *Laboratoire de Recherche en Neuroimagerie* (LREN), Department of Clinical Neurosciences (DNC) at the University Hospital of Lausanne (CHUV).

Key Expertise

- Computational anatomy methods
- Functional MRI
- Research dedicated equipment
- Brain disorders
- Neurodegeneration, stroke, psychiatric diseases
- Univariate and multivariate statistical methods
- MRI physics
- Neuroimaging analysis methods
- Neuroimaging tools.

P28) ICL, Imperial College of Science, Technology and Medicine, United Kingdom (SP8)

ICL was founded in 1907, and is today considered one of the world's leading universities. It was placed 5th in the world in the 2013/14 QS world rankings, and 10th in the world in the Times Higher Education world rankings.

The Scientific Data Management Laboratory

Profile

The Scientific Data Management laboratory focuses on inter-disciplinary research, bridging the gap between data management research and other sciences. Driven by the data management challenges of researchers in different disciplines, the laboratory develops new methods and indexes to analyse the growing amounts of scientific data that is more efficient and more scalable than the state-of-the-art. Through the research of our lab we enable and accelerate new scientific discoveries. Headed by Thomas HEINIS, the lab results are regularly published in top database conferences and journals, such as ACM SIGMOD and VLDB.

Key personnel

Thomas HEINIS (male) is a Lecturer (Assistant Professor) at Imperial College, where his research focuses on scalable data management algorithms for large-scale scientific applications.

Key expertise

- Scientific data management
- Scalable data management
- Large-scale data analysis
- Indexes for scientific data
- Spatial data analysis
- High-dimensional data.

P29) ICM, *L'Institut du Cerveau et de la Moelle Épinière*, France (SP8)

Molecular Basis, Physiopathology and Treatment of Neurodegenerative Diseases Lab

Profile

The research group lead by Alexis BRICE comprises approximately 50 people, and focuses on the phenotypical and genetic characterisation of patients with different neurodegenerative conditions (HD, PD, frontotemporal lobar degenerations, etc.) and has made significant contributions in the field of genetic and physiopathology of these disorders. Professors DURR, BRICE and CORVOL coordinate several national and international research networks in PD (Parkinson's Disease Genetics in France), inherited ataxias and spastic paraplegias (SPATAX network), HD (French network of centres for presymptomatic testing) and FTLD (French research network on FTLD/FTLD-MND). These networks have contributed detailed phenotypical data (including neuroimaging for a subset) and biomaterial (DANN, cells, eventually plasma) for more than 40 000 individuals with neuropsychiatric disorders.

Key Personnel

Alexis BRICE (male) is the Head of the Department of Genetics at the Pitié-Salpêtrière University Hospital, linked to the Paris 6 Medical School. He is also the Coordinator of the National Reference Centre for Neurogenetics, Director of the ICM (Brain and Spine Institute), and Head of a research group.

Key Expertise

- Neurosciences
- Neurodegenerative disorders
- Genetic and phenotypical characterisation of patients
- Genetic and physiopathology of neurodegenerative disorders
- Phenotypical data.

P30) IEM HAS, Institute of Experimental Medicine Hungarian Academy of Sciences, Hungary (SP1, SP6)

Laboratory of Cerebral Cortex Research

Profile

The Laboratory of Cerebral Cortex Research is part of the Hungarian Academy of Sciences' Institute of Experimental Medicine. Research at the lab focuses on the principles that govern the structural and functional organisation of the cerebral cortex, and specifically the

operation of the neuronal microcircuits responsible for mental operations such as conscious perception and memory. Over the past two decades, the lab has made conceptually novel steps toward uncovering:

1) The role of new molecular pathways in communication within nerve cells
2) Basic principles governing connectivity among nerve cells
3) Principles governing the generation of network activity patterns by neuronal circuits.

These findings shed new light not only on the normal operations of the cerebral cortex, but also on several of its disorders at the molecular, cellular and network levels.

Key Personnel

Tamás FREUND (male) is the Director of the Institute of Experimental Medicine, Hungarian Academy of Sciences, and Head of the Department of Neurosciences, Pázmány Péter Catholic University, Budapest.

Szabolcs Káli (male) is a Senior Researcher in the Laboratory of Cerebral Cortex Research at the Institute of Experimental Medicine of the Hungarian Academy of Sciences.

Key Expertise

- Cortical (hippocampal) anatomy, physiology, and function
- Properties, classification and functions of cortical interneurons
- *In vivo* and *in vitro* (slice) physiology, pharmacology, optogenetics
- Single cell recording, labelling, visualisation, and morphological reconstruction
- Anatomical and functional characterisation of synaptic connections
- Conventional light, confocal, and super-resolution microscopy
- Two-photon functional imaging of single cells and networks
- Transmission electron microscopy and tomography
- Quantitative molecular anatomy.

P31) IST, Institute of Science and Technology Austria, Austria (SP1)

Shigemoto Group

Profile

The Shigemoto Group investigates the functional roles of these molecules in the synaptic transmission, neuronal circuits, systematic organization of the brain and animal behaviors, by analyzing their localization, movements, and functions using morphological, electrophysiological, and molecular biological techniques. Special attentions are being made to combine these different techniques efficiently and elucidate the integrated brain functions.

Key Personnel

Ryuichi Shigemoto (male) is Professor at the National Institute for Physiological Sciences, IST Austria.

Key Expertise

- Molecular neuroscience
- Neuronal and glial cells

- Receptors, channels and transporters
- Electrophysiology
- Molecular biology

P32) JSI, *Institut Jozef Stefan*, Slovenia (SP8)

Department of Knowledge Technologies at JSI

Profile

The Department of Knowledge Technologies is part of the Jožef Stefan Institute, a research organisation for basic and applied research in natural sciences and technology. With a total of 962 staff (748 research), JSI is a national institute, complementing the universities and bridging the gap between science and industry. The Department of Knowledge Technologies performs research in advanced information technologies, aimed at managing knowledge for knowledge-based applications, including intelligent data analysis (machine learning, data mining, knowledge discovery in databases), text and web mining, semantic web, social network analysis, language technologies, decision support and knowledge management. It applies these technologies to practical problems in the areas of environmental and life sciences, medicine, economy and marketing. The group's expertise relevant to the HBP includes data mining approaches, such as subgroup discovery and predictive clustering, and their use in medical and health informatics problems.

Key Personnel

- Sašo DŽEROSKI (male) is a Scientific Councillor at the Department of Knowledge Technologies, JSI, and a Professor at Jožef Stefan International Postgraduate School.
- Nada LAVRAČ (female) is the Head of the Department of Knowledge Technologies, and Professor at Jožef Stefan International Postgraduate School, and the University of Nova Gorica.

Key Expertise

- Machine learning
- Data mining
- Knowledge discovery in databases
- Rule induction
- Subgroup discovery
- Predictive clustering
- Structured output prediction
- Computational scientific discovery
- Equation discovery
- Data stream mining
- Ensemble methods
- Ontologies
- Workflows
- Relational data mining

- Text and web mining
- Social network analysis
- Decision support
- Human language technologies
- Applications in biomedicine and life sciences
- Applications in environmental sciences.

P33) INRIA, *Institut National de Recherche en Informatique et en Automatique*, France (SP2, SP4)

INRIA is dedicated to fundamental and applied research in information and communication science and technology (ICST).

The NeuroMathComp Lab: Mathematical and Computational Neuroscience

Profile

The long-term goal of the NeuroMathComp Lab, led by Olivier FAUGERAS, is to unveil the principles that govern the functioning of neuronal assemblies at a variety of spatial and temporal scales. The members of the group have extensive experience in the mathematical modelling of populations of neurons at different levels of biological organisation. One important research topic is the application of probabilistic descriptions to account for emerging properties of these populations, to explain the role of randomness in the functioning of the brain, and to investigate various aspects of the central idea of sparse representations in the neural codes.

Key Personnel

- Olivier FAUGERAS (male) is a Research Director at INRIA, where he leads the NeuroMathComp Laboratory, a joint scientific venture between INRIA, and the JAD Laboratory at UNSA.

Key Expertise

- Models of populations of neurons using the tools of dynamical systems analysis, such as bifurcation theory, equivariant bifurcations theory, dynamical systems with several time scales, canards theory.
- Neural fields and their applications to modelling large cortical areas.
- Stochastic representations of populations of neurons including the application of the theory of stochastic differential equations and stochastic partial differential equations.
- Thermodynamic limits of large populations of neurons, meanfield techniques, large deviations theory, characterisation of finite size effects through concentration inequalities, study of the limit equations through the theory of McKean-Vlasov equations.

Parietal: machine learning for brain mapping (SP2)

Parietal builds tools to model the anatomo-functional structure of the brain. The tools will facilitate the analysis of data from methods such as functional MRI, and will allow the application of non-rigid coregistration techniques, image-based atlas learning methods, brain parcellation and probabilistic model selection, to model building. A key goal is to develop a model of the interactions between spatially remote brain regions, and thus to gain new insights into functional connectivity. Headed by Bertrand THIRION, Parietal is an

INRIA team, and is part of the NeuroSpin neuroimaging platform. The Parietal group has two permanent INRIA researchers, one CEA researcher, and about twelve other members.

Key Personnel

Bertrand THIRION (male) is a Researcher at INRIA, focused on the modelling of inter-brain variability in group studies, the mathematical study of functional connectivity, and the use of machine learning tools for brain activity analysis.

Key Expertise

- Statistical models for brain mapping
- Modelling of brain functional connectivity
- Multivariate analysis methods for brain imaging
- Registration of brain images
- Deep learning methods
- Machine learning
- Functional modalities for brain mapping (fMRI, ASL, EEG, MEG, PET)
- Multi-fractal analysis
- Compressed sensing for MRI reconstruction
- Methods for big data analysis
- Scientific software in Python
- Neuroimaging data analysis software
- Data sharing.

P34) IP, *Institut Pasteur*, France (SP 2, SP12)

The Integrative Neurobiology of Cholinergic Systems Lab at the Pasteur Institute

Profile

The Integrative Neurobiology of Cholinergic Systems Lab at the Pasteur Institute works on the functional analysis of brain circuits, adopting a multi-level approach. Specifically, it aims to understand how nicotine acts on the brain, affects cognition, and causes addiction. The Lab's strength lies in the association of different kinds of complementary expertise, allowing it to address this problem from an integrative point of view. It is led by Uwe MASKOS, and consists of 11 people. In the HBP, the lab will take administrative responsibility for the work of Jean-Pierre CHANGEUX, who will lead the HBP Ethics and Society Programme.

Key Personnel

Jean-Pierre G. CHANGEUX (male) is an honorary Professor at the Pasteur Institute, and at the *Collège de France* in Paris.

Key Expertise

- Allostery
- Nicotinic receptors structure and function
- Cognition modelling

- Ethics and neuroethics
- Ethics committees.

The Human Genetics and Cognitive Functions Group

Profile

Our Group gathers geneticists, neurobiologists and clinicians to explore the relationship between genetics and the susceptibility to psychiatric conditions. We are especially interested in autism spectrum disorders, and our previous studies have revealed the implication of a synaptogenetic pathway, including the synaptic cell adhesion molecules NLGN3, NLGN4X, and NRXN1 and the scaffolding protein SHANK3 — all crucial for the maintenance of functional synapses. Our aim is to identify new susceptibility genes within this pathway, and to characterise the biological factors that regulate it. We explore the genetic/epigenetic hallmarks of affected individuals using high-throughput genotyping and sequencing-based methods, in combination with clinical, neurobiological and neuroimaging data collected from patients, or using cell and animal models.

Key Personnel

Thomas BOURGERON (male) is the Head of the "*Génétique Humaine et Fonctions Cognitives*" unit.

Key Expertise

- Whole genome genotyping, sequencing and annotation
- Human genetics analyses (linkage, association, heritability, mutation screening)
- Brain MRI data analyses (structural and functional MRI analyses, connectivity analyses, computational neuroanatomy)
- Clinical exploration of patients with neurodevelopmental disorders.

P35) UFRA, *Johann Wolfgang Goethe Universität Frankfurt am Main*, Germany (SP7)

Goethe Centre for Scientific Computing

Profile

The Goethe Centre for Scientific computing (G-CSC) is a research centre that forms part of the University's Department of Computer Science. Currently, there are 25 scientists working on the development of models, algorithms and software for numerous challenging applications, including signal processing in neurons, groundwater flow and transport. Special interest is on multi-scale modelling, fast and robust solvers, and high performance computing. The Centre develops the software UG 4 as a general software platform for models based on partial differential equations. Another of its specialities is the development of algorithms and software for the reconstruction of cell morphologies.

Key Personnel

- Gabriel WITTUM (male) is a Professor for Modelling and Simulation at the Goethe-Universität, Frankfurt am Main.

Key Expertise

- Fast numerical solvers

- High performance computing
- Applied mathematics
- Scientific computing
- Three-dimensional simulations
- Software development
- Modelling of biochemical and electrical signals in the brain.

P36) KIT, *Karlsruher Institut für Technologie*, Germany (SP7)

Steinbuch Centre for Computing (SCC)

Profile

The Steinbuch Centre for Computing (SCC) operates the KIT central computing and data centre. This supports the IT demands of the various research programmes within KIT, and also within the Helmholtz Association of German research centres. It has solid experience in distributed computing infrastructures (DCIs), federated identity management and security in DCIs, large scale data processing, storing and archiving, and in HPC. The SCC developed and runs the largest German university cloud storage for sync-and-share, providing access to more than 350 000 students and 100 000 researchers from 29 different institutions. The SCC provides 22 PB disk (+22 PB tape) storage to a diverse range of scientific experiments, hosted at more than 130 institutes on site, and is also operating a Tier-2 HPC system as part of the Germans Gauss Alliance. The SCC successfully participated in several European projects, such as CrossGrid, Int.EU.grid, EUFORIA, EGEE-1, EGEE-2 and EGEE-3, and EGI-Inspire. The SCC has coordinated the G-Eclipse and MMM@HPC projects. Currently, the SCC participates in the EDUAT2020, AARC and INDIGO-DataCloud EU projects. The SCC coordinates the Large-Scale Data Management and Analysis (LSDMA) initiative with the Germany Helmholtz Association. The SCC is a partner in this proposal, because it can contribute its expertise in federated identity and group management, as well as large-scale data and computing infrastructures.

Key Personnel

- Marcus HARDT (male) is a scientist working as part of the Research Group Cloud Computing at SCC, and is the Technical Coordinator of the Large Scale Data Management and Analysis project LSDMA.

Key Expertise

- Computing infrastructure
- Storage infrastructure
- Emerging computer architectures
- Data sharing
- Data archival
- Scientific computing
- High Performance Computing
- Grid computing
- Cloud computing
- Distributed systems

- Multi-scale biomolecular simulation
- Climate simulation and data analysis
- Energy network simulations
- Nanotechnological simulations of materials and proteins.

P37) KI, *Karolinska Institutet*, Sweden (SPs 1, 5, 6, and 12)

The Nobel Institute for Neurophysiology

Profile

The Nobel Institute for Neurophysiology at the Karolinska Institute focuses on the forebrain mechanisms responsible for the nervous system's ability to select and initiate a set of actions, and the evolution of goal-directed movement. One of the main aims is to understand the neuronal microcircuits that subserve this complex mechanism. As model systems, the Institute uses lamprey and mice, to which they apply a range of neurophysiological, molecular and behavioural techniques. The laboratory, led by Sten GRILLNER, is also heavily involved in promoting the development of Neuroinformatics, and in the International Neuroinformatics Coordinating Facility.

Key Personnel

Sten GRILLNER (male) is the founding Chairman of the International Neuroinformatics Coordinating Facility (INCF) and Secretary General of the International Brain Research Organisation (IBRO).

Key Expertise

- Computational neuroscience
- Bionic robots
- Neuroethology
- Neural circuits
- Simulation-based research.

Department of Neurobiology, Care Sciences and Society

Profile

The Department of Neurobiology, Care Sciences and Society at the Karolinska Institute consists of 11 divisions with shared departmental management. Some divisions have a strong focus on experimental laboratory research and doctoral education, while others have a more clinical focus, with a significant proportion of educational activities. Two groups from this department are included in the HBP. Abdul MOHAMMED's lab has published seminal studies on the impact of enriched environment on brain neurotrophins during aging, which is a basis for its continued neurobiological research. The lab uses normal and genetically modified rodents in studies of aging and AD models, and seeks to develop safe and humane behavioural methods. The lab was involved in an EU project that aimed to minimise the stress of behavioural testing, and promote well-being in mice. The lab collaborates on research and teaching in neuroethics with universities in Europe, the USA and Africa. Kevin GRIMES' lab aims to create and manage a high-quality ethics governance program and its supporting structure. It also hopes to design and carry out research on ethical, legal and social viewpoints concerning topics relevant to ethics in science and technology. It shares responsibility for establishing and coordinating the Research Ethics Committee and the

Ethics Legal and Social Aspects committee (ELSA), communicating with major ethical bodies in Europe, and communicating between the Human Brain Project and the European Commission Ethical Review Programme.

Key Personnel

- Abdul MOHAMMED (male) is a Professor of Biological Psychology at Linnaeus University, and Head of the Behavioural Neuroscience Lab at Karolinska Institute's Alzheimer's Disease Research Centre.
- Kevin GRIMES (male) is a veteran clinical and forensic psychologist. He is also the founder of the Science Writing English Editing (www.englishedit.eu).

Key Expertise

- Committee development and coordination
- Scientific identification of viewpoints in ethical, legal and social discourse
- Writing and editing committee materials
- Preliminary policy development reporting
- Design and evaluate secretariat strategies, SOPs, helpful mechanisms and workflow.

P38) KCL, King's College London, United Kingdom (SP12)

Department of Social Science, Health and Medicine

Profile

The Kings College London (KCL) Department of Social Science, Health and Medicine (SSHM) was established at the beginning of 2012. It aims to establish King's as a world leader in social scientific approaches to health and medicine, with innovative research and research-led teaching as the basis for a significant input into global health policy. It undertakes the highest quality research on the social and ethical implications of developments in medicine, science, and health policy. It places this in a global context, with a specific focus on questions of the social determinants of health inequality, and the role and implications of advances in biomedicine and biotechnology. The SSHM includes a number of Laboratories: the Foresight and Responsible Research Innovation Lab (FRRIL), Urban Brain Lab, and the Centre for Synthetic Biology and Innovation (CSynBi). Previous research labs were: BIOS, BIONET.

Key Personnel

Nikolas ROSE (male) is a Professor of Sociology, and Head of the SSHM at King's College London.

Key Expertise

- Transdisciplinary and transnational research on social science
- Extensive knowledge on the issues of biomedicine, ethics & social justice, biotechnology, pharmaceuticals and public policy
- Foresight research: modelling, horizon scanning and scenario planning.

P39) KTH, *Kungliga Tekniska Hoegskolan*, Sweden (SPs 4, 6, and 9)

Department of Computational Biology

Profile

Created in 2006, the Department of Computational Biology (CB) at the KTH School of Computer Science and Communication is the largest computational neuroscience, neuroinformatics, and neurocomputing centre in Sweden. CB is also leading the Swedish INCF national node. Professor Anders LANSER's group, which currently consists of 14 members, is part of CB. His research focuses on attractor memory network models, and Bayesian approaches applied to neocortex, the olfactory cortex, the hippocampal system and the basal ganglia. Jeanette HELLGREN KOTALESKI's group, which is currently made up of around ten people, focuses on using computational modelling to investigate the neural mechanisms underlying information processing, rhythm generation and learning in motor systems, using basal ganglia as the main model system. The group uses methods ranging from simulations of large-scale neural networks, using biophysically detailed and abstract systems-level models, to kinetic models of subcellular processes involved in synaptic plasticity. All CB researchers have good access to HPC tools, via the Centre for Parallel Computers (PDC) at KTH, Sweden's largest national supercomputing centre.

Key Personnel

- Jeanette HELLGREN KOTALESKI (female) is full professor in Neuroinformatics at KTH.

Key Expertise:

- Models of working memory and memory consolidation
- Neuroinformatics
- Neural information processing
- Modelling of locomotion
- Kinetic modelling of synaptic plasticity and neuromodulation
- Computational systems (neuro)biology
- Tools for multi-scale modelling approaches
- Associative memory, brain network dynamics and oscillations
- Brain data analysis
- Connectionist systems and brain-inspired computing
- Supercomputational neuroscience
- Neuromorphic systems
- Basal ganglia, early olfactory and visual processing
- Temporal sequence learning.

Centre for Parallel Computers

Profile

The Centre for Parallel Computers (PDC) is the leading High Performance Computing centre for the Swedish academic community. It is funded by the Swedish Research Council through the Swedish National Infrastructure for Computing (SNIC). PDC operates cutting-edge computer resources for Swedish users, and provides HPC resources to many important research groups, including the Stockholm Brain Institute (Karolinska Institute), Stockholm University, and KTH. With a capacity of more than 2 PF, PDC is the coordinator for the EU-

funded EPiGRAM project, a partner in the European Exascale project CRESTA, and the main Swedish participant in the PRACE and EUDAT.

Key Personnel

- Erwin LAURE (male) is the Leader of PDC, and the co-Director of the OGF Data Area. He is also the former co-Chair and co-Founder of the OGF GIN-Community Group, and a member of the External Advisory Board of the D4Science-II.

Key Expertise

- Low-level access to hardware
- HPC programming environments and tools
- Meta-languages (PyNN)
- Model adaptation to hardware
- Integration with HPC
- Benchmarking
- Computational theory
- Cellular neuroscience
- Network neuroscience
- Cognitive neuroscience.

P40) LENS, *Laboratorio Europeo di Spettroscopie Non Lineari*, Italy (SP1, SP2)

The Pavone Lab: Biophysics and Biophotonics Group

Profile

Francesco PAVONE's lab aims to develop innovative imaging methodologies for an increased understanding of biological events in the brain. We apply new implementations of light-sheet microscopy to resolve neuronal anatomy in whole fixed brains with cellular resolution. We combine the advantages of light-sheet illumination and confocal slit detection to increase image contrast in real time. In living samples, real-time dynamics of brain rewiring are visualised via two-photon microscopy, with the spatial resolution of single synaptic contacts. We also dissect the plasticity of injured brains, using cutting-edge optical methods that specifically ablate single neuronal processes. Finally, random access multi-photon microscopy, combined with new fluorescence probes, allows optical registrations of action potential across populations of neurons. The development and the application of these complementary optical methodologies provide fundamental insights into brain disease, and represent a completely new approach for investigating the physiology of neuronal network.

Key Personnel

Francesco PAVONE (male) is a Professor at the University of Florence, Department of Physics, and Director of the European Laboratory for Non-Linear Spectroscopy.

Key Expertise

- Advanced optics development
- Two-photon *in vivo* microscopy and nanosurgery

- Correlative methods for multi-level imaging
- Optical functional imaging with calcium and voltage-sensitive indicators
- Brain tissue clearing and post-mortem labelling
- Big images (> 1 TB) management and analysis
- Automatic cell localisation
- Light sheet microscopy
- Confocal microscopy
- Light sheet microscopy
- Two-photon microscopy
- Reflectance microscopy
- Immuno-staining
- Tissue clearing
- Tissue transformation
- Teravoxel-sized image visualisation
- Teravoxel-sized image stitching
- Data sharing
- Cell detection and counting
- Viral infection
- Transgenic animals.

P41) LNU, *Linnéuniversitetet*, Sweden (SP11, SP12)

Department of Psychology — Faculty of Health and Life Sciences

Profile

At *Linnéuniversitetet*, research is carried out in biological psychology, clinical psychology, health psychology and educational psychology. The research in biological psychology is led by Professor Abdul MOHAMMED, who is the Principal Investigator of the Successful Ageing and Enrichment (SAGE) research project. This involves collaboration between *Linnéuniversitetet*, *Karolinska Institutet*, Harvard Medical School and the Medical University of South Carolina. The project is interdisciplinary, and involves medical doctors, nurses, psychologists, sports scientists and computer scientists. It examines the impact of physical and mental stimulation on neural plasticity and cognitive function, in people aged between 65—85 years, in Växjö, Sweden and Boston, USA. We study the role of biomarkers, and particularly neurotrophins, in relation to cognitive function in older people. Studies of cognitive function in the lab use Cambridge Neuropsychological Test Automated Battery (CANTAB), the Cog Med program, and eye-tracking equipment. The lab also gives courses in neuroethics to both the clinical psychology program and research education. In addition, the lab supports the HBP Ethics Advisory Board.

Key Personnel

Abdul MOHAMMED (male) is a Professor of Biological Psychology at Linnaeus University, and Head of the Behavioural Neuroscience Lab at Karolinska Institute's Alzheimer's Disease Research Centre.

Key Expertise

- Database collection
- Travel logistics and auditing
- Providing support on facility planning and organising meetings
- Telecommunications with HBP researchers.

P42) MUI, *Medizinische Universität Innsbruck*, Austria (SP11)

Experimental Psychiatry Unit

Profile

As one of the leading medical universities in Austria, Innsbruck Medical University has a strong focus on neuroscience research. The University brings together a number of different disciplines. Its international PhD programme in Neuroscience "Signal Processing in Neurons" (SPIN) provides a strong, up-to-date programme of neuroscience education, and includes a Management Unit for Distance Education. The Experimental Psychiatry Unit is one of the host labs for SPIN, and is headed by Professor Alois SARIA.

Key Personnel

Alois SARIA (male) is full Professor at Innsbruck Medical University, where he leads the Experimental Psychiatry Unit.

Key Expertise

- Organisation of high-level scientific conferences
- Development of new curricula and training programmes
- Design and organisation of scientific training courses, schools and workshops
- Coordination of several Marie Sklodowska-Curie grants.

P43) UoA, *Ethniko Kai Kapodistriako Panepistimio Athinon*, Greece (SP8)

Management of Data, Information, and Knowledge Group

Profile

The Management of Data, Information, and Knowledge (MaDgIK) Group is part of the University of Athens' Department of Informatics & Telecommunications. It has more than 60 members, including five faculty staff, several R&D staff, and students at all educational stages. The Group focuses on several research areas of the Data-Info-Knowledge continuum, such as database and information systems, distributed and parallel systems, cloud computing, sensor-based and stream data management, query optimisation, information search, personalisation and social networks, knowledge discovery and data mining, knowledge representation and reasoning, constraint satisfaction problems, semantic web and linked data, semantic sensor web, digital libraries, and human-computer interaction. The Group participates in several national and European projects that cover the above areas. Much of the research is done in the context of, and inspired by, problems in several application areas, including medical informatics, cultural heritage, museum studies, biodiversity, earth sciences, marine science, the environment and history.

Key Personnel

Yannis IOANNIDIS (male) is a Professor in the Department of Informatics and Telecommunications at the University of Athens, and President and General Director of the "Athena" Research and Innovation Centre.

Key Expertise

- Database and information systems
- Distributed and parallel systems
- Cloud computing
- Workflow management
- Query optimisation
- Information search
- Scientific experiment management
- Scientific databases
- Heterogeneous systems
- Intelligent databases
- Sensor-based and stream data management
- E-health systems
- Personalisation and social networks
- Data curation and validation
- Knowledge discovery and data mining
- Knowledge representation and reasoning
- Constraint satisfaction problems
- Semantic web and linked data
- Semantic sensor web
- Digital libraries and data repositories
- Human-computer interaction
- Database user interfaces
- Complex data visualisation
- E-infrastructures development and management
- Scientific data management
- Data, tools and services sharing
- Open science policies.

P44) NMBU, *Norges miljø- og biovitenskapelige iniversitetet*, Norway (SP4, SP6, SP7)

Computational Neuroscience Group

Profile

The Computational Neuroscience Group at the Norwegian University of Life Sciences (NMBU) has broad experience in multi-scale modelling of the signal-processing properties of neurons and networks in the early visual and somatosensory systems, the generic properties of cortical networks, place-field formation in hippocampus, astrocyte dynamics, and astrocyte-neuron interactions. The Group has accumulated great experience in large-scale simulations of networks of spiking neurons, developing the NEST simulation tool, with a special focus on generating connectivity in large network models. The Group has also carried out extensive work on the modelling of extracellular potentials (LFP, MUA), and has developed new methods and Neuroinformatics tools to model and analyse multielectrode data (iCSD, LFPy, LPA). The Group, which has two core faculty members (Professor Gaute T. EINEVOLL and Associate Professor Hans E. PLESSER), currently hosts around five researchers. It is also an integral part of the multidisciplinary Centre for Integrative Neuroplasticity at the nearby University of Oslo.

Key Personnel

Gaute T. EINEVOLL (male) is a Professor of Physics at NMBU, and founder of the Computational Neuroscience Group (compneuro.umb.no). He is Programme Director and vice-President of the Norwegian national node of the International Neuroinformatics Coordinating Facility (INCF).

Hans EKKEHARD PLESSER (male) is associate professor in informatics at the Norwegian University of Life Sciences. As a core NEST developer since 2001, he has made key contributions to hybrid parallelization, support for advanced and spatially structured connectivity and quality assurance of NEST code. Plesser is a founding member of the NEST Initiative, currently serving as its President, and is chairman of the board of the Norwegian Research School for Neuroscience, and a member of the Scientific Board of the Geilo Winter School in eScience programme. Together with Eilen NORDLIE and Marc-Oliver GEWALTIG, he devised a widely adopted table format for the summary presentation of network models in publications. Plesser has considerable academic management experience, serving as head of the Basic Science Section of his Department since 2010.

Key Expertise

- Multiscale modelling of neurons and neural networks
- Biophysical modelling of electrical population signals (LFP, EEG, MEG)
- Development of tools for analysis of local field potentials (LFPs)
- Electro diffusive modelling of ion dynamics in the extracellular (and intracellular) medium
- Modelling astrocyte dynamics and neuron-astrocyte interaction
- Modelling effects of genetic variation on neuron and network dynamics
- Biophysical modelling of microelectrode array (MEA) signals
- Biophysical modelling of neuronal spikes
- Validation of spike-sorting algorithms
- Modelling of signal processing in early visual pathway

Modelling of signal processing in somatosensory cortex

P45) OFAI, *Oesterreichische Studiengesellschaft für Kybernetik*, Austria (SP10)

Austrian Research Institute for Artificial Intelligence

Profile

Established in 1984 with support of the then Austrian Federal Ministry for Science and Research, OFAI currently employs 22 researchers, plus several scientists from universities on a contractual basis. It has longstanding experience in cooperating with research institutions, SMEs and industry. For example, it has already successfully completed 32 EC-sponsored multinational research projects, either as a partner or as the coordinator. The Institute undertook research in the areas of language technology, machine learning, interaction technologies, and intelligent software agents from the very beginning, and later also focused on the emotional and social aspects of these research areas, and their embodiment in robots. Studying results of brain research and cognitive science further influenced our work considerably. Research topics that are related to the HBP in particular include: "consciousness and awareness: functions, theories, and models", "spatial memory and navigation ability in a physically embodied cognitive architecture", "hierarchies in spatial memory models", "la revolution bayésienne and physically embodied cognitive architectures", "social human-robot interaction", "ethical systems for robots", and "robots for domestic applications, especially for ambient assisted living". Some of these are currently underway, others are planned for the future.

Key Personnel

Robert TRAPPL (male) is Professor Emeritus at the Centre for Brain Research at the Medical University of Vienna.

Key Expertise

- Applied Artificial Intelligence
- Creating personalities for synthetic actors
- Multi-agent systems
- Emotions in humans and artefacts.

P46) RWTH, *Rheinisch-Westfälische Technische Hochschule Aachen*, Germany (SP7)

Virtual Reality Group

Profile

The Virtual Reality Group at RWTH researches new visualisation and virtual reality methods for scientific applications. The group is part of the University's IT Centre, and uses High Performance Computing to develop comprehensive visualisation frameworks for the explorative analysis of complex technical, physical and natural phenomena. Applications include production technology, simulation science, neuroscience, and psychology. The Group maintains one of Europe's most advanced visualisation labs, with a high-resolution five-sided CAVE.

Key Personnel

Torsten KUHLEN (male) is the founder of the Virtual Reality Group at the Centre for Computing and Communication at RWTH Aachen, where he is also Professor of Virtual Reality (VR) in the Department of Computer Science.

Key Expertise

- Immersive visualisation
- Explorative, interactive data analysis
- Virtual reality
- Natural user interfaces
- Direct interaction
- 3D visualisation
- Large data visualisation
- Parallel visualisation algorithms.

P47) UHEI, *Ruprecht-Karls-Universität Heidelberg*, Germany (SPs 5, 9, and 11)

Kirchhoff-Institute for Physics

Profile

The UHEI group explores and implements novel concepts for information processing in massively parallel, mixed-signal VLSI technologies. Founded in 1994 as a spin-off from instrumentation development for particle physics experiments, its previous projects have included bio-inspired vision sensors, sensory substitution systems, analog evolvable hardware devices and very large-scale neuromorphic information processing systems. The group initiated and led the European FACETS project and the Marie-Curie Network on Neural Computation (FACETS-ITN). It led the FP7 integrated project BrainScaleS, one of the foundations for the HBP (BrainScaleS ended 31 March 2015). In the context of BrainScaleS, it pioneered the use of wafer-scale integration for neuromorphic systems, and the PyNN meta-language — a language providing unified access to neural simulators in software and hardware. Among the more than 50 group members are five post-doctoral researchers, twelve PhD students, bachelor's and master's students, and engineers. The group's technical infrastructure includes a microelectronics laboratory, and workshops for electronics and mechanics. The Group has established a renowned German center for the design and construction of microelectronics systems (The Heidelberg ASIC laboratory). The lab has at its disposal a complete design suite for analog and digital chip design, layout and simulation; a clean room for assembling, bonding and testing microelectronics systems; an electronics workshop with technical facilities for soldering, and component mounting; and high frequency and low noise testing facilities. A mechanical workshop with a complete manufacturing workflow from CAD design to computer controlled production machines allows us to construct large-scale mechanical set-ups as required for the NM-PM facility in the framework of HBP. The group also operates Teraflop-scale compute clusters for neural and electronics system simulations, and for the control and analysis of experiments with Neuromorphic computing systems.

Key Personnel

Karlheinz MEIER (male) is the founding Director of the Kirchhoff-Institute for Physics and the ASIC Laboratory for Microelectronics, where he holds a Chair in Experimental Physics.

Key Expertise

- Analog chip design
- Digital chip design
- FGPA design
- System design
- Integration and testing
- Low level access to hardware
- HW system configuration (“mapping and routing”)
- HW system simulation (“ESS”)
- Analysis tools for experiment results
- Model adaptation to hardware
- Integration with the Collaboratory
- Platform operation and user support
- Training, education and community building
- Innovation, industry relations, IPR
- Computational theory.

Multidimensional Image Processing

Profile

The UHEI Multidimensional Image Processing (MIP) group works at the forefront of algorithms development for bioimage analysis, and is spearheading efforts to make advanced machine learning and image analysis methods available to experimental end users. In particular, the group has coordinated the development of ilastik, a framework for image analysis, which in its most recent version allows interactive machine learning on data sets in the order of multiple terabytes. The group is also one of the leading players in the area of automated tracing, that is, the automated extraction of brain circuit topology and connectivity in large volume electron microscopic images. Today, the group maintains active collaborations with most of the leading experimental groups who pursue the study of the connectome, or the quest for a better understanding of neural ultrastructure. These groups have complementary experimental techniques, including three variants of electron microscopy, as well as functional imaging. Besides its head, the group comprises one senior scientist, four post-doctoral researchers, three full-time software developers, five PhD students, and undergraduate students.

Key Personnel

Fred HAMPRECHT (male) is a member of the Interdisciplinary Center for Scientific Computing (IWR) of the University of Heidelberg, and a Professor in its Faculty for Physics and Astronomy.

Key Expertise

- Interactive machine learning for biological image analysis
- Automated tracing/segmentation of connectomics data since 2007
- Principled modelling of image analysis pipelines: clear separation of objective function and optimisation

- Combinatorial optimisation
- Efficient approximate inference in probabilistic graphical models
- Development of user-friendly segmentation and tracking software for biologists.

P48) SU, Sabancı University, Turkey (SP9)

Sabancı University Microelectronics Group and Sabancı University Nanotechnology Research and Application Centre

Profile

Sabancı University Microelectronics Group has extensive research programs in integrated circuits and systems design, fabrication and testing. The group's experience includes high frequency and microwave circuits, low power circuits, readout circuits, analogue and mixed-signal circuits, MEMS and microsystems, biosensors and biomimetic circuits. The Sabancı University Nanotechnology Research and Application Centre (SUNUM), provides valuable additional capabilities to the research infrastructure of the Faculty of Engineering and Natural Sciences (FENS). In collaboration with the research expertise of the Faculty of Engineering and Natural Sciences, SUNUM conducts application oriented, multidisciplinary research programs, bringing together researchers to address applications in electronics, healthcare, structural materials, energy, agriculture, food and defence industries. SU Microelectronics Group has extensive integrated circuits and system design capabilities on different Digital, Analog, Mixed-Signal, RF/Microwave and THz applications, with a project portfolio from National and International Funding Agencies (such as TUBITAK, EU Framework Programs, NSF), and other companies. The Group's research capabilities also include Micro-Electro-Mechanical Systems (MEMS), sensors and actuators, and microsystems for applications such as biosensors, chemical sensors, mechanical sensors, RFMEMS, and IR detectors. The Group has the necessary CAD tools, such as Cadence ADS Design Environments, Coventorware, Momentum, and Comsol. It also has experienced IC technology libraries, based on CMOS and SiGe technologies, from 0.35 µm down to 28 nm scale. In addition, the Group has a board and die-level test and measurement capabilities ranging from DC to 110 GHz operating frequency, with a temperature range of 77K-cryo to 240 C, along with micro/nano fabrication capabilities in 40 m2 area of cleanroom. SUNUM is housed in a state-of-the art, two-storey, 7 500 m2 building, with an 850 m2 clean room (ISO 5), 1 600 m2 for laboratories, and 2 400 m2 for office and general use, all furnished with high tech equipment to support R&D in nanotechnologies. There are 12 multidisciplinary laboratories in the centre. These deal with: micro/nano fabrication (Class 100 clean room), molecular biology, material characterisation, nanoelectronics and nanomagnetics, micro-nano fluidics, surface sciences and energy systems, nano packaging and heterogeneous integration, advanced microscopy, micro and nano systems testing and characterisation, 3D design and fabrication, and tissue engineering and regenerative systems. These laboratories include state-of-the art fabrication and characterisation equipment spanning large application areas, from electron lithography, nanolithography, DNA sequencing, protein analysis, liquid, gas and mass spectroscopy, mK cryo systems, atomic resolution TEM, SEM, FIB, confocal microscopy, and 3D prototyping. SU conducts research in other HBP related areas, including biomedical information processing, brain computer interfaces, image analysis techniques with applications to medical imaging modalities, cognitive psychology, memory and language formation, and vision and sensory information processing.

Key Personnel

- Yasar GÜRBÜZ (male) is a member of the Faculty of Engineering and Natural Sciences (FENS) at Sabancı University, and is also one of the founding faculty members of the

Microelectronics, Electronics Engineering Diploma Programs and Nanotechnology Research and Application Centre.

- Volkan ÖZGÜZ (male) is Director of the Nanotechnology Research and Application Center at Sabancı University.

Key Expertise

- Digital chip design
- FPGA design
- System design, integration and test
- Novel technologies
- Low level access to hardware
- Training, education and community building.

P49) SSSA, *Scuola Superiore di Studi Universitari e di Perfezionamento Sant'Anna*, Italy (SP10)

The BioRobotics Institute

Profile

The BioRobotics Institute at *Scuola Superiore Sant'Anna* is an integrated system aimed at innovative research, education and technological transfer. The Institute wants to act as a link to international centres of knowledge, and to create a new concept of engineers that are scientists, inventors, entrepreneurs, and are able to invent and solve problems, and to create new companies in high technology sectors, such as biomedical engineering, microengineering, robotics and mechatronics.

Key Personnel

Cecilia LASCHI (female) is an Associate Professor of Biorobotics at SSSA, and Leader in the area of soft robotics.

Silvestro Micera (male) is Professor of Bioengineering and Head of the Translational Neural Engineering Area at the Scuola Superiore Sant'Anna and Associate Professor of Bioengineering and Director of the Translational Neural Engineering Laboratory at the *Ecole Polytechnique Federale de Lausanne* (EPFL).

Key Expertise

- Soft robotics
- Bionics and Biomechanics
- Biorobotics
- Implantable neuroprostheses
- Rehabilitation robotics
- Wearable devices
- Neuro-controlled artificial limbs
- Reaching, grasping and locomotion
- Functional electrical stimulation

P50) CWI, *Stichting Centrum voor Wiskunde en Informatica*, The Netherlands (SP5)

The Stichting Centrum voor Wiskunde en Informatica

Profile

The Stichting Centrum voor Wiskunde en Informatica (CWI) is the Dutch national research institute for mathematics and computer science. It is a private, non-profit organisation located at the Science Park, Amsterdam. CWI's mission is twofold: to perform frontier research in mathematics and computer science, and to transfer new knowledge in these fields to society. This is realised by several means. In addition to the standard ways of disseminating scientific knowledge, CWI actively pursues joint projects with external partners, provides consulting services, and stimulates the creation of spin-off companies. Special efforts are made to make research results known to non-specialist circles, ranging from researchers in other disciplines, to the public at large. CWI is headed by Jos BAETEN. CWI also manages the Benelux Office of the W3C, and hosts both the Semantic Web Activity Lead, and the chair of the XHTML and XForms Working Group. CWI has always been very successful in participating in European research programmes (e.g. VITALAS, K-SPACE, QAP, CREDO, MUSCLE, and others) and large scale national research programmes (e.g., programmes BRICKS, MultimediaN, and VL-e; NWO Veni, Vidi, Vici grants). It has extensive experience in managing these collaborative research efforts. CWI is also strongly embedded in Dutch university research; about thirty-five of its permanent senior researchers hold part-time positions as professors at universities, and many projects are carried out in cooperation with university research groups. CWI receives basic funding from the Netherlands Organisation for Scientific Research (NWO), amounting to about two thirds of the Institute's total income. The remaining third is obtained through national research programmes, international programmes, and contract research commissioned by industry. CWI hosts a staff of 235 full-time employees, 50 permanent scientific staff, 135 temporary scientific staff, and 50 support staff.

Key Personnel

Martin KERSTEN (male) is a full Professor in multimedia databases at the University of Amsterdam, and Head of the Information Systems Department at CWI. He is also co-Founder of Data Distilleries B.V.

Key Expertise

- Database management systems
- Column stores
- Scientific data management
- File repositories
- Distributed database processing
- Query optimisation
- Data structures
- Storage optimisation
- Indexing algorithms
- In-memory data processing
- Open-source software distribution
- Building up spin-off companies.

P51) SKU, *Stichting Katholieke Universiteit*, The Netherlands (SP5)

The Donders Institute

Profile

Founded in 2008, the Donders Institute houses the department of Neuroinformatics. Research at the department currently focuses on three major themes: 1) understanding the processing of visual information in the brain at the level of networks of spiking neurons, and its modulation by cognitive factors; 2) developing analysis methods for multivariate data, to extract and confirm inter-cortical network communication, and 3) building predictive models for brain network structure and applying database and machine-learning methods to infer missing data. The Institute also has an experimental lab for conducting optogenetics experiments to support computational studies. DI is a community of 500 researchers spanning the faculties of science, social sciences and medicine, as well as the Donders Centre for Cognitive Neuroimaging.

Key Personnel

Paul TIESINGA (male) is a Professor of Neuroinformatics, and Chair of the Department of Neuroinformatics.

Key Expertise

- Neuroinformatics
- Computational Neuroscience
- Systems Neuroscience
- Predictive Neuroscience
- Nonlinear dynamics
- Atlasing
- Analysis of large-scale, heterogeneous scientific data
- Information theory
- Scientific computing
- Data sharing
- Image analysis & segmentation of MRI data
- Multivariate time series analysis (Granger causality)
- Graph theoretical analysis of networks
- Numerical algorithms and algorithm development
- Data clustering
- Machine learning
- Optimisation
- Statistical mechanics approaches for generating networks
- Neuronal network models for visual and barrel cortex
- Single neuron models, single and multi-compartment
- Spike train analysis
- Neural oscillations.

P52) FZI, *Stiftung FZI Forschungszentrum Informatik am Karlsruher Institut für Technologie*, Germany (SP10)

Interactive Diagnosis and Service Systems

Profile

The FZI Research Centre for Information Technology (FZI) in Karlsruhe is a non-profit independent research centre with about 160 employees. Its core mission is to facilitate technology transfer of innovative solutions in ICT, and to create a link between academia and industry. FZI consists of four interdisciplinary research divisions working in close collaboration. The department of Interactive Diagnosis and Service Systems (IDS) concentrates on the development of intelligent, mobile service robots and supporting technologies. IDS is involved with a significant number of industry partners, e.g. in the areas of Automated Guided Vehicles, manipulation, tele-operated diagnosis and inspection systems. IDS' project experiences allowed them to develop agile sensing devices and algorithms that could cope with complex tasks involving robots and humans, and to fulfil robustness and speed constraints needed in industrial applications. The modular software framework MCA2 was developed at FZI, and is being used in different professional applications, such as robust indoor navigation. Recently, this real time capable framework was extended by introducing defined interfaces to ROS (Robot Operating System). The philosophy of the Software Engineering (SE) division is to look at software engineering in its entirety. We therefore analyse, design, develop, adapt, and evolve complex mobile and multi-platform software systems, in addition to the underlying business processes, from an engineering viewpoint, and with continuous quality assurance in mind. SE has been working in more than 50 cooperative and consulting actions on service-orientated software construction, model-driven software engineering, software quality assessment, and legacy software evolution with national and European industry. SE serves numerous SMEs and large companies, such as Siemens, ABB, Nokia, IBM, Deutsche Telekom, Daimler-Chrysler, and BASF. SE's research contributes regularly to leading technological conferences, including ICSE, WCRE, CSMR, and QoSA.

Key Personnel

Paul LEVI (male) is a Professor for Computer Science (Distributed AI, Computer Vision) and an Executive member of FZI.

Key Expertise

- Swarm robotics
- Sensor data fusion
- Mobile, autonomous systems
- Multi-agent systems
- Machine vision
- Architecture of cognitive systems
- Service robotics
- Quantum field based molecular physics
- Molecular robotics.

P53) TUC, Technical University of Crete, Greece (SP5)

Software Technology and Network Applications

Profile

The Technical University of Crete (TUC) was founded in 1977. The purpose of this state institution is to provide high-quality undergraduate and graduate studies in modern engineering fields, as demanded by the Greek and international job market, to conduct research in cutting edge technologies, and to develop links with Greek and European industry. TUC is committed to staying at the forefront of educational and intellectual development in research and teaching, both in Greece and internationally. The Software Technology and Network Applications group (SoftNet), which is part of TUC's Department of Electronic & Computer Engineering, represents TUC in the HBP. SoftNet's current research activities focus on database management systems, data mining, centralised and distributed data-stream processing, cloud computing, distributed and peer-to-peer systems, and sensor networks. SoftNet members publish regularly in these areas in major international conferences and journals.

Key Personnel

Minos GAROFALAKIS (male) is a Professor of Computer Science in the Department of Electronic and Computer Engineering, and the Director of the Software Technology and Network Applications Laboratory (SoftNet).

Key Expertise

- Big data management and analytics
- Continuous data-stream analysis and mining
- Approximation techniques for big data
- Large-scale distributed data management
- Distributed systems and algorithms
- Data management in the cloud
- Data mining and machine learning
- Database management systems.

P54) TUD, *Technische Universität Dresden*, Germany (SP9)

Endowed Chair of Highly-Parallel VLSI-Systems and Neuromorphic Circuits

Profile

The neuromorphic hardware research chair, established in 1997, has an extensive track record in VLSI circuit design for advanced digital and analogue systems. Led by René SCHÜFFNY, the group consists of two professors, three post-doctoral fellows and twenty PhD students. Its expertise encompasses the design and implementation of multi-processor systems on chips using various deep-submicron (e.g. 28 nm) processes, with a focus on high speed, versatile on- and off-chip digital communication (e.g. 90 GB/s Network-on-chip links). The group also designs and implements neuromorphic hardware and peripheral components for digital control, pulse routing and interfacing. The chair collaborates with industry, and is part of a number of EU projects. The group has also been responsible for the intra-wafer, ASIC and FPGA-based pulse communication networks for wafer-scale neuromorphic systems in the FACETS, FACETS-ITN and BrainScaleS projects.

Key Personnel

Sebastian HÖPPNER (male) is a Project Manager with the Chair of Highly-Parallel VLSI-Systems and Neuromorphic Circuits.

Christian Mayr (male) is Professor in the Institute of Circuits and Systems at Dresden University of Technology.

Key Expertise

- Digital chip design
- FPGA design
- System design, integration and testing
- Novel technologies
- Low level access to hardware
- HW system simulation ("ESS")
- Innovation, industry relations, IPR.

P55) TUGRAZ, *Technische Universität Graz*, Austria (SP9)

The Institute for Theoretical Computer Science

Profile

For the last twenty years, the Institute for Theoretical Computer Science at *Technische Universität Graz* (Graz University of Technology) has been developing theory and computer models to understand computation and learning in biological neural systems and artificial networks of spiking neurons. Headed by Wolfgang MAASS, it has frequently collaborated with experimental neuroscientists on neurobiological experiments that test predictions of theoretical models. For example, in collaboration with Wolf Singer, it tested and verified salient predictions of the liquid computing model, the results of which were published 2009, in PLoS Biology. It has also collaborated with neuromorphic hardware and robotics experts on applications of biologically inspired computing and learning principles. The Institute uses a wide variety of methods, including machine learning and computational complexity theory. Theoretical predictions are validated with the help of several computer clusters. Two of its best-known software developments are the PCSIM software system for the parallel simulation and computational analysis of biological networks of neurons, and the NEVESIM software for event-based simulations of stochastic spike-based networks in continuous time. The Institute has two full Professors (Wolfgang MAASS and Franz AURENHAMMER) and one Associate Professor (Robert LEGENSTEIN). In addition, it has two University Assistants, several postdoctoral fellows and PhD students, a system administrator, and two part-time administrative assistants. It consists of the Maass Lab, the Legenstein Lab (and the Aurenhammer Lab, which will not participate in the HBP).

Key Personnel

Wolfgang MAASS (male) is a Professor of Computer Science, and Head of the Institute for Theoretical Computer Science at the Graz University of Technology.

Key Expertise

- Analysis tools for experiment results
- Training, education and community building
- Benchmarking

- Innovation, Industry relations, IPR
- Computational theory
- Cellular neuroscience
- Network neuroscience
- Cognitive neuroscience.

The Legenstein Lab for Learning Principles in Biological and Bio-inspired Systems

Profile

Robert LEGENSTEIN's lab uses mathematical analysis and computer simulations to investigate fundamental principles of learning and self-organisation in biological neuronal networks and neuromorphic systems. This research is often performed in close collaboration with experimental neuroscientists and experts for neuromorphic hardware. The lab has, for example, worked on the analysis of spike-timing dependent plasticity, both in the context of models for learning in biological systems, and as a paradigm for neuromorphic systems. This work has bridged the gap between biologically plausible plasticity rules and well-established statistical learning methods, such as reinforcement learning and Bayes-optimal learning. Recently, the lab has also contributed to research on learning in novel memristor-based neuromorphic hardware.

Key Personnel

Robert LEGENSTEIN (male) is an Associate Professor at the Institute for Theoretical Computer Science.

Key Expertise

- Analysis tools for experiment results
- Training, education and community building
- Benchmarking
- Innovation, Industry relations, IPR
- Computational theory
- Cellular neuroscience
- Network neuroscience
- Cognitive neuroscience.
- Computational Complexity Theory
- Learning Theory
- Machine Learning.

P56) TUM, *Technische Universität München*, Germany (SP10, SP11)

Robotics and Embedded Systems

Profile

The Robotics and Embedded Systems group is part of the Technische Universität München's (TUM) Department of Informatics. The group is headed by Professor Alois KNOLL, and its primary mission is the research and education of machines for perception, cognition, action and control. More specific research topics include, but are not limited to, algorithms (e.g.

for collision avoidance and path planning), computer architecture for embedded systems, graphics and simulation using the latest rendering devices, motor control, machine learning, natural and spoken language, robot programming languages and controllers, and synthetic biology and statistical algorithms for computer vision.

Key Personnel

Alois KNOLL (male) is a Professor of Computer Science at the Informatics Department of the Technical University of Munich, and Chair of the "Robotics and Embedded systems" research group.

Florian Röhrbein (male) is a research assistant in the Neurorobotics research group in the field of neurobiological learning methods for robotics.

Key Expertise

- Cognitive and sensor-based robotics
- Multi-agent systems
- Data fusion
- Adaptive systems
- Simulation systems
- Embedded systems
- Cyber-Physical systems
- Software development.

Research group on Fusing Augmented Reality

Profile

Headed by Professor Gudrun KLINKER, the group on Fusing Augmented Reality (FAR) focuses on Ubiquitous Augmented Reality — a combination of ubiquitous computing, wearable computing and augmented reality. FAR's research focuses on developing technologies that can place virtual information three-dimensionally into real environments, adapting the information provided to users' location, work context and attentional capabilities. Current work includes the development, use and fusion of tracking technologies in sensor networks, and the use of novel, three-dimensional user interfaces in specific application contexts. Applications developed in the department use a broad range of mobile devices ranging from mobile phones, PDAs and tablet PCs, to HMDs, HUDs, multi-touch displays and steerable laser projectors.

Key Personnel

Gudrun KLINKER (female) is a Professor of Augmented Reality at TUM, and a founding member of the International Symposium on Mixed and Augmented Reality (ISMAR).

Key Expertise

- Computing
- Wearable computing
- Augmented reality
- Sensor networks

Chair of Industrial Design

Profile

The Chair of Industrial Design operates on the field of design and realisation of industrial products, product systems, services and corporate strategies. Research activities at the Chair of Industrial Design focus on social questions, such as ecologically justifiable mass production, or the demographic change. The teaching emphasises universal design, the principles of "new functional design" proclaimed by Professor Fritz FRENKLER, and the scientific approach to design. The Chair of Industrial Design encourages entrepreneurial behaviour and supports TUM start-ups.

Key Personnel

Fritz FRENKLER (male) is a Professor of the newly-created Chair of Industrial Design at TUM. He is also a regional advisor of the ICSID and founding member of iF Universal Design & Service GmbH.

Key Expertise

- Industrial design.

Neuroscientific System Theory

Profile

The Neuroscientific System Theory (NST) group at TUM investigates theory, models, and practical robotic implementations of distributed neuronal information processing. It aims to discover key principles by which large networks of neurons operate, and implement those in technological systems to enhance their real-world performance. Current applications of our research are robust tracking, efficient long-range mapping and navigation, and autonomous micro-helicopter flight stabilisation; current projects explore massively parallel-distributed neural computation and real-time cognitive reasoning based on perception and learning. Details of our research are shown on our project web pages at http://www.nst.ei.tum.de/research/NST.

Key Personnel

Jörg CONRADT (male) is an Assistant Professor of Neuroscientific System Theory at TUM.

Key Expertise

- Distributed local information processing
- Growing and adaptive networks of computational units
- Neuromorphic sensor fusion and distributed actuator networks
- Event-based perception, cognition and action.

P57) TAU, Tel Aviv University, Israel (SP8, SP11)

Department of Statistics and Operations, School of Mathematical Sciences

Profile

Our research group focuses on the statistical aspects of replicability in life sciences, and studies preliminary, basic, pre-clinical, clinical and post clinical studies. As members of the Sagol School of Neuroscience at Tel Aviv University, which combines nine faculties and hospitals, we collaborate with many scientists in these research areas. We also develop statistical tools for the analysis of "Big Data". These are powerful tools for the discovery of

new findings, which we aim to substantiate with rigorous statistical standards (e.g.: False Discovery Rate methods). Our research group is made up of some 14 people (including academics, PhD students, and MSc. students) working on different areas, such as statistics and biology. Our research receives support from an ERC advanced researcher grant, NIH, ERC, HBP and internal grants. We collaborate closely with Israeli hospitals and health systems. As part of the HBP, we plan to develop health informatics methodologies in disease research, such as PD and AD, and to discover new insights from the analysis of the data available to Platforms. These findings may help us understand disease mechanisms, predict the course of a disease, or assist in targeting potential therapeutic options.

Key personnel

Yoav BENJAMINI is a Professor of Applied Statistics at Tel Aviv University, where he also heads the Excellence Centre for Statistical Approaches to Complex Research Problems.

Mira Marcus-Kalish (female) is Senior Research Fellow and a Project Manager at the Interdisciplinary Center for Technology Analysis & Forecasting (ICTAF).

Key expertise

- Pre-processing tools
- Sophisticated algorithms
- Interface tools development
- In-between interactions
- Gait and movement analysis
- Clustering analysis
- Prediction
- Causality
- Replicability
- Actionable informatics.

P58) (blank)

P59) UOXF, The Chancellor, Masters and Scholars of the University of Oxford, United Kingdom (SPs 1, 2, and 10)

The MRC Functional Genomics Unit

Profile

The University of Oxford (UOXF) is the oldest university in the English-speaking world, and is always among the world's top ten universities in various league tables. The Department of Physiology, Anatomy and Genetics is home to the MRC Functional Genomics Unit (FGU). The FGU delivers a potent combination of computational genomics and cellular and model organism experimentation, which is addressing some of the most important questions in neuroscience. The FGU has strength and depth in revealing novel genome and transcriptome functionality, and their contributions to diverse cellular functions and disease. Professor Chris Ponting is Deputy Director of the FGU, and undertakes comparative studies of transcriptomes between different cell types, tissues, developmental stages and species. He is an expert in computational and evolutionary genomics, and is particularly interested in long noncoding RNA function.

Key Personnel

Chris PONTING (male) is Deputy Director of the MRC Functional Genomics Unit, and Professor of genomics at Oxford University.

Key Expertise

- Comparative transcriptomics
- Computational genomics
- Long noncoding RNAs.

Oxford Physiome Lab, in collaboration with the Auckland Bioengineering Institute

Profile

The Auckland Bioengineering Institute (ABI) at the University of Auckland, New Zealand, in collaboration with Oxford University, has been pioneering the development of anatomically and physiologically based models of mammalian organ systems for the past 15 years. This has been carried out under the umbrella of the International Union of Physiological Sciences (IUPS) Physiome Project and, for the last seven years, under the European Framework 7 funded Virtual Physiological Human (VPH) project. For example, a multiscale model of the heart was developed by Professor Peter Hunter (ABI Director and co-Director of Computational Physiology at Oxford) and his team at the ABI, in collaboration with Professors Noble and Paterson from the Department of Physiology, Anatomy and Genetics (DPAG) at Oxford University. Multiscale human Physiome models have now been developed for the circulation system, the musculo-skeletal system, the respiratory system and the digestive system. These models are based on the laws of physics implemented on anatomically accurate tissue geometries with anisotropic, nonlinear and inhomogeneous material properties, and linked to molecular systems biology models.

Key Personnel

Peter HUNTER (male) is the Founder and Director of the Auckland Bioengineering Institute (ABI) at the University of Auckland. He is also co-Director of Computational Physiology at Oxford University, where he holds a visiting professorship.

Mark SAGAR (male) is the Director of the Laboratory for Animate Technologies, based at the Auckland Bioengineering Institute, and Associate Professor at the University of Auckland.

Key Expertise

- Human physiome models
- Implantable devices
- Orthopaedics
- Biomimetics
- Human vision.

P60) HUJI, Hebrew University of Jerusalem, Israel (SP4, SP6)

The Laboratory for Understanding Neurons

Profile

Research at the Laboratory for Understanding Neurons focuses on modelling synaptic plasticity, dendritic and axonal excitability, synaptic integration in dendrites and dendritic spines, and the dynamics of small and mid-size cortical microcircuits. It is also geared to

the development of analytical and computational methods for deciphering information processing at single cell and network levels. Led by Idan SEGEV, the group consists of eight postdoctoral fellows, doctoral and Master's students, with projects focusing on understanding the computational capabilities of single cells and on the characterisation of the link between neuron types and networks dynamics. The laboratory houses a powerful computer cluster (Dual-Core AMD Opteron Processor 2220), personal computers (Macs and PCs) for each of the students, and a direct line to the Blue Brain Project supercomputer.

Key Personnel

Idan SEGEV (male) is a Professor of Computational Neuroscience, and the former Director of the Interdisciplinary Centre for Neural Computation (ICNC) at the Hebrew University of Jerusalem.

Key Expertise

- Cable theory for dendrites
- Compartmental models for 3D reconstructed neurons (humans and rodents)
- Dendritic integration
- Modelling dendritic excitability
- Modelling synaptic plasticity
- Automated modelling of neuronal spiking activity
- Cluster analysis for dendritic structures
- Small-to medium scale realistic network simulations
- Modern graph analysis for network motifs structure
- Multiple objective optimisation methods
- Information theoretical methods for neuronal activity
- Methods for signal analysis.

P61) UABER, University of Aberdeen, United Kingdom (SP6)

Institute of Pure and Applied Mathematics

Profile

The Institute of Pure and Applied Mathematics (IPAM) at the University of Aberdeen is a partnership of two institutes: the Institute of Mathematics (IMA), and the Institute of Complex Systems and Mathematical Biology (ICSMB). The IMA is a centre of excellence in pure mathematics, and specifically in topology and geometry. Other subjects strongly represented at the IMA are group and representation theory and analysis. The unifying research theme of the ICSMB is the study of complex dynamic and its applications. Aberdeen is an international university, serving one of the most dynamic regions in Europe. With over 16 000 students, of more than 120 nationalities, and over 3000 staff, the University is at the forefront of teaching and research in medicine, the humanities and the sciences.

Key Personnel

Ran LEVI (male) is Professor of Mathematics at the University of Aberdeen.

Key Expertise

- Cutting-edge knowledge in pure algebraic topology, geometric topology and algebra

- Expertise in computational topology and the skill to perform high level computations
- High level expertise in applied algebraic topology
- Cutting-edge expertise in applications of applied mathematics methods to neuroscience
- Computing infrastructure.

P62) UEDIN, University of Edinburgh (SP1)

School of Informatics

Profile

The School of Informatics is part of the College of Science and Engineering. The School is one of the largest in the world, and is renowned for both its research and its teaching. The School is the largest department in the UK for research, and is also the highest rated. Its city centre premises include a new purpose-built research centre, the Informatics Forum, which provides teaching facilities and dedicated incubator space for knowledge transfer activities. Our research strengths include database technology, theory and data mining; neural computation and systems biology modelling; probabilistic modelling and machine learning; and naturally inspired computation and robotics. The School is also home to the highly successful ProspeKT and AspeKT initiatives — two important programmes that support the creation of new IT businesses, knowledge creation and knowledge transfer. Within the School of Informatics, Peter BUNEMAN is Professor of Database Systems, and Douglas ARMSTRONG is Professor of Systems Neurobiology.

Key Personnel

Douglas ARMSTRONG (male) is a Professor of Systems Neurobiology at the University of Edinburgh School of Informatics.

Key Expertise

- Systems biology
- Neuroinformatics
- Bioinformatics and biological databases
- Genetic and molecular architecture
- Bio-computational models
- Open-source software
- Databases and programming languages
- Data integration
- Semistructured data
- Data provenance, archiving and annotation.

P63) UMAN, University of Manchester, United Kingdom (SP9, SP11)

Advanced Processor Technology Group

Profile

Led by Professor Steve FURBER, the Advanced Processor Technology (APT) group at the University of Manchester focuses on issues related to the complexity of microelectronic

design. The UK microelectronics design research community has identified four Grand Challenges for research in this area, of which the APT group addresses three: “batteries not included” (minimising the energy demands of electronics; a vital objective for exascale computing); “moore for less” (performance-driven design for next-generation chip technology), and “building brains” (neuro-inspired electronic systems).

Key Personnel

Steve FURBER (male) leads the Advanced Processor Technologies group, and is known internationally for having spearheaded the creation of the ARM microprocessor at Acorn Computer, Ltd.

Key Expertise

- Digital chip design
- FPGA design
- System design, integration and test
- Low level access to hardware
- HW system configuration (“mapping and routing”)
- HW system simulation (“ESS”)
- Model adaptation to hardware
- Unified portal integration
- Platform operation and user support
- Training, education and community building
- Benchmarking
- Innovation, Industry relations, IPR
- Computational theory
- Multidimensional Image Processing.

SpiNNaker Software Group

Profile

Led by David LESTER, and part of the APT group at the University of Manchester, the SpiNNaker Software Group (SSG) focuses on the provision of software support for SpiNNaker, both NM-MC1 and NM-MC2. This is currently performed primarily using the PyNN (neuromorphic standard) language. However, in collaboration with the Simulator Technology team led by DIESMANN in SP6, the Group is well-placed to leverage the emerging convergence in simulator technology to support a wider range of user tools (Neuron, NEST, PyNN, and NineML) on the Neuromorphic Platform. The Group is responsible for the provision of low-level support software i.e. operating system primitives, fixed-point arithmetic libraries, and hardware interactions. It also provides and higher level activities, such as distributed partitioning of data and associated place-and-route algorithms. Whilst much of this is SpiNNaker-specific, other components (such as distributed algorithms for partition) will be of interest to DIESMANN’s group, and the ability to easily link neuromorphics sensors and actuators will be of interest to SP10, and in particular the groups of KNOLL, GEWALTIG AND LEVI. In conjunction with the members of the open calls, we are working with Anders LANSNER to develop bench-marking suites to provide quantifiable data on the neuromorphic design space. We also have a strong interest in validating the SpiNNaker system against other simulator technologies, such as NEST and Brian; this activity

involves interaction with GRUN and DAVISONS' Elephant Team in SP5. The Group has an on-going interest in developments outside of neuromophics; in particular using SpiNNaker as an extensible smart data base system in collaboration with AILAMAKI's Team in SP8, and using the device for other embarrassingly parallel algorithmic experiments.

Key Personnel

David LESTER (male) is a Lecturer at the University of Manchester, specialising in functional programming, computer arithmetic, and more recently in Neuromorphic engineering.

Key Expertise

- Neuromorphic neuroscience
- Computational neuroscience
- Distributed computation
- Computer arithmetic
- Theory
- Statistics
- Sustainable software.

P64) UAM, *Universidad Autónoma de Madrid*, Spain (SP1)

Thalamus Laboratory — Department of Anatomy and Graduate Programme in Neuroscience

Profile

Our laboratory focuses on clarifying cell diversity and the precise wiring of long-range projection neurons (LRPN). These monosynaptically link distant brain regions, and may therefore be pivotal substrates of the widely distributed networks that allow complex perception, cognition and action. We apply electrophysiology and high-resolution single-cell axonal tracing methods. These include juxtacellular injections and single-cell transfection *in vivo*; standard, confocal and transmission electron microscopy; stereology; and 3D reconstruction methods.

Key Personnel

- Francisco CLASCÁ (male) is a Professor in the Department of Anatomy, and the Graduate Program in Neuroscience, at *Universidad Autónoma de Madrid*.

Key Expertise

- Experimental animals and humans
- Mesoscopic anatomy of cortical and thalamic long-range pathways
- Stereological axonal pathways
- Confocal microscopy
- 3D Electron microscopy reconstructions
- Neurochemical characterisation of neurons and synapses
- Micropopulation and single-cell axonal tracing, reconstruction, and quantitative 3D analysis.

P65) UCLM, *Universidad de Castilla - La Mancha*, Spain (SP1)

Synaptic Structure Laboratory

Profile

The Synaptic Structure Laboratory (Syslab) focuses on unravelling several aspects of the neuronal functional structure. This knowledge is crucially important to understanding the basic mechanisms by which the brain functions and, therefore, the consequences deriving from its dysfunction under pathological conditions. The main emphasis of the Laboratory's research is on the fundamental principles that regulate the cellular and subcellular localisation taking place in neuronal signalling processes in the brain. We are particularly focused on understanding how neurotransmission mediated by neurotransmitter receptors and ion channels occurs in normal and pathological conditions. The underlying premise of our work is that a better understanding of the general organising principles for receptors and ion channels will allow the identification of new molecular targets and new therapeutic strategies to treat a wide spectrum of CNS disorders. The Laboratory's methodology is based in the use of immunohistochemical techniques at the light microscopic level, and specifically high-resolution immunohistochemical techniques at the electron microscopic level, combined with quantitative analysis and 3D reconstruction of immunolabelling.

Key Personnel

Rafael LUJÁN (male) leads the Laboratory of Synaptic Structure in the Medical School of *Universidad de Castilla-La Mancha*.

Key Expertise

- Electron microscopy
- Transmission electron microscopy
- 3D reconstruction
- Confocal microscopy
- Pre-embedding immunogold
- Post-embedding immunogold
- SDS-Freeze Fracture replica labelling
- Synaptic and neuronal architecture
- Brain connections
- Pharmaceutical chemistry
- Supramolecular chemistry
- Polimers and dendrimers
- Fluorescence sensors.

P66) UGR, *Universidad de Granada*, Spain (SP10)

The Computational Neuroscience and Neurorobotics Lab

Profile

The Computational Neuroscience and Neurorobotics Lab is part of the Computer Architecture and Technology Department at the University of Granada. The Lab focuses on developing efficient neural simulation engines for real-time closed-loop experiments with

brain-body models. It has participated in three European projects investigating these issues, as part of the FP5, FP6 and FP7 programmes. The Lab's main expertise is in simulating brain modules or neural subsystems such as the cerebellum, and interfacing with real or simulated robots in behavioural experiments. Work at the Lab concentrates on experiment-driven development, and most of the tools it has created have been released under open source licenses. One of the best known is EDLUT — an efficient neural simulator with a strong focus on real-time simulation. The Lab's main equipment consists of local simulation clusters that are used for massive simulations for brain-body configuration studies.

Key Personnel

Eduardo ROS (male) is an associate Professor of Computer Science and Telecomunications at the University of Granada.

Key Expertise

- Computational neuroscience
- Neurorobotics
- Neuro-robot interfaces
- Embedded, real-time neural simulators
- Vision system, cerebellum, motor and sensory subsystems
- Sensory-motor integration
- Embodiment
- Neural substrate of coordinate and accurate movement

P67) UMINHO, Universidade do Minho, Portugal (SPs 1, 2, 5, 6 & 10)

ICVS/3Bs

Profile

The Neuroscience Research Domain at ICVS, headed by Nuno SOUSA, covers the full spectrum of research (from basic to clinical) with a high degree of interdisciplinarity. We are focused on understanding the neurobiological mechanisms implicated in several neurodevelopmental and neurodegenerative disorders, and on evaluating the interplay between the nervous and the immune systems. We benefit from a high-quality research infrastructure and a vast team that guarantees expertise in a broad technical platform; in this way we foster multimodal approaches to the research questions under study. The close interplay with the Clinical Academic Centre allows us to connect the genetic, molecular and cellular approaches to clinical applications within the same infrastructure. ICVS is part of the University of Minho, located in Braga, Portugal.

Key Personnel

Nuno SOUSA (male) is a Professor and Director of the Medical Degree at the School of Health Sciences, University of Minho, and Director of the Clinical Academic Centre at the Hospital de Braga. He also coordinates the Neuroscience Research Domain at ICVS.

Key Expertise

- Neuroanatomical analysis (from 3D reconstruction to confocal)
- Neurobehavioral platform (including new set-ups such as the PhenoWorld)

- Electrophysiology platform (from patch-clamp to *in-vivo* freely moving to portable EEG and neurofeedback)
- Molecular biology facilities (from (epi)genetics to proteomics and lipidomics)
- Optogenetics
- Neuroimaging facilities (from acquisition to post-processing)
- Research facilities for clinical studies and trials.

P68) UPM, *Universidad Politécnica de Madrid*, Spain (SPs 1, 5, 6, and 7)

Laboratorio Cajal de Circuitos Corticales UPM-CSIC

Profile

The *Laboratorio Cajal de Circuitos Corticales UPM-CSIC* (CCCL) is led by Javier DE FELIPE. The laboratory is located at the UPM, and was established in 2008 as a joint research laboratory between *Universidad Politécnica de Madrid* (UPM) and the Cajal Institute (IC-CSIC). It aims to combine experimental studies of the brain with computer science technologies. The lab brings together Neuroinformatics groups from across the UPM that provide expertise in statistics, informatics tools and image analysis. These include expert researchers in neuroscience (neuroanatomy) from the IC-CSIC, and computer scientists. The CCCL has the latest equipment to carry out its on-going research. It is currently engaged in collaborations with research groups from EPFL (Switzerland), Columbia University (USA), *Ruprecht-Karls-Universität Heidelberg* (Germany), University of Cambridge (England), the Royal College of Surgeons (Ireland), and the *Institut Pasteur* (France).

Key Personnel

Javier DE FELIPE (male) is the Director of the *Laboratorio Cajal de Circuitos Corticales* (*Centro de Tecnología Biomédica*, UPM) and of the *Laboratorio de Microorganización de la Corteza Cerebral Normal y Alteraciones de los Circuitos* (*Departamento de Neurobiología Funcional y de Sistemas, Instituto Cajal*, CSIC).

Key Expertise

- Microanatomy of pyramidal neurons, interneurons and glia
- Microanatomical basis for modelling
- 3D quantitative analysis
- Automated electron microscopy
- Confocal microscopy
- Spatial distributions of neurons and synapses
- Neurochemical characterisation of neurons and synapses
- Intracellular injections in fixed tissue
- Project management and coordination.

Computational Intelligence Group

Profile

The Computational Intelligence Group (CIG) was created in 2010, and is led by Professor Pedro LARRAÑAGA and Professor Concha BIELZA. The group's research, both theoretical and

practical, is devoted to modelling (from a statistical and machine learning perspectives), heuristic optimisation, and Neuroinformatics. The main issues in modelling include: data streams, multi-dimensional supervised classification, multi-label classification, clustering in high-dimensional spaces, feature subset selection using methods as Bayesian networks, and regularisation. In heuristic optimisation, we solve complex problems which, for example, have multiple objectives with special emphasis on estimation of distribution algorithms. In Neuroinformatics, we face neuroanatomy issues, like modelling and simulation of dendritic trees, spines or somas; optimal dendritic wiring; spatial distribution of synapses, and the classification of neuron types based on morphological features. In addition, we deal with problems related to neurodegenerative diseases, such as predicting health-related quality of life in PD, and searching for genetic biomarkers in AD. Current collaborations include research groups from Columbia University (USA), George Mason University (USA), *Centro de Investigación y Estudios Avanzados del Instituto Politécnico Nacional* (Mexico), Oxford University (UK), Radboud University Nijmegen (The Netherlands), Aalborg University (Denmark) and King's College Hospital (UK).

Key Personnel

- Pedro LARRAÑAGA (male) is a Professor at the Technical University of Madrid, and founder of the Computational Intelligence research group.

Key Expertise

- Statistics and data mining
- Supervised classification: Bayesian classifiers, K-nearest neighbours, classification trees, logistic regression, support vector machines, ensembles of classifiers, etc.
- Clustering: hierarchical, partitional, probabilistic, affinity propagation
- Probabilistic graphical models: inference and learning with Bayesian networks and Markov random fields
- Large scale (Big Data) machine learning
- Text mining
- Spatial statistics: modelling and sampling
- Heuristic optimisation
- Predictive Neuroinformatics with neuronal morphological data
- Neuron type classification
- Pyramidal neuron statistical modelling: basal and apical arbour, synapses, spines, soma.

CCS - Centre for Computational Simulation

Profile

The Centre for Computational Simulation is a centre that gathers most of the research on Computational Science and Engineering at the UPM. It also includes the research previously performed at CeSViMa (Madrid Visualization and Supercomputing Centre), which is now solely an infrastructure provider. Both Centres are designed to complement one another; CeSViMa manages the services and infrastructure, and the CCS conducts research activities. CCS has over 30 principal researchers in: fundamentals, devoted to new computational models and algorithmics (currently quantum information and computing, but extending into neurocomputing), Big Data analytics, large numerical simulations (mainly computational fluid dynamics), visualisation and data interaction, grid and cloud computing, and energy efficiency in ICT. CCS researchers' work with the Cajal Blue Brain project, and HBP has resulted in activity devoted to interactive/immersive 3D visualisation for neuroscience

applications. As part of these works, the group has developed or co-developed the ESPINA, RTNeuron and Neurite frameworks, which provide novel functionality for image segmentation, 3D volume reconstruction of synapses, cortical column visualisation and mechanical-electrophysiological simulation models.

Key Personnel

- Vicente MARTIN (male) is an Associate Professor of computational science at the *Universidad Autónoma de Madrid,* and the Director of CeSViMa, where he leads the UPM Quantum Information and Computation Group.

Key Expertise

- High performance computing infrastructure and management
- Data and text mining
- Large scale numerical/combinatorial optimisation
- Co-processor computing and algorithms (GPU, MIC)
- Visualisation techniques
- Computational steering and interactive supercomputing
- Scalable algorithms for computational fluid dynamics
- Quantum information algorithms and quantum computing
- Grid and cloud computing.

P69) URJC, *Universidad Rey Juan Carlos*, Spain (SP1, SP7)

Research Group on Modelling and Virtual Reality

Profile

The Research Group on Modelling and Virtual Reality (GMRV) focuses its research on scientific and information visualisation, interaction, exploratory analysis and visual analytics, physically-based simulation and animation, and virtual reality. It was created in 2000 with researchers from the URJC and UPM, and is led by Luis PASTOR. The group is composed of one full professor, two associate professors, six assistant professors, six postdoctoral fellows, two technical staff and eleven PhD students, from both institutions. With an ERC starting grant, GMRV collaborates with numerous European, Spanish and privately funded research programmes, including the Cajal Blue Brain and the HBP, in the areas of computer graphics, VR and visualisation.

Key Personnel

- Luis PASTOR (male) is a Professor of Computer Science and Engineering at the *Universidad Rey Juan Carlos* in Madrid, where he heads the Research Group on Modelling and Virtual Reality.

Key Expertise

- Real-time scientific visualisation and information visualisation
- Virtual reality
- Multimodal interaction and navigation
- 3D real time rendering

- Exploratory analysis and visual analytics
- Content-based retrieval and data filtering.

P70) UNIPV, *Universita degli Studi di Pavia*, Italy (SP1, SP6)

Brain Connectivity Centre, Laboratory of Neurophysiology

Profile

The Laboratory of Neurophysiology, led by Egidio D'ANGELO, investigates plasticity and computation, and generates advanced computational models of the cerebellar network. The group is specialised in single-neuron and neural circuit physiology, single-neuron and neural circuit computation, electrophysiology and imaging, and cerebellum and sensory-motor control. The Laboratory belongs to and directs the Brain Connectivity Centre (BCC), a centre jointly used by the University of Pavia and the IRCCS Neurological Institute C. Mondino. This installs and operates facilities for fMRI, TMS, BCI, and EEG studies. The Laboratory coordinates the PhD in Biomedical Sciences, two EU projects (REALNET and CEREBNET) on basic cerebellar physiology and computation, and three projects on cerebro-cerebellar function and pathology in humans for the Italian Ministry of Health.

Key Personnel

- Egidio D'ANGELO (male) is a full Professor of Physiology at the University of Pavia. He is also director of its PhD programme in Physiology and Neuroscience, and directs the Brain Connectivity Centere for neuroscience research, IRCCS C. Mondino, the European Projects CEREBNET (ITN), and REALNET (ICT).

Key Expertise

- Computational modelling: single neurons
- Computational modelling: microcircuits
- Electrophysiology *in vitro*
- Electrophysiology *in vivo*
- Cellular and tissue functional imaging
- Synaptic transmission and plasticity
- Ionic channels and receptors
- Cerebellum.

P71) UBERN, *Universität Bern*, Switzerland (SP4)

Computational Neuroscience Lab, Department of Physiology (Senn Lab)

Profile

The Senn Lab at the University of Bern uses mathematical models of synapses, neurons and networks to explain aspects of perception and behaviour. It particularly focuses on models of cortical pyramidal neurons and microcircuits that have been investigated experimentally *in vivo* and *in vitro*. Other research at the Lab focuses on the neuronal substrate for learning and memory, and the way the brain learns action sequences from an on-going stream of sensory inputs and a delayed feedback signal. The Lab has developed models of sensory processing and its interaction with cortical top-down signals, which can explain experimental recordings from the visual cortex, obtained during perceptual or classification

tasks. These models highlight key mechanisms by which synapses and neurons enable our brains to deal with learning and memory.

Key Personnel

Walter SENN (male) is a full Professor in the Department of Physiology at the University of Bern, and co-Editor-in-Chief of Biological Cybernetics.

Key Expertise

- Models of synaptic plasticity
- Optimal learning rules
- Dendritic computing.

P72) UNIBI, *Universität Bielefield*, Germany (SP9)

Cluster of Excellence Cognitive Integration Technology, Cognitronics and Sensor Systems

Profile

The Cognitronics and Sensor Systems (CSS) research group, directed by Professor Ulrich RÜCKERT and Dr Mario PORRMANN, is part of the Cluster of Excellence Cognitive Interaction Technology (CITEC) at Bielefeld University. Our common research goal is the systematic design and the demand-oriented implementation of innovative microelectronic circuits and systems. In this field, we are developing microelectronic components and systems in digital and analogue circuit technology, with an emphasis on massively parallel and dynamically reconfigurable system architectures. Particular attention is paid to the optimisation of the resource-efficiency and robustness of respective implementations. The group comprises 28 PhD students, funded by the EU, DFG, BMBF, ESA, and industry.

Key Personnel

Ulrich RÜCKERT (male) is a full Professor at the Cognitive Interaction Technology Centre of Excellence at Bielefeld University, and heads the research group Cognitronics and Sensor Systems.

Key Expertise

- Digital chip design
- FPGA design
- System design, integration and testing
- Low level access to hardware
- HW system configuration (“mapping and routing”)
- HW system simulation (“ESS”)
- Analysis tools for experiment results
- Model adaptation to hardware
- Benchmarking
- Innovation, Industry relations, IPR
- Computational theory
- Cognitive neuroscience.

P73) UKAACHEN, *Universitätsklinikum Aachen*, Germany (SP8)

Department of Psychiatry, Psychotherapy and Psychosomatics

The Department of Psychiatry, Psychotherapy and Psychosomatics is the department with the most inpatient beds of the University Hospital RWTH Aachen. It offers treatment for around 120 inpatients, houses 50 day-care patients and offers numerous highly specialised ambulatory therapeutic interventions. The department is very much focused on research, especially in close collaboration with the *Forschungszentrum Jülich*. It currently comprises a total of eleven professorships; among those are three junior professorships, three joint appointments with Jülich, and one senior professor. The department focuses on the investigation of biological correlates of mental disorders; both with respect to predisposition for a disorder, and early markers and markers for course of illness.

Key Personnel

Frank SCHNEIDER (male) is the Head of the Department of Psychiatry, Psychotherapy and Psychosomatics at the University Hospital Aachen. He is also Vice Dean at the School of Medicine, and Managing Director of the Jülich Aachen Research Alliance (JARA), directing the "Translational Brain Research" section.

Key Expertise

- Biological correlates of psychiatric disorders, especially disturbances of emotion processing and social cognition
- Diagnostic criteria for psychiatric disorders and differential diagnoses
- Assessment of treatment effects
- Functional and structural imaging in psychiatric disorders
- Neurofeedback
- Psychotherapy
- Computational psychiatry.

P74) UKE, *Universitätsklinikum Hamburg-Eppendorf*, Germany (SP10)

Department of Neurophysiology and Pathophysiology

Profile

Work in the Department of Neurophysiology and Pathophysiology (led by Professor Andreas K. ENGEL) focuses on cognitive and sensorimotor functions. These are studied in humans and animal models using neurophysiological and neuroimaging techniques. The group is addressing the neural mechanisms underlying perceptual integration, sensorimotor integration, multisensory interactions, attentional control, response selection, perceptual decision-making, agency, social cognition and awareness. Further topics of interest include the role of synchrony in sensorimotor transformations (which convert signals from various sensory modalities into motor commands), establishing links between synchrony and perceptual states, cross-species comparison of synchronisation phenomena, and the study of synchronisation mechanisms (carried out via recordings in transgenic mice). To understand the mechanisms of cross-modal binding, the group has developed computational models of networks of coupled oscillators. The group's research also focuses on the pathophysiology of neuropsychiatric disorders, such as multiple sclerosis, PD, schizophrenia and autism. It also undertakes interdisciplinary work linking neurophysiology, neuroimaging and technical

applications (neuroprosthetics, brain-computer-interfaces and neurorobotics). Links with other groups have successfully been established as part of several EU-funded ICT projects (Amouse, POP, eSMCs and socSMCs) and networks (Neuro-IT, NeuroVersIT, euCognition, euCogII and euCogIII).

Key Personnel

Andreas K. ENGEL (male) is a Professor of Physiology, and Director of the Department of Neurophysiology and Pathophysiology at UKE.

Key Expertise

- Neuronal dynamics
- Computational modelling
- Data analysis for MEG/EEG
- Neuroprosthetics
- Neuropsychiatric disorders.

P75) UZH, *Universität Zürich*, Switzerland (SP1)

The UZH Functional Imaging and Neurovascular Coupling Group

Profile

The UZH Functional Imaging and Neurovascular Coupling group, headed by Bruno WEBER, investigates the mechanisms governing the regulation of blood flow and metabolism in the brain. Combining *ex vivo* and *in vivo* experiments in the rodent somatosensory cortex, the group is working to close the gap between structural and functional aspects of hemodynamic response. Other studies by the group use immunohistochemical methods and synchrotron-based X-ray computed tomography to study cerebral microvasculature in rat and monkey tissue, and state-of-the-art optical methods to study the 2D and 3D dynamics of blood flow. The experimental data collected in this work serves as a basis for numerical models, simulating the topology of cerebral blood flow.

Key Personnel

Bruno WEBER (male) is a Professor of Multimodal Experimental Imaging at the UZH Medical Faculty.

Key Expertise

(Experimental Animals)

- Microanatomy of cerebrovascular system
- Microanatomical basis for modelling
- Fluid dynamics modelling
- 3D quantitative analysis
- *In vivo* two-photon microscopy
- Intrinsic optical imaging.

P76) UB, *Universitat de Barcelona*, Spain (SP10)

Experimental Virtual Environments for Neuroscience and Technology

Profile

The Experimental Virtual Environments for Neuroscience and Technology (EVENT Lab) is an interdisciplinary lab that carries out research in virtual reality as applied to scientific questions in neuroscience and psychology. In particular, it focuses on the exploitation of virtual reality and robotics in investigating how the brain represents the body, and the perceptual, behavioural and psychological consequences of different self-representations. The EVENT Lab is funded mainly through European projects, including an ERC Senior research project granted to the lab director, ICREA Professor Mel Slater. Co-led by Mel SLATER and Maria V. SANCHEZ-VIRES, the EVENT Lab has a staff of approximately 25 full-time researchers and technicians. The Lab has several head-mounted displays, with head-trackers and full body motion capture systems, and physiological recording devices including EEG. It also has a state-of-the-art high definition four-sided CAVE system, and an emotionally expressive life-sized robot.

Key Personnel

Mel SLATER (male) is a Research Professor at ICREA-University of Barcelona, and part-time Professor of virtual environments at University College London. He also leads the FET consortium Virtual Embodiment and Robotic Re-Embodiment, and is the Scientific Manager of BEAMING.

Key Expertise

- Concepts of body ownership and agency
- ERC award for TRAVERSE project
- Leader of the FET consortium Virtual Embodiment and Robotic Re-Embodiment
- Scientific manager of BEAMING.

P77) UPF, Universitat Pompeu Fabra, Spain (SP4)

Universitat Pompeu Fabra was established as a public university in 1990. The Department of Information and Communication Technologies (DTIC) (ranked 17th in the Times Higher Education World University Ranking 2012) was established in 1999. Its mission was to become one of the leading European university departments in the broad range of fields that has developed around the convergence of ICT with biomedical and cognitive sciences, computation and networks. Since its earliest days, the DTIC has emphasised scientific excellence and internationalisation as core aspects of its activities. The Center for Brain and Cognition (CBC) at DTIC currently hosts six independent research groups, with over 90 researchers and staff. The CBC conducts leading-edge interdisciplinary research in the cognitive neurosciences. It hosts world-leading research on topics such as early bilingual language acquisition, biologically plausible models of cognitive phenomena, probabilistic reasoning, bilingual language production, and multisensory perception. It has access to a broad variety of techniques; from behavioural experiments with humans of all ages, to computational modelling and brain imaging. The Centre hosts academics from diverse backgrounds, including philosophers, linguists, psychologists, biologists, physicists and computer scientists.

The Computational and Theoretical Neuroscience Group

Profile

The Computational Neuroscience Group (CNS), group member of the CBC, investigates neuronal and cortical mechanisms of perception and cognition. CNS has developed a

theoretical framework to deepen our understanding of a great variety of mechanisms and computations underlying higher brain functions. This has been obtained by developing explicit mathematical neurodynamic models of brain function at the level of neuronal spiking and synaptic activity. The analysis of networks of integrate-and-fire neurons (including non-linearities) enables the study of many aspects of brain function, from the spiking activity of single neurons to the effects of pharmacological agents on synaptic currents. CNS has extensive experience in modelling cognitive functions, such as attention and decision-making with biologically realistic models.

The Group has been involved in many international projects. These include: BrainscaleS - Brain-inspired multiscale computation in neuromorphic hybrid systems (2011-2014, FP7-ICT), CORONET - Choreographing Neural Networks: Coupling Activity Dynamics Across Biomimetic Brain Interfaces with Neuromorphic VLSI (2011-2014, FP7-ICT), DYSTRUCTURE - The Dynamical and Structural Basis of Human Mind Complexity: Segregation and Integration of Information and Processing in the Brain (2012-2017, FP7-IDEAS-ERC), INDIREA - Individualised Diagnostics and Rehabilitation of Attention - (2013-2017, FP7-PEOPLE-ITN), and SEMAINE - Simultaneous MEG or fMRI And INtracranial EEG (2014-2016, ERANET NEURON). CNS hosts six Marie Curie Individual Fellowships: NEUCOD, INTERACTIONS, CEMNet, CONSCBRAIN, QTMODEM and NeuArc2Fun (2013-2018). CNS is a partner of the Brain Network Recovery Group (2011 - 2014, funded by the James S. McDonnell Foundation) and of the HBP (FET Flagship).

Key Personnel

Gustavo DECO (male) is a Research Professor at ICREA (*Institució Catalana de Recerca i Estudis Avançats*) and is Professor at Pompeu Fabra University (Barcelona), where he is head of the Computational and Theoretical Neuroscience Group and Director of the Centre of Brain and Cognition.

Key Expertise

- Modelling cognitive functions, such as attention and decision making with biologically realistic models.
- Modelling whole brain activity (as evidenced by EEG, MEG and fMRI).
- Investigation and modelling of how the brain regulates information flow.
- Model-based approach and dynamical system analysis to infer directed intracortical connectivity and intrinsic variability for whole cortical dynamics
- Graph analysis of cortical interactions to uncover functional hubs/modules.
- Interpretation of fMRI/EEG/MEG data for resting-state and task-evoked activity to characterise cortical neural processing in the context of development/aging or disease.

P78) AMU, *Université d'Aix Marseille*, France (SP4)

Institut des Neurosciences de Système

Profile

The *Institut des Neurosciences de Système* (INS) is located on the medical campus of Aix-Marseille University, the largest University in France. INS houses a high-performance computing cluster dedicated to neural modelling, an MEG platform, and a coupled EEG-TMS platform. It also has an epileptic patient unit with stereotactic EEG (sEEG) at La Timone hospital (APHM). INS is directed by Viktor JIRSA, and comprises 27 permanent faculty members, and 70 institute members in total. INS combines expertise from computational, cognitive and clinical neuroscience, and biomedical imaging and signal analysis. In 2011, INS

received the highest grade of excellence (A+) at the end of its four-year evaluation by the National Scientific Evaluation Agency (AERES).

Key Personnel

Viktor JIRSA (male) is the Director of Research (CNRS) and Co-Director of the Institut de Neurosciences des Systèmes (INS). He also heads the Theoretical Neurosciences Laboratory.

Key Expertise

- Computational neuroscience
- Clinical neuroscience
- Large-scale brain modelling
- Nonlinear dynamics theory
- Network theory
- Complex systems.

P79) UBO, *Université de Bordeaux*, France (SP8)

Research Centre in Epidemiology and Biostatistics

Profile

L'Université de Bordeaux (UBO) is a multidisciplinary university of around 50 000 students and 6 600 permanent staff. Its cutting-edge research activities are carried out in 80 research departments, which are associated with major research bodies (CNRS, CEA, INSERM and INRA). UBO is a top education and research organisation (ranked 208th in Shanghai ranking, and third in France), which was recently rewarded the "Campus of Excellence" label by the French government. The Research Centre in Epidemiology and Biostatistics has significant experience in participating in large research projects funded by the French government (i-share cohort, SYRIC BRIO on Cancer, the Labex Vaccine Research Institute), and by the EC (FP6/FP7/H2020 projects: FRAILOMIC, EUROCOORD, CHAIN, NEAT, EYE-RISK and IMI2 EBOVAC), including one ERC Starting Project. Headed by Christophe TZOURIO, the Research Centre has a unique position in France thanks to its critical mass of researchers, the quality of its teams and researchers, and the fact that it is backed by the Institut de Santé Publique et Développement (ISPED). The research topics covered by the Centre include biostatistics, epidemiology of neurological diseases, ageing, HIV and other infectious diseases, cancer, nutrition, and trauma prevention. In addition to the development and use of modern methods in epidemiology and biostatistics, the Research Centre benefits from large cohorts that constitute research platforms, such as the Aquitaine HIV cohort, longitudinal studies in older community-dwelling persons (Paquid/3C), the MeMento on dementia, and the more recent i-Share student cohort. We have close links with hospitals, as several clinicians participate in research teams regarding HIV, trauma prevention, nutrition and ophthalmology.

Key Personnel

Jean-François DARTIGUES (male) is Director of the *Epidémiologie et Neuropsychologie du Vieillissement Cérébral* group at the Inserm centre U 897, *Université de Bordeaux*. He is also responsible for the CMRR of Bordeaux-Aquitaine.

Key Expertise

- Epidemiology of AD and dementia

- Clinical expertise on the diagnosis of dementia
- Constitution of data base with socio-demographic, clinical, neuropsychological, biological and neuroimaging data
- Biostatical analysis of the data base with longitudinal design.

P80) UA, *Universiteit Antwerpen*, Belgium (SP4)

The Theoretical Neurobiology and Neuroengineering Laboratory

Profile

The Theoretical Neurobiology and Neuroengineering Laboratory is an interdisciplinary group. It was founded in 1993, and has been led by Michele GIUGLIANO since 2008. The lab's early pioneering activities on multicompartmental modelling in cerebellar physiology and on Neuroinformatics had a significant impact on the consolidation of computational neurosciences as a discipline. Today, the group consists of four postdoctoral fellows, four doctoral students, and a lab engineer and system administrator. The lab coordinates, or is involved in, several FP7 projects (BRAINLEAP, ENLIGHTENMENT, MERIDIAN) and Marie Curie training networks (NAMASEN, NEUROACT, C7, CEREBNET). It focuses on 1) multi-scale acquisition of in vitro electrophysiological data, related to information processing in cerebellar and cortical-like structures; 2) theoretical modelling and simplification of neuronal cortical dynamics; 3) the creation of tools for data analysis, real-time experiments, and *in silico* simulations; and 4) novel micro- and nanotechnologies for probing or interfacing brain tissue at cellular and microcircuit levels. The lab has access to UA's High Performance Computing core facilities (168 compute nodes, HP BL2x220 G5/G6/G7, for a total of 3360 cores), which is integrated in the Flemish Supercomputer Centrum (VSC) infrastructure.

Key Personnel

Michele GIUGLIANO (male) is a Principal Investigator and a tenured Associate Professor (ZAP-BOF research mandate, Hoofddocent) in the Department of Biomedical Sciences and at the University of Antwerp.

Key Expertise

- Simplified quantitative description of neuronal excitability
- Neuronal dynamical response properties
- Efficient numerical simulation of stochastic ionic permeability
- Molecular modelling of signalling pathways
- Morphological analysis
- Dynamic-clamp and computer-controlled model identification.

P81) UIO, *Universitetet i Oslo*, Norway (SP3, SP5)

Institute of Basic Medical Sciences, Neural Systems Laboratory

Profile

The Institute of Basic Medical Sciences at UIO is the largest Norwegian centre of its kind, covering research on biological processes from the nucleic acid level to whole organisms and human behaviour. Neuroscience is a key area, and one of the largest in the Institute, which has extensive infrastructures for multi-level studies of the brain. The HBP partnership

is centred on the Institute's Neural Systems laboratory, which develops workflows and analytical tools under NORBRAIN, a large-scale national infrastructure supported by the Research Council of Norway. The Neural Systems Laboratory supports advanced informatics developments for brain architecture analysis and brain atlasing. It is integrated with the central University infrastructure and *Uninett Sigma*, the national infrastructure for computational science in Norway. The Laboratory also hosts the Norwegian Node of the International Neuroinformatics Coordinating Facility.

Key Personnel

Jan BJAALIE (male) is the Head of the Institute of Basic Medical Sciences at the University of Oslo, and Chair of the Governing Board of the International Neuroinformatics Coordinating Facility.

Key Expertise

- Neuroanatomy
- Brain architecture
- Brain maps
- Brain connectivity
- Brain projection systems and map transformations
- Three-dimensional digital brain atlasing
- Histology
- Robotic microscopy and slide scanning
- Serial two-photon tomography
- Small animal MR and PET imaging
- Phenotyping of disease models
- Large-scale image management and storage
- Database development
- Computational neuroanatomy tools development
- Data and tools sharing.

Brain Signalling

Profile

The lab studies signalling and information processing in the brain at multiple levels, from synapses, neurons and circuits, to control of behaviour and mental processes, particularly consciousness and memory. The work is fundamentally motivated and guided by a long-term interest in the brain's most unique property: its ability to generate conscious experience. Thus, it primarily studies multilevel electrical and chemical neuronal signalling at time scales of milliseconds to seconds – the type of processes likely to be involved in consciousness. The research is on neurophysiology of the mammalian brain, in particular the cerebral cortex including the hippocampal formation, at three main levels, using a variety of electrophysiological, optical, and computational methods: (1) Single neuron signalling and computation; (2) Functions, dynamics and neuromodulation of neural circuits; (3) Consciousness research in humans and animals, including EEG and TMS experiments. In this research, we also use opportunities to contribute to related areas, including translational medicine - often in fruitful collaborations with experts in these fields.

Key Personnel

Johan Frederik STORM (male) is Professor at the Molecular Medicine, Institute for Basic Medical Sciences of University of Oslo.

Key Expertise

- Electrophysiology of single neuron signaling and computation *in vivo* and *in vitro*
- Computer modelling of single neuron signaling and computation
- Electrophysiology of network signaling and computation *in vivo*
- Computer modelling of network signaling and computation
- Electroencephalography (EEG) in humans and animals
- Transcranial Magnetic Stimulation (TMS) in humans
- Two-photon microscopy/Calcium imaging in animals
- Animal behavioural tasks (whisker /barrel cortex system, vision)
- Clinical neurophysiology
- Anaesthesiology
- Radiology

P82) UCL, University College London, United Kingdom (SPs 2, 3, 4, 6, and 8)

Synaptic Circuitry Group, Department of Pharmacology, UCL School of Pharmacy

Profile

The Synaptic Circuitry Group, led by Alex THOMSON and Audrey MERCER, uses a variety of techniques to study synaptic circuitry.

Key Personnel

Alex THOMSON (female) was Head of the Pharmacology Department and Wellcome Professor of Pharmacology at UCL. She retired in 2014, taking emeritus status.

Audrey MERCER (female) is a Lecturer of Pharmacology, and RCUK Academic Fellow at UCL.

Key Expertise

- Interactions between synaptic cleft-spanning proteins that underpin synapse-formation and specificity
- Contribution of voltage-gated ion channels to the shaping and integration of synaptic inputs
- Properties of cortical circuits and the synaptic connections that form them.

The Wellcome Trust Centre for Neuroimaging

Profile

The Wellcome Trust Centre for Neuroimaging (WTCN) (incorporating the Leopold Muller Functional Imaging Laboratory and the Wellcome Department of Imaging Neuroscience) is an interdisciplinary centre for neuroimaging excellence. It brings together clinicians and scientists who study brain function and structure using neuroimaging techniques. The goal is

to understand how thought and behaviour arise from brain activity, and how such processes break down in neurological and psychiatric disease. The Centre is home to the SPM package, which is a well-established image analysis framework for neuroimaging data. Using this, the Centre seeks to answer fundamental questions about how the brain works, to improve human and animal health. It hosts and trains over 100 clinicians, scientists and support staff, and interacts with over 200 collaborators — both at UCL and throughout the world.

Key Personnel

John ASHBURNER (male) is a Professor of Imaging Science at the Wellcome Trust Centre for Neuroimaging, UCL.

Key Expertise

- Probabilistic generative modelling of 3D medical image data
- Nonlinear optimisation
- Rigid-body 3D image registration
- Diffeomorphic nonlinear 3D medical image registration
- Tissue segmentation of magnetic resonance images
- Pattern recognition and machine learning
- Statistical parametric mapping
- MATLAB and C programming
- DICOM and NIfTI image file formats
- Neuroimaging.

The Space and Memory Lab

Profile

The Space and Memory Lab at the UCL Institute of Cognitive Neuroscience (ICN), headed by Neil BURGESS, has strong expertise in computational neuroscience, virtual reality, human neuropsychology, single-unit electrophysiology in freely moving rodents, and functional neuroimaging, including fMRI and MEG. The Lab's main interest is understanding the neural mechanisms of spatial memory and navigation, with a focus on the functioning of the hippocampus, and its relations to other brain regions. Specific research has considered computational modelling of the activity of place cells, grid cells, boundary vector cells and theta rhythmicity in rodents and humans; their interactions with processing in the striatum; and their contributions to spatial navigation and episodic memory.

Key Personnel

Neil BURGESS (male) is a Professor of Cognitive and Computational Neuroscience, a Wellcome Trust Principal Research Fellow, and Deputy Director of the UCL Institute of Cognitive Neuroscience.

Key Expertise

- Computational neuroscience (spiking neurons, medium scale networks, embodied simulations)
- Functional neuroimaging
- Neuropsychology
- *In-vivo* Electrophysiology

- Matlab and C++ programming
- Virtual reality.

Cacucci Lab

Profile

Its research focuses on the study of hippocampal spatial and memory processing in the rodent, with an emphasis on its post-natal development. Techniques employed range from single neuron extra-cellular recording, to behavioural testing, functional neuroanatomy and in vivo circuit manipulation (e.g. viral tracing, optogenetics, pharmacological manipulations). The Cacucci lab currently employs 3 post-doctoral and 3 doctoral researchers.

Key Personnel

Francesca CACUCCI (female) is Reader in Neuroscience in the department of Neuroscience, Physiology and Pharmacology at UCL.

Key Expertise

- Single neuron extracellular recording
- Functional neuro-anatomy
- Behavioural testing
- Functional neuroimaging
- Computational neuroscience
- Neuropsychology

P83) UU, *Uppsala Universitet*, Sweden (SP8, SP12)

The Centre for Research Ethics and Bioethics

Profile

Uppsala University is a research university in Uppsala, Sweden. Founded in 1477, it is the oldest university in Sweden. The University is one of the best in Northern Europe according to international rankings. The Centre for Research Ethics and Bioethics (CRB) was established by on 1 January 2008, and is part of the Faculty of Medicine. In 2011, Uppsala University conducted an overall evaluation of the University's research, "Quality and Renewal 2011", and the CRB was evaluated as "top quality". CRB research deals with ethical, legal and social aspects of medicine and biology (bioethics), and the application of ethical principles and values to different scientific topics (research ethics). Our research topics cover a wide range of ethical questions related to biobanks and registry research, ethical review, informed consent, medical treatment of patients, nursing, explanations of human consciousness, quality of life, end of life care and others. The methods we use range from analytical philosophical methods, to empirical studies using both qualitative and quantitative methods.

Key Personnel

Kathinka EVERS (female) is a Senior Researcher and Professor of Philosophy at the Centre for Research Ethics and Bioethics (CRB) at Uppsala University. She is also honorary professor at *Universidad Central*, Santiago, Chile.

Key Expertise

- Philosophy of science
- Philosophy of mind
- Philosophy of neuroscience
- Bioethics
- Neuroethics.

P84) WEIZMANN, Weizmann Institute of Science, Israel (SP4)

The Weizmann Institute's Computational Neuroscience Lab

Profile

The Weizmann Institute's Computational Neuroscience Lab, led by Dr Misha TSODYKS, adopts a theoretical approach to modelling brain functions. It is part of the neurobiology department, with which the Lab collaborates on the design of new experiments and the analysis of experimental data. The Lab's main activities are in the fields of learning and memory, space representation in hippocampal formation, visual processing and synaptic transmission in the cortex. It includes one post-doctoral fellow, three PhD students and one research assistant. It is well equipped with computer power, and benefits from the services of the Weizmann Institute Computer Centre.

Key Personnel

Misha TSODYKS (male) is full Professor in the Department of Neurobiology, Weizmann Institute of Science.

Key Expertise

- Mathematical models of short-term synaptic plasticity
- Neural network models of working memory and memory recall
- Attractor neural networks and models of spatial representations
- Synaptic learning rules.

The visual cognition laboratory

Profile

The visual cognition laboratory studies the visual mechanisms and processes used by the brain to understand the world in terms of objects, agents, and the interactions between them. Key topics include object recognition and categorisation, action recognition, and the use of vision to obtain information about agents, their goals, and interactions. The main focus is on computational studies and the modelling of brain processes that allow the brain to attain its goals. The computational models are evaluated by their functional performance, and by their ability to explain and predict empirical data at both physiological and behavioural levels. A major aspect of Lab's studies is to include learning mechanisms that allow the models to learn from visual experience.

Key Personnel

Shimon ULLMAN (male) is a Professor of Computer Science at the Weizmann Institute. He is also member of the Israeli Academy of Science and the Humanities.

Key Expertise

- Computational modelling of visual processing in the brain
- Modelling for cortical circuits
- Modelling and theory of bottom-up and top-down cortical processing.

P85) TUDA, *Technische Universität Darmstadt*, Germany (SP7)

Laboratory for Parallel Programming

Profile

The Laboratory for Parallel Programming's objective is to develop solutions that support simulation scientists in exploiting massive parallelism on modern architectures. The Laboratory specialises in programming tools for application performance analysis and modelling, data-race detection, and parallelism discovery. Further topics include parallel algorithms and cluster resource management. One of the laboratory's key projects is Scalasca, a performance-analysis tool for large-scale parallel applications, which is being jointly developed with the Jülich Supercomputing Centre. The Laboratory's recent contributions to Scalasca are related to automated performance modelling and requirements engineering for HW/SW co-design.

Key Personnel

Felix WOLF (male) is a Professor in the *Technische Universität Darmstadt*'s Department of Computer Science, and Head of the Research Area Parallel Programming.

Key Expertise

- Performance-analysis tools
- Performance-modelling tools.

P86) UNIGE, *Université de Genève*, Switzerland (SP8)

Laboratoire de Neuroimagerie du Vieillissement

Profile

L'Université de Genève (UNIGE) hosts the *Laboratoire de Neuroimagerie du Vieillissement* (LANVIE), which is led by Giovanni B FRISONI. UNIGE is Switzerland's second largest university. It has a strong international reputation, both for the quality of its research (it ranks among the top institutions in the League of European Research Universities), and the excellence of its education. The Faculty of Medicine is well-known at international level, and leads research in partnership with the largest hospital complex in Switzerland, *Les Hopitaux Universitaires de Genève*. Here, the Clinical Medicine Section's research is oriented towards new therapies, improving diagnostic tools, disease prevention, quality of care and patient support.

Key Personnel

Giovanni B. FRISONI (male) is a Professor of Clinical Neuroscience at the University of Geneva, and Head of the Memory Clinic at Geneva University Hospital. He is also Scientific Director at the National Alzheimer's Centre in Brescia, Italy, and Head of the local Laboratory of Neuroimaging and Translational Care Unit.

Key Expertise

- Neurosciences
- Neuroimanging
- AD
- Cognitive decline
- Ageing
- Neurodegenerative diseases
- Biomarkers
- Early diagnosis.

P87) IDIBAPS, *Consorci Institut d'Investigacions Biomediques August Pi I Sunyer*, Spain (SP3)

Cortical networks Group at IDIBAPS

Profile

The Cortical Networks group led by Prof. SANCHEZ-VIVES is in the Systems Neuroscience division, also led by Prof. Sanchez-Vives, at IDIBAPS. IDIBAPS (Institute of Biomedical Research August Pi i Sunyer) is a consortium devoted to translational research, innovation and technological progress in the field of biomedicine, through different programmes. IDIBAPS has a strong track record of working in European projects, especially within the Framework programme. IDIBAPS has experience running EU projects, and in FP7 IDIBAPS dealt with 101 projects, being the coordinator of 29 of them.

Our expertise is the study of the activity that spontaneously emerges from the cortical network, the mechanisms that regulate it, the information it encodes, and the consequences of this activity upon the network. We also concentrate on the altered patterns of the emergent activity in transgenic mice that are models of different neurological disorders. The understanding of these changes reveals the underlying mechanisms and their possible reversion with treatment.

Key Personnel

Maria V. SANCHEZ-VIVES (female) is ICREA Research Professor at Institut d'Investigacions Biomediques August Pi Sunyer in Barcelona where she is head of the Systems Neuroscience group.

Key Expertise

- Study of cortical network dynamics in preparations *in vitro* and *in vivo* (anaesthetized and awake)
- Modelling of cortical circuits
- Mechanisms of generation of rhythmic patterns

P88) IBEC, *Fundacio Institut de Bioenginyeria de Catalunya*, Spain (SP3)

Nanoprobes and nanoswitches

Profile

IBEC (www.ibecbarcelona.eu) is a research institute covering most bioengineering fields, from basic research to medical applications, aiming to act as an international reference in this field. IBEC was established in 2005 by the Government of Catalonia, the University of Barcelona (UB) and the Technical University of Catalonia (UPC) and is located at the Barcelona Science Park (PCB) sharing also facilities with the Bellvitge University Hospital (BUH). IBEC hosts around 250 researchers and technicians from 20 different countries, working in a truly interdisciplinary environment such as engineering, physics and biology, which are part of its own staff or are associated to the UB and UPC or coming from different recruitment programs of research staff (e.g. ICREA and others). These institutions may act as third parties of the Grant Agreement (see Section 7). The model envisaged by IBEC is inspired by a creative, innovative new ecosystem based on interaction between research experts in different technologies (nano-bio-info-cogno) to generate new knowledge and engineering solutions in health technology. The knowledge that exists within the IBEC research groups is structured in three broad areas: nanomedicine, cellular and tissue engineering and ICT for health. IBEC has substantial experience with the coordination, participation, administration and valorization of EU-funded research. IBEC has participated in more than 30 EU research projects, including 9 ERCs projects, and has been involved in coordination actions such as EURONANOBIO, Nano2market or the High-Level Group on Key Enabling Technologies on Nanobiotechnology, in addition to be Core member of the EIT-Health initiative. Moreover, IBEC is one of the Spanish research centres of excellence awarded with the 'Severo Ochoa' grant. Within IBEC, the team "Nanoprobes and Nanoswitches" (www.ibecbarcelona.eu/nano) led by Prof. Pau GOROSTIZA is focused on developing nanoscale tools to study biological systems, including the light-regulated drugs included in this proposal. In particular, the laboratory is involved in the design, synthesis and characterization (chemical, photophysical, biological *in vitro* and *in vivo*) of bioactive photoswitchable compounds such as light regulated peptide inhibitors of protein-protein interactions, and small molecule photoswitchable ligands of endogenous receptor proteins, with special relevance in the central nervous system.

Key Personnel

Pau GOROSTIZA (male) is a ICREA Research Professor and the Group Leader of Nanoprobes and Nanoswitches Lab.

Key Expertise

- Design of light-regulated ligands (agonists, antagonists, modulators) of receptor proteins, including photochromic and pharmacological properties
- *In vitro* characterisation of light-regulated ligands using electrophysiology in cell lines and cultured neurons
- *In vitro* characterisation of light-regulated ligands using high-throughput motility assays in small aquatic animals

P89) DZNE, *Deutsches Zentrum für Neurodegenerative Erkrankungen EV*, Germany (SP3)

Functional anatomy and plasticity of memory

Profile

The lab of E DÜZEL uses multimodal imaging including FMRI, PET, MR-PET, EEG and MEG to dissect the functional anatomy and molecular regulation of memory processes in the human

brain. The work spans from basic research in healthy individuals to the effects of neurological disorders and neurodegenerative diseases as well as the effects of aging on memory. We have pioneered the functional imaging of laminar activity in human memory circuits as well as the comparative use of PET and functional imaging in memory processing in humans. Within the DZNE our group coordinates the multicentre structural and functional imaging of large DZNE cohorts in longitudinal studies.

Key Personnel

Emrah DÜZEL (male) is the speaker of the Magdeburg site of the German Center for Neurodegenerative Diseases (Helmholtz-Society) and director of the Institute of Cognitive Neurology and Dementia Research at the Univ. of Magdeburg. He has retained a 25% part time position at the UCL Institute of Cognitive Neuroscience.

Key Expertise

- The cognitive neuroscience of memory in young and old age
- Functional anatomy of memory circuits
- Functional and structural imaging of the human brain
- Imaging at ultrahigh field (7T) of laminar level functional activity in the human brain
- Electrophysiology and electromagnetic imaging of cognitive processes using EEG and MEG
- Coordination of imaging in large cohort (standardisation, quality monitoring)

P90) UBER, *Humbolt-Universität zu Berlin*, Germany (SP3)

Larkum laboratory

Profile

The Larkum laboratory focuses on the influence of feedback signals in the brain, and on their effect on dendritic / neuronal processing, which are at the heart of cognitive processes. Understanding the special influence of feedback inputs at the cellular level is likely to reveal deeper insight about the underlying principles of intelligence itself. This will have implications for the design of neural networks to accomplish many tasks that are at present out of the reach of computer science. This laboratory is part of the Neurocure Center for excellence, which brings together a viral vector core, joint and shared spinning disc confocal facilities, and 2-photon imaging facilities, with the labs own resources for imaging calcium signals *in vitro* and *in vivo* in dendrites.

Key Personnel

Matthew LARKUM is the PI in this lab at Humboldt University in Berlin and is part of the Neurocure center for excellence.

Key Expertise

- Nanostimulation and behavioural perception
- Visual and somatosensory cortex
- Two-photon imaging

P91) INFN, *Istituto Nazionale di Fisca Nucleare*, Italy (SP3)

APE parallel/distributed computing lab

Profile

Since 1984, the APE Lab of INFN has co-designed applications, system software and hardware of several generations of parallel/distributed computing systems, dedicated to scientific simulations and digital signal processing. The APE lab developed several generations of custom processors and interconnects and invented several parallelization algorithms. Multiple industrial spin-offs have been generated by the APE lab research line.

Key Personnel

Pier Stanislao PAOLUCCI (male) is a permanent Staff Researcher at INFN APE lab.

Key Expertise

- Parallelisation/distribution techniques for numerical applications and digital signal processing
- Design & development of hardware interconnects
- Design & development of numerical/digital signal processors
- Development of system software for parallel/distributed platforms

P92) ISS, *Istituto Superiore di Sanità*, Italy (SP3)

Unit of Complex Systems Modelling

Profile

The Unit of Complex Systems Modelling (CSM) in the Department of Technologies and Health is a component of the ISS (Italian Institute of Health), the technical and scientific governmental institution of the Italian National Health Service, with activities in research, control and training in relation to public health in Italy. The CSM unit (neural.iss.infn.it) covers a range of cross-disciplinary subjects in biological systems, grounded on specific competences in theoretical and computational physics. The main scientific contributions of the unit originate from the study of the collective dynamics of neuronal networks, from which innovative theory-inspired analyses have been developed to characterize the evoked and spontaneous activity of *in vitro* and *in vivo* cortical cell assemblies.

Key Personnel

Maurizio MATTIA (male) is a permanent staff Researcher at the Department of Technologies and Health of ISS.

Key Expertise

- Nonlinear dynamics
- Statistical mechanics and stochastic processes for neuronal network dynamics and plasticity
- Analysis of nonlinear time series from cortical multichannel recordings
- Electronic implementation of neuronal network models
- Development of large-scale spiking neuronal network simulations

P93) KNAW, *Koninklijke Nederlandse Akademie van Wetenschappen – Knaw*, The Netherlands (SP2, SP3)

Molecular Visual Plasticity

Profile

The Levelt lab studies the mechanisms regulating cortical plasticity and development, with a special interest the involvement of inhibitory innervation. Levelt has investigated the involvement of selected signalling pathways and disease genes in cortical plasticity and development. Forward and reverse genetics approaches and iTRAQ based proteomics have been used to identify novel candidate plasticity genes. This approach also resulted in the discoveries of novel roles of TrkB/BDNF-signaling in the development and plasticity of the visual cortex (Heimel et al. 2010, Saiepour et al. 2014).

The lab has made an important contribution to the field by employing *in vivo* two-photon microscopy to show for the first time that inhibitory synapses are rapidly removed from excitatory neurons during experience induced plasticity in the mouse visual cortex (van Versendaal et al. 2012). Later, the lab demonstrated that this disinhibition does not enhance plasticity through an instructive but through a permissive mechanism (Saiepour et al. 2015). His current work focuses on the role of thalamic and cortical inhibition in the onset of critical periods of cortical plasticity and the control of perceptual learning mechanisms. Head-fixed behavioural paradigms have been developed in the Levelt laboratory allowing the chronic imaging of calcium signals in specific neuronal subsets during perceptual learning.

Key Personnel

Christiaan LEVELT (male) is head of the department of Molecular Visual Plasticity at the NIN and special professor of Molecular and Cellular Mechanisms of Cortical Development and Plasticity at VU University, Amsterdam.

Key Expertise

- *In vivo* two-photon microscopy
- Mouse behaviour
- *In vivo* electrophysiology
- Optical imaging (calcium/intrinsic signal)
- Slice physiology
- Molecular biology

Vision and Cognition Group

Profile

The Vision & Cognition group at the NIN investigates how neurons in different brain areas work together during visual cognition, i.e. during tasks that require thinking with the visual brain. The strength of the group's approach is that it is strongly theory driven and multidisciplinary. Specifically, the group uses neurophysiological recordings from mice and rhesus monkeys trained to do cognitive tasks, neural network studies on the interactions between brain areas and psychological and imaging techniques that probe cognition in human observers.

Key Personnel

Pieter ROELFSEMA (male) is opinion leader in the field of visual cognition and attention. He is the general director of the Netherlands Institute for Neuroscience.

Key Expertise

- Cortical mechanisms of visual perception
- Memory
- Plasticity
- Perceptual organisation
- Cognitive processing in early visual cortex
- Recording of single units in humans

P94) MRC, Medical Research Council, United Kingdom (SP3)

Object vision and population-code representation

Profile

The MRC Programme "Object vision and population-code representation" was launched in 2009 under the leadership of Dr Nikolaus KRIEGESKORTE. The Programme uses a combination of computational modelling, functional magnetic resonance imaging, and cell recording to understand how humans perceive the visual world and recognise objects.

Key Personnel

Nikolaus KRIEGESKORTE (male) is a Programme Leader at the Medical Research Council's Cognition and Brain Sciences Unit in Cambridge, UK.

Key Expertise

- Deep neural net modelling
- High-resolution functional magnetic resonance imaging
- Novel statistical analyses and visualisations of brain-activity data, including searchlight information mapping and representational similarity analyses

P95) UMIL, *Universita Degli Studi Di Milano*, Italy (SP3)

Integrated Thalamo-Cortical Function (ITCF)

Profile

The Integrated Thalamo-Cortical Function (iTCf) research group (www.thalamocortical.org) led by Dr. Marcello MASSIMINI is located at the Department of Biomedical Clinical Sciences (DIBIC) at the University of Milan (www.unimi.it). Research activity of the members of UMIL, from the cellular level to the patient, has been devoted to understanding what changes in thalamocortical networks (in terms of spontaneous activity, sensory transmission, internal information integration) across states of vigilance. The group pioneered the application of TMS/EEG and intracortical stimulations/recordings in humans to study cortical excitability, effective connectivity and complexity in different conditions, including sleep, anaesthesia, coma and after stroke. On this topic the members of the lab have participated in several national and international projects and have published on high-ranking journals such as Science, PNAS, Brain, Current Biology and Science Translational Medicine.

Key Personnel

Marcello MASSIMINI (male) is Associate Professor of Physiology at the University of Milan.

Key Expertise

- High density (hd) EEG recordings in wakefulness and sleep
- TMS/EEG recordings in sleep, anaesthesia and coma
- Pre-surgical intracranial electrical stimulation/recordings in patients
- Scalp hd-EEG recordings during intracranial electrical stimulation/recordings
- Development of automated tools for TMS, hd-EEG and intracranial data analysis

P96) ULG, *Universite de Liege*, Belgium (SP3)

Coma Science Group

Profile

Our team assesses the recovery of neurological disability and of neuronal plasticity in severely brain damaged patients with altered states of consciousness by means of multimodal functional neuroimaging It aims at characterising the brain structure and the residual cerebral function in patients who survive a severe brain injury: patients in coma, vegetative state, minimally conscious state and locked in syndrome as contrasted to pharmacologically modulated alterations of consciousness.

Key Personnel

Steven LAUREYS (male) is founding director of the Coma Science Group (CSG) at the GIGA Research and Neurology Department of the University and University Hospital of Liège, Belgium. He is Research Director at the Belgian National Fund for Scientific Research (FNRS) and board-certified in neurology and in palliative medicine.

Key Expertise

- Behavioural clinimetric evaluation of patients with disorders of consciousness (DOC)
- Multimodal imaging of residual brain function in DOC (PET, MRI, EEG, EEG-TMS) using passive and active paradigms
- Multimodal imaging of residual brain function during general anaesthesia in humans
- Medical and ethical implications of the study of DOC

P97) UvA, *Universiteit van Amsterdam*, The Netherlands (SP3)

Faculty of Science, Swammerdam Institute of Life Sciences (SILS), Cognitive and Systems Neuroscience Group

Profile

The UvA is one of the largest universities in the Netherlands with around 22.000 students, ranked top-50 in the QS World University Rankings 2015 and is LERU-member. Its Center for Neuroscience includes the Dept. of Cognitive & Systems Neuroscience (CSN; 19 researchers; 8.0 FTE permanent staff, incl. a data analytics engineer). CSN participates in UvA's Research Priority Program Brain & Cognition and focuses on brain mechanisms of sensory integration, perception and memory and motivation.

Key Personnel

Cyriel PENNARTZ (male) is full professor and heads the Department of Cognitive & Systems Neuroscience.

Key Expertise

- Computational Neuroscience: network modelling
- Computational Neuroscience: advanced data analytics
- Mouse brain: *in vivo* ensemble recordings, multi-neuron Ca2+ imaging
- Mouse brain: *in vivo* two-photon targeted patch clamp; optogenics
- Mouse brain: behavioural and cognitive studies
- Human brain: neuroimaging and electrophysiology
- Behavioural and Systems Neurophysiology in other species (rats, ferrets)
- Brain disease: human studies & animal models, intracranial recordings
- Surgery & immunohistology

P98) UGLA, University of Glasgow, United Kingdom (SP3)

The Muckli Group

Profile

The Muckli group is part of the University of Glasgow's Institute of Neuroscience and Psychology, and the Centre for Cognitive Neuroimaging (CCNi). The CCNi is equipped with 3T fMRI, MEG, TMS, EEG, and RIcompatible EEG. By the end of 2016, the University of Glasgow will open an Imaging Centre of Excellence, including 7T fMRI. The Muckli group studies visual and cognitive neurosciences using fMRI. They measure the role of cortical feedback in prediction, using retinotopic mapping to identify regions of V1 receiving no sensory stimulation, to isolate feedback. They use multivariate pattern classification to decode the information content of top-down signals to distinct cortical layers.

Key Personnel

Lars MUCKLI (male) is Professor of Visual and Cognitive Neurosciences, Centre for Cognitive NeuroImaging (CCNi), School of Psychology, Institute of Neuroscience & Psychology, Colleges of Science & Engineering and Medical, Veterinary & Life Sciences, University of Glasgow, UK.

Key Expertise

- High-field, high-resolution functional brain imaging
- Layer specific fMRI
- Visual cortex
- Cortical feedback/predictive coding
- Multivariate tools for 'brain reading'

P99) UHAM, University of Hamburg, Germany (SP3)

Biological Psychology and Neuropsychology (BPN)

Profile

The unit Biological Psychology and Neuropsychology was established with the move of Prof. Dr. Brigitte RÖDER to the University of Hamburg. BPN investigates multisensory interactions and age dependent neuroplasticity in healthy and clinical populations. The main methods

include behavioural paradigms, non-invasive electrophysiological methods and brain imaging. BPN is part of the SFB 936 and the Hamburg Center for Neuroscience (HCNS).

Key Personnel

Brigitte RÖDER (female) is a full professor for Biological Psychology and Neuropsychology at the University of Hamburg.

Key Expertise

- Behavioural experiments, eye-body movement tracking, ERP/EEG, (f)MRI
- Multisensory research
- Neuroplasticity in humans
- Prospective studies from infant age to older individuals
- Retrospective studies in permanently blind or deaf humans as well as individuals after sensory restitution
- Adult plasticity following physical activity

P100) USFD, University of Sheffield, United Kingdom (SP3)

Sheffield Robotics

Profile

Sheffield Robotics (SR) was founded in 2011 as a cross-disciplinary institute across both Universities in Sheffield. Sheffield Robotics has one of the largest portfolios of ongoing publicly-funded robotics research in the UK, supported by both the UK Research Councils and the European Union. We are also building research partnerships with leading industrial, commercial, and government organisations in order to ensure the real world relevance and impact of our research. A key theme of SR is the development of brain-based and biomimetic robots both as a means to create useful assistive and field robot systems and to tests theories in biology.

Key Personnel

Tony J. PRESCOTT (male) chairs Cognitive Neuroscience at the University of Sheffield (2007-) and is Director of Sheffield Robotics (2011-). He is Co-founder of the Living Machines international conference series.

Key Expertise

- Systems Computational Neuroscience
- Brain-based and Biomimetic Robots
- Machine Learning
- Sensorimotor Control, Memory and Decision-making

P101) UWE, University of the West of England, Bristol, United Kingdom (SP3)

Bristol Robotics Laboratory (BRL)

Profile

BRL is a joint research institute for the University of Bristol and University of the West of England (UWE) tasked to understand the science, engineering and social role of robotics and embedded intelligence. BRL consists of over 150 members of staff, researchers and technicians in 3500m2 of laboratory space. Facilities include mechanical and electrical manufacture, rapid prototyping suite, and 3D motion capture equipped test arenas. Total external research funding grants active at BRL is currently EUR 5 Million per year.

The neurorobotics research group (within the BRL) use embodied models to study tactile sensorimotor processes and their neural correlates. This involves close collaboration with neuroscientists from across Europe through EU funded projects (ICEA, BIOTACT) and RCUK funding (Whiskerbot, BELLA).

Key Personnel

Anthony Pipe (male) is full Professor and Deputy Director of BRL with 20 years of experience in robotics research and teaching.

Key Expertise

- Robotics hardware development (electro-mechanical integration)
- Adaptive control and advanced sensory processing
- Machine vision
- Embedded real-time computing and architecture design
- Embedded reconfigurable computing
- Biomimetic tactile sensing and manipulation
- Soft-bodies robots
- Simultaneous Localisation and Mapping (SLAM)

P102) SURREY, University of Surrey, United Kingdom (SP4)

Computational Neuroscience and Learning Lab (Gruening Lab), NICE Research Group, Department of Computer Science

Profile

The Gruening Lab at the University of Surrey uses computational simulations and mathematical modelling to bridge the gap between neural scale bottom-up approaches (How do synaptic plasticity rules "conspire" to yield goal-oriented behaviour at systems scale) and top-down system-scale approaches (How does the pursuit of a systems-scale goal utilise and constrain synaptic scale plasticity?) towards understanding the functioning of nervous systems. One important focus of research activity lies on the development and computational exploration of spiking neural network learning algorithms that are both biologically plausible, technically performant, and implementable on HBP's neuromorphic systems. The lab currently consists of four members, including two postdocs, and disposes over state-of-the-art workstations and simulation servers.

Key Personnel

André GRÜNING (male) is Senior Lecturer (Associate Professor) in Computational Intelligence at the University of Surrey. He is also a board member of the European Neural Network Society (ENNS).

Key Expertise

- Simplified models of networks of spiking neurons
- Functional utilisation of synaptic plasticity
- Computational modelling
- Mathematical modelling
- Goal-oriented learning
- Learning algorithms for spiking neural networks
- Software development in C, C++ and Python

P103) TUT, *TTY-Saatio*, Finland (SP4)

Computational Neuroscience Lab

Profile

Computational Neuroscience Research Group works to unravel the molecular, cellular and network level mechanisms underlying excitability, neurotransmission, and plasticity. The Group is established in 2004 and led by Marja-Leena LINNE (http://www.cs.tut.fi/sgn/cns/). The Group uses both wet-lab and computational modelling approaches to study neural mechanisms, as well as developing theoretical methodology for computational modelling and simulation of neural systems. One of the Group's important goals is to identify the key mechanisms by which astrocytes modulate neuronal excitability and plasticity. In addition to synaptic and cellular mechanisms, the group has experience in addressing the effects of small and medium-scale structural organisation to network dynamics using the tools from complex networks theory. The consequences of stochasticity and noise in neuronal phenomena are taken into account in modelling when appropriate. The work has implications not only to understanding the basic mechanisms of network activity and plasticity for learning and memory in the brain but also to the disrupted mechanisms leading to neuronal dysfunctions such as in Alzheimer's disease.

The Group involves seven researchers and is located at Tampere University of Technology in Finland. The group is affiliated with two institutes: BioMediTech (http://www.biomeditech.fi/), a biomedical research institute at the University of Tampere, and European Institute of Theoretical Neuroscience (EITN) in Paris.

Key Personnel

Marja-Leena LINNE (female) is an electrical engineer and Principal Investigator at the Department of Signal Processing at Tampere University of Technology (TUT). She is Head of Computational Neuroscience Research Group at TUT. She is also a Board member of international organizations INCF and OCNS.

Key Expertise

- Computational and theoretical neuroscience
- Modelling the structure and function of neurons and astrocytes

- Modelling synaptic transmission and plasticity
- Modelling network growth and structure-function relationship
- Stochastic modelling and simulation methodology
- Dynamical systems theory
- Electrophysiology of *in vitro* systems
- Neuron-glia interactions
- Training students to master interdisciplinary topics in neuroscience

P104) ULEEDS, University of Leeds, United Kingdom (SP4)

Computational Neuroscience Group (Leeds University)

Profile

The computational neuroscience group in Leeds employs two permanent staff (COHEN, DE KAMPS) and has three postdoctoral fellows and approximately a dozen PhD students. Topics of study are *C. elegans*; theory and implementation of mean field techniques, in particular population density techniques; machine learning. The group has a wide range of expertise in using established neural simulators such as NEST, BRIAN and NEURON, as well as developing their own: MIIND. These techniques are applied to problems of cognitive neuroscience, in language and visual attention. The group also has experience in machine learning: multilayer perceptrons, EM algorithms and Boltzmann machines. It is currently exploring the application of Deep Learning on patient records.

Key Personnel

Marc DE KAMPS (male) is Lecturer in the School of Computing, University of Leeds.

Key Expertise

- Theory of Stochastic Differential Equations
- Development of theory and implementation of mean field techniques, in particular population density techniques
- Simulator development: MIIND
- Use of established simulators such as NEURON, NEST, etc.
- Parallel implementation of large-scale networks in C/C++ using MPI, with Python and XML interfaces
- Large-scale models of cognition
- Machine Learning

P105) UPMC, *Université Pierre et Marie Curie – Paris 6*, France (SP4)

Institut de la Vision

Profile

The Institut de la Vision is one of the most important research centres in Europe on eye diseases. Conceived as a place of gathering and exchanges, it brings together in a single building researchers, clinicians and industrial partners. The Institute's goal is to discover,

test and develop treatments and technological innovations of tomorrow in order to prevent or limit visual impairment and to improve the autonomy and the quality of life of patients.

It harbours, aside from the research centre, a clinical investigation centre, a rare disease reference center and innovative new companies. The building, 6000 m2, houses more than 15 research teams (Inserm - UPMC - CNRS) working on different eyesight problems: retina imaging, AMD (age-related macular degeneration), glaucoma, diabetic retinopathies, retinitis pigmentosa, etc.

Key Personnel

Olivier MARRE (male) is a research fellow at the Vision Institute (UPMC, INSERM, CNRS) in Paris, France, working in the team headed by Serge Picaud.

Key Expertise

- Neuroscience
- Vision, Ophthalmology
- Computational neuroscience
- Pharmacology
- Optogenic therapy
- Gene therapy
- Medical device
- Retinal prosthesis
- Disease prevention, diet, nutricament, taurine, phototoxicity
- Handicap
- Retinal information processing
- Animal models
- Glaucoma, Usher syndrome, retinitis pigmentosa, age-related macular degeneration, diabetic retinopathy

P106) UoS, University of Sussex, United Kingdom (SP9)

Computational Neuroscience and Neuromorphic Computing Group

Profile

The Computational Neuroscience and Neuromorphic Computing Group led by Thomas NOWOTNY conducts research in a variety of areas. Central topics in the group are the use of neuromorphic computing for data analysis and machine learning, researching chemical sensing in both technical applications and in animals, hybrid brain-computer systems, and high performance computing methods, such as GPU accelerated computing. Currently, the group is receiving funding from the EPSRC, EU FP7 (Marie Curie and HBP Ramp-Up), and HFSP. The group sits in the wider context of the Centre for Computational Neuroscience and Robotics (CCNR), hosted by the School of Engineering and Informatics and the School of Life Sciences. The CCNR at the University of Sussex was established in 1996 and brings together groups from Informatics and Biology and Environmental Sciences. The strong research portfolio includes evolutionary and adaptive robotics, insect and robot navigation, modelling neural systems, evolutionary electronics, theory of natural and artificial evolution, applications of evolutionary computing and stochastic search, novel ANN

mechanisms for generating adaptive behaviour, machine learning in robotics, GPU accelerated neural networks and other related research areas. The groups have enjoyed substantial funding from research councils EPSRC, BBSRC, EU Framework Programmes, AHRB, Arts Council, British National Space Centre, Wellcome, Nuffield, Leverhulme, HFSP, CSIRO, and direct from industry, including BT, HP, Xilinx, Intel, Algorithmix, Astrium, Rolls Royce, MathEngine, SKB, NaturalMotion, Infonic, and the MASA group. They collaborate with many other companies and have strong links with leading research groups around the world in related areas.

Key Personnel

Thomas NOWOTNY (male) is a Professor of Informatics at the School of Engineering and Informatics of the University of Sussex and the Director for Research and Knowledge Exchange of the School.

Key Expertise

- Applications of neuromorphic computing to data analysis
- Chemical sensing and e-Noses
- GPU-accelerated computing
- Computational neuroscience
- Olfaction
- Hybrid brain-computer systems (e.g. dynamic clamp)

P107) MU, Middlesex University Higher Education Corporation, United Kingdom (SP9)

Department of Computer Science

Profile

The Department has extensive experience of European funding including Framework Programmes, and non- European funding. For example, the Department is leading the FP7 collaborative project VALCRI – Visual Analytics for Sense-making in Criminal Intelligence Analysis - worth € 13 million to the consortium. The group has substantial experience with large scale language systems, and with neural systems. This includes developing real virtual agents on neuromorphic platforms.

Key Personnel

Christian HUYCK (male) is Professor of Artificial Intelligence at Middlesex University in the School of Science and Technology.

Key Expertise

- Development of neural models and synaptic plasticity models
- Development of large-scale neural systems
- Implementation of systems on neuromorphic platforms
- Large-scale software development
- Natural language processing, including neural NLP

P108) UCBL, *Université Lyon 1 Claude Bernard*, France (SP2)

Lyon Neuroscience Research Center (CRNL, UCBL/INSERM U1028/CNRS UMR5292) – DYCOG Team (Brain Dynamics and Cognition)

Profile

The DYCOG Team at CRNL pursues fundamental research on the neurophysiological substrates of perceptual and cognitive functions in Humans, and develops new clinical tools for diagnosis, prognosis, and rehabilitation. This research is backed up with advanced methods in electrophysiology and neuroimaging that are in constant development and improvement in the team (integrated into, e.g., the ELAN software package (http://elan.lyon.inserm.fr/, or Brain TV). DYCOG strategy is to uncover fine neurophysiological markers of specific (normal and abnormal) brain processes in different aspects of cognition (from perception to social cognition.

CRNL website: http://crnl.univ-lyon1.fr/index.php/fr

DYCOG website: http://www.lyon.inserm.fr/821/

Key Personnel

Jean-Philippe LACHAUX (male) is INSERM Research Director and member of the DYCOG Team at CRNL.

Key Expertise

- Combination of multiple levels of investigation (EEG, MEG, intracerebral EEG, functional and structural MRI)
- Brain oscillations and neurophysiological correlates of dynamic mental processes
- Signal processing
- Cognitive psychology (perception, attention, social cognition, etc.)
- Brain computer interfaces, real-time electrophysiology
- Clinical investigation of epilepsy

P109) POLITO, *Politecnico di Torino*, Italy (SP9)

The Electronic Design Automation Group (EDA)

Profile

The EDA (http://eda.polito.it) group is part of The Department of Control and Computer Engineering (DAUIN), which is the point of reference in Politecnico di Torino for the area of Information and Communication Technologies (ICT), which studies the methodologies and technologies used for the management, processing and transmission of information.

EDA is aimed at the design and development of automated techniques for complex systems. Benefiting from tight interdisciplinary collaborations with other research institutions and with industry experts, our research activities span three main application domains:

- VLSI-CAD, design Automation for standard digital CMOS ICs, Beyond-CMOS circuits and Electrical Energy Systems (EES), with particular emphasis on computer-aided design (CAD) algorithms, electrical modelling and circuit-level simulation of Graphene-based devices, and modelling, design and simulation of EES systems with charge allocation/distribution policies.
- Bioinformatics, with special regards to the design, development and acceleration of SW and HW-SW solutions for the automated management, analysis and interpretation of complex biological and medical data from various sources. Among them, gene

expression data and gene regulatory networks, Next Generation Sequencing (NGS) data, biological and medical images.

- Smart City with particular emphasis on IoT devices for energy monitoring and control applications, distributed software architectures for ambient intelligence and for network interoperability, software solutions for simulating and optimising energy demand response, Virtual and Augmented reality applications for interactive visualization of energy information.

Key Personnel

Enrico MACII (male) is a Full Professor of Computer Engineering at Politecnico di Torino.

Key Expertise

- Embedded system design
- Software for multicore systems
- Electronic Design Automation tools
- Wireless sensor networks
- Internet of Things (protocols and applications)

P110) UGENT, *Universiteit Gent*, Belgium (SP10)

Data Science Lab

Profile

Data Science Lab is the newly formed lab within the Electronics and information Systems Department. It consists of three former groups known as Reservoir Lab (HBP partner in the Ramp-Up Phase and expert in machine learning, brain-inspired computation and robotics), SySTems (decision theory, system modelling and control theory) and MultimediaLab (multimedia, semantic data, natural language modelling, etc.). As such, it combines the department's expertise with respect to system modelling, data and signal analysis and data representation. Data Science Lab counts 13 professors and some 80 scientists (PhD students and postdocs) in total.

Key Personnel

Joni DAMBRE (female) is a tenured professor at Ghent University and head of the UGent Reservoir Lab (Engineering Faculty).

Key Expertise

- Reservoir computing
- Feedforward and recurrent neural networks
- Supervised machine learning and deep learning
- Unsupervised machine learning and deep regenerative models
- Reinforcement learning
- Compliant robotics

P111) KUL, *Katholieke Universiteit Leuven*, Belgium (SP2)

Laboratory for neuro- and Psychophysiology

Profile

Our research group investigates neural processes underlying visual cognition, mainly of extrastriate or higher order cortices, of human and non-human primates. The main tools are single-cell and multiple cell recordings, human and awake monkey fMRI, stimulation and inactivation studies, behavioural studies and modelling.

Key Personnel

Wim VANDUFFEL is professor at the Neuroscience department of KU Leuven.

Key Expertise

- Cognition
- Visual perception
- Attention and reward processing
- fMRI in human subjects
- fMRI in awake behaving non-human primates
- Electrophysiology in non-human primates
- Microstimulation/optogenetics in non-human primates

P112) UNIBAS, *Universität Basel*, Switzerland (SP2)

Human Genomics

Profile

The lab of Sven CICHON has a long-standing experience in the analysis of genetically complex traits and imaging genetics. The lab has made significant contributions to the identification of genetic factors contributing to a broad range of brain phenotypes. There is a particularly strong expertise on technological aspects of monitoring different types of genomic and epigenomic variation as well as in analysis concepts of genetically complex/ multifactorial brain phenotypes. The success of the lab depends on a strong collaboration with clinical and biostatistical/bioinformatics groups, in particular at the Universities of Bonn and Heidelberg/Mannheim, and on participation in a number of large, international consortia aiming at genetic mega-analyses in complex neuropsychiatric (Psychiatric Genomics Consortium - PGC) and imaging genetics (ENIGMA) phenotypes. Since 2010, Sven CICHON is also heading a research group at the Research Center Juelich, Germany, dedicated to genomic imaging.

Key Personnel

Sven CICHON (male) is Director of the Division of Medical Genetics, University Hospital Basel and Head, Research Group “Human Genomics”, Dept. of Biomedicine, University of Basel.

Key Expertise

- Analysis of genetically complex as well as monogenic traits
- Psychiatric genetics
- Imaging genetics
- Genome-wide association studies

P113) VU, *Stichting VU-VUmc*, The Netherlands (SP1, SP2)

Mansvelder lab - Integrative Neurophysiology

Profile

The Mansvelder lab is one of the few in the world that study morphological and physiological properties of microcircuits in the human neocortex. In a series of papers, the Mansvelder lab published among the very first high quality and quantitative data-sets on the physiology, morphology and plasticity of human pyramidal neurons and excitatory synapses in the human neocortex, along with careful comparisons to the rodent system from which most of our insights derive. In collaboration with the lab of Idan SEGEV, the Mansvelder lab published the very first data driven models on the function of human neurons within the framework of HBP.

Key Personnel

Huib MANSVELDER (male) is full professor and heads the department of Integrative Neurophysiology.

Key Expertise

- High-end cellular and synaptic physiology of human neurons and synapses
- Digital reconstruction of human cortical microcircuit morphology
- Linking morphology and physiological data
- Two-photon imaging of subcellular calcium dynamics and neuronal circuit activity
- Synaptic plasticity
- Neuromodulation of cortical circuits
- Data driven cellular level reconstruction and validation
- Data driven subcellular level reconstruction and validation

P114) SIB, *Institut Suisse de Bioinformatiquefondation ISB* (Swiss Institute of Bioinformatics), Switzerland (SP1)

Computational Biophysics

Profile

The group is interested in the structure-function relationship of membrane proteins. Using molecular mechanics simulations, the group aims at understanding the microscopic mechanisms underlying the functions of proteins involved in the membrane transport of various substrates. A central topic of study concerns the elucidation of gating mechanisms regulating the activity of potassium channels in excitable cells.

Key Personnel

Simon BERNÈCHE (male) is Group Leader at the Swiss Institute of Bioinformatics.

Key Expertise

- Structure and functions of ion channels and receptors
- Molecular dynamics simulations of membrane systems
- Potential of mean force calculations and methodological development

- Multi-scale using Markov chain random walk
- Development of detailed kinetic models

P115) EBRI, *European Brain Research Institute Rita Levi-Montalcini Fondazione*EBRI*, Italy (SP1)

EBRI

Profile

EBRI was founded in 2005 by the Nobel Laureate Rita Levi-Montalcini. Launched as an interdisciplinary research centre, it was designed to spearhead Italian neuroscience investigating fundamental questions of the development and functional organisation of the brain, and to showcase translational neuroscience with tangible output and patient benefit. Despite its young age, EBRI has already been able to secure a number of very competitive research grants from the EC (ERC, Cooperation, Marie Curie), the American Alzheimer's Association, and the Italian Health Minister.

EBRI is part of the Neuroscience campus enveloping Fondazione Santa Lucia, the Cell Biology and Neurobiology Institute (CNR), and two Telethon groups. EBRI currently provides flourishing environment to seven research groups whose scientific interest and endeavours encompass development of recombinant antibodies, synaptic transmission and plasticity, neurotrophin factors neurodegenerative disease, stem cells, adult neurogenesis, CNS mRNA metabolism, genomics and bioinformatics, super resolution imaging, opto and chemogenetic approaches for the identification of microcircuit involved in cognitive functions and computational neuroscience.

Key Personnel

Enrico CHERUBINI (male) Enrico Cherubini is the Scientific Director of EBRI.

Key Expertise

- Functional validation of intrabodies, with biochemical, electrophysiological, immunohistochemical techniques
- *In vivo* and *in vitro* synaptic physiology
- Microcircuitry involved in cognitive functions assessed by behavioural tests using opto- and chemogenetic tools
- mRNA metabolism
- Super resolution imaging of fluorophore targeted intrabodies
- Microarray and bioinformatics

P116) SNS, *Scuola Normale Superiore*, Italy (SP1)

Bio@SNS laboratory of Biology

Profile

The main scientific focus of research at Bio@SNS Laboratory of Biology, directed by Prof. Antonino CATTANEO, Full professor of Neurobiology at SNS, is the study of the brain, investigating aspects of brain functions and mechanisms during development, in the adult and in ageing. Research programs include the molecular and cellular basis of neural development and stem cell biology, neurotrophic biology, synaptic plasticity, neurodegeneration, neuroinflammation and ageing. A strong focus of the BioSNS Lab is

represented by of the study protein misfolding processes that underlie many neurodegenerative diseases, Alzheimer's and Parkinson's disease in particular. Unique animal models for the study of neurodegeneration and ageing have been developed by scientists at BioSNS. Biophysical approaches for the single particle tracking of receptors and molecules in neurons are being developed to study neurotrophins and their receptors.

Major advancements in neurosciences rely heavily on new methods, and for this reason the broad scientific aims in Neurobiology are accompanied by a strong effort in the development of new cutting edge experimental methods and technologies, in the fields of genomics, recombinant antibodies, optogenetics, molecular imaging.

Key Personnel

Antonino CATTANEO (male) is the Bio@SNS Director.

Key Expertise

- Biochemistry
- Cell biology
- Molecular biology
- Electrophysiology (*in vitro* and *in vivo*) experiments
- Tissue culture facilities
- Animal house for mice and fish
- Advanced imaging microscopy (light microscope and fluorescence, Leica TCS SL Confocal microscope, two photon microscope)
- Recombinant protein expression and purification

P117) UM, *Universiteit Maastricht*, The Netherlands (SP2)

Maastricht Brain Imaging Center

Profile

The Cognitive Neuroscience (CN) department combines psychophysical and cognitive paradigms with cutting edge functional neuroimaging to derive detailed and biologically inspired models of human perception, cognition and behaviour. All CN research is embedded in the Faculty of Psychology and Neuroscience - which houses 31 labs for multimodal imaging and other psychological research, including fMRI (3 Tesla), TMS, EEG, NIRS, eye movement, virtual reality and psychophysical labs - and in the Maastricht Brain Imaging Center which has been established in 2005 and now hosts 3 T (2x), 7T and 9.4T fMRI scanners for human imaging.

Key Personnel

Rainer GOEBEL (male) is Full Professor for Cognitive Neuroscience at Universiteit Maastricht.

Key Expertise

- Neuroscience applications of ultra-high field functional MRI
- Dedicated hardware (coils, motion capture cameras, stimulation devices)
- Optimised MR sequence
- Human fMRI

- Advanced data analysis and modelling methods for (f)MRI data and other neural signals

Appendix 6: Consortium Partners' HBP Third Parties

Partner #	Short Name	Third parties involved in the Project
1	EPFL	**Tasks to be subcontracted:** Benchmarking and validation of neurorobotics models (in T10.3.4) and of physics and light simulation (in T10.5.8) will be undertaken by a linked third party, because this capability does not exist within the Consortium. SP(s): SP10 Neurorobotics Platform Timing: continuous during FPA Management software development, legal services and consulting services are minor tasks which will be subcontracted, as this approach is more cost effective. SP(s): SP11 Central Services Timing: continuous during FPA ***Benchmarking and validation of neurorobotics models, physics and light simulation*** This benchmarking and validation work, undertaken within Task 10.3.4 (neurorobotics models) and Task 10.5.8 (physics and light simulation), is essential for the HBP's Neurorobotics Platform. Because the necessary competence does not exist within the HBP Core Project, this work will be undertaken by a linked third party, Cyberbotics. Its work for T10.3.4 involves accurate calibration of simulated robots against the characteristics of their real-life counterparts; in other words, to ensure that the former are as realistic a replication of the latter as possible. The work for T10.5.8 helps to ensure that physical phenomena and light are reproduced as accurately as possible in the Platform's virtual environment, in which its simulated robots operate. Cyberbotics was founded as a spin-off company from the EPFL in 1998 to refine and market the Webots software created by the EPFL. Cyberbotics develops simulations for a range of major industrial companies and participates in EU and Swiss national research projects. SP(s): SP10 (WP10.3, T10.3.4 and WP10.5, T10.5.8) ***Management software development and operations:*** EMDESK and Open ERP development will be outsourced to specialised vendors. The subcontracting under this task has two objectives The first objective is to license the EMDESK reporting and project tracking system. The other part of this subcontract is to pay a subcontractor for strategic modifications to both EMDESK and the planned Odoo Enterprise Resource Planning (ERP) software. EMDESK was used during the Ramp-Up Phase and has proven to be a worthwhile expenditure. This investment also allows the operational intelligence and training built up during the Ramp-Up Phase to be further utilised as much of the reporting is done directly by project teams. Based on an evaluation done during the Ramp-Up Phase, Odoo is the premier open source ERP system. There is a wide network of professional services companies and the system is open source so it can be updated and modified by the SP11 team themselves. This flexibility will help to ensure the most cost-effective use of Coordinator IT and subcontracting resources. Liferay development will be outsourced to specialised vendors. The object of this subcontract is to provide enhancement, extension and customisation of the public facing HBP website and Intranet portal used

Partner #	Short Name	Third parties involved in the Project
		for HBP communication and coordination. Both the public facing website and then Intranet site have been essential in the Ramp-Up Phase to communicate with the public, the HBP scientific community and the wider non-HBP scientific community. As is necessary in any forward-thinking communication strategy, the function and styling of these sites must be continuously updated to ensure engagement with the user audience. SP(s): SP11 (WP11.3; T11.3.4 and WP 11.5; T 11.5.3)
2	AALTO	**No third parties involved**
3	LUMC	**Contribution in kind provided by 3rd parties (against payment, art. 16 of the FPA):** Prof. Boudewijn LELIEVELDT has a dual professor appointment: mainly at the partner LUMC, but in part also at Delft University of Technology. It is foreseen that some effort will be performed by Delft University of Technology for the methodological development of t-SNE against payment.
4	AUEB	**No third parties involved**
5	BSC	**Contribution in kind provided by 3rd parties (free of charge, art.17 of the FPA)** The BSC is a consortium that is composed of the following member institutions: Universitat Politècnica de Catalunya (UPC), Spanish Council for Scientific Research (CSIC), as well as the Spanish and the Catalan governments. As part of the charter of this consortium, each member institution must contribute resources either in cash or in kind. Both UPC and CSIC contribute in kind by making human resources available to work on projects free of charge. The relationship between BSC and CSIC /UPC (respectively) is defined in an agreement with each institution that was established prior to the start of this project. ***UPC (Universitat Politècnica de Catalunya):*** The High Performance Computing research group of the Computer Architecture Department at the Universitat Politècnica de Catalunya (UPC) is a leading research group in Europe in topics related to high performance processor architectures, runtime support for parallel programming models and performance tuning applications for supercomputing. There is a signed Collaboration Agreement between the UPC and the BSC establishing the framework of the relationship between these two entities. According to this agreement, several professors of the UPC are made available to the BSC to work on projects. Specifically for the HBP project: Prof Jesus Labarta, Prof Eduard Ayguadé, Dr Xavier Martorell David Carreras and Judit Gimenez are professors at the UPC. They carry out their research activities in association with the Barcelona Supercomputing Center - Centro Nacional de Computación (BSC) on the BSC premises. Some work in WP7 will be carried out at the Barcelona Supercomputing Center-Centro Nacional de Supercomputación (BSC-CNS) will be contributed by UPC free of charge. Aside from the professors mentioned, no other UPC staff will be dedicated to the project. ***Consejo Superior de Investigaciones Científicas (CSIC):*** The objective of the Spanish Council for Scientific Research (CSIC) is to promote, coordinate, develop and disseminate the scientific and technology research of a multidisciplinary nature, with the aim of contributing to the pursuit of higher knowledge as well as economic, social and cultural development in Spain. It also promotes training of personnel and consultancy to public and private institutions. CSIC researchers carry out their work at universities and research centres based in Spain with

Partner #	Short Name	Third parties involved in the Project
		which CSIC actively collaborates. This collaboration takes place within the framework of long-term agreements, ensuring that CSIC researchers are fully integrated into teams and research projects. CSIC has signed collaboration agreements with several entities, including the BSC. Specifically for the HBP project: Dr Rosa Badía is a CSIC researcher affiliated with the BSC. She carries out her research in association with the Barcelona Supercomputing Centre - Centro Nacional de Computación (BSC) on the BSC premises. Work in WP7 will be carried out at the Barcelona Supercomputing Centre-Centro Nacional de Supercomputación (BSC-CNS) will be contributed by CSIC
6	BAUW	**No third parties involved**
7	BUW	**No third parties involved**
8	BSMJ	**No third parties involved**
9	CF	**No third parties involved**
10	CNRS	**No third parties involved**
11	CEA	**No third parties involved**
12	CNR	**No third parties involved**
13	CINECA	**No third parties involved**
14	DTU	**No third parties involved**
15	UoD	**No third parties involved**
16	DMU	**Tasks to be subcontracted:** Ombudsperson: The Ombudsperson has to be independent of the HBP and therefore must not be a partner or a member of the consortium. At the same time this position is likely to require some support and resources. It was estimated that €2000 per month would be sufficient to provide some secretarial support and cover costs, including travel costs, where required. External expertise: The complexity of the ethical issues within the HBP is such it is impossible to know in advance all areas of expertise which are likely to be required. The EAB has been constituted with a view to the various areas of expertise but it cannot cover all possible areas. In order to quickly find reliable answers, subcontracting is likely to be required. SP(s): SP12 (WP12.45; T12.4.1, T12.4.2)
17	ENS	**No third parties involved**
18	ETHZ	**No third parties involved**
19	FT	**Tasks to be subcontracted:** Execution of citizen consultations in European countries. The Citizen Consultations will be going on each second year of the FPA duration and will each of the involve consultations in a number of European member states. These will make use of different methods each time and involve a changing amount of European member states and a changing amount of citizens in each state. For each round of Citizen Consultation there will be a closed call for tender to find collaborators in the countries, which can make the operational work in each country. Because we will use different methods along the way subcontracting is the best solution – compared to including the operators as partners. Call for tenders will be made to subcontract collaborators in 5-6 European countries, which are to execute national citizen consultations. The subcontractors will have responsibility for translation of relevant material, recruitment of national citizens for the

Partner #	Short Name	Third parties involved in the Project
		consultation, execution of the citizen meetings (core of the consultations), and reporting results to FT. Subcontractors will work according to precise manuals, made by FT, and will receive training in execution of the consultations. The costs for subcontracts are, thus, only for the mere execution of the meetings – all planning and instructions are made by the HBP partner FT. Subcontracting is needed, since it would not be reasonable to include these collaborators as partners because of the limited time and budget for their engagement in the work. National collaborators are crucial to have, since it is needed to have the citizen consultations be made in national languages. Besides, local conditions often play important roles for setting up citizen consultations. SP(s): SP12 (WP12.3; T12.3.1) Timing: A round of subcontracting each second year of the full duration of the FPA. For the first SGA one round of tendering.
20	JUELICH	**No third parties involved**
21	FORTISS	**No third parties involved**
22	FG	**No third parties involved**
23	FCHAMP	**No third parties involved**
24	UDUS	**No third parties involved**
25	UH	**No third parties involved**
26	HITS	**No third parties involved**
27	CHUV	**Tasks to be subcontracted:** IT costs for installation, upgrade, maintenance. Advantage: reducing total cost of own built infrastructure and shortening the production time. SP(s): SP8 Timing: continuous during FPA **Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA)** The McGill Centre for Integrative Neuroscience (MCIN), the Laboratory of Neuro Imaging (LONI) of the University of Southern California will provide privileged access to public datasets, software (CBRAIN, LONI pipeline), computing resources (Grid) and expertise in distributed computing for large-scale data. We expect that expertise from companies outside medicine (not yet defined), where data mining is currently used, will interact with the Medical Informatics developers to facilitate this functionality, which will be a priority of early development of this part of the platform. These companies will provide software for data mining.
28	ICL	**No third parties involved**
29	ICM	**Contribution in kind provided by third parties (free of charge, art. 17 of the FPA)** Master Agreement with the AP-HP, CNRS, Inserm & UPMC: The ICM is based on a partnership between the public and private sectors to perform its missions. In March 2011, the ICM signed an agreement with its academic partners Assistance Publique- Hôpitaux de Paris (AP-HP Pitié Salpêtrière), Centre National de la Recherche Scientifique (CNRS UMR 7225), Institut National de la Recherche Medicale (Inserm U 1127) and the University of Paris Pierre and Marie Curie (UPMC P6 UMR S 1127) making resources available and sharing IP. Therefore the ICM gathered the critical mass in neurosciences in the

Partner #	Short Name	Third parties involved in the Project
		same building and benefit from the excellent expertise of the public research teams working on the common research objectives and in the framework of the common research strategy.
30	IEM HAS	**No third parties involved**
31	IST	**No third parties involved**
32	JSI	**No third parties involved**
33	INRIA	**No third parties involved**
34	IP	**No third parties involved**
35	UFRA	**No third parties involved**
36	KIT	**No third parties involved**
37	KI	**No third parties involved**
38	KCL	**No third parties involved**
39	KTH	**No third parties involved**
40	LENS	**Contribution in kind provided by 3rd parties (against payment and/or free of charge, art. 16 and 17 of the FPA):** The European Laboratory for Non Linear Spectroscopy (LENS) was established in 1991 at the University of Florence as an independent scientific research centre with a clear international vocation, aimed to promote and facilitate the exchange of ideas, scientific themes, and technical skills. Since the beginning, LENS has been associated with universities and research centres, both Italian and foreign, public and private, by means of agreements. The main one is the University of Florence. LENS may use in kind contributions by University of Florence in particular for the seconded persons and infrastructures according to art. 16 and 17 of the Model Framework Partnership Agreement. The recruitment of staff by University of Florence will depend on the presence in the infrastructure of the high specialized qualifications requested by the work in progress of the FPA -ten year project.
41	LNU	**No third parties involved**
42	MUI	**Tasks to be subcontracted:** Subcontractors will be local providers at the education programme event venues for the events outlined and professional companies in media productions for the online material as well as infrastructure and licensing for interactive online courses. SP(s): SP11 Central Services Timing: continuous during the FPA Software development and operations: HBP Education Programme website Liferay web development. The object of this subcontract is to provide enhancement, extension and customisation of the education website used for public engagement, communication and coordination of the Education Programme activities. The public facing HBP Education Programme website was essential to Education Programme activities in the RAMP-UP Phase. Based on the Ramp-Up success, the function and styling of the Education Programme website must be continuously updated to add additional functions needed for expansion of Education Programme activities in SGA1. SP(s): SP11 (WP11.8; T11.8.1, T11.8.3) **Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA):**

Partner #	Short Name	Third parties involved in the Project
		Several international scientific non-profit organisations (International Brain Research Organisation, Federation of European Neuroscience Societies, Society for Neuroscience (US) and the International Society for Neurochemistry) have already expressed interest in collaborating with HBP. Their contribution may be educational material, joint training events or travel grants for students to attend HBP schools or workshops. For teaching in the HBP curriculum, advanced schools, at training events and for seeking expert opinion on methods of education we will invite external experts in addition to experts from HBP beneficiaries. Travel and subsistence costs of external experts will be covered. The target group of the HBP Education Programme is young researchers (masters students already carrying out research, PhD students and researchers who have received their doctoral degree within the past three years at the time of their application for training). To enable young researchers coming from within the HBP for trans-national access to and training about research infrastructure, travel and subsistence costs will be covered under the same criteria for giving financial support to third parties. The persons or categories of persons that may receive financial support are: • Young researchers not employed by an HBP beneficiary, coming from all over the world • Young researchers are masters students already carrying out their research, PhD students and researchers who have received their doctoral degree within the past three years at the time of their application for training Criteria for giving financial support: • An application must be submitted according to the guidelines defined for specific education and training events • Selection by one or more scientists with an expertise on the specific topics of the educational events based on academic decision Monitoring process: • Proof of participation through daily attendance sheets • Presentation of own research if such presentations are part of the event programme • A short report by the recipient summarising the scientific content most important and beneficial to her/him The maximum amount of financial support for each third party: • Young researchers travelling from Europe: ○ Travel: max. € 450.00 ○ Subsistence: max. € 120.00 per night for a maximum of 6 nights • Young researchers coming from outside Europe: ○ Travel: max. € 1000.00 ○ Subsistence: max. € 120.00 per night for a maximum of six nights
43	UoA	**No third parties involved**
44	NMBU	**No third parties involved**
45	OFAI	**No third parties involved**
46	RWTH	**No third parties involved**
47	UHEI	**No third parties involved**

Partner #	Short Name	Third parties involved in the Project
48	SU	**No third parties involved**
49	SSSA	**No third parties involved**
50	CWI	**No third parties involved**
51	SKU	**No third parties involved**
52	FZI	**No third parties involved**
53	TUC	**No third parties involved**
54	TUD	**No third parties involved**
55	TUGRAZ	**No third parties involved**
56	TUM	**Tasks to be subcontracted:** Software development and operations: Development of partner and reviewer database for the calls for Expression of Interest; official communication panel; statistic and report. SP(s): SP11 (WP11.2, T11.2.4)
57	TAU	**Contribution in kind provided by 3rd parties (against payment, art. 16 of the FPA):** We envision that databases might be made available by Ichilov Hospital at Tel Aviv
58	(blank)	
59	UOXF	**No third parties involved**
60	HUJI	**Tasks to be subcontracted:** CFS: The subcontracting costs are costs of certificate on the Finance Statements (CFS) that needs to be provided together with the report as the amount requested for both SP4 and SP6 for HUJI is higher than €375,000. SP(s): SP4 (WP4.1, T4.1.1)
61	UABER	**No third parties involved**
62	UEDIN	**No third parties involved**
63	UMAN	**Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA):** ARM Limited (a microprocessor IP company) may support the work through in-kind contribution of microprocessor and related IP that will be used free of charge on NM-MC-2.
64	UAM	**No third parties involved**
65	UCLM	**No third parties involved**
66	UGR	**Tasks to be subcontracted:** Some low-level software development tasks are planned to be subcontracted (they are not research tasks, but rather technical support). Also, some tasks related to robotic fabrication, customization, related drivers, etc., are planned to be subcontracted. SP(s): SP10 Timing: SGA1 and beginning of SGA2
67	UMINHO	**Contribution in kind provided by 3rd parties (against payment, art. 16 of the FPA):** UMinho, through the School of Health Sciences (ECS) and the Life and Health Science Research Institute (ICVS), research Unit integrated in the ECS, has set up a Clinical Academic Center (Centro Clínico Académico – Braga, Associação, 2CA-Braga) in partnership with Hospital

Partner #	Short Name	Third parties involved in the Project
		de Braga and Hospital CUF Porto. 2CA-Braga is a legal entity registered on 03-01-2012 as a Private Non-Profit Association. The creation of the 2CA-Braga, with a focus on research, education, training and care in a clinical setting, and open to collaboration with other hospitals of the region, was envisaged to enhance the clinical research activities developed by the ECS/ICVS. In this project part of the work will be carried out using resources in-kind available at 2CA-Braga, in particular to what concerns the MRI scanner and its related equipment, and the Clinical Pathology Laboratory equipment for biological samples processing and analysis. The in-kind contributions of 2CA-Braga will be made available against payment under article 16 of the Model Framework Partnership Agreement.
68	UPM	**Contribution in kind provided by 3rd parties (against payment, art. 16 of the FPA):** The Laboratorio Cajal de Circuitos Corticales UPM-CSIC (CCCL) is a research laboratory managed by UPM and the Cajal Institute (IC-CSIC) that is located at UPM. CSIC (legal name: Agencia Estatal Consejo Superior de Investigaciones Científicas) is a Spanish non-profit public research institution. In the HBP, CSIC will provide resources to UPM in the form of personnel. Therefore, in the frame of the project, CSIC will be considered as a third party under Art. 11 of the Annotated Model Grant Agreement. The link between UPM and CSIC is based on a collaboration agreement between both organisations to carry out research activities. Personnel from CSIC will be working on UPM premises.
69	URJC	**Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA):** As a result of a close collaboration with the Universidad Politécnica de Madrid (UPM), we plan to share and integrate tools and models developed by UPM and URJC.
70	UNIPV	**No third parties involved**
71	UBERN	**No third parties involved**
72	UNIBI	**No third parties involved**
73	UKAACHEN	**No third parties involved**
74	UKE	**No third parties involved**
75	UZH	**No third parties involved**
76	UB	**No third parties involved**
77	UPF	**Contribution in kind provided by 3rd parties (free of charge, art.17 of the FPA):** ICREA (Institució Catalana de Recerca i Estudis Avançats) will provide resources (professor/researcher) free of charge to Universitat Pompeu Fabra as a third party (Article 12 Grant Agreement). ICREA is a foundation supported by the Catalan Government and guided by a Board of Trustees which aims to recruit top scientists for the Catalan R&D system: scientists capable of leading new research groups, strengthening existing groups, and setting up new lines of research. Following the rules of ICREA, although the salary costs of Prof. Gustavo DECO are paid by ICREA, he is assigned to physically work at in Universitat Pompeu Fabra, department of Information and Communication Technologies and considered a member of Universitat Pompeu Fabra. The terms and conditions of this cooperation between ICREA and Universitat Pompeu Fabra are reflected in a bilateral agreement between the two parties. The beneficiary, Universitat Pompeu Fabra, is free to use these resources at will. They are therefore

Partner #	Short Name	Third parties involved in the Project
		assimilated as "own resources" of the beneficiary, and will be charged to the project without being considered as a receipt. The cost will be declared by the beneficiary and will be recorded in the accounts of the third party. These accounts will be available for auditing if required.
78	AMU	**Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA):** Aix-Marseille University (AMU) is the beneficiary of the project. AMU uses the in-kind contributions provided by its third party, Protisvalor Méditerranée SAS (PVM), as defined in the Article 17 of the Model Framework Partnership Agreement. PVM, being in charge of the financial handling of the HBP FPA contribution dedicated to AMU, will handle some means and expenses necessary for the fulfilment of AMU tasks described in this document. These include amongst others the following tasks: hiring the non-permanent personnel, buying the necessary consumables and/or equipment to execute the EU-GA, reimbursing the travel and accommodation costs for the researchers involved in the project, or any other expenses necessary for its execution.
79	UBO	**No third parties involved**
80	UA	**No third parties involved**
81	UIO	**No third parties involved**
82	UCL	**No third parties involved**
83	UU	**No third parties involved**
84	WEIZMANN	**No third parties involved**
85	TUDA	**No third parties involved**
86	UNIGE	IRCCS Fatebenefratelli **Third Party Description:** The IRCCS (Istituto di Ricovero e Cura a Carattere Scientifico-Research and Care Institute) San Giovanni di Dio Fatebenefratelli is the National Centre for Research and Care of Alzheimer's disease. About 4,500 persons with Alzheimer's disease (AD) or associated disorders and 1,700 with mental disorders are treated yearly. The IRCCS Fatebenefratelli is acknowledged as a leading European centre in the field of Alzheimer's and other mental diseases, with particular regard to neuroimaging research, and has strong connections with leading academic centres in North America and elsewhere. Research conducted at the Laboratory of Alzheimer's Neuroimaging and Epidemiology focuses on causal factors in disorders of memory, cognition and behaviour, and their progression over time. Researchers working at the Laboratory have first-hand knowledge of the issues involved with archiving/retrieval of neuroimages and make extensive use of computationally intensive image analysis algorithms. The goal is to develop innovative diagnostic tools that help the recovery of patients with cognitive impairment. Headed by Giovanni B. Frisoni, the research facility has a staff of 27 including four post-docs, six Ph.D. students, fifteen fellows and 2 project managers. **Contribution in kind provided by 3rd parties:** The IRCCS Fatebenefratelli will devote staff effort and equipment (the neuGRID infrastructure plus other machines if needed). **Tasks to be subcontracted:** The IRCCS Fatebenefratelli will contribute to the following tasks: **Research initiatives:** will instantiate and coordinate interactions with the main European and international research initiatives interested in

Partner #	Short Name	Third parties involved in the Project
		getting connected to the MIP network and platform. Operatively, the task will compile a list of research studies and consortia efforts focused on neurodegenerative disease to be outreached and recruited. This task priority will be to focus on data sources and initiatives that are willing to become federated partners through the MIP. Sources of the highest priority include: EMIF-AD, PharmaCOG, BiomarkAPD, ARWIBO, GAAIN, EGI-MoBrain, etc. **Training and user engagement:** will expand the Liferay Knowledge Base (KB) platform (http://193.204.145.212:8080/liferay/) developed during the ramp-up phase. Aim of this task will be to develop a dedicated Specific Support Center (SSC) for user assistance including active learning, training, support (e.g.: via Redmine or other issue tracking tools), and education facilities. The SSC will cover support and training on all aspects of the whole knowledge chain from designing a scientific experiment, to uploading or accessing data, customizing algorithm pipelines, running analyses, visualizing, checking results, and carrying out statistics. By using web services, the SSC will provide users its services at any time irrespective of their geographic location. This task will massively cooperate with other subtasks of SP8, to build and provide courses to end-users. Development of the MIP SSC's outreach to users will be twofold: i) by means of educational and informative static materials to be made available to new and potentials users; ii) by means of in-person and remote training courses.
87	IDIBAPS	**The Hospital Clínic i Provincial de Barcelona (HCPB)** HCPB has a legal link to the IDIBAPS implying collaboration that is not limited to the action and it is reflected on the statutes of the beneficiary. The HCPB is a university tertiary hospital located in Barcelona. It is a public institution with a long reputation of excellence in care provision, training and research at national and international level. HCPB is a community hospital that employs around 4,000 workers (23% doctors, 55% nurses and 22% clerical and other supportive staff). As a Tertiary Hi-tech Hospital, the goals are around consolidating an organisation that stimulates knowledge and its translation to mainstream services, together with an adequate innovation in technology that ensures the development of the most advanced work practices. The priority is set in innovation on new models of organising care provision. HCPB has pursued the creation of an integrated care model of service integration aiming at maximising cooperation among professionals, levels of care and institutions. **Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA):** ***Institució Catalana de Recerca I Estudis Avançats (ICREA)*** ICREA will provide resources (professor/teacher) free of charge to the Graphene Core 1 Project as a third party (Article 12 of the Grant Agreement). ICREA is a foundation supported by the Catalan Government and guided by a Board of Trustees which aims to recruit top scientists for the Catalan R&D system: scientists capable of leading new research groups, strengthening existing groups, and setting up new lines of research. Following the rules of ICREA, although the salary costs of Dr. SANCHEZ-VIVES are paid by ICREA, she is assigned to physically work at IDIBAPS, and considered a member of IDIBAPS. The terms and conditions of this cooperation between ICREA and IDIBAPS are reflected in a bilateral agreement between the two parties. The beneficiary IDIBAPS is free to use these resources at will. They are therefore assimilated as 'own resources' of the beneficiary, and will be charged to the project without being considered as a receipt. The cost will be

Partner #	Short Name	Third parties involved in the Project
		declared by the beneficiary and it will be recorded in the accounts of the third party. These accounts will be available for auditing if required.
88	IBEC	**Contribution in kind provided by 3rd parties (free of charge, art. 17 of the FPA):** ***Institució Catalana de Recerca I Estudis Avançats (ICREA)*** ICREA will provide resources (professor/researcher) free of charge to IBEC as a third party (Article 12 Grant Agreement). ICREA is a foundation supported by the Catalan Government and guided by a Board of Trustees which aims to recruit top scientists for the Catalan R&D system: scientists capable of leading new research groups, strengthening existing groups, and setting up new lines of research. Following the rules of ICREA, although the salary costs of Prof. Pau GOROSTIZA are paid by ICREA, he is assigned to physically work at IBEC (leading the 'Nanoprobes and nanoswitches' laboratory) and considered a member of IBEC. The terms and conditions of this cooperation between ICREA and IBEC are reflected in a bilateral agreement between the two parties. The beneficiary, IBEC, is free to use these resources at will. They are therefore assimilated as 'own resources' of the beneficiary, and will be charged to the project without being considered as a receipt. The cost will be declared by the beneficiary and it will be recorded in the accounts of the third party. These accounts will be available for auditing if required.
89	DZNE	**No third parties involved**
90	UBER	**No third parties involved**
91	INFN	**No third parties involved**
92	ISS	**No third parties involved**
93	KNAW	**No third parties involved**
94	MRC	**No third parties involved**
95	IMIL	**No third parties involved**
96	ULG	**Centre Hospitalier Universitaire de Liège (University of Liège Hospital)** Clinical, MRI, EEG and EEG-TMS performed in University Hospital in post-coma patients (personnel and other direct costs). Medical transportation, overnight stay and clinical assessments performed in University Hospital of post-coma patients.
97	UvA	**No third parties involved**
98	UGLA	**No third parties involved**
99	UHAM	**No third parties involved**
100	USFD	**No third parties involved**
101	UWE	**No third parties involved**
102	SURREY	**No third parties involved**
103	TUT	**Contribution in kind provided by 3rd parties (against payment, art. 16 of the FPA):** Dr. Marja-Leena LINNE will continue to collaborate with Assoc. Prof. Ausra SAUDARGIENE (Vtautas Magnus University, Kaunas, Lithuania), similarly to what has already been successfully realised in 2014-2015, in HBP T4.3.4. The cooperation is external support in nature, meaning the following: Prof. Marja-Leena LINNE is an expert on plasticity and learning rules and algorithms, specifically detailed biophysical rules that are going to

Partner #	Short Name	Third parties involved in the Project
		be used and further developed in the project, as well as astroglial regulation of plasticity and learning. Prof. LINNE therefore has all key expertise necessary to fulfil the goals of T4.2.2, both biological and theoretical. Prof. Saudargiene is an expert in phenomenological models of plasticity. Prof. SAUDARGIENE's group will provide additional insight into the project. Strictly speaking on existing phenomenological plasticity and learning rules and their computational implementations. This cooperation is selected because it is expected to speed up the project, specifically the validation of novel models developed by Prof. LINNE. Speeding up will be achieved because Prof. SAUDARGIENE has obtained extensive experience in implementing some of the models that will be used as test tools to validate the developed novel models. The costs for cooperation are claimed by the project participant (Dr. LINNE). Only the amount actually incurred by the third party will be claimed. Other collaborations that greatly support the Task 4.2.2 are established within the HBP Ramp-Up Phase during years 2014 and 2015. These are internal HBP collaborations.
104	ULEEDS	**No third parties involved**
105	UPMC	**INSERM** The Institut de la Vision is a Joint Research Center (Unité Mixte de Recherche UMRS 968) joining the French National Institute of Health and Medical Research (Inserm) currently hiring the PIs, the National Center for Scientific Research (CNRS) and the University Pierre and Marie Curie (UPMC). In order to facilitate the administrative management of the research, a General Management Delegation was assigned to UPMC. That is why UPMC is the beneficiary for this project. However, Inserm has to be added as a third party so the beneficiary UPMC can charge costs incurred by the third party in carrying out the project for permanent staff or temporary staff hired to work on the project, in accordance with the provisions of the grant agreement. INSERM is the French National Health Institute. Mr MARRE is employed by INSERM but he works in a joint research unit ('Unité Mixte de Recherche'), which is laboratory recognised and supported by both INSERM and UPMC. Therefore, INSERM should be identified as a UPMC linked third party following the Art. 14 of the EC-GA. ***Description of the Third Party organisation:*** Founded in 1964, the French National Institute of Health and Medical Research (Inserm) is a public scientific and technological institute which operates under the joint authority of the French Ministry of Health and French Ministry of Research. As the only French public research institute to focus entirely on human health, in 2008 Inserm took on the responsibility for the strategic, scientific and operational coordination of biomedical research. This key role as coordinator comes naturally to Inserm thanks to the scientific quality of its teams and its ability to conduct translational research, from the laboratory to the patient's bed. Institut de la Vision is a Joint Research Centre (Unité Mixte de Recherche UMRS 968) joining the French National Institute of Health and Medical Research (Inserm) currently hiring the PIs, the National Centre for Scientific Research (CNRS) and the University Pierre and Marie Curie (UPMC). In order to facilitate the administrative management of the research, a General Management Delegation was assigned to UPMC. That is why UPMC is the beneficiary for this project. However, Inserm has to be added as a third party so the beneficiary UPMC can charge costs incurred by the third party in carrying out the project for permanent staff or temporary staff hired to work on the project, in

Partner #	Short Name	Third parties involved in the Project
		accordance with the provisions of the grant agreement.
106	UoS	**No third parties involved**
107	MU	**No third parties involved**
108	UCBL	**No third parties involved**
109	POLITO	**No third parties involved**
110	UGENT	**No third parties involved**
111	KUL	**No third parties involved**
112	UNIBAS	**University Hospital Basel (USB)** The University of Basel includes the University Hospital Basel (USB) as a linked third party (third party with a legal link). The affiliation is based on the fact that the University of Basel is in charge of all aspects regarding education and research carried out at University Hospitals. The legal basis is given by the public laws establishing the University of Basel and the University Hospitals as well as the bilateral contracts (performance agreements, Leistungsvereinbarungen) between the University of Basel and its University Hospitals. The University Hospital Basel (USB) will carry out the work described in Annex I. The University of Basel – mandating its University Hospitals regarding education and research – is in charge of all aspects concerning contract management, accounting, controlling, financial reporting, exploitation of intellectual property and audit management. The practice to delegate the financial project management to the Finance Department of the University of Basel is accepted by the Swiss National Science Foundation for the national projects. It is also part of the accounting rules of the University of Basel as shown in the notes of the yearly financial statements.
113	VU	**No third parties involved**
114	SIB	**No third parties involved**
115	EBRI	**No third parties involved**
116	SNS	**No third parties involved**
117	UM	**No third parties involved**

Table 42: HBP Core Project Partners' Third Parties

Appendix 7: Critical Infrastructure for the HBP

Infrastructure Type	Description	Used for SP	Details of use	Platform	State	Partner	PI	Estimated Contributing Value (EUR)	Time to Replace (Est.)	Available from (date)	Available until (date)
Supercomputing/HPC	MareNostrum: 1.1 petaflops				ES	BSC	Rosa M. BADIA Javier BARTOLOME	870 000			
Supercomputing/HPC	HBP Development Supercomputer hosted at CSCS (BBP5) paid by Swiss national funding				CH	CSCS (ETHZ)	Thomas SCHULTHESS	23 000 000			
Supercomputing/HPC	JUQUEEN Blue Gene/Q Supercomputer				DE	JUELICH	Thomas LIPPERT	19 000 000			
Supercomputing/HPC	Pre-Exascale HBP Supercomputer				DE	JUELICH	Thomas LIPPERT	50 000 00			
Supercomputing/HPC	Exascale HBP Supercomputer				DE	JUELICH	Thomas LIPPERT	10 000 000			
Supercomputing/HPC	HPC cluster				DE	JUELICH	Thomas LIPPERT	200 000			
Supercomputing/HPC	Big Data HPC cluster system				IT	CINECA	Giovanni ERBACCI	1 500 000			
Supercomputing/HPC	Follow on of the previous Big Data HPC cluster system				IT	CINECA	Giovanni ERBACCI	1 500 000			
Supercomputing/HPC	Fermi System IBM BG/Q (2.1 PFlop/s system)				IT	CINECA	Giovanni ERBACCI	4 000 000			
Supercomputing/HPC	Next Tier 0 System after the Fermi System (5 times the performance of				IT	CINECA	Giovanni ERBACCI	7 000 000			

	Fermi)					
Supercomputing/HPC	Further evolution of Tier 0 System and Big Data Infrastructure (expected performance in excess of 50PFlops)		IT	CINECA	Giovanni ERBACCI	12 000 000
Supercomputing/HPC	Blue Brain Project computing and storage infrastructure, acquired 2011 -2013 paid by Swiss national funding		CH	EPFL	Henry MARKRAM	18 600 000
Supercomputing/HPC	Magerit-2 supercomputer: 4000 Power 7 cores + 1000 Intel (mostly Xeon E5-2670 cores) + Infiniband+ special coprocessing nodes for testing purposes (GPU+Xeon Phi)		ES	UPM CeSViMa	Vicente MARTIN	1 000 000
Cloud Systems	Largest German university cloud storage for sync-and share. Provides 22 PB disk (+22 PB tape) storage		DE	KIT Steinbuch Centre for Computing	Marcus HARDT	
Cloud Systems	neuGRID: State-of-the-art facilities to access and manage big imaging and non imaging data, sophisticated image processing algorithms, adequate computational power, and training and help for the non expert user.		CH	HUG	Giovanni FRISONI	4 300 000

Cloud Systems	EXAREME: Platform for distribute data-flow processing on cluster and cloud infrastructures		GR	UOA	Yannis IOANNIDIS	900 000
Neuromorphic Systems	“Physical-Model (PM)” system		DE	UHEI	Karlheinz MEIER	
Neuromorphic Systems	IT Infrastructure for integrated circuit design, Software Licences from Europractice Program		DE	TUD	René SCHÜFFNY	300 000
Neuromorphic Systems	pCluster ClusterServer 4HE 128Core XE5-2670 / 1024GB Ram (= 8GB Ram per Core) + Masternode and Filer 12 TB diskspace		AT	TUGRAZ	Wolfgang MAASS	75 000
Neuromorphic Systems	18 cruncher 19, DUALXeon 6Core 2.6GHz/ 96GB DDR3		AT	TUGRAZ	Wolfgang MAASS	118 000
Neuromorphic Systems	1 x nCluster 15 x Sun Fire X4600M2 480GB RAM 240 CPUS + Masternode and Filer		AU	TUGRAZ	Wolfgang MAASS	251 000
Neuromorphic Systems	26 Linux Workstations for the scientific offices. 2Gb- 4GB Ram Dual Core Intel Cpus 2.6 Ghz		AT	TUGRAZ	Wolfgang MAASS	15 000
Neuromorphic Systems	1 x Matlab Cluster (64 Cores). Dual XEON DualCore E5430 2,66GHZ each 16GB RAM per core		AT	TUGRAZ	Wolfgang MAASS	50 000
Neuromorphic Systems	SpiNNaker machine – NM-MC-1		UK	UMAN	Dave LESTER/ Steve FURBER	3 600 000

Table 43: HBP Core Project Partners' Key Infrastructure Contributions

Appendix 8: Risk Detection & Mitigation

The Project Lifecycle Framework has different problem-detection strategies in its various phases:

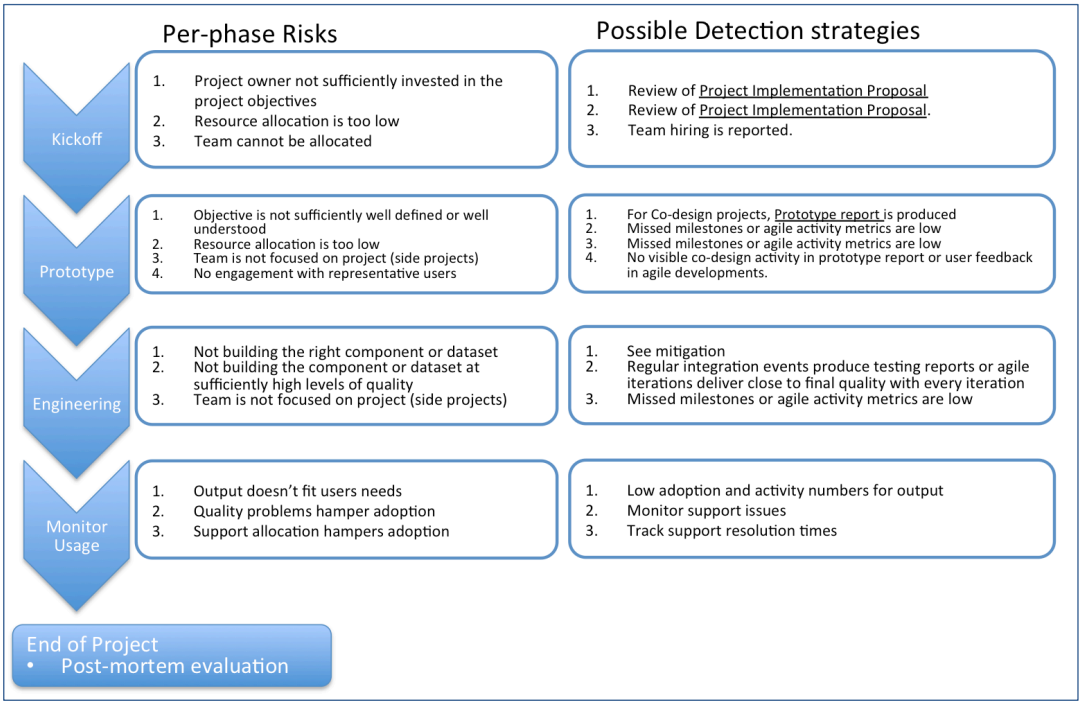

Figure 15: Project Lifecycle Framework problem detection strategies

The Project Lifecycle Framework also has mitigation strategies in specific phases.

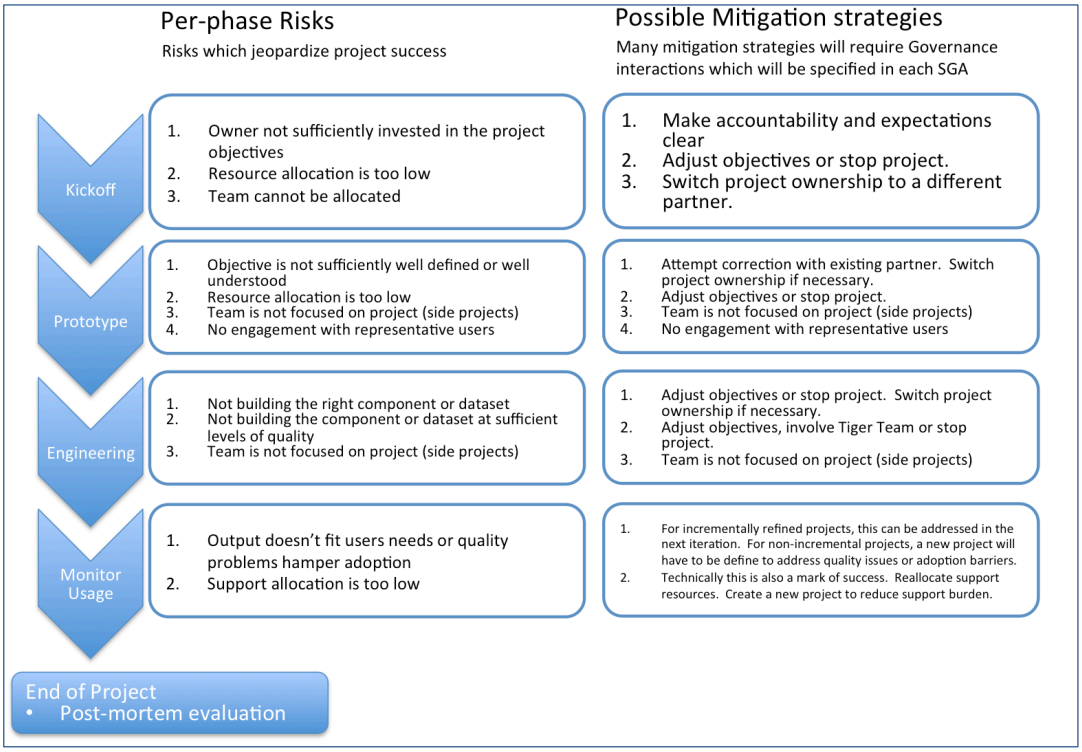

Figure 16: Project Lifecycle Framework mitigation strategies

Appendix 9: Glossary

Action Potential	A short-lasting electrical event in which the membrane potential of a cell rapidly rises and falls, following a consistent trajectory of depolarisation and hyperpolarisation.
Axon	A long projection of a neuron that conducts electrical impulses away from the principle cell body.
Blue Brain Project	An EPFL project launched in 2005, with the goal of creating the workflows and tools necessary to build and simulate brain models. As proof of concept, the project has successfully built and simulated a cellular-level model of the rat cortical column.
BlueGene	An IBM supercomputer. The BlueGene/P used in the EPFL Blue Brain Project is a massively parallel, tightly interconnected machine with 16,384 processors, 56 Teraflops of peak performance, 16 Terabytes of distributed memory and a 1 Petabyte file system. The Blue Brain team provides enough computing power to simulate at least 60 rat cortical columns.
Brain atlas	A work of reference (e.g., the Allen Mouse Atlas), often available as an online public resource showing how one or more data sets (e.g., gene expression data) map to specific regions and sub-regions of the brain.
BrainScaleS	An EU-funded research project that integrates in vivo experimentation with computational analysis to investigate how the brain processes information on multiple spatial and temporal scales, and to implement these capabilities in neuromorphic technology.
Cable Theory	Mathematical models making it possible to calculate the flow of electric current (and accompanying voltage), assuming passive neuronal fibres such as axons and dendrites are cylindrical cable-like structures.
Connectome	The complete connectivity map between neurons, including the locations of all synapses.
Core Project (CP)	The component of the HBP FET Flagship Initiative responsible for coordinated research and development critical to building and operating the HBP Platforms, and for the overall governance and coordination of the Flagship Initiative. The Core Project will be governed by the Framework (FPA), executed by the partners listed in the FPA, and funded by the European Commission through the FET Flagship Programme. The Core Project will be articulated in several (probably three) phases, each regulated by a Specific Grant Agreement between the Partners and the European Commission.
Core Project Objective (CPO)	One of the 12 objectives of the Core Project, defined in the Research Roadmap.

Dendrite	The branched projections of a neuron that conduct electrochemical signals received from other neurons to the soma of the principal neuron.
Diffusion Tensor Imaging (DTI)	A technique that enables the measurement of the restricted diffusion of water in tissue to produce neural tract images. It also provides useful structural information.
DIR	Directorate (see section 2.3.2.5.2)
EAB	Ethics Advisory Board, created by merging the original HBP Research Ethics Committee (REC) and Ethics, Legal and Social Aspects Committee (ELSA).
ECOG	Intracranial electro-corticogram. A technique in which electrodes are placed directly on the exposed surface of the brain to record electrical activity.
EEG	Electroencephalography. The recording of electrical activity on the surface of the scalp. EEG measures voltage fluctuations resulting from ionic current flows within the neurons of the brain.
Electrophysiology	The study of the electrical properties of excitable biological cells and tissues.
Exascale	Refers to a supercomputer with a performance of 1018 flops. The first computers with this level of performance are expected to become available during the second half of this decade.
Executable Systems Specification (ESS)	An engineering approach to large-scale system design in which specifications are implemented as a complete software model of the device under construction. The ESS approach makes it possible to verify the hardware design without building a physical system.
FACETS	A European research project (2005-2010) that pioneered an integrated workflow for neuromorphic computing, leading from neurobiology and brain modelling to neuromorphic hardware.
Flop/s	Floating Point Operations Per Second. A measure of computer performance. The largest current supercomputers have a performance in the order of Petaflops (1015 flops). Exascale supercomputers planned for the end of the decade would have a performance in the order of Exaflops (1018 flops).
fMRI	Functional Magnetic Resonance Imaging.
FO	Flagship Objective (see 2.1.1.4)
Framework Partnership Agreement (FPA)	The agreement between the Commission and the other signatories regulating the execution of the Core Project in the FET Flagship Initiative, and defining the Research Roadmap for the whole Initiative.
Functional Magnetic Resonance Imaging	An MRI procedure that measures brain activity by detecting functional changes associated with changing blood flow.
Glia	Non-neuronal cells that maintain homeostasis, form

	myelin, and provide support and protection for neurons in the nervous system.
HBP Flagship Initiative	One of the two Flagship Initiatives launched and managed by the EU FET Flagship Programme. The HBP Flagship Initiative will be responsible for implementing the Action Plan and Research Roadmap defined in this document. It will consist of a Core Project and Partnering Projects.
High-Performance Computing (HPC)	The use of parallel processing to run an applications programme efficiently, reliably and quickly. The term HPC is sometimes used as a synonym for supercomputing.
Hodgkin and Huxley Model	A set of differential equations describing an electrical circuit model for the non-linear dynamics of ion channels and the cell membrane of neurons.
Human Brain Project (HBP)	Short name of the HBP Flagship Initiative.
In silico	A process or an experiment performed on a computer or via computer simulation.
In vitro	Studies in experimental biology conducted using components of an organism that have been isolated from their usual biological context.
In vivo	Studies using a whole, living organism as opposed to a partial or dead organism.
Innovation and Technology Transfer Committee (ITTC)	The Innovation and Technology Transfer Committee is responsible for defining and implementing HBP policies on issues related to intellectual property, acting in an advisory body to the SIB and the Directorate.
Innovation and Technology Transfer Committee (ITTC)	The Innovation and Technology Transfer Committee is responsible for defining and implementing HBP policies on issues related to intellectual property, acting in an advisory body to the RB and the ExCo.
International Neuroinformatics Coordinating Facility (INCF)	An international science organisation, the purpose of which is to facilitate worldwide cooperation of activities and infrastructures in neuroinformatics-related fields.
Ion channel	Proteins controlling the passage of ions through the cell membrane. Ion channels are targets for neuromodulatory systems and for drugs. The distribution of ion channels determines the electrical behaviour of the cell.
iPSC	Induced Pluripotent Stem Cell, a type of stem cell that can be used to generate neurons and other kinds of cell for use in research.
ITTC	Innovation and Technology Transfer Committee.
KnowledgeSpace	A community-driven wiki integrated in the HBP Neuroinformatics Platform. The KnowledgeSpace provides an encyclopaedic view of the latest data, models and literature for all levels of brain organisation.

Localiser	A (usually simple) task used in conjunction with fMRI to characterise the neuronal circuitry responsible for a specific cognitive or behavioural capability.
Magnetic Resonance Imaging (MRI)	A medical imaging technique allowing the visualisation detailed internal structures. Nuclear magnetic resonance (NMR) is used to image nuclei of atoms inside the body.
MCELL	A widely used simulator from the Computational Neurobiology Lab, SALK Institute, USA. Mcell is used in reaction diffusion simulations of molecular interactions.
Mechanistic	Refers to an explanation that identifies the causal chain of physical or chemical events leading from an initial cause (e.g., a gene defect) to its consequences (e.g., a change in behaviour). In clinical research, knowledge of such cascades is a precondition for rational drug design.
Microcircuit	A neural circuit lying within the dimensions of the local arborisations of neurons (typically 200–500 μm).
Molecular Dynamics	A form of computer simulation using approximations of known physics to estimate the motion of atoms and molecules.
Multi-level	Refers to a description of the brain that takes account of its different levels of organisation.
Multi-scale	Refers to a simulation technique that reproduces the different levels of organisation of a complex phenomenon, switching dynamically between different levels of detail according to the needs of the simulation.
Neuroinformatics	The academic discipline concerned with the use of computational tools to federate, organise and analyse neuroscience data.
Neuromorphic	Refers to a method for emulating the structure and function of neurons and neuronal circuits in electronics.
Neuromorphic Computing System	A computing system comprising a neuromorphic computing device, a software environment for configuration and control, and the capability to receive input and to generate output.
Neuron	An electrically excitable cell that processes and transmits information by electrical and chemical signalling.
NEURON	A well-established environment for the empirically based simulations of neurons and networks of neurons. Developed by Michael Hines, Yale University, USA.
Neurorobotic System	A robotic system comprised of a controller, a body, actuators and sensors, whose controller architecture is derived from a model of the brain.
Operational Phase	The remaining 7½ years of the HBP, following the conclusion of the Ramp-Up phase.

Optogenetics	The combination of genetic and optical methods to control specific events in targeted cells of living tissue. Optogenetics provides the temporal precision (millisecond-timescale) needed to keep pace with functioning intact biological systems.
Organelles	Specialised subunits performing a specialised function within a cell.
Partnering Project (PP)	The component of the HBP FET Flagship Initiative responsible for developing new ideas, approaches and technologies that are proposed spontaneously by independent research groups, adding novel capabilities to the Platforms and using the Platforms to address questions beyond the capabilities of any individual laboratory. Funding for the Partnering Projects will come from outside the FET Flagship Programme (e.g., from regional and national sources, other sources of EU funding, and industry).
PET	An imaging technique that produces a three-dimensional image of functional processes in the body, using pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer).
Petascale	Refers to a supercomputer with a performance of 1015 flops. In November 2011, the Japanese K computer became the first machine to achieve a peak performance of more than 10 Petaflops.
Plasticity	The ability of a synapse, a neuron or a neuronal circuit to change its properties in response to stimuli or the absence of stimuli.
PLI	Polarised Light Imaging.
Polarised Light Imaging (PLI)	An imaging technique making it possible to identify the orientation of fibres in histological sections of the brain. Often used for imaging post mortem samples from the human brain.
Predictive Neuroinformatics	The use of computational techniques to discover statistical regularities in the relationships between two neuroscience data sets, and the exploitation of these regularities to predict parameter values where experimental measurements are not available.
Proteome	The set of all the proteins expressed by a cell.
Ramp-Up Phase	The first 2½ years of the HBP.
Receptor	A protein molecule that receives and transmits chemical information across membranes.
Reconstruction	A computer model of the brain or of parts of the brain derived from sparse data by exploiting interdependencies between data sets spanning different levels of biological organisation.
SB	Stakeholder Board (see 2.3.2.5.1)
SIB	Science and Infrastructure Board (see 2.3.2.5.5)
Simulation	The imitation or replication of a complex real-world process.

Soma	The cell body or the compartment in a cell that houses the nucleus.
Specific Grant Agreement (SGA)	An agreement between the European Commission and the signatories regulating a specific phase of the Core Project.
SpiNNaker	A UK-funded research project, the goal of which is to build neuromorphic computing systems based on many-core chips with efficient bi-directional links for asynchronous spike-based communication.
Steering	Refers to interactive control of a simulation using real-time (usually visual) feedback from the simulation.
STEPS	A simulator for stochastic reaction-diffusion systems in realistic morphologies, from the Theoretical Neurobiology group, University of Antwerp, Belgium.
Subproject (SP)	The highest level of subunit within the HBP, charged with coordinating the Initiative's activities in a given area of scientific, technical or managerial work. The HBP Flagship Initiative consists of 10 Subprojects dedicated to scientific research and infrastructure work, one Subproject responsible for social and ethical matters, and one dedicated to providing central services (coordination, dissemination, outreach, education, central IT services, etc.). Subprojects bring together work performed by the Core Project, by Partnering Projects and by collaborations with other national, European or international projects and initiatives.
Supercomputer	A computer with performance close to the highest performance attainable at a given time.
Synapse	A structure between two neurons allowing them to communicate via chemical or electrical signals.
SyNAPSE	A research project funded by the US agency DARPA with the aim of building energy efficient, compact neuromorphic systems based on modern component technologies.
Terascale	Refers to a supercomputer with a performance of 10^{12} flops.
Transcriptome	The set of information required to fully represent all cDNA expressed by a cell during translation of the genome.
Very Large Scale Integration (VLSI)	The integration of very large numbers of transistors on a single silicon chip. VLSI devices were initially defined as chips with more than 10,000 transistors. Current systems may contain more than 2,000,000.
Workflow	Term used in management engineering and in computer science to describe a sequence of steps leading to a well-defined outcome.
Work Package (WP)	A component of a Subproject covering a specific area of scientific, technical or managerial work. Work Package Deliverables and Milestones for a given phase of the

	HBP will be defined in the SGA for that phase.

Appendix 9: References

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