EUROPEAN COMMISSION

Directorate-General for Communications Networks, Content and Technology

Digital Excellence and Science Infrastructure
Emerging & Disruptive Technologies

AMENDMENT Reference No AMD-650003-389

Framework Partnership: 650003 — HBP FPA

The parties agree to amend the Framework Partnership Agreement as follows ('**Amendment**'):

1 . Addition of a new partner

The following new partner is added:

- UNIVERSITA DEGLI STUDI DI TORINO (UNITO) — as from 1 December 2021

This implies the **following changes** to the **Framework Partnership Agreement:**

• The new partner and the 'accession date' is added to the **Preamble**:

  " *UNIVERSITA DEGLI STUDI DI TORINO (UNITO)*, *established in VIA GIUSEPPE VERDI 8, TORINO 10124, Italy, VAT number: IT02099550010, — as from 1 December 2021*"

Moreover, this implies the following **automatic changes** to the **Specific Agreement(s)**:

• The new partner and the 'accession date' is added to the **Preamble** as inactive partner:

  "*UNIVERSITA DEGLI STUDI DI TORINO (UNITO)*, *established in VIA GIUSEPPE VERDI 8, TORINO 10124, Italy, VAT number: IT02099550010, — as 'partner not carrying out action tasks' as from 1 December 2021*"

2 . Change of Annex 1 (action plan/implementation strategy)

Annex 1 of the **Framework Partnership Agreement** is changed and replaced by the Annex 1 attached to this Amendment.

All other provisions of the Agreement and its Annexes remain unchanged.

This Amendment **enters into force** on the day of the last signature.

This Amendment **takes effect** on the date on which the amendment enters into force, except where a different date has been agreed by the parties (for one or more changes).

Please inform the other members of the consortium of the Amendment.

SIGNATURES

For the coordinator   For the Commission

Enclosures:
                        Annex 1 Action plan to the FPA

EUROPEAN COMMISSION

Directorate-General for Communications Networks, Content and Technology

CNECT.C – Digital Excellence and Science Infrastructure
C.4 – Emerging & Disruptive Technologies

ANNEX 1 (part A)

Framework Partnership Agreement

NUMBER — 650003 — HBP FPA

Table of Contents

1.1. The project summary

Project Number [1]	650003	Project Acronym [2]	HBP FPA

One form per project

General information	
Project title [3]	Human Brain Project Framework Partnership Agreement
Starting date [4]	
Duration in months [5]	62
Call (part) identifier [6]	H2020-FETFLAG-2014
Topic	FETFLAG-1-2014 2014: Framework Partnership Agreement
Fixed EC Keywords	
Free keywords	mouse brain, human brain, transcriptome, simulation, reconstruction, neuroinformatics, biological signatures of disease, high performance computing, neuromorphic computing, neurorobotics

Abstract [7]

Understanding the human brain is one of the greatest scientific challenges of our time. Such an understanding can provide profound insights into our humanity, leading to fundamentally new computing technologies, and transforming the diagnosis and treatment of brain disorders. Modern ICT brings this prospect within reach. The HBP Flagship Initiative (HBP) thus proposes a unique strategy that uses ICT to integrate neuroscience data from around the world, to develop a unified multi-level understanding of the brain and to diseases, and ultimately to emulate its computational capabilities. The goal is to catalyse a global collaborative effort. A Core Project will build and operate a tightly integrated network of six ICT platforms, providing HBP researchers and the scientific Community with unique resources and capabilities: multi-level atlases and high-fidelity reconstructions of the mouse and human brains, tools and workflows for brain simulation, high performance computing infrastructure, interactive supercomputing, a federated network of anonymised clinical data, Neuromorphic Computing Systems, and Neurorobotics capabilities closing the loop between brain simulations and the environment. Partnering Projects will enable independent research groups to expand the capabilities of the Platform, and use them to address otherwise intractable problems in neuroscience, computing and medicine. Collaborations with other national, European and international initiatives will create synergies, maximizing returns on research investment. This document outlines the concept underlying the HBP Flagship Initiative, describes mechanisms providing for effective governance of the Initiative and proposes a detailed Research Roadmap, showing the allocation of specific activities to the Core Project, the Partnering Projects and external collaborations. The document will form the basis for the Framework Partnership Agreement governing the Core Project.

1.2. List of Beneficiaries

Project Number [1]	650003	Project Acronym [2]	HBP FPA

List of Beneficiaries					
No	Name	Short name	Country	Project entry date[8]	Project exit date
1	EBRAINS	EBRAINS	Belgium	01/03/2020	
2	AALTO KORKEAKOULUSAATIO SR	AALTO	Finland		12/12/2020
3	ACADEMISCH ZIEKENHUIS LEIDEN	LUMC	Netherlands		
4	ATHENS UNIVERSITY OF ECONOMICS AND BUSINESS - RESEARCH CENTER	AUEB	Greece		
5	BARCELONA SUPERCOMPUTING CENTER-CENTRO NACIONAL DE SUPERCOMPUTACION	BSC	Spain		
6	BAUHAUS-UNIVERSITAET WEIMAR	BAUW	Germany		12/12/2020
7	BERGISCHE UNIVERSITAET WUPPERTAL	BUW	Germany		
8	Bloomfield Science Museum Jerusalem (BSMJ)	BSMJ	Israel		12/12/2020
9	CARDIFF UNIVERSITY	CF	United Kingdom		12/12/2020
10	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS	CNRS	France		
11	COMMISSARIAT A L ENERGIE ATOMIQUE ET AUX ENERGIES ALTERNATIVES	CEA	France		
12	CONSIGLIO NAZIONALE DELLE RICERCHE	CNR	Italy		
13	CINECA CONSORZIO INTERUNIVERSITARIO	CINECA	Italy		
14	DANMARKS TEKNISKE UNIVERSITET	DTU	Denmark		
15	DEBRECENI EGYETEM	UoD	Hungary		12/12/2020
16	DE MONTFORT UNIVERSITY	DMU	United Kingdom		
17	ECOLE NORMALE SUPERIEURE	ENS	France		
18	EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZUERICH	ETHZ	Switzerland		
19	FONDEN TEKNOLOGIRADET	FT	Denmark		
20	FORSCHUNGSZENTRUM JULICH GMBH	JUELICH	Germany		
21	FORTISS GMBH	FORTISS	Germany		

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry date[8]	Project exit date
22	FRAUNHOFER GESELLSCHAFT ZUR FOERDERUNG DER ANGEWANDTEN FORSCHUNG E.V.	Fraunhofer	Germany		
23	FUNDACAO D. ANNA SOMMER CHAMPALIMAUD E DR. CARLOS MONTEZ CHAMPALIMAUD	FCHAMP	Portugal		12/12/2020
24	HEINRICH-HEINE-UNIVERSITAET DUESSELDORF	UDUS	Germany		
25	HELSINGIN YLIOPISTO	UH	Finland		12/12/2020
26	HITS GGMBH	HITS	Germany		
27	CENTRE HOSPITALIER UNIVERSITAIRE VAUDOIS	CHUV	Switzerland		
28	IMPERIAL COLLEGE OF SCIENCE TECHNOLOGY AND MEDICINE	ICL	United Kingdom		
29	INSTITUT DU CERVEAU ET DE LA MOELLE EPINIERE	ICM	France		
30	KIRSERLETI ORVOSTUDOMANYI KUTATOINTEZET	IEM HAS	Hungary		
31	INSTITUTE OF SCIENCE AND TECHNOLOGY AUSTRIA	IST	Austria		12/12/2020
32	INSTITUT JOZEF STEFAN	JSI	Slovenia		12/12/2020
33	INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET AUTOMATIQUE	INRIA	France		
34	INSTITUT PASTEUR	IP	France		
35	JOHANN WOLFGANG GOETHE-UNIVERSITATFRANKFURT AM MAIN	UFRA	Germany		12/12/2020
36	KARLSRUHER INSTITUT FUER TECHNOLOGIE	KIT	Germany		12/12/2020
37	KAROLINSKA INSTITUTET	KI	Sweden		
38	KING'S COLLEGE LONDON	KCL	United Kingdom		
39	KUNGLIGA TEKNISKA HOEGSKOLAN	KTH	Sweden		
40	LABORATORIO EUROPEO DI SPETTROSCOPIE NON LINEARI	LENS	Italy		
41	LINNEUNIVERSITETET	LNU	Sweden		
42	MEDIZINISCHE UNIVERSITAT INNSBRUCK	MUI	Austria		
43	ETHNIKO KAI KAPODISTRIAKO PANEPISTIMIO ATHINON	UoA	Greece		

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry date[8]	Project exit date
44	NORGES MILJO-OG BIOVITENSKAPLIGE UNIVERSITET	NMBU	Norway		
45	OSTERREICHISCHE STUDIENGESELLSCHAFTFUR KYBERNETIK VEREIN	OFAI	Austria		12/12/2020
46	RHEINISCH-WESTFAELISCHE TECHNISCHE HOCHSCHULE AACHEN	RWTH	Germany		
47	RUPRECHT-KARLS-UNIVERSITAET HEIDELBERG	UHEI	Germany		
48	SABANCI UNIVERSITESI	SU	Turkey		12/12/2020
49	SCUOLA SUPERIORE DI STUDI UNIVERSITARI E DI PERFEZIONAMENTO S ANNA	SSSA	Italy		
50	STICHTING NEDERLANDSE WETENSCHAPPELIJK ONDERZOEK INSTITUTEN	CWI	Netherlands		
51	STICHTING RADBOUD UNIVERSITEIT	SKU	Netherlands		
52	FZI FORSCHUNGSZENTRUM INFORMATIK	FZI	Germany		
53	POLYTECHNEIO KRITIS	TUC	Greece		12/12/2020
54	TECHNISCHE UNIVERSITAET DRESDEN	TUD	Germany		
55	TECHNISCHE UNIVERSITAET GRAZ	TUGRAZ	Austria		
56	TECHNISCHE UNIVERSITAET MUENCHEN	TUM	Germany		
57	TEL AVIV UNIVERSITY	TAU	Israel		
58	THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE	UCAM	United Kingdom		30/06/2016
59	THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD	UOXF	United Kingdom		
60	THE HEBREW UNIVERSITY OF JERUSALEM	HUJI	Israel		
61	THE UNIVERSITY COURT OF THE UNIVERSITY OF ABERDEEN	UABER	United Kingdom		23/12/2019
62	THE UNIVERSITY OF EDINBURGH	UEDIN	United Kingdom		
63	THE UNIVERSITY OF MANCHESTER	UMAN	United Kingdom		

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry date[8]	Project exit date
64	UNIVERSIDAD AUTONOMA DE MADRID	UAM	Spain		
65	UNIVERSIDAD DE CASTILLA - LA MANCHA	UCLM	Spain		
66	UNIVERSIDAD DE GRANADA	UGR	Spain		
67	UNIVERSIDADE DO MINHO	UMINHO	Portugal		
68	UNIVERSIDAD POLITECNICA DE MADRID	UPM	Spain		
69	UNIVERSIDAD REY JUAN CARLOS	URJC	Spain		
70	UNIVERSITA DEGLI STUDI DI PAVIA	UNIPV	Italy		
71	UNIVERSITAET BERN	UBERN	Switzerland		
72	UNIVERSITAET BIELEFELD	UNIBI	Germany		16/07/2020
73	UNIVERSITAETSKLINIKUM AACHEN	UKAACHEN	Germany		
74	UNIVERSITAETSKLINIKUM HAMBURG-EPPENDORF	UKE	Germany		
75	UNIVERSITAT ZURICH	UZH	Switzerland		12/12/2020
76	UNIVERSITAT DE BARCELONA	UB	Spain		
77	UNIVERSIDAD POMPEU FABRA	UPF	Spain		
78	UNIVERSITE D'AIX MARSEILLE	AMU	France		
79	UNIVERSITE DE BORDEAUX	UBO	France		
80	UNIVERSITEIT ANTWERPEN	UA	Belgium		
81	UNIVERSITETET I OSLO	UiO	Norway		
82	UNIVERSITY COLLEGE LONDON	UCL	United Kingdom		
83	UPPSALA UNIVERSITET	UU	Sweden		
84	WEIZMANN INSTITUTE OF SCIENCE	WEIZMANN	Israel		
85	TECHNISCHE UNIVERSITAT DARMSTADT	TUDA	Germany		
86	UNIVERSITE DE GENEVE	UNIGE	Switzerland		12/12/2020
87	UNIVERSITY OF GLASGOW	UGLA	United Kingdom	01/04/2016	
88	MEDICAL RESEARCH COUNCIL	MRC	United Kingdom	01/04/2016	03/10/2017
89	UNIVERSITAET HAMBURG	UHAM	Germany	01/04/2016	
90	HUMBOLDT-UNIVERSITAET ZU BERLIN	UBER	Germany	01/04/2016	
91	KONINKLIJKE NEDERLANDSE AKADEMIE VAN WETENSCHAPPEN - KNAW	KNAW	Netherlands	01/04/2016	

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry date[8]	Project exit date
92	ISTITUTO NAZIONALE DI FISICA NUCLEARE	INFN	Italy	01/04/2016	
93	CONSORCI INSTITUT D'INVESTIGACIONS BIOMEDIQUES AUGUST PI I SUNYER	IDIBAPS	Spain		
94	UNIVERSITA DEGLI STUDI DI MILANO	UMIL	Italy	01/04/2016	
95	FUNDACIO INSTITUT DE BIOENGINYERIA DE CATALUNYA	IBEC	Spain	01/04/2016	
96	ISTITUTO SUPERIORE DI SANITA	ISS	Italy	01/04/2016	
97	UNIVERSITE DE LIEGE	ULG	Belgium	01/04/2016	
98	UNIVERSITEIT VAN AMSTERDAM	UvA	Netherlands	01/04/2016	
99	DEUTSCHES ZENTRUM FUR NEURODEGENERATIVE ERKRANKUNGEN EV	DZNE	Germany	01/04/2016	
100	THE UNIVERSITY OF SHEFFIELD	USFD	United Kingdom	01/04/2016	
101	UNIVERSITY OF THE WEST OF ENGLAND, BRISTOL	UWE	United Kingdom	01/04/2016	
102	UNIVERSITY OF SURREY	SURREY	United Kingdom	01/04/2016	12/12/2020
103	TAMPEREEN KORKEAKOULUSAATIO SR	TUT	Finland		
104	UNIVERSITY OF LEEDS	ULEEDS	United Kingdom	01/04/2016	12/12/2020
105	SORBONNE UNIVERSITE	SUxUPMC	France		12/12/2020
106	THE UNIVERSITY OF SUSSEX	UoS	United Kingdom	01/04/2016	
107	MIDDLESEX UNIVERSITY HIGHER EDUCATION CORPORATION	MU	United Kingdom	01/04/2016	12/12/2020
108	UNIVERSITE LYON 1 CLAUDE BERNARD	UCBL	France	01/04/2016	
109	POLITECNICO DI TORINO	POLITO	Italy	01/04/2016	
110	UNIVERSITEIT GENT	UGent	Belgium	01/04/2016	
111	KATHOLIEKE UNIVERSITEIT LEUVEN	KUL	Belgium	01/04/2016	
112	UNIVERSITAT BASEL	UNIBAS	Switzerland	01/04/2016	
113	STICHTING VU	VU	Netherlands	01/04/2016	
114	SIB INSTITUT SUISSE DE BIOINFORMATIQUE	SIB	Switzerland	01/04/2016	12/12/2020
115	FONDAZIONE EUROPEAN BRAIN RESEARCHINSTITUTE RITA LEVI	EBRI	Italy	01/04/2016	12/12/2020
116	SCUOLA NORMALE SUPERIORE	SNS	Italy	01/04/2016	12/12/2020

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry date[8]	Project exit date
117	UNIVERSITEIT MAASTRICHT	UM	Netherlands	01/04/2016	
118	THE UNIVERSITY OF HERTFORDSHIRE HIGHER EDUCATION CORPORATION	HERTS	United Kingdom	01/09/2016	
119	UNIVERSITATSKLINIKUM BONN	UKB	Germany	01/06/2018	12/12/2020
120	IDRYMA IATROVIOLOGIKON EREUNON AKADEMIAS ATHINON	BRFAA	Greece	01/05/2018	
121	CONVELOP - COOPERATIVE KNOWLEDGE DESIGN GMBH	CONVELOP	Austria	01/04/2018	
122	CHARITE - UNIVERSITAETSMEDIZIN BERLIN	Charite	Germany	01/04/2018	
123	EUROPEAN MOLECULAR BIOLOGY LABORATORY	EMBL	Germany	01/07/2018	
124	SICHH SWISS INTEGRATIVE CENTER FOR HUMAN HEALTH SA	SICHH	Switzerland	01/04/2018	
125	UNIVERSITE GRENOBLE ALPES	UGA	France		
126	CENTRE HOSPITALIER UNIVERSITAIRE DE GRENOBLE	CHUGA	France	01/04/2018	
127	UNIVERSITAETSKLINIKUM FREIBURG	UKLFR	Germany	01/04/2018	
128	L'AZIENDA SOCIO SANITARIA TERRITORIALE (ASST) GRANDE OSPEDALE METROPOLITANO NIGUARDA	CERCE	Italy	01/04/2018	12/12/2020
129	UNIVERSITATSMEDIZIN GREIFSWALD KORPERSCHAFT DES OFFENTLICHEN RECHTS	UMG	Germany	01/04/2018	12/12/2020
130	UNIVERSITAT TRIER	UT	Germany	01/12/2018	
131	CENTRE HOSPITALIER REGIONAL ET UNIVERSITAIRE DE LILLE	CHULILLE	France	01/12/2018	
132	HOCHSCHULE STRALSUND	HOST	Germany	15/06/2019	
133	ATHINA-EREVNITIKO KENTRO KAINOTOMIAS STIS TECHNOLOGIES TIS PLIROFORIAS, TON EPIKOINONION KAI TIS GNOSIS	ATHENA	Greece	01/09/2019	
134	ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE	EPFL	Switzerland		
135	FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA	IIT	Italy	01/10/2020	
136	POLITECNICO DI MILANO	POLIMI	Italy	01/10/2020	
137	UNIVERSITA DEGLI STUDI DI NAPOLI FEDERICO II	UNINA	Italy	01/10/2020	

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry date[8]	Project exit date
138	CENTRE HOSPITALIER REGIONAL DE MARSEILLE ASSISTANCE PUBLIQUE-HOPITAUX MARSEILLE	APHM	France	01/10/2020	
139	UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA	UNIROMA1	Italy	01/10/2020	
140	GEORG-AUGUST-UNIVERSITAT GOTTINGEN STIFTUNG OFFENTLICHEN RECHTS	UGOE	Germany	01/10/2020	
141	ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM	EMC	Netherlands	01/10/2020	
142	SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI DI TRIESTE	SISSA	Italy	01/10/2020	
143	MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN EV	MPIEA	Germany	01/10/2020	
144	INGLOBE TECHNOLOGIES SRL	INGLOBE	Italy	01/06/2021	
145	AI2LIFE SRL	AI2LIFE	Italy	01/06/2021	
146	ROBOTNIK AUTOMATION SLL	ROB	Spain	01/06/2021	
147	BIOMAX INFORMATICS AG	BIOMAX	Germany	01/06/2021	
148	ALPINE INTUITION SARL	AIS	Switzerland	01/06/2021	
149	AUTONOMYO SARL	AUTONOMYO	Switzerland	01/06/2021	
150	BIT & BRAIN TECHNOLOGIES SL	BITBRAIN	Spain	01/06/2021	
151	GENERAL EQUIPMENT FOR MEDICAL IMAGING SA	OCV	Spain	01/05/2021	
152	UNIVERSITA DEGLI STUDI DI TORINO	UNITO	Italy	01/12/2021	

1. Project number

The project number has been assigned by the Commission as the unique identifier for your project. It cannot be changed. The project number **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

2. Project acronym

Use the project acronym as given in the submitted proposal. It can generally not be changed. The same acronym **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

3. Project title

Use the title (preferably no longer than 200 characters) as indicated in the submitted proposal. Minor corrections are possible if agreed during the preparation of the grant agreement.

4. Starting date

Unless a specific (fixed) starting date is duly justified and agreed upon during the preparation of the Grant Agreement, the project will start on the first day of the month following the entry into force of the Grant Agreement (NB : entry into force = signature by the Commission). Please note that if a fixed starting date is used, you will be required to provide a written justification.

5. Duration

Insert the duration of the project in full months.

6. Call (part) identifier

The Call (part) identifier is the reference number given in the call or part of the call you were addressing, as indicated in the publication of the call in the Official Journal of the European Union. You have to use the identifier given by the Commission in the letter inviting to prepare the grant agreement.

7. Abstract

8. Project Entry Month

The month at which the participant joined the consortium, month 1 marking the start date of the project, and all other start dates being relative to this start date.

9. Work Package number

Work package number: WP1, WP2, WP3, ..., WPn

10. Lead beneficiary

This must be one of the beneficiaries in the grant (not a third party) - Number of the beneficiary leading the work in this work package

11. Person-months per work package

The total number of person-months allocated to each work package.

12. Start month

Relative start date for the work in the specific work packages, month 1 marking the start date of the project, and all other start dates being relative to this start date.

13. End month

Relative end date, month 1 marking the start date of the project, and all end dates being relative to this start date.

14. Deliverable number

Deliverable numbers: D1 - Dn

15. Type

Please indicate the type of the deliverable using one of the following codes:
R	Document, report
DEM	Demonstrator, pilot, prototype
DEC	Websites, patent fillings, videos, etc.
OTHER	
ETHICS	Ethics requirement
ORDP	Open Research Data Pilot
DATA	data sets, microdata, etc.

16. Dissemination level

Please indicate the dissemination level using one of the following codes:
  PU   Public
  CO   Confidential, only for members of the consortium (including the Commission Services)
  EU-RES Classified Information: RESTREINT UE (Commission Decision 2005/444/EC)
  EU-CON Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC)
  EU-SEC Classified Information: SECRET UE (Commission Decision 2005/444/EC)

17. Delivery date for Deliverable

Month in which the deliverables will be available, month 1 marking the start date of the project, and all delivery dates being relative to this start date.

18. Milestone number

Milestone number:MS1, MS2, ..., MSn

19. Review number

Review number: RV1, RV2, ..., RVn

20. Installation Number

Number progressively the installations of a same infrastructure. An installation is a part of an infrastructure that could be used independently from the rest.

21. Installation country

Code of the country where the installation is located or IO if the access provider (the beneficiary or linked third party) is an international organization, an ERIC or a similar legal entity.

22. Type of access

  TA-uc if trans-national access with access costs declared on the basis of unit cost,
  TA-ac if trans-national access with access costs declared as actual costs, and
  TA-cb if trans-national access with access costs declared as a combination of actual costs and costs on the basis of unit cost,
  VA-uc if virtual access with access costs declared on the basis of unit cost,
  VA-ac if virtual access with access costs declared as actual costs, and
  VA-cb if virtual access with access costs declared as a combination of actual costs and costs on the basis of unit cost.

23. Access costs

Cost of the access provided under the project. For virtual access fill only the second column. For trans-national access fill one of the two columns or both according to the way access costs are declared. Trans-national access costs on the basis of unit cost will result from the unit cost by the quantity of access to be provided.

The Human Brain Project - Framework Partnership Agreement (HBP-FPA): Amendment 12

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List of Figures

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Evolution of the Consortium and Third Parties

The HBP FPA Consortium originally included 86 Partners.

Amendment 1 (signed by EC on 12 July 2016)

During the preparation of the SGA1 work plan, there were a number of changes in the Consortium composition as described below.

- 15 Partners were added through the Call for Expression of Interest on Systems and Cognitive Neuroscience, organised between May and July 2015:
  - P87: UGLA (University of Glasgow)
  - P88: MRC (Medical research Council)
  - P89: UHAM (University of Hamburg)
  - P90: UBER (Humboldt-Universitaet zu Berlin)
  - P91: KNAW (Koninklijke Nederlandse Akademie van Wetenschappen – Knaw)
  - P92: INFN (Istituto Nazionale di Fisica Nucleare)
  - P93: IDIBAPS (Consorci Institut d'Investigacions Biomediques August Pi i Sunyer)
  - P94: UMIL (Universita Degli Studi Di Milano)
  - P95: IBEC (Fundacio Institut de Bioenginyeria de Catalunya)
  - P96: ISS (Istituto Superiore di Sanita)
  - P97: ULG (Universite de Liege)
  - P98: UvA (Universiteit van Amsterdam)
  - P99: DZNE (Deutsches Zentrum fuer Neurodegenerative Erkrankungen)
  - P100: USFD (University of Sheffield)
  - P101: UWE (University of the West of England, Bristol)
- 16 additional partners are returning from the Ramp-Up Phase. This will allow continuity between the phases:
  - P102: SURREY (University of Surrey): SURREY was a partner in the HBP Ramp-Up Phase. SURREY will continue to have an active role in the SGA1 under T4.3.3: Functional plasticity for multi-compartment neurons.
  - P103: TUT (TTY-Saatio): TUT was a partner in the HBP Ramp-Up Phase. TUT will continue to have an active role in the SGA1 under T4.2.2: Network models including neuron-glia interactions.
  - P104: ULEEDS (University of Leeds): ULEEDS was a partner in the HBP Ramp-Up Phase. ULEEDS will continue to have an active role in the SGA1 under T4.1.3: Mean-field and population models.
  - P105: UPMC (Universite Pierre et Marie Curie - Paris 6): UPMC was a partner in the HBP Ramp-Up Phase. UPMC will continue to have an active role in the SGA1 under T4.4.2: Models of low-level vision.
  - P106: UoS (University of Sussex): UoS was a partner in the HBP Ramp-Up Phase (Application subproject). UoS will continue being part of the Neuromorphic Platform as early users and will have a role in T9.5.3: Platform coordination.
  - P107: MU (Middlesex University Higher Education Corporation): MU was a partner in the HBP Ramp-Up Phase (Application subproject). MU will continue being part of the Neuromorphic Platform as early users and will have an active role in T9.5.3: Platform coordination and T9.5.4: Platform application.

- o P108: UCBL (Universite Lyon 1 Claude Bernard): UCBL was a partner in the HBP Ramp-Up Phase. UCBL will continue to have an active role in the SGA1 under T2.5.3 Human intracranial electrophysiology data and tools.

- o P109: POLITO (Politecnico di Torino): POLITO was a partner in the HBP Ramp-Up Phase. POLITO will continue being part of SP9 with an active role in the SGA1 under T9.3.2: Next generation system development (Software) and T9.5.3: Platform coordination.

- o P110: UGENT (Universiteit Gent): The first periodic review of the HBP Ramp-Up Phase recommended strengthening physical robotics. Therefore, UGENT, a partner in the Ramp-Up Phase, will have an active role in SGA1 under T10.4.5: Real-time robot control with reservoir networks.

- o P111: KUL (Katholieke Universiteit Leuven): KUL was a partner in the HBP Ramp-Up Phase. KUL will continue to have an active role in the SGA1 under T2.4.1 Multi-scale processing in space, time and frequency and T2.7.1 Ethics and Innovation.

- o P112: UNIBAS (Universitat Basel): UNIBAS was a partner in the HBP Ramp-Up Phase. UNIBAS will continue to have an active role in the SGA1 under T2.1.1 Imaging Genomics of the Human Brain.

- o P113: VU (Stichting VU-VUMC): VU was a partner in the HBP Ramp-Up Phase. VU will continue to have an active role in the SGA1 under T1.2.2: Cell Types, Synapses, and their Quantitative Characterisation in the Human Brain; T2.2.2: Cell types, synapses, and their quantitative characterization in the human brain and T2.2.6: Morphological and functional connectivity of human cortical microcircuits.

- o P114: SIB (Institut Suisse de Bioinformatiquefondation ISB): SIB was a partner in the HBP Ramp-Up Phase. SIB will continue to have an active role in the SGA1 under Active role in T1.1.5: K Channel Kinetics: Modulation of action potential propagation by K channels.

- o P115: EBRI (European Brain Research Institute Rita Levi-Montalcini Fondazione EBRI): EBRI was a partner in the HBP Ramp-Up Phase. EBRI will continue to have an active role in the SGA1 under Proposed active role in SGA1 under T1.1.2: Exploiting the IACT antibody platform the isolation of small antibody domains for next generation brain imaging and mapping and T1.1.4: Generation of In Vivo Functional Data on Interactions Between Neuroligin and Neuroxin Synaptic Proteins, and their Use for Computational Modelling of Trans-synaptic Signalling.

- o P116: SNS (Scuola Normale Superiore): SNS was a partner in the HBP Ramp-Up Phase. SNS will continue to have an active role in the SGA1 under T1.1.2: Exploiting the IACT antibody platform the isolation of small antibody domains for next generation brain imaging and mapping and T1.1.4: Functional in vivo interaction data between synaptic proteins of the neuroligin and the neuroxin families, and their use for the computational modelling of trans-synaptic signalling.

- o P117: UM (Universiteit Maastricht): UM was a partner in the HBP Ramp-Up Phase. UM will continue to have an active role in the SGA1 under T2.4.2: The role of attention in perception and learning; T2.4.4: Development of an Empirically-Derived Brain Atlas on Sensorimotor Integration and T2.6.5: Co-design of the HBP atlas based Big Data Analytics.

- P58: UCAM (University of Cambridge) withdrew from the HBP Consortium on 30 June 2016 for the following reasons: The PI considered that resources were not in line with requested project deliverables; increased workload requirement by the HBP ethics requirements; assessment complicated by non-EU country involvement. In addition, the PI could not apply for new HBP research grant funding for research work expansion as they were already an HBP member. No mitigation of risk was necessary as no project budget was allocated in SGA1.

- Inclusion of the following linked third parties:

- o Cyberbotics Sarl (CYBER), linked to P1 EPFL.

- o Hospital Clinic I Provincial de Barcelona (HCPB), linked to P93 IDIBAPS.

- o Centre Hospitalier Universitaire de Liege (ULG), linked to P97 ULG.

- o Institut National de la Sante et de la Recherche Medicale (INSERM), linked to P105 SUxUPMC.

- o University Hospital Basel (USB), linked to P112 UNIBAS.

- P118: HERTS (The University of Hertfordshire) inclusion as of 1 September 2016 due to the move of a Principal Investigator (PI) from the University of Sussex (P106 UoS) to HERTS.

- Inclusion of Institut National de la Sante et de la Recherche Medicale (INSERM), linked to P108 UCBL.

Amendment 3 (signed by EC on 27 November 2017)

- P88: MRC (Medical research Council) termination as of 30 June 2017 due to a move of the Principal Investigator (PI) Nikolaus KRIEGESKORTE. The work planned by MRC in the remainder of SGA1 is taken over by UGLA (T3.1.1 and T3.1.5), UvA (T3.3.3 and T3.5.3) and UBER (T3.1.4)

- P16: DMU (Montfort University) removal of Third Parties (subcontracting section for Ombudsperson). SP12 decided to not have a permanent Ombudsperson via subcontracting, since it may not be used, considering that the governing structures in HBP have been increased and fine-tuned, which reduces the breadth of issues that the Ombudsperson will be needed for. The Ombudsperson SOP will be revised to reflect the changing role. It will include rules about the selection of and interaction with an Ombudsperson. All SP12 partners agree to this solution and all are willing to contribute to the costs of activating the Ombudsperson if needed.

- P20: JUELICH (Forschungszentrum Jülich GmbH) had Institute for Research in Biomedicine Barcelona (IRB) listed as a Third Party (in kind contributions against payment not used on partner's premises) since the beginning of SGA1 (April 2016); it is therefore added here to align with SGA1.

- P27: CHUV (Hospices Cantonaux CHUV) inclusion of four hospitals as Third Parties (in kind contributions against payment not used on partners' premises) in the context of the MIP demo sites:

  o ASST Grande Ospedale Metropolitano Niguarda – Milan

  o University Hospital – CHU Lille

  o Universitätsklinikum Freiburg

  o Tel Aviv Sourasky Medical Center (Israel)

  Further details can be found in Appendix 6: Consortium Partners' Third Parties.

- P42: MUI (Medizinische Universitat Innsbruck) removal of Third Parties (in kind contributions free of charge) as they were referring to financial support to third parties, which is not applicable in SGA1 (Art.13). These collaborations with external institutions and NGO's are now described in Section 2.2.2.3.6 Contributions to Education and Training section.

- P87: UGLA (University of Glasgow) inclusion of Third Party (Subcontracting) to compensate the loss of expertise resulting from MRC withdrawal. In order to avoid delays, a competitive tender process will take place in SGA1 and may continue in SGA2.

- P112: UNIBAS (Universitaet Basel) inclusion of Third Party (subcontracting) for the lab work to provide the necessary robotics and devices for processing of the SNP-Chips and methylation Chips.

Amendment 4 (signed by the EC on 9 July 2018)

Following the Calls for Expression of Interest for SGA2 (non-MIP related), four new beneficiaries joined the HBP consortium:

- P119: UKB (Universitätsklinikum Bonn); winning Proposal of the CEoI on "Comparative single cell analyses of principal neurons and Interneurons in mice and humans".

- P120: BRFAA (BIOMEDICAL RESEARCH FOUNDATION, ACADEMY OF ATHENS) winning Proposal of the CEoI on "Modelling allosteric drugs" for CDP6 in SP8.

- P121: CONVELOP (convelop cooperative knowledge design gmbh); winning Proposal of the CEoI on "Coordination of gender equality activities".

- P122: CHARITE (Charité Universitätsmedizin Berlin); winning Proposal of the CEoI on "Co-designing the HBP digital infrastructure for advancing the understanding of multilevel brain organisation" for CDP8.

Several existing beneficiaries have new teams joining, following the Calls for Expression of Interest for SGA2 (non-MIP related).

One new beneficiary joined due to the move of a Principle Investigator.

- P123: EMBL (European Molecular Biology Laboratory) inclusion as of 1 July 2018 due to the move of a Principal Investigator (PI) from the Ruprecht-Karls Universität Heidelberg (P47 UHEI) to EMBL.

A new Director General has been nominated.

Amendment 5 (signed by the EC on 19 December 2018)

Following the MIP Calls for Expression of Interest for SGA2, six new beneficiaries joined the HBP consortium:

- P124: SICHH (Swiss Integrative Center for Human Health); winning Proposal of the CEoI on "Testing pathophysiological models of brain diseases".
- P125: UGA (Universite Grenoble Alpes); winning Proposal of the CEoI on "Federated analysis of human intracerebral stimulation and recording data".
- P126: CHUGA (Centre Hospitalier Universitaire Grenoble Alpes); winning Proposal of the CEoI on "Federated analysis of human intracerebral stimulation and recording data".
- P127: (UKLFR Epilepsiezentrum, Universitätsklinikum Freiburg, University Medical Center); winning Proposal of the CEoI on "Federated analysis of human intracerebral stimulation and recording data".
- P128: CERCE (ASST Grande Ospedale Metropolitano Niguarda Ca'Granda); winning Proposal of the CEoI on "Federated analysis of human intracerebral stimulation and recording data".
- P129: UMG (Medical University Greifswald); winning Proposal of the CEoI on "Testing pathophysiological models of brain diseases".

Several existing beneficiaries have new teams joining, following the MIP Calls for Expression of Interest for SGA2: P12 CNR, P22 FG, P38 KCL, P73 UKAACHEN, P78 AMU, P108 UCBL, P122 CHARITE

Two new beneficiaries have also joined the HBP Consoritum:

- P130: UT (University of Trier), as of 1st of December due to the move of a Principle Investigator from P46 RWTH
- P131: CHULILLE (Centre Hospitalier Universitaire de Lille). The selection process is already approved by the DIR, the SB and the EC

Alignment of third parties as per SGA2 Amendment 1 (see Appendix 6), particularly, the inclusion of the following linked third parties:

- Institut National de la Sante et de la Recherche Medicale (INSERM), linked to P78 AMU and to P125 UGA

Amendment 6 (signed by the EC on 26 November 2019)

Changes in the HBP Consortium:

- P61: UABER (The University Court of The University of Aberdeen) Termination as of 1st January 2019 (inactive partner in SGA2)
- P132: HOST (Hochschule Stralsund) Addition of new partner due to the move of a Principal Investigator (PI) from the University of Surrey – UK (P102 SURREY) to HOST - GE
- P133: ATHENA (Athena Research and Innovation Center) Addition of new partner approved by the DIR and SIB

Appendix 5 – HBP Core Project Partner Details: partners updates

Appendix 6 - Third parties updates:

- P27 CHUV – new subcontracting

- P68 UPM – new in-kind contributions provided by third parties against payment - Fundación General UPM
- P117 UM – new subcontracting

Amendment 7 (signed by the EC on 2 March 2020)

Changes in the HBP Consortium:

- P134: EBRAINS (EBRAINS) Addition of new partner to be the future Coordinator of the HBP.

Amendment 8 (signed by the EC on 11 August 2020)

Changes in the HBP Consortium: Following the 1st round of CEoI for SGA3, several new partners, third parties and units from existing partners are added:

- List of CEoI:
  - 1: "Validation and Interference"
  - 3: "Whole-brain multi-parametric imaging using invasive and non-invasive recordings"
  - 4: "Rodent micro-circuits"
  - 5: "Data and models for studying the neural basis of cognition"
  - 6: "Data and models for the understanding of consciousness"
  - 10: "Preparing Cellular-Level Models for Portable HPC Simulation using Arbor"
- P135: IIT (Fondazione Istituto Italiano di Tecnologia) – CEoI 1
- P136: POLIMI (Politecnico di Milano) – CEoI 4
- P137: UNINA (University of Naples Federico II) – CEoI 4
- P138: APHM (Assistance Publique – Hôpitaux de Marseille) – CEoI 3
- Third Party: in kind contributions against payment (PVM)
- P139: UNIROMA1 (Sapienza University) – CEoI 5
- P140: UGOE (University of Goettingen) – CEoI 10
- P141: EMC (Erasmus Medical Center) – CEoI 10
- P142: SISSA (Scuola Internazionale Superiore di Studi Avanzati) – CEoI 10
- P143: MPIEA (Max Planck Society) – CEoI 6
- New units from existing partners: P10 CNRS (new unit) and Linked Third Party: Université Paris-Sarclay, P11 CEA (new unit), P29 ICM (new unit) and Linked Third Party: INSERM, P76 UB (new unit) and Third party: in-kind contributions free of charge (UGH), P77 UPF (new unit) and Third party: subcontracting, P78 AMU (new units), P111 KUL (new unit).

Note: leaving dates below are dates indicated by the organisations, but the official date is the date of submission of the amendment as implementable by the participant portal.

- P72: UNIBI (Universität Bielefield) Termination as of 1st June 2020 (inactive partner in SGA3).
- Linked Third Parties' updates as per SGA3:
  - CYBER (Cyberbotics Sarl) – P1 EPFL. Termination as of 31st April 2020.
  - ULH (Centre Hospitalier Universitaire de Liege) – P97 ULG. Termination as of 31st April 2020.
  - INSERM (Institut National de la Sante et de la Recherche Medicale) - P105 SUxUPMC. Termination as of 31st March 2020.
  - INSERM (Institut National de la Sante et de la Recherche Medicale) - P125 UGA. Termination as of 31st May 2020.

- Existing active third parties updated accordingly.

- Work Plan (Section 2.3.1) updated to reflect change from Subproject structure in SGA1 & SGA2 to one based on Work Packages in SGA3.

- Governance update for aligment with SGA3 and transition to EBRAINS.

- Renaming and merging the Scientific and Clinical Advisory Boards (SAB and CAB) into the Science and Infrastructure Board (SIAB).

Amendment 9 (signed by the EC on 17 December 2020)

Changes in the HBP Consortium: Following the EC willingness to update the HBP Consortium and in the context of the amendment to the Consortium Agreement and the inclusion of the standard contractual clauses (SCCs) for Brexit, we have taken the opportunity to revise the HBP Consortium in its last phase and invite inactive partners to withdraw.

Withdrawals: due to lack of active role in the last phase of the HBP (SGA3)

- P2 AALTO, Aalto Korkeakizlusaatio SR (Finland)

- P6 BAUW, Bauhaus-Universitaet Weimar (Germany)

- P8 BSMJ, Bloomfield Science Museum Jerusalem (Israel)

- P9 CF, Cardiff Universtiy (United Kingdom)

- P15 UoD, Debreceni Egyetem (Hungary)

- P23 FCHAMP, Fundação Anna de Sommer Champalimaud e Dr. Carlos Montez Champalimaud (Portugal)

- P25 UH, Helsingin yliopisto (Finland)

- P31 IST, Institute of Science and Technology Austria (Austria)

- P32 JSI, Institut Jozef Stefan (Slovenia)

- P35 UFRA, Johann Wolfgang Goethe-Universität Frankfurt am Main (Germany)

- P36 KIT, Karlsruher Institut für Technologie (Germany)

- P45 OFAI, Österreichische Studiengesellschaft für Kybernetik (Austria)

- P48 SU, Sabanci University (Turkey)

- P53 TUC, Polytechnio Kritis (Greece)

- P75 UZH, Universität Zürich (Switzerland)

- P86 UNIGE, Université de Genève (Switzerland)

- P102 SURREY, University of Surrey (United Kingdom)

- P104 ULEEDS, University of Leeds (United Kingdom)

- P105 SUxUPMC, Sorbonne Université (France)

- P107 MU, Middlesex University Higher Education Corporation (United Kingdom)

- P114 SIB, Institut Suisse de Bioinformatique (Switzerland)

- P115 EBRI, European Brain Research Institute Rita Levi-Montalcini (Italy)

- P116 SNS, Scuola Normale Superiore (Italy)

- P119 UKB, Universitätsklinikum Bonn (Germany)

- P128 CERCE, l'Azienda Socio – Sanitaria Territoriale (ASST) Grande Ospedale Metropolitano Niguarda (Italy)

- P129 UMG, Universitätsmedizin Greifswald Körperschaft des Öffentlichen Rechts (Germany)

Third parties updates:

- P57 TAU: use of in-kind contributions provided by third parties against payment (TASMC)
- P122 CHARITE: subcontracting

Amendment 10 (signed by the EC on 9 March 2021)

Changes in the HBP Consortium:

- Change of Coordinator from EPFL to EBRAINS, as of 1 March 2021. EPFL changes Partner number from P1 to P134 and EBRAINS from P134 to P1 (automatic change, as Coordinator must be P1).

Amendment 11 (signed by the EC on 16 June 2021)

Changes in the HBP Consortium:

- New partners and new units are added via CEoI Application of functional architectures supporting advanced cognitive functions to address AI and automation problems of industrial and commercial relevance:
  - P12 CNR
  - P68 UPM
  - P135 IIT
  - P144 INGLOBE
  - P145 AI2LIFE
  - P146 ROB
- New unit added via CEoI High-level neuro-symbolic processing for guidance of goal-directed behaviour:
  - P51 SKU
- New partners added via CEoI Engagement of Industry, SMEs and start-ups:
  - P147 BIOMAX
  - P148 AIS
  - P149 AUTONOMYO
  - P150 BITBRAIN
  - P151 OCV

Other changes (EC Requests):

- Removal of references to SGA4
- Appendix 5: HBP Core Project Partner Details – Partners short descriptions revised, units' descriptions and key personnel moved to SGA3
- Appendix 6: HBP Beneficiaries' Third Parties: moved to SGA3 (only Linked Third Parties remain in the FPA)

Amendment 12

Changes in the HBP Consortium:

- Following the 3rd round of CEoI for SGA3, one new partner and new units from existing Partners are added for the CEoI "COVID-19 and its impact on the brain and mental health":
  - P20 JUELICH (existing unit)
  - P26 HITS (existing unit)
  - P70 UNIPV (new unit and existing unit)*

*UNIPV is involved in the two selected proposals from the CEoI "COVID-19 and its impact on the brain and mental health"

Other changes (EC requests):

- Removal of references to SGA4

- Removal of the counting of terminated Partners

- Addition of cross references between SPs' tables of Main Objectives / Deliverables per SGA

2.1 Excellence

2.1.1 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.

2.1.2 Concept and Objectives

2.1.2.1   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 organisation 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 visualisation 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.

2.1.2.2   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: 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.
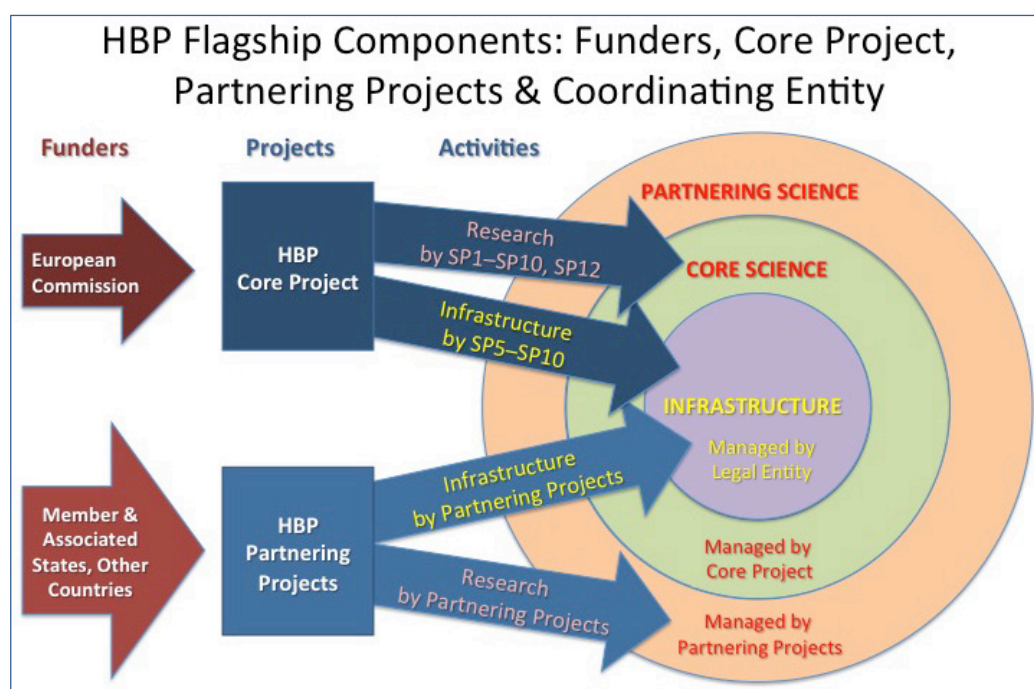
Figure 1: HBP Flagship Components

2.1.2.3   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.

2.1.2.3.1   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.

2.1.2.4   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.

2.1.2.5   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.

2.1.2.6   Actions foreseen under this FPA to achieve the objectives

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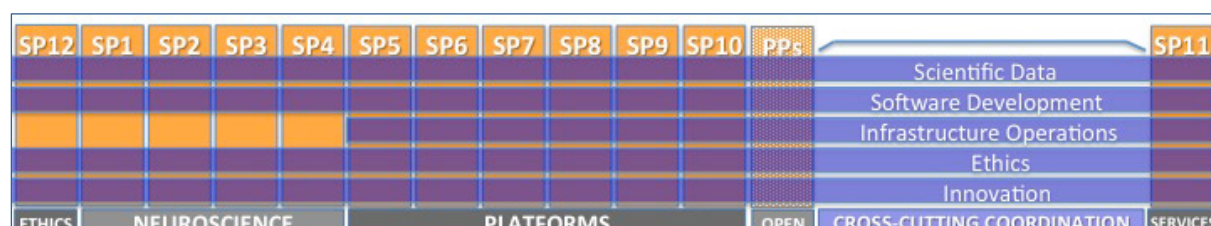
Figure 2: HBP Activity Clusters: Scientific Research, Software Development & Infrastructure Operations

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 – Management and Coordination) 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 2.1.2.7).

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, but they also underline the increased importance attached to the Project's role as a provider of European scientific research infrastructure.

2.1.2.6.2   Management and Coordination

SP11 (Management and Coordination) 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.

2.1.2.7   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 organised 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 organisation 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.

2.1.2.7.1 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 2.1.2.7) 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:

Table 1: Structure of the different service components in the Research Infrastructure.

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			

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 Section 2.3.2.14). For example, the Scientific Coordination 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.

2.1.2.7.2   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 harmonised with the specific needs of established co-design activities, user programmes and software service support efforts in following SGAs.

2.1.2.8   Gender Balance in the HBP

2.1.2.8.1   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).

2.1.2.8.2 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 studied (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

2.2.1 Expected 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 several HBP platforms.

IMP 3.5: Experimental and computational characterisation 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 Section 2.3.2.6) from executive direction (by the Directorate – see Section 2.3.2.5), from overall supervision and confirmation of resource allocation (by the Stakeholder Board – see Section 2.3.2.3), and also from supervisory auditing and control (via the Audit Committee – see Section 2.3.2.12). 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 Section 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 Science and Infrastructure Advisory Board (SIAB – see Section 2.3.2.9.2).

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 Section 2.3.2.3), once the HBP Legal Entity (see Section 2.3.2.4) is created.

At the implementation level, the HBP's Project Coordination Office (PCO – see Section 2.3.2.7) 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 2.1.2.7.2) 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 Section 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 2.3.2.9.2). 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 Section 2.3.2.7) 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 authorised 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 Section 2.3.2.7) 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

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 2.2.1 and 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 Section 2.3.2.5).

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, maximising 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 Science and Infrastructure Advisory Board (SIAB – see Section 2.3.2.9.2). 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 Section 2.3.2.4).

The main objective of the innovation management framework is to help the Flagship to document, assess and govern results, and maximise 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 Software, Infrastructure and Scientific 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.
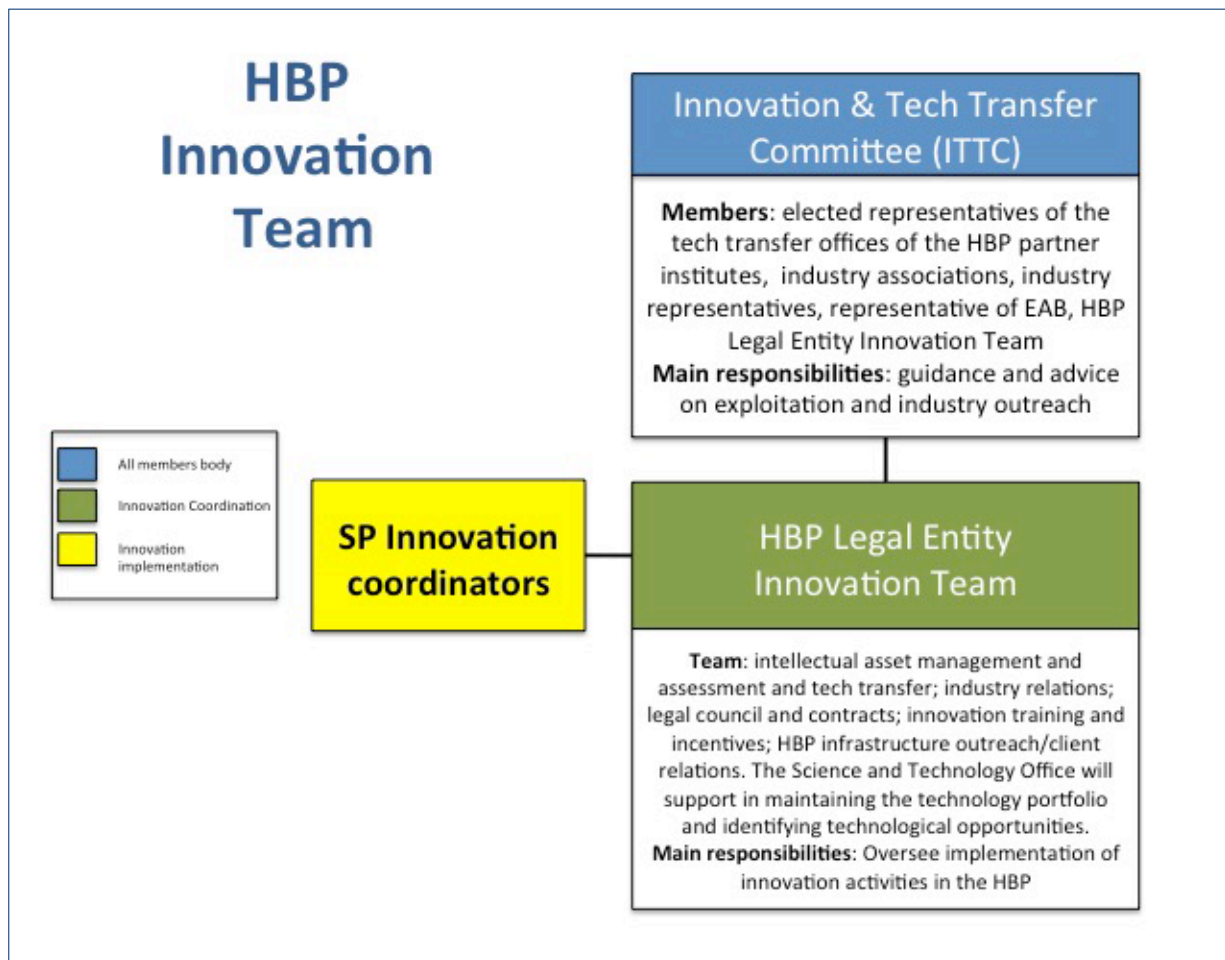
Figure 3: The Innovation Team

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 organising 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 Software, Infrastructure and Scientific 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 2.3.2.14)

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.

Table 2: Timeframe for Implementation of HBP Innovation Support Activities

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

SGA	Governance	Infrastructure	Innovation Support	Specific Activities
			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

SGA	Governance	Infrastructure	Innovation Support	Specific Activities
			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

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.

Collaborations with HBP Partners, and external institutions and NGO's, are essential to carry out the tasks to which MUI is contractually bound. Those cooperations include actively integrating external institutions and NGO's to education programme activities. This may be adding a representative of the aforementioned as speakers to an educational event, to jointly organise an event such as for example at FENS meetings or by helping members of external institutions and NGO's getting access to HBP Education Programme activities. Vice versa, NGO's and external institutions are helping the HBP Education programme with the promotion of its activities via their networks which can be seen as beneficial for the whole HBP.

Curriculum

The new EP academic curriculum comprises five separate courses. It includes detailed user material, mandatory lectures and workshops on innovation (including responsible innovation) for all young researches participating in HBP-related research. Formal examinations and a multi-university certification process are planned. Teaching will be based on innovative forms of online education, in

which online lectures are complemented by face-to-face workshops. The courses are being developed and taught by senior scientists from within and outside the Project. The commitment of the Course Directors and associated teachers will be supported by a limited financial contribution from the EP budget. The courses 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. Course 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. Advanced schools 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 2.3.2.7) 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 Student Conference to the student with the best poster.

The HBP Curriculum and respective courses 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

2.3.1.1 Work Plan in SGA3

In order to improve focus and efficiency in SGA3, the HBP switched from a Work Plan based around 12 discipline-based Subprojects (described below) and eight cross-disciplinary Co-Design Projects to one based on nine cross-disciplinary Work Packages. The rationale for the change is given in the SGA3 Grant Agreement in Section 1.4.4 "From SGA2 into SGA3: Change in implementation". See also Section 1.4.5 "How the SGA2 Subprojects relate to the SGA3 Work Packages". The SGA3 Work Packages are:

- WP1: The human multiscale brain connectome and its variability – from synapses to large-scale networks and function

- WP2: Networks underlying brain cognition and consciousness

- WP3: Adaptive networks for cognitive architectures: from advanced learning to neurorobotics and neuromorphic applications

- WP4: EBRAINS Data Services

- WP5: EBRAINS Modelling Services

- WP6: EBRAINS Computing Services

- WP7: Management and Coordination

- WP8: Communication, Outreach and Exploitation

- WP9: Responsible Research and Innovation

Descriptions of the SGA3 Work Packages and their objectives can be found in the SGA3 Grant Agreement, Part A.

Table 3: How SGA1 and SGA2 Subprojects relate to the SGA3 WPs

SGA1/2 SPs vs SGA3 WPs	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9
SP1	X		X						
SP2	X	X	X	X					
SP3		X	X						
SP4	X	X	X	X					
SP5	X			X	X	X			
SP6	X		X		X				
SP7				X	X	X			
SP8	X			X	X				
SP9			X		X	X			
SP10			X		X				
SP11				X		X	X	X	
SP12	X	X	X	X			X		X

2.3.1.2   Work Plan in SGA1 and SGA2

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 organisation 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 organisational principles of spatial and temporal brain architecture. Addressing the multi-scale organisation 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.

2.3.1.3   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 & characterisation 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.

Table 4: Main Objectives / Deliverables per SGA for SP1: Mouse Brain Organisation (= Table 29*)

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, fibre 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 behaviours. Spatial organisation 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 organisation 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.
	M103-M114	Fully integrated multi-level map of the mouse brain including data from the Core Project, Partnering Projects and collaborations

* See cross reference table in Section A1.4.5SP1: Main Objectives / Deliverables per SGA.

2.3.1.4   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 organisation 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 authorised 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

Table 5: Main Objectives / Deliverables per SGA for SP2: Human Brain Organisation (= Table 30*)

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.
	M103-M114	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.

* See cross reference table in Section A1.5.5SP2: Main Objectives / Deliverables per SGA.

2.3.1.5   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 emphasised 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 organisation 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 organisation when brain state changes. Infer properties of awake resting states from the multi-scale organisation 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. Characterise through a perturbational approach the multi-scale organisation (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 dendritic feedback mechanisms for the integration of feedback in rodents 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

Table 6: Main Objectives / Deliverables per SGA* for SP3: Systems and Cognitive Neuroscience
(= Table 31**)

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).
	M103-M114	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.

* Timings for attainment of these objectives are approximate and need to be confirmed by the partners undertaking the work.
** See cross reference table in Section A1.6.4 SP3: Main Objectives / Deliverables per SGA

2.3.1.6   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 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.

- 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.

Table 7: Main Objectives / Deliverables per SGA for SP4: Theoretical Neuroscience (= Table 32*)

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.
	M103-M114	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.

* See cross reference table in Section A1.7.5 SP4: Main Objectives / Deliverables per SGA.

2.3.1.7 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, organised 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

Table 8: Main Objectives / Deliverables per SGA for SP5: Neuroinformatics (= Table 33*)

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

Phase	Months	Main Objective(s) / Deliverable(s)
		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 centres. 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.
	M103-M114	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 centres 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.

* See cross reference table in Section A1.8.5 SP5: Main Objectives / Deliverables per SGA.

2.3.1.8   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 standardise 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

Table 9: Main Objectives / Deliverables per SGA for SP6: Brain Simulation Platform (= Table 34*)

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.
	M103-M114	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.

* See cross reference table in Section A1.9.5 SP6: Main Objectives / Deliverables per SGA.

2.3.1.9   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

Table 10: Main Objectives / Deliverables per SGA for SP7: High-Performance Analytics & Computing Platform (= Table 35*)

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
	M103-M114	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

* See cross reference table in Section A1.10.5 SP7: Main Objectives / Deliverables per SGA.

2.3.1.10   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 harmonising heterogeneous clinical databases, data anonymisation, ontology-based query interfaces, federated search and distributed analysis of clinical data.

- Establish agreements or MoUs, in consultation with authorised representatives of involved HBP Partners, for access to hospital data, centralised 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

Table 11: Main Objectives / Deliverables per SGA for SP8: Medical Informatics Platform (= Table 36*)

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 MIP infrastructure developed in academia to industry for its industrialization, commercialization 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-SGA3 below).

Phase	Months	Main Objective(s) / Deliverable(s)
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.
	M103-M114	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.

* See cross reference table in Section A1.11.5 SP8: Main Objectives / Deliverables per SGA.

2.3.1.11   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

Table 12: Main Objectives / Deliverables per SGA for SP9: Neuromorphic Computing Platform (NM)
(= Table 39*)

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.

Phase	Months	Main Objective(s) / Deliverable(s)
		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)
	M103-M114	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)

* See cross reference table in Section A1.12.5 SP9: Main Objectives / Deliverables, per SGA.

2.3.1.12   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 standardise 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

Table 13: Main Objectives / Deliverables per SGA for SP10: Neurorobotics Platform (= Table 40*)

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.
	M103-M114	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.

* See cross reference table in Section A1.13.5 SP10: Main Objectives / Deliverables per SGA.

2.3.1.13　Subproject 11: Management and Coordination

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

Table 14: Main Objectives / Deliverables per SGA for SP11: Management and Coordination

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-M114	Launch HBP as durable European Research Infrastructure

2.3.1.14   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.

Table 15: Main Objectives / Deliverables per SGA for SP12: Ethics and Society (=Table 41*)

SGA	Deliverable	Due date
SGA1	SP12 first "opinions" report	End of SGA1 Y1
	SP12 second "opinions" report	End of SGA1 Y2
	SP12 first activities report	End of SGA1 Y1
	SP12 second activities report	End of SGA1 Y1
SGA2	SP12 first "opinions" report	End of SGA2 Y1
	SP12 second "opinions" report	End of SGA2 Y2
	SP12 first activities report	End of SGA2 Y1
	SP12 second activities report	End of SGA2 Y1
SGA3	SP12 first "opinions" report	End of SGA3 Y1
	SP12 second "opinions" report	End of SGA3 Y2
	SP12 first activities report	End of SGA3 Y1
	SP12 second activities report	End of SGA3 Y2

* See cross reference table in Section A1.14.5 SP12: Main Objectives / Deliverables per SGA.

2.3.2 Management structures and procedures

2.3.2.1   The FET Flagships Governance Framework

2.3.2.1.1 Board of Funders

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

The role of this Board is essential for defining and planning the financial support for 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 Flagships, with the aim of maximising synergies and helping the Flagships to meet their objectives. They may also focus on the selection and integration mechanisms for bringing PPs into 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 with innovation policies at national and European level.

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

2.3.2.2   HBP Core Project Governance: Underlying Factors and Principles

The HBP governance should ensure a clear "separation of powers", 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. The HBP should ensure that its governance structure is transparent and simple; fairly represents Partner organisations, funders and other stakeholders; and provides adequate accountability to all these parties; as well as including appropriate mechanisms for resolving conflicts.

Described below is the HBP governance structure for the Core Project, in which the principle of "separation of powers" (or system of "checks and balances") is achieved by allocating specific responsibilities to different bodies.

The General Assembly (GA), representing the HBP Partner organisations in the Consortium, was the ultimate decision-making body at the start of SGA1. It was replaced by the Stakeholder Board (SB), which represents the HBP Partner organisations but with one representative for each country. The transfer of overall authority, from the GA to the SB, took place during the first months of SGA1. The SB is therefore now the ultimate decision-making body of the HBP Core Project.

The Science and Infrastructure Board (SIB) represents the scientists and engineers in the project and is a body responsible for scientific decisions and management of the work done in the science and infrastructure WPs. The SIB is responsible for developing a work plan for a given SGA and related budget estimates for the different component activities, and proposing these to the Directorate.

The Directorate (DIR) is responsible for executive management, representation, communication and coordination of the HBP. It prepares and implements the decisions of the SB. The Directorate is led by a Director-General (DG) and includes – amongst other members - the Chair and up to two Vice-Chairs of the Science and Infrastructure Board (SIB). It reviews the work plan and budget proposed by the SIB for achievability and compatibility with the long-term HBP objectives, as set out in the FPA. In the event that it deems external input desirable, for example in case of disparities or incompatible budget estimates, the Directorate will consult with the HBP's external advisory bodies, and then recommend possible solutions to the 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 SB, thereby providing the necessary "separation of powers".

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) at any given time. 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.

The structure of the current HBP governance can be seen in Figure 4 and a summary of the responsibilities of the different governing bodies can be found in the following sub-sections. The operational rules of these governing bodies are further detailed in the FPA Consortium Agreement (FPA CA), the Governance Handbook, and the Terms of Reference and/or Standard Operating Procedures of the various bodies shown in the Figure.
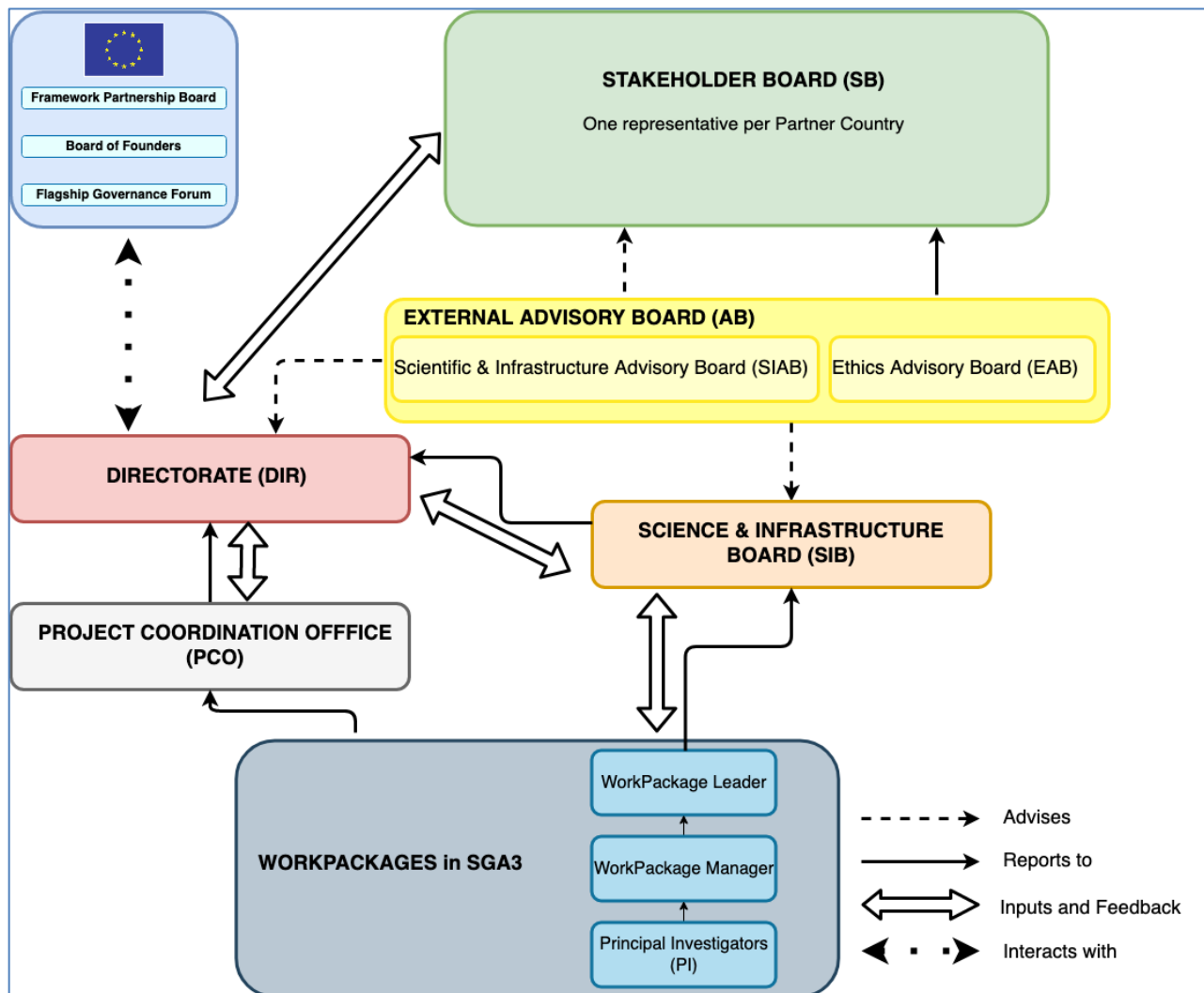
Figure 4: HBP governance structure

2.3.2.3   The Stakeholder Board (SB)

The SB exercises ultimate authority over the HBP and replaced the General Assembly in SGA1 as the ultimate decision-making body.

The main responsibilities of the SB are:

1) To approve the work plan and budget proposals before submission to the EC.

2) To decide upon material changes to the work plan and to approve Amendments to the FPA and the SGA, which include but are not limited to:

   a) Changes to the budget allocation to HBP Partner organisations

   b) Changes to the membership of the Consortium, and on the accession of individual Partners to the FPA, as well as their withdrawal or termination from the FPA

c) Changes to Tasks or Work Packages, reallocations of work or changes of the leader or deputy leader of a Work Package or Task

d) Proposals to change the Coordinator

3) To supervise the SB committees created to address special issues for the SB. The SB may modify the mandate of its committees and appoint or dismiss its members.

4) To appoint, suspend or dismiss the members of the DIR (including the Director General), the SIB (including its Chair and Vice-Chairs), and all Advisory Bodies.

5) To declare an HBP Partner organisation to be a Defaulting Partner.

2.3.2.3.1   SB composition

The Stakeholder Board is composed of one Member for each country participating in the HBP. Where there is more than one HBP Partner organisation in a country, those HBP Partner organisations will nominate a single Member to represent them. A Member of the SB represents all HBP Partner organisations of that country. Each SB Member is responsible for communicating HBP-related information to the individual HBP Partner organisations that he/she represents.

When all the Partner organisations in a country are inactive (meaning that they are not funded or part of the workplan of an SGA), the country concerned will not have a Member on the SB, but may attend its meetings as a non-voting Observer.

SB Members should have the expertise and experience necessary to understand the aims and work of the HBP, while being free of conflicts of interests. They therefore cannot be directly funded as scientists or administrators by the grants received from the European Commission through the SGAs. SB Members cannot also be members of any other governing body or advisory body of the HBP Core Project.

The SB elects its Chair from among the Members representing the eight countries that receive the largest national shares of the overall budget for the current SGA. The Chair may be re-elected for a subsequent SGA phase, providing the requisite criteria are still met.

2.3.2.4   EBRAINS AISBL - the HBP Legal Entity

The EBRAINS AISBL (Partner name: EBRAINS) replaces the EPFL in the role of the Coordinator of the HBP with effect 1 March 2021, as per FPA Amendment 10. The EBRAINS AISBL is a member of the Consortium and a Legal Entity created with the objective of coordinating the HBP and managing an enduring European scientific research infrastructure.

Strategic decisions for the EBRAINS AISBL are taken by the Board of Directors, whose Founding Members are those serving on the SB of the HBP. This reflects the desire to avoid duplication of structures and ensure smooth transition between the HBP and the Legal Entity.

The EBRAINS AISBL is headed by a Chief Executive Officer (CEO) who also serves as the Director General (DG) of the HBP (see Section 2.3.2.5.3). The composition of the AISBL's Management Board reflects both the scientific as well as RI legacy of the HBP. The CEO is supported by the Executive Director (see Section 2.3.2.5.3) and reports to the AISBL Board of Directors. As a Partner in the Consortium, the EBRAINS AISBL is responsible for recruiting its own staff, but it will employ members of the staff of the Project Coordination Office under the terms of an agreement between the original Coordinator, the EPFL, and the EBRAINS AISBL. The HBP project coordination role will continue to be fulfilled primarily by the HBP Project Coordination Office, which will become part of the EBRAINS AISBL.

The EBRAINS AISBL is responsible for developing a sustainable operational model for the EBRAINS Research Infrastructure built by the HBP. In order to achieve this, it cooperates closely with the SIB in shaping the current and future infrastructure and service provisions of EBRAINS. It puts forward its own suggestions with respect to the future development of EBRAINS, including the related timelines for service offerings. It is responsible for the promotion of EBRAINS services, outreach and communication, as well as relations with user communities.

Its responsibilities include:

- Managing, via the DG and in partnership with the SIB, the establishment, operation and improvement of the EBRAINS Research Infrastructure (RI).

- Ensuring an effective interface with the scientific community, including through advanced functionality of the EBRAINS website.

- Promoting recognition for the excellence of the EBRAINS services by, for example, seeking to be included on the ESFRI Roadmap, an effort pursued jointly with the SIB.

- Ensuring that the EBRAINS RI responds to changing needs and expectations of the scientific community in close working dialogue with Members and Associate Members of the EBRAINS AISBL.

- Building a viable post-2023 operating model, based on diverse sources of revenue.

- Working with companies and other partners to promote downstream applications of HBP technology and discoveries.

- Creating a legal and intellectual property framework for the exploitation of the EBRAINS Research Infrastructure.

- Concluding agreements or MoUs with other research initiatives and the industry.

- Engaging in promoting science, research and innovation through projects that are complementary to the HBP.

- Overseeing training programmes for Research Infrastructure users.

2.3.2.5 The Directorate (DIR)

The HBP Directorate (DIR) is the Executive Governance Body of the HBP, leading Core Project management and proposing, subject to SB approval, the strategy for the EBRAINS Research Infrastructure. The DIR reports to the SB. The DIR takes decisions by consensus whenever possible, or by vote if necessary.

The Directorate is responsible for:

- Ensuring that the HBP Consortium fulfils its obligations as set out in the FPA and the SGA;

- Ensuring that the decisions of the SB are implemented appropriately;

- Ensuring effective development of the EBRAINS Research Infrastructure, acting for this purpose as the interface between EBRAINS AISBL and the SIB;

- Reviewing, approving or rejecting proposals, budgets and recommendations made by the SIB, in relation to the SGA, the Scientific and Infrastructure Work Plans and related budgets, and submitting approved proposals, budgets and recommendations to the SB for decision;

- Reviewing, approving or rejecting recommendations from the SIB and/or PCO for amendments to existing agreements (including the FPA, SGA and Consortium Agreement), and submitting approved recommendations to the SB for decision;

- Approving or rejecting proposals of the SIB and/or PCO for changes to the composition of the Consortium and submitting approved proposals to the SB for decision;

- Monitoring that the approved Scientific and Infrastructure Work Plans are implemented appropriately, that Milestones are met, in order to produce the planned Deliverables and Outputs;

- Adopting all audit reports and ensuring the implementation of the requested measures;

- When appropriate, requesting the SIB to take measures in relation to a breach of SGA obligations, and/or ii) referring the issue to the SB;

- Representing the HBP in external meetings and dissemination activities, and maintaining close relations with key stakeholders;

- Actively communicating the Project's objectives and achievements.

- Prior to rejecting a proposal or recommendation or submitting a proposal or recommendation to the SB, consulting, whenever possible, with the appropriate HBP Advisory Board(s)

2.3.2.5.1 DIR composition, roles and nomination

- **Director-General (DG):** the DG chairs and leads the Directorate. The DG is appointed by the SB. In SGA3, the DG and the CEO of EBRAINS AISBL will be one and the same person. The DG is responsible for:

  - Leading the Directorate and its activities, preparing its work programme and ensuring that it serves the strategic needs of the Project and that its views are well communicated to the SB;

  - Ensuring that the DIR takes all necessary decisions to secure the HBP's legacy in the form of a state-of-the-art, durable EBRAINS Research Infrastructure;

  - Approving the nomination of new Members of the DIR, for approval by the SB;

  - Functioning as the DIR's liaison with the EC and representing the HBP at the Board of Funders.

- **Executive Director (ExD):** the ExD serves as deputy to the DG and head of the HBP's Project Coordination Office (PCO). The ExD is employed by the Coordinator and is nominated as member of the DIR by the DG. The ExD's responsibilities include:

  - Leading the Management and Coordination activities of the Project and the Project Coordination Office (PCO) to ensure a smooth and efficient governance, and proper representation of the partners of the Project in the governing bodies;

  - Contributing to the establishment of the EBRAINS Research Infrastructure.

- **Scientific Research Director (SRD)**, the SIB's Chair (ex officio). The SRD is elected by the SIB members and appointed by the SB. The SRD is the overall scientific leader of the HBP. The responsibilities of the SRD are:

  - Leading the Project's scientific research activities, in particular:

    Leading the development of HBP's long- and short-term scientific strategy, in the form of its scientific roadmap and work plan;

    Fostering and promoting the HBP's high-level publications;

    Serving as the Project's primary contact for scientific collaborations; initiating and establishing international collaborations and representing the interests of the HBP within these collaborations.

  - Briefing the DIR and the SB on the scientific progress of the Project and any issues encountered, at intervals determined by the SB and the DIR Chairs.

  - Representing the SIB in the DIR and, conversely, representing the DIR in the SIB. Bringing proposals from the SIB to the DIR and communicating requests from the DIR to the SIB.

  - Representing the project's scientific research activities and vision internally and externally.

  - ESFRI Roadmap: together with the IDD, the EBRAINS AISBL and the PCO, making sure that the EBRAINS Research Infrastructure attaining ESFRI status reflects the needs and scientific visions of the neuroscientific community, leading the scientific case of the ESFRI proposal.

- **Infrastructure Development Director (IDD)**, the SIB's first Vice-Chair (ex officio). The IDD is elected by the SIB members and appointed by the SB. The IDD is responsible for the coordination of the design, development and upgrading of the EBRAINS Research Infrastructure. In close collaboration with Research Infrastructure stakeholders, the IDD is also responsible for the sustainability of the Research Infrastructure. The IDD's specific responsibilities include:

  - Infrastructure strategy: driving the development of a coherent HBP Research Infrastructure that meets the needs of the research community, supports a broad range of research methodologies and facilitates data sharing, ICT services and collaborative research harnessing multiple

- ESFRI Roadmap: together with the SRD, EBRAINS AISBL and the PCO, leading the definition of a vision for the EBRAINS Research Infrastructure attaining ESFRI status and overseeing its implementation by HBP governing bodies.

- User support: leading a support structure to help external users and developers to use and contribute to the EBRAINS Research Infrastructure; supporting the EBRAINS AISBL in developing an extensive and diverse user base for EBRAINS services going beyond the HBP.

- **Software Development Director (SDD)**, the SIB's second Vice-Chair (ex officio). The SDD is elected by the SIB members and appointed by the SB. The SDD is responsible for:

  - Defining the Project's Software Development strategy.

  - Coordinating the Project's software development activities and ensuring appropriate implementation of the work plan.

  - Defining software development quality standards and coordinating their implementation.

  - Ensuring inter-operability of EBRAINS with other initiatives at the software level, together with the IDD.

- **Innovation Director (InD)**, nominated by the DG. The Innovation Director (InD) is responsible for:

  - Developing the HBP's innovation strategy and leading its execution, with the support of the HBP Innovation Team.

  - Building an innovation ecosystem around the HBP and EBRAINS Research Infrastructure, facilitating the scaling up of technology transfer.

  - Guiding the Innovation Team in approaching key target users, thus contributing to raising interest in HBP-developed technology.

- **Ethics Director (EthD)** is proposed by the Ethics Advisory Board (EAB). The Ethics Director is responsible for:

  - Representing ethics-related activities and processes on the HBP Directorate.

  - Coordinating HBP Partner organisations to prepare and respond to ethics reviews.

  - Leading HBP interactions with ethics audits.

  - Working with the HBP Directorate and PCO to ensure that ethics-related activities and Standard Operating Procedures (SOPs) are appropriately integrated in HBP management structures.

  - Working with all WPs and ensuring that ethics and compliance management issues are addressed appropriately

  - Overseeing ethics-related activities.

2.3.2.6   The Science and Infrastructure Board (SIB)

The SIB provides the scientific leadership of the HBP. In close partnership with EBRAINS AISBL, the SIB sets out to achieve the development and implementation of the HBP's collaborative and sustainable EBRAINS Research Infrastructure. The SIB Panel, a subgroup of the SIB (see below), directs the implementation of the Science and Infrastructure work plan, fulfilling the necessary executive functions to that end.

The composition of the SIB should enable effective scientific leadership of the HBP, taking into account both past and ongoing developments, and future challenges to the development of a sustainable infrastructure. Its Members shall represent the breadth and scope of the scientific disciplines involved in the Project. The SIB will consist of both SGA2 Subproject (SP) representatives and Work Package Leaders (WP leaders) of SGA3. While WP leaders have the responsibility to lead and coordinate their

Work Packages, SP representatives, who do not have such coordinating role, contribute to the board through their expertise and leadership quality, and are representatives of different scientific fields.

2.3.2.6.1 SIB Leadership

The SIB chair shall hold the position of the Scientific Research Director (SRD). The SRD is the overall scientific leader of the HBP, Chair of the SIB and an ex officio member of the DIR and the SIB Panel. The first SIB vice chair shall hold the position of the Infrastructure Development Director (IDD). The IDD leads planning and development of the EBRAINS RI under the HBP and is a vice-chair of the SIB and an ex officio member of the DIR and the SIB Panel. The second vice-chair shall hold the position of the Software Development Director (SDD). The SDD coordinates the HBP's software development activities, is a vice-chair of the SIB, and an ex officio member of the DIR and the SIB Panel.

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

2.3.2.6.2 SIB Membership

The SIB will comprise:

- One representative of each SGA2 scientific and infrastructure Subproject (SP1-10), still active in SGA3, elected by the SGA2 PIs, still involved in SGA3, of their respective SPs.
- One representative of each SGA3 Work Package (WP1-6), elected by the WP PIs.

If the representative of an SGA2 SP and an SGA3 WP is the same person, both are represented by only one person, and the total number of members reduces accordingly.

The SIB may invite guests to its meetings or ask experts to contribute.

2.3.2.6.3 SIB Panel

The SIB Panel is a subgroup of the SIB, and will comprise:

- one representative of each SGA3 Science and Infrastructure Work Package (WP1-6),
- the Science Research Director, the Infrastructure Development Director and the Software Development Director.

If the position of the SRD, IDD or SDD and any of the SGA3 WP leaders is with the same person, both are represented by only one person, and the total number of members reduces accordingly.

2.3.2.6.4 Roles and Responsibilities of the SIB

The SIB oversees the implementation of the scientific and infrastructure work plan by the work packages, and proposes to the DIR the scientific and infrastructure roadmaps, related budget allocations together with the mid- and long-term strategy of SGA3 and beyond.

The SIB shall be responsible for the following:

1) Ensuring that the science and infrastructure WPs achieve the objectives set out in the SGA and defining proposals to the DIR for appropriate action when SGA objectives may not be met.

2) Proposing adjustments to the list of Partners in the HBP.

3) Developing and proposing scientific concepts for research and infrastructure development beyond SGA3, including towards bringing EBRAINS to the ESFRI Roadmap.

4) Proposing changes to the scientific and infrastructure work plans to account for scientific and technological advances inside and outside the HBP.

5) Initiating and participating in outreach activities.

6) Establishing and contributing to international collaborations.

7) Reviewing and approving scientific Partnering Projects and their Associated Members, ensuring that the Partnering Projects contribute to the Strategic Flagship Objectives.

8) Engaging the entire community of HBP researchers in a dynamic dialogue with the DIR to foster bottom-up input in project decision-making.

9) Engaging with scientific communities, Member States and funding agencies, in close collaboration with the EBRAINS AISBL.

2.3.2.6.5 Roles and responsibilities of the SIB Panel

The SIB panel prepares and coordinates, on behalf of the SIB, science and infrastructure activities in SGA3 on a daily basis. It prepares decisions of the SIB. The SIB Panel shall be responsible for the following:

1) Monitoring that the scientific and infrastructure WPs achieve the objectives, milestones and deliverables set out in SGA3.

2) Monitoring changes in the performance of a WP's work.

3) Identifying corrective actions when a WP fails to implement adequate corrective actions itself with regard to fulfilment of SGA commitments.

4) Proposing Calls for Expression of Interest, in accordance with the procedure outlined in the FPA.

5) Monitoring ICEI applications, and presenting them to the DIR.

6) Contributing to an effective communication of science and research activities, supported by the PCO.

2.3.2.7   Project Coordination Office (PCO)

The PCO, employed by the Coordinator and headed by the Executive Director, manages and coordinates the Core Project and acts as the intermediary between the HBP Partner organisations and the European Commission. It:

- Maintains the Consortium Plan (budget) and administers the EU contribution.

- Coordinates the compilation of the SGA work plans and related budgets, prior to review by the DIR and decision by the SB.

- Coordinates the planning, writing and timely submission of SGA and FPA Amendments to the European Commission.

- Monitors and supports the implementation of the SGA work plan by the WPs.

- 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 and keeps the DIR informed about it. Coordinates common infrastructure procurement and technology choices.

- Monitors and facilitates the integration of Partnering Projects (PPs) in the HBP.

- Provides central management, coordination, and support across the Core Project.

- Collects, reviews and submits Reports and Deliverables to the DIR and the European Commission.

- Supports the EBRAINS Research Infrastructure by building and operating the Collaboratory (Portal for the RI, collaborative tools), and other coordination software and tools.

2.3.2.8   Arbitration

In case of any conflicts between the positions of the DIR or the SIB and the position of the EBRAINS AISBL regarding HBP matters, the necessary arbitration would be performed by the SB.

2.3.2.9   Advisory Boards (AB)

The ABs are independent from the HBP and should provide it with an external advice. Their members should not receive funding from the HBP as beneficiaries of the Grant.

2.3.2.9.1   Ethics Advisory Board (EAB)

The EAB is a high-level body that advises the SB and can be consulted by the DIR and the SIB on specific ethical, regulatory, social and philosophical issues raised by HBP research. It reports to the DIR.

Composition: 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 appointed and dismissed by the SB.

2.3.2.9.2   Scientific and Infrastructure Advisory Board (SIAB)

The SIAB is a high-level body that advises the SB and can be consulted by the DIR and the SIB, on issues of scientific, technical and clinical importance for the aim and objectives of the Human Brain Project. Moreover, the SIAB will advise on the development of the EBRAINS Research Infrastructure, user engagement, and embedding the HBP in the international neuroscience landscape. The SIAB is a merger of the former Science Advisory Board (SAB) and Clinical Advisory Board (CAB).

Composition: Scientists at the top of disciplines of current and future interest to the HBP, but with no participation or interest in the HBP. The membership of the SIAB is adjusted to ensure expertise, geographical, and gender balance. Its members provide independent expertise, can be proposed by the SIB and are appointed and dismissed by the SB.

2.3.2.10   Ombudsperson

The Ombudsperson is an external person responsible for investigating issues in relation with Research Integrity. Beneficiaries of EU Grants under the H2020 programme must comply with the European Code of Conduct for Research Integrity. When issues arise regarding Research Integrity (misconduct, harmful or dishonest practices), researchers can contact their institutions and/or the Ombudsperson, as an independent actor. Institutions, Work Packages and researchers should declare any complaint or case regarding Research Integrity to the HBP Core Project, even when a satisfactory solution has been implemented. The Ombudsperson is appointed by the SB and reports to the DIR; he/she does not receive funding from the HBP Grant, but can, in cases requiring more in-depth evaluation and action, be contracted by the HBP to solve the issue, on the decision of the DIR. In this case, he/she can receive payment from the HBP under a specific contract.

2.3.2.11   Data Protection Officer (DPO)

The HBP will, at all times, have a DPO to facilitate the implementation of the EU General Data Protection Regulation and other applicable data protection laws in the frame of the HBP. The DPO advises the Core Project and should be proactive in updating the DIR on all matters relating to Data Protection. This includes:

- Monitoring compliance with data protection and privacy legislation. In particular, performing all tasks as required by Articles 37-39 of the General Data Protection Regulation (GDPR).

- Consultation on data processing activities, in particular, providing advice and recommendations on compliance with applicable laws and data protection issues, in addition to acting as a contact point for data subjects and the supervisory authorities.

- Working with partners across the project to develop policies and procedures including Data Protection Impact Assessments (DPIA), Data Use Agreements and Access Policies, data processing and data sharing agreements.

2.3.2.12   Audit Committee

Where external quality control of an HBP Deliverable, impartial investigation of alleged underperformance by an element within the HBP, oversight of HBP financial matters, prevention of deviation from the work plan and/or expected underperformance, or a compliance check is required, the HBP governance 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.

2.3.2.13   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 WP concerned. A formal request includes a standard time limit on proposal for corrective action from the WP. Possible outcomes:

    a) The WP 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 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 SB.

5) In the case of c) above, the DIR can propose to the SB to change a Task, a WP or change the Partners and/or leaders involved.

2.3.2.14   Cross-Cutting Coordination Committees

To ensure the smooth running of the HBP, there is a need for permanent and/or ad-hoc committees, which undertake particular coordination responsibilities. Committees can be mandated by any governing body; to which they report for the duration of their activities. The committees have a chair and a clear mandate.

2.3.2.15   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.

2.3.2.15.1 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.

2.3.2.15.2 Software, Infrastructure and Scientific 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.
- Maximise 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.

2.3.2.15.3 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.

Table 16: Technology Readiness Levels (TRLs)

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

Technology Readiness Level	Expected Properties
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

2.3.2.15.4 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 Software, Infrastructure and Scientific 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.

Software, Service or Data Development lifecycle
Project granularity set in SGA. Outputs can be software, services or data

Kickoff
- Assign ownership and accountability
- Identify implementation details with Project Implementation Proposal

Prototype
- Identify solutions to key problems and demonstrate those solutions in prototype form.
- Initial Samples of data or preliminary user testing should be possible
- Enhance detail and certainty with the Project Prototype Report (for Co-design projects)

Engineering
- Deliver the Minimum Viable Product or Minimum Viable Increment (to an existing product) as quickly as possible
- Engage with representative user base as soon as possible, ideally during early stages of Engineering effort.

Monitor Usage
- Determine MVP or MVI value
- Determine additional quality enhancements or features which drive adoption via interaction with users.

Agile Incremental Improvement
Wherever possible the project should produce incremental improvements in base functionality. This implies that there will be multiple cycles through the last 3 parts of the project with the same team. Once the initial MVP is delivered usage monitoring should be continuous

End of Project
- Post-mortem evaluation

Figure 5: 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

- Determine which Project Lifecycle Framework model will be used:

  Agile development - multiple passes through the Project lifecycle, $\leq$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.

Mapping to Technology Readiness Levels

Project Lifecycle phases
Select the project scope to try address incremental improvements

TRL phases
Select the project scope to try address incremental improvements

Kick-off

Prototype

Engineering

Monitor Usage

TRL 1	Project Initiation
TRL 2	Conceptualization
TRL 3	PoC Implementation
TRL 4	Prototype Component
TRL 5	Prototype Integration
TRL 6	Prototype to Real-world Integration
TRL 7	Operational Integration
TRL 8	Deployment
TRL 9	Production

Figure 6: 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.
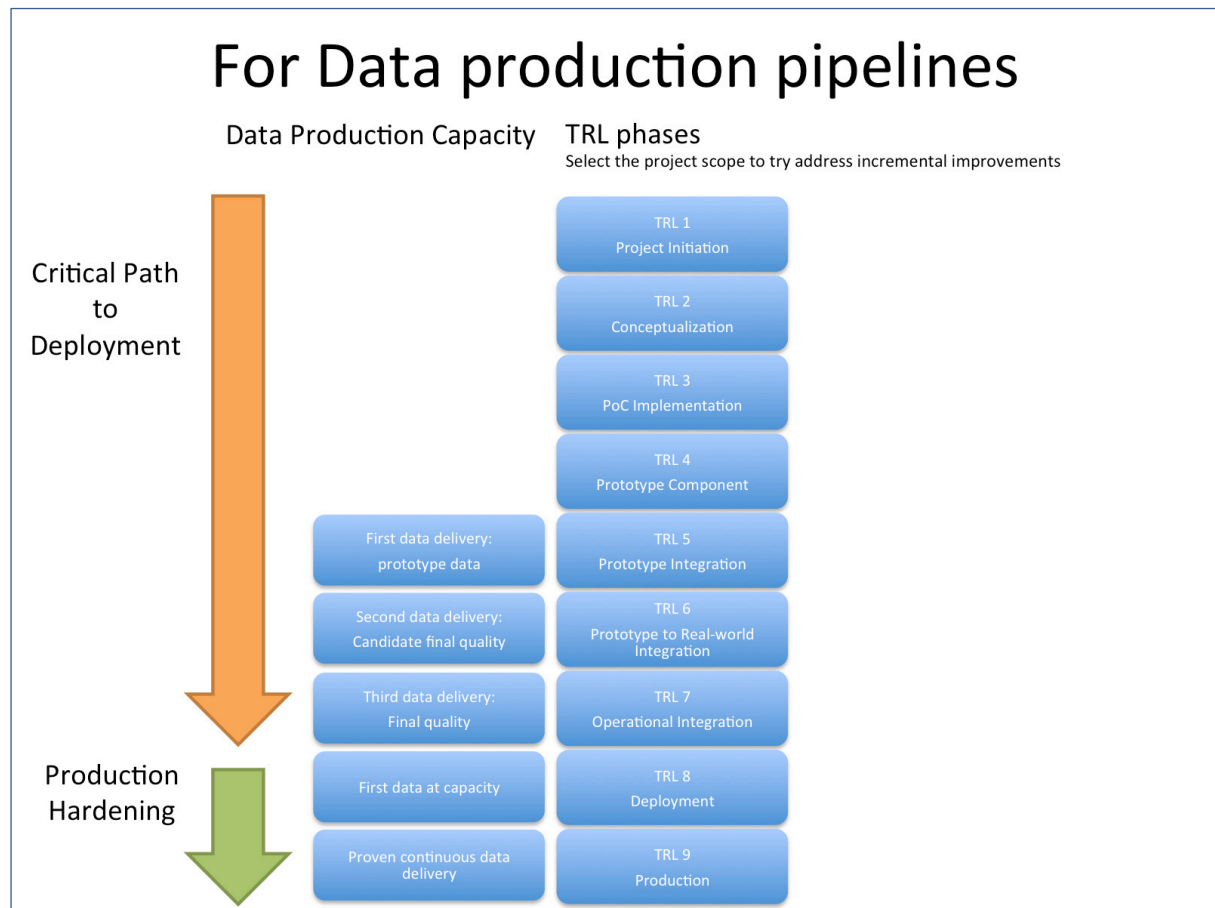
Figure 7: Data deliveries from data projects

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.

2.3.2.15.5 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.

Table 17: Data Accessibility Criteria

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.

2.3.2.15.6 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.

Table 18: HBP Key Performance Indicators (KPIs)

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

Flagship Objective	Key Performance Indicator (KPI)	Alignment with HBP Flagship Objectives (FOs)
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
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 organised by the HBP Education Programme	FO6
Education Programme	Number of Schools organised by the HBP Education Programme	FO6
Education Programme	Number of academic attendees at Schools organised 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

Flagship Objective	Key Performance Indicator (KPI)	Alignment with HBP Flagship Objectives (FOs)
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
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

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

2.3.2.15.7 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.

2.3.2.15.8 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 Software, Infrastructure and Scientific 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 Software, Infrastructure and Scientific 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.

- Organisational: higher-level strategic risks. Can be detected with high-level KPIs. In most cases, mitigation of these risks will require larger strategic organisational action.

- External: these risks are the result of external factors and can't be detected with KPIs. Mitigation strategies might also require broader strategic organisational action.

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

Table 19: Risks and Contingency Plans

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	Organisational	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	SP5 - SP10	High	Medium	Implementation	Discussions with possible Partners have begun. If deployment of large	The risk for multi-petaflop capabilities will be cleared with the installation of a multi-petaflop

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
required supercomputing power					supercomputing resources is delayed, the Project will use the resources already available.	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 /Organisational	If data volumes are insufficient, Project can build lower fidelity reconstructions until the data becomes available. Project could reallocate additional financial resources to SP1 and SP2, and/or to bring in new research groups.	This risk will fall gradually as the volume of available data increases, allowing the construction of progressively more accurate models. The risk 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 organisations 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	SP8	High	Medium	Implementation	The project has used the Ramp Up Phase Competitive Call to diversify its portfolio of candidate algorithms, improving its chances	This risk can be considered cleared with the delivery of efficient algorithms and their

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
generate unique biological signatures of disease					of success. Following the Project Lifecycle, kick-off and prototype activities should address key scientific issues. See Project Lifecycle for detection and mitigation details.	incorporation into the Medical Informatics Platform, planned for Month 30.
Delays in neuromorphic computing hardware development	SP9	Medium	Medium	Implementation	Experiments are routinely planned using software simulations of neuromorphic computing hardware. This strategy minimises the consequences of delays in hardware development. See Project Lifecycle for detection and mitigation details.	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 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	SP9	Low	High	Implementation	Project will seek early indications if the target industries do not show enough interest	This risk will only be cleared in the operational phase, when the Platforms begin to be used by

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
Neuromorphic Computing Platform from potential applications developers.					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.	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 a major contribution to the HBP.	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 HBP or whose contribution is not yet proportional to their standing in the European science.	This risk should be cleared by time the HBP presents its proposal for the Operational Phase.
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	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.

not employed by HBP partners)						

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 overruns in major infrastructure (CAPEX or operating costs)	All SPs	Medium	High	Implementation	This is a risk in large projects. HBP infrastructure 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.	This risk will be present for the whole duration of 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	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	This risk will be present for the whole duration of the HBP, and will grow as the Project gains visibility.

Risk	SP	Probability	Impact	Risk Category	Contingency plans	End of the risk
particular, animal experimentation) possibly leading to the introduction of new legal restrictions					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.	
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 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.	This risk will be present for the whole duration of the HBP, and will grow as the Project gains visibility.

2.3.2.15.9 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 four 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 2023, planned EU contribution of EUR 150 million

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). Limited funding will be assigned to Course Directors 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. Furthermore, the Education Programme Office will work to exploit the possibilities offered by the European Institute of Innovation & Technology.

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. Currently, the estimated value of the resources made available as co-funding contribution by Partners amounts to EUR 556 million. The most important is Major equipment and Research Facility with EUR 366 million or 66% of the total resources made available. The partners contributing the most to this category are JUELICH with EUR 81 million (HPC, visualisation and characterisation 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 190 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.

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

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
P1	EBRAINS	70	1.2		
P2	AALTO (terminated)				
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 (terminated)			Projection-based multi-user virtual reality display systems	1.0
P7	BUW	32	0.2		
P8	BSMJ (terminated)				
P9	CF (terminated)				
P10	CNRS	358	4.63	Computational clusters. National (and potentially European) HPC resources Patch-clamp experimental setup (microscope, anesthesia appara- tus, animal fixture, electronics, computers)	0.9 0.25
P11	CEA	40	2.25	2 clinical systems Non-human primate electrophysiology lab / Deep Imaging Platform	1.6 0.5
P12	CNR	341	1.66	Computing lab space and logistics.	0.3
P13	CINECA	3,000	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 (terminated)	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				

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
P20	JUELICH	3,101	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 (terminated)				
P24	UDUS	100	0.5	Lightcycle PCR, Tissuescope.	1.7
P25	UH (terminated)				
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	3.6	0.02		
P30	IEM HAS	50	0.3	2 *in vitro* electrophysiology setups. Animal facility and gene technology unit.	0.1
P31	IST (terminated)			SP5 confocal microscope. Ultima 4 two photon – confocal – uncaging system.	0.6
P32	JSI (terminated)	100	0.5	Computing cluster with 1024 cores.	0.1
P33	INRIA				
P34	IP				
P35	UFRA (terminated)	200	0.1		
P36	KIT (terminated)				
P37	KI	600	3.54	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	1.6

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
				facility. Patch clamp system. Animal housing facility, Biochemical laboratory, Electron microscopy centre.	
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 (terminated)	20	0.2		
P46	RWTH	200	0.1	Cave for immersive visualisation. High-resolution display.	0.6
P47	UHEI	6	0.05	Heidelberg University + Helmholtz Association, Normalverfahren, Collaborative Research Centres	2.9
P48	SU (terminated)			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	136	0.1	Computing or storage infrastructures.	0.31
P52	FZI	200	2.2	FZI Living Lab Service Robotics. IT Infrastructure of FZI. Computing and storage resources.	0.2
P53	TUC (terminated)				
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	UCAM				

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
	(terminated)				
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 (terminated)	60	0.5		
P62	UEDIN				
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
				LST Living Lab facilities (4-6 months utilisation, EUR 30,000), Tools to experiment with Neurorobotics Platform regarding robots supporting memory deficit (EUR 10,000).	0.04
P69	URJC			Lab space	0.2
P70	UNIPV	346	1.1	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	1.6

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
				laboratory. MRI laboratory. TMS/BCI laboratory. Laboratory supplies	0.04
P71	UBERN		0.1		
P72	UNIBI (terminated)	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. The Institute of Computational Neuroscience (ICNS) provides a combination of high-end PCs, a powerful centralised compute-server with 32 cores and 768 GB main memory, as well as extensive cloud storage and backup facilities (> 200 TB).	0.8
P75	UZH (terminated)				
P76	UB	15	0.07		
P77	UPF	33	0.24		
P78	AMU	83.7	0.72	INS houses a high-performance computing cluster dedicated to neural modelling. 7t MRI	0.1 8
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	3.2	0.06	Multiphoton and confocal microscopes. Lasers. Electrophysiology rigs. High Performance Computing Cluster (Grace)	1.3

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
				with more than 10,000 Intel Haswell cores connected by Intel Truescale Infiniband. Protein production laboratory. NMR. Microcalorimetry and SPR facilities.	
P83	UU		0.3	Lab space	0.2
P84	WEIZMANN				
P85	TUDA				
P86	UNIGE (terminated)	40	0.3	NeuGRID.	4.3
P87	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)
P88	MRC (terminated)				
P89	UHAM			Three EEG labs, access to MRI scanner, IT infrastructure, six behavioural testing rooms	
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	KNAW	40	0.29	Two photon microscopes, behavioural set-up, two slice patch clamp electrophysiology set-ups, Two *in vivo* electrophysiology/imaging set-ups, transgenic and conventional mouse facilities, monkey facility, molecular biology laboratory, IT	0.35
P92	INFN	90	0.49	Existing experimental computing set-up and subsequent upgrades (1-4)	0.46

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
P93	IDIBAPS				
P94	UMIL	86	0.42	Navigated Brain Stimulation System (NBS), TMS compatible EEG amplifier, air-cooled NBS, other UMIL contribution (overheads not withheld)	0.97
P95	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
P96	ISS	136	0.64	HPC server and HPC co-processing board	0.02
P97	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	
P98	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	
P99	DZNE	18	0.12	MR-PET, access to 7Tesla, Memory Clinic of the DZNE Magdeburg, technical infrastructure and computing cluster at DZNE Bonn	Cannot be estimated
P100	USFD	2	0.01	iCub humanoid robot and real-time computing cluster	0.23
P101	UWE			Bristol Robotics Laboratory	~30.0

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
P102	SURREY (terminated)			Three high-performance simulation servers	0.02
P103	TUT	15	0.13	Computing infrastructure	0.1
P104	ULEEDS (terminated)				
P105	SUxUPMC (terminated)	38.6	0.15		
P106	UoS			UoS HPC equipment is available for supporting computational work	0.01
P107	MU (terminated)				
P108	UCBL				
P109	POLITO				
P110	UGENT	156		State of the art supercomputing facility, team to support researchers by providing a stable and state of the art high performance computing	
P111	KUL	96	0.2	3T scanner and technical infrastructure (animal housing, ICT, software and set-ups)	5.3
				Acquisition of data: Neuroport 128 channel recording system	0.15
				Surgery-related costs including hybrid depth electrodes	0.05
P112	UNIBAS		0.8		
P113	VU			Research and technical infrastructure	5.0
P114	SIB (terminated)			Cluster of compute nodes	0.15
P115	EBRI (terminated)	59	0.20		
P116	SNS (terminated)	69	0.43		
P117	UM				
P118	HERTS				
P119	UKB (terminated)				
P120	BRFAA			100-processor Apple Cluster (Intel Xeon Six Core, 2.66 GHz), available for	

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
				molecular modelling applications and drug design studies. The Cournia lab is equipped with an IBM 36-processor Blade Server (Intel Xeon Six Core, 2.66 GHz).	
P121	CONVELOP				
P122	CHARITE	36	0.13	support and facilitie through the Berlin Data Integration Center that is funded with €7Mio per Year until 2020	0.05
P123	EMBL				
P124	SICHH	7	0.03		
P125	UGA	22	0.12		
P126	CHUGA	12	0.08		
P127	UKLRF	4	0.03		
P128	CERCE (terminated)	7	0.05		
P129	UMG (terminated)	12	0.16		
P130	UT	6	0.04		
P131	CHULILLE	(not quantifiable)		(not quantifiable)	
P132	HOST	3	0.02		
P133	ATHENA	10	0.06		
P134	EPFL	14,000	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. Low-power wearables design and interconnectivity to HBP Development Supercomputer. Such availability of EPFL equipment or research facilities is subject to legal restrictions (if any).	109
P135	ITT	12	0.06	RED Icub and Robotic laboratory (1 month utilisation, EUR 30,000), Technical EEG room and Technical EEG staff (EUR 40,000), Experimental Facilities and	0.01

P No	Partner	Human resources (PMs)	Estimated value (Mio€)	Major equipment / Research facility	Estimated value (Mio€)
				Sensorised Facilities (1 month duration, EUR 30,000)	
P136	POLIMI	30	0.09		
P137	UNINA	8	0.05		
P138	APHM	15	0.09		
P139	UNIROMA1	48	0.16	Systems for depth multi-electrode recording and EEG/ECoG. Multisite stimulation system	0.03
P140	UGOE	22.5	0.15	Computer cluster, KUKA robot arms	1.8
P141	EMC	17	0.14	Specialized computing cluster (maintenance and management costs)	0.13
P142	SISSA	5	0.02	Access to the SISSA's HPC facilities	0.00
P143	MPIEA	15	0.1	MEG scanning and MRI scanning	0.2
P144	INGLOBE	17	0.06		
P145	AI2LIFE	6.4	0.02		
P146	ROB			Mobile platforms, localisation and navigations systems, sensors (EUR 60,000), mobile robotic arm (EUR 40,000)	0.1
P147	BIOMAX	12	0.08		
P148	AIS	0.6	0.03	Computing infrastructure facility	0.02
P149	AUTONOMYO			Device	0.03
P150	BITBRAIN	15	0.08		
P151	OCV			Prototype's component costs, safety / regulatory 60601 testing, subcontracting and others	0.09
P152	UNITO	5.00	0.03		
Total		**28,901.57**	**190.31**		**366.04**

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 503 million. Of this sum, EUR 374 million from national funding sources, EUR 111 million from European funding sources, and EUR 17 million from international funding organisations.

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

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P1	EBRAINS				
P2	AALTO (terminated)				
P3	LUMC		2	0.2	
P4	AUEB		0.2		
P5	BSC		1.4		
P6	BAUW (terminated)				
P7	BUW				
P8	BSMJ (terminated)				
P9	CF (terminated)		32	4	3
P10	CNRS		1		
P11	CEA				
P12	CNR		4		0.2
P13	CINECA		3		
P14	DTU		0.8		
P15	UoD (terminated)		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				

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P23	FCHAMP (terminated)				
P24	UDUS		1.4		0.7
P25	UH (terminated)				
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 (terminated)			0.1	
P32	JSI (terminated)		0.3	0.1	
P33	INRIA		2		
P34	IP				
P35	UFRA (terminated)		1.4		
P36	KIT (terminated)				
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 (terminated)		0.4		
P46	RWTH		0.8		
P47	UHEI		26		

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P48	SU (terminated)		2		
P49	SSSA				
P50	CWI				
P51	SKU		0.2		
P52	FZI				
P53	TUC (terminated)				
P54	TUD			1.3	
P55	TUGRAZ		0.1	0.1	
P56	TUM		0.5	0.8	
P57	TAU			0.1	0.1
P58	UCAM (terminated)				
P59	UOXF		0.5	0.7	
P60	HUJI		1.5		3.7
P61	AUBER (terminated)		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 (terminated)		0.5		

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P73	UKAACHEN		0.5		
P74	UKE		0.9		
P75	UZH (terminated)				
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		2.0	0.2	
P83	UU				
P84	WEIZMANN			1.6	
P85	TUDA				
P86	UNIGE (terminated)			0.2	0.3
P87	UGLA			1.5	
P88	MRC (terminated)				
P89	UHAM	0.26	4.07		2.81
P90	UBER		0.42	1.01	
P91	KNAW		0.06	0.14	
P92	INFN				
P93	IDIBAPS				
P94	UMIL				
P95	IBEC	0.04	0.31	0.34	
P96	ISS				
P97	ULG				
P98	UvA	0.83	0.73	0.25	

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P99	DZNE		1.9		
P100	USFD			0.6	
P101	UWE		6.0		
P102	SURREY (terminated)				
P103	TUT	0.8	0.99		
P104	ULEEDS (terminated)				
P105	SUxUPMC (terminated)				
P106	UoS			0.05	
P107	MU (terminated)				
P108	UCBL		1.43		
P109	POLITO				
P110	UGENT	0.4			
P111	KUL	5.8	0.9		
P112	UNIBAS				
P113	VU				
P114	SIB (terminated)		0.1		
P115	EBRI (terminated)				
P116	SNS (terminated)				
P117	UM				
P118	HERTS				
P119	UKB (terminated)				
P120	BRFAA				
P121	CONVELOP				
P122	CHARITE				

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P123	EMBL				
P124	SICHH				
P125	UGA				
P126	CHUGA				
P127	UKLRF				
P128	CERCE (terminated)				
P129	UMG (terminated)				
P130	UT				
P131	CHULILLE				
P132	HOST				
P133	ATHENA				
P134	EPFL		190	2.5	0.8
P135	ITT				
P136	POLIMI				
P137	UNINA				
P138	APHM				
P139	UNIROMA1				
P140	UGOE				
P141	EMC		3.96	0.45	
P142	SISSA				
P143	MPIEA				
P144	INGLOBE				
P145	AI2LIFE				
P146	ROB				
P147	BIOMAX				
P148	AIS				
P149	AUTONOMYO				

P No	Partner	Regional resources (Mio€)	National resources (Mio€)	European resources (Mio€)	International resources (Mio€)
P150	BITBRAIN				
P151	OCV				
P152	UNITO				
Total		9.33	365.57	111.74	17.01

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 122 Partner organisations in 19 countries (16 of which have currently active Partners in SGA3). The majority of Partners are universities, public/non-profit private research organisations or non-profit organisations. At the moment, there are ten SMEs in the FPA Consortium: HITS, CONVELOP, INBLOBE, AI2LIFE, ROBOTNIK, BIOMAX, ALPINE INTUITION, AUTONOMYO, BITBRAIN and ONCOVISION. Other organisations participate in the Flagship Initiative primarily through the Partnering Projects. EBRAINS replaces the EPFL as Coordinator of the HBP with effect 1 March 2021 (see Section 2.3.2.4 EBRAINS AISBL - the HBP Legal Entity).

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

Table 22: Partners' expertise and experience for implementing the Work Plan (SGA1 & SGA2)

P No.	Acronym	Country	SP-1 Mouse Brain	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-11 Management and Coordination	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
1	EBRAINS	BE												X	X		
2	AALTO term*	FI															
3	LUMC	NL								X							
4	AUEB	GR								X							
5	BSC	ES							X								
6	BAUW term*	DE															
7	BUW	DE							X								
8	BSMJ term*	IL															
9	CF term*	UK															
10	CNRS	FR			X		X				X						
11	CEA	FR	X			X											
12	CNR	IT			X		X										
13	CINECA	IT							X								
14	DTU	DK										X					
15	UoD term*	HU															
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 term*	PT															
24	UDUS	DE	X														
25	UH term*	FI															
26	HITS	DE					X										
27	CHUV	CH								X							
28	ICL term*	UK					X			X							
29	ICM	FR								X							
30	IEM HAS	HU	X				X										
31	IST term*	AT															
32	JSI term*	SI															
33	INRIA	FR	X		X												
34	IP	FR	X											X			
35	UFRA term*	DE															
36	KIT term*	DE															
37	KI	SE	X				X	X						X			
38	KCL term*	UK												X			
39	KTH	SE			X		X				X	X					
40	LENS	IT	X	X													
41	LNU	SE												X		X	
42	MUI	AT													X	X	
43	UoA	GR								X							
44	NMBU	NO			X		X	X									
45	OFAI term*	AT															
46	RWTH	DE							X								
47	UHEI	DE				X					X				X		X
48	SU term*	TR															

P No.	Acronym	Country	SP-1 Mouse Brain	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-11 Management and Coordination	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
49	SSSA	IT										X					
50	CWI	NL					X										
51	SKU	NL					X										
52	FZI	DE										X					
53	TUC term*	GR															
54	TUD	DE									X						
55	TUGRAZ	AT									X						
56	TUM	DE										X					X
57	TAU	IL								X					X	X	
58	UCAM term*																
59	UOXF	UK		X								X					
60	HUJI	IL				X		X									
61	UABER term*																
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								X
69	URJC	ES	X						X								
70	UNIPV	IT	X					X									
71	UBERN	CH			X												
72	UNIBI term*																
73	UKAACHENN	DE		X						X							
74	UKE	DE		X								X					
75	UZH term*	CH															
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 term*	CH															
87	UGLA	UK			X												
88	MRC term*																
89	UHAM	DE			X												
90	UBER	DE			X												
91	KNAW	NL		X	X												
92	INFN	IT			X												
93	IDIBAPS	ES			X												
94	UMIL	IT			X												
95	IBEC	ES			X												
96	ISS	IT			X												
97	ULG	BE			X												

P No.	Acronym	Country	SP-1 Mouse Brain	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-11 Management and Coordination	SP-11 Dissemination	SP-11 Education	SP-11 Innovation management
98	UvA	NL			X												
99	DZNE	DE	X	X	X												
100	USFD	UK			X												
101	UWE	UK			X												
102	SURREY *term**	UK															
103	TUT	FI				X											
104	ULEEDS *term**	UK															
105	SUxUMPC *term**	FR															
106	UoS	UK									X						
107	MU *term**	UK															
108	UCBL	FR		X													
109	POLITO	IT									X						
110	UGENT	BE					X					X					
111	KUL	BE		X													
112	UNIBAS	CH		X													
113	VU	NL	X	X													
114	SIB *term**	CH															
115	EBRI *term**	IT															
116	SNS *term**	IT															
117	UM	NL		X													
118	HERTS	UK									X						
119	UKB *term**	DE															
120	BRFAA	GR								X							
121	CONVELOP	AT													X		
122	CHARITÉ	DE					X										
123	EMBL	DE					X										
124	SICHH	CH								X							
125	UGA	FR								X							
126	CHUGA	FR								X							
127	UKLRF	DE								X							
128	CERCE *term**	IT															
129	UMG *term**	DE															
130	UT	DE						X									
131	CHULILLE	FR								X							
132	HOST	GE			X												
133	ATHENA	GR								X							
134	EPFL	CH	X		X	X	X	X	X	X	X	X		X	X	X	X

* Terminated Partners

Table 23: Active partners' expertise and experience for implementing the Work Plan (SGA3)

P No.	Acronym	Country	WP1 - The human multiscale brain connectome and its variability	WP2 - Networks underlying brain cognition and consciousness	WP3 - Adaptive networks for cognitive architectures	WP4 - EBRAINS Data Services	WP5 - EBRAINS Modelling Services	WP6 - EBRAINS Computing Services	WP7 - Management and Coordination	WP8 - Communications, Outreach and Innovation	WP9 - Responsible Research and Innovation
P1	EBRAINS	BE				X	X	X	X	X	
P4	AUEB	GR				X					
P5	BSC	ES				X		X			
P7	BUW	DE					X				
P10	CNRS	FR	X	X		X	X	X			
P11	CEA	FR	X	X		X		X			
P12	CNR	IT	X	X	X	X	X				
P13	CINECA	IT				X	X				
P16	DMU	UK			X	X					X
P18	ETHZ	CH				X	X	X			
P19	FT	DK				X		X			X
P20	JUELICH	DE	X	X	X	X	X	X	X	X	
P21	FORTISS	DE				X	X				
P24	UDUS	DE	X			X					
P26	HITS	DE					X				
P27	CHUV	CH				X					
P29	ICM	FR	X								
P30	IEM HAS	HU	X								
P33	INRIA	FR	X	X		X					
P34	IP	FR					X				
P37	KI	SE	X		X	X					
P39	KTH	SE	X		X	X	X	X			
P40	LENS	IT	X	X				X			
P41	LNU	SE				X			X		X
P42	MUI	AT								X	
P44	NMBU	NO		X	X	X	X				
P46	RWTH	DE					X				
P47	UHEI	DE				X	X	X	X	X	
P49	SSSA	IT			X		X				
P50	CWI	NL				X					
P51	SKU	NL				X	X				
P52	FZI	DE				X					
P54	TUD	DE						X			
P55	TUGRAZ	AT			X						
P56	TUM	DE				X	X	X	X		
P57	TAU	IL	X							X	
P59	UOXF	UK			X						
P60	HUJI	IL	X								
P62	UEDIN	UK	X				X				
P63	UMAN	UK				X	X	X			
P64	UAM	ES		X							
P66	UGR	ES			X		X				
P68	UPM	ES	X		X	X		X		X	
P69	URJC	ES						X			

P No.	Acronym	Country	WP1 - The human multiscale brain connectome and its variability	WP2 - Networks underlying brain cognition and consciousness	WP3 - Adaptive networks for cognitive architectures	WP4 - EBRAINS Data Services	WP5 - EBRAINS Modelling Services	WP6 - EBRAINS Computing Services	WP7 - Management and Coordination	WP8 - Communications, Outreach and Innovation	WP9 - Responsible Research and Innovation
P70	UNIPV	IT	X		X	X	X				
P71	UBERN	CH		X	X						
P74	UKE	DE	X								
P76	UB	ES		X							
P77	UPF	ES	X	X							
P78	AMU	FR	X	X		X	X				
P81	UIO	NO		X		X		X			
P82	UCL	UK	X								
P83	UU	NO	X	X	X						X
P85	TUDA	DE						X			
P87	UGLA	UK		X							
P90	UBER	DE	X	X							
P91	KNAW	NL	X	X	X						
P92	INFN	IT		X							
P93	IDIBAPS	ES		X							
P94	UMIL	IT		X							
P95	IBEC	ES	X	X							
P96	ISS	IT		X							
P97	ULG	BE		X							
P98	UvA	NL		X	X			X			
P99	DZNE	DE	X	X							
P100	USFD	UK			X						
P101	UWE	UK		X	X						
P103	TUT	FI	X								
P106	UoS	UK			X		X				
P108	UCBL	FR	X			X					
P111	KUL	BE		X		X					
P112	UNIBAS	CH	X				X				
P113	VU	NL	X								
P117	UM	NL		X	X						
P118	HERTS	UK			X						
P121	CONVELOP	AT									X
P122	CHARITE	DE	X				X				
P123	EMBL	DE				X					
P125	UGA	FR	X	X		X					
P130	UT	DE				X	X				
P132	HOST	DE			X						
P133	ATHENA	GR				X	X	X			
P134	EPFL	CH	X	X	X	X	X	X	X	X	
P135	IIT	IT	X		X						
P136	POLIMI	IT	X								
P137	UNINA	IT	X								
P138	APHM	FR	X								
P139	UNIROMA1	IT		X							
P140	UGOE	DE					X				
P141	EMC	NL					X				

P No.	Acronym	Country	WP1 - The human multiscale brain connectome and its variability	WP2 - Networks underlying brain cognition and consciousness	WP3 - Adaptive networks for cognitive architectures	WP4 - EBRAINS Data Services	WP5 - EBRAINS Modelling Services	WP6 - EBRAINS Computing Services	WP7 - Management and Coordination	WP8 - Communications, Outreach and Innovation	WP9 - Responsible Research and Innovation
P142	SISSA	IT					X				
P143	MPIEA	DE		X							
P144	INGLOBE	IT			X						
P145	AI2LIFE	IT			X						
P146	ROB	ES			X						
P147	BIOMAX	GE				X					
P148	AIS	CH					X				
P149	AUTONOMY	CH					X				
P150	BITBRAIN	ES					X				
P151	OCV	ES	X								
P152	UNITO	IT					X				

Tables 23 and 24 below provides a breakdown of the partners by country and their distribution across Subprojects in SGA1 & SGA2 and across Work Packages in SGA3. 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.

Table 24: Number of beneficiaries in each Subproject (SGA1 & SGA2), by country

	SP1	SP2	SP3	SP4	SP5	SP6	SP7	SP8	SP9	SP10	SP11	SP12	TOTAL
Austria	1								1	1	2		5
Belgium		1	1	1	1					1	1		6
Denmark										1		1	2
Finland				1						2			3
France		4		4	1	2		5	1			1	18
Germany	1	5	3	2	4	2	8	3	5	5	2		40
Greece					1			4					5
Hungary	2						1						3
Israel				1				1			2		4
Italy	4	1	3	2		3	1	1	1	1			17
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	1		15
Sweden	1			1	1	2		1	1	1	1	3	12
Switzerland	4	1		2	1	1	2	4	1	1	1		20
Turkey										1			1
United Kingdom	1	2		3	1	2		4	4	1	1	2	25
TOTAL	19	18	16	18	14	15	14	17	15	17	11	7	

Table 25: Number of beneficiaries in each Work Package (SGA3), by country

	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	TOTAL
Austria			1					1	1	3
Belgium		2		1				1		4
Denmark				1		1			1	3
Finland	1									1
France	8	5		6	3	2				24
Germany	6	4	4	8	10	4	3	2		41
Greece				2	1	1				4
Hungary	1									1
Israel	2							1		3
Italy	6	6	6	3	5	2				28
Netherlands	2	3	5	1	1	1				13
Norway		2	1	2	1	1				7
Spain	4	5	3	2	3	2		1		20
Sweden	3	1	3	3	1	1	1		2	15
Switzerland	2	2	2	3	5	2	1	1		18
United Kingdom	3	2	6	2	3	1			1	18
TOTAL	**38**	**32**	**31**	**34**	**33**	**18**	**5**	**7**	**5**	

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

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 Section 2.3.2.6), aided by the Project Coordination Office (see Section 2.3.2.7), 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

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 Section 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: HBP Beneficiaries' Third Parties

2.5 Responsible Research and Innovation

2.5.1 Ethics 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 2.3.2.7). 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 Section 2.3.2.9.1) 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 organisations 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 organisational and scientific details (e.g. adjustments to management structures and procedures, ethical authorisations 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 2.3.2.14).

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

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 Ombudsperson

The Ombudsperson 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 Ombudsperson has the right to access all information and members of the HBP, and is bound by a non-disclosure agreement. The Ombudsperson has the right to attend and speak at all governance bodies of the HBP, including the right to add items to agendas. The Ombudsperson can raise PORE issues and thereby involve SP12 and the EAB in investigations and recommendations. The Ombudsperson 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" 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 authorised 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 set. 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

#	Issue Name	H2020 Category	SP	Responsible	Status	Action	Target date
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

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.
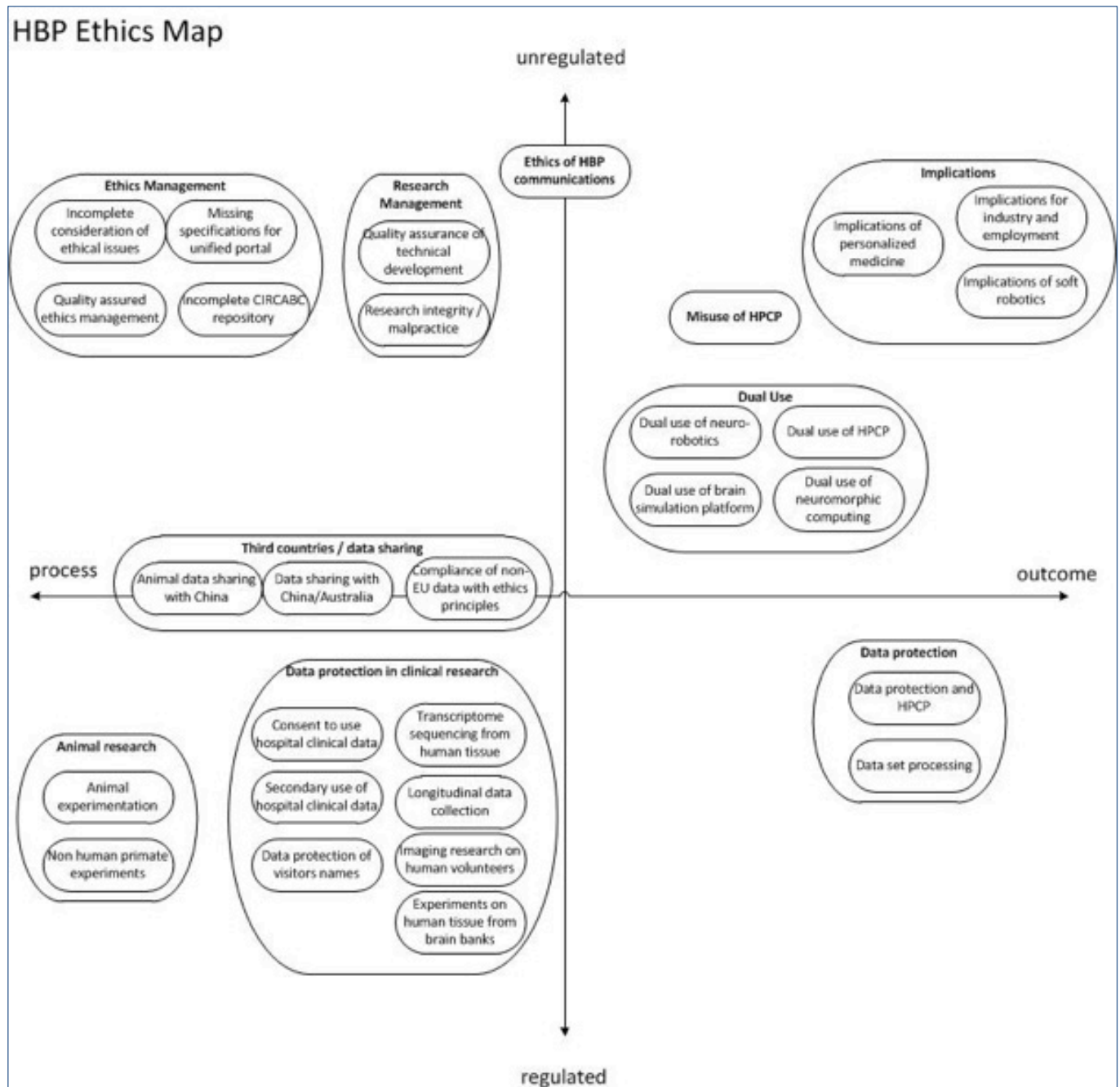
Figure 8: Graphical overview of the current content of the HBP Ethics Map

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

Table 27: 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 humans, including research staff?	☐Yes ☒No
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.	

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.

Table 28: HBP FPA - Ethics Issues and Requirement Descriptions

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.

Ethics Issue Category	Ethics Requirement Description	Actions / Plans by HBP
		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 Management and Coordination 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 mechanisms 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 appropriate ethics standards and guidelines to be organised, including when the R&D is carried out outside the Core Project.	This monitoring of appropriate ethics standards is the remit the Compliance Management task. The principle 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.

Ethics Issue Category	Ethics Requirement Description	Actions / Plans by HBP
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

Ethics Issue Category	Ethics Requirement Description	Actions / Plans by HBP
		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 (BoD – predecessor of the SIB).
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*

Ethics Issue Category	Ethics Requirement Description	Actions / Plans by HBP
		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 Ombudsperson is described at the beginning of this FPA in section 2.5.1.3.10 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 PPs, that ethical and legal compliance is of high priority for the long term sustainability of the initiative.	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 2.5.1.3.3) who will be elected by the EAB and who will be a member of the Directorate, thus ensuring the presence of ethics on all 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	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.

Ethics Issue Category	Ethics Requirement Description	Actions / Plans by HBP
	provided in the Description of Actions of the successive SGAs	
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.

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 ongoing 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 modelling (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 & characterisation 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

Table 29: Main Objectives / Deliverables per SGA for SP1: Mouse Brain Organisation (= Table 4*)

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, fibre 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 behaviours. Spatial organisation 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 organisation 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.
	M103-M114	Fully integrated multi-level map of the mouse brain including data from the Core Project, Partnering Projects and collaborations

* See cross reference table in Section 2.3.1.3 Subproject 1: 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 organisation 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 authorised 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

Table 30: Main Objectives / Deliverables per SGA for SP2: Human Brain Organisation (= Table 5*)

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.
	M103-M114	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.

* See cross reference table in Section 2.3.1.4 Subproject 2: 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 organisation, 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 emphasised 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 organisation 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 characterising 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 characterised 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 characterised 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 standardised 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 organisation 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 organisation when brain state changes. Infer properties of awake resting states from the multi-scale organisation 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. Characterise through a perturbational approach the multi-scale organisation (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 dendritic feedback mechanisms in rodents 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

Table 31: Main Objectives / Deliverables per SGA* for SP3: Systems and Cognitive Neuroscience (= Table 6**)

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).
	M103-M114	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.

*Timings for attainment of these objectives are approximate and need to be confirmed by the partners undertaking the work.
** See cross reference table in Section 2.3.1.5 Subproject 3: Systems and Cognitive Neuroscience.

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 characterisation 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 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.

- 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

Table 32: Main Objectives / Deliverables per SGA for SP4: Theoretical Neuroscience (= Table 7*)

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.
	M103-M114	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.

* See cross reference table in Section 2.3.1.6 Subproject 4: 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.

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 <u>Core Project</u> 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. <u>Partnering Projects</u> 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, organised 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.

A1.8.5   SP5: Main Objectives / Deliverables per SGA

Table 33: Main Objectives / Deliverables per SGA for SP5: Neuroinformatics (= Table 8*)

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 centres. Integrate vascular and glial data and predictions. Release multilevel human brain atlas with structural and

Phase	Months	Main Objective(s) / Deliverable(s)
		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.
	M103-M114	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 centres 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.

* See cross reference table in Section 2.3.1.7 Subproject 5 Neuroinformatics Platform.

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 <u>Core Project</u> 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 organisation 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. <u>Partnering Projects</u> 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 organisation 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]

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.

- 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 standardise 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

Table 34: Main Objectives / Deliverables per SGA for SP6: Brain Simulation Platform (= Table 9*)

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.
	M103-M114	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.

* See cross reference table in Section 2.3.1.8 Subproject 6: 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

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

Table 35: Main Objectives / Deliverables per SGA for SP7: High-Performance Analytics & Computing Platform (= Table 10*)

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
	M103-M114	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

* See cross reference table in Section 2.3.1.9 Subproject 7: 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 harmonising heterogeneous clinical databases, data anonymization, ontology-based query interfaces, federated search and distributed analysis of clinical data.

- Establish agreements/MoUs, in consultation with authorised representatives of involved HBP Partners, for access to hospital data, centralised 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

Table 36: Main Objectives / Deliverables per SGA for SP8: Medical Informatics Platform (= Table 11*)

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-SGA3 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

Phase	Months	Main Objective(s) / Deliverable(s)
		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.
	M103-M114	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.

* See cross reference table in Section 2.3.1.10 Subproject 8: 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).

The University of Southern California (USC) can provide privileged access to public USC datasets. USC provided information regarding the variables in datasets (provenance, instruments, coding system, etc). This information was used for the harmonisation of the clinical data with research data.

A1.11.7   SP8: Impact and Innovation Potential

2.5.2.1.1   Scientific Impact

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: 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 <u>Neuromorphic Computing Platform</u> 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 <u>Brain Simulation Platform</u> 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 <u>High Performance Computing Platform</u>, 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 <u>Brain Simulation Platform</u>. 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 <u>Core Project</u> 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).

Table 37: Development roadmap for Physical Model Neuromorphic Computing Systems (PM-NCS)

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 (*)	**50 Wafers** 50M Neurons 13B Synapses	**Structured Neurons**	65nm CMOS **30 cm Wafers** Wafer-on-PCB	**Torus Architecture**	System construction cost (in addition to the

System Version	Unit Numbers / HW cost	Neuroscience Features	Technologies	Infrastructure	System construction costs
construction start possible in month 100		Up to 16000 syn. inputs 6-bit synapses STP, STDP Plasticity Processor x1.000-x10.000 acc.	**FPGA-less**	**On-wafer digital links** 100TFlop local cluster	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	

(*) The choice between options a and b will depend on the result of technology R+D on wafer-PCB embedding

Table 38: Development Roadmap for Many Core Neuromorphic Computing Systems (MC-MCS)

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

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

Table 39: Main Objectives / Deliverables per SGA for SP9: Neuromorphic Computing Platform (NM)
(= Table 12*)

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)
	M103-M114	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)

* See cross reference table in Section 2.3.1.11 Subproject 9: Neuromorphic Computing Platform

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 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 <u>Brain Simulation Platform</u> running slower than real time, and to emulated models on the <u>Neuromorphic Computing Platform</u> 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 <u>Core Project</u> 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. <u>Partnering Projects</u> 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 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, <u>biologically inspired robots</u> have mainly come from academic research. However, recent advances in humanoid and four-legged robots have led 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.
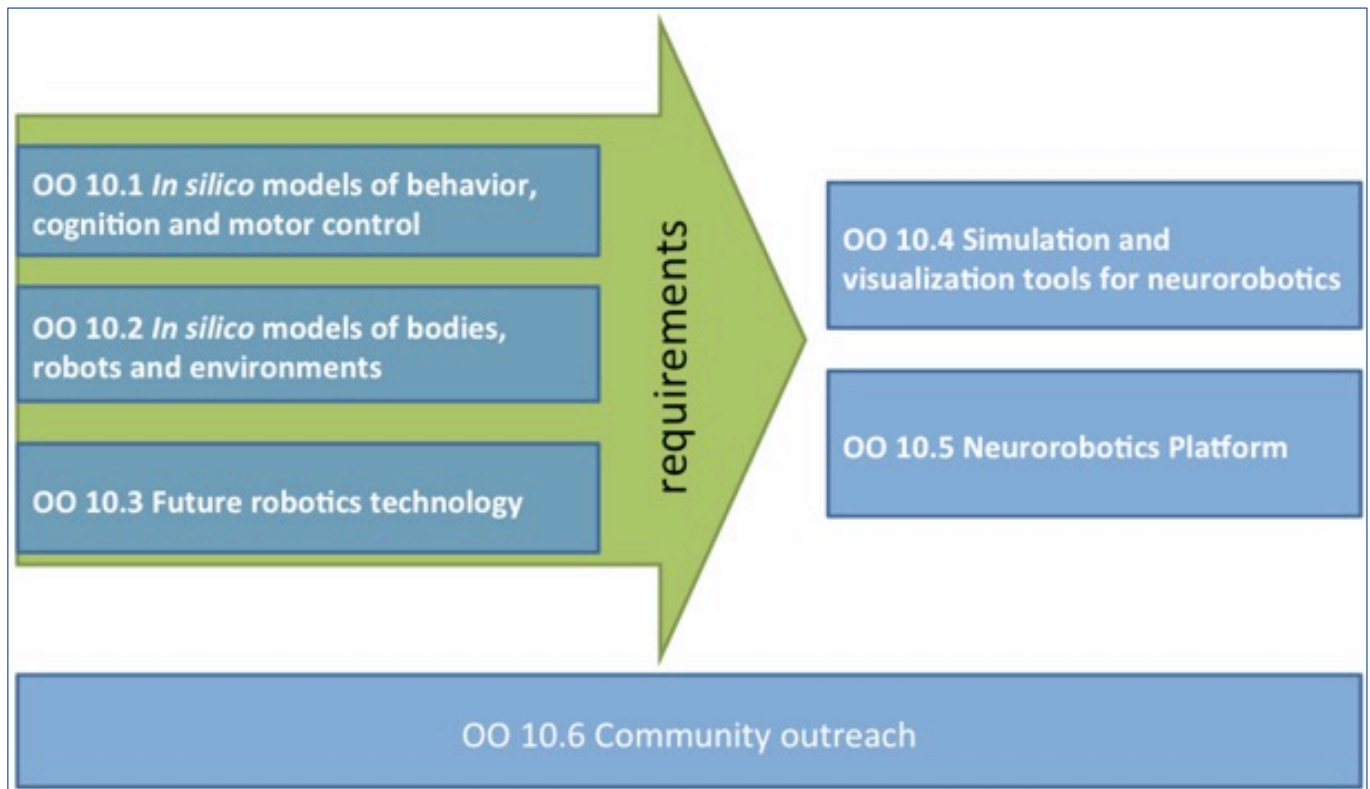
A1.13.4   SP10: Operational Objectives

Figure 9: 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 standardise 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

Table 40: Main Objectives / Deliverables per SGA for SP10: Neurorobotics Platform (= Table 13*)

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.
	M103-M114	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.

* See cross reference table in Section 2.3.1.12 Subproject 10: 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.

Table 41: Main Objectives / Deliverables per SGA for SP12: Ethics & Society (= Table 15*)

SGA	Deliverable	Due date
SGA1	SP12 first "opinions" report	End of SGA1 Y1
	SP12 second "opinions" report	End of SGA1 Y2
	SP12 first activities report	End of SGA1 Y1
	SP12 second activities report	End of SGA1 Y2
SGA2	SP12 first "opinions" report	End of SGA2 Y1
	SP12 second "opinions" report	End of SGA2 Y2
	SP12 first activities report	End of SGA2 Y1
	SP12 second activities report	End of SGA2 Y2
SGA3	SP12 first "opinions" report	End of SGA3 Y1
	SP12 second "opinions" report	End of SGA3 Y2
	SP12 first activities report	End of SGA3 Y1
	SP12 second activities report	End of SGA3 Y2

* See cross reference table in Section 2.3.1.14 Subproject 12: Ethics and 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 Management and Coordination 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

The Human Brain Project (HBP) Flagship[1] 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 co-funding contributions to the Flagship[2]. 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 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.

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[1] https://www.humanbrainproject.eu/

[2] Such co-funding contributions, from organisations in the Core and Partnering Projects, include access to research infrastructures, experimental facilities and use of technical equipment, extra personnel, etc.

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 Section 2.3.2.6) 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:

Table 42: Benefits of Participating in the HBP as a Partnering Project

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[3]	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[4]	Yes
Direct funding from the core project	No	No	Yes

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[3] Inclusion of published results by permission only. Work not funded by the CP will be clearly identified.

[4] Unless otherwise agreed in an agreement.

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, 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 organisation 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 organisation 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 organisation 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: Management and Coordination

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).
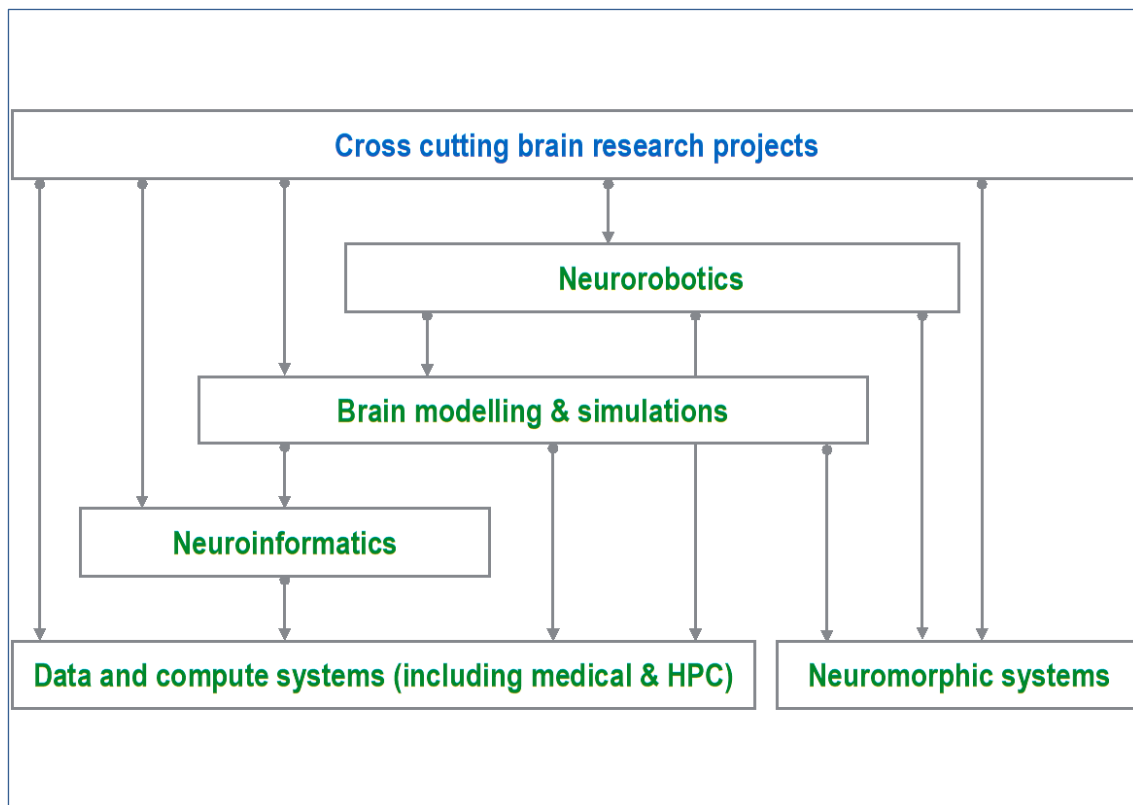
Figure 10: Relationship between the ICT infrastructure "Platforms" developed in the HBP.

(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 through 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.

Table 43: Overview of the HBP Timeline, RI Development and Adoption Cycle.

	HBP Project Phase		
	Ramp-Up	**SGA1**	**SGA2**
Timeframe	10/2013—09/2016	04/2016—03/2018	04/2018—03/2020
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

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.
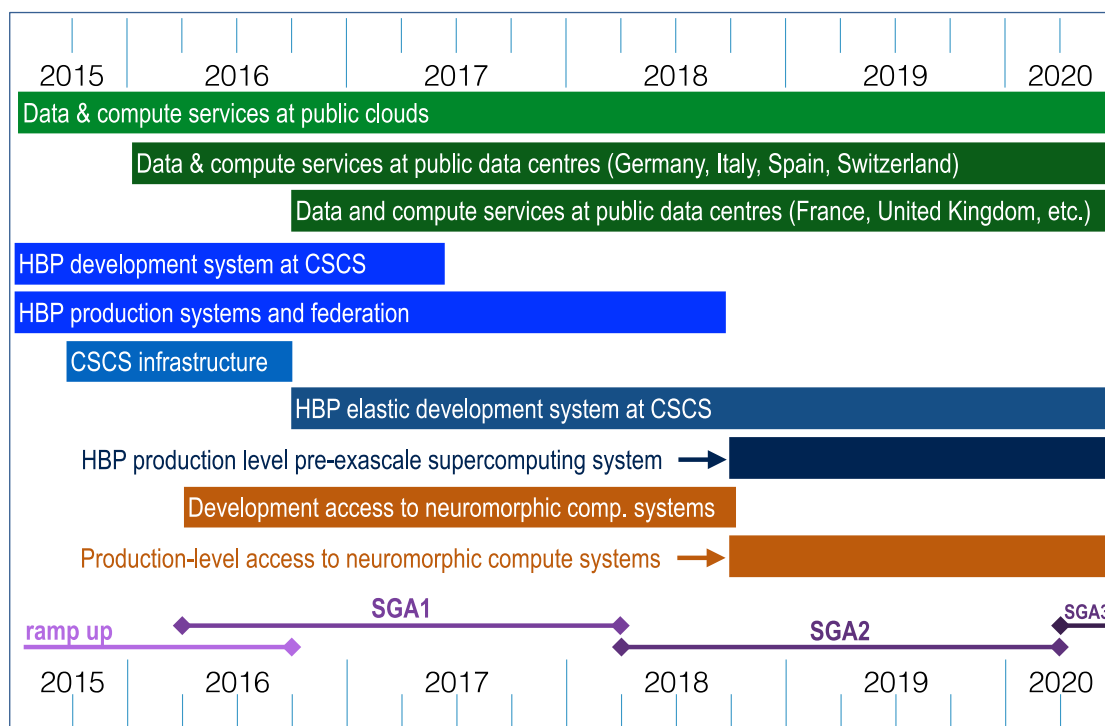
Figure 11: Timeline of the base infrastructure for the HBP

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 organisational 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 organised 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 12: 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 Opensource 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.
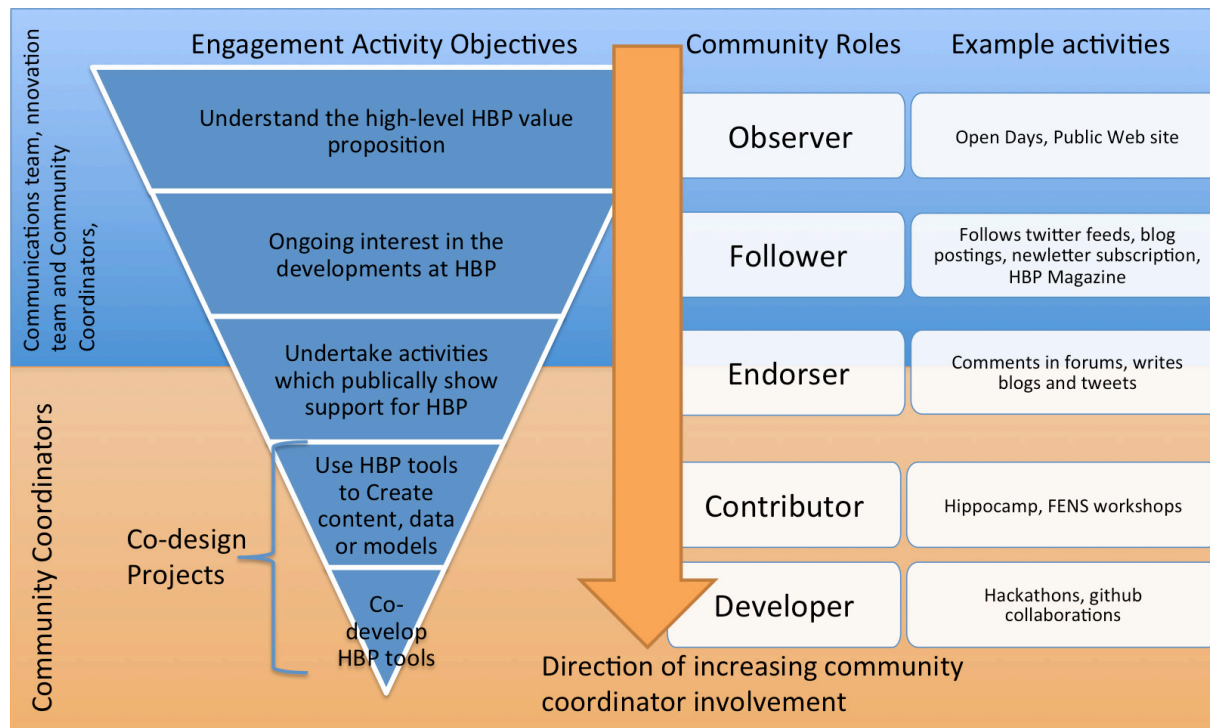

Figure 13: Community Engagement "Funnel"

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.

1) 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.

2) 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 2.1.2.7. 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

For details of each Partner's participating labs and key personnel in each funding period of the Project please refer to the corresponding Grant Agreement:

- Ramp-Up Phase (Oct 2013 to Mar 2016): §2.2.2. Descriptions of the partners & Appendix I – Detailed descriptions of key personnel
- SGA1 (Apr 2016 to Mar 2018): §4.1 Participants (applicants)
- SGA2 (Apr 2018 to Mar 2020): Appendix 4: Participants (applicants)
- SGA3 (Apr 2020 to Mar 2023): Annex B: Members of the Consortium

P1) EBRAINS, EBRAINS, Belgium and Switzerland (SGA3: WP7 & WP8), former P134

Active HBP Partner: SGA3

EBRAINS is an AISBL (*Association Internationale Sans But Lucratif*) under Belgian Law. Its mission is to coordinate the Human Brain Project in SGA3 and to build the future EBRAINS Research Infrastructure in the longer term. EBRAINS is located in Brussels but it has a Swiss branch in Geneva (ex-EPFL Project Coordination Office) to facilitate the transition and continuity of coordination activities during SGA3.

P2) AALTO, *Aalto-Korkeakoulusäätiö*, Finland (SP10)

Active HBP Partner: RUP, SGA1, SGA2

AALTO withdrew from the HBP Consortium at the end of 2020.

P3) LUMC, *Academisch Ziekenhuis Leiden - Leids Universitair Medisch Centrum*, The Netherlands (SP8)

Active HBP Partner: RUP (CEoI), SGA1

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, www.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.

P4) AUEB, Athens University of Economics and Business, Greece (SP8; SGA3: WP4)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Information Processing Lab was founded in 1998 and is part of the Division of Information Systems and Databases of the Department of Informatics at the Athens University of Economics and Business. The Lab supports the research and teaching of the Department of Informatics.

P5) BSC, Barcelona Supercomputing Centre - *Centro Nacional de Supercomputación*, Spain (SP7; SGA3: WP4, WP6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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*.

P6) BAUW, *Bauhaus-Universitaet Weimar*, Germany (SP10)

Active HBP Partner: SGA1, SGA2

BAUW withdrew from the HBP Consortium at the end of 2020.

P7) BUW, *Bergische Universität Wuppertal*, Germany (SP7; SGA3: WP5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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 High Performance Computing / Software Engineering Group focuses on efficient numerical algorithms for computer simulation in the sciences.

P8) BSMJ, Bloomfield Science Museum Jerusalem, Israel (SP11)

Active HBP Partner: RUP, SGA1, SGA2

BSMJ withdrew from the HBP Consortium at the end of 2020.

P9) CF, Cardiff University, United Kingdom (SP8)

Active HBP Partner: SGA1, SGA2

CF withdrew from the HBP Consortium at the end of 2020.

P10) CNRS, *Centre National de la Recherche Scientifique*, France (SPs 4, 6, and 9; SGA3: WPs1, 2, 4 and 6)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI), SGA3

The Department of *Neurosciences Intégratives et Computationnelles, Information et Complexité* of the Neuro-PSI is a multidisciplinary research unit combining experimental and theoretical neuroscience.

The Bioinformatics: Structures and Interactions group (CNRS-IBCP, Lyon) is one of ten that form the *Institut de Biologie et Chimie des Protéines* (IBCP), an institute centred on molecular microbiology and structural biochemistry.

The Centre Giovanni Borelli aims at producing both fundamental mathematical results, algorithms and software tools, technologies for large scale data acquisition and analysis.

P11) CEA, *Commissariat à l'Énergie Atomique et aux Énergies Alternatives*, France (SPs 2 and 5; SGA3: WPs 1, 2, 4 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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 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.

The INSERM-CEA Cognitive Neuroimaging Unit is a research group directed by Stanislas DEHAENE at NeuroSpin. The unit investigates high-level cognitive functions and consciousness at different scales of observation in the human and non-human primate (NHP) brain.

P12) CNR, *Consiglio Nazionale Delle Ricerche*, Italy (SPs 4, 6 and 8; SGA3: WPs1, 2, 3, 4 and 5)

Active HBP Partner: RUP (CEoI), SGA1, SGA2 (CEoI), SGA3

The Italian National Research Council (CNR) carries out, promotes, transfers and improves research activities, and their applications for the scientific, technological, economic and social development of the country. CNR Institutes are distributed all over Italy.

The National Institute of Optics (INO) performs pure and applied research, technology transfer, consulting, metrology and testing services, and training activities.

The Pezzulo Lab is part of the Institute of Cognitive Sciences and Technologies, National Research Council (CNR). The lab focuses on computational modelling and the analysis of neural data.

IN-CNR is part of the Neuroscience Institute of National Research Council, established via an agreement between the Neuroscience Department of Parma University and the Neuroscience Institute of CNR.

P13) CINECA, *Consorzio Interuniversitario Cineca*, Italy (SP7; SGA3: WPs 4 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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 facility for supercomputing and one of the largest HPC centres in Europe. It has an HPC & Data Analytics environment equipped with cutting-edge technology and supported by highly-qualified personnel. I

P14) DTU, *Danmarks Tekniske Universitet*, Denmark (SP10)

Active HBP Partner: SGA1, SGA2

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.

P15) UoD, *Debreceni Egyetem*, Hungary (SP1)

Active HBP Partner: SGA1, SGA2

UoD withdrew from the HBP Consortium at the end of 2020.

P16) DMU, De Montfort University, United Kingdom (SP12; SGA3: WPs 3, 4 and 9)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

DMU's School of Computer Science and Informatics has teaching, learning and research/commercial activities that broadly span computer science, computer security, software engineering, computing for business as well as games programming, artificial intelligence, robotics and mathematics.

The Centre for Computing and Social Responsibility sits within the SCSI and is the only research centre in the UK specialising in the ethical and social issues of computing and information systems.

P17) ENS, *École Normale Supérieure*, France (SP6)

Active HBP Partner: RUP, SGA1, SGA2

The ENS is a leading publicly funded higher education institution in France. 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, it developed new video microscopy techniques using nano-semiconductor particles, also known as quantum dots.

P18) ETHZ, *Eidgenössische Technische Hochschule Zürich*, Switzerland (SP7; SGA3: WPs 4, 5 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Swiss National Supercomputing Centre (CSCS) partners with Swiss universities and research institutions to provide scientists with the computing infrastructure and expertise they need, from cutting-edge supercomputers, to a full range of services delivered by an international team of 100 personnel. CSCS is an autonomous unit of the Swiss Federal Institute of Technology in Zurich (ETH Zurich).

P19) FT, *Fonden Teknologirådet*, Denmark (SP12; SGA3: WPs 4, 6 and 9)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P20) JUELICH, *Forschungszentrum Jülich GmbH*, Germany (SPs 2, 4, 5, 6, 7 and 9; SGA3: WPs 1, 2, 3, 4, 5, 6, 7 and 8)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Institute of Neuroscience and Medicine — Structural and Functional Organisation of the Human Brain (INM-1) is developing a 3D model of the human 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 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.

The Institute of Neuroscience and Medicine — Brain and Behavior (INM-7) is developing novel methods for mapping the regional organization of the human brain into cortical areas.

The Computational Biomedicine Institute (INM-9/IAS-5) develops multi-scale molecular simulation and data-mining approaches to predict structural and energetic aspects of neurological pathways.

The Functionality of Cortical Circuits (INM-10) group investigates the structural and functional aspects of synaptic transmission and its modulation.

The Jülich Supercomputing Centre (JSC) has long-standing expertise in operating supercomputers of the highest performance and co-designs innovative high performance computing technology.

P21) FORTISS, *Fortiss GmbH*, Germany (SP10; SGA3: WPs 4 and 5)

Active HBP Partner: SGA1, SGA2, SGA3

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*). Fortiss' mission is to facilitate research and technology transfer in software-intensive systems and services, thereby triggering future-ready innovation.

P22) FG, *Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V.*, Germany (SPs 7, 8 and 9)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI)

The Fraunhofer Institute für Zuverlässigkeit und Mikrointegration (IZM) is a world leader in microelectronics and microsystem packaging.

The Fraunhofer Institute for Algorithms and Scientific Computing (SCAI) conducts research in the field of computer simulations for product and process development.

P23) FCHAMP, *Fundaçao D. Anna Sommer Champalimaud E Dr Carlos Montez Champalimaud*, Portugal (SP2)

Active HBP Partner: RUP, SGA1, SGA2

FCHAMP withdrew from the HBP Consortium at the end of 2020.

P24) UDUS, *Heinrich Heine Universität Düsseldorf*, Germany (SP2; SGA3: WPs 1 and 4)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Cécile and Oskar Vogt Institute of Brain Research is one of Germany's major centres of neuroscience, and has a long and prominent history in brain mapping.

The Institute of Anatomy I is integrated into the preclinical training of students in the human and dental medicine sectors.

The Institute of Systems Neuroscience is dealing with the integrated investigation and modelling of structures, function and connectivity of the human brain.

P25) UH, *Helsingin yliopisto*, Finland (SP10 until SGA1, SP2 in SGA2)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

UH withdrew from the HBP Consortium at the end of 2020.

P26) HITS, *HITS gGmbH*, Germany (SP6; SGA3: WP5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P27) CHUV, *Hospices Cantonaux, Centre Hospitalier Universitaire Vaudois*, Switzerland (SP8; SGA3: WP4)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The *Laboratoire de recherche en neuroimagerie* (LREN) studies the role of human brain structure and function in neurological disorders and healthy aging.

The CHUV Department of Clinical Neuroscience (DNC) is a university hospital department of international standard open to all patients suffering from diseases of the nervous system.

The Direction des Systèmes d'information (DSI) is the IT department of CHUV, which mission is to develop and operate the CHUV information systems.

P28) ICL, Imperial College of Science, Technology and Medicine, United Kingdom (SP8 until the end of SGA1; SP5 in SGA2)

Active HBP Partner: SGA1, SGA2

P29) ICM, *L'Institut du Cerveau et de la Moelle Épinière*, France (SP8; SGA3 WP1)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Molecular Basis, Physiopathology and Treatment of Neurodegenerative Diseases Lab focuses on the phenotypical and genetic characterisation of patients with different neurodegenerative conditions (HD, PD, frontotemporal lobar degenerations, etc.).

The Motivation, Brain and Behavior (MBB) group aims at disclosing the biopsychological determinants of behavior.

P30) IEM HAS, Institute of Experimental Medicine Hungarian Academy of Sciences, Hungary (SPs 1 and 6; SGA3: WP1)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P31) IST, Institute of Science and Technology Austria, Austria (SP1)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

IST withdrew from the HBP Consortium at the end of 2020.

P32) JSI, *Institut Jozef Stefan*, Slovenia (SP8)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

JSI withdrew from the HBP Consortium at the end of 2020.

P33) INRIA, *Institut National de Recherche en Informatique et en Automatique*, France (SPs 2 and 4; SGA3: WPs 1, 2 and 4)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

INRIA is dedicated to fundamental and applied research in information and communication science and technology (ICST). The MathNeuro Inria Project-Team addresses key questions in Neuroscience using adapted mathematical tools.

P34) IP, *Institut Pasteur*, France (SPs 2 and 12; SGA3: WP5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Integrative Neurobiology of Cholinergic Systems Lab at the Pasteur Institute works on the functional analysis of brain circuits. It aims to understand how nicotine acts on the brain, affects cognition, and causes addiction.

The Human Genetics and Cognitive Functions Group gathers geneticists, neurobiologists and clinicians to explore the relationship between genetics and the susceptibility to psychiatric conditions.

P35) UFRA, *Johann Wolfgang Goethe Universität Frankfurt am Main*, Germany (SP7)

Active HBP Partner: RUP, SGA1, SGA2

UFRA withdrew from the HBP Consortium at the end of 2020.

P36) KIT, *Karlsruher Institut für Technologie*, Germany (SP7)

Active HBP Partner: RUP, SGA1, SGA2

KIT withdrew from the HBP Consortium at the end of 2020.

P37) KI, *Karolinska Institutet*, Sweden (SPs 1, 5, 6, and 12; SGA3: WPs 1, 3 and 4)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

The Department of Neurobiology, Care Sciences and Society consists of 11 divisions. Some 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.

P38) KCL, King's College London, United Kingdom (SPs 8 and 12)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI), SGA3

KCL withdrew from the SGA3 as of the beginning of 2021.

P39) KTH, *Kungliga Tekniska Hoegskolan*, Sweden (SPs 4, 6, 9 and 10; SGA3: WPs 1, 3, 4, 5 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Department of Computational Biology (CST) at the KTH School of Computer Science and Communication is the largest computational neuroscience, neuroinformatics, and neurocomputing centre in Sweden. The CST also leads the Swedish INCF national node.

The PDC Center for High Performance Computing is the leading supercomputing centre for the Swedish academic community, and provides HPC resources to many important research groups, including the Stockholm Brain Institute (Karolinska Institute), Stockholm University, and KTH.

P40) LENS, *Laboratorio Europeo di Spettroscopie Non Lineari*, Italy (SPs 1 and 2; SGA3: WPs 1, 2 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

LENS is an interdisciplinary research center within the University of Florence.

The Biophysics and Biophotonics group aims at develop innovative imaging and analytical 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.

P41) LNU, *Linnaeus University*, Sweden (SPs 11 and 12; SGA3: WPs 4, 7 and 9)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

In the LNU's Department of of Chemistry and Biomedical Sciences, within the Faculty of Health and Life Sciences & Office of External Relations, research is carried out in biochemistry, theoretical chemistry, galenic pharmacy and physical chemistry.

P42) MUI, *Medizinische Universität Innsbruck*, Austria (SP11; SGA3: WP8)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Medical University of Innsbruck stands for outstanding performance in the fields of science, research, teaching and patient care. Together with the university hospital, it is our vision to be the leading centre of medicine in Western Austria. We employ highly qualified teachers to provide our students with the best possible training. The research results of scientists at the Medical University of Innsbruck are published to international acclaim.

P43) UoA, *Ethniko Kai Kapodistriako Panepistimio Athinon*, Greece (SP8)

Active HBP Partner: RUP, SGA1, SGA2

The Management of Data, Information, and Knowledge (MaDgIK) Group focuses on 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.

P44) NMBU, *Norges miljø- og biovitenskapelige iniversitetet*, Norway (SPs 4, 6 and 7; SGA3: WPs 2, 3, 4 and 5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Computational Neuroscience Group has 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, astrocyte-neuron interactions, large-scale simulations of networks of spiking neurons, developing the NEST simulation tool, and generating connectivity in large network models.

P45) OFAI, *Oesterreichische Studiengesellschaft für Kybernetik*, Austria (SP10)

Active HBP Partner: SGA1, SGA2

OFAI withdrew from the HBP Consortium at the end of 2020.

P46) RWTH, *Rheinisch-Westfälische Technische Hochschule Aachen*, Germany (SP7; SGA3: WP5)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI), SGA3

The Virtual Reality Group at RWTH researches new visualisation and virtual reality methods for scientific applications. The group 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.

P47) UHEI, *Ruprecht-Karls-Universität Heidelberg*, Germany (SPs 5, 9, and 11; SGA3: WPs 4, 5, 6, 7 and 8)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Kirchhoff-Institute for Physics at UHEI implements information processing in massively parallel, mixed-signal VLSI technologies, including bio-inspired vision sensors, sensory substitution systems, analog evolvable hardware devices and very large-scale neuromorphic information processing systems.

The UHEI Multidimensional Image Processing (MIP) group develops algorithms for bioimage analysis, and makes advanced machine learning and image analysis methods available to experimental end users.

P48) SU, Sabancı University, Turkey (SP9)

Active HBP Partner: RUP, SGA1, SGA2

SU withdrew from the HBP Consortium at the end of 2020.

P49) SSSA, *Scuola Superiore di Studi Universitari e di Perfezionamento Sant'Anna*, Italy (SP10; SGA3: WPs 3 and 5)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

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.

P50) CWI, *Stichting Nederlandse Wetenschappelijk Onderzoek Instituten*, The Netherlands (until 31 Dec 2017: *Stichting Centrum voor Wiskunde en Informatica* (SGA1: SP5; SGA3: WP3)

Active HBP Partner: RUP, SGA1, SGA3

The Stichting Centrum voor Wiskunde en Informatica (CWI) is the Dutch national research institute for mathematics and computer science. Its mission is to perform frontier research in mathematics and computer science, and to transfer new knowledge in these fields to society.

P51) SKU, *Stichting Katholieke Universiteit*, The Netherlands - The Donders Institute (SP5; SGA3: WP4)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

Radboud University Nijmegen is a broad public research university. Its neuroscience research activities are organized in The Donders Institute for Brain, Cognition and Behaviour. Our research includes cognition and behavior in humans as well as on the neuronal substrate, including the genetic, molecular and cellular processes that underlie cognition and behaviour. We cover the full spectrum of research 'from Molecule to Man'.

P52) FZI, *Stiftung FZI Forschungszentrum Informatik am Karlsruher Institut für Technologie*, Germany (SP10; SGA3: WP3)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

The mission of the FZI Research Centre for Information Technology (FZI) is to facilitate technology transfer of innovative solutions in ICT, and to create a link between academia and industry.

The department of Interactive Diagnosis and Service Systems (IDS) concentrates on the development of intelligent, mobile service robots and supporting technologies.

The Software Engineering (SE) division analyses, designs, develops, adapts, and evolves complex mobile and multi-platform software.

P53) TUC, Technical University of Crete, Greece (SP5)

Active HBP Partner: RUP, SGA1

TUC withdrew from the HBP Consortium at the end of 2020.

P54) TUD, *Technische Universität Dresden*, Germany (SP9; SGA3: WP6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Endowed Chair of Highly-Parallel VLSI-Systems and Neuromorphic Circuits group has an extensive track record in VLSI circuit design for advanced digital and analogue systems. 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).

P55) TUGRAZ, *Technische Universität Graz*, Austria (SP9; SGA3: WP3)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Institute of Theoretical Computer Science at *Technische Universität Graz* (Graz University of Technology) develops theory and computer models to understand computation and learning in biological neural systems and artificial networks of spiking neurons.

The Legenstein Lab for Learning Principles in Biological and Bio-inspired Systems uses mathematical analysis and computer simulations to investigate fundamental principles of learning and self-organisation in biological neuronal networks and neuromorphic systems.

P56) TUM, *Technische Universität München*, Germany (SPs 10 and 11; SGA3: WPs 3, 4, 5 and 7)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Robotics and Embedded Systems group is part of the TUM Department of Informatics. Its primary mission is the research and education of machines for perception, cognition, action and control.

The Research group on Fusing Augmented Reality focuses on Ubiquitous Augmented Reality — a combination of ubiquitous computing, wearable computing and augmented reality.

The Chair of Industrial Design operates on the field of design and realisation of industrial products, product systems, services and corporate strategies.

The Neuroscientific System Theory (NST) group at TUM investigates theory, models, and practical robotic implementations of distributed neuronal information processing.

P57) TAU, Tel Aviv University, Israel (SPs 8 and 11; SGA3: WPs 1 and 8)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Department of Statistics and Operations Research, School of Mathematical Sciences, has expertise in a broad range of theoretical and applied statistics. We have been at the forefront of research on statistical aspects of replicability in life sciences, including preliminary, basic, pre-clinical, clinical and post clinical studies. We are actively involved in research on efficient and reliable study design for both exploratory and confirmatory research.

P58) UCAM, University of Cambridge

Active HBP Partner: RUP

UCAM withdrew from the HBP Consortium on 30 June 2016.

P59) UOXF, The Chancellor, Masters and Scholars of the University of Oxford, United Kingdom (SPs 1, 2 and 10; SGA3: WP3)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI), SGA3

The University of Oxford (UOXF) is the oldest university in the English-speaking world.

The MRC Functional Genomics Unit (FGU) delivers a combination of computational genomics and cellular and model organism experimentation, to address some of the most important questions in neuroscience.

The Oxford Physiome Lab, with the Auckland Bioengineering Institute (NZ), develops anatomically and physiologically based models of mammalian organ systems.

The Human Information Processing Lab studyes the neural and computational mechanisms of human decision-making, using behavioural testing, modelling and functional brain imaging.

P60) HUJI, Hebrew University of Jerusalem, Israel (SPs 4 and 6; SGA3: WP1)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P61) UABER, University of Aberdeen, United Kingdom (SP6)

Active HBP Partner: SGA1

UABER withdrew from the HBP Consortium on 1 January 2019.

P62) UEDIN, University of Edinburgh (SP1; SGA3: WPs 1 and 5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The School of Informatics' research strengths include database technology, theory and data mining; neural computation and systems biology modelling; data sciences including probabilistic modelling and machine learning; and naturally inspired computation and robotics.

P63) UMAN, University of Manchester, United Kingdom (SPs 9 and 11; SGA3: WPs 4, 5 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Advanced Processor Technology (APT) group focuses on issues related to the complexity of microelectronic design. It addresses three Grand Challenges: "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).

The SpiNNaker Software Group (SSG) focuses on the provision of software support for SpiNNaker, both NM-MC1 and NM-MC2.

P64) UAM, *Universidad Autónoma de Madrid*, Spain (SP1; SGA3: WP2)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Cellular Connectomics 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.

P65) UCLM, *Universidad de Castilla - La Mancha*, Spain (SP1)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

The Synaptic Structure Laboratory (Syslab) focuses on unravelling several aspects of the neuronal functional structure. This knowledge is important to understanding the basic mechanisms by which the brain functions and 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.

P66) UGR, *Universidad de Granada*, Spain (SP10; SGA3: WPs 3 and 5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Computational Neuroscience and Neurorobotics 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.

P67) UMINHO, *Universidade do Minho*, Portugal (SPs 1, 2, 5, 6 and 10)

Active HBP Partner: SGA1, SGA2

The Neuroscience Research Domain at ICVS 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.

P68) UPM, *Universidad Politécnica de Madrid*, Spain (SPs 1, 5, 6, 7 and 11; SGA3: WPs 1, 4, 6 and 8)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The *Laboratorio Cajal de Circuitos Corticales* aims to combine experimental studies of the brain with computer science technologies.

The Computational Intelligence Group is devoted to modelling (from a statistical and machine learning perspectives), heuristic optimisation, and neuroinformatics.

The Centre for Computational Simulation does research in Computational Science and Engineering.

The Center for Technology Innovation drives technology-based entrepreneurship and exploitation of research results.

P69) URJC, *Universidad Rey Juan Carlos*, Spain (SPs 1 and 7; SGA3: WP5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P70) UNIPV, *Universita degli Studi di Pavia*, Italy (SPs 1 and 6; SGA3: WPs 1, 3, 4 and 5)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Brain Connectivity Centre, Laboratory of Neurophysiology, 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 Department of Chemistry joined the HBP via the CEoI "COVID-19 and its impact on the brain and mental health" with the proposal "BRAVE - Protecting the brain from COVID-19-mediated neurodegeneration through inflammasome inhibition" (in WP5).

Research at the Department of Chemistry's Colombo Lab aims to explore the links between protein sequence, structure, conformational dynamics and molecular recognition to identify the atomistic determinants of defined biological (mis)functions.

P71) UBERN, *Universität Bern*, Switzerland (SP4; SGA3: WPs 2 and 3)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P73) UKAACHEN, *Universitätsklinikum Aachen*, Germany (SP8)

Active HBP Partner: SGA1, SGA2 (CEoI)

The Department of Psychiatry, Psychotherapy and Psychosomatics offers treatment for around 120 inpatients, houses 50 day-care patients and offers numerous highly specialised ambulatory therapeutic interventions. With the *Forschungszentrum Jülich,* it 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.

P74) UKE, *Universitätsklinikum Hamburg-Eppendorf*, Germany (SP10 until end of SGA1; SP2, CDP8 from SGA2; SGA3: WP1)

Active HBP Partner: RUP (CEoI), SGA1, SGA2 (CEoI), SGA3

The Department of Neurophysiology and Pathophysiology studies cognitive and sensorimotor functions in humans and animal models using neurophysiological and neuroimaging techniques.

The Institute of Computational Neuroscience advances understanding of fundamental organizational principles of brain function and structure by computational analysis and modeling and translates these findings into clinical applications.

P75) UZH, *Universität Zürich*, Switzerland (SP1)

Active HBP Partner: RUP, SGA1, SGA2

UZH withdrew from the HBP Consortium at the end of 2020.

P76) UB, *Universitat de Barcelona*, Spain (SP10; SGA3: WP2)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The Experimental Virtual Environments for Neuroscience and Technology (EVENT Lab) 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 Math-Neuro Action (MNA) lab investigates the mechanisms that explain how the brain controls behavior, with emphasis on how sensory information is incorporated to neural dynamics and on how movements and decisions emerge in situated environments.

P77) UPF, *Universitat Pompeu Fabra*, Spain (SP4; SGA3: WPs 1 and 2)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The [Center for Brain and Cognition](link) (CBC) at UFP conducts leading-edge interdisciplinary research in the cognitive neurosciences.

The Computational Neuroscience Group (CNS), investigates neuronal and cortical mechanisms of perception and cognition.

The Theoretical and Cognitive Neuroscience Group (TCN) focuses on investigating how we perceive and decide and uncovering the neuronal mechanisms that define and limit our cognition and self.

P78) AMU, *Université d'Aix Marseille*, France (SPs 4 and 8; SGA3: WPs 1, 2, 4 and 5)

Active HBP Partner: RUP (CEoI), SGA1, SGA2 (CEoI), SGA3

The *Institut des Neurosciences de Système* (INS) combines expertise from computational, cognitive and clinical neuroscience, and biomedical imaging and signal analysis.

Institute of Neuroscience of the Timone (INT) bridges levels of organization of the nervous system to understand the neural underpinnings of behavior and as well as neurological and psychiatric diseases.

The Centre for Magnetic Resonance in Biology and Medicine (CRMBM) explores the morphology, metabolism and pathophysiology of human diseases and associated animal models (rodents).

The Fresnel Institute promotes specialises in biomedical molecular imaging.

P79) UBO, *Université de Bordeaux*, France (SP8)

Active HBP Partner: RUP, SGA1, SGA2

L'Université de Bordeaux (UBO) is a multidisciplinary university with 80 research departments, associated with major research bodies (CNRS, CEA, INSERM and INRA).

The Research Centre in Epidemiology and Biostatistics works on biostatistics, epidemiology of neurological diseases, ageing, HIV and other infectious diseases, cancer, nutrition, and trauma prevention.

P80) UA, *Universiteit Antwerpen*, Belgium (SP4)

Active HBP Partner: SGA1, SGA2

The Theoretical Neurobiology and Neuroengineering Laboratory has done pioneering work in multicompartmental modelling in cerebellar physiology and neuroinformatics, which has had a significant impact on the consolidation of computational neurosciences as a discipline.

P81) UIO, *Universitetet i Oslo*, Norway (SPs 3 and 5; SGA3: WPs 2, 4 and 6)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

The UIO is the largest and highest ranked institution of research and higher education in Norway.

The Neural Systems laboratory supports advanced informatics developments for brain architecture analysis and brain atlasing, and hosts the Norwegian Node of the INCF.

The Brain Signalling 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.

P82) UCL, University College London, United Kingdom (SPs 2, 3, 4, 6, and 8; SGA3: WP1)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI), SGA3

The Synaptic Circuitry Group uses a variety of techniques to study synaptic circuitry.

The Wellcome Trust Centre for Neuroimaging studies how thought and behaviour arise from brain activity, and how such processes break down in neurological and psychiatric disease.

The Space and Memory Lab investigate the neural mechanisms of spatial memory and navigation, with a focus on the functioning of the hippocampus, and its relations to other brain regions.

The Cacucci Lab focuses on the study of hippocampal spatial and memory processing in the rodent.

The Biomolecular Modelling Group develops sampling simulation algorithms to investigate ligand binding, allosteric effects and the mechanism of activation of signalling proteins in atomic details.

The Spatial Cognition Lab studies the neural basis of spatial cognition using a variety of human brain imaging methods and electrophysiological methods with rodents.

The Department of Neuroinflammation and the Department of Experimental & Translational Medicine joined the HBP via the CEoI "COVID-19 and its impact on the brain and mental health", with the proposal "MODEL - Advanced Modeling Of Magnetic Resonance Imaging Data To Study The Biophysical Underpinning Of Neurological Symptoms Of Long-COVID" (in WP1). The group working on MODEL-COV is specialised in advanced quantitative Magnetic Resonance Imaging of the central nervous system. In this project, the group will provide and elaborate data to develop integrated models of the effects of COVID-19 on the brain. This will involve a collaboration with the University of Pavia, to implement virtual brain models of the COVID-19 brain, as well as classification of alterations using AI and the Medical Informatics Platform.

P83) UU, *Uppsala Universitet*, Sweden (SPs 8 and 12; SGA3: WPs 1, 2, 3 and 9)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

Uppsala University it is the oldest university in Sweden.

The Centre for Research Ethics and Bioethics (CRB) 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).

P84) WEIZMANN, Weizmann Institute of Science, Israel (SP4)

Active HBP Partner: RUP, SGA1, SGA2

The Weizmann Institute's Computational Neuroscience Lab adopts a theoretical approach to modelling brain functions, in the fields of learning and memory, space representation in hippocampal formation, visual processing and synaptic transmission in the cortex.

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.

P85) TUDA, *Technische Universität Darmstadt*, Germany (SP7; SGA3: WP6)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

The Laboratory for Parallel Programming creates methods, tools, and algorithms that support the development and deployment of parallel software systems in various stages of their life cycle. The laboratory specialises in programming tools for application performance modelling and parallelism discovery, parallel algorithms, scheduling algorithms for cluster resource management systems, and deep neural networks.

P86) UNIGE, *Université de Genève*, Switzerland (SP8)

Active HBP Partner: RUP (via CEoI?), SGA1, SGA2

UNIGE withdrew from the HBP Consortium at the end of 2020.

P87) UGLA, University of Glasgow, United Kingdom (SP3; SGA3: WP2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

The Muckli group is part of the Institute of Neuroscience and Psychology, the Centre for Cognitive Neuroimaging and the Imaging Centre of Excellence. It studies visual and cognitive neurosciences using fMRI, measures the role of cortical feedback in prediction, using retinotopic mapping to identify regions of V1 receiving no sensory stimulation, to isolate feedback, and uses multivariate pattern classification to decode the information content of top-down signals to distinct cortical layers.

P88) MRC, Medical Research Council

Active HBP Partner: SGA1 (CEoI)

MRC withdrew from the HBP Consortium on 3 October 2017.

P89) UHAM, University of Hamburg, Germany (SP3)

Active HBP Partner: SGA1 (CEoI)

The Biological Psychology and Neuropsychology unit 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).

P90) UBER, *Humbolt-Universität zu Berlin*, Germany (SP3; SGA3: WPs 1 and 2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

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. 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 resources for imaging calcium signals *in vitro* and *in vivo* in dendrites.

P91) KNAW, *Koninklijke Nederlandse Akademie van Wetenschappen – Knaw*, The Netherlands (SPs 2 and 3; SGA3: WPs 1, 2 and 3)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

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.

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.

P92) INFN, *Istituto Nazionale di Fisica Nucleare*, Italy (SP3; SGA3: WP2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

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.

P93) IDIBAPS, *Consorci Institut d'Investigacions Biomediques August Pi I Sunyer*, Spain (SP3; SGA3: WP2)

Active HBP Partner: SGA1(CEoI), SGA2, SGA3

The Consorci Institut D'Investigacions Biomediques August Pi i Sunyer (IDIBAPS) is a public research centre dedicated to translational research in the field of biomedicine.

The Cortical Networks Group studies the activity generated by the cerebral cortex network, both spontaneous and evoked, the mechanisms that regulate it, the information it encodes, and the consequences of this activity upon the network.

P94) UMIL, *Universita Degli Studi Di Milano*, Italy (SP3; SGA3: WP2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

The Integrated Thalamo-Cortical Function (iTCf) group, in the Biomedical Clinical Sciences Department, studies changes in thalamocortical networks (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.

P95) IBEC, *Fundacio Institut de Bioenginyeria de Catalunya*, Spain (SP3; SGA3: WPs 1 and 2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

IBEC is a bioengineering research institute and its "Nanoprobes and Nanoswitches" group develops nanoscale tools to study biological systems. It is involved in the design, synthesis and characterisation (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.

P96) ISS, *Istituto Superiore di Sanità*, Italy (SP3; SGA3: WP2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

The Unit of Complex Systems Modelling (CSM) is part of the technical and scientific institution of the Italian National Health Service. It covers a range of cross-disciplinary subjects, including the collective dynamics of neuronal networks, from which innovative theory-inspired analyses have been developed to characterise the evoked and spontaneous activity of *in vitro* and *in vivo* cortical cell assemblies.

P97) ULG, *Universite de Liege*, Belgium (SP3; SGA3: WP2)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

The GIGA Consciousness Unit studies human consciousness and its modifications; assessing pathological, pharmacological and physiological modifications of conscious awareness in both patients and healthy subjects. Its expertise ranges from the assessment of brain function in (1) general anesthesia, controlled sedation and hallucinatory drugs to (2) brain death, coma, "vegetative" unresponsive, minimally responsive, locked-in and near-death patients to (3) hypnosis, meditation and dream-like states.

P98) UvA, *Universiteit van Amsterdam*, The Netherlands (SP3; SGA3: WPs 2, 3 and 6)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

The UvA's Swammerdam Institute for Life Sciences includes the Department of Cognitive & Systems Neuroscience, which participates in UvA's Research Priority Program Brain & Cognition and focuses on brain mechanisms of sensory integration, perception and memory and motivation.

P99) DZNE, *Deutsches Zentrum für Neurodegenerative Erkrankungen EV, Germany* (SP3; SGA3: WPs 1 and 2)

Active HBP Partner: SGA1 (CEoI), SGA2 (CEoI), SGA3

E DÜZEL lab 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.

PRECISE (J SCHULTZE & M BEYER) focuses on developing and applying new single-cell high-throughput genomics technologies to unravel new biology in the fields of neuroscience and immunology.

P100) USFD, University of Sheffield, United Kingdom (SP3; SGA3: WP3)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

Sheffield Robotics has a large portfolio of ongoing robotics research, supported by the UK Research Councils and the European Union, and active membership of 200 researchers. SR is building research partnerships with leading industrial, commercial, and government organisations to ensure the real world relevance and impact of its research. A key theme 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.

P101) UWE, University of the West of England, Bristol, United Kingdom (SP3; SGA3: WPs 2 and 3)

Active HBP Partner: SGA1 (CEoI), SGA2, SGA3

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.

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).

P102) SURREY, University of Surrey, United Kingdom (SP4)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

SURREY withdrew from the HBP Consortium at the end of 2020.

P103) TUT, Tampere University, Finland (SP4; SGA3: WP1)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

Computational Neuroscience Research Group works to unravel the molecular, cellular and network level mechanisms underlying excitability, neurotransmission, and plasticity. It uses 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 goals is to identify the key mechanisms by which astrocytes modulate neuronal excitability and plasticity.

P104) ULEEDS, University of Leeds, United Kingdom (SP4)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

ULEEDS withdrew from the HBP Consortium at the end of 2020.

P105) SUxUPMC, *Sorbonne Université*, France (until 31 Dec 2017: *Université Pierre et Marie Curie – Paris 6)*, (SP4)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

SUxUPMC withdrew from the HBP Consortium at the end of 2020.

P106) UoS, University of Sussex, United Kingdom (SP9; SGA3: WPs 3 and 5)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

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.

P107) MU, Middlesex University Higher Education Corporation, United Kingdom (SP9)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

MU withdrew from the HBP Consortium on at the end of 2020.

P108) UCBL, *Université Lyon 1 Claude Bernard*, France (SPs 2 and 8; SGA3: WPs 1 and 4)

Active HBP Partner: RUP (CEoI), SGA1, SGA2 (CEoI), SGA3

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 is backed up with advanced methods in electrophysiology and neuroimaging. 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.

P109) POLITO, *Politecnico di Torino*, Italy (SP9)

Active HBP Partner: RUP, SGA1, SGA2

The EDA group develops automated techniques for complex systems in three main application domains: VLSI-CAD (design Automation for standard digital CMOS ICs, Beyond-CMOS circuits and Electrical Energy Systems); Bioinformatics (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; and Smart City (with particular emphasis on IoT devices).

P110) UGENT, *Universiteit Gent*, Belgium (SPs 5 and 10, plus CDP8)

Active HBP Partner: RUP, SGA1, SGA2 (CEoI)

Data Science Lab consists of three former groups: Reservoir Lab (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.).

The Brain connectivity and modelling lab focuses on methodological and computational aspects of neuroscience research and on the dynamical networks subserving function.

P111) KUL, *Katholieke Universiteit Leuven*, Belgium (SP2; SGA3: WPs 2 and 4)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

The Laboratory for Neuro- and Psychophysiology 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.

The Research Group Experimental Neurosurgery and Neuroanatomy is specialized in electrophysiological recordings in human patients; specifically, in drug resistant epilepsy patients.

P112) UNIBAS, *Universität Basel*, Switzerland (SP2; SGA3: WPs 1 and 5)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

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.

P113) VU, *Stichting VU-VUmc*, The Netherlands (SPs 1 and 2; SGA3: WP1)

Active HBP Partner: RUP, SGA1, SGA2, SGA3

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.

P114) SIB, *Institut Suisse de Bioinformatiquefondation ISB* (Swiss Institute of Bioinformatics), Switzerland (SP1)

Active HBP Partner: RUP (CEoI), SGA1

SIB withdrew from the HBP Consortium at the end of 2020.

P115) EBRI, *European Brain Research Institute Rita Levi-Montalcini Fondazione*EBRI*, Italy (SP1)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

EBRI withdrew from the HBP Consortium on at the end of 2020.

P116) SNS, *Scuola Normale Superiore*, Italy (SP1)

Active HBP Partner: RUP (CEoI), SGA1, SGA2

SNS withdrew from the HBP Consortium at the end of 2020.

P117) UM, *Universiteit Maastricht*, The Netherlands (SP2; SGA3: WPs 2 and 3)

Active HBP Partner: RUP (CEoI), SGA1, SGA2, SGA3

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.

P118) HERTS, University of Hertfordshire, United Kingdom (SP9; SGA3: WP3)

Active HBP Partner: SGA1, SGA2, SGA3

The BioMachineLearning unit is part of the Biocomputation Research Group at the Centre for Computer Science and Informatics Research. It develops neuromorphic algorithms for neuromorphic olfaction. We leverage event-based approaches that are directly derived from brain circuits to unlock the potential of energy-efficient neuromorphic computing. We validate our algorithms for event-based sensing, inference and control in embodied neuromorphic implementations, applied to robotic gas-based navigation.

P119) UKB, *Universitätsklinikum Bonn*, Germany (SP2)

Active HBP Partner: SGA2 (CEoI)

UKB withdrew from the HBP Consortium at the end of 2020.

P120) BRFAA, Biomedical Research Foundation of the Academy of Athens, Greece (SP8 plus CDP6)

Active HBP Partner: SGA2 (CEoI)

BRFAA houses a 100-processor Apple Cluster (Intel Xeon Six Core, 2.66 GHz), which is available for molecular modelling applications and drug design studies. The Cournia lab is also equipped with an IBM 36-processor Blade Server (Intel Xeon Six Core, 2.66 GHz). Molecular dynamics codes (GROMACS, NAMD, AMBER, etc.) complemented by enhanced sampling algorithms are fully supported and optimised for these platforms.

P121) CONVELOP, convelop cooperative knowledge design gmbh, Austria (SP11; SGA3: WP9)

Active HBP Partner: SGA2 (CEoI), SGA3

SME specialized in the design, implementation and evaluation of strategies, programmes and measures at the interface of science, technology, innovation and human resources with a special focus on equal opportunities, gender and diversity. Customers are universities, ministries, managing authorities for European structural & investment funds, and international projects.

P122) CHARITÉ, *Charité Universitätsmedizin Berlin*, Germany (SPs 5 and 8, plus CDP8; SGA3: WPs 1 and 5)

Active HBP Partner: SGA2 (CEoI), SGA3

The Berlin Institute of Health supports research and development work on The Virtual Brain and provides access to BIH scientific-technological platforms: Multiscale Genomics, Digital Medicine, Clinical-Translational Sciences, Humanized Modelsystems and Cell Engineering. In addition, Prof. Ritter's group has access to the Charité Department of Neurology for patient recruitment, the Berlin Center for Advanced Imaging and the Supercomputing Center Jülich.

P123) EMBL, European Molecular Biology Laboratory, Germany (SP5; SGA3: WP4)

Active HBP Partner: SGA2 (CEoI), SGA3

The Kreshuk Group specializes in developing machine learning algorithms and tools for automatic segmentation, classification and analysis of biological images. The PI Anna Kreshuk changed affiliation from UHEI (P47) to EMBL (P123) during SGA2.

P124) SICHH, Swiss Integrative Center for Human Health, Switzerland (SP8)

Active HBP Partner: SGA2 (CEoI)

The Swiss Integrative Center for Human Health (SICHH), a spin-off of the University of Fribourg, is an academic competence center focused on research and development for the benefit of human health. The center provides research services at an academic excellence level. Its vision leans on integrative innovation, bringing expertise of highly-skilled specialists in Information Technology (IT), neurology, life science, physics and chemistry under the same roof.

P125) UGA, *Université Grenoble Alpes*, France (SP8; SGA3: WPs 1, 2 and 4)

Active HBP Partner: SGA2 (CEoI), SGA3

The Grenoble Institute of Neuroscience (GIN) was created in 2007 and the research teams specializing in the study of physiological processes or in pathologies of the nervous system and in the development of innovating techniques to explore them.

P126) CHUGA, *Centre Hospitalier Universitaire Grenoble Alpes*, France (SP8)

Active HBP Partner: SGA2 (CEoI)

The Clinical Investigation Centre - Innovative Technology is a research structure which aims to accompany the maturation of innovative medical devices from their design to their multicenter clinical assessment. The final goal is to demonstrate the Medical Service associated to IT. CIC-IT belongs to the national network of CIC-IT (Tech4Health platform) and to the French labeled node of the European Clinical Research Infrastructures Network (ECRIN) in the Medical Device field.

P127) UKLFR, *Universitaetsklinikum Freiburg*, Germany (SP8)

Active HBP Partner: SGA2 (CEoI)

The UKLFR epilepsy center performs brain surgery and brain stimulation techniques for epilepsy. It is part of the Freiburg Excellence Cluster BrainLinks-BrainTools devoted to interdisciplinary research between Medicine, Microsystems Technology, Informatics and Neurobiology and clinical applications of emerging technologies, in brain-computer interfacing, seizure-detection based closed-loop intervention systems, seizure prediction and analyses of neurophysiological epilepsy biomarkers.

P128) CERCE, *ASST Grande Ospedale Metropolitano Niguarda Ca'Granda*, Italy (SP8)

Active HBP Partner: SGA2 (CEoI)

CERCE withdrew from the HBP Consortium at the end of 2020.

P129) UMG, The Medical University of Greifswald, Germany (SP8)

Active HBP Partner: SGA2 (CEoI)

UMG withdrew from the HBP Consortium at the end of 2020.

P130) UT, *Universität Trier*, Germany (SP8; SGA3: WPs 4 and 5)

Active HBP Partner: SGA2 (CEoI), SGA3

The *Human-Computer Interaction Group* is part of the Department IV - Computer Science and Business Informatics. The group focuses on interdisciplinary research topics in the human-computer interaction and virtual reality domains. The group develops and investigates interactive data visualization and analysis methods, interaction concepts for virtual and augmented reality, as well as design approaches for interactive systems using formal modelling approaches.

P131) CHULILLE, *Centre Hospitalier Universitaire de Lille*, France (SP8)

Active HBP Partner: SGA2 (CEoI)

University hospital of Lille (CHULILLE) is a bench-mark university hospital for primary care, teaching, innovation and research, serving the six million inhabitants of the region (les Hauts de France). Its vocation is to develop innovations and to treat serious pathologies requiring the state-of-the-art medico-technical platforms, specialized expertise and multidisciplinary care. It is a complex of 10 hospitals on a unique medical campus, gathering 16 University Hospital centers, employing 15,900 people.

P132) HOST, Hochschule Stralsund, Germany (SP4; SGA3: WP3)

Active HBP Partner: SGA2, SGA3

The Faculty of Electrical Engineering at the University of Applied Science Stralsund comprises c.20 academic staff and offers degrees related to Computer Science and Electrical Engineering. Its expertise relevant to the HBP includes artificial and computational intelligence and biological modelling. Its research infrastructure includes compute clusters suitable for the simulation of neural networks relevant to Task 433, and the central IT of the university provides access to HPC in case required.

P133) ATHENA, Athena Research and Innovation Center, Greece (SGA3: WPs 4, 5 and 6)

Active HBP Partner: SGA3

The Management of Data, Information, and Knowledge (MaDgIK) group focuses on Database and Information Systems, Distributed and Parallel Systems, Cloud Computing, Sensor-based and Stream Data Management, Query Optimization, Information Search, Personalization and Social Networks, Knowledge Discovery & Data Mining, Knowledge Representation and Reasoning, Constraint Satisfaction Problems, Semantic Web and Linked Data, Semantic Sensor Web, Digital Libraries, and Human-Computer Interaction.

P134) EPFL, *École Polytechnique Fédérale de Lausanne*, Switzerland (SPs 1, 4, 5, 6, 7, 8, 9, 10 and 11; SGA3: WPs 1, 2, 3, 4, 5, 6, 7 and 8), former P1 Coordinator until 1 March 2021

Active HBP Partner: RUP, SGA1, SGA2 (CEoI), SGA3

The Blue Brain Project (BBP) uses detailed modelling and simulation as tools to systematically integrate data about the brain.

The Data-Intensive Applications and Systems (DIAS) Laboratory focuses on database systems and applications.

The Laboratory of Computational Neuroscience focuses on theoretical and computational neuroscience.

The Microelectronic Systems Laboratory is as part of the Institute of Electrical Engineering.

The Biorobotics Laboratory (BIOROB) works on neuromechanical models of animal locomotion, and dynamical system control for articulated robots and exoskeletons.

The Translational Neural Engineering Laboratory (TNE) develops neurotechnologies that restore sensorimotor function in people affected by different kinds of disabilities.

The International Paraplegic Foundation Chair in Spinal Cord Repair designs innovative interventions to restore sensorimotor functions after neurological disorders.

The Laboratory of Psychophysics uses TMS, EEG, and mathematical modelling to study visual information processing in humans.

The Computer Vision Laboratory focuses on shape and motion recovery from images.

The Laboratory of Computational Chemistry and Biochemistry focuses on *ab initio* MD methods and their application to systems of chemical and/or biological interest.

The Embedded Systems Laboratory (ESL) focuses on design and optimization of high-performance embedded systems and nano-scale architectures.

P135) IIT, *Fondazione Istituto Italiano di Tecnologia*, Italy (SGA3: WP1)

Active HBP Partner: SGA3 (CEoI)

Fondazione Istituto Italiano di Tecnologia (IIT) is a public research institute that conducts cutting-edge research and transfers technology to companies and clinical institutions.

The Center for Neuroscience and Cognitive Systems studies with systems level neuroscience in human subjects and in animal models, including psychophysical techniques, functional imaging, trans-cranial stimulation and computational approaches.

P136) POLIMI, *Politecnico di Milano*, Italy (SGA3: WP1)

Active HBP Partner: SGA3 (CEoI)

The Politecnico di Milano trains engineers, architects and industrial designers. POLIMI participates in the RisingNet project with the Neuroengineering and Medical Robotics Laboratory NearLab of the Department of Electronics, Information and Bioengineering. The NearLab (5 faculties, 4 Post doc researchers and 15 PhD students) is equipped with relevant instrumentation (biosignal devices acquisitions, motion capture systems, robots, haptic interfaces, …).

P137) UNINA, University of Naples Federico II, Italy (SGA3: WP1)

Active HBP Partner: SGA3 (CEoI)

The University of Naples Federico II (UNINA) is one of the oldest and largest academic institutions in the world. The proposed research will be carried out at the Department of Mathematics and Applications "R.Caccioppoli" of the School of Polytechnic and Basic Sciences of UNINA

P138) APHM, *Assistance Publique – Hôpitaux de Marseille*, France (SGA3: WP1)

Active HBP Partner: SGA3 (CEoI)

Within the **Clinical Neuroscience Department of APHM**, the Clinical Neurophysiology and Epileptology department is specialized in rare and complex epilepsies management. It coordinates and hosts the preoperative assessment of children and adults with DRFE.

The **Medical Imaging Department of APHM** comprises the nuclear medicine and radiology departments.

P139) UNIROMA1, Sapienza University, Italy (SGA3 WP2)

Active HBP Partner: SGA3 (CEoI)

The Motor Control and Cognition Lab is equipped to record up to 256 channels of electrophysiological data and behavioural parameters and has access to a computing cluster for intensive analysis of neural data sets. Facilities include: two awake NHP labs for multiple electrode recording; magnetic and electric stimulation systems; EEG/ECoG recording system; fully equipped surgical operating theatre; main NHP facility housing up to 15 NHPs.

P140) UGOE, University of Goettingen, Germany (SGA3 WP5)

Active HBP Partner: SGA3 (CEoI)

Founded in 1737, the Georg-August-Universität Göttingen is a research university of international renown with strong focuses in research-led teaching. The University is distinguished by the rich diversity of its subject spectrum, its excellent facilities for the pursuit of scientific research, and the outstanding quality of the areas that define its profile. The name of Göttingen is associated with more than 40 Nobel Prize winners who have lived and worked here.

P141) EMC, Erasmus Medical Center, Netherlands (SGA3 WP5)

Active HBP Partner: SGA3 (CEoI)

The Dept. of Neuroscience of the Erasmus Medical Centre (EMC) in Rotterdam is the oldest neuroscience department in the Netherlands and was founded in 2001. In this project, EMC will participate with two groups: Mario NEGRELLO (EMC-MN) and Christos STRYDIS (EMC-CS).

P142) SISSA, *Scuola Internazionale Superiore di Studi Avanzati*, Italy (SGA3 WP5)

Active HBP Partner: SGA3 (CEoI)

SISSA is a world-recognized international research and PhD school. It scored first place in Italy, seventh in Europe and among the Top 50 "Young Universities" in the world, according to the 2019 Nature Index. SISSA operates as a post-graduate University in the three main areas of physics, mathematics and neurosciences.

P143) MPIEA, Max Planck Society, Germany (SGA3: WP2)

Active HBP Partner: SGA3 (CEoI)

The Max Planck Society conducts basic research in the natural sciences, life sciences, and humanities at its 84 Max Planck Institutes and facilities in Germany. The Max Planck Institute for Empirical Aesthetics is a newly established interdisciplinary institute. A joint effort of researchers in the humanities and sciences which aims at unraveling the cognitive and affective mechanism involved in aesthetic appreciation and their neural, physiological and behavioral correlates.

P144) INGLOBE, Inglobe Technologies Srl (SGA3: WP3)

Active HBP Partner: SGA3 (CEoI)

Inglobe Technologies Srl is an italian SME focused on the development of Natural Interfaces and Mixed Reality (MR) solutions. With more than 12 years of experience in the emerging market of Mixed Reality, the Team of Inglobe has introduced in the market first of a kind MR Applications and commercialised one of the first 3D Tracking SDKs for mobile devices and Smartglasses.

P145) AI2LIFE, AI2Life Srl (SGA3: WP3)

Active HBP Partner: SGA3 (CEoI)

AI2Life srl (www.ai2life.com) is a spin-off company of the Institute of Cognitive Sciences and Technologies (ISTC) of the italian National Research Council (CNR) engaged in the technology transfer of its know-how related to the design, prototyping, engineering, production and commercialization of human-centred AI technological innovations, aimed at supporting the digital transformation and the competitiveness of industrial stakeholders.

P146) ROB, Robotnik Automation SSL (SGA3: WP3)

Active HBP Partner: SGA3 (CEoI)

Robotnik provides mobile robotic solutions, with a large portfolio of mobile robot platforms and manipulators. It specialises in: a) autonomous logistics systems to transport different loads and designed

to work safely with people around; b) mobile robotic inspection and maintenance systems to reach hard-to-access areas autonomously or under remote control; c) mobile security and defense platforms that can operate in dangerous environments; and d) autonomous farming robots.

P147) BIOMAX, Biomax Informatics (SGA3: WP4)

Active HBP Partner: SGA3 (CEoI)

Biomax Informatics provides computational solutions for better decision making and knowledge management in the life sciences. The solutions help customers generate value by integrating information from proprietary and public resources to enable a knowledge-based approach to developing innovative life science products. Biomax' worldwide customer community includes clinics, companies and research organizations with a focus on drug discovery, diagnostics, fine chemicals, food and plant production.

P148) AIS, Alpine Intuition Sarl (SGA3: WP5)

Active HBP Partner: SGA3 (CEoI)

Alpine Intuition enables SMEs to benefit from the Artificial Intelligence (AI) revolution. Alpine Intuition is building "Isquare", one of the first community driven AI platforms where customers can choose from a variety of state-of-the-art AI models built by the community and provided as API services running on a cloud or on-site. Alpine Intuition also provides expertise in linking physical devices with cloud-based environments and has developed proofs-of-concept in computer vision, machine learning and robotics simulations.

P149) AUTONOMYO, Autonomyo Sàrl (SGA3: WP5)

Active HBP Partner: SGA3 (CEoI)

Autonomyo uses advanced robotic technology to address walking issues for people with neurological disorders, in partnership with well-established academic institutions such as the Ecole Polytechnique Fédérale de Lausanne and the Centre Hospitalier Universitaire Vaudois. The core of Autonomyo's technology is based on advanced mechanical design of powered exoskeleton and on key control strategies allowing an impressive symbiosis between the exoskeleton and the user.

P150) BITBRAIN, Bit&Brain Technologies SL (SGA3: WP5)

Active HBP Partner: SGA3 (CEoI)

P150 BITBRAIN, Bit&Brain Technologies SL (SGA3: WP5)

Bitbrain is a spin-off of a University of Zaragoza neurotechnology research team, pioneering brain-computer interface applications outside laboratory investigation settings. Bitbrain has three business areas: 1) hardware: providing the first family of EEG and biosensor high reliable equipment able to be used by non-expert personal; 2) software: a human behaviour research platform that integrates more than 35 research sensor modalities and produces emotional/cognitive and visual metrics; and 3) cognitive training for medical and wellness uses.

P151) OCV, Oncovision / General Equipment for medical Imaging SA (SGA3: WP1)

Active HBP Partner: SGA3 (CEoI)

Oncovision is an innovative molecular vision company revolutionizing personalized patient care. Its proprietary IP-protected medical imaging devices have been successfully used by physicians, radiologists, surgeons and oncologists in 150,000+ patients, in 35+ countries. Its awards include "Most Innovative SME of Spain", "Model Global Company" and "Best breast molecular imaging technology in

Europe". Its pipeline is expanded technology transfer from the world-leading Institute for Instrumentation in Molecular Imaging I3M of Valencia, Spain.

P152) UNITO, Università Degli Studi di Torino, Italy (SGA3:WP5)

Active HBP Partner: SGA3 (CEoI)

P152 UNITO and the Department of Drug Science and Technology (DSTF) joined the HBP via the CEoI "COVID-19 and its impact on the brain and mental health" with the proposal "BRAVE - Protecting the brain from COVID-19-mediated neurodegeneration through inflammasome inhibition" (in WP5). The DSTF uses a multidisciplinary and technological approach in its efforts to design and develop new bio-active molecules and their metabolites, study the mechanisms underlying their action, develop new drugs of natural and synthetic origin, develop innovative drug delivery strategies as well as nanotechnologies.

Appendix 6: HBP Beneficiaries' Third Parties

The Table below identifies Linked Third Parties (as defined in Article 19 of the FPA).

For details of each Partner's related Third Parties in each funding period of the Project, please refer to the corresponding Grant Agreement:

- Ramp-Up Phase (Oct 2013 to Mar 2016): §2.3.3 Sub-contracting and §2.3.3 Third parties (other than subcontractors)

- SGA1 (Apr 2016 to Mar 2018): §4.2 Third parties involved in the project (including use of third party resources)

- SGA2 (Apr 2018 to Mar 2020): §4.2 Third Parties involved in the Project (Including Use of Third Party Resources)

- SGA3 (Apr 2020 to Mar 2023): §4.2 Third Parties involved in the Project (Including Use of Third Party Resources)

In addition to the Linked Third Parties, the Grant Agreements identify other types of Third Party and Subcontracting, including:

- In-kind contributions provided by 3rd parties against payment (as defined in Article 16 of the FPA)

- Contribution in kind provided by 3rd parties free of change (as defined in Article 17 of the FPA)

- Subcontracting (as defined in Article 18 of the FPA)

Table 44: HBP Core Project Partners' Third Parties

Partner #	Third parties involved in the Project
P1 EBRAINS	
P2 AALTO (terminated)	
P3 LUMC	
P4 AUEB	
P5 BSC	
P6 BAUW (terminated)	
P7 BUW	
P8 BSMJ (terminated)	
P9 CF (terminated)	
P10 CNRS	**Added in FPA Amendmnet 8 for SGA3** **Linked Third Party (Article 19 FPA):** **University Paris-Saclay** Université Paris-Saclay offers a complete and varied range of Bachelor's, Master's and Doctorate degrees, whose quality is recognized internationally thanks to the reputation of its research and the commitment of its teaching staff. Its constituent faculties and component institutions further expand this offer with cutting-edge thematic training in science and engineering, life sciences and health, social sciences and humanities. With 275 laboratories shared with the CEA, CNRS, IHES, inrae, inria, inserm, Onéra, Université Paris-Saclay represents 13% of the French research potential. Paris-Saclay is part of of the programme Cluster of excellent science and technology Paris-Saclay which includes different scientific governmental and private institutions (NEURO SPIN, CEA) and Grandes écoles (Polytechnique, Central Supérlec). This contribution will take place at the Paris-Saclay Institute of Neuroscience (NeuroPSI) laboratory, a joint research unit (JRU)

	between the CNRS, the beneficiary, and Paris-Saclay University. CNRS and UPSaclay are linked by a legal agreement that goes further the cooperation within this specific project. SGA3: WP2
P11 CEA	
P12 CNR	
P13 CINECA	
P14 DTU	
P15 UoD (terminated)	
P16 DMU	
P17 ENS	
P18 ETHZ	
P19 FT	
P20 JUELICH	
P21 FORTISS	
P22 FG	
P23 FCHAMP (terminated)	
P24 UDUS	
P25 UH (terminated)	
P26 HITS	
P27 CHUV	
P28 ICL	
P29 ICM	**Added in FPA Amendment 8 for SGA3** **Linked Third Party (Article 19 FPA):** INSERM (**Institut national de la santé et de la recherche médicale**) French National Institute of Health and Medical Research (Inserm) is the only public research institution solely focused on human health and medical research in France. It conducts fundamental and translational research projects through 339 research units, run by around 13,000 scientists. Link between ICM and INSERM: Convention 2011. INSERM is PI's employer.
P30 IEM HAS	
P31 IST (terminated)	
P32 JSI (terminated)	
P33 INRIA	
P34 IP	
P35 UFRA (terminated)	
P36 KIT (terminated)	
P37 KI	
P38 KCL	
P39 KTH	
P40 LENS	

Partner #	Third parties involved in the Project
P41 LNU	
P42 MUI	
P43 UoA	
P44 NMBU	
P45 OFAI (terminated)	
P46 RWTH	
P47 UHEI	
P48 SU (terminated)	
P49 SSSA	
P50 CWI	
P51 SKU	
P52 FZI	
P53 TUC (terminated)	
P54 TUD	
P55 TUGRAZ	
P56 TUM	
P57 TAU	
P58 UCAM (terminated)	
P59 UOXF	
P60 HUJI	
P61 UABER (terminated)	
P62 UEDIN	
P63 UMAN	
P64 UAM	
P65 UCLM	
P66 UGR	
P67 UMINHO	
P68 UPM	
P69 URJC	
P70 UNIPV	
P71 UBERN	
P72 UNIBI (terminated)	
P73 UKAACHEN	
P74 UKE	
P75 UZH (terminated)	
P76 UB	
P77 UPF	
P78 AMU	**Linked Third Party (Article 19 FPA):**

Partner #	Third parties involved in the Project
	INSERM (**Institut national de la santé et de la recherche médicale**) AMU and INSERM jointly host the "Institut de Neurosciences des Systèmes (INS)" research unit (UMR_S 1106). UMR means *Joint Research Units (JRU) (i.e. research laboratories created and owned by two or more different legal entities in order to carry out research)*. The status and management of the unit, which employs staff from both establishments, is defined by a framework agreement. SGA2: SP4 (WP4.2 & WP4.5) SGA3: WP1
P79 UBO	
P80 UA	
P81 UIO	
P82 UCL	
P83 UU	
P84 WEIZMANN	
P85 TUDA	
P86 UNIGE (terminated)	
P87 UGLA	
P88 MRC (terminated)	
P89 UHAM	
P90 UBER	
P91 KNAW	
P92 INFN	
P93 IDIBAPS	<u>Linked Third Party (Article 19 FPA):</u> **HCPB (The Hospital Clínic i Provincial de Barcelona)** 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. SGA2: No costs foreseen SGA3: WP2
P94 UMIL	
P95 IBEC	
P96 ISS	
P97 ULG	<u>Linked Third Party (Article 19 FPA):</u> **ULH (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. SGA1: no costs foreseen SGA2: no costs foreseen SGA3: Terminated

Partner #	Third parties involved in the Project
P98 UvA	
P99 DZNE	
P100 USFD	
P101 UWE	
P102 SURREY (terminated)	
P103 TUT	
P104 ULEEDS (terminated)	
P105 SUxUPMC (terminated)	
P106 UoS	
P107 MU (terminated)	
P108 UCBL	**Linked Third Party (Article 19 of the FPA):** **INSERM (Institut National de la Santé et de la Recherche Médicale)** UCBL and INSERM jointly host the "CRNL" research unit. The status and management of the unit, which employs staff from both establishments, is defined by a framework agreement (contrat quadriennal). INSERM is covered by special clause 10, "Affiliates", e.g. a legal entity that is under the direct or indirect control of the beneficiary, or under the same direct or indirect control as the beneficiary. Its costs will be declared by the beneficiary and they will be recorded in the accounts of the **linked third party** and available for auditing if required. SGA1: SP2 (WP2.5) SGA2: SP2 (WP2.1, WP2.2 & WP2.6) SGA3: WP1 & WP4
P109 POLITO	
P110 UGENT	
P111 KUL	
P112 UNIBAS	**Linked Third Party (Article 19 of the FPA):** **USB (University Hospital Basel)** 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 of the SGAs. 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. SGA1: SP2 (WP2.1) SGA2: SP2 (WP2.3 & WP2.4) SGA3: WP1 & WP5
P113 VU	
P114 SIB (terminated)	

Partner #	Third parties involved in the Project
P115 EBRI (terminated)	
P116 SNS (terminated)	
P117 UM	
P118 HERTS	
P119 UKB (terminated)	
P120 BRFAA	
P121 CONVELOP	
P122 CHARITE	
P123 EMBL	
P124 SICHH	
P125 UGA	**Linked Third Party (Article 19 of the FPA):** **INSERM (Institut National de la Santé et de la Recherche Médicale)** Founded in 1964, Inserm is a public scientific and technological institute which operates under the joint authority of the French Ministries of Health and Research. The institute is dedicated to biomedical research and human health, and is involved in the entire range of activities from the laboratory to the patient's bedside. It also partners with the most prestigious research institutions in the world that are committed to scientific challenges and progress in these fields. INSERM and UGA will provide the SEEMIP database and brain atlas from the CCEP analysis. It will interact with other SP2 partners for the cross-validation of the CCEP atlas with DTI atlases developed in HBP. UGA will interact with CNR, CERCE, AMU and UCBL for the collection of SEP data in Grenoble. SGA2: SP8 (WP8.8) SGA3: Terminated
P126 CHUGA	
P127 UKLFR	
P128 CERCE (terminated)	
P129 UMG (terminated)	
P130 UT	
P131 CHULILLE	
P132 HOST	
P133 ATHENA	
P134 EPFL	**Linked Third Party (Article 19 FPA):** **CYBER (Cyberobotics)** *Benchmarking and validation of neurorobotics models, physics and light simulation* 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. SGA1: SP10 (WP10.3 and WP10.5); SGA2: SP10 (WP10.4) SGA3: Terminated
P135 IIT	
P136 POLIMI	
P137 UNINA	

Partner #	Third parties involved in the Project
P138 APHM	
P139 UNIROMA1	
P140 UGOE	
P141 EMC	
P142 SISSA	
P143 MPIEA	
P144 INGLOBE	
P145 AI2LIFE	
P146 ROB	
P147 BIOMAX	
P148 AIS	
P149 AUTONOMYO	
P150 BITBRAIN	
P151 OCV	
P152 UNITO	

Appendix 7: Critical Infrastructure for the HBP

Table 45: HBP Core Project Partners' Key Infrastructure Contributions

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 Fermi)				IT	CINECA	Giovanni ERBACCI	7 000 000			
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,				CH	EPFL	Henry MARKRAM	18 600 000			

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)
	acquired 2011 -2013 paid by Swiss national funding										
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			

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)
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			

Appendix 8: Risk Detection & Mitigation

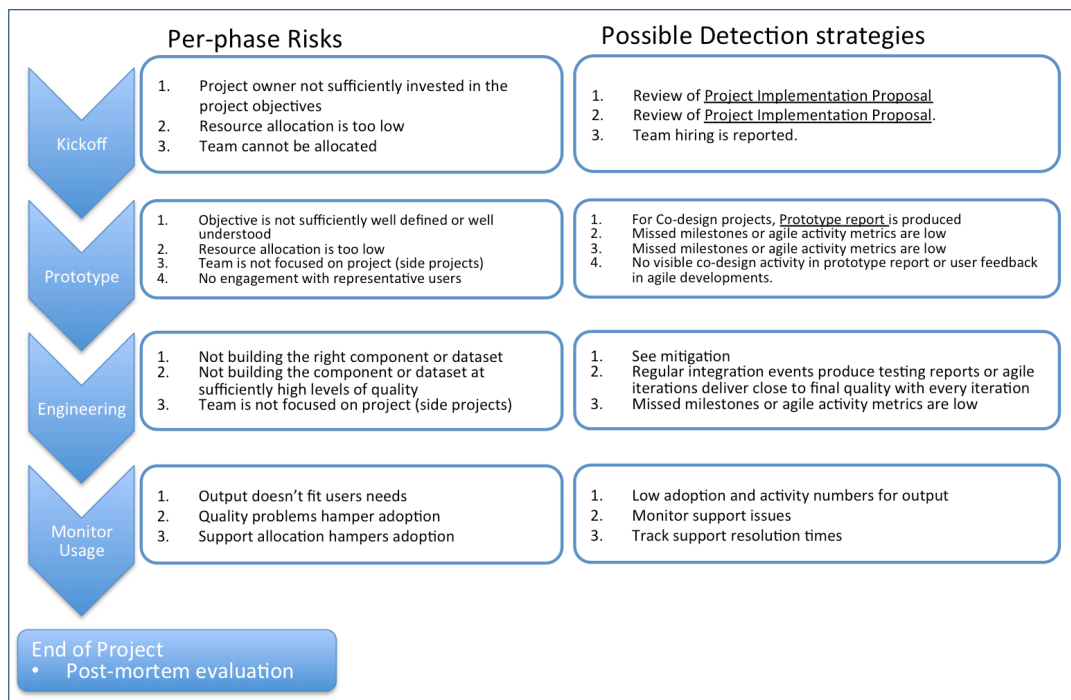The Project Lifecycle Framework has different problem-detection strategies in its various phases:

Figure 14: Project Lifecycle Framework problem detection strategies

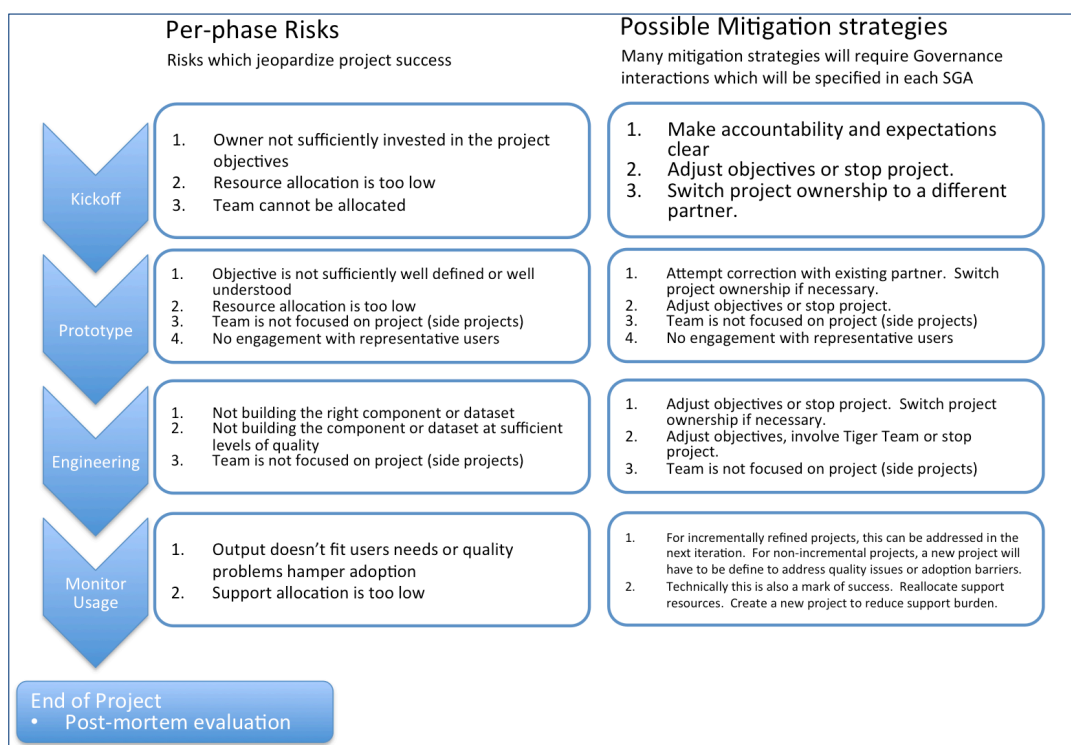The Project Lifecycle Framework also has mitigation strategies in specific phases.

Figure 15: 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 2.1.2.4)
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 Section 2.3.2.3)
SIB	Science and Infrastructure Board (see Section 2.3.2.6)
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 Management and Coordination (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.

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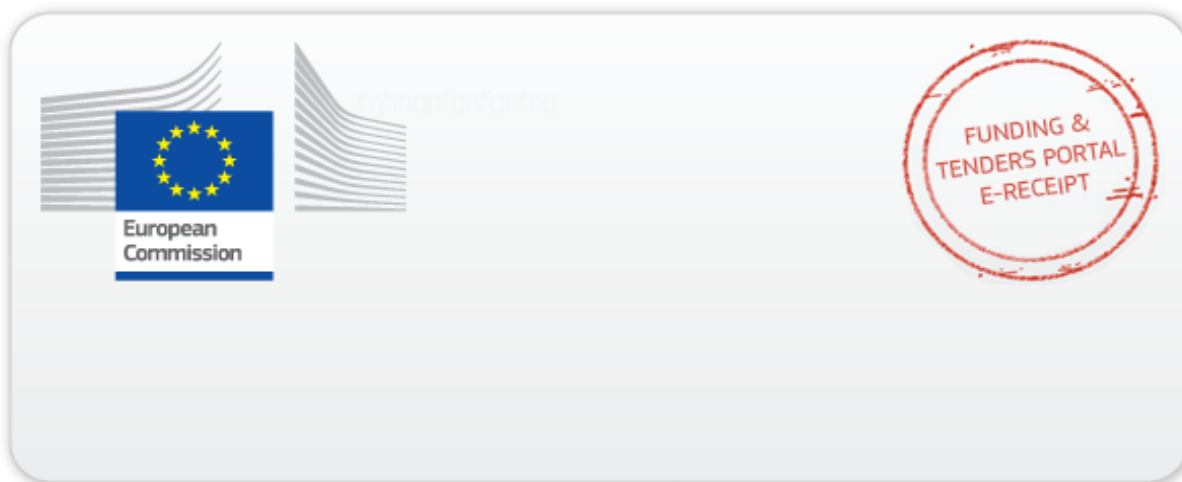
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