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Abstract:	This Deliverable describes progress made in the development of the Neuroinformatics Platform in M1-M12. It focuses on the tools to be incorporated in the Platform, and the brain atlases and predictive informatics as specified in Deliverable D5.8.1.
Keywords:	Neuroinformatics Platform, KPIs, brain atlas, predictive neuroinformatics

Document Status

Version	Date	Status	Comments
1	20 Oct 2014	Draft	Template received from the Scientific Writing & Editorial Services Team
2	19 Nov 2014	Draft	Nearing completion; adding additional sections requested by the European Commission
3	9 Dec 2014	Draft	Sent to the Scientific Writing & Editorial Services Team

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1. Introduction

1.1 The Human Brain Project (HBP)

The Human Brain Project (HBP) is a major international scientific research project, involving over 100 academic and corporate entities in more than 20 countries. Funded by the European Commission (EC), the ten-year, EUR 1 billion Project was launched in 2013 with the goal "to build a completely new ICT infrastructure for neuroscience, and for brain-related research in medicine and computing, catalysing a global collaborative effort to understand the human brain and its diseases and ultimately to emulate its computational capabilities."

The fields of neuroscience, medicine and information technology each have important roles to play in addressing this challenge, but the knowledge and data that each is generating have been very fragmented. The HBP is driving integration of these different contributions.

During the Ramp-Up Phase, the HBP will collect strategic data, develop theoretical frameworks, and perform technical work necessary for the development of six Information and Communication Technology (ICT) Platforms during the Operational Phase. The ICT Platforms, offering services to neuroscientists, clinical researchers and technology developers, comprise Neuroinformatics (a data repository, including brain atlases and analysing tools); Brain Simulation (building ICT models and multi-scale simulations of brains and brain components); Medical Informatics (bringing together information on brain diseases); Neuromorphic Computing (ICT that mimics the functioning of the brain); and Neurorobotics (allowing testing of brain models and simulations in virtual environments). A High Performance Computing Platform will support these Platforms.

1.2 HBP Subproject 5: Neuroinformatics Platform

The Neuroinformatics Platform provides an informatics infrastructure and analysis tools. The Platform must serve both “power users” and less skilled casual users, because the goals of the Human Brain Project can only be met by active collaboration between biologists, scientific modellers and computer scientists. The Platform is intended to make a large body of neuroscience data easily discoverable and accessible to the broad scientific community. It provides tools to compare and analyse data sets, allowing scientists to derive new knowledge about the brain. A unified description of neuroscience data is key to achieve meaningful data integration and enable powerful searching. For this purpose, key aspects of experimental data sets, calculated models and information extracted from the literature are captured by a common data model. The model is based on ontologies, which provide a straightforward mechanism to integrate new information and allow for the model to evolve over time. Moreover, the definition and implementation of data standards is a key mechanisms for facilitating multi-scale data integration. Finally, the Platform provides programmatic and graphic interfaces to register data in this common framework.

The Platform catalyses collaboration through the use of common tools and data curation interfaces. Furthermore, detailed brain atlases provide users with a powerful spatial navigation resource, to guide them through a large amount of information and to facilitate data discovery.

To enable these goals to be achieved, a number of different components will be built and made available:

- DataSpace: an easy-to-use global data federation tool, unifying access to diverse neuroscience data repositories.
- KnowledgeGraph: the core database for registering, searching, accessing and tracking the provenance of all data artefacts throughout the HBP – including biological and *in silico* data.

- KnowledgeSpace: a community encyclopaedia, ontology store and data index. The KnowledgeSpace was known in earlier documents as the "Brainpedia".
- Ontologies and Data standards: these are used to develop and curate common ontologies and data standard for Project wide use.
- Data mining infrastructure, to help find and analyse neuroscience data.
- 3D Brain Atlas Builder: tools to organise, anchor, and annotate data to standard anatomical ontologies and 3D reference spaces.
- Tools for structural data analysis: EM and fluorescent image segmentation and annotation analyse synapse distribution (3DSynapsesSA), morphology reconstruction (3DPyrStructure, 3DSomaMS).
- Tools for functional data analysis: spike train analysis.
- Predictive neuroinformatics: tools to allow brain-wide connectivity prediction (brain addressing system).
- Brain atlases: accessible repositories of mouse brain and human brain data.

1.3 Purpose of this Document

This report will describe progress in the development of the Neuroinformatics Platform, the tools to be incorporated in the Platform, the brain atlases and predictive informatics.

1.4 Structure of this Document

The remainder of this chapter provides an SP-level overview, highlighting the SP's main accomplishments and issues encountered in the period M1-M12. Subsequent chapters look at accomplishments and issues within individual Work Packages of the SP:

- WP5.1: Tools for Brain Atlases (including the Brain Atlas Builder)
- WP5.2: Tools for Structural Data Analysis
- WP5.3: Tools for Functional Data Analysis
- WP5.4: Predictive Neuroinformatics
- WP5.5: Brain Atlases
- WP5.6: Neuroinformatics Platform: Integration and Operations
- WP5.7: Neuroinformatics Platform: User Support and Community Building
- WP5.8: Scientific Coordination

The Annexes present in tabular form what the Subproject planned to achieve in this period and what it actually achieved, including the Subproject's Scientific Key Performance Indicators (SKPIs).

1.5 Overview of Subproject 5: Achievements

In the first Year, SP5 has developed and delivered a detailed initial specification of the Neuroinformatics Platform (D5.8.1), the tools for brain atlases, structural and functional analysis tools and predictive neuroinformatics. In addition, initial atlas services tools and services are up and running, and the Platform is well on its way to its initial alpha deployment in M18. The 10 Milestones due in the Period (M1-M12) have all been achieved. The requirements (e.g. Platform, predictive neuroinformatics, user support and documentation) and tools (e.g. structural, functional, atlas) have all been specified. The data model for both the mouse and rat brain atlases have been shared with the Allen Brain Institute and the INCF Software Center,

respectively. They consist of 1) one or more image volumes, 2) delineations of anatomical structures present in the image volumes, and 3) surface meshes modelling anatomical structures, based on the delineations.

Ensuring the integration of a diverse number of efforts is challenging and requires a substantial number of meetings. SP5 has held 19 meetings (via video conference or in-person) with Partners from other SPs, especially with SPs 1, 2 and 6. In addition, we have regular meetings (mostly via video conference) with all Partners in the SP, which are well attended. The Science & Technology Office (STO), which reviews our Quarterly Reports, Periodic Report and Deliverables, attends these meetings when possible. SP5 has an excellent interaction with the STO.

The SP5 Partners have progressed well with their scientific and technical work in this Period. The Partners are now all familiar with EMDESK and their reporting duties, so this will become timelier. Many personnel have joined us during this Period, including a Scientific Project Coordinator (shared with SP6). She is helping to improve with the interaction with the Partners.

The data federation infrastructure for neuroscience repositories has been developed and deployed in the Amazon cloud and provides a metadata catalogue for diverse, globally distributed data repositories. Several key data repositories (including CINECA and EPFL) have joined this federation and are making initial datasets available through the DataSpace interface. Work is still required to ensure a clean interface between the Document Service in the Unified Portal (the web interface to all the HBP Platforms) and the DataSpace.

The KnowledgeSpace has been launched and the governance model agreed to. The KnowledgeSpace is being established as a collectively owned cooperative effort led by INCF, NIF and HBP. Content from existing INCF, NIF and HBP resources, including Neurolex (www.neurolex.org) will be imported into a new deployment hosted by EPFL. NIF and INCF are contributing to the development, data import and curation of ontologies. The first target data set to be imported is a collection of cortical neuron morphologies. Key ontologies under development include Protocol and Data type ontologies.

The KnowledgeGraph is the core database for tracking the provenance of all data artefacts throughout the HBP – including biological and *in silico* data. The standard data model has been established, based on the W3C provenance standards, and is implemented in the Unified Portal. A REST API will provide core semantic and spatial search functionality.

This work is being undertaken in close collaboration with the Unified Portal (UP) team. The multi-search service is a component of the UP that is being created via a combined effort by the Neuroinformatics and UP teams. This service is intended to provide unified search indexes across all services provided by the UP and Neuroinformatics Platform. This work will also define a standard API for populating the index. This service is being implemented on top of ElasticSearch, an open source, horizontally scalable search index.

Integrating prior knowledge from neuroscience literature is a key challenge for SP5. To start to approach this challenge, the data mining team has established a pipeline for analysing large corpora of abstracts and full-text documents, using modified open source technologies from IBM's Watson technologies deployed on EPFL infrastructure. This enables natural language processing (NLP) of the text and mining of specific assertions and quantitative observations. This has made it possible to mine statements about brain connectivity in the mouse brain into a connectivity matrix that is entirely literature-derived. This can now serve as a tool for computational modellers to identify specific literature that can help validate brain connectivity properties between specific brain areas.

The initial 3D atlasing services (including data registration workflows) have been constructed and deployed for internal testing. These include the ability to navigate very large volumetric datasets, view slices of these data at arbitrary cutting angles, anchor datasets at specific xyz coordinates and display search results. These services are currently deployed at EPFL and all

data has been replicated to EPFL for convenience. We are currently investigating deployment at the CINECA and Juelich data centres, in order to be close to other large datasets.

The structural and functional analysis teams have made substantial progress in delivering the first versions of their analysis frameworks. In the case of the structural analysis, the ESPINA tool has been made fully open source, as of version 2.0, and is publically available (http://cajalbbp.cesvima.upm.es/espina/). An early version of the Elephant electrophysiology analysis toolkit is also available in open source form (https://github.com/NeuralEnsemble/elephant).

Atlas datasets for Mouse, Rat and Human atlases have been integrated into the brain atlas viewing services, with initial semantic navigation (browsing by brain region) enabled. Further data overlays are in the process of being registered and integrated through the registration workflows.

Several examples of predictive neuroscience have also been implemented for predicting cellular morphological properties and brain connectivity. These examples are meant to prototype the analysis and prediction process that can ultimately feed into specific model-building workflows.

Significant progress has been made in developing important community relationships and collaborations. A collaboration with the Allen Institute has been instrumental in ensuring close access to data and technical information for integrating the Allen Mouse Brain Atlas. This collaboration is also being extended to include standards and quality measures for morphological reconstructions, electrophysiological characterisations and a high-resolution common coordinate framework for atlasing. An important collaboration has also been established with the Britton Chance Center for Biomedical Photonics in Wuhan, China. This group produces large numbers of very high quality, high-resolution 3d volumetric scans of rodent brains (including both mouse and rat). These scans include information about cell densities, vasculature, dendritic morphologies, whole-brain axons and connectivity. This collaboration will focus on extracting features from these datasets and organising them in brain atlases. Another important collaboration has been established with the Australian Research Council Center of Excellence for Integrative Brain Function. Planning is underway to hold a joint workshop to develop data sharing and modelling collaborations. Discussions have also been held with numerous other organisations and national governments and work is underway to plan specific workshops or establish agreements to develop collaborations.

1.6 Overview of Subproject 5: Problems

The Neurinformatics Platform Specification, D5.8.1, due in M6, was submitted in October 2014 (M13). The delay in providing this document was due primarily to a delay in receiving details of a roadmap for delivering specific data. However, the core specification was complete at M6 and, consequently, there have been no delays in the progress of Platform development. For D5.8.2, we received the template from the Scientific Writing & Editorial Services Team in October 2014, as a complete D5.8.1 was required to create the template.

The Milestones due in this period were all achieved on time, but the reporting of them in EMDESK was sometimes slightly delayed by a few weeks. The Partners are now all familiar with the reporting requirements of their Milestones in EMDESK.

The delays experienced with the Deliverables or with the reporting of the Milestones have not had any impact on the SP. The SP is on track and working towards the alpha release in M18.

1.7 Overview of Subproject 5: The Next 6 Months

The SP is on track and will achieve D5.8.3 and the associated Milestones for the alpha/internal release of the Neuroinformatics Platform in M18.

The upcoming Deliverable and Milestones that will be achieved by M18 are:

- Deliverable D5.8.3: Neuroinformatics Platform v1 – preliminary release for internal Consortium use (prototype)
- Milestone M87: Alpha version of atlas registration and navigation tools including Knowledge Graph
- Milestone M91: Alpha release of structural analysis tools
- Milestone M95: Alpha release of functional analysis tools
- Milestone M101: Alpha versions of mouse and human atlases released
- Milestone M105: Neuroinformatics Platform ready for internal release
- Milestone M109: Alpha release of user documentation.

2. Neuroinformatics Platform: Software

2.1 Software Development Methodology

One of the goals of Human Brain Project's ICT Platforms is "…to produce immediately valuable outputs for neuroscience, medicine and computing". To achieve this goal, the Neuroinformatics Platform (NIP) team must produce the right software for scientific customers. Because many of the requirements for scientific tools are not known ahead of time, building the right software can only be achieved cost-effectively through close collaboration between software development teams and scientific customers.

The Agile software development methodologies attempt to provide a viable approach for the cost-effective delivery of complex and risky software projects. The principles are captured in the Agile Manifesto (http://agilemanifesto.org/):

- Individuals and interactions over processes and tools.
- Working software over comprehensive documentation.
- Customer collaboration over contract negotiation.
- Responding to change over following a plan.

There are many methodologies that are built on the principles above. The NIP is being developed using the Scrum Agile methodology. In Scrum, a shippable increment of the Platform is produced at the end of each iteration, also known as a sprint. A sprint has a fixed duration, typically 2 weeks.

At the beginning of the development, the Product Owner, with the help of the team, transforms this specification into small increments called User Stories and containers of stories called Epics. These are collected in the product Backlog, which can be considered as an ordered list of requirements.

At the beginning of each iteration, the team looks at the stories with the highest priority and decides which of them can be implemented in the Iteration. At the end of each iteration, the team demonstrates to the Product Owner and the Users that the stories are completely implemented, tested and documented.

Before any deployment, a number of quality criteria must be met. For the core services of the NIP, the code is reviewed by at least one team member. Continuous build processes validate any change in the code base by ensuring that all regression tests are successful and that the Platform is successfully deployed in our development environment. To meet production quality, tests must cover at least 85% of the code.

One of the goals of working with small Iterations is to have rapid feedback from the Users. At the end of each iteration, a working Neuroinformatics Platform is released within the Unified Portal. It allows the Users and stakeholders to see the software capabilities at any time during the Ramp-Up Phase. As a first step, before the Neuroinformatics Platform reaches the Minimum Viable Product (MVP) state, internal Users have to test a subset of features. These Users will be people involved in the HBP Consortium. Once the MVP state is reached, more Users will begin testing the Platform.

The feedback of the Users concerning each iteration is addressed when the Backlog is discussed with the stakeholders and the Product Owner. Integrating this feedback is vital for the Neuroinformatics Platform. It reduces the risk of the final delivery failing to correspond to the Users' expectations

In the Scrum methodology, the Backlog is the container of all Backlog items. Backlog items are usually User Stories that deliver User-visible functionality. However, they might also be bugs to be fixed or tasks to be performed. Every Backlog item has an effort estimate and a priority.

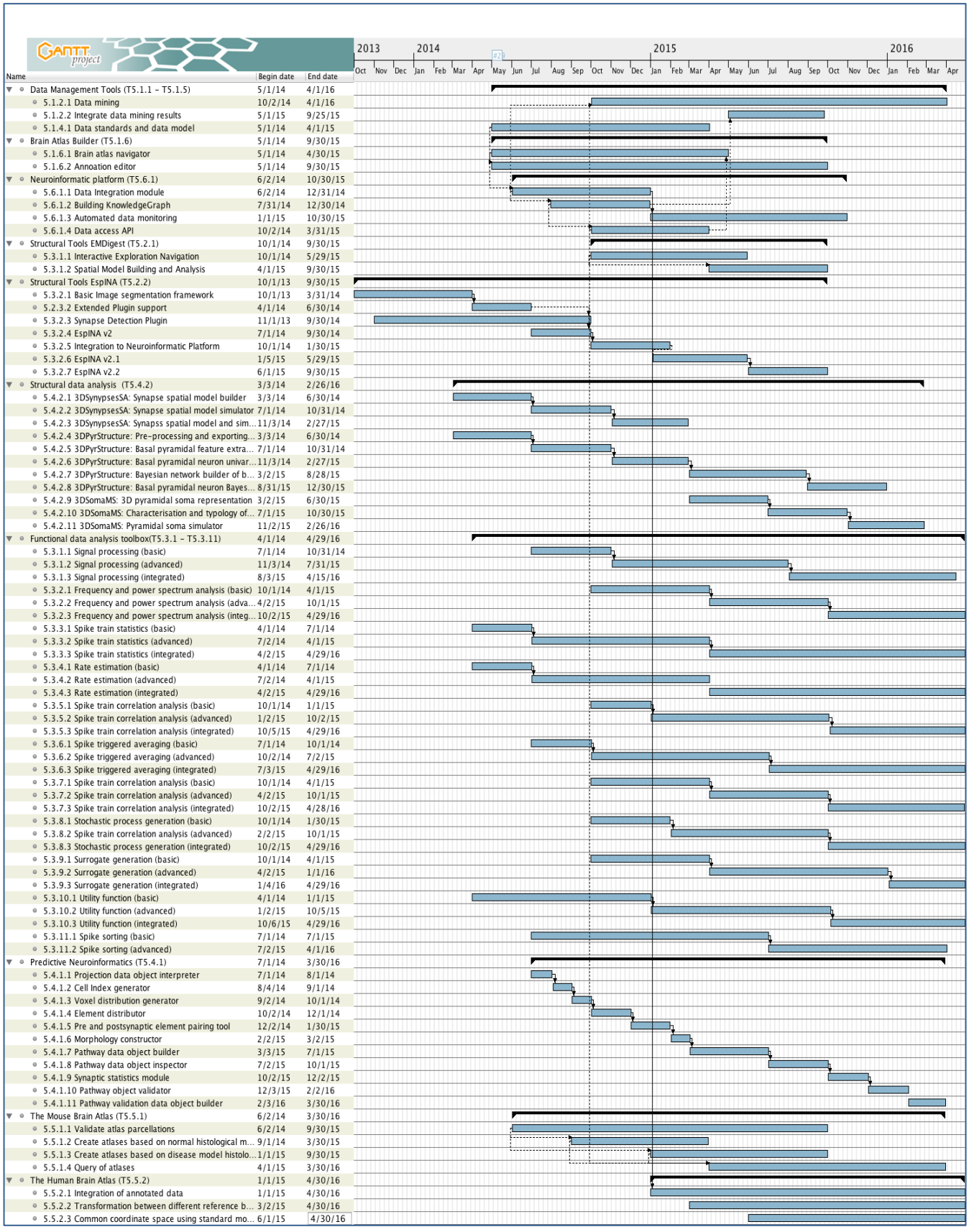
The Backlog is available to the stakeholders at all times and is regularly reviewed by the Product Owner and the stakeholders to determine whether some modification to the Backlog contents or priorities have to be made.

2.2 Software Deployment

The Neuroinformatics Platform is a hub providing access to all the tools developed by SP5 Partners. The Platform also provides Application Programming Interfaces (APIs) to publish, search and access datasets in the Knowledge Graph. The Neuroinformatics Platform itself is deployed as a part of the Unified Portal (SP6).

Software	Deployment plan	Open source
Knowledge Graph	Component of NIP, deployed on UP. Database service running at EPFL	PLANNED
Data integration API	Component of NIP, deployed on UP	
Data access API & Search	Component of NIP, deployed on UP	
Volumetric data service	Component of NIP, deployed on servers with large volumetric data.	PLANNED
Atlas Viewer	Component of NIP, deployed on UP	PLANNED
EspINA	Standalone http://cajalbbp.cesvima.upm.es/espina/	YES
EMDigest	Integrated in Unified Portal	
Elephant	Deployed via iPython https://github.com/NeuralEnsemble/elephant	YES
3DSynapsesSA	Component of NIP, deployed on UP	PLANNED
3DPyrStructure	Component of NIP, deployed on UP	PLANNED
3DSomasMS	Component of NIP, deployed on UP	PLANNED
Functional Data Analysis Toolbox	Component of NIP, deployed on UP	PLANNED
Brain addressing system	Accessible through web interface (TBD)	
Data Space	Amazon Cloud (DataSpace.incf.org)	YES
Knowledge Space	EPFL infrastructure	YES

3. Neuroinformatics Platform: Functionality Schedule



Name	Begin date	End date
Data Management Tools (T5.1.1 – T5.1.5)	5/1/14	4/1/16
5.1.2.1 Data mining	10/2/14	4/1/16
5.1.2.2 Integrate data mining results	5/1/15	9/25/15
5.1.4.1 Data standards and data model	5/1/14	4/1/15
Brain Atlas Builder (T5.1.6)	5/1/14	9/30/15
5.1.6.1 Brain atlas navigator	5/1/14	4/30/15
5.1.6.2 Annoation editor	5/1/14	9/30/15
Neuroinformatic platform (T5.6.1)	6/2/14	10/30/15
5.6.1.1 Data Integration module	6/2/14	12/31/14
5.6.1.2 Building KnowledgeGraph	7/31/14	12/30/14
5.6.1.3 Automated data monitoring	1/1/15	10/30/15
5.6.1.4 Data access API	10/2/14	3/31/15
Structural Tools EMDigest (T5.2.1)	10/1/14	9/30/15
5.3.1.1 Interactive Exploration Navigation	10/1/14	5/29/15
5.3.1.2 Spatial Model Building and Analysis	4/1/15	9/30/15
Structural Tools EspINA (T5.2.2)	10/1/13	9/30/15
5.3.2.1 Basic Image segmentation framework	10/1/13	3/31/14
5.2.3.2 Extended Plugin support	4/1/14	6/30/14
5.3.2.3 Synapse Detection Plugin	11/1/13	9/30/14
5.3.2.4 EspINA v2	7/1/14	9/30/14
5.3.2.5 Integration to Neuroinformatic Platform	10/1/14	1/30/15
5.3.2.6 EspINA v2.1	1/5/15	5/29/15
5.3.2.7 EspINA v2.2	6/1/15	9/30/15
Structural data analysis (T5.4.2)	3/3/14	2/26/16
5.4.2.1 3DSynypsesSA: Synapse spatial model builder	3/3/14	6/30/14
5.4.2.2 3DSynypsesSA: Synapse spatial model simulator	7/1/14	10/31/14
5.4.2.3 3DSynypsesSA: Synapss spatial model and sim…	11/3/14	2/27/15
5.4.2.4 3DPyrStructure: Pre-processing and exporting…	3/3/14	6/30/14
5.4.2.5 3DPyrStructure: Basal pyramidal feature extra…	7/1/14	10/31/14
5.4.2.6 3DPyrStructure: Basal pyramidal neuron univar…	11/3/14	2/27/15
5.4.2.7 3DPyrStructure: Bayesian network builder of b…	3/2/15	8/28/15
5.4.2.8 3DPyrStructure: Basal pyramidal neuron Bayes…	8/31/15	12/30/15
5.4.2.9 3DSomaMS: 3D pyramidal soma representation	3/2/15	6/30/15
5.4.2.10 3DSomaMS: Characterisation and typology of…	7/1/15	10/30/15
5.4.2.11 3DSomaMS: Pyramidal soma simulator	11/2/15	2/26/16
Functional data analysis toolbox(T5.3.1 – T5.3.11)	4/1/14	4/29/16
5.3.1.1 Signal processing (basic)	7/1/14	10/31/14
5.3.1.2 Signal processing (advanced)	11/3/14	7/31/15
5.3.1.3 Signal processing (integrated)	8/3/15	4/15/16
5.3.2.1 Frequency and power spectrum analysis (basic)	10/1/14	4/1/15
5.3.2.2 Frequency and power spectrum analysis (adva…	4/2/15	10/1/15
5.3.2.3 Frequency and power spectrum analysis (integ…	10/2/15	4/29/16
5.3.3.1 Spike train statistics (basic)	4/1/14	7/1/14
5.3.3.2 Spike train statistics (advanced)	7/2/14	4/1/15
5.3.3.3 Spike train statistics (integrated)	4/2/15	4/29/16
5.3.4.1 Rate estimation (basic)	4/1/14	7/1/14
5.3.4.2 Rate estimation (advanced)	7/2/14	4/1/15
5.3.4.3 Rate estimation (integrated)	4/2/15	4/29/16
5.3.5.1 Spike train correlation analysis (basic)	10/1/14	1/1/15
5.3.5.2 Spike train correlation analysis (advanced)	1/2/15	10/2/15
5.3.5.3 Spike train correlation analysis (integrated)	10/5/15	4/29/16
5.3.6.1 Spike triggered averaging (basic)	7/1/14	10/1/14
5.3.6.2 Spike triggered averaging (advanced)	10/2/14	7/2/15
5.3.6.3 Spike triggered averaging (integrated)	7/3/15	4/29/16
5.3.7.1 Spike train correlation analysis (basic)	10/1/14	4/1/15
5.3.7.2 Spike train correlation analysis (advanced)	4/2/15	10/1/15
5.3.7.3 Spike train correlation analysis (integrated)	10/2/15	4/28/16
5.3.8.1 Stochastic process generation (basic)	10/1/14	1/30/15
5.3.8.2 Spike train correlation analysis (advanced)	2/2/15	10/1/15
5.3.8.3 Stochastic process generation (integrated)	10/2/15	4/29/16
5.3.9.1 Surrogate generation (basic)	10/1/14	4/1/15
5.3.9.2 Surrogate generation (advanced)	4/2/15	1/1/16
5.3.9.3 Surrogate generation (integrated)	1/4/16	4/29/16
5.3.10.1 Utility function (basic)	4/1/14	1/1/15
5.3.10.2 Utility function (advanced)	1/2/15	10/5/15
5.3.10.3 Utility function (integrated)	10/6/15	4/29/16
5.3.11.1 Spike sorting (basic)	7/1/14	7/1/15
5.3.11.2 Spike sorting (advanced)	7/2/15	4/1/16
Predictive Neuroinformatics (T5.4.1)	7/1/14	3/30/16
5.4.1.1 Projection data object interpreter	7/1/14	8/1/14
5.4.1.2 Cell Index generator	8/4/14	9/1/14
5.4.1.3 Voxel distribution generator	9/2/14	10/1/14
5.4.1.4 Element distributor	10/2/14	12/1/14
5.4.1.5 Pre and postsynaptic element pairing tool	12/2/14	1/30/15
5.4.1.6 Morphology constructor	2/2/15	3/2/15
5.4.1.7 Pathway data object builder	3/3/15	7/1/15
5.4.1.8 Pathway data object inspector	7/2/15	10/1/15
5.4.1.9 Synaptic statistics module	10/2/15	12/2/15
5.4.1.10 Pathway object validator	12/3/15	2/2/16
5.4.1.11 Pathway validation data object builder	2/3/16	3/30/16
The Mouse Brain Atlas (T5.5.1)	6/2/14	3/30/16
5.5.1.1 Validate atlas parcellations	6/2/14	9/30/15
5.5.1.2 Create atlases based on normal histological m…	9/1/14	3/30/15
5.5.1.3 Create atlases based on disease model histolo…	1/1/15	9/30/15
5.5.1.4 Query of atlases	4/1/15	3/30/16
The Human Brain Atlas (T5.5.2)	1/1/15	4/30/16
5.5.2.1 Integration of annotated data	1/1/15	4/30/16
5.5.2.2 Transformation between different reference b…	3/2/15	4/30/16
5.5.2.3 Common coordinate space using standard mo…	6/1/15	4/30/16

4. Tools for Brain Atlases (WP5.1)

4.1 Tools for Brain Atlases: Introduction

The HBP will create a general-purpose, open-source software framework, allowing researchers to build and navigate multi-level atlases of the brain of any species. These tools will allow researchers to upload and access multi-level information about any part of the brain. The information will provide a shared DataSpace (T5.1.1), data mining tools (T5.1.2, T5.1. 3), data standards (T5.1.4) and a generic "Atlas Builder" (T5.1.6), which make it possible to build, manage and query such atlases. In addition, the Project will also create and manage an HBP "Knowledge Space" – a community-driven Wiki that provides an encyclopaedic view of the latest data, models and literature for all levels of brain organisation (T5.1.5).

4.2 Tools for Brain Atlases: Functions

Function	Description
SP5-FR-001	HBP-CORE: minimal metadata specifications
SP5-FR-002	Data standards and data model
SP5-FR-003	KnowledgeGraph – database built on HBP-CORE data model and ontologies
SP5-FR-005	LabSpace – semantic wiki for organising and curating summaries of individual laboratory data sets
SP5-FR-006	Data sharing interface
SP5-FR-007	Automated data monitoring pipeline

4.3 Tools for Brain Atlases: Main Achievements

SP5-FR-001

Complete. Specifications HBP-MIN to describe experimental data and data derived from analysis run on the Platform. Validation by SP5 and SP6.

SP5-FR-002

First iteration done. Implementation of HBP-MIN in PostgreSQL, which constitutes the Knowledge Graph. Development of the seven ontologies needed to register neuroscience data. Implementation of data standards covering all data currently made available to SP5, i.e. morphology, electrophysiology, regional composition and connectivity.

SP5-FR-003

Complete first iteration of web interface to manually register data to Knowledge Graph and upload files using services provided by Unified Portal infrastructure.

SP5-FR-005

Preparation of HBP-MIN metadata for all raw laboratory data used by SP6 for cellular and circuit modelling. All metadata are described by ontologies.

4.4 Tools for Brain Atlases: Main Problems

None encountered.

4.5 Tools for Brain Atlases: The Next 6 Months

SP5-FR-002

Define additional data standard to register expected data delivered by SP1, SP2 and SP3.

SP5-FR-003

Tests web registration interface with data producer and build second generation based on user feedback. Develop a web interface to register data manually extracted from Literature.

SP5-FR-005

Implement services to manage different ontologies versions that are used in data registration.

SP5-FR-006

Ontology-driven search to retrieve registered data.

SP5-FR-007

Implement Spark to run mining algorithms on data retrieved form the Knowledge Graph.

5. Tools for Structural Data Analysis (WP5.2)

5.1 Tools for Structural Data Analysis: Introduction

Much of the structural data produced by modern neuroscience takes the form of image stacks from light and electron microscopy, MRI, PET, etc. As many of these techniques produce terabytes of data in a single session, the best way to unlock the information they contain is through automatic image processing. The HBP will develop tools for this (T5.2.1, T5.2.2), which it will share with the community via the INCF. The tools will include software to automate the extraction of cell densities and distributions; the reconstruction of neuron morphologies; the determination of subcellular properties such as synapse and organelle geometry, size and location; and the identification of the long-range fibre tracts underlying connectivity.

This chapter covers the following specific tools:

- Analysis of experimental data obtained by EM and light microscopy (EMDigest)
- Segmentation and annotation of brain tissue microscopy stacks (EspINA).
- Analysis of synapse distribution (3DSynapsesSA).
- Reconstruction of neuron morphology of neurons (3DPyrStructure).
- Reconstruction of soma morphology (3DSomaMS).

5.2 Tools for Structural Data Analysis: Functions

Function	Description
SP5-FR-014	EMDigest: authentication and authorisation
SP5-FR-015	EMDigest: data references
SP5-FR-016	EMDigest: filter and compare service
SP5-FR-017	EspINA: authentication and authorisation
SP5-FR-018	EspINA: data references
SP5-FR-019	EspINA: load microscopy images
SP5-FR-020	EspINA: load/store segmentation data
SP5-FR-021	EspINA: collaborative segmentation
SP5-FR-022	EspINA: segmentation tools
SP5-FR-023	EspINA: segmentation classification
SP5-FR-024	EspINA: segmentation inspection
SP5-FR-025	EspINA: stereological counting frame definition
SP5-FR-026	EspINA: synaptic apposition surface
SP5-FR-027	EspINA: neuron structure data
SP5-FR-028	EspINA: neuron structure analysis
SP5-FR-029	EspINA: stack visualisation
SP5-FR-030	EspINA: interactive visualisation
SP5-FR-031	EspINA: user interaction
SP5-FR-032	EspINA: export scenes to common 3D formats

5.3 Tools for Structural Data Analysis: Main Achievements

SP5-FR-014

Completed. No specific authentication function is needed.

SP5-FR-015

Local data support available. EMDigest is already operative (up to the implemented functionalities) using local data; a preliminary test has been conducted in using Data Space repositories.

SP5-FR-016

Completed (pending integration with DataSpace). Current version supports all functional requirements specified by SP5-FR-016 working with local data repositories.

SP5-FR-017

Complete for current data structures. No authentication required except for the access to common repositories.

SP5-FR-018

Complete. ESPINA already support remote repository access to DataSpace-compliant structures. Nonetheless, the extension of structural/semantic information will require extending this remote storage feature.

SP5-FR-019

Completed. ESPINA supports both MetaImage (MHD/MHA) and multi-image TIFF file reading for both electron and light microscopy images.

SP5-FR-020

Completed (pending accessibility API). The tool provides backwards compatibility to previous ESPINA versions and provides its own .seg format. Future released versions will be distributed with the .seg management API to provide developers to programmatically exploit ESPINA files.

SP5-FR-021

Tasks accomplished. The following feature has been already implemented:

- Load two different analysis of the same stack for the current session in order to merge segmented data.

SP5-FR-022

Tasks accomplished and new methods. The following features are already implemented:

- ROI limits segmentation algorithms.
- Segmentation tools: growing seed, and manual segmentation.
- Assisting tools using image training: mitochondria, myelin and postsynaptic density.
- Segmentation manipulation: manual segmentation.

SP5-FR-023

Completed (up to current semantic ontology). Segmented objects can be annotated according to a predefined (but extensible) taxonomy. Category membership can be changed for any segmented object.

SP5-FR-024

Completed. Segmented objects are visible using 2D and 3D representations. In addition, creation parameters and additional information can also be reported visually.

SP5-FR-025

Stereological counting frame can be defined as an orthogonal element and be modified in both 3D and 2D views. The stereological counting frame information is exported in the .seg format.

SP5-FR-026

Completed. ESPINA can generate a SAS structure for any segmentation categorised as a synapse. All the relevant metrics of the SAS structures are computed and available for analysis or export in its own report.

SP5-FR-027

Completed. Segmented object provide morphological and location information: centroid, Feret diameter, distances to the edges of the stack, text notes and taxonomical tag information.

SP5-FR-028

Completed. ESPINA exports tabular analysis information in both .csv and .xls formats. The reported fields can be manually selected.

SP5-FR-029

Stack visualisation includes mechanisms to specify voxel dimensions as well as to modify contrast, brightness, opacity and stain of the stack.

SP5-FR-030

Major functionalities completed. Interactive visualisation features allow major requested operations: Channel and crosshair visibility, selective segmentation visualisation and criteria-base colouring and grouping.

SP5-FR-031

Major functionalities completed. User interaction features include done/undone operations (for basic operations and some selected plugin extensions), interactive visualisation controls, contextual menus and operation cancellation.

SP5-FR-032

Basic output formats are supported.

5.4 Tools for Structural Data Analysis: Main Problems

None encountered.

5.5 Tools for Structural Data Analysis: The Next 6 Months

SP5-FR-016

Integration with DataSpace repository will be the main goal during this time. Additionally and beyond the scope of the original proposal, a new file format will be designed for saving the state and results of an analysis carried in EMDigest.

SP5-FR-021

The management of multi-stack features is only partially supported and there are no analysis tools to exploit multiple stacks. Along this following period some preliminary tests will be conducted.

SP5-FR-022

Future features:

- New assisting tools: Cell nuclei identification in light microscopy.
- Advanced segmentation manipulation: Morphological modification tools, Boolean operators, split tool and hole filling.
- Manual segmentation using contours.

SP5-FR-025

Adaptive stereological frame will be implemented.

SP5-FR-029

Stack visualisation needs to be modified in order to change properties of multiple visualised stacks.

SP5-FR-030

New interactive visualisation requirements will be included along user feedback is received.

SP5-FR-031

Complete do/undo operations for the remaining plugins. Produce more documented APIs and user documentation (user manuals and video tutorials).

6. Tools for Functional Data Analysis (WP5.3)

6.1 Tools for Functional Data Analysis: Introduction

Understanding of brain function depends on data from a wide range of techniques. It is important that simulation results be comparable against this data. To meet this need, the HBP will develop new tools and techniques to compare data from simulations against data from experiments. These will include tools for population analysis (measurement of local field potentials, EEG, fMRI, MEG etc., via T5.3.1) and tools for the analysis of single cell activity (T5.3.2). Some of these tools will build on previous work in the BrainScaleS project.

6.2 Tools for Functional Data Analysis: Main Achievements

6.2.1 Specifications for toolbox

Complete. Supplied specifications of the toolbox indicating anticipated analysis functionality, the toolbox design layout, and the method of integration into the Unified Portal (UP). The toolbox will be developed as an open-source Python library ('Elephant', from 'ELEctroPHysiology ANalysis Toolkit'), which will then be integrated as a collection of "Task" components into the UP. The name 'Functional Data Analysis Toolbox' (FDAT) is used to refer to this set of UP components. The Neo library was selected as the data object model for all analysis work.

6.2.2 Contacted analysis software developers

Complete. Several developers of analysis software known within the Python electrophysiology community (including developers of the Neo project) have been contacted, and are now actively involved in discussions related to the design of Elephant, and have begun to contribute code. A joint workshop is planned for later this Year or early 2015.

6.2.3 Implementation of toolbox

Initial release complete. A first set of prototype analysis functions has been implemented and assembled for an initial internal release, available as a branch of the Project repository. Implemented function prototypes include: spike train statistics (e.g., CV, FF, mean rate, peri-event time histogram), spike train correlations (e.g. cross-correlation), advanced higher-order correlation analysis (e.g. CuBIC, Staude et al. 2010), surrogate data methods for hypothesis testing (e.g., spike dithering), stochastic models of independent and correlated spike trains, as well as supporting functions, such as e.g. time-binning of spike data.

6.2.4 Applied use-case of initial release

Complete. The initial release of the Elephant toolbox was successfully tested in the context of a three-hour practical exercise based on IPython notebooks during the 2014 HBP summer school in Alpbach. The course enabled the students to perform interactive hands-on analysis of simulated and biological spike train data using the developed tools.

6.2.5 Recruitment of personnel

The hiring of 2 full-time programmers/scientists and the hiring of an additional, temporary computer scientist is complete.

6.3 Tools for Functional Data Analysis: Main Problems

6.3.1 Acquisition of experimental Partners to supply a test data set

Despite problems in finding HBP Partners that are able to contribute electrophysiological data sets very early on, WP5.3 has made contacts with experimentalists to get their assistance in integrating selected existing data sets into the Platform for testing and use-case implementation for demonstration.

6.3.2 Recruitment delays

Our Partner CNRS-UNIC experienced a delay of several months in recruiting personnel, due in part to a hired candidate who withdrew only days before the planned start date. However, we expect to make up the delay entirely within the second Year of the Project.

6.4 Tools for Functional Data Analysis: The Next 6 Months

6.4.1 Integrate prototype functions of initial release into main branch of Elephant repository

Required: additional tests.

6.4.2 Implement and integrate further analysis functions according to the toolbox specifications

Missing analysis functionality: z-score, signal filtering, power spectrum, spike-triggered average, SPADE (previously called FIM). Prototypes outside the Elephant repository are already available for all missing functions.

Further requirements for practical work: Helper functions to accelerate productivity with the Neo data model (e.g., NeoFilter class) developed in M1-M12.

6.4.3 Implement initial version of spike sorting component to wrap existing libraries under a common umbrella

6.4.4 UP integration of Elephant as FDAT components

All necessary information for access and use of the portal has now been gathered in M1-M12 during personal and video-conference meetings with the Unified Portal (UP) team, and practically exercised in the scope of a workshop organised by the UP team during the HBP summit. A software developer has been explicitly hired (temporarily) for this process to expedite the integration process.

6.4.5 Construction of use-cases using UP technologies

The teaching modules developed as Use Cases for the Elephant standalone base library will serve as the basis for the first UP-integrated Use Cases.

7. Predictive Neuroinformatics (WP5.4)

7.1 Predictive Neuroinformatics: Introduction

The HBP will make a major effort to develop new tools for Predictive Neuroinformatics, using machine learning and statistical modelling techniques to extract rules describing the relationships between datasets for different levels of brain organisation. A statistical model will make it possible to derive a "global neuronal addressing system" that can predict the targets and the course of long-range axonal projections from specific types of neurons to their targets in the rest of the brain (T5.4.1). A second important goal will be to develop algorithms that use the statistical structure of neuronal and synaptic geometries to synthesise model neurons and synapses (T5.4.2) computationally.

7.2 Predictive Neuroinformatics: Functions

Function	Description
SP5-FR-036	3DSynapsesSA: authentication and authorisation
SP5-FR-037	3DSynapsesSA: data analysis
SP5-FR-039	3DPyrStructure: neuron selection
SP5-FR-040	3DPyrStructure: generation of descriptive analysis
SP5-FR-041	3DPyrStructure: Bayesian network generation
SP5-FR-042	3DSomaMS: authentication and authorisation
SP5-FR-043	3DSomaMS: selection of soma
SP5-FR-044	3DSomaMS: 3D representation
SP5-FR-045	3DSomaMS: generate table with quantitative characterisation
SP5-FR-046	3DSomaMS: reconstruction of the soma

7.3 Predictive Neuroinformatics: Main Achievements

7.3.1 Brain Addressing System

We have initiated SP1-SP5 collaboration and formulated procedures for obtaining and ingesting experimental data of the thalamocortical projection from VPM to barrel cortex needed to specify this Use Case.

We have generated a pilot Matlab data structure that specifies the parameters of a projection. A pilot (standalone) version of Function 5.4.1.1 was written in python to generate an HDF5 file containing the specification of these parameters and read it into a matlab structure that the pipeline can use. A pilot version of Function 5.4.1.2 (Cell Index generator) and a pilot version of Function 5.4.1.3 (Voxel distribution generator) were integrated in the pathway generation pipeline. We are evaluating three schemes (Poisson, Ising, LASSO) for generating the pre/post synaptic element distribution, in order to pick the best one.

7.3.2 3DSynapsesSA

SP5-FR-036

Complete. R source and its packages do not need any authentication or authorisation system.

SP5-FR-037

Prototype finished. This is a component in R language that reads xyz coordinates of the synapses and outputs its visualisation, fitted spatial models using statistical tests and common graphs to analyse the data distribution.

7.3.3 3DPyrStructure

SP5-FR-039

Complete offline but not within the HBP Platform. Neurons layer can be selected, common statistics can be retrieved, and data can be exported to other file formats.

SP5-FR-040

Complete offline but not within the HBP Platform. The component can perform descriptive analyses over different types of selected variables (discrete, continuous, angular), which are then saved.

7.3.4 3DSomaMS

SP5-FR-042

Complete. R source and its packages do not need any authentication or authorisation system.

SP5-FR-043

Complete offline but not within the HBP Platform. The component can read and process somas; VRML files can be interpreted.

SP5-FR-044

Complete offline but not within the HBP Platform. The component can store soma and output data. Also, 3D data (transformed into a ply file) is displayed as a polyhedron.

SP5-FR-046

In progress. The pre-processing and repair of the soma is being supervised by the user.

7.4 Predictive Neuroinformatics: Main Problems

7.4.1 Brain Addressing System

None encountered.

7.4.2 3DSynapsesSA

None encountered.

7.4.3 3DPyrStructure

The PhD student (Ignacio Leguey) working full-time hired by the HBP for this component has been recently granted by the Spanish Ministry and will leave the HBP Project in September 2014. A new PhD student is about to be hired.

7.4.4 3DSomaMS

None encountered.

7.5 Predictive Neuroinformatics: The Next 6 Months

7.5.1 Brain Addressing System

Collect and ingest the data from the Clasca group to advance the experimental component of the Use Case.

After making a choice regarding best algorithm for element distribution, we will implement as a pipeline of independent matlab functions, that is, generate second version of 5.4.1.1-5.4.1.3 and implementing 5.4.1.4-5.4.1.6.

7.5.2 3DSynapsesSA

SP5-FR-037

Upload and test the component in the HBP Platform.

7.5.3 3DPyrStructure

SP5-FR-039

Upload and test the R component in the HBP Platform.

SP5-FR-040

Upload and test the R component in the HBP Platform.

SP5-FR-041

Develop a Bayesian network with continuous and discrete variables from the selected subset of neurons.

7.5.4 3DSomaMS

SP5-FR-043

Upload and test the R component in the HBP Platform.

SP5-FR-044

Upload and test the R component in the HBP Platform.

SP5-FR-045

Develop a quantitative characterisation of somas.

SP5-FR-046

Validate pre-processing and repair of the soma.

8. Brain Atlases (WP5.5)

8.1 Brain Atlases: Introduction

The HBP will use the tools just described to build multi-level atlases of the mouse and human brains (T5.5.1 and T5.5.2 respectively). The design will encourage research groups outside the Project to deposit data in the atlases, enabling global collaboration to integrate data across scales in a single atlas for each species.

8.2 Brain Atlases: Main Achievements

8.2.1 The Mouse Brain Atlas

- MS99: Brain Atlas requirements fully specified (M6): complete. Requirements for rodent brain atlases: mouse and rat. Specification of volumetric data sets (template and structural delineations), mesh representation of structures, and standardised space.
- MS100: Initial population of brain atlas: initial data models and ontologies (M12): Complete. Data model for the mouse and rat brain atlases. Specification of the ontologies of brain structures used for the mouse and rat brain.
- Atlas template packages, first release, and basic version: complete. Mouse brain 3D template package and Rat brain 3D template package, including volumetric template with one (mouse) or seven (rat) imaging modalities, volumetric parcellations of structures, and meshes of structures.
- Validation of atlas parcellations for the atlas template packages for mouse and rat is complete.
- Rodent brain image data collection, first collection: complete. Collections of experimental image data and normal material from mouse and rat brain available for anchoring to atlas templates, using AligNII tool (WP5.1).

8.2.2 The Human Brain Atlas

- A maximum probability map was generated from updated cytoarchitectonic probabilistic maps (Amunts, Jülich). It is ready for registration (in terms of: making it known) in the Data Space of the UP.
- A pipeline for 3D reconstruction of a rat brain volume based on high-resolution Polarised Light Imaging (PLI) has been setup (Axer, Jülich), which will allow for registration of a PLI volume in the UP Data Space until M18.
- 250 brain sections of the human hippocampal target region were analysed by PLI and transferred into high-resolution fibre orientation maps.
- High resolution scans of histological slices from 2 human *post mortem* brains have been processed. One has been 3D reconstructed and published (“BigBrain”); another one is subject to refinement after a successful initial reconstruction has been completed. The first dataset has been registered in the UP Data Space.
- A human infant template has been prepared for registration in the UP Data Space (G. Dehaene), including MR data, atlas delineations and labels.
- A processing pipeline for 3D reconstruction of rat brain volumes from receptor autoradiographs has been established (Zilles, Jülich), and methods for registration into the Waxholm space have been coordinated between Jülich (Zilles) and Oslo (Bjaalie).

8.3 Brain Atlases: Main Problems

Integration of large datasets from remote sites between the DataSpace and the Unified Portal Document Service is not yet clearly defined in technical terms. Network connections and middleware solutions have to be investigated together with other SPs in the near future to find a standard. For the time being, EPFL will replicate datasets directly to the UP Document Service.

8.4 Brain Atlases: The Next 6 Months

8.4.1 The Mouse Brain Atlas

- SP5.5 Atlas template packages, second release.
  - Addition of subdivisions of the hippocampus in rat, defined based on MRI, DTI, cyto- and chemoarchitecture.
- SP5.5 Creation of atlases based on normal histological material
  - Anchor selections of data to the atlas templates with use of AligNII tool (WP 5.1).
  - Muscarinic M2 receptor distributions, rat (Month 18)
  - Combined cyto- and myeloarchitecture (Month 18)

8.4.2 The Human Brain Atlas

- Registration of ~100 cytoarchitectonically defined human brain regions (in MNI ICBM152casym space) in the UP Data Space
- Registration of the human infant template in the UP Data Space
- Registration of a first 3D reconstruction containing Muscarinic M2 receptor distributions from 500 histological sections of the rat brain in the UP Data Space

9. Neuroinformatics Platform: Scientific Coordination (WP5.8)

9.1 Scientific Coordination: Internal Meetings

This table lists meetings between SP staff.

Date	Description	Location	Participants	Comments
15/10/2013	SP5	EPFL, Switzerland	John Richard Walker (EPFL), Sean Hill (EPFL), Guy Willis (EPFL)	
21/10/2013-22/10/2013	WP5.2	Madrid, Spain	Javier Defelipe (UPM), José M. Peña (UPM), Pascal Fua (EPFL), Luis Baumela (UPM), Ángel Merchan (UPM), Jorge PEÑA (UPM), Félix de las Pozas (UPM)	
05/11/2013	SP5	Skype	Sonja Grün (JUELICH), Paul Tiesinga (SKU), Martin Telefont (EPFL), Martina Reske (JUELICH), Jan Bjaalie (UIO)	
28/11/2013	SP5	Skype	Sonja Grün (JUELICH), Martin Telefont (EPFL), Jan Bjaalie (UIO)	
17/12/2013	WP5.3	Skype	Sonja Grün (JUELICH), Michael Denker (JUELICH), Andrew Davison (CNRS)	
07/01/2014	WP5.3	Skype	Sonja Grün (JUELICH), Andrew Davison (CNRS), Michael Denker (JUELICH)	
10/01/2014	WP5.4	Skype	Paul Tiesinga (SKU), Pedro Larrañaga (UPM), Bakker Rembrandt (SKU), Concha Bielza (UPM)	
13/01/2014	SP5	Skype	Sonja Grün (JUELICH), Michael Denker (JUELICH), Alper Yegenoglu (JUELICH), Andrew Davison (CNRS), Martin Telefont (EPFL), Sten Grillner (KI), Jan Bjaalie (UIO)	
11/02/2014	WP5.4	Skype	Paul Tiesinga (SKU), Bakker Rembrandt (SKU), Pedro Larrañaga (UPM)	
09/04/2014	SP5	Skype	Katrien Van Look (EPFL), Sean Hill (EPFL), Paul Tiesinga (SKU), Jan Bjaalie (UIO), Martin Telefont (EPFL), Michael Denker (JUELICH), Andrew Davison (CNRS), Catherine Zwahlen (EPFL), José M. Peña (UPM)	
05/05/2014	SP5	Skype	Katrien Van Look (EPFL), Andrew Davison (CNRS), Sonja Grün (JUELICH), Jan Bjaalie (UIO), Paul Tiesinga (SKU), Sean Hill (EPFL), Martin Telefont (EPFL), Catherine Zwahlen (EPFL), José M. Peña (UPM)	

Date	Description	Location	Participants	Comments
07/05/2014	WP5.3	Video conference	Martina Reske (JUELICH), Sonja Grün (JUELICH), Andrew Davison (CNRS), Michael Denker (JUELICH), Alper Yegenoglu (JUELICH)	
08/05/2014	WP5.3	Video conference	Martina Reske (JUELICH), Michael Denker (JUELICH), Andrew Davison (CNRS), Alper Yegenoglu (JUELICH), Sonja Grün (JUELICH)	
22/05/2014	WP5.3	Video conference	Martina Reske (JUELICH), Michael Denker (JUELICH), Sonja Grün (JUELICH), Andrew Davison (CNRS), Alper Yegenoglu (JUELICH)	
26/05/2014	SP5	Video conference	Katrien Van Look (EPFL), Sean Hill (EPFL), Martin Telefont (EPFL), Xavier Vasques (EPFL), Jan Bjaalie (UIO), Sonja Grün (JUELICH), Alper Yegenoglu (JUELICH), Michael Denker (JUELICH), Sten Grillner (KI), Paul Tiesinga (SKU), Catherine Zwahlen (EPFL), José M. Peña (UPM)	
03/06/2014	WP5.3	Video conference	Martina Reske (JUELICH), Michael Denker (JUELICH), Sonja Grün (JUELICH), Andrew Davison (CNRS), Alper Yegenoglu (JUELICH)	
10/06/2014	WP5.3	Video conference	Martina Reske (JUELICH), Michael Denker (JUELICH), Andrew Davison (CNRS), Alper Yegenoglu (JUELICH), Sonja Grün (JUELICH)	
23/06/2014	SP5	Video conference	Katrien Van Look (EPFL), Andrew Davison (CNRS), Paul Tiesinga (SKU), Bakker Rembrandt (SKU), Sonja Grün (JUELICH), Martina Schmalholz (UHEI), Alper Yegenoglu (JUELICH), Martin Telefont (EPFL), Xavier Vasques (EPFL), Sean Hill (EPFL), Jan Bjaalie (UIO), Catherine Zwahlen (EPFL), José M. Peña (UPM)	
03/07/2014	WP5.3	Video conference	Martina Reske (JUELICH), Andrew Davison (CNRS), Michael Denker (JUELICH), Alper Yegenoglu (JUELICH), Sonja Grün (JUELICH)	
10/07/2014	WP5.3	Video conference	Martina Reske (JUELICH), Sonja Grün (JUELICH), Michael Denker (JUELICH), Andrew Davison (CNRS), Alper Yegenoglu (JUELICH)	
26/08/2014	WP5.4	Leiden, the Netherlands	Paul Tiesinga (SKU), Pedro Larrañaga (UPM), Bakker Rembrandt (SKU)	An in-person meeting at the INCF Neuroinformatics 2014 conference

Date	Description	Location	Participants	Comments
08/09/2014	SP5	Video conference	Katrien Van Look (EPFL), Andrew Davison (CNRS), Jan Bjaalie (UIO), Pedro Larrañaga (UPM), Sean Hill (EPFL), Catherine Zwahlen (EPFL), Martin Telefont (EPFL), Xavier Vasques (EPFL), Sonja Grün (JUELICH), Bakker Rembrandt (SKU), José M. Peña (UPM), Concha Bielza (UPM)	
29/09/2014	SP5	Heidelberg, Germany	Katrien Van Look (EPFL), Sonja Grün (JUELICH), Michael Denker (JUELICH), Alper Yegenoglu (JUELICH), Jean-Denis Courcol (EPFL), Martina Schmalholz (UHEI), Martin Telefont (EPFL), Xavier Vasques (EPFL), Catherine Zwahlen (EPFL), Pedro Larrañaga (UPM), Sean Hill (EPFL), Jan Bjaalie (UIO), Bakker Rembrandt (SKU), Sten Grillner (KI), José M. Peña (UPM), Concha Bielza (UPM), Tsolmongerel Papilloud (EPFL), Jeffrey Grethe (UCAL)	

9.2 Scientific Coordination: HBP Meetings

This table lists meetings between this SP and other SPs.

Date	Description	Location	Participants	Comments
22/10/2013	SP5 & SP2	Video conference	Marshall Elaine (UEDIN), Sean Hill (EPFL), Jan Bjaalie (UIO)	
05/11/2013	SP5 & SP1	Skype	Bruno Weber (UZH), Martin Telefont (EPFL)	
18/11/2013	WP5.2 & SP1	Skype	Javier Defelipe (UPM), José M. Peña (UPM), Martin Telefont (EPFL), Sean Hill (EPFL), Daniel Keller (EPFL), Ángel Merchan (UPM)	
25/11/2013-28/11/2013	WP5.2 & SP1	Madrid, Spain	Javier Defelipe (UPM), José M. Peña (UPM), Ángel Merchan (UPM), Carlos Becker (EPFL), Pol Monso (EPFL), Luis Baumela (UPM), Jorge PEÑA (UPM), Félix de las Pozas (UPM), Angel Rodriguez (UPM), Juan Morales (UPM), Antonio LaTorre (UPM)	
29/11/2013	SP5 & SP7	UPM, Spain	Vicente Martin (UPM), Luis Pastor (URJC), José M. Peña (UPM), Juan Hernando (EPFL)	
12/12/2013	WP5.2 & WP7.3	Skype	José M. Peña (UPM), Luis Pastor (URJC), Felix Schürmann (EPFL), Stefan Eilemann (EPFL), Juan Hernando (EPFL)	
20/12/2013	WP5.2 & WP7.3	Skype	José M. Peña (UPM), Luis Pastor (URJC), Pascal Fua (EPFL), Torsten Kuhlen (RWTH)	
27/02/2014-28/02/2014	WP5.4 & SP1	Madrid, Spain	Paul Tiesinga (SKU), Francisco Clasca (UAM), Javier Defelipe (UPM), Pedro Larrañaga (UPM), Bakker Rembrandt (SKU), Concha Bielza (UPM), Ignacio Leguey (UPM), Angeles Evangelio, Javier Rodriguez, Ángel Merchan (UPM)	
13/05/2014	SP5 & SP2	EPFL, Switzerland	Huibert Mansvelder (VU), Martin Telefont (EPFL)	
14/05/2014	SP5 & SP2	Skype	Katrin Amunts (JUELICH), Sean Hill (EPFL), Jeffrey Christopher Muller (EPFL), Xavier Vasques (EPFL)	
16/06/2014	SP5 & SP6	JUELICH, Germany & video conference	Andrew Davison (CNRS), Jeffrey Christopher Muller (EPFL), Sonja Grün (JUELICH), Michael Denker (JUELICH), Alper Yegenoglu (JUELICH)	
26/06/2014	SP5 & SP6	Video conference	Jeffrey Christopher Muller (EPFL), José M. Peña (UPM)	
03/07/2014	SP5 & SP8	CHUV, Switzerland	Ferath Kherif (CHUV), Xavier Vasques (EPFL), Catherine Zwahlen (EPFL)	

Date	Description	Location	Participants	Comments
07/07/2014	SP5 & SP1	Milan, Italy	Ryuichi Shigemoto (IST), Francesco Pavone (LENS), Szabolcs Kali (IEM HAS), Michele Migliore (CNR), Sten Grillner (KI), Sean Hill (EPFL), Paul Tiesinga (SKU), Jan Bjaalie (UIO), Sabine Rehberger-Schneider (UHEI), Martina Schmalholz (UHEI), Alberto Muñoz (UPM), Enrico Cherubini (EBRI)	An in-person meeting during the 9th FENS Forum of Neuroscience
09/07/2014	SP5, SP1 & SP2	Video conference	Xavier Vasques (EPFL), Jan Bjaalie (UIO), Pablo Toharia Rabasco (URJC), José M. Peña (UPM), Tsolomongerel Papilloud (EPFL), Dmitri Darine (UIO), Gergely Csúcs (UIO), Angel Rodriguez (UPM), Juan Morales (UPM)	Video conference
15/07/2014	SP5 & SP1	Video conference	Jan Bjaalie (UIO), Paul Tiesinga (SKU), Martin Telefont (EPFL), Francisco Clasca (UAM), Szabolcs Kali (IEM HAS), José M. Peña (UPM), Yury Katkov (EPFL), Attila Gulyas (IEM HAS)	
17/07/2014	SP5, SP1, SP2, SP3, SP4, SP6, SP7, SP8, SP9, SP10 & SP11	Video conference		Organised by the STO. A list of attendees was not recorded.
19/08/2014	SP5, SP1, SP7 & SP9	Madrid, Spain	Javier Defelipe (UPM), Karlheinz Meier (UHEI), Luis Pastor (URJC), Pedro Larrañaga (UPM), José M. Peña (UPM), Gonzalo León (UPM), Óscar Herreras (external collaborator, IC-CSIC), members of the Cajal Cortical Circuits Laboratory, additional Spanish representatives of SP5 & SP7	
21/08/2014	SP5 & SP1	Zürich, Switzerland	Bruno Weber (UZH), Martin Telefont (EPFL)	

9.3 Scientific Coordination: External Meetings

This table lists meetings between this SP and Partners outside the HBP.

Date	Description	Location	Participants	Comments
14/10/2013	Novartis	EPFL, Switzerland	Annika Hjelm (EPFL), Sean Hill (EPFL)	
14/10/2013	Karolinska Institutet authorities	Stockholm, Sweden	Sten Grillner (KI)	
15/10/2013	SGENIA	Madrid, Spain	José M. Peña (UPM)	
28/10/2013	HBP: Spanish participation; external meeting. Audience: Spanish participants and Spanish funding agency	Madrid, Spain	Paula Barrera (UPM), Javier Defelipe (UPM), Pilar Flores Romero (UPM), Francisco Clasca (UAM), Mel Slater (UB), Gustavo Deco (UPF), José M. Peña (UPM), Pedro Larrañaga (UPM), Jesus Labarta (BSC), Sergi Girona (BSC), Francesca Arcara (BSC), Vicente Martin (UPM), Luis Pastor (URJC), Eduardo Ros (UGR), Annika Hjelm (EPFL)	
31/10/2013	NEXTLIMIT	Madrid, Spain	José M. Peña (UPM)	
20/11/2013	Royal Institute of Technology	Stockholm, Sweden	Sten Grillner (KI)	
27/11/2013	Elsevier	Video conference	Richard Frackowiak (CHUV), Bogdan Draganski (UNIL), Ferath Kherif (CHUV), Sean Hill (EPFL), Anastasia Ailamaki (EPFL), Tea Danelutti (CHUV)	
27/11/2013	Novartis	Video conference	Annika Hjelm (EPFL), Sean Hill (EPFL), Chris Ebell (EPFL), David Horrigan (EPFL)	
28/11/2013	Goldman Sachs	Video conference	Annika Hjelm (EPFL), Sean Hill (EPFL)	
03/12/2013	Ministry of Education and Research, Government Offices of Sweden	Stockholm, Sweden	Sten Grillner (KI)	
09/12/2013	Novartis	EPFL, Switzerland	Annika Hjelm (EPFL), Sean Hill (EPFL), Chris Ebell (EPFL), Amanda Pingree (EPFL)	
11/04/2014	Karolinska Institutet authorities	Stockholm, Sweden	Sten Grillner (KI)	

Date	Description	Location	Participants	Comments
12/05/2014	National Science Foundation and the National Institutes of Health	Washington DC, USA	Sean Hill (EPFL)	
19/05/2014	European Space Agency	Madrid, Spain	Sean Hill (EPFL)	
11/06/2014	IBM Research	New York, USA	Sean Hill (EPFL)	
19/06/2014	Google – Eric Schmidt, the Executive Chairman	EPFL, Switzerland	Sean Hill (EPFL)	
25/06/2014	ab medic	Milan, Italy	Sean Hill (EPFL)	
24/09/2014	Oracle	EPFL, Switzerland	Sean Hill (EPFL), Catherine Zwahlen (EPFL), Martin Telefont (EPFL), Kathleen Elsig (EPFL), Julian Shillcock (EPFL)	
28/09/2014-30/09/2014	Representatives of the international brain initiatives - US, China, Japan and Australia	Heidelberg, Germany	Annika Hjelm (EPFL), Sean Hill (EPFL), Chris Ebell (EPFL), Kathleen Elsig (EPFL)	

9.4 Scientific Coordination: Monitoring & Quality Control

SP5 has met regularly (mainly via video conference), as well as with other SPs and external parties. For internal monitoring and quality control, the STO is invited to every SP5 meeting and receives all emails sent to SP5. The STO also reviews our periodic reports and deliverables.

9.5 Scientific Coordination: Additional Comments

Talks given by the Partners at conferences and workshops are listed in the Annex of the M1-M12 periodic report.

9.6 Scientific Coordination: The Next 6 Months

We will continue with our regular meetings; these are listed (along with the agenda and minutes) on the Collaboration Portal and EMDESK, so that all the HBP Partners can join if they wish. We had a recent (November 2014) in-person meeting in Jülich, Germany and plan to continue/increase the frequency of these in the future.

Annex A: Milestones

No.	Milestone Name	WP	Month Due	Month Achieved	See Page
MS86	Atlas tools fully specified; digital brain atlas registration services pre-alpha 1 deployed on Project servers; Data Space pre alpha deployed on public cloud	5.1	6	6	10
MS89	Structural analysis tools fully specified	5.2	6	6	10
MS93	Functional analysis tools fully specified	5.2	6	6	10
MS97	Predictive Neuroinformatics requirements specified	5.4	6	6	10
MS99	Brain atlas requirements fully specified	5.5	6	6	10
MS104	Neuroinformatics Platform fully specified	5.6	6	6	10
MS108	Requirements for user support and documentation fully specified	5.7	6	6	10
MS90	Initial structural analysis tools released (focus on EM segmentation)	5.2	12	12	10
MS94	Initial functional analysis tools released (focus on spike sorting and LFP analysis)	5.3	12	12	10
MS100	Initial data models and ontologies for ion channels, single cells, synaptic and microcircuit data registered with data space and annotated	5.5	12	12	10

Annex B: Subproject Functions

SP5's current KPI information can be viewed on the STO's KPI website via this link:

https://flagship.kip.uni-heidelberg.de/jss/CollectKPI?uI=268&s=UJuR3AgTezrb&um=sPO&oSP=5

No.	Function Name	Start (plan)	Start (actual)	Complete (plan)	Complete (actual)	See Page
5.1.2.1	Data mining	Oct 2014		April 2016		
5.1.2.2	Integrate data mining results	May 2015	-	Sept 2015		
5.1.4.1	Data standards and data model	May 2014		April 2015		
5.1.6.1	Brain atlas navigator	May 2014		April 2015		
5.1.6.2	Annotation editor	May 2014		Sept 2015		
5.2.1.1	Interactive exploration navigation	Oct 2014		May 2015		
5.2.1.2	Spatial model building and analysis	April 2015	-	Sept 2015		
5.2.2.1	Basic image segmentation framework	Oct 2013		March 2014		
5.2.2.2	Extended plug-in support	April 2014		June 2014		
5.2.2.3	Synapse detection plug-in	Nov 2013		Sept 2014		
5.2.2.4	EspINA v2	July 2014		Sept 2014		
5.2.2.5	Integration with Neuroinformatics Platform	Oct 2014		Jan 2015		
5.2.2.6	EspINA v2.1	Jan 2015	-	May 2015		
5.2.2.7	EspINA v2.2	June 2015	-	Sept 2015		
5.3.1.1	Signal processing (basic)	July 2014		Oct 2014		
5.3.1.2	Signal processing (advanced)	Nov 2014		Aug 2015		
5.3.1.3	Signal processing (integrated)	Aug 2015	-	April 2016		
5.3.2.1	Frequency and power-spectrum analysis (basic)	Oct 2014		April 2015		
5.3.2.2	Frequency and power-spectrum analysis (advanced)	April 2015	-	Oct 2015		
5.3.2.3	Frequency and power-spectrum analysis (integrated)	Oct 2015	-	April 2016		

No.	Function Name	Start (plan)	Start (actual)	Complete (plan)	Complete (actual)	See Page
5.3.3.1	Spike train statistics (basic)	April 2014		July 2014		
5.3.3.2	Spike train statistics (advanced)	July 2014		April 2015		
5.3.3.3	Spike train statistics (integrated)	April 2015	-	April 2016		
5.3.4.1	Rate estimation (basic)	April 2014		July 2014		
5.3.4.2	Rate estimation (advanced)	July 2014		April 2015		
5.3.4.3	Rate estimation (integrated)	April 2015	-	April 2016		
5.3.5.1	Spike train correlation analysis (basic)	Oct 2014		Jan 2015		
5.3.5.2	Spike train correlation analysis (advanced)	Jan 2015	-	Oct 2015		
5.3.5.3	Spike train correlation analysis (integrated)	Oct 2016	-	April 2016		
5.3.6.1	Spike triggered averaging (basic)	July 2014		Oct 2014		
5.3.6.2	Spike triggered averaging (advanced)	Oct 2014		July 2015		
5.3.6.3	Spike triggered averaging (integrated)	July 2015	-	April 2016		
5.3.7.1	Frequent itemset mining (basic)	Oct 2014		April 2015		
5.3.7.2	Frequent itemset mining (advanced)	April 2015	-	Oct 2015		
5.3.7.3	Frequent itemset mining (integrated)	Oct 2015	-	April 2016		
5.3.8.1	Stochastic process generation (basic)	Oct 2014		Jan 2015		
5.3.8.2	Stochastic process generation (advanced)	Jan 2015	-	Oct 2015		
5.3.8.3	Stochastic process generation (integrated)	Oct 2015	-	April 2016		
5.3.9.1	Surrogate generation (basic)	Oct 2014		April 2015		
5.3.9.2	Surrogate generation (advanced)	April 2015	-	Jan 2016		

No.	Function Name	Start (plan)	Start (actual)	Complete (plan)	Complete (actual)	See Page
5.3.9.3	Surrogate generation (integrated)	Jan 2015	-	April 2016		
5.3.10.1	Utility functions (basic)	April 2014		Jan 2015		
5.3.10.2	Utility functions (advanced)	Jan 2015	-	Oct 2015		
5.3.10.3	Utility functions (integrated)	Oct 2015	-	April 2016		
5.3.11.1	Spike sorting	July 2014		July 2015		
5.3.11.2	Spike sorting (integrated)	July 2015	-	April 2016		
5.4.1.1	*Projection* data object interpreter	July 2014		Aug 2014		
5.4.1.2	Cell Index generator	Aug 2014		Sept 2014		
5.4.1.3	Voxel distribution generator	Sept 2014		Oct 2014		
5.4.1.4	Element distributor	Oct 2014		Dec 2014		
5.4.1.5	Pre and postsynaptic element pairing tool	Dec 2014		Feb 2015		
5.4.1.6	Morphology constructor	Feb 2015	-	Mar 2015		
5.4.1.7	*Pathway* data object builder	Mar 2015	-	July 2015		
5.4.1.8	*Pathway* data object inspector	July 2015	-	Oct 2015		
5.4.1.9	Synaptic statistics module	Oct 2015	-	Dec 2015		
5.4.1.10	*Pathway* object validator	Dec 2015	-	Feb 2015		
5.4.1.11	*Pathway validation* data object builder	Feb 2015	-	Mar 2015		
5.4.2.1	Synapse spatial model builder	Mar 2014		Jun 2014		

No.	Function Name	Start (plan)	Start (actual)	Complete (plan)	Complete (actual)	See Page
5.4.2.2	Synapse spatial model simulator	July 2014		Oct 2014		
5.4.2.3	Synapse spatial model and simulation plotter	Nov 2014		Feb 2015		
5.4.2.4	Pre-processing and exporting pyramidal neuron data	Mar 2014		June 2014		
5.4.2.5	Basal pyramidal neuron feature extractor	July 2014		Oct 2014		
5.4.2.6	Basal pyramidal neuron univariate analyser	Nov 2014		Feb 2015		
5.4.2.7	Bayesian network builder of basal pyramidal neurons	Mar 2015	-	Aug 2015		
5.4.2.8	Basal pyramidal neuron Bayesian network reasoner	Sep 2015	-	Dec 2015		
5.4.2.9	3D pyramidal soma representation	Mar 2015	-	June 2015		
5.4.2.10	Characterisation and typology of pyramidal somas	July 2015	-	Oct 2015		
5.4.2.11	Pyramidal soma simulator	Nov 2015	-	Feb 2016		
5.5.1.1	Validate atlas parcellations	June 2014		Sept 2015		
5.5.1.2	Create atlases based on normal histological material	Sept 2014		Mar 2015		
5.5.1.3	Create atlases based on disease model histological material	Jan 2015	-	Sept 2015		
5.5.1.4	Query of atlases	April 2015	-	Mar 2016		
5.5.2.1	Integration of annotated data	Jan 2015	-	April 2016		
5.5.2.2	Transformation between different reference…	Mar 2015	-	April 2016		
5.5.2.3	Common coordinate space using standard mo….	June 2015	-	April 2016		
5.6.1.1	Data integration module	June 2014		Dec 2014		
5.6.1.2	Building a Knowledge Graph	July 2014		Dec 2014		
5.6.1.3	Automated data monitoring pipeline	Jan 2015	-	Oct 2015		
5.6.1.4	Data access API	Oct 2014		March 2015		

Annex C: Scientific Key Performance Indicators (SKPIs)

SP5's current KPI information can be viewed on the STO's KPI website via this link:

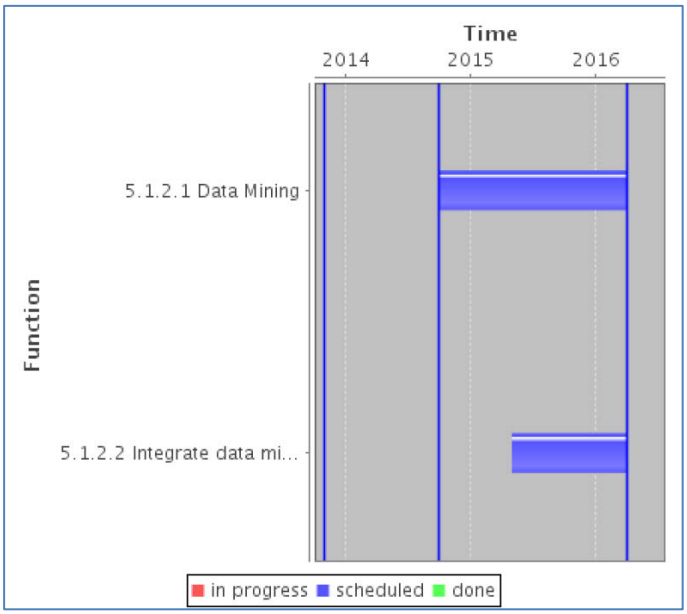
https://flagship.kip.uni-heidelberg.de/jss/CollectKPI?uI=268&s=UJuR3AgTezrb&um=sPO&oSP=5

Task	KPI	ID	M12 Target	M12 Actual
5.1.2	Number of completed functions	SP5-SKPI-001	-	
5.1.4	Percentage of data covered for current data provider	SP5-SKPI-002	50%	
5.1.6	Number of completed functions	SP5-SKPI-003	-	
5.3.1	Number of completed functions	SP5-SKPI-004	1	
5.3.2	Number of completed functions	SP5-SKPI-005	1	
5.3.3	Number of completed functions	SP5-SKPI-006	1	
5.3.4	Number of completed functions	SP5-SKPI-007	1	
5.3.5	Number of completed functions	SP5-SKPI-008	1	
5.3.6	Number of completed functions	SP5-SKPI-009	1	
5.3.7	Number of completed functions	SP5-SKPI-010	-	
5.3.8	Number of completed functions	SP5-SKPI-011	-	
5.3.9	Number of completed functions	SP5-SKPI-012	-	
5.3.10	Number of completed functions	SP5-SKPI-013	1	
5.3.11	Number of completed functions	SP5-SKPI-014	-	
5.4.1	Number of completed functions	SP5-SKPI-015	3	
5.4.2	Number of completed functions	SP5-SKPI-016	4	
5.5.1	Number of completed functions	SP5-SKPI-017	-	
5.6.1	Number of completed functions	SP5-SKPI-018	-	

WP5.1 Tools for brain atlases

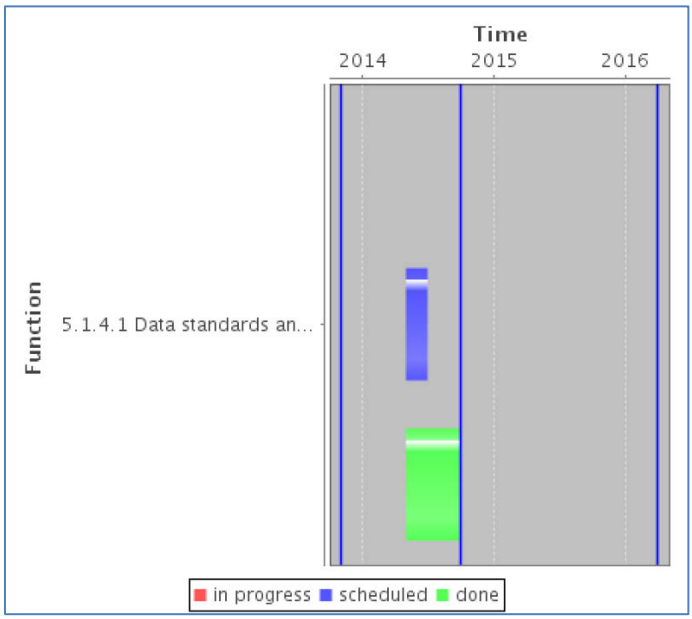
Data Management Tools (T5.1.1 - T5.1.5)

- 5.1.2.1 Data Mining. Planned: 2014/10/01 - 2016/03/31 edited by pare Test case: data a defined sets of tools and a series of parameters are generated, that can be used in simulations; Requires functions 5.6.1.4, 5.6.1.1
- 5.1.2.2 Integrate data mining results. Planned: 2015/05/01 - 2016/03/31 Test C population of the database with results derived from analysis and linked to the appropriate ontologies; requires function 5.1.2.1
- Responsible: catherine.zwahlen@epfl.ch



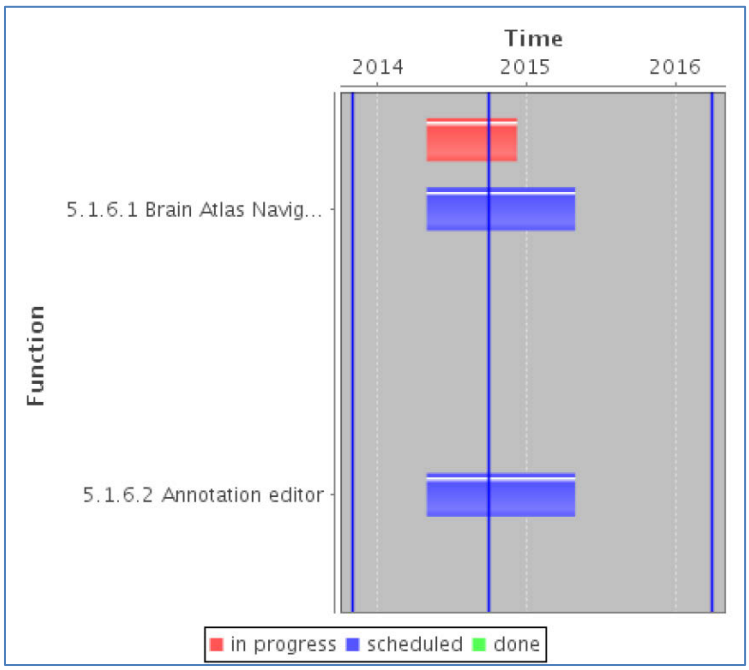
Data standards (T5.1.4)

- 5.1.4.1 Data standards and models. Planned: 2014/05/01 - 2014/06/30 Test c specifications allowing a developer to build an interface for uploading selected data types and their associated metadata.
- Responsible: catherine.zwahlen@epfl.ch



3D Brain Atlas Builder (T5.1.6)

- 5.1.6.1 Brain Atlas Navigator. Planned: 2014/05/01 - 2015/04/30 Test C
  navigate through the brain in different planes using a web browser. The navigator will allow the user to create a brain atlas from a stack of high-resolution 2D images.
- 5.1.6.2 Annotation editor. Planned: 2014/05/01 - 2015/04/30 Test ca
  annotate specific 2D images within the atlas. The annotations are searchable. Requires function 5.1.6.1
- Responsible: catherine.zwahlen@epfl.ch

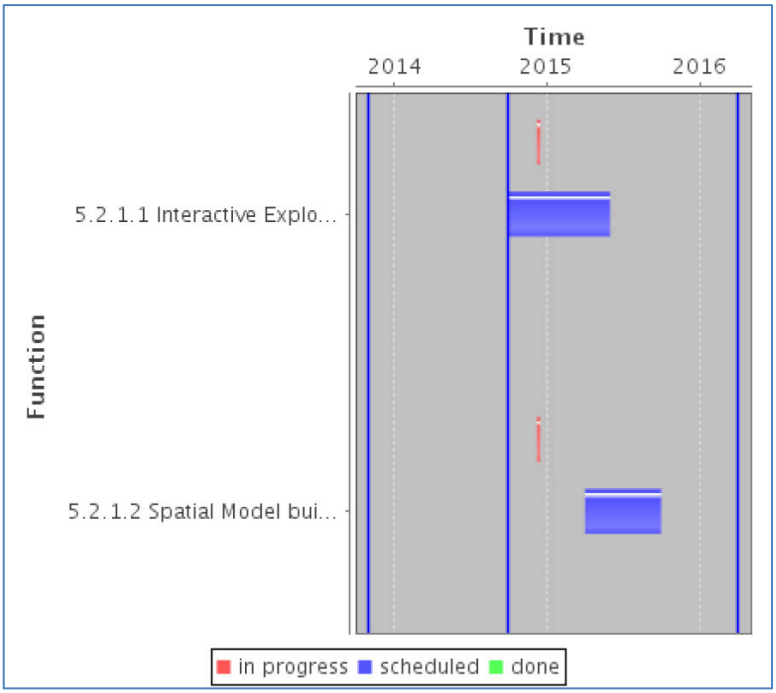


WP5.2 Tools for structural data analysis

EMDigest (T5.2.1)

Tools for structural data analysis

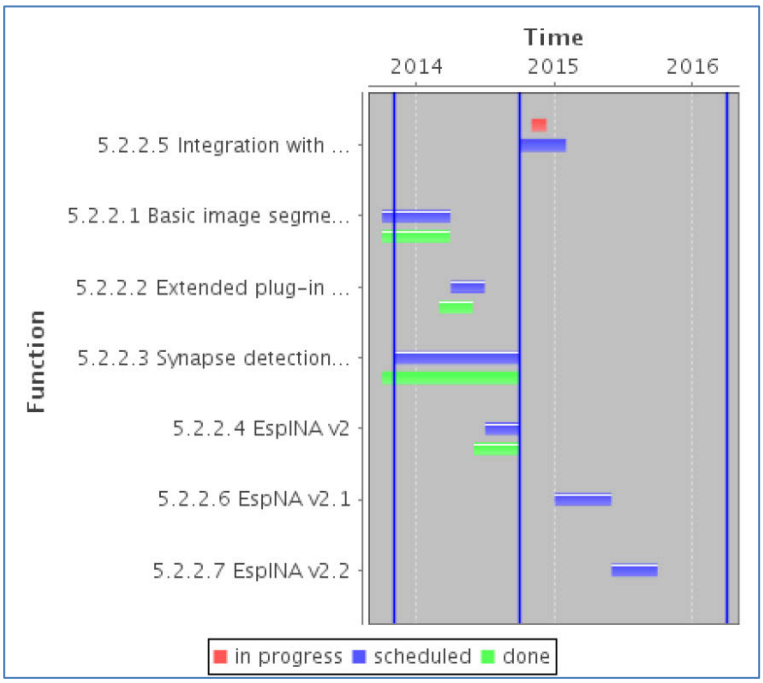
- 5.2.1.1 Interactive Exploration Navigation. Planned: 2014/10/01 - 2015/05/31 Test Ca
  will perform interactive filtering of experimental EM data, visualizing and interacting with the obtained results in a user-driven exploratory navigation and analysis process. Test Case B: The user may report the results of the analysis session in a standard spreadsheet format or using XML-based formats (compliant with the Neuroinformatics Platform); requires function 5.2.2.1 (EspINA tool).
- 5.2.1.2 Spatial Model building and Analysis. Planned: 2015/04/01 - 2015/09/30 Test Ca
  user will perform statistical data analysis on experimental EM data using pattern identification algorithms and will perform statistical tests about the population under study. Test Case B: A user will export model patterns in a XML exchangeable format; requires function 5.2.1.1
- Responsible: catherine.zwahlen@epfl.ch



Segment (T5.2.2)

Structural Tools: EspINA

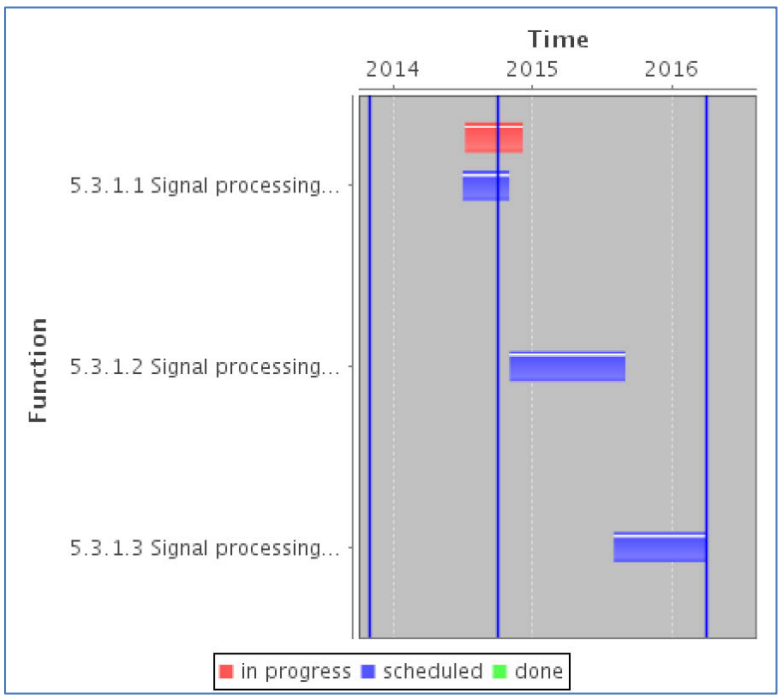
- 5.2.2.1 Basic image segmentation framework. Planned: 2013/10/01 - 2014/03/31 Test Ca
  user may open raw images and previous EspINA versions to perform manual segmentation or using the default automatic algorithms and filters. Test Case B: The user may produce spreadsheet results of the segmented structures. Test CCase C: The user can create a new segmentation clicking on an identified structure on the sample.
- 5.2.2.2 Extended plug-in support. Planned: 2014/04/01 - 2014/06/30 Test Ca
  may develop new image segmentation algorithms. The user may load the plug-in elements that implement these algorithms and using them inside EspINA. Test Case B: Users may refined the segmented objects produced by any automatic segmentation algorithm and re-execute the algorithm again. Requires function 5.2.2.1.
- 5.2.2.3 Synapse detection plug-in. Planned: 2013/11/01 - 2014/09/30 Test Ca
  an interactive assisted synapse detection algorithm i,plemented as an EspINA plug-in. Requires function 5.2.2.2
- 5.2.2.4 EspINA v2. Planned: 2014/07/01 - 2014/09/30 Test C
  logical counting frames. Test Case B: Users may segment larger EM stacks (>1GiB). The user can simultaneously explore multiple channels/views of the same sample. The user may modify channel visibility and opacity properties. Test Case D: The user may limit the area where the context-aware segmentation tool will be applied. Test Case F: The user may compute the synaptic apposition surface of any post synaptic density. Test case G: The user may use extended edition tools: dilatation, erode, planar split and fill holes. Requires function 5.2.2.2
- 5.2.2.5 Integration with Neuroinformatics Platform. Planned: 2014/10/01 - 2015/01/31 Test ca
  : Users may storage and recover raw images and segmentation files from the Data Space. Test Case B: The user may export metadata information from EspINA framework into the Knowledge Graph. Requires function 5.2.2.4
- 5.2.2.6 EspNA v2.1. Planned: 2015/01/01 - 2015/05/31 Test c
  annotation categories or load predefined ontology hierarchies. Test case B: The user may define different types of stereological counting frames to the analysis. These counting frames may be orthogonal or adaptive. Test Case C: The user may use orthogonal and manual regions of interest for the application of different assisted tools. Test Case D: The user may define tags to extend metadata information associated to the segmented objects and structures. The user may filter and query the segmented objects according to these tags. Test Case E: The user can obtain the stereo logical inclusion information of any segmentation. Test Case F: The user may import/export data from/to other tools. This included 3D scenes. Test Case G: The user can import a new segmentation from a stack of images containing its binarization. Requires function 5.2.2.5
- 5.2.2.7 EspINA v2.2. Planned: 2015/06/01 - 2015/09/30 Test Ca
  with multiple stacks in tiling or comparative mode. Test Case B: Users may define skeletons of segmented structures to identify dendrite and axonal processes. Test Case C: The user may manage multiple region of interest and combine their application. Test Case D: The user can obtain statistical information about the structures in the analysis and apply some simple data analysis algorithms to create the custom reports. Test Case E: Contributors may use extended pug-in architecture: new report extensions and new color engine. Requires function 5.2.2.6
- Responsible: pascal.fua@epfl.ch Responsible: jmpena@fi.upm.es



WP5.3 Tools for the analysis of functional data

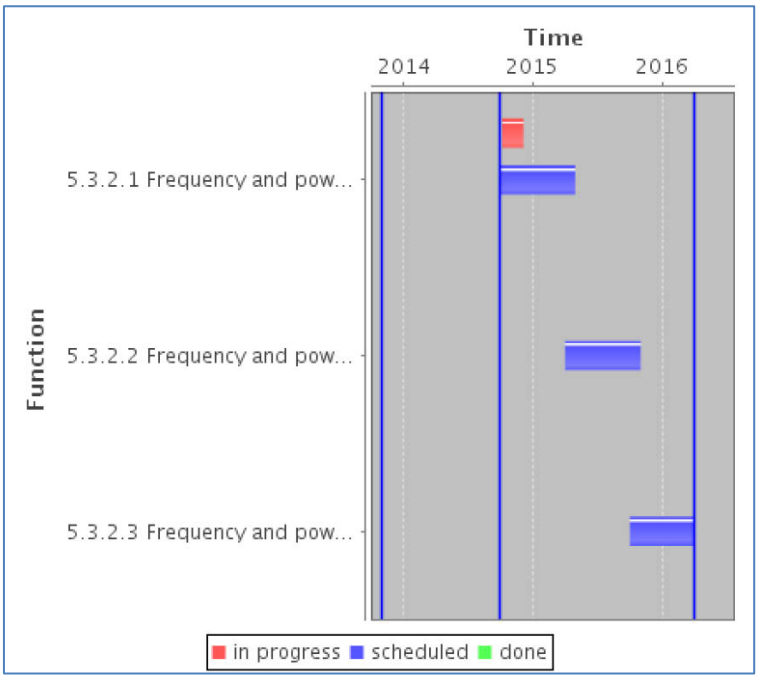
FDAT - Signal processing (T5.3.1)

- 5.3.1.1 Signal processing (basic). Planned: 2014/07/01 - 2014/10/31 Test ca
  calculate the z-score of a given signal. Test Case B: A user can filter the frequency of signals.
- 5.3.1.2 Signal processing (advanced). Planned: 2014/11/01 - 2015/08/31 Test ca
  calculate the analytic signal (phase and amplitude). Requires Function 6.3.1.1
- 5.3.1.3 Signal processing (integrated). Planned: 2015/08/01 - 2016/03/31 Test ca
  of 5.3.1 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.1.1 and 5.3.1.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



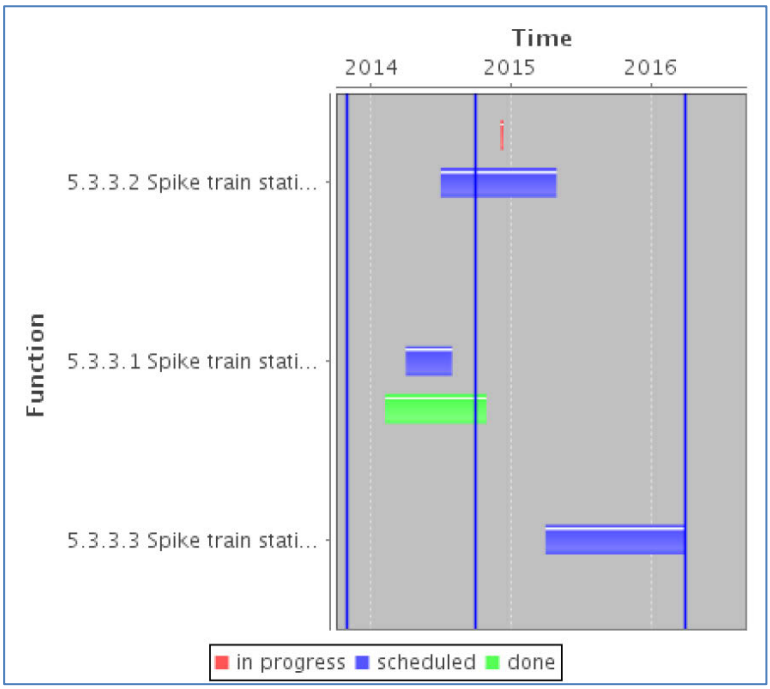
FDAT - Frequency and power-spectrum analysis (T5.3.2)

- 5.3.2.1 Frequency and power-spectrum analysis (basic). Planned: 2014/10/01 - 2015/04/30 Test case A: A user can calculate the Fourier transform of a signal. test case B: A user can calculate the power spectrum of a signal.
- 5.3.2.2 Frequency and power-spectrum analysis (advanced). Planned: 2015/04/01 - 2015/10/31 Test case A: A user can calculate the coherence between two signals. Test case B: A user can calculate the coherency between two signals. requires Function 5.3.2.1
- 5.3.2.3 Frequency and power-spectrum analysis (integrated). Planned: 2015/10/01 - 2016/03/31 Test case: All functions of 5.3.2 are fully tested and integrated into the HBP platform. Requires Functions 5.3.2.1 and 5.3.2.2
- Responsible: pascal.fua@epfl.ch Researcher: jmeyer@fi.upm.es



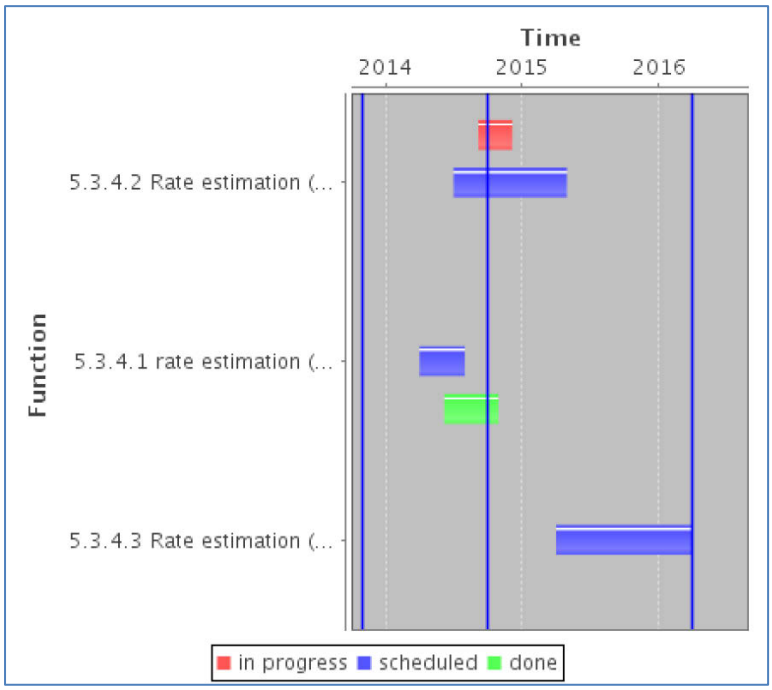
FDAT - Spike train statistics (T5.3.3)

- 5.3.3.1 Spike train statistics (basic). Planned: 2014/04/01 - 2014/07/31 Test ca
  calculate the time series of inter-spike intervals. Test Case B: A user can calculate the co-efficient of variation and the FANO factor.
- 5.3.3.2 Spike train statistics (advanced). Planned: 2014/07/01 - 2015/04/30 Test Ca
  calculate train metrics, e.g. Victor-Purpura or van Rossum spike distances. Requires Function 5.3.3.1
- 5.3.3.3 Spike train statistics (integrated). Planned: 2015/04/01 - 2016/03/31 Test C
  functions of 5.3.3 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.3.1 and 5.3.3.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



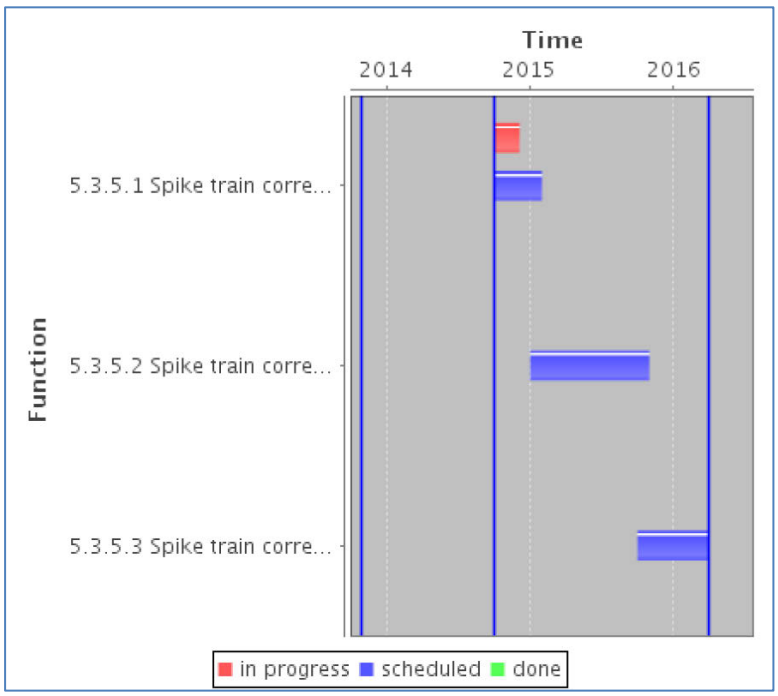
FDAT - Rate estimation (T5.3.4)

- 5.3.4.1 rate estimation (basic). Planned: 2014/04/01 - 2014/07/31 Test C
  calculate the discretely binned presentation of spike trains.
- 5.3.4.2 Rate estimation (advanced). Planned: 2014/07/01 - 2015/04/30 Test C
  create a continuous rate estimate using convolution of spikes with smooth kernels, such as Gaussian windows. Requires Function 5.3.4.1
- 5.3.4.3 Rate estimation (integrated). Planned: 2015/04/01 - 2016/03/31 Test C
  of 5.3.4 are fully tested and integrated into the HBP Platform
- Responsible: andrew.davison@unic.cnrs-gif.fr



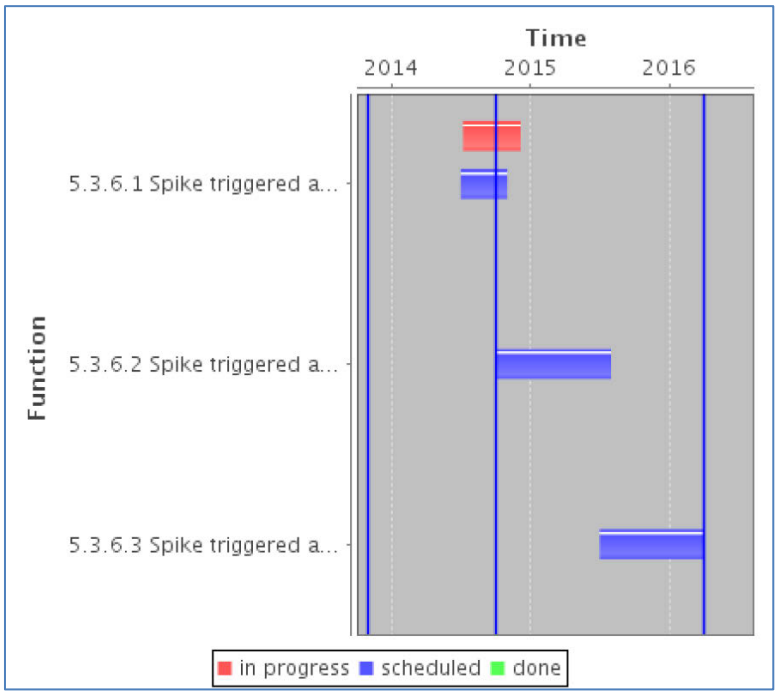
FDAT - Spike train correlation analysis (T5.3.5)

- 5.3.5.1 Spike train correlation analysis (basic). Planned: 2014/10/01 - 2015/01/31 Test Ca
  user can calculate the covariance between two parallel spike trains. Test Case B: A user can calculate the cross-correlation histogram between two parallel spike trains.
- 5.3.5.2 Spike train correlation analysis (advanced). Planned: 2015/01/01 - 2015/10/31 Test Ca
  A: A user can calculate matrices of correlation between multiple parallel spike trains. Test Case B: A user can calculate matrices of correlation coefficients between multiple parallel spike trains. Requires Function 5.3.5.1
- 5.3.5.3 Spike train correlation analysis (integrated). Planned: 2015/10/01 - 2016/03/31 Test Case: All functions of 5.3.5 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.5.1 and 5.3.5.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



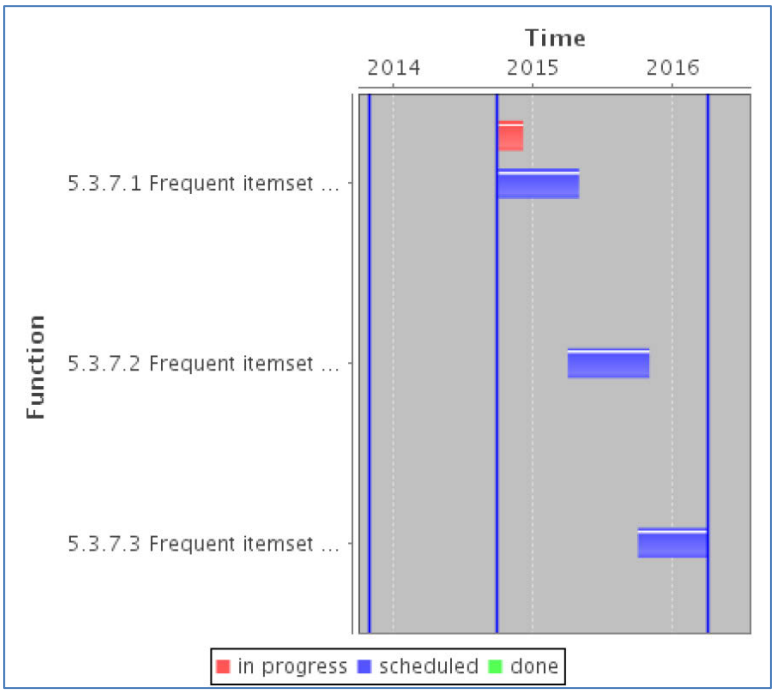
FDAT - Spike-triggered averaging (T5.3.6)

- 5.3.6.1 Spike triggered averaging (basic). Planned: 2014/07/01 - 2014/10/31 Test C
  can calculate the spike-triggered average.
- 5.3.6.2 Spike triggered averaging (advanced). Planned: 2014/10/01 - 2015/07/31 Test ca
  user can calculate the spike-field coherence. Requires Function 5.3.6.1
- 5.3.6.3 Spike triggered averaging (integrated). Planned: 2015/07/01 - 2016/03/31 Test Case: All functions of 5.3.6 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.6.1 and 5.3.6.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



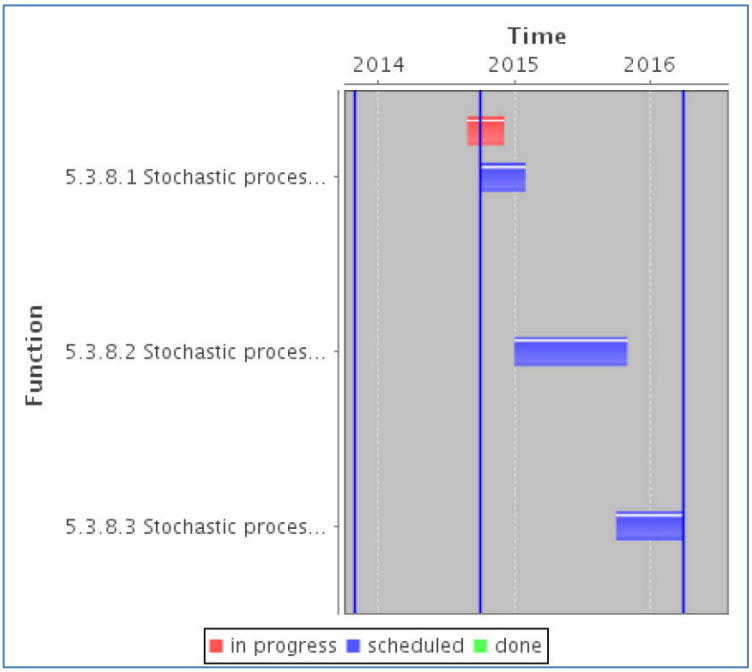
FDAT - Spike pattern analysis using frequent item set mining (FIM) (T5.3.7)

- 5.3.7.1 Frequent itemset mining (basic). Planned: 2014/10/01 - 2015/04/30 Test Ca
  detect frequent patterns in synchronously active neurons.
- 5.3.7.2 Frequent itemset mining (advanced). Planned: 2015/04/01 - 2015/10/31 Test C
  user can evaluate significance of observed spike patterns. Requires Function 5.3.7.1
- 5.3.7.3 Frequent itemset mining (integrated). Planned: 2015/10/01 - 2016/03/31 Test Ca
  Functions of 5.3.7 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.7.1 and 5.3.7.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



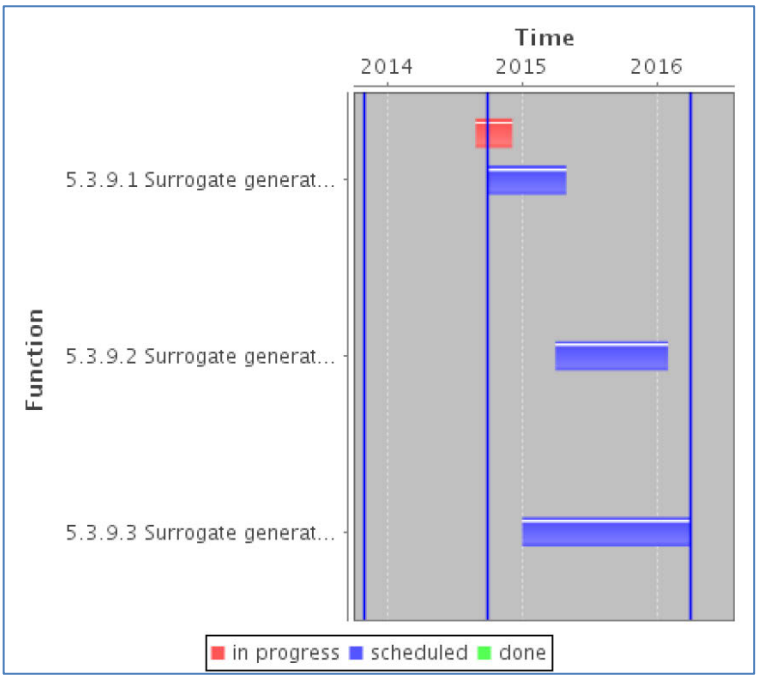
FDAT - Stochastic process generation (T5.3.8)

- 5.3.8.1 Stochastic process generation (basic). Planned: 2014/10/01 - 2015/01/31 Test Ca
  user can generate one or more independent Poisson distributed time series. Test case B: A user can generate one or more independent Gamma distributed time series.
- 5.3.8.2 Stochastic process generation (advanced). Planned: 2015/01/01 - 2015/10/31 RTest C
  A: A user can generate correlated sets of (multiple) multidimensional Poisson processes according to the SIP (single interaction process) model. Test Case B: A user can generate correlated sets of (Multiple) multidimensional Poisson processes according to the MIP (multiple interaction process) model. Requires Function 5.3.8.1
- 5.3.8.3 Stochastic process generation (integrated). Planned: 2015/10/01 - 2016/03/31 Test Ca
  All Functions of 5.3.8 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.8.1 and 5.3.8.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



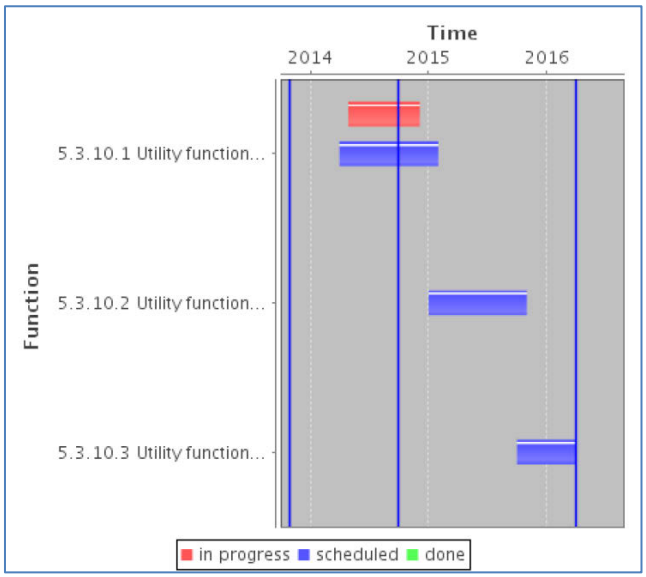
FDAT - Surrogate generation (T5.3.9)

- 5.3.9.1 Surrogate generation (basic). Planned: 2014/10/01 - 2015/04/30 Test Ca
  obtain surrogates by uniformly dithering times around the original position. Test Case B: A user can obtain surrogates by randomly shuffling times around the original position.
- 5.3.9.2 Surrogate generation (advanced). Planned: 2015/04/01 - 2016/01/31 test Ca
  can obtain surrogates by uniformly shifting each trial by a random time offset. Requires Function 5.3.9.1
- 5.3.9.3 Surrogate generation (integrated). Planned: 2015/01/01 - 2016/03/31 Test C
  functions of 5.3.9 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.9.1 and 5.3.9.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



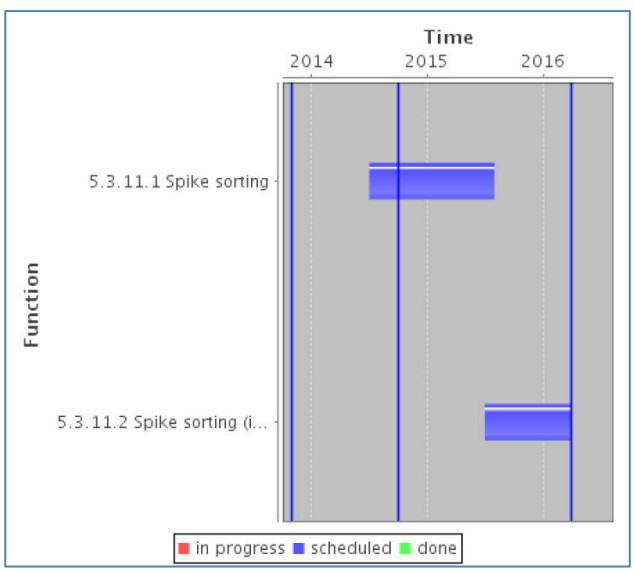
FDAT - Utility functions (T5.3.10)

- 5.3.10.1 Utility function (basic). Planned: 2014/04/01 - 2015/01/31 Test ca
  create a histogram of values. Test Case B: A user can calculate statistical measures such as mean, standard deviation, variance, and standard error of mean.
- 5.3.10.2 Utility function (advanced). Planned: 2015/01/01 - 2015/10/31 Test Ca
  select subsets of data (such as specific electrodes, specific neurons and specific time windows). Requires Functions 5.3.10.1
- 5.3.10.3 Utility function (integrated). Planned: 2015/10/01 - 2016/03/31 Test ca
  of 5.3.10 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.10.1 and 5.3.10.2
- Responsible: andrew.davison@unic.cnrs-gif.fr



FDAT - Spike sorting (T5.3.11)

- 5.3.11.1 Spike sorting. Planned: 2014/07/01 - 2015/07/31 Test Ca
  sorting algorithm based on Neo compatible data and obtains results in a Neo data structure.
- 5.3.11.2 Spike sorting (integrated). Planned: 2015/07/01 - 2016/03/31 Test Ca
  5.3.11 are fully tested and integrated into the HBP Platform. Requires Functions 5.3.11.1
- Responsible: andrew.davison@unic.cnrs-gif.fr

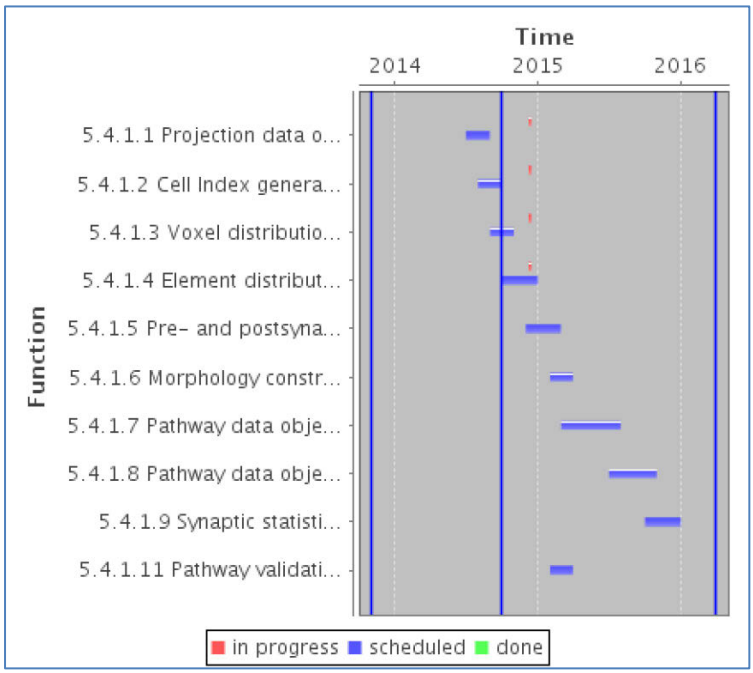


WP5.4 Predictive neuroinformatics

T5.4.1 Neuronal addressing system

Neuronal addressing system

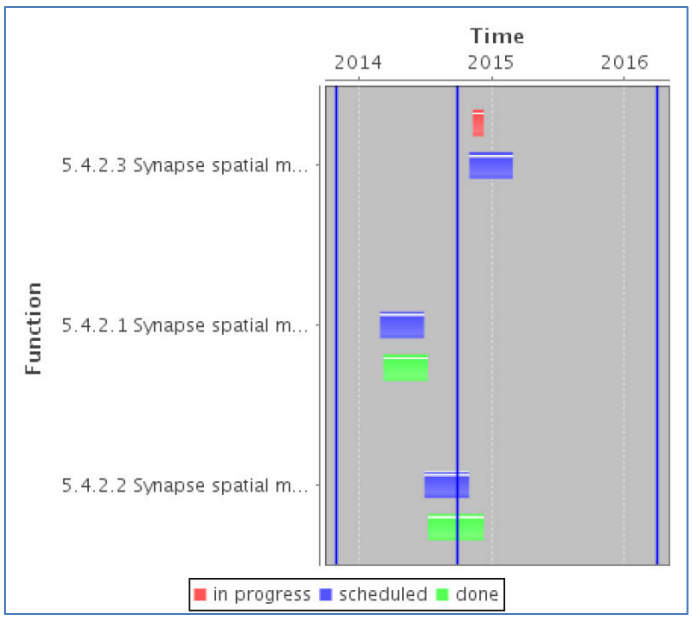
- 5.4.1.1 Projection data object interpreter. Planned: 2014/07/01 - 2014/08/31 Test c
  Successfully translation of Projection data object interpreter into internal Matlab data structure used by subsequent functions in the pipeline.
- 5.4.1.2 Cell Index generator. Planned: 2014/08/01 - 2014/09/30 Test Ca
  of number of cells specified by the Projection data object into internal Matlab data structure used by subsequent functions in the pipeline. Requires function 5.4.1.1
- 5.4.1.3 Voxel distribution generator. Planned: 2014/09/01 - 2014/10/31 Test C
  ingestion of voxelization of the postsynaptic brain area into internal Matlab data structure and indexed pre- or postsynaptic cells specified by the Cell index generator and subsequent generation of the probability of an pre- or post-synaptic element for each voxel. Requires functions 5.4.1.1 and 5.4.1.2
- 5.4.1.4 Element distributor. Planned: 2014/10/01 - 2014/12/31 Test Ca
  output of voxel distribution generator and the generation for each voxel of the realized post- or presynaptic element. Requires function 5.4.1.1, 5.4.1.2, and 5.4.1.3
- 5.4.1.5 Pre- and postsynaptic element pairing tool. Planned: 2014/12/01 - 2015/02/28 Test Ca
  Successful ingestion of pre- and postsynaptic elements generated by the element distributor and the generation of pairs of pre- and postsynaptic elements for all elements. Requires functions 5.4.1.1, 5.4.1.2, and 5.4.1.4
- 5.4.1.6 Morphology constructor. Planned: 2015/02/01 - 2015/03/31 Test C
  ingestion of pre- or postsynaptic elements generated by the element distributor (and prior generated elements); the generation of a morphology using these elements as seed points optimizing a weighted sum of wire length and path length. Requires Functions 5.4.1.1, 5.4.1.2, and 5.4.1.4
- 5.4.1.7 Pathway data object builder. Planned: 2015/03/01 - 2015/07/31 Test Ca
  ingestion of output of the pre- and postsynaptic element pairing tool and the Morphology constructor. Generation of the pathway, specified for each synapse, the identity of presynaptic cell and axon branch by which it is made and the identity of the postsynaptic cell and the dentritic branch on which it is made. Test Case B: Select a projection data object and turn it into a pathway data object. requires functions 5.4.1.1, 5.4.1.2, 5.4.1.5, and 5.4.1.6
- 5.4.1.8 Pathway data object inspector. Planned: 2015/07/01 - 2015/10/31 Test Ca
  ingestion of a pathway data object and extraction of components for other functions that validate or statistically characterize the pathway. Requires Function 5.4.1.7
- 5.4.1.9 Synaptic statistic module. Planned: 2015/10/01 - 2015/12/31 Test c
  ingestion of a Pathway data object and extraction of relevant components via Pathway data object inspector. Determination of the distribution of branch order for the pre- and postsynaptic elements. (Additional functionality will be added). Requires Functions 5.4.1.1, 5.4.1.7, and 5.4.1.8
- 5.4.1.10 Pathway object validator. Planned: 2015/12/01 - 2015/02/28 Test c
  ingestion of a projection data object and Pathway data object and extraction of relevant components via Pathway data object inspector and determination of their pertinent statistics via synaptic statistics module. Requires Functions 5.4.1.1, 5.4.1.7, and 5.4.1.9
- 5.4.1.11 Pathway validation data object builder. Planned: 2015/02/01 - 2015/03/31 Test ca
  Successful ingestion of the output of Pathway object validator and packaging of the outcome of statistical comparisons between desired and generated statistics for use in summary functions. Requires Functions 5.4.1.1, 5.4.1.7, and 5.4.1.10
- Responsible: p.tiesinga@science.ru.nl



T5.4.2 Neuronal structural design and predictions

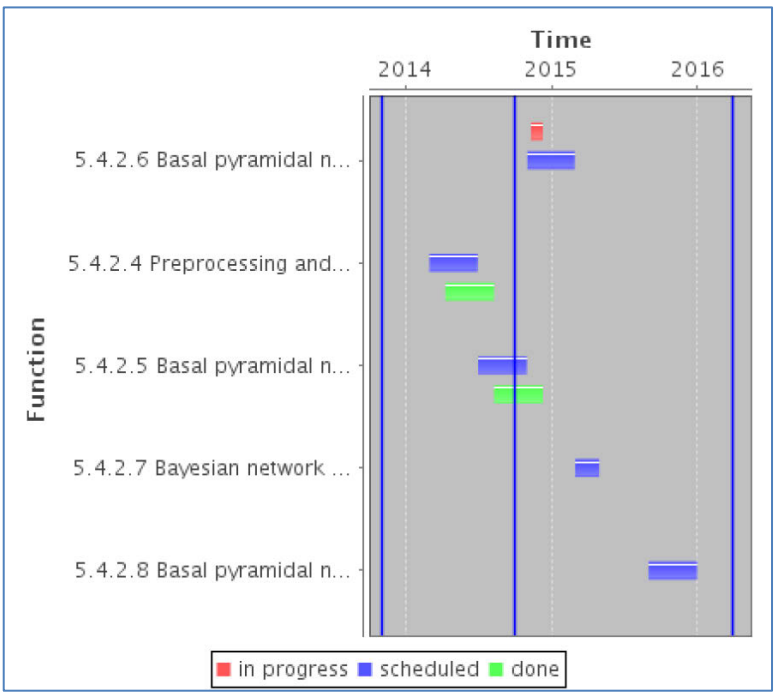
3DSynapsesSA

- 5.4.2.1 Synapse spatial model builder. Planned: 2014/03/01 - 2014/06/30 Test C analyses whether the pattern defined by synapses coordinates follows a complete spatial randomness (CSR) or a random sequential adsorption (RSA) process.
- 5.4.2.2 Synapse spatial model simulator. Planned: 2014/07/01 - 2014/10/31 Test ca runs 3D CSR or RSA processes simulations with the same characteristics of the synapses he is studying. Requires Function 5.4.2.1
- 5.4.2.3 Synapse spatial model and simulation plotter. Planned: 2014/11/01 - 2015/02/28 Test Case. A user compares the simulations with the real samples using statistical tests and graphically represents G,F, K, and L functions of simulation patterns and real samples. Requires Functions 5.4.2.1, 5.4.2.2
- Responsible: plarranaga@fi.upm.es



3DPyrStructure

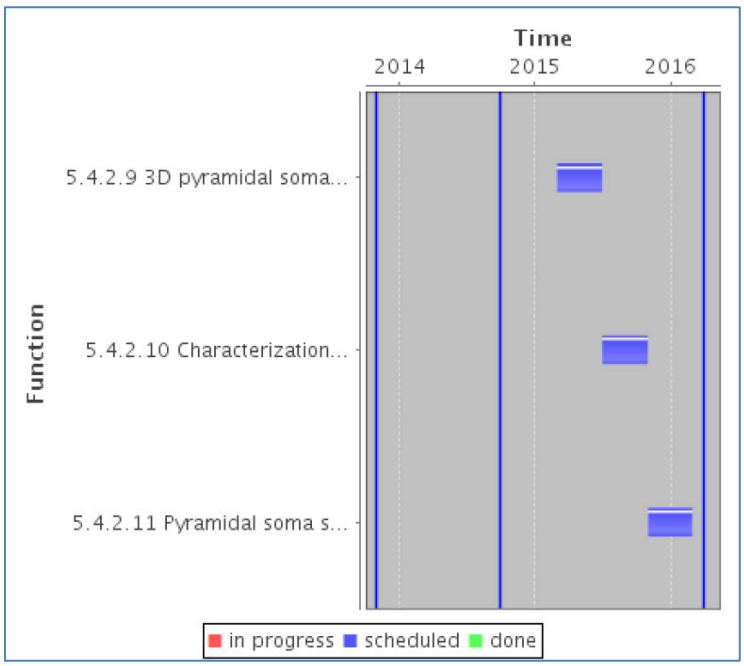
- 5.4.2.4 Preprocessing and exporting pyramidal neuron data. Planned: 2014/03/01 - 2014/06/30 Test Case: A user can perform basic checks in the data of pyramidal neurons and should change the Neurolucida format (.DAT) to R using the windows command prompt.
- 5.4.2.5 Basal pyramidal neuron feature extractor. Planned: 2014/07/01 - 2014/10/31 Test Ca
  A user selects the different features to be measured and this function returns their values. Requires Function 5.4 2.4
- 5.4.2.6 Basal pyramidal neuron univariate analyser. Planned: 2014/11/01 - 2015/02/28 Test Case: A user obtains with this function a univariate descriptive analysis of the morphological neuron measures. Requires Functions 5.4.2.4 and 5.4.2.5
- 5.4.2.7 Bayesian network builder of basal pyramidal neurons. Planned: 2015/03/01 - 2015/04/30 A uservobtains a bayesian network model as a multivariate graphical representation (directed acyclic graph) whose nodes represent the morphological variables and the arcs the conditional probabilistic dependencies among them. Requires Functions 5.4.2.4, 5.4.2.5, and 5.4.2.6
- 5.4.2.8 Basal pyramidal neuron Bayesian network reasoner. Planned: 2015/09/01 - 2015/12/31 Test Case: A user asks queries to the model, i.e. the probability of some variables given other variables fixed to some values (evidence). The user receives these probabilities in numerical and graphical formats attached to each node in the directed acyclic graph. Requires functions 5.4.2.4, 5.4.2.5, 5.4.2.6, and 5.4.2.7
- Responsible: plarranaga@fi.upm.es



3DSomaMS

- 5.4.2.9 3D pyramidal soma representation. Planned: 2015/03/01 - 2015/06/30 UTest C
  can repair, reconstruct and supervise a soma image for a correct pre-processing (cut of dendrites, filling holes, convex hull and smoothing). He then obtains a representation of the soma as a 3D polyhedron.
- 5.4.2.10 Characterization and typology of pyramidal somas. Planned: 2015/07/01 - 2015/10/31 Test Case: A user stores the soma morphological quantitative characteristics. Then he obtains an automatic typology of the soma shapes according to a cluster algorithm and individual somas within each group can be displayed. Requires Function 5.4.2.9

- 5.4.2.11 Pyramidal soma simulator. Planned: 2015/11/01 - 2016/02/28 Test Ca
  set the parameters for the optimization process, which transforms the simulated soma characteristics into a 3D soma image. Requires Functions 5.4.2.9, 5.4.2.10
- Responsible: plarranaga@fi.upm.es

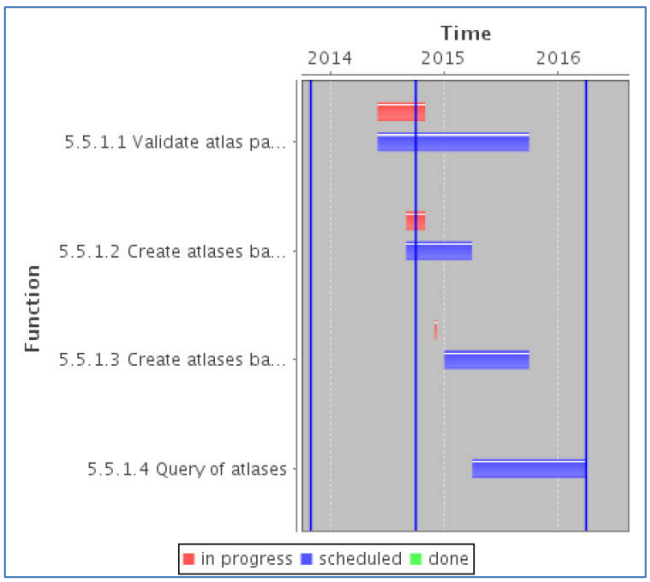


WP5.5 Brain atlases

T5.5.1 The Mouse Brain Atlas

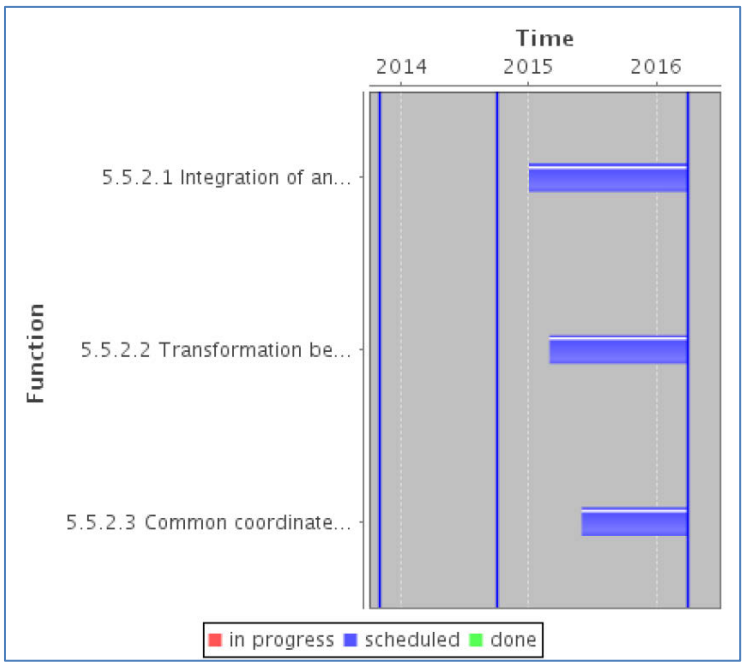
Mouse Brain Atlas

- 5.5.1.1 Validate atlas parcellations. Planned: 2014/06/01 - 2015/09/30
- 5.5.1.2 Create atlases based on normal histological material. Planned: 2014/09/01 - 2015/03/31
- 5.5.1.3 Create atlases based on diseased model histological material. Planned: 2015/01/01 - 2015/09/30
- 5.5.1.4 Query of atlases. Planned: 2015/04/01 - 2016/03/31
- Responsible: j.g.bjaalie@medisin.uio.no



Human Brain Atlas

- 5.5.2.1 Integration of annotated data. Planned: 2015/01/01 - 2016/03/31
- 5.5.2.2 Transformation between different references.... Planned: 2015/03/01 - 2016/03/31
- 5.5.2.3 Common coordinate space using standard mo.... Planned: 2015/06/01 - 2016/03/31
- Responsible: k.amunts@fz-juelich.de

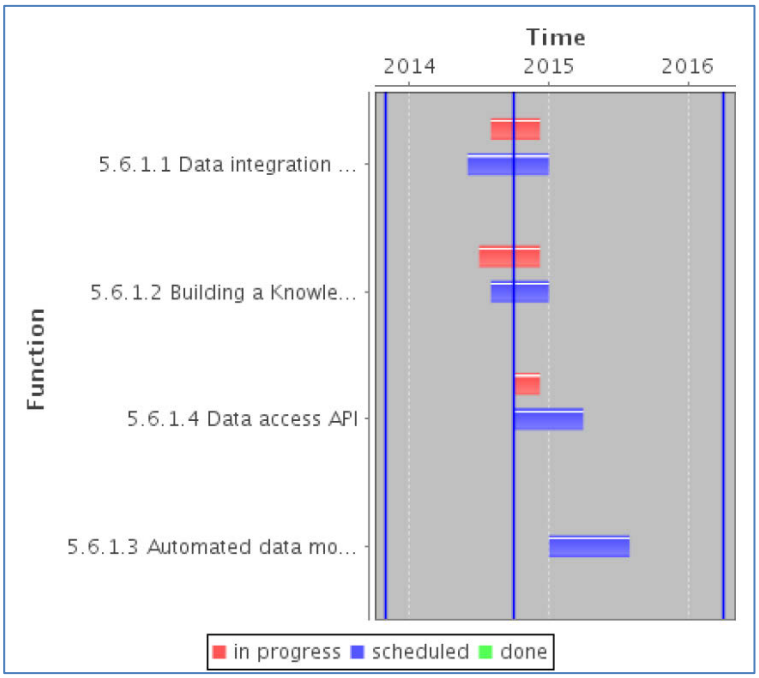


WP5.6 Neuroinformatics Platform: integration and operation

T5.6.1 Integration, website construction, maintenance & administration

Neuroinformatics Platform: Integration and operation

- 5.6.1.1 Data integration module. Planned: 2014/06/01 - 2014/12/31 Test C successfully stored in a database with links to the appropriate ontologies and links to the original raw data. Test Case B: data from a specific lab can successfully be retrieved via a database-querying tool. Requires function 5.1.4.1, shared Data Space (T5.1.1)
- 5.6.1.2 Building a Knowledge Graph. Planned: 2014/08/01 - 2014/12/31 Test Ca retrieve all linked information relevant to their query. Requires function 5.6.1.1
- 5.6.1.3 Automated data monitoring pipeline. Planned: 2015/01/01 - 2015/07/31 :Test Cas Data uploaded in the DataSpace are automatically integrated and made available for querying. Requires function 5.6.1.2, shared Data Space (T5.1.1)
- 5.6.1.4 Data access API. Planned: 2014/10/01 - 2015/03/31 A user and obtains the relevant data in the format of choice (e.g. JSON, csv files). Requires function 5.6.1.2, 5.6.1.3
- Responsible: catherine.zwahlen@epfl.ch



Annex D: Glossary

2D image	High-resolution bitmap image, currently supported formats: TIFF, JPEG, PNG; work in progress: Yokogawa CV1000, CZI. The list of the supported formats relies on OME Bio-Formats library.
3D data	Coming from a soma confocal microscopy image contains 3D points and the edges that join them (the faces). This data contains the 3D representation of the soma that is computed and statistically analysed to obtain the quantitative characterisation.
3D stack	A series of 2D consecutive images from a tissue sample or preparation obtained vie electron or light microscopy.
3D template package	A general 3D template package consists of an MRI template (NIfTI file), a delineations template (NIfTI file, produced from MRI template) and meshes (STL files, produced from delineations template).
AligNII	Browser-based anchoring tool.
Anchoring	The process of positioning (translate, rotate, scale) 2D images in 3D space defined by a 3D template package. Through region-by-region anchoring, several positions could be stored for each 2D image.
Annotations	Vector drawings (SVG) superimposed on 2D images.
Brain addressing system	Builds connectivity matrices. Neurons in the source area send out axons that terminate on the dendrites and soma of neurons in the target area. Each neuron has dendrites and an axon, both of which can be described in terms of a branching structure. An instantiated synaptic connection is characterised by the index of the sending neuron, the index of receiving neuron, the index of axonal branch of the sending neuron and index of the dendritic branch of the receiving neuron between which the synapse is made.
Brain atlas	A collection (usually a stack) of 2D images anchored to a 3D template package.
Complete spatial randomness (CSR)	AKA homogeneous Poisson process. 'Reference' or 'benchmark' model of a random point pattern.
Converter	A server-side process of creating pyramids, previews and thumbnails from 2D images.
Data file	A file that contains data common to electrophysiological recordings. This includes in particular, but is not limited to, spike time data, discretely sampled continuous signal data (such as LFP or measures of the stimulus), and trigger events. In the context of the Unifying Portal, data files represent an artefact.
Delineations	Boundaries of structures in the brain shown in the context of brain atlas space.
Dendritic basal arbour	The part of the neuron that includes the general features of the neuron observed from the apical dendrite, such as the layout of the basal dendritic trees and their features.
Dendritic & soma data	Contains properties of dendritic specification and quantitative characterisation of the soma.
F function	Cumulative distribution function of the empty space distance.
G function	Cumulative distribution function of the nearest-neighbour distance for a typical point in the pattern.
HDF5	A hierarchical file format designed to store numerical data.
Hybrid Bayesian network	A Bayesian network that combines continuous, discrete and in this case, also angular variables.

K function	Ripley's function, expected number of other points of the process within a distance r of a typical point of the process divided by the intensity.
L function	Commonly used transformation of K function making visual assessment of the graph much easier.
Local field potential (LFP)	The continuous low-pass filtered signal from an extracellular recording electrode (high cut of the filter typically in the range of 100-500 Hz).
Metadata	The data available and recorded, either in an automated fashion or by the user, before, during and after an experiment providing additional information relevant in interpreting and relating the electrophysiological and behavioural recordings.
Optimisation data	Contains the data corresponding to a 3D soma shape generated by simulation.
PAB	Metadata in the hierarchical form: Project -> Animal(s) -> Block(s).
Pathway data object	Contains an instantiation of a connection matrix.
Pathway validation data object	Contains the validation data of a pathway data object
Preview	A downscaled copy of 2D image.
Projection data object	Contains the statistics of the projection between two areas and can be accessed in the atlas by referring to the sending as well as receiving area.
Random sequential adsorption (RSA)	Spatial process where the pattern is constructed by placing spheres in three-dimensional space iteratively and randomly, with their radii following a probability density function. If any newly generated sphere intersects with an existing sphere, the new sphere is rejected and another sphere with a different centre and radius is generated. This process is stopped when the required number of spheres is reached.
Sample	The original tissue preparation from which a 3D stack is obtained.
Segmentation	A set of different segmented structures.
Segmented structure	A set of 3D voxels corresponding to a biological structure (either cell or sub-cell entities) annotated with its corresponding semantic information.
Soma	Represented by several morphological characteristics. Somas are described by a set of statistical distributions which represent their main properties as height, width, volume, etc.
Spatial point pattern	Realisation of a spatial point process.
Spatial point process	Mathematical model that describes the arrangement of objects irregularly or randomly distributed in space forming patterns.
Spike	The action potential of a neuron and its time point of the firing. Spikes are measured by an extracellular recording electrode in the vicinity of a neuron. Spikes are detected as a threshold crossing-event on the electrode signal that displays a typical spike waveform (to distinguish it from recording artefacts).
Spike sorting	The process of assigning labels to the individual spikes in an electrophysiological recording in order to group those spikes that are likely to have originated from a single neuron. Labels are assigned on the basis of the similarity of observed spike waveforms in the analogue signal.

Stereological counting frame/counting frame	Inclusive/exclusive boundaries of the 3D stack to be considered in the counting of segmented structures.
Synaptic apposition surface (SAS)	The surface between the active zone and the postsynaptic density representing the area of the synaptic junction.
Template	Data set specifying a brain atlas space, i.e., a 3-D coordinate system of the brain.

Annex E: References

[1] Amunts K, Lepage C, Borgeat L, Mohlberg H, Dickscheid T, Rousseau M-E, Bludau S, Bazin P-L, Lewis LB, Oros-Peusquens A-M, Shah NJ, Lippert T, Zilles K, Evans AC (2013). BigBrain: An ultrahigh-resolution 3D human brain model. *Science* 340 (6139): 1472-1475. DOI: 10.1126/science.1235381

[2] Amunts K, Lindner A, Zilles K (2014). The Human Brain Project: Neurowissenschaftliche Perspektiven und Beiträge aus Deutschland. *Neuroforum* 2/14: 222-229.

[3] Amunts K, Lindner A, Zilles K (2014). The human brain project: neuroscience perspectives and German contributions. *e-Neuroforum* 5: 43–50. DOI: 10.1007/s13295-014-0058-4

[4] Anton-Sanchez L, Bielza C, Merchan-Pérez A, Rodríguez JR, DeFelipe J, Larrañaga P (2014). Three-dimensional distribution of cortical synapses: a replicated point pattern-based analysis. *Frontiers in Neuroanatomy* 8 (85). DOI: 10.3389/fnana.2014.00085

[5] Bielza C, Benavides-Piccione R, Lopez-Cruz PL, Larrañaga P, DeFelipe J (2014). Branching angles of pyramidal cell dendrites follow common geometrical design principles in different cortical areas. *Scientific Reports* 4 (5909). DOI: 10.1038/srep05909

[6] Morales J, Benavides-Piccione R, Dar M, Fernaud I, Rodríguez A, Anton-Sanchez L, Larrañaga P, Bielza C, DeFelipe J, Yuste R (2014). Random positioning of dendritic spines in human cerebral cortex. *Journal of Neuroscience* 34 (30): 10078-10084. DOI: 10.1523/JNEUROSCI.1085-14.2014

[7] Papp EA, Leergaard TB, Calabrese E, Johnson GA, Bjaalie JG (2014). Waxholm Space atlas of the Sprague Dawley rat brain. *Neuroimage* 97, 374-386.