SP5 Neuroinformatics Platform - Results for SGA2 Year 1 (D5.8.1 – SGA2)

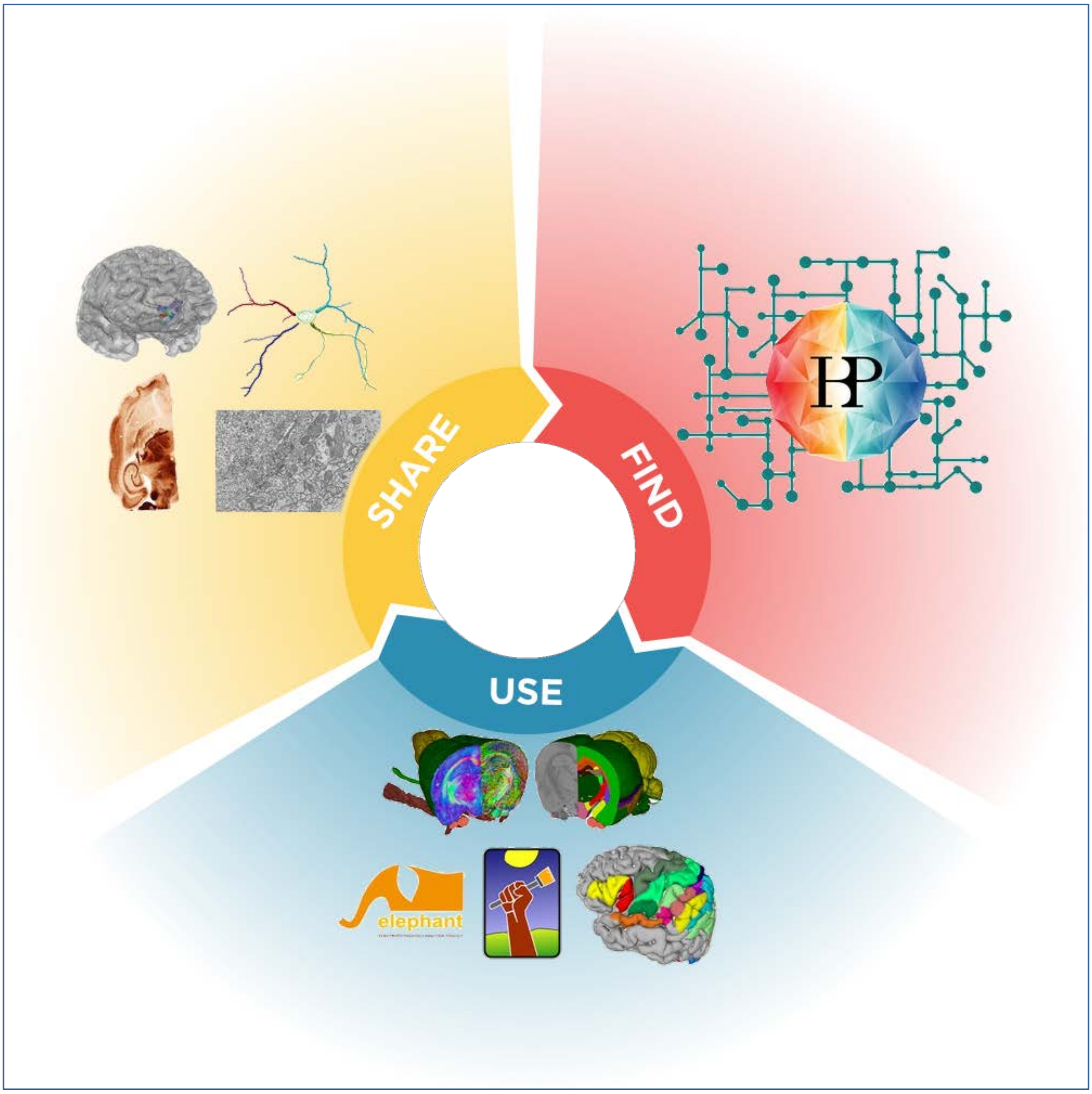

Figure 1: The corner pillars of the Neuroinformatics Platform

The Neuroinformatics Platform provides an infrastructure for neuroscientists who wish to collaboratively curate, analyse, share, and re-use large-scale neuroscience data, ultimately contributing to making research data Findable, Accessible, Interoperable and Reusable (FAIR). Go to https://www.humanbrainproject.eu/en/explore-the-brain/ to find out how you can contribute.

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Description in GA:	For consistent presentation of HBP results, SGA2 M12 Deliverables describing the accomplishments of an entire SP or CDP have been prepared according to a standard template, which focuses on Key Results and the outputs that contribute to them. Project management elements such as Milestones and Risks will be covered, as per normal practice, in the SGA2 Year 1 Report.
Abstract:	The Neuroinformatics Platform aims to ensure that the data needed to build brain models can be brought together, annotated, made accessible and prepared for analysis. The Platform includes an online Knowledge Graph with a search interface to make the data in HBP data storage discoverable and accessible. 3D brain atlases

	are provided as tools for navigation and exploration, and as entry points for finding and analysing data, based on location. Tools and workflows for analysis of structural and brain activity data are being developed and made available, together with the corresponding data. All data made available through the Platform are curated by a dedicated team and mapped into the HBP Knowledge Graph and the atlases. New versions of the atlases are released on a regular basis, together with workflows supporting feature extraction from images, based on atlas regions as well as deep analysis of activity data. Overall, the Platform makes solutions for sharing and advanced analysis of data available to the entire neuroscience community, creating new opportunities for collaborative data analysis, re-analysis of new combinations of data and reproducible science. The Neuroinformatics Platform also hosts the HBP High-Level Support Team, which delivers support to all HBP Platform users.
Keywords:	Data sharing; data curation; data management; reference atlas; rodent; human; spatial registration; image analysis; electrophysiology; neuronal activity; prediction; infrastructure; neuroinformatics
Target Users/Readers:	Scientists, Companies and other potential users of HBP results.

Table of Contents

1. Overview 6
2. Introduction 6
3. Key Result KR5.1 “A well-defined, well-documented and proven metadata curation approach which makes HBP data and models FAIR (Findable, Accessible, Interoperable, Re-usable) in a consistent and user-friendly way.” 8
3.1 Outputs 8
3.2 Validation and Impact 10
3.3 Components contributing to KR5.1 11
4. Key Result KR5.3 “Complete workflow going from heterogeneous experimental image data to extracted quantitative features defined in rodent atlas space, available for general use” 12
4.1 Outputs 12
4.2 Validation and Impact 14
4.3 Components contributing to KR5.3 16
5. Key Result KR5.4 “A well-defined, well-documented and proven approach for assigning spatial metadata to HBP data and models.” 16
5.1 Outputs 16
5.2 Validation and Impact 18
5.3 Components contributing to KR5.4 19
6. Key Result KR5.6 “Interactive exploration of function, connectivity, cytoarchitecture and receptor architecture at sub-laminar resolution in the Big Brain template space.” 20
6.1 Outputs 20
6.2 Validation and Impact 21
6.3 Components contributing to KR5.6 22
7. Key Result KR5.7 “Queries for structural parcellations, genetics, and activity for user-defined regions of interest” 22
7.1 Outputs 23
7.2 Validation and Impact 24
7.3 Components contributing to KR5.7 24
8. Key Result KR5.9 “A user-driven, data-sharing and data-management infrastructure accelerating scientific progress by providing access to large collections of curated, heterogeneous neuroscience data” 25
8.1 Outputs 25
8.2 Validation and Impact 27
8.3 Components contributing to KR5.9 28
9. Key Result KR5.11 “HBP-specific workflows developed to fully leverage the current state-of-the-art in computer vision with regards to object detection and segmentation problems. Active and transfer learning methods will be developed to lower the requirements to the necessary amount of training data.” 30
9.1 Outputs 30
9.2 Validation and Impact 31
9.3 Components contributing to KR5.11 32
10. Key Result KR5.12 “Comprehensive analysis toolbox to support analysis workflows for electrophysiological activity data from experiments and simulations, including support for HPC and visualisation capabilities” 33
10.1 Outputs 33
10.2 Validation and Impact 34
10.3 Components contributing to KR5.12 35
11. KR5.13 “The neural activity resource (NAR) as a central mechanism to register, annotate and browse activity data sets within the HBP” 36
11.1 Outputs 36
11.2 Validation and Impact 38
11.3 Components contributing to KR5.13 39
12. Key Result KR5.14 “HBP and non-HBP affiliated researchers using interoperable platforms” 39

12.1 Outputs 39
12.2 Validation and Impact 41
12.3 Components contributing to KR5.14 42
13. Conclusion and Outlook 44

Table of Tables

Table 1: Overview of Components with releases or major updates related to Key Result KR5.1....11
Table 2: Overview of Components with releases or major updates related to Key Result KR5.3....16
Table 3: Overview of Components with releases or major updates related to Key Result KR5.4....19
Table 4: Overview of Components with releases or major updates related to Key Result KR5.6....22
Table 5: Overview of Components with releases or major updates related to Key Result KR5.7....24
Table 6: Overview of Components with releases or major updates related to Key Result KR5.9....28
Table 7: Overview of Components with releases or major updates related to Key Result KR5.11....32
Table 8: Overview of Components with releases or major updates related to Key Result KR5.12....35
Table 9: Overview of Components with releases or major updates related to Key Result KR5.13....39
Table 10: Overview of Components with releases or major updates related to Key Result KR5.14....43

Table of Figures

Figure 1: The corner pillars of the Neuroinformatics Platform 1
Figure 2: Overview of the data curation process in the Human Brain Project 9
Figure 3: Analytical workflow for automated quantification and spatial analysis....13
Figure 4: Component Composition Predictor illustrations 14
Figure 5: Interactive atlas viewer....21
Figure 6: Neural Activity Visualiser 37
Figure 7: Embedding Neo Visualizer 37

1. Overview

The Neuroinformatics Platform aims to ensure that the data needed to build brain models can be brought together, annotated, made accessible and prepared for analysis. The Platform includes an online Knowledge Graph with a search interface to make the data in HBP data storage discoverable and accessible. 3D brain atlases are provided as tools for navigation and exploration, and as entry points for finding and analysing data, based on location. Tools and workflows for analysis of structural and brain activity data are being developed and made available, together with the corresponding data. These resources are accessible through the HBP public website https://www.humanbrainproject.eu/en/explore-the-brain/ and HBP Collaboratory https://collab.humanbrainproject.eu/#/collab/47.

Researchers outside the HBP can now use the Platform to share their data and annotate it online before uploading it to the Platform storage. All data made available through the Platform are curated by a dedicated team and mapped into the HBP Knowledge Graph and the atlases. New versions of the atlases are released on a regular basis, together with workflows supporting feature extraction from images, based on atlas regions as well as deep analysis of activity data. New releases of interactive atlas viewers, tools for spatial registration of data to the atlases, and activity data viewers have been provided.

Overall, the Platform makes solutions for sharing and advanced analysis of data available to the entire neuroscience community, creating new opportunities for collaborative data analysis, re-analysis of new combinations of data and reproducible science. The Neuroinformatics Platform also hosts the HBP High-Level Support Team, which delivers support to all HBP Platform users.

In the coming year, we will further improve Platform usability, make it more visible on the web and release more tutorials to help users to make the most of its features.

2. Introduction

The Neuroinformatics Platform provides the neuroscience community with a service for sharing research data and giving access to curated data for analysis and re-analysis in new combinations. The Platform delivers integrated, multi-level, data-enriched atlases of the human, mouse and rat brains, together with the tools and services required to spatially register datasets, navigate the atlases and perform queries. Access to the tools required for collaborative workflows to analyse and view structural data and activity data are provided through the HBP Collaboratory.

This document provides an overview of Key Results (KRs), including releases, prototypes, demonstrations, major updates, and impacts of tools and services delivered between April 2018 and March 2019, or soon thereafter. To avoid repetition, we have merged some of the KRs, as indicated below. KR5.8 (Tools to enable complete workflows from metadata annotation, data curation, and spatial integration in reference atlases to viewing of multi-level data) involves tools that are described under the various KRs they support.

- **KR5.1: Making HBP data and models FAIR** - Section 3
  - The Curation service develops routines for submission of data and models to the HBP data storage, with metadata available for search in the HBP Knowledge Graph. The **minimal metadata standards** required for making neuroscientific datasets and computational models discoverable have been updated with a modular design that allows users to express their metadata in a flexible and extensible graph structure. This new feature allows enrichment of method-specific metadata related to already published datasets. A new methods ontology, with significant coverage of terms, has been introduced, and a more efficient and consistent **process for curation and metadata management** (Curation Workflow 2.0) has been prepared for use from April 2019. A new **Knowledge Graph Editor**, to be released in April 2019, will allow data contributors to enter metadata through an online system in preparation for curation.

- **KR5.3: Workflow from image data to extracted features** – Section 4 (includes KR5.5: Prediction-based cell-type specific mesoconnectome)
    - o We released key software to enable a workflow going from heterogeneous experimental image data to extracted quantitative features, defined in rodent atlas space. The new workflow delivers **combined feature extraction and quantification from serial images in regions of interest defined by a 3D reference atlas**. The Connectomic Composition Predictor (CCP) tool, a Jupyter notebook tool available in the Collaboratory, has also been updated to provide **predictions for a cell-type specific mesoconnectome** at the region level.
- **KR5.4: Assigning spatial metadata to HBP data and models** – Section 5
    - o The HBP brain **reference atlases** have been updated. The Waxholm space atlas of the rat brain, downloaded more than 2,000 times per year, has benefitted from a new release with complete representation of auditory structures. A new version of a key tool for **2D image registration to 3D reference atlases** has also been released.
- **KR5.6: Interactive exploration of function, connectivity, cytoarchitecture and receptor architecture at sub-laminar resolution** - – Section 6
    - o Over the last few months, there has been a large increase in the number of users of the **HBP interactive atlas viewer**, the HBP's default tool for online browsing of 3D reference atlases. This tool hosts different reference templates and parcellations for the human, mouse and rat brains. The tool's new release supports mobile devices and has improved integration with other platform services. It is capable of showing spatial locations (such as intracerebral EEG contact points) and other spatial metadata available from the HBP Knowledge Graph.
- **KR5.7: Queries for structural parcellations, genetics, and activity for user-defined regions of interest** – Section 7
    - o The **JuGEx** (JuBrain Gene Expression), an integrated framework of the AllenBrain and JuBrain atlases for statistical analysis of differential gene expression relative to cytoarchitectonic brain areas in the adult human brain, has been updated. A first version of the **Gene Regulatory Network Explorer** that can be used to learn and visualise Bayesian networks (or other graph structures) is now available.
- **KR5.9: A user-driven, data-sharing and data-management infrastructure** - Section 8
    - o The **Collaboratory** is being re-engineered. The first of in total four planned releases features a new Collaboratory with an XWiki based user interface, fully public Collabs, and the possibility for collaborative editing of documents through OnlyOffice. Additionally, the **HBP Knowledge Graph** has been extended and the required tools for high-quality meta-data management has been released.
- **KR5.11: Workflows to leverage state-of-the-art computer vision to object detection and segmentation problems** – Section 9 (including KR5.10: Machine learning-based image analysis tools)
    - o The first version of a voxel segmentation workflow has been introduced in ilastik, the main tool for machine learning-based image analysis employed by the Neuroinformatics Platform. The new workflow will reduce the labelling effort for 3D segmentation. Progress has been made on running ilastik on HPC clusters and a prototype of a new back-end allowing our users to run pre-trained CNN-based classifiers directly from ilastik is in place.
- **KR5.12: Toolbox to support analysis workflows for electrophysiological activity data** – Section 10
    - o The Elephant tool for **analysis of activity data** has been updated with a novel method for analysing activity patterns in large-scale spike data.
- **KR5.13: The neural activity resource (NAR) to register, annotate and browse HBP activity data sets** – Section 11

- o A **new neural activity** has been implemented based on Neo, the package for representing electrophysiology data in Python, which allows reading a wide range of file formats. Metadata schemas for intracellular electrophysiology have been released through the Neuroshapes project and deployed within the HBP Knowledge Graph.

- **KR5.14: HBP and non-HBP affiliated researchers using interoperable platforms** (including KR5.2: A discoverability portal that links data and models to literature) – Section 12
  - o The **High-Level Support Team** has been launched and is now accessible via the main HBP website. The team specialized support in 10 areas, covering all platforms of HBP. **KnowledgeSpace** has been integrated into TrainingSpace, https://training.incf.org/, an online hub that provides links to courses, tools, and data, to provide another forum in which it can be discovered, and it provides training resources and links to tools that complement the data discoverable through KnowledgeSpace**. The Virtual Brain** has joined HBP and aims to implement a web-interface through the Neuroinformatics Platform. The Hybrid Virtual Brain C Code has been released and several tutorials have been made available.

3. Key Result KR5.1 "A well-defined, well-documented and proven metadata curation approach which makes HBP data and models FAIR (Findable, Accessible, Interoperable, Re-usable) in a consistent and user-friendly way."

The curation service develops the routines for submission of data and models to the HBP data storage, with metadata available for search in the HBP Knowledge Graph. It makes sure that high-quality data and computational models reach the neuroscience community. The HBP curation team develops the workflows, standards and curation routines to ensure that all data and computational models published through the Neuroinformatics Platform are Findable, Accessible, Interoperable and Reusable (FAIR). FAIR data enables Platform users to find, reuse and combine data in new ways to advance research and innovation.

3.1 Outputs

3.1.1 Overview of Outputs

- Output 1: Optimised data curation service:
  - o MINDS v 0.2.1 - Revised metadata schema with increased flexibility for tagging different types of neuroscience data. Released November 2018 (C2284, C2285).
  - o Curation Workflow 2.0 – Revised curation workflow to increase the efficiency of the curation process. Released February 2019 (C2241, C2284, C2522, C2523, C2285). Updated documentation, supporting material, and tutorials for data providers made available via the HBP Collaboratory. Released February 2019 (C2240, C2242, C2284).
- Output 2: Ontology development – Methods ontology. Released March 2019 (C2285).

3.1.2 Output 1: Optimised data curation service

MINDS v 0.2.1 – MINDS is the minimal metadata standard required for making neuroscientific datasets and computational models discoverable. It is a key step towards the goal of integrating multi-scale and multi-modal neuroscience data. The revised version of MINDS (released in November 2018) introduces a "modular design allowing users to express their metadata in a graph structure that is both flexible and extensible". The new feature allows "enrichment of method-specific metadata" to already published datasets. Through a collaboration with teams in the US BRAIN Initiative and the INCF's Neuroshapes, HBP MINDS contributes to creating a unified standard that will facilitate the global exchange of related data. MINDS is available as a metadata spreadsheet via the following link:

https://collab.humanbrainproject.eu/#/collab/7574/nav/57658?state=uuid%3D392c27a0-7464-4e4b-a23b-6dba46dcd9d5

Curation Workflow 2.0 – Version 2.0 of the curation workflow (released in February, 2019) builds on the version introduced in SGA1 and delivers a "*more efficient and consistent process for curation and metadata management*". It is delivered as a service to all data providers (Figure 2). The new workflow is divided into two distinct activities:

1) Curation support, now with a single entry point for all internal and external users curation-support@humanbrainproject (monitored via the new ticketing system provided by the High-Level Support Team, HLST, described under KR5.14 – Section 12), and
2) The curation process, delivering a systematic review before data and metadata are made discoverable through the HBP Knowledge Graph (described under KR5.9 – Section 8). Information about the new Curation Workflow is available via the following link: https://collab.humanbrainproject.eu/#/collab/7574/nav/281006

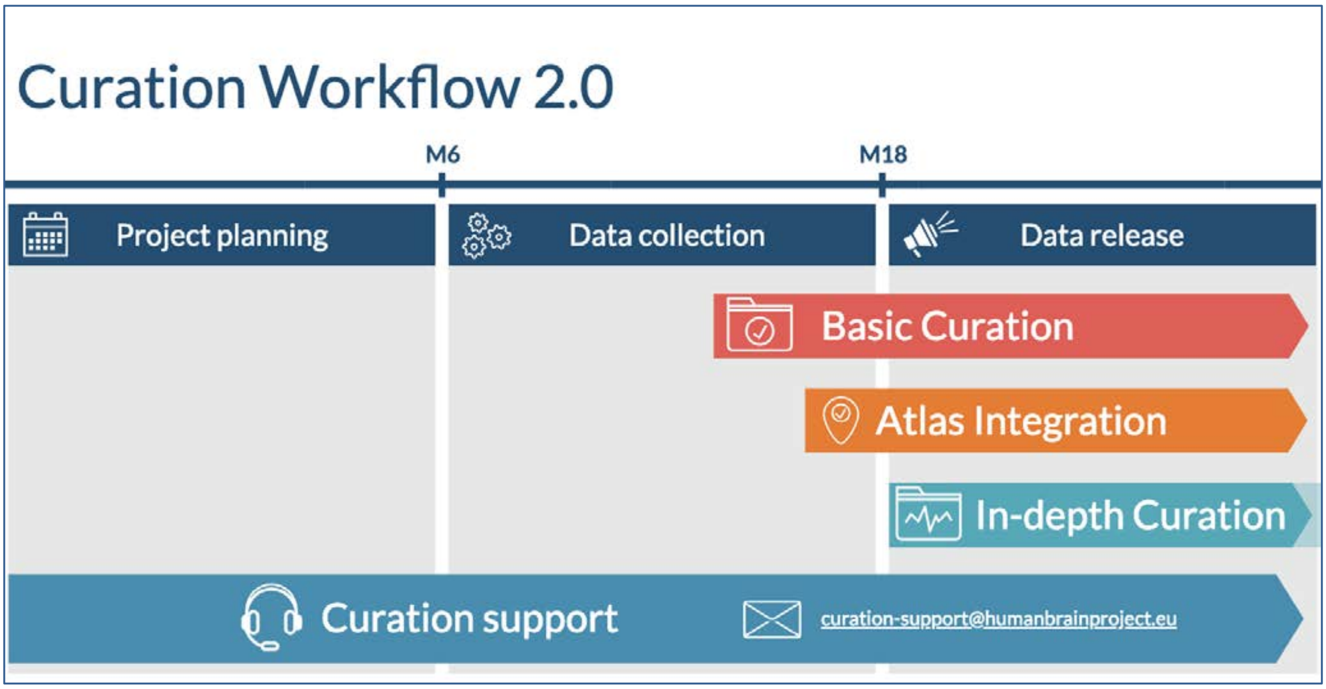

Figure 2: Overview of the data curation process in the Human Brain Project

Metadata are added and curated through a three-step process (basic curation, atlas curation, and in-depth activity data curation). With metadata searchable through the HBP Knowledge Graph, data organised and stored in HBP storage are made Findable, Accessible, Interoperable, and Re-usable (FAIR). A detailed report on the 175 datasets from SGA1 that have been published in the HBP Knowledge Graph is provided in the SGA2 Deliverable D5.1.1 (D28.1 D72) - Completion of SGA1 data/model curation into NIP meta data database.

3.1.3 Ouput 2: Ontology development

The standardisation of metadata builds on the use of ontologies. A new Methods ontology (released March, 2019) will be implemented in the HBP Knowledge Graph in April-May 2019. The Parcellation (brain structure names) has already been implemented in the HBP Knowledge Graph, to be reported in detail later, when more complete.

Ontology development is a continuously ongoing process, not typically expressed as "releases". The curation team has collaboratively developed a workflow for enriching existing ontologies according to HBP needs, with a primary focus on three ontologies, for which technical documentation is available via the following links:

- Methods ontology (https://github.com/SciCrunch/NIF-Ontology/tree/methods)
- Parcellation ontology (https://github.com/SciCrunch/NIF-Ontology/tree/parcellation)
- Neuron ontology (https://github.com/SciCrunch/NIF-Ontology/tree/neurons)

All three ontologies have significant coverage of the terms in their domain. Unified standards are achieved through integration into InterLex and the NIF-ontology, both products of the Neuroscience Information Framework which is involved in the ontology development for the US BRAIN Initiative. This integration makes it much simpler for domain experts to contribute new terms and update existing ones. InterLex enables the building of streamlined workflows for term look up, creation, and review. Importantly, integration will make it simpler for ontology developers to get resolvable identifiers for their ontology terms and make them visible to the larger community, while the long-term impact of the integration will give users the ability to maintain their own versions of terminologies without becoming disconnected from the rest of the community.

3.2 Validation and Impact

3.2.1 Actual Use of Output(s)

The new version of MINDS has been extensively tested and will be fully integrated into the online system for entering metadata, Knowledge Graph editor (see KR5.9, Section 8) by April 2019.

Curation Workflow 2.0 was highlighted in the HBP Newsletter (March 2019: https://mailchi.mp/d31687cc524a/hbp-newsletter-marchl-598477) and on Twitter https://twitter.com/hbpneuroinf. The single entry curation support ticketing system was released on 1 February 2019 and is operational. Curation Workflow 2.0 introduces a FAIR-ness index, to demonstrate that applying the new version of MINDS can lead to an increased FAIR-ness score for data.

The new ontologies have been integrated into the KnowledgeSpace ontology and are employed by the HBP Knowledge Graph and the HBP curation team.

3.2.2 Potential Use of Output(s)

The new version of MINDS will increase the quality of the datasets published in the HBP Knowledge Graph (see KR5.9 – Section 8).

Curation Workflow 2.0 will decrease the time spent on the curation process by curators and data providers.

The ontologies support the curation process and leads to a higher FAIR-ness score for data discoverable through the HBP Knowledge Graph.

The ontologies will be available in a public repository, so other initiatives/projects can use them. This will create a semantic link between HBP and other projects that could result in future integration of data/models.

3.2.3 Publications

- P1745: Lillehaug, S., Yetman, M.J., Puchades, M.A., Checinska, M.M., Kleven, H., Jankowsky, J.L., Bjaalie, J.G. & Leergaard, T.B. (2019) Brain-wide distribution of reporter expression in five transgenic tetracycline-transactivator mouse lines. *Scientific Data*, **6**, 190028. doi: 10.1038/sdata.2019.28

- o Demonstration of proof of concept, first data publication with data curated by HBP curation team and DOIs assigned by the HBP Knowledge Graph (Output 1).

3.2.4 Measures to Increase Impact of Output(s): disseminations

A set of short, intuitive infographics was developed to explain key steps of the HBP data curation service: https://collab.humanbrainproject.eu/#/collab/7574/nav/281006 (Output 1). In addition, a two day introductory course on ontology engineering was co-organised with INCF in January 2019 (https://www.med.uio.no/imb/english/research/networks/neuroinformatics/courses/ontology.html; Output 2)

The HBP curation services will be presented at several neuroscience conferences worldwide, as well as in HBP Newsletters and on Twitter (https://twitter.com/hbpneuroinf). A recent presentation for the International Brain Initiative (Shanghai, March 2019) confirmed community interest in the approach developed by the HBP (Outputs 1 and 2).

3.3 Components contributing to KR5.1

Table 1: Overview of Components with releases or major updates related to Key Result KR5.1

ID	Component Name	Type	Contact	Info on releases and major updates
C2240	Tutorials, training and supervision in assignment of spatial metadata	service	Trygve LEERGAARD (UIO)	Release March 2019: Updated data integration guide https://collab.humanbrainproject.eu/#/collab/7574/nav/57656
C2241	Validation and approval of semantic and image-derived spatial metadata assigned to experimental rodent brain data before final entry in Knowledge Graph	service	Trygve LEERGAARD (UIO)	Release Feb 2019: Curation Workflow 2.0 https://collab.humanbrainproject.eu/#/collab/7574/nav/281006
C2242	Optimised procedures for anchoring of 2D and 3D image data to reference atlas	service	Trygve LEERGAARD (UIO)	Release Feb 2019: Curation Workflow 2.0 https://collab.humanbrainproject.eu/#/collab/7574/nav/329069
C2284	Metadata used to enrich SGA2 data and models	service	Krister ANDERSSON (UIO)	Release Feb 2019: Curation Workflow 2.0 https://collab.humanbrainproject.eu/#/collab/7574/nav/281006
C2285	Ontology for data/model discoverability annotation	dataset	Mathew ABRAMS (KI)	Release March 2019: Methods ontology https://github.com/SciCrunch/NIF-Ontology/tree/methods Neuron ontology https://github.com/SciCrunch/NIF-Ontology/tree/neurons Parcellation ontology https://github.com/SciCrunch/NIF-Ontology/tree/parcellation
C2522	Support for data upload and download	service	Jan BJAALIE (UIO)	Release Feb 2019: Curation Workflow 2.0

				https://collab.humanbrainproject.eu/#/collab/7574/nav/281006 User support: curation-support@humanbrainproject
C2523	Support for data transfer	service	Jan BJAALIE (UIO)	Release Feb 2019: Curation Workflow 2.0 https://collab.humanbrainproject.eu/#/collab/7574/nav/281006 User support: curation-support@humanbrainproject

4. Key Result KR5.3 "Complete workflow going from heterogeneous experimental image data to extracted quantitative features defined in rodent atlas space, available for general use"

Microscopic studies of different brain cells, their axonal connections, and expression of proteins and signalling molecules, is fundamental to many basic neuroscience studies of healthy, ageing, and pathological brains. The capacity to efficiently and accurately enumerate and compare different cellular parameters in specific anatomical regions between different groups of mouse or rat models is relevant for efforts to study brain architecture, development of computational models and evaluation of potentially therapeutic interventions. To map, model and understand the vastly complex brain, and conduct statistically powerful experimental analyses of animal models of brain disease more efficiently, it is necessary to collect and share data from entire brains and also ensure that measurements are reproducible and comparable. To this end, the HBP has developed analytical workflows for automated quantification and spatial analysis of labelling in large series of section images from rodent brains, and methods for predicting neural connectivity based on sparse tract tracing and gene expression data.

4.1 Outputs

4.1.1 Overview of Outputs

- Output 1: Tools and procedures for extracting cellular and neural features from high-resolution rodent brain images. Released November 2018 and March 2019 (C3074)
- Output 2: Connectomic Composition Predictor v 2.0. Released March 2019 (C935)

4.1.2 Output 1: Tools and procedures for extracting cellular neural features from high resolution rodent brain images

To extract and quantify different types of morphological features visualised in serial 2D images with variable signal strength and quality, several tools were combined to create a new analytical workflow for automated quantification and spatial analysis of microscopic labelling in serial section images from rodent brains (Figure 3).

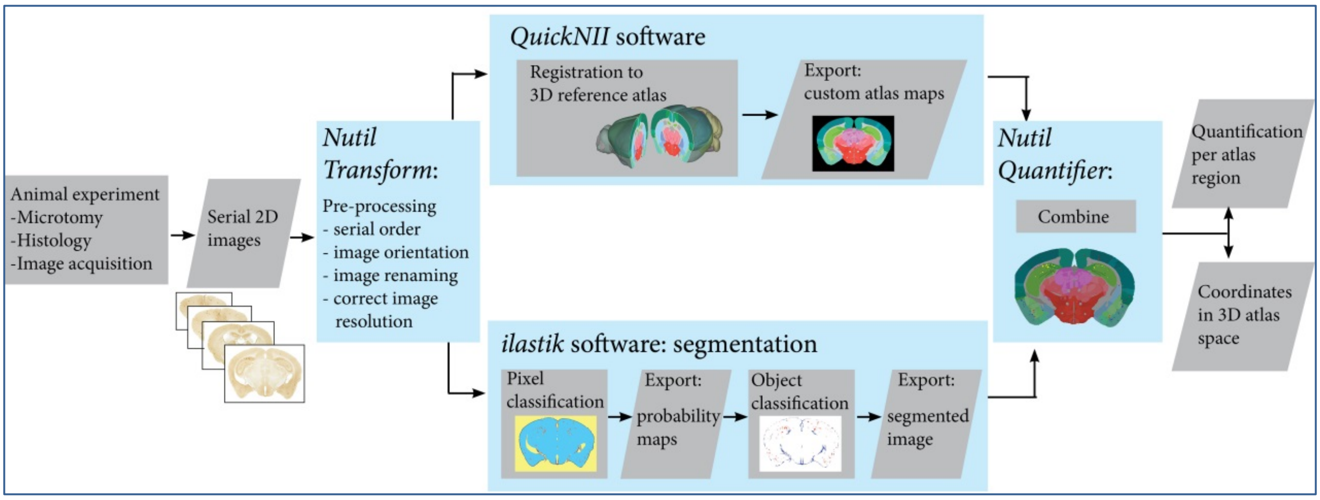

Figure 3: Analytical workflow for automated quantification and spatial analysis

The new workflow combines: 1. Registration of 2D images to 3D atlases with the *QuickNII* tool, which generates custom atlas maps defining anatomical regions of interest in each section; 2. Advanced automated image segmentation using the machine learning tool *ilastik,* which is based on Random Forest Algorithm for supervised classification. Finally, the segmented images are analysed on a whole brain and at the regional level, using the registered brain atlas maps in the *Nutil* software. Thereby, whole brain features and region level features such as number of and area occupied by objects are derived, enabling quantitative regional analysis as a semi-automatic pipeline.

The QuickNII tool (see KR5.4, Section 5) is used to spatially register serial 2D images cut in any plane of orientation to a 3D reference atlas. The tool has been extensively evaluated at several international test sites.

The ilastik tool (see KR5.11, Section 9), is adapted for segmentation of high-resolution 2D images and has been successfully tested on a range of histological mouse brain image data, including immunolabeled neurons and anterograde tract-tracing data.

The Neuroscience Data Utility Toolkit, Nutil v0.30 (http://www.nesys.uio.no/nutil/) is used for region-wise object counting and extraction of spatial coordinates from segmented microscopic images. Nutil was developed and extensively tested on a range of serial 2D images. Successful results were achieved for region-wise quantification of amyloid plaque load in immunostained serial sections from transgenic Alzheimer's disease mouse models, counting of immunolabeled amyloid plaques across entire mouse brains.

In addition, an alternative workflow was developed for rapid evaluation of spatial locations and semi-quantitative recording of features that are difficult to extract using image analysis. This workflow also employs custom atlas plates generated using QuickNII, but is based on the annotation feature of the LocaliZoom tool, in combination with 3D visualisation using the MeshView viewer (https://collab.humanbrainproject.eu/#/collab/5401/nav/42067) (released in November 2018). The MeshView tool (released in March 2019) is made available through NITRC.org, where new feature implementations and updates will be available.

Guidelines for use of the above analytic approaches, combinations of tools for feature extraction and quantitative analysis are in preparation and will be released via the HBP Collaboratory pages. A preliminary version is available here:

- https://collab.humanbrainproject.eu/#/collab/5401/nav/42303

and here for use of the Nutil software:

- https://collab.humanbrainproject.eu/#/collab/9129/nav/69017.

To next make the extracted feature data available for general use, we will utilize MINDS (see KR5.1, Section 3) to develop a metadata schema suited for making derived data elements available via the HBP Knowledge Graph.

Currently, no other tools combine feature extraction and quantification from serial images in regions of interest defined by a 3D reference atlas. Several steps of the workflow can be automated and will allow efficient and unbiased analysis of large amounts of histological data.

4.1.3 Output 2: Connectomic Composition Predictor

The Connectomic Composition Predictor (CCP) tool is a Jupyter notebook tool that delivers a predicted mesoconnectome, based on tract tracing data from the Allen Institute. Version 2.0 of the tool, released in March 2019 (https://collab.humanbrainproject.eu/#/collab/8650/nav/299443), has been updated to (1) provide predictions for the cell-type specific mesoconnectome at the region level, which is (2) extrapolated for visualisation purposes to a volumetric representation. The predictions are validated by a number of measures, including box plots indicating precision, recall and F-score. The actual predictions are compared to the data in the form of images of coronal slices and cortical flat maps (see examples in Figure 4). The current state of the art is the prediction of binary connectivity for an older version of the Allen Brain Atlas using wild-type mouse data (e.g. Ji *et al*,, 2014[1]). Here, we go beyond the state of the art by making non-binary predictions of the connection strength, using the latest version of the Common Coordinate Framework (CCF 3.0), which includes cortical layers, and including the results from cre mouse lines to make the predictions cell-type specific. Next, we will develop a more spatially-resolved volumetric prediction augmented with inferred relevant genes, derived from single-cell RNA sequences, that will allow high-resolution mesoconnectome predictions. For this, we will use techniques used by other researchers in this area (e.g. Li *et al*., 2017[2]), who are mining gene expression data.

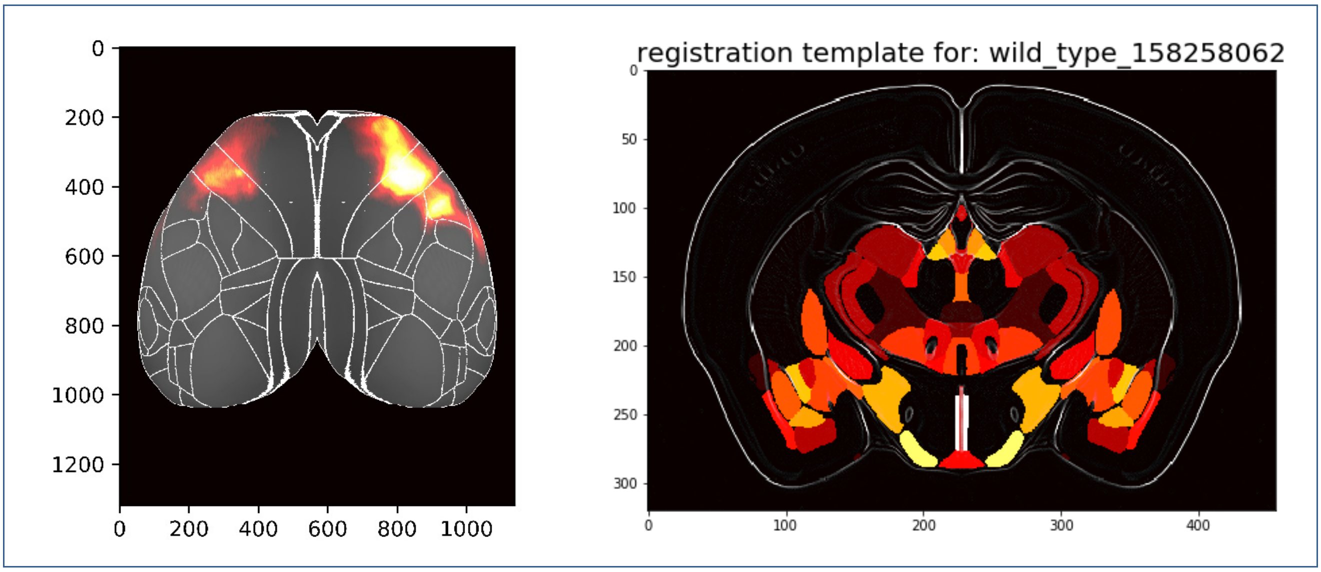

Figure 4: Component Composition Predictor illustrations

Left: Illustration of the flatmap representation produced by CCP (adapted from allensdk Python module provided by the Allen Institute). The 3D labelled volume of cortical areas in a tracer experiment is projected in 2D, with borders between cortical areas indicated by the white lines. Right: Example coronal section produced by CCP representing predictions for the regionalised connectivity, the colour code reflects the strength of the connectivity to that particular cortical area.

4.2 Validation and Impact

[1] Ji, S., Fakhry, A. & Deng, H. (2014) Integrative analysis of the connectivity and gene expression atlases in the mouse brain. *Neuroimage*, **84**, 245-253. doi: 10.1016/j.neuroimage.2013.08.049

[2] Li Y, Chen H, Jiang X, Li X, Lv J, Peng H, Tsien JZ, Liu T. (2017). Discover mouse gene coexpression landscapes using dictionary learning and sparse coding. Brain Struct Funct 222:4253-4270.

4.2.1 Actual Use of Output(s)

Since the above reported releases are new, a broader user community has not yet coalesced. Examples of use so far include:

- Quantification of amyloid plaque load in transgenic Alzheimer's disease mice with the analytical workflow (in collaboration with the JPND project CrossSeeds), article submitted. We have contact with interested test sites and have worked extensively with a research group at the Jackson Laboratory, Maine, USA.
- Mapping of neural network changes in conditional transgenic mouse lines, in which cortical arealization development has been experimentally manipulated (project collaboration, Michele Studer, University of Nice, France), in progress.
- Investigation of topographical organisation in mouse subcortical pathways, in progress.
- Mapping of the brain-wide distribution of somatostatin expressing interneurons in mice (project collaboration, Menno P. Witter, Norwegian University of Science and Technology), in progress.

4.2.2 Potential Use of Output(s)

The feature-extracting workflow has attracted considerable interest when presented at conferences. It is generally useful for neuroscientists who need to quantify labelled objects in serial microscopic sections. The workflow will be employed to analyse images registered in the HBP research infrastructure and generate derived data which is useful for validating, tuning and expanding computational models of brain function.

The connectomic composition predictor will be useful for students and neuroscientists who want to understand mouse brain mesoscopic connectivity, computational neuroscientists who want to incorporate whole brain connectivity patterns in their simulations, and translational neuroscientists who want to link gene expression patterns to distortions in connectivity. For the release of CCP version 2.0, we included three use cases that illustrate the potential use of the output.

4.2.3 Publications

A manuscript documenting the concept and practical use of the analytical workflow combining ilastik – QuickNII – Nutil tools has been submitted and is currently being reviewed (Output 1).

4.2.4 Measures to Increase Impact of Output(s): disseminations

The feature extracting workflows and accompanying tools (Output 1), as well as the Connectomic Composition Predictor (Output 2), have been disseminated mainly through open Collabs (see Section 4.1.2), conferences and courses. We plan to participate in the Neuroinformatics congress (August 2019), Nordic Neuroscience meeting (September 2019), and the Society for Neuroscience annual meeting (October 2019).

The analytical workflow (Output 1) was demonstrated in a course for PhD students at University of Oslo in 2018: IMB9345 - Neuroscience data integration through use of digital brain atlases. Iterations of this course are planned for 2019, including:

- University of Oslo PhD Course (IMB9345), 17-18 June (https://www.uio.no/studier/emner/medisin/med/IMB9345)
- One-day course at the INCF 2019 conference, 31 August, Warsaw, Poland

- The CAJAL advanced training programme, whole brain imaging, 9-13 September, Bordeaux, France (https://www.fens.org/Training/CAJAL-programme/CAJAL-courses-2019/WBI-2019/).

4.3 Components contributing to KR5.3

Table 2: Overview of Components with releases or major updates related to Key Result KR5.3

ID	Component Name	Type	Contact	Info on releases and major updates
C935	Connectomic composition predictor (rodent)	software	Paul TIESINGA (SKU)	Release March 2019: Connectomics composition predictor (CCP) 2.0 https://collab.humanbrainproject.eu/#/collab/8650/nav/299443
C3074	Nutil software for brain atlasing workflows: pre- and post-processing of microscopic image data	software	Jan BJAALIE (UIO)	Release March 2019: version 0.30 http://www.nesys.uio.no/nutil

5. Key Result KR5.4 “A well-defined, well-documented and proven approach for assigning spatial metadata to HBP data and models.”

One key goal of the HBP’s Neuroinformatics Platform is to organise a large part of the neuroscientific data it hosts by their location relative to atlases of the mouse, rodent and human brains, thereby providing a topographically organised information system. To achieve this goal, curation of new datasets has to address the structured preparation of their metadata (Tier 1 curation), and also specifically assign a proper definition of their location in the brain (Tier 2 curation). Such location assignment can be based on the level of brain regions, relative to a reference parcellation, or in terms of spatial coordinates, relative to a reference coordinate space. This Key Result establishes the standards and methods to assign such location information to data. The resulting tools will be used in the Curation Workflow, but are also be accessible to external users of the HBP research infrastructure.

5.1 Outputs

5.1.1 Overview of Outputs

- Output 1: Updated and improved brain atlases
    - Updated human brain atlas with new core datasets included. Released March 2019 (C773, C2264)
    - Updated and improved Waxholm Space reference atlas of the rat brain, accepted for publication March 2019, projected release April-May 2019 (C2169)
- Output 2: Optimised tools and procedures for registration of brain-image data to reference atlases. Released: December 2018, projected release: May 2019 (C2242, C2244, C2265, C2277, 2371)

5.1.2 Output 1: Updated and improved brain atlases

The rodent and human atlases provide the framework for topological organization of neuroscientific data. They consist of several reference template and parcellations that can be accessed via the HBP Knowledge Graph or interactively explored in the HBP atlas viewer. The HBP curation teams continuously link datasets in the HBP Knowledge Graph to brain regions and coordinates of reference templates (Atlas curation), so more and more data can be explored relative to these atlases. The human and rodent anatomical atlases used by HBP have been improved and expanded.

Several core datasets that constitute the Human Brain Atlas have undergone metadata curation and are now searchable and available for download through the HBP Knowledge Graph in their recent version of March 2019. This includes the different volumetric, coronal, axial and sagittal serial sections of the Big Brain microscopic brain model[3] (Amunts *et al*. 2013), and an updated version of the JuBrain probabilistic cytoarchitectonic atlas with new individual probabilistic maps (C2264). Both the Big Brain and the cytoarchitectonic atlas are integrated in the HBP Atlas Viewer described in KR5.6, Section 6.

The Waxholm Space atlas of the rat brain v.3, with complete coverage of the auditory system, has been completed and documented in an article preliminary accepted for publication (Osen *et al*., Neuroimage)[4]. The new atlas version is, as of March 2019, temporarily available in a private Collab (https://collab.humanbrainproject.eu/#/collab/9126/nav/69000) before it is transferred to its public location at https://www.nitrc.org/projects/whs-sd-atlas in May 2019. Contact curation-support@humanbrainproject for access to the private Collab.

5.1.3 Output 2: Optimised tools and procedures for registration of brain image data to reference atlases

It is not always possible to assign anatomical location in an automated way to different types of data. . Therefore, we are developing interactive tools to assign locations in the HBP atlases to 1D, 2D and 3D datasets. These tools are used in the Curation Workflow, but are also made available to neuroscientists inside and outside the Project to help them put their data into an anatomical context.

QuickNII is a tool for 2D image registration to a 3D reference atlas. After its first release in SGA1, it was extensively tested internationally (see Actual Use of Outputs, Section 5.2.1). Based on user feedback, basic image manipulation functions have been added. QuickNII v2.1 (C2277) was released in December 2018, together with updated user documentation (RRID: SCR_016854/ https://www.nitrc.org/projects/quicknii). A manuscript presenting the tool is currently in revision, and video tutorials and further dissemination efforts are in preparation. Work is now in progress to make the tool more user friendly and interoperable with other tools, with a next release planned for March 2020.

The non-linear warping tool for optimising the spatial registration of 2D image data to a custom atlas reference image generated with QuickNII (developed during SGA1) will be further developed as an extension of the QuickNII tool (in progress, release planned for March 2020). By adding a non-linear registration step after QuickNII registration, the coordinates of the 2D images and derived objects of interest will increase in precision.

The volumetric spatial alignment tool landmark-reg (C2371), developed during SGA1 to map 3D images to a 3D reference atlas, has been re-implemented to fully embed the volumetric atlas viewer NeHuBa (C2265). This new version is more intuitive to use and responds to user feedback that we collected in hands-on workshops in 2017 and 2018. Besides entering corresponding landmarks, it

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[3] Amunts, K., et al. (2013). BigBrain: An Ultrahigh-Resolution 3D Human Brain Model. Science, 340 (1639), pp 1472-1475. DOI: 10.1126/science.1235381

[4] Osen et al. Waxholm Space atlas of the rat brain auditory system: Three-dimensional delineations based on magnetic resonance and diffusion tensor imaging

allows direct adjustment of position, orientation and scale of an incoming image to a high-resolution template using an interactive drag and drop feature in a superimposed view. This is particularly efficient for producing a first, coarse alignment before refining with landmarks. This major update of the software is an important step towards a significantly more unified viewer architecture, since it shares a software component with the interactive atlas viewer, thus reducing the codebase and facilitating compatibility of data formats. A beta release of the new implementation of landmark-reg is planned for May 2019 and will be described in more detail in SGA2 Deliverable D5.3.1 (D30.1, D74)) “New Release of interactive spatial alignment tool”.

5.2 Validation and Impact

5.2.1 Actual Use of Output(s)

The Waxholm Space atlas of the rat brain is widely used, with more than 5,000 downloads since it was introduced at NITRC.org in May 2017 and 5,500 downloads from its previous host, the INCF Software Center.

The QuickNII tool is being evaluated at several test sites around the world, including the Korea Brain Research Institute (Korea), Jackson Laboratory (USA) and the Macquarie University (Australia). So far, 64 users have been trained in registration of serial images to murine atlases using QuickNII, 19 of these during SGA2. QuickNII has been used to map image data from 126 rodent specimens (31 data sets) to atlas space.

The new implementation of landmark-reg expected to be released in May 2019, having been validated and employed by several internal users to perform different Atlas Curation tasks with volumetric datasets generated from Polarised Light Imaging (PLI) and light microscopy.

5.2.2 Potential Use of Output(s)

The tools and workflow for mapping image data to reference atlas will be relevant for a wide range of neuroscientists who have a need to assign and analyse anatomical location in their data.

While QuickNII is a core tool for Tier 2 curation of section image data from rodent brain, landmark-reg will become a core tool for Tier 2 curation of volumetric human data, in particular for the task of integrating high-resolution multimodal volumes of interest to the Big Brain reference space. We expect it to be used frequently by curation teams, starting in the second half of 2019.

5.2.3 Publications

- P1530: Bjerke, I.E., Ovsthus, M., Andersson, K.A., Blixhavn, C.H., Kleven, H., Yates, S.C., Puchades, M.A., Bjaalie, J.G. & Leergaard, T.B. (2018) Navigating the Murine Brain: Toward Best Practices for Determining and Documenting Neuroanatomical Locations in Experimental Studies. *Front Neuroanat*, **12**, 82. DOI: 10.3389/fnana.2018.00082.
    - o Recommendations for improved assignment of anatomical location with use of HBP tools and workflows (C2244; Output 2).

5.2.4 Measures to Increase Impact of Output(s): disseminations

The HBP tools and workflows will be described in several manuscripts which are in preparation. In addition, the atlases and the tools will be promoted at several conferences (Nordic Neuroscience meeting 2019, Neuroinformatics 2019 and Society for Neuroscience Annual Meeting 2019). The use of the tools for registration of data to the reference atlases will be taught at several workshops, including:

- PhD Course (IMB9345), 17-18 June, University of Oslo, Norway (https://www.uio.no/studier/emner/medisin/med/IMB9345),
- A one day course in connection with INCF 2019 conference, 31 August, Warsaw, Poland, and
- The CAJAL advanced training programme, whole brain imaging, 9-13 September, Bordeaux, France (https://www.fens.org/Training/CAJAL-programme/CAJAL-courses-2019/WBI-2019/).

We have also proposed an educational course addressing the HBP Human Brain Atlas at the Organisation for Human Brain Mapping (OHBM) Conference 2019 in Rome, which would include the use of this tool.

5.3 Components contributing to KR5.4

Table 3: Overview of Components with releases or major updates related to Key Result KR5.4

ID	Component Name	Type	Contact	Info on releases and major updates
C773	SP2 - Selected multimodal regional maps with cognitive features	Research	Simon EICKHOFF (JULEICH)	Release Oct 2018: Selected multimodal regional maps with cognitive features https://www.humanbrainproject.eu/en/explore-the-brain/search/?q=Selected%20multimodal%20regional%20maps%20with%20cognitive%20features&facet_type[0]=Project#Project/86b122d4358357d834a87ce618a55de0
C2169	Expanded and improved Waxholm Space rat brain reference atlas (with additional and corrected structure delineations) based on co-registered multimodal data	dataset	Trygve LEERGAARD (UIO)	Internal Release April 2018: Waxholm Space atlas of the rat brain v.3 (Private Collab) https://collab.humanbrainproject.eu/#/collab/9126/nav/69000 (contact curation-support@humanbrainproject.eu for access). The new atlas will be moved to https://www.nitrc.org/projects/whs-sd-atlas in May 2019.
C2242	Optimised procedures for anchoring of 2D and 3D image data to reference atlas	service	Trygve LEERGAARD (UIO)	Release Feb 2019: Curation Workflow 2.0, released: February 2019: https://collab.humanbrainproject.eu/#/collab/7574/nav/329069)
C2244	Best practice recommendations for assignment of anatomical location to experimental rodent brain data	report	Trygve LEERGAARD (UIO)	Nov 2018: Publication: Bjerke et al (2018). Navigating the murine brain: Towards best practices for determining and documenting neuroanatomical locations in experimental studies. Frontiers in Neuroanatomy, 12:82, 2018. https://doi.org/10.3389/fnana.2018.00082
C2264	Curation of new cytoarchitectonic mappings into human atlas	service	Timo DICKSCHEID (JUELICH)	Release May 2019: Whole Human Brain Cytoarchitectonic and Maximum Probability Maps https://www.humanbrainproject.eu/en/explore-the-

				brain/search/?facet_type[0]=Dataset#Project/a684eceee76fc522773286a895bc8436
C2265	Support for visual landmarks in 3D atlas viewer	software	Timo DICKSCHEID (JUELICH)	Release Oct 2018: NeHuBa https://neuroglancer.humanbrainproject.eu
C2277	QuickNII software (v3.0) with updated functionality	software	Jan BJAALIE (UIO)	Release Dec 2018: QuickNII v 2.1 (RRID: SCR_016854) https://www.nitrc.org/projects/quicknii
C2371	Web-based multi-resolution three-planar viewer for large image volumes	software	Timo DICKSCHEID (JUELICH)	Release Oct 2018: NeHuBa https://neuroglancer.humanbrainproject.eu

6. Key Result KR5.6 "Interactive exploration of function, connectivity, cytoarchitecture and receptor architecture at sub-laminar resolution in the Big Brain template space."

A unique aspect of HBP's multilevel Brain Atlas is that it describes brain anatomy at different spatial resolutions, going from the millimetre to the micrometre scale, and provides access to regional characterisations of brain structure, function and connectivity. A particularly challenging problem is the integration of different data modalities at the level of different cortical layers, which are only resolved at the resolution of tens to few hundreds of micrometres. To date, there is no framework available that would allow interactive exploration of brain anatomy at this level. This Key Result addresses this problem, aiming to provide explorative access to microscopic resolution multimodal data through visual interaction with the high-resolution Big Brain template.

6.1 Outputs

6.1.1 Overview of Outputs

- Output 1: HBP Interactive Atlas Viewer Release, October 2018 (C2265, C2371, C2802)

6.1.2 Output 1: HBP Interactive Atlas Viewer

The Interactive Atlas Viewer (https://jubrain.humanbrainproject.eu) is the HBP's default tool for online browsing of reference atlases in 3D, and currently hosts different reference templates and parcellations for the mouse, rodent and human brains.

It has received four incremental releases during the last year. This iterative release pattern allows major features to be developed, tested and implemented, without disrupting the continuous rollout of smaller improvements to the UI and in performance. Over this period, we improved the integration of the Viewer with other Platform services by fetching and displaying metadata directly from the HBP Knowledge Graph, and improved the overall usability by new features, including novel previews for region-specific multimodal data and display of 3D landmarks. The viewer is now capable of showing spatial locations, such as sEEG contact points that are accessed through the spatial search service. We optimised the overall codebase, reduced the average loading time by a factor of 2, and improved the overall responsiveness of the application. Finally, the Atlas Viewer now supports recent Android mobile devices, and can be used on many phones and tablet devices.

Figure 5: Interactive atlas viewer

The HBP interactive atlas viewer is now available on Android devices

6.2 Validation and Impact

6.2.1 Actual Use of Output(s)

The HBP Interactive Atlas Viewer attracted a significant number of users between 1 April, 2018 and 18 February 2019.

- Total number of page leaves to neuroglancer viewer from anywhere on the public web page: 6,997
- Total number of page leaves to neuroglancer viewer from /en/explore-the-brain/atlases: 3,799 (Bigbrain: 2128, Jubrain; 833, Waxholm: 504, AMBA: 334)
- Total number of page leaves to neuroglancer viewer from /en/explore-the-brain/: 2,835 (Bigbrain: 1,854, Jubrain: 523, Waxholm: 286, AMBA: 172)
- User number of page leaves to neuroglancer viewer from the HBP Knowledge Graph search: 244

6.2.2 Potential Use of Output(s)

The HBP Interactive Atlas Viewer has the potential to become an entry point to multilevel brain data, allowing navigation through available data, based on their location in terms of brain regions and spatial coordinates. The spectrum of potential users ranges from education and training to searches for data in the context of specific research questions.

6.2.3 Publications

None

6.2.4 Measures to Increase Impact of Output(s): disseminations

The HBP Human Brain Atlas and associated tools were presented by Timo Dickscheid at the annual meeting of the Organization for Human Brain Mapping (OHBM) in June 2018, in Singapore (~2,000 attendees), as well as during the HBP School "The HBP Human Brain Atlas: Neuroscientific basis, tools and applications", which was organized in Jülich/Maastricht/Düsseldorf on 3-7 September 2018.

We will continue to teach the use of the Interactive Atlas Viewer in conferences and workshops, including the 2019 CAJAL course on whole brain imaging (https://www.fens.org/Training/CAJAL-programme/CAJAL-courses-2019/WBI-2019/) in Bordeaux. We have submitted a proposal for an educational course on the HBP Human Brain Atlas at the Organization for Human Brain Mapping (OHBM) Conference 2019 in Rome, which would include the use of this tool.

As mobile devices are becoming the computing device of choice for millions, we continue to work on the mobile readiness of the Interactive Atlas Viewer. We have largely enabled use on android devices and are now directing our focus to IOS devices that currently do not support the required standard WebGL2. Once Apple adds support for WebGL2 to its mobile devices, we will release the Atlas Viewer for this platform.

6.3 Components contributing to KR5.6

Table 4: Overview of Components with releases or major updates related to Key Result KR5.6

ID	Component Name	Type	Contact	Info on releases and major updates
C2265	Support for visual landmarks in 3D atlas viewer	software	Timo DICKSCHEID (JUELICH)	Release Oct 2018: NeHuBa https://neuroglancer.humanbrainproject.eu
C2371	Web-based multi-resolution three-planar viewer for large image volumes	software	Timo DICKSCHEID (JUELICH)	Release Oct 2018: NeHuBa https://neuroglancer.humanbrainproject.eu
C2802	Adoption of 3D atlas viewer to a unified viewer architecture	software	Timo DICKSCHEID (JUELICH)	Expected release Summer 2019. This component has been described in detail in SGA2 Deliverable D5.4.1 (D31.1, D75)

7. Key Result KR5.7 "Queries for structural parcellations, genetics, and activity for user-defined regions of interest"

Some data modalities, like local recordings of brain function over time or expression of genes in different parts of the brain, cannot be adequately explored by superimposing their images with a reference. Instead, they often require very specific analytical tools that would make it possible, for example, to understand whether their signals in different regions of the brain differ significantly or not. This Key Result implements software interfaces that allow a first set of such specific analysis tools to be connected to brain atlases. This allows users to explore and select brain regions in the atlas and, from there, to smoothly access the appropriate tool to inspect such specific data modalities.

7.1 Outputs

7.1.1 Overview of Outputs

- Output 1: HiBOP - HBP atlas viewer software interface. Described in SGA2 Deliverable D2.7.3 (D14.3, D120)
- Output 2: JuGEx - HBP atlas services integration (C2802). Described in SGA2 Deliverables D2.7.1 (D14.1, D16) and D5.4.1 (D31.1, D75). Planned release: Summer 2019.
- Output 3: Gene Regulatory Network Explorer. Initial release: January 2019 (C2380)

7.1.2 Output 1: HiBOP - HBP atlas viewer software interface

HiBOP is an expert desktop application designed to display, process and analyse iEEG recording data in anatomical context. Developers of the HiBOP software for expert analysis of iEEG data (LYON) worked extensively with those of the HBP Atlas Viewer (JUELICH) on a first proof-of-principle implementation of a software interface between the two systems, which allows a direct transition from HiBOP to the Interactive Atlas Viewer. Their work is further detailed in the CDP3 Deliverable D2.7.3 (D14.3, D120).

7.1.3 Output 2: JuGEx - HBP atlas services integration

JuGEx (JuBrain Gene Expression) is an integrated framework for the AllenBrain and JuBrain atlases, allowing statistical analysis of differential gene expression, relative to cytoarchitectonic brain areas in the adult human brain.[5] It was originally released as a Matlab software[6]. We have continued ton integrate JuGEx with the HBP atlas services. It has been rewritten as a RESTful backend service on the Neuroinformatics Platform, with an interactive plugin for the Interactive Atlas Viewer as a user interface (C2802). For more information, see SGA2 Deliverables D2.7.1 (D14.1, D16) and D5.4.1 (D31.1, D75).

7.1.4 Output 3: Gene Regulatory Network Explorer

A first version of the Gene Regulatory Network Explorer (C2380) was made available in January 2019 (https://neurosuites.com/morpho/ml_bayesian_networks). The Gene Regulatory Network Explorer can be used to learn and visualise Bayesian networks or other graph structures. It includes some tools to make it easier to visualise big graphs, with thousands of nodes, by exploring the neighbourhoods of any nodes of interest.

In this version, users can learn the structure and parameters of Bayesian Networks without the need to download any software. They are also able to visualise bigger networks than with any other Bayesian network visualiser, thanks to the use of GPU acceleration. Our version of the Fast Greedy Equivalence Search, which can be accessed through the link above, beats the state of the art in

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[5] Sebastian Bludau, Thomas W. Mühleisen, Simon B. Eickhoff, Michael J. Hawrylycz, Sven Cichon, Katrin Amunts (2018) Integration of transcriptomic and cytoarchitectonic data implicates a role for *MAOA* and *TAC1* in the limbic-cortical network. *Brain Structure and Function.* DOI:10.1007/s00429-018-1620-6

[6] http://www.fz-juelich.de/SharedDocs/Downloads/INM/INM-1/DE/jugex.html;jsessionid=6D74AC7447670FD861F86B87E326D3EF?nn=2163780

speed to learn the structure of very big Bayesian networks (>10K nodes) with competitive accuracies. We will be releasing more functionality throughout the coming year and expect the fully functional Gene Regulatory Network Explorer to be released in February 2020.

7.2 Validation and Impact

7.2.1 Actual Use of Output(s)

The Gene Regulatory Network Explorer is currently used internally by the Computational Intelligence Group at Universidad Politécnica de Madrid to validate algorithms for learning gene regulatory networks, by comparing structure in examples with known real structures, and as a quick way for testing various algorithms for learning Bayesian networks on available data.

7.2.2 Potential Use of Output(s)

The Gene Regulatory Network Explorer provides a graphical interface for common algorithms to learn Bayesian networks and visualise graphs, making it well-suited for non-experts to rapidly learn and explore rough Maximum Likelihood models. The main use we are building towards is doing differential analysis of multiple networks learnt under different experimental conditions, to explore how gene regulation changes depending on those conditions.

7.2.3 Publications

- P1740: Bielza, C., Larrañaga, P., (2019). Data-Driven Computational Neuroscience. Cambridge University Press
    - Book pending publication related to the Gene Regulatory Network explorer (Output 3).

7.2.4 Measures to Increase Impact of Output(s): disseminations

Concha Bielza participated in a panel discussion at the 9th International Conference on Probabilistic Graphical Models in Prague in September 2018 (http://pgm2018.utia.cz/?id=16) where she discussed the use of Probabilistic Graphical Models in neuroscience, including the use of Bayesian networks for the study of Gene Regulation (Output 3).

The Gene Regulatory Network Explorer was further presented at a poster session at the 3rd HBP Student Conference in Ghent, 2019 (Bernaola, N., Bielza, C., Larrañaga P., "Using Bayesian Networks to learn Gene Regulatory Networks").

7.3 Components contributing to KR5.7

Table 5: Overview of Components with releases or major updates related to Key Result KR5.7

ID	Component Name	Type	Contact	Info on releases and major updates
C2380	Regulatory networks explorer	software	Bojan MIHALJEVIC (UPM)	Release Feb 2020: Gene Regulatory Network Explorer https://neurosuites.com/morpho/ml_bayesian_networks

C2802	Adoption of 3D atlas viewer to a unified viewer architecture	software	Timo DICKSCHEID (JUELICH)	Expected release Summer 2019. This component has been described in detail in SGA2 Deliverable D5.4.1 (D31.1, D75)

8. Key Result KR5.9 “A user-driven, data-sharing and data-management infrastructure accelerating scientific progress by providing access to large collections of curated, heterogeneous neuroscience data”

The HBP has developed the basic building blocks of a data-sharing and data-management infrastructure. A Knowledge Graph (KG) Editor allows data providers to submit their data/meta-data to the HBP curation team. Once validated, the data becomes publicly searchable via the KG Search (UI/API) and can be referenced via a provided DOI. The goal is for the HBP Knowledge Graph to become the “go-to” reference for neuroscience FAIR datasets. The infrastructure also offers optimised access to large image datasets stored centrally in the HBP research infrastructure and referenced by the HBP Knowledge Graph, to avoid having to download GB/TB-sized images for interactive browsing.

The HBP Collaboratory offers protected workspaces for teams to develop reproducible workflows, and potentially share their work publicly. It is also a more general solution for collaborative edition of documentation (rich text, wiki or MS Office-type documents) and a user-friendly file repository. The research infrastructure provides cloud computing for the reproducible workflows.

8.1 Outputs

8.1.1 Overview of Outputs

- Output 1: HBP Knowledge Graph v2.2 and various integrated tools. Released in March 2019 (C1469, C1474, C1477, C2239, C2619, C2822).
- Output 2: Collaboratory - Coordination release, March 2019 (C372, C373, C374, C540, C532, C2482, C2617).
- Output 3: Container Orchestration PaaS. Released in December 2018 (C1489).
- Output 4: Atlasing Foundation. Release of requirements document and proof of concept based on Distributed, Versioned, Image-oriented Dataservice (DVID), March 2019 (C1461).

8.1.2 Output 1: HBP Knowledge Graph

The **HBP Knowledge Graph**, available at https://kg.humanbrainproject.eu, is a meta-data management solution, consisting of various tools to enable its users to collaboratively annotate data. It is fed with metadata from the Curation Workflow (KR5.1, Section 3) through the Knowledge Graph Editor. The HBP Knowledge Graph focuses on the support of highly dynamic and community-driven metadata annotation processes. Because of its permissive editing policies, combined with automated reflection mechanisms, the system encourages the iterative development of annotation standards.

Knowledge Graph v2.2 (C2822) was released in March 2019 and includes the KG Service, Spatial Search, KG Editor and KG Search UI releases.

KG Service (C1474) provides mechanisms to manage and query linked meta-data. Its APIs are used by external clients (e.g. via KG Python API – C1477), as well as by the other Knowledge Graph tools.

Spatial Search (C2239) has been integrated into KG Service as part of the latest release of the HBP Knowledge Graph. It ensures that spatially anchored information registered into the HBP Knowledge Graph is also properly indexed in the Spatial Search engine. Spatial Search is used as a backend service of the HBP Knowledge Graph and allows the location of spatially anchored datasets within specific brain volumes. It provides the infrastructure for indexing and querying references based on coordinates and 3-dimensional geometries.

After the successful initial integration into the HBP Knowledge Graph, further work will involve increasing the search precision, performance optimisation, addition of more complex filter geometries, etc.

KG Editor (formerly known as the "Data Workbench" – C1469) is the editor and meta-data management tool of the HBP Knowledge Graph. Besides the possibility to add, edit and remove meta-data directly in the HBP Knowledge Graph, it also provides advanced data management capabilities such as reconciliation of different data sources, support for ontologies, visualisation of dependencies and role-based review and publication mechanisms.

To meet the requirements of the curation pipeline workflows, and to validate the usability of the solution, the HBP curation teams were involved throughout the development process.

The **KG Search UI** (C2619) provides a public search interface for the published (meta) data. Originally released in SGA1, this Component has since been improved in terms of UI/UX, responsiveness and performance.

8.1.3 Output 2: Collaboratory

The Collaboratory is an extendable collaborative platform which brings the independent collections of software and services provided by the HBP into a cohesive and productive ecosystem for scientific projects.

The Collaboratory is being re-engineered to replace homemade features with standard open-source solutions. Spread over four distinct releases during 2019, this new version will gain in maturity as users' feedback is incorporated.

The user interface and core engine (C540) are replaced with XWiki, an extensible wiki platform that brings full-text search and versioning: https://wiki.humanbrainproject.eu.

The Collaboratory Storage (C373, C532 & C2617) becomes Collaboratory Drive and is now based on Seafile, a state-of-the-art document repository: https://drive.humanbrainproject.eu.

The HBP Identity Service (C374) based on MITREid Connect is replaced by KeyCloak, an OpenID Connect and SAML compatible authentication and authorisation service.

The Document App (C2617) based on Etherpad is replaced by OnlyOffice, a collaborative document editing solution, compatible with Microsoft Office documents: https://office.humanbrainproject.eu.

Contact support@humanbrainproject.eu for user access and support.

8.1.4 Output 3: Container Orchestration PaaS

The Container Orchestration PaaS (C1489) provides a self-service container platform as a service, based on the OpenShift Kubernetes distribution, deployed on top of the Pollux OpenStack platform hosted at CSCS. It was released on a production platform in December 2018: https://openshift.hbp.eu/.

This platform integrates with the Collaboratory identity service, providing access for all accredited HBP members to an easy-to-use container environment. The platform is also closely integrated with the HBP GitLab instance to provide a way to implement continuous integration pipelines and workflows. The tight integration with the Collaboratory will allow HBP members to deploy and publish their applications in the Software Catalogue.

8.1.5 Output 4: Atlasing Foundation

An image service is being developed to give access to high-resolution 3D images of brain atlases. The images are stored in the form of pre-processed image chunks in HBP central storage to optimize delivery of an optimized subset of the image at one of the selectable resolutions upon request by a viewer (typically running in a user's browser) or by an analysis tool.

Requirements (C1461) for a REST API delivering rich URL-indexed image, voxel, time series and geometric data have been collected from the client apps within HBP, i.e. viewers and data analytic applications. The requirements have been released in a public collab for the image service https://collab.humanbrainproject.eu/#/collab/48122/nav/331995

A proof-of-concept has been built based on DVID (Distributed, Versioned, Image-oriented Dataservice) developed at the Janelia Research Campus. Sample code using the PoC is available in the same collab: https://collab.humanbrainproject.eu/#/collab/48122/nav/330283 . Performance issues are being assessed.

8.2 Validation and Impact

8.2.1 Actual Use of Output(s)

The **HBP Knowledge Graph,** with its Search UI, allows anyone, inside the HBP or outside it, to explore data and models created inside and outside the HBP and download published data. Other Knowledge Graph tools are for more specialised use. Users of the **KG Service,** including the **Spatial Search,** are developers of other systems making use of the APIs of the system, whereas the **KG Editor** until now has mainly been used in the Curation Workflow (KR5.1, Section 3) for metadata registration and publication.

The **Collaboratory** is currently used by multiple stakeholders: coordinators manage their projects through collabs, scientists use its notebooks to run jobs and analysis, students participate in MOOCs through the Collaboratory, researchers publish collabs as interactive papers. Currently, 900 HBP users and 3,000 external users are registered.

The Container Orchestration PaaS is used by HBP developers to test and deploy applications in self-service mode.

8.2.2 Potential Use of Output(s)

We plan to increase continually the size of the **HBP Knowledge Graph** user groups. For instance, the **KG Editor** was extended and will now be available directly to data producers as well. The Knowledge Graph's various components and the overall data management system can be applied in various places within the HBP (e.g. reuse of spatial search, integration of model catalogue, etc.)

The **Collaboratory's** aim is to be a science-agnostic, Open Science platform with an extensible architecture focused on integrating powerful open-source solutions. It has the potential to be used by other Open Science projects.

The **Container Orchestration PaaS** will help HBP accredited users to reduce the engineering costs of application deployments by managing common pain points: SSL certificate creation, auto-scaling, self-healing mechanism, monitoring.

8.2.3 Publications

- P1745: Lillehaug, S., Yetman, M.J., Puchades, M.A., Checinska, M.M., Kleven, H., Jankowsky, J.L., Bjaalie, J.G. & Leergaard, T.B. (2019) Brain-wide distribution of reporter expression in five transgenic tetracycline-transactivator mouse lines. *Scientific Data*, **6**, 190028. doi: 10.1038/sdata.2019.28
  - o Demonstration of proof of concept, first data publication with data curated by HBP curation team and DOIs assigned by the HBP Knowledge Graph (Output 1).

8.2.4 Measures to Increase Impact of Output(s): disseminations

The HBP Knowledge Graph (Output 1) and Collaboratory (Output 2) provide the backbone of the data sharing and data management infrastructure of the Neuroinformatics Platform. As such, they are showcased at all conferences and events where the Neuroinformatics Platform is presented. The main events of the past year were ICT 2018 (December 2018, Vienna), the Society for Neuroscience meeting (September 2018, San Diego) and the Bernstein Conference (September 2018, Berlin). Other dissemination channels are through Twitter (https://twitter.com/hbpneuroinf) and HBP Newsletters (https://www.humanbrainproject.eu/en/follow-hbp/newsletter).

In order to increase the impact of the HBP Knowledge Graph and the data shared, we apply search engine optimisations and promote discoverability by external systems (e.g. https://developers.google.com/search/docs/data-types/dataset). Plans also involve an active use of Twitter when new datasets are released.

8.3 Components contributing to KR5.9

Table 6: Overview of Components with releases or major updates related to Key Result KR5.9

ID	Component Name	Type	Contact	Info on releases and major updates
C373	Collaboratory Storage Service	service	Allan FRANCANI (EPFL)	Release March 2019: Coordination release https://drive.humanbrainproject.eu User documentation: https://manual.seafile.com/develop/web_api_v2.1.html User access and support: support@humanbrainproject.eu
C374	HBP Identity Service	service	Allan FRANCANI (EPFL)	Release March 2019: Coordination release https://iam.humanbrainproject.eu User documentation: https://www.keycloak.org/documentation.html User access and support: support@humanbrainproject.eu
C532	Collaboratory Storage UI	service	Allan FRANCANI (EPFL)	Release March 2019: Coordination release https://drive.humanbrainproject.eu User documentation: https://manual.seafile.com/ User access and support: support@humanbrainproject.eu

C540	Collaboratory Web UI	service	Allan FRANCANI (EPFL)	Release March 2019: Coordination release https://wiki.humanbrainproject.eu User documentation: https://www.xwiki.org/xwiki/bin/view/Documentation/ User access and support: support@humanbrainproject.eu
C1461	Large-Scale Image Service	service	Marc MORGAN	Release March 2019: Proof of Concept https://collab.humanbrainproject.eu/#/collab/48122/nav/330275
C1469	Knowledge Graph Editor	service	Oliver SCHMID (EPFL)	Release March 2019: v2.2 https://kg.humanbrainproject.eu/editor
C1474	Knowledge Graph Service	service	Oliver SCHMID (EPFL)	Release March 2019: v2.2 https://kg.humanbrainproject.eu
C1477	Knowledge Graph Python API	service	Oliver SCHMID (EPFL)	Release March 2019: v2.2 https://kg.humanbrainproject.eu
C1489	HBP Standard Deployment service	service	Fabrice GAILLARD (EPFL)	Release Dec 2018: M09 https://openshift.hbp.eu User documentation: https://collab.humanbrainproject.eu/#/collab/38996
C2239	Advanced Spatial Data Exploration	service	Anastasia AILAMAKI (EPFL)	Release Feb 2019: v2.2 https://kg.humanbrainproject.eu
C2482	Collaboratory	service	Allan FRANCANI (EPFL)	Release March 2019: Coordination release https://wiki.humanbrainproject.eu User documentation: https://www.xwiki.org/xwiki/bin/view/Documentation/ User access and support: support@humanbrainproject.eu
C2617	Document App	service	Allan FRANCANI (EPFL)	Release March 2019: Coordination release https://office.humanbrainproject.eu User documentation: https://helpcenter.onlyoffice.com/ONLYOFFICE-Editors/index.aspx User access and support: support@humanbrainproject.eu
C2619	Knowledge Graph Search UI	service	Oliver SCHMID (EPFL)	Release October 2018: v2.0 https://kg.humanbrainproject.eu/webapp
C2822	Knowledge Graph	service	Oliver SCHMID (EPFL)	Release March 2019: v2.2 https://kg.humanbrainproject.eu

9. Key Result KR5.11 "HBP-specific workflows developed to fully leverage the current state-of-the-art in computer vision with regards to object detection and segmentation problems. Active and transfer learning methods will be developed to lower the requirements to the necessary amount of training data."

Computer vision is developing faster than ever before, constantly pushing the state-of-the-art in object detection and segmentation. These methods are, however, not directly accessible to neuroscientists who might wish to apply them for brain image analysis. The two main barriers are the expertise required to apply the new methods and the amount of training data they need. This Key Result aims to alleviate both.

9.1 Outputs

9.1.1 Overview of Outputs

- Output 1: ilastik as part of the HBP infrastructure. Releases planned for summer 2019 and January 2020 (C2234)
- Output 2: ilastik and the brain atlases. Released March 2019 and another release planned for January 2020 (C2235)
- Output 3: Voxel Segmentation Workflow plugin for ilastik. Released March 2019 (C2282)
- Output 4: PyTorch back-end for ilastik. Releases planned for Summer 2019 and January 2020 (C2236)

9.1.2 Output 1: ilastik as part of the HBP infrastructure

ilastik is an interactive tool for machine learning-based image segmentation, counting and tracking. Since ilastik requires no computational expertise, it is particularly well suited for serving the imaging analysis needs of the diverse range of neuroscientists in the HBP. The goal of this output is to integrate ilastik with the rest of the Neuroinformatics Platform and allow users to run image analysis tasks using HBP datasets and HBP computing infrastructure (C2234).

The main release is planned for January 2020. We are currently working on the remote execution of ilastik computational tasks steered by the client-side viewer. The source code can be found at https://github.com/ilastik/tiktorch/tree/alpha. An alpha release is planned for Summer 2019.

The current state-of-the-art is executing ilastik locally, communicating with other tools through files. This project will allow for integration with the rest of the HBP research infrastructure and for the exploitation of HBP high-performance computing resources for the neuroimage analysis tasks.

9.1.3 Output 2: ilastik and the brain atlases

This Output will allow users to integrate features automatically extracted by ilastik classifiers with the brain atlases provided by the Neuroinformatics Platform (C2235, also see KR5.4, Section 5).

The first version was released as part of the March 2019 release of ilastik (version 1.3.3, available for download at https://www.ilastik.org/download). We have added support for user-defined image masks to the ilastik pixel and object classification workflows. These masks represent a parcellation of the original input image and allow to collect features and their statistics per mask region. After the first release, we will work on closer integration with the HBP Knowledge Graph. After testing by a group of advanced users, necessary corrections will be introduced before the final release in January 2020.

This project will allow neuroscientists without computational expertise to detect features in their images and analyse their spatial distribution in the context of brain atlases provided by the HBP.

9.1.4 Output 3: Voxel Segmentation Workflow plugin for ilastik

An image-based classifier is developed to segment structures like cells or synapses using state of the art ML techniques and delivered it as a plugin for ilastik (C2282). We addressed the lack-of-training data problem by developing an interactive labelling pipeline, where the labels produced by the annotator are immediately used to improve the predictor, which is then used to speed up further annotation.

Our plugin is currently available at https://github.com/ilastik/ilastik/pull/1892, awaiting integration into the next major software release of ilastik. It enables fast, ML-assisted segmentation of image stacks by training a classifier in an interactive manner. We developed a new active learning (AL) algorithm for this purpose. Existing ones ignore the fact that navigation in 3D volumes can be daunting. Our algorithm exploits geometric priors to identify the voxels to be annotated so as to optimize the performance gain with minimal user intervention.

Evaluation on Electron Microscopy image stacks of neural tissue and Magnetic Resonance volumes revealed a marked performance increase for our approach, compared to several widely accepted baselines, details of which can be found in Konyushkova *et al*. 2015[7].

9.1.5 Output 4: PyTorch back-end for ilastik

The aim is to integrate cutting-edge image analysis algorithms developed from the voxel segmentation plugin into ilastik. We have developed a prototype of the deep learning back-end for ilastik, based on PyTorch (C2236). It allows ilastik users to run inference and training tasks directly from ilastik. An alpha release is planned for Summer 2019. The workflows will be modified according to user feedback and released for a larger audience in January 2020.

A prototype can be found at https://github.com/ilastik/tiktorch/tree/alpha.

Generic detection and segmentation algorithms exist but require significant expertise for training and application to new data. This backend will allow ilastik users to access cutting-edge segmentation methods directly in ilastik, in a user-friendly GUI, without the need to write code.

9.2 Validation and Impact

9.2.1 Actual Use of Output(s)

As the first releases (Output 2 and 3) were in March 2019, with ilastik version 1.3.3, the Components have not attracted users yet. Ilastik, however, is a popular tool for image segmentation,

[7] Konyushkova, K., Sznitman, R. and Fua, P., Introducing Geometry in Active Learning for Image Segmentation, International conference in Computer Vision, Santiago, Chile, December 2015

classification and tracking. The current user base across all communities and applications is measured in thousands (~15,000 downloads for January and February 2019 combined). The main use cases are in the life sciences, primarily in biology for microscopy image analysis. With such a large user base, the tools developed here will benefit much once released.

9.2.2 Potential Use of Output(s)

Output 1 (“ilastik as part of the HBP infrastructure”) will allow HBP users to interactively train ilastik workflows directly on HBP data and, once configured, to run large-scale image analysis jobs using HBP computing infrastructure.

The ilastik - Brain Atlases feature (Output 2) will allow HBP users to run completely integrated workflows, combining ilastik results with brain parcellation and other overlays contained in HBP Brain Atlases.

Once released, the Voxel Segmentation Workflow for ilastik (Output 3) will facilitate the reconstruction of complex 3D structures from image stacks, by bootstrapping the deployment of ML into the early phase of annotation, where very little labelled data is available. It can be used on any type of image stacks, ranging from electron microscopy, through light microscopy, to MRI and CT scans.

The PyTorch backend (Output 4) will greatly simplify the deployment of neural network-based classifiers for users without computational expertise. We envision it to become a simple route to connect cutting-edge bioimage analysis research with practitioners in the field.

9.2.3 Publications

none

9.2.4 Measures to Increase Impact of Output(s): disseminations

The prototype of the new ilastik development (Output 2) was demonstrated at the EMBL Conference “Images to Knowledge with ImageJ and Friends” (December 2018, Heidelberg, Germany) and at the 3rd Neubias Conference (February 2019, Luxembourg). The tools were received enthusiastically by the bioimage analysis community.

Our plan to enable remote computation with the ilastik back-end has been presented at developer and user conferences in the bioimage analysis community (I2K 2018 and NEUBIAS 2019) and generated a lot of interest and support from the community.

9.3 Components contributing to KR5.11

Table 7: Overview of Components with releases or major updates related to Key Result KR5.11

ID	Component Name	Type	Contact	Info on releases and major updates
C2234	Ilastik user interaction modes	service	Anna KRESHUK (EMBL)	Alpha release planned for Summer 2019
C2235	Integration of ilastik with the KnowledgeGraph and Neuroinformatic Platform	service	Anna KRESHUK (EMBL)	Release March 2019: ilastik 1.3.3beta1 https://www.ilastik.org/download

C2236	Extension of ilastik image analysis workflows	software	Anna KRESHUK (EMBL)	Alpha release planned for Summer 2019
C2282	Segmentation tools	software	Pascal FUA (EPFL)	Release March 2019: v1.0 https://github.com/etrulls/ilastik_al/releases/tag/v1.0

10. Key Result KR5.12 "Comprehensive analysis toolbox to support analysis workflows for electrophysiological activity data from experiments and simulations, including support for HPC and visualisation capabilities"

The primary result of neuronal network simulations performed in the HBP is simulated brain activity that reflects the concerted activity of vast numbers of brain cells on multiple scales. This data is complemented by experimental data recorded using a broad range of measurement techniques. The goal of KR5.12 is to provide the resources needed to make qualified statements about the comparability and validity of the developed models, compared to real brains. We provide generic data structures and analysis methods that enable scientists to perform exactly the same type of analyses of artificial brains as those typically performed on biological data. These methods are the basis of model validation at the network activity level. A special emphasis is placed on novel methods that exploit the availability of large parallel data streams to extract the correlative structure hidden within the activity data.

10.1 Outputs

10.1.1 Overview of Outputs

- Output 1: Electrophysiological Analysis Toolkit – Elephant v0.6.1. Released in March 2019 (C348)
- Output 2: Software library Elephant Visualisation. Release planned for Autumn 2019 (C2122)
- Output 3: Software library Neo v0.7.1. Released in December 2018 (C361)

10.1.2 Output 1: Electrophysiological Analysis Toolkit (Elephant)

Elephant (C348) is an open-source software library that provides analysis methods for activity data from experiment and simulation, in particular parallel spike trains and population activity time series data. Elephant release v0.6.0 (Oct 12, 2018), available at https://github.com/NeuralEnsemble/elephant, contains a newly added, novel analysis method for the analysis of activity patterns in large-scale spike data (Russo et al., 2017), complementing an array of methods for the comprehensive investigation of concerted activity from different angles within a single framework not available in other tools. A follow-up release v.0.6.1 (March 31, 2019) encompasses a compatibility and bug-fix release of the library following changes and enhancements to the data model in the 0.7 release of the Neo library. Work on an improved documentation system containing interactive material for Elephant is ongoing and expected to become available by summer 2019.

10.1.3 Output 2: Elephant Visualisation

Elephant Visualisation (C2122) represents a complementary library for Elephant to provide functionality related to visualization of data and analysis results. Work on prototyping the library has begun by working in two directions. Firstly, the library will provide functions to visualize Neo data objects. A first function to flexibly visualize Neo spike trains along with basic spike train statistics obtained from Elephant has been developed. Secondly, the library will provide static and interactive visualizations of analysis results. To this end, in collaboration with RWTH Aachen, a prototype data model and interactive viewer for correlation results was developed, that is able to display time-variant graph structure obtained from pair-wise correlation measures based on force-directed graph layouting. The planned scope of standardized and interactive visualizations for analysis results is currently not available to researchers. We expect to release the initial version of the Elephant Visualization in in autumn 2019, but development work can already be monitored at https://github.com/INM-6/viziphant.

10.1.4 Output 3: Neo

Neo (C361) is a package for representing electrophysiology data in Python, together with support for reading a wide range of neurophysiology file formats. It is essential to guarantee interoperability of HBP tools independent of the data sources. It is developed as a community open-source project, with contributors from both inside and outside the HBP. Version 0.7.0 was released on 27 November 2018, with contributions from 14 people (of whom four are HBP members). The main focus of this release was improving and fixing bugs in the IO modules - see release notes for more details: https://neo.readthedocs.io/en/latest/releases/0.7.0.html. Version 0.7.1 was released on 13 December 2018, providing minor bug fixes. The test suite was increased from 992 tests (release 0.6.0) to 1,003 tests. Neo is available at https://github.com/NeuralEnsemble/python-neo.

10.2 Validation and Impact

10.2.1 Actual Use of Output(s)

Elephant is successively validated through HLST-supported interactions, such as the analysis of spatial activity in SWAP (in particular, C2051, C2053), or the current-source density analysis of simulated LFP. Elephant constitutes the backend to the HBP “NetworkUnit” validation library developed in SP6 (see publications validating the use of Elephant). Close interactions to developers of a complementing validation library on the single neuron level, “NeuronUnit”, have been established, opening up for closer interlinkage between individual open source components of the libraries in the future.

Elephant contains contributions from 25 developers, has 46 stars and 56 forks (on Github).

Neo is widely used within the HBP and in the wider neuroscience community, directly and as a dependency of tools such as PyNN and Elephant. The Neo project has 120 stars and 135 forks on Github, and is a dependency for 85 other repositories. At the time of writing, the project homepage had received 156 unique visitors in the preceding 14 days.

10.2.2 Potential Use of Output(s)

The **Elephant** library strives to provide a growing number of analysis tools to easily enable researchers to probe their data, interactively, via scripts, or as backend. By increasing the focus on distributed architectures this includes also computationally demanding methods.

The **Elephant Visualisation** intends to facilitate interactive work by transforming JupyterLab notebooks from a generic Python environment to a visual workbench for activity data analysis, spanning experimental data and simulations. Preliminary prototyping is in progress.

Neo is already widely used, but we expect its usage numbers to increase by a factor of at least 10 over the coming three years, as a series of performance improvements on large datasets, currently in development, are released, and measures are taken to proactively disseminate information about the tool.

10.2.3 Publications

- P1627: Trensch, G., Gutzen, R., Blundell, I., Denker, M., and Morrison, A. (2018). Rigorous Neural Network Simulations: A Model Substantiation Methodology for Increasing the Correctness of Simulation Results in the Absence of Experimental Validation Data. *Frontiers in Neuroinformatics* **12**, 81. doi: 10.3389/fninf.2018.00081
- P1628: Gutzen, R., von Papen, M., Trensch, G., Quaglio, P., Grün, S., and Denker, M. (2018). Reproducible Neural Network Simulations: Statistical Methods for Model Validation on the Level of Network Activity Data. *Frontiers in Neuroinformatics* **12**, 90. doi: 10.3389/fninf.2018.00090
    - o These papers demonstrate the practical use of the HBP Validation Library NetworkUnit (developed in SP6) in model validation on the level of network activity dynamics, which is directly based on the analysis capabilities of the Elephant library (Output 1).

10.2.4 Measures to Increase Impact of Output(s): disseminations

Both Elephant, the HBP NetworkUnit validation library and Neo (Output 1 and 3) have been featured at various workshops and conferences the past year, including the Bernstein Conference Workshop "Practical approaches to research data management and reproducibility" (Berlin, September 2018), the HBP CodeJam#9 Workshop (Palermo, November 2018) and the German Neuroscience meeting (Goettingen, March 2019). Another major event was the third annual 2½ week spring school on Advanced Neural Data Analysis (ANDA) for young scientists arranged in Juelich in April 2019, which was dominated by a practical part that employed Elephant and related tools.

10.3 Components contributing to KR5.12

Table 8: Overview of Components with releases or major updates related to Key Result KR5.12

ID	Component Name	Type	Contact	Info on releases and major updates
C348	Elephant	software	Michael DENKER (JUELICH)	Release Dec 2018: 0.6.0 https://pypi.org/project/elephant/0.6.0 Documentation: https://github.com/NeuralEnsemble/elephant/releases/tag/v0.6.0 Release March 2019: 0.6.1 https://pypi.org/project/elephant/0.6.1 Documentation: https://github.com/NeuralEnsemble/elephant/releases/tag/v0.6.1

C361	Neo (enhancements including support for optophysiology recordings)	software	Andrew DAVISON (CNRS)	Release Nov 2018: Neo 0.7.0 https://pypi.org/project/neo/0.7.0 Documentation: https://neo.readthedocs.io/en/latest/releases/0.7.0.html
C2051	T3.2.5 (1) High-efficiency analysis of (perturbed) SWA/transitions on single areas	research	Pier Stanislao PAOLUCCI	See SGA2 D3.6.1 (D20.1, D17) for more details
C2053	T3.2.5 (3) High-efficiency, multi-area wave propagation analysis	research	Pier Stanislao PAOLUCCI	See SGA2 D3.6.1 (D20.1, D17) for more details
C2122	Elephant Visualisation	software	Michael DENKER (JUELICH)	Autumn 2019: Target initial release Development at: https://github.com/INM-6/viziphant

11. KR5.13 “The neural activity resource (NAR) as a central mechanism to register, annotate and browse activity data sets within the HBP”

Recordings of neural activity are typically performed to answer specific hypotheses, but such data may in addition be reused by other scientists, potentially in combination with other data from other labs, to answer different questions that were not considered by the original lab.

Such reuse requires that the data are thoroughly annotated with detailed information (“metadata”) about the experimental conditions (the same applies to details of the model and simulation, for simulated data). This annotation is done by data providers and by curators (see "In depth" curation under KR 5.1, Section 3). To ensure that the annotations are consistent across different data sets, the HBP develops metadata schemas (used to structure metadata within the HBP Knowledge Graph, see KR 5.9, Section 8), together with tools to make it easy to find, understand, and reuse neural activity data (whether for further analysis, for model building or for model validation). The set of metadata schemas, software and web services related specifically to neural activity recordings collectively form the Neural Activity Resource.

11.1 Outputs

11.1.1 Overview of Outputs

- Output 1: Neural Activity Resource metadata tools (C1463) - Web app (work in progress), Python library (released May 2018) and HBP Knowledge Graph schemas (work in progress).
- Output 2: Neo Viewer - Viewer for time-series data in the NAR. Software component and web service. Released January 2019 (C2124)

11.1.2 Output 1: The Neural Activity Resource

The Neural Activity Resource (NAR) provides tools and documents to support the creation, curation and use of in-depth metadata about neural activity datasets (from experiments and simulations). The new tools under development are (i) a web app for viewing in-depth metadata (stored in the HBP Knowledge Graph); (ii) a Python library for searching, creating, downloading such metadata for use in modelling, simulation and data analysis; (iii) metadata schemas in SHACL format, for validating metadata.

The web app has not been formally released, but is available at https://nar-browser-app.brainsimulation.eu/app/ (HBP identity account required - contact support@humanbrainproject.eu to request access). Development has focused on improved testing, fixing bugs, and tracking changes in Knowledge Graph schemas. Version 0.1.0 of the NAR Python library was released on 2018-05-15. Notable improvements since this release are support for MINDS and for brain simulation metadata. A Jupyter notebook demonstrating the library is available at https://collab.humanbrainproject.eu/#/collab/1635/nav/78122 (HBP identity account required).

Metadata schemas using the W3C SHACL standard have been developed for intracellular electrode recordings and for two-photon calcium imaging. Schemas for multi-electrode array and EEG recordings are under development. The intracellular recording schemas have been released through the Neuroshapes project (https://incf.github.io/neuroshapes/) and deployed within the HBP Knowledge Graph.

11.1.3 Output 2: Neo Viewer

Neo Viewer v 1.0 (released in January 2019) is a web service and accompanying Javascript package for visualizing neural activity data (analog signals, spike trains etc.) in a web browser. Its key features are: (i) it supports a wide range of file formats (those supported by the Neo library); (ii) can be easily deployed by data providers or consumers (available as a Docker container), so as to match server resources to user demand.

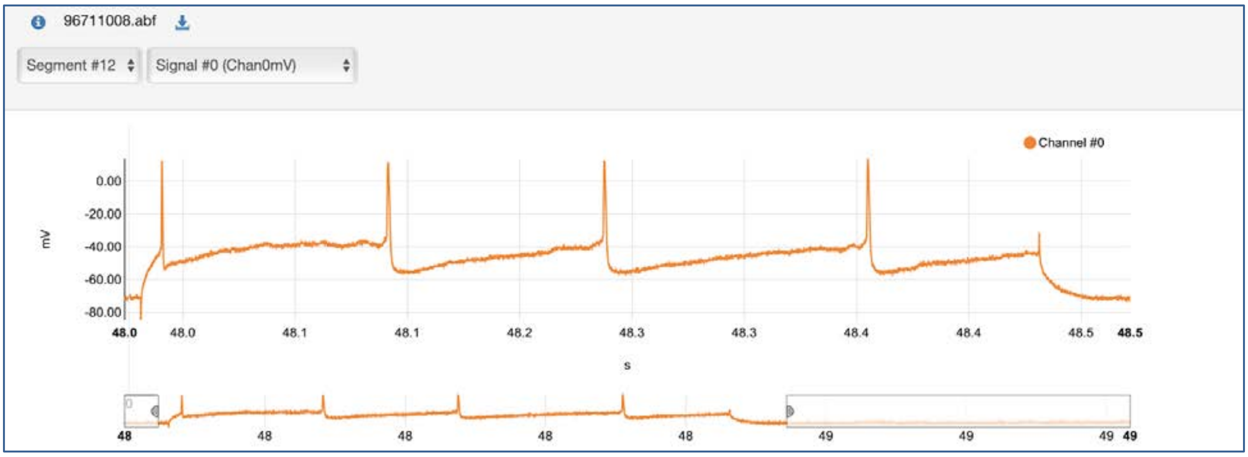

Figure 6: Neural Activity Visualiser

Screenshot of the neural activity visualiser, showing a recording from a neuron in hippocampus CA1, in Axon Binary Format. The datafile is registered with the HBP Knowledge Graph, read directly from archival storage at the CSCS supercomputer centre (provided through the ICEI project), and converted to JSON by the Neo Viewer web service so that it can be displayed by the Javascript app.

```
<div ng-app="neo-visualizer">
    <visualizer-view
        source="https://object.cscs.ch/v1/AUTH_c0a333ecf7c045809321ce9d9ecdfdea/Migliore_2018_CA1/exp_dat
        height=400>
    </visualizer-view>
</div>
```

Figure 7: Embedding Neo Visualizer

Code snippet demonstrating how easily the Javascript app can be used within a web page.

A demonstration of the web service is available at https://neo-viewer.brainsimulation.eu. Related visualisation tools are available from the Geppetto project (https://geppetto.readthedocs.io/) and the Allen Institute Cell Types database (http://celltypes.brain-map.org/). The main advantages of

Neo Viewer over Geppetto are that it is much lighter and easier to use, and that it supports a very wide range of data formats. The Allen Institute database supports interactive visualisation, but it is customised for the specific protocols used in the Allen Institute and it is not distributed for use with other data outside the Allen Institute database.

11.2 Validation and Impact

11.2.1 Actual Use of Output(s)

The **NAR tools** are used primarily within the Tier 3 curation activity (see KR 5.1, Section 3). The Python client is publicly available on Github, with sample Jupyter notebooks available in the Collaboratory, and it is being evaluated by Brain Simulation Platform developers (Migliore lab, CNR) for use in online use cases.

The **Neo Viewer** is already being used in the HBP, as part of a series of “live papers” being released to accompany traditional journal articles about the modelling results from the Brain Simulation Platform. The first live paper released is available at: https://humanbrainproject.github.io/hbp-bsp-live-papers/2018/migliore_et_al_2018/migliore_et_al_2018.html, and uses the Neo Viewer in the “Electrophysiological Traces” section; i.e., all the electrophysiology recordings used in the published article can be visualised interactively in the web browser.

11.2.2 Potential Use of Output(s)

The **NAR tools** are potentially of use to anyone wishing to reuse neural activity datasets shared through the HBP Neuroinformatics Platform, either directly or through the Brain Simulation Platform online use cases. We expect that, once the Python API has stabilised, it will be the primary tool for interacting with the HBP Knowledge Graph for data-driven model building, simulation, and validation, or for advanced data analysis.

The **Neo Viewer** could be used by any neuroscientist wishing to share electrophysiology data, whether from experiment or simulation, and by anyone wishing to inspect such shared data. We plan to rapidly improve its performance and capabilities. It could be adopted by other data sharing initiatives outside the HBP.

11.2.3 Publications

None

11.2.4 Measures to Increase Impact of Output(s): disseminations

The NAR tools (Outputs 1 and 2) were presented at a Bernstein Conference workshop "Practical approaches to research data management and reproducibility" (Berlin, September 2018) as well as at the HBP CodeJam #9 Workshop (January 2019, Italy).

11.3 Components contributing to KR5.13

Table 9: Overview of Components with releases or major updates related to Key Result KR5.13

ID	Component Name	Type	Contact	Info on releases and major updates
C1463	Neural Activity Resource Development (API, WebApp, MetaData DB)	service and software	Andrew DAVISON (CNRS)	Release May 2018: nartools v0.1.0 https://github.com/HumanBrainProject/neural-activity-resource/releases/tag/0.1.0 Documentation: https://github.com/HumanBrainProject/neural-activity-resource/blob/master/client/README.md
C2124	Viewer for time-series data in the NAR	service and software	Andrew DAVISON (CNRS)	Release Feb 2019: 1.0.0 https://github.com/NeuralEnsemble/neo-viewer Documentation: https://neo-viewer.brainsimulation.eu

12. Key Result KR5.14 "HBP and non-HBP affiliated researchers using interoperable platforms"

Here, we report on the recent achievements in:

1) Building a community-based, data-driven encyclopaedia for neuroscience that provides an interface between current brain research concepts and the data, models, and literature,
2) Delivering user support to users of all HBP Platforms through the newly established High-Level Support Team, and
3) Building the links to The Virtual Brain, the platform allowing for personalised brain simulations by linking computational neuroscience with individual brain imaging data.

12.1 Outputs

12.1.1 *Overview of Outputs*

- Output 1: KnowledgeSpace, latest release March 2019 (C2186.)
- Output 2: HBP single entry support point: High level support team established in October 2018 (C3085), Front line ticketing system released in December 2018 (C3084).
- Output 3: The Virtual Brain: TVB-HBP interface (C3046, released August 2018; C3047, latest release March 2019), The Virtual Brain EduPack, latest update February 2019 (C3049)

12.1.2 *Output 1: KnowledgeSpace*

KnowledgeSpace, available from http://knowledge-space.org, is a community-based, data-driven encyclopaedia for neuroscience that provides a unique, global interface between current brain research concepts and the data, models, and literature that support or weaken their definition. KnowledgeSpace has been integrated into TrainingSpace, https://training.incf.org/, an online hub that provides links to courses, tools, and data, to provide another forum in which it can be discovered, and it provides training resources and links to tools that complement the data discoverable through KnowledgeSpace (release March 2019). The updates furthermore covered improved search functionality and user interface. Data and models available via KnowledgeSpace have reached over 1 million records and the encyclopaedia content has been enhanced to complement the ontology-based definitions of concepts with summary content from Wikipedia. Work continues to improve the specificity of the literature results from PubMed associated with brain research concepts on concept pages. Links from KnowlegeSpace to atlas representations and analysis tools have been added to the website.

12.1.3 Output 2: HBP single support entry point

The High Level Support Team (HLST) was established following an extensive preparation process and approval by the HBP governing bodies. The HLST represents a single entry point for HBP research infrastructure user support. Users submit requests through the ticketing system and a qualified team routes the requests to dedicated personnel in the HLST or forwards it to the Platform if the request cannot be treated by the HLST. In total, 35 staff members from the various Platforms provide user support within one of the more general services: front line support, operations support, or specialized support actions related to various HBP Platforms. These support actions comprise 8 separate tasks - Data Curation support, support for Jupyter Notebook users, Functional Data Analysis support, Brain Simulation Platform support, Medical Informatics Platform support, Neuromorphic Computing support, Neurorobotics Community Managements and Simulation and Data Analytics Workflow support.

Anyone can submit a request for HBP infrastructure support by means of email to support@humanbrainproject.eu or, for HBP-members, through the web interface: https://support.humanbrainproject.eu/.

12.1.4 Output 3: The Virtual Brain

Interface TVB with Brain Simulation Platform

The Virtual Brain (TVB) is an open-source simulation platform that was introduced into the HBP in April 2018 following a Call for Expressions of Interest (CEoI) in Codesigning the Human Brain Project (HBP) digital infrastructure for advancing the understanding of multilevel brain organisation. TVB provides a user-friendly environment that allows personalised brain simulations, by linking computational neuroscience with individual brain imaging data.

To allow fast, parallelised C implementation of the TVB model on the Jureka supercomputer (FZJ), we released a C-Code for a modified Wong-Wang model that includes some optimisations for speeding up computation-time. The code was released in August 2018 at https://github.com/BrainModes/The-Hybrid-Virtual-Brain.

A tutorial, "Inferring multi-scale neural mechanisms with brain network modelling", is available at https://www.youtube.com/watch?v=rAyAiQ83B9U.

Interface TVB with Neuroinformatics Platform

The goal is to implement a web interface for HBP's Neuroinformatics Platform that enables users to create a brain network model by selecting an atlas and (structural and diffusion) MRI data sets. The TVB model construction pipeline is installed in the backend on a high-performance computer, and constructs brain network models using the data/atlas/parameters specified via the web interface. Implementation of the multimodal processing pipeline is publicly accessible and usable via a web interface on the NIH's NSG Server http://www.nsgportal.org. The pipeline is also functional on the Jureca supercomputer (FZJ); but there is no public access yet, as it is undergoing testing). The full code is available at: (https://github.com/BrainModes/TVB-empirical-data-pipeline). An online video tutorial, "Inferring multi-scale neural mechanisms with brain network modelling", is available at https://www.youtube.com/watch?v=j7r8WZ5ls64&list=PLVtblERyzDeIATvaoHp-bBtksF25zm8p1&t=2s&index=7

The Virtual Brain EduPack (C3049) develops TVB tutorials for novice and advanced users.

Currently the following tutorials are available:

- TVB Made Easy, August 2018 –7 tutorial videos: https://www.youtube.com/playlist?list=PLVtblERyzDeIATvaoHp-bBtksF25zm8p1
- The Virtual Brain Node #6 Workshop, August 2018, Berlin, 11 Tutorial Videos: https://www.youtube.com/playlist?list=PLVtblERyzDeIlUsOx-_DQ5bXDKecoIdly
- Student workshop The Virtual Brain at Bernstein Center for Computational Neuroscience Berlin, February 2019, 4 Online Lectures: https://www.youtube.com/playlist?list=PLVtblERyzDeLeknnDG2fAHTuf5o9RgH5c

12.2 Validation and Impact

12.2.1 Actual Use of Output(s)

The user base of **KnowledgeSpace** (Output 1) from April 2018 to March 2019 was 2,896 users, with 65.97% from outside Europe and 34.03% from within Europe. We are unable to discern which European users are part of the HBP and which are from the wider neuroscience community. The top 10 countries using KnowledgeSpace are: USA, France, India, UK, Germany, Canada, China, Brazil, Italy and Japan (based on Google Analytics for the website).

Since December 2018, around 300 support tickets have been opened and resolved through the **HLST** front line (Output 2). A large number of agents facilitates quick qualified response, appropriate routing of tickets to dedicated specialists which is also reflected in high user satisfaction in surveys (>4/5 stars). The majority of the requests came from the HBP, but the number of external users showing interest in HBP offering (students, individual researchers, attendants of courses and lay public) is growing.

The majority of requests deal with relatively simple issues, e.g. getting access to the Collaboratory, the HBP, feedback with regards to Jupiter notebooks and other HBP tools/services. Other requests deal with implementation of new features for HBP researchers aimed on implementation of use cases or expansion of infrastructure, e.g. for Medical Informatics Platform (hospitals in Plovdiv, UK Aachen, research centres Neurospin and Creactive). Several external users have requested data curation services. With regards to brain simulation, the HLST is involved into implementation of use cases concerning HBP neuroscientists using Elephant tool for hippocampus LFP simulation and development of live paper on basal ganglia in the Brain Simulation Platform (BSP). Furthermore, the Simulation and Data Analytics Workflow Support action is involved in implementation of Learning-to-learn (L2L) workflow using Fenix/ICEI resources at ETHZ-CSCS. The L2L workflow is a machine learning use case including simulations, optimization and analysis of a biologically realistic neuronal model of a single cortical micro-column. Neurorobotics Platform (NRP) community management shows active use of NRP Platform forum and continuous growth of user base.

TVB (Output 3) has experienced an increase in the number of downloads since it was introduced into HBP and has recently reached more than 19,000 downloads. The Hybrid Virtual Brain C-Code has already resulted in several publications (e.g.: Aets *et al*. 2018[8], Zimmermann *et al*. 2018[9] and Schirner *et al*. 2018[10]):

The Virtual Brain EduPack tutorials have been viewed more than 2,000 times.

12.2.2 Potential Use of Output(s)

KnowledgeSpace's encyclopaedia component is approximately 75% complete and currently has 14 data sources completely integrated (100%). Work continues to further strengthen the integration between data and literature references in PubMed. KnowledgeSpace can be used by other large-scale projects as a place to expose and integrate their work into a larger framework. Repositories connected to KnowledgeSpace have to demonstrate that they are FAIR and that the data contained within them is FAIR.

The **HLST** started in October 2018 and is now well established and prepared to increase its capacity, following intensification of outreach activities.

12.2.3 Publications

The use of Hybrid Virtual Brain C-Code was demonstrated in several publications during its development before TVB was introduced in the HBP (see Actual Use of Output(s) for examples).

12.2.4 Measures to Increase Impact of Output(s): disseminations

In-person demonstrations of **KnowledgeSpace** (Output 1) have been conducted at FENS (July 2018, Berlin), Society for Neuroscience (September 2018, San Diego), INCF Congress on Neuroinformatics (August 2018, Montréal) to solicit community feedback on progress and feature requests. Furthermore, a survey was conducted with the Faculty for Undergraduate Neuroscience to get feedback on what would be needed for them to use KnowledgeSpace as part of their teaching.

Information about **HLST** (Output 2) has been sent out via the HBP internal and external newsletters (January 2019). Specialised HLST services will be showcased on a regular basis through the HBP newsletters and other communication channels, including Twitter. Other measures include workshops for direct interaction with potential users: NRP workshop (February 2019), Digital brain atlasing course (June 2019), Data Curation and Activity Data analysis workshop (late 2019); and showcasing at the international events (Society for Neuroscience, HBP Summit, Neuroinformatics meeting in Warsaw, September 2019).

TVB (Output 3) has a large number of users and has recently reached more than 19,000 downloads. To further increase impact and dissemination, we plan to integrate TVB into the TrainingSpace to provide users with training via this centralised resource.

12.3 Components contributing to KR5.14

[8] Aerts H, et al. (2018). Modeling Brain Dynamics in Brain Tumor Patients Using the Virtual Brain. *eNeuro* 5(3). pii: ENEURO.0083-18.2018. doi: 10.1523/ENEURO.0083-18.2018.

[9] Zimmermann et al. (2018). Differentiation of Alzheimer's disease based on local and global parameters in personalized Virtual Brain models. *Neuroimage Clin.* 19, pp 240-251. doi: 10.1016/j.nicl.2018.04.017.

[10] Schirner M, McIntosh AR, Jirsa V, Deco G, Ritter P (2018). Inferring multi-scale neural mechanisms with brain network modelling. *Elife*, 7. pii: e28927. doi: 10.7554/eLife.28927.

Table 10: Overview of Components with releases or major updates related to Key Result KR5.14

ID	Component Name	Type	Contact	Info on releases and major updates
C2186	Expansion of data, model, and literature content	service	Mathew ABRAMS (KI)	Release March 2019: KnowledgeSpace 2.0 https://knowledge-space.org
C2187	Atlas representations	service	Mathew ABRAMS (KI)	Expected release March 2020 https://knowledge-space.org
C2188	Links to analysis tools	service	Mathew ABRAMS (KI)	Expected release March 2020: https://knowledge-space.org
C3046	BSP-TVB pipeline	software	Petra RITTER (CHARITE)	Release Aug 2018: Hybrid Virtual Brain - C implementation of TheVirtualBrain reduced Wong Wang model for HPC https://github.com/BrainModes/The-Hybrid-Virtual-Brain Release Aug 2018: Online Video tutorial "Inferring multi-scale neural mechanisms with brain network modelling" URL: https://www.youtube.com/watch?v=rAyAiQ83B9U
C3047	NIP-TVB pipeline	software	Petra RITTER (CHARITE)	Latest version release March 2019 (Initial version release August 2015) TVB empirical data pipeline: Software is running via this HPC web-server: http://www.nsgportal.org/ Code and user documentation: https://github.com/BrainModes/TVB-empirical-data-pipeline Online Video tutorial "An automated pipeline for constructing personalized virtual brains from multimodal neuroimaging data" URL: https://www.youtube.com/watch?v=j7r8WZ5ls64&list=PLVtblERyzDeIATvaoHp-bBtksF25zm8p1&t=2s&index=7 Release: 18 August 2018
C3049	EduPack	report	Daniele MARINAZZO (UGENT)	Release Aug 2018: TVB Made Easy – youtube channel with 7 tutorial videos: https://www.youtube.com/playlist?list=PLVtblERyzDeIATvaoHp-bBtksF25zm8p1 Made available Feb 2019: Student workshop The Virtual Brain at Bernstein Center for Computational Neuroscience Berlin – Four Online Lectures: https://www.youtube.com/playlist?list=PLVtblERyzDeLeknnDG2fAHTuf5o9RgH5c

				Release Aug 2018: TVB Node#6 Berlin one day workshop videos: https://www.youtube.com/playlist?list=PLVtblERyzDeIlUsOx-_DQ5bXDKecoldly
C3084	Front Line Support Ticketing System	admini-strative	Roman VOLCHENKOV (UIO)	Release Dec 2018: https://www.humanbrainproject.eu/en/hbp-platforms/support/ User documentation: https://zammad-user-documentation.readthedocs.io/en/latest/
C3085	High Level Support Team (HLST)	admini-strative	Roman VOLCHENKOV (UIO)	https://www.humanbrainproject.eu/en/hbp-platforms/support/

13. Conclusion and Outlook

The HBP is at a turning point, marked by a transition from intra-project co-design in previous project phases, to a co-design process involving the research and development communities that the Research Infrastructure will serve. In this regard, the **HBP data sharing service**, introduced in April 2017, has been instrumental. The service of making HBP data and models discoverable and accessible includes data curation and metadata enrichment, Knowledge Graph search, and Fenix-provided storage. It has been developed extensively over the last year and now reaches out to communities beyond the HBP. An important openness measure has been the newly established High-Level Support Team (HLST). In the context of the data sharing service, the HLST has contributed by providing front-line support with a ticketing system, and by offering Special Support Actions for data curation user support and Jupyter notebook user support.

The data sharing service is being gradually improved through an agile process. This has resulted in the recent release of more efficient curation workflows and more relevant ontologies for metadata. Through dissemination activities, we have received feedback indicating high interest in learning more about the HBP’s approaches to data curation and storage, and in trying out the main HBP Neuroinformatics Platform product offering available the broader community: the HBP Knowledge Graph. Usability testing of the Knowledge Graph user interface revealed several opportunities for improving navigation and user experience. Implementation of an improved user interface is ongoing and will continue with new releases over the coming months. The first article citing data curated and shared through the HBP Knowledge Graph, with DOIs for the shared data, was recently published in the Nature journal “Scientific Data”. FAIRness scores for data will be introduced in the second half of the current project phase, together with curation education events aimed at educating researchers in developing sound plans for sharing and managing data.

The HBP also reaches out to large user communities with its **Brain Atlases**. One category of Atlas comprises the experimental researchers who submit their data to curation, with a view to having the exact location of the data verified (structure names or spatial coordinates in the HBP Atlases) and making the data discoverable through the Atlases. Another category of users involves researchers who seek to find, analyse, and interpret data in the context of discovery driven or hypothesis driven research projects, often combining their own data with numerous other data categories found through the atlases. HBP atlas resources include the reference atlases - volumetric reference volumes, maps and region ontologies -, the tools used to register data to the reference atlases and thereby enrich them, and the tools used to explore and retrieve data from these enriched atlases. The Human Brain Atlases continue to be expanded, with 14 new probabilistic cytoarchitectonic maps added in the first year of SGA2, as well as updated bundle maps. The Rat Brain Reference Atlas will be released publicly in May, with a complete representation of auditory structures. This Atlas has been downloaded at a rate of about 2,500 times per year over the last 4 years. Key tools for registration of data to the atlases have been improved and will continue to be a priority for further development during the remainder of the current project phase, enabling higher accuracy and efficiency in the registration of data to Atlases. Active dissemination of the tool for interactive alignment of high-resolution data to the Big Brain template from a browser will be initiated, initially addressing the brain imaging community in Europe. The Interactive Atlas Viewer has received four incremental releases during the last year and is now the default tool for online browsing of the HBP Atlases in 3D.

The HBP Atlas Services include tools and workflows for **machine learning based segmentation of high-resolution 2D and 3D images in atlas space**. The HBP employs the widely used ilastik tool for image segmentation, classification and tracking. The new service under preparation will allow HBP users to interactively train ilastik workflows directly on HBP data and, once configured, to run large-scale image analysis jobs using the HBP computing infrastructure. Ilastik's brain atlases feature has now been tested extensively and will be released in the second year of the present phase. It will allow HBP users to run completely integrated workflows, combining ilastik results with brain parcellation and other overlays contained in HBP brain atlases.

The HBP analysis services enable researchers to work with **dynamic functional data f**rom experiments and simulations by providing the tools and services to integrate and analyse activity data. The Elephant analysis library and the underlying Neo data model have seen continuous development efforts, including new functionality and the initial development of a corresponding visualisation component planned for release in the second year of the present phase. Importantly, the visualisation component will include a formalisation of data types for data analysis results that provides a basis for recording rigorous provenance information for analysis workflows. In the remainder of the period, the focus will be on stability (release of Elephant v1.0), in-depth documentation, parallelisation, and improved support for optical imaging data.

The **High-Level Support Team** (HLST) started in October 2018 and is now well established and prepared to increase its capacity, following intensification of outreach activities. Ten areas of specialised support have been established, covering all HBP research infrastructure Platforms. Services will be showcased on a regular basis through the HBP newsletters and other communication channels. Openness measures include workshops for direct interaction with potential users and presence at upcoming international meetings.