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Abstract:	This Deliverable is the annual compound of HBP deliveries and results (outputs and outcomes) from Subproject SP6 – Brain Simulation Platform. The complete live catalogue of HBP deliveries is accessible online at the HBP portal. The main deliveries from April 2017 to March 2018 are: • Multi-scale molecular dynamics simulation and modelling approaches that inform models of subcellular signalling • Data-driven scaffold models to bootstrap community use and contribution • Advanced tools for data-driven modelling and simulation • Brain Simulation Platform – version 2 • Massive-open online course on simulation neuroscience
Keywords:	Brain Simulation Platform; co-design; data-driven; scaffold models; simulation neuroscience; MOOC; multiscale models; community

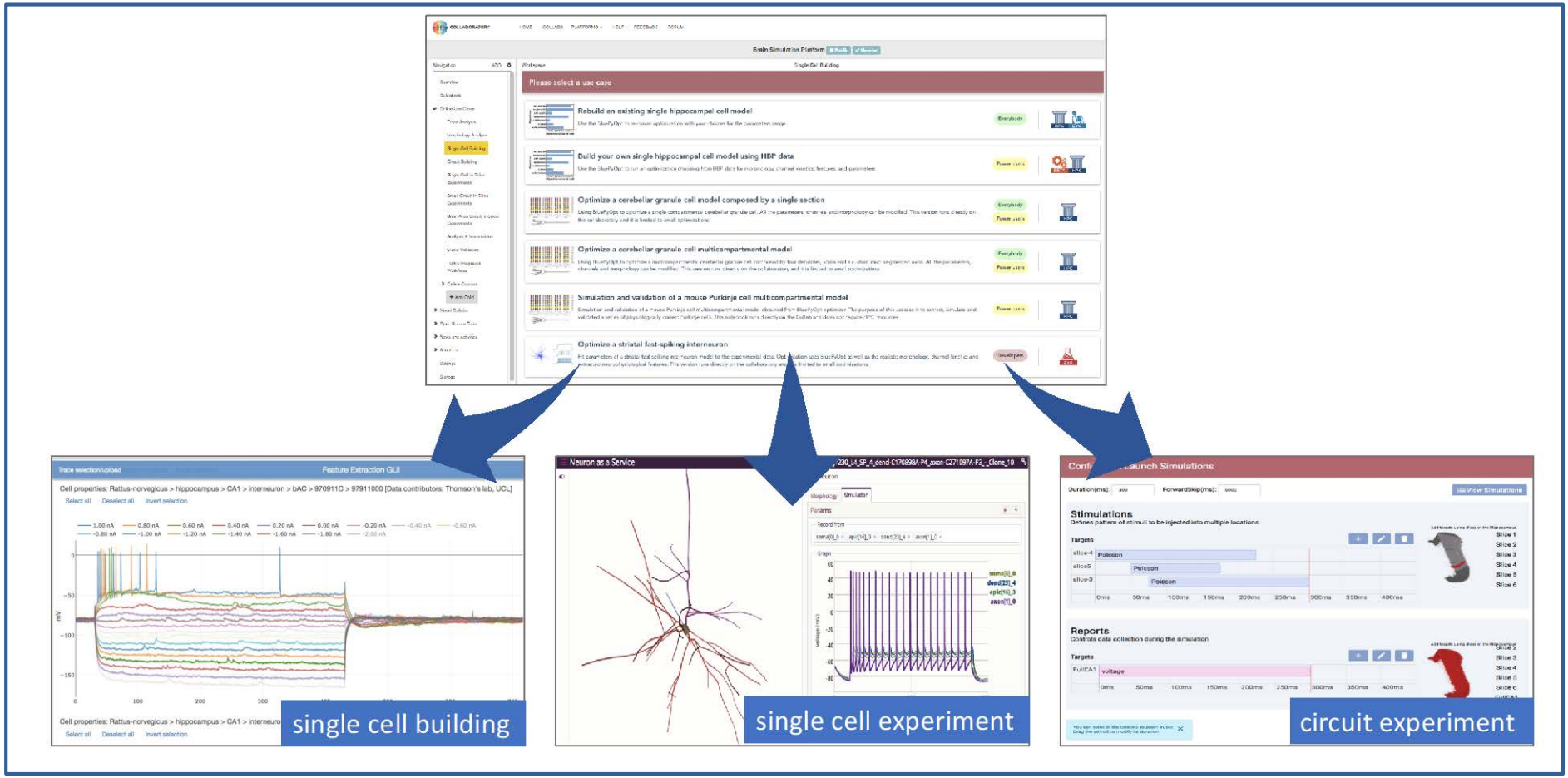

Figure 1: New version of the HBP Brain Simulation Platform

Illustration of the new version of the HBP Brain Simulation Platform. It is based on a new modular design integrating the feedback from previous reviews and ongoing co-design activities, and caters to a wide variety of uses, thus serving the wider community.

Audience:	(Potential) Platform users
Work-Package(s):	SGA1 WPs 6.1, 6.2, 6.3, 6.4 and 6.5
Planned Due Date:	SGA1 M24 / 31 MAR 2018

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Summary of Changes 21 September 2018	Annex 4: Life Cycle Model for Data-Driven Models was updated with a clarification on the community engagement strategy and opportunities in the lifecycle model for data-driven models.

Table of Contents

List of Figures

List of Tables

Introduction

The goal of SP6 is to catalyse a global community effort to systematically integrate neuroscience knowledge through the construction of data-driven models of brain tissue at different levels of biological detail. To achieve this goal, SP6 is building the HBP Brain Simulation Platform (BSP), which is made available through an HBP Collaboratory, where researchers from within and outside of the HBP can participate. The primary strategy developed for the BSP is to provide workflows for brain building that leverage state-of-the-art approaches and technologies for using neuroscience data to inform the construction of brain models. Many of the underlying technologies are developed by the partners as matching support or as open-sourced technologies developed by researchers outside of the HBP, to then be customised and integrated into the BSP. Co-design drivers, aimed at constructing specific scaffold brain models, guide the BSP development work performed in SP6. Scaffold models are framework brain models that allow for the continuous integration of neuroscience data by the community in a standardised manner.

For the period M13-M24 the following Key Results have been achieved:

Multi-Scale Molecular Dynamics Simulation and Modelling Approaches that Inform Models of Subcellular Signalling in Both a Qualitative and Quantitative Manner

Brain function is dependent, at the same time, on mechanisms at the subcellular, cellular, network and whole brain level. To inform and constrain model parameters used for such subcellular level models, molecular level simulations have been used to predict inaccessible parameters for biochemical cascades relevant for plasticity. Furthermore, to bridge levels of biological scales, first attempts of integrating subcellular models with a cellular level model of a striatal principal neuron have been made. Novel tools for molecular simulations of neuronal biomolecules and drugs have been developed and tested.

Data-Driven Scaffold Models to Bootstrap Community Use and Contribution

In the HBP Work Plan, several model systems, from subcellular cascades to individual neurons to entire brain regions, serve as scientific co-design drivers for the BSP. In this phase, all model systems, from human neurons to the selected brain regions of the hippocampus, cerebellum and basal ganglia, as well as the whole mouse brain network level model, have been refined, leading to new model versions. Also, for the first time, a somatosensory microcircuit of a mouse was built, leveraging the Blue Brain Cell Atlas and somatosensory microcircuit previously developed by the Blue Brain Project for the rat, and data coming from SP1. Lastly, an important achievement in this phase is the definition of a Life Cycle Model for all these modelling efforts, formalising the requirements they need to comply to, depending on the life cycle phase; this is an important prerequisite for community use and contribution. All models have been integrated into the HBP Model Catalog.

Advanced Tools for Data-Driven Modelling and Simulation

Where available, the BSP builds on best-in-class community software and contributes to its extension and maturation. During the last 12 months, SP6 successfully improved the scalability and usability of the major community simulators NEST, NEURON/CoreNeuron and STEPS, leading to new major releases of these tools. Where necessary for a highly integrated ecosystem, SP6 iteratively co-develops new software with the science drivers. A specific outcome of the last year is the advanced single neuron modelling workflow. This now addresses better pre-processing of the input data and efficient post-processing of large amounts of single cell models, as well as a generalised atlas-aware circuit building workflow as a prerequisite of structured brain region modelling.

Brain Simulation Platform – Version 2

Version 2 of the Brain Simulation Platform has been designed and deployed, and continuously updated over the last 12 months. It is based on a new modular design integrating the feedback from previous reviews and ongoing co-design activities, and caters to a wide variety of uses, thus serving the community even better. In particular, it now features mature functionality for the creation of single cell models, for *in silico* experimentation with single cells and scaffold

microcircuit and brain region models, and a validation framework used to validate models against a growing set of experimental data in an automated and repeatable manner. The seamless integration with the Neuroinformatics Platform has been made possible through the Blue Brain Nexus technology that was open-sourced and is now used to integrate neuroscience data in the HBP. The BSP is tightly integrated with the Neuroinformatics Platform and the High Performance Analytics and Computing Platform, and well prepared for the transition to the HBP Joint Platform.

Massive Open Online Course on Simulation Neuroscience

A major result in this period is the successful deployment of a first massive open online course (MOOC) on "Simulation neuroscience: reconstruction of a single neuron" that combines the power of a worldwide digital learning platform (edX.org) with the HBP's Collaboratory and the new version of the BSP. Since its worldwide launch in November 2017 it has attracted almost 6000 inscriptions (+100/week), leading to more than 500 active learners and >230 users to the BSP. The success of this first MOOC encouraged us to make MOOCs a major component of SP6's outreach strategy.

1. Results

1.1 Multiscale Molecular Dynamics Simulation and Modelling Approaches that Inform Models of Subcellular Signalling in Both a Qualitative and Quantitative Manner

Brain function depends simultaneously on processes at the subcellular, cellular, network and whole brain level. These levels interact continuously. For instance, synaptic plasticity is typically controlled by neuronal activity in the network, but co-activated neuromodulatory systems play important roles for shaping such plasticity. The temporal activation patterns of receptor-induced cascades thus need to be described quantitatively to enhance our understanding of phenomena such as learning, neuromodulation and homeostasis in the brain. Also, the subcellular level is a bridge to drug discovery processes, actively carried out now in the HBP via the Co-Design Project CDP6, as most brain diseases are treated with drugs affecting membrane receptors in one way or another. Thus, research and method development facilitating the building of subcellular level models and their integration with the cellular level, furthers greatly our understanding of the casual chain of events linking the molecular level with the cellular and network levels. Particularly important are model predictions from quantitative multiscale models. These may provide novel hypotheses that experimental groups in turn can verify or disprove, greatly improving our understanding of neuronal function and dysfunction. However, subcellular model parameters are often hard to get. Parallel strategies thus need to be explored and developed, such as using molecular level simulations to inform models of receptor-induced cascades. Here, we use molecular simulation to inform established kinetic models of neuronal cascades.

Parameter Prediction Using Molecular Level Simulations

To enhance the capability to predict subcellular model parameters, we have continued developing further such molecular level simulation approaches, both with regard to approaches to predict parameters and software tools. So far, we focused on adenylyl cyclases (AC), in particular AC5, which is prevalent in the striatum, the brain region most heavily neuromodulated by dopamine and acetylcholine. These neuromodulatory systems control AC5 via the G-proteins, Golf and Gi, respectively (see Figure 2). Molecular dynamics approaches were used to investigate the binding rates of these G proteins, as well as the activities of the complexes formed when either one of Gi or Golf or both, are bound to AC5. The resulting predictions are in line with the interpretation that the transient dopamine and acetylcholine signalling give rise to a strong synergistic detection of such transients.

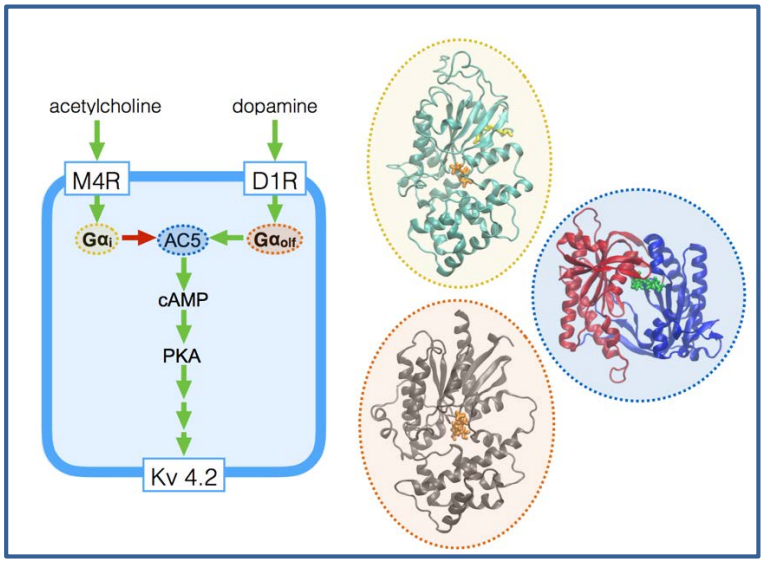

Figure 2: Scheme of the control of cAMP signalling

Scheme of the control of cAMP signalling by a dopaminergic and cholinergic receptor cascade, along with snapshots from molecular dynamics simulations of the proteins involved in it. Simulations predicted effects of G protein binding to AC5.

Proof of Concept of Multiscale Simulation of a Dopamine Receptor-Induced Cascade in a Model of a Striatal Neuron

As a proof of concept of multiscale simulations, a model of a dopamine receptor-induced cascade was integrated with a detailed neuron model of a striatal principal neuron, and the dynamics of membrane excitability was investigated and compared to experimental data. A prediction from this modelling study is that co-release of glutamate could play a significant role in the dorsal striatum. The reason is that the time course of the dopamine neuromodulation is difficult to reconcile with the experimentally observed effects of dopamine transients (see Lindroos *et al.*, 2018).

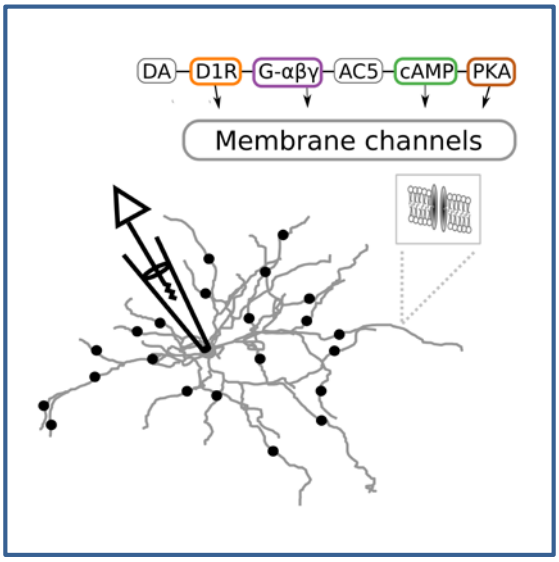

Figure 3: Control of membrane excitability by a dopaminergic receptor-induced cascade

Illustration of the control of membrane excitability by a dopaminergic receptor-induced cascade. For example, PKA-dependent phosphorylation of Kv4.2 channels increase excitability.

Novel Tools for Molecular Simulations of Neuronal Biomolecules and Drugs

Tools for molecular simulation, such as the SDA Brownian dynamics software, have greatly advanced. Furthermore, a new platform of advanced tools was developed to analyse molecular dynamics (MD) trajectories mimicking the procedures followed by human experts. We have developed a specific database of dynamics of membrane proteins involved in the transmission of

neural signals. A new method, combining QM and MD simulations has been developed to explore the ability of drugs to adopt bioactive conformations and we are using it to create a 4D library of accessible conformations of CNS bioactive drugs. In a test system, a new and rather accurate scheme was implemented to calculate rate constants of ligands detaching from proteins. A novel, highly scalable, HPC-based QM/MM interface, to investigate enzymatic reactions, is currently tested.

These novel tools, along with established methods, were applied to adenylyl cyclase (AC) (Figure 2), responsible for cAMP production. A combined molecular modelling and bioinformatics approach allowed identification of the binding sites of AC-regulating proteins (Tong, Wade & Bruce 2016), whereas co-evolution-driven molecular approaches (manuscript *in preparation*) and molecular dynamics provided the molecular basis for the effect (stimulating or inhibiting) of AC's cellular partners, along with previously unrecognised key effects of key post-translational modifications for the AC cascade.

1.1.1 Achieved Impact

- A novel, unprecedented massively parallel, open-source code for QM/MM is being completed. It is expected to be finished by the end of the year. It will then be used during the next years to calculate velocity constants required for the modelling of subcellular cascades. This work has also been supported by other EU grants and it involves several researchers from different European countries.
- The Brownian dynamics software package SDA (http://mcm.h-its.org/sda) has been downloaded 88 times during the M13-M24 period. In July 2017, a new version of the code was released publicly with a number of new and updated tools for analysing simulation data. The main simulation code has seen two major improvements: 1) a new treatment for modelling diffusion close to confining surfaces, such as the cellular membranes found in pre- and post-synaptic regions, and 2) a new adaptive-resolution solute model that allows a 90% reduction in the computational cost of simulating crowded cell-like conditions, without loss of accuracy. These updates are registered in the HBP software catalog and are available to internal HBP members. They will be released to the wider community following the publication of manuscripts that are in preparation.
- New platform of advanced tools to analyse MD trajectories mimicking the procedures followed by human experts. This approach is now used to investigate neuroreceptors, such as the muscarinic receptor, studied by Prof. Zilles in SP2.
- Experimental groups outside of the HBP have started to investigate subcellular model predictions (see Yapo *et al.,* 2018) and further collaborations are expected.
- Publications during M13-M24:
  - Balbi, P., Massobrio, P., & Hellgren Kotaleski, J. (2017). A single Markov-type kinetic model accounting for the macroscopic currents of all human voltage-gated sodium channel isoforms. *PLoS Comput Biol, 13*(9), e1005737. doi:10.1371/journal.pcbi.1005737
  - Brocke, E., Djurfeldt, M., Bhalla, U. S., Kotaleski, J. H., & Hanke, M. (2017). Multirate method for co-simulation of electrical-chemical systems in multiscale modeling. *Journal of Computational Neuroscience, 42*(3), 245-256. doi:10.1007/s10827-017-0639-7
  - Bruce, N. J., Ganotra, G. K., Kokh, D. B., Sadiq, S. K., & Wade, R. C. (2018). New approaches for computing ligand–receptor binding kinetics. *Current Opinion in Structural Biology, 49*, 1-10. doi:https://doi.org/10.1016/j.sbi.2017.10.001
  - Frezza, E., Martin, J., & Lavery, R. (2018). A molecular dynamics study of adenylyl cyclase: the impact of ATP and G-protein binding. *PLOS ONE* (accepted, 29 March 2018)
  - Lindroos, R., Dorst, M. C., Du, K., Filipovic, M., Keller, D., Ketzef, M., Kozlov, A. K., Kumar, A., Lindahl, M., Nair, A. G., Perez-Fernandez, J., Grillner, S., Silberberg, G., & Hellgren Kotaleski, J. (2018). Basal Ganglia Neuromodulation Over Multiple Temporal and Structural

Scales-Simulations of Direct Pathway MSNs Investigate the Fast Onset of Dopaminergic Effects and Predict the Role of Kv4.2. *Front Neural Circuits, 12*, 3. doi:10.3389/fncir.2018.00003

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- Ranft, J., Almeida, L. G., Rodriguez, P. C., Triller, A., & Hakim, V. (2017). An aggregation-removal model for the formation and size determination of post-synaptic scaffold domains. *PLoS Comput Biol, 13*(4), e1005516. doi:10.1371/journal.pcbi.1005516
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- Tarenzi, T., Calandrini, V., Potestio, R., Giorgetti, A., & Carloni, P. (2017). Open Boundary Simulations of Proteins and Their Hydration Shells by Hamiltonian Adaptive Resolution Scheme. *J Chem Theory Comput, 13*(11), 5647-5657. doi:10.1021/acs.jctc.7b00508
- Yapo, C., Nair, A. G., Clement, L., Castro, L. R., Hellgren Kotaleski, J., & Vincent, P. (2017). Detection of phasic dopamine by D1 and D2 striatal medium spiny neurons. *J Physiol, 595*(24), 7451-7475. doi:10.1113/JP274475

1.1.2 Component Dependencies

Table 1

Component dependencies of Key Result "Multiscale molecular dynamics simulation and modelling approaches that inform models of subcellular signalling in both a qualitative and quantitative manner".

Component ID	Component Name	HBP Internal	Comment
210	SDA	No	Simulator for Brownian dynamics simulations of the diffusional association in a continuum aqueous solvent. Freely available to academic researchers.
1046	Brownian dynamics simulations	Yes	Essential for predicting e.g. molecule binding rates.
1001	QM/MM simulations for prediction of reaction kinetics	Yes	The component is going to be publicly available by the end of the year. Two publications will document the novel software.
765	Subcellular model of timing-dependent reward/dopamine plasticity	No	Model deposited in BioModels database in SBML format: MODEL1603270000, component from SGA1 was used.
766	Integration of subcellular models in single neuron models	No	Multiscale model, component from SGA1, deposited in ModelDB; accession no: 237653). Re-uses components above with IDs 89 and 765. Described in: https://collab.humanbrainproject.eu/#/collab/489/nav/5364

1.2 Data-Driven Scaffold Models to Bootstrap Community Use and Contribution

Life Cycle Model for Brain Models

We formalised a life cycle for modelling artefacts and related data that reconciles the intended goal for structured open and reproducible science, while at the same time not overburdening the model bootstrapping that needs to be flexible in early phases (attached in Annex: Life Cycle Model for Data-Driven Models, and it will be integrated into the HBP's Data Management Plan); see Figure 4. A model classified within a certain life cycle stage may not be fully compliant with all the requirements set forth by the respective phase. This may happen, especially during the introduction of this new Life Cycle Model, or when a model moves from one phase to the next. SP6 management established a process to track this and to prioritise SP6 activities accordingly.

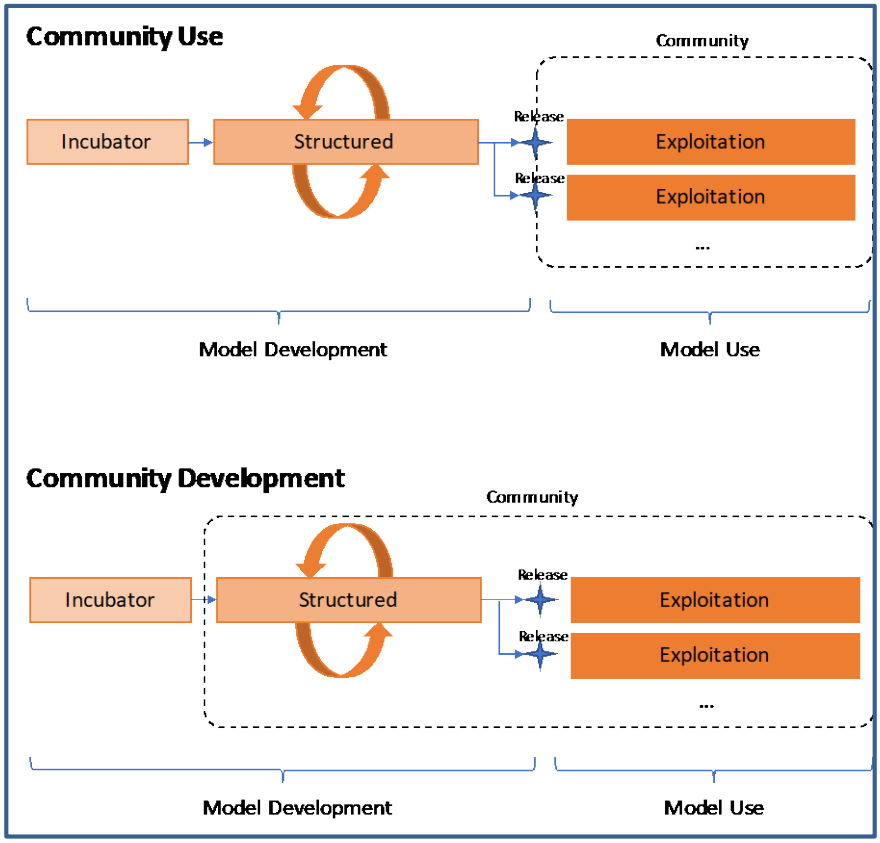

Figure 4: Life Cycle Model for brain models formalised during M13-M24.

Scaffold Single Neuron Models for Human

After the important achievement of the first computational models of human neurons in 2016, several additional advances were accomplished in this phase. On the one hand, a new multi-feature analysis was applied to human L2/3 pyramidal cells revealing two disctinct classes of cells in human, versus a single class of this type of cell in mice (Deitcher *et al.,* 2017). On the other hand, the first detailed compartmental models of dendritic and axonal excitability of human L2/3 pyramidal neurons (including Ca-, Na- and NMDA-spikes) has been developed with detailed models for their synaptic inputs (AMPA- and NMDA-receptors) and passive cable models of their dendritic spines. The modelling of active properties of human neurons is proceeding to adhere to the structured phase of the newly defined HBP modelling life cycle.

Scaffold Cerebellum Model

A first cerebellum scaffold model has been completed. This first scaffold is the result of a new model construction pipeline that consists of two phases, *neuron placement* and *connectivity*. In *neuron placement* the user can define neuronal densities, locating them in space, generate appropriate morphologies of the axons and dendrites. In the *connectivity* phase, the neuron

elements are connected together. The scaffold network model is constructed serially, connecting the three main cerebellar subnetworks, the granular layer, molecular layer and DCN, and inserting the best neuron models available and connecting them accordingly. The simplification of these models has been started (Rössert *et al.,* 2017; Gemignani, Casellato, Pedrocchi and D'Angelo, in progress) and the simplified models are going to be used to make the first functional test on the scaffold network model. The cerebellum modelling is proceeding to adhere to the structured phase of the newly defined HBP modelling life cycle.

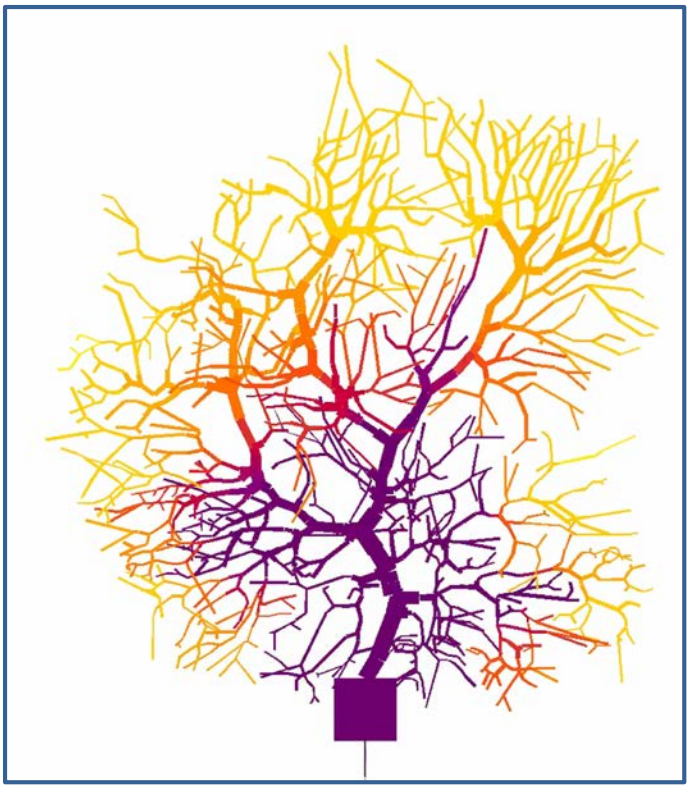

Figure 5: Purkinje cell calcium response to excitatory synaptic activation.

The activation/deactivation of dendritic calcium channels is triggered by spontaneous firing and by an excitatory burst, generated by granule cells and distributed over 100 randomly selected synapses located on spiny dendrites. The colour scheme ranges from purple, where the current is zero, to yellow where it is highest in a soma - apical dendrites fashion.

Scaffold Hippocampus Microcircuit and CA1 Region Model

Significant progress was made in the development of hippocampal single cell and local circuit models. A new generation of optimised rat neuronal models was built and analysed (Migliore *et al.,* 2018, submitted) and the first set of optimised models for the mouse hippocampus was generated. The validation suite for hippocampal neurons was extended with new tests and integrated with the validation framework developed for the Brain Simulation Platform. Optimised neurons were used to build new versions of the rat hippocampal CA1 scaffold circuit model. A new release of this model was finalised in June 2017; a second release has been completed at the end of SGA1, which includes several refinements of the single neuron models, cell placement and synaptic physiology. The simplification of cellular and circuit models is in progress, using the method from Rössert *et al.,* 2017. The hippocampus modelling is proceeding to adhere to the structured phase of the newly defined HBP modelling life cycle, with community modelling involvement.

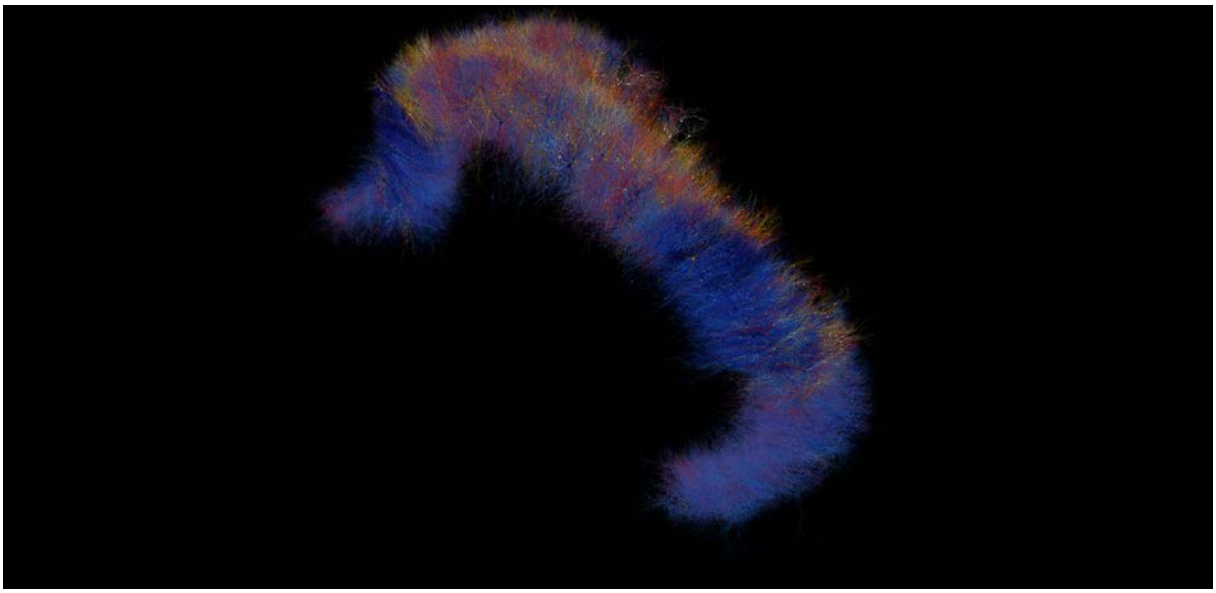

Figure 6: Cellular model of a rat hippocampus CA1 region

Snapshot from a movie showing spontaneous activity generated in the current release of the cellular model of a rat hippocampus CA1 region. For clarity, only a few thousands of the ~800,000 cells composing the entire CA1 region are plotted.

Scaffold Basal Ganglia Model

A first scaffold microcircuit model of the striatum has been achieved. Also, a preliminary code to define separate functional channels in the striatum has been developed. The code allows different connectivity between neurons of the same channel, relative to neurons belonging to different channels. The striatal neurons are placed with a density of 72,000 cells per mm^3. The dendritic ramifications of each cell is based on detailed reconstructions of the two types of medium spiny neurons expressing D1 and D2 receptors, respectively, and with an axonal arbor for each cell. Similarly, fast-spiking interneurons are simulated, as well as cholinergic neurons. The basal ganglia modelling is proceeding to adhere to the structured phase of the newly defined HBP modelling life cycle. A model of a striatal principal neuron has been released to the public.

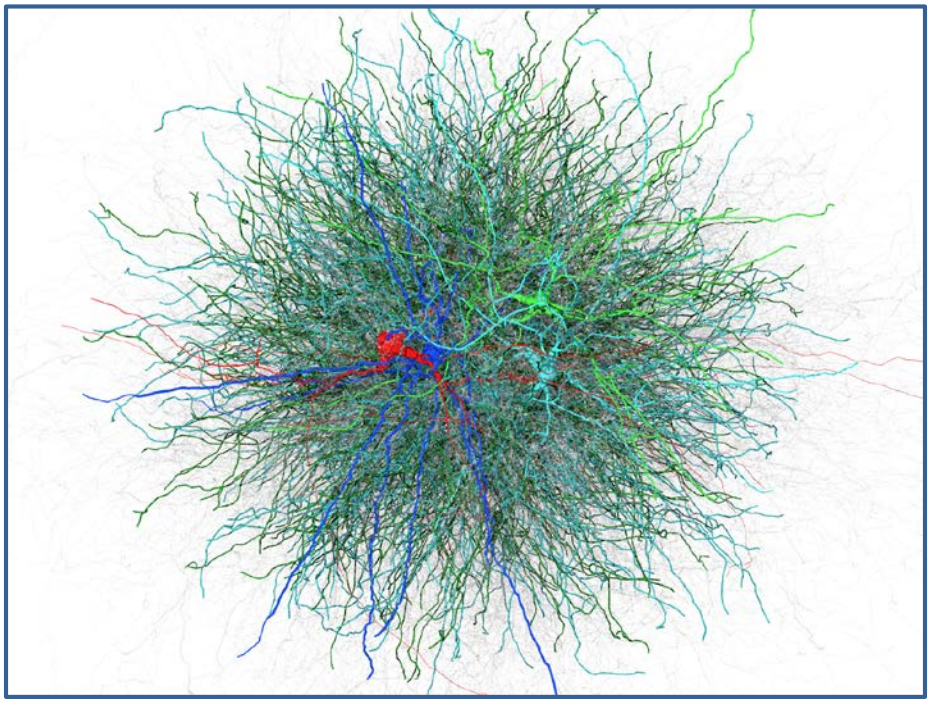

Figure 7: Cell placement for building the striatal microcircuit.

Neurons with their somata placed within a 50 um cube are shown – medium spiny neurons (green and cyan), fast-spiking interneurons (blue), cholinergic interneurons (red) and axons (grey). Cell density is 72,000 neurons per cubic millimetre.

Scaffold Somatosensory Cortex Microcircuit for Mouse

Based on Markram *et al.*, 2015, that laid out a process for reconstructing and simulating a neocortical microcircuit, which was applied to reconstruct a rat microcircuit, a new scaffold microcircuit model of the somatosensory cortex of the mouse has been built. This model combines specific datasets obtained for mouse somatosensory cortex (such as layer height, cell distribution, bouton densities, post-synaptic potential amplitudes), models of neuronal electrophysiology constrained to mouse primary visual cortex data from the Allen Cell Types Database, and datasets that were algorithmically transformed from rat to mouse. As such, it represents a proof of concept of a cross-species data integration strategy. For example, rat morphologies were scaled according to the ratio of heights of the mouse and rat circuits to match mouse proportions, and neurite diameters were transformed to match branch order dependencies of mouse V1 data (Allen Cell Types Database). The microcircuit model features 45,891 neurons (7 hypercolumn modules of ~6555 cells each) and ~116 million synapses. The somatosensory cortex microcircuit modelling is proceeding to adhere to the structured phase of the newly defined HBP modelling life cycle. Initial simulations of local-field-potential and the associated currents have been made available to other partners in the HBP (SP4) researching these topics.

Scaffold Whole Brain Network Level Model for Mouse

In parallel to the aforementioned cellular level models for specific brain regions, a data driven network level model (using point neurons) of an entire mouse brain is pursued, which integrates whole brain datasets, such as the Allen Institute Meso-Scale Connectome into a common space defined by the Allen Brain Mouse Atlas and which is based on the EPFL/BBP Cell Atlas. The most recent addition to this model is the refinement of the thalamo-cortical pathway. This pathway mediates the sensory information from the periphery to the cortex. Several studies have shown that this information is represented both in the thalamus and the somatosensory cortex, which implies direct connections. Based on data from Hunnicutt *et al.*, 2014, we extended the SP6 Whole Mouse Brain reconstruction workflow, creating a detailed map of the thalamic projections as an addition to the model. A first version of this brain model has been integrated into the Neurorobotics Platform. The whole brain modelling is proceeding to adhere to the structured phase of the newly defined HBP modelling life cycle.

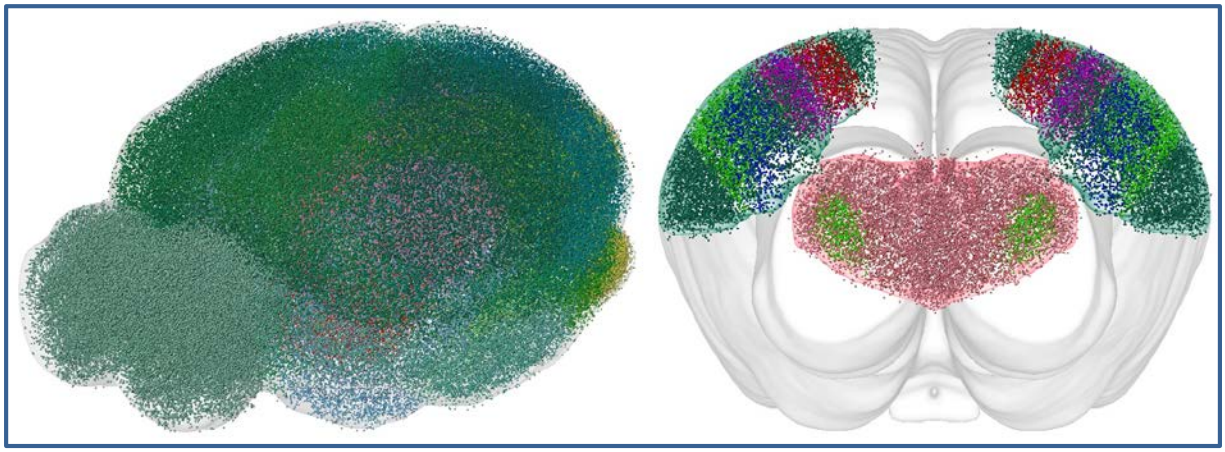

Figure 8: Visualisation of cell placement in whole mouse brain model

Left image, Point neuron mouse brain: This is a 3D representation of the data-driven reconstructed point neuron mouse brain. One percent of the neurons are shown; the colour corresponds to brain regions as defined by the Allen Brain Atlas. Right image, Extract from the brain model: Refinement of the thalamo-cortical regions targeted during SGA1, in particular the VPM-VPL regions of the thalamus and their projection to the somatosensory cortex.

Additional Results from Models in the Incubator Phase

- **Investigation of Generic Properties of Active Dendrites** - New generic insights into the interactions between dendritic NMDA spikes and local dendritic inhibition in principal neurons of neocortex and striatum (using rodent data) were gained; see Figure 9. Such generic insights

are most likely valid also for the quantitative understanding of human neurons. NMDA spikes/plateaus are highly sensitive to dendritic inhibition; sparse, weak inhibition can finely tune synaptic plasticity both locally at the dendritic branch level and globally at the level of the neuron's output. This result is very important since modelling these interactions is key to understanding dendritic biophysics and to properly implement realistic neuronal models of principal neurons in the brain regions studied within the HBP. Model predictions are quite similar in neocortical and striatal principal neurons (Du *et al.*, 2017; Doron *et al.*, 2017). Several of the model predictions were furthermore experimentally verified (Du *et al.*, 2017).

- **Data-Driven Modelling of Ca2+-Dependent Cascades Controlling Synaptic Signalling and Homeostasis** – a Ca2+ cascade was simulated in a dendritic spine with the goal to better understand the role of GABA receptor regulation.
- **Subcellular Signalling Parameters from Molecular Simulation** – in addition to predictions on cAMP signalling described above, similar approaches have been applied to different receptor-ligand complexes.
- **Data-Driven Modelling of G Protein-Coupled Receptor-Dependent Cascades** – in collaboration with external groups, subcellular model predictions have been tested and model components further improved (Yapo *et al.*, 2017; see above).
- **Multiscale Simulations** – dopamine-dependent neuromodulation of medium spiny neurons of the direct pathway of the striatum predicted the role of Kv4.2 for controlling the membrane excitability (Lindroos *et al.*, 2018; see above).

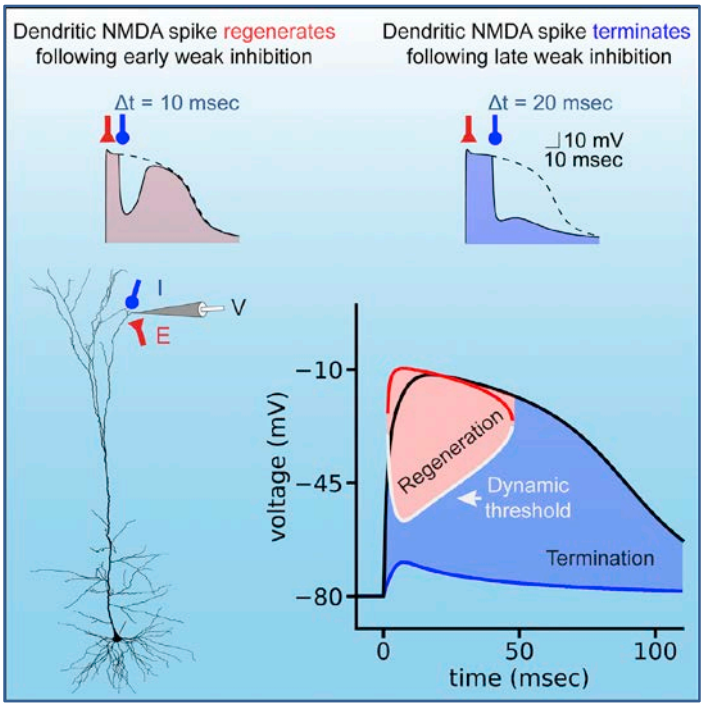

Figure 9: Timed synaptic inhibition shapes NMDA spikes

Timed synaptic inhibition shapes NMDA spikes, influencing local dendritic processing and global I/O properties of cortical neurons. The NMDA spike is a nonlinear dendritic phenomenon involved in synaptic plasticity and in shaping the I/O properties of neurons. Doron *et al.*, 2017 used a theoretical approach to study the fine-tuned and powerful modulation of the NMDA spike by timed synaptic inhibition. They provide a mechanistic explanation for the interaction between timed inhibition and excitation, and explore the implications for dendritic and somatic computations.

1.2.1 Achieved Impact

- A Life Cycle Model for data-driven brain models has been formalised, elaborating a common set of requirements (in terms of integration with the Brain Simulation Platform, BSP) and availability to the community. All data-driven models that are currently used to co-design the

BSP have been transitioned into this new Life Cycle Model making it clear to the community how and when it can engage with the respective modelling activities.

- The aforementioned models allowed us to actively engage multiple communities, e.g.:
  - Through meetings and courses in order to foster applications in neurorobotics, neuromorphic hardware, medical informatics. For example, the Erice School gathered 80 participants on "Multiscale Brain Modelling".
  - In cooperation with the EITN (SP4), a community workshop took place in Paris on 23-24 May 2017 entitled "HBP Hippocamp 2017: Collaborative and Integrative Modelling of Hippocampus". The workshop featured speakers from both the HBP (SPs 1, 4, 6) and the broader community, and in addition to the talks, it included intense discussions on many topics relevant to large-scale collaborative modelling and community convergence.
- The aforementioned models also succeeded to drive the BSP to a level of functionality and modularity that attracts and enables external users. Together with the 1st Simulation Neuroscience MOOC teaching the use of the BSP for the data-driven modelling of single neurons, these dissemination activities are a major source for new registrations to the HBP platforms.
- Peer-reviewed models and respective data have been made available to the community for use, and in several cases models have been made available even before publication e.g. as Use Cases in the Brain Simulation Platform. See Annex: Summary of Dissemination Status of SP6 SGA1 model components and Annex: Summary of Data use in SP6 SGA1 model components for details.
- Publications during M13-M24:
  - Deitcher, Y., Eyal, G., Kanari, L., Verhoog, M. B., Atenekeng Kahou, G. A., Mansvelder, H. D., de Kock, C. P. J., & Segev, I. (2017). Comprehensive Morpho-Electrotonic Analysis Shows 2 Distinct Classes of L2 and L3 Pyramidal Neurons in Human Temporal Cortex. *Cerebral Cortex, 27*(11), 5398-5414. doi:10.1093/cercor/bhx226
  - Doron, M., Chindemi, G., Muller, E., Markram, H., & Segev, I. (2017). Timed Synaptic Inhibition Shapes NMDA Spikes, Influencing Local Dendritic Processing and Global I/O Properties of Cortical Neurons. *Cell Rep, 21*(6), 1550-1561. doi:10.1016/j.celrep.2017.10.035
  - Du, K., Wu, Y. W., Lindroos, R., Liu, Y., Rozsa, B., Katona, G., Ding, J. B., & Kotaleski, J. H. (2017). Cell-type-specific inhibition of the dendritic plateau potential in striatal spiny projection neurons. *Proc Natl Acad Sci U S A, 114*(36), E7612-E7621. doi:10.1073/pnas.1704893114
  - Gal, E., London, M., Globerson, A., Ramaswamy, S., Reimann, M. W., Muller, E., Markram, H., & Segev, I. (2017). Rich cell-type-specific network topology in neocortical microcircuitry. *Nature Neuroscience, 20*(7), 1004-1013. doi:10.1038/nn.4576
  - Gandolfi, D., Cerri, S., Mapelli, J., Polimeni, M., Tritto, S., Fuzzati-Armentero, M. T., Bigiani, A., Blandini, F., Mapelli, L., & D'Angelo, E. (2017). Activation of the CREB/c-Fos Pathway during Long-Term Synaptic Plasticity in the Cerebellum Granular Layer. *Front Cell Neurosci, 11*, 184. doi:10.3389/fncel.2017.00184
  - Grillner, S., von Twickel, A., & Robertson, B. (2017). The blueprint of the vertebrate forebrain - With special reference to the habenulae. *Seminars in Cell & Developmental Biology*. doi:10.1016/j.semcdb.2017.10.023
  - Masoli, S., & D'Angelo, E. (2017). Synaptic Activation of a Detailed Purkinje Cell Model Predicts Voltage-Dependent Control of Burst-Pause Responses in Active Dendrites. *Front Cell Neurosci, 11*, 278. doi:10.3389/fncel.2017.00278

- Masoli, S., Rizza, M. F., Sgritta, M., Van Geit, W., Schurmann, F., & D'Angelo, E. (2017). Single Neuron Optimization as a Basis for Accurate Biophysical Modeling: The Case of Cerebellar Granule Cells. *Front Cell Neurosci, 11*, 71. doi:10.3389/fncel.2017.00071
- Mercer, A., & Thomson, A. M. (2017). Cornu Ammonis Regions-Antecedents of Cortical Layers? *Front Neuroanat, 11*, 83. doi:10.3389/fnana.2017.00083
- Palesi, F., De Rinaldis, A., Castellazzi, G., Calamante, F., Muhlert, N., Chard, D., Tournier, J. D., Magenes, G., D'Angelo, E., & Gandini Wheeler-Kingshott, C. A. M. (2017). Contralateral cortico-ponto-cerebellar pathways reconstruction in humans in vivo: implications for reciprocal cerebro-cerebellar structural connectivity in motor and non-motor areas. *Sci Rep, 7*(1), 12841. doi:10.1038/s41598-017-13079-8
- Parmar, K., Stadelmann, C., Rocca, M. A., Langdon, D., D'Angelo, E., D'Souza, M., . . . Magnims study group (2018). The role of the cerebellum in multiple sclerosis-150 years after Charcot. *Neuroscience & Biobehavioral Reviews*. doi:10.1016/j.neubiorev.2018.02.012
- Perez-Fernandez, J., Kardamakis, A. A., Suzuki, D. G., Robertson, B., & Grillner, S. (2017). Direct Dopaminergic Projections from the SNc Modulate Visuomotor Transformation in the Lamprey Tectum. *Neuron, 96*(4), 910-924 e915. doi:10.1016/j.neuron.2017.09.051
- Suryanarayana, S. M., Robertson, B., Wallen, P., & Grillner, S. (2017). The Lamprey Pallium Provides a Blueprint of the Mammalian Layered Cortex. *Current Biology, 27*(21), 3264-3277 e3265. doi:10.1016/j.cub.2017.09.034
- Zuccolo, E., Lim, D., Kheder, D. A., Perna, A., Catarsi, P., Botta, L., . . . D'Angelo, E., Guerra, G., & Moccia, F. (2017). Acetylcholine induces intracellular Ca(2+) oscillations and nitric oxide release in mouse brain endothelial cells. *Cell Calcium, 66*, 33-47. doi:10.1016/j.ceca.2017.06.003

1.2.2 Component Dependencies

Table 2

Component dependencies for Key Result "Data-driven scaffold models to bootstrap community use and contribution".

Component ID	Component Name	HBP Internal	Comment
1029	Models of nonlinear human neurons	Yes	Life cycle phase: structured Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/human-neurons/ Link to model inventory (R3b): https://collab.humanbrainproject.eu/#/collab/9747/nav/73393 Link to public Collab: https://collab.humanbrainproject.eu/#/collab/528/nav/4669
827, 3023	Cerebellar scaffold model (and cerebellar cell models)	Yes	Life cycle phase: structured Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/cerebellum/ Link to model inventory (R3b): https://collab.humanbrainproject.eu/#/collab/9136/nav/69076 Link to public cerebellum Collab: https://collab.humanbrainproject.eu/#/collab/9135/nav/69068

			Link to public cerebellum microcircuit Collab: https://collab.humanbrainproject.eu/#/collab/8124/nav/61648
891	Circuit model of area CA1 of the rat hippocampus	Yes	Life cycle phase: structured Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/hippocampus/ Link to model inventory (R3b): https://collab.humanbrainproject.eu/#/collab/9821/nav/73921
972	Scaffold basal ganglia model (striatum)	Yes	Life cycle phase: structured Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/basal-ganglia/ Link to model inventory (R3b): https://collab.humanbrainproject.eu/#/collab/7840/nav/59620 Link to public Collab: https://collab.humanbrainproject.eu/#/collab/9102/nav/68835
3011	Scaffold somatosensory cortex microcircuit (mouse)	Yes	Life cycle phase: structured Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/mouse-sscx/ Link to model inventory (R3b): https://collab.humanbrainproject.eu/#/collab/9138/nav/69095 Link to public Collab: https://collab.humanbrainproject.eu/#/collab/9137/nav/69090
827	Whole brain network-level model for mouse	Yes	Life cycle phase: structured Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/whole-mouse-brain-model/ Link to model inventory (R3b): https://collab.humanbrainproject.eu/#/collab/9875/nav/74309
1137	Data-driven modelling of Ca2+-dependent cascades controlling synaptic signalling and homeostasis	Yes	Life cycle phase: incubator Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/inhibition-and-calcium-cascades/ Link to model inventory (R3a): https://collab.humanbrainproject.eu/#/collab/9141/nav/69119
559	Subcellular signalling parameters from molecular simulation	Yes	Life cycle phase: incubator Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/molecular-models/ Link to model inventory (R3a): https://collab.humanbrainproject.eu/#/collab/9104/nav/68847
762	Data-driven modelling of G protein-coupled	Yes	Life cycle phase: incubator

	receptor-dependent cascades		Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/signalling-cascades Link to model inventory (R3a): https://collab.humanbrainproject.eu/#/collab/9323/nav/70371 Link to public Collabs: CaMKII: https://collab.humanbrainproject.eu/#/collab/9065/nav/68534 MGLuRd: https://collab.humanbrainproject.eu/#/collab/9064/nav/68529 Workflow: https://collab.humanbrainproject.eu/#/collab/9148/nav/69157 Modelling related to neuromodulation: https://collab.humanbrainproject.eu/#/collab/489/nav/5364
766	Multiscale modelling (integration of subcellular models in single neuron models)	Yes	Life cycle phase: incubator Link to HBP public website (R1): https://www.humanbrainproject.eu/en/brain-simulation/multiscale-modelling Link to model inventory (R3a): https://collab.humanbrainproject.eu/#/collab/9475/nav/71489 Link to public Collab: https://collab.humanbrainproject.eu/#/collab/489/nav/5364

1.3 Advanced Tools for Data-Driven Modelling and Simulation

The Brain Simulation Platform (BSP) is based on a variety of advanced software tools for the generation and simulation of models at different scales. Where available, the BSP builds on best-in-class community software and contributes to its extension and maturation. At the same time, a major contribution of the BSP is to provide a tightly integrated ecosystem of workflows allowing end-to-end modelling at scale, and necessary functionality not found in community software is being co-developed with the science drivers. These tools, currently at TRL 6-7, become available through the BSP, furthermore, their open-sourcing is pursued, thus benefitting the computational neuroscience community in multiple ways.

Advanced Single Cell Modelling Workflow

One of the core scientific workflows for detailed data-driven modelling of brain tissue is the generation of accurate biophysical models of individual cells. While the building of individual cell models for a variety of brain regions was successfully addressed previously in the HBP (BluePyOpt), the newly achieved result is that the pre- and post-processing of these electrical models for the use in large-scale brain region models has been substantially improved during the last year.

On the pre-processing side, several new features have been integrated in the open-source software for morphology analysis and in the analysis of electrical traces, which are the pre-requisite for effective single cell modelling. For example, the morphology analysis tool (NeuroM) now features an improved cut plane analysis and improved tutorials; for the analysis of electrical traces, new feature extraction algorithms have been added and new software has been devised that allows feature analyses over a large number of traces to e.g. extract population features.

On the post-processing side, there have been two major improvements. First, the focus was on maturing a pre-existing software tool (BluePyMM) that allows to generalise an individual electrical cell model into any number of morphological variants. This functionality now has become a core workflow step for the hippocampus modelling. Second, the models resulting from the single cell building workflow can now be automatically validated against relevant experimental data, thanks to the development of a model validation framework and of several cell type specific test suites.

Improved Circuit Building Workflow

In co-design with the modelling of diverse and larger brain areas, the circuit building workflow has been extended to include i) atlas-aware positioning of cells (based on volumetric density profiles), ii) atlas-aware placement of cells defining the orientation in space, and iii) atlas-aware projection and connectivity algorithms. This now enables the building of curved brain regions and a variety of areas including nuclei. This workflow is implemented by extending the pre-existing software tools, BrainBuilder, placement hints and projectionizer.

Scale-Out and Usability of Community Simulators

Simulators useful for the molecular, subcellular, cellular and network levels have been significantly improved.

SDA - Development of tools for estimating kinetic and thermodynamic parameters for constraining neuronal signalling cascades. The software has been updated to include an adaptive resolution solute model that is able to reproduce the accuracy of the full resolution model, in the important regions of a simulation, while reducing the computational cost by up to 90%. Additionally, a model for a Brownian dynamics treatment of diffusion near confining surfaces has been tested and validated, and is being integrated in the SDA simulator.

STEPS – Together with the community-code owners of the simulator STEPS, the Okinawa Institute of Science and Technology (OIST), the main focus was to make the tool as easy as possible to use by the HBP scientists. As such, the documentation of the tool has been reviewed and updated, the tool has been deployed on the majority of the HBP supercomputers via the Nix package manager. To further ease its use, the tool has already been packaged using Docker container technology for easy delivery and fully interfaced with the Jupyter notebook. On the scientific development side, several updates of the distributed Gillepsie algorithms have been carried out to further increase the scalability of the simulator, enabling it to model a full neuron. The STEPS simulator is now deployed as part of the Brain Simulation Platform's foundation software on the various HPAC HPC systems. Its scalability has been considerably increased, so that scientists can start modelling very large models up to a full neuron, using a coupled Reaction-Diffusion and eField solvers.

NEURON/CoreNeuron – Major memory saving and massive scale-out has been previously achieved in the CoreNeuron software that contains the core elements of the more general NEURON simulator, necessary for simulations at scale. As expected, CoreNeuron software was released on GitHub in 2017, it includes 688 software commits provided by 10 contributors as of 1 February 2017. In addition to the milestones described here, a number of functionalities have been added to support scientific use case requests, making CoreNeuron ready for scientific exploitation and discovery. CoreNeuron is now deployed on a majority of the HBP HPC supercomputers via Nix software packaging system and available to users through the BSP.

NEST – In the NEST simulator, a new core simulator technology has been developed that makes the administrative data overhead independent of the number of parallel processes used in a simulation. While the previous technology had manageable overheads up to some 10^6 parallel processes, the overheads became infeasible for larger systems. Our achievements have eliminated this memory wall. At the same time, scaling behaviour for large simulations has been significantly improved: simulations not only require less memory, they also run faster. For the usability of NEST, the NEST Instrumentation App has been improved, which provides a graphical user interface for connecting stimulation and recording devices to specific neuron populations, and likewise selecting populations for recording spike and membrane recordings, written in JavaScript for Collaboratory integration.

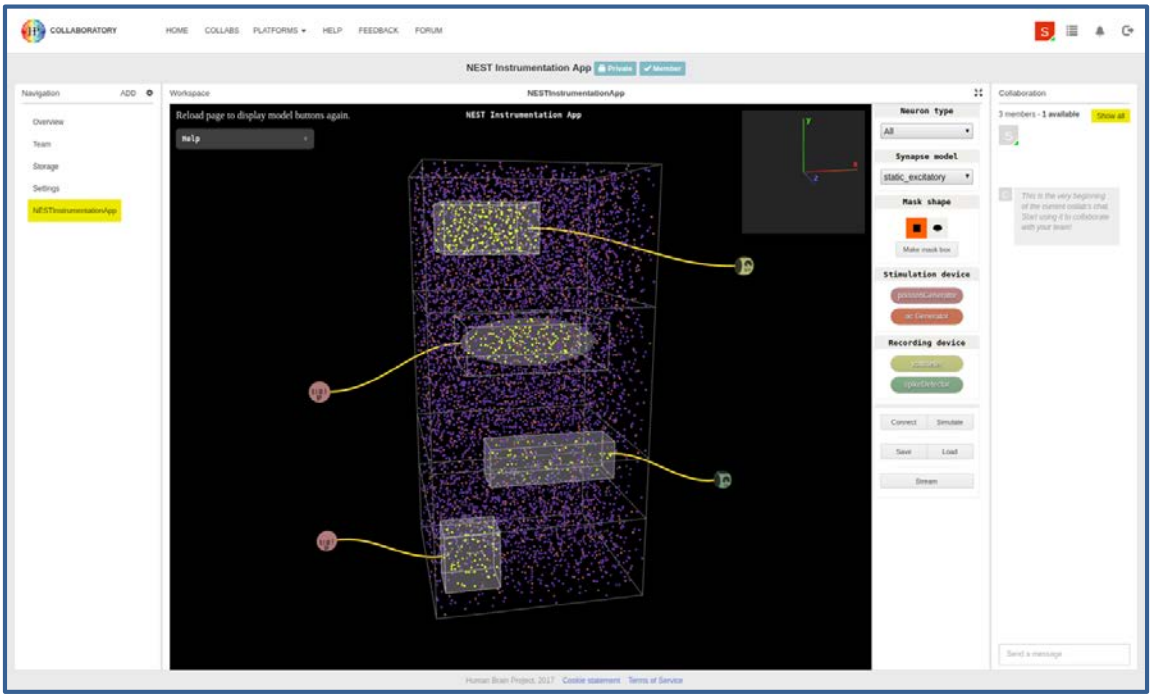

Figure 10: NEST instrumentation app in the HBP Collaboratory

This image illustrates a stimulation and recording configuration for a simplified model of a cortical microcolumn (Potjans-Diesmann model). Two stimulating devices (left), each providing Poisson spike-train input, are connected to an ellipsoidal neuronal population in layer 4 and a cubic population in layer 6, respectively. Membrane potential traces are recorded from a cuboid population in layer 2/3 and spike trains from a cuboid population in layer 5.

Community Formats

Key progress has been achieved in this period with respect to harmonisation of scaffold model representations inside the BSP and promoting interoperability with modelling software ecosystems in SP9 and SP10, and the community at large. In particular, SP6 has played a leading role in the development of a new, high-performance file format for large-scale circuit models at cellular and network levels, being co-developed as a collaboration between the partner EPFL/BBP and the Allen Institute for Brain Science. To support the use of this model format in SP9 and SP10, prototype support in the PyNN unifying simulator API has been developed.

1.3.1 Achieved Impact

- Standardised deployment of simulators on HBP HPAC computing systems using the Nix package manager.
- Improved scalability and usability of open-source simulators that immediately benefit the entire computational neuroscience community.
  - Release of SDA: 7.2.2 (July 2017) - https://www.h-its.org/downloads/sda7
  - Release of STEPS: 3.3 (April 2018) - https://github.com/CNS-OIST/STEPS
  - Release of CoreNeuron: 0.9.1 (February 2018) - https://github.com/BlueBrain/CoreNeuron
  - Release of NEST: 2.14.0 (October 2017) - http://github.com/nest/nest-simulator; branch with 5g kernel: https://github.com/jakobj/nest-simulator/tree/5g
- Improved software ecosystem for the generation of single neuron models at scale, i.e. when many cells need to be modelled e.g. as the foundation of a brain region model, and for the generation of generalised curved brain regions. These improvements directly enable collaborative modelling, such as done for the hippocampus led by the HBP and engaging an outside community.

- Improved open-source tools for morphology and electrical trace analysis that increase usability and thus adoption; this also forms the basis for the successful massively-open online course that was released using the BSP. For more details on the open sourcing strategy, please see Annex: Open Sourcing Strategy.
- Harmonisation of model representations used by the tools underpinning the BSP and the Allen Institute for Brain Science. The format has a name "SONATA" and will serve to maintain synergies between the tools and workflows developed by the HBP and the Allen Institute, and likely will attract a larger community around it. The working URL is https://github.com/BlueBrain/sonata
- Publications during M13-M24:
  - Ippen, T., Eppler, J. M., Plesser, H. E., & Diesmann, M. (2017). Constructing Neuronal Network Models in Massively Parallel Environments. *Front Neuroinform, 11*, 30. doi:10.3389/fninf.2017.00030
  - Jordan, J., Ippen, T., Helias, M., Kitayama, I., Sato, M., Igarashi, J., . . . Diesmann, M., & Kunkel, S. (2018).Extremely Scalable Spiking Neuronal Network Simulation Code: From Laptops to Exascale Computers. *Front Neuroinform, 12*, 2. doi:10.3389/fninf.2018.00002
  - Plesser, H. E. (2017). Reproducibility vs. Replicability: A Brief History of a Confused Terminology. *Front Neuroinform, 11*, 76. doi:10.3389/fninf.2017.00076
  - Schmidt, M., Bakker, R., Hilgetag, C. C., Diesmann, M., & van Albada, S. J. (2017). Multi-scale account of the network structure of macaque visual cortex. *Brain Struct Funct*. doi:10.1007/s00429-017-1554-4

1.3.2 Component Dependencies

Table 3

Component dependencies for Key Result "Advanced tools for data-driven modelling and simulation".

Component ID	Component Name	HBP Internal	Comment
193	NeuroM	No	Open-source software for analysis of single cell morphologies.
203	eFEL	No	Open-source software for analysis of electrical traces from experimental recordings or simulated models.
202	BluePyOpt	No	Open-source software for single cell electrical model building.
3018	BluePyEFE	Yes	Software for the feature extraction from a large number of traces. Open-sourcing is in preparation and will be done as soon as the supportive publication is ready.
3019	BluePyMM	(Yes)	Software for the generalisation of electrical models to morphological variants. Open-sourcing is in preparation and will be done as soon as the supportive publication is ready.
196	BrainBuilder	Yes	Software for defining cell properties and location based on atlas volumetric data.
3020	Placement hints	Yes	Software for defining cell orientation and placement depending on spatial constraints in an atlas-aware volumetric space.
195	Morphology repair and diversification framework	Yes	Software for repairing morphology reconstruction artefacts and generating a diversified population of neuron morphologies.

209	NEST - The neural simulation tool	No	Open-source simulator for large-scale networks of point neurons.
207	CoreNeuron	No	Optimised version of NEURON simulator used for empirically-based simulations of neurons and networks of neurons.
208	NEURON	No	Open-source simulator for single cells to large-scale networks of morphologically-detailed neurons.
206	STEPS	No	Open-source simulator for single compartment to large-scale reaction-diffusion models.
210	SDA	No	Simulator for Brownian dynamics simulations of the diffusional association in a continuum aqueous solvent. Freely available to academic researchers.
1680	Python client for the Model Validation service	No	Python library for structured model validation tests. Development brought forward from SGA2.

1.4 Brain Simulation Platform Version 2 - Web Accessible Suite of Highly Integrated Model Building, Simulation and Validation Tools

We have created a suite of highly integrated tools targeting average users with little technical background. They are easily accessible from the web and implemented as intuitive use case-driven interfaces, allowing to recreate previous models or use them as a starting point for new models and experiments; users are seamlessly connected to HPC systems or to massive open online course platforms, allowing easy training at different levels. The tool for single cell model building and that for *in silico* microcircuit experimentation, in particular, are unique in the field. They offer services, flexibility, usability and robustness that are way beyond the state of the art in the field; see Figure 11. On the technical side, a deeper integration with the Neuroinformatics Platform has been achieved with respect to the ability to register model artefacts in its Knowledge Graph, as well as with the HPAC Platform with respect to a structured packaging of the Brain Simulation Platform's foundation software and its deployment to various HPC systems.

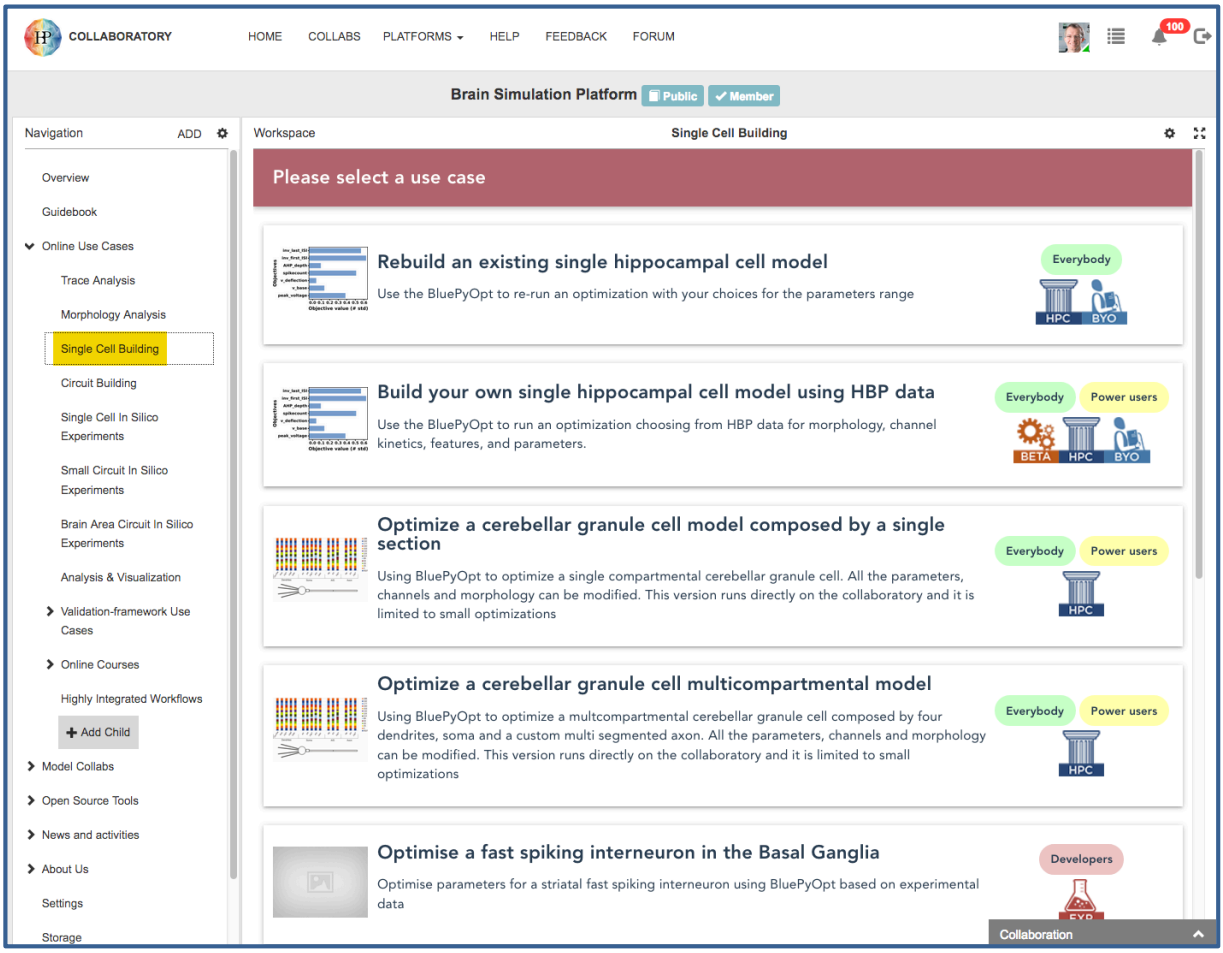

Figure 11: Screenshot of version 2 of the Brain Simulation Platform.

Single Cell Model Builder and *In Silico* Single Cell Experimentation

The Single Cell Model Builder allows an average user to build, through the Collaboratory, a morphologically and biophysically accurate neuron model using a complete and self-consistent pipeline. The process involves electrophysiological feature extraction from voltage traces (either recorded or simulated), model parameter optimisation and *in silico* experiments using the optimised model cell (Neuron as a Service); see Figure 12.

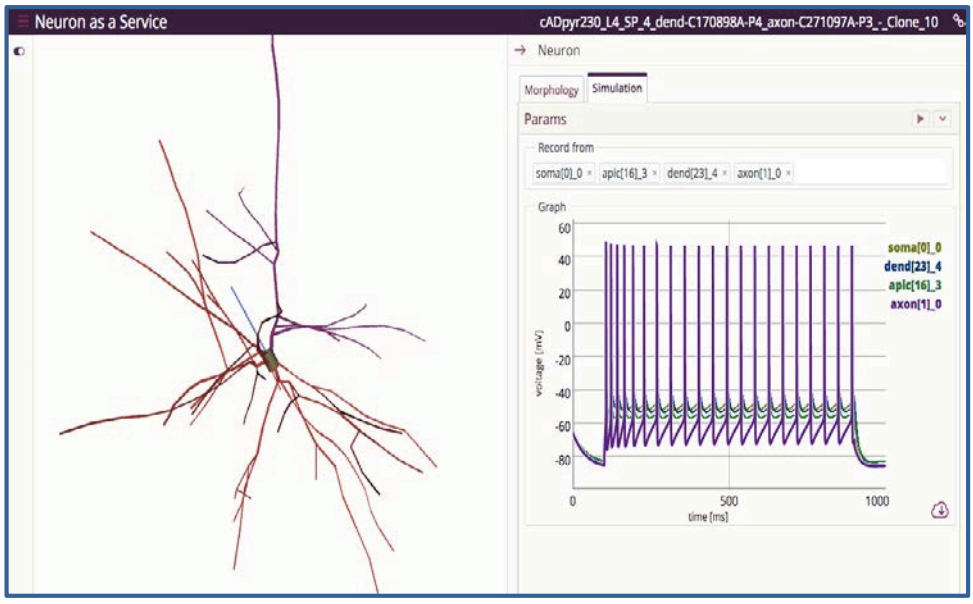

Figure 12: Screenshot of the Brain Simulation Platform's Neuron as a Service functionality.

In Silico Microcircuit Experimentation

The *in silico* microcircuit experimentation allows a user to build, through the Collaboratory, an experiment against a biophysically detailed model of a microcircuit of the hippocampus; see Figure 13. The process involves several steps, in which the user is freed from most of the details of the complex workflow going on behind the scene, to setting up a simulation environment, configuring the proper files, transferring files between sites and configuring/launching HPC jobs.

These tools can be effectively exploited by a wide range of potential users, from students interested in learning modelling, to experimentalists interested in building a realistic model of their own cell or circuit, to more experienced modellers interested to collaborate with HBP partners in using or building upon data and models already available in the HBP Model Catalog.

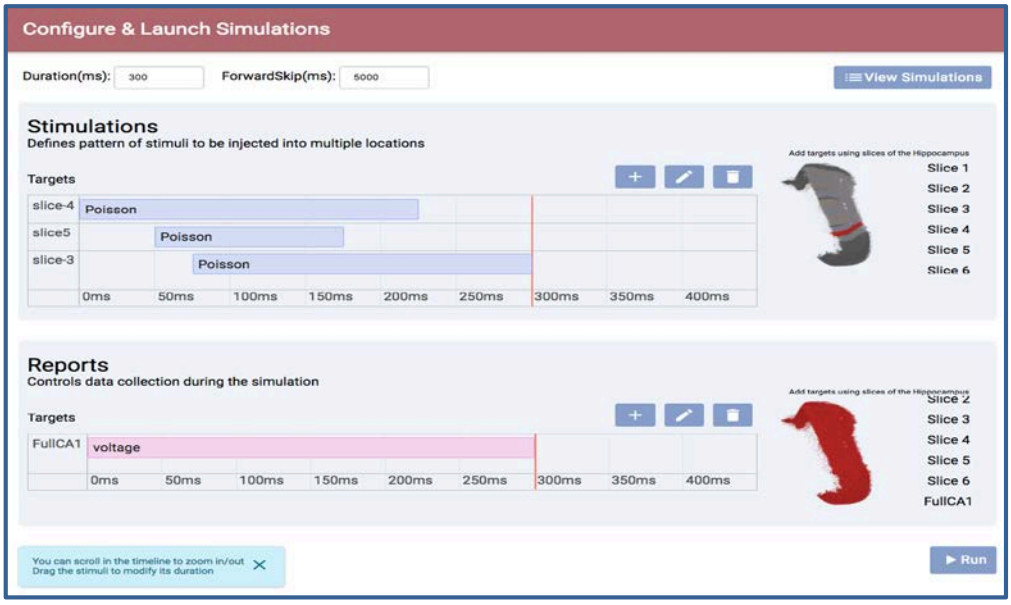

Figure 13: Screenshot of the Brain Simulation Platform's Experiment Builder.

Model Catalog and Validation Framework

Automated model validation is an important Brain Simulation Platform feature to support a transparent and reproducible community process for data-driven modelling. During the last 12 months, two new Collaboratory apps, the Model Catalog app and the Model Validation app, and a Python client (https://pypi.python.org/pypi/hbp_validation_framework/0.3.0) were developed and released, based on feedback from early users of the prototypes.

Figure 14: Results of running a validation test, as viewed in the Model Validation app.

1.4.1 Achieved Impact

- As of June 2017, version 2 of the Brain Simulation Platform (https://collab.humanbrainproject.eu/#/collab/1655/nav/28538) is available to the community, providing a novel modular and use case-oriented logic. In order to track numerical impact, we introduced systematic tracking with version 2 of the Platform. Since 16 June 2017 (and as of 23 March 2018), we see the following adoption:
- Cloned use cases: 6915
  - Unique users (who cloned use cases): 403
  - Number of use cases added to an existing Collab: 2200
  - Number of use cases cloned to a newly created Collab: 4715
- The new modular version of the Brain Simulation Platform has enabled novel teaching on simulation neuroscience. On the one hand, it is the foundation of the MOOC on "Simulation neuroscience: reconstruction of a single neuron" (see Key Result in Section 1.5). On the other hand, the 14-week EPFL master-level course "In silico Neuroscience" (BIOENG-450, http://edu.epfl.ch/coursebook/en/in-silico-neuroscience-BIOENG-450) has been updated to perform its tutorial using the HBP Collaboratory and Brain Simulation Platform.
- The release of the Validation Framework tools has allowed the scaffold model teams to begin systematically integrating validation tests into their workflows. The GUI and Python tools allow

a user to find and run validation tests relevant to their model, register the results and to contribute new tests. This is an important prerequisite for community engagement, as it became clear in outreach events that model adoption by the community will heavily depend on effectively communicating validation results of the model, and thus transmitting trust.

- Guided by the feedback from the hippocampus community outreach events, preliminary work has been done on generating validation tests for the hippocampus scaffold model developed in SP6 from data available from community neuroinformatics resources, specifically http://hippocampome.org and http://mariannebezaire.com.
- Based on a key result of SP5, namely the HBP Knowledge Graph leveraging the open-source Blue Brain Nexus technology, SP6 was able to synergistically develop schemas for deep integration with the HBP Knowledge Graph for modelling artefacts required by the Brain Simulation Platform; these schemas are made available to the community under: https://github.com/INCF/neuroshapes/tree/master/modules/simulation/src/main/resources/schemas/neurosciencegraph/simulation

1.4.2 Component Dependencies

Table 4

Component dependencies for Key Result "Brain Simulation Platform version 2 - web accessible suite of highly integrated model building, simulation and validation tools".

Component ID	Component Name	HBP Internal	Comment
946	Engineering support to build data-driven models	No	This component provides a user-friendly interface to allow users an easy extraction of electrophysiological activity features, needed for data-driven model construction.
994	Web hosting, deployment, monitoring and updating of platform services for data-driven models	Yes	This component provides the services needed to deploy, monitor, update and host the web applications developed for support to data-driven models.
953	Brain Simulation Platform access	Yes	This component provides a user-friendly interface to access the Brain Simulation Platform services.
947	Support of open-source tools for configuration of data-driven model	No	This component will provide a user-friendly interface to configure and launch optimisation processes on remote HPC systems.
3014	Neuron as a Service	Yes	A web graphical user interface to experiment with a single cell neuron model.
3015	Bsp-usecase-wizard	No	This component initialises the Collabs created for the students with the necessary notebooks for the exercises; open-sourcing is underway and will be completed before M24.
213	JS Simulation Configuration	No	A web component to configure simulation on a detailed circuit model using Neuron.
3013	Model Catalog web app	No	Collaboratory app for searching, viewing, creating and editing information about models, and registering model code for model validation experiments.

720	Model validation test suites	Yes	A collection of Python libraries implementing validation tests for different model types and brain regions. Libraries currently include HippoUnit, CerebUnit, BasalUnit, MorphoUnit and NetworkUnit.
721	Model Validation Service	No	Web service giving access to catalogs of models and validation tests, and to a database of test results.
722	Model validation web app	No	Browser app for searching, browsing, creating and editing model validation tests, and for visualisation of validation test results.

1.5 1st Massive Open Online Course on Simulation Neuroscience deployed using HBP's Collaboratory and Brain Simulation Platform

A major result in this period is the successful deployment of a first massive open online course (MOOC) on "Simulation neuroscience: reconstruction of a single neuron" that combines the power of worldwide digital learning platforms (edX.org) with the HBP's Collaboratory and Brain Simulation Platform (BSP). Not only does this achievement provide a path for the effective introduction of advanced brain modelling capabilities to students around the world and the research community at large, but it also represents a novel way of integrating practical hands-on learning (learning the skill by doing) into this novel type of teaching. The resounding success of this first course makes this a prime example of successful outreach and will represent a major pillar of SP6's outreach strategy going forward. The coupling of the HBP Collaboratory and Brain Simulation Platform with the online learning platform (see Figure 15), has been made possible by developing specific glue components, and by the re-worked BSP that is now more modular, allowing users to easily take any BSP online use case as a starting point for their work.

The course is a 6-week course, free-of-charge and self-paced. It has ~700min of lectures and tutorials, practice/graded quizzes, practice/graded assignments using the HBP Collaboratory. Through partner EPFL it is possible to obtain a certificate. A first beta test with a restricted number of attendees (250) was launched in June 2017 and a worldwide public launch on edX.org was done in November 2017.

This key result goes beyond the originally planned and committed Work Plan. The *development* of the MOOC was achieved through substantial in-kind contribution by partner EPFL/BBP, stemming from a donation to partner EPFL/BBP. The deployment was made possible through an intense collaboration with several partners within the HBP consortium (SP5 and SP7), to make the necessary integration with the HBP Collaboratory Framework.

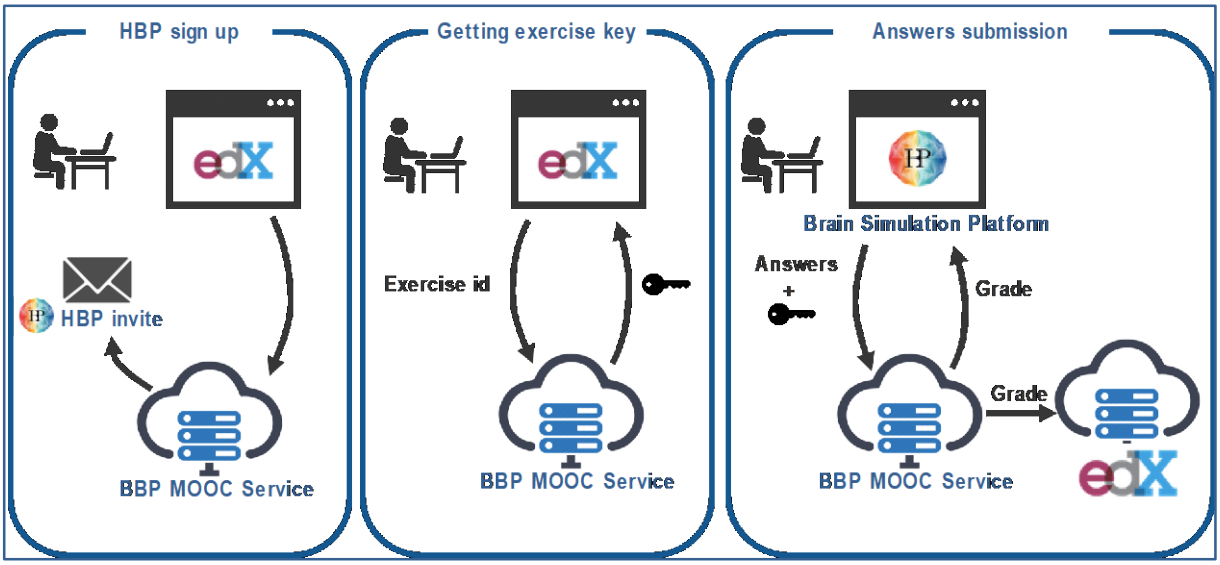

Figure 15: Schematic of linking the edX.org with the HBP Collaboratory

Schematic of the underlying technical components that were developed for linking a worldwide MOOC platform (edX.org) with the HBP's Collaboratory and Brain Simulation Platform that allows a seamless integration of the lecture and the exercise components.

1.5.1 Achieved Impact

- Successfully linked the Brain Simulation Platform with the worldwide platform for online eduction (edX.org) by having deployed a first massive open online course on "Simulation neuroscience: reconstruction of a single neuron" that links a worldwide digital learning platform with the interactive access to advanced modelling and simulation capabilities https://www.edx.org/course/simulation-neuroscience-epflx-simneurox
- Beta release in June 2017 was limited to 250 inscriptions and led to 165 active learners; worldwide launch in November 2017 led to ~6,000 inscriptions (currently about ~100 new inscriptions/week) and ~500 active learners as of March 2018, leading to >230 active users in the HBP Collaboratory from the MOOC alone.

1.5.2 Component Dependencies

Table 5

Component dependencies for Key Result "1st massively-open online course on simulation neuroscience deployed using HBP's Collaboratory and the Brain Simulation Platform".

Component ID	Component Name	HBP Internal	Comment
193	NeuroM	No	Using this software is part of the exercises.
202	BluePyOpt	No	Using this software is part of the exercises.
203	eFEL	No	Using this software is part of the exercises.
3015	bsp-usecase-wizard	No	This component initialises the Collabs created for the students with the necessary notebooks for the exercises; open-sourcing is underway and will be completed before M24.
3017	MOOC neurons and synapses 2017	No	A public GitHub repository containing all the notebooks needed for the exercises.

3016	MOOC service	Yes	A web service managing the submission of answers to the MOOC exercises and the interaction with the EdX platform.

2. Component Details

The following is a list of the newly released internal *software* components for this Deliverable. For a list of *model* components, please see Section 1.2.2 and the online Model Catalog: https://collab.humanbrainproject.eu/#/collab/1655/nav/75901.

2.1 BluePyEFE

Field Name	Field Content	Additional Information
ID	3018	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	A pipeline to extract electrophysiological features from a population of traces	
Latest Release	0.0.1	2018-01-19
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Unchecked	
Validation – Users	Yes	Internal Users: Luca Bologna
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Closed source, contact software owner	
Component Access URL	https://bbpcode.epfl.ch/code/analysis/BluePyEfe	
Technical documentation URL		
Usage documentation URL		
Component dissemination material URL		

2.2 BluePyMM

Field Name	Field Content	Additional Information
ID	3019	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	An electrical model generalisation and validation pipeline	
Latest Release	0.6	2018-03-27
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Unchecked	
Validation – Users	Yes	Internal user: Carmen Iupascu
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	LGPLv2/LGPLv3 (in preparation)	
Component Access URL	https://github.com/BlueBrain/BluePyMM	
Technical documentation URL		
Usage documentation URL	https://github.com/BlueBrain/BluePyMM/blob/master/notebook/BluePyMM.ipynb	
Component dissemination material URL		

2.3 BluePyOpt

Field Name	Field Content	Additional Information
ID	202	
Component Type	Software	
Contact	COURCOL, Jean-Denis	

Component Description	The Blue Brain Python Optimisation Library (BluePyOpt) is an extensible framework for data-driven model parameter optimisation that wraps and standardises several existing open-source tools.	
Latest Release	1.6	10/2017
TRL	9	
Location	Data hosted by other non-HBP 3rd party	
Format	Software	
Curation Status	Not applicable	
Validation - QC	Pass	QA Owner: Alexander Dietz
Validation – Users	Yes	External users: Used by 100+ users in the single cell modelling MOOC
Validation – Publications	Yes	https://doi.org/10.3389/fninf.2016.00017
Privacy Constraints	No Privacy Constraint	
Sharing	Anonymous	
License	LGPLv3	
Component Access URL	https://github.com/BlueBrain/BluePyOpt	
Technical documentation URL	http://bluepyopt.readthedocs.io/en/latest/	
Usage documentation URL	http://bluepyopt.readthedocs.io/en/latest/	
Component dissemination material URL	https://doi.org/10.3389/fninf.2016.00017	

2.4 BrainBuilder

Field Name	Field Content	Additional Information
ID	196	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	A component to build circuit and brain region based on volumetric atlas	
Latest Release	0.5.10	2018-03-06
TRL	3	
Location	data hosted by task providing dataset	

Format	Software	
Curation Status	Not applicable	
Validation - QC	Unchecked	
Validation – Users	Yes	Internal user: Armando Romani, Eilif Muller
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Closed source, contact software owner	
Component Access URL	https://bbpcode.epfl.ch/code/#/admin/projects/nse/brainbuilder	
Technical documentation URL		
Usage documentation URL		
Component dissemination material URL	NA	

2.5 Brain Simulation Platform access

Field Name	Field Content	Additional Information
ID	953	
Component Type	Service	
Contact	MIGLIORE, Michele	
Component Description	This component provides a user friendly interface to access Brain Simulation Platform services	
Latest Release	1.0.0 Feb.2018	
TRL	7	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	Not applicable	
Validation - QC	Pass	
Validation – Users	Yes	Validation method: Google analytics
Validation – Publications	No	

Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	Apache v2.0	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/40558	
Technical documentation URL	https://github.com/antonelepfl/usecases/blob/dev/README.md	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL		

2.6 Brownian dynamics simulations

Field Name	Field Content	Additional Information
ID	1046	
Component Type	data	
Contact	BRUCE, Neil	
Component Description	Predicted rate constants of G protein association to AC5 obtained from Brownian dynamics simulations	
Latest Release	1.0 March 2018	
TRL	NA	
Location	HPC Platform	(see component 559)
Format	text files	
Curation Status	PLA Registered	
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	
License	Release License Unspecified	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9104/nav/68847	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9104/nav/68847	
Usage documentation URL	https://www.humanbrainproject.eu/en/brain-simulation/molecular-models/	

Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/molecular-models/	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/molecular-models/	

2.7 Bsp-usecase-wizard

Field Name	Field Content	Additional Information
ID	3015	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	This component initializes the Collabs created for the students with the necessary notebooks for the exercises; open sourcing is underway and will be completed before M24.	
Latest Release	0.0.1	2018-03-27
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA responsible: Alexander Dietz
Validation – Users	Yes	Internal users:92 External users: 315 from use case statistics
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	LGPLv3 in progress	
Component Access URL	https://github.com/BlueBrain/bsp-usecase-wizard (in progress)	
Technical documentation URL		
Usage documentation URL		
Component dissemination material URL	Not Available	

2.8 Cerebellar cell models

Field Name	Field Content	Additional Information
ID	3023	
Component Type	model	
Contact	MASOLI Stefano	
Component Description	The cerebellum microcircuit is built with three main cells, granule cells, Purkinje cells, Golgi cells and interneurons. All these cell models are optimised and validated.	
Latest Release	SGA1 M24 31/03/2018	
TRL	NA	In "Structured Phase" according to Life Cycle Model for data-driven models (see section 5)
Location	HPC platform (CSCS), BSP platform	
Format	py, mod	
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	Granule mono model https://collab.humanbrainproject.eu/#/collab/9136/nav/77077?state=model.4214dd50-08cb-49ea-8e38-e1d96f6ead69 Granule multi model https://collab.humanbrainproject.eu/#/collab/9136/nav/77077?state=model.03318cde-d679-45ab-bf05-1d3d524ec293 Purkinje cell model https://collab.humanbrainproject.eu/#/collab/9136/nav/77077?state=model.079ea5bf-2d0c-4977-bc5d-4aee3d9ca4f5
Validation - QC	Pass	
Validation – Users	Yes	Stefano Masoli, Martina Rizza,
Validation – Publications	Yes	Masoli S, D'Angelo E. Synaptic Activation of a Detailed Purkinje Cell Model Predicts Voltage-Dependent Control of Burst-Pause Responses in Active Dendrites. Front Cell Neurosci. 2017 Sep 13;11:278. doi: 10.3389/fncel.2017.00278 Masoli S, Rizza MF, Sgritta M, Van Geit W, Schürmann F, D'Angelo E. Single Neuron Optimization as a Basis for Accurate Biophysical Modeling: The Case of Cerebellar Granule Cells. Front Cell Neurosci.

		2017 Mar 15;11:71. doi: 10.3389/fncel.2017.00071
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Release License Unspecified	License will be defined for exploitation phase releases according to Life Cycle Model for data-driven models (see section 5)
Component Access URL	Registered to HBP Model Catalog Granule mono model https://collab.humanbrainproject.eu/#/collab/9136/nav/77077?state=model.4214dd50-08cb-49ea-8e38-e1d96f6ead69 Granule multi model https://collab.humanbrainproject.eu/#/collab/9136/nav/77077?state=model.03318cde-d679-45ab-bf05-1d3d524ec293 Purkinje cell model https://collab.humanbrainproject.eu/#/collab/9136/nav/77077?state=model.079ea5bf-2d0c-4977-bc5d-4aee3d9ca4f5	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9136/nav/69076	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/375/nav/3408	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/cerebellum/	

2.9 Cerebellar scaffold model

Field Name	Field Content	Additional Information
ID	827	
Component Type	model	
Contact	D'Angelo Egidio	
Component Description	To develop a scaffold model of the mouse cerebellum including different cerebellar neurons, geometry- and statistical-based connection rules, layers and full cerebellar network models.	
Latest Release	SGA1 M24 31/03/2018	
TRL	NA	In "Structured Phase" according to Life Cycle Model for data-driven models (see section 5)
Location	BSP platform	

Format	Py, pyNEST	hdf5, gdf/dat
Curation Status	Uploaded to an approved HBP data repository location Registered to HBP Model Catalog	
Validation - QC	Pass	
Validation – Users	Yes	Stefano Casali, Jean Denis Courcol, Elisa Marenzi, Claudia Casellato
Validation – Publications	NA	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Release License Unspecified	License will be defined for exploitation phase releases according to Life Cycle Model for data-driven models (see section 5)
Component Access URL		
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/8444/nav/70360	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/66853	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/cerebellum/	

2.10 Circuit model of area CA1 of the rat hippocampus

Field Name	Field Content	Additional Information
ID	891	
Component Type	model	
Contact	ROMANI, Armando	
Component Description	This component comprises cellular and circuit models of area CA1 of the rat hippocampus. It contains optimised models of pyramidal cells and several classes of interneurons based on morphological and electrophysiological data from UCL, a medium-scale model of the hippocampal CA1 microcircuit, and a full-scale 3-dimensional circuit model of the CA1 region. The models were built using a customized version of the pipeline developed at the Blue Brain Project.	
Latest Release	20180309 (03/09/2018)	
TRL	NA	In “Structured Phase” according to Life

		Cycle Model for data-driven models (section 5)
Location	HPC platform (CSCS)	
Format	Various file formats (.asc, .mod, custom formats)	
Curation Status	Uploaded to an approved HBP data repository location /Registered in HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/9821/nav/78121?state=model.47606e45-6efc-49ad-b61d-efcd26d9bb46
Validation - QC	Checked	Guided by the feedback from the hippocampus community outreach events, preliminary work has been done on generating validation tests for the hippocampus scaffold model developed in SP6 from data available from community neuroinformatics resources, specifically http://hippocampome.org and http://mariannebezaire.com.
Validation – Users	Yes	Community involvement for definition of validation suite; see Hippocamp events.
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	
License	Release License Unspecified	License will be defined for exploitation phase releases according to Life Cycle Model for data-driven models (see section 5)
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9821/nav/78121?state=model.47606e45-6efc-49ad-b61d-efcd26d9bb46	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9821/nav/73921	

Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/594/nav/5317	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/hippocampus/	

2.11 CoreNeuron

Field Name	Field Content	Additional Information
ID	207	
Component Type	Software	
Contact	DELALONDRE, Fabien	
Component Description	Optimised version of NEURON simulator used for empirically-based simulations of neurons and networks of neurons	
Latest Release	0.9.1 (Feb. 2018)	
TRL	6	
Location	Data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	Simulation results are compared against NEURON simulation results
Validation – Users	Yes	Scientists of partners EPFL/BBP and CNR
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Anonymous	
License	BSD – 3	
Component Access URL	https://github.com/BlueBrain/CoreNeuron	
Technical documentation URL	https://github.com/BlueBrain/CoreNeuron/blob/master/README.md	
Usage documentation URL	https://github.com/nrnhines/ringtest	
Component dissemination material URL	https://github.com/BlueBrain/CoreNeuron/blob/master/README.md	

2.12 Data-driven modelling of Ca2+-dependent cascades controlling synaptic signalling and homeostasis

Field Name	Field Content	Additional Information
ID	1137	
Component Type	model	
Contact	SERNA MARTINEZ, Pablo	
Component Description	This component studies morphological changes and energetic states of multi-molecular assemblies, particularly gephyrin, and it uses Hodgkin-Huxley and cable theory formalism to study the Calcium dependent cascades and their effects on tuning inhibition.	
Latest Release	2018.03 & 28/03/2018	
TRL	NA	In "Incubator Phase" according to Life Cycle Model for data-driven models (section 5)
Location	HBP Model Catalog	
Format	Python and neuron files	Python3, neuron, STEPS
Curation Status	Uploaded to an approved HBP data repository location /Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/9141/nav/77337?state=model.4595af27-857f-4113-8ae1-14bcb129edda
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	
License	Attribution, https://creativecommons.org/licenses/by/4.0	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9141/nav/77337?state=model.4595af27-857f-4113-8ae1-14bcb129edda	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9141/nav/69119	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/8844/nav/66860	

Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/inhibition-and-calcium-cascades/	

2.13 Data-driven modelling of G-protein coupled receptor-dependent cascades

Field Name	Field Content	Additional Information
ID	762	
Component Type	Model	Ongoing work
Contact	HELLGREN KOTALESKI, Jeanette	Andrei Kramer <andreikr@kth.se>
Component Description	Scaffold models of GPCR cascades is being created. The workflow for model building will successively be more and more automatised with regard to parameter search given the provided data. Current work at the end of SGA1 relates to a workflow for CaMKII signalling and the endocannabinoid signalling via Gq protein coupled receptor cascades.	
Latest Release	M24 - 2018.03	The date was used as the version number
TRL	NA	In "Incubator Phase" according to Life Cycle Model for data-driven models (section 5)
Location	Private Collab, also HPC platform (CSCS)	Link to model inventory (R3a): https://collab.humanbrainproject.eu/#/collab/9323/nav/70371 Link to Collabs with corresponding model components: CaMKII: https://collab.humanbrainproject.eu/#/collab/9065/nav/68534 MGLuRd: https://collab.humanbrainproject.eu/#/collab/9064/nav/68529 Workflow: https://collab.humanbrainproject.eu/#/collab/9148/nav/69157
Format	sbml	http://sbml.org/Main_Page
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/9064/nav/77085?state=model.ca485e6

		3-38c0-445e-8076-775df6609342
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No privacy constraints	
Sharing	Consortium	
License	Attribution NonCommercial, ShareAlike, https://creativecommons.org/licenses/by-nc-sa/4.0/	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9064/nav/73791	
Technical documentation URL	NA	Ongoing work
Usage documentation URL	NA	Ongoing work
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/signalling-cascades	

2.14 eFEL

Field Name	Field Content	Additional Information
ID	203	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	Electrophys Feature Extraction Library	
Latest Release	2.13	2017-11-14
TRL	9	
Location	Data hosted by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	
Validation – Users	Yes	External Users: Google BigQuery report 350,000 downloads since creation
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	

Sharing	Anonymous	
License	LGPLv2/LGPLv3	
Component Access URL	https://github.com/BlueBrain/eFEL	
Technical documentation URL	http://efel.readthedocs.io/en/latest/	
Usage documentation URL	http://efel.readthedocs.io/en/latest/	
Component dissemination material URL		

2.15 Engineering support to build data-driven models

Field Name	Field Content	Additional Information
ID	946	
Component Type	Service	
Contact	MIGLIORE, Michele	
Component Description	This component provides a user-friendly interface to allow user an easy extraction of electrophysiological activity features, needed for data-driven model construction	
Latest Release	1.0.0 Feb.2018	
TRL	7	
Location	data hosted by task providing dataset, by Collaboratory storage and by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA Owner: Jean-Denis Courcol, “Checkpoint Quality Assurance”
Validation – Users	Yes	Validation method: BSP analytics log Counts: 71 (43 external, 28 internal)
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	Apache v2.0	

Component Access URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/40558	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/19/nav/2108?state=software,Feature_Extraction_Graphical_User_Interface	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL		

2.16 Human neurons

Field Name	Field Content	Additional Information
ID	1029	
Component Type	Model	Ongoing work
Contact	SEGEV, Idan	Idan Segev idan.segev@mail.huji.ac.il, Guy Eyal guy1eyal@gmail.com
Component Description	Integrating a wide range of anatomical and physiological data on human pyramidal cells, we built, and provide, the most comprehensive models of human neurons available today. These models demonstrate that human cortical neurons have distinctive biophysical and computational properties.	
Latest Release	passive dendrite models	Oct 2016 (Eyal *et al.*, eLife)
TRL	NA	In "Structured Phase" according to Life Cycle Model for data-driven models (section 5)
Location	Data hosted by Collaboratory storage	https://collab.humanbrainproject.eu/#/collab/528/nav/4671
Format	hoc, nmodl	https://www.neuron.yale.edu/neuron/
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/9747/nav/77288?state=model.4aaa0411-f626-4537-b2d1-91c8e43a158a
Validation - QC	Pass	
Validation – Users	Yes	Citations to paper
Validation – Publications	Yes	https://dx.doi.org/10.7554%2FeLife.16553
Privacy Constraints	No privacy constraints	

Sharing	anonymous	
License	All Rights Reserved, Copyright	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/528/nav/4671	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9747/nav/73393	Model inventory: Human Neurons; includes current work on active dendrite models
Usage documentation URL	https://dx.doi.org/10.7554%2FeLife.16553	eLife publication covering passive dendrite models
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/human-neurons/	

2.17 Integration of subcellular models in single neuron models

Field Name	Field Content	Additional Information
ID	766	
Component Type	model	
Contact	HELLGREN KOTALESKI, Jeanette	
Component Description	The SGA1 task 6.1.4 has integrated a subcellular scaffold model into models of one main neuron type in striatum. Neuron models incorporating subcellular models will make it possible to investigate the role of neuromodulation and its consequences for synaptic integration in active dendrites, etc. The model was published 2018, see doi: 10.3389/fncir.2018.00003	
Latest Release	1.02_SGA1-m24 03/27/2018	
TRL	NA	In “Incubator Phase” according to Life Cycle Model for data-driven models (section 5)
Location	HPC platform (CSCS)	
Format	Py, mod, json, swc	
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/9475/nav/76936?state=model.2e2b7998-45b0-4075-9a59-beae74939f85
Validation - QC	Unchecked	

Validation – Users	No	
Validation – Publications	Yes	doi: 10.3389/fncir.2018.00003
Privacy Constraints	No constraints	
Sharing	Anonymous	
License	**CC BY-NC 4.0**	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9475/nav/76936?state=model.eac5bc60-89da-4d16-8a4f-143315a86f3b	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9475/nav/71489	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/489/nav/4316	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/multiscale-modelling	

2.18 JS Simulation Configuration

Field Name	Field Content	Additional Information
ID	213	
Component Type	Software component	
Contact	COURCOL, Jean-Denis	
Component Description	A Web component to configure simulation on detailed circuit model using Neuron.	
Latest Release	1.0.0	Feb.2018
TRL	7 (expected by the end of SGA1)	
Location	Data hosted by HPC platform	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA Owner: Alexander Dietz
Validation – Users	Yes	Internal Users: M.Migliore, Stefano Antonel
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	BSD-3-Clause	

Component Access URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/26424	
Technical documentation URL	Work in progress	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Work in progress	

2.19 Model Catalog web app

Field Name	Field Content	Additional Information
ID	3013	
Component Type	Service	
Contact	Davison, Andrew	
Component Description	A Collaboratory app for searching, viewing, creating and editing information about models, and registering model code for model validation experiments. The Model Catalog is part of the Brain Simulation Platform Validation Framework, but can also contain models from other sub-projects, and from external Collaboratory users.	
Latest Release	v1.0	31/03/2018
TRL	6	
Location	data hosted by other non-HBP 3rd party	Commercial cloud provider (EU-based)
Format	NA	
Curation Status	NA	
Validation - QC	Pass	Agile Quality Assurance
Validation – Users	Yes	Sara Saray, Alexander Kozlov, Armando Romani, Luca Bologna, Alexander Dietz, Morgane Bourdonnais, Katherine Frégnac, Katrien Van Look… (>20 people in total)
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	Apache v2 license	

Component Access URL	The app can be installed in any Collab, so it is not possible to give a single URL	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Not applicable	

2.20 Model validation service

Field Name	Field Content	Additional Information
ID	721	
Component Type	Service	
Contact	Davison, Andrew	
Component Description	The Model Validation Service REST API allows modellers to find validation tests that are suitable for the species, structure (single cell, brain region, etc.) and spatial/temporal scale being modelled. It also allows modellers to define and upload new validation test definitions. It provides a database of validation experiment results, and a web-services API for querying the database and uploading new results.	
Latest Release	v1.0	31/03/2018
TRL	6	
Location	data hosted by other non-HBP 3rd party	Commercial cloud provider (EU-based)
Format	Web service	
Curation Status	Not applicable	
Validation - QC	Pass	Agile Quality Assurance
Validation – Users	Yes	Sara Saray, Alexander Kozlov, Armando Romani, Luca Bologna, Alexander Dietz
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	Apache v2 license	
Component Access URL	https://validation-v1.brainsimulation.eu	

Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Not applicable	

2.21 Model validation test suites

Field Name	Field Content	Additional Information
ID	720	
Component Type	Software	
Contact	Davison, Andrew	
Component Description	A collection of Python libraries implementing validation tests for different model types and brain regions. Libraries currently include HippoUnit, CerebUnit, BasalUnit, MorphoUnit, NetworkUnit	
Latest Release	Hippounit: v1.0, BasalUnit: v1.0, MorphoUnit: v1.0.	31/03/2018
TRL	5	
Location	data hosted by other non-HBP 3rd party	GitHub
Format	NA	
Curation Status	NA	
Validation - QC	Pass	Agile Quality Assurance
Validation – Users	Yes	Sara Saray, Alexander Kozlov, Armando Romani, Luca Bologna, Alexander Dietz
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	BSD-3-Clause	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/8123/nav/61654	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/8123/nav/61654	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Not available	

2.22 Model validation web app

Field Name	Field Content	Additional Information
ID	722	
Component Type	Service	
Contact	Davison, Andrew	
Component Description	A Collaboratory app for searching, browsing and viewing validation test definitions and the results of model validation experiments.	
Latest Release	v1.0	31/03/2018
TRL	6	
Location	data hosted by other non-HBP 3rd party	Commercial cloud provider (EU-based)
Format	Web app	
Curation Status	Not applicable	
Validation - QC	Pass	Agile Quality Assurance
Validation – Users	Yes	Sara Saray, Alexander Kozlov, Armando Romani, Luca Bologna, Alexander Dietz
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	Apache v2 license	
Component Access URL	The app can be installed in any Collab, so it is not possible to give a single URL	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Not applicable	

2.23 MOOC neurons and synapses 2017

Field Name	Field Content	Additional Information
ID	3017	
Component Type	Software	

Contact	COURCOL, Jean-Denis	
Component Description	A public GitHub repository containing all the notebooks needed for the exercises	
Latest Release	0.0.1 2018-02-16	
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA Owner: Alexander Dietz
Validation – Users	Yes	External Users > 5000 from EdX analytics
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	LGPLv3	
Component Access URL	https://github.com/BlueBrain/MOOC-neurons-and-synapses-2017	
Technical documentation URL	https://github.com/BlueBrain/MOOC-neurons-and-synapses-2017	
Usage documentation URL	https://github.com/BlueBrain/MOOC-neurons-and-synapses-2017	
Component dissemination material URL	https://github.com/BlueBrain/MOOC-neurons-and-synapses-2017	

2.24 MOOC service

Field Name	Field Content	Additional Information
ID	3016	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	A web service managing the submission of answers to the MOOC exercises and the interaction with EdX platform	
Latest Release	0.0.1 2018-03-16	
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	

Curation Status	NA	
Validation - QC	Pass	QA Owner: Alexander Dietz
Validation – Users	Yes	External users: > 5000 from Edx Analytics
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Closed source, contact software owner	
Component Access URL	https://github.com/BlueBrain/mooc-grading-service	
Technical documentation URL	https://github.com/BlueBrain/mooc-grading-service	
Usage documentation URL	https://github.com/BlueBrain/mooc-grading-service	
Component dissemination material URL	Not Available	

2.25 Morphology repair and diversification framework

Field Name	Field Content	Additional Information
ID	195	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	A framework to repair morphology reconstruction and to generate a diversified population based on a smaller population	
Latest Release	0.1.3	2017-10-30
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	
Validation – Users	Yes	Internal Users: Armando Romani, Eilif Muller
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	

Sharing	Consortium	
License	Closed source, contact software owner	
Component Access URL	https://bbpcode.epfl.ch/code/#/admin/projects/platform/bbp-morphology-workflow	
Technical documentation URL		
Usage documentation URL		
Component dissemination material URL	Not Available	

2.26 NEST – The Neural Simulation Tool

Field Name	Field Content	Additional Information
ID	209	
Component Type	Software	
Contact	DIESMANN, Markus	
Component Description	NEST-The Neural Simulation Tool- is a highly scalable Simulator for networks of point or few-compartment spiking neuron models. It includes multiple synaptic plasticity models, gap-junctions, and rate-based models. NEST also provides techniques to define complex network structure.	
Latest Release	NEST 2.14.0 20 Oct 2017	DOI 10.5281/zenodo.882971
TRL	7	
Location	Hosted by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	Continuous Integration and Code Review Process
Validation – Users	Yes	See D11.3.3, Sec.6.3
Validation – Publications	Yes	Over 40 publications based on NEST simulations in 2016 and 2017, see http://www.nest-simulator.org/publications
Privacy Constraints	No privacy constraint	
Sharing	Anonymous	

License	GPL v2 or later	https://www.gnu.org/license/gpl.html
Component Access URL	http://github.com/nest/nest-simulator	
Technical documentation URL	http://nest.github.io/nest-simulator/	
Usage documentation URL	http://www.nest-simulator.org/documentation/	
Component dissemination material URL	http://www.nest-simulator.org	See guidance below

2.27 NeuroM

Field Name	Field Content	Additional Information
ID	193	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	A neuronal morphology analysis tool	
Latest Release	1.4.5	2017-11-12
TRL	9	
Location	Data hosted by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA Owner Alexander Dietz
Validation – Users	Yes	External Users: > 5000 as part of EdX analytics
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Anonymous	
License	BSD 3-clause	
Component Access URL	https://github.com/BlueBrain/NeuroM	
Technical documentation URL	http://neurom.readthedocs.io/en/stable/	
Usage documentation URL	http://neurom.readthedocs.io/en/stable/	
Component dissemination material URL		

2.28 NEURON

Field Name	Field Content	Additional Information
ID	208	
Component Type	Software	
Contact	DELALONDRE, Fabien	
Component Description	NEURON is a simulation environment for modelling networks of neurons with complex branched anatomy including extra-cellular potential near membranes and biophysical properties such as multiple channel types, inhomogeneous channel distribution and ionic accumulation.	
Latest Release	7.5 (Sept 2017)	
TRL	9	
Location	Data hosted by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	Neuron is tested against a test suite of models from ModelDB
Validation – Users	Yes	Michael Hines (author of NEURON) and community users of NEURON
Validation – Publications	Yes	https://neuron.yale.edu/neuron/static/bib/usednrn.html
Privacy Constraints	No privacy constraint	
Sharing	anonymous	
License	BSD-3	
Component Access URL	https://neuron.yale.edu/neuron/	
Technical documentation URL	https://neuron.yale.edu/neuron/static/py_doc/index.html	
Usage documentation URL	https://neuron.yale.edu/neuron/static/docs/neuronpython/index.html	
Component dissemination material URL	https://www.neuron.yale.edu/phpBB/	

2.29 NEURON as a Service

Field Name	Field Content	Additional Information
ID	3014	
Component Type	Software	
Contact	COURCOL, Jean-Denis	
Component Description	A web application to run an experiment on a single neuron model using the NEURON simulator as a backend.	
Latest Release	0.0.16	2018-03-28
TRL	7	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA Owner: Alexander Dietz
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Closed source, contact software owner	
Component Access URL	https://bbpcode.epfl.ch/browse/code/nse/BlueNaaS/?h=refs/heads/master)	
Technical documentation URL		
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Not Available	

2.30 Placement Hints

Field Name	Field Content	Additional Information
ID	3020	
Component Type	Software	
Contact	COURCOL, Jean-Denis	

Component Description	Software for defining cells orientation and placement depending on spatial constraints in an atlas aware volumetric space	
Latest Release	0.0.1	2018-02-13
TRL	3	
Location	data hosted by task providing dataset	
Format	NA	
Curation Status	NA	
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	Consortium	
License	Closed source, contact software owner	
Component Access URL	https://bbpcode.epfl.ch/code/building/placementAlgorithm	
Technical documentation URL		
Usage documentation URL		
Component dissemination material URL	Not Available	

2.31 Python client for the model validation service

Field Name	Field Content	Additional Information
ID	1680	
Component Type	Software	
Contact	Davison, Andrew	
Component Description	A Python client for the Model Validation service. It enables searching the catalogues of models and validation tests, downloading test definitions, registering models and validation tests with the catalogue, running validation experiments, and registering the results of model validation experiments with the service.	
Latest Release	v0.4.0	31/03/2018
TRL	6	

Location	data hosted by other non-HBP 3rd party	GitHub
Format	NA	
Curation Status	NA	
Validation - QC	Pass	Agile Quality Assurance
Validation – Users	Yes	Sara Saray, Alexander Dietz
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	BSD-3-Clause	
Component Access URL	https://pypi.python.org/pypi/hbp_validation_framework/0.4.0 https://github.com/HumanBrainProject/hbp-validation-client	
Technical documentation URL	http://hbp-validation-client.readthedocs.io/en/master/	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL	Not available	

2.32 QM/MM simulations for prediction of reaction kinetics

Field Name	Field Content	Additional Information
ID	1001	
Component Type	Software	
Contact	ursula.roethlisberger@epfl.ch, p.carloni@fz-juelich.de	
Component Description	Massively parallel QM/MM interface for hybrid molecular dynamics simulations	
Latest Release	To be released version 1.0.0	Project is currently under development
TRL	5	Currently performing validation tests on the real-world, published systems
Location	data hosted by other non-HBP 3rd party	gitlab.com

Format	Modular library	Library that is linked against the CPMD and a MM code to provide necessary means of communication for hybrid simulations
Curation Status	N/A	
Validation - QC	Unchecked	
Validation – Users	No	User tests will begin after the publication of the interface
Validation – Publications	No	Publications are being prepared
Privacy Constraints	No privacy constraint	
Sharing	anonymous	The interface is going to be distributed as a free open-source library that can be linked against CPMD code to enable QM/MM workflow
License	LGPLv3	CPMD has a free for academic institutions proprietary license and the first MM code that has QM/MM capabilities is GROMACS, which is distributed under LGPLv2.1 license
Component Access URL	https://www.dropbox.com/s/kbuvefgbtli2jga/MiMiC.tar.gz?dl=0	Will be available after the initial release of the project
Technical documentation URL	TBA	Will be available after the initial release of the project
Usage documentation URL	TBA	Will be available after the initial release of the project
Component dissemination material URL	TBA	Will be available after the initial release of the project

2.33 Scaffold basal ganglia model (striatum)

Field Name	Field Content	Additional Information
ID	972	

Component Type	model	
Contact	GRILLNER, Sten	
Component Description	Models of different types of interneurons and projection neurons in striatum will be built based on detailed morphology and membrane properties, distributed in geometrically defined populations. The model neurons will be synaptically connected via GABAergic synapses in a striatal microcircuit as shown experimentally.	
Latest Release	SGA1 M24 & 21/03/2018	
TRL	NA	In "Structured Phase" according to Life Cycle Model for data-driven models (section 5)
Location	HPC platform (CSCS)	
Format	Python, JSON, SWC files	Runs on the Collaboratory server via web-based interface
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/7840/nav/76935?state=model.1a9298bc-6ed4-45a7-8f3f-e822ff262aa9
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	Internal HBP use
License	Release License Unspecified	License will be defined for exploitation phase releases according to Life Cycle Model for data-driven models (see section 5)
Component Access URL	https://collab.humanbrainproject.eu/#/collab/7840/nav/76935?state=model.1a9298bc-6ed4-45a7-8f3f-e822ff262aa9	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/7840/nav/59620	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/376/nav/3413	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/basal-ganglia/	

2.34 Scaffold somatosensory cortex microcircuit (mouse)

Field Name	Field Content	Additional Information
ID	3011	
Component Type	model	
Contact	SOOD, Vishal	
Component Description	Scaffold somatosensory cortex microcircuit for mouse	
Latest Release	1.0.0 & 15/03/2018	
TRL	NA	In "Structured Phase" according to Life Cycle Model for data-driven models (section 5)
Location	HPC Platform (CSCS)	
Format	H5 files	H5py - hdfview
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/9138/nav/77967?state=model.bc7a2946-3d5c-4c4e-9fab-7f2991b65736
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	(HBP internal)
License	Release License Unspecified	Open sourcing in preparation (likely license: CC BY-NC-SA 4.0) as required due to in-kind contribution
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9138/nav/77967?state=model.bc7a2946-3d5c-4c4e-9fab-7f2991b65736	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9138/nav/69095	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/9137/nav/69090	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/mouse-sscx/	

2.35 SDA

Field Name	Field Content	Additional Information
ID	210	
Component Type	Software	
Contact	BRUCE, Neil	
Component Description	Software package containing a Brownian dynamics simulator and associated preparation and analysis tools	
Latest Release	7.2.3 March 2018	Internal HBP release. Current public release: 7.2.2 July 2017
TRL	8	
Location	data hosted by other HBP party	
Format	NA	
Curation Status	NA	
Validation - QC	Unchecked	
Validation – Users	Yes	https://mcm.h-its.org/sda/doc/doc_sda7/references.html
Validation – Publications	Yes	https://mcm.h-its.org/sda/doc/doc_sda7/references.html
Privacy Constraints	No privacy constraint	
Sharing	Anonymous	
License	Closed source, contact software owner	
Component Access URL	https://mcm.h-its.org/sda	
Technical documentation URL	https://mcm.h-its.org/sda/doc/doc_sda7/doc.html	
Usage documentation URL	https://mcm.h-its.org/sda/doc/doc_sda7/doc.html	
Component dissemination material URL		

2.36 STEPS

Field Name	Field Content	Additional Information
ID	206	

Component Type	Software	
Contact	DELALONDRE, Fabien	
Component Description	Stochastic Engine for Pathway Simulation developed by OIST university in collaboration with the Blue Brain Project	
Latest Release	3.2 (Oct. 2017)	
TRL	8 (5)	Higher number refers to general STEPS; number in brackets refers to parallel STEPS functionality now part of STEPS
Location	Data hosted by other non-HBP 3rd party	
Format	library with python scripting interface	
Curation Status	Not Applicable	
Validation - QC	Pass	
Validation – Users	Yes	Users from partner EPFL/BBP and scientists at site of code owner (Okinawa Institute for Science and Technology - OIST)
Validation – Publications	Yes	W. Chen and E. De Schutter (2017). Parallel STEPS: Large Scale Stochastic Spatial Reaction-Diffusion Simulation with High Performance Computers. Front. Neuroinform. 11:13. doi: 10.3389/fninf.2017.00013. Article
Privacy Constraints	No	
Sharing	Anonymous	
License	GPL – 2	
Component Access URL	https://github.com/CNS-OIST/STEPS	
Technical documentation URL	http://steps.sourceforge.net/manual/manual_index.html	
Usage documentation URL	http://steps.sourceforge.net/manual/manual_index.html	
Component dissemination material URL		

2.37 Subcellular model of timing dependent reward/dopamine plasticity

Field Name	Field Content	Additional Information
ID	765	
Component Type	Model	
Contact	HELLGREN KOTALESKI, Jeanette	
Component Description	In reward learning, the integration of NMDA-dependent calcium and dopamine by striatal projection neurons leads to potentiation of corticostriatal synapses through CaMKII/PP1 signalling. In order to elicit the CaMKII/PP1-dependent response, the calcium and dopamine inputs should arrive in temporal proximity and must follow a specific (dopamine after calcium) order. In this computational study, we propose that these temporal requirements emerge as a result of the coordinated signalling via two striatal phosphoproteins, DARPP-32 and ARPP-21. Model published 2016; doi: 10.1371/journal.pcbi.1005080	
Latest Release	2017-11-15; see also doi: 10.1371/journal.pcbi.1005080	See BioModels, https://www.ebi.ac.uk/biomodels-main/MODEL1603270000
TRL	NA	The model built and released before the Life Cycle Model defined. Used as component for the multiscale work in second half of SGA1 (see component 766). The subcellular modelling work defined to be in the 'incubator' phase.
Location	Data hosted by other non-HBP third party	
Format	SBML	
Curation Status	Uploaded to an approved HBP data repository location/Registered to the Model Catalog	See https://collab.humanbrainproject.eu/#/collab/9475/nav/76936?state=model.7f9611e5-8bd8-47da-b0d3-e8d8d5d4b15d
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	Yes, doi: 10.1371/journal.pcbi.1005080	

Privacy Constraints	No	
Sharing	Anonymous	
License	CC BY-NC 4.0	
Component Access URL	https://www.ebi.ac.uk/biomodels-main/MODEL1603270000	
Technical documentation URL	doi: 10.1371/journal.pcbi.1005080	
Usage documentation URL	doi: 10.1371/journal.pcbi.1005080	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/signalling-cascades	

2.38 Subcellular signalling parameters from molecular simulation

Field Name	Field Content	Additional Information
ID	559	
Component Type	model	
Contact	Bruce, Neil; Carloni, Paolo	
Component Description	Predicted structural models and estimates of kinetic and thermodynamic parameters describing the formation and stability of stimulatory and inhibitory G protein binding to adenylyl cyclase 5.	
Latest Release	1.0, March 2018	
TRL	NA	In “Incubator Phase” according to Life Cycle Model for data-driven models (section 5)
Location	HPC Platform (CSCS)	
Format	pdb (http://www.wwpdb.org/documentation/file-format-content/format33/v3.3.html), xtc (http://manual.gromacs.org/current/online/xtc.html)	VMD, pymol, chimera
Curation Status	Uploaded to an approved HBP data repository location/Registered in the HBP Model Catalog	
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	

License	Release License Unspecified	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/9104/nav/68847	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/9104/nav/68847	
Usage documentation URL	https://www.humanbrainproject.eu/en/brain-simulation/molecular-models/	
Component dissemination material URL	https://www.humanbrainproject.eu/en/brain-simulation/molecular-models/	

2.39 Support of open-source tools for configuration of data-driven model

Field Name	Field Content	Additional Information
ID	947	
Component Type	Service	
Contact	MIGLIORE, Michele	
Component Description	This component will provide a user-friendly interface to configure and launch optimisation processes on remote HPC systems	
Latest Release	1.0.0 Feb.2018	
TRL	7	
Location	data hosted by task providing dataset, by HPC platform, by Collaboratory storage and by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	QA Owner: Alexander Dietz, “Checkpoint Quality Assurance”
Validation – Users	Yes	Validation method: BSP analytics log Counts: 77 (28 external, 49 internal)
Validation – Publications	No	
Privacy Constraints	No privacy constraint	
Sharing	public authenticated	
License	Apache v2.0	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/66898	

Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/19/nav/2108?state=software,Hodgkin_Huxley_Neuron_Builder_CDP2_P1	
Usage documentation URL	https://collab.humanbrainproject.eu/#/collab/1655/nav/18580	
Component dissemination material URL		

2.40 Web hosting, deployment, monitoring and updating of platform services for data-driven models

Field Name	Field Content	Additional Information
ID	994	
Component Type	Service	
Contact	MIGLIORE, Michele	
Component Description	This component provides the services needed to deploy, monitor, update and host the web applications developed for support to data-driven models	
Latest Release	1.0.0 Feb.2018	
TRL	7	
Location	data hosted by task providing dataset, by HPC platform, by Collaboratory storage and by other non-HBP 3rd party	
Format	NA	
Curation Status	NA	
Validation - QC	Pass	
Validation – Users	Yes	Validation method: BSP analytics log Counts: 89 (external 51, internal 38)
Validation – Publications	No	
Privacy Constraints	no privacy constraint	
Sharing	public authenticated	
License	Apache v2	
Component Access URL	https://collab.humanbrainproject.eu/#/collab/19/nav/2108?state=software,Hodgkin_Huxley_Neuron_Builder_CDP2_P1	
Technical documentation URL	https://collab.humanbrainproject.eu/#/collab/19/nav/2108?state=software,Hodgkin_Huxley_Neuron_Builder_CDP2_P1	

Usage documentation URL	NA	
Component dissemination material URL	NA	

2.41 Whole brain network-level model for mouse

Field Name	Field Content	Additional Information
ID	827	
Component Type	model	
Contact	RODARIE, Dimitri	
Component Description	This model is a point neuron representation of the whole mouse brain reconstructed through the BBP data-driven workflow (see Collab for more details). It is stored in a unique file which structure corresponds to a dictionary, each field having its own description to explain its purpose. The file comprises the position, and orientation of its cells, associated with their labelled Morphological and Electrical type. It contains also the E-types point neuron parameters used to simulate the model with Nest. The connections and synapse parameters of only 1% of the neurons are stored, split in 10 subgroups, to keep the file portable.	
Latest Release	0.5.0 & 15/02/2018	
TRL	NA	In “Structured Phase” according to Life Cycle Model for data-driven models (section 5)
Location	HPC platform (CSCS)	
Format	H5 files	H5py - hdfview
Curation Status	Uploaded to an approved HBP data repository location/Registered to HBP Model Catalog	https://collab.humanbrainproject.eu/#/collab/521/nav/76972?state=model.111bc309-ba88-4aa9-9ea1-1c9dcaf75a13
Validation - QC	Unchecked	
Validation – Users	No	
Validation – Publications	No	
Privacy Constraints	No Privacy Constraint	
Sharing	consortium	

License	Release License Unspecified	License will be defined for exploitation phase releases according to Life Cycle Model for data-driven models (see section 5)
Component Access URL	https://collab.humanbrainproject.eu/#/collab/521/nav/76972?state=model.111bc309-ba88-4aa9-9ea1-1c9dcaf75a13	

3. Conclusion and Outlook

The Key Result "Multi-scale molecular dynamics simulation and modelling approaches that inform models of subcellular signalling in both a qualitative and quantitative manner" achieved during month 13-24 supports SP6's objective "Scaffold models of molecular level principal neurons, cellular level reconstructions of selected cortical and sub-cortical regions (6a)". While we have been working towards using molecular level simulations to inform models of receptor-induced cascades since the start of the HBP, during the second half of SGA1 this has materialised in significant and novel insights, and a proof of concept of a multi-scale model was realised using a dopamine receptor-induced cascade integrated into a detailed neuron model of a striatal principal neuron.

So far, we have focused on a particular system, the adenylyl cyclase (AC), with particular reference to the type 5. In the particular case of AC5, novel insights were gained regarding the formation of, and activity of, the ternary complex consisting of two types of G-proteins and the AC5 molecule. This highlights the fact that theoretical approaches can predict data when current experimental techniques have difficulties in measuring for instance, reaction kinetics, binding affinities, enzyme activities, etc. A preliminary 'workflow' for parameter estimation, as well as model sensitivity analysis, has also been developed using a calcium-dependent signalling as a test case.

During SGA2, we will enhance and mature this modelling workflow, so that a population of models are generated for particular datasets as a general rule, instead of only working with one particular model instance with specific parameters. The workflow will also be tested on G-protein-dependent cascades.

The Key Result "Data-driven scaffold models to bootstrap community use and contribution" achieved during month 13-24 supports the SP6 objectives "Scaffold models of molecular level principal neurons, cellular level reconstructions of selected cortical and sub-cortical regions (6a)", "Network level models of the whole mouse brain (6b)" and "Simplified models exported for implementation in neuromorphic computing systems (6c)". While we have been working on detailed models of selected regions of the rodent brain since the start of the HBP, it has now been possible to have the first scaffold models of three main brain microcircuits (hippocampus, cerebellum and basal ganglia), in addition to the previously published somatosensory microcircuit model. In collaboration with SP1, a first mousified version of the latter has been developed. We have continually refined the process of systematically simplifying the cellular level reconstructions, by adding in particular validated and optimised support for automatically simplifying morphologically-detailed microcircuit models to point neuron versions suitable for the NEST simulator, effectively making information contained in cellular level models usable for network level models. The network level model of the whole mouse brain (point neurons) has also been further advanced. The work has progressed exploiting a close collaboration among the HBP partners from multiple Sub Projects, mainly coordinated through CDP1 and CDP2.

A critical introduction during this period was the definition of a Life Cycle Model (see Annex) for data-driven models. On the one hand, this answers to reviewer feedback on data and model availability, and an improved data management plan. On the other hand, this provides a mechanism to track and drive the deep integration of the respective models with the HBP

Platforms. This effort will continue during SGA2. A major focus during SGA2 will be the active engagement of communities outside the HBP, around the first scaffold models and to enable the community at large to complement and expand the HBP's modelling efforts. From the early community experience we could gather during SGA1 on the hippocampus, a standardised modelling approach with a transparent validation framework and the possibility to systematically simplify these models automatically, are key ingredients to cater to the diverse interests in the community.

The Key Results "Advanced Tools" and "Brain Simulation Platform - version 2" achieved during month 13-24 support all of SP6's objectives, but specifically "Initial version of Brain Simulation Platform incorporating algorithms and workflows for reconstruction and simulation of subcellular, cellular, microcircuit and meso-circuit (brain region/system) levels (6d)" and "Tools and protocols for *in silico* experimentation and model validation (6e)". While we have been working on improving best-in-class community software to the scale and detail required by the HBP's modelling efforts, as well as integrating them into a single ecosystem allowing for collaborative modelling and *in silico* experimentation, we achieved a major step forward during the second half of the SGA1 period: all community simulators selected by SP6 (NEST, NEURON, STEPS) have been scaled to massively-parallel execution capability and a systematic deployment on the HBP's HPAC Platforms has been adopted. The re-designed and newly released version of the Brain Simulation Platform makes it much easier to leverage the Platform's functionality for related research by external scientists with deep workflow knowledge. By focusing on its most mature workflows, namely single cell modelling and *in silico* experimentation on microcircuits, a solid user experience for those external users is provided, without limiting the advanced co-design with the internal science drivers.

The Brain Simulation Platform is strongly dependent on the Neuroinformatics (SP5) and High Performance Analytics and Computing (SP7) Platforms. As functionalities of these underlying Platforms ramp up on the way to a Joint Platform, intermediate solutions developed to make the Brain Simulation Platform fully functional today will successively be replaced. More specifically, the integration of typed data and models into the Neuroinformatics Platform will be completed so as to allow the Brain Simulation Platform's use cases to programmatically discover and ingest any available and compatible data. Additionally, the communication services allowing the interaction with all the available HPC systems belonging to the HPAC Platform (SP7) will be finalised in order to allow the interaction with these systems through the UNICORE framework. This integration process is closely managed by regular multi-SP conference calls. In addition to the deep integration with the Joint Platform, a major focus during the SGA2 period will be to bring additional workflows (e.g. reconstruction of brain regions) from the co-design prototype stage to the same maturity level as e.g. the single cell model building today, and therefore allowing the community at large to contribute to the building of models.

Lastly, the Key Result "Massive open online course on simulation neuroscience" represents a major step forward for the dissemination and community engagement for the Brain Simulation Platform, and probably for the HBP Platforms as a whole. With the worldwide launch of the first course on single neuron modelling in November 2017 (and as of March 2018), almost 6,000 inscriptions (+100/week) have been attracted, which have led to 500 active learners and more than 230 users of the Brain Simulation Platform. This success is enabled by workflows developed in co-design with the HBP internal science drivers, which then matured and were made readily available in the re-designed version 2 of the Brain Simulation Platform.

During the timeframe of SGA2, additional courses will be developed in line with the development roadmap of mature Platform functionality, specifically on *in silico* experimentation and brain region reconstruction. While the science drivers in the HBP will be most instrumental to demonstrate that *in silico* experimentation represents a powerful method for addressing scientific questions that cannot be addressed experimentally, the MOOCs will be a critical component to train the community and next generation scientists, to enable them to do alike.

4. Annex: Life Cycle Model for Data-Driven Models

Version 1; this version and future refinements will be integrated into the HBP's Data Management Plan.

We defined a Life Cycle Model for data-driven modelling artefacts that reconciles the intended goal for open and reproducible science, and it aims at the same time to not overburden the modelling process that needs to be flexible in early phases (*incubator*). In later stages, modelling gains more structure by adopting community standards such as version control systems, a distinction between release versions and development versions of a model, automated concurrent validation, standard data formats with open APIs (etc.). Such a model is then referred to as *structured*; see Figure 16.

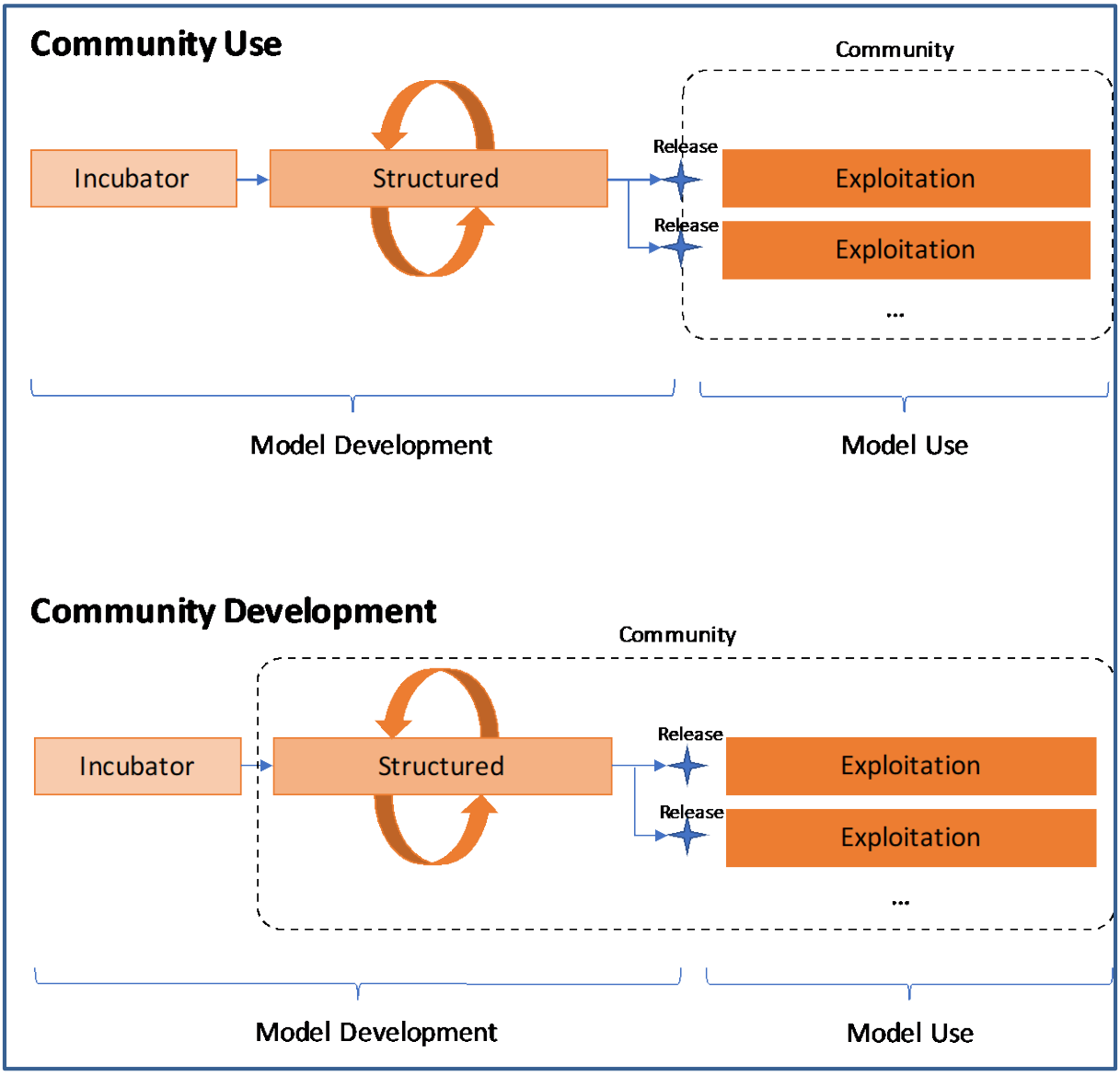

Figure 16: Schematic overview of the phases in the Life Cycle Model

Schematic of the life cycle model for brain model artefacts and related data. Presented are two ways of implementing this life cycle: 1) the model development is done inside a limited collaboration and the model is shared for use with the community at large (upper panel); 2) the actual model development is done as a community project (lower panel).

As illustrated in Figure 16, we distinguish two types of communities: 1) community use, i.e. scientists that would like to use the model or would like to contribute to a validation of a model; 2) community development, i.e. scientists that get involved in the actual creation of the model. Our experience working with the community indicates that the model user community is in

principle larger than the community willing to contribute to the building of a model. From a management point of view, managing a model building community is much more involved than a model user community. In practice, it is reasonable to assume that the community process starts with (1) and then recruits committed contributors for (2) over time.

It should be noted that this life cycle process is the recommended way of categorising and structuring modelling activities in the HBP, but it cannot claim to capture all possible scenarios. For example, it is certainly conceivable that a model might go from an unstructured form to publication and external exploitation right away; however, in this Life Cycle Model this is not recommended.

The specific properties of the model life cycle phases are described in Table 6: Properties of the different life cycle phases.

Table 6: Properties of the different life cycle phases.

	Incubator Phase	Structured Phase	Exploitation Phase
What type of models?	• Initial modelling steps • Typically, work in progress • Not all approaches developed yet • Few collaborators	• Mature and structured modelling process • Work in progress but with clear model releases • Typically, several collaborators • Clarified rules for contributions	• Scientific publication (for crediting) is out • Model can be made available to others for use • Data can be made available to others for use
Community involvement	• Typically closed set of collaborators	• Development can be driven by closed set of collaborators • Development can be driven as community project	• Fully available to the community
Required HBP integration	• Appearance on public HBP website in accordance with template (R1) • Appearance on Brain Simulation Platform in accordance with template (R2) • Structured inventory (spreadsheet) of data and model artefacts deposited in an Internal HBP Model Collab every 6 months (R3a) • Data for model building continually aggregated in an Internal HBP Model Collab/HBP data store for staging (R4a) • Data for model validation continually aggregated in an Internal HBP Model Collab/HBP data store for staging (R5a) • Model artefacts mirrored to internal HBP Collab/HBP data store every 6 months (R6a)	• R1 & R2 • Structured inventory of data used deposited in an Internal HBP Model Collab upon each model release (R3b) • Data for model building registered in NIP Knowledge Graph and privately accessible (R4b) • Data for model validation registered in NIP Knowledge Graph and privately accessible (R5b) • Model artefacts registered in HBP Model Catalog/NIP Knowledge Graph and mirrored to internal HBP Collab/store upon each model release (R6b) • End user license terms in case of	• R1 & R2 • Inventory of data used accessible through HBP Collaboratory (R3c) • Data for model building registered in NIP Knowledge Graph and publicly available (R4c) • Data for model validation registered in NIP Knowledge Graph and publicly available (R5c) • Model artefacts registered in HBP Model Catalog/NIP Knowledge Graph upon each model release and publicly available (R6c) • End user license terms for model use (R7b) • Model artefacts available for BSP use cases (R10)

		community development (R7a)	
Optional properties		• Harmonised, standardised model representations (R8) • Validation implemented through BSP's Validation Framework (R9) • Model artefacts available for BSP use cases (R10)	• Harmonised, standardised model representations (R8) • Validation implemented through BSP's Validation Framework (R9) • Functionality for model building, simulation and analysis available as BSP use cases (R11)
SP6 SGA1 community use models	• Parameter prediction with molecular dynamics (T6.1.1) • Intracellular signalling cascades involved in plasticity (T6.1.2) • Interaction of excitatory and inhibitory currents in spines (T6.1.3) • Multiscale modelling integrating intracellular signalling cascades (T6.1.4)	• Human neurons (T6.2.1) • Somatosensory cortex (T6.2.2) • Cerebellum (T6.2.3) • Basal Ganglia (T6.2.5) • Whole mouse brain (T6.2.6)	• eLife Passive human cell models
SP6 SGA1 community development models		• Hippocampus (T6.2.4) [currently still community on invitation]	

Dependency on Other HBP Platform Developments

The above listed HBP Integration Requirements are subject to the technical availability of underlying functionality of the various HBP Platforms (e.g. Neuroinformatics Platform's Knowledge Graph ready for data ingest) and possible prioritisation by other teams (e.g. data curation team). If the functionality is not yet available or ingest is scheduled for completion in the future, data and model artefacts may be put into a staging area for subsequent ingest and registration.

Compliance with HBP Integration Requirements

A model classified within a certain life cycle phase may not be fully compliant with all the requirements set forth by the respective phase. This may happen especially during the introduction of this new life cycle model or when a model moves from one phase to the next. SP6 management will track respective compliance/non-compliance and use this as a management tool to coordinate and prioritise SP6 activities.

Relevance to Other Modelling Activities in the HBP

This Life Cycle Model may be applicable to other modelling efforts with similar complexity and longevity of models, such as mouse body models in SP10.

Relation to External Repositories

The above life cycle requirements are not meant to exclude publishing of data and model artefacts in external community repositories (e.g. neuromorpho, ModelDB, etc.). However, publishing according to the above requirements in the HBP Platforms should be the priority, and mirroring in public repositories can be seen as a desirable optional activity.

Outlook to SGA2

In SGA2, there are three explicit community tasks, for cortex, cerebellum and hippocampus, respectively. Their goal is to transfer the lessons learned for community management of the hippocampus during SGA1 into the respective communities of cortex and cerebellum. As a goal of SGA2, the hippocampus will become a community structured modelling process, while cortex and cerebellum will focus on pushing the internal results to exploitation as soon as possible to form a model user community, and accept specific contributions (i.e. structured, but non-community modelling, and run a managed exploitation phase with the goal to attract model contributors).

5. Annex: Summary of Dissemination Status of SP6 SGA1 model components

Life Cycle Stage, Publication Status, Dissemination Status of SP6 SGA1 model components; this is an extract and summary of the information provided in the online Model Inventories for each model linked in sections 1.2.2 and section 2.

Table 7

Brain Region	Species	Type	Artefact Name	Life Cycle Stage	Publication	Dissemination Status
SIGNALLING CASCADES (Component ID: 762)						
General	-	General	CaMKII/PP2B/CaM cascade	Incubator	Unpublished	HBP Internal release 2018.03
Basal ganglia	-	MSN	Endocannabinoid pathway	Incubator	Unpublished	HBP Internal release 2018.03
Ca2+-dependent cascades controlling synaptic signalling and homeostasis (Component ID: 1137)						
General	-	Spine Model	Dendritic spine model with inhibition (python)	Incubator	Unpublished	HBP Internal release 2018.03
General	-	Spine Model	Dendritic spine model with inhibition (NEURON)	Incubator	Unpublished	HBP Internal release 2018.03
General	-	Reaction Model	Simplified Ca-dependent cascade model	Incubator	Unpublished	HBP Internal release 2018.03
General	-	Reaction Model	Full Ca-dependent cascade model	Incubator	Unpublished	HBP Internal release 2018.03
MULTISCALE (Component ID: 766)						
Striatum	Mouse	Single Cell Model	Medium spiny neuron (dMSN); electrophysiology and subcellular signalling	Incubator	Lindroos *et al.*, 2018	Anyone at ModelDB
Striatum	Mouse	Data	Morphology dMSN, cell WT-P270-20	Incubator	Lindroos *et al.*, 2018	Anyone at ModelDB

Striatum	Mouse	Data	Validation Data – CA transient	Incubator	Lindroos *et al.*, 2018	Anyone at ModelDB
Striatum	Mouse	Data	Validation Data - Electrophysiology	Incubator	Lindroos *et al.*, 2018	Anyone at ModelDB
Striatum	Mouse	Data	Ion channel models MSN	Incubator	Lindroos *et al.*, 2018	Anyone at ModelDB
Striatum	Mouse	Reaction Model	Subcellular cascades	Incubator	Lindroos *et al.*, 2018	Anyone at ModelDB
HUMAN NEURONS (Component ID: 1029)						
Cortex	Human	Single Cell Models	Layer 2/3 pyramidal cells Passive model HL2/3 0603Cell03 Passive model HL2/3 0603Cell08 Passive model HL2/3 0603Cell11 Passive model HL2/3 1303Cell03 Passive model HL2/3 1303Cell05 Passive model HL2/3 1303Cell06	Structured	Eyal *et al.*, 2016	Model & data publicly available to anyone with HBP community account
STRIATUM SCAFFOLD (Component ID: 972)						
Striatum	Mouse	Single Cell Models	Optimised single neuron model MSN D1, cell YJ150915_c6 Optimised single neuron model MSN D2, cell YJ150915_c7 Optimised single neuron model FS, cell 161205_FS1 Optimised single neuron model ChIN, cell CIN-2016-05-04_slice2_Cell3	Structured	Unpublished	Publicly available for Single Cell Building/Model Validation Use Case to anyone with HBP community account

Striatum	Mouse	Data	Repaired morphologies MSN D1 Repaired morphologies MSN D2 Repaired morphologies FS Repaired morphologies ChIN	Structured	Unpublished	Publicly available for Single Cell Building/Model Validation Use Case to anyone with HBP community account
Striatum	Mouse	MSN FS ChIN	Striatum microcircuit	Structured	Unpublished	Publicly available for Single Cell Building/Model Validation Use Case to anyone with HBP community account
CEREBELLUM SCAFFOLD (Component ID: 3023)						
Cerebellum	Rat	Single Cell Models	Granule mono compartmental model Granule multi compartmental model	Structured	Masoli *et al.*, 2017a	Model publicly available to anyone with HBP community account
Cerebellum	Rat	Data	Granule mono morphology Granule multi morphology	Structured	Masoli *et al.*, 2017a	Data publicly available to anyone with HBP community account
Cerebellum	Rat	Data	Granule mono Calcium buffer Granule mono Ca channel Granule mono Ka channel Granule mono Kca channel Granule mono Kir channel Granule mono Leak1 channel Granule mono Leak2 channel Granule mono Persistent Na channel Granule mono Km channel Granule mono Kv channel Granule mono Transient Na channel Granule mono Resurgent Na channel	Structured	Masoli *et al.*, 2017a	Data publicly available to anyone with HBP community account
Cerebellum	Rat	Data	Granule multi Calcium buffer Granule multi Ca channel	Structured	Masoli *et al.*, 2017a	Data publicly available to anyone with HBP community account

			Granule multi Ka channel Granule multi Kca channel Granule multi Kir channel Granule multi Km channel Granule multi Kv channel Granule multi Leak1 channel Granule multi Leak2 channel Granule multi Na channel			
Cerebellum	Mouse	Single Cell Model	Purkinje multi compartmental model	Structured	Masoli *et al.*, 2017b	Model publicly available to anyone with HBP community account
Cerebellum	Mouse	Data	Purkinje cell p43 mouse morphology	Structured	Masoli *et al.*, 2017b	Data publicly available to anyone with HBP community account
Cerebellum	Mouse	Data	Purkinje multi Cav2.1 channel Purkinje multi Cav3.1 channel Purkinje multi Cav3.2 channel Purkinje multi Cav3.3 channel Purkinje multi CDP5 calcium buffer Purkinje multi HCN1 channel Purkinje multi Kca1.1 channel Purkinje multi Kca2.2 channel Purkinje multi Kca3.1 channel Purkinje multi Kir2.3 channel Purkinje multi Kv1.1 channel Purkinje multi Kv1.5 channel Purkinje multi Kv3.3 channel Purkinje multi Kv3.4 channel Purkinje multi Kv4.3 channel Purkinje multi Leak channel Purkinje multi Nav1.6 channel	Structured	Masoli *et al.*, 2017b	Data publicly available to anyone with HBP community account
HIPPOCAMPUS CA1 SCAFFOLD (Component ID: 891)						
Hippocampus	Rat	Single Cell Models	Inter neurons: 27 single cell models optimised using BluePyOpt	Structured	Unpublished	Available for *in silico* experimentation to anyone with HBP community account

Hippocampus	Rat	Single Cell Models	Pyramidal cells: 17 single cell models optimised using BluePyOpt	Structured	Unpublished	Available for *in silico* experimentation to anyone with HBP community account
Hippocampus (CA1)	Rat	Network Model	Hippocampus CA1 model	Structured	Unpublished	HBP Internal releases: Network model 20160322 (RUP M30) Network model 20160630 Network model 20170630b Network model 20170630c Network model 20180219 Network model 20180309
SOMATOSENSORY CORTEX SCAFFOLD (Component ID: 3011)						
Somatosensory cortex	Rat	Single Cell Models	1035 cells (5 for each of the 207 different morpho-electrical types of the 6 layers)	Structured	Markram *et al*. 2015	Publicly accessible for download Available for *in silico* experimentation to anyone with HBP community account
Somatosensory cortex	Mouse	Single Cell Models	L1 NGC L2 inverted pyramidal cell L23 Chandelier Cell L4 MC dNAC L5 tufted pyramidal cell L6 inverted pyramidal cell	Structured	Unpublished	Models available for *in silico* experimentation to anyone with HBP community account
Somatosensory cortex	Mouse	Microcircuit Model	Somatosensory cortex microcircuit	Structured	Unpublished	HBP Internal release: M24 release
WHOLE MOUSE BRAIN NETWORK-LEVEL SCAFFOLD MODEL (Component ID: 827)						
Whole mouse brain	Mouse	Network Model	Generated cell position, orientation, properties for point neuron models and connectome	Structured	Unpublished	HBP Internal release: M24 release
Whole mouse brain	Mouse	Network Model	Cell counting and densities	Structured	Unpublished	HBP Internal release: M24 release

6. Annex: Summary of Data use in SP6 SGA1 model components

Summary of data use in SP6 SGA1 model components; this is a summary of the information provided in the online Model Inventories. For full information please refer to online Model Inventories linked for each model in sections 1.2.2 and section 2.

Table 8

Model Name	Data Use in Model	Data Source	HBP Funded
SIGNALLING CASCADES (Component ID: 762)			
Spine Model	Morphological data on gephyrin scaffolds	ENS	No
Ca2+-dependent cascades controlling synaptic signalling and homeostasis (Component ID: 1137)			
CaMKII/PP2B/CaM cascade	Dose response or time series data of substances and similar	Literature	No
Endocannabinoid pathway	Dose response or time series data of substances and similar	Literature	No
MULTISCALE (Component ID: 766)			
Medium spiny neuron (dMSN); electrophysiology and subcellular signalling	Dendritic CA transients	Day *et al.* 2008,	No
	Single cell electrophysiology	Planert *et al.,* 2013	No
	Cascades	Literature	No
HUMAN NEURONS (Component ID: 1029)			
Human Neurons	Morphology, electrophysiology, spine sizes	HBP RUP/HBP SGA1 (Task 1.2.1, T1.2.2, T2.2.6)	Yes
STRIATUM SCAFFOLD (Component ID: 972)			
MSN D1 & D2 Neuron Models	Morphologies	Neurmorpho.org	No
	Electrophysiology	HBP SGA - task 1.2.3, task 6.1.4	Yes
FS Neuron Model	Morphologies	Neurmorpho.org	No
	Electrophysiology	HBP SGA - task 1.2.3	Yes

ChIN Neuron Model	Eorphologies	HBP SGA - task 1.2.3	Yes
	Electrophysiology	HBP SGA - task 1.2.3	Yes
CEREBELLUM SCAFFOLD (Component ID: 3023)			
Purkinje cell model	Morphology	Egidio D'Angelo, Stefano Masoli, SP1 (http://neuromorpho.org)	Yes
	Channel kinetics	Masoli *et al.*, 2015, Masoli and D'Angelo 2017 T6.2.4, T1.2.4	Yes
Granule cell model optimisation	Morphology reconstruction	Diwakar *et al.*, 2009 & D'Angelo *et al.*, 2001, D'Angelo lab T6.2.4, T1.2.4	Yes
	Channel electrophysiology data	Diwakar *et al.*, 2009 & D'Angelo *et al,.* 2001, D'Angelo lab T6.2.4, T1.2.4	Yes,
	Single Cell electrophysiology	D'Angelo lab SGA1 T1.2.4, SP1 – HBP RUP	Yes
Golgi Cell model optimisation	Morphology reconstruction	Vervaeke *et al.,* 2010	No
	Channel electrophysiology data	Solinas *et al.*, 2007 D'Angelo lab	No
	Single Cell electrophysiology	D'Angelo lab SGA1 T1.2.4, SP1 – HBP RUP	Yes
Stellate Cell model optimisation	Morphology reconstruction	D'Angelo lab, SP1	Yes
	Single Cell electrophysiology	D'Angelo *et al.*, 2002 T1.2.4	Yes
Scaffold Cerebellum	Positioning and connectome of different neuron types in a layered-volume	Solinas *et al.,* 2010	No
HIPPOCAMPUS CA1 SCAFFOLD (Component ID: 891)			
Scaffold Hippocampus CA1	Morphology reconstruction + locations (rat)	HBP RUP/SGA1	Yes
	Morphology reconstructions + locations (mouse)	HBP RUP (Task 1.2.4) + SGA1 (Task 1.2.5)	Yes
	Paired recordings (mouse)	HBP SGA1 (Task 1.2.6)	Yes
	Atlas (rat)	Ropireddy *et al.*, 2012	Yes
SOMATOSENSORY CORTEX SCAFFOLD (Component ID: 3011)			
Scaffold Somatosensory Cortex Microcircuit (mouse)	Morphology reconstruction	EPFL/BBP	No

	Layer thickness + C57-NeuN-Feb-2018 + C57-interneurons-Feb-2018 + C57 Somatosensory Synaptic Density	HBP-SGA1 (UPM)	Yes
	Cell models	Allen Institute	no
WHOLE MOUSE BRAIN NETWORK-LEVEL SCAFFOLD MODEL (Component ID: 827)			
Whole mouse brain	Nissl stains & parcellation & AAV tracer stains,	Allen Brain Atlas	No
	Whisker inputs & projections,	Zembrzycki *et al.*, (2013)	No
	Thalamus input, sensory input mapped to thalamus,	Hunnicutt *et al.*, (2014)	No
	Motor neuron tracing data,	Zembrzycki *et al.*, (2013)	No
	Calcium imaging	European Laboratory for Non-Linear Spectroscopy, EPFL Neuroprosthetics laboratory	No

7. Annex: Open Sourcing Strategy

This annex summarises open sourcing strategy of SP6/BSP at the end of SGA1.

Constraints

- Naive open sourcing without common file format nor sufficient maturity and documentation does not lead to community convergence
- BSP functionality has been enabled in the first place by leveraging a large amount of in-kind background/side-ground contribution; if HBP had to build this from scratch, much larger resource numbers (3-5x) would have to be dedicated to software engineering
- Given current resources in SP6 for scientific software engineering, tradeoffs have to be made in terms of priorities
  - Generalise background contribution software to general applicability
  - Harden software tools, improve documentation and ease of use for the average user + combine with outreach strategy
  - Co-design & maintenance of platform foundation software for power users to deliver on science objectives of the project

Goals

- Responsible open source strategy to ensure usability and community adoption readiness at the time of release and efficient use of resources to achieve community convergence
- Deliver functionality as early as possible, e.g. through delivery “as a Service” in order to allow the community to benefit even before a tool is open sourced
- For maximal convergence and synergy, implement a phased approach around mature functionality useful for the wide community (not just power users) and supported by outreach (MOOC1, MOOC2, MOOC3) – see Figure 1
  - Phase 1: Cell Building (SGA1)
  - Phase 2: *In silico* Experimentation (SGA1 + SGA2)
  - Phase 3: Circuit Building (SGA2 + SGA3)
- Build ecosystem around recently developed open (and performant) circuit and simulation data format: SONATA
- Leverage open source efforts from in-kind contributions such as open sourcing by EPFL/BBP to compensate HBP’s overall shift away from a simulation-focused mission to a wider set of goals

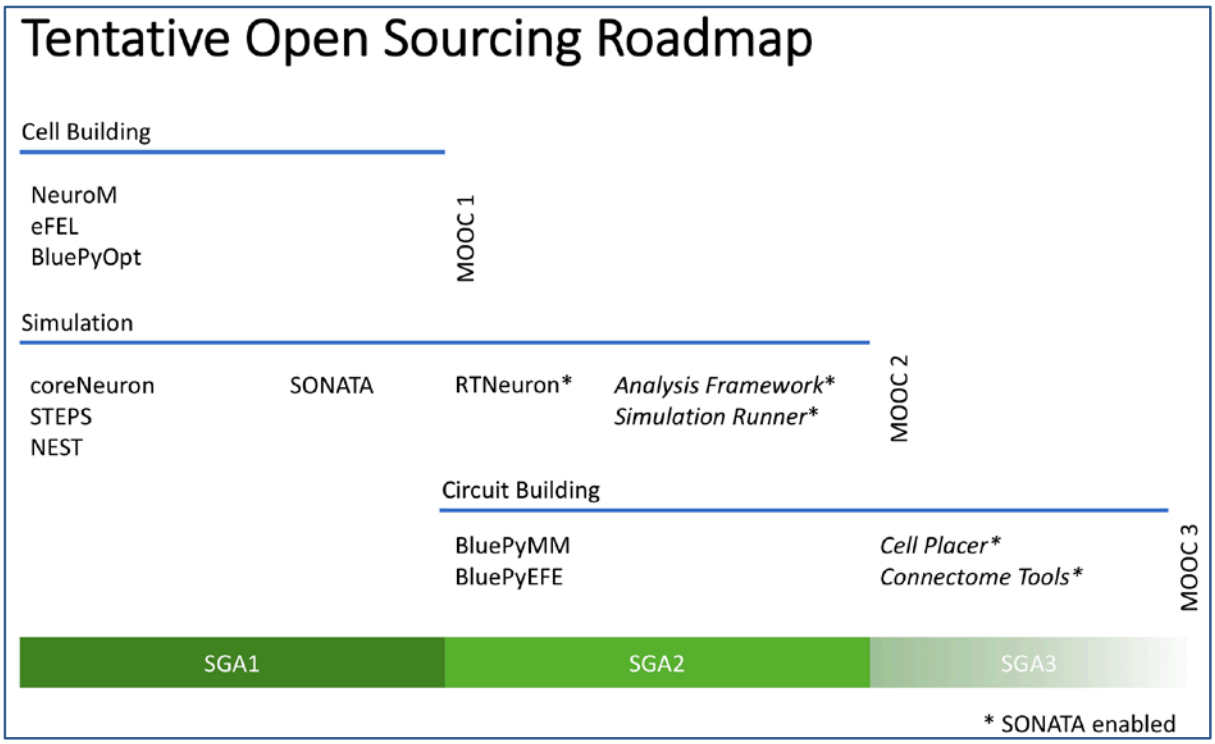

Figure 17 Tentative Open Sourcing Roadmap