# *EBRAINS modelling workflows implementation status at M21 (D5.5 – SGA3)*

M21 status on installed workflows and simulation engines including tools interconnected according to EBRAINS architecture specification, closed-loop simulation solutions, and new release of tools interconnected by EBRAINS APIs.

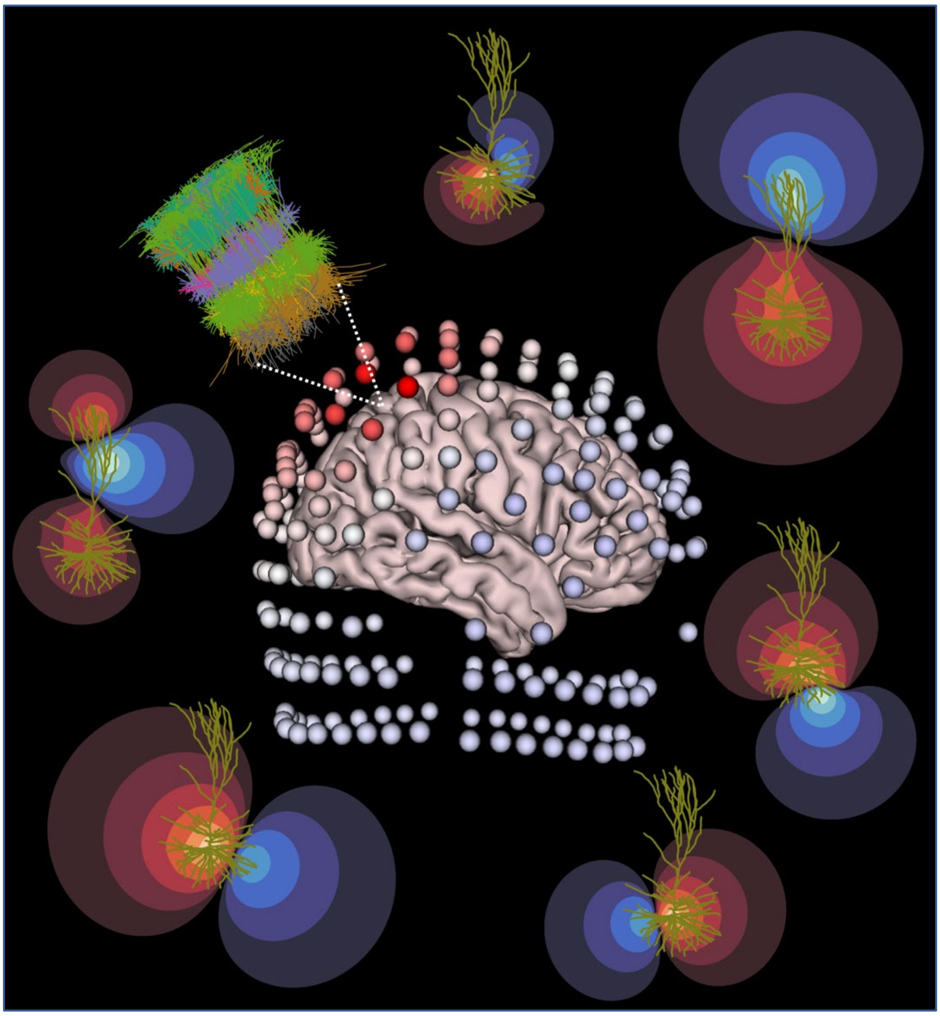

**Figure 1: Illustration of the dipole nature of the EEG signal as predicted by computer models.**

The EEG signal measured on the surface of the head originates from large numbers of synaptic inputs to populations of neurons. In principle, each synaptic input causes a complex pattern of current sources and sinks, but the EEG contribution from single cells, or even large neural populations can be represented with high accuracy by single current dipoles. This lays the ground for accurate simulation of EEG signals, also from more high-level simulations of neural activity, like point neuron networks or firing rate models (Næss *et al.* 2021[1])https://doi.org/10.1016/j.neuroimage.2020.117467.

---

[1] Næss, S., *et al.*, Biophysically detailed forward modeling of the neural origin of EEG and MEG signals. NeuroImage, 2021. 225: p. 117467. (P2604)

| | | | |
|---|---|---|---|
| Project Number: | 945539 | Project Title: | HBP SGA3 |

| | |
|---|---|
| Document Title: | EBRAINS modelling workflows implementation status at M21 |
| Document Filename: | D5.5 (D52) SGA3 M21 ACCEPTED 220520.docx |
| Deliverable Number: | SGA3 D5.5 |
| Deliverable Type: | Other |
| Dissemination Level: | PU = Public |
| Planned Delivery Date: | SGA3 M21 / 31 Dec 2021 |
| Actual Delivery Date: | SGA3 M21 23 Dec 2021; accepted 20 May 2022 |
| Author(s): | Felix SCHÜRMANN, EPFL (P134) |
| Compiled by: | Felix SCHÜRMANN, EPFL (P134), Katrien VAN LOOK, EPFL (P134) |
| Contributor(s): | Luca Leonardo BOLOGNA, CNR (P12)<br>Claudia CASELLATO, UNIPV (P70)<br>Jean-Denis COURCOL, EPFL (P134)<br>Benjamin CUMMING, ETHZ (P18)<br>Egidio D'ANGELO, UNIPV (P70)<br>Giulia D'ARRIGO, HITS (P26)<br>Andrew DAVISON, CNRS (P10)<br>Michael DENKER, JUELICH (P20)<br>Robin Gilbert DE SCHEPPER, UNIPV (P70)<br>Sandra DIAZ, JUELICH (P20)<br>Markus DIESMANN, JUELICH (P20)<br>Gaute EINEVOLL, NMBU (P44)<br>Anne ELFGEN, JUELICH (P20)<br>Jan FOUSEK, AMU (P78)<br>Sonja GRÜN, JUELICH (P20)<br>Espen HAGEN, NMBU (P44)<br>Jeanette HELLGREN KOTALESKI, KTH (P39)<br>Johannes HJORTH, CNRS (P10)<br>Adam HOSPITAL, IRB Barcelona<br>Brent HUISMAN, JUELICH (P20)<br>Viktor JIRSA, AMU (P78)<br>James KING, EPFL (P134)<br>Wouter KLIJN, JUELICH (P20)<br>Juliette MARTIN, CNRS (P10)<br>Michele MIGLIORE, CNR (P12)<br>Abigail MORRISON, JUELICH (P20)<br>Torbjørn Vefferstat NESS, NMBU (P44)<br>Lena ODEN, JUELICH (P20)<br>Petra RITTER, CHARITE (P122)<br>Óscar David ROBLES SÁNCHEZ, URJC (P69)<br>Giulia ROSSETTI, JUELICH (P20)<br>Dennis TERHORST, JUELICH (P20)<br>Werner VAN GEIT, EPFL (P134)<br>Rebecca WADE, HITS (P26)<br>Huifang WANG, AMU (P78)<br>Benjamin WEYERS, UT (P130) |
| WP QC Review: | Anne ELFGEN, JUELICH (P20) |
| WP Leader / Deputy Leader Sign Off: | Susanne KUNKEL, NMBU (P44) |
| T7.4 QC Review: | Guy WILLIS, EBRAINS (P1) |
| Description in GA: | M21 status on installed workflows and simulation engines including tools interconnected according to EBRAINS architecture specification, closed-loop simulation solutions, and new release of tools interconnected by EBRAINS APIs. |
| Abstract: | This report presents the status of tools and workflows for modelling and simulation in EBRAINS at the end of 2021. It contains a brief guide to each of the available and planned tools/workflows with links to further information, recent changes since the M9 Deliverable and an outlook for the remainder of SGA3. |
| Keywords: | Modelling, simulation, data analysis, model validation, visualisation, molecular, subcellular, single neuron, network, whole brain, software libraries, web apps, workflows. |
| Target Users/Readers: | Computational neuroscience community, computer scientists, Consortium members, funders, general public, HPC community, neuroinformatics specialists, neuroscience community, neuroscientists, platform users, researchers, students. |

## Table of Contents

## Table of Tables

## Table of Figures

# 1. Overview

EBRAINS is a new digital research infrastructure, created by the EU-funded Human Brain Project (HBP), that gathers and makes available an extensive range of data and tools for brain-related research. It draws on cutting-edge neuroscience, big data, computing, robotics and related technologies to help translate the latest scientific discoveries into innovation in medicine and industry, for the benefit of patients and society.

EBRAINS's ambition is to provide the neuroscience community at large with an open, state-of-the-art capability that fosters collaborative brain science, opens the way to ground-breaking discovery and aims to secure Europe's leading position in the dynamically growing field of multidisciplinary brain research and its exploitation.

This document provides an update on the implementation status of the EBRAINS modelling workflows at SGA3 Project Month 21 (M21). The document is organised in the spirit of "release notes", providing users with a summary of the developments that have occurred since M9  For a full description of this part of EBRAINS and the tools included here, please consult the earlier Deliverable D5.2[2] (EBRAINS modelling workflows implementation status at M9), which provides useful background.

# 2. Status Summary of Modelling Workflows in EBRAINS

## 2.1 Integration of Tools in EBRAINS

The integration of modelling tools and workflows into the EBRAINS infrastructure has progressed well. A central accomplishment has been the transition to a single EBRAINS platform from the previously separated HBP platforms and Collaboratory 1, which were successfully decommissioned in September 2021.

From a user perspective, this integration now means that EBRAINS is a single-entry point for a diverse set of modelling workflows and proposes a set of common usage idioms, improving the overall user experience:

- **Knowledge Graph Integration** – Applications and workflows consuming data from the EBRAINS Knowledge Graph and deposit their outputs into the Knowledge Graph respectively. This allows easy reuse of one's own or other users' results and enables better chaining of workflows.
- **Handling of User Data with Collaboratory/Drive+Bucket** – Workflows accepting data provided by the user via the Collaboratory/Drive and Collaboratory/Bucket, which provide a convenient low-volume store and a safe large-volume store. This provides a robust, safe whilst flexible means to work with data on the EBRAINS infrastructure.
- **Workflow Customisation with Collaboratory/Lab** – Workflows requiring a large amount of flexibility and adaptability are typically implemented in Python notebooks. Using the Collaboratory/Lab services users are enabled to derive their own variant of such workflows. Embracing the community standard of Python notebooks in a JupyterLab environment delivers state-of-the-art functionality to the user, with added value due to the integration with other EBRAINS services.

Using the EBRAINS Collaboratory's Identity and Access Management system, the applications and workflows can use a single set of credentials, can be deployed on dedicated virtual machines managed by EBRAINS, and can use scalable and interactive HPC provided to EBRAINS via FENIX. For the status of service integration, please consult Table 1, which summarises the status and interdependencies between the different tools and services.

---

[2] https://sos-ch-dk-2.exo.io/public-website-production/filer_public/bc/40/bc400294-0104-4ec3-b463-72803255b686/d52_d49_sga3_m9_accepted_210303.pdf

## Table 1: Interdependencies between EBRAINS tools and services.

| | | Other SCs | | | | | | | | | | SC3 | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | IAM | JupyterLab | Collaboratory/Drive | KG | Prov Service | Curated Data | Neuromorphic | VMs | Scalable HPC | Interactive HPC | Model Catalog | Electrical Model Building Toolset | PyNN | NESTML | Snudda | Brain Scaffold Builder | NEST | Arbor | NEURON/coreNEURON | Multiscale, multi-simulator, co-simulation | Neo | Elephant | LFPy | Elephant Visualization (Viziphant) | Validation Test Libraries | SimDaVis - Insite | BluePyEfe | BluePyOpt | TVB | NRP | CSCS Openshift | CSCS Pollux Storage | Neuron as a Service (aka BlueNaaS aka Single Cell In Silico Experiment Tool) | Feature Extraction Tool (NeuroFeatureExtract) |
| app | Subcellular Web App | 🟨 |  |  | 🟨 | 🟨 | 🟨 |  | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟨 |  |  |  |  |  | 🟩 | 🟩 |  |  |
| app | Feature Extraction Tool (NeuroFeatureExtract) | 🟨 |  |  | 🟨 | 🟨 | 🟨 |  | 🟩 |  |  |  |  |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |
| app | **Hodgkin-Huxley Neuron Builder (HHNB)** | 🟩 |  | 🟨 | 🟨 | 🟨 | 🟨 |  | 🟩 |  | 🟩 | 🟩 |  |  |  |  |  |  |  | 🟩 |  | 🟩 |  |  |  |  |  |  | 🟩 |  |  |  |  | 🟩 | 🟩 |
| app | NEST Desktop | 🟨 |  |  | 🟨 | 🟨 |  |  | 🟩 |  |  | 🟨 |  |  |  |  |  | 🟩 |  |  | 🟩 |  | 🟨 |  |  |  | 🟩 |  |  |  | 🟨 |  |  |  |  |
| app | The Virtual Brain (TVB) | 🟩 | 🟩 | 🟩 | 🟩 | 🟨 | 🟩 | 🟨 | 🟩 | 🟩 | 🟩 | 🟨 |  |  |  |  |  | 🟩 |  |  | 🟩 |  | 🟩 |  |  | 🟨 |  |  |  |  | 🟨 | 🟩 | 🟩 |  |  |
| app | **SDA** | 🟨 |  |  | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app | ArDOCK | 🟨 |  |  | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app | CGMD Platform | 🟨 | 🟨 | 🟨 | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app | SSB Platform/METNET | 🟨 | 🟨 | 🟨 | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app | MoDEL-CNS | 🟨 | 🟨 | 🟨 | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app | BioExcel-CV19 | 🟨 | 🟨 | 🟨 | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app | **Small Circuit In Silico Experiments Tool (Rat Hippocampus CA1)** | 🟨 |  |  | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟩 |  |  |  |
| app | **Brain Areas Circuit In Silico Experiments Tool (Rat Hippocampus CA1)** | 🟨 |  |  | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟩 |  |  |  |
| app | **Neuron as a Service (aka BlueNaaS aka Single Cell In Silico Experiment Tool)** | 🟨 |  |  | 🟨 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟩 |  |  |  |
| app | **SimVisSuite** | 🟨 |  |  |  |  |  |  | 🟨 |  | 🟨 |  |  |  |  |  |  |  |  |  | 🟨 |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  |
| app | **SimDaVis - Insite** | 🟨 |  |  |  |  |  |  | 🟨 | 🟨 |  |  |  |  |  |  |  | 🟩 | 🟨 |  | 🟩 |  | 🟨 |  |  |  | 🟩 |  |  |  |  |  |  |  |  |
| app | Neuromorphic Computing Job Manager App | 🟩 | 🟩 | 🟨 | 🟨 | 🟨 | 🟨 | 🟩 | 🟩 | 🟨 |  |  |  | 🟩 |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app (Jupyter) | **Rebuild an Existing Single Hippocampal Cell Model** | 🟩 | 🟩 | 🟩 | 🟩 | 🟨 | 🟩 |  |  |  | 🟩 | 🟩 |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |
| app (Jupyter) | **Build Your Own Single Hippocampal Cell Model Using HBP Data** | 🟩 | 🟩 | 🟩 | 🟩 | 🟨 | 🟩 |  |  |  | 🟩 | 🟩 |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |
| app (Jupyter) | **Synaptic Events Fitting** | 🟩 | 🟩 | 🟩 | 🟩 | 🟨 | 🟩 |  |  |  | 🟩 |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| app & service | Model Catalog | 🟩 | 🟩 | 🟩 | 🟩 | 🟨 | 🟨 | 🟨 | 🟩 | 🟨 |  |  |  |  |  |  |  |  |  |  | 🟨 | 🟨 | 🟨 |  |  | 🟩 |  |  |  |  |  |  |  |  |  |
| library | Electrical Model Building Toolset |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟩 |  | 🟩 |  | 🟨 |  |  |  | 🟩 | 🟩 |  |  |  |  |  |  |
| library | PyNN |  | 🟩 |  |  |  |  | 🟩 |  | 🟨 |  |  |  |  | 🟨 |  |  | 🟩 | 🟨 | 🟩 | 🟨 | 🟩 |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |
| library | **NESTML** |  | 🟩 |  | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  | 🟩 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| library | **Snudda** |  | 🟨 | 🟨 |  |  | 🟨 |  |  | 🟩 |  |  |  |  |  | 🟩 |  |  |  | 🟩 |  |  |  |  |  | 🟩 |  | 🟩 | 🟩 |  |  |  |  |  |  |
| library | Brain Scaffold Builder |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  | 🟩 | 🟩 | 🟩 | 🟨 |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |
| library | **NEST** |  | 🟩 |  |  |  |  |  | 🟩 | 🟩 | 🟨 |  |  | 🟩 | 🟩 |  | 🟩 | 🟩 | 🟨 |  | 🟩 | 🟨 |  | 🟨 |  |  | 🟨 |  |  | 🟨 | 🟨 |  |  |  |  |
| library | **Arbor** |  | 🟨 |  |  |  |  |  | 🟨 | 🟨 | 🟨 |  |  |  |  |  | 🟩 | 🟨 | 🟩 |  | 🟩 |  |  | 🟨 |  | 🟨 |  |  |  |  |  |  |  |  |  |
| library | **NEURON/coreNEURON** |  | 🟩 |  |  |  |  |  |  | 🟩 |  |  |  | 🟩 |  |  | 🟩 |  |  | 🟩 | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| library | Multiscale, multi-simulator, co-simulation | 🟨 | 🟩 | 🟨 | 🟨 | 🟨 | 🟨 |  | 🟨 | 🟩 | 🟩 |  |  | 🟨 | 🟨 |  | 🟨 | 🟩 | 🟩 | 🟨 | 🟩 | 🟩 | 🟩 | 🟩 | 🟨 |  | 🟩 |  |  | 🟩 | 🟨 |  |  |  |  |
| library | Neo |  | 🟩 |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| library | Elephant |  | 🟩 |  |  | 🟨 |  |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  | 🟩 | 🟩 |  |  | 🟩 |  |  |  |  |  |  |  |  |  |  |
| library | **LFPy** |  | 🟨 |  |  | 🟩 |  |  | 🟩 | 🟩 | 🟩 |  |  |  |  |  | 🟨 | 🟨 | 🟩 | 🟩 | 🟩 | 🟩 | 🟩 |  |  |  |  | 🟨 | 🟨 | 🟨 |  |  |  |  |  |
| library | Elephant Visualization (Viziphant) |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟨 | 🟩 | 🟩 |  |  |  |  |  |  |  |  |  |  |  |  |
| library | Validation Test Libraries |  | 🟨 |  |  |  |  |  |  | 🟨 |  |  | 🟩 | 🟩 | 🟨 | 🟨 |  | 🟩 | 🟨 | 🟩 | 🟨 | 🟩 | 🟩 | 🟨 | 🟨 |  |  |  |  |  |  |  |  |  |  |
| library | **Molecular Level Tools (Apps and Scripts) e.g. MD-IFP, PIPSA** |  | 🟨 | 🟩 | 🟩 |  | 🟩 |  | 🟩 | 🟩 | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| library/workflow | Subcellular Model Building Toolset |  | 🟨 | 🟨 | 🟨 |  |  |  | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 🟨 |  |  |  |  |  |  |  |  |  |
| workflow/app | **Jupyter Notebook for Computing Dissociation Rates Using tauRAMD Method** |  | 🟨 | 🟨 | 🟨 |  |  |  | 🟨 | 🟨 | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| workflow/app | JN and Scripts for Using Molecular Level Tools (to Port from HBP to EBRAINS Platform) |  | 🟨 | 🟩 | 🟩 |  | 🟩 |  | 🟩 | 🟩 | 🟨 | 🟨 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**Green indicates that the tool or service in the left-hand column uses, or can easily be run on, the tool or service listed in the columns. Yellow means that such integration is planned, partial, or in progress. It should be noted that this table is meant to guide the user as to which use scenarios are possible, i.e. not all combinations are desirable/useful nor are they planned (for example, libraries would typically not integrate with IAM, but the applications using the libraries would).**

Technically speaking, this integration process requires re-factoring of services and workflows to interoperate with the aforementioned EBRAINS's core services and deployment to dedicated EBRAINS resources. While it is of course possible to use the majority of the modelling and simulation tools standalone because of their open-source nature, the integration with EBRAINS allows their operation as part of an ecosystem reflecting the need for more complex scientific workflows of today's science. The ability to run the tools directly on EBRAINS's elastic and supercomputing resources furthermore frees users to provision costly infrastructure. For more details on the EBRAINS-wide integration process run by the HBP's Technical Coordination team, please refer to the SGA3 Deliverables D5.3 and D5.4.

## 2.2 Improvements and Additions to Tools

Alongside the aforementioned integration, additional improvements and additions have been accomplished for M21. For example, the migration from Python 2.x to Python 3.6+ for packages using Python was accomplished, which became necessary due to the sunsetting of Python 2.

All improvements of the underlying software packages and libraries done in the context of the HBP have also been released separately in their respective open-source repositories, specifically NEST 3.0 and 3.1, NEURON 7.8.2 and 8.0, Neo 0.10.0 (smaller release), Elephant (major release), new releases for ViSimpl, NeuroTessMesh and NeuroScheme (SimVisSuite), NEST Desktop, SimDaVis - Insite, Elephant Visualization (Viziphant) and Validation Test Libraries.

In addition, the Model Catalog is now available as a "community app" in the EBRAINS Collaboratory.

Finally, there are five new tools/services listed in this Deliverable, which were not listed in the earlier M9 Deliverable (D 5.2). These are:

- CNS Ligands – this website has been introduced as a platform designed to efficiently generate and parameterise bioactive conformers of ligands binding to neuronal proteins for molecular dynamics simulations.
- GRALL - the Glycine Receptor Allosteric Ligand Library (GRALL) is the first database of allosteric modulators of a human synaptic receptor with a structural annotation based on their binding site on the receptor.
- Single Cell Modelling Workflows – these workflows consist of an ensemble of Jupyter notebooks for single cell modelling and data analysis.
- BioExcel-CV19 - a standalone web app and a new webserver resource for providing molecular dynamics simulation data; it is a collaboration between HBP, Fenix and BioExcel.
- MMCG Platform – the webserver automatises and speeds up the hybrid Molecular-Mechanics/Coarse-Grained (MM/CG) simulations set-up of G-Protein coupled receptors/ligand complexes.

# 3. How to Read this Document

EBRAINS Modelling Workflows can be categorised by:

- Type (web app, software library, command-line application, web service),
- Model scope (molecular and subcellular mechanisms, single neurons, networks, whole brain),
- Abstraction level (statistical modelling, systems biology, point neuron models, biophysical neuron models, population modelling, etc.),
- Role in the modelling and simulation life cycle (essentially the activity by a scientist while creating, exploring and validating a model).

Below we give a brief introduction to the available and planned tools and services, grouping them by activity. Where tools and services have multiple features with different levels of maturity, the icon indicates the most mature features.

Table 2 explains the icons used in Section 4 to document the type, maturity, modelling scope and abstraction layer of each tool or workflow. Furthermore, we have added icons for the support and training channels, making it easier for a user to see what type of resources are available to help users of a given tool/workflow (Table 3). In particular, we identify where there are online training resources, such as the Massive Open Online Course or online tutorials; in-person meetings, such as summer schools or user group meetings; and other electronic support channels, such as user forums or dedicated support channels (e.g. via the HBP's High Level Support Team).

While the general description of most tools/workflows can be found in the M9 Deliverable D5.2[3], Section 5 provides an update on results achieved since M9 (December 2020) and future plans. Summary tables for all the tools, workflows and services can be found in the Annex.

Table 2: Legend for icons for each tool or service that were already used in D5.2.

| Type | | Availability/maturity | | Scope | | Modelling abstraction level | |
|---|---|---|---|---|---|---|---|
| web app | 💻 | mature, available now (TRL 7-9) | ✓ | molecular | ⠿ | nanoscale | NS |
| command-line tool or library | ⚙ | prototype available (TRL 5-6) | 🔧 | subcellular | ⇄ | systems biology | SB |
| | | in progress / future work | 📋 | single neurons | Ẍ | point neuron models | PT |
| | | | | networks | ⅄ | biophysical models | BI |
| | | | | whole brain | 👤 | population models | PP |
| | | | | | | statistical models | ST |

Table 3: New icons added in D5.5 showing user engagement channels for each tool or service.

| User engagement channels | |
|---|---|
| online training/course/MOOC | 🎓 |
| workshop/summer school (in person) | 👥 |
| electronic support | 🎧 |

# 4. Recent Changes and Future Plans

## 4.1 Building Models

### *4.1.1 ArDOCK*

| | |
|---|---|
| **Type:** web app<br>**Scope:** molecular | 💻✓⠿<br>🎧 |
| **Abstraction level:** nanoscale<br>**Status:** available for use<br>**Homepage & more information:**<br>• https://ardock.ibcp.fr/ | |

---

[3] https://sos-ch-dk-2.exo.io/public-website-production/filer_public/bc/40/bc400294-0104-4ec3-b463-72803255b686/d52_d49_sga3_m9_accepted_210303.pdf

## Recent Changes

No changes since M9.

## Outlook

This component of the toolset developed in the HBP Collaboratory v1[4] will be made available on the EBRAINS platform.

# *4.1.2 Molecular Level Toolset*

| | |
|---|---|
| **Type:** workflows/scripts/tools/apps<br>**Scope:** molecular | |
| **Abstraction level:** nanoscale<br>**Status:** available on the EBRAINS Collaboratory<br>**Homepage & more information:**<br>• https://humanbrainproject.github.io/hbp-sp6-guidebook/online_usecases/molecular_level/molecular_level.html | |

## Recent Changes

Migration of guidebooks and Jupyter notebooks to the EBRAINS Collaboratory. New scripts have been developed to compute dissociation rate constants with the tauRAMD method[5] [6].

## Outlook

Further scripts for computing molecular binding kinetic parameters are in development. We are working on using FENIX resources for the more computationally demanding parts of the scripts and have been allocated ICEI-FENIX resources for this purpose. Molecular-level tools are in the process of being added to the EBRAINS Services listings.

# *4.1.3 CNS Ligands*

| | |
|---|---|
| **Type:** web app<br>**Scope:** molecular | |
| **Abstraction level:** nanoscale<br>**Status:** available for use<br>**Homepage & more information:**<br>• http://mmb.irbbarcelona.org/webdev/slim/CNS/public/<br>• https://search.kg.ebrains.eu/?facet_type[0]=Software&q=csn%20ligands#696d987f-128d-467b-a91b-1056a4f7dc7e | |

The CNS ligands website[7] has been introduced as a platform designed to efficiently generate and parameterise bioactive conformers of ligands binding to neuronal proteins for molecular dynamics simulations. The CNS ligands database presents the results in a graphical user interface, displaying small molecule properties, analyses and generated 3D conformers. All data produced by the project is available to download. CNS ligands will help to improve understanding of neuronal signalling cascades by protein structure-based simulations, calculating thermodynamics and kinetics constants of the molecular processes.

---

[4] https://wiki.ebrains.eu/bin/view/Collabs/computation-of-protein-association-rates

[5] https://kbbox.h-its.org/toolbox/methods/molecular-simulation/-random-acceleration-molecular-dynamics-ramd/

[6] initial version: https://wiki.ebrains.eu/bin/view/Collabs/protein-ligand-unbinding-rates

[7] http://mmb.irbbarcelona.org/webdev/slim/CNS/public/

### Recent Changes

The first dataset of bioactive conformers of ligands binding to neuronal proteins has been published in the CNS ligands database, including 71 interesting molecules for the central nervous system.

### Outlook

New bioactive conformations for ligands binding to neuronal proteins will be progressively added.

## 4.1.4 GRALL

| | |
|---|---|
| **Type:** web app<br>**Scope:** molecular | 💻 ✔ ⠿<br>🗣 |
| **Abstraction level:** nanoscale<br>**Status:** available for use<br>**Homepage & more information:**<br>• https://ifm.chimie.unistra.fr/grall | |

The Glycine Receptor Allosteric Ligand Library GRALL[8] is the first database of allosteric modulators of a human synaptic receptor with a structural annotation based on their binding site on the receptor. GRALL offers a collection of 218 chemical entities with documented modulatory activities at homomeric glycine receptors (GlyR) α1 and α3, which includes agonists, antagonists, positive and negative allosteric modulators and a large number of experimentally inactive compounds. This collection provides information on the chemical structure, the direction of modulation, the potency, the 3D molecular structure and quantum-mechanical charges of a large number of biologically active compounds at a human synaptic receptor. Most importantly, a large fraction of modulators in GRALL comes with a structural annotation of their ligand-binding site on the receptor, which was assigned using a level of confidence from 1 (highest) to 5 (lowest) depending on the quality of the evidence supporting the annotation. This information, which is currently missing in popular drug banks like ChEMBL, PubChem, or Binding DB provides a stringent benchmark that is expected to boost the development of predictive *in silico* strategies for allosteric drug design.

### Recent Changes

The GRALL library has been made publicly available as a web-accessible database at the following link: https://ifm.chimie.unistra.fr/grall. A documentation presenting the database, its general purpose, and how to use it has been added to the web page along with the EBRAINS logo.

### Outlook

GRALL is a unique contribution to the field of neuropharmacology, which is constantly in progress. We encourage researchers to submit missing information or new modulatory ligands via the pre-formatted form available from the GRALL website.

## 4.1.5 Subcellular Web App

| | |
|---|---|
| **Type:** web app<br>**Scope:** subcellular | 💻 ✔ ⇄<br>👥 🗣 |
| **Abstraction level:** reaction-diffusion systems<br>**Status:** available for use, EBRAINS integration in progress<br>**Homepage & more information:**<br>• https://subcellular.humanbrainproject.eu<br>• https://humanbrainproject.github.io/hbp-sp6-guidebook/online_usecases/subcellular_level/subcellular_app/subcellular_app.html | |

---

[8] https://ifm.chimie.unistra.fr/grall

## Recent Changes

The application scalability has been improved to support up to 10 million data points. It has been migrated to EBRAINS and a database backup/restore on EBRAINS has been created. In addition, the migration from a MongoDB database to PostgreSQL has been done. Recent changes also include the visualisation of reactivity networks, a new geometry editor for subcellular components, the addition of a Tetops solver[9] and the integration of additional BioNetGen solvers.

## Outlook

The improvement of a Python API to load models, configure and run simulation load models is planned.

### 4.1.6 *Subcellular Model Building Toolset*

| | |
|---|---|
| **Type:** library<br>**Scope:** subcellular models | |
| **Abstraction level**: molecular/subcellular<br>**Status:** in progress | |

## Recent Changes

The SBtab format was chosen and a toolchain was written to process this format. This includes a conversion tool that automatically creates Ordinary Differential Equation (ODE) code for many languages. Any subcellular reaction network model can now be converted to an ODE and solved using any of the commonly available solvers in many languages (C, R, Julia, MATLAB, GNU Octave). The models created in this way are suitable for parameter estimation tasks, as we have put emphasis on model parameters and model inputs, right from the beginning. We have also developed Bayesian parameter estimation tools as part of this set. We are using ABS sampling (R), SMMALA (C) and conventional optimisation (MATLAB). Some of these results are also described in Santos *et al.* 2020[10] and some modules are used in collaboration with a Partnering Project[11]. We have written a R package that uses the GNU scientific library in C (the programming language) to solve a series of ODE problems in parallel (this is in a working state, but is currently being further developed to include more features).

## Outlook

We are currently working on increasing the performance of this toolset. We do this by interfacing R (high-level) with C (lower-level) when solving initial value problems (ODEs), new features will include more convenience: instead of calling the solver with an initial value problem (as argument) we will provide an interface where the user specifies a simulation experiment, with a structure and terminology that is closer to systems biology. All toolset components are on GitHub, and most have a web presence, either through GitHub pages, readthedocs.io or independent. We will attempt to unify the tools in one place if that is feasible.

---

[9] Tetops solver is a reference to "TetopSplit" solver from STEPs : http://steps.sourceforge.net/manual/diffusion.html#Simulation-with-TetOpSplit .

[10] Santos, J. P. G. *et al.* (2020) A Modular Workflow for Model Building, Analysis, and Parameter Estimation in Systems Biology and Neuroscience. BioRxiv. (P2991)

[11] Church, T. W. *et al.* (2021) AKAP79 enables calcineurin to directly suppress protein kinase A activity. eLife e10:e68164 (P2992)

### 4.1.7 Feature Extraction Tool (NeuroFeatureExtract)

**Type:** web app
**Scope:** single neurons

**Abstraction level:** biophysical models
**Status:** available on EBRAINS
**Homepage & more information:**

- https://hbp-bsp-hhnb.cineca.it/efelg/
- https://ebrains-cls-interactive.github.io/
- https://search.kg.ebrains.eu/instances/Software/348d66fb-8e82-4e1b-b266-db886d6ca1b9

#### Recent Changes

The GUI of the NeuroFeatureExtract (NFE) has been updated with a more user-friendly layout. Functionalities to allow the users to configure feature extraction parameters (e.g. spike threshold, voltage correction) have been added, as well as the possibility to group the uploaded data files by cell id and tag them with relevant metadata. The possibility to upload data files in JSON format has been integrated. The Guidebook has been updated. The available dataset has been moved to the CSCS container and the relevant metadata have been created and made available for the integration of the NFE with the Hippocampus Hub[12].

#### Outlook

The tool will be supported and maintained going forward with special emphasis on fulfilling community requests. Whenever possible, the integration with the EBRAINS Knowledge Graph will be tightened (with respect to the relevant information on the data to be used for the feature extraction and the provenance tracking engine).

### 4.1.8 Hodgkin-Huxley Neuron Builder (HHNB)

**Type:** web app
**Scope:** single neurons

**Abstraction level:** biophysical models
**Status:** available on EBRAINS
**Homepage & more information:**

- https://hbp-bsp-hhnb.cineca.it/hh-neuron-builder/
- https://ebrains-cls-interactive.github.io/index.html
- https://kg.ebrains.eu/search/instances/Software/0295cfba-f9d6-4743-be2b-4628f7c5ab58

#### Recent Changes

The GUI of the Hodgkin-Huxley Neuron Builder (HHNB) has been updated with a more user-friendly layout. A number of APIs and front end components have been developed to integrate the HHNB with the Hippocampus Hub[13]. The code has been restructured for a more efficient execution. The Guidebook has been updated.

#### Outlook

The tool will be supported and maintained going forward with special emphasis on fulfilling community requests. Whenever possible, the integration with the EBRAINS Knowledge Graph will be finalised (e.g. as for data fetching and provenance tracking) and the number of HPC systems available for model optimisation will be increased.

---

[12] https://www.hippocampushub.eu/
[13] https://www.hippocampushub.eu/

## 4.1.9 Electrical Model Building Toolset

| **Type:** command-line tool or library<br>**Scope:** single neurons | |
|---|---|
| **Abstraction level:** biophysical neuron models<br>**Status:** mature, available on HPC, JupyterLab<br>**Homepage & more information:**<br>BluePyOpt:<br>• https://github.com/BlueBrain/BluePyOpt<br>• https://kg.ebrains.eu/search/instances/Software/d2918247-8f25-4252-8efb-906e8190d5cd<br>eFEL:<br>• https://github.com/BlueBrain/eFEL<br>• https://kg.ebrains.eu/search/instances/Software/42c9ca46-1689-4494-85b5-33f6dffc1ac7<br>BluePyEfe:<br>• https://github.com/BlueBrain/BluePyEfe | |

### Recent Changes

The eFEL documentation was extensively revised to add information on many eFeatures. Python 2 support was dropped and installable Python wheels for MS Windows for feel were added on PyPi.

In BluePyOpt and BluePyMM, the tests were moved to PyTest and Python 2 support was dropped. BluePyEfe was made compatible with newer versions of NWB data standard.

### Outlook

For BluePyEfe, support for other standardised formats will be added. Integration with LFPy is in the advanced stages and will be made open source soon. The core algorithm of BluePyMM is being re-thought to support very large neuron networks (>10 million neurons).

In the longer term, we will work on the integration of BluePyOpt with Arbor and the configuration system of BluePyEfe will be reworked to accommodate more general use cases. BluePyMM will support the SONATA network description format.

## 4.1.10 PyNN

| **Type:** command-line tool or library<br>**Scope:** networks | |
|---|---|
| **Abstraction level:** point neuron models, biophysical neuron models<br>**Status:** mature, available now on HPC, JupyterLab, neuromorphic<br>**Homepage & more information:**<br>• http://neuralensemble.org/PyNN/<br>• https://kg.ebrains.eu/search/instances/Software/bb06ac59-9ada-4b1d-a00a-e2fcafb031f8 | |

### Recent Changes

PyNN v0.9.6 added support for the Brian 2 simulator. The latest release of PyNN (v0.10.0) brings support for NEST v3 and NEURON v8, together with a number of bug fixes and minor improvements.

### Outlook

Within the next year, we will release PyNN 1.0, at which point the API for point neuron models will be considered stable. We will also begin releasing development versions of what will become PyNN 2.0[14], with the major change being support for multi-compartmental neuron models, with

---

[14] http://neuralensemble.org/docs/PyNN/2.0/

implementations for NEURON and Arbor. This will greatly facilitate cross-simulator comparisons for morphologically and biophysically detailed neuronal network models.

### *4.1.11 NESTML*

**Type:** command-line tool or library
**Scope:** single neurons, networks

**Abstraction level:** point neuron models
**Status:** mature, available on HPC, JupyterLab
**Homepage & more information:**

- https://nestml.readthedocs.io
- https://kg.ebrains.eu/search/instances/Software/95472c51-772c-42dd-a427-553851f83c2b

#### Recent Changes

The next major release of NESTML (version 4.0) containing improvements to equations and kernels handling has taken place, as well as two minor releases of ODE-toolbox (2.2 and 2.3), containing bug fixes and feature enhancements. Training materials, in the form of Jupyter (Python) notebooks, have been created for the synaptic plasticity rules feature. Several spike-timing dependent plasticity rule model variants have also been implemented as part of this.

#### Outlook

We are planning for seamless integration with the NEST simulator using the “just-in-time compilation” paradigm. This would simultaneously enable the integration of NESTML with NEST Desktop, allowing models to be created and edited directly via the NEST Desktop graphical user interface.

We aim to support a third-factor “Clopath” synaptic plasticity rule in NESTML and as part of this, implement support for differential equations with delay. In addition, we plan to support third-factor neuromodulated (e.g. dopamine-modulated) plasticity rules.

Finally, we plan to ramp-up the SpiNNaker platform target project.

### *4.1.12 Snudda*

**Type:** command-line tool or library
**Scope:** networks

**Abstraction level:** biophysical neurons
**Status:** prototypes available, integration in process
**Homepage & more information:**

- https://github.com/Hjorthmedh/Snudda
- https://search.kg.ebrains.eu/instances/e9390ad8-3167-43bd-b04d-fcfdccb59ac1

#### Recent Changes

A new methods paper for Snudda was published (Hjorth *et al.* 2021[15]) describing the underlying methods and how to use the software with examples using both Jupyter notebooks and command-line tools. Additional code has been added to facilitate input tuning for different neuron types, as different excitable neurons require different amounts of input in the network. Online documentation of the code has been created and is now available at https://snudda.readthedocs.io/en/latest/.

---

[15] Hjorth, J. J. J., Hellgren Kotaleski, J., & Kozlov, A. (2021). Predicting Synaptic Connectivity for Large-Scale Microcircuit Simulations Using Snudda. *Neuroinformatics*, *19*(4), 685-701. (P2899)

The Snudda framework has been extended to handle neuromodulation in a more generalised way, allowing for greater flexibility and simulation of multiple neuromodulators simultaneously. The methods are described in a methods paper (Frost Nylen *et al*. 2021)[16].

## Outlook

Work is ongoing for optimising the dynamics of the synapses, both for external input from cortex/thalamus and for intra-striatal synapses. Tools are being created to optimise the synapses; not only on single compartment models, but also on detailed electrophysiological models with full morphology. Tools are also being designed to allow for specifying population units and to introduce ablation of connectivity for virtual experiments.

Updated SONATA support and a tighter integration with the EBRAINS services is planned for the future. We plan to continuously update the network model, including adding new morphologies and neuron models.

# *4.1.13 Brain Scaffold Builder*

**Type:** command-line tool or library
**Scope:** networks

**Abstraction level:** multi-scale networks with spatial features, biophysical neurons, point neurons
**Status:** prototypes available
**Homepage & more information:**

- https://github.com/dbbs-lab/bsb

## Recent Changes

We have enriched the reconstruction algorithms, in order to work with complex network topologies, cell morphologies and many other spatial and n-point problems. Further connectivity strategies have been added. Multiple adapters to different simulators are provided (NEURON - RRID:SCR_005393; NEST - RRID:SCR_002963; Arbor - 10.5281/zenodo.4428108)[17] [18].https://github.com/dbbs-lab/bsb; https:/bsb.readthedocs.io/

A Blender module has been completed. It contains a complete pipeline for rendering videos of the network activity or of microscopic variables on a single machine or a cluster.

We have generated the first computational model of the entire cerebellar cortical microcircuit. It includes both the granular and molecular layer, in which multi-compartmental neuron models were wired through a connectome, defined by the anisotropy of dendritic and axonal processes through principled rules. The model was then used to simulate network dynamics and validated against naturalistic inputs[19].

## Outlook

A major new version is coming soon with improved design and public interfaces, support for LFP simulations and more support for community supported data formats, for both network description and simulation results.

Long-term plans include optimising the algorithms, parallel reconstruction for full-scale cerebellum, application to other brain regions and improving the public API, based on user feedback.

---

[16] Frost Nylen, J. (2021). Dopaminergic and Cholinergic Modulation of Large Scale Networks in silico Using Snudda. *Frontiers in Neural Circuits*, 15. https://doi.org/10.3389/fncir.2021.748989 (P2972)

[17] https://github.com/dbbs-lab/bsb

[18] https://bsb.readthedocs.io/

[19] De Schepper et al. (2021). Scaffold modelling captures the structure-function-dynamics relationship in brain microcircuits. BioRXiv. (P2967)

## 4.1.14 *The Virtual Brain (TVB)*

**Type:** command-line tool or library & web app
**Scope:** whole brain

**Abstraction level:** population models
**Status:** mature, available, EBRAINS integration well advanced
**Homepage & more information:**

- https://www.thevirtualbrain.org/tvb/zwei
- https://kg.ebrains.eu/search/instances/Software/316edfdb-abd7-4451-b54e-21b746838ec0

### Recent Changes

In the last few months, the focus has been on enabling large parameter sweeps on HPC, creating workflows with TVB enabling the showcases in the HBP’s WP1 (The human multiscale brain connectome and its variability – from synapses to large-scale networks and function) and extending RateML to homogeneously treat Python and CUDA code generation.

We also focused on improving information security of TVB with HPC backend. A detailed security concept has been developed and implemented for TVB Web at EBRAINS:

PRD OpenShift: https://thevirtualbrain.apps.hbp.eu/

The data protection concept is presently under discussion with all relevant stakeholders (Data Protection Officers, infrastructure operators and service providers).

### Outlook

We will focus on the generation of adaptors for data ingestion from the EBRAINS Knowledge Graph and the multi-level Human Brain Atlas, as well as graphic user interfaces, which will support the Showcases in the HBP’s WP1.

Additionally, support for high-resolution simulations with neural fields is in development and its integration into parameter inference schemes is ongoing.

We will continue focusing on data protection; in particular, as part of the recently awarded EBRAINS awarded Call Service for Sensitive Data (SSD) project “Health Data Cloud”[20]https://www.healthdatacloud.eu/.

## 4.1.15 *Single Cell Modelling Workflows*

**Type:** workflows / Jupyter notebooks
**Scope:** biophysical models

**Abstraction level:** biophysical models
**Status:** available on EBRAINS
**Homepage & more information:**

- https://ebrains-cls-interactive.github.io/
- https://ebrains.eu/service/cls-interactive

The Single Cell Modelling Workflows consists of an ensemble of Jupyter notebooks for single cell modelling and data analysis. The notebooks are grouped into three main topics ("Trace Analysis", "Single Cell Modelling" and "Morphology") and allow a user-friendly construction and optimisation of hippocampal and cerebellar single cell models implemented in NEURON, the fitting of individual synaptic events, the configuration and test of different synaptic plasticity models and induction protocols, and the visualisation and analysis of neural morphologies.

---

[20] **Error! Hyperlink reference not valid.**

## Recent Changes

The Jupyter notebooks “Build your own single hippocampal cell model using HBP data”, “Rebuild an existing single hippocampal cell model”, “Synaptic plasticity”, “Mono compartmental cerebellar granule cell optimisation”, “multi-compartmental cerebellar granule cell optimisation”, “Custom axon cerebellar granule cell simulation”, “Simulation and validation of a mouse Purkinje cell multi-compartmental model” have all been migrated to Python 3 and integrated into EBRAINS.

## Outlook

The tool will be supported and maintained going forward, with special emphasis on fulfilling community requests.

# 4.2 Running Simulations

## *4.2.1 CGMD Platform*

| | |
|---|---|
| **Type:** web app<br>**Scope:** networks | 💻 ✔ ⅄<br>🧠 |
| **Abstraction level:** course-grained molecular dynamics<br>**Status:** available for use, EBRAINS integration in progress<br>**Homepage & more information:**<br>• https://molsim.sci.univr.it/mermaid/begin.php | |

## Recent Changes

The web server is online, working and already available via the EBRAINS Collaboratory[21].

## Outlook

The next steps will include the embedding of the server within the EBRAINS platform, as well as on the Google Collaboratory. More features will also be added in the longer term.

## *4.2.2 SSB Platform*

| | |
|---|---|
| **Type:** web app and standalone app<br>**Scope:** subcellular | 💻 📋 ⇄<br>👥 🧠 |
| **Abstraction level:** combined molecular and systems biology simulation<br>**Status:** in development | |

## Recent Changes

We finalised the realisation of a set of stand-alone Jupyter notebooks for the simulation protocol. The web application with the basic services was implemented on the Google Collaboratory (link not public yet).

## Outlook

The Jupyter notebooks will be integrated into the EBRAINS platform. In the longer term, we plan to develop a webserver to be implemented in the EBRAINS platform.

---

[21] https://wiki.ebrains.eu/bin/view/Collabs/molecular-tools-cgmd-platform/

### 4.2.3 MoDEL-CNS

| | |
|---|---|
| **Type:** web app<br>**Scope:** subcellular | |
| **Abstraction level:** atomistic molecular dynamics<br>**Status:** beta version publicly available online and within the EBRAINS infrastructure<br>**Homepage & more information:**<br>• http://mmb.irbbarcelona.org/MoDEL-CNS/<br>• https://wiki.ebrains.eu/bin/view/Collabs/molecular-tools-model-cns/ | |

#### Recent Changes

Extended help documentation: https://mmb.irbbarcelona.org/MoDEL-CNS/#/help.

#### Outlook

The collection of MD trajectories and flexibility analysis is being extended thanks to the use of ICEI/FENIX resources (CSCS Piz Daint supercomputer). The available set of analyses will be extended as well, adding new protein family-specific studies.

Jupyter notebooks retrieving information from the MoDEL-CNS REST API will be developed and integrated in the EBRAINS platform using the integrated Jupyter Lab tool.

### 4.2.4 BioExcel-CV19

| | |
|---|---|
| **Type:** web app<br>**Scope:** subcellular | |
| **Abstraction level:** atomistic molecular dynamics<br>**Status:** beta version publicly available online and within the EBRAINS infrastructure<br>**Homepage & more information:**<br>• https://bioexcel-cv19.bsc.es/#/<br>• https://wiki.ebrains.eu/bin/view/Collabs/molecular-tools-bioexcel-cv19 | |

BioExcel-CV19 is a platform designed to provide web access to atomistic-MD trajectories for macromolecules involved in the COVID-19 disease. It is a side project of the previously presented MoDEL-CNS platform, redesigned to tackle COVID-19 related MD simulations.

The project is part of the open access initiatives promoted by the worldwide scientific community to share information about COVID-19 research.

The BioExcel-CV19 web server interface presents the resulting trajectories, with a set of quality control analyses and system information. All data produced by the project are available to download from an associated programmatic access API.

#### Recent Changes

More than 350 COVID-related atomistic MD simulations taken mostly from the COVID-19 Molecular Structure and Therapeutics Hub[22] have been uploaded.

#### Outlook

The collection of MD trajectories and flexibility analysis is being extended with direct connection to groups in the field generating such data. The available set of analyses is going to be extended as well, using feedback received from the same groups. Jupyter notebooks retrieving information from

---

[22] https://covid.molssi.org/

the BioExcel-CV19 REST API will be developed and integrated in the EBRAINS platform using the integrated Jupyter Lab tool.

## 4.2.5 SDA

**Type:** web app and standalone app
**Scope:** molecular

**Abstraction level:** nanoscale
**Status:** available for use
**Homepage & more information:**

- https://mcm.h-its.org/sda
- https://websda.h-its.org/
- https://search.kg.ebrains.eu/?facet_type[0]=Software&q=SDA#a65c722a-71e9-4eba-bce6-fdc7ef736dc3

### Recent Changes

SDA 7.3.0, which was released in December 2020, has added functionality for the modelling of the interactions of proteins with surfaces, allowing inclusion of protein-surface hydrodynamic interactions and long-range electrostatic interactions. Minor releases (currently on SDA 7.3.3) have been done with additional examples and bug fixes.

### Outlook

Planned developments are aimed at combining molecular dynamics and Brownian dynamics simulations to compute association rate constants for protein-ligand binding accounting for molecular flexibility. Listing as a tool on the EBRAINS Services web page is in process.

## 4.2.6 Single Cell In Silico Experiment Tool (BlueNaaS)

**Type:** web app
**Scope:** single neurons

**Abstraction level:** biophysical models
**Status:** available on EBRAINS
**Homepage & more information:**

- https://blue-naas-bsp-epfl.apps.hbp.eu/#/
- https://humanbrainproject.github.io/hbp-sp6-guidebook/online_usecases/single_cell_in_silico/single_cell_clamp/single_cell_clamp.html

### Recent Changes

Running single-cell *in silico* experiments is a central application on EBRAINS for users to explore existing neuron models. This service is now fully migrated to EBRAINS. Furthermore, the API was modified to support the EBRAINS Live Papers, which make frequent use of this neuron simulation services for a variety of Live Papers.

### Outlook

The application will be maintained, but no more features will be added.

## 4.2.7 Small Circuit In Silico Experiments Tool (Rat Hippocampus CA1)

| | |
|---|---|
| **Type:** web app<br>**Scope:** networks | |
| **Abstraction level:** biophysical neurons<br>**Status:** available, EBRAINS integration almost done<br>**Homepage & more information:**<br>• https://bsp-rat-ca1.humanbrainproject.eu/circuits/rat-ca1<br>• https://humanbrainproject.github.io/hbp-sp6-guidebook/online_usecases/small_circuit_in_silico_experiments/pair_recording_app/pair_recording_app.html | |

### Recent Changes

This service has been deployed on a dedicated site, in an EBRAINS-compatible manner (i.e. leveraging the services of the EBRAINS infrastructure, such as the EBRAINS authentication system). The service's functionality has been improved: the possibility to run longer simulations (up to 30 s) has been added, as well as the support for the SONATA format, in view of a Massive Open Online Course that will make use of this service.

### Outlook

An additional functionality to replay spikes from existing simulations will be added. The integration of a simulation campaign concept will be considered, which would allow to chain more complex simulation-analysis workflows.

## 4.2.8 Brain Areas Circuit In Silico Experiments Tool (Rat Hippocampus CA1)

| | |
|---|---|
| **Type:** web app<br>**Scope:** networks | |
| **Abstraction level:** biophysical neurons<br>**Status:** available, EBRAINS integration done<br>**Homepage & more information:**<br>• https://simulation-launcher-bsp-epfl.apps.hbp.eu/index.html#/circuits/hippo_hbp_sa_full_ca1<br>• https://humanbrainproject.github.io/hbp-sp6-guidebook/online_usecases/brain_area_circuit_in_silico_experiments/hippocampus/configure_run_brainregion_preconf_model_data/configure_run_brainregion_preconf_model_data.html | |

### Recent Changes

This service has been integrated with EBRAINS, allowing users to run low-barrier *in silico* experiments on detailed brain tissue models on EBRAINS HPC systems.

The service's functionality has been improved with support for the SONATA format, with additional support for projections (Schaffer collateral), as well as with new visualisation utilities. Additionally, this application has been extended, so it can be run with dynamically generated neural circuits.

### Outlook

We will investigate moving from one *in silico* experiment at a time to parameter sweeping experiments.

## 4.2.9 *NEST*

**Type:** command-line tool or library
**Scope:** networks

**Abstraction level:** point neuron models
**Status:** mature, available on HPC, Fenix/ICEI resources and on JupyterLab, integration in EBRAINS well advanced
**Homepage & more information:**

- https://nest-simulator.org
- https://kg.ebrains.eu/search/instances/Software/c3d23fd5-4370-487b-9231-e0f8e8a1e9e6

### Recent Changes

In the past months, NEST 3.0 and NEST 3.1 were released[23] with contributions by some 40 developers. NEST 3 boosts the productivity of brain scientists by making it much easier to construct complex network models in a computer. Using NEST 3, a single line of code can achieve what required dozens of lines of code in earlier versions. This allows researchers to explore a wide range of model variants and makes it easier to validate models, contributing to reliable and reproducible research. Performance improvements enable ever-larger simulations, including the efficient storage of steadily growing amounts of simulation data. Availability through the EBRAINS JupyterLab enables users to exploit EBRAINS simulation capabilities seamlessly with other EBRAINS integrated tools and services. Additionally, work in three different Research Infrastructure voucher projects is extending the simulator:

1) A new class of connection types is being implemented for modelling ternary connections as for example established by astrocyte cells[24];

2) The construction of large-scale spatially structured networks is optimised for hybrid parallelisation with the Japanese Whole Brain Model (Doya, Igarashi *et al.*[25]); and

3) Connectivity generation is being implemented in NEST directly from network specifications in the HBP-co-developed SONATA format, to allow for data formats compatibility and more direct validations of models and simulators[26].

A RESTful API now provides simulation services to NEST Desktop and the EBRAINS Neurorobotics Platform, as well as enabling NEST simulations from the EBRAINS Jupyter services. The very successful virtual NEST Conference 2021[27] attracted an international audience showing the broad field of applications of NEST and boosting community collaboration.

### Outlook

For the mid-term, developers are working towards a higher integration of NESTML-generated model code and HPC back-end access. This will allow users to extend the list of available models more easily and to access NEST from front end services like Jupyter and NEST Desktop through EBRAINS middleware services. Work is ongoing to integrate documentation in the EBRAINS tools and to establish interfaces to the joint co-simulation framework. In parallel, maintenance and support of users, joint voucher projects and the operational integration into EBRAINS will continue.

---

[23] See full release notes at https://nest-simulator.readthedocs.io/en/latest/release_notes
[24] AstroNeuronNets voucher project lead by Dr. Jugoslava Acimovic (Tampere University, Finland)
[25] EXABRAINPREP voucher project lead by Dr. Jun Igarashi (RIKEN, Japan)
[26] NESTSONATA voucher project lead by Dr. Anton Arkhipov (Allen Institute, USA)
[27] NEST Conference 2021 – https://nest-initiative.org/conference-2021

### 4.2.10 *Arbor*

| | |
|---|---|
| **Type:** command-line tool or library<br>**Scope:** single neurons, networks | |
| **Abstraction level:** biophysical models<br>**Status:** releases available, including for HPC, package is selected as prototype for EBRAINS Spack CD, integration in EBRAINS well advanced<br>**Homepage & more information:**<br>• arbor-sim.org<br>• docs.arbor-sim.org<br>• https://kg.ebrains.eu/search/instances/Software/80d205a9-ffb9-4afe-90b8-2f12819950ec | |

## Recent Changes

The Arbor-GUI: a tool to visually construct, inspect, verify and execute single cell simulations, has been released. The range of file formats supported has been expanded and now includes Neurolucida, NeuroML morphologies and Arbor's ACC format. Additionally, simulations are now stoppable and resumable, enabling users to steer and interact with the simulation in real-time; this facilitates co-simulation. Runtime loading of user-specified mechanisms through the Arbor Mechanism ABI is supported, enabling users to more easily share optimised mechanism components. Other recent changes are that the CI has been significantly expanded, including Python binary wheel building, and Spack file and Spack testing have been added, which facilitate the roll-out through Spack-based EBRAINS CD. There are new examples in the documentation, many provided by users. Post-event functionality to support models with STDP synapses has been added. Finally, cooperation with our 'HBP Calls for Expression of Interest' (CEoI) partners has expanded significantly, resulting in numerous improvements.

## Outlook

For NeuroML, we plan to expand the current support of morphologies with support for dynamics and networks, and to allow users to specify networks with higher-level primitives, roughly in the spirit of NeuroMLlite, possibly feeding back into that project. We aim to work towards scientific submissions for our CEoI partners (Fippa and Arborio). In terms of the recipe file format, we plan to enable the long-term storage and composability of simulations and facilitate moving from desktop to HPC environments. We also plan to integrate with parameter estimators, such as the Learning2Learn framework. Finally, we are planning for EBRAINS integration (Arbor is part of the Spack prototype, which should be the main method of CD to the EBRAINS Lab environment before the end of the year), plus a regular release cycle for Arbor.

### 4.2.11 *NEURON/CoreNEURON*

| | |
|---|---|
| **Type:** command-line tool or library<br>**Scope:** single neurons, networks | |
| **Abstraction level:** biophysical<br>**Status:** stable, available on HPC and JupyterLab<br>**Homepage & more information:**<br>• https://github.com/BlueBrain/CoreNeuron<br>• https://github.com/neuronsimulator/nrn<br>• https://kg.ebrains.eu/search/instances/Software/dbe2802c-ebe5-4963-a02d-508e07c4be31 | |

## Recent Changes

During the past year, NEURON has had two major releases[28], 7.8.2 and 8.0[29]. These are the last two releases which will support automake for building and Python 2 compatibility. As part of ongoing efforts to modernise NEURON/CoreNEURON, much work has been done to improve the portability and stability of the NEURON Python Wheel. This includes notably adding support for Windows via Windows Subsystem for Linux (WSL). Many more tests have been added to NEURON's continuous integration (CI) framework, which include the suite of legacy tests that had been run manually in the past. This has increased the code coverage and will help prevent regressions in the future. In addition, improvements have been made to facilitate profiling and performance analysis of NEURON and CoreNEURON. When building a custom *special*, fully-fledged binary code is generated, rather than relying on wrapper scripts. This binary can be used more easily in debuggers and profiler applications. Also, instrumentation with Caliper and Likwid is available to help target future optimisations.

To allow migration of additional models for NEURON to CoreNEURON, NMODL now supports mod files with CONSTRUCTOR and DESTRUCTOR functions. In addition, a new feature, 'psolve-direct', allows for NEURON and CoreNEURON to exchange data via direct memory-transfer back and forth during runtime, enabling a seamless integration of NEURON and CoreNEURON. This allows control to be returned to the interpreter following some CoreNEURON executions, so that certain actions can be taken before returning to CoreNEURON to continue the simulation. In preparation for work on running models for GPU, Eigen library support for solving linear systems has been extended.

## Outlook

NEURON 8.1 is in preparation. Firstly, this will drop support for auto tools and Python 2. Secondly, this will introduce GPU offloading support in Python Wheels, which is currently under development. Thirdly, buffering report data in GPU memory for bulk transfer back to main memory will be made possible. This will allow scientists to collect more data with reduced interruptions to the solver, leading to improved performance. For NMODL, we are investigating native language support for Random Number Generation which will reduce the need for VERBATIM blocks and improve code generation. Lastly, we will finalise support for dynamic selection of MPI libraries during runtime so that the same executable can, for example use either MVAPICH or OpenMPI, on a given system.

# *4.2.12 Neuromorphic Computing Job Manager App*

| | |
|---|---|
| **Type:** web app, command-line app and library<br>**Scope:** networks | 💻⚙✔⅄<br>☁🎓👥🧠 |
| **Abstraction level:** point neurons<br>**Status:** stable, available on the EBRAINS Collaboratory and as a standalone web app<br>**Homepage & more information:**<br>• https://electronicvisions.github.io/hbp-sp9-guidebook/using_the_platform.html | |

## Recent Changes

The neuromorphic computing job queue system has been migrated to use the latest version of the EBRAINS authentication system. The web app has been entirely rewritten using a more modern Javascript framework, and is now available both as a stand-alone web app [30] https://job-manager.hbpneuromorphic.eu/and as a "community app", that can be installed in any Collab.

---

[28] The two NEURON releases are available here: https://github.com/neuronsimulator/nrn/releases

[29] https://nrn.readthedocs.io/en/8.0.0/changelog.html

[30] https://job-manager.hbpneuromorphic.eu/

## Outlook

In the near future, it will become possible to select the model/simulation code from the Collaboratory Drive and from the Data Proxy service (“Buckets”), and to copy simulation outputs to the same locations with a single click. We are currently working on migrating all job records (including provenance metadata) to the EBRAINS Knowledge Graph, facilitating workflows that combine HPC and neuromorphic computing.

### *4.2.13 Multiscale Co-Simulation Framework*

| | |
|---|---|
| **Type:** command-line tool or library<br>**Scope:** networks, whole brain | |
| **Abstraction level:** point models, biophysical models, population models<br>**Status:** in progress<br>**Homepage & more information:**<br>• https://github.com/multiscale-cosim | |

## Recent Changes

Basic tool development for deployment of workflows, design of the communication protocol, maturation and operational support of existing workflows.

- Alpha release of the deployment tools and orchestration framework[31]https://github.com/multiscale-cosim/EBRAINS-RichEndpoint.
- Versions 0.1 data exchange protocol, transformation standards and design protocol[32].
- Operational support and development TVB-NEST workflows, NEST desktop, NRP, TVB-NEST co-simulation, Elephant, Learning 2 learn, OpenAI.
- New versions in the LFPy toolset: LFPykit[33]http://lfpykit.rtfd.io/, LFPy[34]http://lfpy.rtfd.io/, hybridLFPy[35]http://hybridlfpy.rtfd.io/.

## Outlook

We are planning a production release of infrastructure for two-way coupling of NEST and TVB, and the next version of coupling APIs and standards. Also, a production version of the orchestration software for coupled applications (for one- and two-way co-simulation and analysis) on FENIX, HPC resources and local PCs is planned.

In the long term, we will work on the NEST-Arbor multiscale, two-way, co-simulation infrastructure and the infrastructure for LFP forward-model calculations as a one-way co-simulation. Finally, the first phase of CI/CD, multi-scale model provenance tracking and curation, and EBRAINS Knowledge Graph integration is planned.

---

[31] https://gitub.com/multiscale-cosim/EBRAINS-RichEndpoint

[32] https://drive.ebrains.eu/smart-link/0f8dc477-db70-495c-b500-dd83d271715a/

[33] LFPykit.rtfd.io

[34] LFPy.rtfd.io

[35] hybridLFPy.rtfd.io

### 4.2.14 The Virtual Brain (TVB)

#### Recent Changes

The whole-brain simulator TVB has been integrated with the micro-scale simulators NEST and Annarchy[36]. Two preprints report on the technical details: Schirner *et al.* 2021[37] describes the technical implementation of TVB-NEST co-simulation. Meier et al. 2021[38] shows a use case for multi-scale co-simulation. TVB co-simulation is accessible via the EBRAINS website[39]https://www.ebrains.eu/service/the-virtual-brain.

#### Outlook

We are planning model validation/reproducibility using the two different co-simulation approaches, i.e. TVB-NEST versus TVB-Annarchy. We are also planning to validate model predictions on patient data (Parkinson's Disease and deep brain stimulation). See also Section 4.1.14.

### 4.2.15 MMCG Platform

<table>
<tr><td><b>Type:</b> web app<br><b>Scope:</b> networks</td><td>💻 ✔ ⅄<br>🗣</td></tr>
<tr><td colspan="2"><b>Abstraction level:</b> hybrid molecular mechanics/coarse-grained molecular dynamics<br><b>Status:</b> available for use, EBRAINS integration in progress<br><b>Homepage & more information:</b><br>• https://mmcg.grs.kfa-juelich.de/<br>• https://ebrainsaisbl.sharepoint.com/Users/vanlook/Dropbox/Mac/Downloads/•%09https:/mmcg.grs.kfa-juelich.de/documentation</td></tr>
</table>

The Hybrid MM/CG Webserver automatises and speeds up the hybrid Molecular-Mechanics/Coarse-Grained (MM/CG) simulations set-up of G-Protein coupled receptors/ligand complexes. The server allows for equilibration of the systems, either fully automatically or interactively. It allows the visualisation of results online (using both interactive 3D visualisations and analysis plots), helping the user to identify possible issues and modify the set-up parameters accordingly.

#### Recent Changes

The web server is online, working and already available via the EBRAINS Collaboratory[40].

#### Outlook

The next steps will include the improvement of the documentation to make it accessible also to non-experts and the embedding of the server within the EBRAINS platform, as well as on the Google Collaboratory. More features requested by the users, like the possibility of running longer simulations and more computational power, will be added in the longer term.

## 4.3 Data Analysis

---

[36] https://annarchy.readthedocs.io/en/latest/

[37] Schirner, M., *et al.*, Brain Modelling as a Service: The Virtual Brain on EBRAINS. arXiv, 2021. 2102.05888. (P2973)

[38] Meier, J. M., *et al.*, Virtual deep brain stimulation: Multiscale co-simulation of a spiking basal ganglia model and a whole-brain mean-field model with The Virtual Brain. bioRxiv, 2021. doi: https://doi.org/10.1101/2021.05.05.442704 (P2974)

[39] https://www.ebrains.eu/service/the-virtual-brain

[40] https://wiki.ebrains.eu/bin/view/Collabs/hybrid-mmcg-webserver/Webserver

## 4.3.1 *Neo*

**Type:** command-line tool or library
**Scope:** all

**Abstraction level:** all
**Status:** mature, available now on HPC, JupyterLab, neuromorphic
**Homepage & more information:**

- http://neuralensemble.org/neo/
- https://neo.readthedocs.io/
- https://kg.ebrains.eu/search/instances/Software/b0d73040-6547-447d-a1be-6761c209973f

### Recent Changes

Neo v0.10.0 was released. New features include a further simplification of the data model by removing specific containers of data objects, which is expected to facilitate interoperability with EBRAINS tools and services, as well as improved file handling by providing seven new IO handlers and improvements to six existing handlers, in order to broaden the scope of data providers handled by Neo[41].

### Outlook

The next release of Neo (v0.11.0) will focus on further stabilisation of the API and improved functionality for user-side processing of data, work on overhauling and updating the documentation (including improved tutorials), and further improvements for the wide range of IO modules, in particular the standard Neurodata Without Borders (NWB:N) and Neuroscience information exchange (NIX) formats. The release of Neo v1.0 is planned for 2022. At this point, the API will be considered stable and backwards compatibility maintained.

## 4.3.2 *Elephant*

**Type:** command-line tool or library
**Scope:** all

**Abstraction level:** all
**Status:** mature, available now on HPC, JupyterLab, neuromorphic
**Homepage & more information:**

- https://python-elephant.org
- https://elephant.readthedocs.io
- https://kg.ebrains.eu/search/instances/Software/f3685e37-cb34-4010-a528-468564482257

### Recent Changes

Elephant received a new major release, 0.10.0, on 4 March 2021, which provided several new functionalities. With a new implementation of the ASSET analysis, Elephant saw its first inclusion of code that makes use of GPUs for acceleration. In addition, the restructured object-oriented code base of ASSET allowed the creation of an alternative back end based on the Helmholtz Analytics Toolkit (Heat) for parallelisation, which is currently evaluated as a prototype and is anticipated for a future release. In addition, several functions for the analysis of phase synchronisation were added, in addition to work on documentation and tutorials. Full details can be seen in the release notes42.

---

[41] https://neo.readthedocs.io/en/stable/releases/0.10.0.html
[42] https://elephant.readthedocs.io/en/v0.10.0/release_notes.html

## Outlook

Current work focuses towards the 0.11.0 release, which will include, in particular, a highly optimised implementation of the SPADE method, and a reworked module for spike train generation. Work on Elephant will further address re-factoring and speed optimisations, including the use of HPC and GPU resources. A new package to track micro-scale provenance and introduce data analysis objects for performed analysis operations will be integrated. Analysis plug-ins for the co-simulation framework will be developed.

## 4.3.3 LFPy

**Type:** command-line tool or library
**Scope:** single neurons, networks

**Abstraction level:** biophysical neuron models
**Status:** mature, available on HPC and JupyterLab
**Homepage & more information:**

- https://lfpy.readthedocs.io/
- https://lfpykit.readthedocs.io/

### Recent Changes

LFPy was originally designed as a Python interface to NEURON, with the ability to set-up and control simulations of multicompartment neurons, and to calculate different brain signals like extracellular potentials, and EEG and MEG measurements from the simulated neural activity. LFPy's functionality to calculate such signals was not originally available for other neural simulators. To facilitate interoperability across simulators, we moved the parts of LFPy responsible for calculating brain signals into a free-standing Python package called LFPykit that is independent of the neural simulation software (that is, NEURON and LFPy). LFPykit has been demonstrated to work with Arbor, and is now a dependency for LFPy-2.2 and hybridLFPy, a package for calculating LFPs/EEGs from spiking point neuron network models. Demonstrations for these tools are available on EBRAINS[43] [44] https://wiki.ebrains.eu/bin/view/Collabs/lfpy-showcasehttps://wiki.ebrains.eu/bin/view/Collabs/hybridlfpy-showcase.

### Outlook

We plan to include additional examples of how to use LFPykit with different neural simulators like NEURON, LFPy and Arbor. We are also using LFPykit and LFPy to develop methods to simulate brain signals, like LFPs and EEGs, directly from large-scale point neuron network models and neural field/mass models. Our aim is to deal with forward-model predictions as a linear and time-invariant causal system, mapping spikes/spike rates to the corresponding signals. These methods will be interfaced with NEST and TVB in tools available through the EBRAINS platform.

## 4.3.4 *The Virtual Brain (TVB)*

### Recent Changes

We have further developed the TVB image-processing pipelines that extract structural connectomes and functional time series from MRI scans to constrain TVB models. The Container pipelines are accessible via the EBRAINS portal45.https://www.ebrains.eu/service/the-virtual-brain

The latest addition is provenance tracking with DataLad. Versioning and documentation of all processing steps guarantee full reproducibility of our workflows. Details can be found in the preprint by Schirner *et al.*[46] that describes the technical implementation of TVB-NEST co-simulation.

To protect personal health data, data protection mechanisms such as access control, encryption and sandboxing have been implemented. We have developed a comprehensive data protection concept for brain simulation in the cloud. Service agreements and processes are currently being developed to open the "Virtual Brain Cloud" EBRAINS Facility Hub to external users.

---

[43] https://wiki.ebrains.eu/bin/view/Collabs/lfpy-showcase
[44] https://wiki.ebrains.eu/bin/view/Collabs/hybridlfpy-showcase
[45] https://www.ebrains.eu/service/the-virtual-brain
[46] Schirner, M., et al., Brain Modelling as a Service: The Virtual Brain on EBRAINS. arXiv, 2021. 2102.05888. (P2973)

We applied successfully for the HBP Call Service for Sensitive Data (SSD) with the Health Data Cloud concept[47],https://www.healthdatacloud.eu/ and this work will now be further advanced within the HBP.

### Outlook

TVB end-to-end workflows will be integrated with the new Service for Sensitive Data – EBRAINS Health Data Cloud.

See also Sections 4.1.14 and 4.2.14.

# 4.4 Visualisation

## *4.4.1 SimVisSuite*

| | |
|---|---|
| **Type:** desktop app<br>**Scope:** single neurons, networks | |
| **Abstraction level:** point neuron models, biophysical neuron models<br>**Status:** prototypes available, integration in EBRAINS well advanced<br>**Homepage & more information:**<br>Visimpl:<br>• https://vg-lab.es/visimpl/<br>• https://kg.ebrains.eu/search/instances/Software/6f8b4c7d-31f6-49b5-a843-2e0b4421be6f<br>NeuroTessMesh:<br>• https://github.com/vg-lab/NeuroTessMesh<br>• https://kg.ebrains.eu/search/instances/Software/4aa7fc48-101c-4f8f-bd6e-559486c133a3<br>Neuroscheme:<br>• https://github.com/vg-lab/NeuroScheme<br>• https://kg.ebrains.eu/search/instances/Software/a5f69883-eb34-4dd5-bc44-30e5d4718f27 | |

### Recent Changes

There are new releases for ViSimpl, NeuroTessMesh and NeuroScheme that contribute to the stability of the tools after removing bugs. ViSimpl has been successfully integrated with the *in situ* pipeline. Documentation of the tools at ReadTheDocs[48], including manuals and runbooks, have been created and published.

### Outlook

On one hand, we plan to advance with the testing and integration of the tools to complete the deployment. On the other hand, we plan to enhance the integration with the *in situ* pipeline, improving the data management.

## *4.4.2 NEST Desktop*

| | |
|---|---|
| **Type:** web app<br>**Scope:** networks | |
| **Abstraction level:** point neuron models<br>**Status:** mature, available as standalone app<br>**Homepage & more information:**<br>• https://nest-desktop.apps.hbp.eu/#/ | |

---

[47] https://www.healthdatacloud.eu/

[48] https://visimpl-documentation.readthedocs.io/en/latest/

- https://nest-desktop.readthedocs.io
- https://github.com/nest-desktop/nest-desktop
- https://search.kg.ebrains.eu/?facet_type[0]=Software&q=nest%20desktop#b1f7faf5-aafe-4675-a1cb-532326f10b5c

### Recent Changes

NEST Desktop 3.0 was released in August 2021, along with NEST 3.0. This enables the use of NEST 3.0 through the NEST Desktop user interface. NEST Desktop has also been completely reimplemented in Vue.js for the 3.0 release, due to reducing overhead induced by the previous framework. The result is a more reliable and lightweight application and code base. NEST Desktop is usable through EBRAINS (https://nest-desktop.apps.hbp.eu/#/).

In terms of documentation, we extended the user and developer documentation on ReadTheDocs[49] with documentation for lecturers, who intend to use NEST Desktop as a tool in computational neuroscience courses.

We used NEST Desktop in the summer terms of 2020 and 2021 and in the winter term of 2020/2021, for an online course on computational neuroscience at Freiburg University; which enabled the course to happen, despite the fact that no in person teaching was possible due to COVID-19. In these courses, we received positive feedback on the tool and its applicability. In an online survey, we received positive qualitative feedback, as well as good results for usability (SUS score of 58) and user experience (UEQ around 1.0 on all sub-scales) in quantitative evaluations. In addition, a publication[50] in eNeuro on NEST Desktop has been published in November 2021.

### Outlook

Next steps include final integration of the SimDaVis framework for *in situ* visualisation in the next major release and working on the integration of Elephant, to enable complex data analysis of simulated data. We also plan to consider enabling users to create Neuron models via NESTML in the user interface of NEST Desktop.

## *4.4.3 SimDaVis - Insite*

**Type:** command-line tool or library
**Scope:** networks

**Abstraction level:** point neuron models, biophysical models
**Status:** prototype available
**Homepage & more information:**

- https://vrgrouprwth.github.io/insite
- https://kg.ebrains.eu/search/instances/Software/eb0b86a5-eb49-4a87-9128-6ca592293218

### Recent Changes

NEST API endpoints were updated to better reflect the naming scheme that is used by NEST. The metadata database was shifted into existing components to reduce the number of dependencies that users must install. The first version with full NEST support was successfully released. The user documentation was updated to describe all endpoints, reflect changes and make searching easier. The pipeline was updated to be compatible with NEST 3.0 master branch. To accomplish this, functionality that was formerly provided via a NEST fork for Insite was merged into the official NEST code base. An unreleased prototype implementation for Arbor was developed supporting spike data and morphological information. Endpoints for Arbor were added to the new version of the API.

---

[49] https://nest-desktop.readthedocs.io

[50] Weyers, B., et al. (2021) NEST Desktop, an Educational Application for Neuroscience. eNeuro 8 (6) ENEURO.0274-21.2021; DOI: https://doi.org/10.1523/ENEURO.0274-21.2021 (P2980)

## Outlook

In the short term, full support of the functionality that the Arbor simulator provides, and public release of Insite that supports Arbor will be a focus. The major aspect of the long-term plan is the full integration into the EBRAINS infrastructure. This integration would allow users to start simulations remotely on EBRAINS-managed HPC resources and connect to them using the specified REST API for analysis and visualisation purposes. Additionally, access to data from one more abstraction level will be provided, by adding support for TVB into the Insite pipeline. Furthermore, we plan to integrate basic steering capabilities into the pipeline to enable interactive supercomputing. This will depend greatly on the steering functionality provided by the simulator and we cannot estimate this yet.

# *4.4.4 Elephant Visualization (Viziphant)*

**Type:** command-line tool or library
**Scope:** all

**Abstraction level:** all
**Status:** prototype available
**Homepage & more information:**

- https://viziphant.readthedocs.io
- https://github.com/INM-6/viziphant

## Recent Changes

Viziphant is currently feature-complete to receive a new release 0.2.0, concurrently with the upcoming Elephant release 0.11.0. The current release candidate includes new plotting functionality for Elephant modules such as GPFA or ASSET, as well as API improvements. It was tested in multiple tutorials held at the GDR Neuralnet School, Lyon and at the Nix-Neo-Elephant Workshop, which was part of the INCF Training Week.

## Outlook

We will work on further maturation of the package and increasing the number of visualisations made available by the package. The integration of the package into tutorials of the Elephant documentation will be further improved. To simplify interaction with the Neo and Elephant libraries for interactive work, work continues on a first prototype of a visual variable inspector for JupyterLab based on the Viziphant base functionality. Also, making visualisations available to users, and work on providing a visual inspector for Neo objects and analysis results in the JupyterLab environment have been started.

# 4.5 Validating Models Against Experimental Data

## *4.5.1 Validation Test Libraries*

**Type:** library
**Scope:** all

**Abstraction level:** all
**Status:** mixed. Some mature, available on HPC, JupyterLab, others in progress
**Homepage & more information:**
NetworkUnit:

- https://github.com/INM-6/NetworkUnit
- https://kg.ebrains.eu/search/instances/Software/e3566d6b-fed9-4f5d-b704-04e6eda76c99

MorphoUnit:

- https://github.com/appukuttan-shailesh/morphounit
- https://kg.ebrains.eu/search/instances/Software/860c230e-56cf-4f49-bdb7-cd438a3de0e2

HippoUnit:

- https://github.com/KaliLab/hippounit
- https://kg.ebrains.eu/search/instances/Software/fd369ab8-c788-4c7b-89ec-594aa3e46c24

CerebUnit:

- https://cerebtests.readthedocs.io/

Validation Framework - Python Client:

- https://hbp-validation-client.readthedocs.io/en/master/#
- https://kg.ebrains.eu/search/instances/Software/c053931f-ddd1-4416-8b3e-5506677c4bda

### Recent Changes

Incremental updates have been made to several of the existing test suites. NetworkUnit is receiving new capabilities for parallelisation of tests, as well as an extended repertoire of statistical tests, which will enter the upcoming 0.2 release. A second manuscript of a use case scenario utilising NetworkUnit is currently in progress. HippoUnit has been updated to be compatible with the latest version of the NEURON simulator (v8), while retaining backwards compatibility. A study demonstrating the functionality and scientific value of using HippoUnit was published in *PLoS Computational Biology*[51].

### Outlook

We plan to extend the various validation suites and publish results derived from these. Meanwhile, in addition to creating more validation tests at the level of single cells (different tests based on cell type), work has started to create tests for synapses between cells. This will then be followed by creating tests for subcellular mechanisms. CerebUnit will also be extended to measure sensitivity, specificity and accuracy of the validation test. We also intend to look into developing newer test suites, such as for testing whole brain models. We are currently also working on a study to demonstrate how models can be compared using the VF tools. Future work on NetworkUnit will include tests for the spatial organisation of population signals, contributing to the Showcases on evaluating slow wave analysis, as well as providing improved documentation. In addition, HippoNetworkUnit, a Hippocampus-CA1 dedicated validation unit is currently under further development, to include tests for the Bezaire *et al.* (2006)[52] model against experimental results reported from physiological experiments. Previous work on this validation unit included anatomical validation tests for microcircuit models of Hippocampus-CA1 developed at the EPFL Blue Brain Project, to compare their axonal boutons distributions with experimental values. A first release of the unit can be found at https://zenodo.org/record/3886484.

---

[51] https://journals.plos.org/ploscompbiol/article/comments?id=10.1371/journal.pcbi.1008114 (P2993)
[52]

We intend to disseminate the utility of incorporating the validation services in the modelling and reviewing workflows, via publications, hackathons and workshops on model validation. This will help familiarise the community with the test suites and their usage, and promote community-driven development of model validation test suites.

### 4.5.2 *Model Catalog*

| | |
|---|---|
| **Type:** web app, REST API<br>**Scope:** all | |
| **Abstraction level:** all<br>**Status:** mature; available now as a standalone web app, a Collaboratory app and a REST API<br>**Homepage & more information:**<br>• https://model-catalog.brainsimulation.eu/docs/<br>• https://validation-v2.brainsimulation.eu/docs | |

#### Recent Changes

The Model Catalog is now available both as a "community app" in the EBRAINS Collaboratory and as a standalone web app. The advantage of installing the app in a Collab is that the app's configuration (filtering by brain region, cell type, model scope, etc.) is saved on a per-Collab basis. The landing page of the app has been revised and it now highlights featured models and shows statistics about the models in the Catalog. Behind the scenes we have introduced extensive end-to-end testing using Cypress, which has led to a more responsive and consistent user experience. Version 1 of the Model Catalog app is no longer available due to the shutdown of the HBP Collaboratory.

#### Outlook

With the upcoming release of version 3 of the EBRAINS Knowledge Graph and the migration to OpenMINDS schemas, the web service will need to be updated accordingly; this work is underway. Both the web service and app will be extended to link models with simulations generally, rather than only those simulations performed for model validation, as is the case at present.

# 5. Related Tools and Services

http://modeldb.science/https://www.opensourcebrain.org/https://www.ebi.ac.uk/biomodels/https://portal.bluebrain.epfl.ch/https://www.nsgportal.org/https://portal.brain-map.org/At present, EBRAINS services and the tools described above are more complementary than in competition. For example, the Neuroscience Gateway provides simplified access to US-funded HPC resources, while EBRAINS provides the same for European HPC resources, through the ICEI project. Similarly, the field will be best served by promoting interoperability between ModelDB, OpenSourceBrain and EBRAINS. An example of this strategy can be found in the newly released Hippocampus Hub (www.hippocampushub.eu), which was developed by HBP Partners with external funding and connected to EBRAINS via an HBP Facility Hub. This Hub provides the hippocampus community, or more specifically those who want to build models of the hippocampus, with a seamless view to the data from the diverse data portals and can funnel those data to model building workflows on EBRAINS. Similar hubs for other communities (e.g. cerebellum, basal ganglia) are under way.

# Annex - Summary Tables of EBRAINS Tools, Workflows and Services

## Building Models

Table 4: Tools and services for building models across the diverse scales as part of EBRAINS.

| Tool or service | Characteristics | Modelling abstraction level | Purpose |
|---|---|---|---|
| ArDOCK | 💻 ✔ ⁙ 🎧 | **NS** | Detect potential interaction sites on the surface of a protein. |
| Molecular Level Toolset | ⚙ 🔧 ⁙ 🎓 👥 🎧 | **NS** | Set-up, run and analyse molecular level calculations, e.g. tauRAMD calculations to compute dissociation constants. |
| CNS Ligands | 💻 ✔ ⁙ 🎧 | **NS** | Efficiently generate and parameterise bioactive conformers of ligands binding to neuronal proteins for molecular dynamics simulations. |
| GRALL | 💻 ✔ ⁙ 🎧 | **NS** | Search for allosteric modulators of the human glycine receptor with a structural annotation of their ligand-binding site. |
| Subcellular Web App | 💻 ✔ ⇄ 👥 🎧 | **SB** | Create and simulate brain molecular networks. |
| Subcellular Model Building Toolset | ⚙ 🔧 ⇄ 🎧 | **SB** | Construct, simulate and validate subcellular models. |
| Feature Extraction Tool (NeuroFeatureExtract) | 💻 ✔ ⚲ 👥 🎧 | **BI** | Extract a wide variety of electrophysiological features from experimental recordings. |
| Hodgkin-Huxley Neuron Builder (HHNB) | 💻 ✔ ⚲ 👥 🎧 | **BI** | Optimise a single cell model against experimental data on HPC resources. |
| Electrical Model Building Toolset | ⚙ ✔ ⚲ 🎓 👥 🎧 | **BI** | Build and validate biophysically detailed electrical neuron models. |
| PyNN | ⚙ ✔ ⅄ 🎧 | **PT BI** | Build simulator-independent spiking neuronal networks and simulation experiments. |
| NESTML | ⚙ ✔ ⚲ 🎓 👥 🎧 | **PT** | Build simulator-independent point neuron and synaptic plasticity models. |
| Snudda | ⚙ 🔧 ⅄ 👥 🎧 | **BI** | Build networks of biophysically detailed neurons where the connectivity is based on the neuron morphologies. |
| Brain Scaffold Builder | ⚙ 🔧 ⅄ 👥 🎧 | **BI** | Rapidly construct biologically realistic network models. |
| The Virtual Brain (TVB) | 💻 ⚙ ✔ 🧠 🎓 👥 🎧 | **PP** | Construct and simulate personalised brain network models. |
| Single Cell Modelling Workflows | ⚙ ✔ ⚲ 👥 🎧 | **BI** | Build biologically detailed single cell models. |

# Running Simulations

Table 5: Tools and services part of EBRAINS for running simulations, for the diverse scales.

| Tool or service | Characteristics | Modelling abstraction level | Purpose |
|---|---|---|---|
| CGMD Platform | 💻 ✔ ⅄ 🧠 | **NS** | Prepare, run and analyse coarse-grained molecular dynamics simulations. |
| SSB Platform | 💻 📋 ⇄ 👥 🧠 | **NS SB** | Predict the downstream effects upon ligand binding/disease associated variants, such as protein/metabolite concentrations/dose response curves, and explore metabolic networks using automated bio-mathematical models. |
| MoDEL-CNS | 💻 🔧 ⇄ 🎓 👥 🧠 | **NS** | Access atomistic-MD trajectories for relevant signal transduction proteins in a web browser. |
| BioExcel-CV19 | 💻 🔧 ⇄ 🎓 👥 🧠 | **NS** | Web server resource for providing molecular dynamics simulation data. Currently, set-up to provide simulation trajectories for Covid-19 studies, but is also applicable to brain-related (and other) studies. |
| SDA | 💻 ✔ ⁙ 🎓 👥 🧠 | **NS** | Simulate diffusional association of proteins. Compute bimolecular association rate constants. |
| Single Cell *In Silico* Experiment Tool (BlueNaaS) | 💻 ✔ ⚲ 🎓 👥 🧠 | **BI** | Neuron as a Service: Simulate and visualise detailed single neuron models in a web browser. |
| Small Circuit *In Silico* Experiments Tool (Rat Hippocampus CA1) | 💻 ✔ ⅄ 🎓 👥 🧠 | **BI** | Run simulation experiments with a small hippocampal neural circuit. |
| Brain Areas Circuit *In Silico* Experiments Tool (Rat Hippocampus CA1) | 💻 ✔ ⅄ 🎓 🧠 | **BI** | Run simulation experiments with a full-scale model of the hippocampus CA1 region. |
| NEST | ⚙ ✔ ⅄ 🎓 👥 🧠 | **PT** | Run highly-scalable simulations of point neuron networks. |
| Arbor | ⚙ ✔ ⅄ 🎓 👥 🧠 | **BI** | Run scalable, high-performance simulations of multi-compartment neurons in large networks. |
| NEURON/CoreNEURON | ⚙ ✔ ⅄ 🎓 👥 🧠 | **BI** | Run scalable, high-performance simulations of multi-compartment neurons in large networks in the well-established NEURON simulation environment. |
| Neuromorphic Computing Job Manager App | 💻 ⚙ ✔ ⅄ 🎓 👥 🧠 | **PT** | Run simulation experiments with point neuron networks on the BrainScaleS and SpiNNaker neuromorphic computing systems. |
| Multiscale Co-Simulation Framework | ⚙ 🔧 ⅄ 💡 🧠 | **PT BI PP** | Connect simulation tools at runtime to enable multiscale co-simulations. |
| The Virtual Brain (TVB) | 💻 ⚙ ✔ 💡 🎓 👥 🧠 | **PP** | Simulate personalised brain network models locally, on the EBRAINS Collaboratory, or directly on HPC for large parameter explorations. |
| MMCG Platform | 💻 ✔ ⅄ 🧠 | **NS** | Set-up hybrid molecular mechanics/coarse grain simulations. |

# Data Analysis

Table 6: Tools and services part of EBRAINS for data analysis, for the diverse scales.

| Tool or service | Characteristics | Modelling abstraction level | Purpose |
|---|---|---|---|
| Neo | ⚙ ✔<br>🎓 👥 🧠 | SB PT BI PP ST | Load, save, annotate and manipulate electrophysiology and imaging data from experiment and simulation in a standardised framework. |
| Elephant | ⚙ ✔<br>🎓 👥 🧠 | SB PT BI PP ST | Analyse neuronal activity data from experiment and simulation using high-performance, well-tested methods. |
| LFPy | ⚙ ✔ ⅄<br>👥 🧠 | BI PP | Calculate electric and magnetic brain signals from multi-compartment neuron models and networks. |
| The Virtual Brain (TVB) | 💻 ⚙ ✔ 💡<br>🎓 👥 🧠 | PP | Load, analyse, visualise and explore experimental and simulated brain activity time series. |

# Visualisation

Table 7: Tools and services part of EBRAINS for visualisation, for the diverse scales.

| Tool or service | Characteristics | Modelling abstraction level | Purpose |
|---|---|---|---|
| SimVisSuite | 💻 🔧 ⅄<br>👥 🧠 | PT BI PP | Interactively visualise and analyse network and neuron-level simulations. |
| NEST Desktop | 💻 ✔ ⅄<br>👥 🧠 | PT | Build, run, visualise and analyse simulations with the NEST simulator in a web-based GUI. |
| SimDaVis - Insite | ⚙ 🔧 ⅄<br>🧠 | SB PT BI PP ST | Continuously access simulation data at runtime. |
| Elephant Visualization (Viziphant) | ⚙ 📋<br>🎓 👥 🧠 | SB PT BI PP ST | Visualise analysis results in Jupyter notebooks. |

# Validating Models Against Experimental Data

Table 8: Tools and services part of EBRAINS for validating models, for the diverse scales.

| Tool or service | Characteristics | Modelling abstraction level | Purpose |
|---|---|---|---|
| Validation Test Libraries | ⚙ ✔ 🔧 ⧗ ⅄<br>⇄ 💡<br>🎓 👥 🧠 | SB PT BI PP ST | Develop and run structured, quantitative model validation tests. |
| Model Catalog | 💻 ⚙ ✔ ⧗ ⅄<br>⇄ 💡<br>🎓 👥 🧠 | SB PT BI PP ST | Explore and visualise computational models, validation tests and validation results. |