

Computational neuroscience with EBRAINS

Andrew Davison, CNRS

HBP Young Researchers Event 2022

EBRAINS - a digital European Infrastructure for next-generation basic & clinical neuroscience

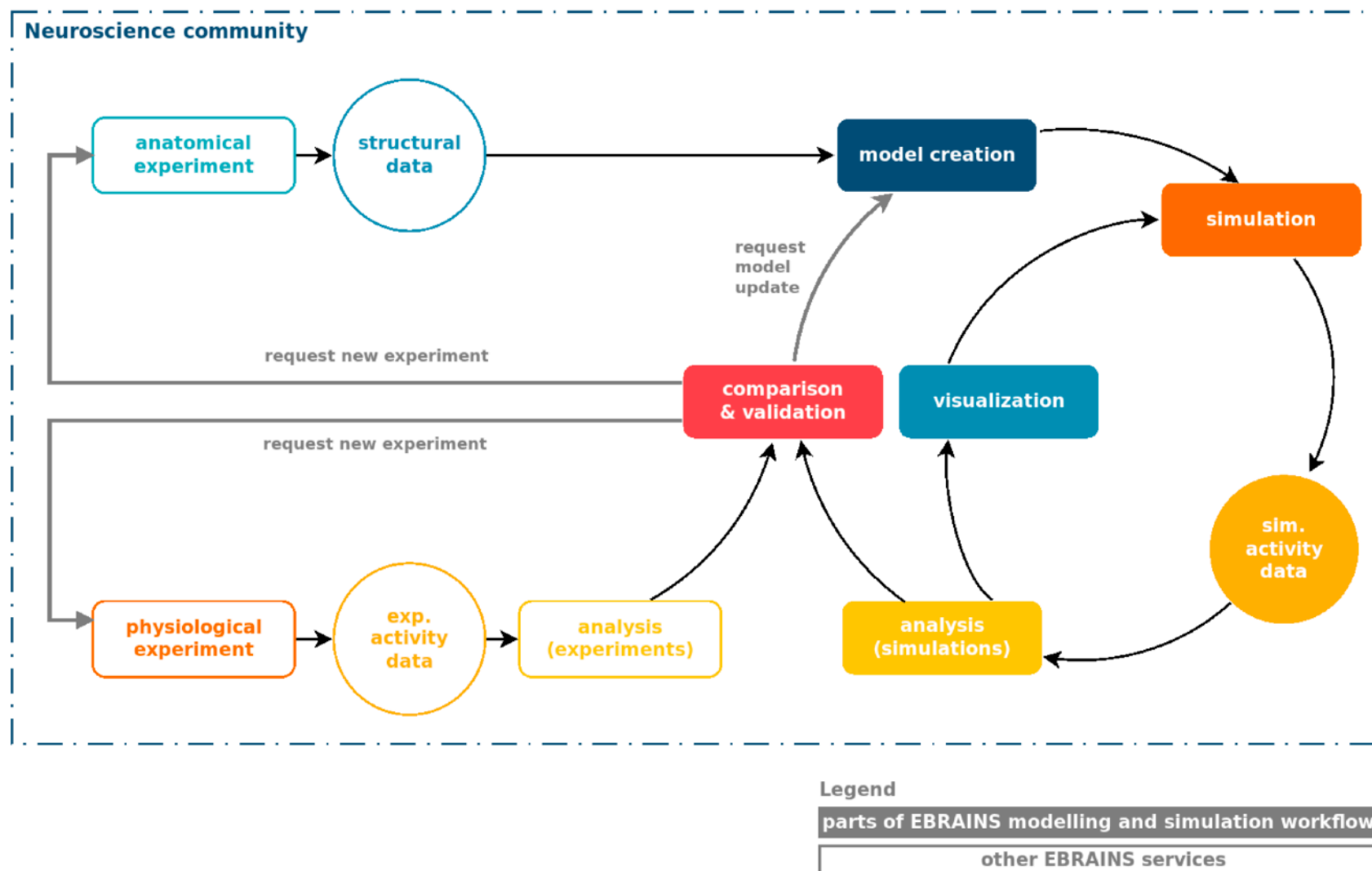
Copenhagen, 16th May 2022



Co-funded by
the European Union



Modelling and simulation lifecycle



Challenges in computational neuroscience

- compute power
 - big data - recordings from more neurons, increased resolution...
 - multiscale simulation - from molecular to whole brain
- software complexity, software quality
 - increasing power, decreasing understandability?
 - student- and scientist-developed tools with limited software engineering training
- collaboration
 - power of multidisciplinary approaches, increasing specialization
- reproducibility
 - workflow complexity, entropy of computational environments..

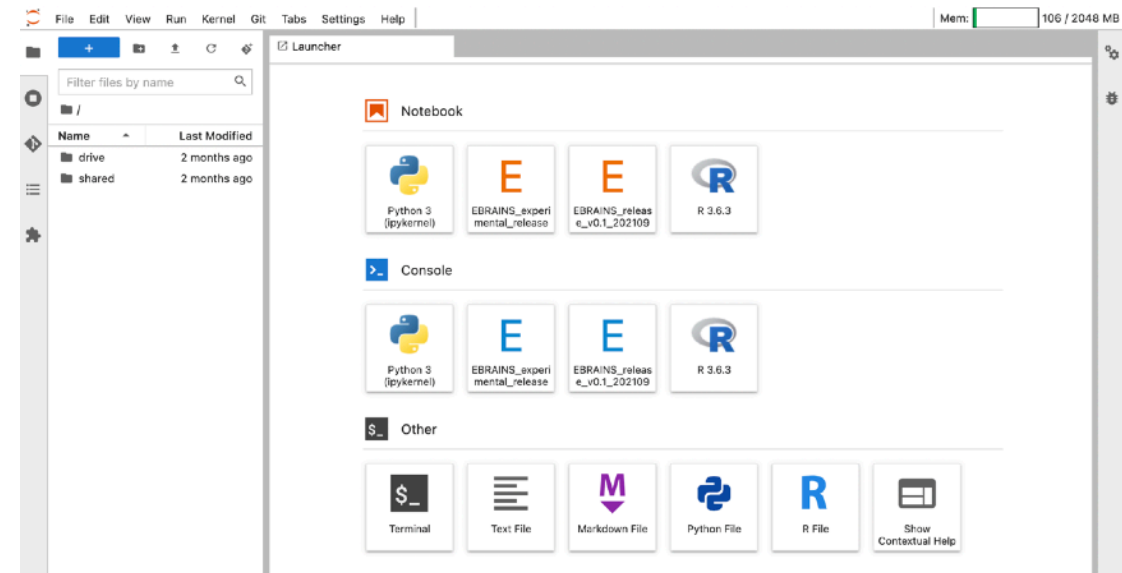
How EBRAINS addresses these challenges

- compute power
 - EBRAINS Lab (Jupyter Lab hosted in HPC centres)
 - federated HPC resources in CH, DE, FR, IT, ES (Fenix)
 - Neuromorphic computing systems (SpiNNaker, BrainScaleS)
- software complexity, software quality
 - Knowledge Graph (find software)
 - software quality standards
 - testing, continuous integration
- collaboration
 - EBRAINS Collaboratory
- reproducibility
 - standardized workflows
 - standard EBRAINS software collection releases

A brief overview of computing resources in EBRAINS

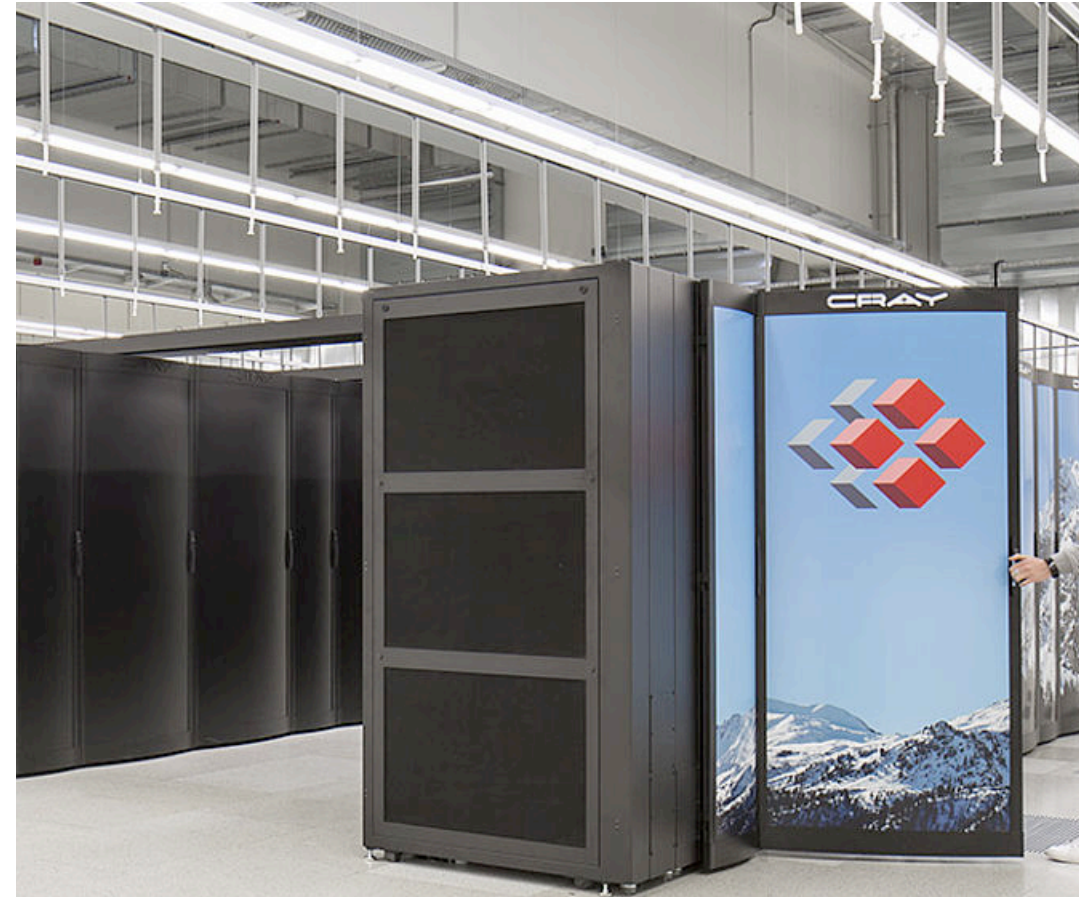
The Lab

- gives EBRAINS users the ability to develop and run programs in the cloud from their web browser, without needing to install anything on their local machine.
- offers a pre-installed programming environment and all of the EBRAINS tools and libraries which can be run from it.
- runs on EBRAINS servers provided by HPC centres across Europe.
- gives users a JupyterLab user interface to manage, edit and run their Jupyter Notebooks.



HPC

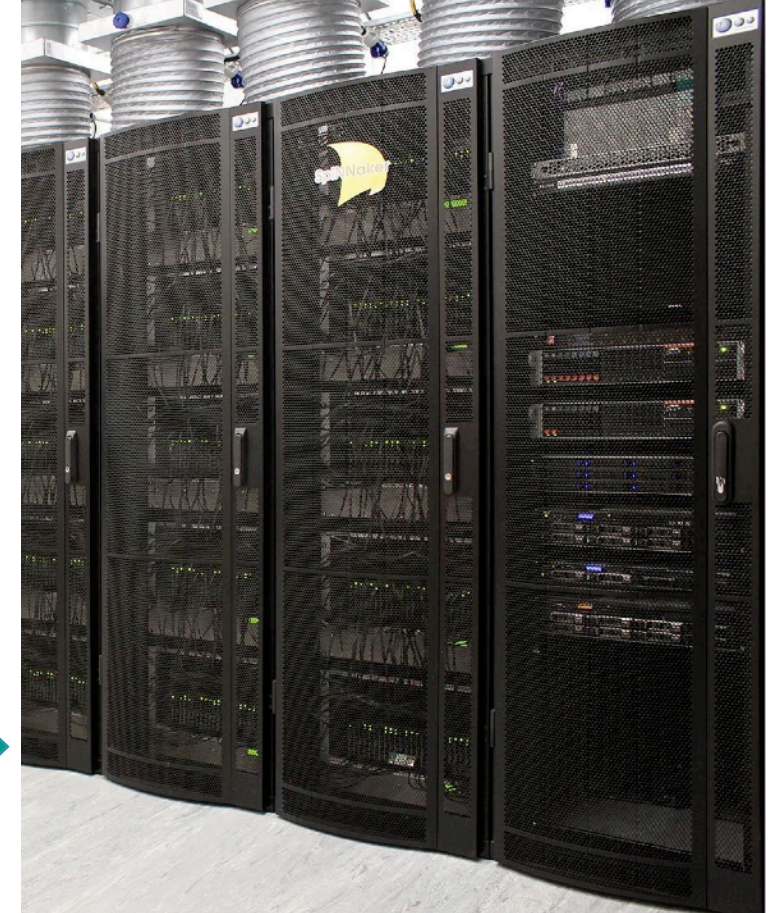
- Five European supercomputing centres, namely BSC (Spain), CEA (France), CINECA (Italy), CSCS (Switzerland) and JSC (Germany), agreed to align their services to facilitate the creation of the Fenix Infrastructure.
- The distinguishing characteristic of this e-infrastructure is that data repositories and scalable supercomputing systems are in close proximity and well integrated.
- Most EBRAINS services run on the Fenix Infrastructure.



Neuromorphic computing













- The BrainScaleS system is based on physical (analogue) emulations of neuron, synapse and plasticity models with digital connectivity, running up to ten thousand times faster than real time.
- The SpiNNaker system is based on numerical models running in real time on custom digital multicore chips using the ARM architecture.



A brief overview of computational neuroscience software and web services in EBRAINS

Finding the right tool...

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		point neuron models	PT
				networks		biophysical models	BI
				whole brain		population models	PP
						statistical models	ST

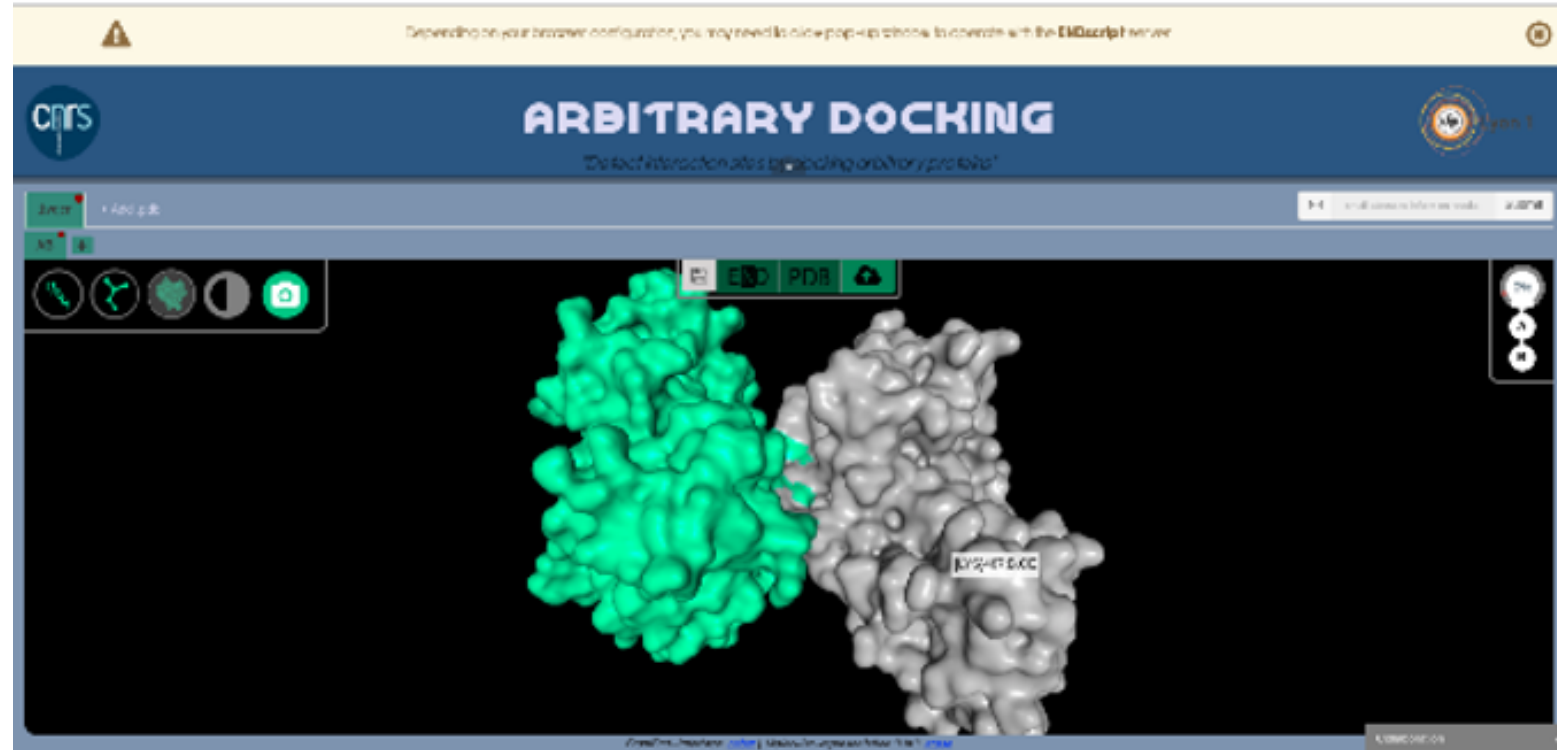
Workflow Stage: model building, simulation, data analysis, visualisation, model validation

Building Models



ArDOCK

- Detect potential interaction sites on the surface of a protein.
- <https://ardock.ibcp.fr/>



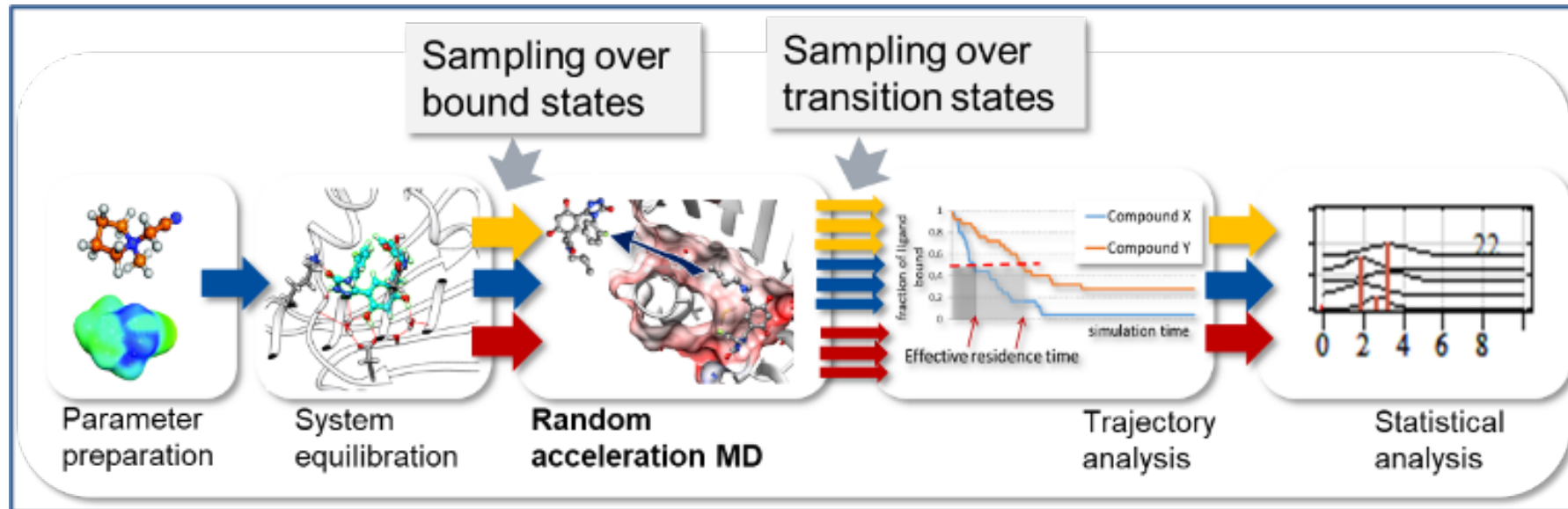
NS

Molecular Level Toolset

- Set up, run and analyse molecular level calculations, e.g. tauRAMD calculations to compute dissociation constants.
- https://humanbrainproject.github.io/hbp-sp6-guidebook/online_usecases/molecular_level/molecular_level.html

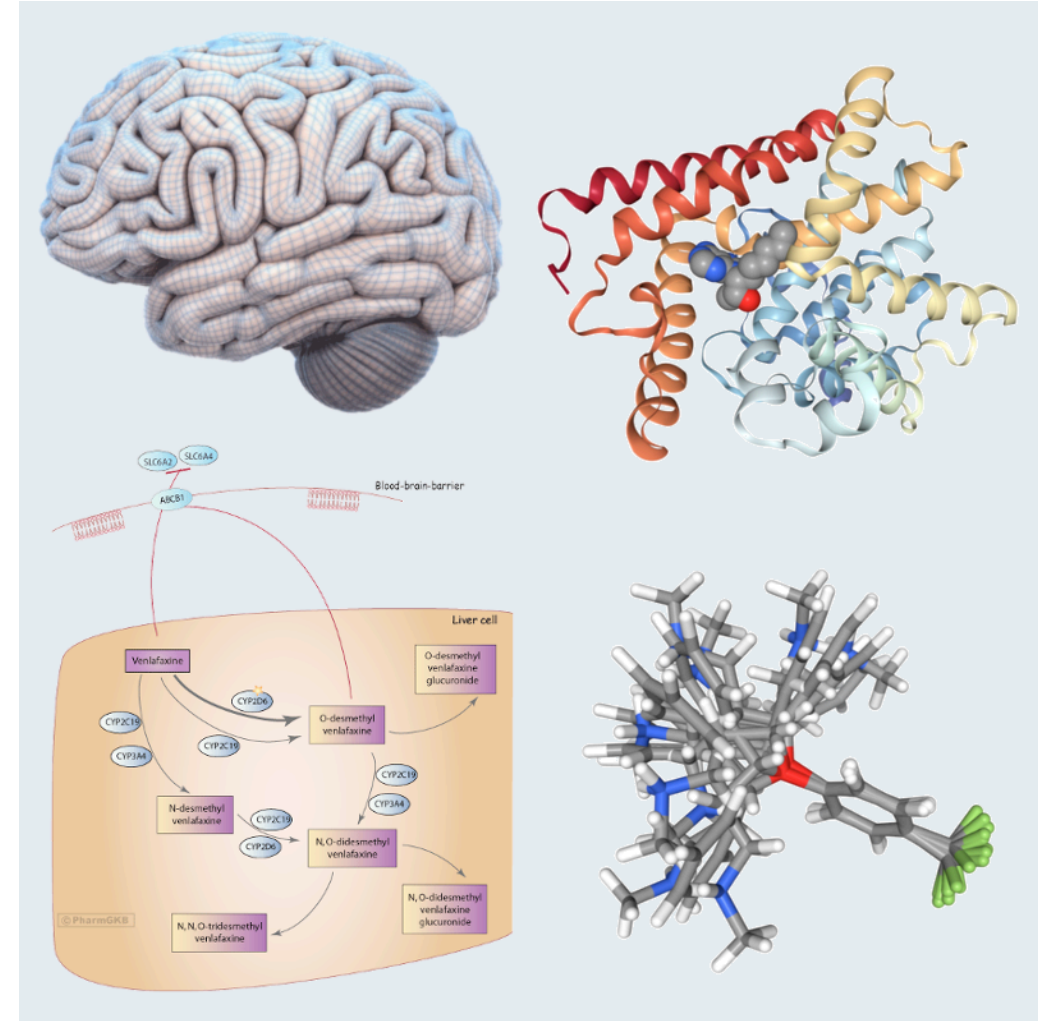


NS



CNS Ligands

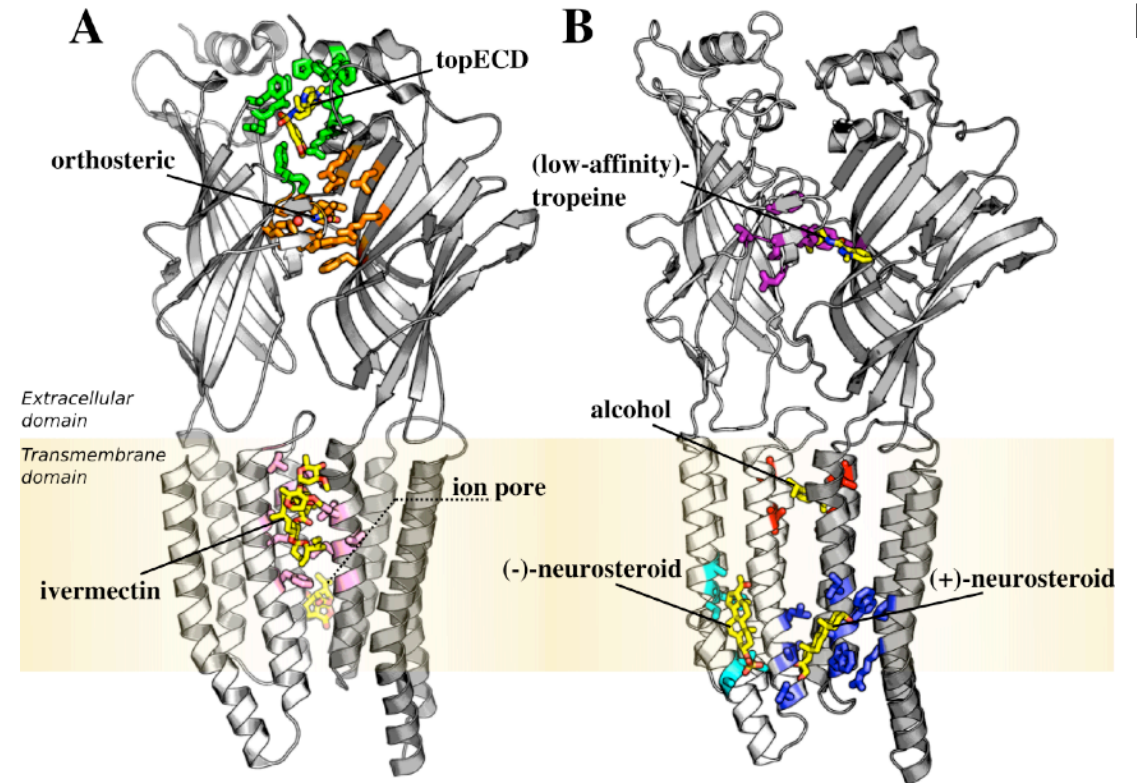
- a platform designed to efficiently generate and parameterise bioactive conformers of ligands binding to neuronal proteins for molecular dynamics simulations
- <http://mmb.irbbarcelona.org/webdev/slim/CNS/public/>



NS

GRALL

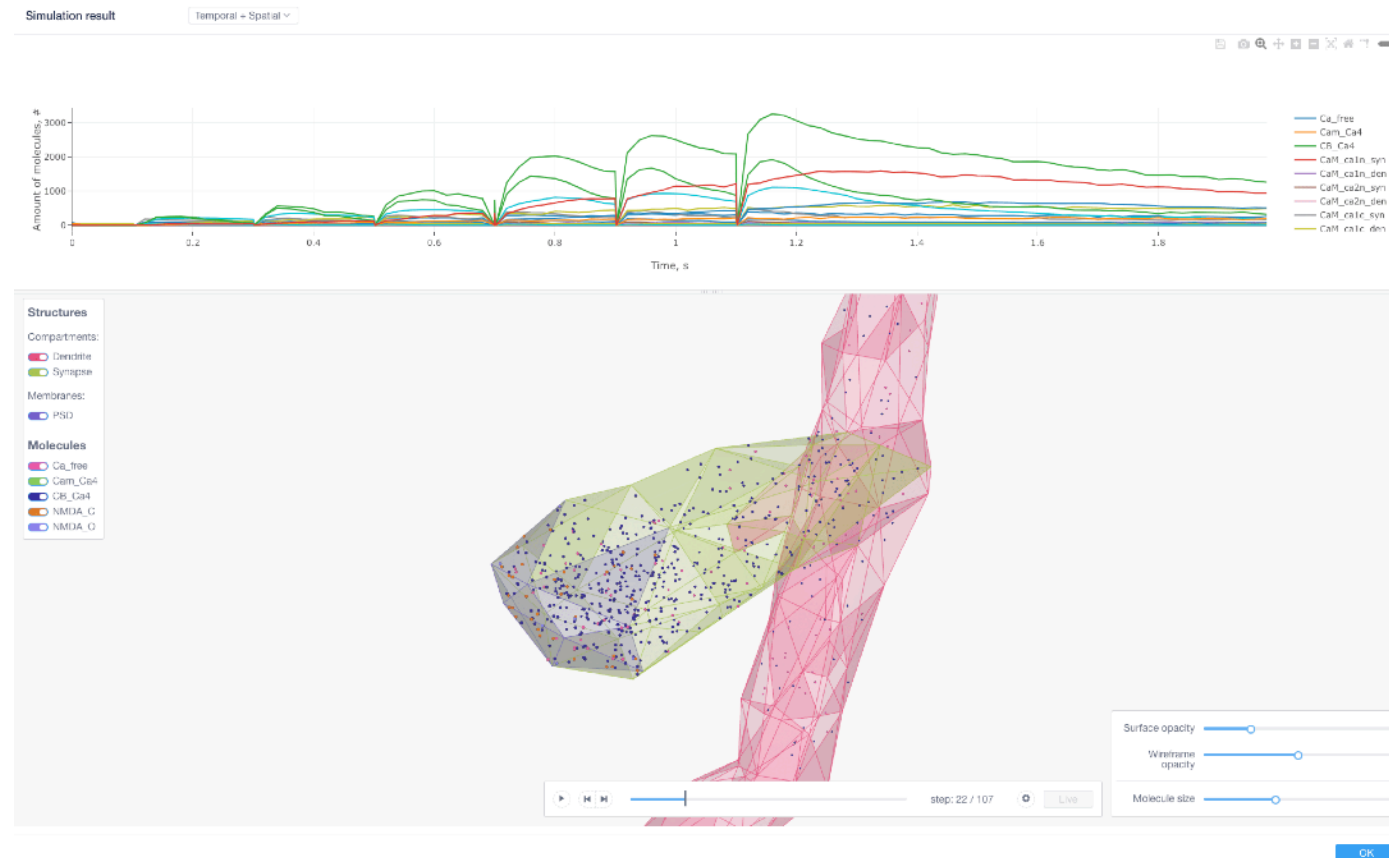
- The Glycine Receptor Allosteric Ligand Library GRALL8 is the first database of allosteric modulators of a human synaptic receptor with a structural annotation based on their binding site on the receptor.
- <https://ifm.chimie.unistra.fr/grall>



NS

Subcellular Web App

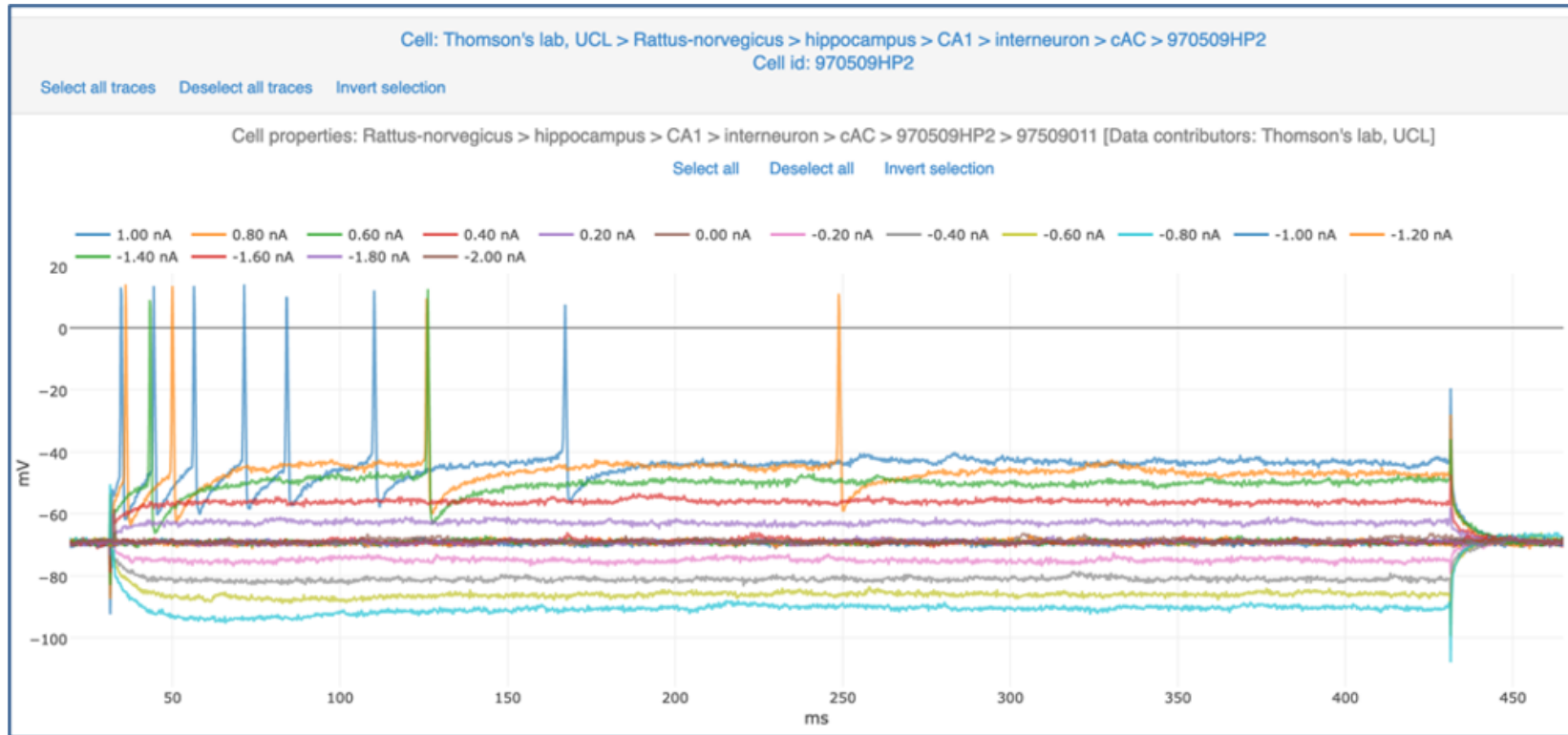
- Create and simulate brain molecular networks.
- <https://subcellular.humanbrainproject.eu/>



SB

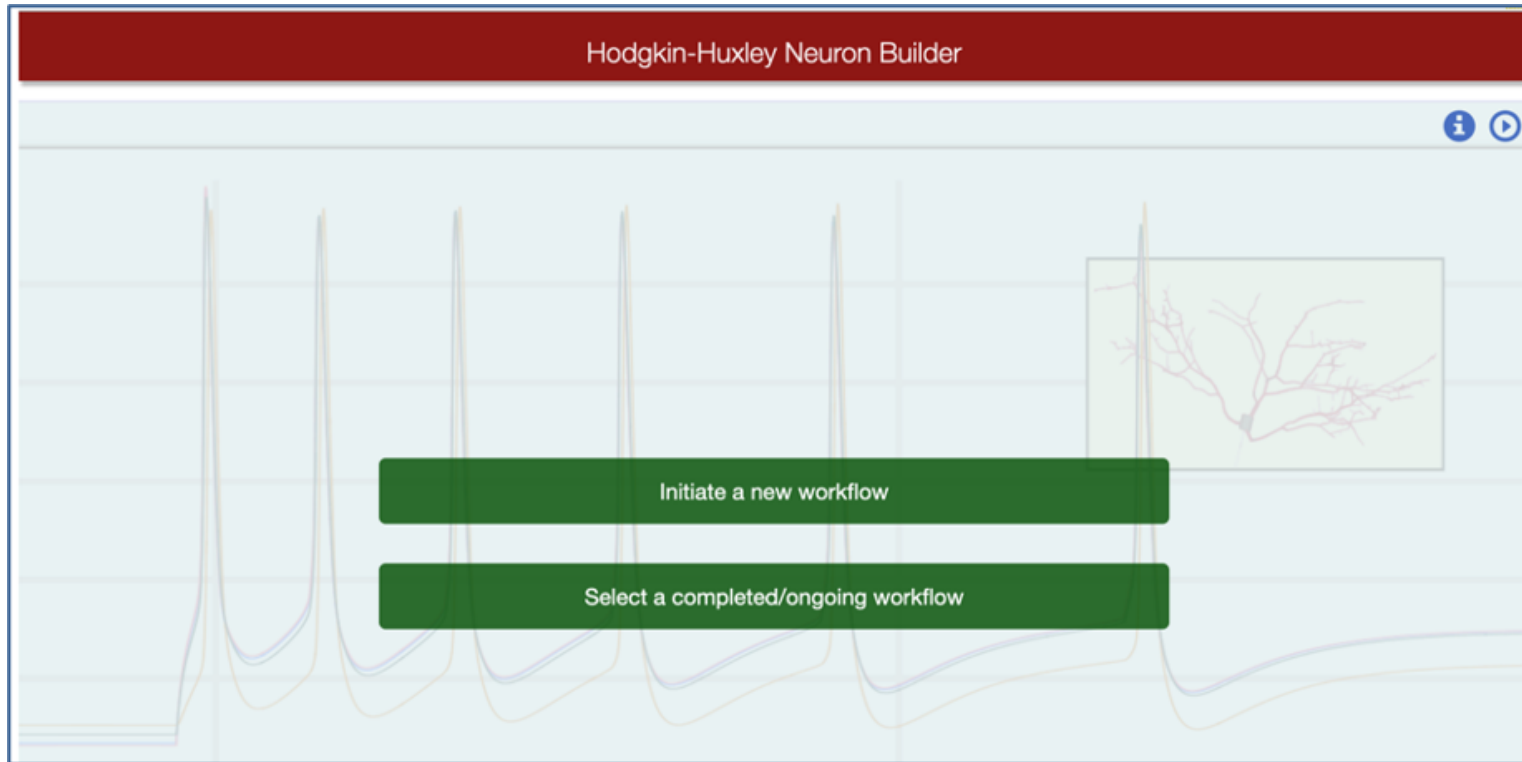
NeuroFeatureExtract

- Extract a wide variety of electrophysiological features from experimental recordings.
- <https://ebrains-cls-interactive.github.io/>



Hodgkin-Huxley Neuron Builder

- Optimise a single cell model against experimental data on HPC resources.
- <https://ebrains-cls-interactive.github.io/>



BI

Electrical Model Building Toolset

- Build and validate biophysically detailed electrical neuron models.

- BluePyOpt:

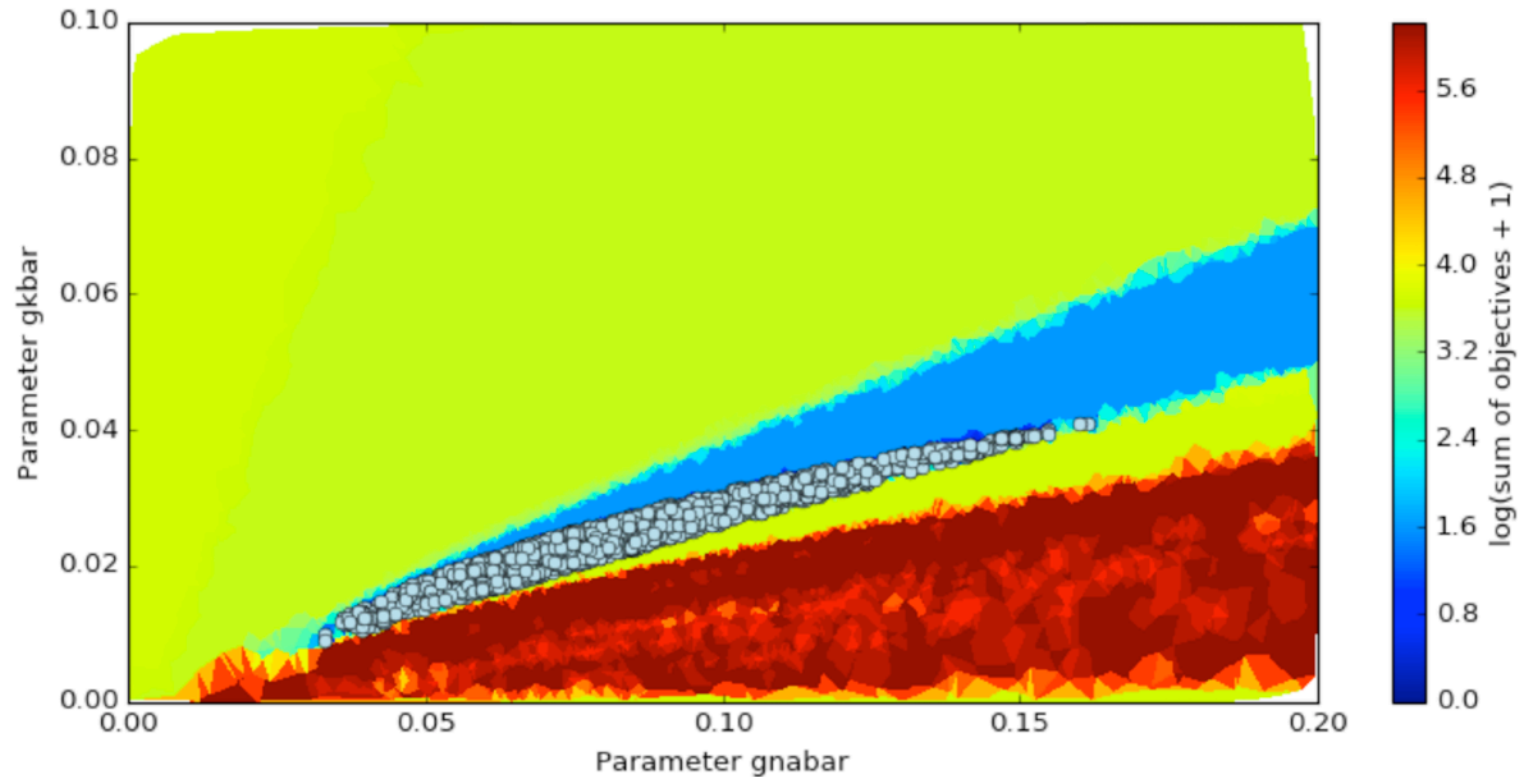
- <https://github.com/BlueBrain/BluePyOpt>

- eFEL

- <https://github.com/BlueBrain>

- BluePyEfe

- <https://github.com/BlueBrain/BluePyEfe>

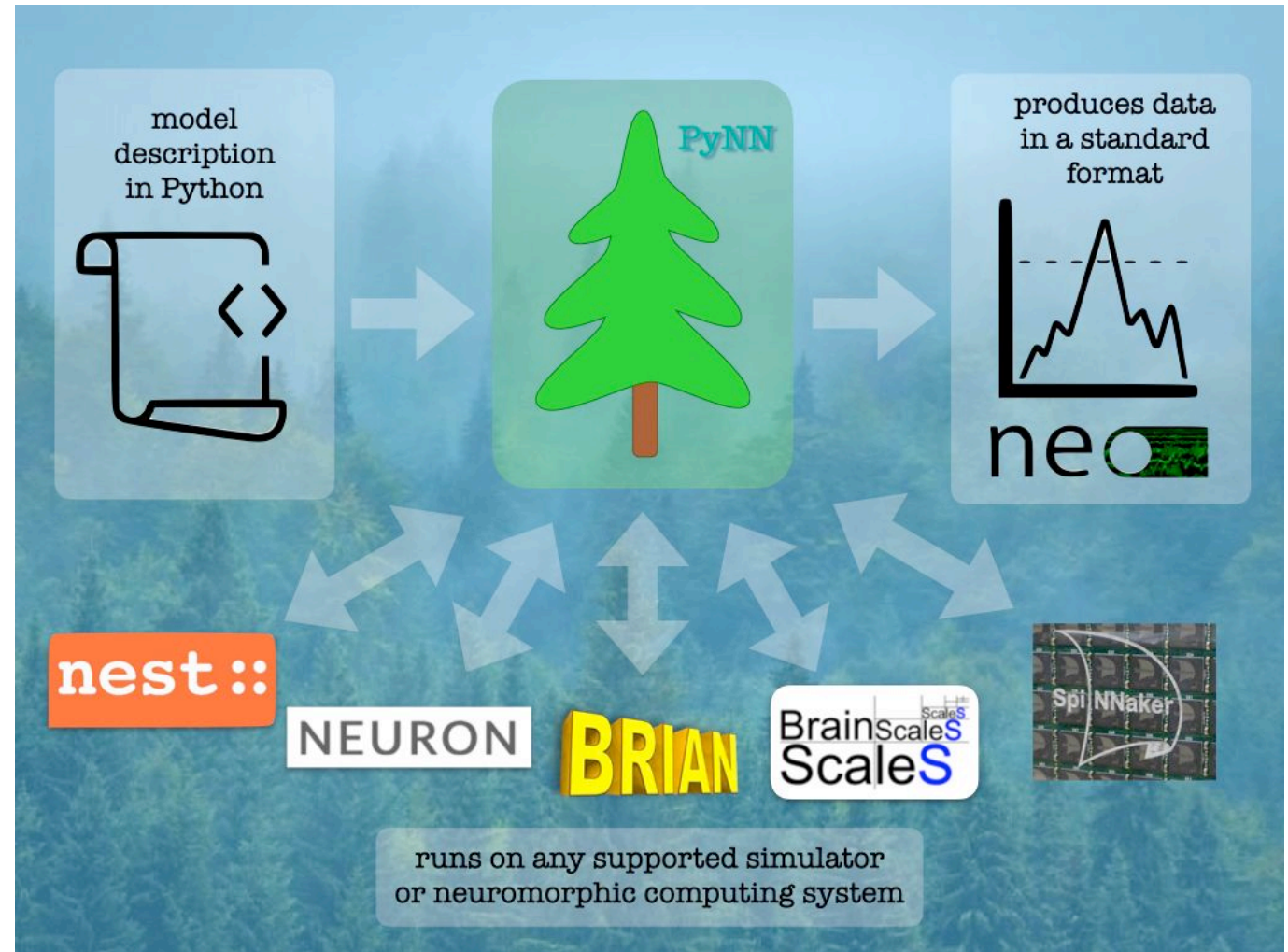


BI

PyNN

- Build simulator-independent spiking neuronal networks and simulation experiments.
- <https://ebrains.eu/service/pynn>

Hands-on
Session

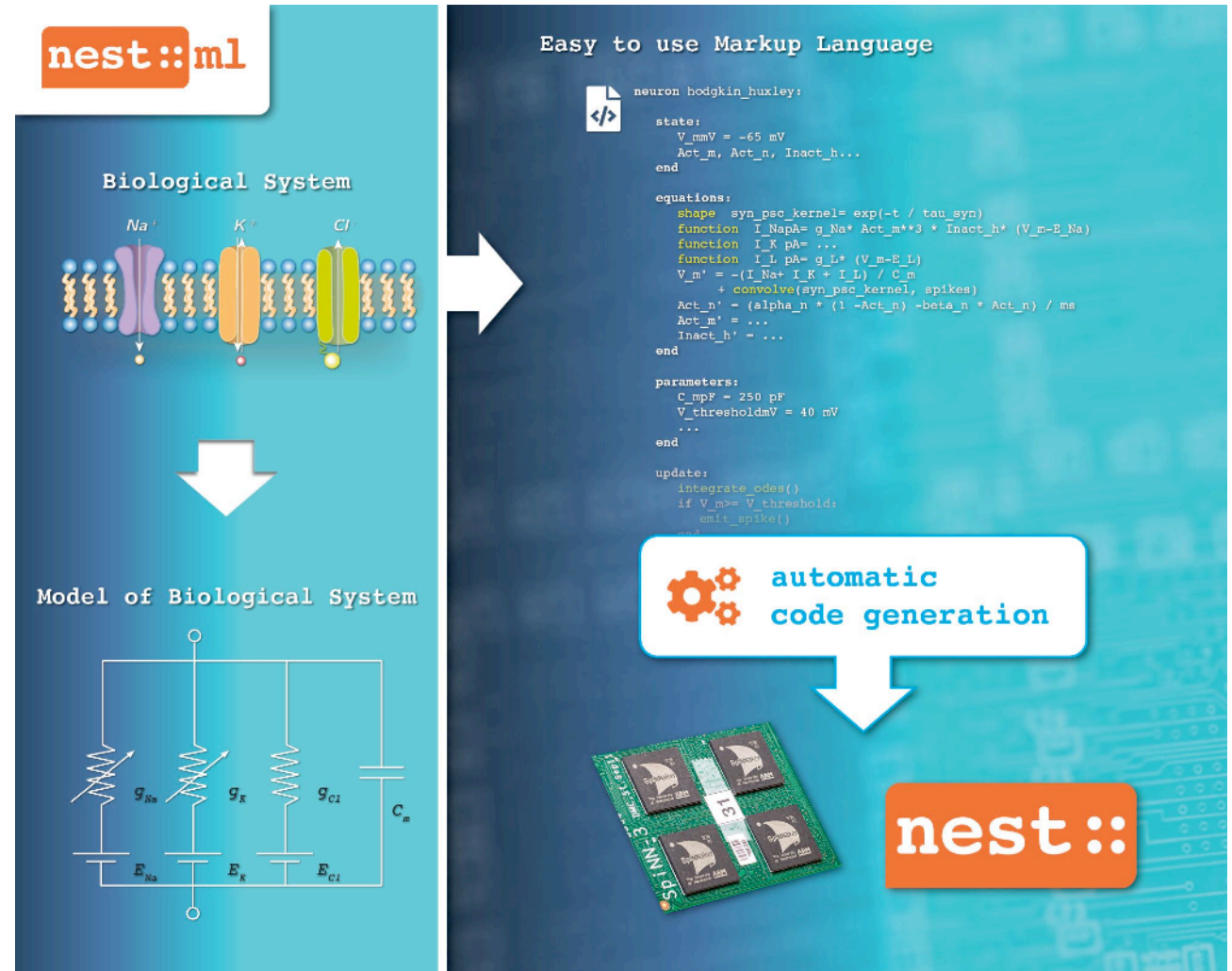


PT

BI

NESTML

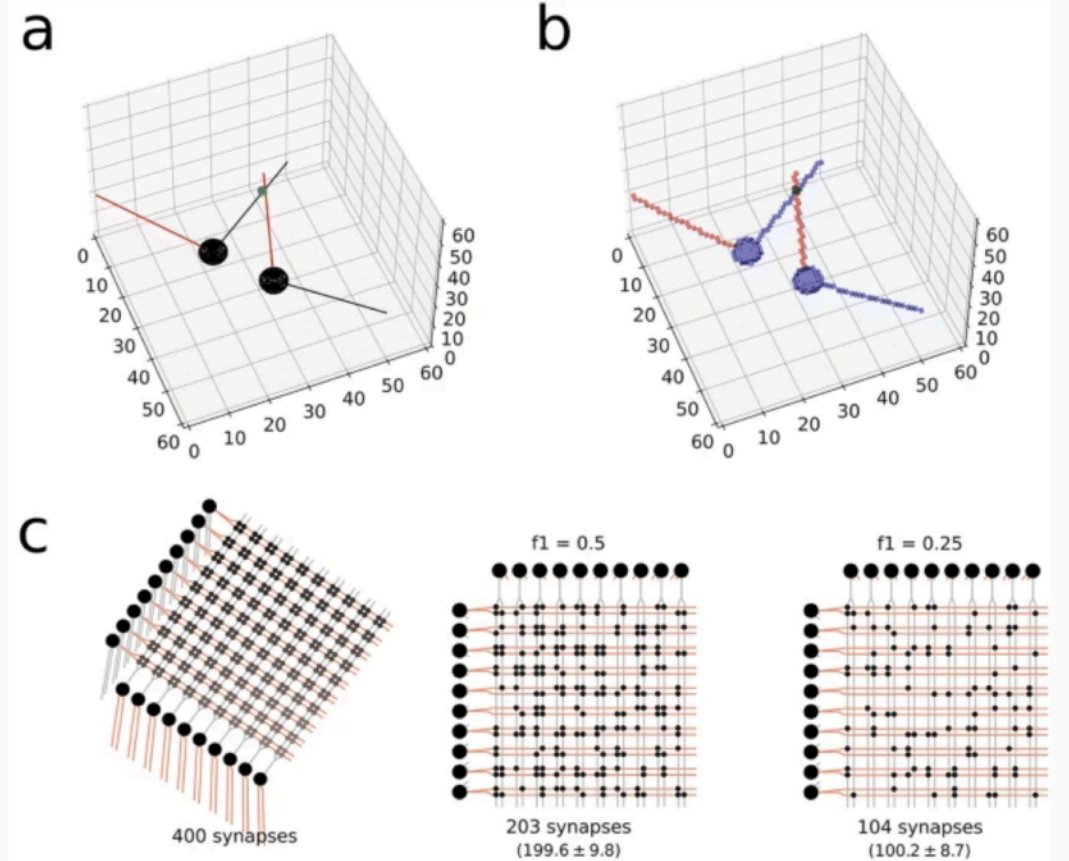
- Build simulator-independent point neuron and synaptic plasticity models.
- <https://ebrains.eu/service/nestml>



Snudda

- Build networks of biophysically-detailed neurons where the connectivity is based on the neuron morphologies.
- <https://github.com/Hjorthmedh/Snudda>

Fig. 3

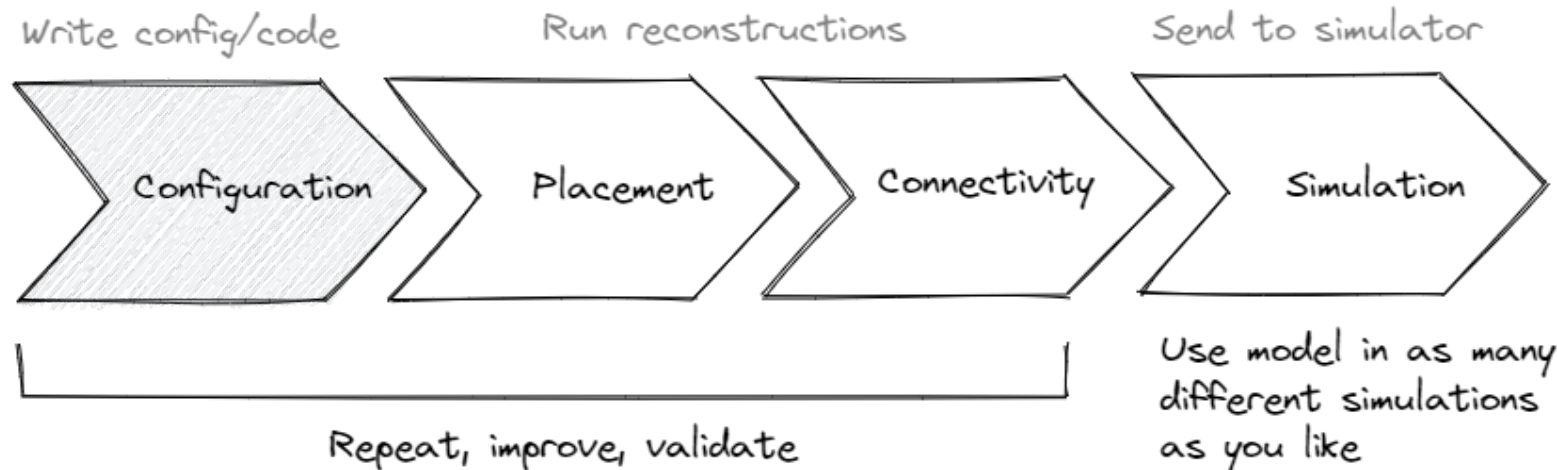


BI

Brain Scaffold Builder

- Rapidly construct biologically realistic network models.
- <https://github.com/dbbs-lab/bsb>

BSB

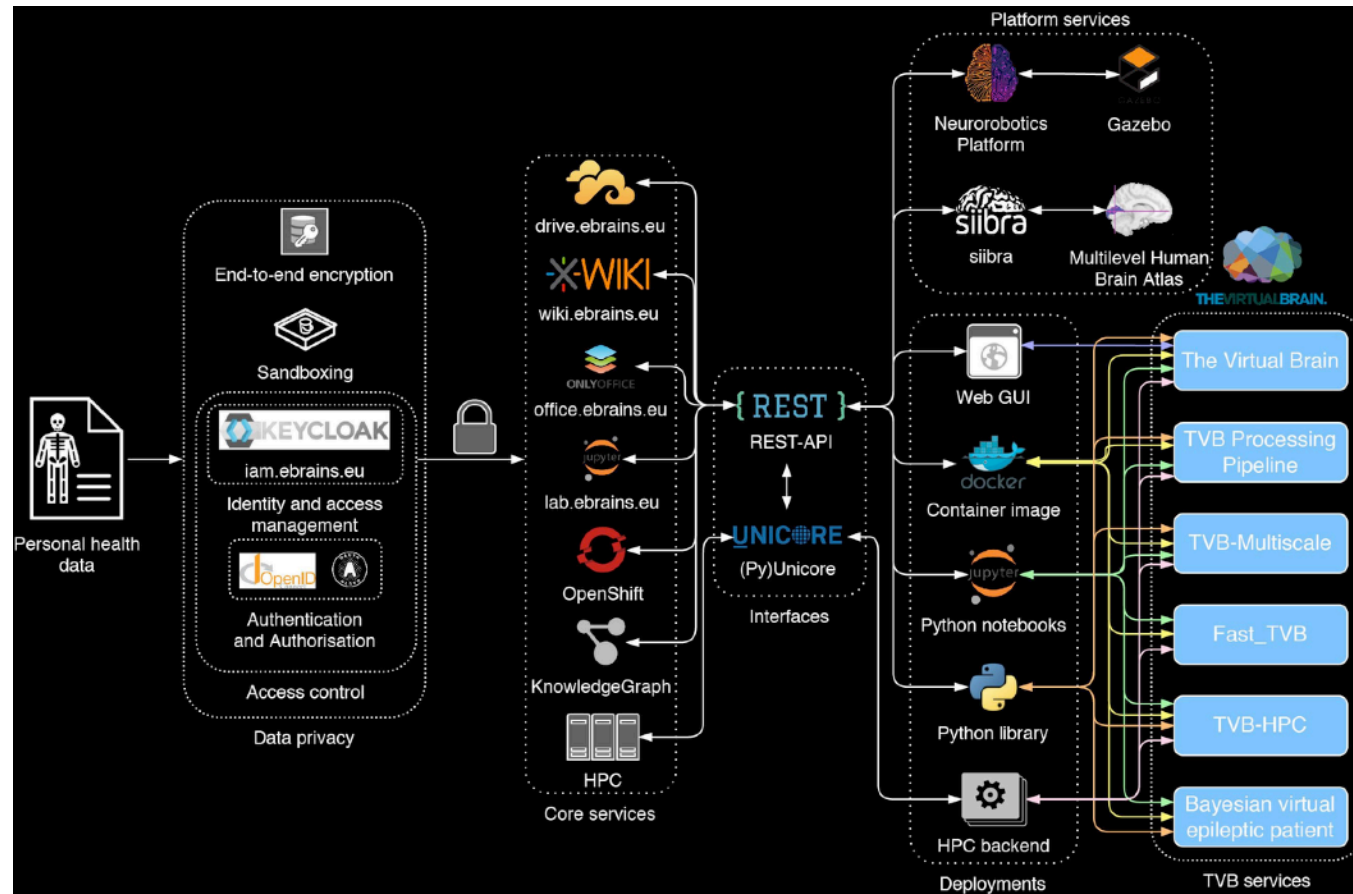


BI

PT

The Virtual Brain (TVB)

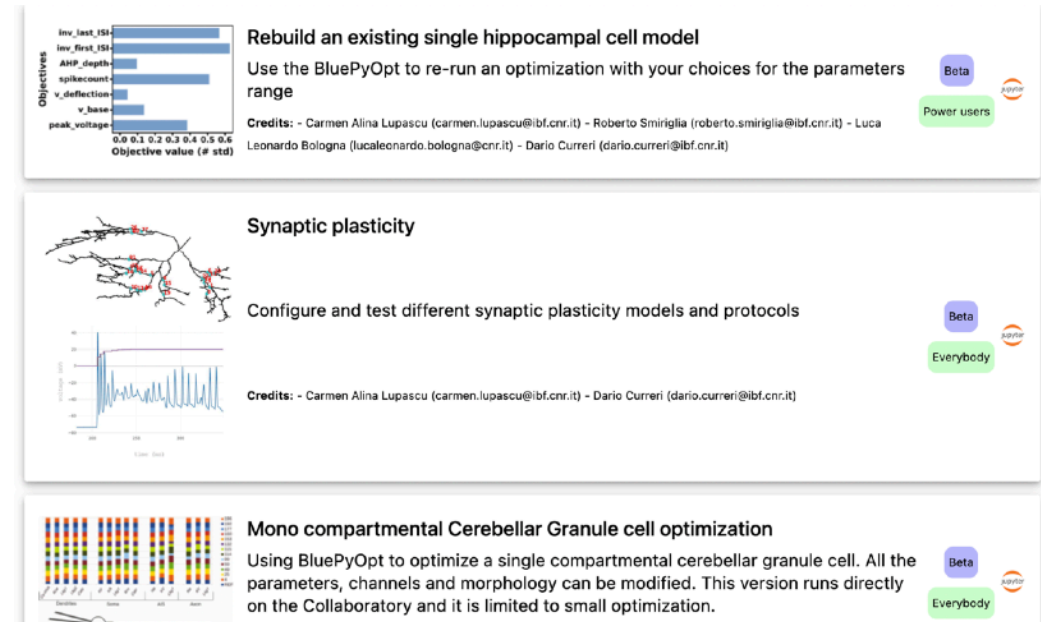
- Construct and simulate personalised brain network models.
- <https://ebrains.eu/service/the-virtual-brain>



PP

Single Cell Modelling Workflows

- an ensemble of Jupyter notebooks for single cell modelling and data analysis. The notebooks 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.
- <https://ebrains.eu/service/cls-interactive>



Rebuild an existing single hippocampal cell model
Use the BluePyOpt to re-run an optimization with your choices for the parameters range
Credits: - Carmen Alina Lupascu (carmen.lupascu@ibf.cnr.it) - Roberto Smiraglia (roberto.smiraglia@ibf.cnr.it) - Luca Leonardo Bologna (lucaleonardo.bologna@cnr.it) - Dario Curreri (dario.curreri@ibf.cnr.it)
Beta
Power users

Synaptic plasticity
Configure and test different synaptic plasticity models and protocols
Credits: - Carmen Alina Lupascu (carmen.lupascu@ibf.cnr.it) - Dario Curreri (dario.curreri@ibf.cnr.it)
Beta
Everybody

Mono compartmental Cerebellar Granule cell optimization
Using BluePyOpt to optimize a single compartmental cerebellar granule cell. All the parameters, channels and morphology can be modified. This version runs directly on the Collaboratory and it is limited to small optimization.
Beta
Everybody

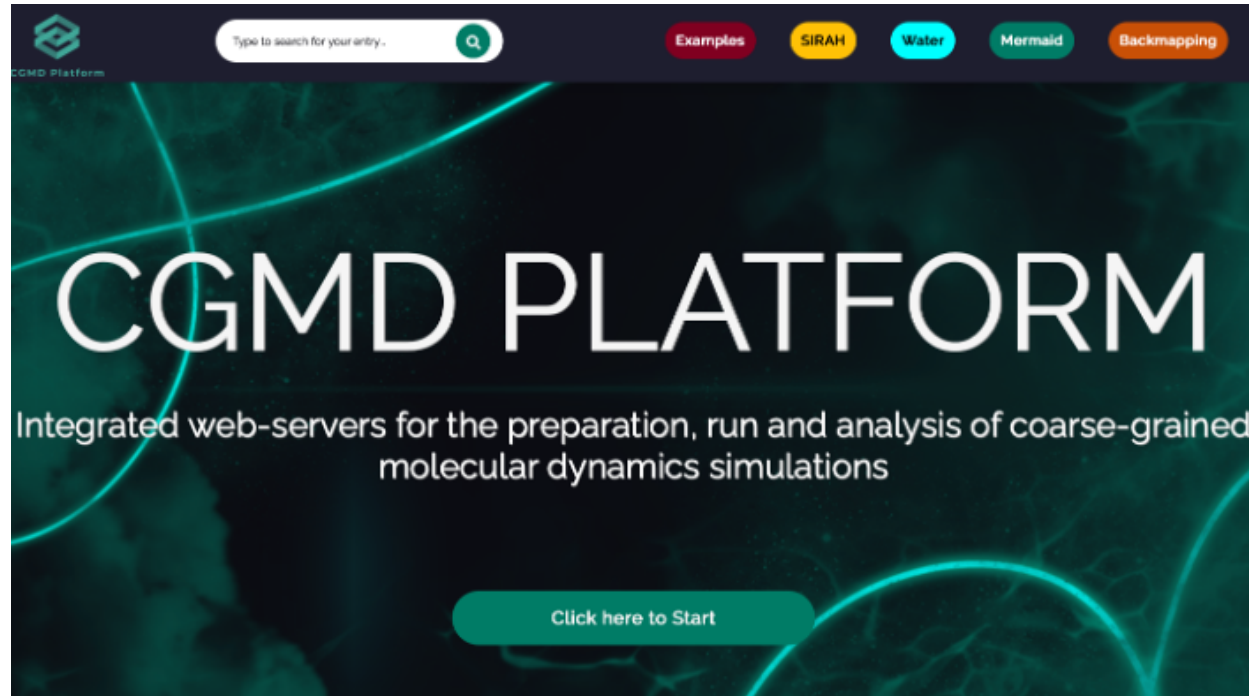


BI

Running Simulations

CGMD Platform

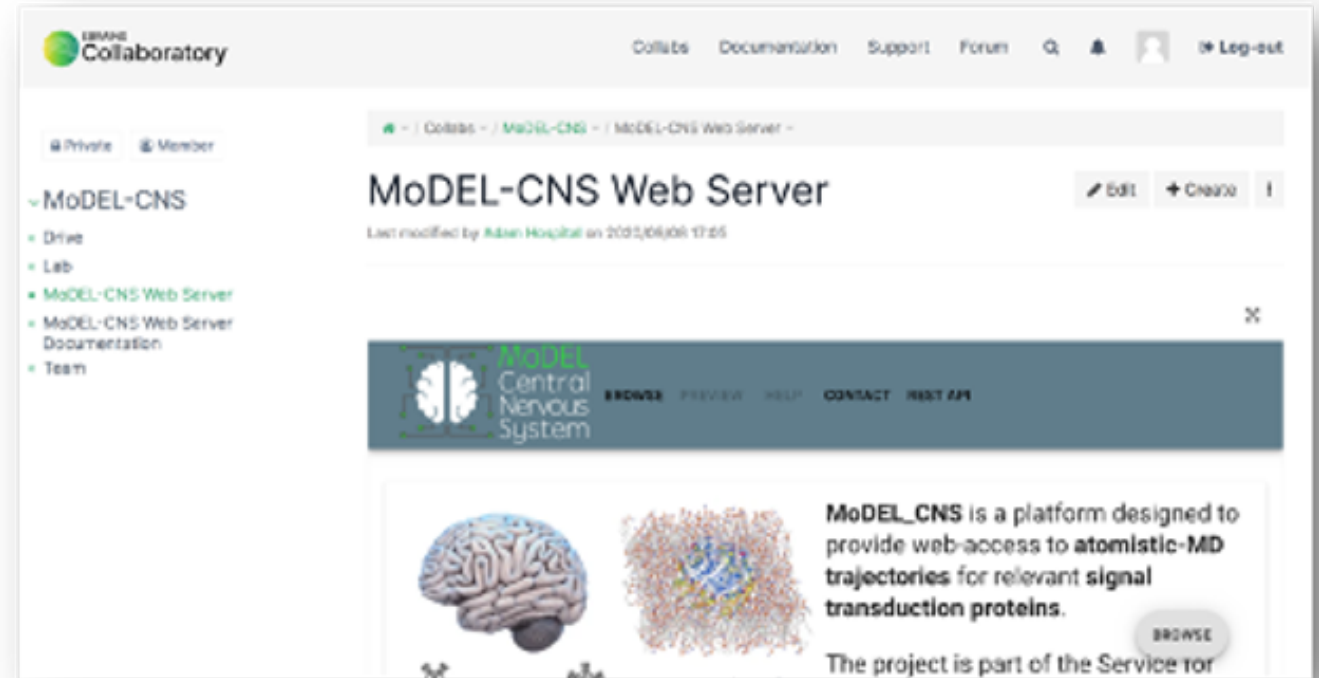
- Prepare, run and analyse coarse-grained molecular dynamics simulations.
- <https://molsim.sci.univr.it/mermaid/begin.php>



NS

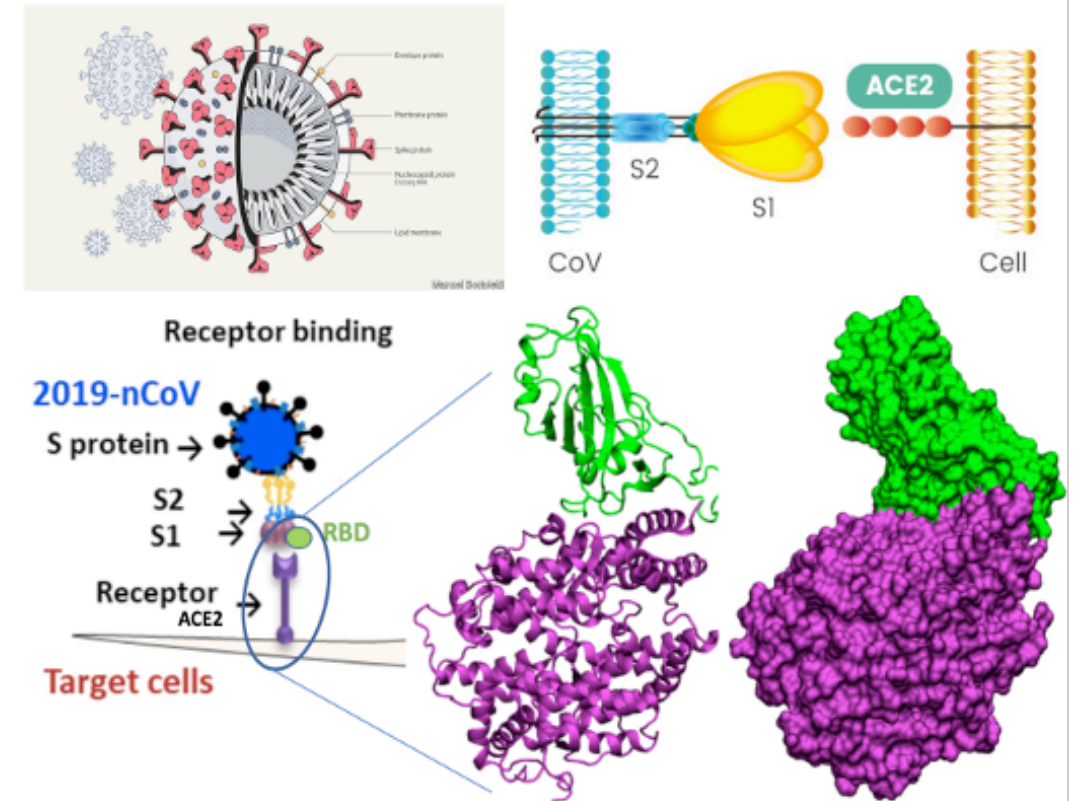
MoDEL-CNS

- Access atomistic-MD trajectories for relevant signal transduction proteins in a web browser.
- <http://mmb.irbbarcelona.org/MoDEL-CNS/>
- <https://wiki.ebrains.eu/bin/view/Collabs/molecular-tools-model-cns/>



BioExcel-CV19

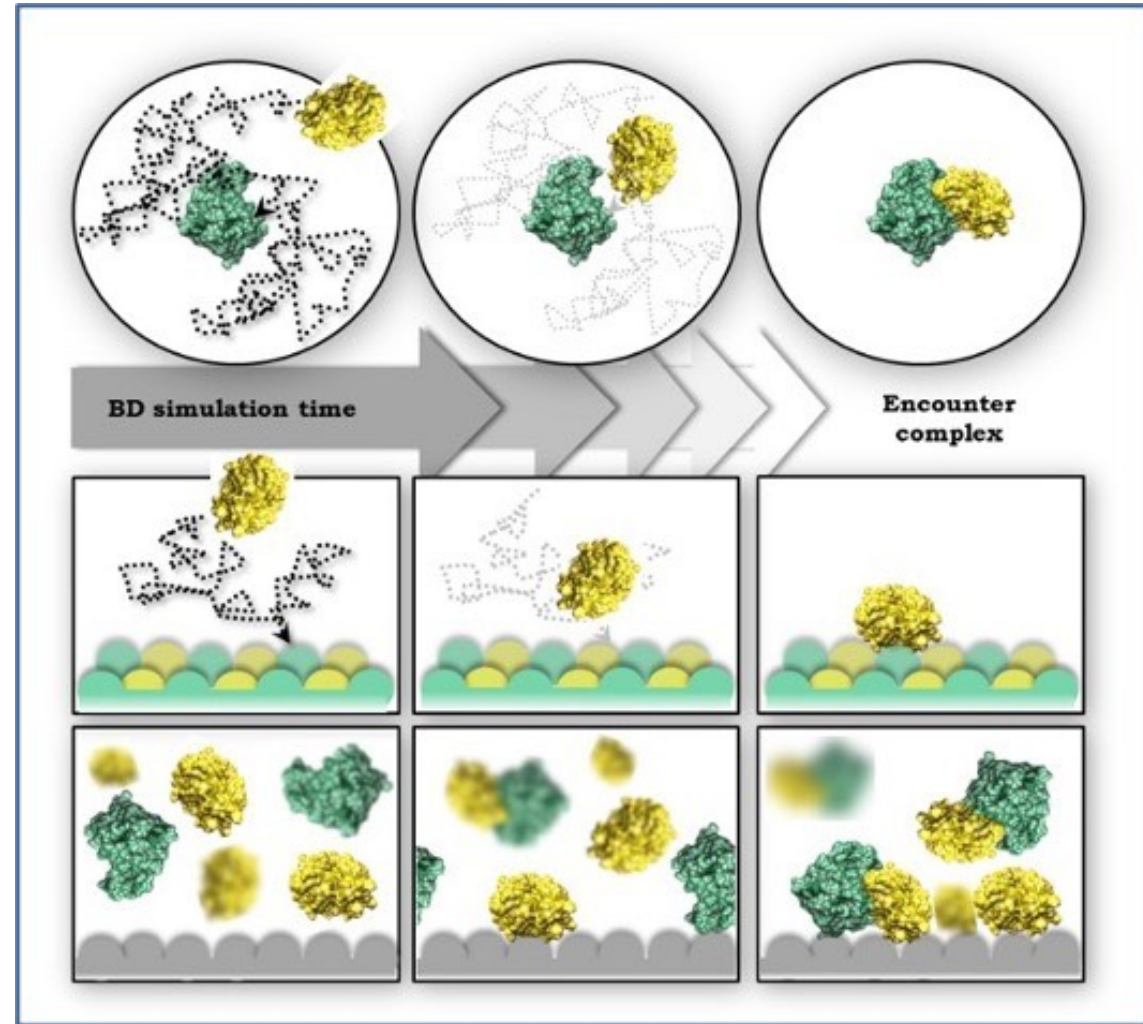
- a platform designed to provide web access to atomistic-MD trajectories for macromolecules involved in the COVID-19 disease. It is a side project of the previously presented MoDEL-CNS platform, redesigned to tackle COVID-19 related MD simulations.
- <https://bioexcel-cv19.bsc.es/#/>
- <https://wiki.ebrains.eu/bin/view/Collabs/molecular-tools-bioexcel-cv19>



NS

SDA

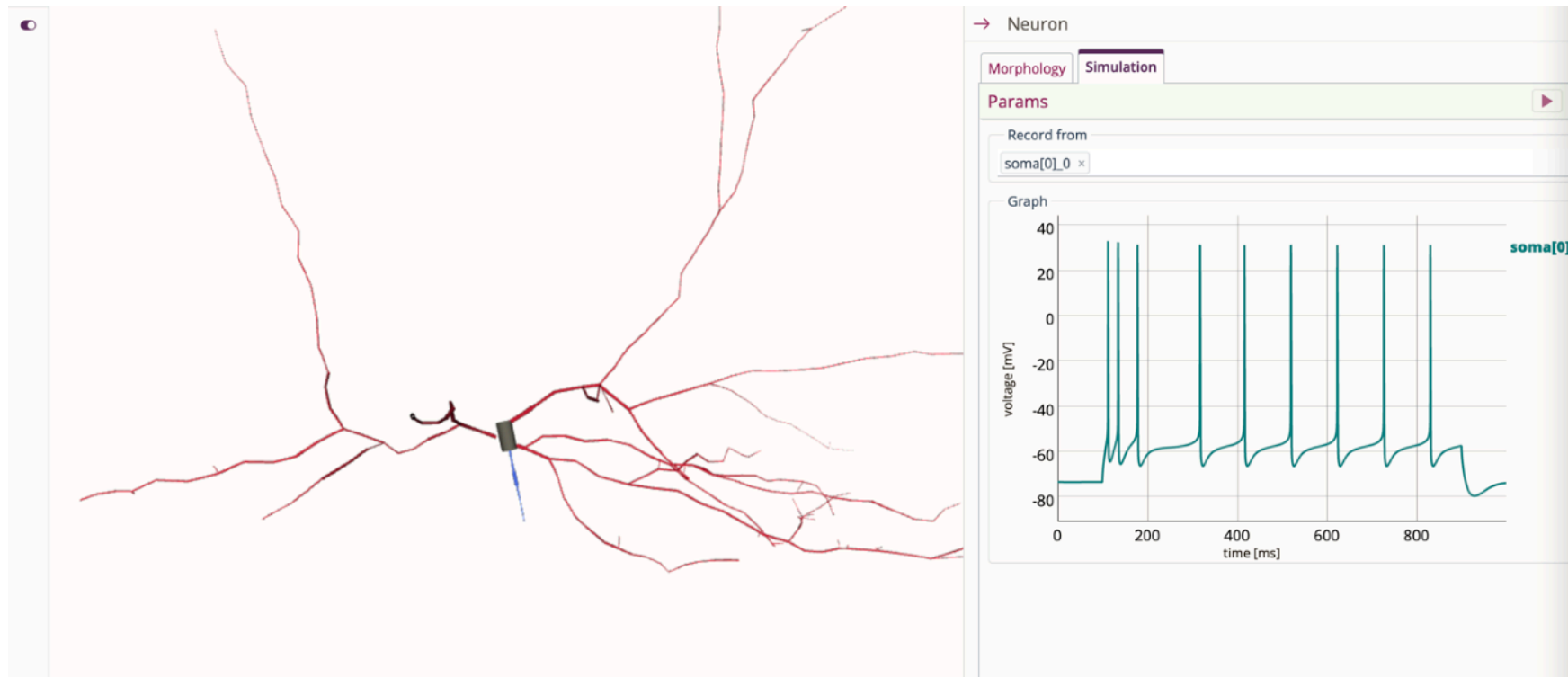
- Simulate diffusional association of proteins. Compute bimolecular association rate constants.
- <https://mcm.h-its.org/sda>
- <https://websda.h-its.org/>



NS

Single Cell In Silico Experiment Tool (BlueNaaS)

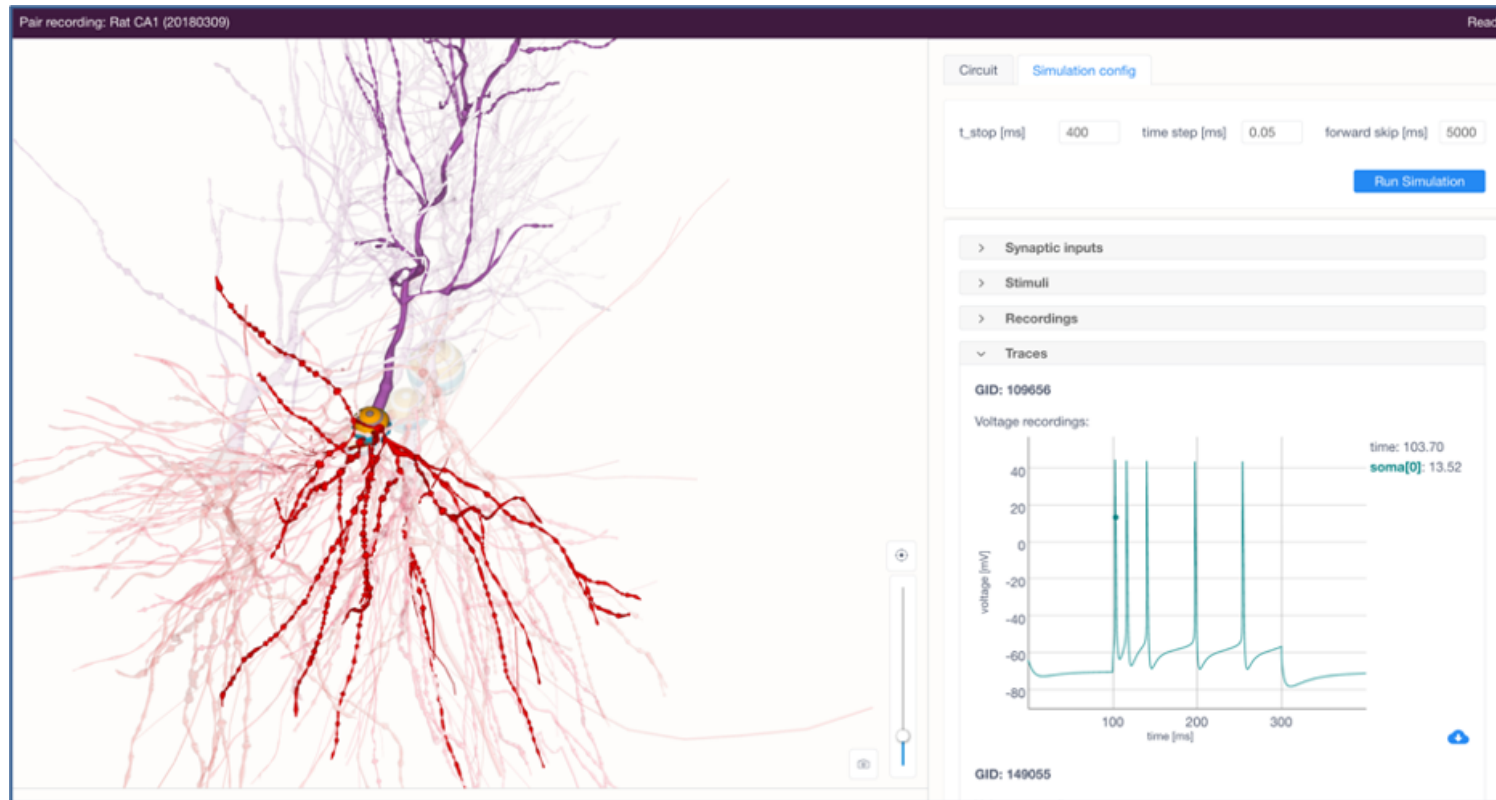
- Neuron as a Service: Simulate and visualize detailed single neuron models in the web browser.
- <https://blue-naas-bsp-epfl.apps.hbp.eu/#/>



BI

Small Circuit In Silico Experiment Tool

- Run simulation experiments with a small hippocampal neural circuit.
- <https://bsp-rat-ca1.humanbrainproject.eu/circuits/rat-ca1>



BI

Brain Areas Circuit In Silico Experiment Tool

- Run simulation experiments with a full-scale model of the hippocampus CA1 region.
- https://simulation-launcher-bsp-epfl.apps.hbp.eu/index.html#/circuits/hippo_hbp_sa_full_ca1

Run Simulation

Define Population to Simulate: BC
Subpopulation of neurons to be simulated (CircuitTarget)*

Duration: 300
Total duration of the simulation (ms)

Stimulations
Defines pattern of stimuli to be injected into multiple locations

0 ms	50 ms	100 ms	150 ms	200 ms	250 ms	300 ms	350 ms	400 ms
BC (Poisson)								

Reports
Controls data collection during the simulation

0 ms	50 ms	100 ms	150 ms	200 ms	250 ms	300 ms	350 ms	400 ms
BC (Voltage)								

Connection Manipulation (expert users only)
Controls the connection between populations

Projection Manipulation (expert users only)
Controls the projection in the circuit

Continue

NEST

- Run highly-scalable simulations of point neuron networks.
- <https://ebrains.eu/service/nest-simulator>

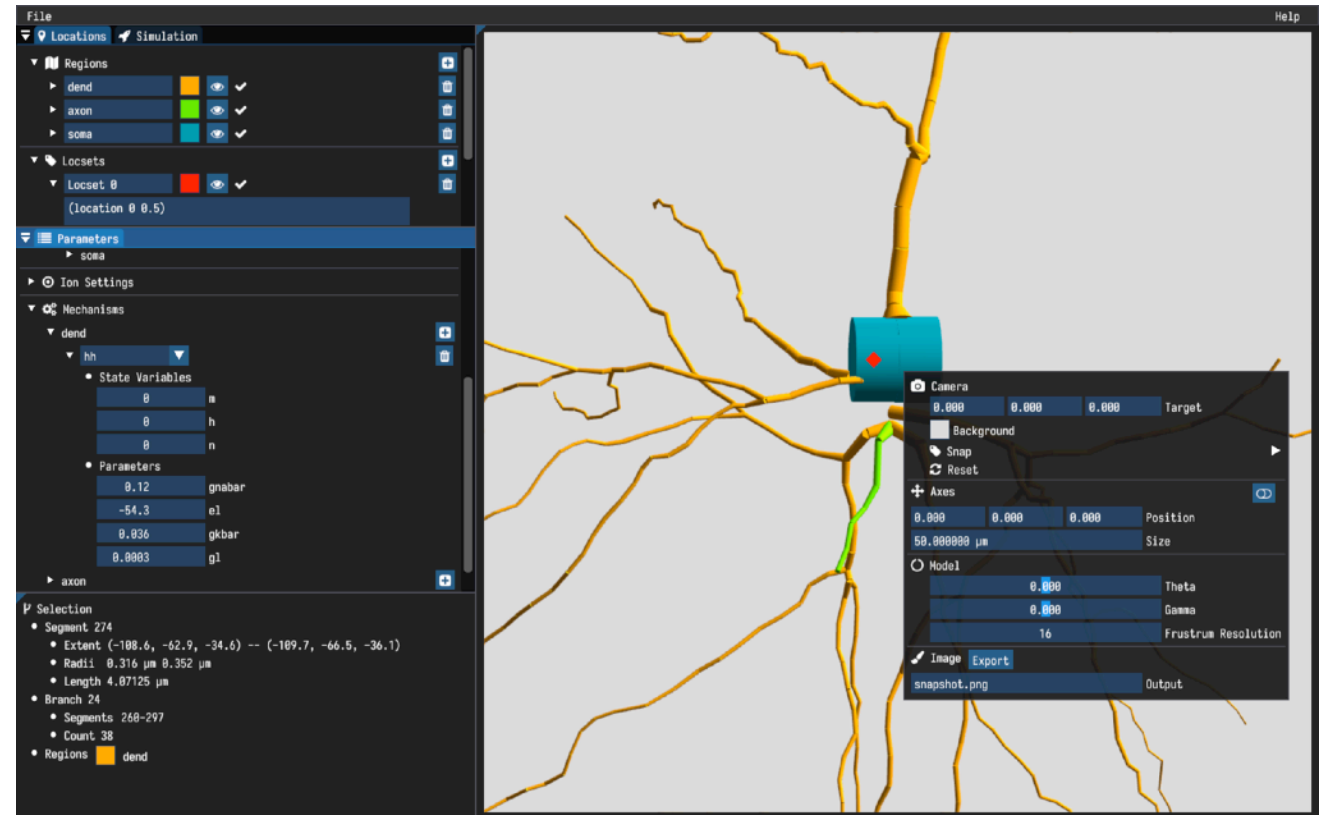


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Arbor

- Run scalable, high-performance simulations of multi-compartment neurons in large networks.
- <https://ebrains.eu/service/arbor>



BI

Neuromorphic Computing Job Manager app

- Run simulation experiments with point neuron networks on the BrainScaleS and SpiNNaker neuromorphic computing systems.
- <https://ebrains.eu/service/neuromorphic-computing>

The screenshot shows the EBRAINS Collaboratory JobManager interface. The top navigation bar includes links for Collabs, Documentation, Support, Forum, and a Log-in button. The main content area displays the JobManager page, which lists simulation jobs. A sidebar on the left shows the 'NMC Collab copy template' with links to 'About template', 'BrainScaleS', 'JobManager', and 'SpiNNaker'. The job list table has columns for ID, Status, System, Code, Submitted on, and Submitted by. Three jobs are listed, all with a 'finished' status.

ID	Status	System	Code	Submitted on	Submitted by
156732	finished	SpiNNaker	""" A population of integrate-and-firing neurons w...	2021/05/17 07:52:47	kindler
156589	finished	BrainScaleS	from neo.io import NeoMatlabIO import pynn_brainsc...	2021/05/12 11:18:42	kindler
156588	finished	BrainScaleS	from neo.io import NeoMatlabIO import pynn_brainsc...	2021/05/12 10:26:33	kindler

The 'Create Job' form includes fields for Hardware Platform (set to NM-PM1), Code (containing a Python script for a neuron simulation), Command, Hardware Config, and Input Files. There are 'Cancel' and 'Submit' buttons at the bottom.

Create Job

Hardware Platform
NM-PM1

Code

```
from pyNN.utility import get_script_args  
  
simulator_name = get_script_args(1)[0]  
exec("import pyNN.%s as sim" % simulator_name)  
  
sim.setup()  
  
neurons = sim.Population(1000, sim.IF_cond_exp, {'tau_m': 10.0})  
inputs = sim.Population(200, sim.SpikeSourcePoisson, {'rate': 100.0})  
neurons[100].record()
```

Command

Hardware Config

Input Files + -

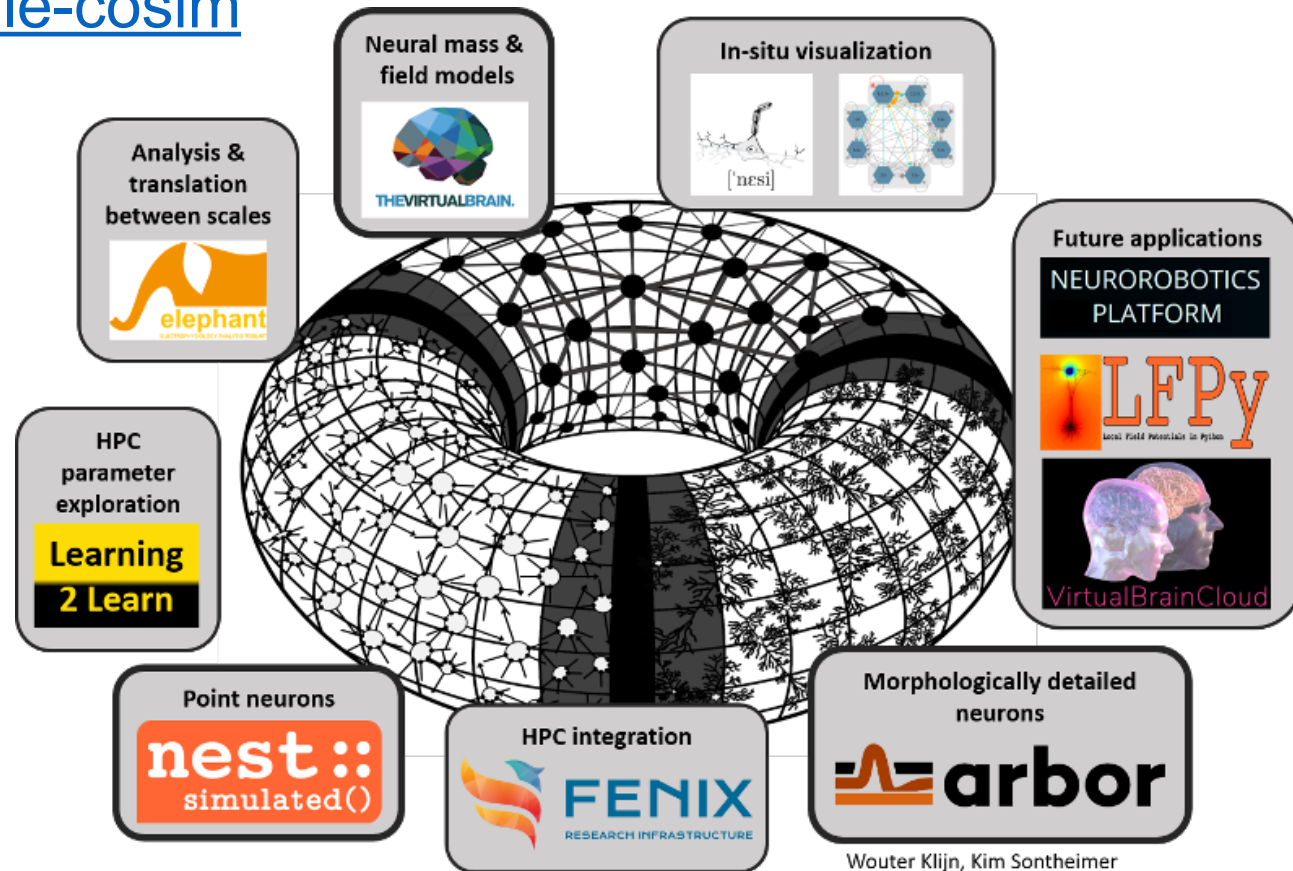
Cancel Submit



PT

Multiscale Co-Simulation Framework

- Connect simulation tools at runtime to enable multiscale co-simulations.
- <https://github.com/multiscale-cosim>



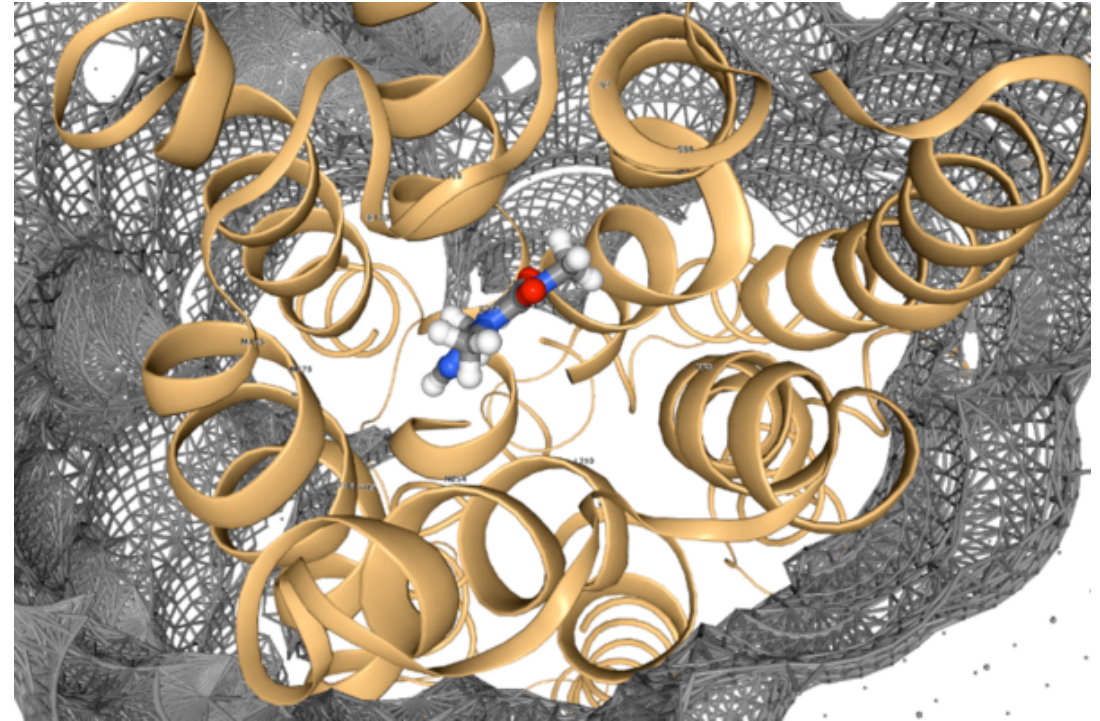
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MMCG Platform

- The Hybrid MM/CG Webserver automates and speeds up the hybrid Molecular-Mechanics/Coarse-Grained (MM/CG) simulations set-up of G-Protein coupled receptors/ligand complexes.
- <https://mmcg.grs.kfa-juelich.de/>

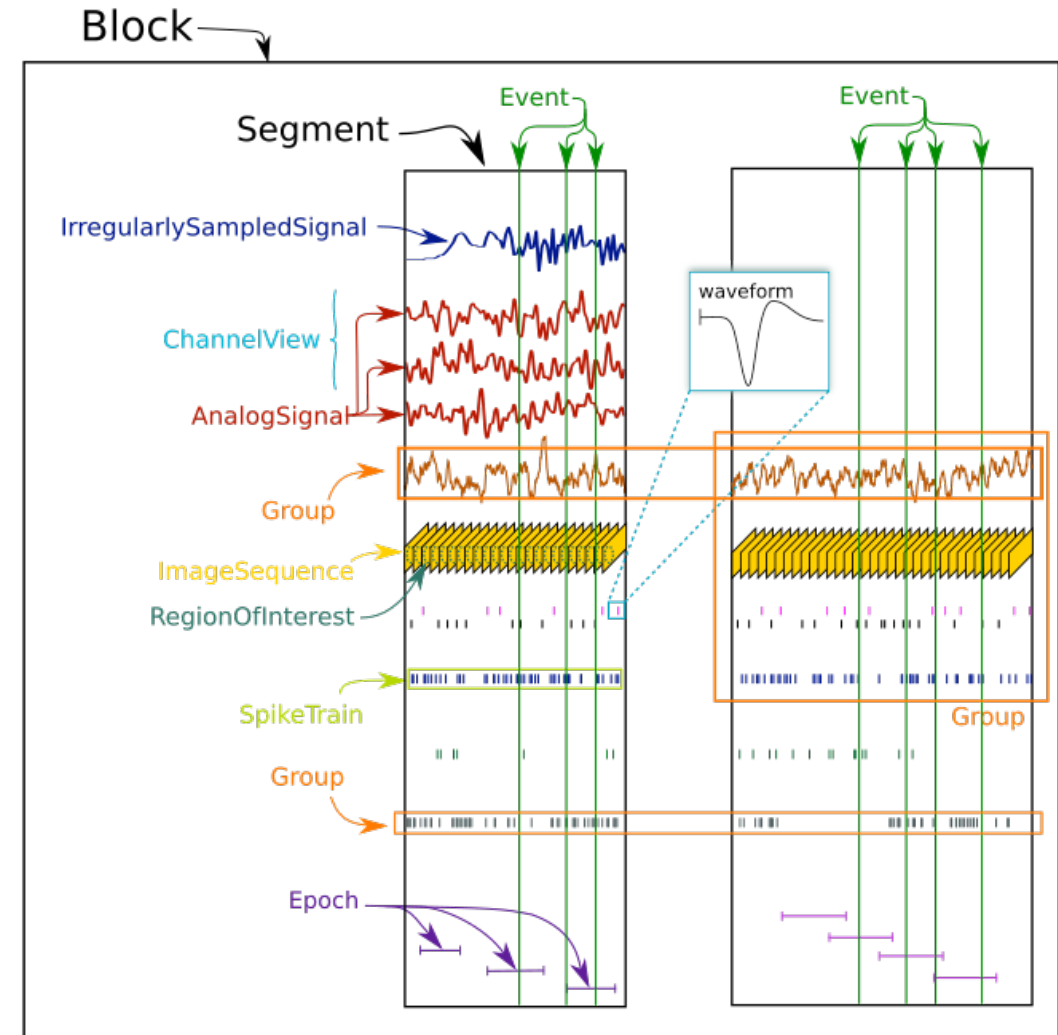


NS

Data Analysis

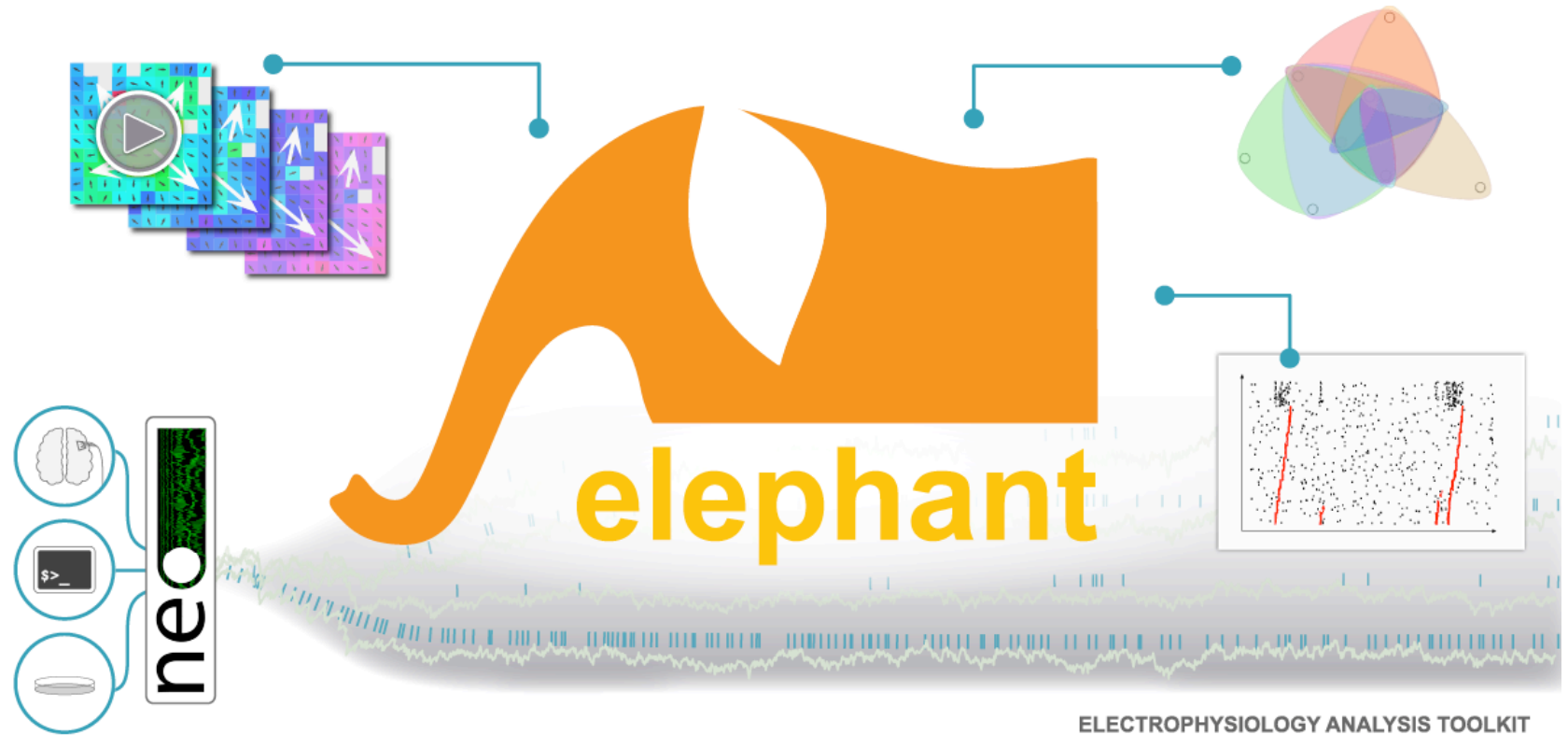
Neo

- Load, save, annotate and manipulate electrophysiology and imaging data from experiment and simulation in a standardised framework.
- <http://neuralensemble.org/neo/>



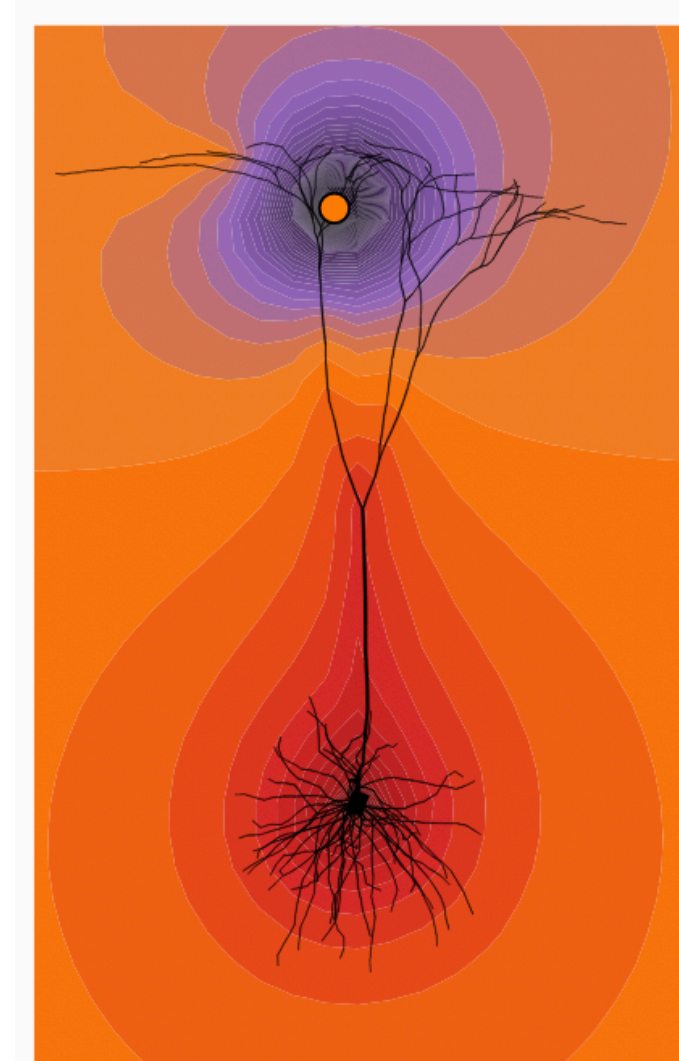
Elephant

- Analyse neuronal activity data from experiment and simulation using high-performance, well-tested methods.
- <https://ebrains.eu/service/elephant>



LFPy

- Calculate electric and magnetic brain signals from multi-compartment neuron models and networks.
- <https://lfp.py.readthedocs.io/>



BI

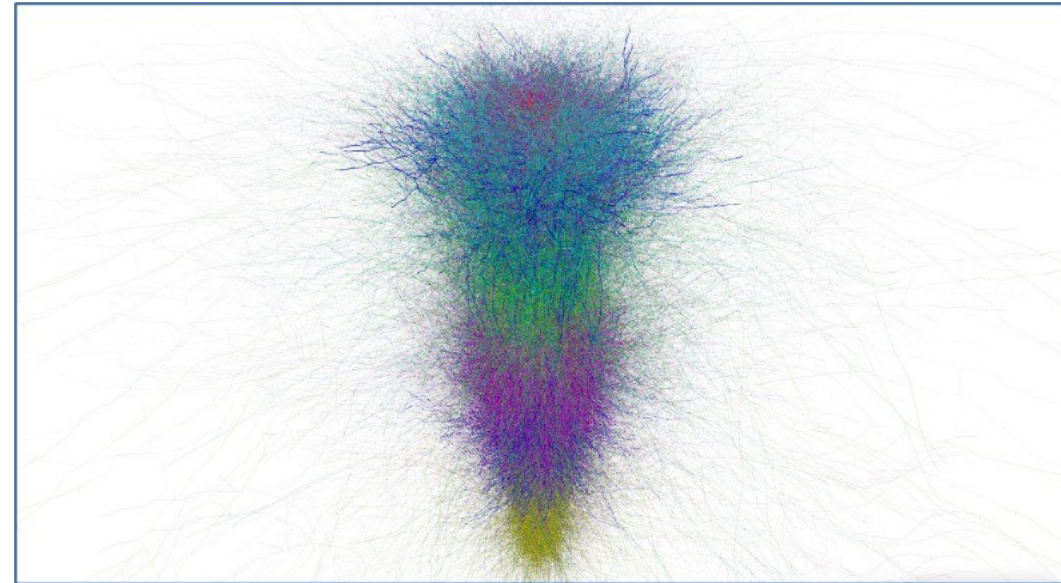
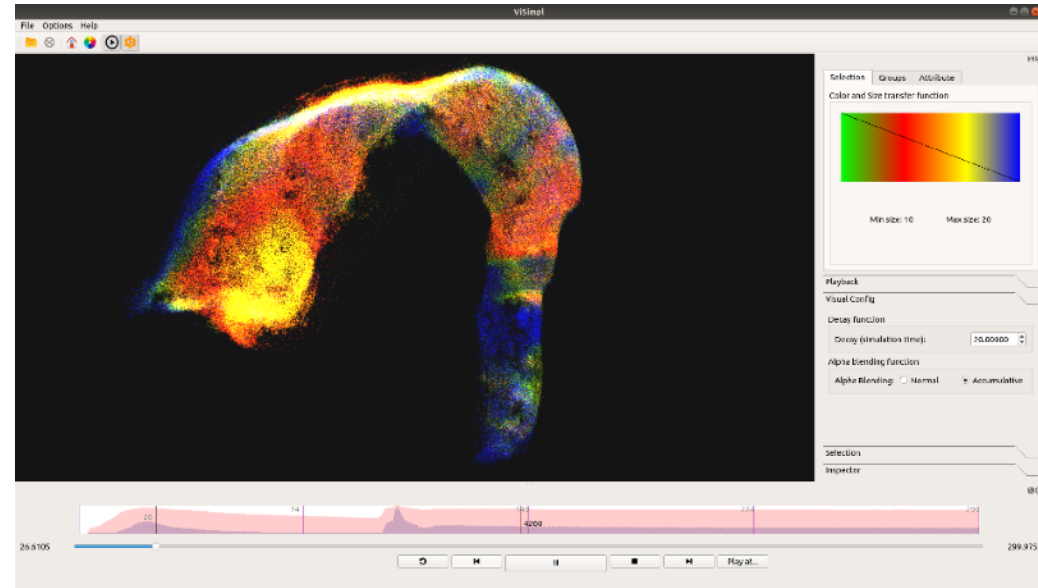
Visualisation



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SimVisSuite

- Interactively visualise and analyse network and neuron-level simulations.
- <https://ebrains.eu/service/neuroscheme>
- <https://ebrains.eu/service/neurotessmesh>
- <https://ebrains.eu/service/visimpl>

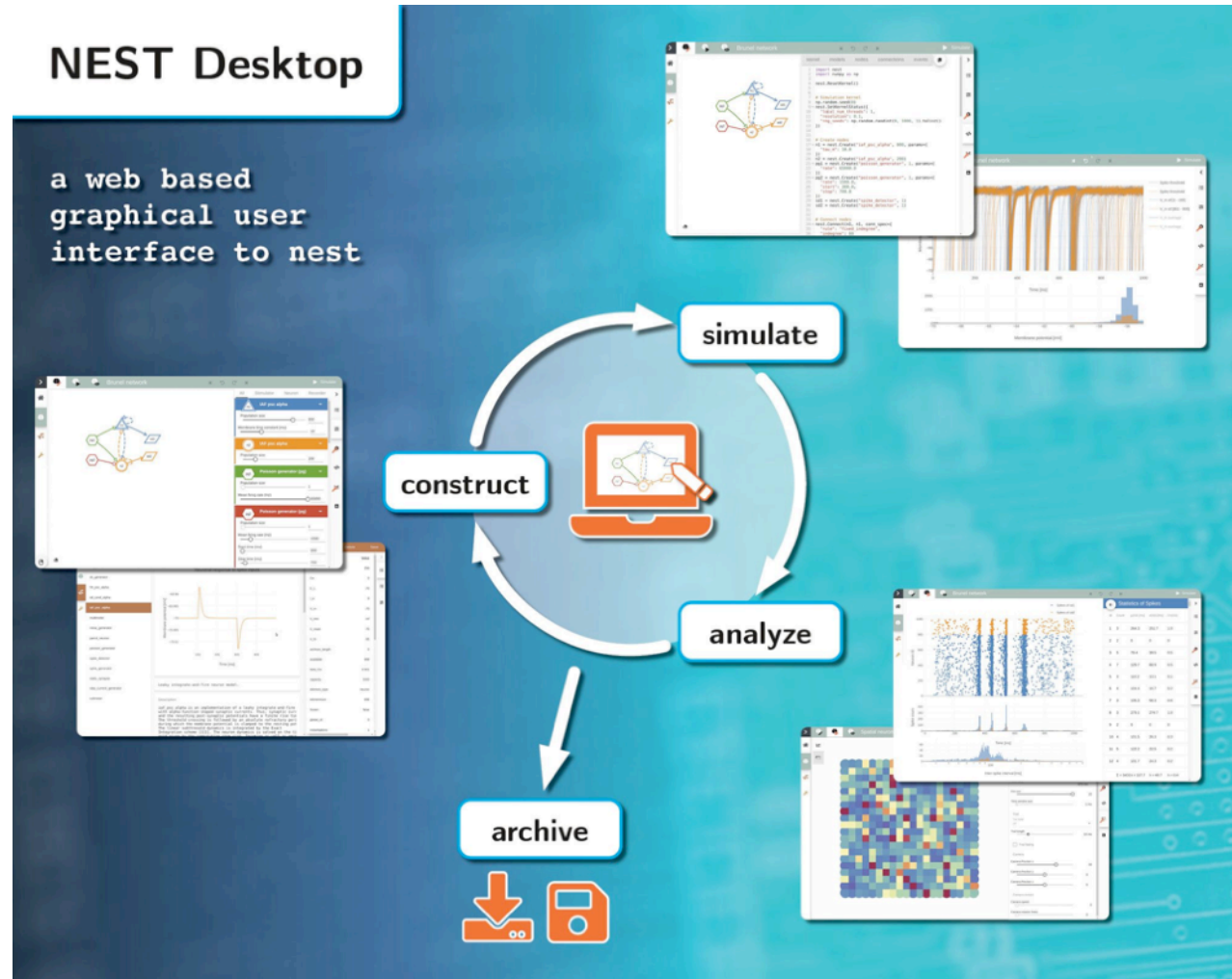


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BI

NEST Desktop

- Build, run, visualise and analyse simulations with the NEST simulator in a web-based GUI.
- <https://ebrains.eu/service/nest-desktop>



PT

SimDaVis - Insite

- Continuously access simulation data at runtime.
- <https://vrgroupwrth.github.io/insite>

The screenshot displays the Insite API documentation interface. On the left is a sidebar menu with categories: Insite, Installation via docker, Installation without docker, Integration into NEST simulation, NEST API, and Nest. Under the 'Nest' category, several endpoints are listed, including 'Get Node Collections' which is currently selected.

The main content area shows the details for the 'Get Node Collections' endpoint:

- Get Node Collections**
Retrieves an list of all node collections. Returned are the node collection IDs, which nodes are part of the collection and which model is used by the collection.
- Responses**
 - > 200 Operation successful.
 - > 500 Operation failed due to server error.

Below this, the 'Get Nodes In Node Collection' endpoint is shown:

- Get Nodes In Node Collection**
Retrieves the list of all nodes within the specified node collection.
- PATH PARAMETERS**
 - `nodeCollectionId` (required): integer <uint64> The identifier of the node collection

On the right, two panels show response samples for these endpoints:

- GET /nest/nodeCollections/**
Response sample (200):

```
{  - {    "nodeCollectionId": 0,    + "nodes": { - },    + "model": { - }  }}
```
- GET /nest/nodeCollections/{nodeCo**
Response sample (200):

```
{  - {    "nodeCollectionId": 0,    + "nodes": { - },    + "model": { - }  }}
```



PT

BI

Elephant Visualisation (Viziphant)

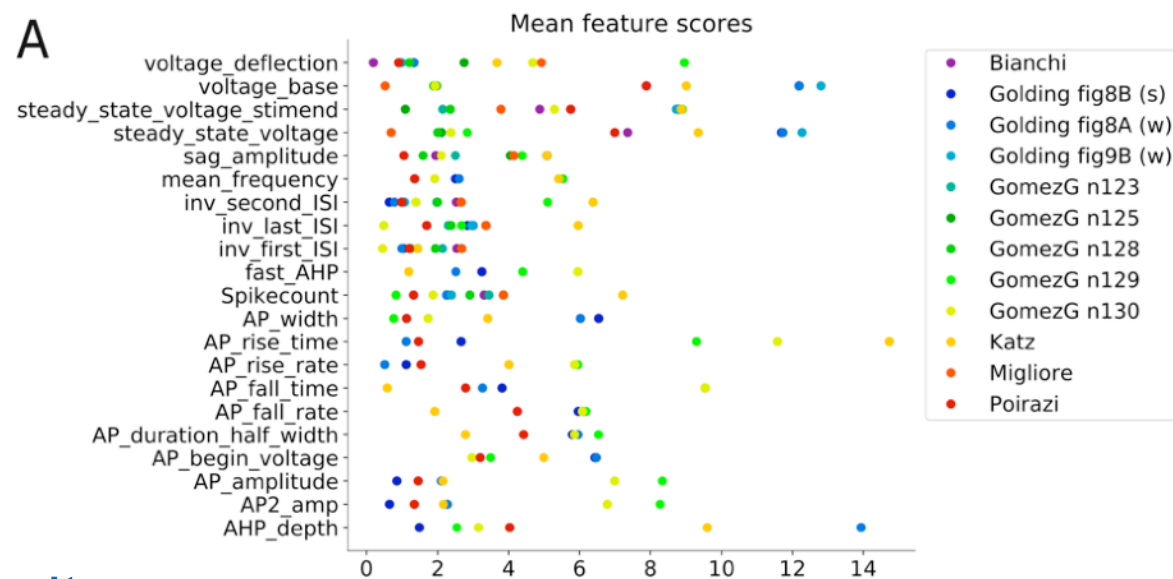
- Visualise analysis results in Jupyter notebooks.
- <https://viziphant.readthedocs.io/>



Validating Models Against Experiment Data

Validation Test Libraries

- Develop and run structured, quantitative model validation tests.
- NetworkUnit:
 - <https://github.com/INM-6/NetworkUnit>
- MorphoUnit:
 - <https://github.com/appukuttan-shailesh/morphounit>
- HippoUnit:
 - <https://github.com/KaliLab/hippounit>
- CerebUnit:
 - <https://cerebtests.readthedocs.io/>



Model Catalog

- Explore and visualise computational models, validation tests and validation results.
- <https://model-catalog.brainsimulation.eu/docs/>
- <https://validation-v2.brainsimulation.eu/docs>
- Python Client: <https://hbp-validation-client.readthedocs.io/>

Models			Tests		
<input type="checkbox"/> Name	Author	Brain region	<input type="checkbox"/> Name	Author	Brain region
<input type="checkbox"/> CA1_pyr_cACpyr_mpg141208_B_idA_20170915151855	Rosanna Migliore	hippocampus	<input type="checkbox"/> BluePyOpt-eFEL Evaluator	Shailesh Appukuttan	hippocampus
<input type="checkbox"/> CA1_int_cNAC_970911C_20180120154902	Rosanna Migliore	hippocampus	<input type="checkbox"/> CA1 laminar-distribution-synapses Neyman-Test	Pedro Garcia-Rodriguez	basal ganglia
<input type="checkbox"/> Surface potential models	Maria Telenczuk, Bartosz Telenczuk and Alain Destexhe	cerebral cortex	<input type="checkbox"/> PROPOSAL_Hippocampus_APPropagationAxonTest_BasketCell	Sara Saray	hippocampus
<input type="checkbox"/> CA1_pyr_cACpyr_mpg141208_B_idA_20190328144006	Rosanna Migliore	hippocampus	<input type="checkbox"/> Davison2000 Mitral - Run Time	Shailesh Appukuttan	
<input type="checkbox"/> Hippocampal formation as a hierarchical generative model	Giovanni Pezzulo	hippocampus	<input type="checkbox"/> Basal Ganglia MSN D2 Type Morphology Soft Constraints	Shailesh Appukuttan	striatum
<input type="checkbox"/> CA1_int_cNAC_060314AM2_20190328165336	Rosanna Migliore	hippocampus	<input type="checkbox"/> Hippocampus_SomaticFeaturesTest_CA1_pyr_cACpyr	Sara Saray	hippocampus
<input type="checkbox"/> CA1_pyr_cACpyr_mpg150305_A_idB_20190305112012	Rosanna Migliore	hippocampus	<input type="checkbox"/> HippoCircuit - Total Boutons	Armando Romani, Shailesh Appukuttan	hippocampus
<input type="checkbox"/> CA1_int_cAC_970627BHP1_20180120160112	Rosanna Migliore	hippocampus			
<input type="checkbox"/> CA1_pyr_cACpyr_oh140807_A0_idA_20190305112828	Rosanna Migliore	hippocampus			



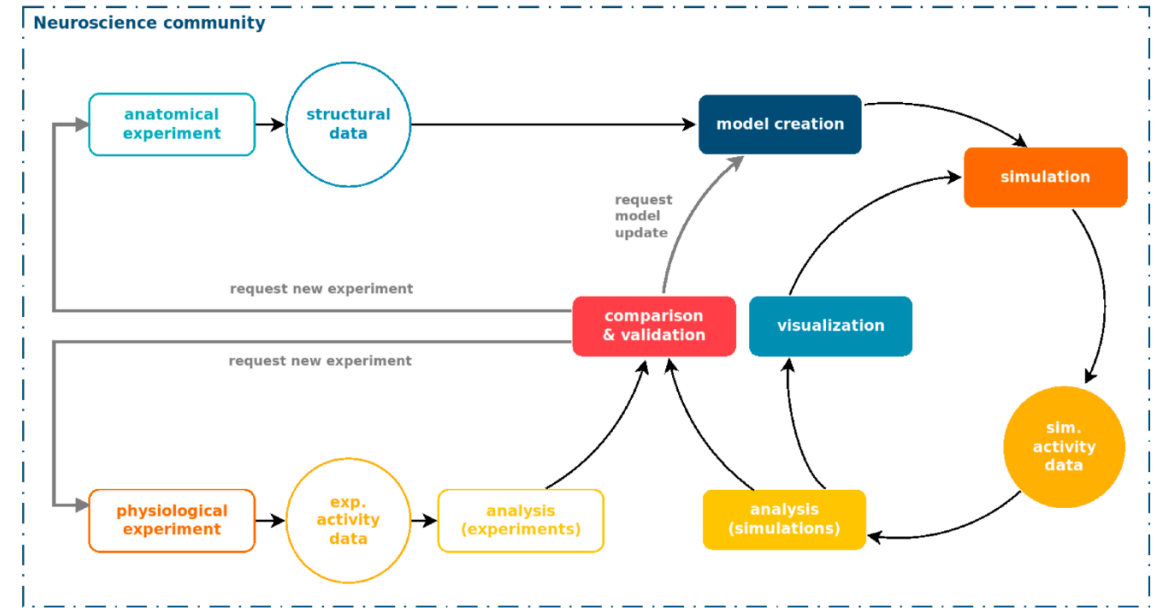
Integrated Workflows



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Computational workflows

- Most research projects use multiple computational tools and services, with data and metadata being passed between them.
- EBRAINS is developing a standardized workflow system based on the Common Workflow Language (CWL), that will allow automation of workflows running on local computers, HPC, and neuromorphic systems.
- Workflow outputs and provenance information can be captured in the Knowledge Graph and published as FAIR datasets.



Hands-on
Session

Summary

- EBRAINS offers many hardware and software resources for modelling and simulation
- From molecular to whole-brain scale (and bodies/environment - see next talk!)
- Focus on software quality, reproducibility
- Curated releases of EBRAINS software collection - every six months - interoperability testing
- Tools combined in automated workflows



Thank you

- The tools and services shown in this presentation have been developed by 100s of people, in many institutions. Please see the individual tool links for details.

www.humanbrainproject.eu

www.ebrains.eu



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