Standards and Tools in Neuroscience

A summary of the Open Source Brain workshop, September 2019

Ankur Sinha
Ph.D. candidate: UH Biocomputation Group, UK,
Volunteer: Fedora Project.

Journal club

2019-10-04

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The problem statement

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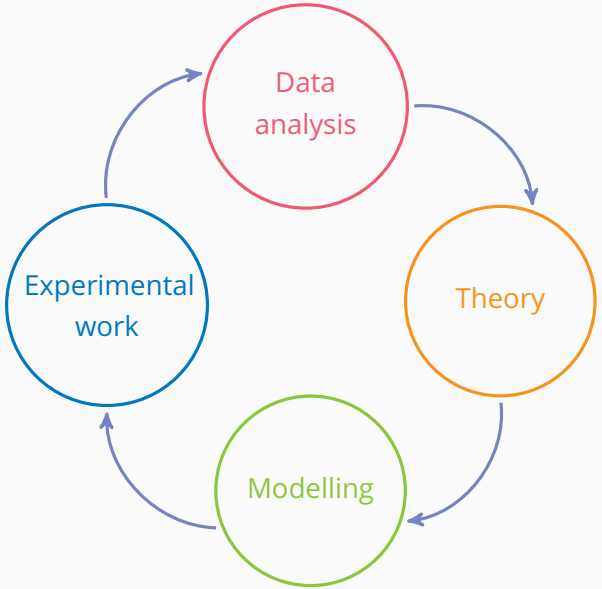
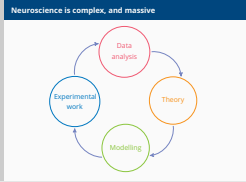
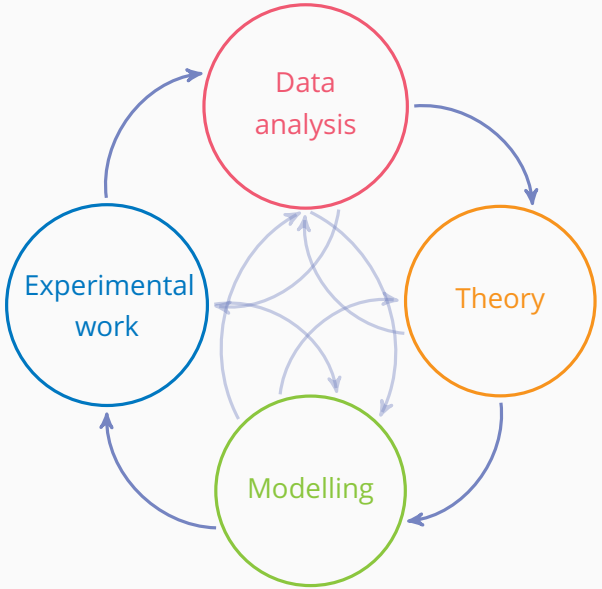
Neuroscience is complex, and massive

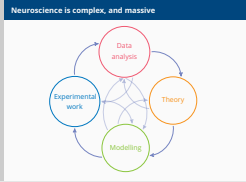




1. A simplified diagram. Actually a lot more complex
2. It is so massive that you can speak to another neuroscientist and not understand a word of what they say—we specialise
3. We won't even discuss dissemination to a non scientific audience today—a completely different problem.

Neuroscience is complex, and massive





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Free/Open Neuroscience

Free/Open science:
Scientific material should be easily, openly accessible to all.

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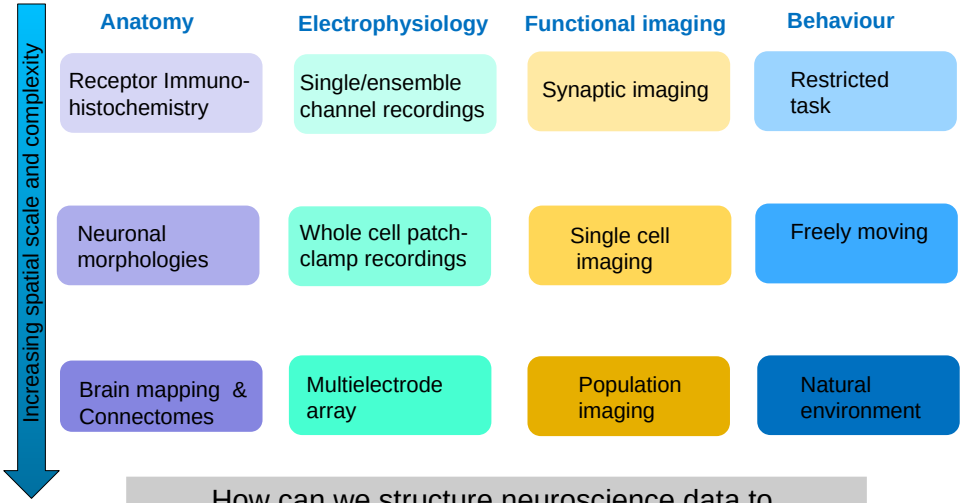
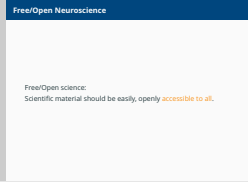
Experimental neuroscience data is heterogeneous, multiscale and analysis is complex



How can we structure neuroscience data to facilitate reuse?



Models of brain function span multiple spatial scales

Behaviour

Brain

Network

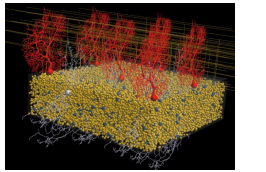
Neuron

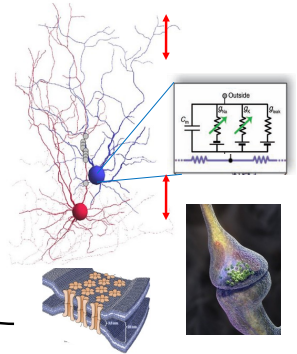
Synapse

Molecular assemblies

Genes

Biologically detailed multi-scale models of brain function.





Free/Open Neuroscience

Free/Open science:
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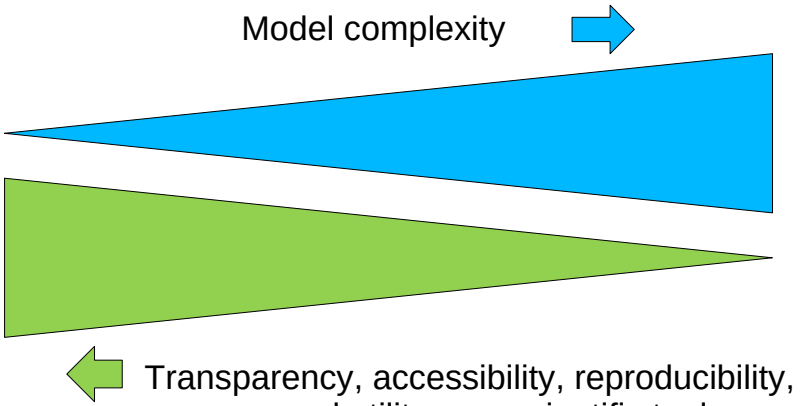
A scaling problem



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Standards: the common tongue

Standards: the common tongue

NWB:N 2.0: An Ecosystem for Neurophysiology Data Standardization

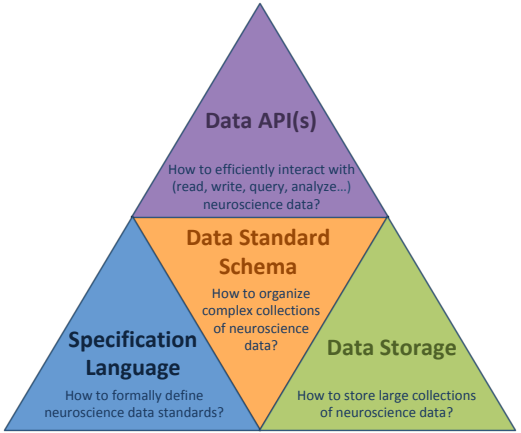
Oliver Rübel
Computational Research Division, Lawrence Berkeley National Laboratory

Open Source Brain Workshop
Alghero, Sardinia
September 10, 2019

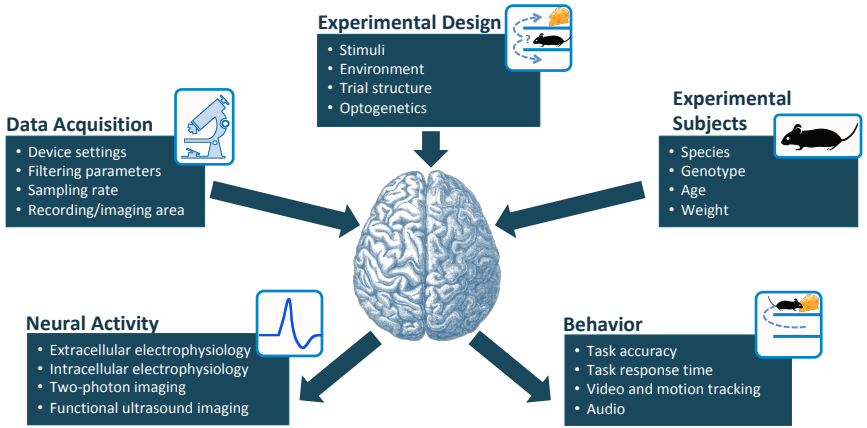
NEURODATA WITHOUT BORDERS

BERKELEY LAB
LAWRENCE BERKELEY NATIONAL LABORATORY

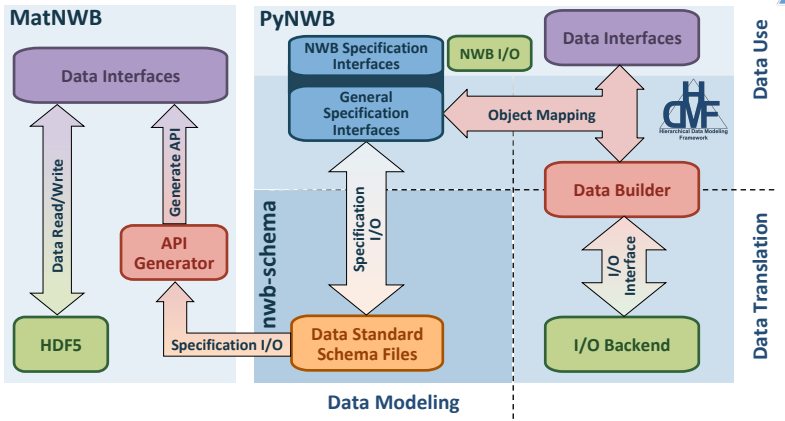
Main components of the NWB:N ecosystem



NWB:N supports complex collections of data required for understanding the brain

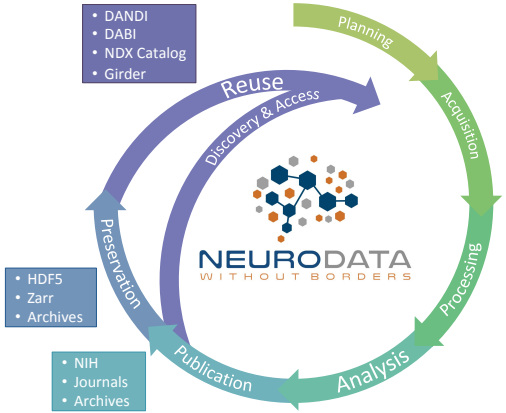


Advanced software architecture for data standardization



Neurophysiology Tools

NWB:N technologies at the heart of the neurodata lifecycle and applications



Electrophysiology	Optical Physiology
DataJoint, NWB Tutorials	
OpenEphys, Plexon, Neuralynx, Intan, TDT, SpikeGadgets, SpikeGLX	MiniScope ScanImage
PyNWB, MatNWB, HDMF, HDF5 tools/libs	
SpikeInterfaces MountainSort, KiloSort, npzsorting BrainStorm WaveClust, UltraMegaSort2000, KiloSort Kluster	NoRMCorre CNMF-E CELLMax EXTRACT
NWB-Explorer (OpenSourceBrain) NWB-JupyterWidgets	
BrainStorm, RAVE, Neo, SpikeWidgets, EcogVis, ephys-viz, …	CaImAn

NEURODATA WITHOUT BORDERS

BERKELEY LAB
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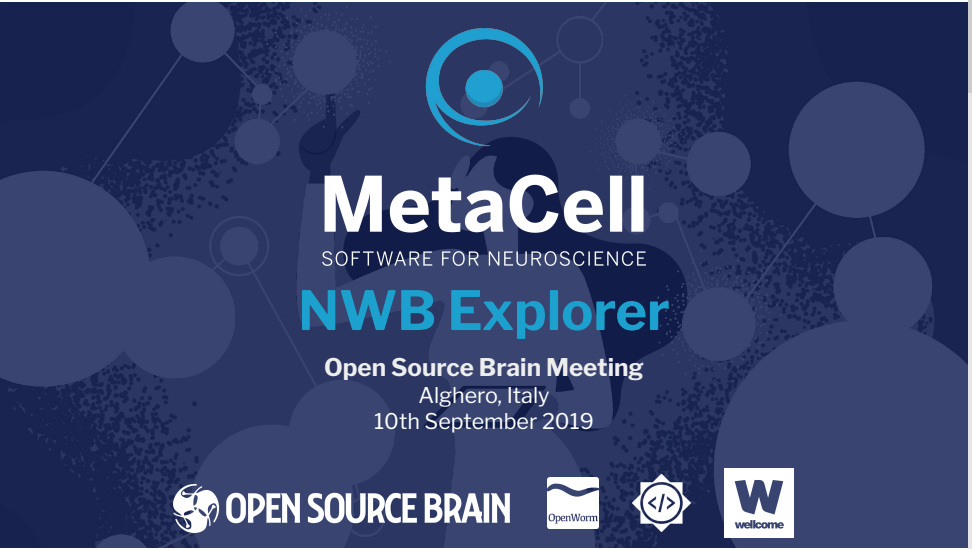
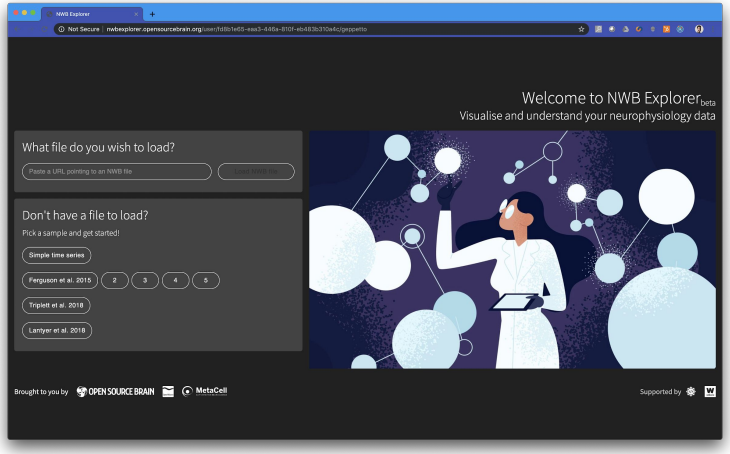

MetaCell
SOFTWARE FOR NEUROSCIENCE
NWB Explorer
Open Source Brain Meeting
Alghero, Italy
10th September 2019
OPEN SOURCE BRAIN
OpenWorm
wellcome



NWB EXPLORER

DEMO

Try it out at

https://nwbexplorer.opensourcebrain.org

Creating cortical models across scales in NeuroML

Padraig Gleeson
p.gleeson@ucl.ac.uk
University College London

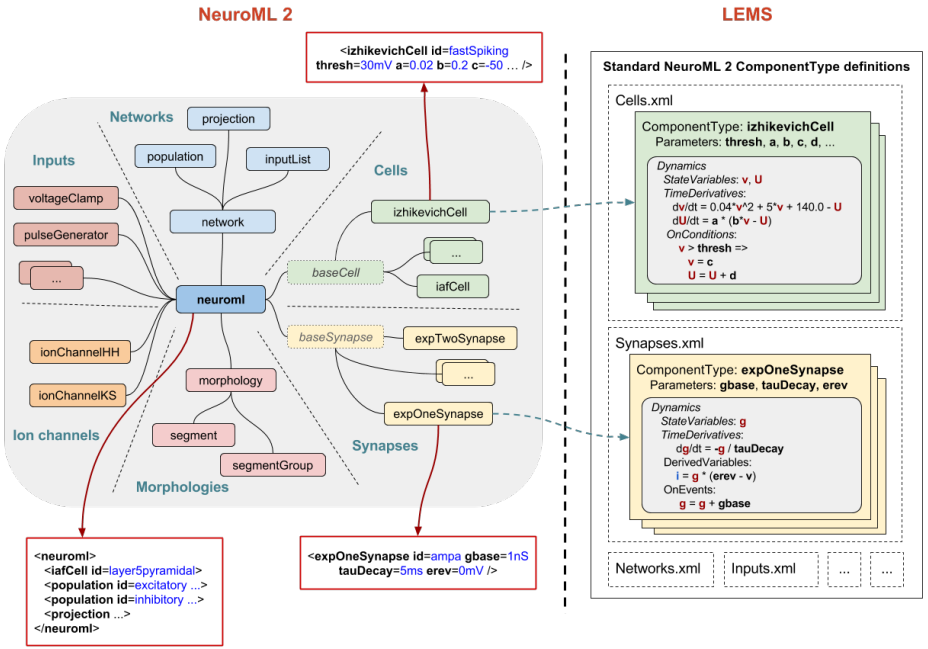
Open Source Brain workshop 2019

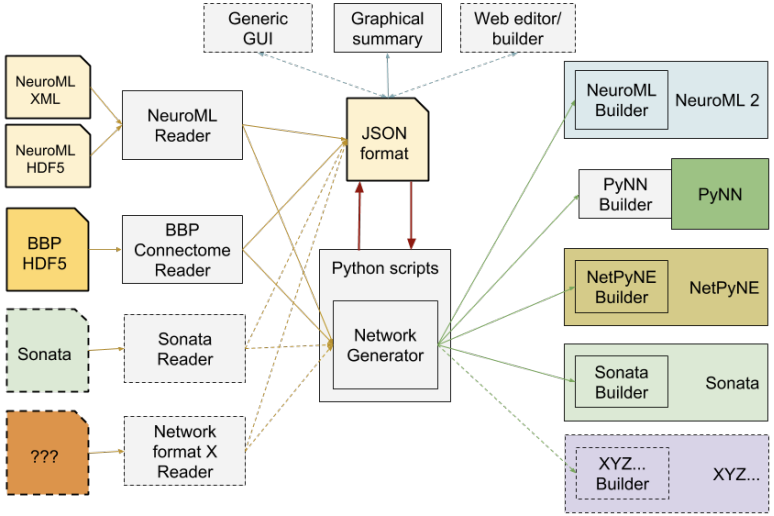
11th Sept 2019

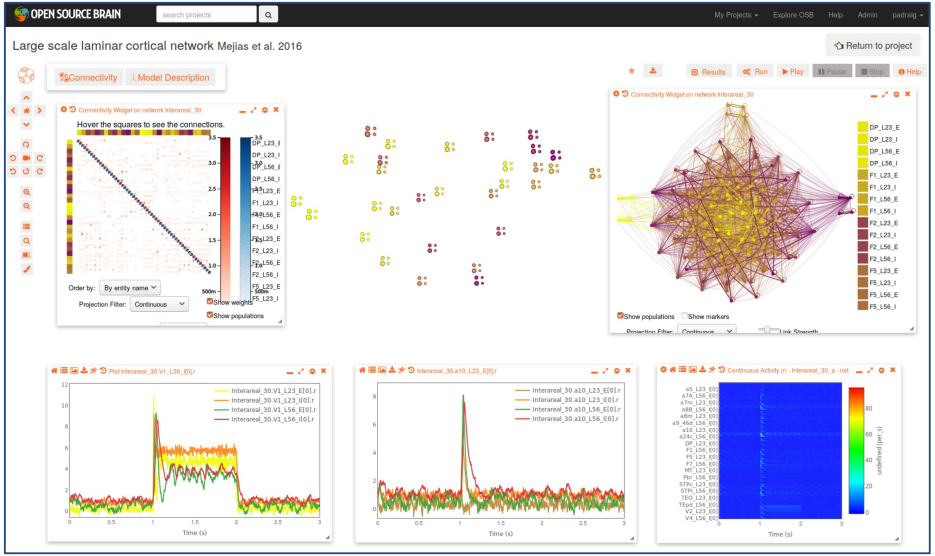
OPEN SOURCE BRAIN [NeuroML]

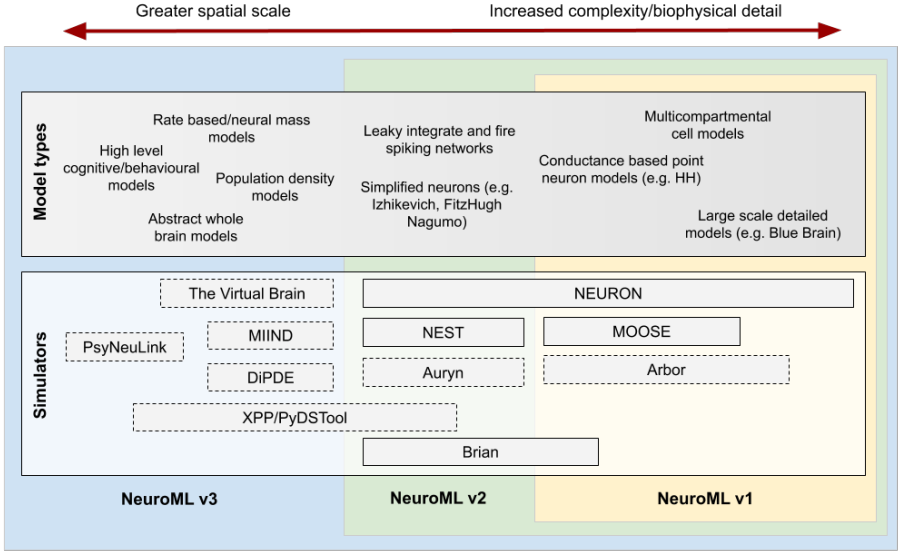
wellcome

Standards: the common tongue


NeuroML 2
LEMS
<izhikevichCell id=fastSpiking thresh=30mV a=0.02 b=0.2 c=-50 ... />
Networks
projection
Inputs
population
inputList
Cells
voltageClamp
network
izhikevichCell
pulseGenerator
baseCell
...
iafCell
neuroml
baseSynapse
expTwoSynapse
ionChannelHH
morphology
...
ionChannelKS
expOneSynapse
Ion channels
segment
Synapses
segmentGroup
Morphologies
<neuroml>
<iafCell id=layer5pyramidal>
<population id=excitatory ...>
<population id=inhibitory ...>
<projection ...>
</neuroml>
<expOneSynapse id=ampa gbase=1nS tauDecay=5ms erev=0mV />
Standard NeuroML 2 ComponentType definitions
Cells.xml
ComponentType: izhikevichCell
Parameters: thresh, a, b, c, d, ...
Dynamics
StateVariables: v, U
TimeDerivatives:
dv/dt = 0.04*v^2 + 5*v + 140.0 - U
dU/dt = a * (b*v - U)
OnConditions:
v > thresh =>
v = c
U = U + d
Synapses.xml
ComponentType: expOneSynapse
Parameters: gbase, tauDecay, erev
Dynamics
StateVariables: g
TimeDerivatives:
dg/dt = -g / tauDecay
DerivedVariables:
i = g * (erev - v)
OnEvents:
g = g + gbase
Networks.xml
Inputs.xml
...
...


Generic GUI
Graphical summary
Web editor/ builder
NeuroML XML
NeuroML HDF5
NeuroML Reader
JSON format
BBP HDF5
BBP Connectome Reader
Python scripts
Network Generator
Sonata
Sonata Reader
???
Network format X Reader
NeuroML Builder
NeuroML 2
PyNN Builder
PyNN
NetPyNE Builder
NetPyNE
Sonata Builder
Sonata
XYZ... Builder
XYZ...


OPEN SOURCE BRAIN
search projects
My Projects
Explore OSB
Help
Admin
padraig
Large scale laminar cortical network Mejias et al. 2016
Return to project
Connectivity
Model Description
Results
Run
Play
Pause
Stop
Help
Connectivity Widget on network Interareal_30
Hover the squares to see the connections.
Order by:
By entity name
Projection Filter:
Continuous
Show weights
Show populations
Show markers
Plot Interareal_30.V1_L56_E[0].r
Interareal_30.a10_L23_E[0].r
Continuous Activity (t) - Interareal_30_a - net
Time (s)



OPEN SOURCE BRAIN NeuroML

wellcome

INCF SIG on Standardised Representations of Network Structures

> This SIG deals with the various tools and formats for creating and sharing representations of biological neuronal networks, and will work towards ensuring these are as interoperable and usable as possible for computational neuroscientists.

Contact info: p.gleeson@uc.ac.uk

Members

Anton Arkhipov, Allen Institute, USA
Tom Close, Monash University, Australia
Sharon Crook, Arizona State University, USA
Kael Dai, Allen Institute, USA
Andrew Davison, UNIC, CNRS, France
Lia Domide, Codemart, Romania & Aix-Marseille Université, France
Salvador Durá-Bernal, SUNY Downstate Medical Center, USA
Viktor Jirsa, Aix-Marseille Université, France
Padraig Gleeson, University College London, UK

Converting simulator specific formats to NeuroML2

Open Source Brain Meeting 2019

Boris Marin

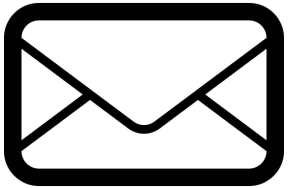
boris.marin@ufabc.edu.br

Universidade Federal do ABC

Standards: the common tongue

Converting NMODL to NeuroML

The Simple™, OSB sponsored way of converting models to NeuroML2



mailto:p.gleeson@ucl.ac.uk

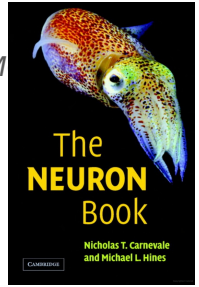
Standards: the common tongue

The *NEURON* simulator

Defining models in *NEURON*

https://www.neuron.yale.edu/neuron/

- Cells, Networks: *hoc* language (accessible from Python)
  - morphologies
  - synaptic connections
  - *.hoc* files
- Ion Channels (membrane mechanisms): *NM*
  - *.mod* files

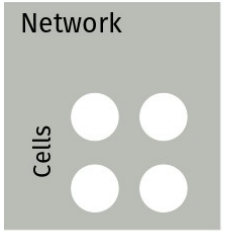


Standards: the common tongue

What is NeuroML, and why should I care?

Why can OSB process any NeuroML2 file?

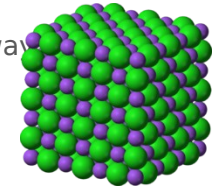
- NML is *structured* (not unlike a *Type System*)



It is all about **Structure**

Structure in NeuroML / NMODL

- A *Type System* (composability rules) is what grants NML its superpowers
- `nmodl` is also powerful, but can be used as a general purpose language
  - `VERBATIM` blocks
  - many different ways of achieving same goal
  - prone to *unstructuredness*
- OSB could in theory treat `nmodl` the same way as NML...
  - .... if only people stuck to "good practices"!



Standards: the common tongue

Levels of Abstraction

NeuroML2

```
<ionChannelHH id="kChan" conductance="10pS" species="k">

    <gateHHrates id="n" instances="4">
      <forwardRate type="HHExpLinearRate" rate="0.1per_ms" midpoint="-55mV" scale="10mV"/>
      <reverseRate type="HHExpRate" rate="0.125per_ms" midpoint="-65mV" scale="-80mV"/>
    </gateHHrates>

  </ionChannelHH>
```

NMODL

```
BREAKPOINT {
        SOLVE states METHOD cnexp
        gk = gkbar * n ^ 4
        ik = gk * (v-ek)
}
INITIAL{
        n = alpha(v) / (alpha(v) + beta(v))
}
DERIVATIVE states{
        n' = (1 - n) * alpha(v) - n * beta(v)
}
```

```
FUNCTION alpha(Vm(mV))(/ms){
        LOCAL x
        UNITSOFF
        x = (Vm + 55) / 10
        if(fabs(x) > 1e-6){
                alpha=0.1*x/(1-exp(-x))
        }else{
                alpha=0.1/(1-0.5*x)
        }
        UNITSON
}
```


Standards: the common tongue

Levels of Abstraction

Declarative vs Imperative

- NeuroML2 operates (at least syntactically) closer to the level of abstraction employed by electrophysiologists
- The gory details exist, but elsewhere: *LEMS*
  - i.e. what to do with α, β; the definition of an `ExpRate`; how all of that is converted to conductances/currents...
- But we seldom need (want!) to interact with that level (look under the hood)

```
<Network ...>
    <Cell ...>
        <Channel ...>
            <Gate ...>
                <Rate ...>
```

```
SOLVE{...} METHOD euler
...
DERIVATIVE {...}
...
FUNCTION trap(v){...}
```

Standards: the common tongue

Levels of Abstraction

NetPyNE: structured network specification

i)
```
popParams['EXC_L2'] = {
'cellType':   'PYR',
'cellModel':  'simple',
'yRange':     [100, 400],
'numCells':   50}
```

ii)
```
popParams['EXC_L5'] = {
'cellType':   'PYR',
'cellModel':  'complex',
'yRange':     [700, 1000],
'density':    80e3}
```

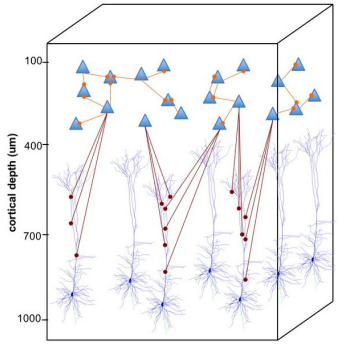
iii)
```
cellParams['PYR_simple'] = {
'conds': {'cellType': 'PYR',
          'cellModel': 'simple'},
'secs':  {'soma':
           'geom': {'diam': 18, 'L': 18},
           'mechs': {'hh':
                     {'gnabar': 0.12,
                      'gkbar': 0.036,
                      'gl':    0.003,
                      'el':    -70}}}}
```

iv)
```
importCellParams(
label =   'PYR_complex',
conds =   {'cellType':  'PYR',
           'cellModel': 'complex'},
fileName = 'L5_pyr_full.hoc',
cellName = 'PYR_L5')
```

vi)
```
synMechParams['AMPA'] = {
'mod':  'Exp2Syn',
'tau1':  0.8,
'tau2':  5.3,
'e':     0}
```

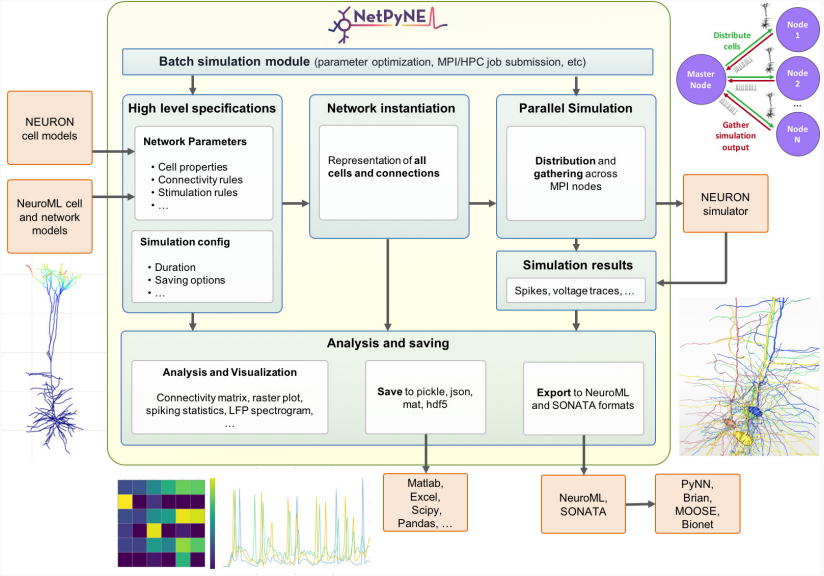
vii)
```
connParams['L2->E2'] = {
'preConds':    {'y':  [100, 400]},
'postConds':   {'pop': 'EXC_L2'},
'probability': '1*exp(-dist_3D/200)',
'weight':       0.4,
'delay':        5,
'synMech':      'AMPA'}
```

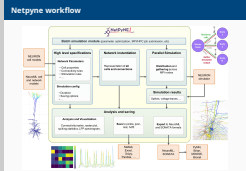
viii)
```
connParams['E2->L5'] = {
'preConds':    {'pop': 'EXC_L2'},
'postConds':   {'y':    [700,1100],
                'cellModel': 'complex'},
'convergence': 25,
'weight':      '0.001 * post_ynorm',
'delay':       'dist_3D/propVelocity',
'sec':         'allDend',
'synMech':     'AMPA',
'synsPerConn': 3}
```



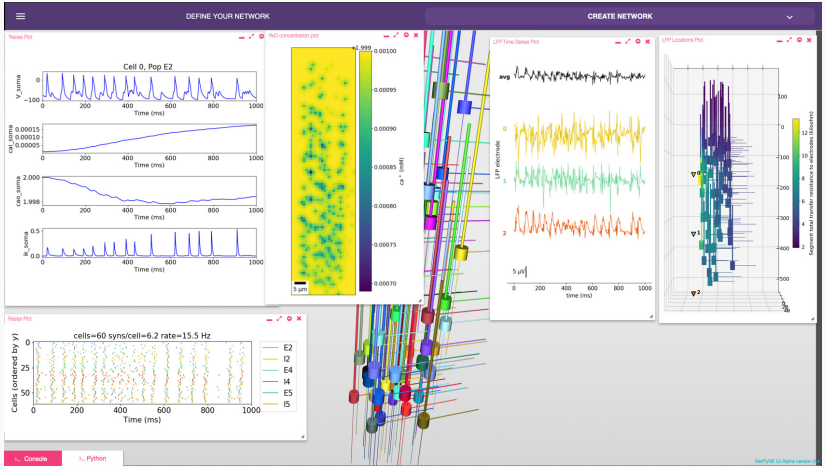
Dura-Bernal, Salvador, et al. "NetPyNE, a tool for data-driven multiscale modeling of brain circuits." Elife 8

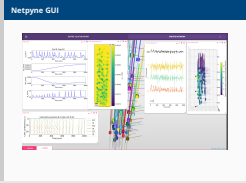
Netpyne workflow





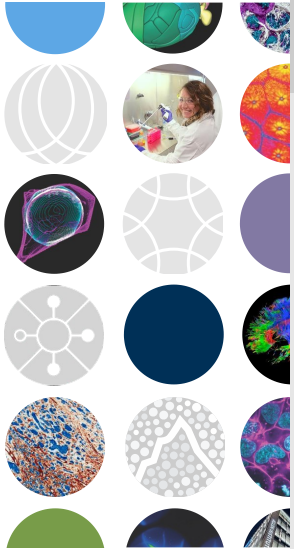
Netpyne GUI

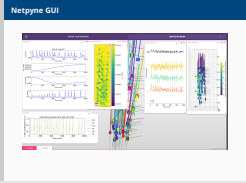

DEFINE YOUR NETWORK
CREATE NETWORK
Cell 0, Pop E2
V_soma
Time (ms)
cai_soma
cao_soma
ik_soma
Ca2+ concentration plot
LFP Time Series Plot
LFP Locations Plot
LFP electrode
Raster Plot
cells=60 syns/cell=6.2 rate=15.5 Hz
Cells (ordered by y)
E2
I2
E4
I4
E5
I5
Console
Python

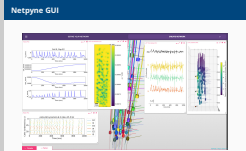

Netpyne GUI

Large-scale Datasets and Modeling Tools from the Allen Institute for Brain Science

Yazan N. Billeh
yazanb@alleninstitute.org

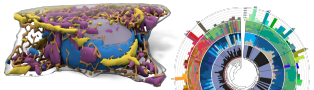






ALLEN INSTITUTE | ALLEN INSTITUTE for BRAIN SCIENCE | ALLEN INSTITUTE for CELL SCIENCE | ALLEN INSTITUTE for IMMUNOLOGY | THE PAUL G. ALLEN FRONTIERS GROUP

- Established 2003 by Paul G. Allen
- South Lake Union, Seattle, WA
- 500 employees++



hard problems
complexity
foundational biology

→

big science

team science

open science

→

data
knowledge
tools

CORE PRINCIPLES

Team Science

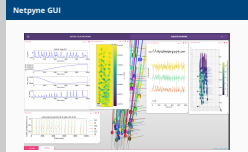
Interdisciplinary teams working towards common goal

Big Science

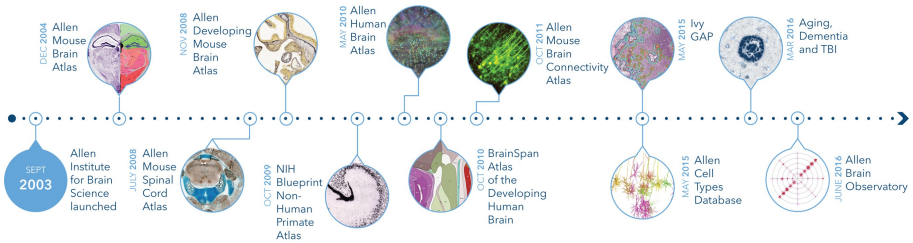
Large-scale projects with robust, massive data

Open Science

All resources available online at brain-map.org or allencell.org

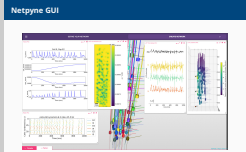


Allen Institute - Online Public Resources
www.brain-map.org



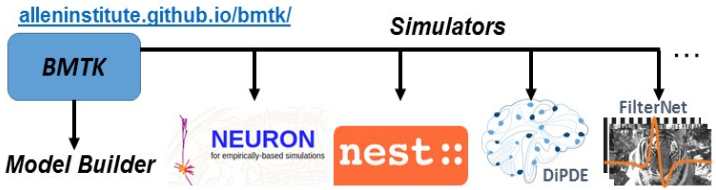
All data are:

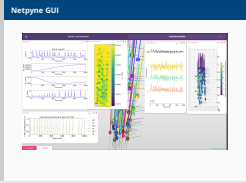
- publicly accessible via API as soon as they pass QC
- freely available without any commercial restrictions



Our Models and Modeling Software Are Freely Available to the Community

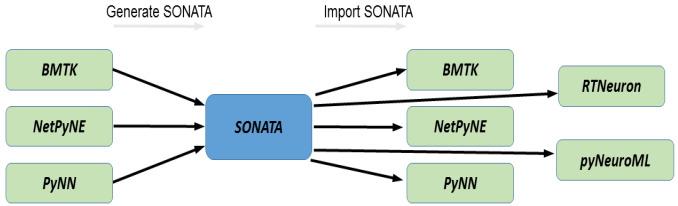
Brain Modeling ToolKit (BMTK): https://alleninstitute.github.io/bmtk/

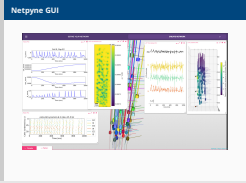




Our Models and Modeling Software Are Freely Available to the Community

Scalable Open Network Architecture TemplAte (SONATA):
https://github.com/AllenInstitute/sonata
An interface between SONATA and the NWB format has been developed as well





Human Brain Project

How model standardization enables new tools and applications in neuroscientific research

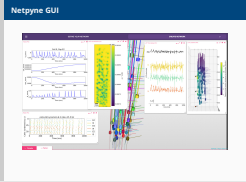
Insights from the HBP

Yann Zerlaut
Neuroinformatics team / group of A. Davison
Centre National de la Recherche Scientifique, France

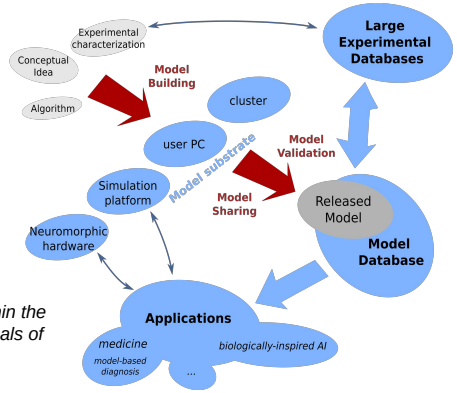
UNIC

cnrs

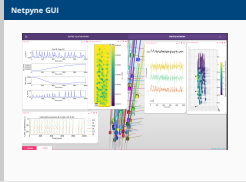
Open Source Brain Meeting 2019, Alghero

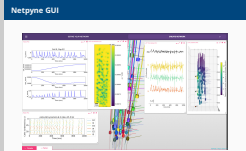


Motivation



Model production pipeline within the infrastructure and research goals of the Human Brain Project





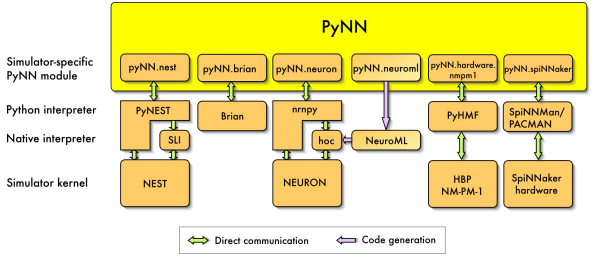
PyNN A unified interface for neuronal network simulators

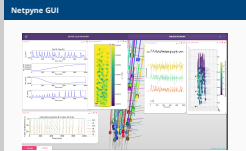
Simulator-independent environments for developing neuroscience models:

- keep the advantages of having multiple simulators or hardware devices
- but remove the translation barrier.

Three (complementary) approaches:

- GUI (e.g. neuroConstruct)
- XML-based language (e.g. NeuroML, NineML)
- interpreted language (e.g. Python)





Sonata (pyNN support)

Large-scale simulation of biophysically-detailed neuronal circuits
→ sets specific constraints

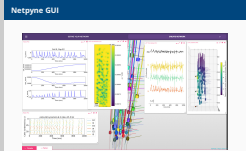
the SONATA Data Format emerges as the standard optimized for performance for simulation, analysis and visualization of large-scale circuits
(joint initiative of Blue Brain Project and the Allen Institute for Brain Science)

Export to Sonata format

```
from pyNN.network import Network
from pyNN.serialization import export_to_sonata

sim.setup()
...
# create populations, projections, etc.
...

# add populations and projections to a Network
net = Network(pop1, pop2, ...., prj1, prj2, ...)

export_to_sonata(net, "sonata_output_dir")
```

Import from Sonata format

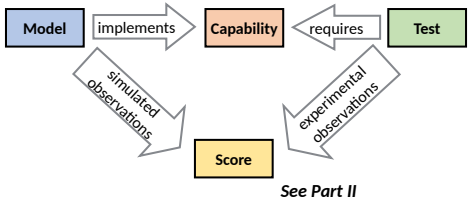
```
from pyNN.serialization import import_from_sonata, load_sonata_simulation_plan
import pyNN.neuron as sim

simulation_plan = load_sonata_simulation_plan("simulation_config.json")
simulation_plan.setup(sim)
net = import_from_sonata("circuit_config.json", sim)
simulation_plan.execute(net)
```



SciUnit

https://github.com/scidash/sciunit

Include a validation framework in model development



See Part II

✓ **What is SciUnit?**

*A **Test**-driven framework for formally validating scientific models against data.*

*It employs the concept of **Capabilities**.*

✓ **What are Tests?**

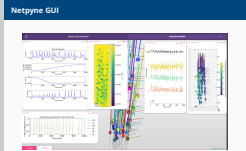
A procedure intended to establish the quality, performance, or reliability of a model

✓ **What are Capabilities?**

- *interfaces through which the model and the validation framework communicate*
- *implemented as methods (functions) within the model*

Requires the participation of modellers:

- ✓ support to wrap your models for SciUnit
- ✓ add/request new tests to the library
- ✓ critique existing tests
- ✓ suggest new features



Test Packages

The overall test suite has been divided into a number of components, some containing validation tests specific to particular brain regions, others more generic. All validation tests are written in Python, using the SciUnit framework. Some of these are listed below:

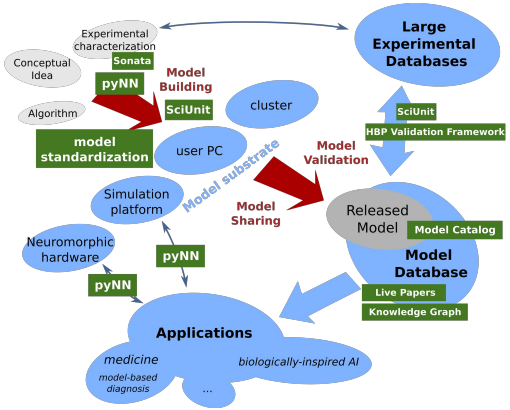
Test suites for specific brain regions

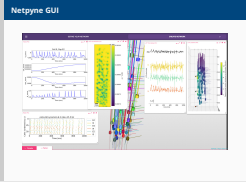
- ***HippoUnit***: `https://github.com/KaliLab/hippounit`
- ***HippoNetworkUnit***: `https://github.com/pedroernesto/HippoNetworkUnit`
- ***CerebUnit***: `https://github.com/lungsi/cerebellum-unit`
- ***BasalUnit***: `https://github.com/appukuttan-shailesh/basalunit`

Test suites for model features, independent of cell type or brain region

- ***MorphoUnit***: `https://github.com/appukuttan-shailesh/morphounit`
- ***NetworkUnit***: `https://github.com/mvonpapen/simrest_validation`
- ***eFELUnit***: `https://github.com/appukuttan-shailesh/eFELunit`

Summary

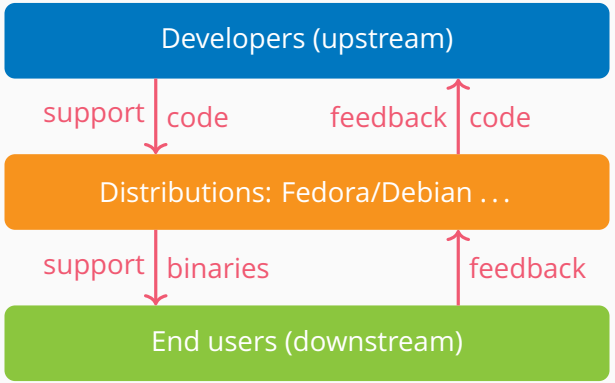

Experimental characterization
Sonata
Conceptual Idea
pyNN
Model Building
SciUnit
Algorithm
model standardization
user PC
cluster
Large Experimental Databases
SciUnit
HBP Validation Framework
Model Validation
Model substrate
Simulation platform
Model Sharing
Released Model
Model Catalog
Model Database
Live Papers
Knowledge Graph
Neuromorphic hardware
pyNN
pyNN
Applications
medicine
model-based diagnosis
...
biologically-inspired AI

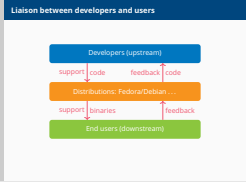

Netpyne GUI

NeuroFedora: marketing pitch

NeuroFedora: marketing pitch

Liaison between developers and users





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Blog: neuroblog.fedoraproject.org
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