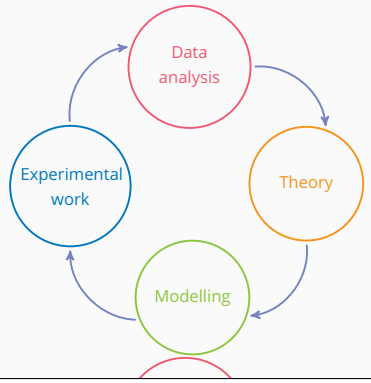
Standards and Tools in Neuroscience

A summary of the Open Source Brain workshop, September 2019

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

The problem statement

Neuroscience is complex, and massive



Free/Open Neuroscience

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

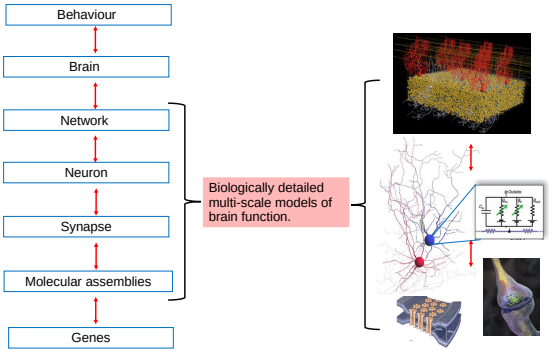
Experimental neuroscience data is heterogeneous, multiscale and analysis is complex

Increasing spatial scale and complexity

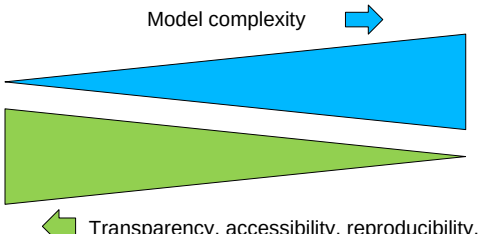
Anatomy	Electrophysiology	Functional imaging	Behaviour
Receptor Immuno-histochemistry	Single/ensemble channel recordings	Synaptic imaging	Restricted task
Neuronal morphologies	Whole cell patch-clamp recordings	Single cell imaging	Freely moving
Brain mapping & Connectomes	Multielectrode array	Population imaging	Natural environment

How can we structure neuroscience data to facilitate reuse?

Models of brain function span multiple spatial scales



A scaling problem



Transparency, accessibility, reproducibility, reuse…..and utility as a scientific tool

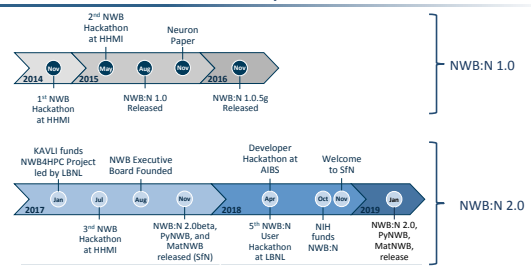
Standards: the common tongue

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

A brief history of NWB:N



Overview

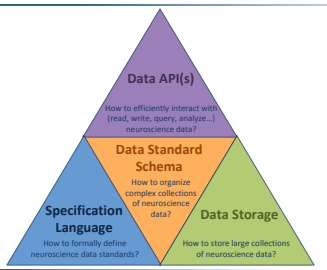
Motivation: Lack of standards for neurophysiology data and related metadata is the single greatest impediment to fully extracting return-on-investment from neurophysiology experiments, impeding interchange and reuse of data and reproduction of derived conclusions

NWB:N – An Ecosystem for Neuroscience Data Standardization

- The NWB:N data standard defines a unified data format for neurophysiology data, focused on the dynamics of groups of neurons measured under a large range of experimental conditions
- NWB:N is more than just a file format but it defines an ecosystem of tools, methods, and standards for storing, sharing, and analyzing complex neurophysiology data

Goal: With NWB:N we aim to develop a next generation data format and software ecosystem that will enable standardization, sharing, and reuse of neurophysiology data and analyses, enhancing discovery and reproducibility

Main components of the NWB:N ecosystem



Specification language

Goal: Enable the formal definition and programmatic interpretation of neuroscience data standards

Format specification language: Schema for defining hierarchical data schemas

Main primitives of the specification language:

- **Object primitives:**
  - **Group:** A group is a collection of objects i.e. subgroups, datasets, links
  - **Dataset:** n-dimensional array with associated data type, dimensions, etc.
  - **Attribute:** small metadata dataset defined on a Group or Dataset
  - **Link:** Like a POSIX soft link to given target neurodata_type (specifying a Group or Dataset)
- **Data type specifications**
  - **Basic data types:** strings (ascii, utf8), numeric types (float, int, uint, bool etc.) etc.
  - **Compound data types:** build complex data type, similar to structs
  - **Isodatetime:** ISO8061 datetime string, e.g. 2018-09-28T14:43:54.123+02:00
  - **Object reference:** Like a link to given neurodata_type but stored as values of a dataset (or attribute)
  - **Region reference:** Links to regions (i.e., select subsets) of datasets stored as as values of a dataset (or attribute)
- **Namespace specification:**
  - Used to define a namespace for format specifications
  - Needed to define and avoid collisions between extensions and to enable the creation of new data standards

Data storage

Primary function: Map NWB:N primitives (Groups, Datasets, Attributes etc.) to storage

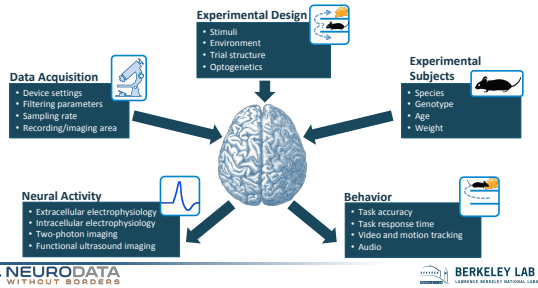
NWB:N uses HDF5 as its main file storage backend:

- Supports large-scale storage of complex data collections in a single file
- Optimized for performance (parallel I/O, advanced I/O filters etc.)
- Supported across platforms and programming languages (Matlab, Python, C/C++, Fortran, R…)
- Targets long-term support

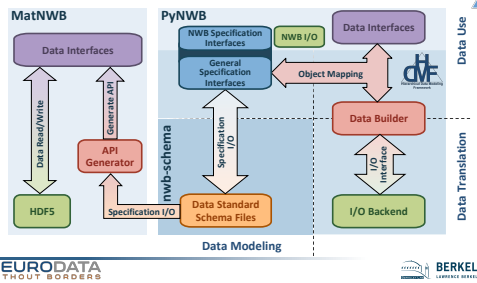
NWB:N supports advanced I/O features:

- Lazy data load → Fast file open and efficient memory usage even for very large files
- Chunking → Optimize data layout, storage, and I/O
- I/O filter → E.g, use compression to reduce storage cost
- Self-contained data storage → Store all data in a single file (e.g. for sharing)
- Modular data storage → Store data across multiple files and integrated via external links
- Iterative data write → Support data streaming, reduce memory usage, and optimize I/O

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

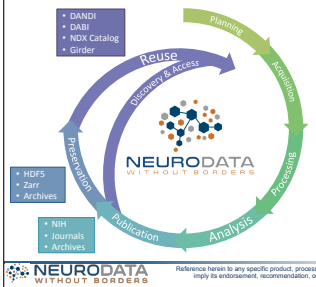


Advanced software architecture for data standardization



Neurophysiology Tools

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



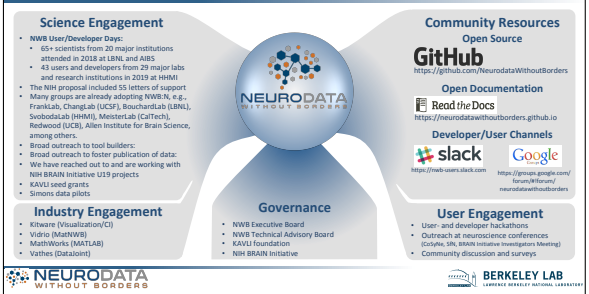
Electrophysiology	Optical Physiology
DataJoint, NWB Tutorials	
OpenEphys, Plexon, Neuralynx, Intan, TDT, SpikeGadgets, SpikeGLX	MiniScope ScanImage
PyNWB, MatNWB, HDMF, HDF5 tools/libs	
SpikeInterfaces MountainSort, KiloSort, npsorting BrainStorm WaveClust, UltraMegaSort2000, KiloSort Kluster	NoRMCorre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

NEURODATA WITHOUT BORDERS

Reference herein to any specific product, process, or service does not constitute or imply its endorsement, recommendation, or favoring by NWB or LBNL.

BERKELEY LAB

Community engagement and outreach



NEURODATA WITHOUT BORDERS

BERKELEY LAB

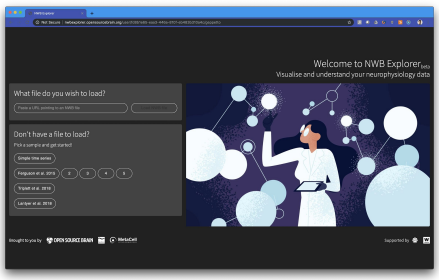
MetaCell

SOFTWARE FOR NEUROSCIENCE

NWB Explorer

Open Source Brain Meeting
Alghero, Italy
10th September 2019

OPEN SOURCE BRAIN



NWB EXPLORER

DEMO

Try it out at

https://nwbexplorer.opensourcebrain.org

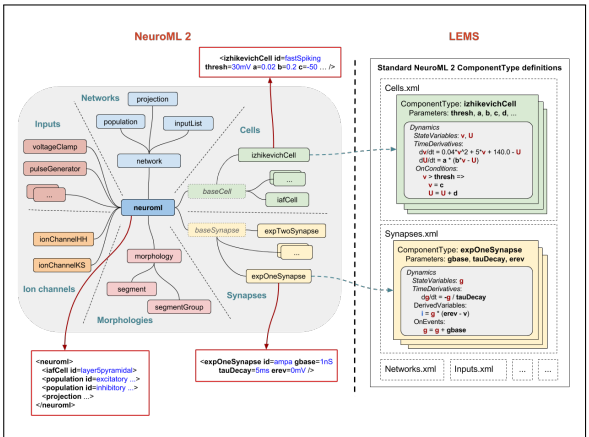
Creating cortical models across scales in NeuroML

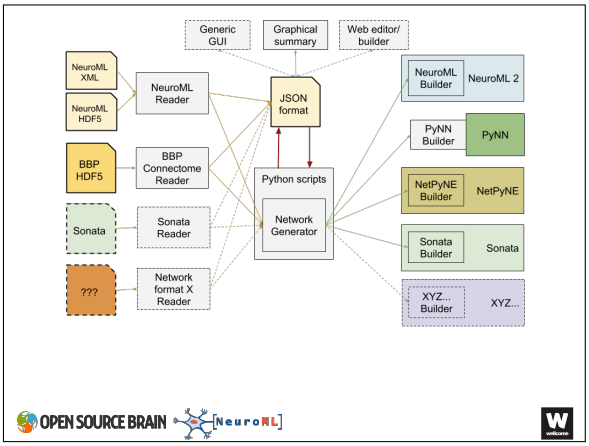
Padraig Gleeson
p.gleeson@ucl.ac.uk
University College London

Open Source Brain workshop 2019

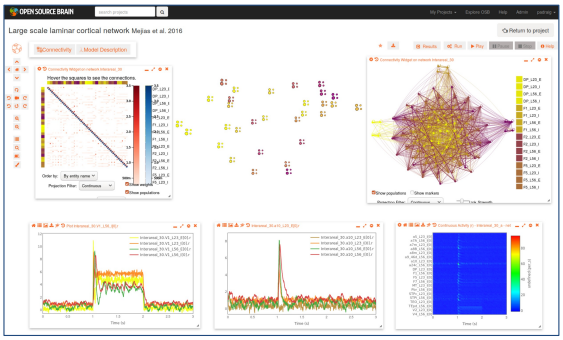
11th Sept 2019

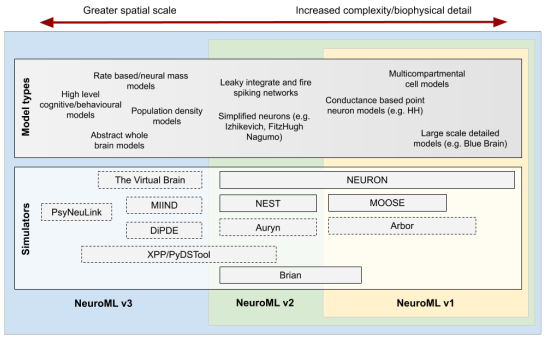
OPEN SOURCE BRAIN NeuroML



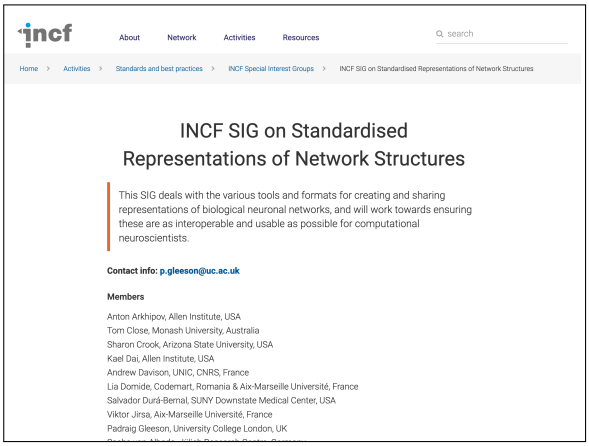


OPEN SOURCE BRAIN NeuroML





OPEN SOURCE BRAIN NeuroML



Converting simulator specific formats to NeuroML2

Open Source Brain Meeting 2019

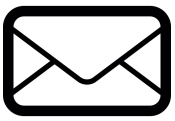
Boris Marin

boris.marin@ufabc.edu.br

Universidade Federal do ABC

Converting NMODL to NeuroML

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



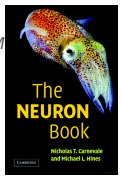
mailto:p.gleeson@ucl.ac.uk

The *NEURON* simulator

Defining models in *NEURON*

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

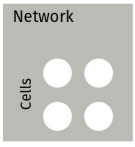
- Cells, Networks: *hoc* language (accessible from Python)
  - morphologies
  - synaptic connections
  - *.hoc* files
- Ion Channels (membrane mechanisms): *NM*
  - *.mod* files



What is NeuroML, and why should I care?

Why can OSB process any NeuroML2 file?

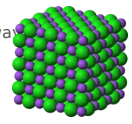
- NML is *structured* (not unlike a *Type System*)



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 wa NML...
  - .... if only people stuck to "good practices"!



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
}
```

Levels of Abstraction

Declarative vs Imperative

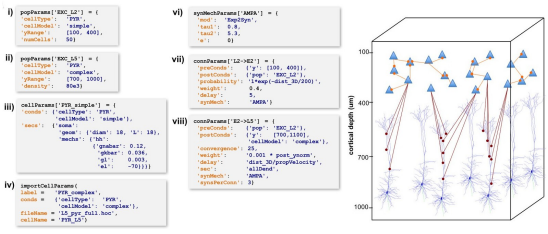
- NeuroML2 operates (at least syntactically) closer to the level of abstraction employed by electrophysiologists
- The gory details exist, but elsewhere: *LEMS*
  - i.e. what to do with α, β; the definition of an `ExpRate`; how all of that is converted to conductances/currents...
- But we seldom need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

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

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

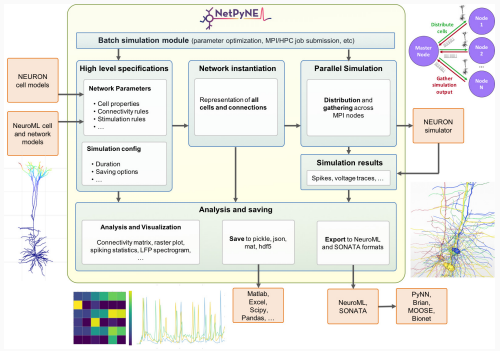
Levels of Abstraction

NetPyNE: structured network specification

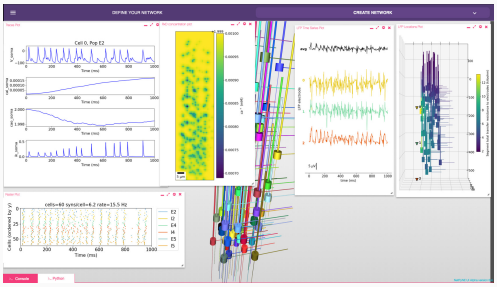


Dura-Bernal, Salvador, et al. "NetPyNE, a tool for data-driven multiscale modeling of brain circuits." Elife 8

Netpyne workflow



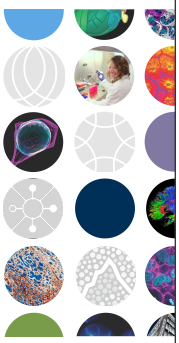
Netpyne GUI



ALLEN INSTITUTE

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

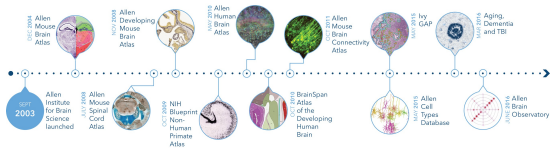
Big Science

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

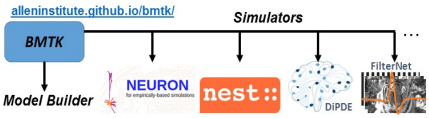


All data are:

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

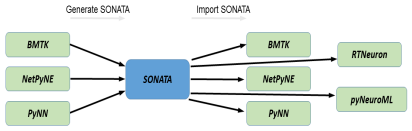
Our Models and Modeling Software Are Freely Available to the Community

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

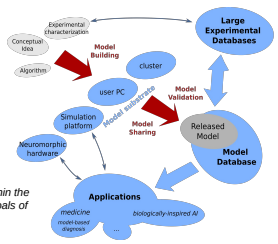
How model standardization enables new tools and applications in neuroscientific research

Insights from the HBP

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

Open Source Brain Meeting 2019, Alghero

Motivation



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

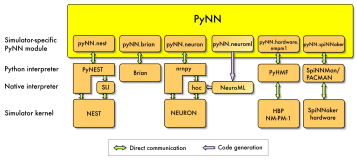
PyNN — A unified interface for neuronal network simulators

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

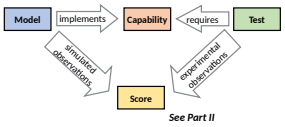
```
from pyNN.serialization import import_from_sonata, load_sonata_simulation_plan
import pyNN.neuron as sim

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:

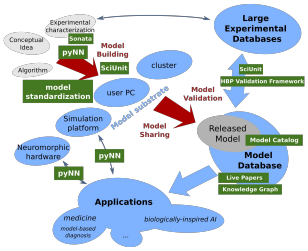
Test suites for specific brain regions

- ***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

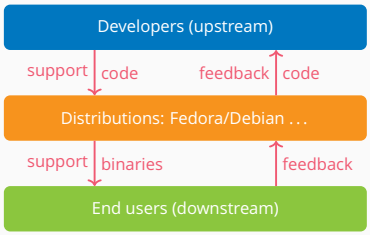
- ***MorphoUnit***: `https://github.com/appukuttan-shailesh/morphounit`
- ***NetworkUnit***: `https://github.com/mvonpapen/simrest_validation`
- ***eFELUnit***: `https://github.com/appukuttan-shailesh/eFELunit`

Summary



NeuroFedora: marketing pitch

Liaison between developers and users



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“Live” ISO now ready to download (demo)
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