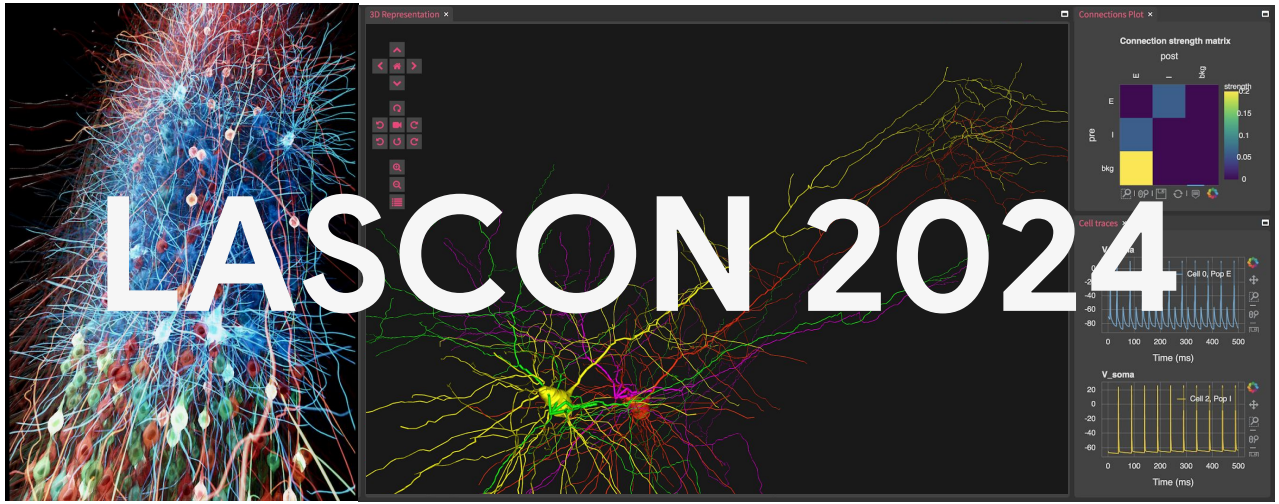
Network Modelling with NetPyNE

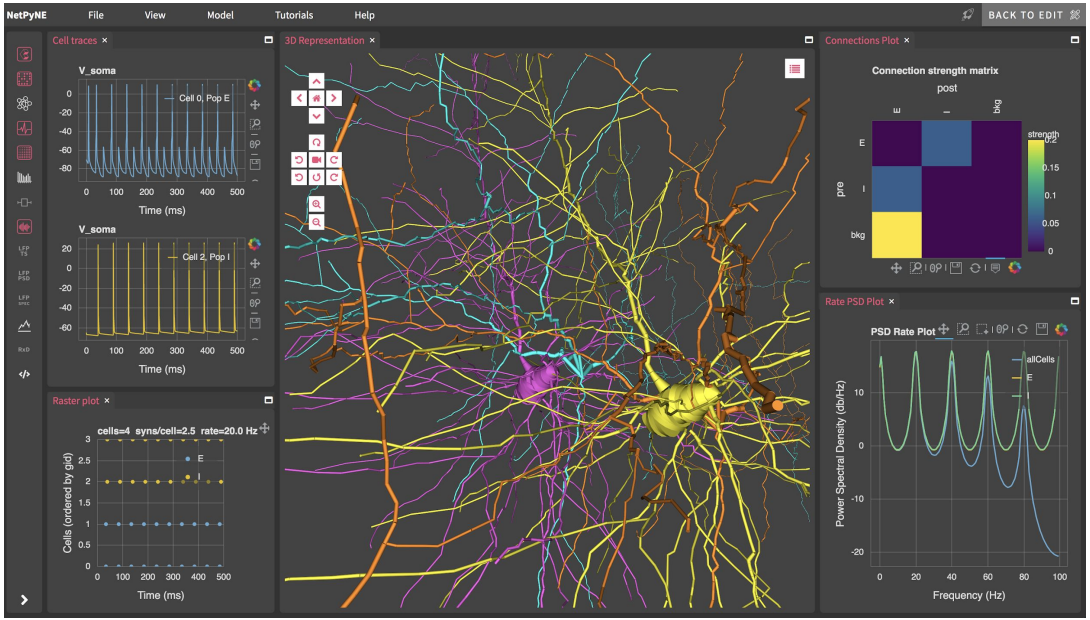


Valery Bragin, State University of New York (SUNY) Downstate vbragin19@gmail.com
PI: Salvador Dura-Bernal, PhD
Assistant Professor, State University of New York (SUNY) Downstate

Lab web: dura-bernal.org

NetPyNE

A python package to facilitate the development, parallel simulation, optimization and analysis of biological neuronal networks using the NEURON simulator.



Funded by:

National Institutes of Health

Motivation

Separate model parameters from standardized implementation

Standardize format – easy to read, interpret, edit, share, reproduce, etc

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

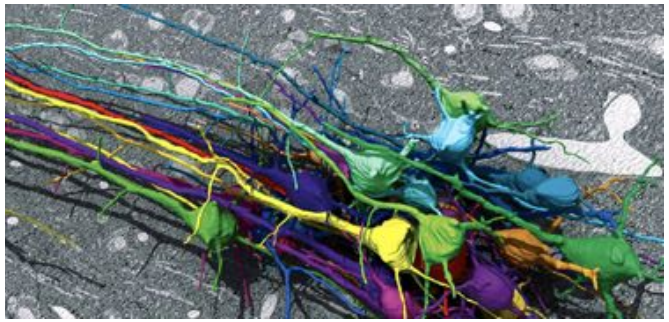
```
for gid in range(pop.numCells):
      cell = sim.Cell()
      cell.y = numpy.random(100,400)
      cell.type = 'PYR'
      pc.cell(gid, h.NetCon(v_soma, threshold))
```

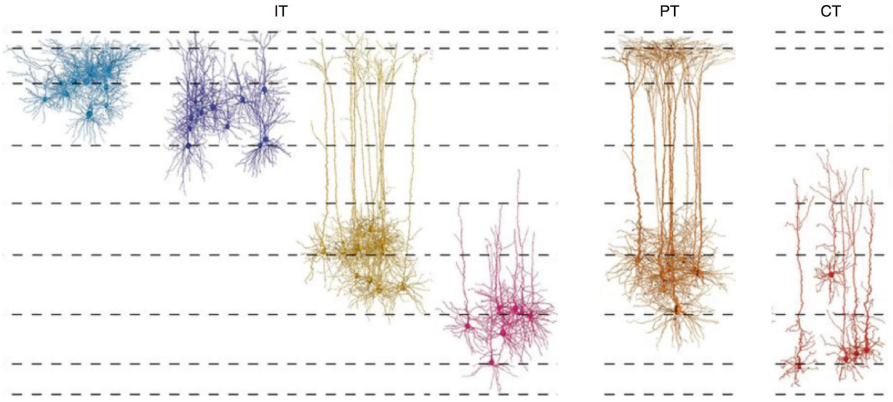
Standard, efficient and tested backend implementation

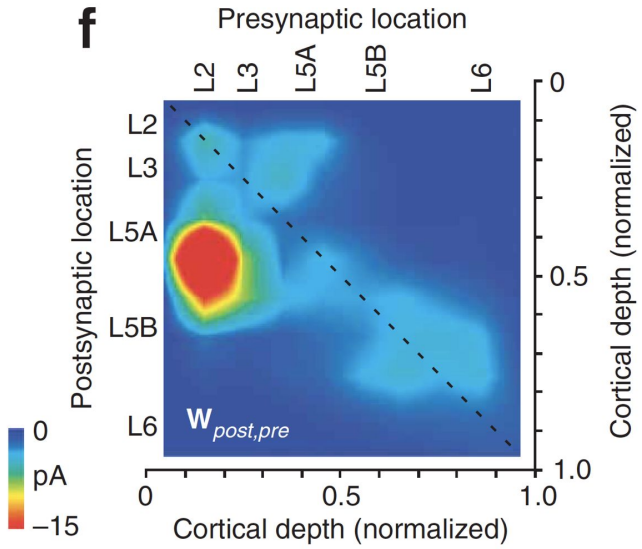
Potentially very different implementations (arbitrary functions, variables, file names etc.)

Motivation

Facilitate incorporation of experimental data at multiple scales







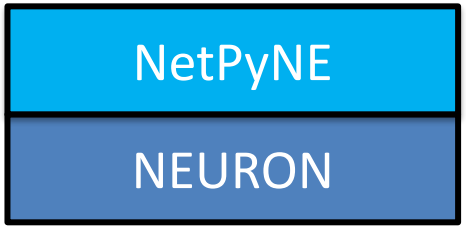
NetPyNE High-Level Specifications

NEURON

```
# add exc connection
postSyn1 = h.ExpSyn(postCell.dend(0.5))
postSyn1.tau = 2
postSyn1.e = -90

pre1Con = h.NetCon(preCell1.soma(0.5)._ref_v,
                   postSyn1,
                   sec=preCell1.soma)
pre1Con.delay = 1
pre1Con.weight[0] = 0.001
pre1Con.threshold = 0
```

NetPyNE High-Level Specifications




```
## Cell connectivity rules
netParams.connParams['S->M'] = {
        'preConds': {'pop': 'S'},
        'postConds': {'pop': 'M'},
        'probability': 0.5,
        'weight': 0.01,
        'delay': 5,
        'synMech': 'exc'}
```

```
# add exc connection
postSyn1 = h.ExpSyn(postCell.dend(0.5))
postSyn1.tau = 2
postSyn1.e = -90

pre1Con = h.NetCon(preCell1.soma(0.5)._ref_v,
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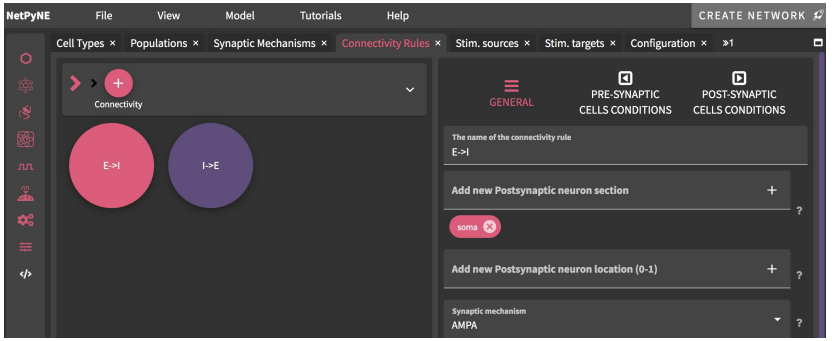
NetPyNE High-Level Specifications

NetPyNE GUI

NetPyNE

NEURON

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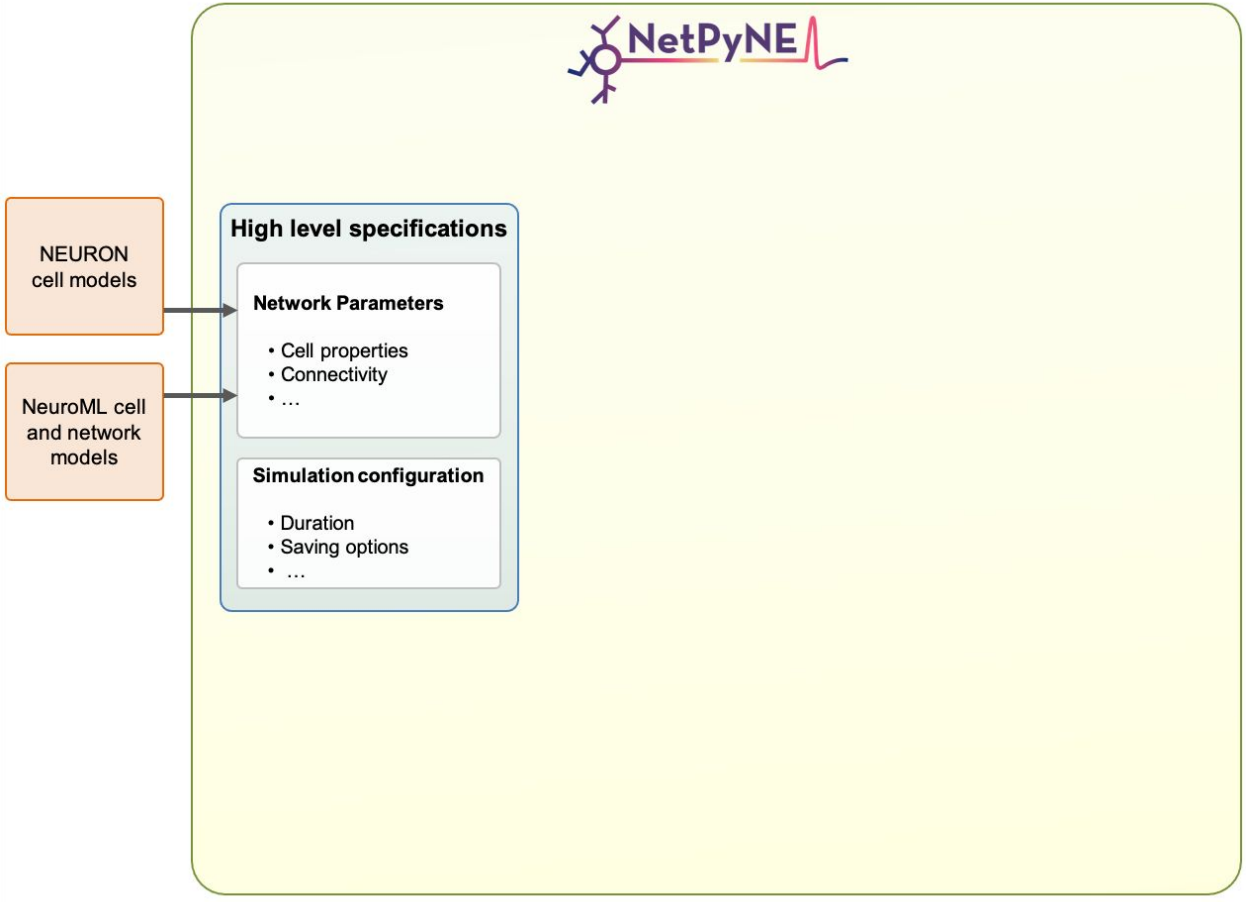
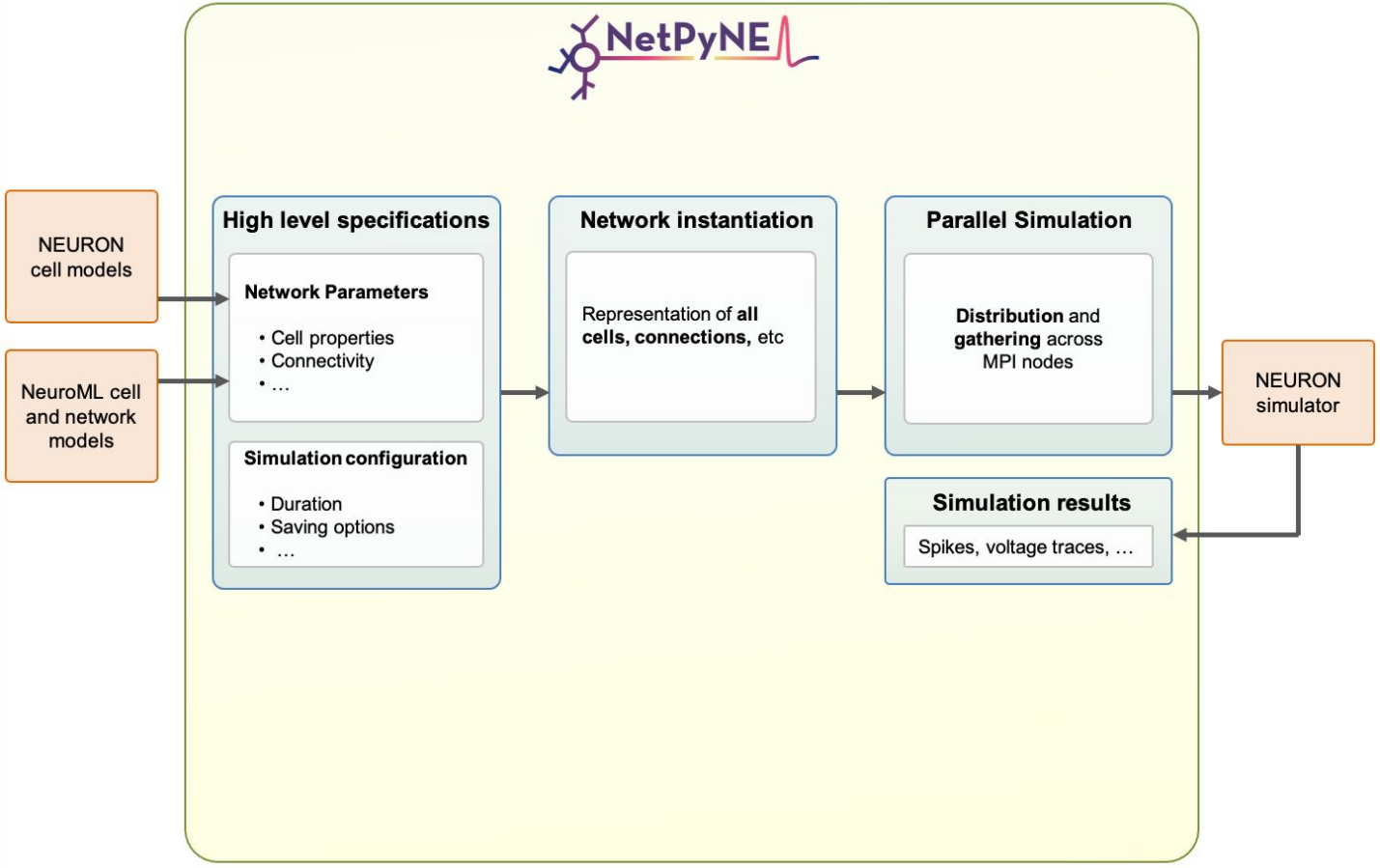

NetPyNE
NEURON cell models
NeuroML cell and network models
High level specifications
Network Parameters
• Cell properties
• Connectivity
• …
Simulation configuration
• Duration
• Saving options
• …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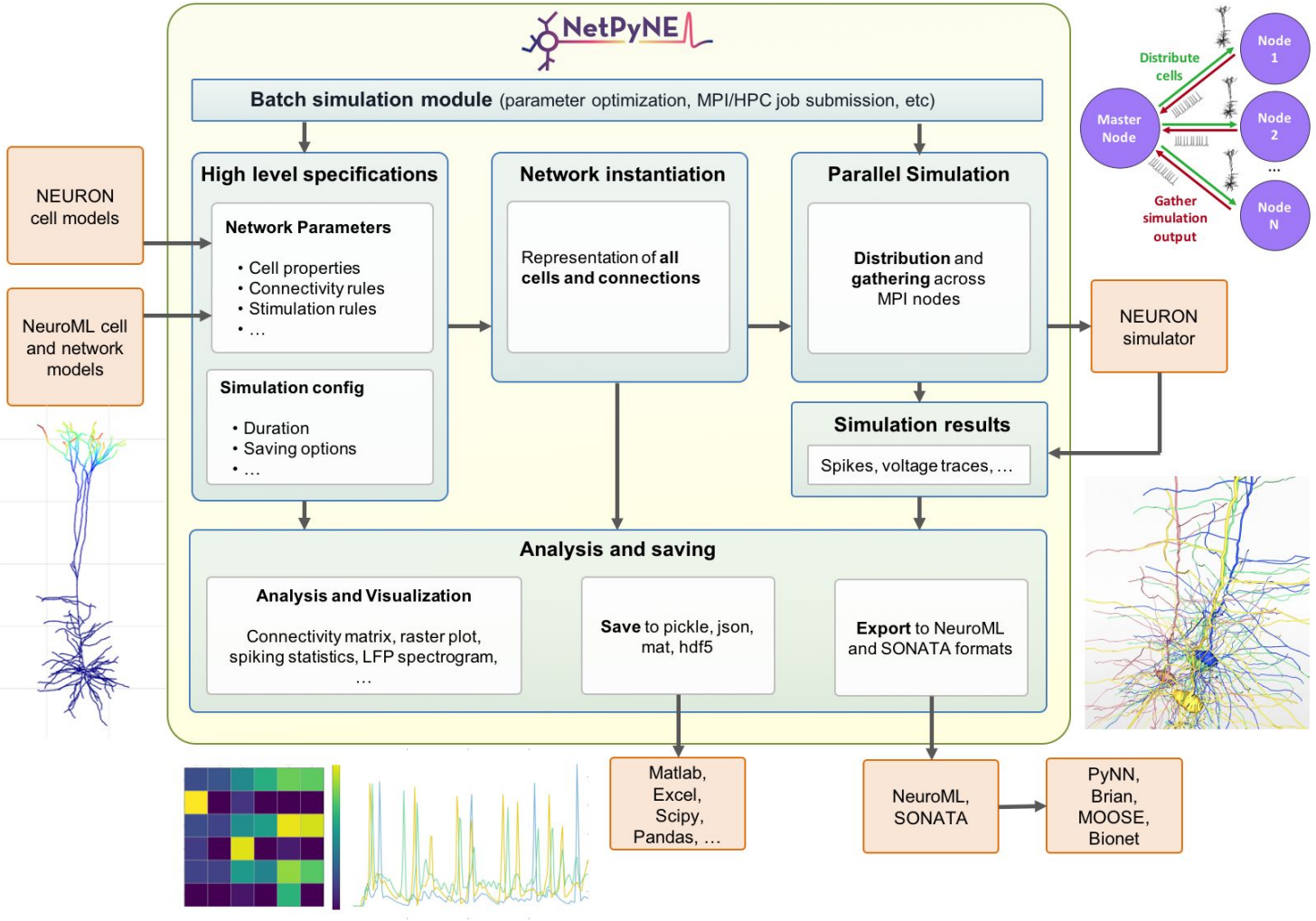
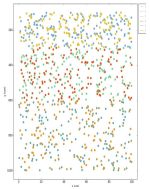
Network instantiation
Representation of all cells, connections, etc
Parallel Simulation
Distribution and gathering across MPI nodes
Simulation results
Spikes, voltage traces, …
NEURON simulator


NetPyNE
Batch simulation module (parameter optimization, MPI/HPC job submission, etc)
NEURON cell models
NeuroML cell and network models
High level specifications
Network Parameters
• Cell properties
• Connectivity rules
• Stimulation rules
• …
Simulation config
• Duration
• Saving options
• …
Network instantiation
Representation of all cells and connections
Parallel Simulation
Distribution and gathering across MPI nodes
Distribute cells
Gather simulation output
Master Node
Node 1
Node 2
Node N
NEURON simulator
Simulation results
Spikes, voltage traces, …
Analysis and saving
Analysis and Visualization
Connectivity matrix, raster plot, spiking statistics, LFP spectrogram, …
Save to pickle, json, mat, hdf5
Export to NeuroML and SONATA formats
Matlab, Excel, Scipy, Pandas, …
NeuroML, SONATA
PyNN, Brian, MOOSE, Bionet

High level specifications

A **standardized, declarative** Python format (JSON-like, lists and dicts) to define:

Populations: cell type, number of neurons or density, spatial extent, ...

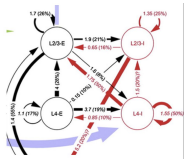


***Cell properties*:** Morphology, biophysics, molecular processes ...

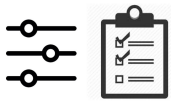
***Synaptic mechanisms*:** Time constants, reversal potential, ...

***Stimulation*:** Spike generators, current clamps, spatiotemporal patterns, ...

***Connectivity rules*:** conditions of pre- and post-synaptic cells, functions, ...



***Simulation configuration*:** duration, saving and analysis, visualization, ...



High level specifications

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')
```

v)
```
rxdParams['regions'] = {
 'cyt': {'cells':      'all',
         'secs':       'soma',
         'nrn_region': 'i'}}

rxdParams['species'] = {
 'ca':    {'regions': 'cyt',
           'charge':  2,
           'initial': 1e-4},
 'buf':   {'regions': 'cyt',
           'initial': 1e-4},
 'cabuf': {'regions': 'cyt',
           'initial': 0}}

rxdParams['reactions'] = {
 'buffering': {'reactant': '2*ca+buf',
               'product':   'cabuf',
               'rate_f':    1e6,
               'rate_b':    1e-2}}

rxdParams['rates'] = {
 'degradation': {'species': 'buf',
                 'rate': '-1e-3*buf'}}
```

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

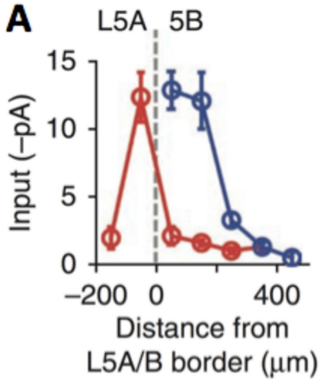
vii)
```
connParams['L2->E2'] = {
 'preConds':    {'y': [100, 400]},
 'postConds':   {'pop': 'EXC_L2'},
 'probability': '1*exp(-dist_3D/200)',
 'weight':       0.4,
 'delay':        5,
 'synMech':      'AMPA'}
```

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}
```

High level specifications

Connectivity

- **Flexible connectivity rules** based on pre- and post-synaptic cell properties (eg, type or location).
- Connectivity **functions** available: probabilistic, convergent, divergent, custom, ...
- Parameters (eg, probability, weight, delay) as a **function of pre/post-synaptic spatial properties**, eg, delays or probability that depend on distance between cells or cortical depth.
- Easily add synapses with **learning** mechanisms (STDP and RL) and **gap junctions.**

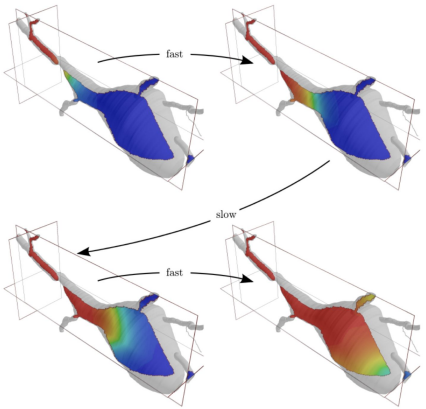


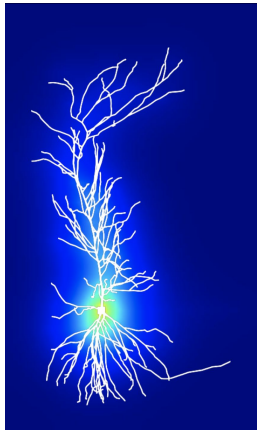
NetPyNE facilitates building models based on experimental data

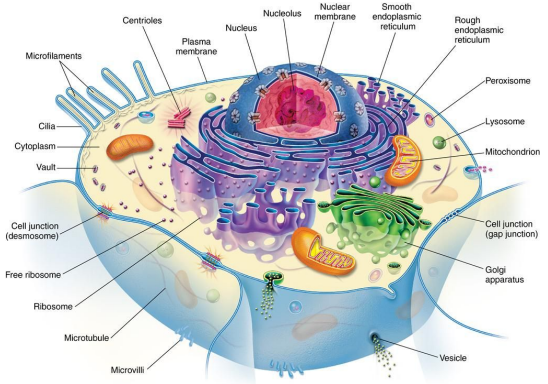
High level specifications

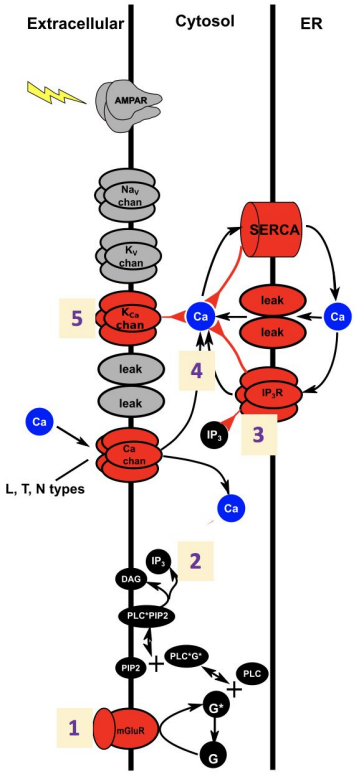
Molecular reaction-diffusion (RxD)

- Intra- and extracellular **diffusion** of ions, proteins (eg, calcium, potassium, IP3, ...)
- Cell internal structures/**organelles** (eg, endoplasmic reticulum, mitochondria,...)
- Molecular **processes** (eg, phosphorylation, buffering, 2nd messenger cascades,...
- **Interaction** with cell and network scales (eg, firing, plasticity, ...)



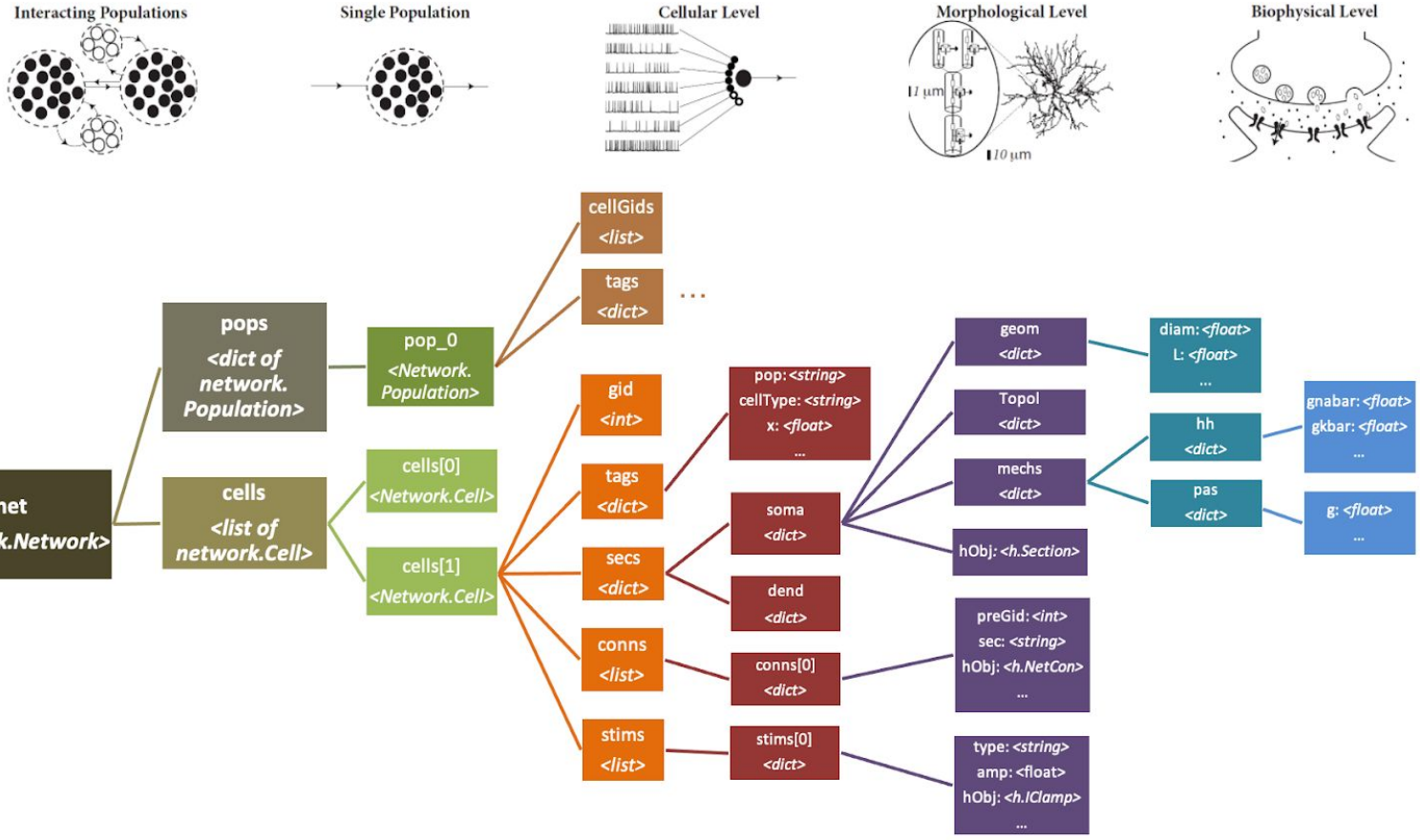






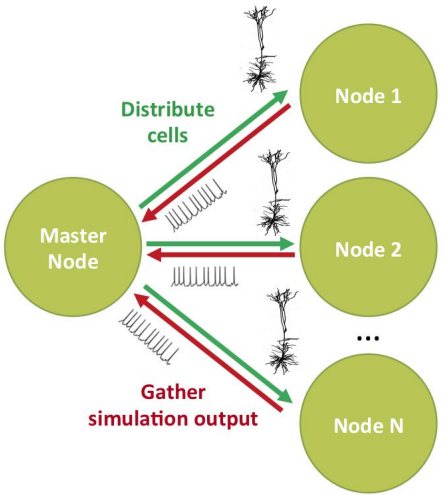
Network instantiation

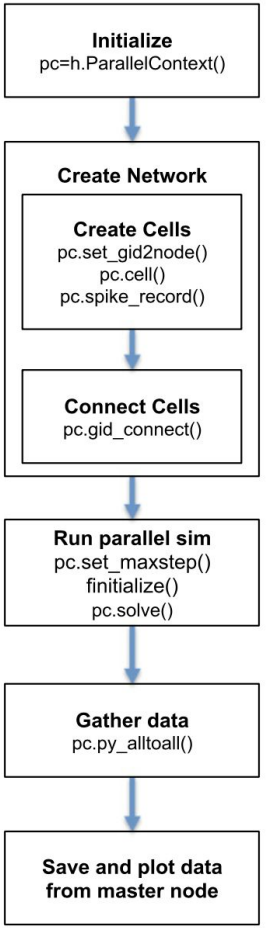
(*sim.net*)



Parallel Simulation

- Set up for MPI **parallel simulation** across multiple nodes (via NEURON simulator).
- Takes care of balanced **distribution** of cells and **gathering** of simulation output from nodes.

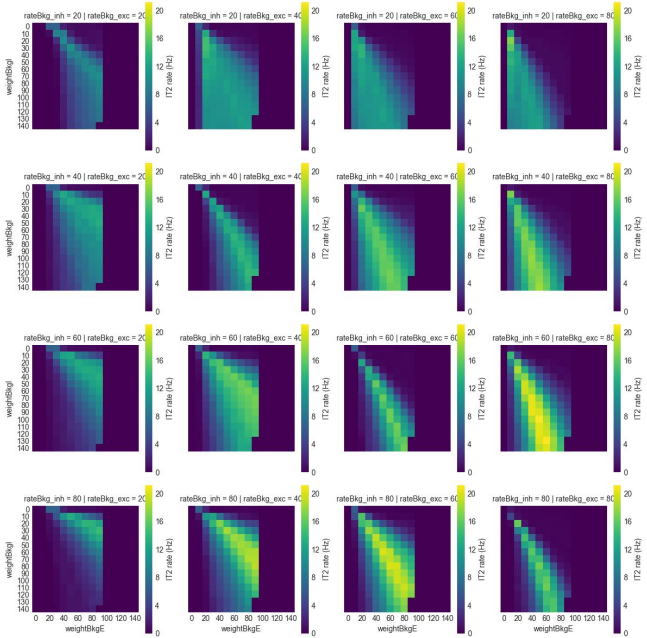




Parallelized parameter exploration

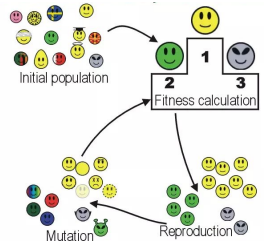
- **Easy specification** of parameters values to explore in batch simulations (param sweep and evolutionary)
- **Pre-defined, configurable** setups to automatically **submit jobs** in multicore machines (Bulletin board) or supercomputers (SLURM or PBS Torque)

SDSC SAN DIEGO SUPERCOMPUTER CENTER

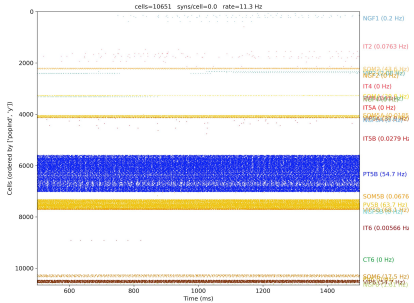


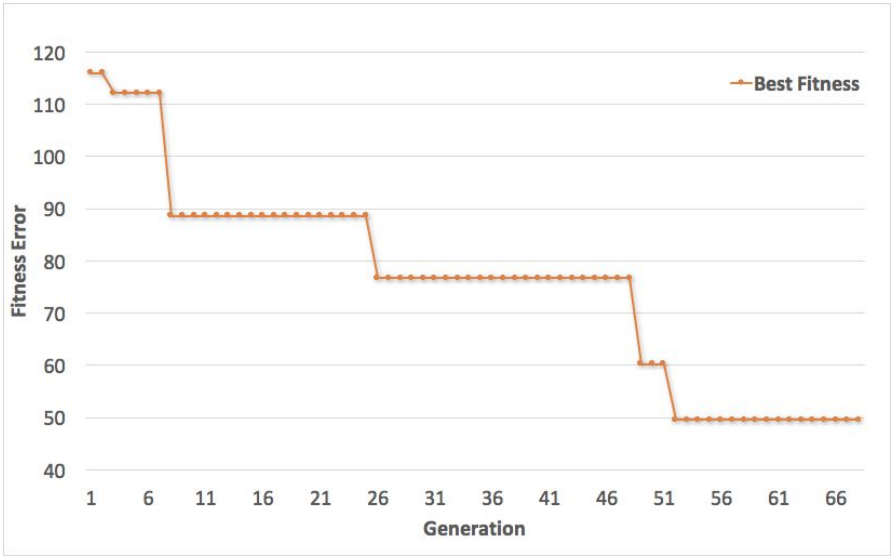
Parallelized parameter exploration

- Evolutionary algorithm optimization (for networks)

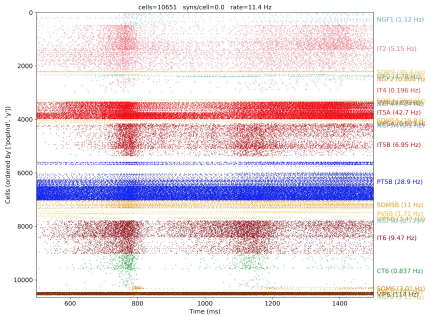


Initial candidate

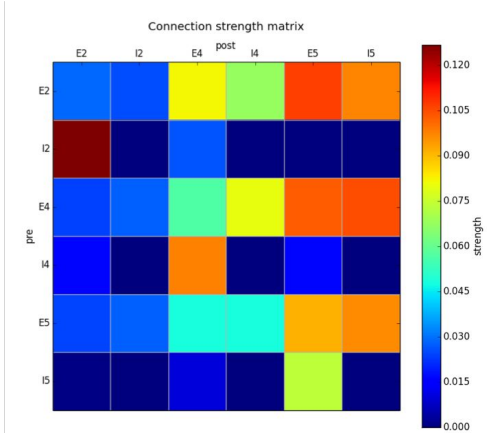


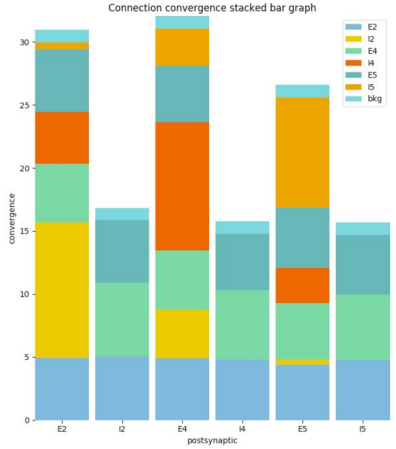


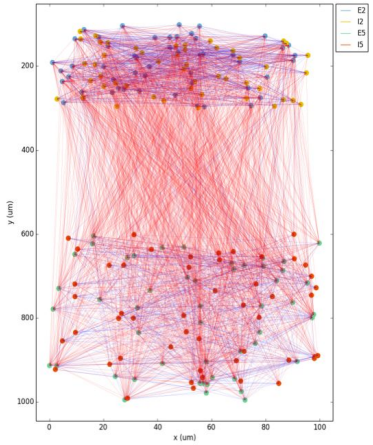
Final candidate

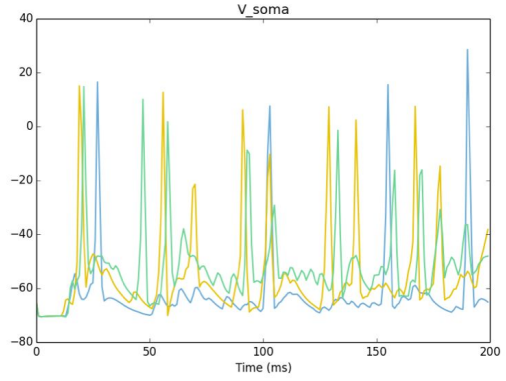


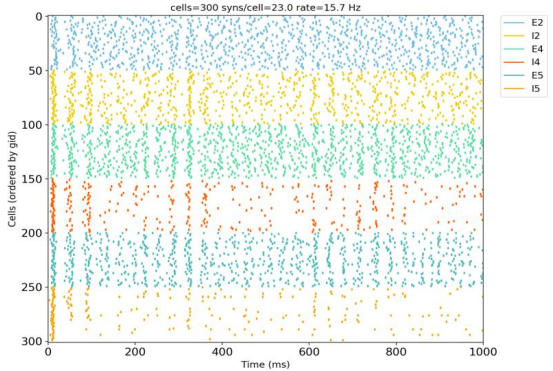
Simulation Analysis

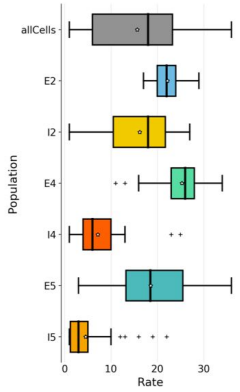






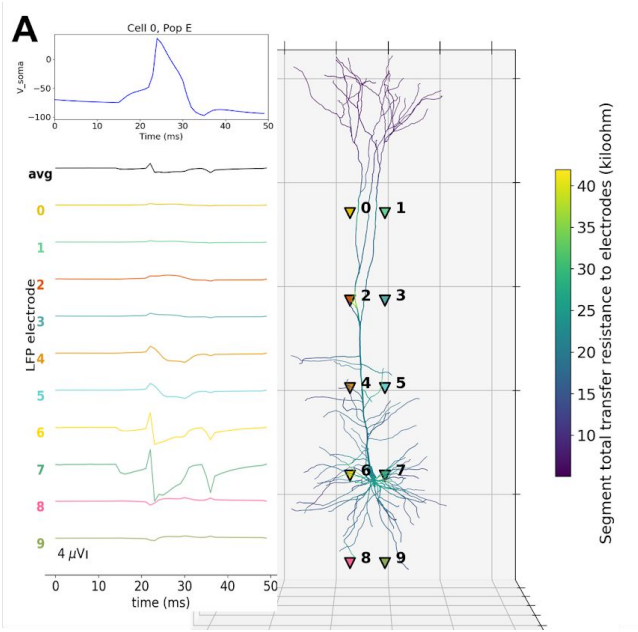




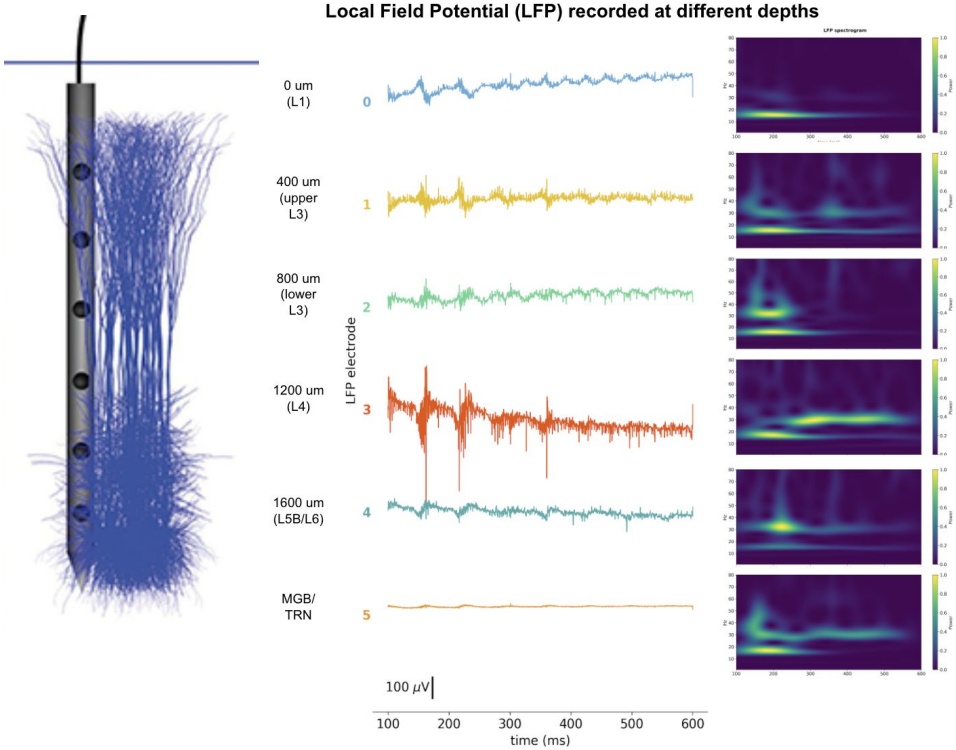


Local Field Potentials

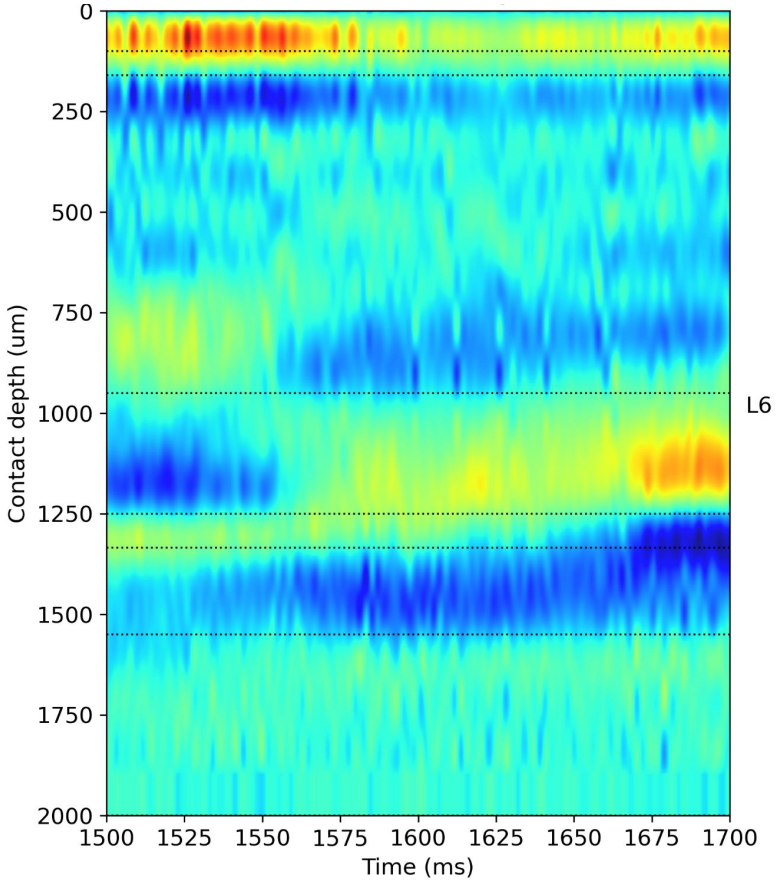
Single cell



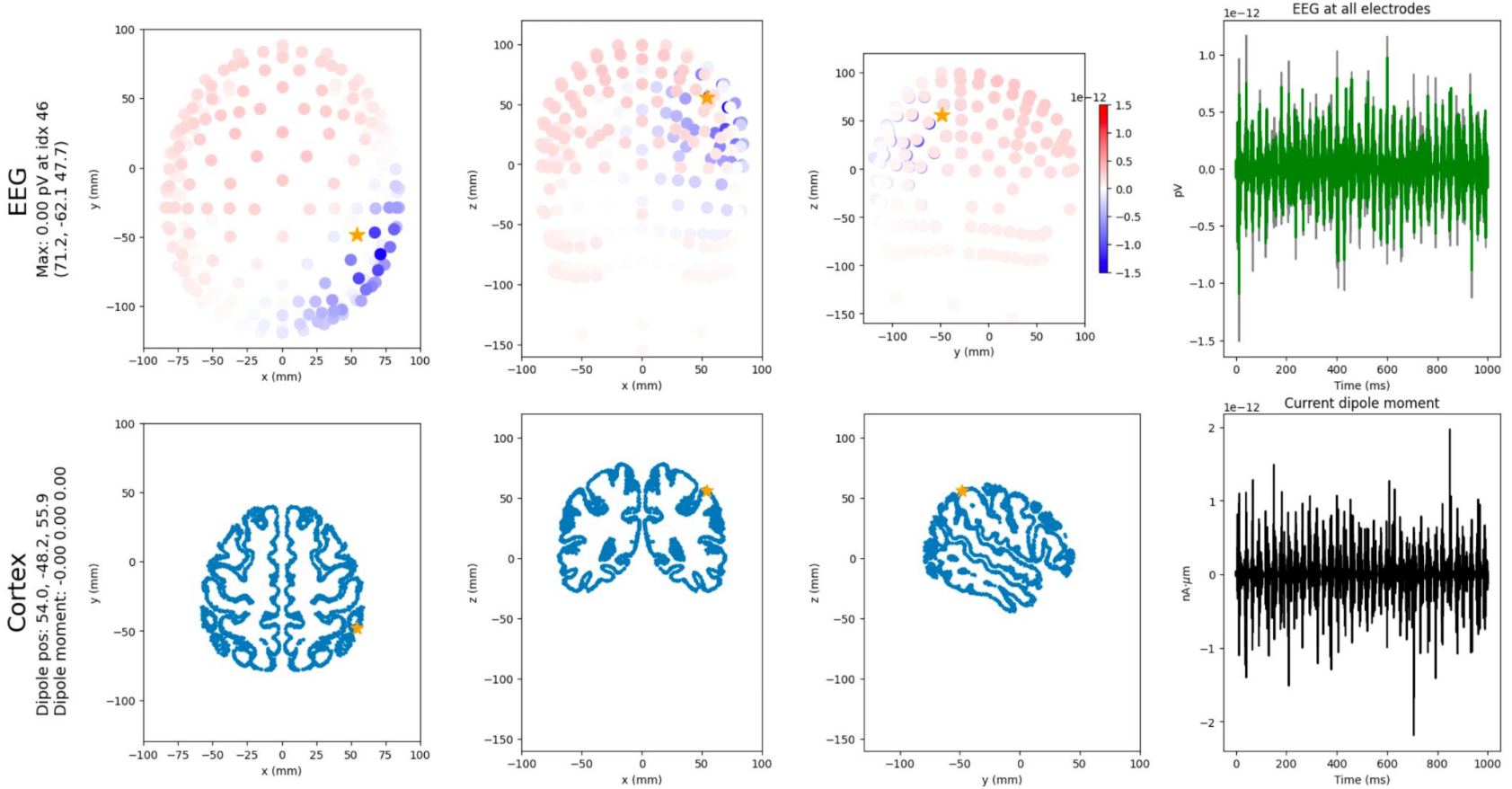
Network



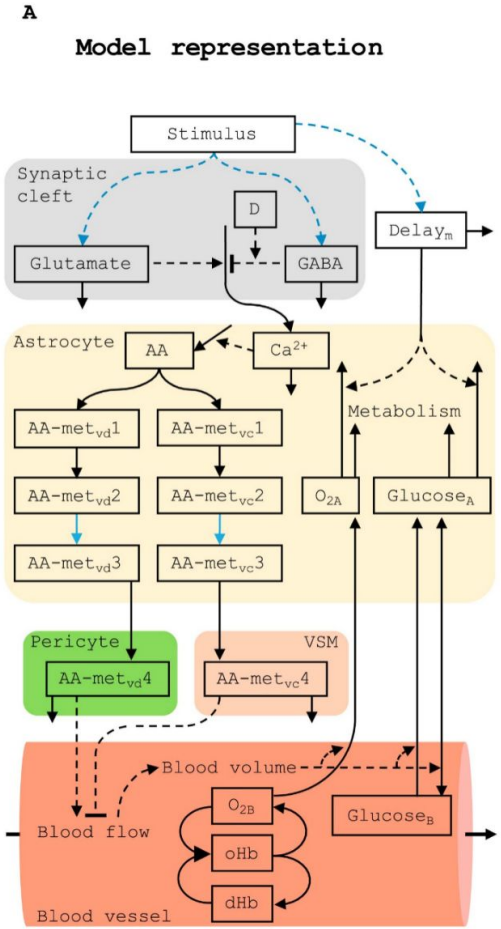
Current Source Density

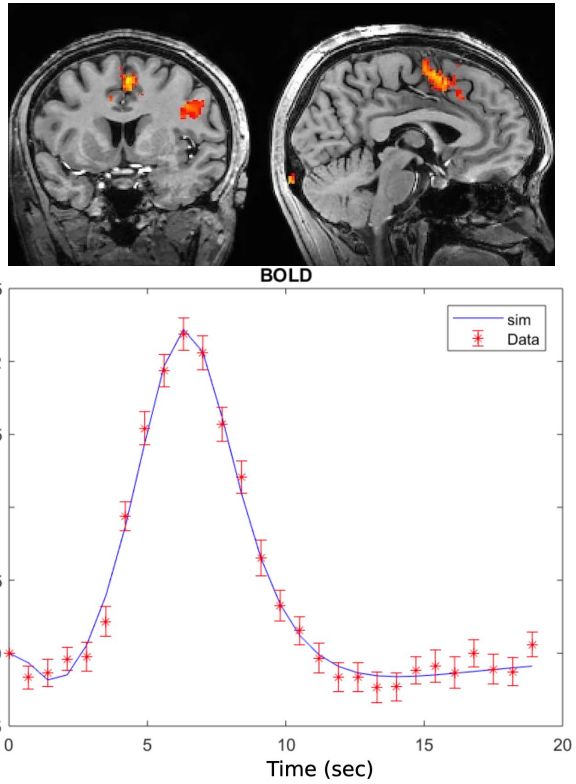


Current dipoles and EEG



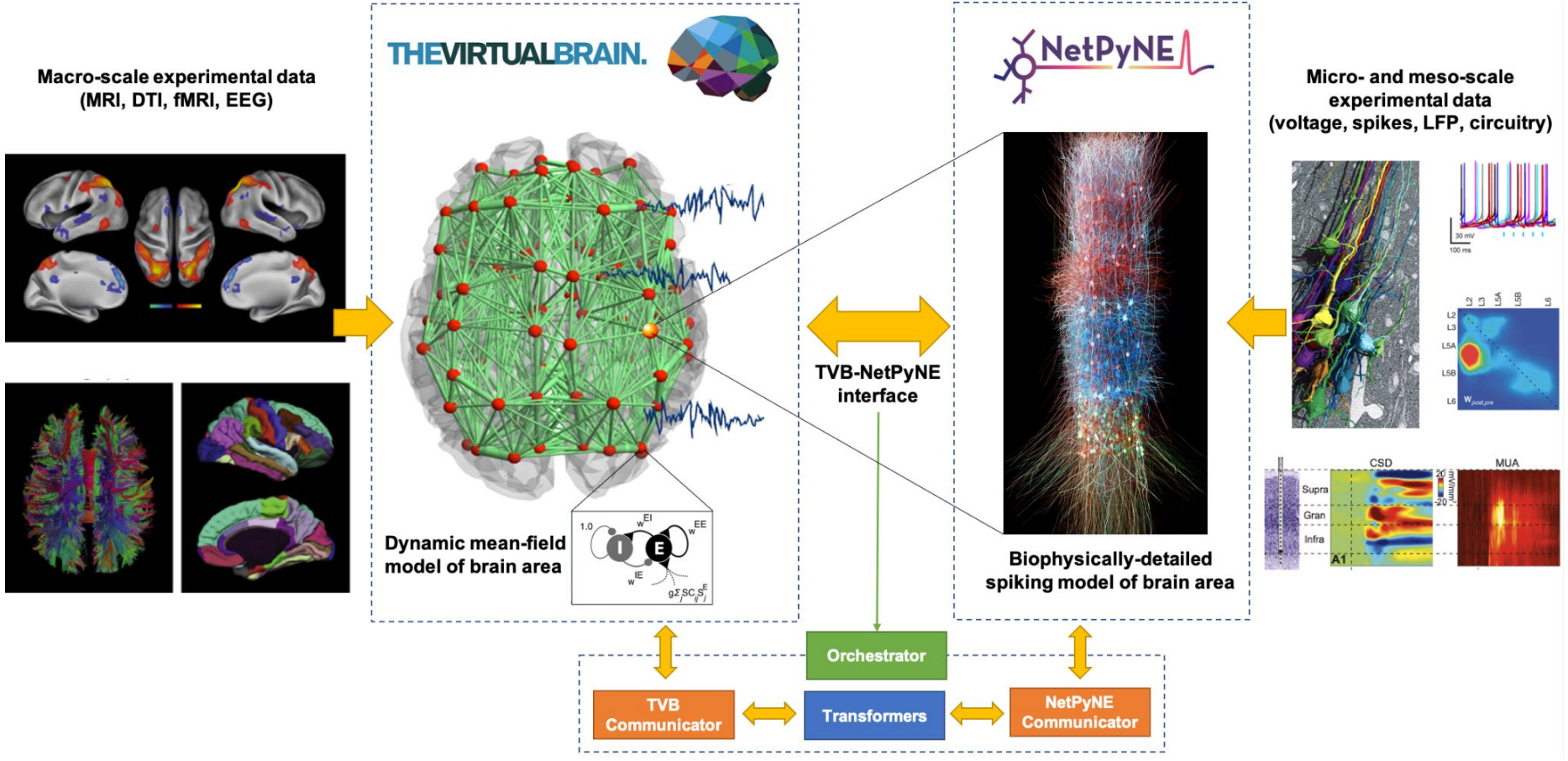
Neurovascular coupling model (BOLD / fMRI)



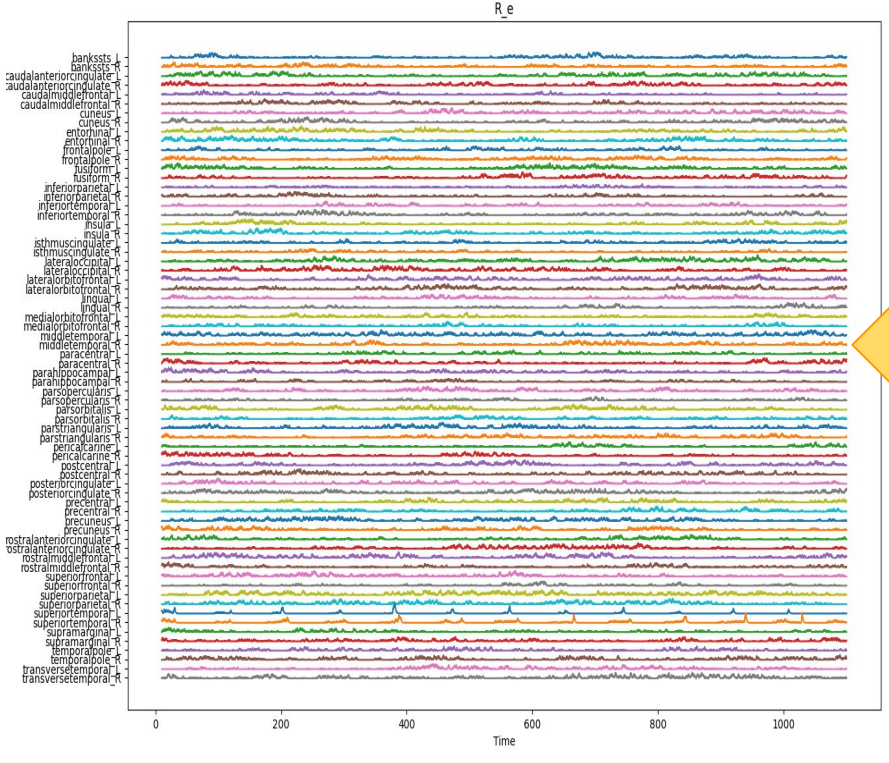


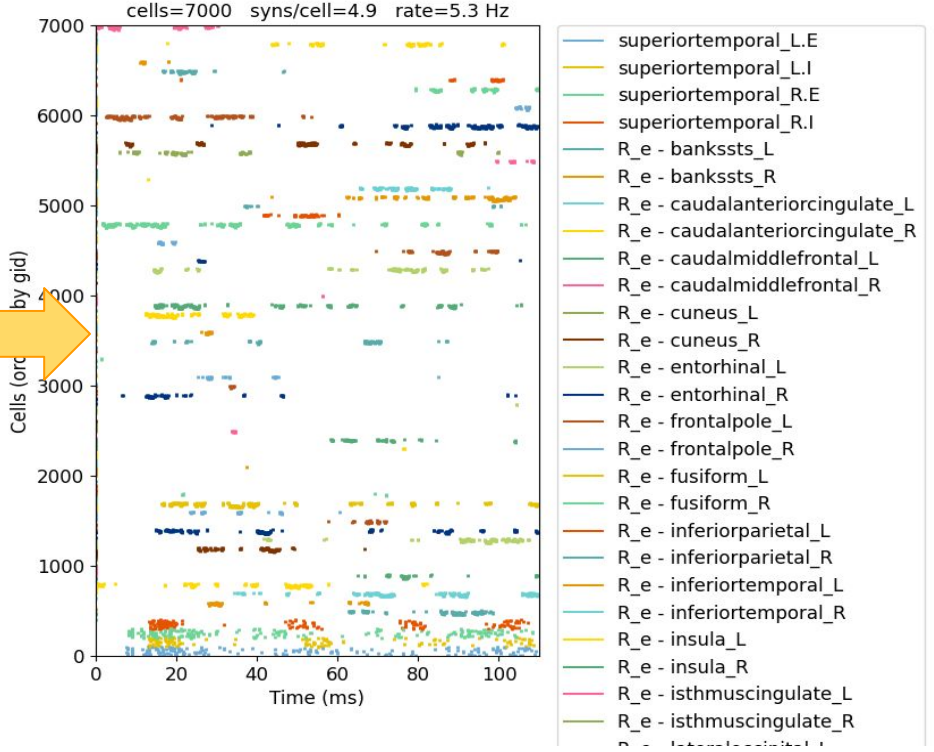
Sten S, et.al. Neural inhibition can explain negative BOLD responses: A mechanistic modelling and fMRI study. Neuroimage. 2017 Sep 1;158:219–31.

TVB-NetPyNE co-simulation

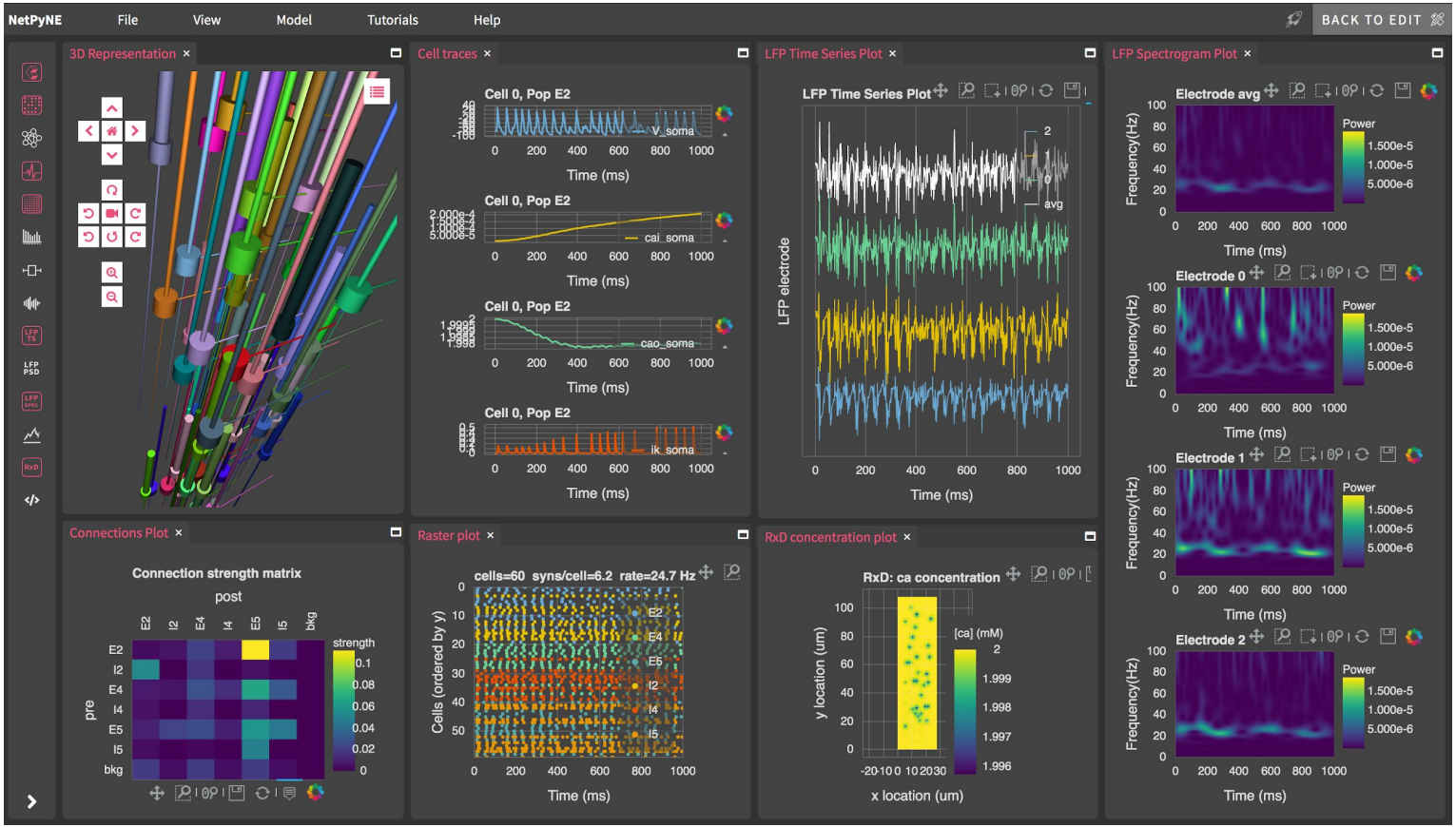


TVB-NetPyNE Example





GUI for Development, Simulation, Analysis



Useful for

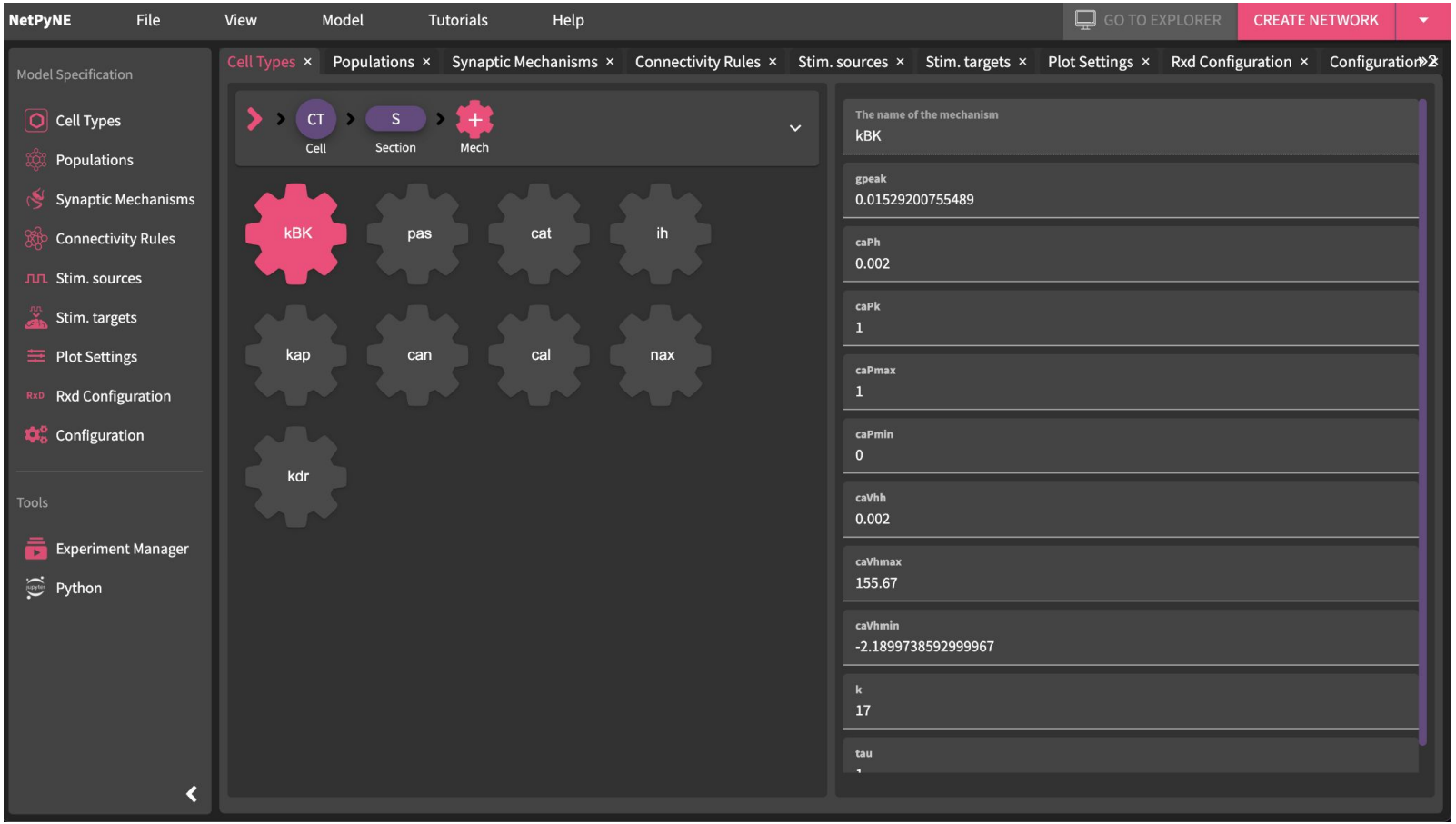
· Students/begin

· Model prototyp

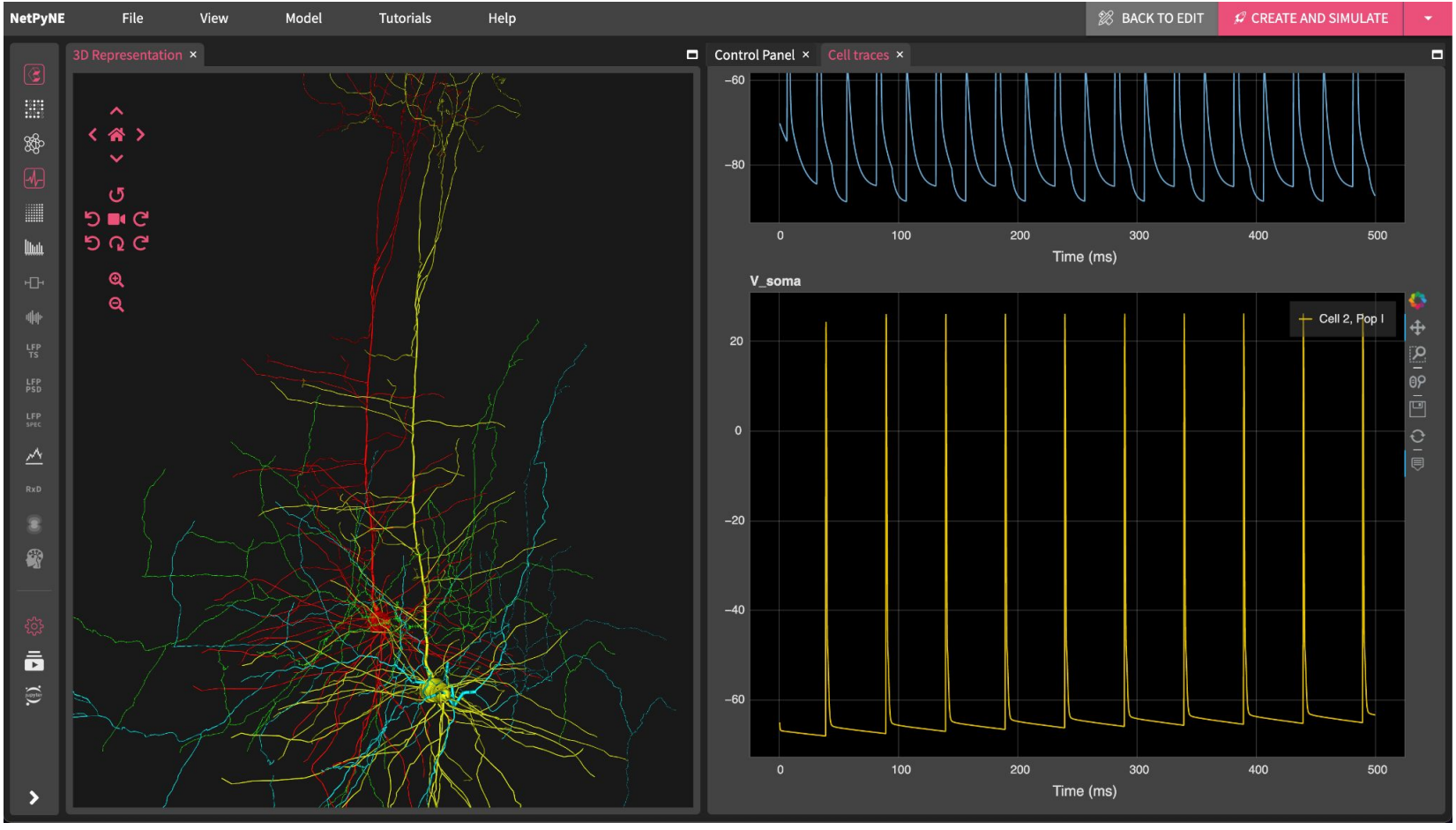
· Exploring/Visua

(interactive in sy

GUI for Development, Simulation, Analysis



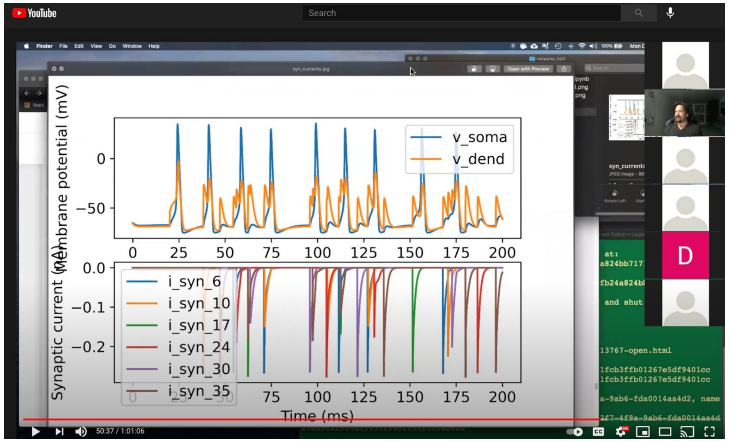
GUI for Development, Simulation, Analysis



Documentation, tutorials and examples

http://netpyne.org

- All learning resources:
  - **Documentation**
  - Jupyter Notebook Tutorials
  - Video tutorials (40+ hours)
  - Package reference
- Example models
- Q&A Forum
- Mailing List

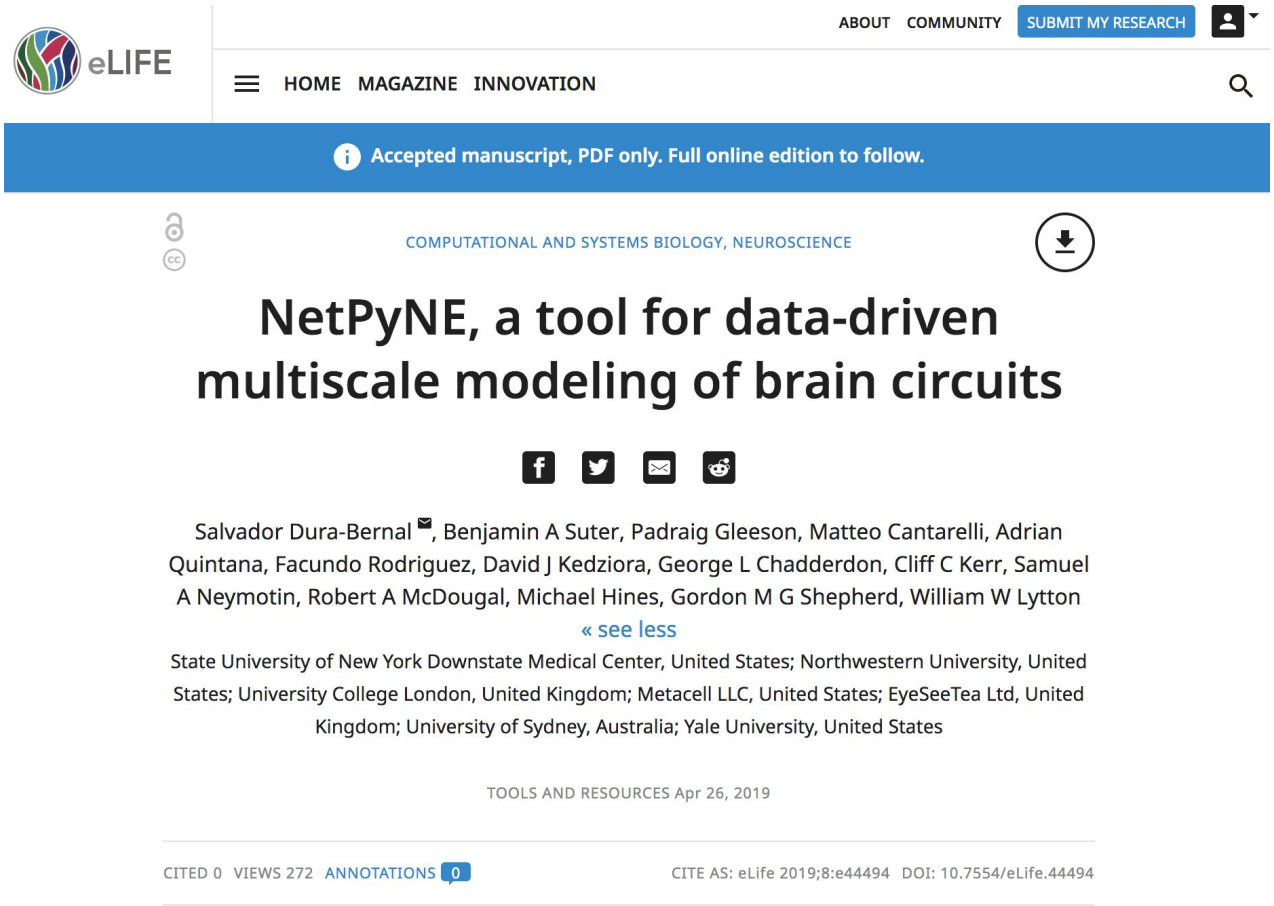


★ NetPyNE Q&A forum 66 members

NetPyNE (www.netpyne.org) is a high-level python interface to NEURON that facilitates the development, parallel simulatio
enables users and developers to post questions, answers and comments about the tool.
Our previous Q&A forum with many posts can be found here: https://www.neuron.yale.edu/phpBB/viewforum.php?f=45

zirui.w...@gmail.com			**LFP signal baseline offset, fluctuate below baseline 0** — Hello, I am usir
maliha....@gm... , vbra...@gma...	2		**Specify colours in rasterplot** — Hi Maliha, You can use `popColors` parar
zirui.w...@gma..., Eugenio Urda...	2		**how to reset kernel in netpyne** — Hi Zirui, to get different results you sho
bh...@rice.e..., ... Gin Estrella Cr...	4		**Problem with importing cells** — I'm somewhat glad to hear that I'm not t

NetPyNE tool: Publication in eLife



eLIFE

ABOUT COMMUNITY SUBMIT MY RESEARCH

HOME MAGAZINE INNOVATION

Accepted manuscript, PDF only. Full online edition to follow.

COMPUTATIONAL AND SYSTEMS BIOLOGY, NEUROSCIENCE

NetPyNE, a tool for data-driven multiscale modeling of brain circuits

Salvador Dura-Bernal, Benjamin A Suter, Padraig Gleeson, Matteo Cantarelli, Adrian Quintana, Facundo Rodriguez, David J Kedziora, George L Chadderdon, Cliff C Kerr, Samuel A Neymotin, Robert A McDougal, Michael Hines, Gordon M G Shepherd, William W Lytton

« see less

State University of New York Downstate Medical Center, United States; Northwestern University, United States; University College London, United Kingdom; Metacell LLC, United States; EyeSeeTea Ltd, United Kingdom; University of Sydney, Australia; Yale University, United States

TOOLS AND RESOURCES Apr 26, 2019

CITED 0 VIEWS 272 ANNOTATIONS 0

CITE AS: eLife 2019;8:e44494 DOI: 10.7554/eLife.44494

NetPyNE-based papers

http://netpyne.org/about.html#publications

- Hasegan D, Deible M, Earl C, D'Onofrio D, Hazan H, Anwar H, Neymotin SA. **Multi-timescale biological learning algorithms train spiking neuronal network motor control** bioRxiv 2021.11.20.469405, *2021*. doi: https://doi.org/10.1101/2021.11.20.469405.
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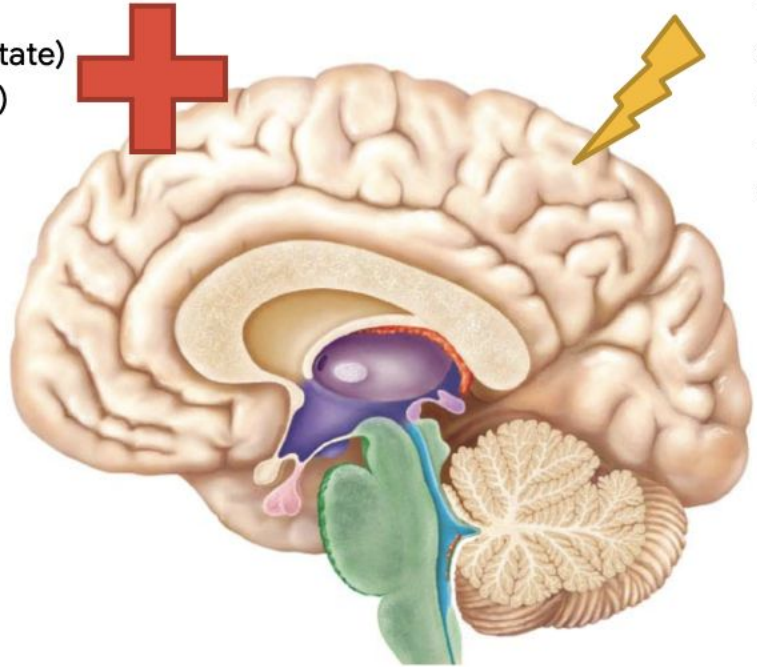
Growing community (>80 models, >40 Labs)

- Schizophrenia (TU Berlin, Brown)
- Ischemic stroke (Yale, Downstate)
- Epilepsy (Cincinatti, Brown, Downstate)
- Chronic Pain (Okinawa, Downstate)
- Depression (Brown)
- Parkinson's (Edinburgh)

- TMS / tDCS / tACS (Duke, Toronto)
- Optogenetics (Sydney)
- Electrical stimulation (Downstate)
- Ketamine (Brown)
- EEG/MEG (Puerto Rico, Brown, Rice)
- fMRI (Linkopig)



- PFC (Sao Paulo)
- Thalamus (UCL, Missouri)
- Olfactory Bulb (Palermo)
- Striatum (Dublin)
- Amygdala (Princeton)
- Hippocampus (Sao Paulo)

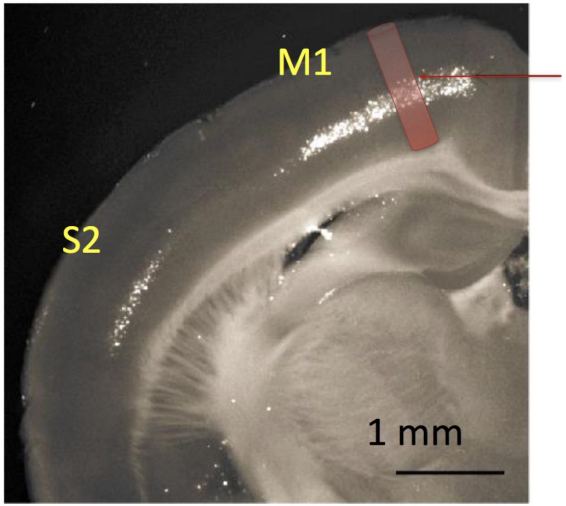
- M1 and S1 (Downstate)
- A1 (NKI)
- V1 (Queensland, Sao Paulo)
- Claustrum (Singapore)
- Cerebellum (Sao Paulo)
- Spinal Cord (Northeastern)

- Cardiac circuits (Jefferson, Downstate, Pavia)

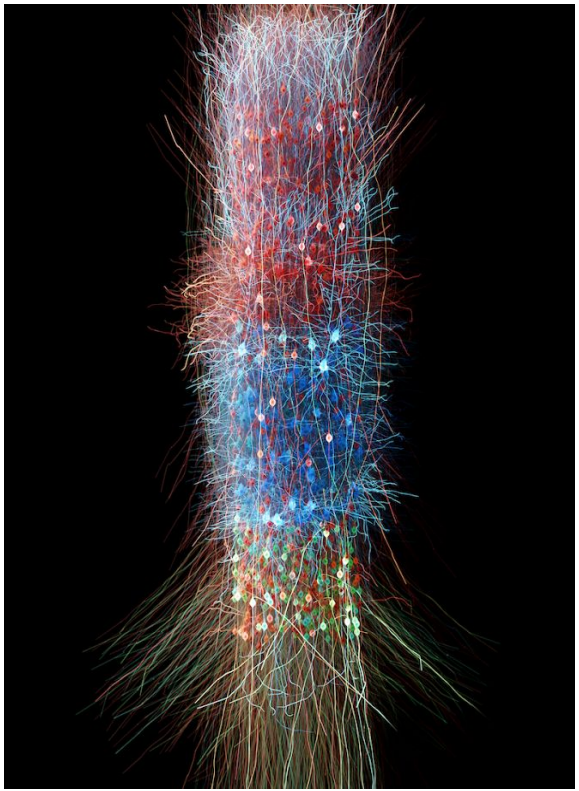
- Enteric / gastrointestinal circuits (Melbourne)

Data-driven model of motor cortex (M1) circuits

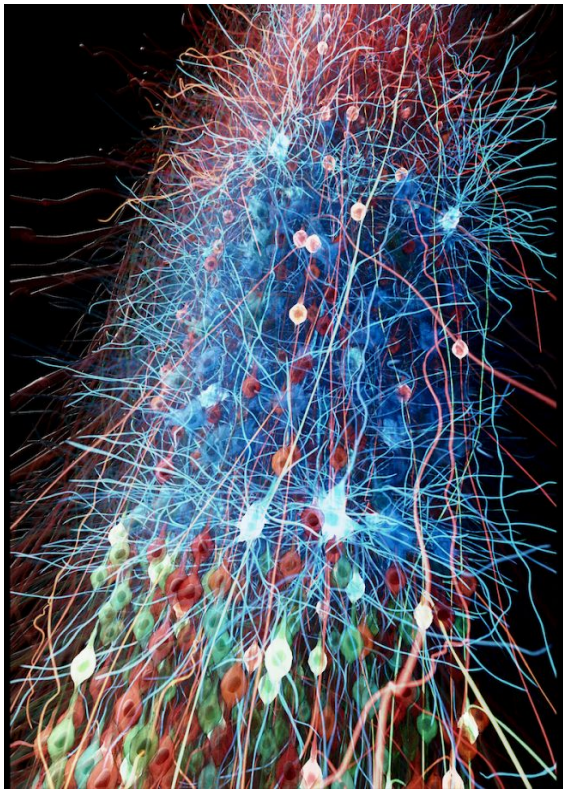
300 um diameter column



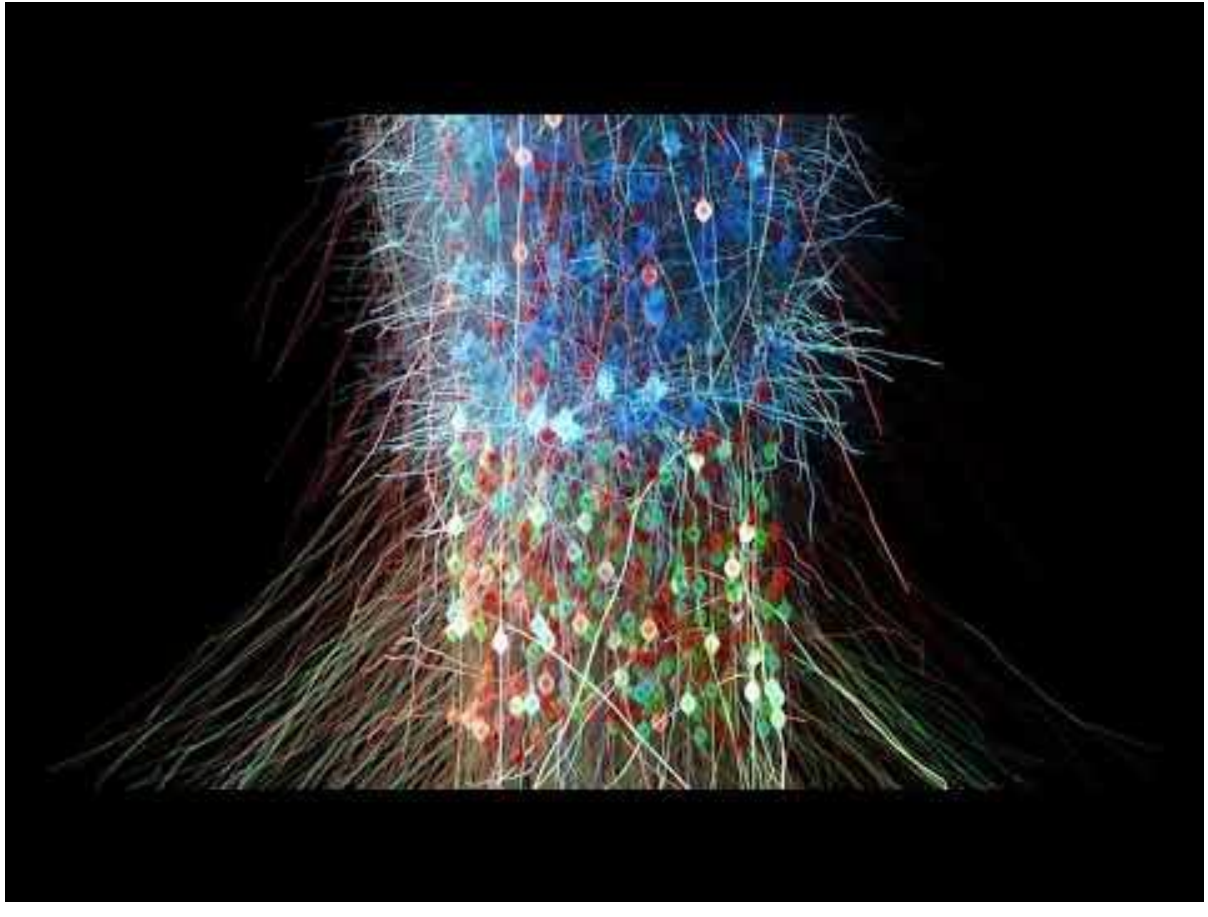
10,000 neurons



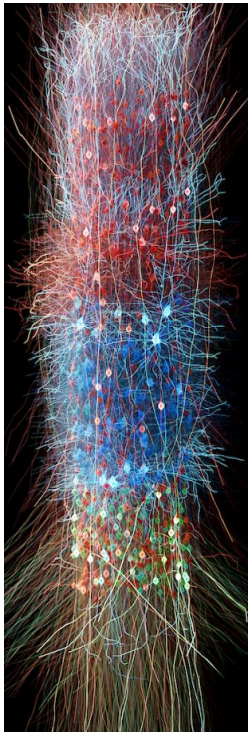
30 million connections

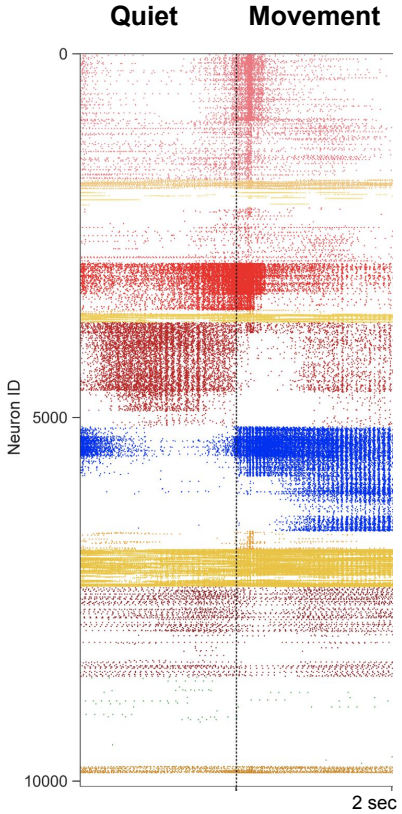


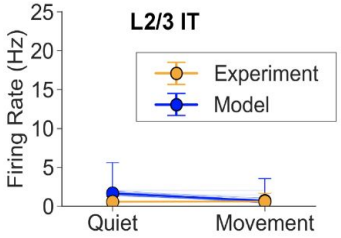
Data-driven model of motor cortex (M1) circuits

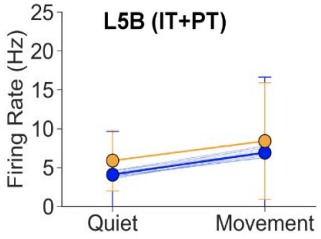


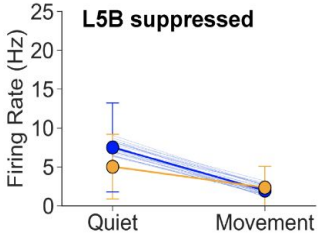
M1 model validated against in vivo data



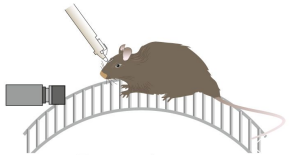


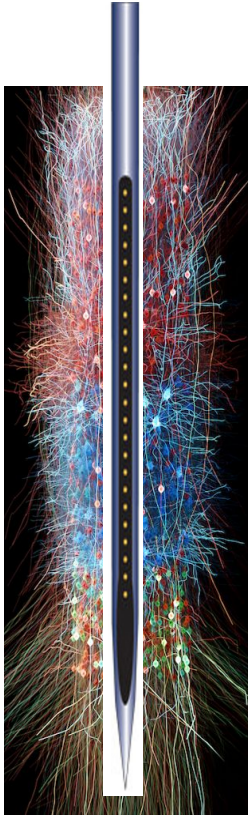




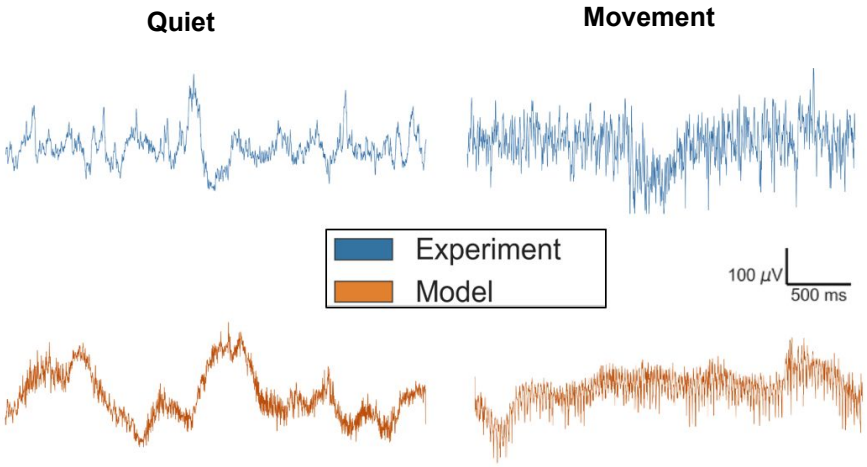


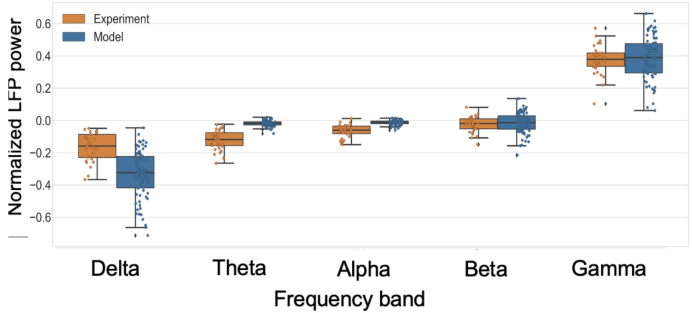
M1 model validated against in vivo data



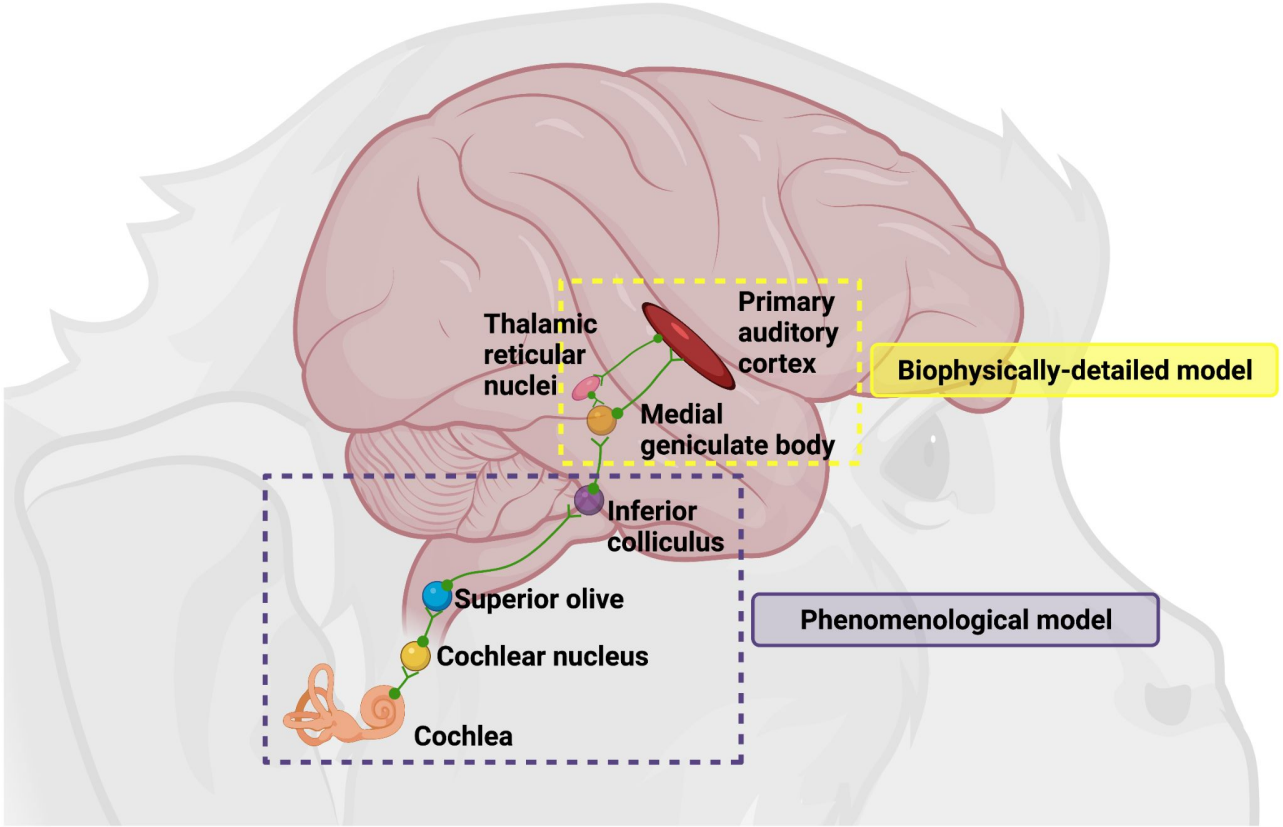


Local Field Potentials (LFPs)



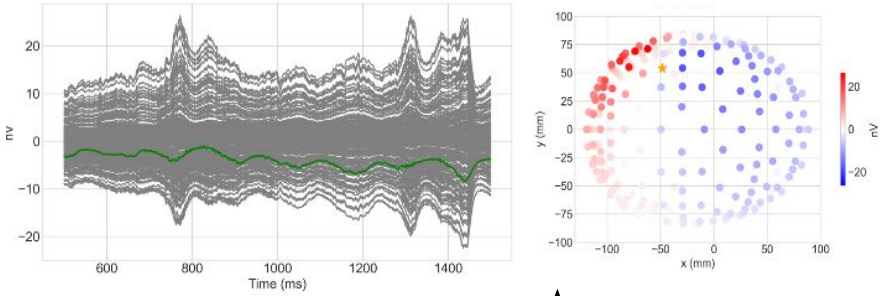


Macaque auditory thalamocortical model

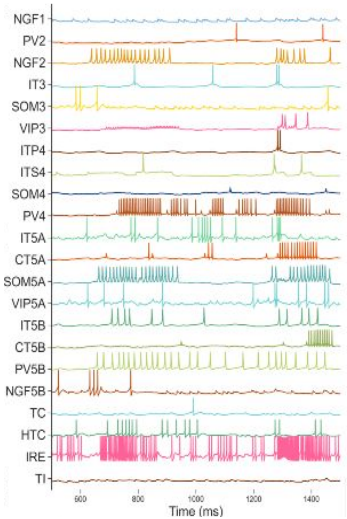


A1 model recordings at multiple scales/modalities

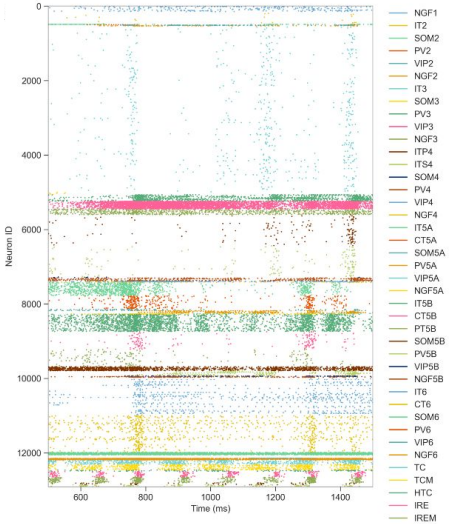
EEG



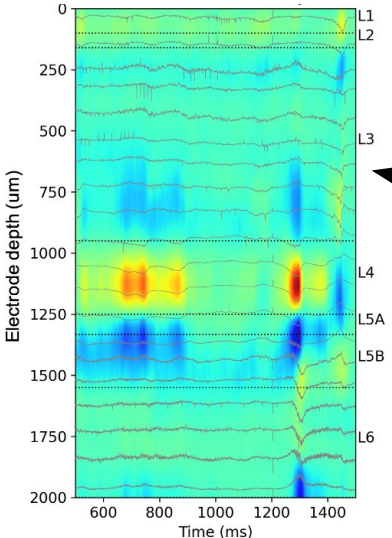
Membrane Voltage

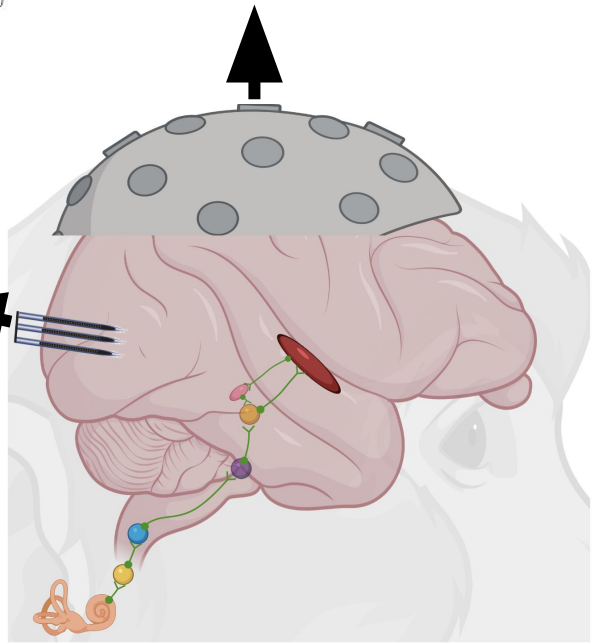


Spikes

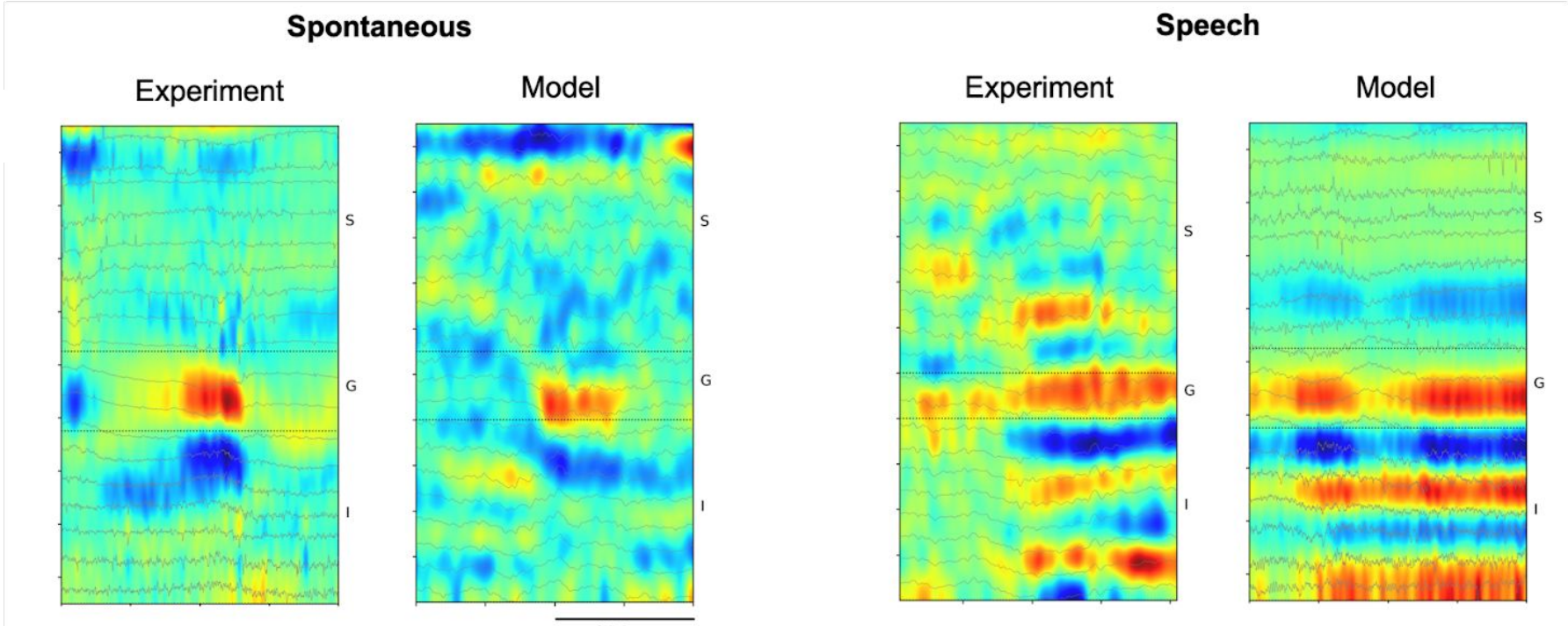


LFP / CSD



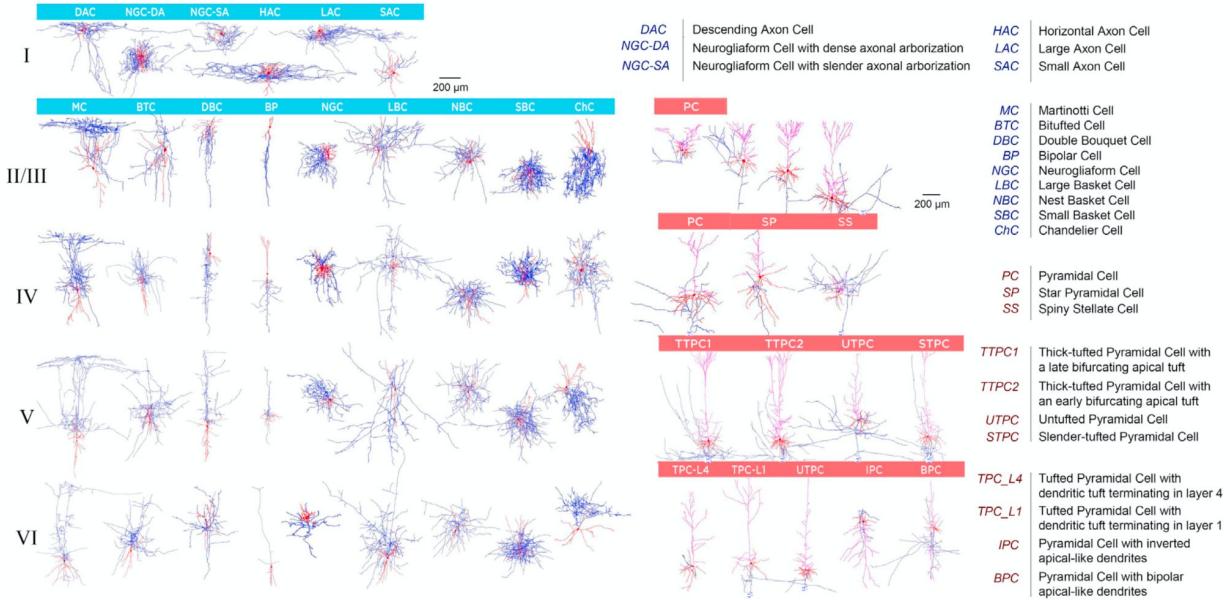


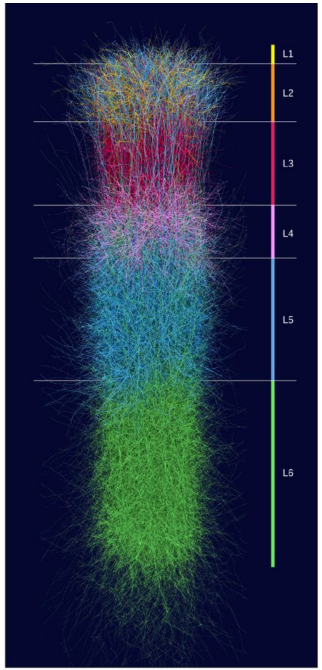
A1 model validated against in vivo data



Somatosensory thalamocortical circuits

- **Highly detailed model: 31k cells, 37M synapses, 207 cell types, 1941 pathways**
- **Original model by EPFL Blue Brain Project**

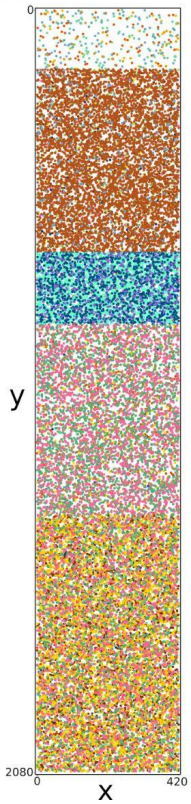


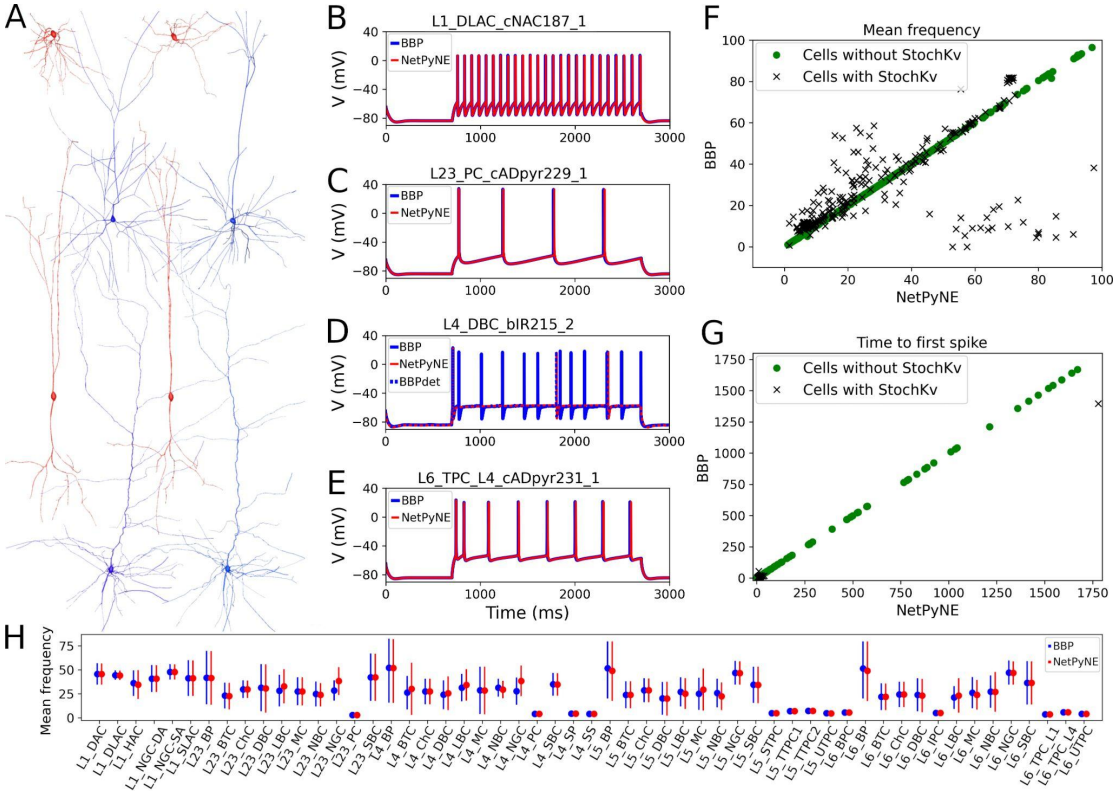


Markram et al, 2015

Somatosensory thalamocortical circuits

- **Reimplemented in NetPyNE**

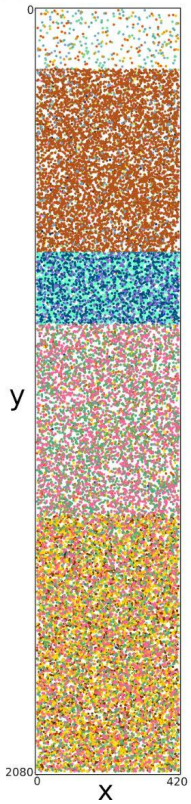


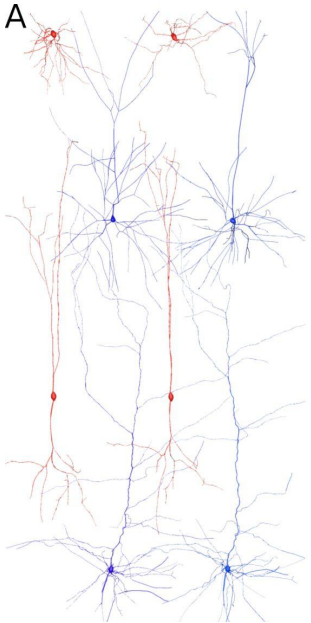


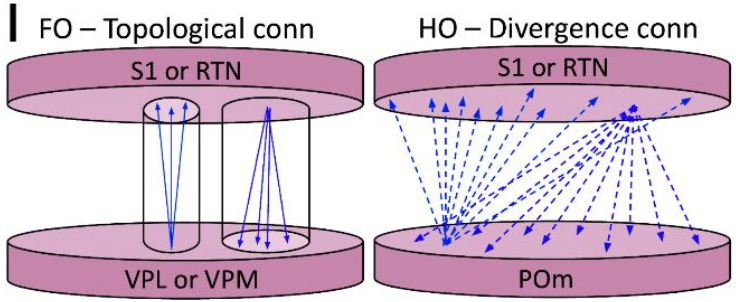
Borges et al, 2021 (CNS, Frontiers, In Prep)

Somatosensory thalamocortical circuits

- **Reimplemented in NetPyNE**
- **Replicated cell properties and connectivity**
- **Extended to include thalamus**

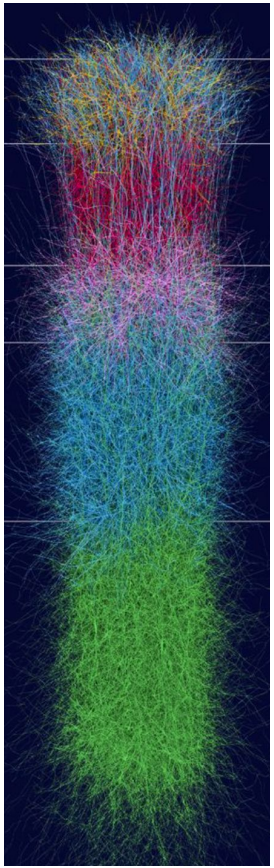


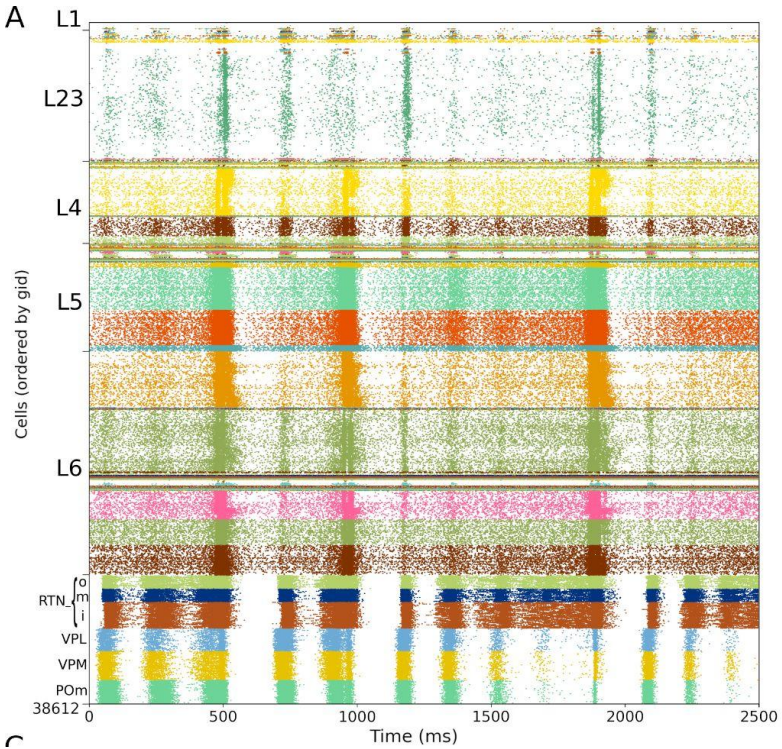


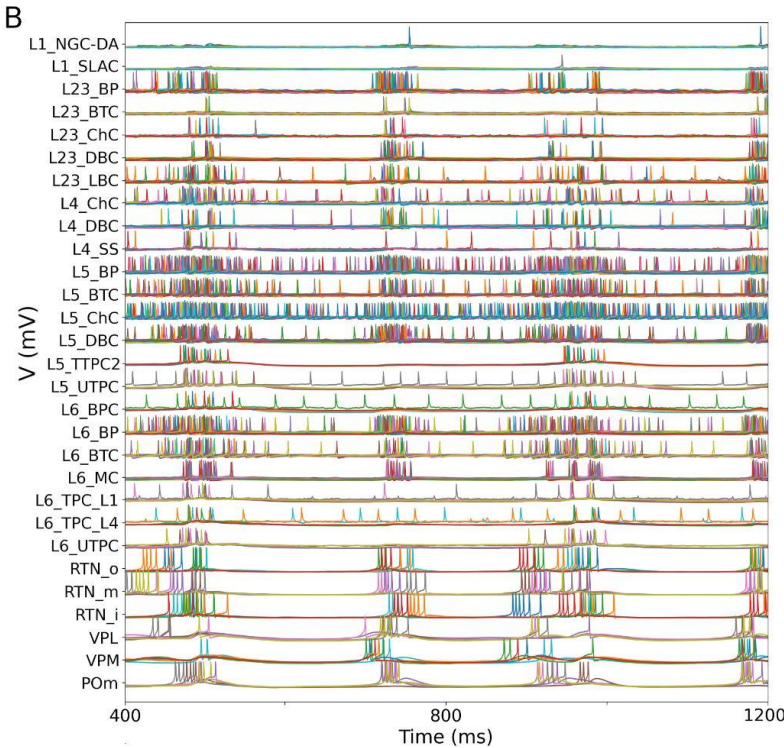


Borges et al, 2021 (CNS, Frontiers, In Prep)

Somatosensory thalamocortical circuits







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NIH U01EB017695, 2014-2021 (M1)

NIH R01DC012947, 2012-2023 (A1)

NIH R01EB022889, 2016-2020 (HNN/NetPyNE)

NIH R01MH086638, 2010-2021 (NEURON RxD)

NYS DOH01-C32250GG, 2017-2022 (M1)

NSF XSEDE TG-IBN160014, 2017-2021 (M1)

SUNY DOWNSTATE Medical Center