Allen Institute Large-scale Datasets and Modeling Tools

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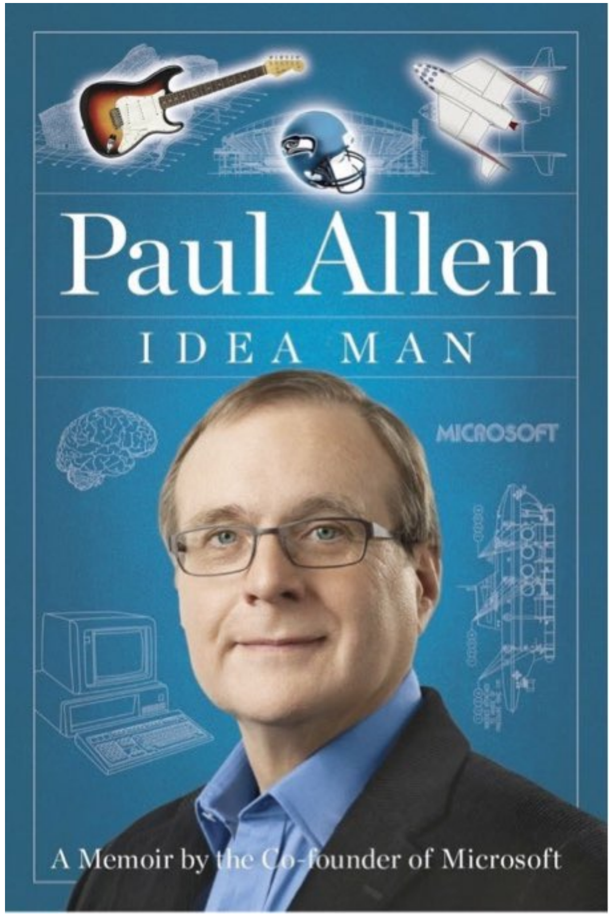
Associate Investigator

A Brief History

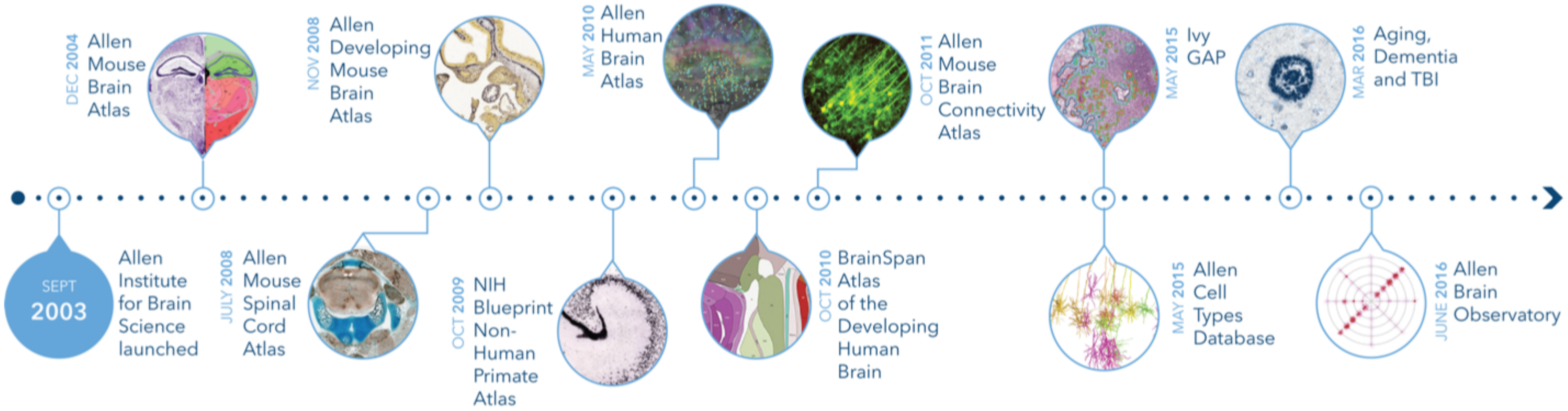
- An independent, non-profit medical research organization, founded in 2003, supporting basic research in the brain sciences

- Culture between a university and a biotech startup, focused on a handful of large projects that can be done at scale and that require tight interactions across disciplines

- Ten-year program initiated in 2012 for building cellular-level observatories for mice and human cortex



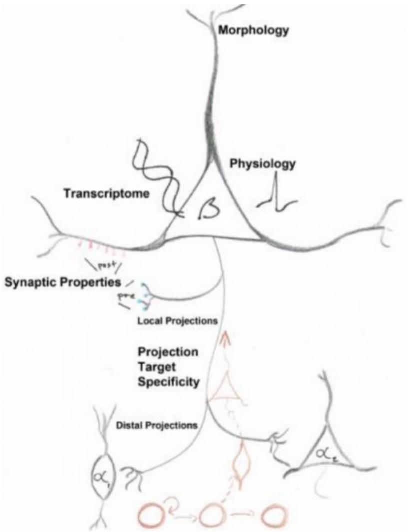
Allen Institute - Online Public Resources
www.brain-map.org

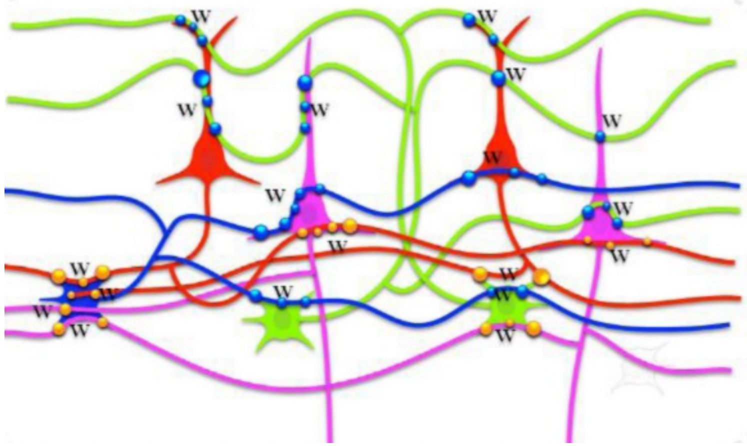


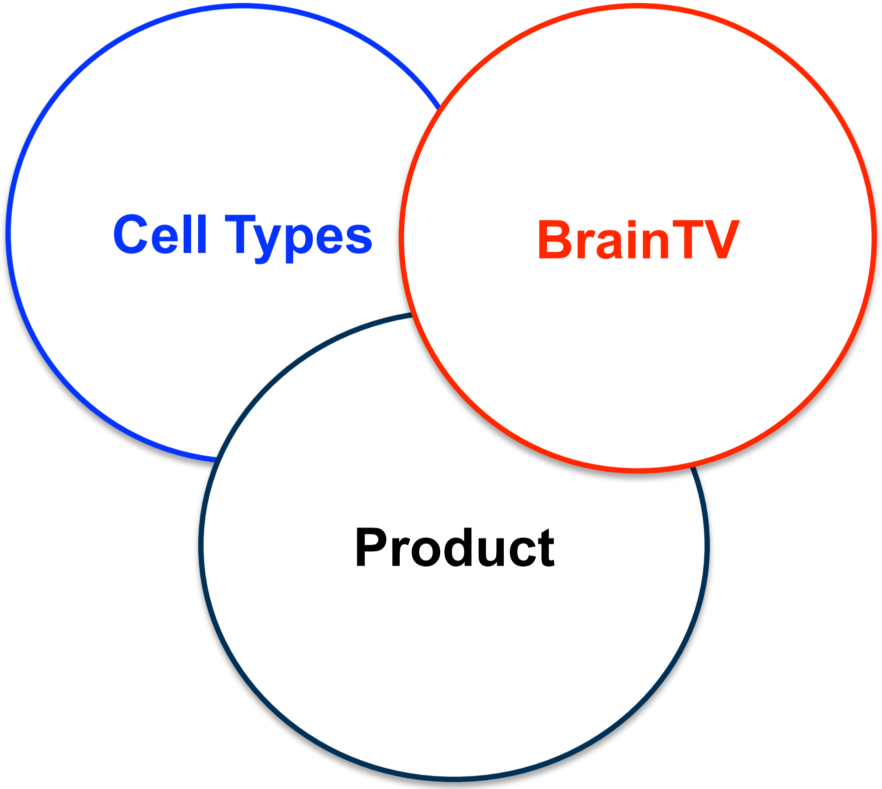
All data are

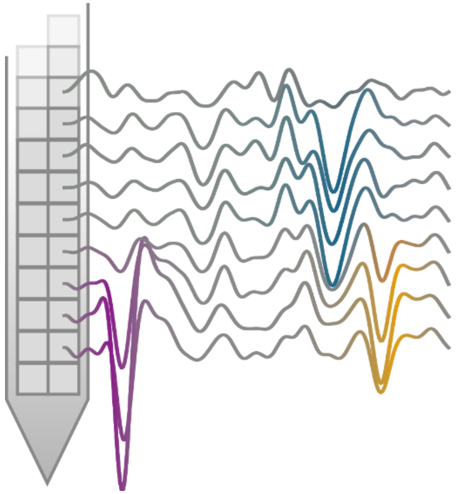
- publicly accessible via API as soon as they pass QC
- freely available without any commercial restrictions
- accessible 1-2 years prior to any publications

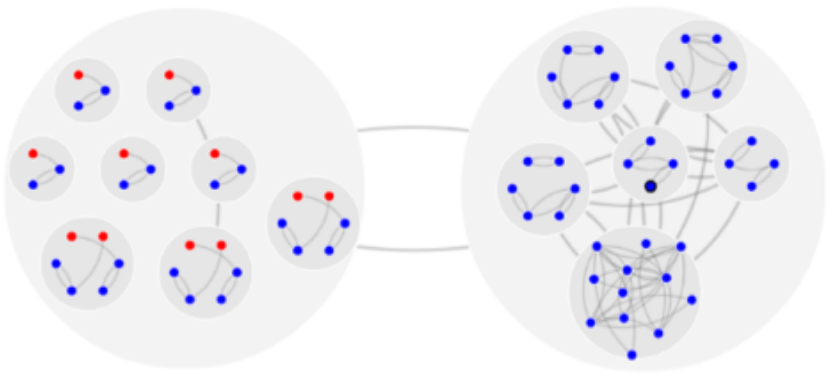
Institute Programs

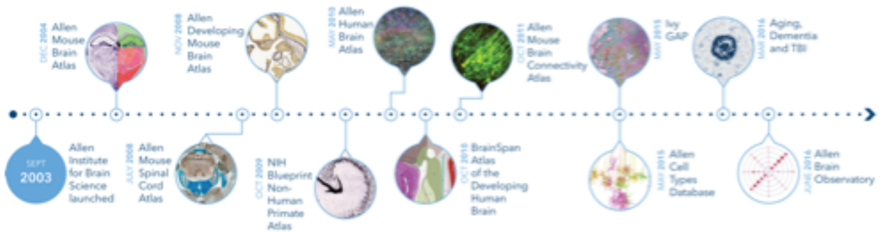


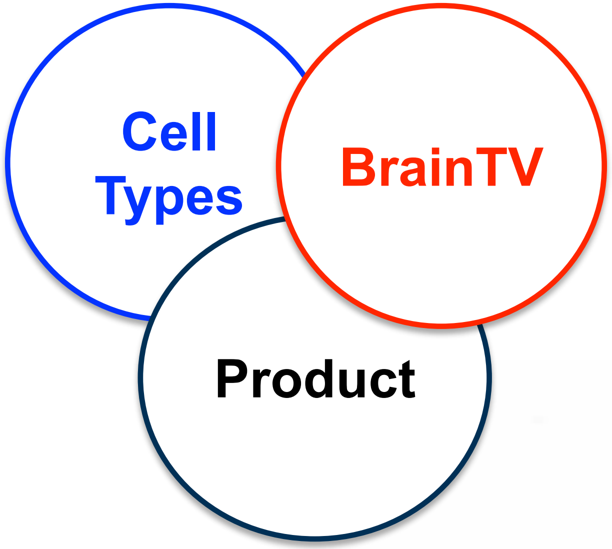






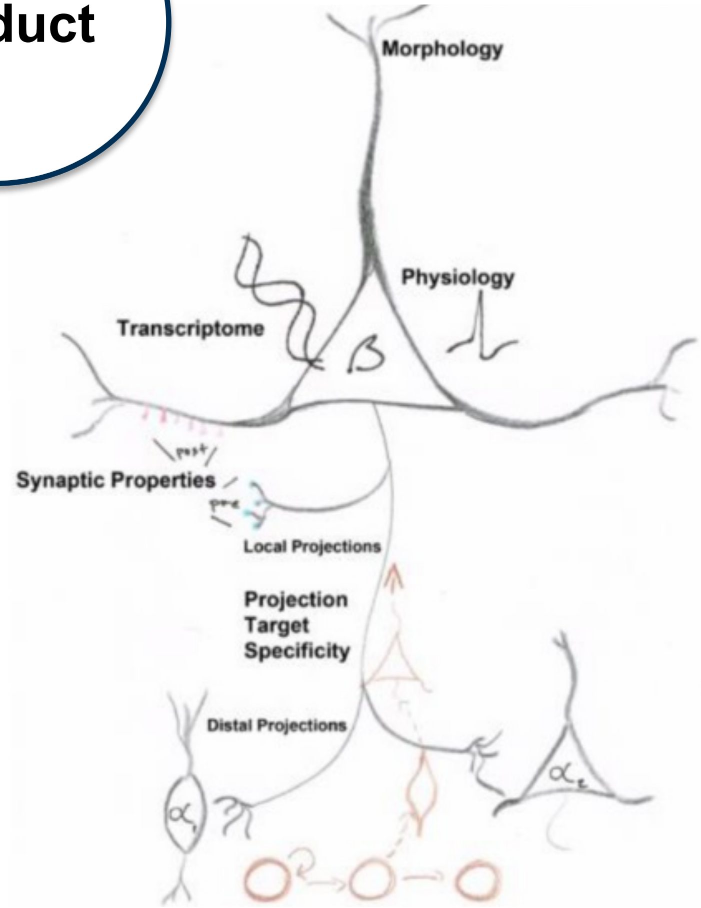


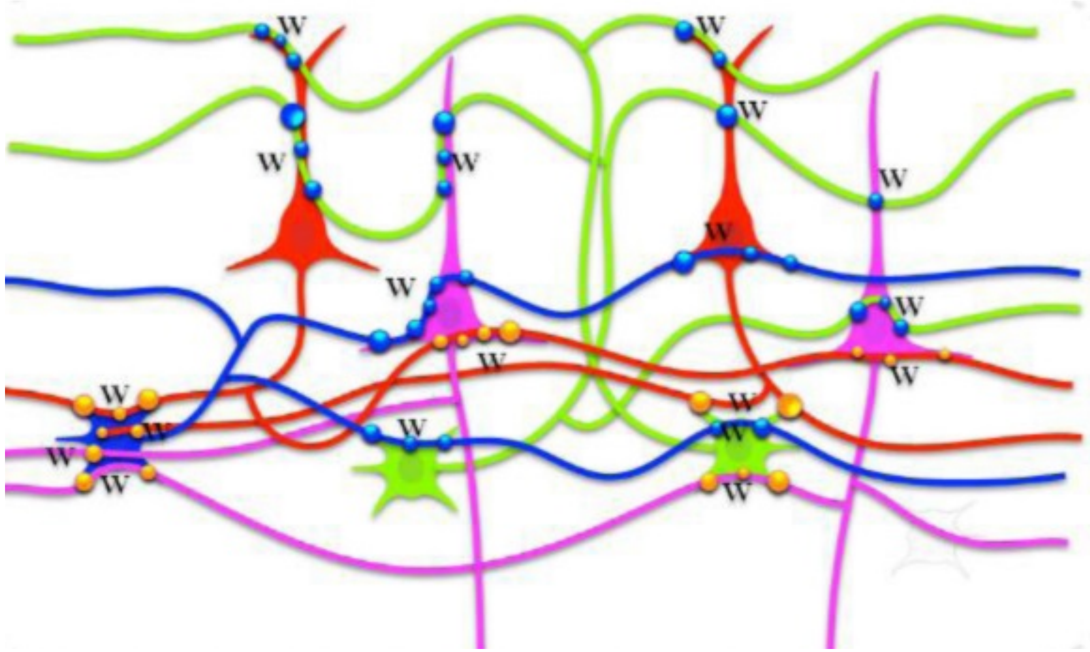




Cell Types Program

Characteristics of cells and connections



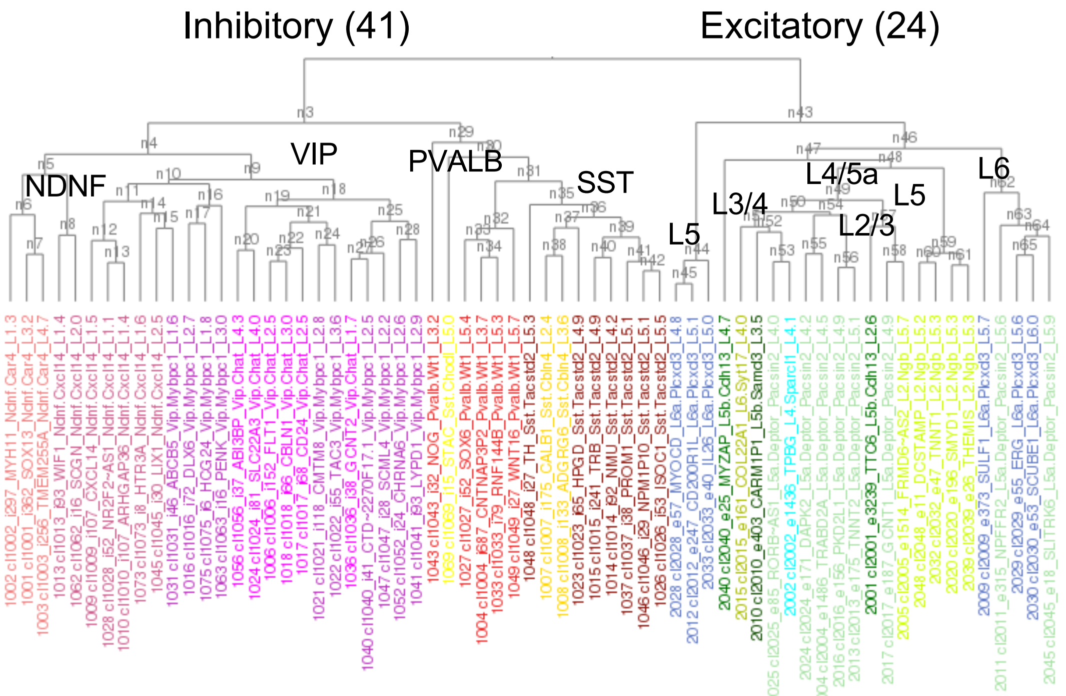


Transcriptomics (Mouse and Human)

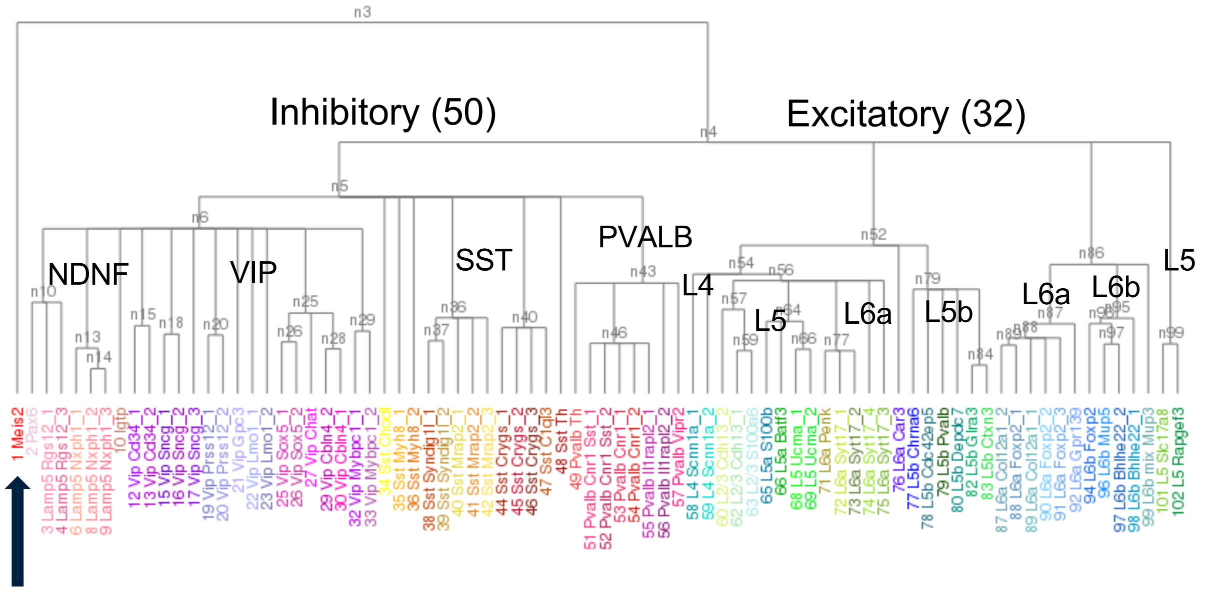
Deliverables: Single-cell transcriptomic data for mouse and human cortical cells, transcriptomic cell type taxonomy.

Scope: Tens of thousands of cells.

Human temporal cortex



Mouse visual cortex



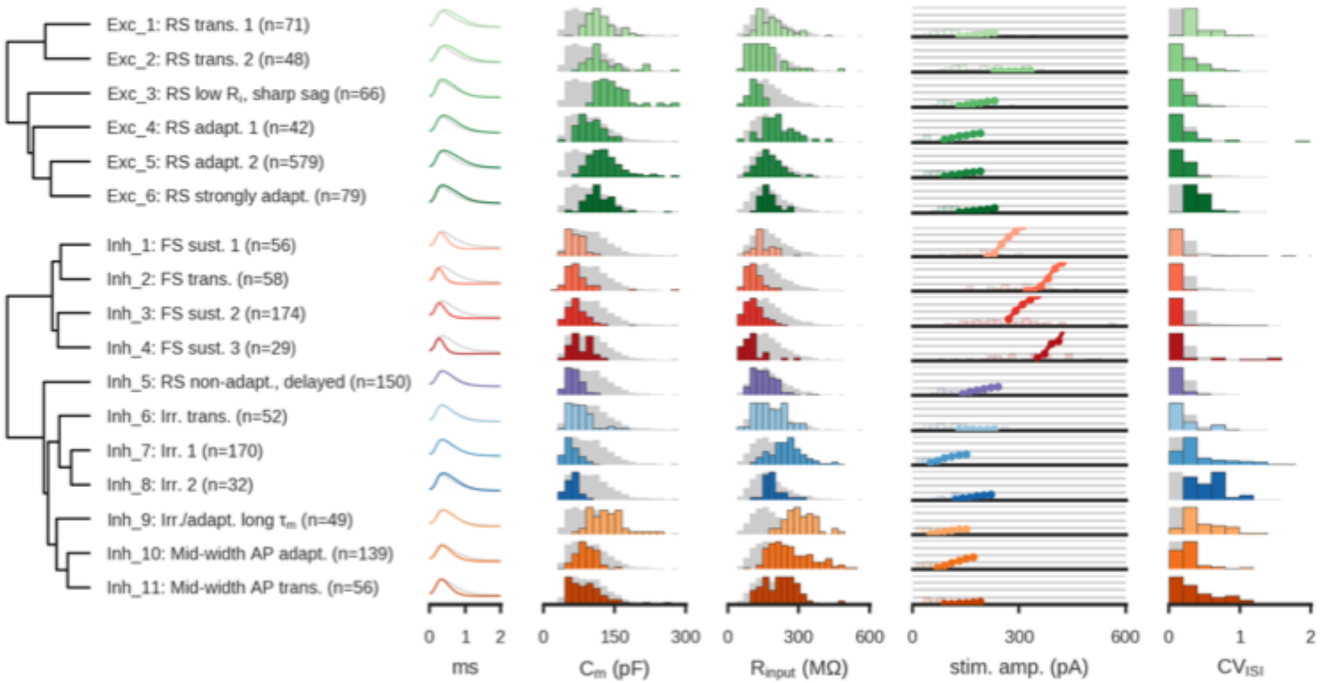
Rare type in deep layer 6 has not yet been sampled in human

Electrophysiology and Morphology of Neurons *in Vitro* (Mouse and Human)

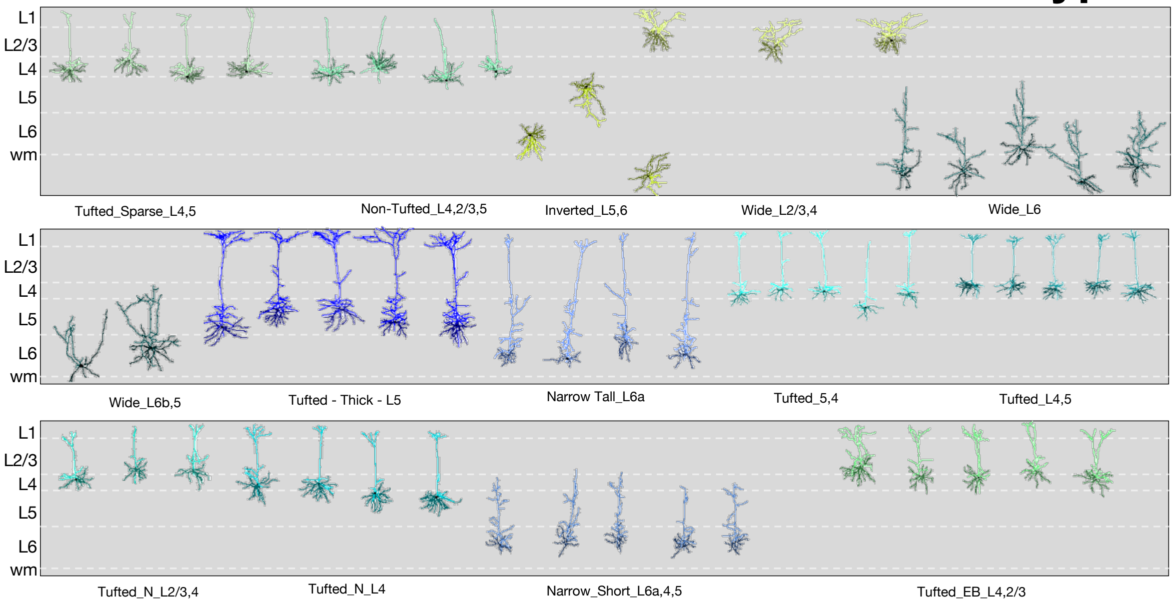
Deliverables: Ephys and morphology data, as well as models, for cortical cells; morphological and physiological classification of cell types.

Scope: Thousands of cells in the mouse visual cortex and human middle temporal gyrus (MTG).

e-types



m-types

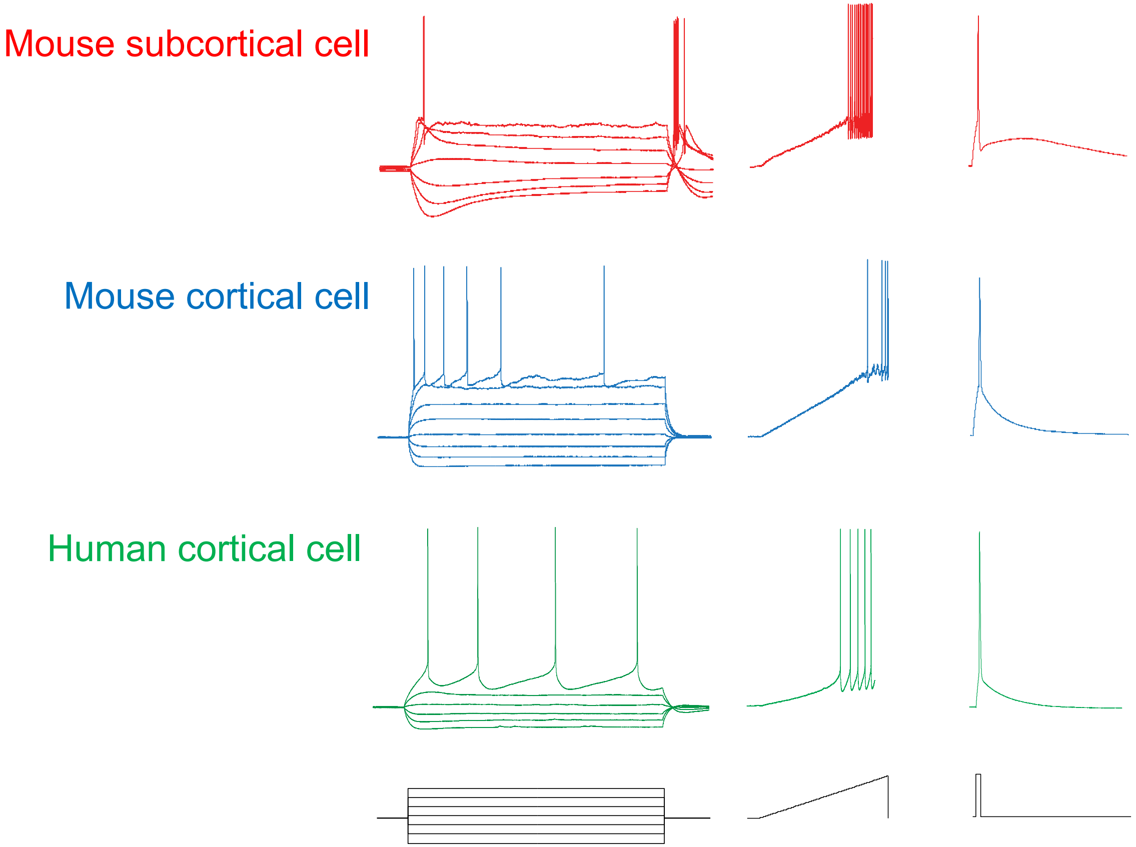


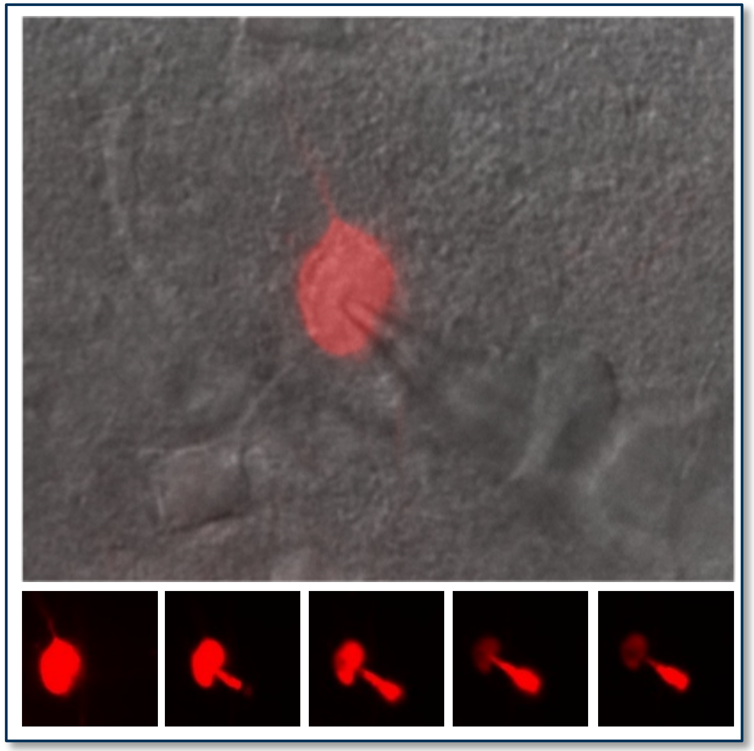
http://celltypes.brain-map.org

Mouse and Human Patch-Seq

Deliverables: Transcriptomic, ephys, and morphology data, as well as models, for mouse and human cortical cells.

Scope: Thousands of neurons in mouse and human.

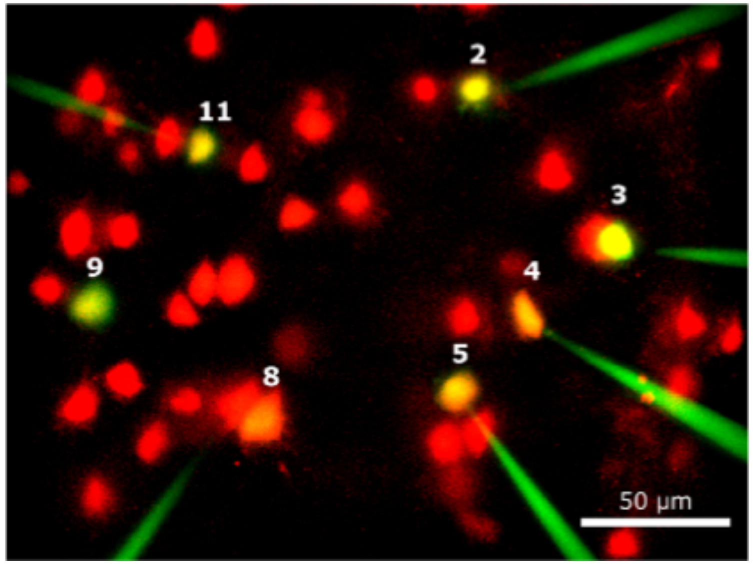


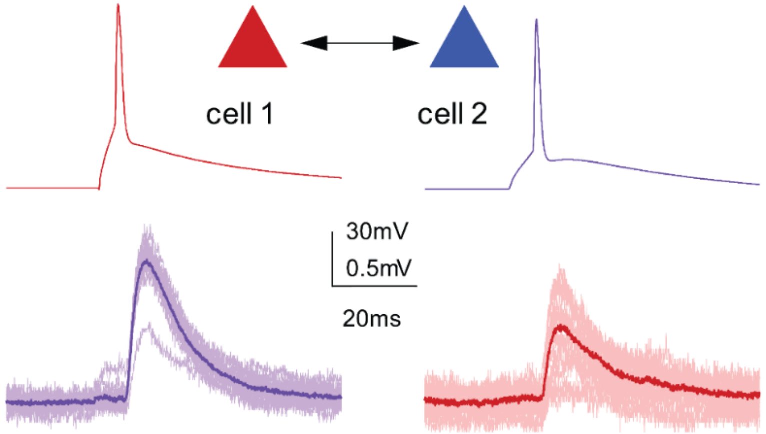


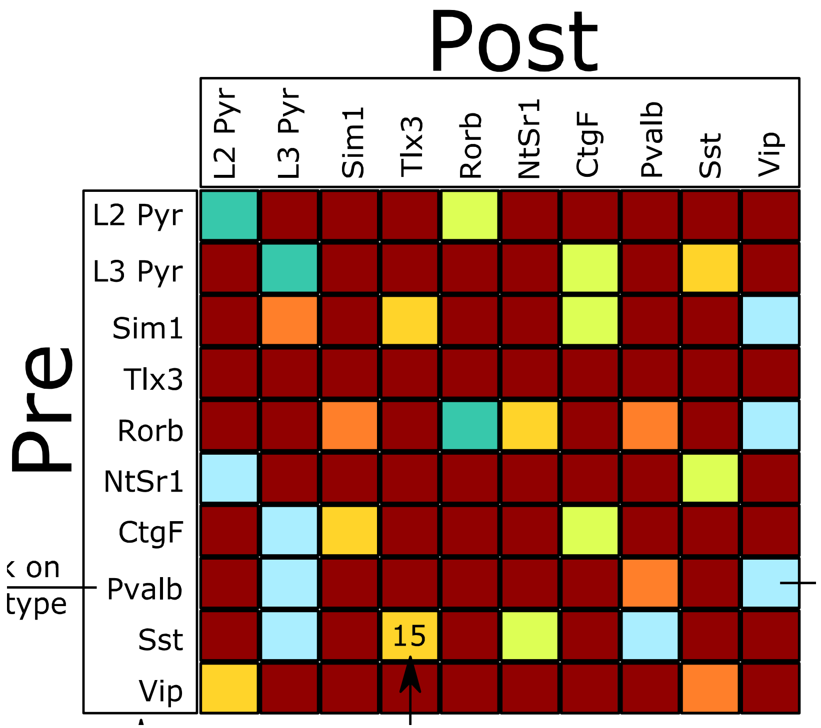
Mouse and Human Synaptic Physiology

Deliverables: Connection probabilities, synaptic strength, and short-term plasticity properties for connections between cortical cell types in mouse and human.

Scope: Initially 50-100 connections per matrix element; approximately 10x10 matrix (i.e., ~10 “cell types”) in mouse and as close to this plan as possible in human. Expand to study specific cell types and correspondence of transcriptome to connectivity in later years.



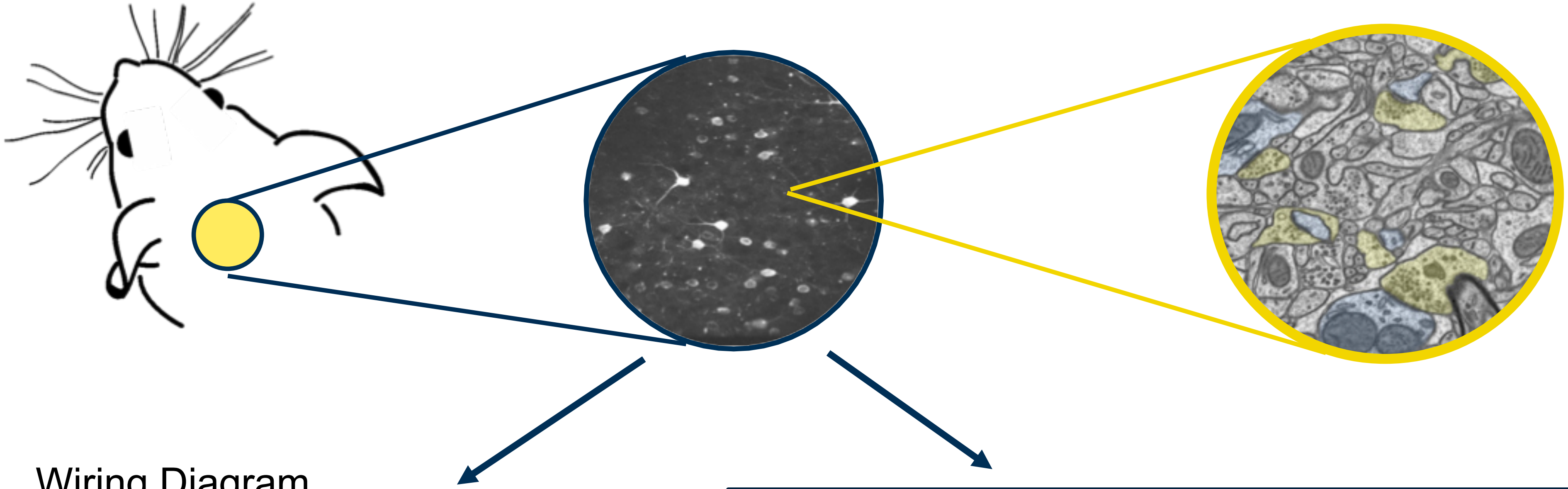




Mouse and Human EM Connectomics

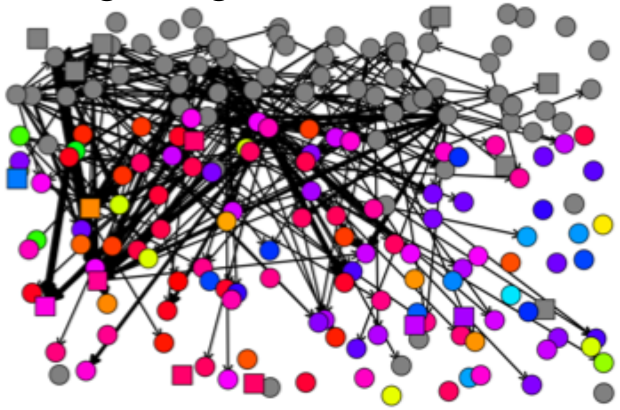
Deliverables: Reconstruction of neuronal morphologies and the connectivity matrix in the local cortical circuit – 1 mm^3 in mouse V1 and 2 mm^3 in human MTG.

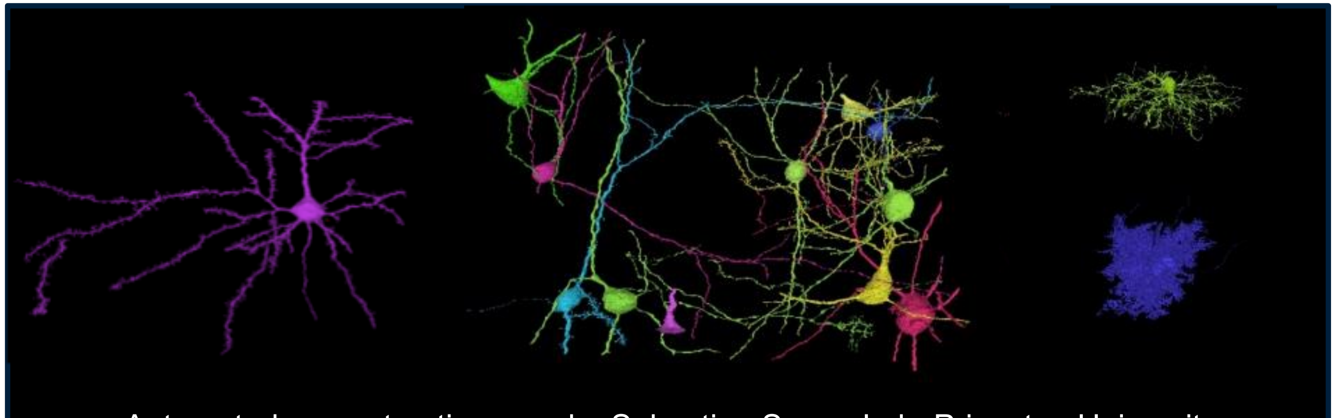
Scope: ~100,000 neurons (in the mouse, most of the neurons would be functionally characterized *in vivo*).



Cell Types

Wiring Diagram

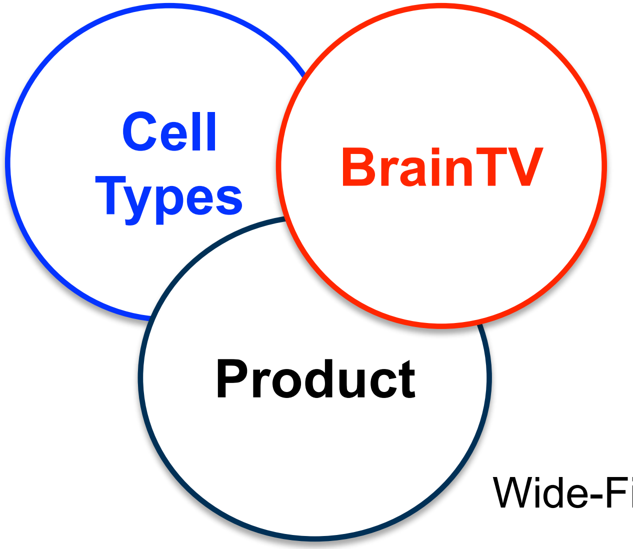




Automated reconstructions are by Sebastian Seung Lab, Princeton University

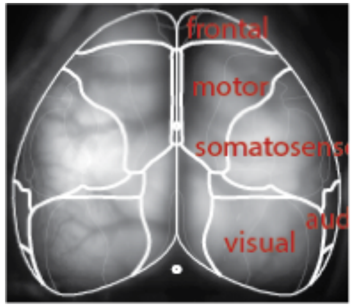
Ca^{2+} imaging is by Andreas Tolias lab, Baylor and by the Allen Institute

BrainTV Program

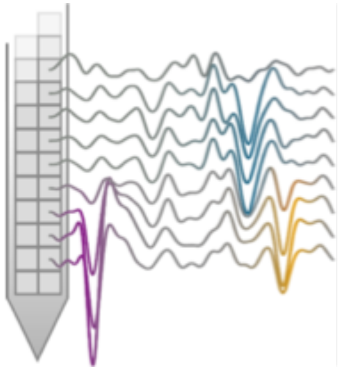


Activity and Computations in Cortical Circuits *in Vivo*

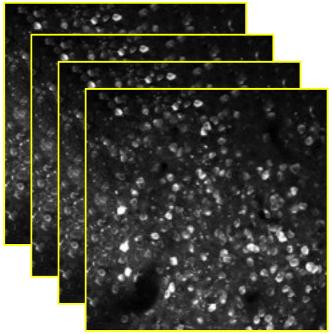
Wide-Field Imaging



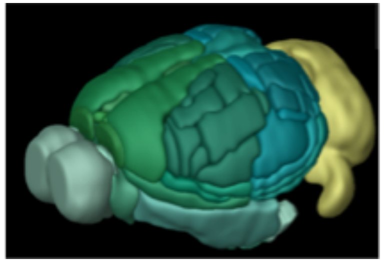
Ephys – Neuropixels Probes



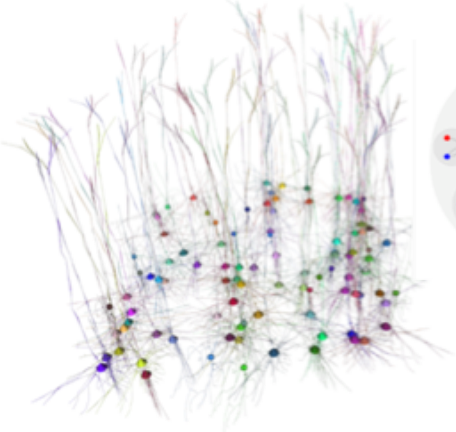
2p cellular imaging



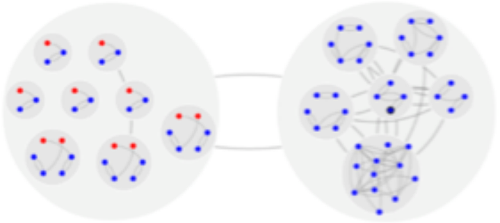
Population Statistics &
Machine Intelligence Networks



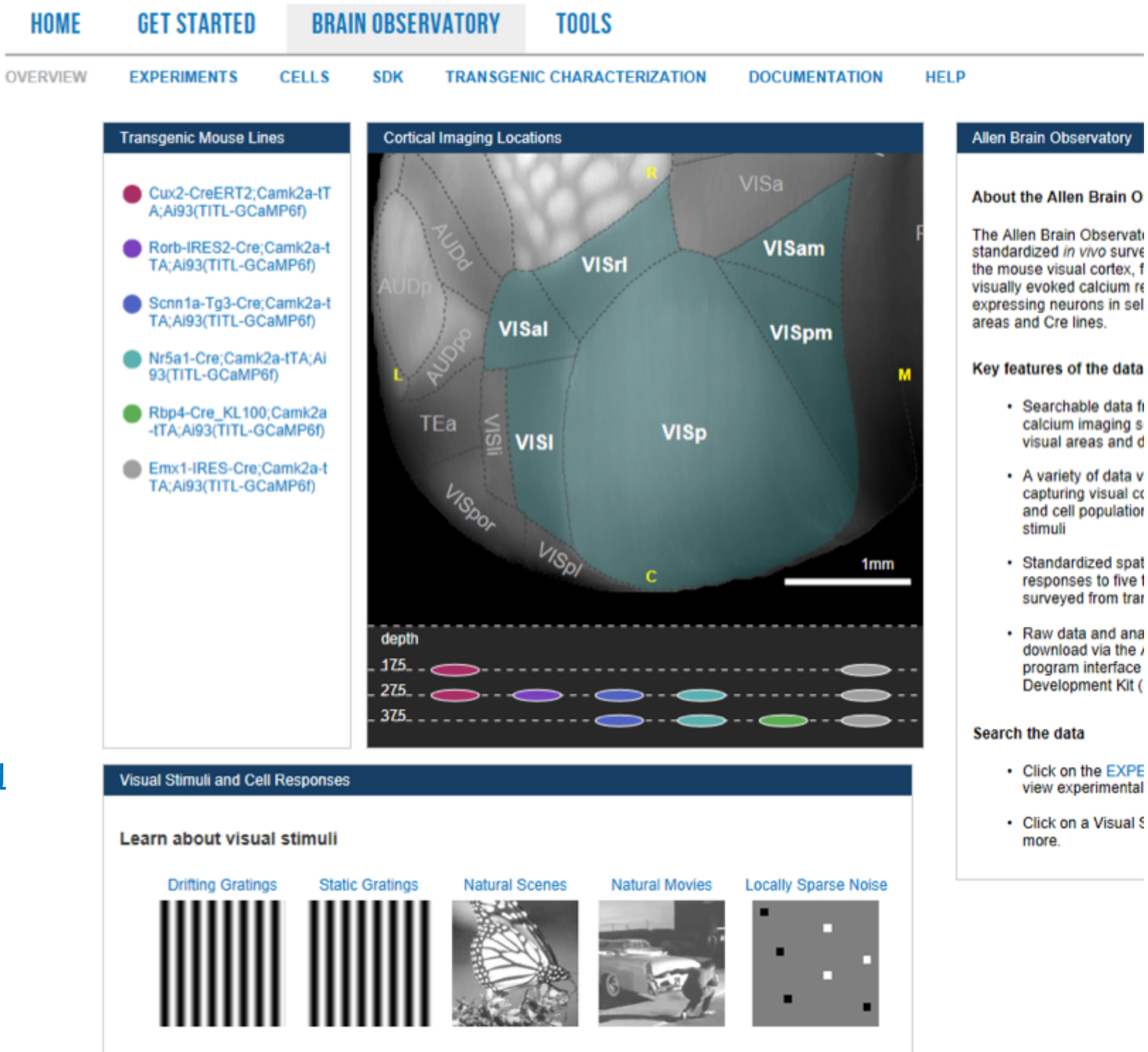
Biophysical Modeling



Point Neuron &
Filter Networks



Visual Coding



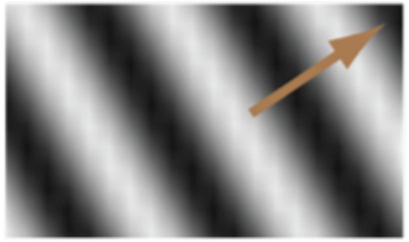
Deliverables:
Ophys and ephys data for neuronal responses in the mouse cortex in vivo.

Scope:
Tens of thousands of cells for ophys; tens of thousands of units for ephys; ~10 cortical areas.

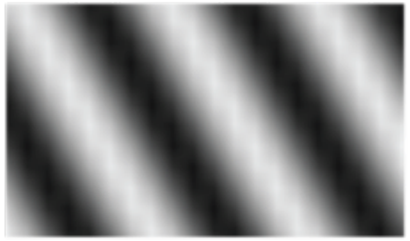
Allen Brain Observatory
http://observatory.brain-map.org/visualcoding

Allen Brain Observatory – in Vivo Ca^{2+} Imaging

Drifting Gratings



Static Gratings

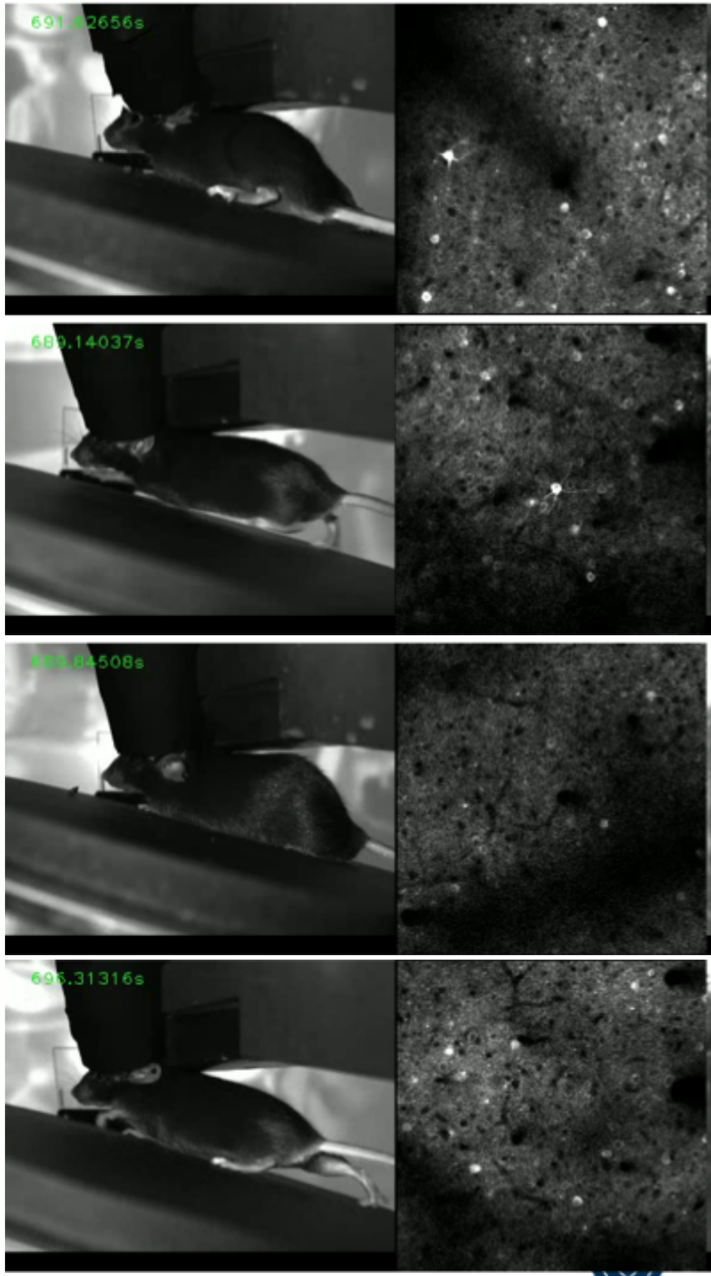


Locally sparse noise

Natural Scenes

Natural Movies

Spontaneous Activity

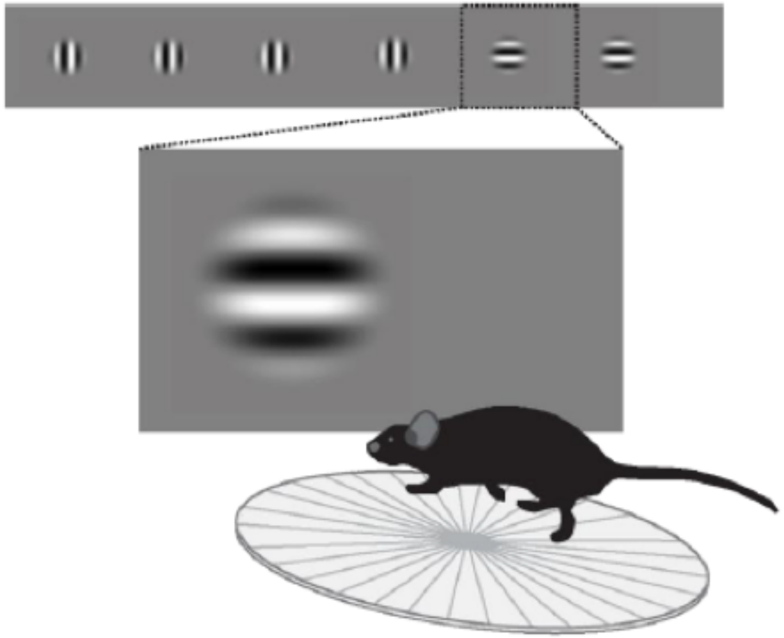


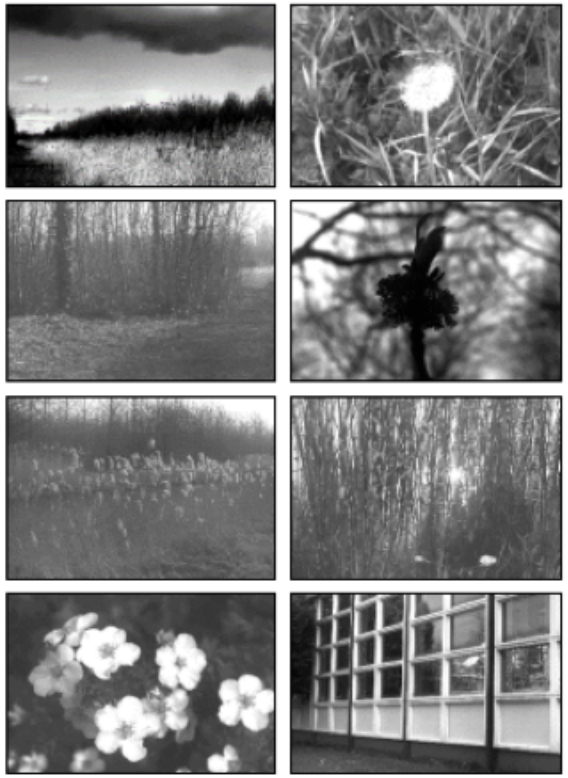
One location – V1 – Cux2 – Layer 2/3

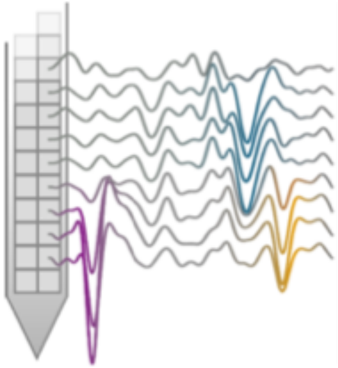
Visual Behavior

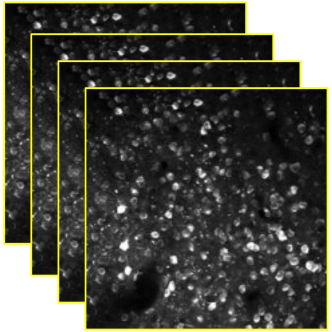
Deliverables:
Ophys and ephys data for single-cell responses in the mouse cortex in vivo, in the context of a change detection behavior.

Scope:
Tens of thousands of cells for ophys; tens of thousands of units for ephys.









Models of V1 and of Multiple Cortical Areas

V1 Models

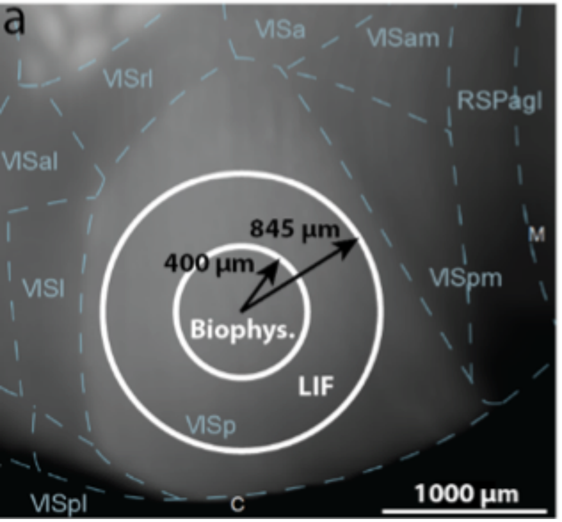
Deliverables: A series of models of the V1 cortical column, employing biophysical and point-neuron approaches.

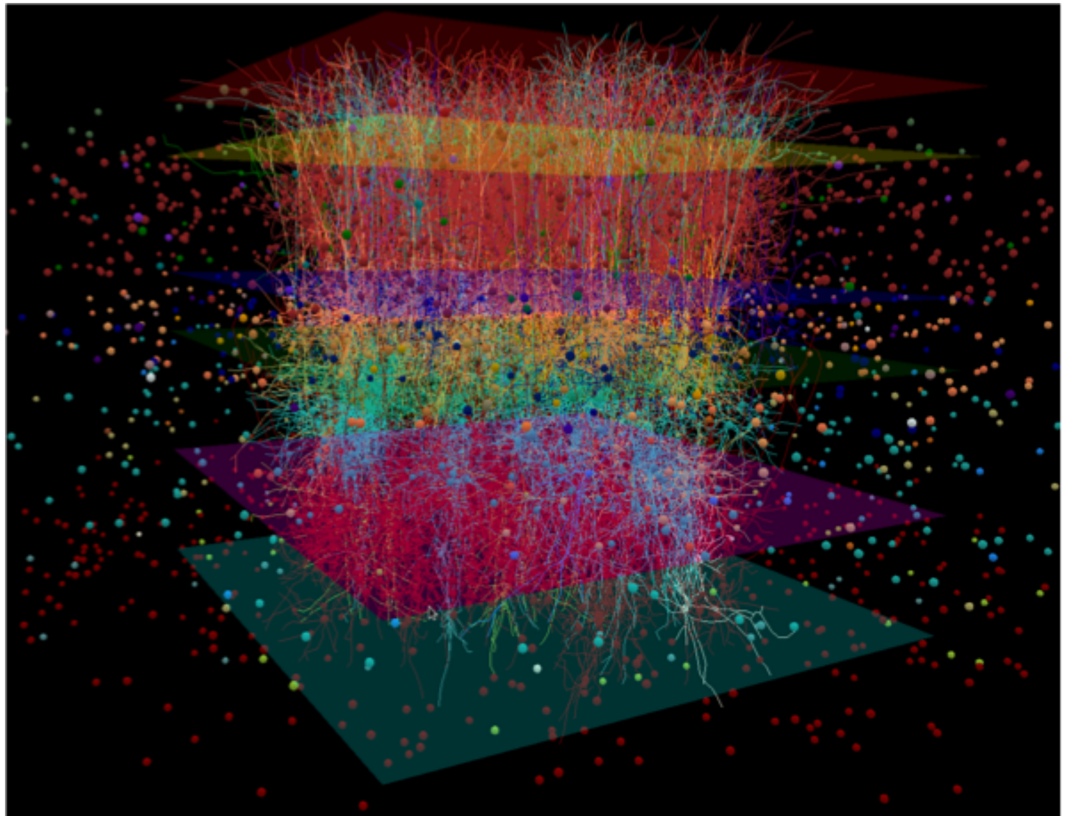
Scope: Representation of all cortical layers in V1, ~200,000 cells.

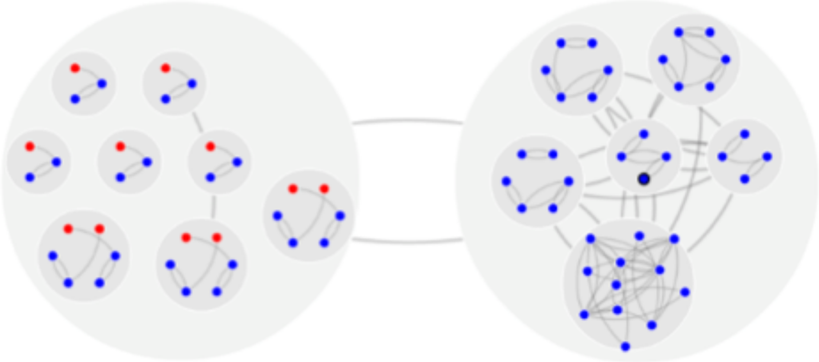
Cortex Models

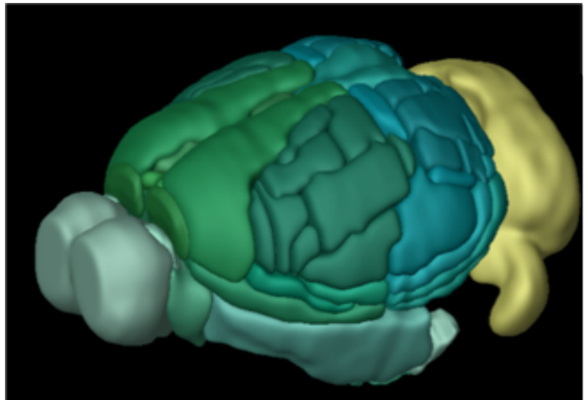
Deliverables: A series of models of multiple cortical areas in the context of behavior, employing point-neuron and machine intelligence approaches.

Scope: Several visual and, potentially, a number of non-visual areas.

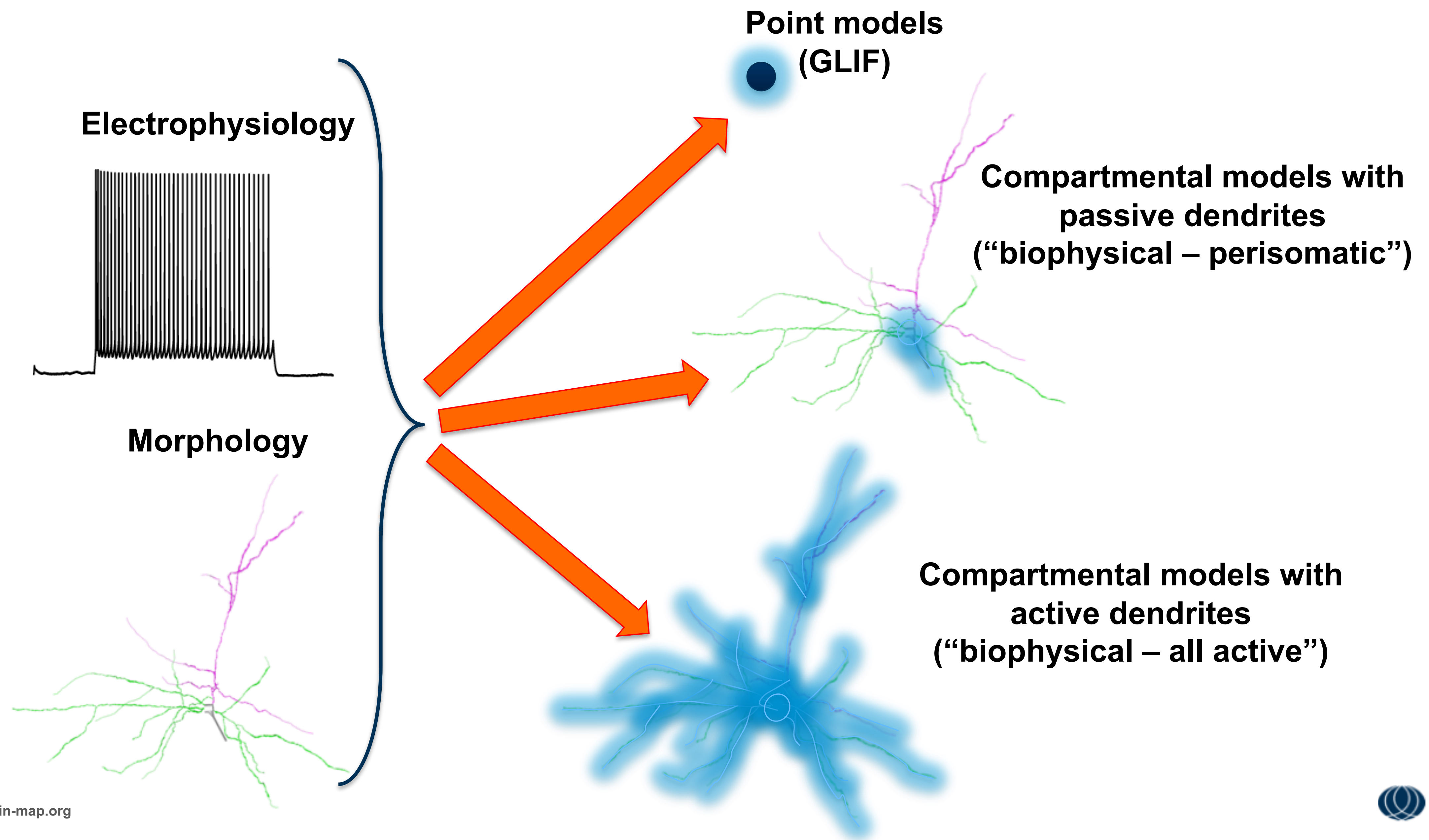




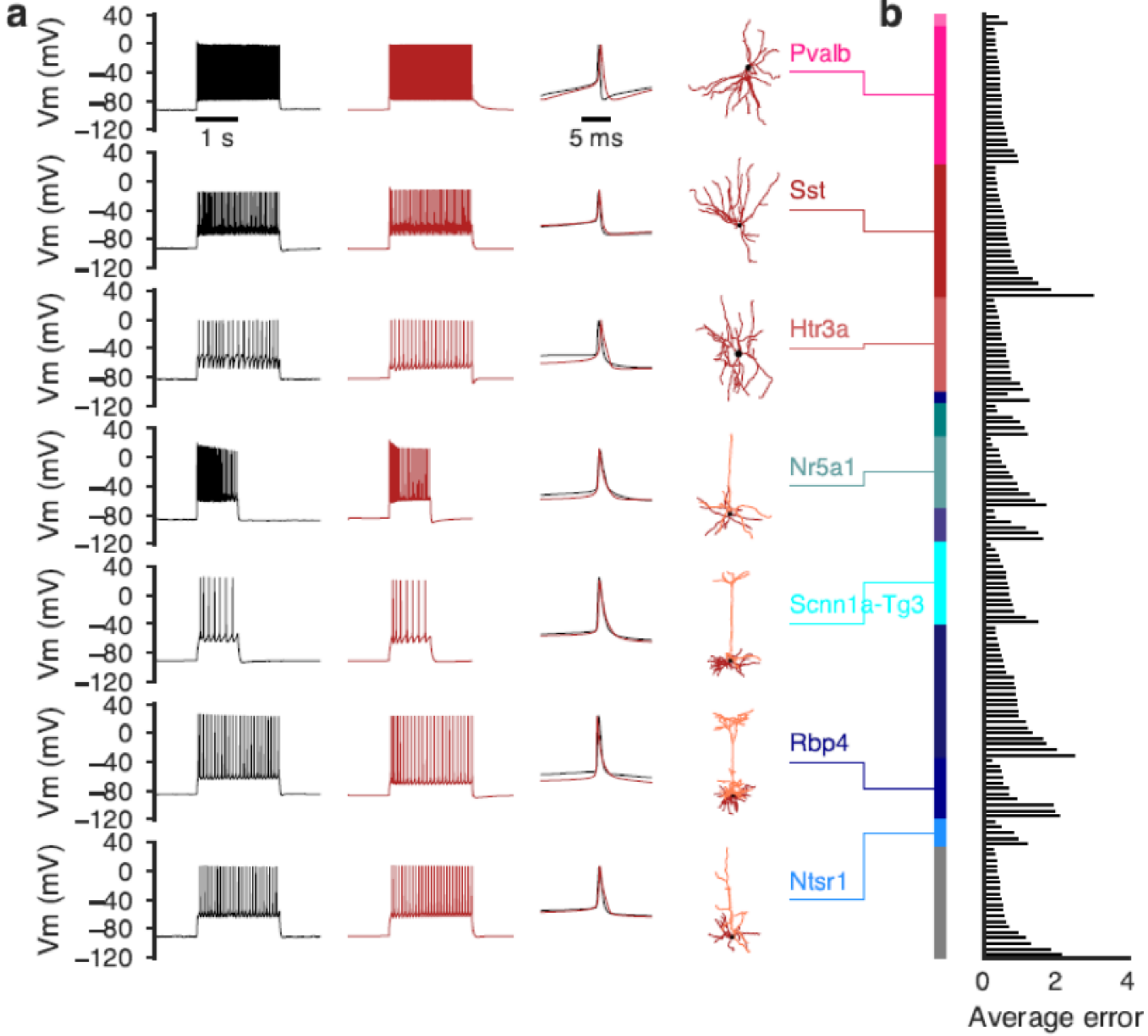




From Slice Data to Neuronal Models



Biophysical Models of Individual Neurons



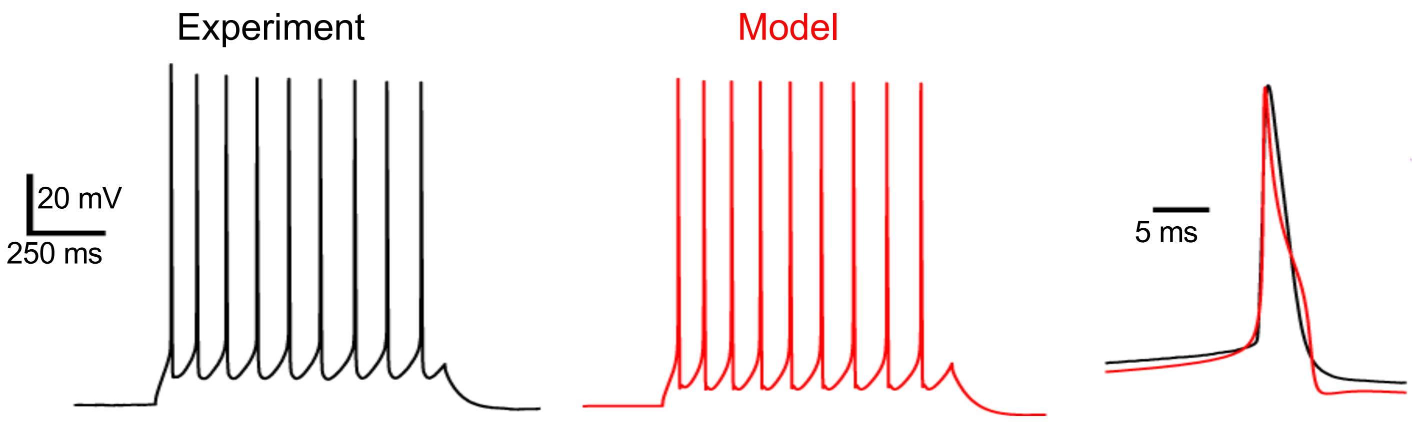
Gouwens et al.,

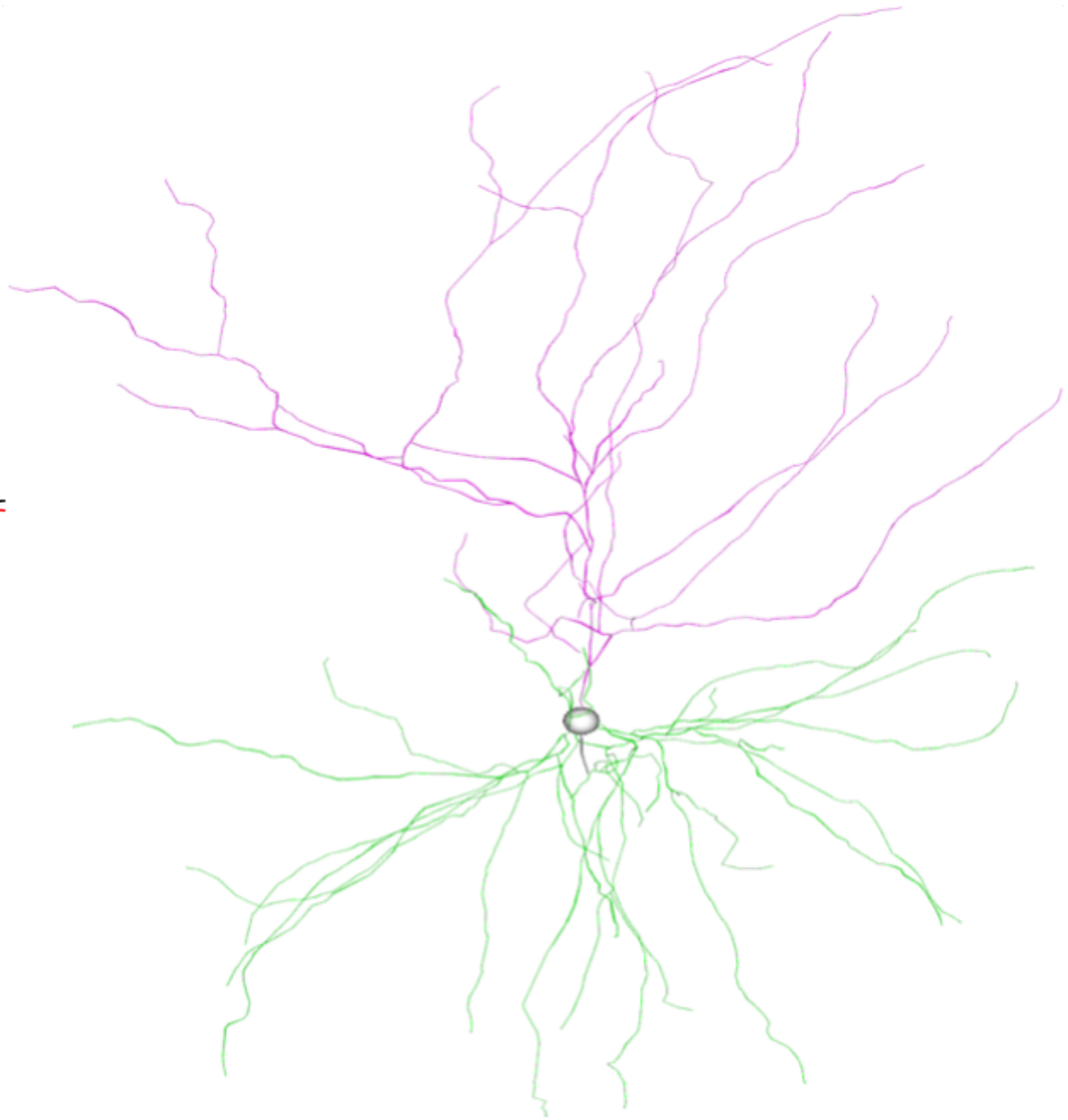
Nature Communications, in press.

Teeter et al.,

Nature Communications, in press.

Biophysical Models of Human Cells



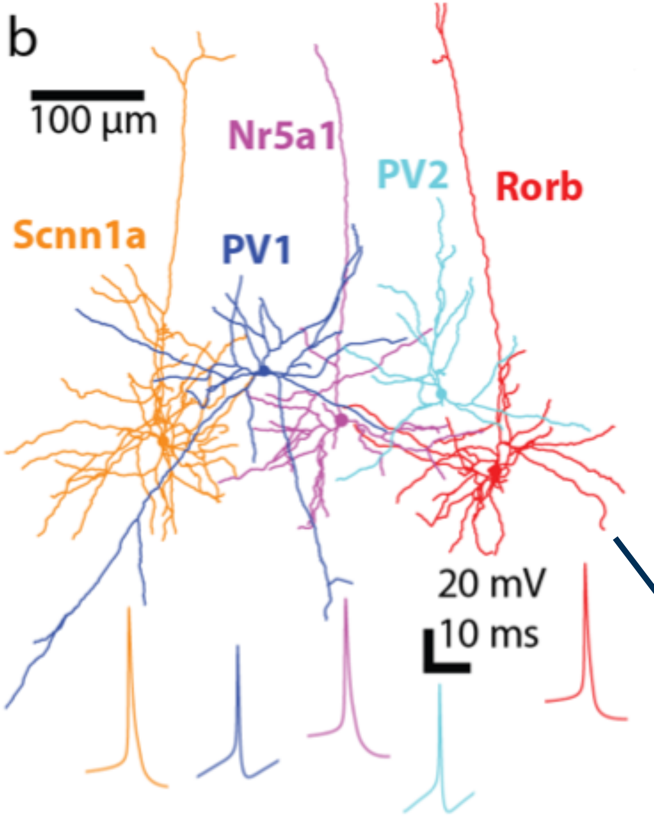


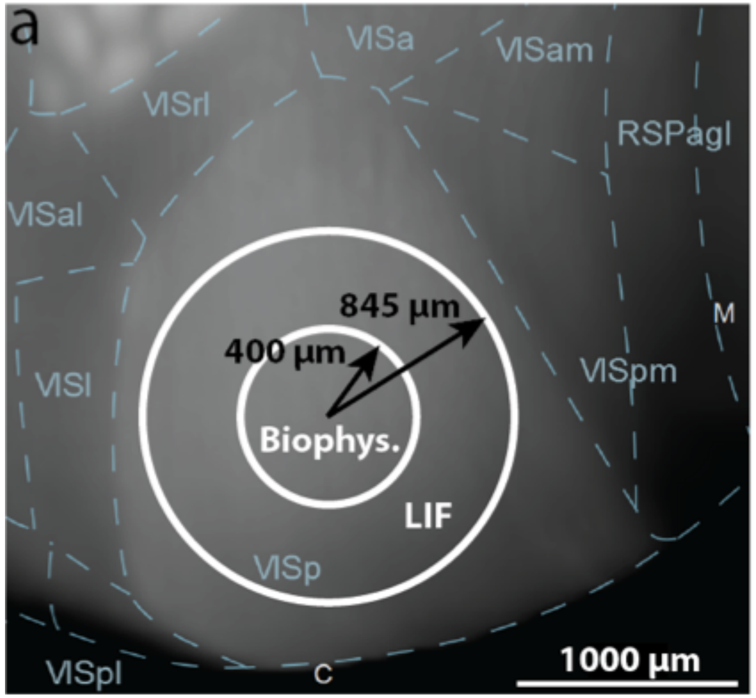
- The same optimization procedure as for mouse cells has worked successfully for the human neurons
- 43 biophysical models of human neurons are currently available in the Allen Cell Types Database

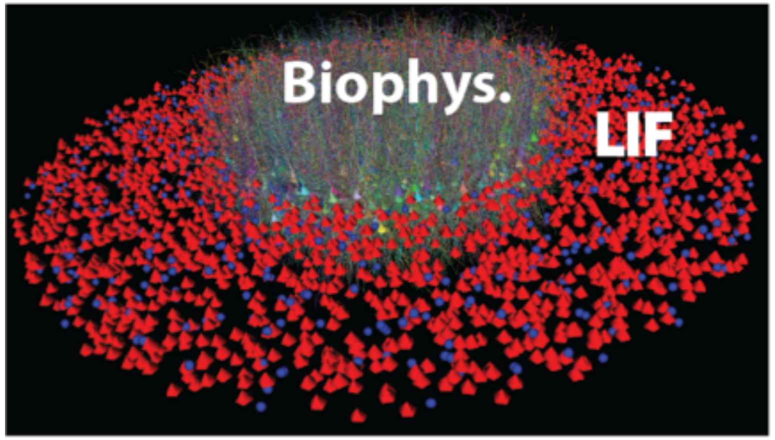
Biophysical Model of the Layer 4 of Mouse V1

Models of Individual Cells

`celltypes.brain-map.org`



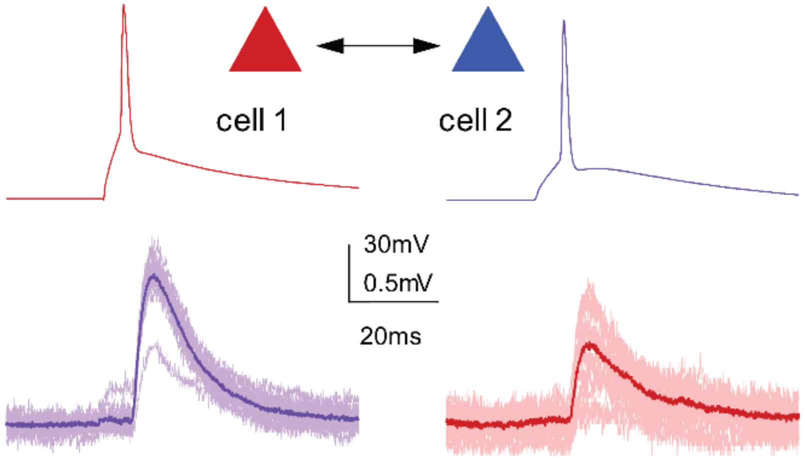




10,000 biophysically detailed neurons

35,000 LIF point neurons

Connectivity and Synaptic Properties



Wu et al., Mol. Brain (2009)

Perin et al., PNAS (2011)

Ko et al., Nature (2011)

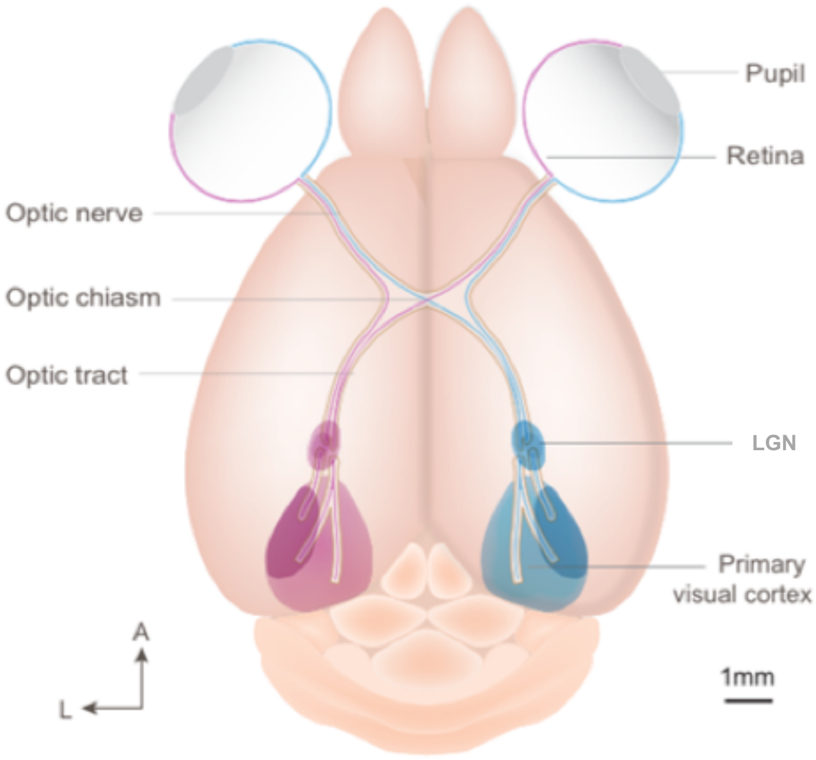
Cossell et al., Nature (2015)

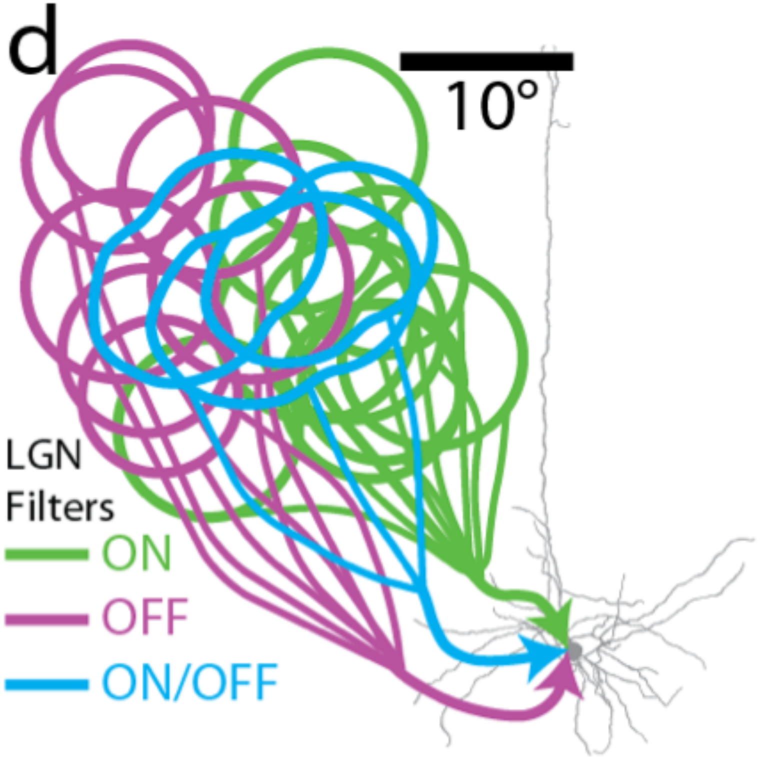
Lee et al., Nature (2016)

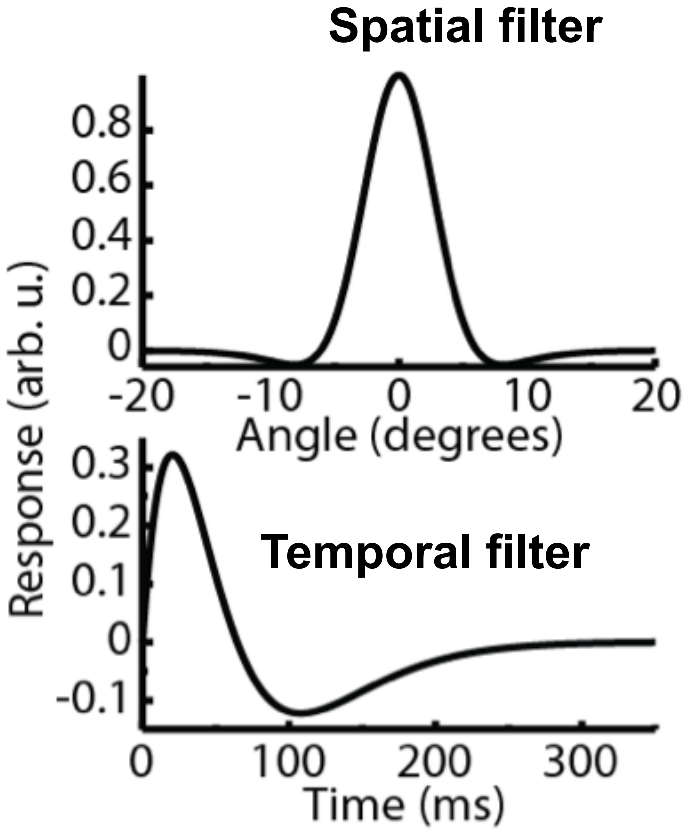
…

Model of Thalamic Inputs

- 9,000 LGN filters
- **3 ‘types’: ON, OFF, ON/OFF**
- Retinotopy based connectivity rules from LGN to L4.

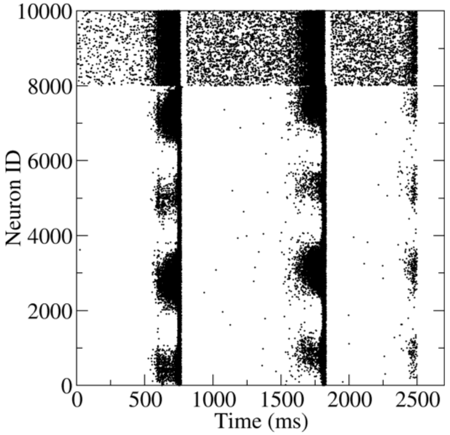


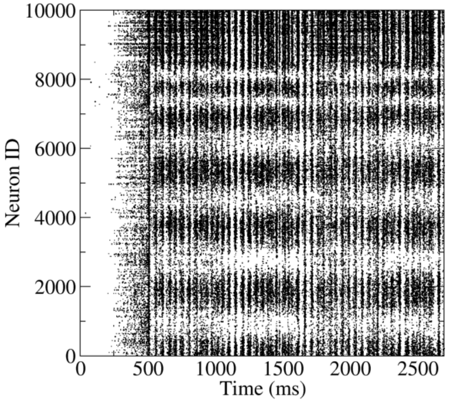




Model Tuning and Production Runs

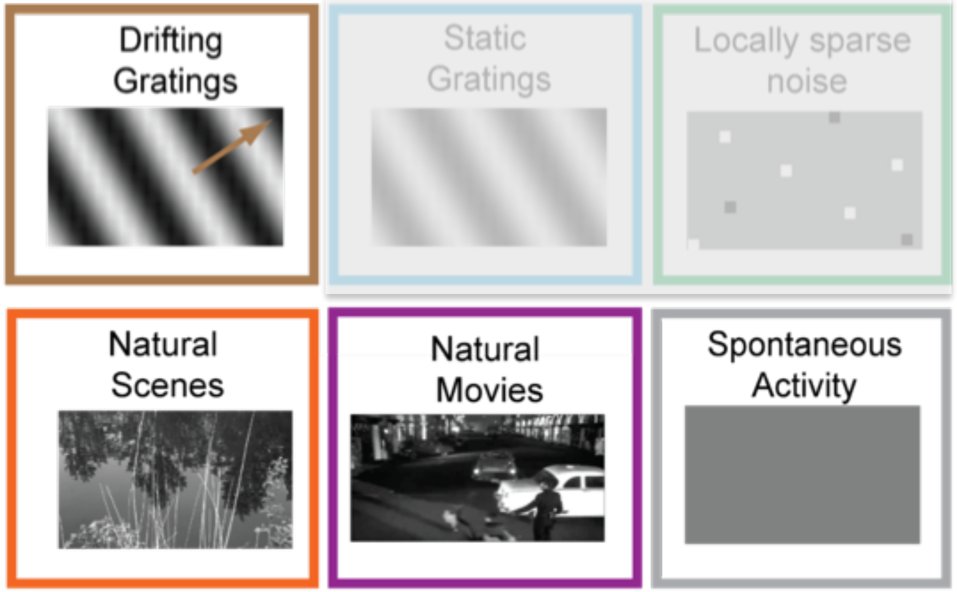
- **3 model instantiations (“3 mice”: M1, M2, M3)**
- **For each, sample alternative connectivity rules**





Test data:

- Spontaneous activity (20 trials)
- Gratings (8-32 conditions, 10 trials each)
- Natural Images (10 images, 100 trials each)
- Natural Movies (3 movies, 10 trials each)
- Full-field flashes (2 conditions, 10 trials each)
- Moving Bars (4 conditions, 10 trials each)

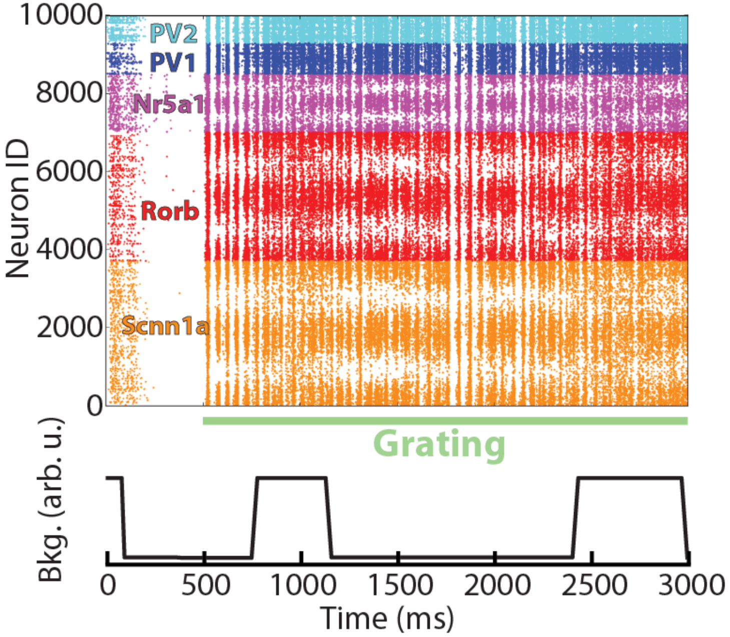


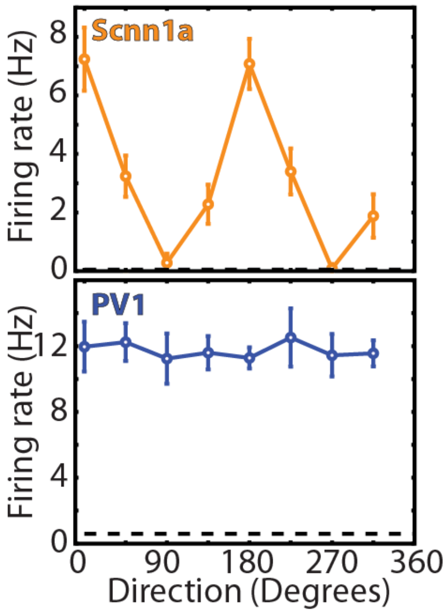
Training data:

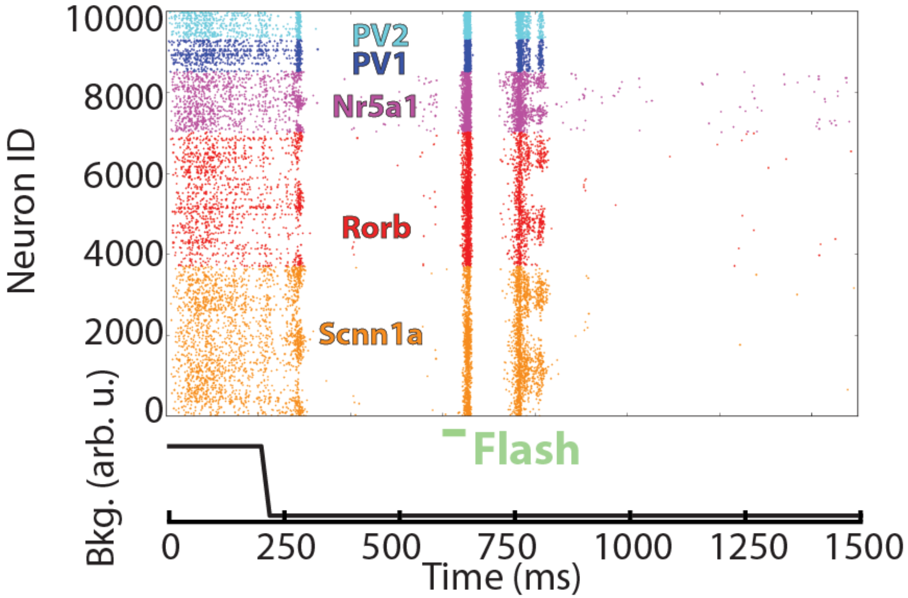
- Spont. rate from 1 trial
- Peak rates for 1 grating trial (a single SF/TF/orientation)
- Peak response to a full-field flash from 1 trial

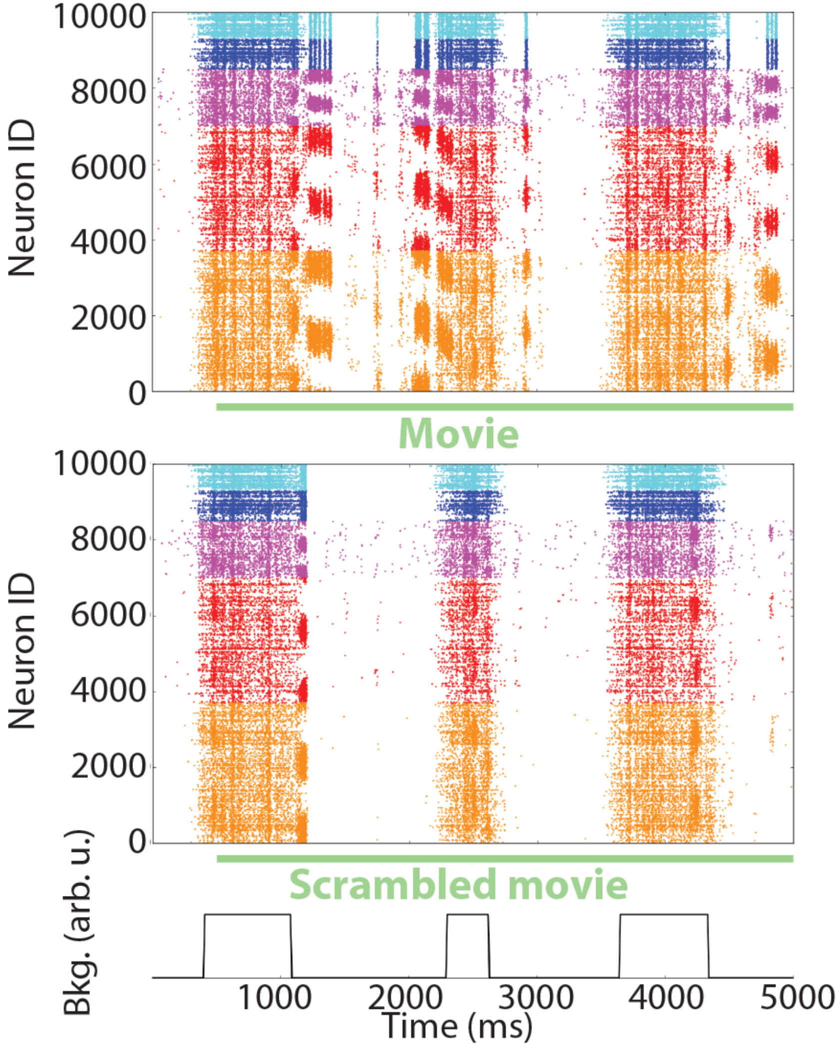
Total number of simulations: ~3,600
Total simulated time: ~3 hours
Computational costs: ~6 months on 1,500 processors

Model Responses

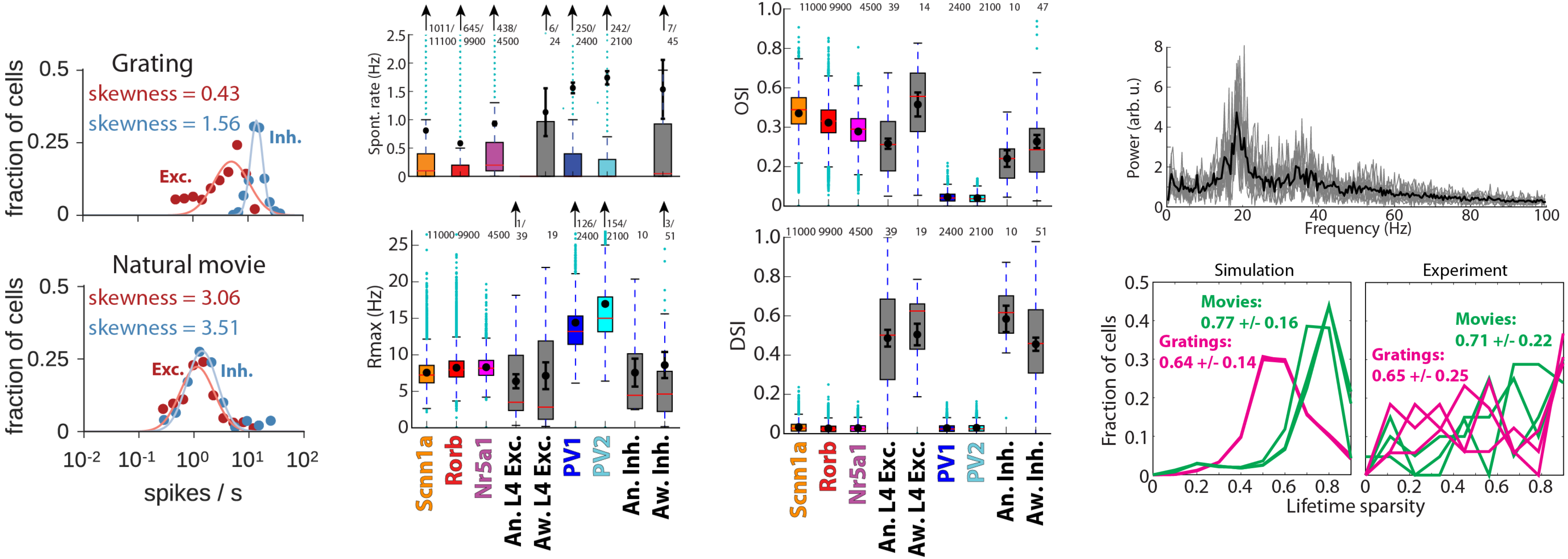




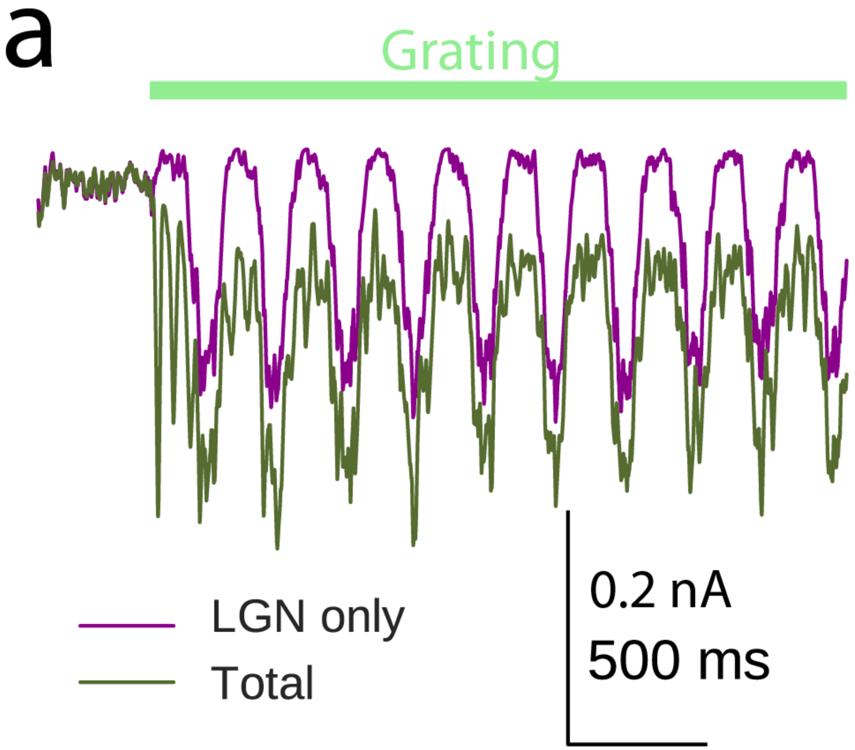


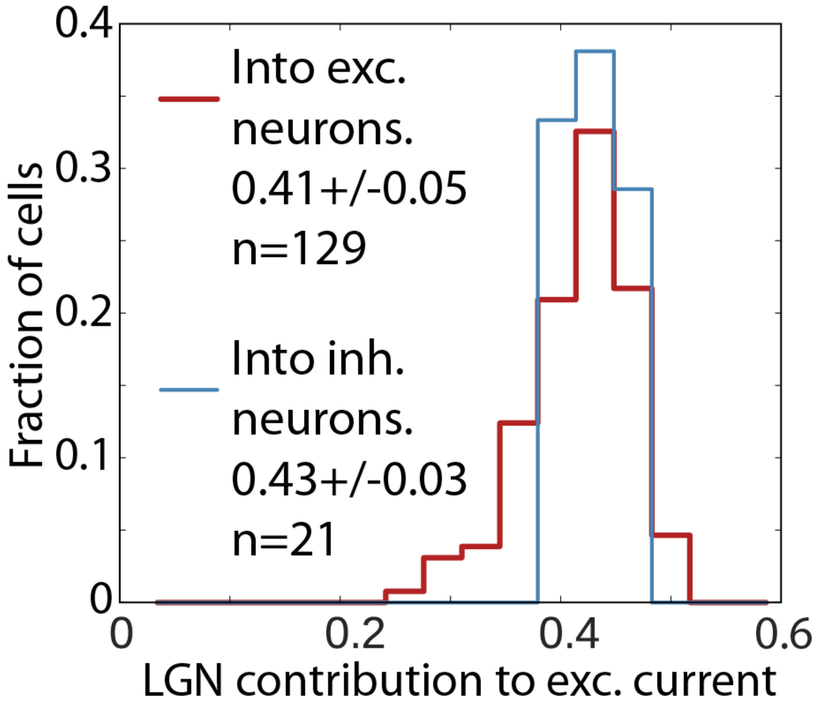


Benchmarking the Model against Experiments



Cortical Amplification





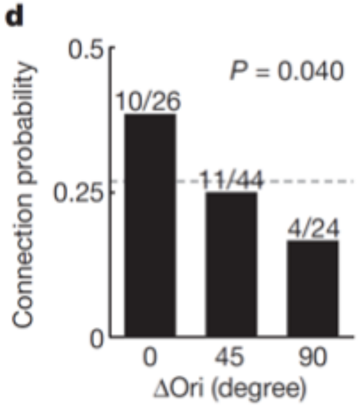
Experiment (2 Hz):

0.36 +/- 0.02

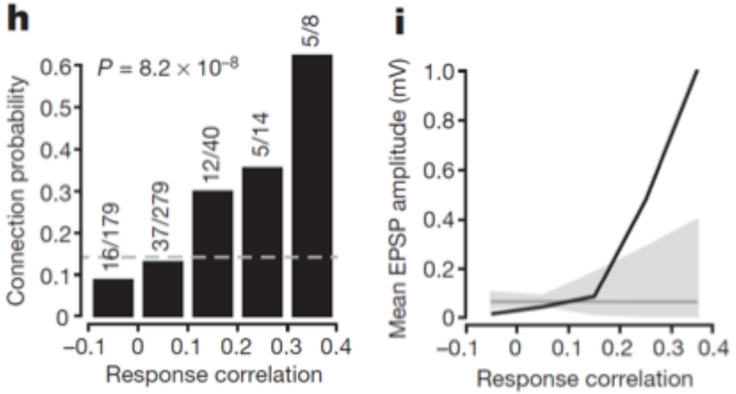
for exc. neurons

(Lien and Scanziani, *Nature Neurosci.*, 2013)

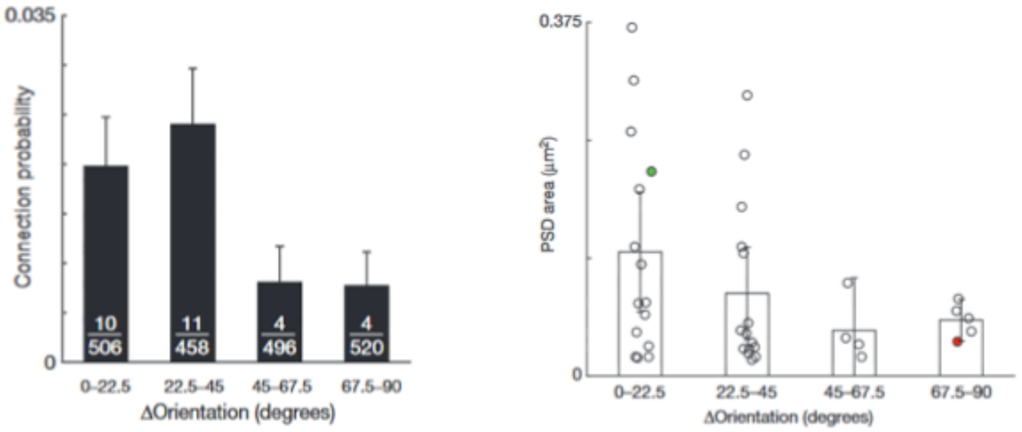
Like-to-Like Connectivity



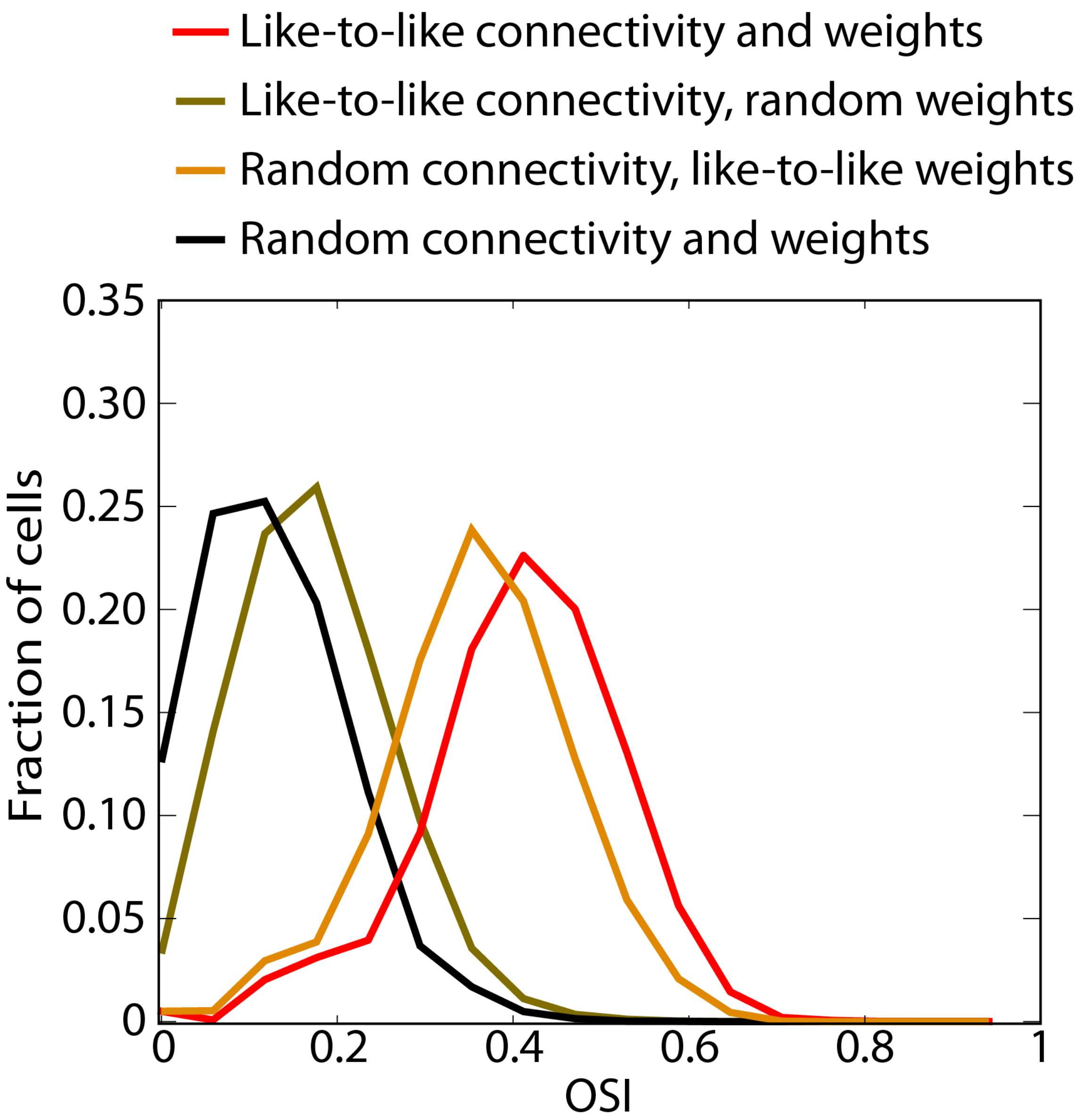
Ko et al., Nature (2011)



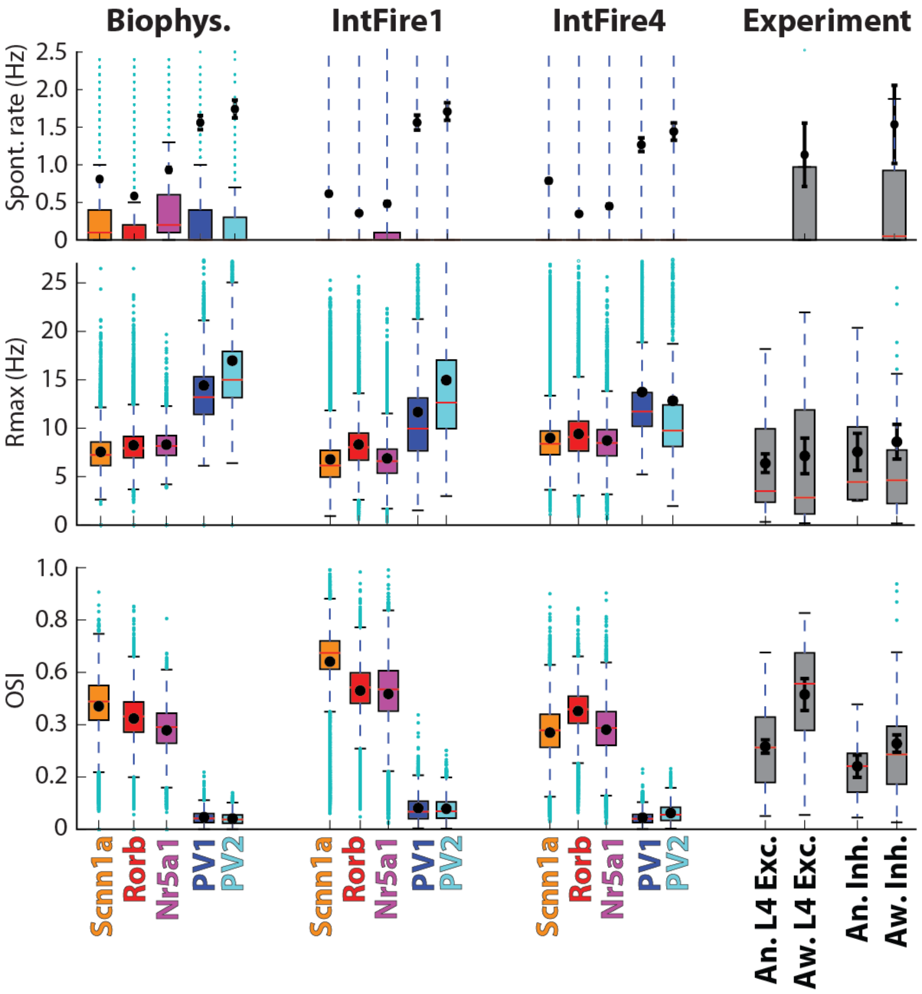
Cossell et al., Nature (2015)

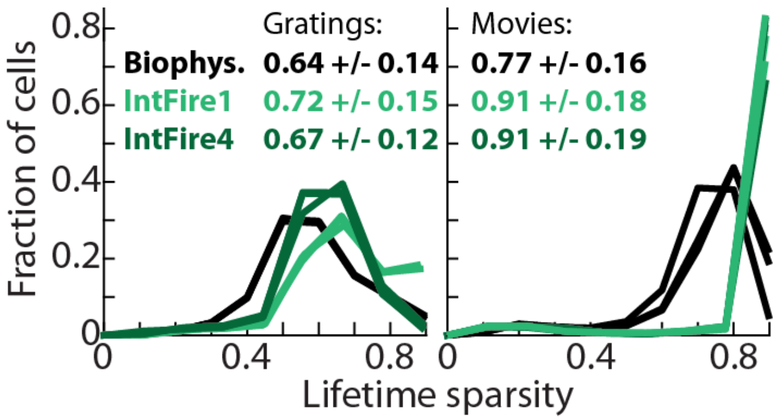


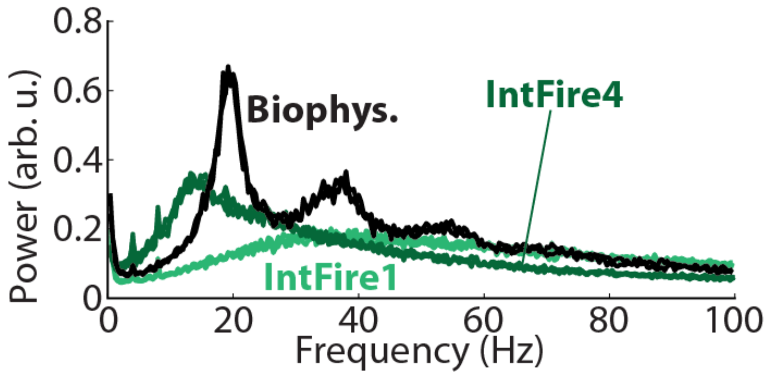
Lee et al., Nature (2016)

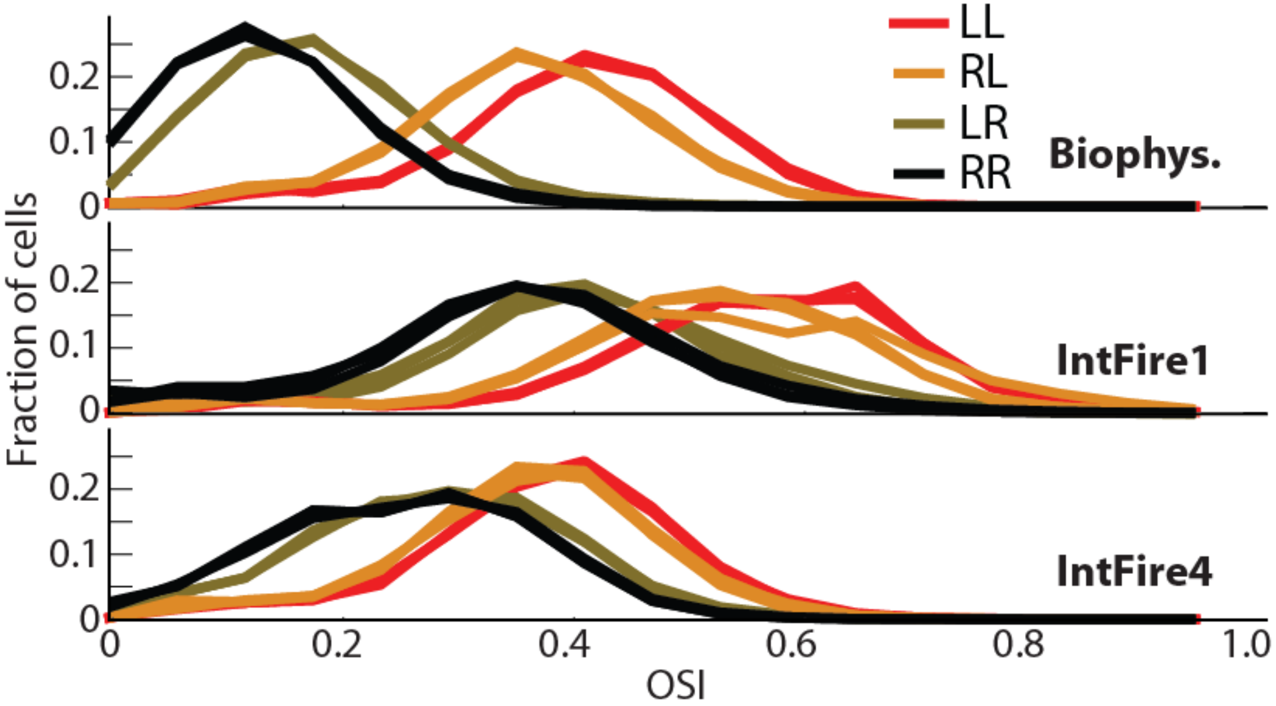


Replacing Biophysical Cells by Point-Neuron Models

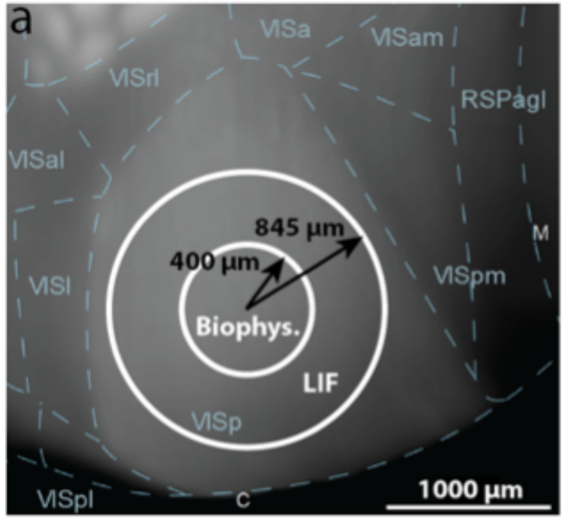








Biophysically Detailed Model of Mouse V1



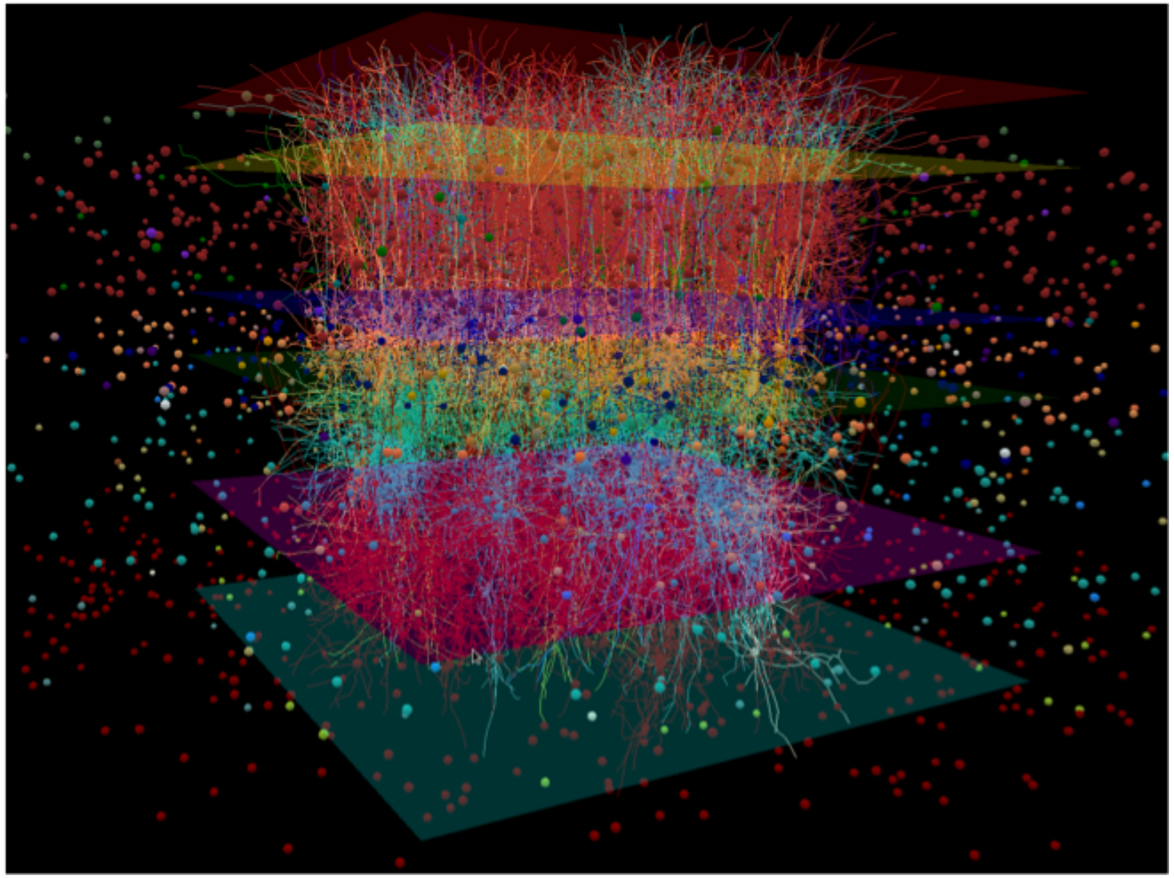
Cell Type	L1 Htr3a
N of cells	978
N of models	2

Cell Type	L2/3 Cux2	L2/3 PV	L2/3 SST	L2/3 Htr3a
N of cells	12689	640	459	1107
N of cell models	1	3	4	8

Cell Type	L4 Scnn1a	L4 Rorb	L4 Nr5a1	L4 other E	L4 PV	L4 SST	L4 Htr3a
N of cells	3072	2620	1248	3194	1025	553	270
N cell models	6	11	9	5	2	2	1

Cell Type	L5 Rbp4	L5 other E	L5 PV	L5 SST	L5 Htr3a
N of cells	6010	1448	673	594	98
N of cell models	9	18	10	5	4

Cell Type	L6 Ntsr1	L6 PV	L6 SST	L6 Htr3a
N of cells	12893	1052	1056	192
N of cell models	5	4	3	2

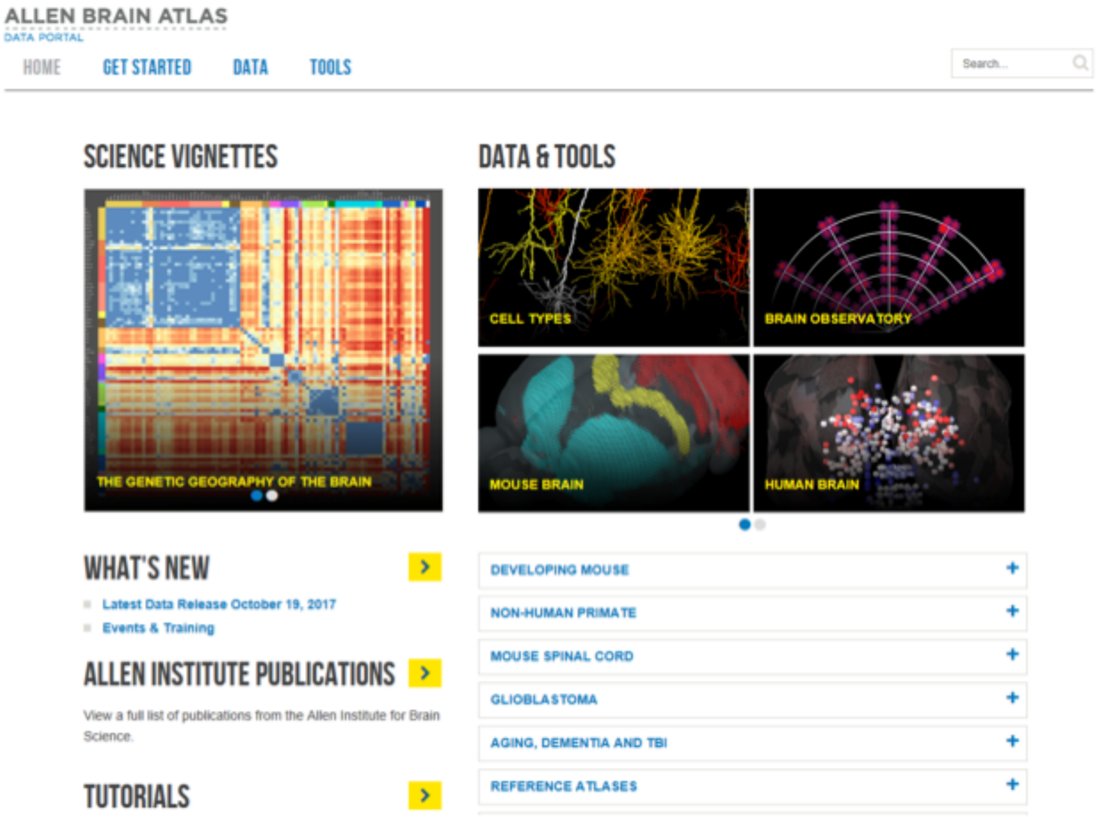


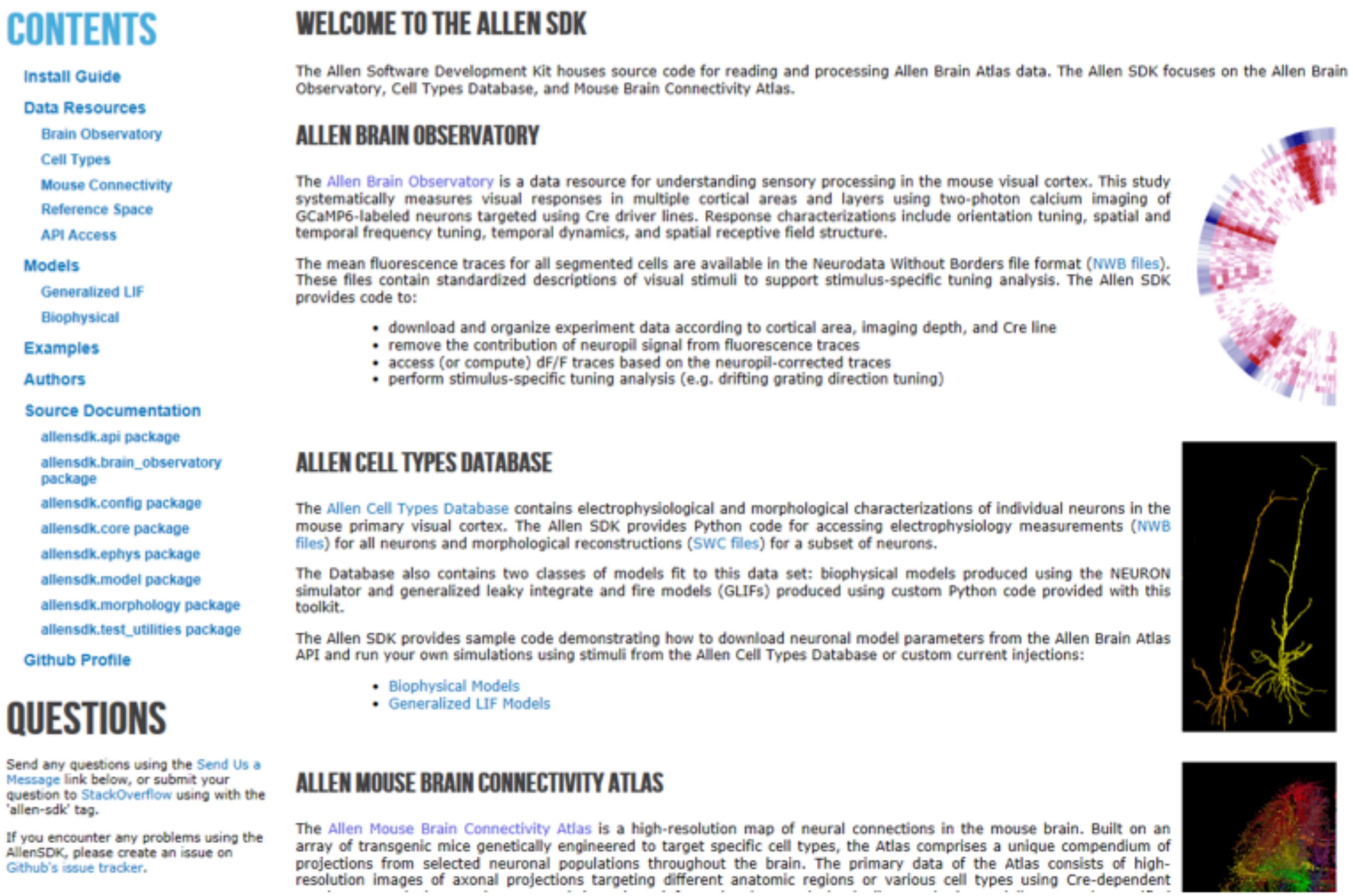
The model contains 51,978 biophysical cells (114 unique models); point-neuron models for the rest; 230,000 cells in total.

Allen Institute's Databases and Allen Software Development Kit (Allen SDK)

http://brain-map.org/

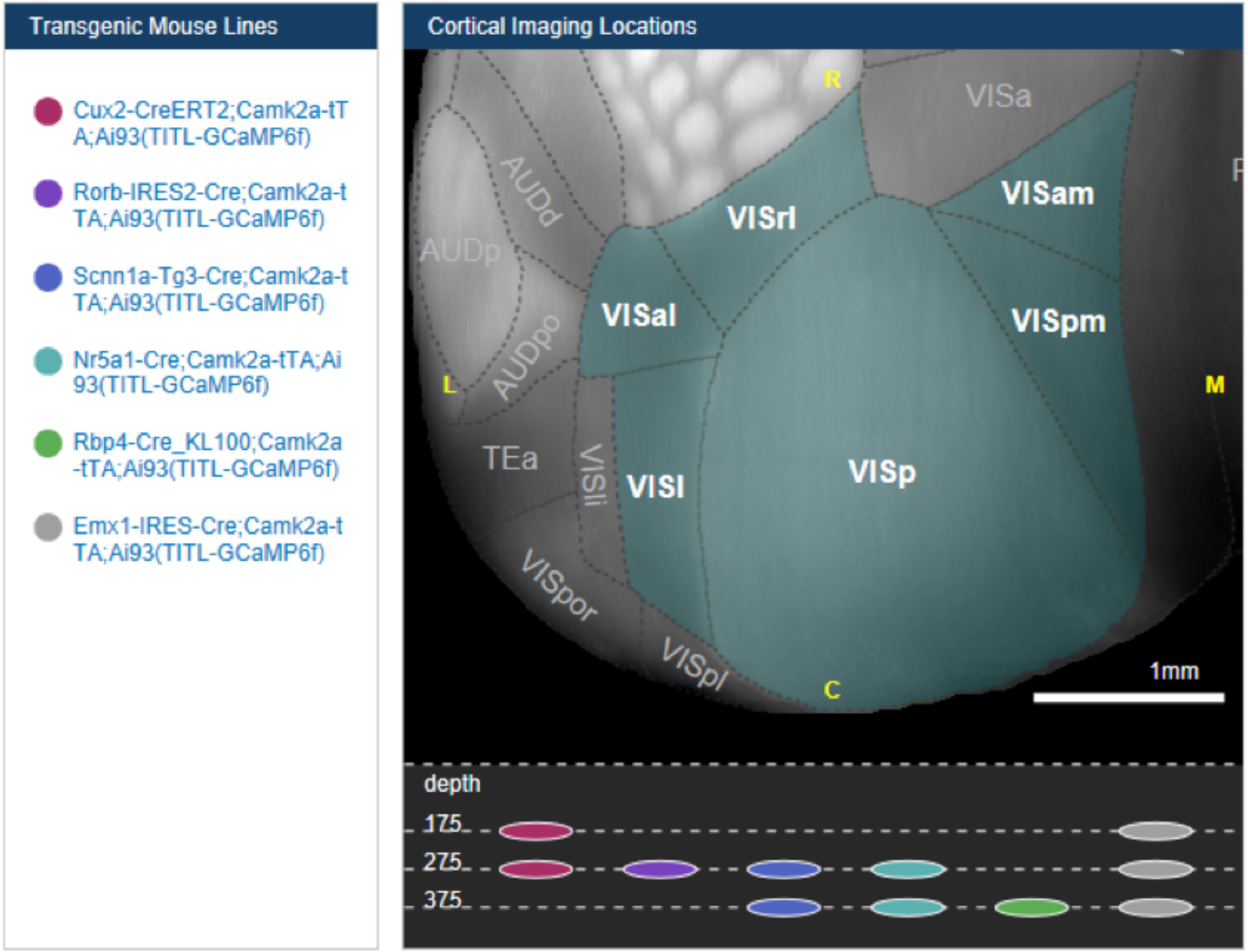
http://alleninstitute.github.io/AllenSDK/





Allen Brain Observatory

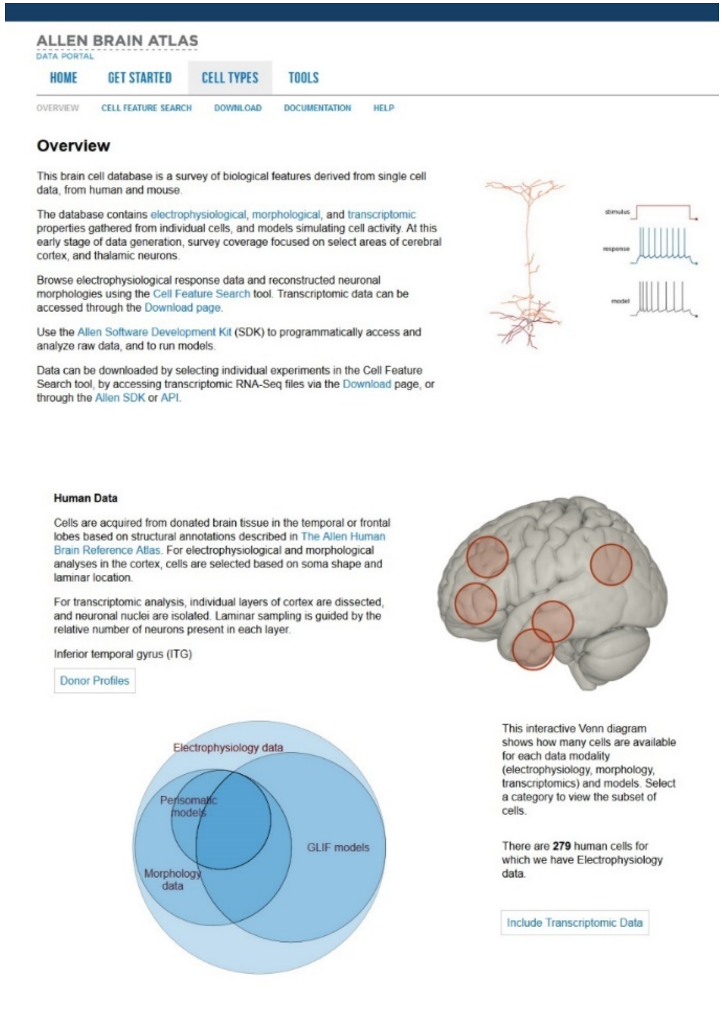
http://observatory.brain-map.org/visualcoding

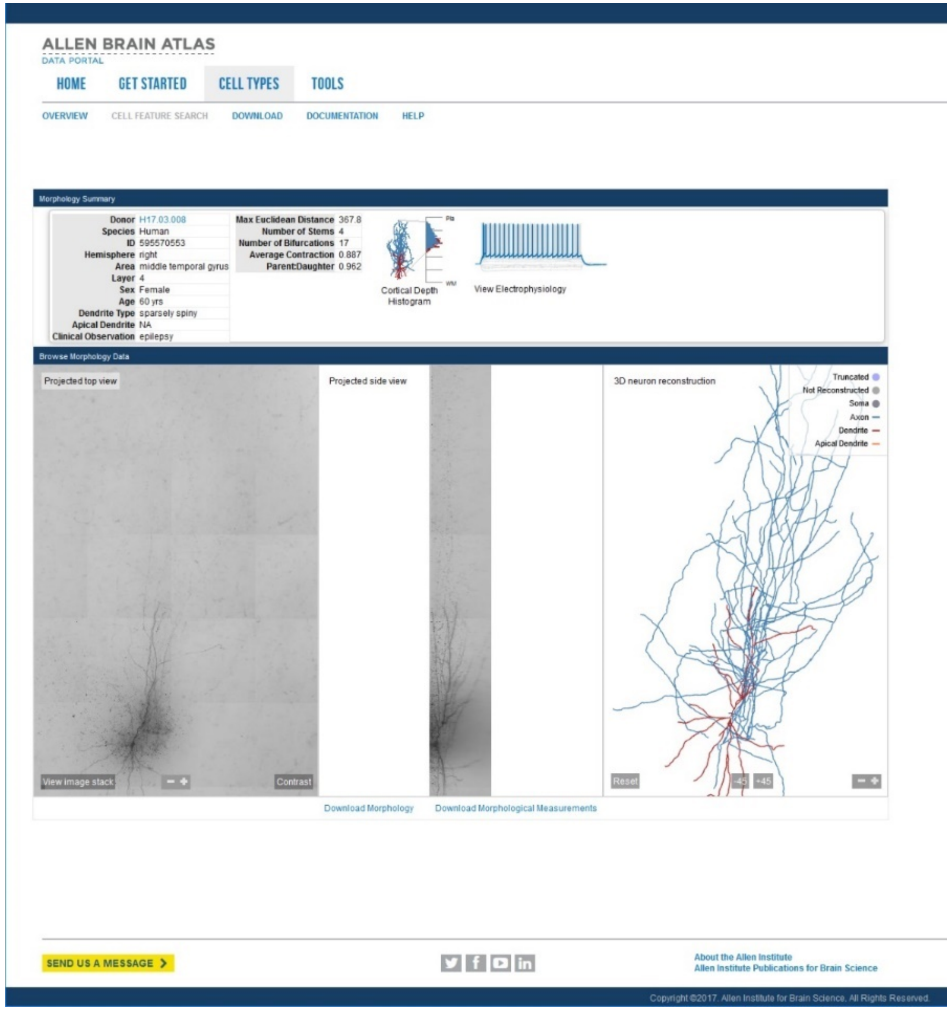


- Mouse Visual Cortex
- 6 Cre lines
- 6 areas
- 181 datasets
- ~45,000 neurons

Allen Cell Types Database

http://celltypes.brain-map.org





- Mouse and Human Cortical Neurons
- 1058 mouse and 279 human cells with ephys recordings
- 295 mouse and 107 human morphology reconstructions
- 712 mouse and 157 human cells with GLIF models
- 205 mouse and 43 human cells with biophysical models

The Dynamic Brain Summer Workshop at Friday Harbor Lab

UNIVERSITY of WASHINGTON
COMPUTATIONAL NEUROSCIENCE TRAINING PROGRAM

ALLEN INSTITUTE for BRAIN SCIENCE

Summer Workshop on the Dynamic Brain

https://github.com/AllenInstitute/SWDB_2017

In [1]:
```
import os
import sys
import pandas as pd
import numpy as np
import random

from modelingsdk.builder.networks import SynNetwork

from matplotlib import pyplot as plt
import matplotlib.image as mpimg
%matplotlib inline
```

Modeling biophysically detailed cells with NEURON

In this tutorial, we will create a network of 8 cells. Four of these cells will be biophysically detailed and four will be Leaky-Intergrate-and-Fire (LIF) models.

<img src="../../Modeling/biophysical_notebook/schematics_png/Full_figure.png" alt=Drawing style="width: 500px;">

Build recurrent network

For building the 8 node network, we will save the nodes (neurons) and edges (connections) separately.

In [2]:
```
# Output file names
directory_name = 'network/recurrent_network/'

# Create direcoty if it doesn't exist
if not os.path.exists(directory_name):
    os.makedirs(directory_name)
```

We will explore the directory structure of how files are being saved later. Just know for now that we will be creating files ans saving them in a directory called "network".

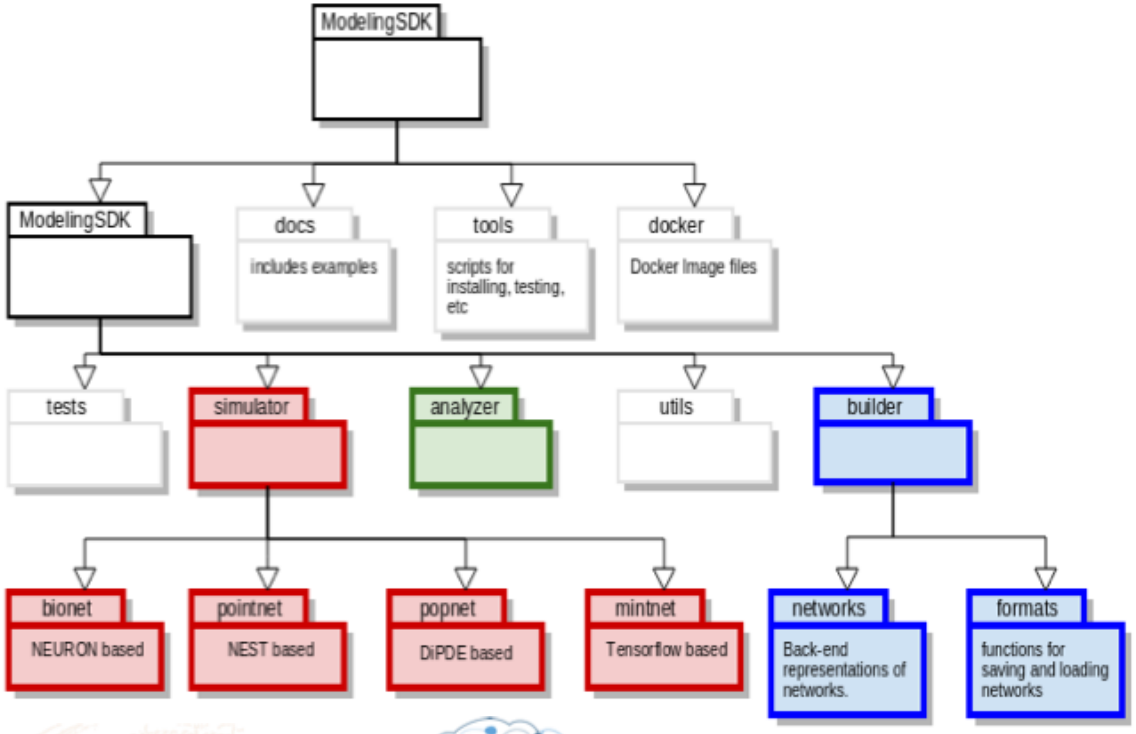
Building Nodes

In this section we will be creating the nodes only. They are not receiving input nor connected to each other yet. The schematic below illustrates where we will be.

Brain Modeling ToolKit (BMTK)

Deliverables:
A software suite for building, simulating and analyzing models at different levels of resolution.

Scope:
Software for 4 levels of resolution (biophysical, point neuron, population statistics, machine intelligence).



builder - An API for building large networks

simulator - A collection of interfaces for quickly running network simulations on a variety of simulators.

analyzer - Functions for analyzing and visualizing network and simulation data.

NEURON for empirically-based simulations

nest::

DiPDE

TensorFlow

https://alleninstitute.github.io/bmtk/

THANK YOU

We wish to thank the Allen Institute for Brain Science founders,
Paul G. Allen and Jody Allen, for their vision, encouragement and support.

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