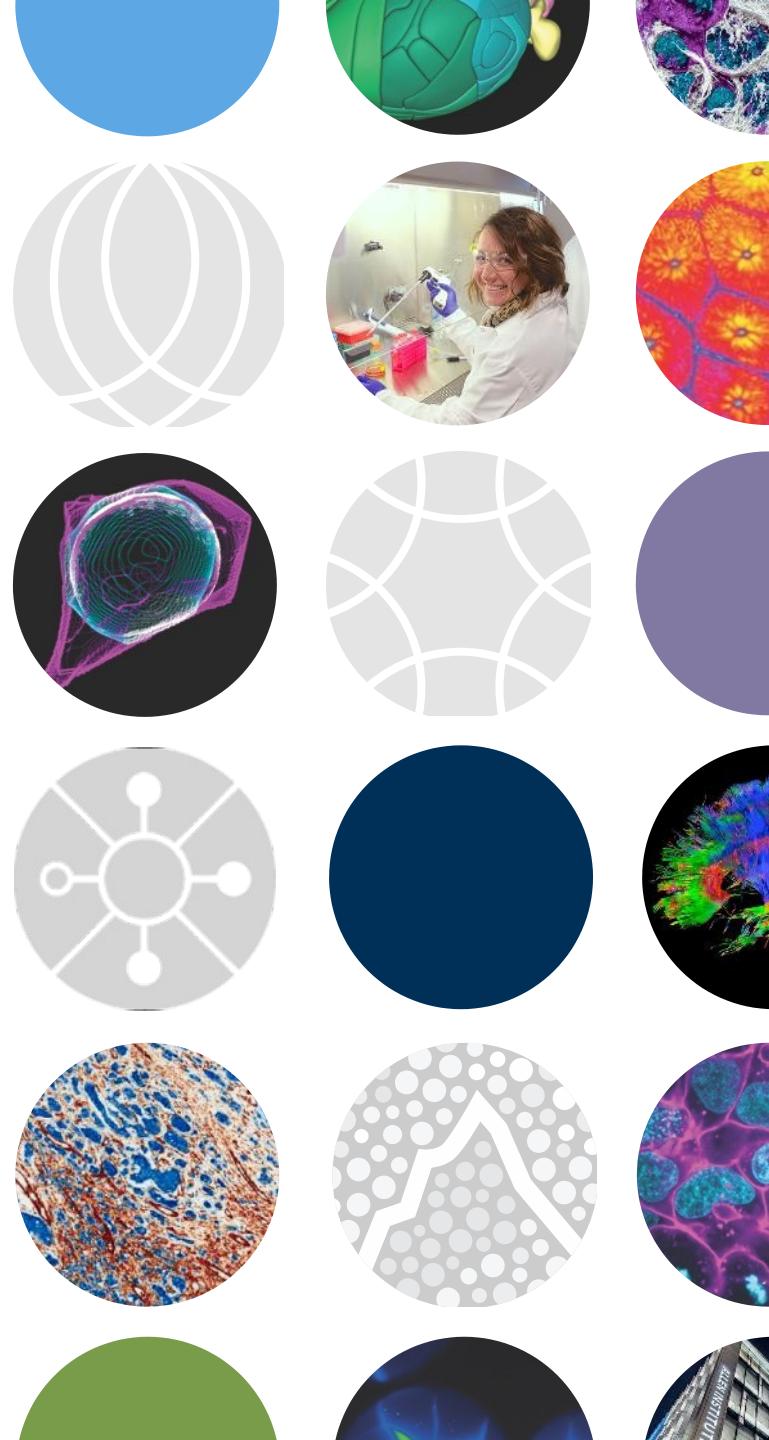




Large-scale Datasets and Modeling Tools from the Allen Institute for Brain Science

Yazan N. Billeh

yazanb@alleninstitute.org





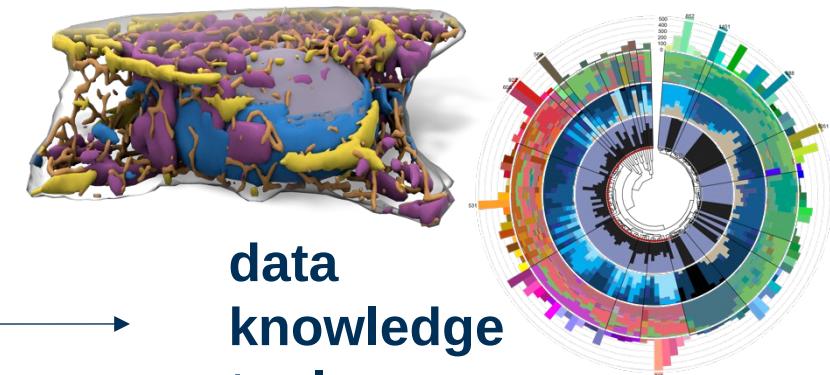
hard problems
complexity
foundational biology



big science
team science



open science



CORE PRINCIPLES

Team Science

Interdisciplinary teams working towards common goal



Big Science

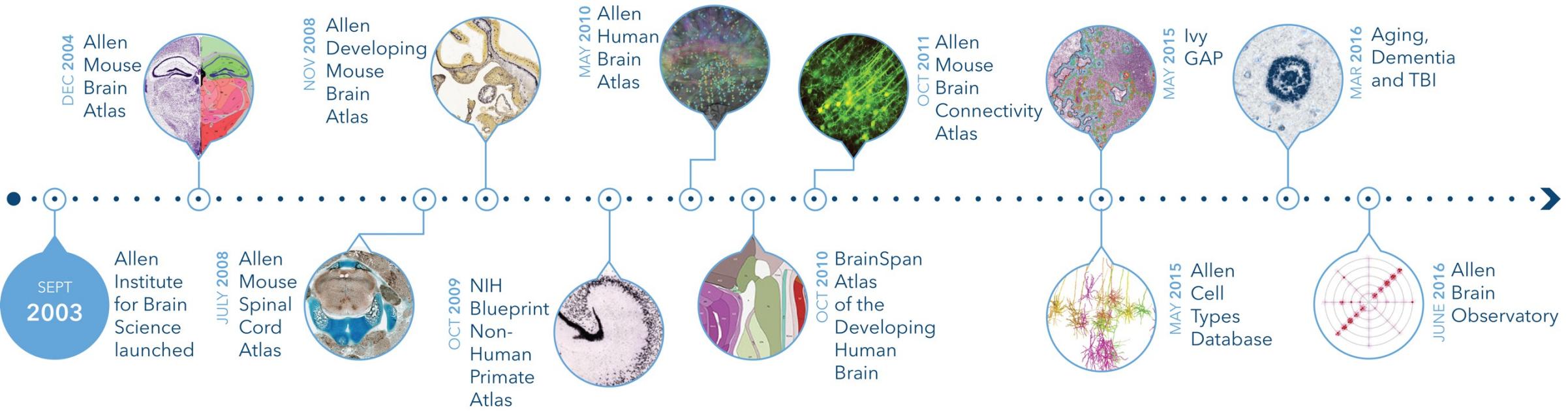
Large-scale projects with robust, massive data

Open Science

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

Allen Institute - Online Public Resources

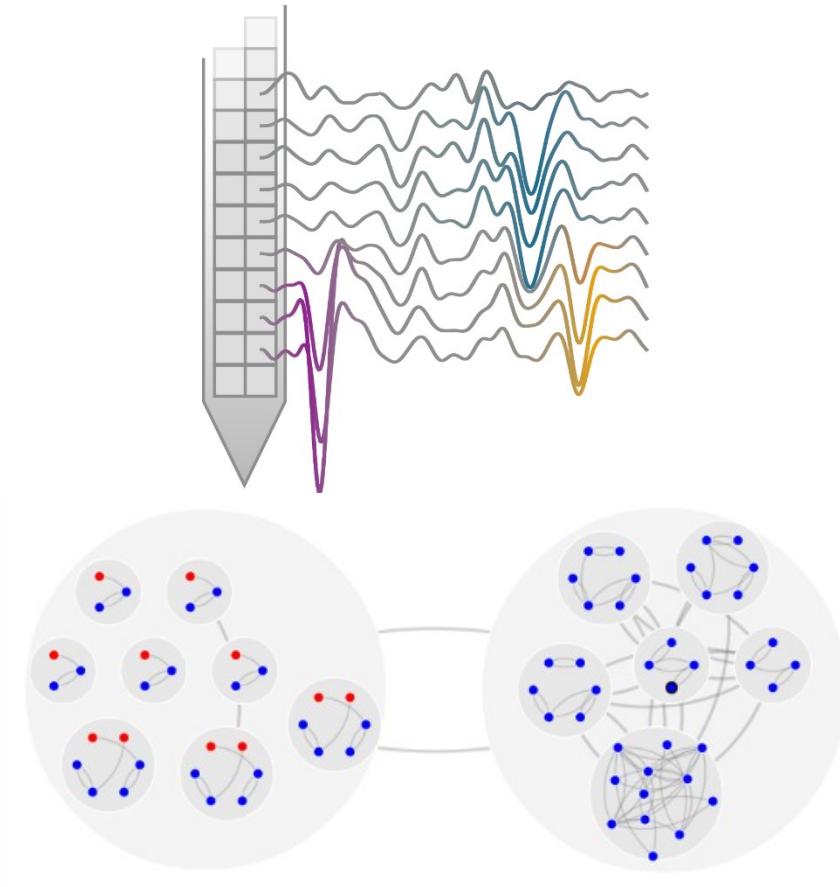
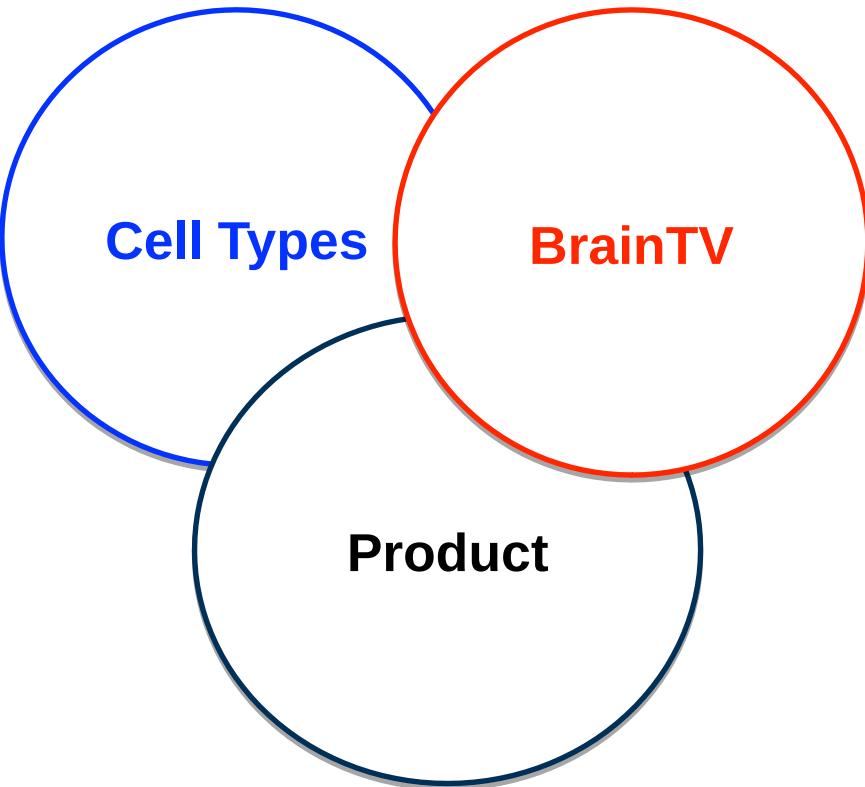
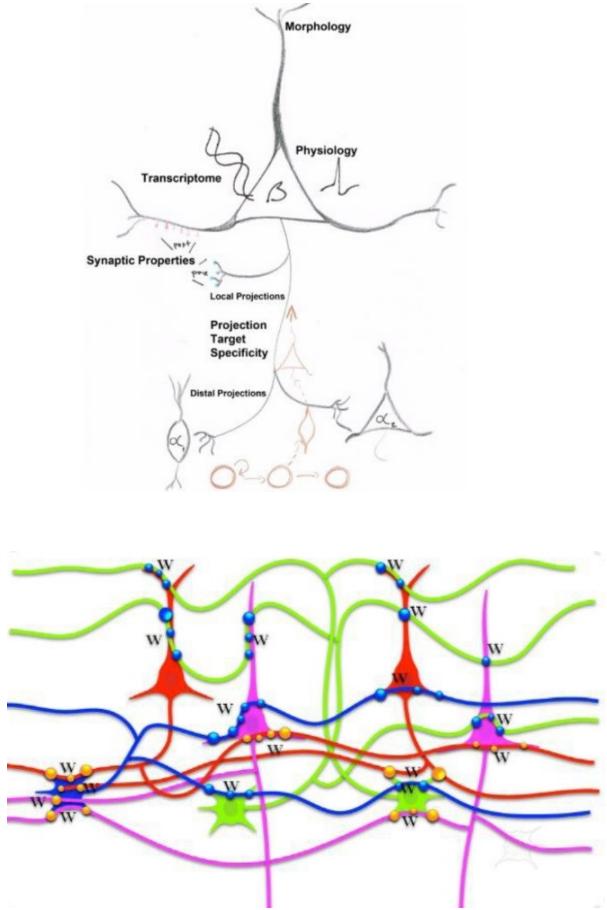
www.brain-map.org



All data are:

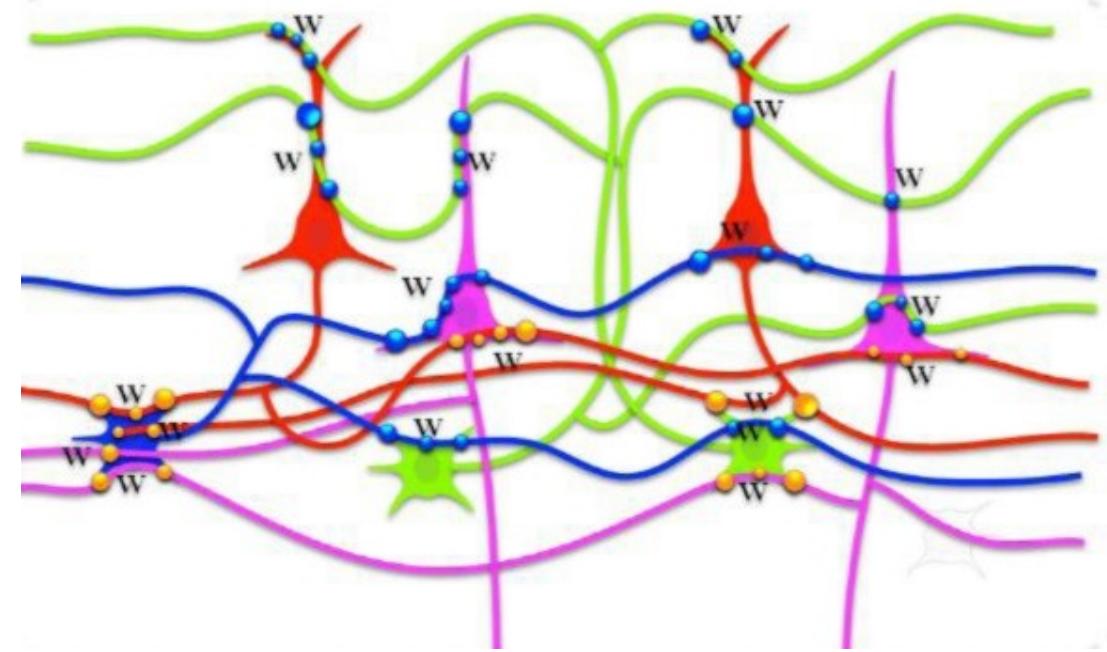
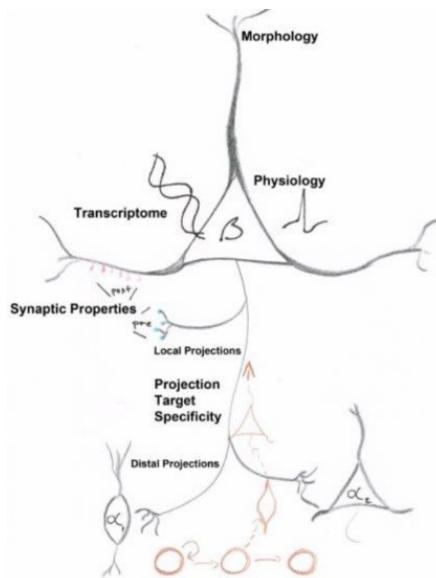
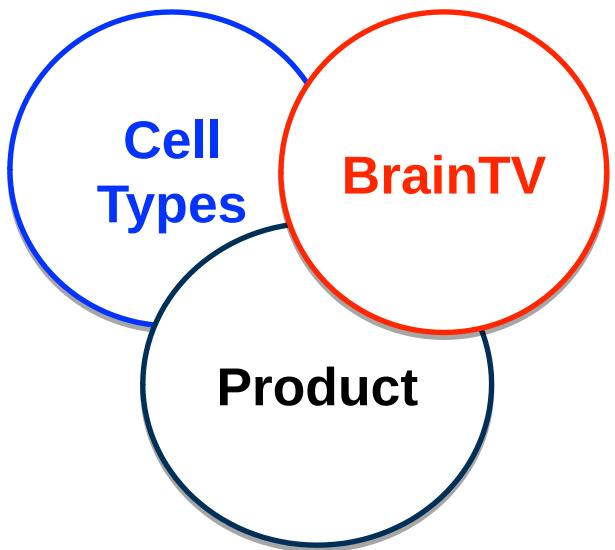
- publicly accessible via API as soon as they pass QC
- freely available without any commercial restrictions

Institute Programs



Cell Types Program

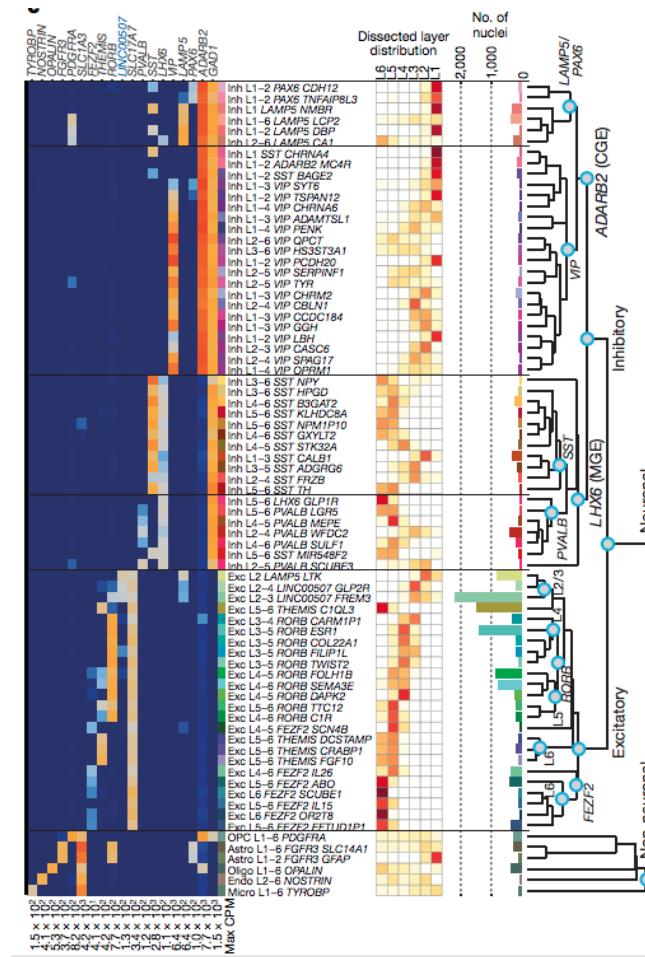
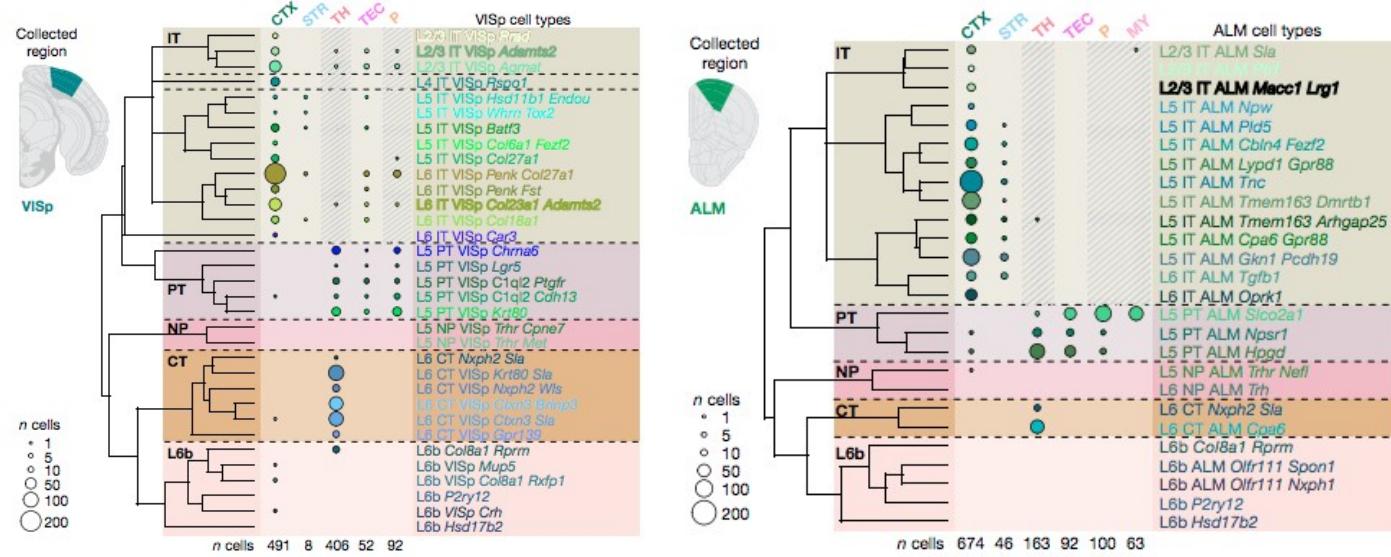
Characteristics of cells and connections



Transcriptomics (Mouse and Human)

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

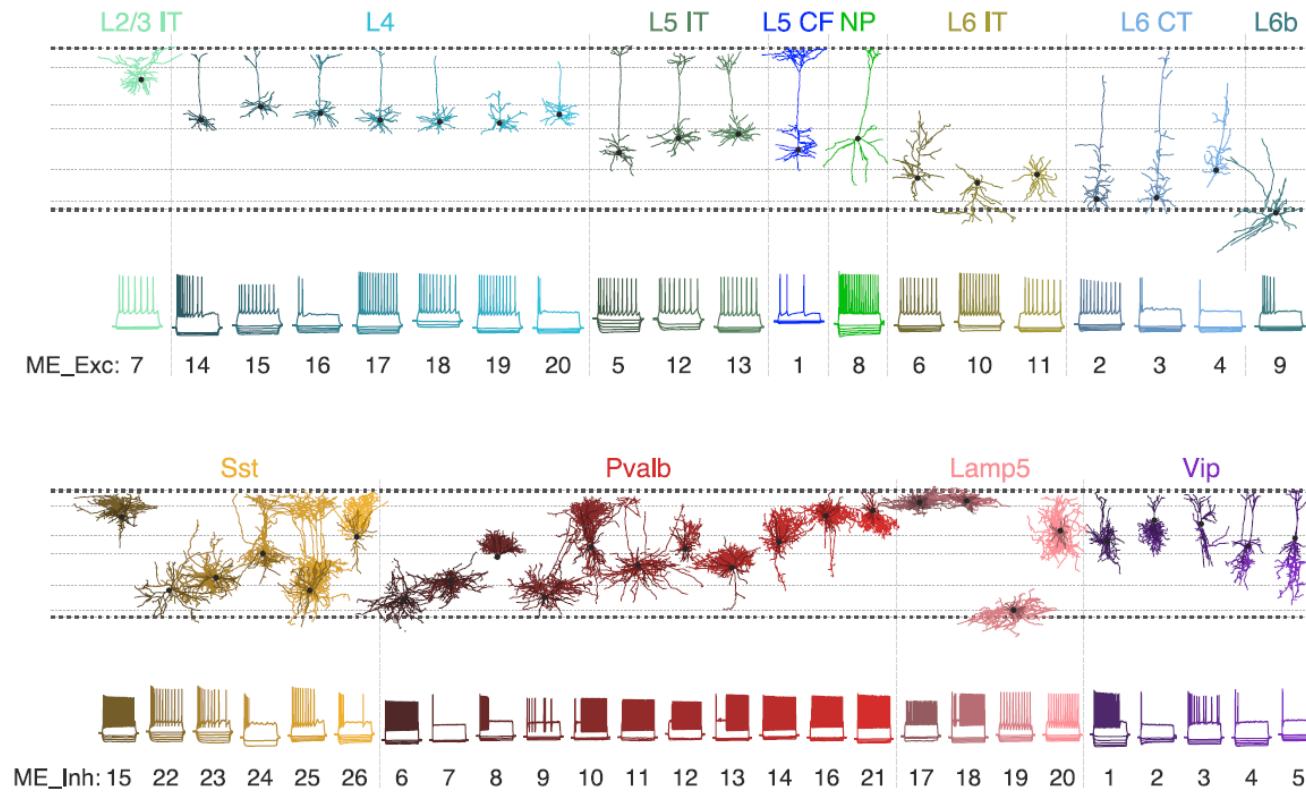
Scope: Tens of thousands of cells.



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

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

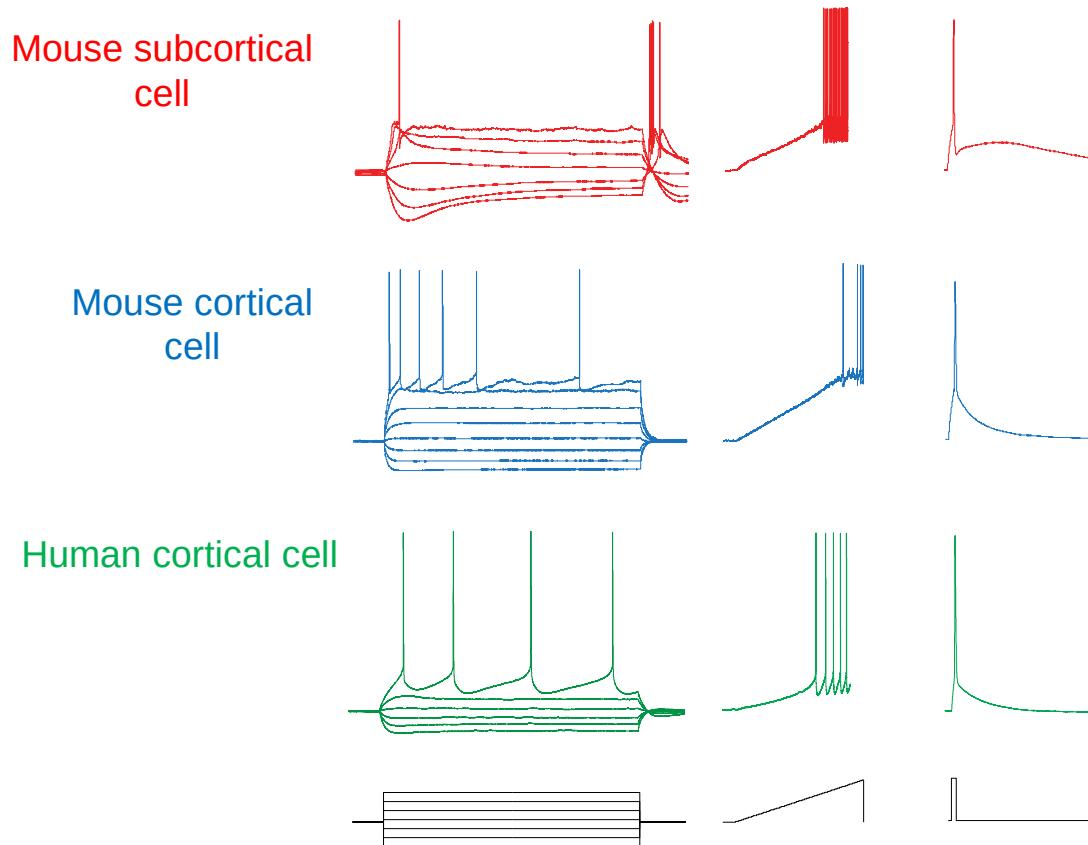
Scope: Thousands of cells in the mouse visual cortex and human middle temporal gyrus (MTG).



Mouse and Human Patch-Seq

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

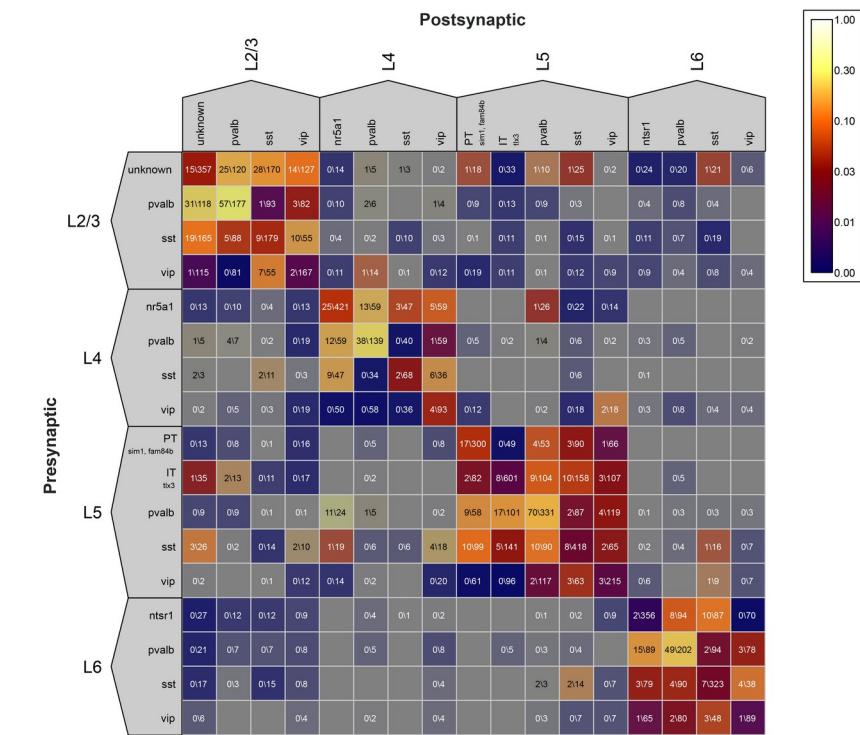
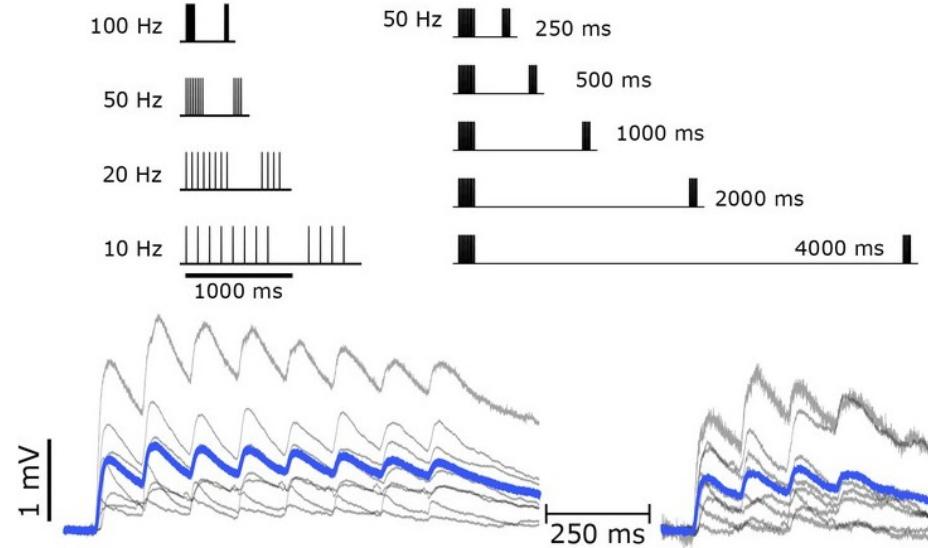
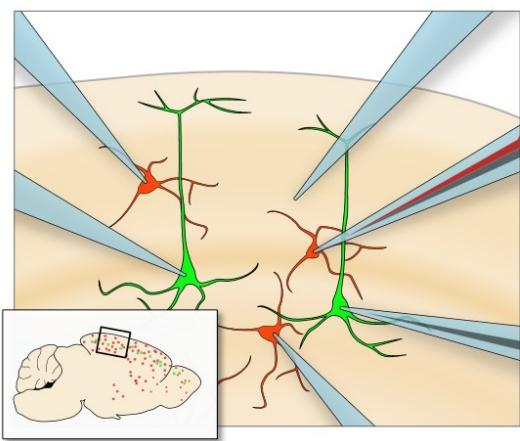
Scope: Thousands of neurons in mouse and human.



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: 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.

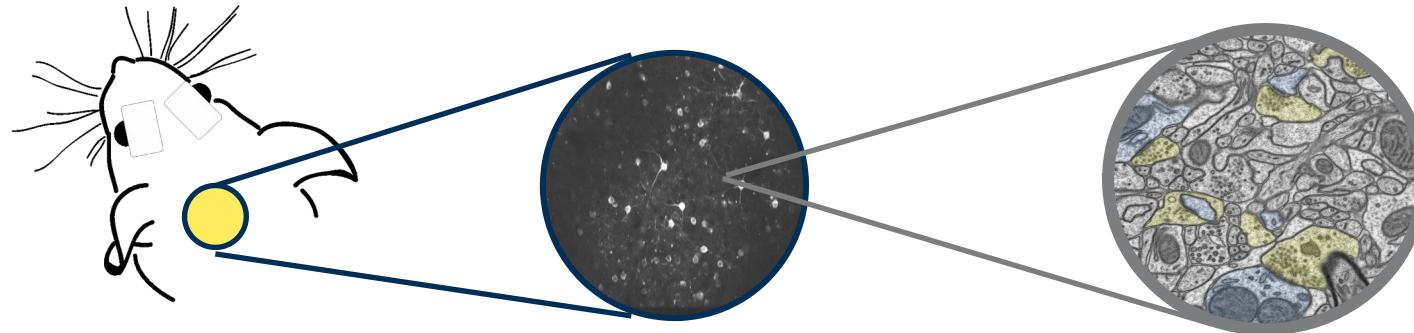
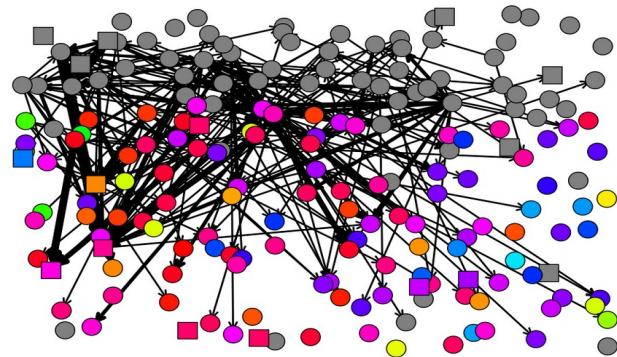


Mouse and Human EM Connectomics

Deliverables: Reconstruction of neuronal morphologies and the connectivity matrix in the local cortical circuit – 1 mm³ in mouse V1 and 2 mm³ in human MTG.

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

Wiring
Diagram



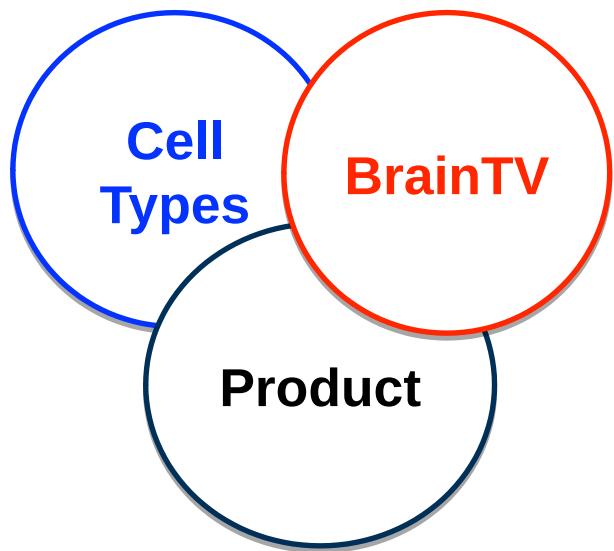
Cell Types



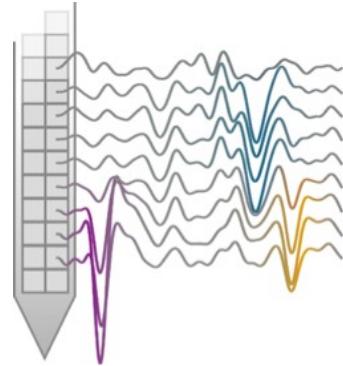
Automated reconstructions are by Sebastian Seung Lab, Princeton

BrainTV Program

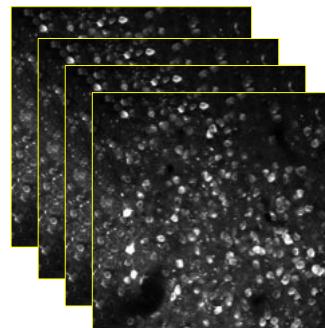
Activity and Computations in Cortical Circuits *in Vivo*



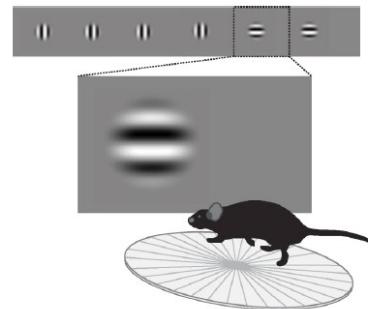
Ephys - Neuropixels Probes



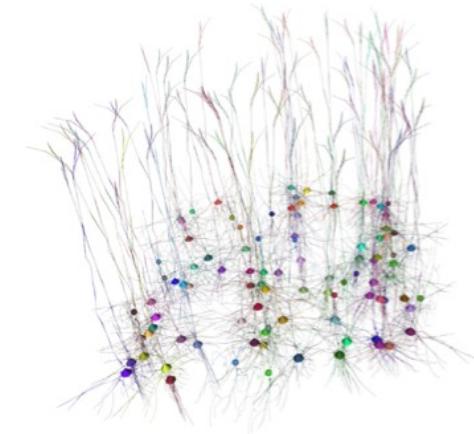
2p Cellular Imaging



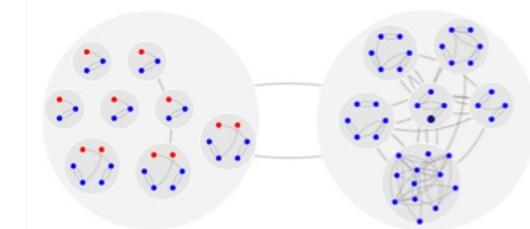
Visual Behavior



Biophysical Modeling



Point Neuron & Filter Networks



Visual Coding

Deliverables:

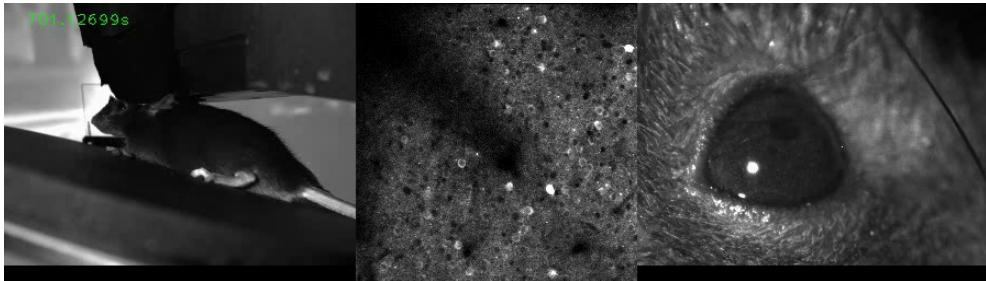
O-phys data for neuronal responses
in the mouse cortex *in vivo*.

Scope:

Over sixty thousands cells recorded

Allen Brain Observatory

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



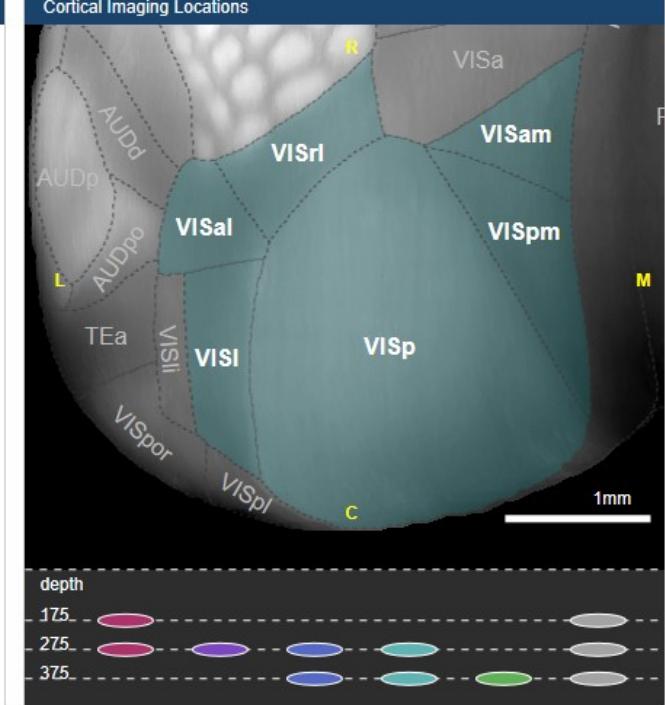
HOME GET STARTED BRAIN OBSERVATORY TOOLS

OVERVIEW EXPERIMENTS CELLS SDK TRANSGENIC CHARACTERIZATION DOCUMENTATION HELP

Transgenic Mouse Lines

- Cux2-CreERT2;Camk2a-tTA;Ai93(TITL-GCaMP6f)
- Rorb-IRES2-Cre;Camk2a-tTA;Ai93(TITL-GCaMP6f)
- Scnn1a-Tg3-Cre;Camk2a-tTA;Ai93(TITL-GCaMP6f)
- Nr5a1-Cre;Camk2a-tTA;Ai93(TITL-GCaMP6f)
- Rbp4-Cre_KL100;Camk2a-tTA;Ai93(TITL-GCaMP6f)
- Emx1-IRES-Cre;Camk2a-tTA;Ai93(TITL-GCaMP6f)

Cortical Imaging Locations



depth

175

275

375

Visual Stimuli and Cell Responses

Learn about visual stimuli

Drifting Gratings Static Gratings Natural Scenes Natural Movies Locally Sparse Noise



Allen Brain Observatory

About the Allen Brain Observatory

The Allen Brain Observatory is a standardized *in vivo* survey of the mouse visual cortex, focused on visually evoked calcium responses from neurons expressing Cre lines.

Key features of the data

- Searchable data for calcium imaging studies across visual areas and depths
- A variety of data visualizations capturing visual cortical activity and cell population responses to different stimuli
- Standardized spatial distribution of responses to five types of stimuli surveyed from three depths
- Raw data and analysis tools available for download via the program interface or Development Kit (DK)

Search the data

- Click on the EXPERIMENT view experimental details
- Click on a Visual STIMULUS to learn more.

Allen Brain Observatory – *in Vivo* Electrophysiology

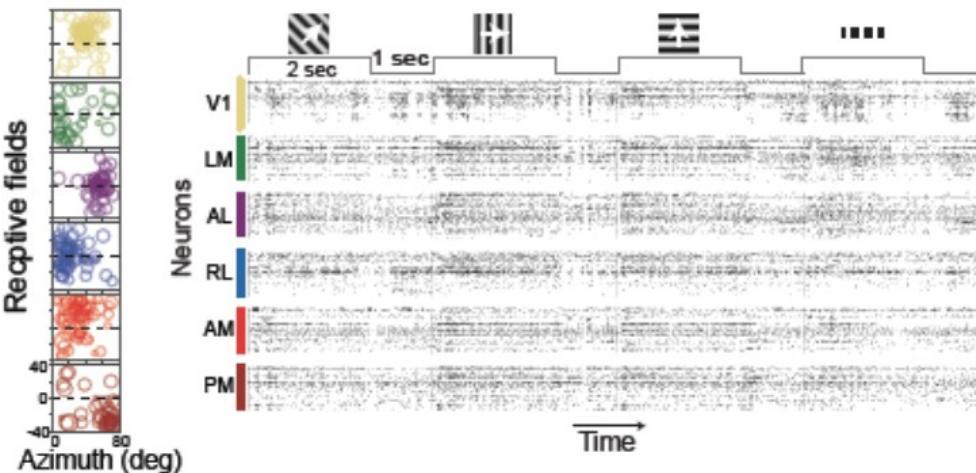
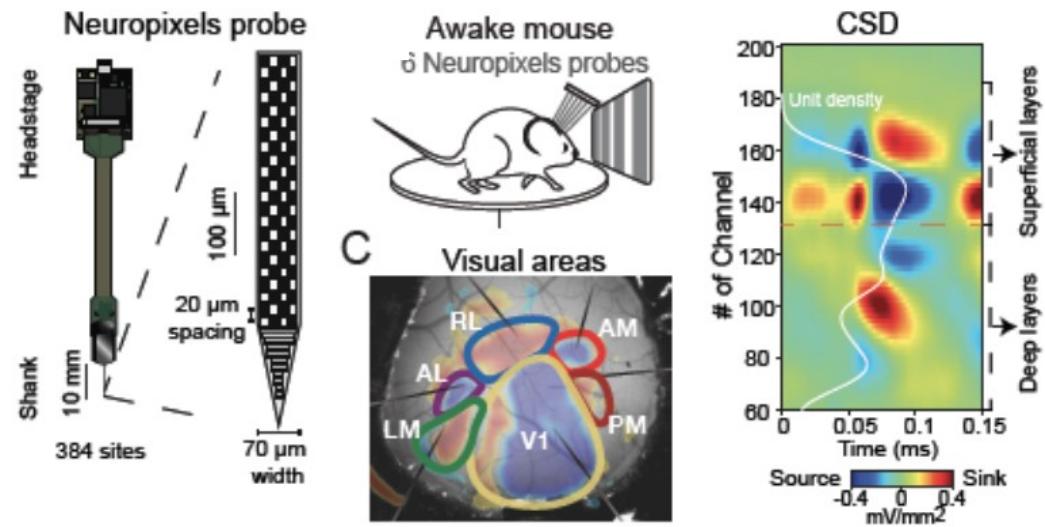
Deliverables:

E-phys data for neuronal responses in the mouse cortex *in vivo*.

Scope:

Tens of thousands of units for E-phys; subcortical areas also

First Release: October 2019



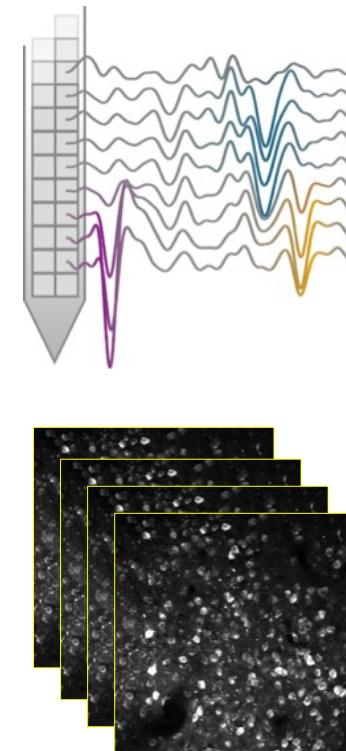
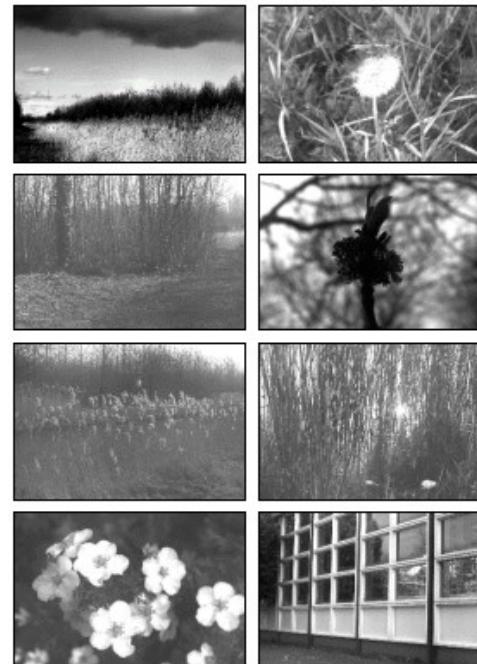
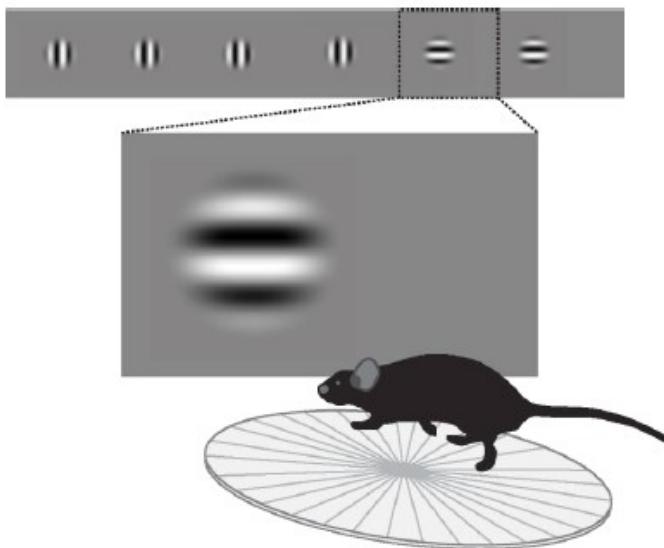
Visual Behavior

Deliverables:

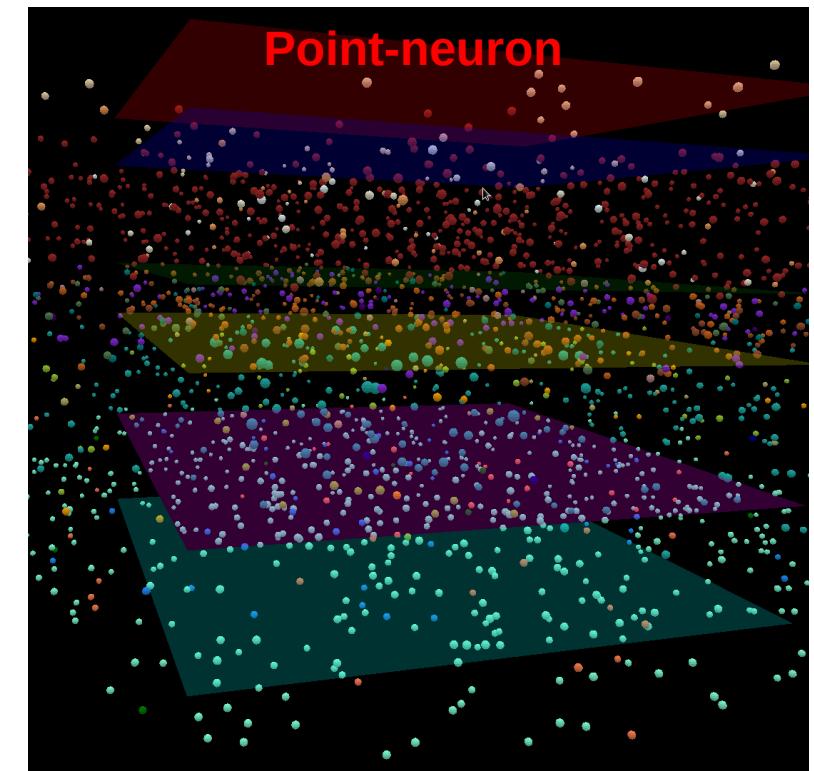
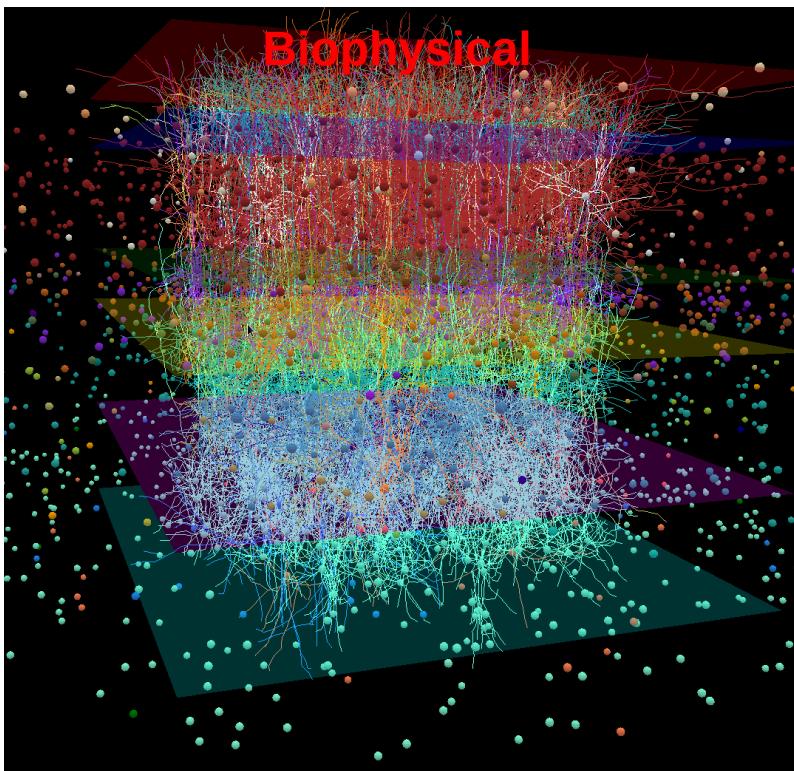
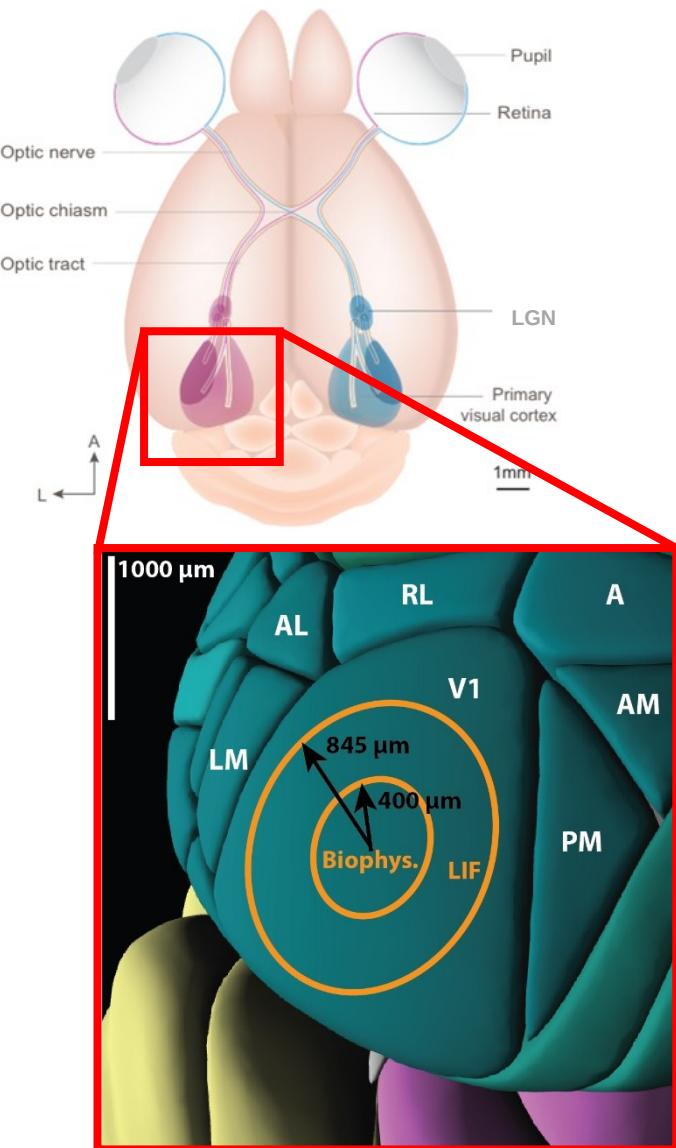
O-phys and E-phys data for single-cell responses in the mouse cortex *in vivo*, in the context of a change detection behavior.

Scope:

Tens of thousands of cells for O-phys; tens of thousands of units for E-phys.



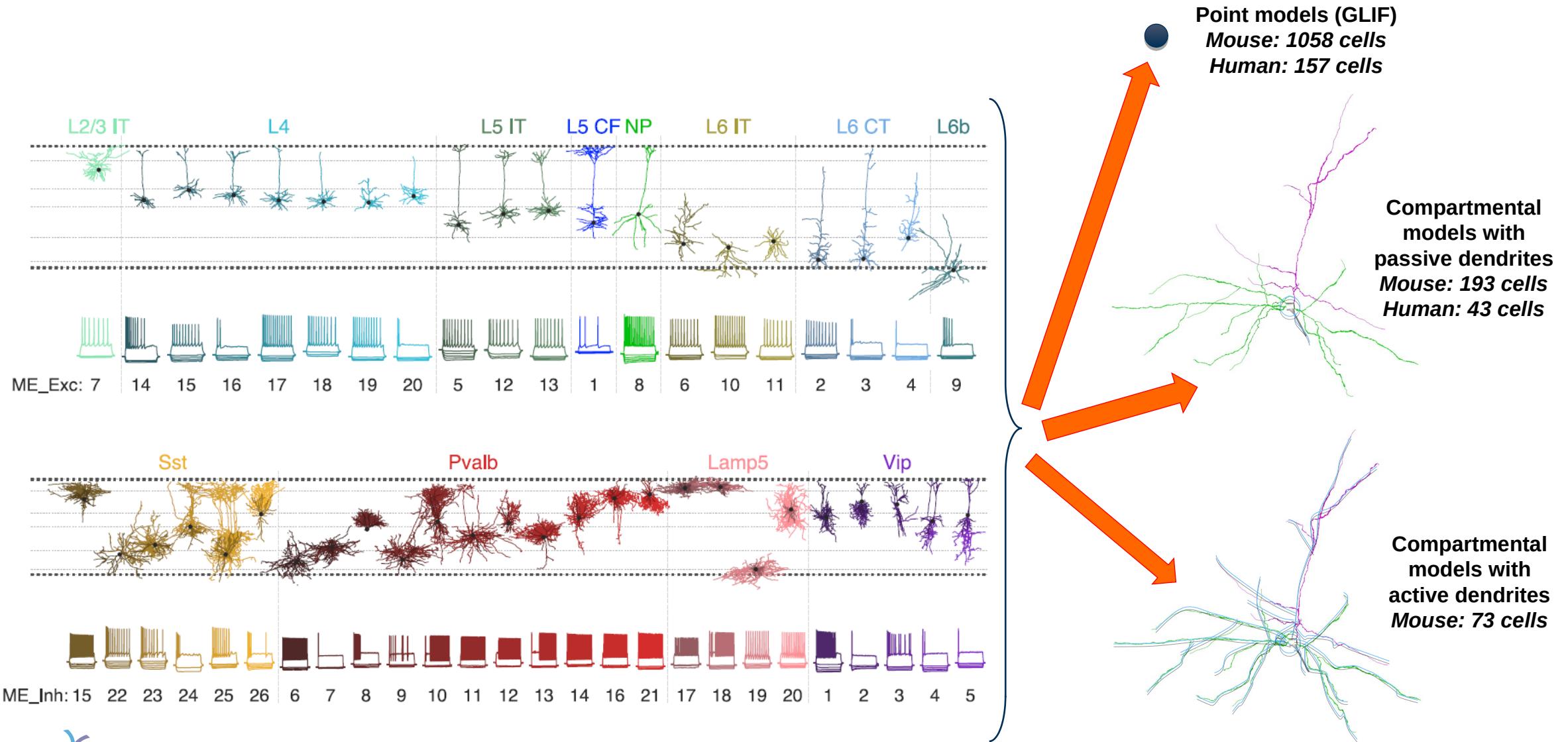
Model of the Mouse Primary Visual Cortex (V1)



- **230,924** cells total
- **17 cell classes**
- **One-to-one** mapping between the biophysical and point-neuron models

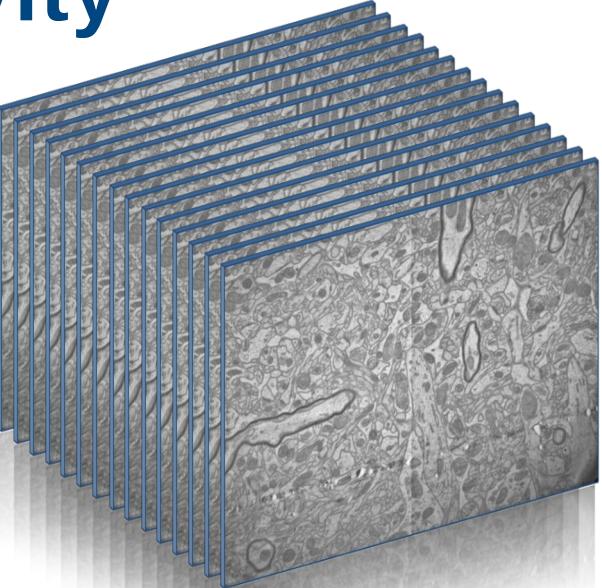
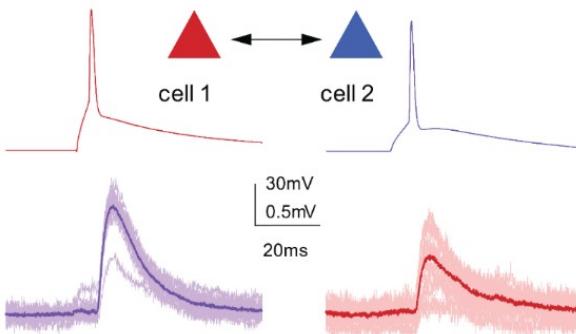
Models of Individual Neurons

Allen Cell Types Database: celltypes.brain-map.org



Connectivity

Electron Microscopy Connectomics



Multi-patch synaptic physiology

Connection probabilities

Target

Source	i1HTR	E2/3	i2/3 PV	i2/3 SST	i2/3 HTR	E4	i4 PV	i4 SST	i4 HTR	E5	i5 PV	i5 SST	i5 HTR	E6	i6 PV	i6 SST	i6 HTR	
i1HTR	0.656	0.356	0.093	0.068	0.464	0.148				0.148	0	0		0.148				
E2/3	0	0.16	0.395	0.182	0.105	0.016	0.083	0.083	0.083	0.083	0.081	0.102		0				
i2/3PV	0.024	0.411	0.451	0.03	0.22	0.05	0.05	0.05	0.05	0.07	0.073							
i2/3SS T	0.279	0.424	0.857	0.082	0.77	0.05	0.05	0.05	0.05	0.021		0						
i2/3HT R	0	0.087	0.02	0.625	0.028	0.05	0.05	0.05	0.05	0								
E4	0.14	0.1	0.1	0.1	0.243	0.43	0.571	0.571	0.104	0.101	0.128	0.05	0.032					
i4PV		0.25	0.05	0.05	0.05	0.437	0.451	0.03	0.22	0.088	0.091	0.03	0.03					
i4SST	0.241	0.25	0.05	0.05	0.05	0.351	0.857	0.082	0.77	0.026	0.03	0	0.03					
i4HTR		0.25	0.05	0.05	0.05	0.351	0.02	0.625	0.028	0	0.03	0.03	0.03					
E5	0.017	0.021	0.05	0.05	0.05	0.007	0.05	0.05	0.05	0.116	0.083	0.063	0.105	0.047	0.03	0.03	0.03	
i5PV	0	0	0.102				0	0.034	0.03	0.03	0.455	0.361	0.03	0.22	0.03	0.01	0.01	0.01
i5SST	0.203	0.169		0.017			0.056	0.03	0.006	0.03	0.317	0.857	0.04	0.77	0.03	0.01	0.01	0.01
i5HTR								0.03	0.03	0.03	0.03	0.125	0.02	0.625	0.02	0.03	0.01	0.01
E6	0						0			0.012	0.01	0.01	0.01	0.026	0.145	0.1	0.1	
i6PV	0.1						0.1			0.1	0.03	0.03	0.03	0.1	0.08	0.1	0.08	
i6SST								0.03	0.03	0.03	0.03	0.1	0.05	0.05	0.05	0.1	0.05	0.05
i6HTR								0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.1	0.05	0.05	0.03

Synaptic Strength, unitary PSP (mV)

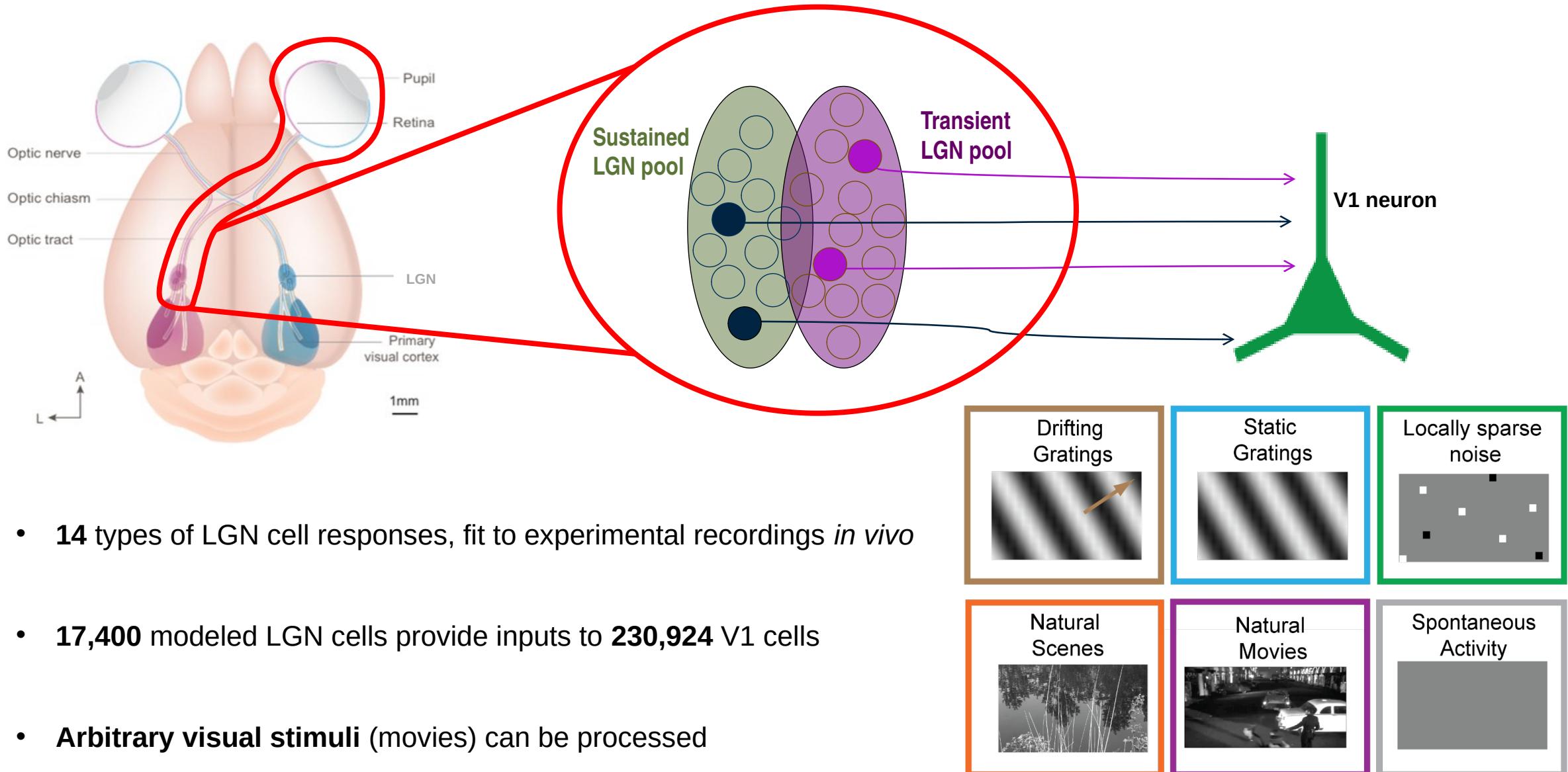
Target

Source	i1HTR	E2/3	i2/3 PV	i2/3 SST	i2/3 HTR	E4	i4 PV	i4 SST	i4 HTR	E5	i5 PV	i5 SST	i5 HTR	E6	i6 PV	i6 SST	i6 HTR
i1HTR	1.73	0.53	0.48	0.57	0.78	0.42				0.42	0	0		0.42			
E2/3	0	0.36	1.49	0.86	1.31	0.34	1.39	0.69	0.91	0.74	1.32	0.53		0			
i2/3PV	0.37	0.48	0.68	0.42	0.41	0.56	0.68	0.42	0.41	0.2	0.79						
i2/3SS T	0.47	0.31	0.5	0.15	0.52	0.3	0.5	0.15	0.52	0.22		0					
i2/3HT R	0	0.28	0.18	0.32	0.37	0.29	0.18	0.32	0.37	0							
E4	0.78	1.39	0.69	0.91	0.91	0.83	1.29	0.51	0.51	0.63	1.25	0.52	0.91	0.96			
i4PV	0.56	0.68	0.42	0.41	0.64	0.68	0.42	0.41	0.73	0.94	0.42	0.41					
i4SST	0.39	0.3	0.5	0.15	0.52	0.29	0.5	0.15	0.52	0.28	0.45	0.28	0.52				
i4HTR	0.29	0.18	0.32	0.37	0.29	0.18	0.32	0.37	0	0.18	0.33	0.37					
E5	0.76	0.47	1.25	0.52	0.91	0.38	1.25	0.52	0.91	0.75	1.2	0.52	1.31	0.4	2.5	0.52	1.31
i5PV	0	0	0.51			0	0.94	0.42	0.41	0.81	1.19	0.41	0.41	0.81	1.19	0.41	0.41
i5SST	0.31	0.25		0.39		0.28	0.45	0.28	0.52	0.27	0.4	0.4	0.52	0.27	0.4	0.4	0.52
i5HTR						0.29	0.18	0.33	0.37	0.28	0.18	0.33	0.37	0.28	0.18	0.33	0.37
E6	0					0				0.23	2.5	0.52	1.31	0.94	3.8	0.52	1.31
i6PV	0.81					0.81				0.81	1.19	0.41	0.41	0.81	1.19	0.41	0.41
i6SST							0.27	0.4	0.4	0.52	0.27	0.4	0.4	0.52	0.27	0.4	0.4
i6HTR							0.28	0.18	0.33	0.37	0.28	0.18	0.33	0.37	0.28	0.18	0.33

Axonal delays

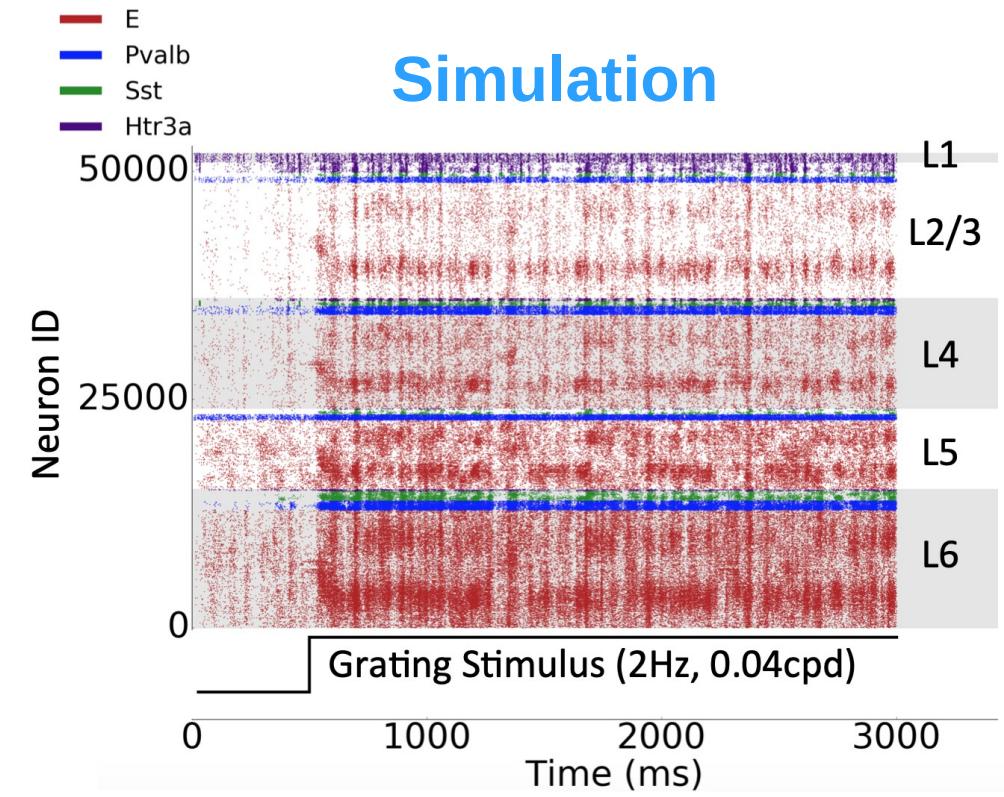
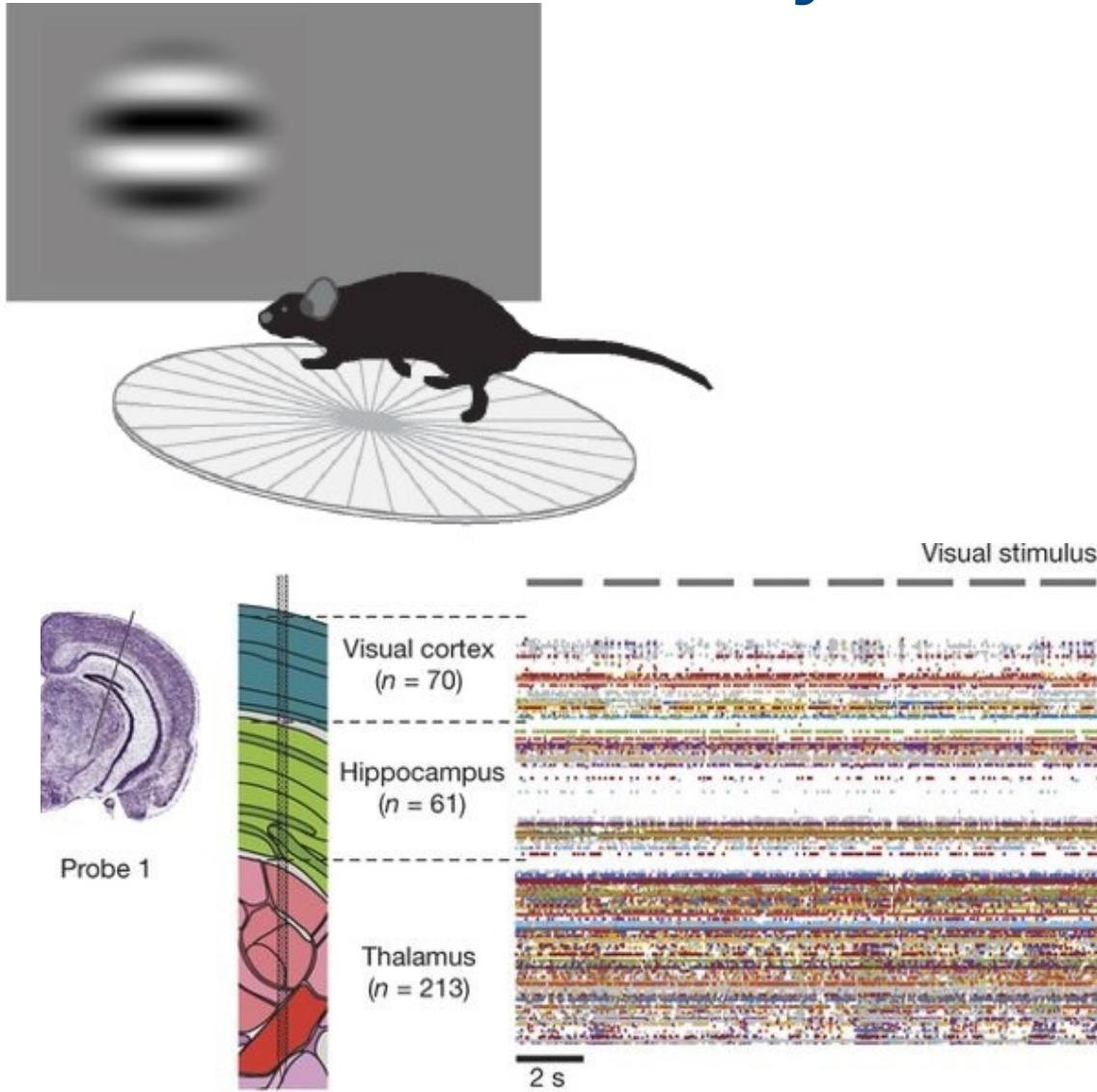
Synaptic targeting of dendrites

Filter-based Visual Inputs into the V1 model



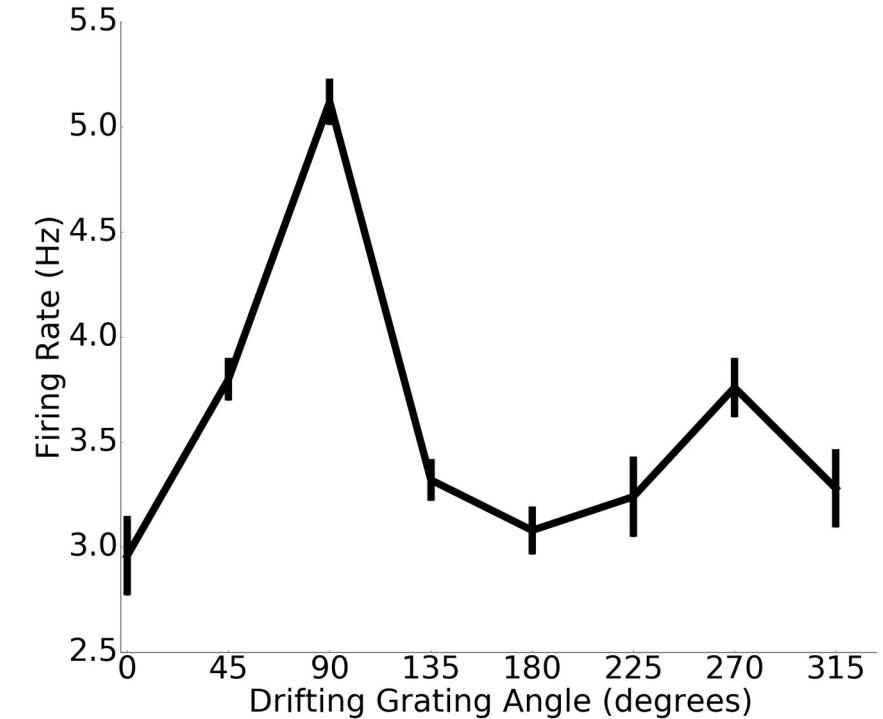
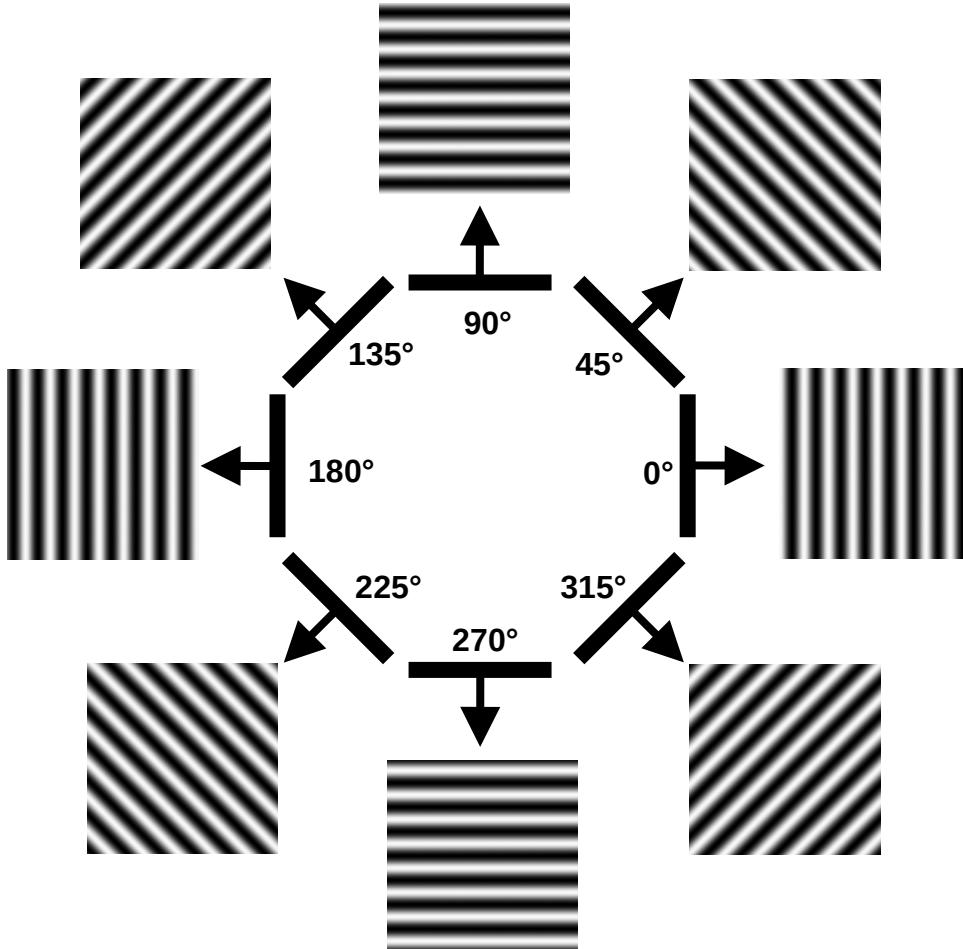
Recording Brain Activity *in Vivo*

Allen Brain Observatory: observatory.brain-map.org



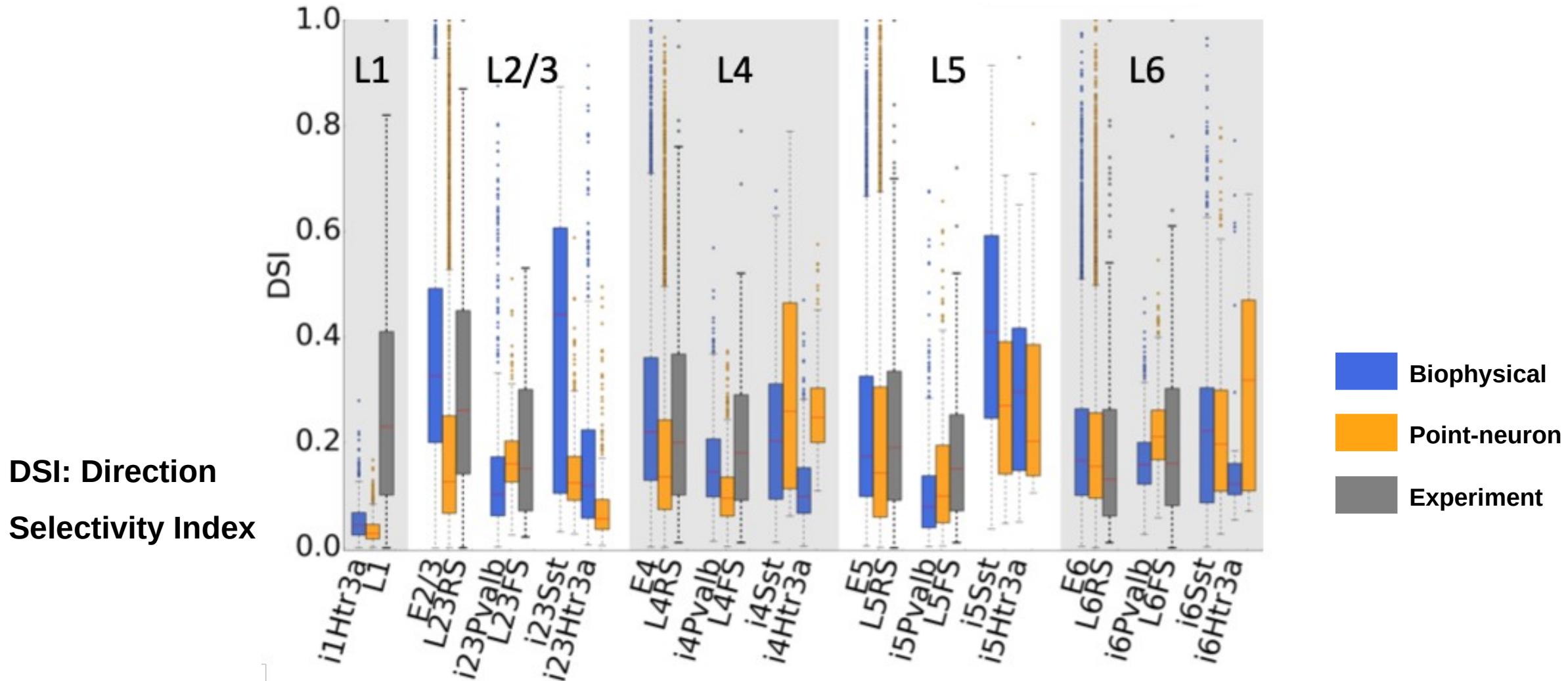
Comparison with Recordings *in Vivo*

Example: Direction Selectivity



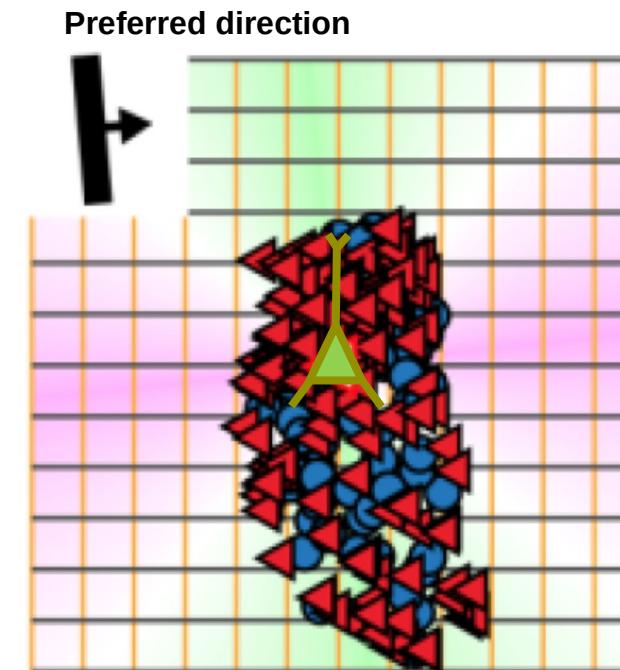
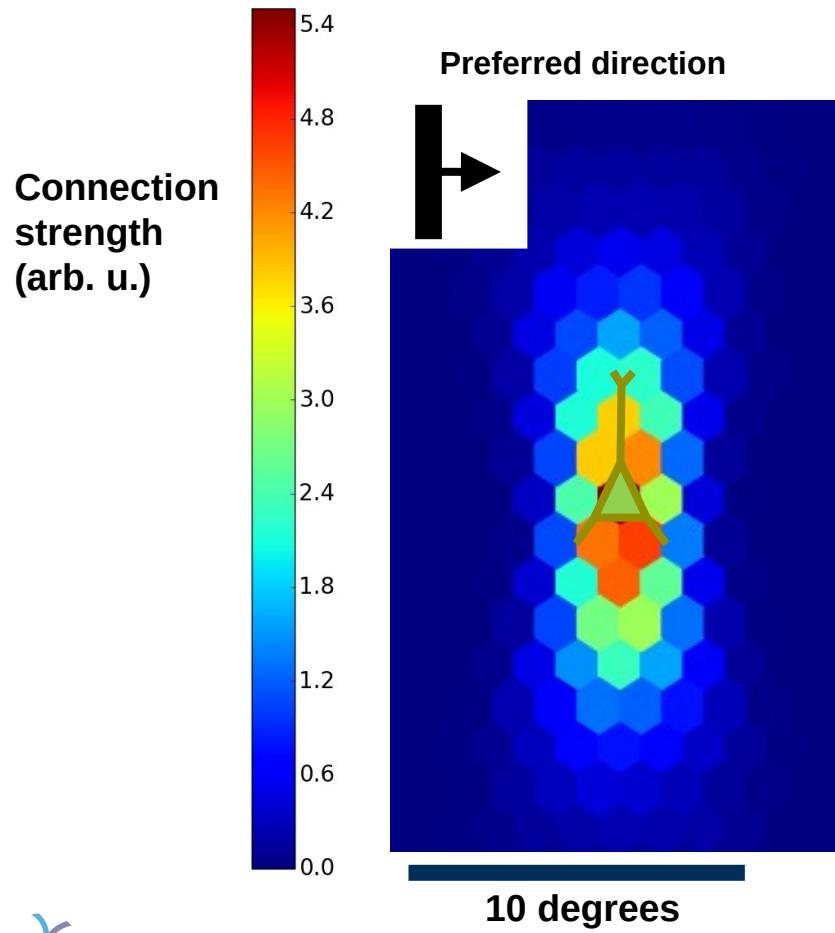
Comparison with Recordings *in Vivo*

Example: Direction Selectivity



Predicting the Logics of Neural Connectivity

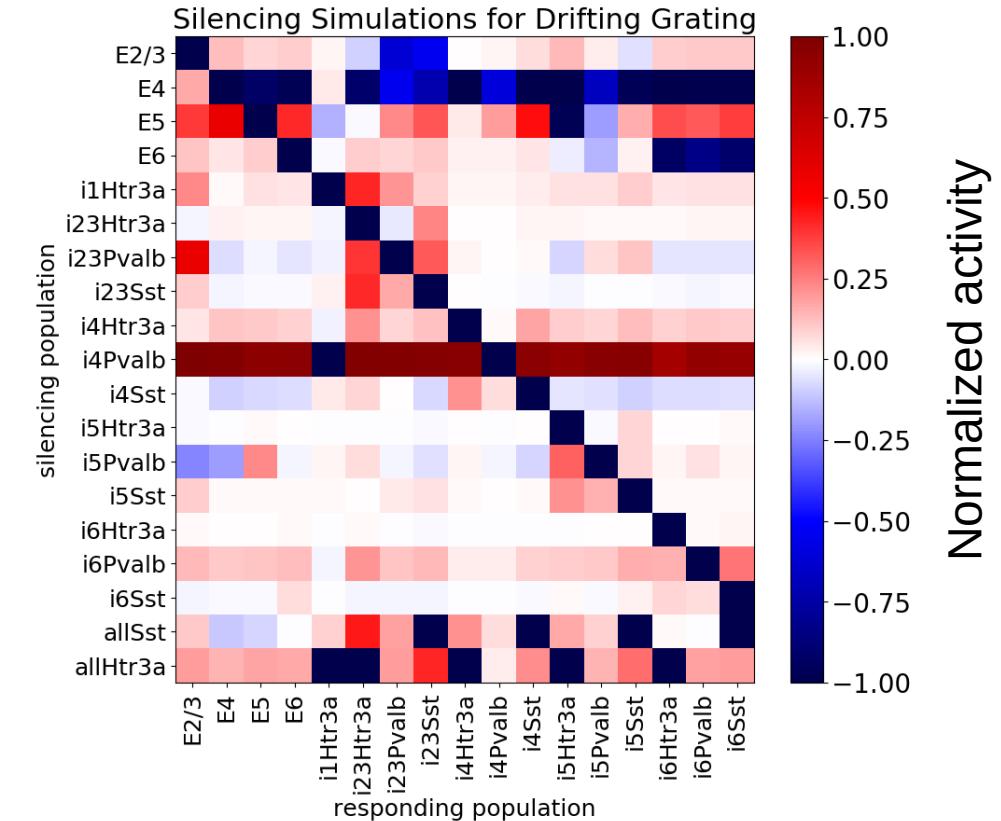
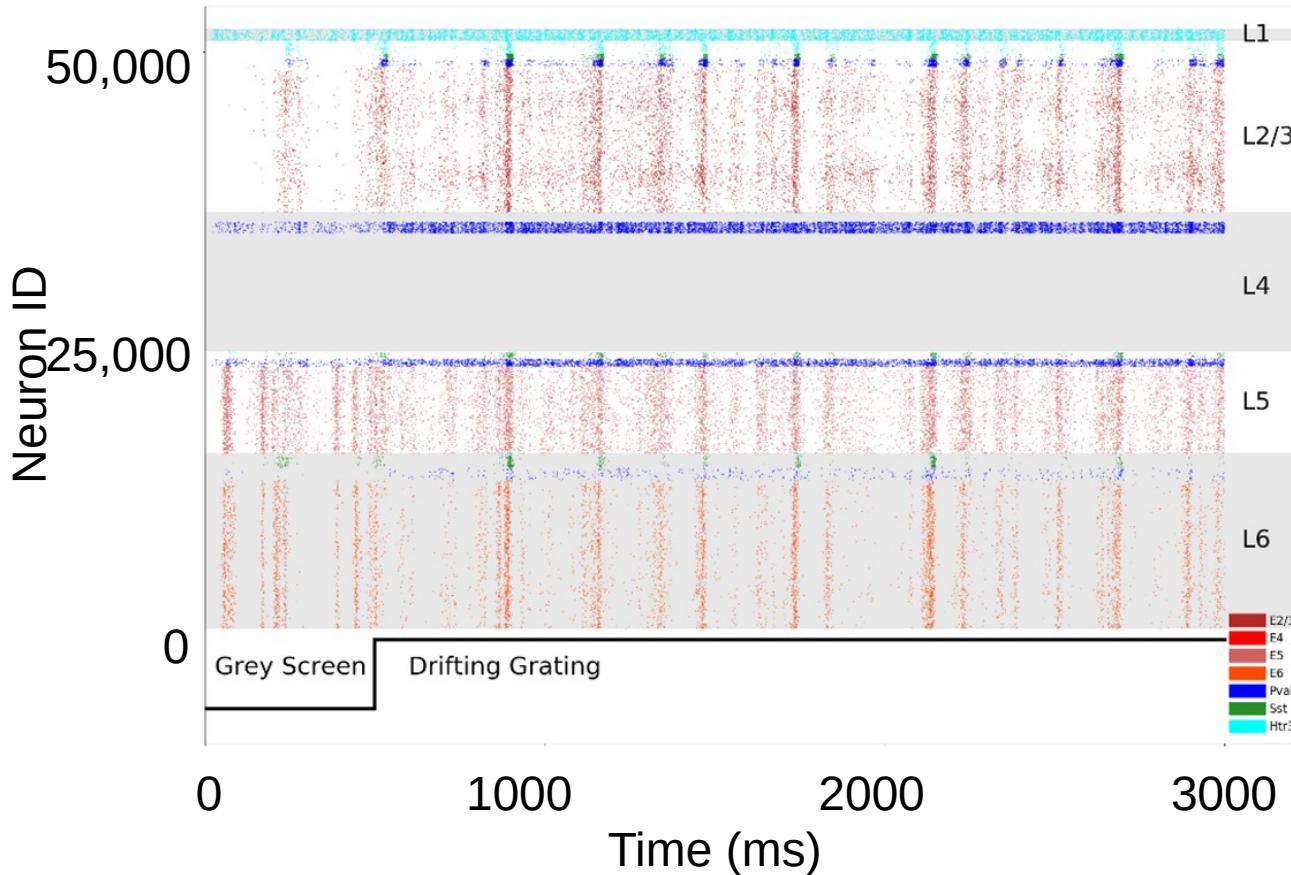
Distribution of connections in the Visual Space



Rossi et al., *BioRxiv*, 2019

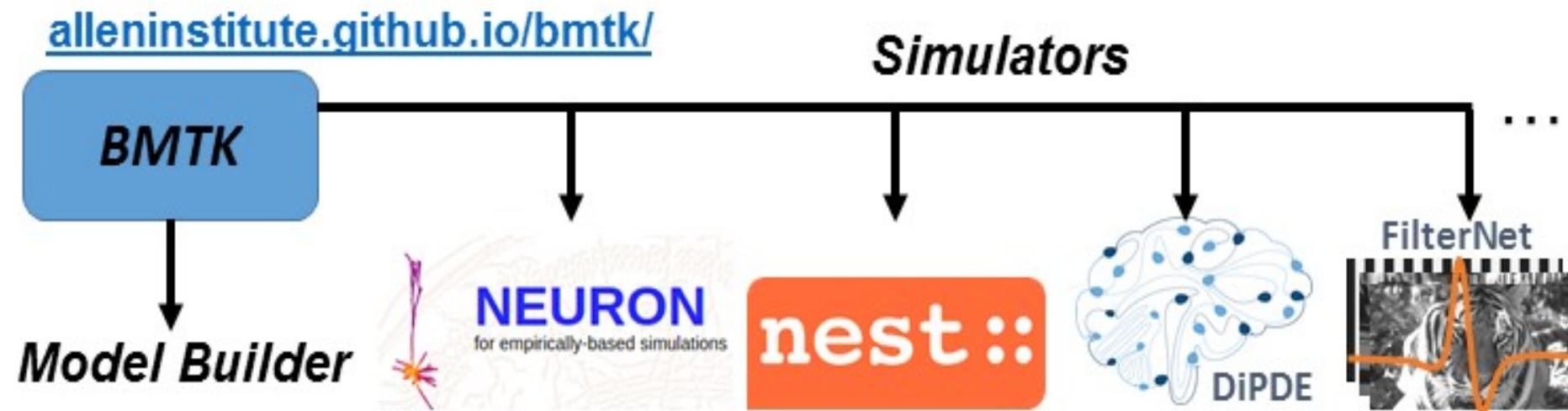
Predicting Cell-Type Specific Effects of Optogenetic Perturbations

Perturbation: Silence Layer 4 Excitatory Neurons



Our Models and Modeling Software Are Freely Available to the Community

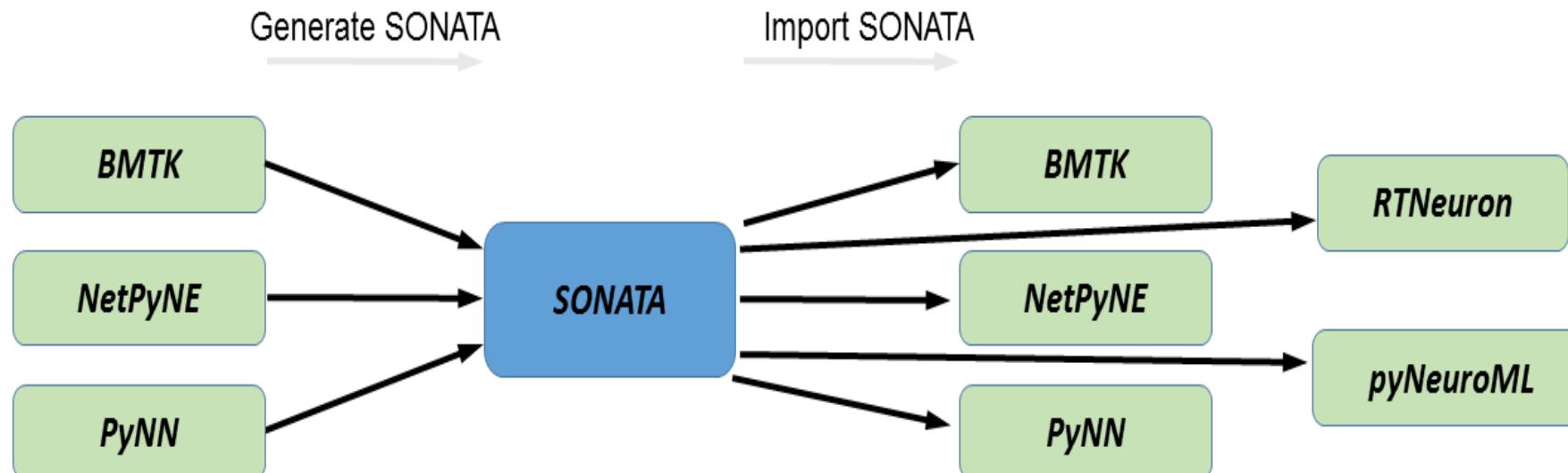
Brain Modeling ToolKit (BMTK): <https://alleninstitute.github.io/bmtk/>



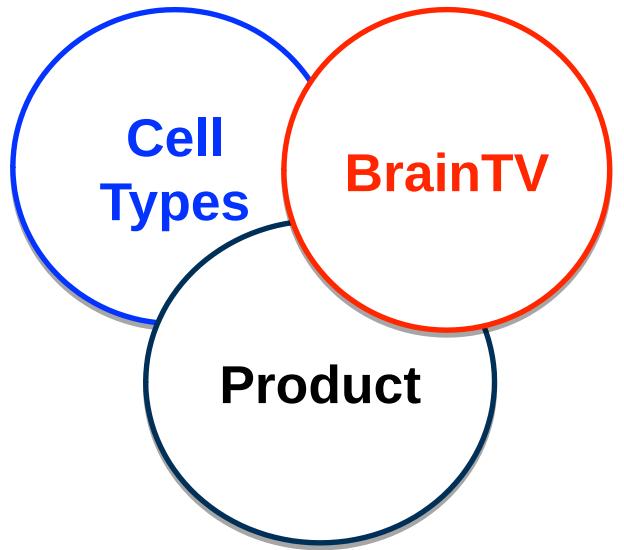
Our Models and Modeling Software Are Freely Available to the Community

Scalable Open Network Architecture TemplAte (SONATA):
<https://github.com/AllenInstitute/sonata>

An interface between SONATA and the NWB format has been developed as well



Product Program



<http://brain-map.org/>

The screenshot shows the homepage of the Allen Brain Map website. At the top, there is a navigation bar with links for "ALLEN BRAIN MAP", "Atlases and Data", "Explore", "Technical Resources", "Allen Institute", and "Updates & Support". Below the navigation bar, a dark banner features the text "Accelerating progress toward understanding the brain." and several circular images of brain tissue and neural structures. The main content area is titled "Allen Brain Atlases and Data" and contains three cards:

- CELL TYPES DATABASE**: A database of biological features derived from single cells, from both human and mouse.
[View Data →](#)
- BRAIN OBSERVATORY**: A new approach to open data, featuring a survey of *in vivo* recordings from the mouse visual cortex.
[View Data →](#)
- MOUSE BRAIN CONNECTIVITY ATLAS**: A brain-wide map of neural projections, including cell class-specific data.
[View Atlas →](#)

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

<http://brain-map.org/>

The screenshot shows the homepage of the Allen Brain Map website. At the top, there is a dark banner with the text "Accelerating progress toward understanding the brain." Below the banner, the main navigation menu includes "ALLEN BRAIN MAP", "Atlases and Data", "Explore", "Technical Resources", "Allen Institute", and "Updates & Support". The main content area features three large circular images: one showing a brain network, another showing a brain slice, and a third showing a microscopic view of neurons. Below this, a section titled "Allen Brain Atlases and Data" contains three cards: "CELL TYPES DATABASE" (with a grayscale neuron image), "BRAIN OBSERVATORY" (with a grayscale image of brain tissue), and "MOUSE BRAIN CONNECTIVITY ATLAS" (with a grayscale image of a brain slice with colored tracers). Each card has a "View Data" button.



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

WELCOME TO THE ALLEN SDK

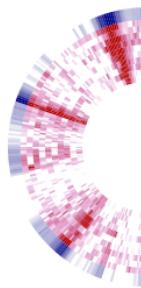
The Allen Software Development Kit houses source code for reading and processing Allen Brain Atlas data. The Allen SDK focuses on the Allen Brain Observatory, Cell Types Database, and Mouse Brain Connectivity Atlas.

ALLEN BRAIN OBSERVATORY

The [Allen Brain Observatory](#) is a data resource for understanding sensory processing in the mouse visual cortex. This study systematically measures visual responses in multiple cortical areas and layers using two-photon calcium imaging of GCaMP6-labeled neurons targeted using Cre driver lines. Response characterizations include orientation tuning, spatial and temporal frequency tuning, temporal dynamics, and spatial receptive field structure.

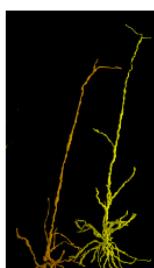
The mean fluorescence traces for all segmented cells are available in the Neurodata Without Borders file format ([NWB files](#)). These files contain standardized descriptions of visual stimuli to support stimulus-specific tuning analysis. The Allen SDK provides code to:

- download and organize experiment data according to cortical area, imaging depth, and Cre line
- remove the contribution of neuropil signal from fluorescence traces
- access (or compute) dF/F traces based on the neuropil-corrected traces
- perform stimulus-specific tuning analysis (e.g. drifting grating direction tuning)



ALLEN CELL TYPES DATABASE

The [Allen Cell Types Database](#) contains electrophysiological and morphological characterizations of individual neurons in the mouse primary visual cortex. The Allen SDK provides Python code for accessing electrophysiology measurements ([NWB files](#)) for all neurons and morphological reconstructions ([SWC files](#)) for a subset of neurons.



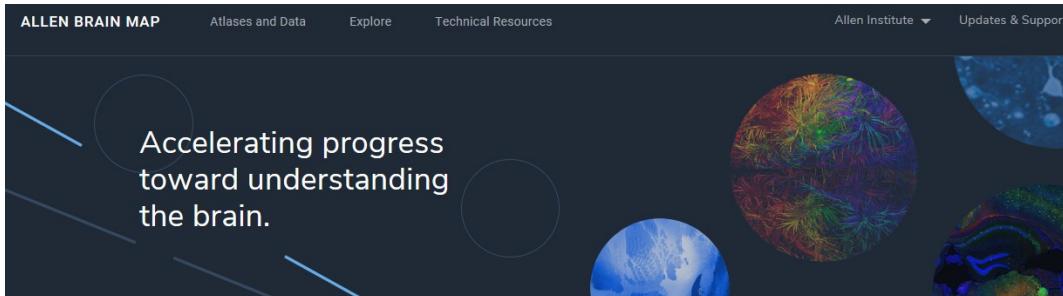
The Database also contains two classes of models fit to this data set: biophysical models produced using the NEURON simulator and generalized leaky integrate and fire models (GLIFs) produced using custom Python code provided with this toolkit.

The Allen SDK provides sample code demonstrating how to download neuronal model parameters from the Allen Brain Atlas API and run your own simulations using stimuli from the Allen Cell Types Database or custom current injections:

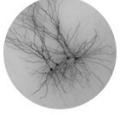
- Biophysical Models
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Our Data, Models, and Software Are Freely Available

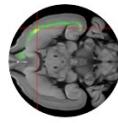
<http://brain-map.org/>



Allen Brain Atlases and Data

 **CELL TYPES DATABASE**
A database of biological features derived from single cells, from both human and mouse.
[View Data →](#)

 **BRAIN OBSERVATORY**
A new approach to open data, featuring a survey of in vivo recordings from the mouse visual cortex.
[View Data →](#)

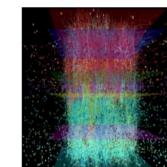
 **MOUSE BRAIN CONNECTIVITY ATLAS**
A brain-wide map of neural projections, including cell class-specific data.
[View Atlas →](#)



Computational Modeling & Theory

The Allen Institute for Brain Science has an active research program focused on modeling the activity and information on the creation and use of brain-wide, circuit-level and cell-level biophysical models, modeling

Network models



Modeling the mammalian cortex: All layers of mouse V1

Biologically realistic models of the mouse primary visual cortex at multiple levels, and used to make predictions about structure-function



Modeling the mammalian cortex: Layer IV of mouse V1

Biologically realistic models of the cortical lamina (Layer IV) at multiple levels, from biophysically detailed and point-neuron levels, to explore model simulations with a battery of visual stimuli. Learn more about the model

MCModels: Whole brain voxel-scale connectivity model

MCModels is a Python package providing mesoscale conne

Single neuron models

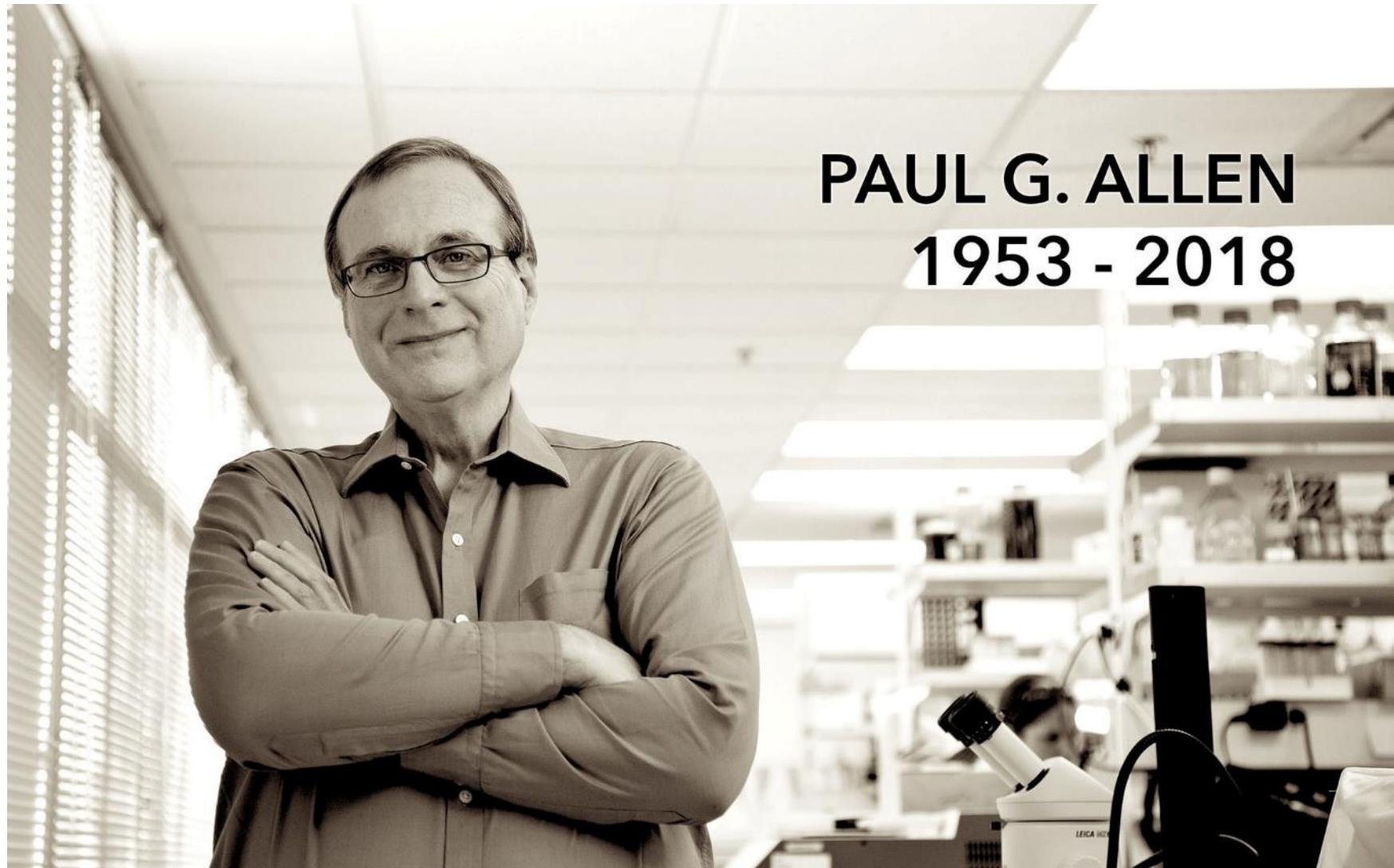


Perisomatic biophysical single neuron models

Biophysically detailed perisomatic action models are optimi

THANK YOU

We wish to thank the Allen Institute founder, Paul G. Allen, for his vision, encouragement, and support.



PAUL G. ALLEN
1953 - 2018

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