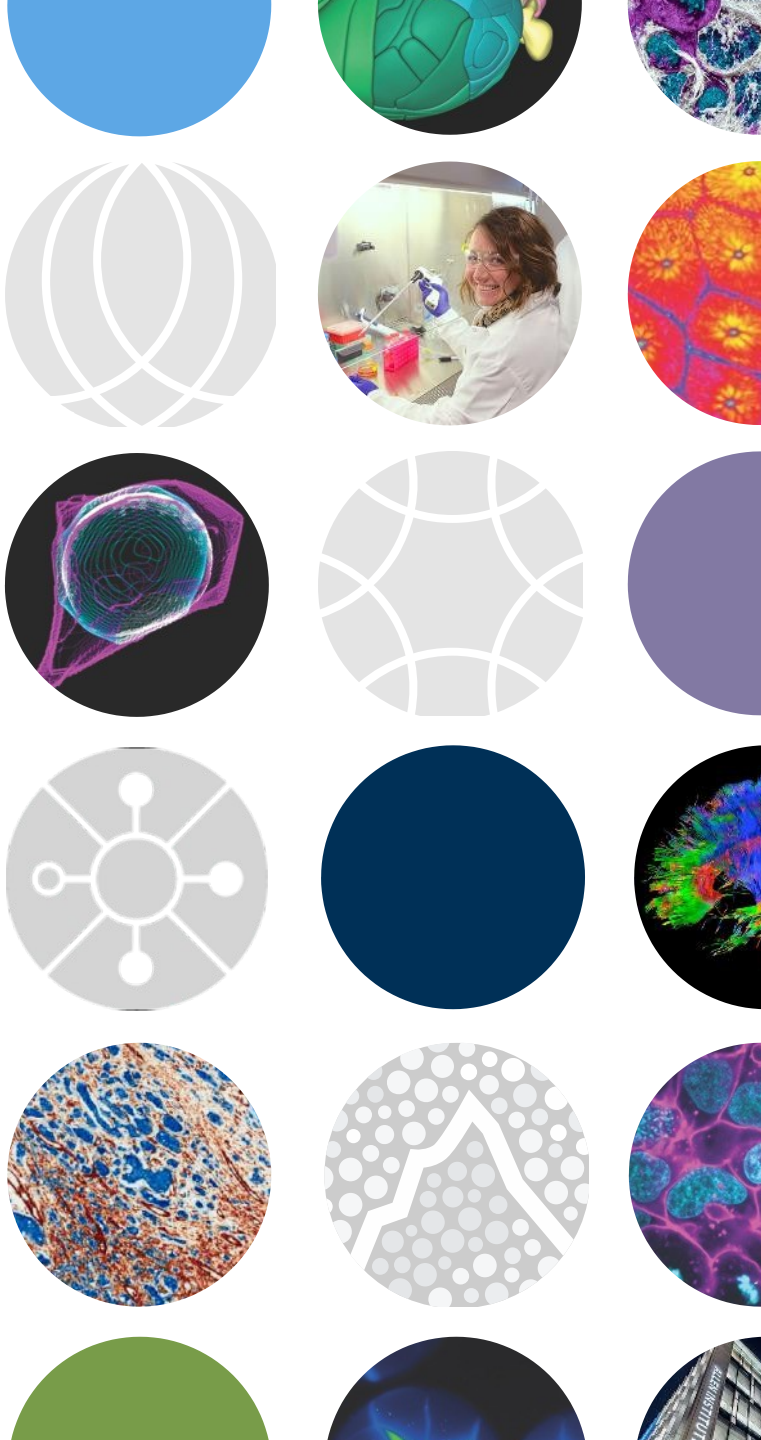


Large-scale Datasets and Modeling Tools from the Allen Institute for Brain Science

Yazan N. Billeh
yazanb@alleninstitute.org

ALLEN INSTITUTE

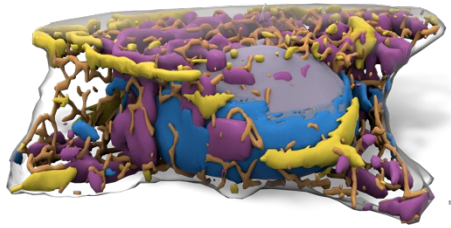
ALLEN INSTITUTE for BRAIN SCIENCE

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

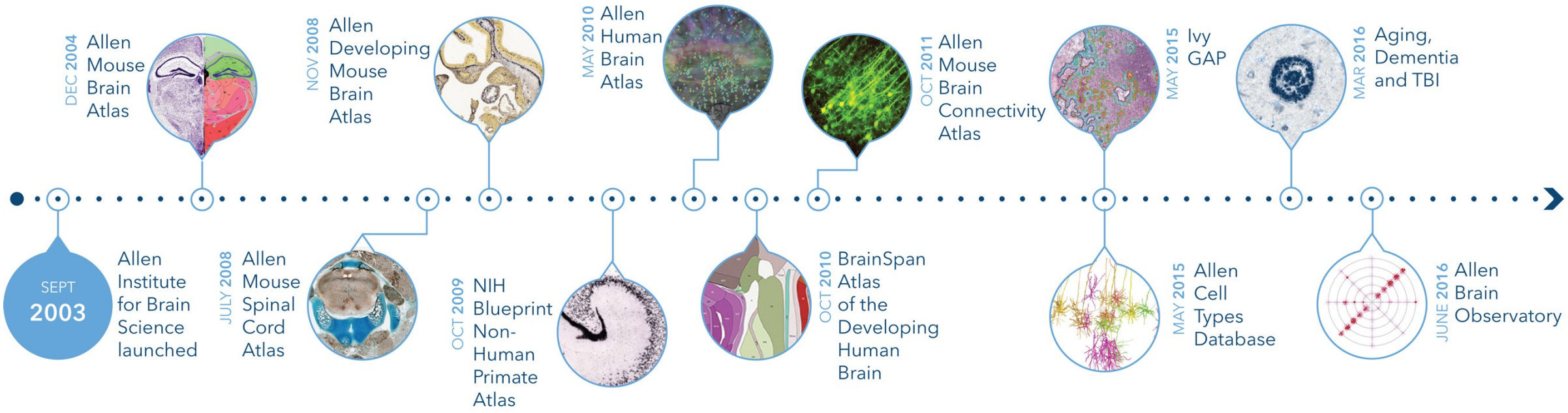
Big Science

Large-scale projects with robust, massive data

Open Science

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

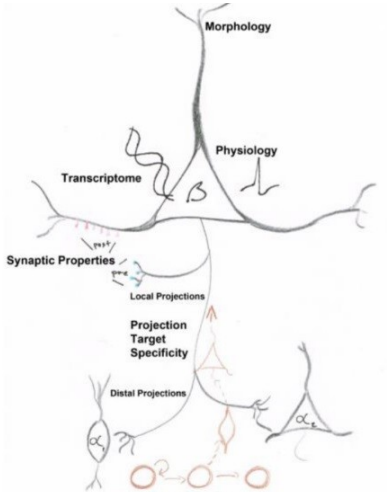
Allen Institute - Online Public Resources
www.brain-map.org

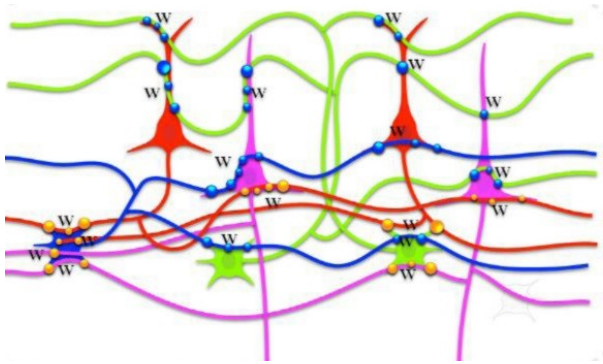


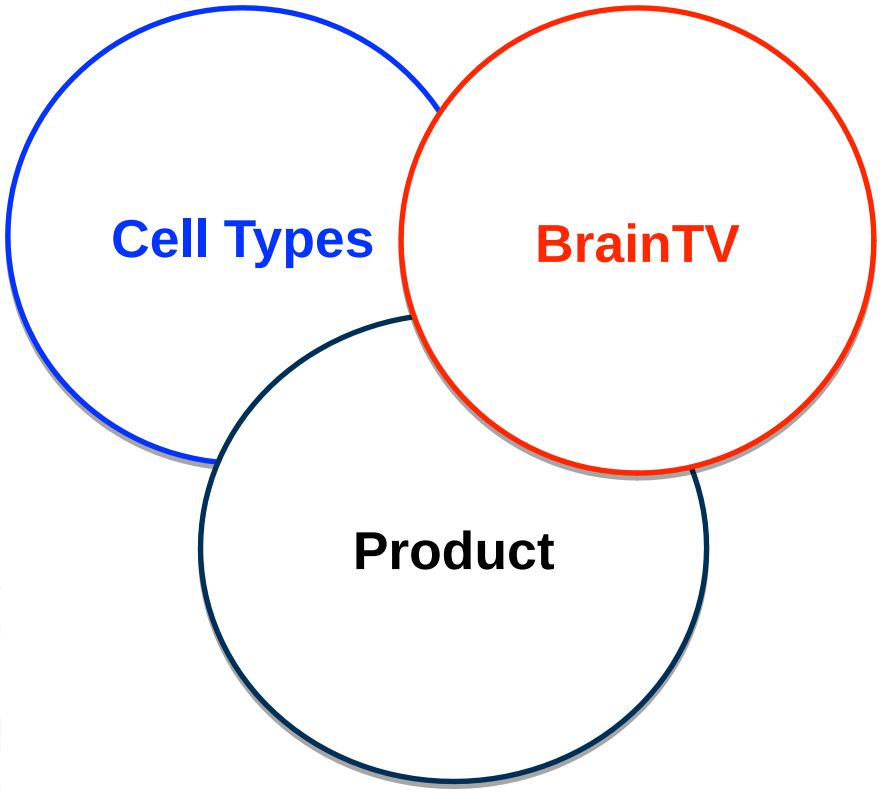
All data are:

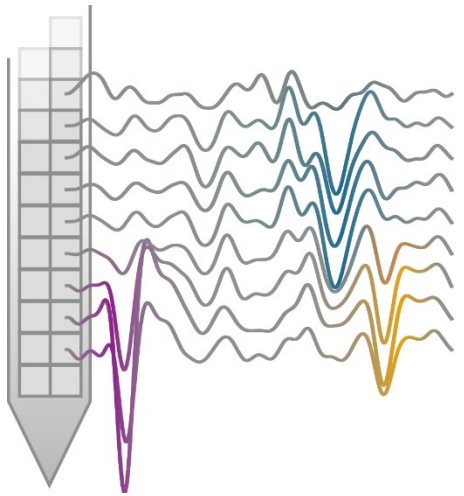
- publicly accessible via API as soon as they pass QC
- freely available without any commercial restrictions

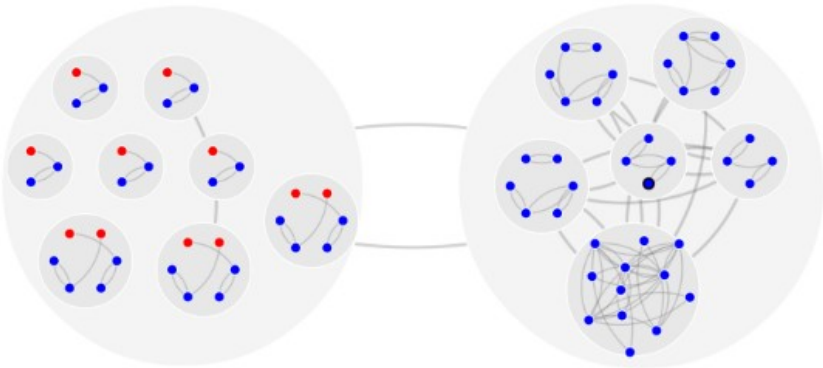
Institute Programs





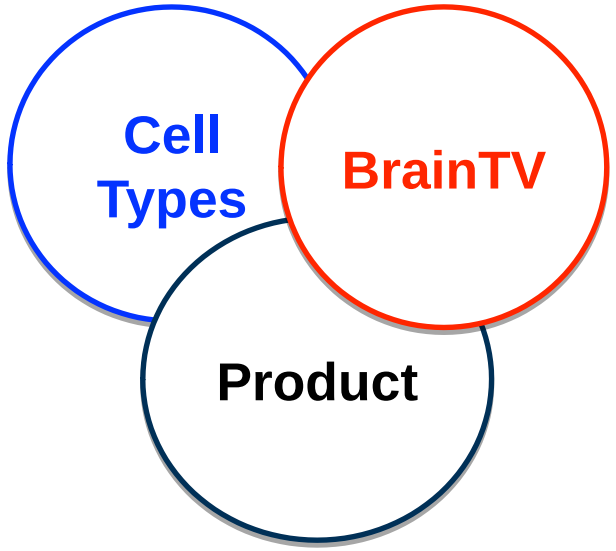


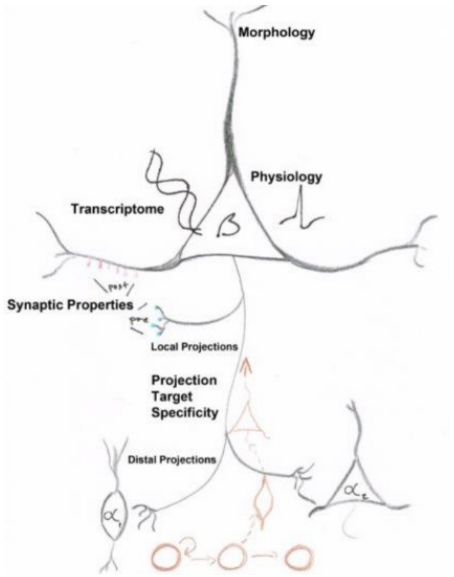


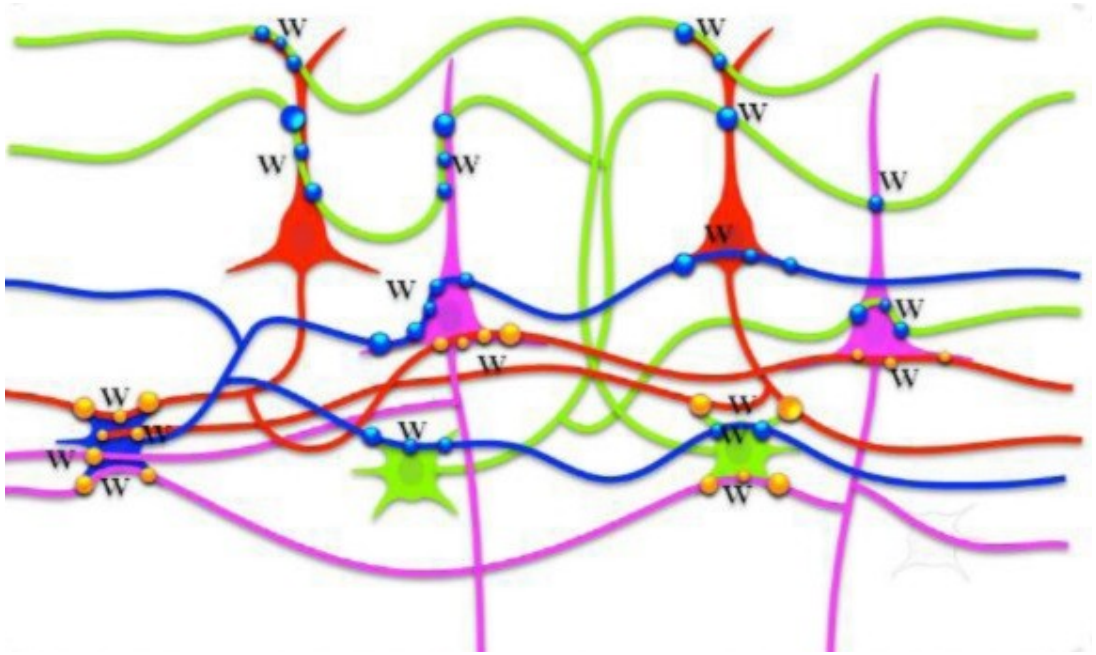


Cell Types Program

Characteristics of cells and connections



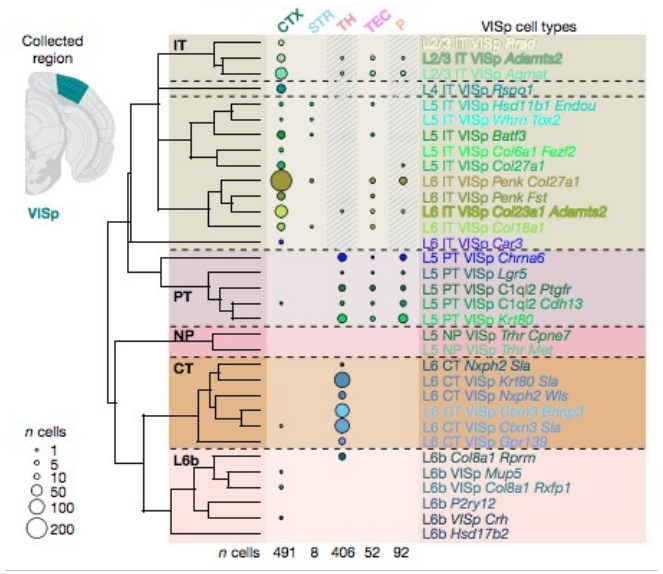


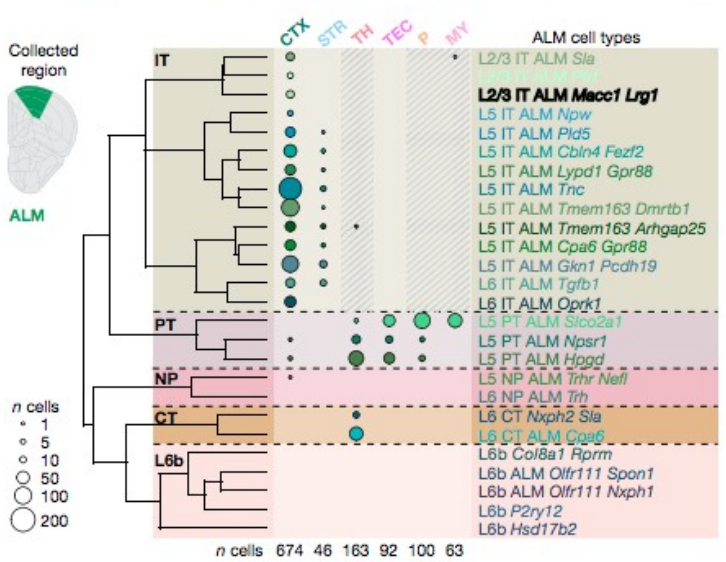


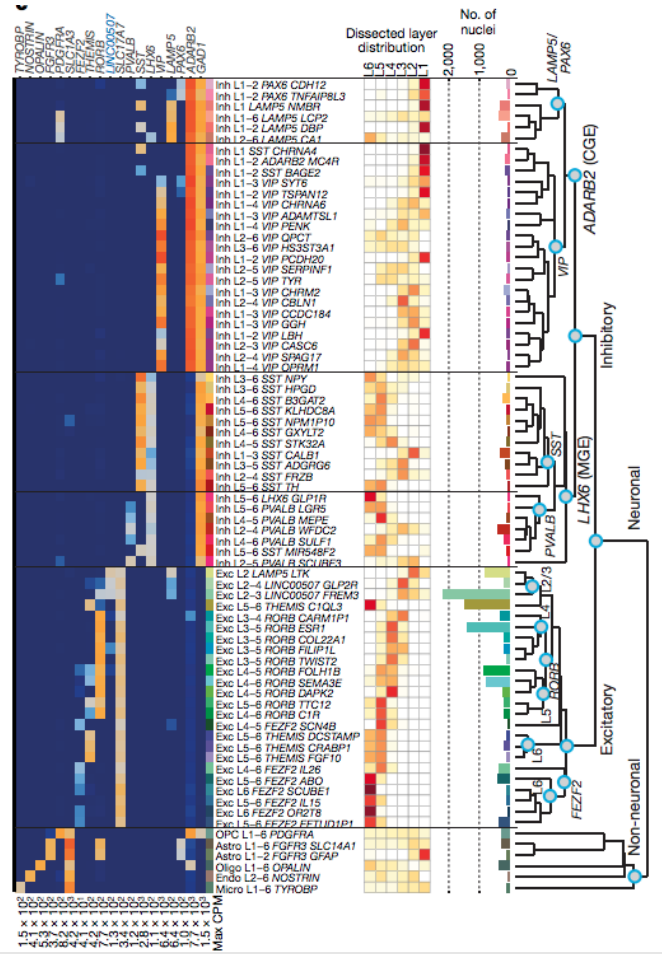
Transcriptomics (Mouse and Human)

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

Scope: Tens of thousands of cells.





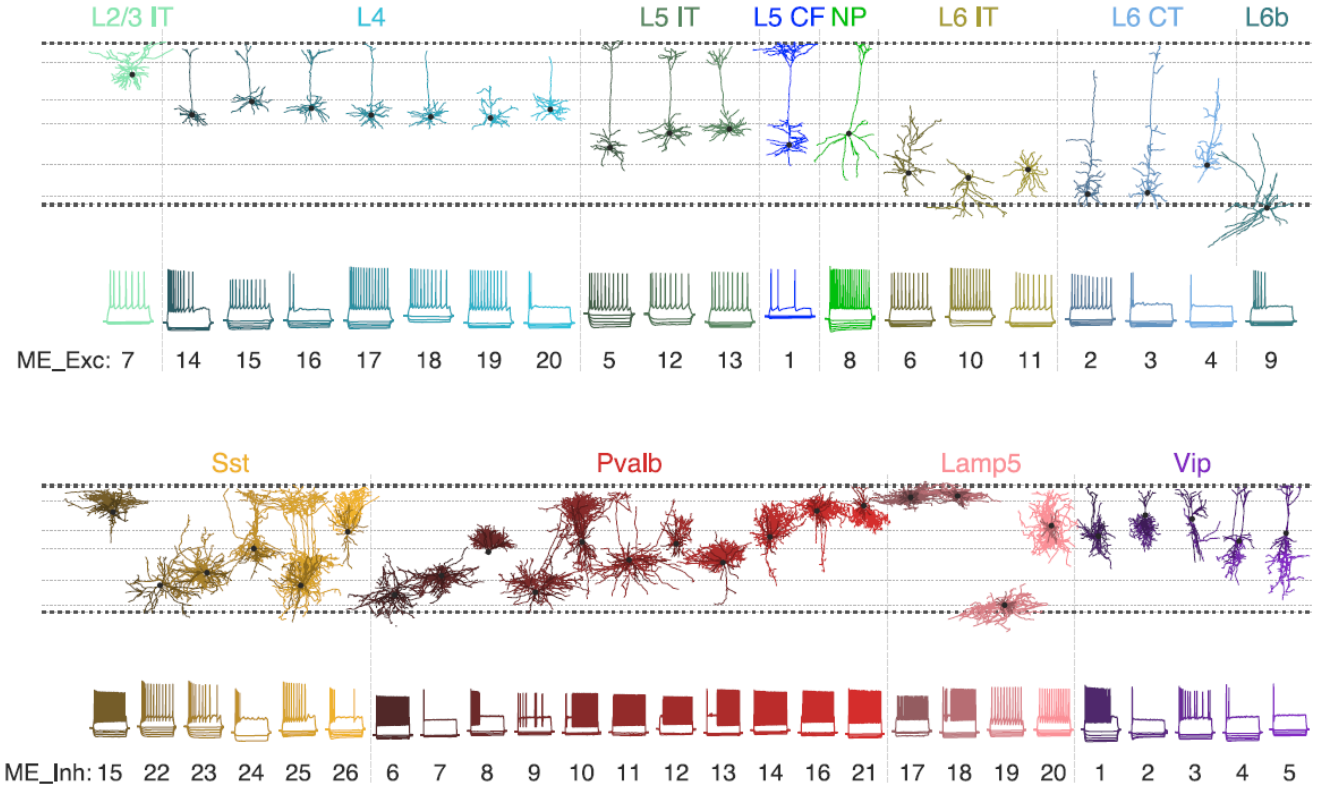


Tasic et al., *Natutre*, 2018; Hodge, Bakken,et al., *Nature*, 2019

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).



Gouwens et al., *Nature Neurosci.*, 2019

Mouse and Human Patch-Seq

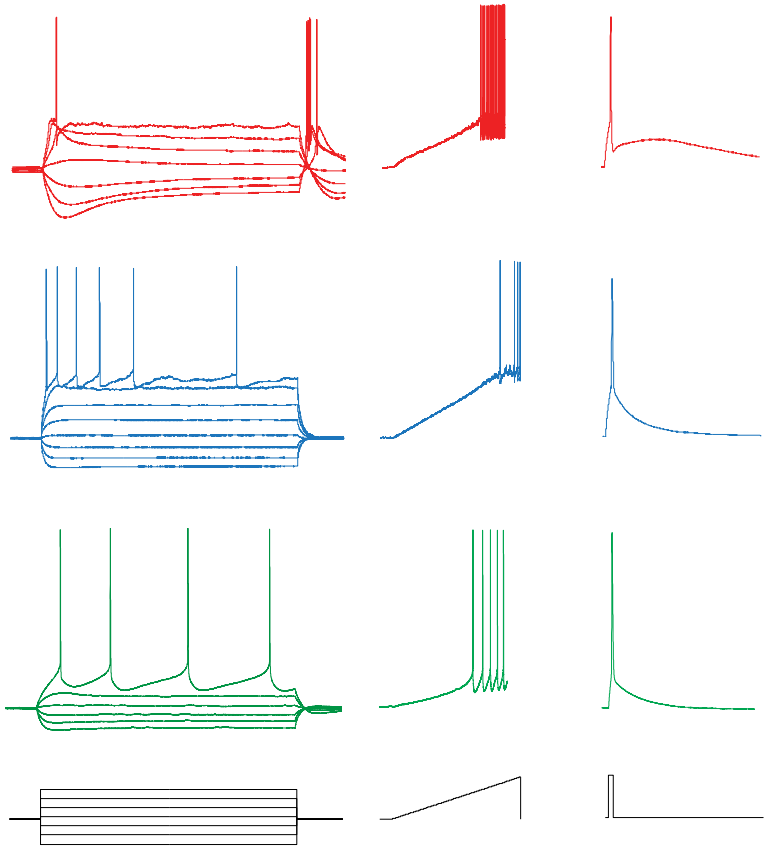
Deliverables: Transcriptomic, E-phys, and morphology data, as well as models, for mouse and human cortical cells.

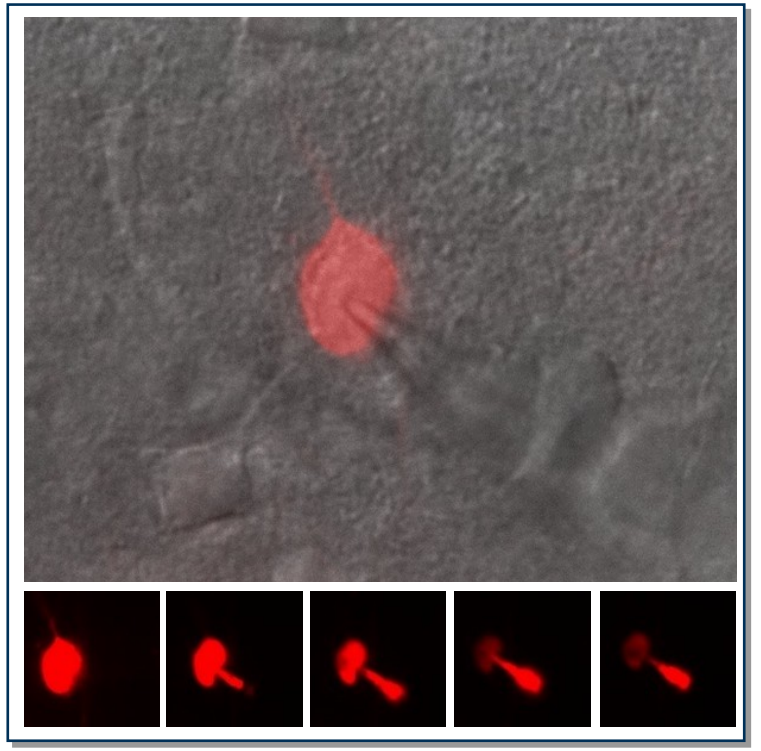
Scope: Thousands of neurons in mouse and human.

Mouse subcortical cell

Mouse cortical cell

Human cortical cell

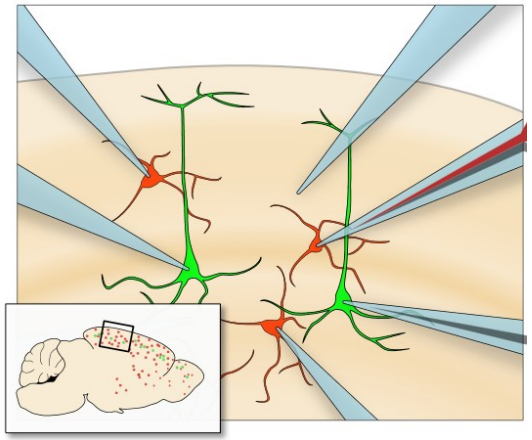


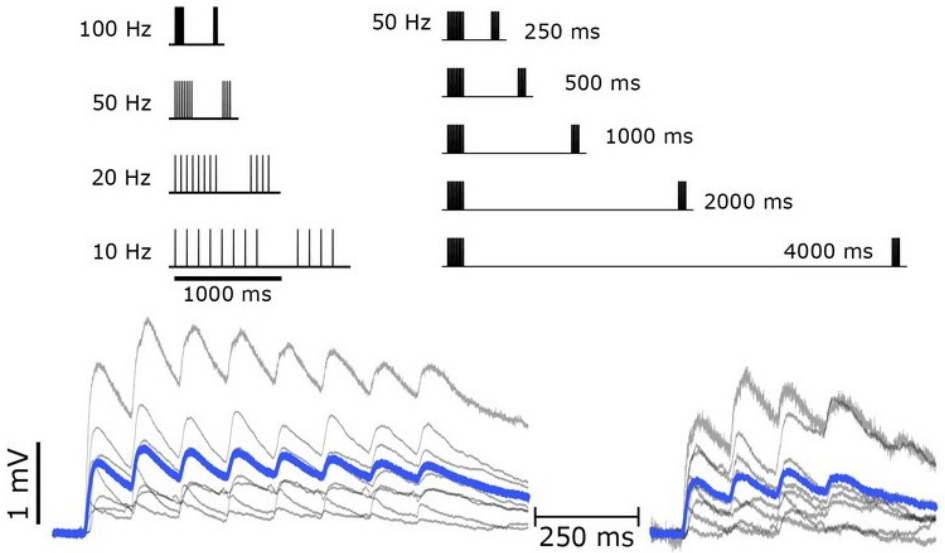


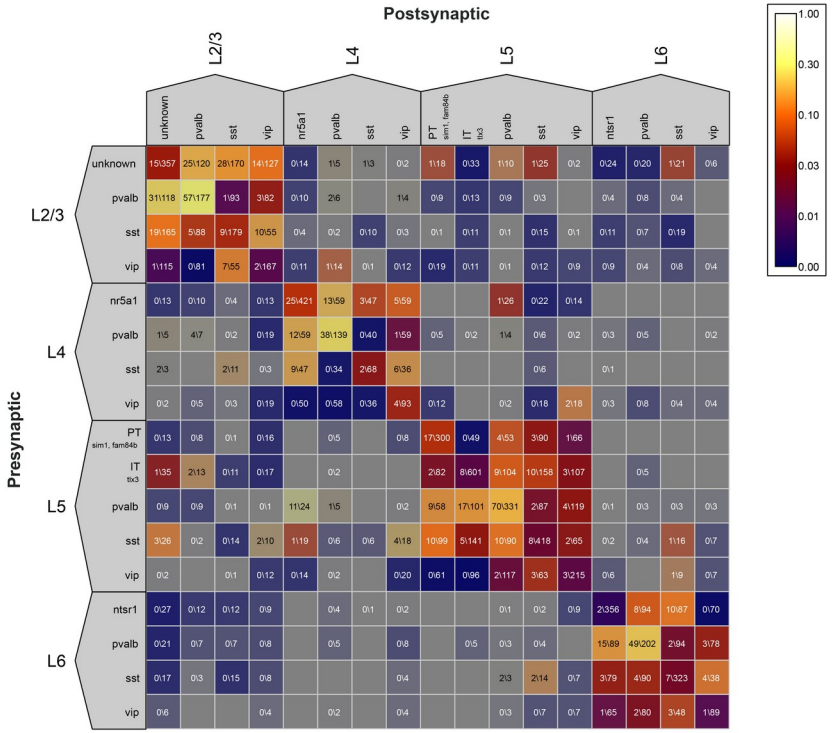
Mouse and Human Synaptic Physiology

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.





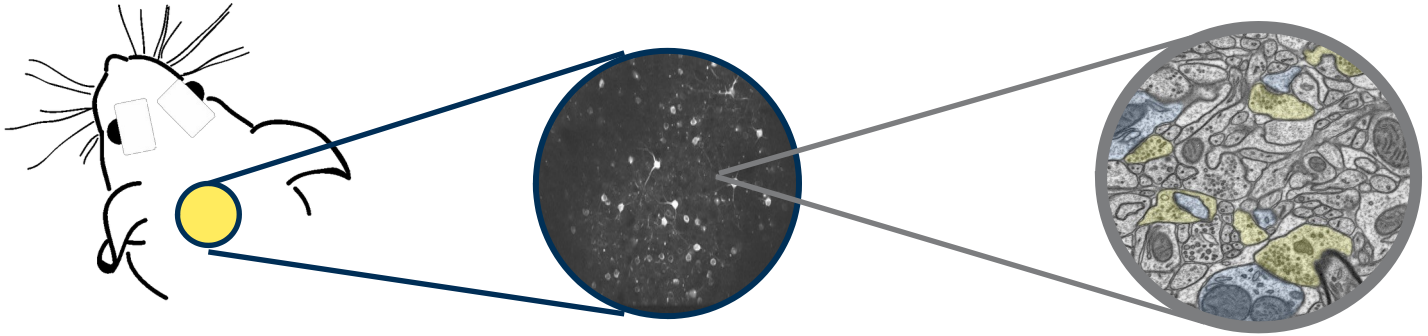


Seeman et al., *eLife.*, 2018

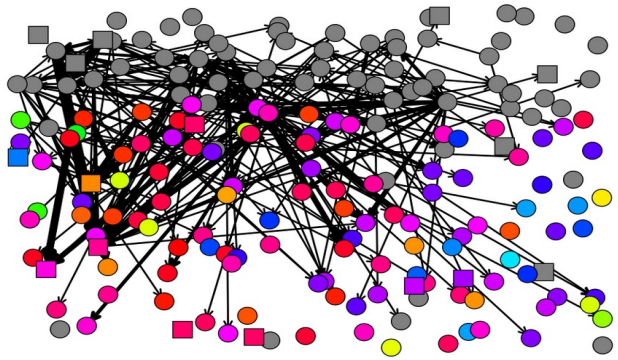
Mouse and Human EM Connectomics

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, many of the neurons would be functionally characterized *in vivo*).



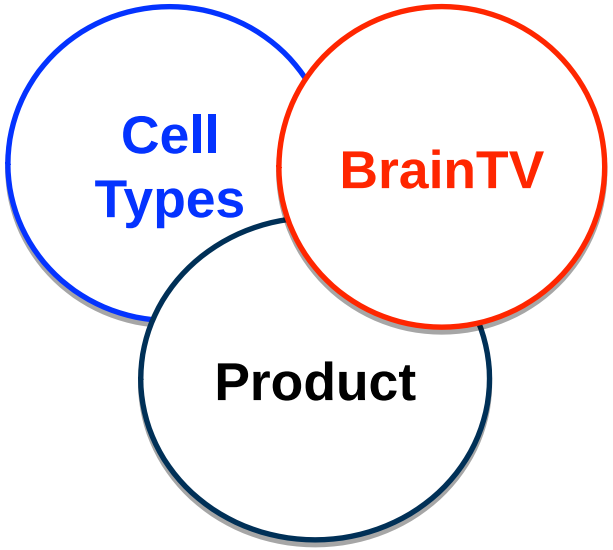
Wiring Diagram



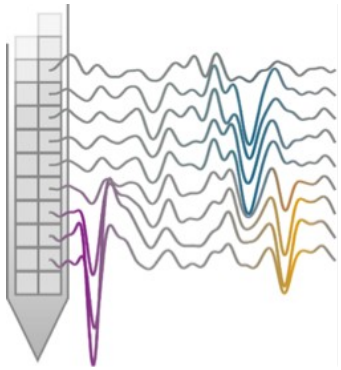
Cell Types

BrainTV Program

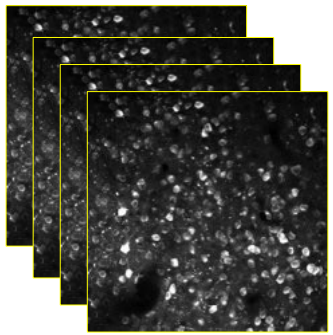
Activity and Computations in Cortical Circuits *in Vivo*



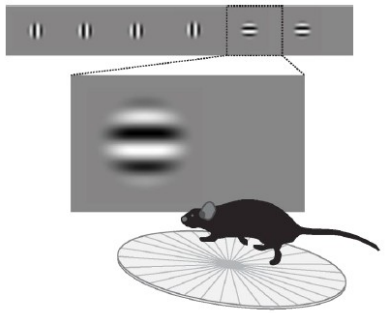
Ephys – Neuropixels Probes



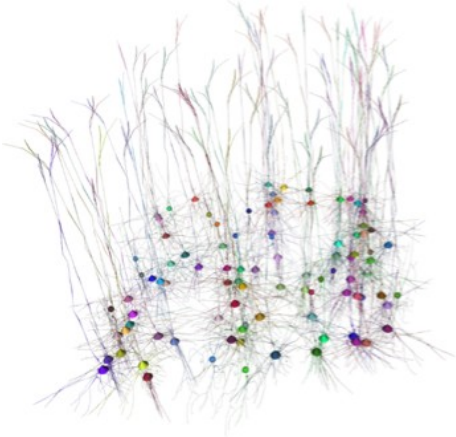
2p Cellular Imaging



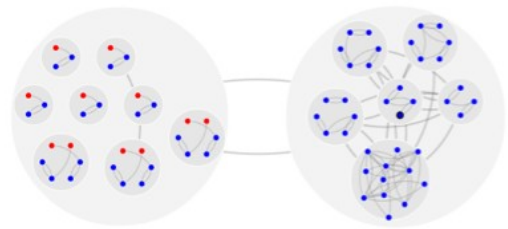
Visual Behavior



Biophysical Modeling



Point Neuron & Filter Networks

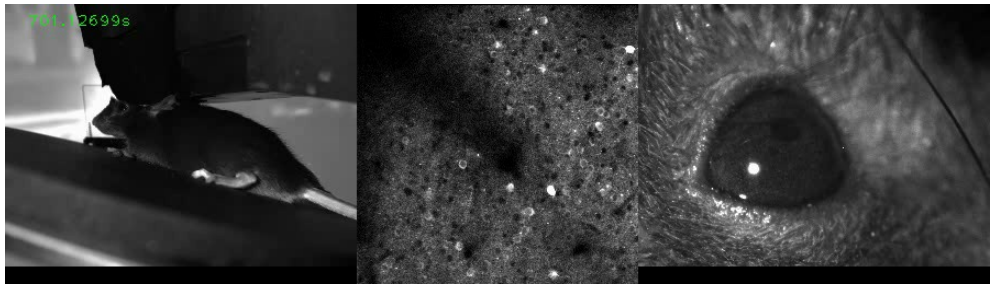


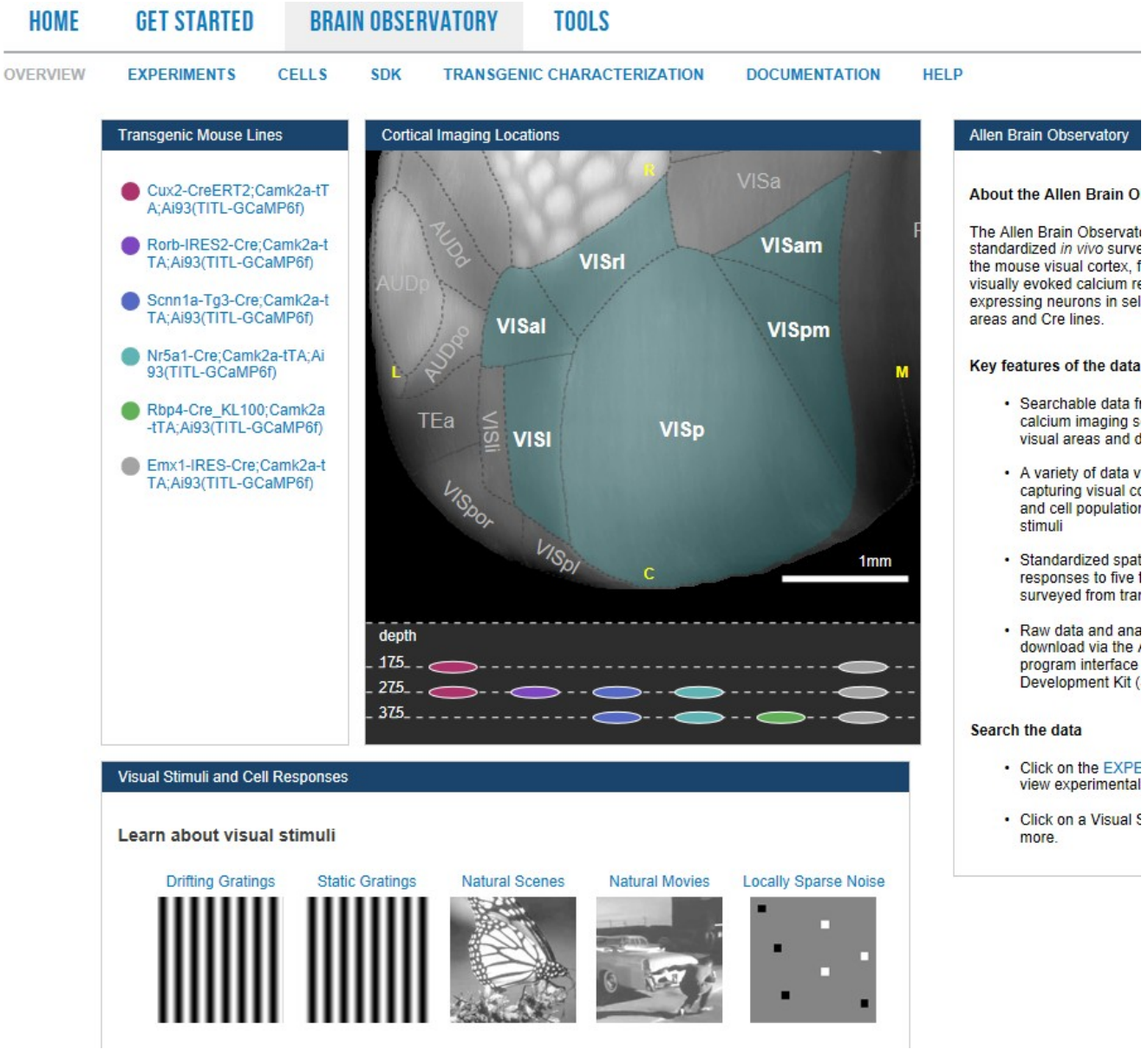
Visual Coding

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





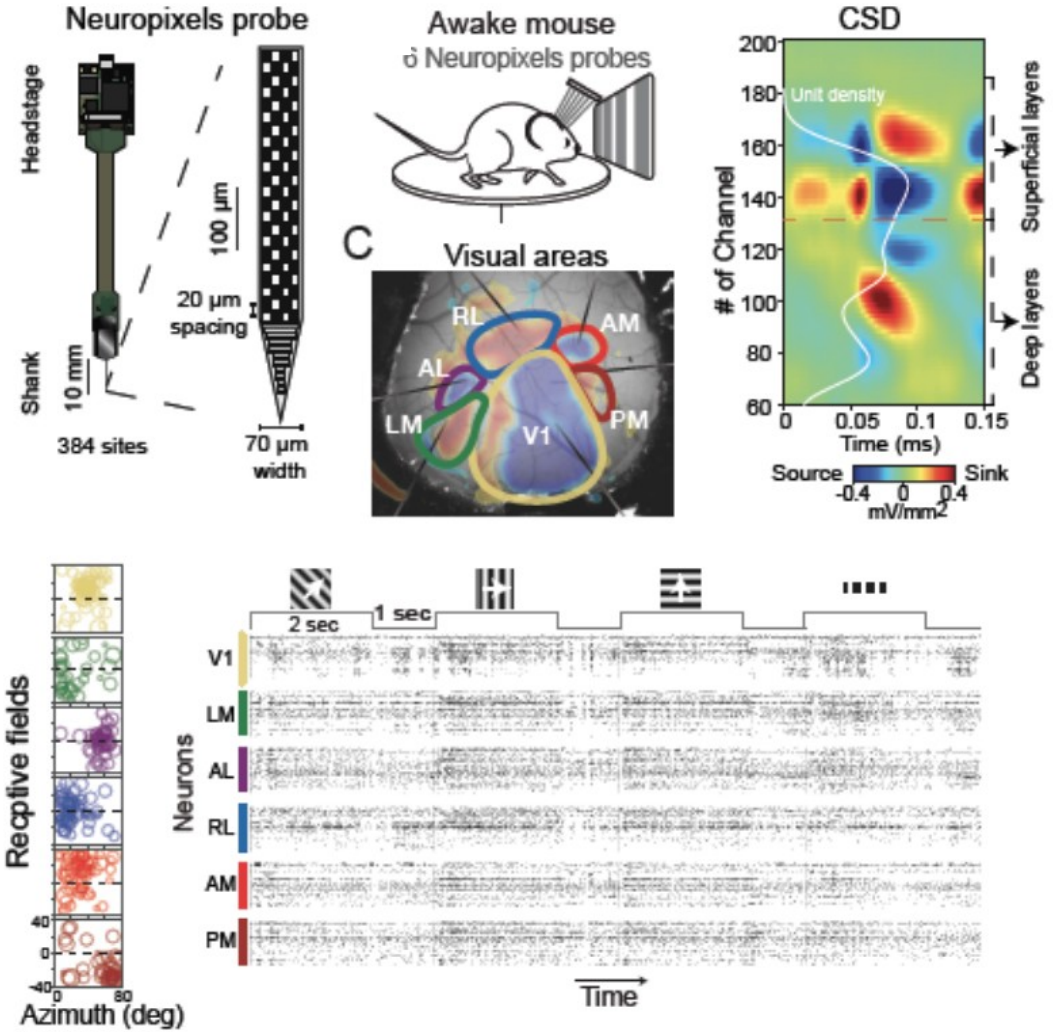
de Vries et al., *Nat. Neuro*, 2019;

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

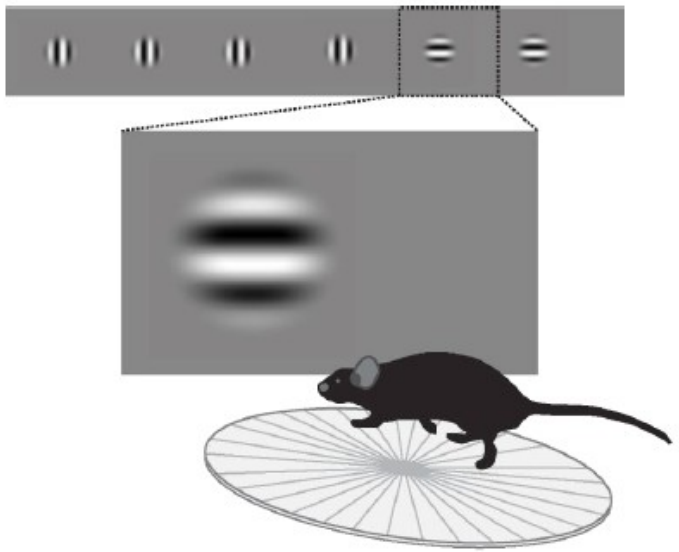


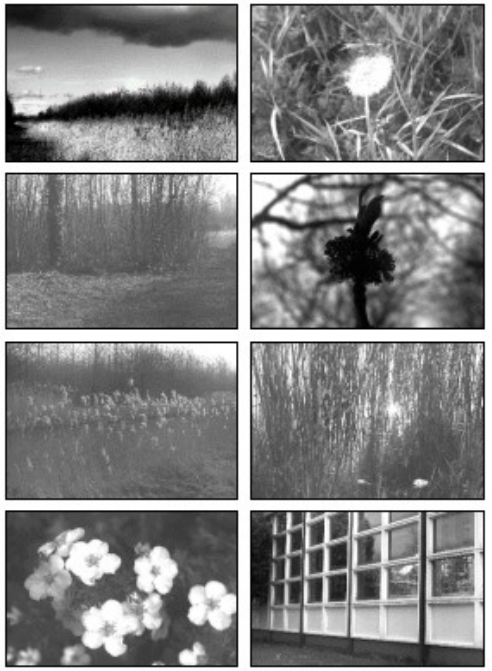
Jun et al., *Nature* , 2017

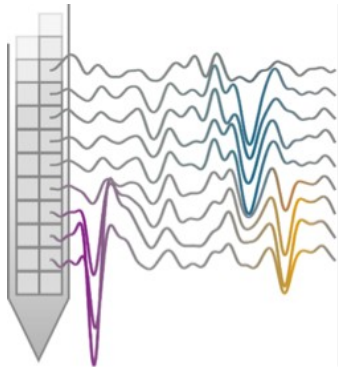
Visual Behavior

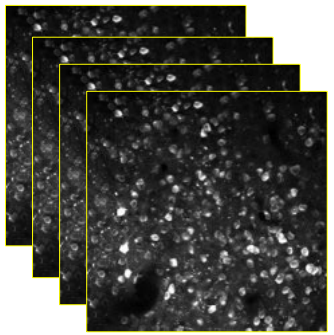
Deliverables:
O-phys and E-phys data for single-cell responses in the mouse cortex *in vivo*, in the context of a change detection behavior.

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



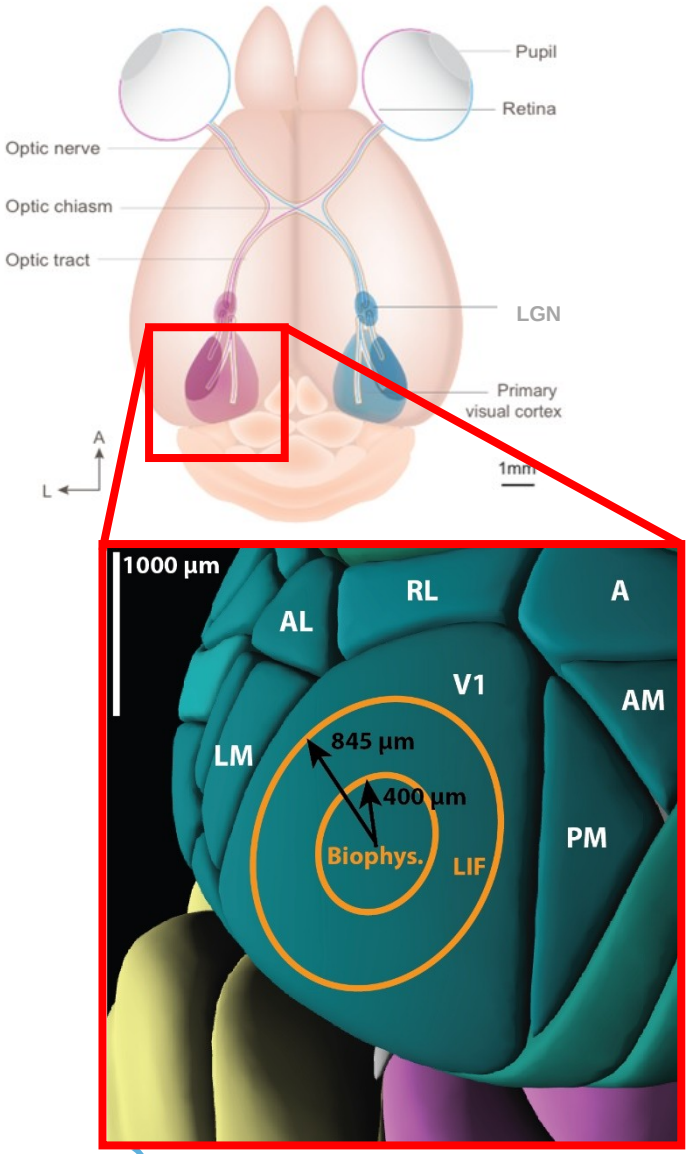


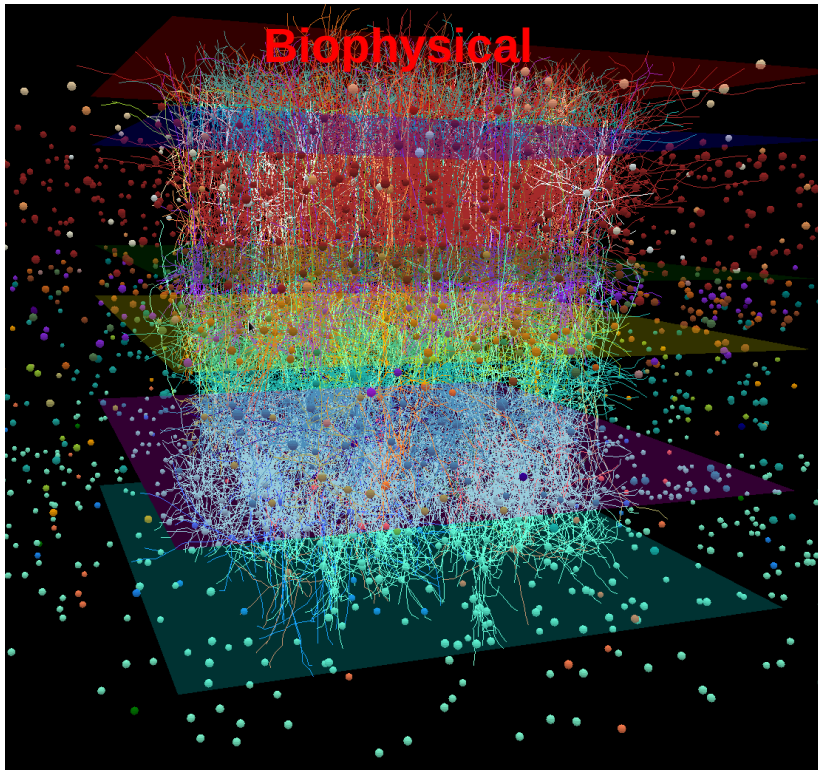


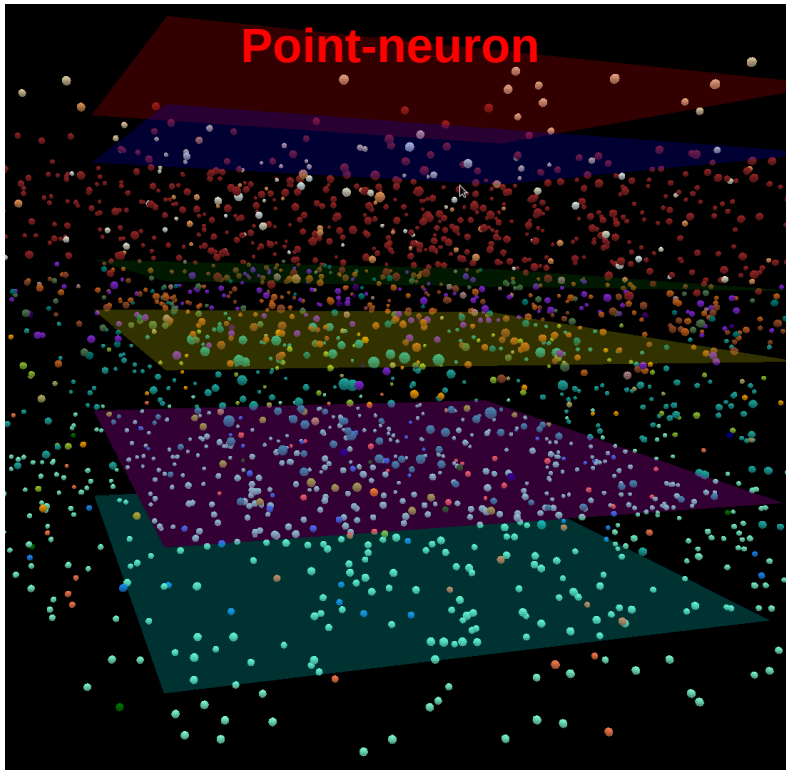


Garrett et al., *BioRxiv*, 2019

Model of the Mouse Primary Visual Cortex (V1)



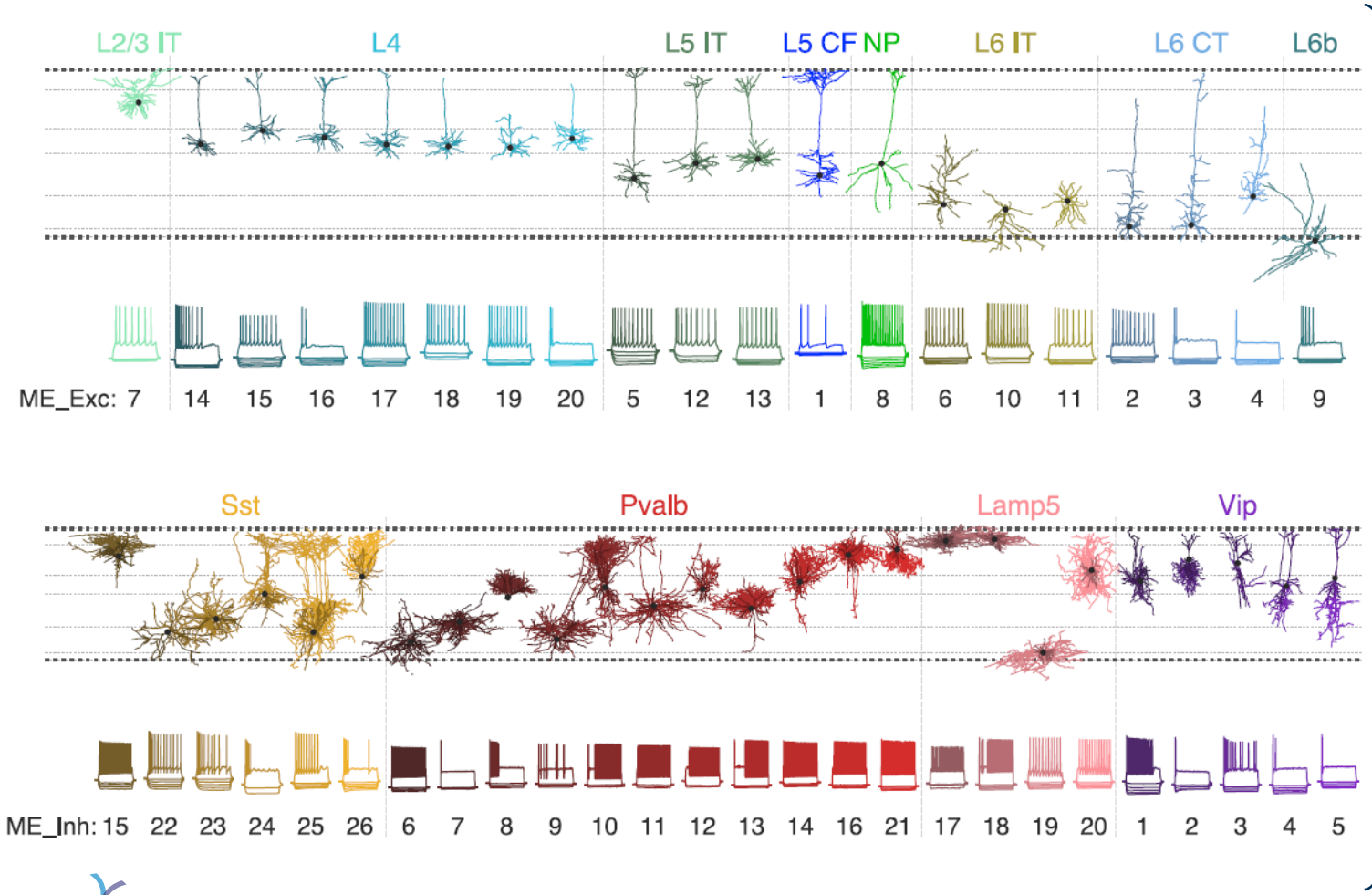




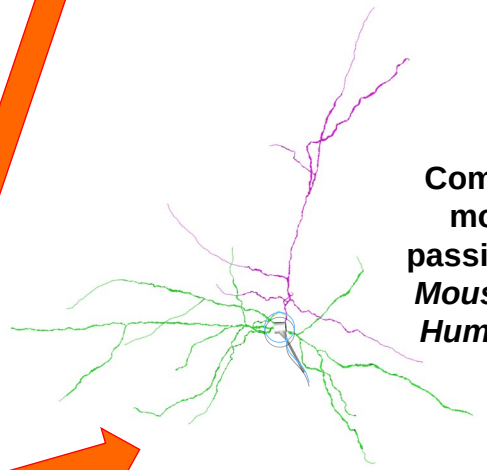
- **230,924** cells total
- **17 cell classes**
- **One-to-one** mapping between the biophysical and point-neuron models

Arkhipov et al., *PLOS Comp. Bio.*, 2018; Billeh et al., *BioRxiv*, 2019

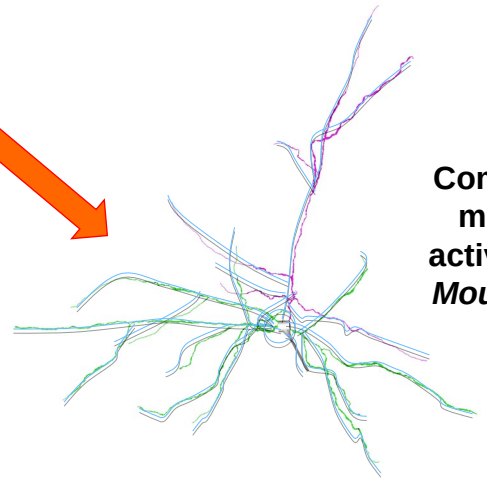
Models of Individual Neurons
Allen Cell Types Database: celltypes.brain-map.org



Point models (GLIF)
Mouse: 1058 cells
Human: 157 cells



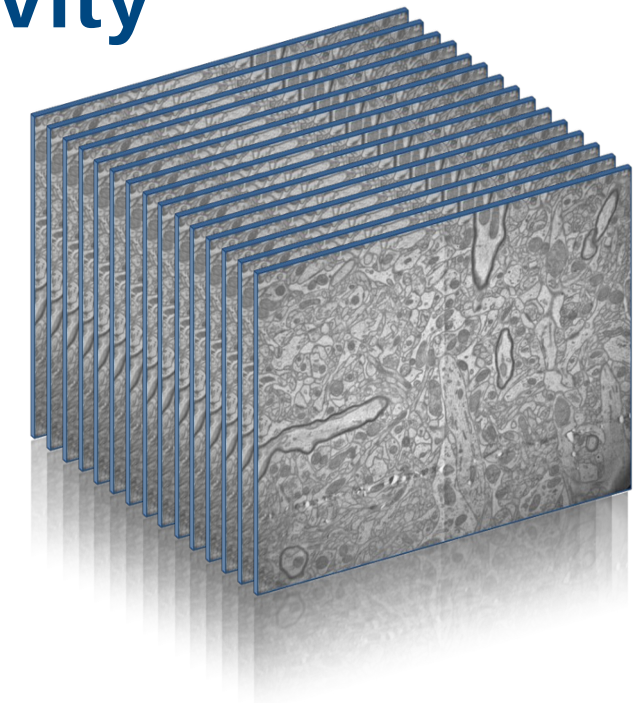
Compartmental models with passive dendrites
Mouse: 193 cells
Human: 43 cells

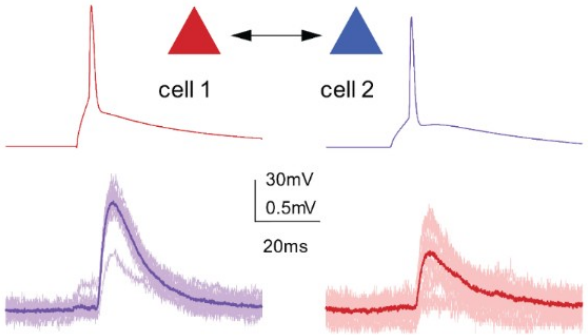


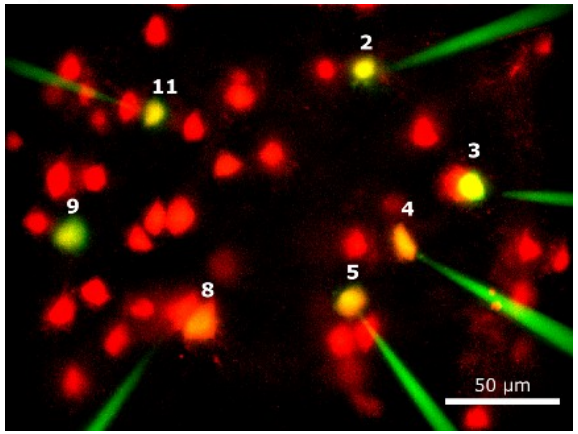
Compartmental models with active dendrites
Mouse: 73 cells

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						
i2/3SST	0.279	0.424	0.857	0.082	0.77	0.05	0.05	0.05	0.05	0.021		0					
i2/3HTR	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	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
i6HTR										0.03	0.03	0.03	0.03	0.1	0.05	0.05	0.03

Synaptic Strength, unitary PSP (mV)

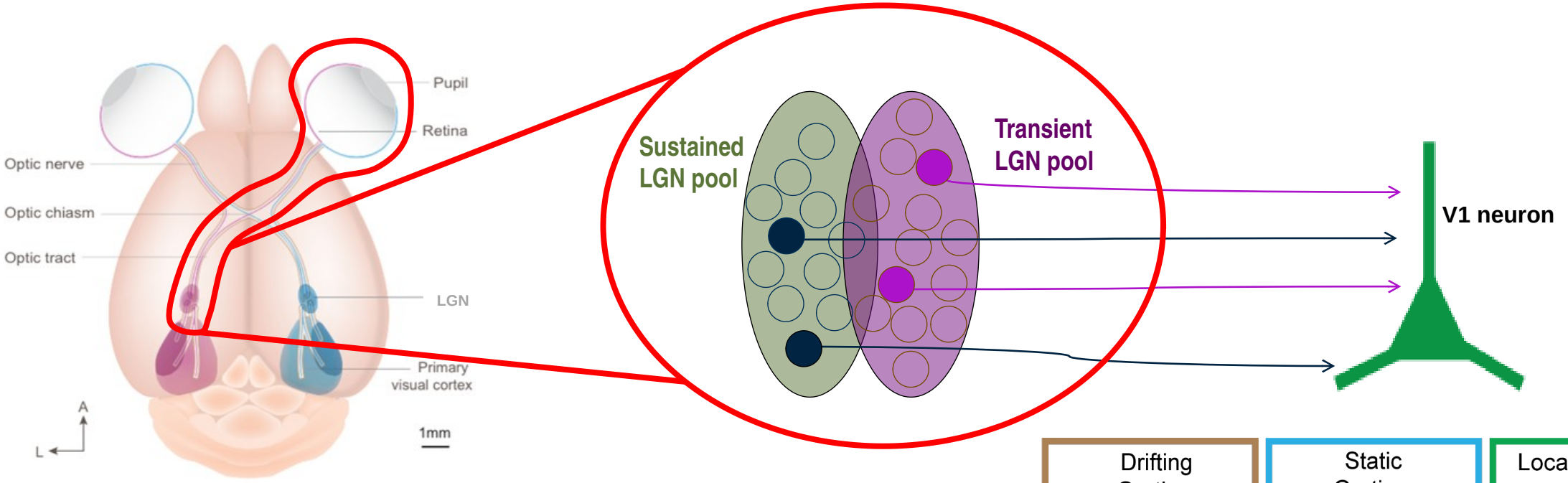
Target

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						
i2/3SST	0.47	0.31	0.5	0.15	0.52	0.3	0.5	0.15	0.52	0.22		0					
i2/3HTR	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	0.83	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
i6HTR										0.28	0.18	0.33	0.37	0.28	0.18	0.33	0.37

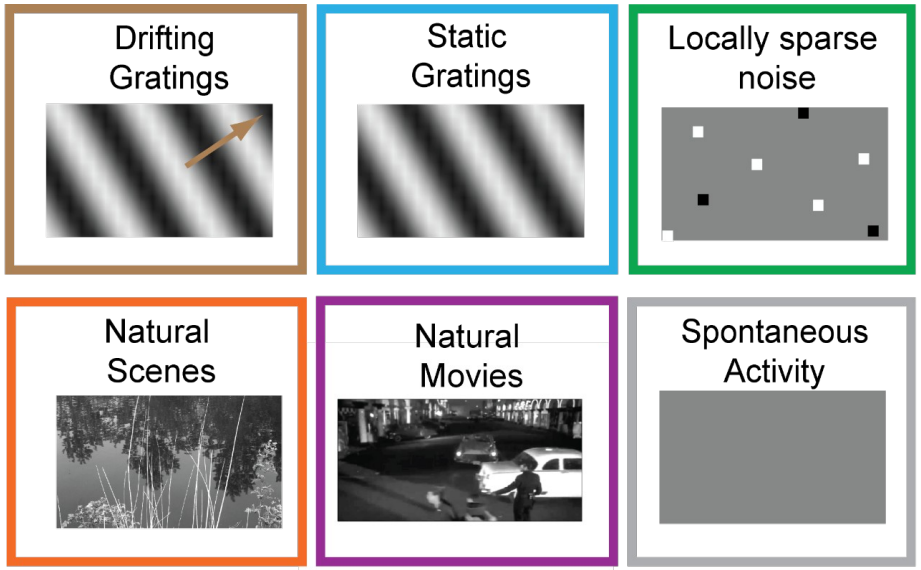
Axonal delays
Synaptic targeting of dendrites

Lee et al., *Nature*, 2016; Seeman et al., *eLife*, 2018; Billeh et al., *BioRxiv*, 2019

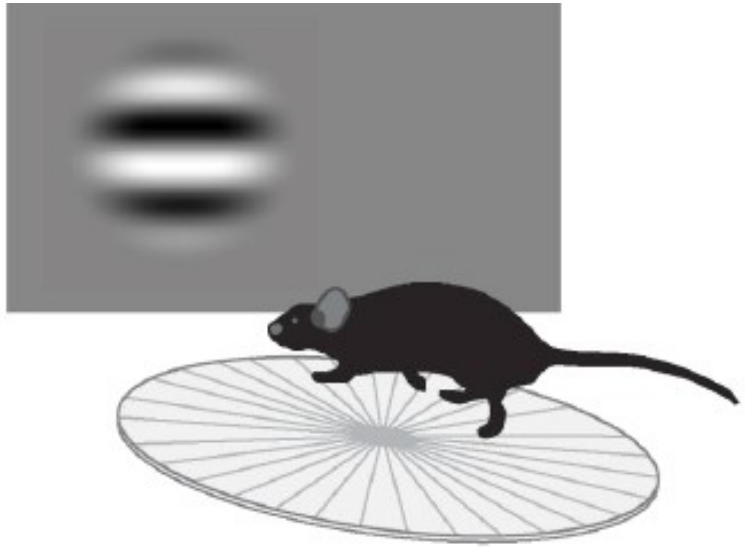
Filter-based Visual Inputs into the V1 model

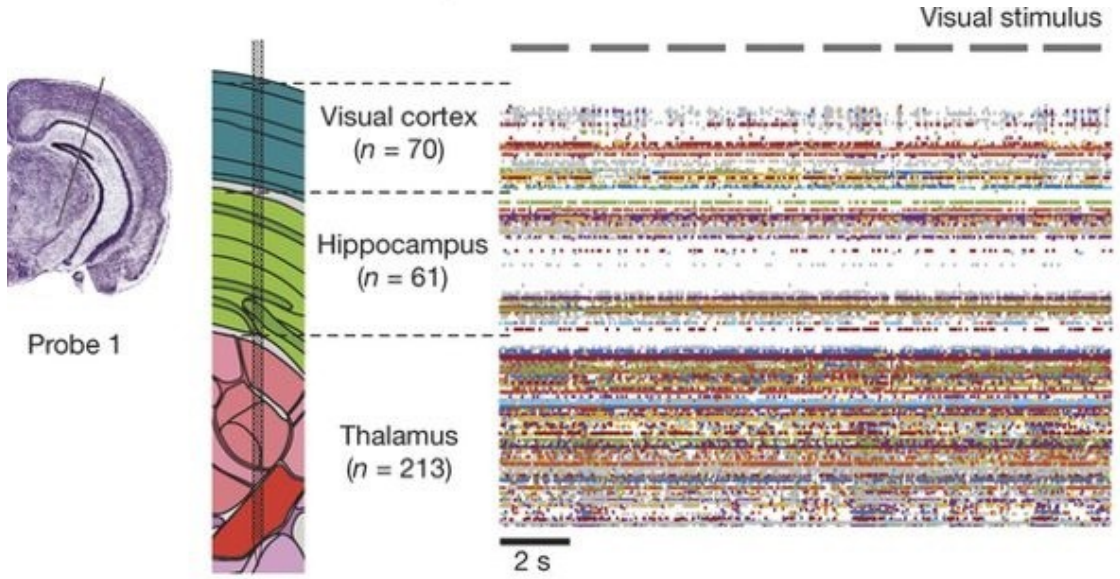


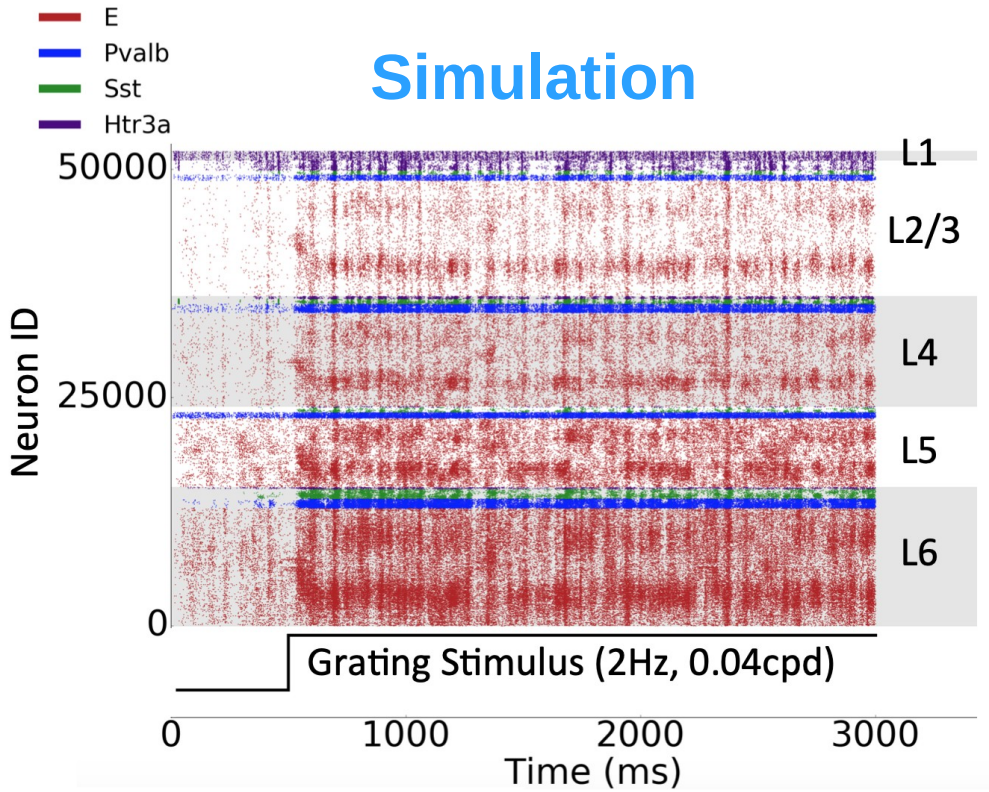
- **14** types of LGN cell responses, fit to experimental recordings *in vivo*
- **17,400** modeled LGN cells provide inputs to **230,924** V1 cells
- **Arbitrary visual stimuli** (movies) can be processed



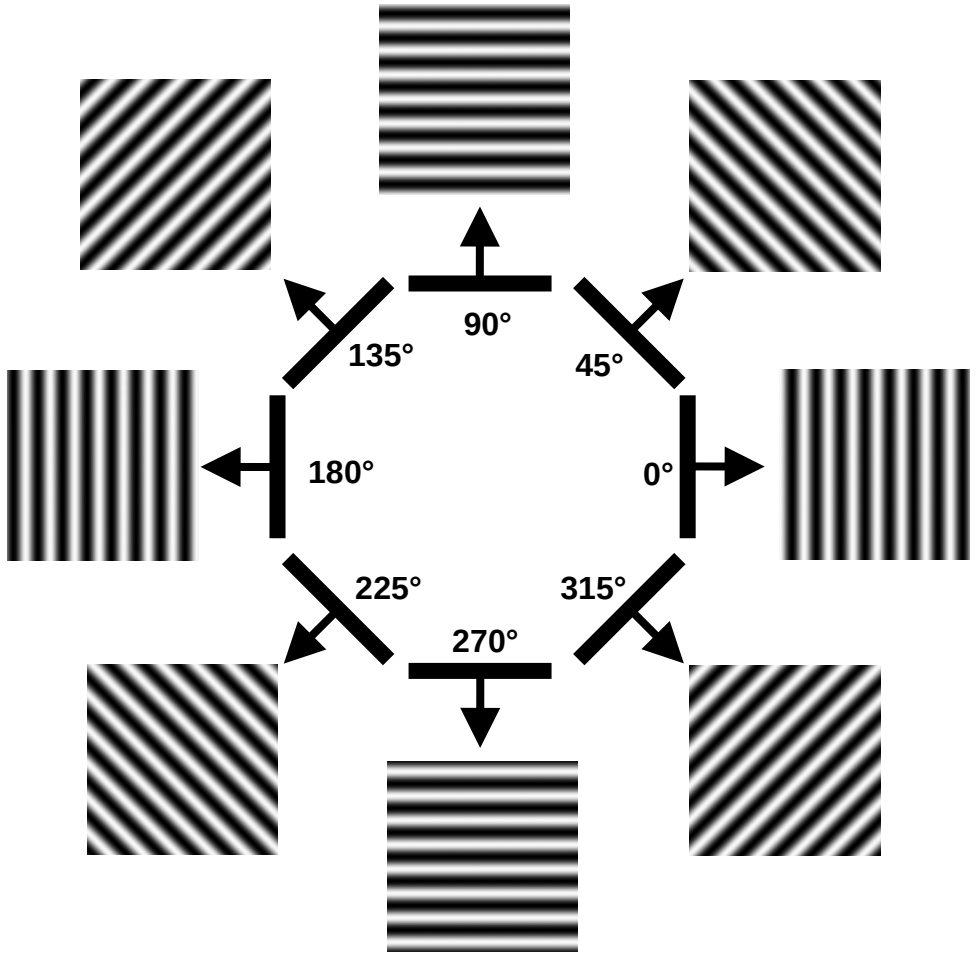
Recording Brain Activity *in Vivo*
Allen Brain Observatory: observatory.brain-map.org

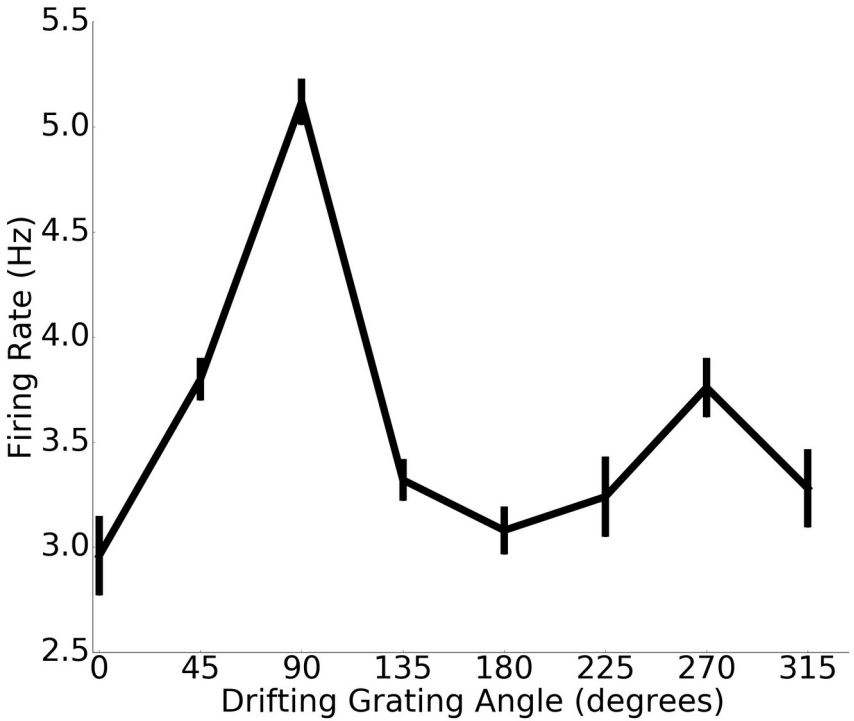






Comparison with Recordings *in Vivo* Example: Direction Selectivity

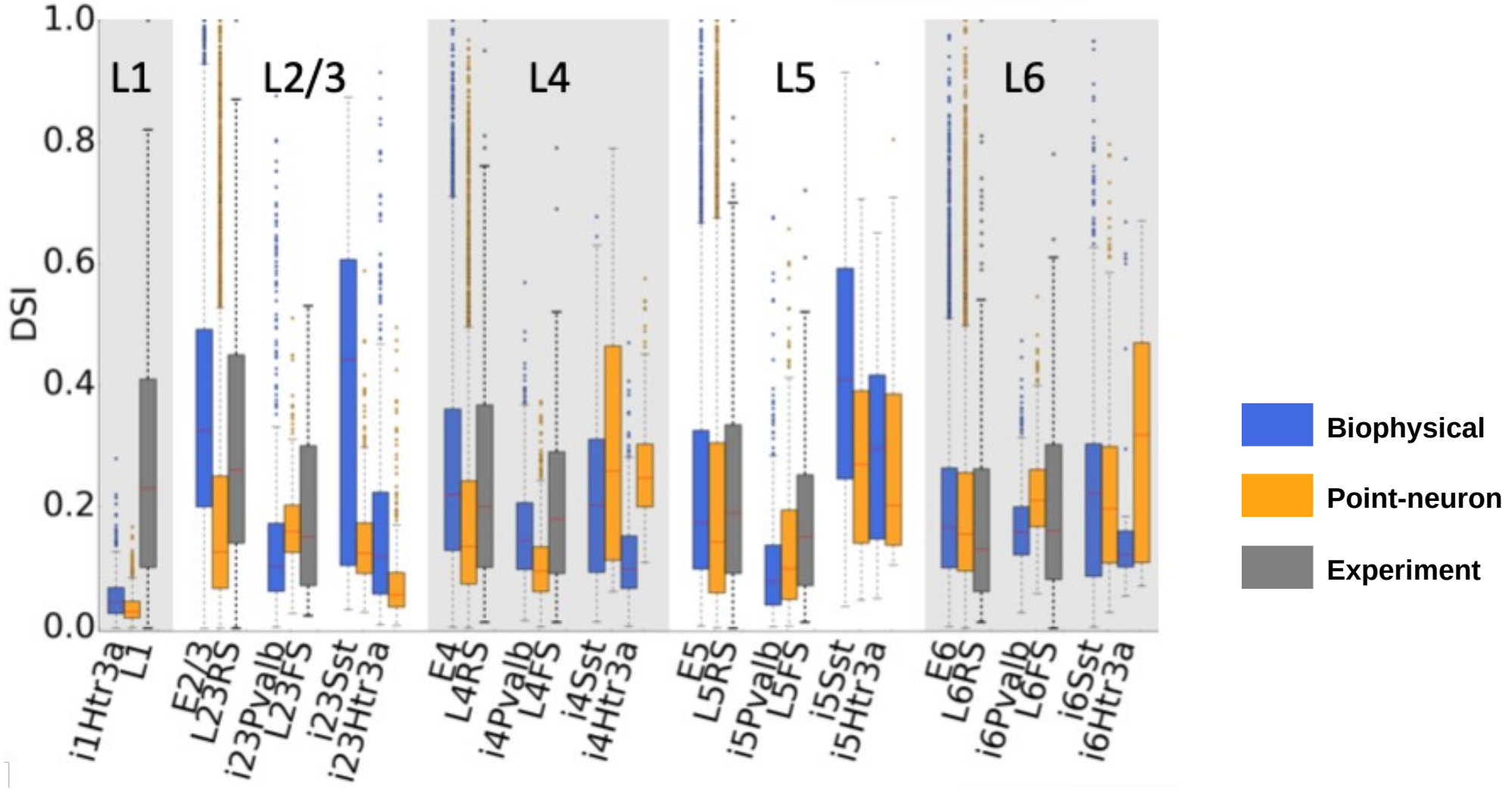




Billeh et al., *BioRxiv*, 2019

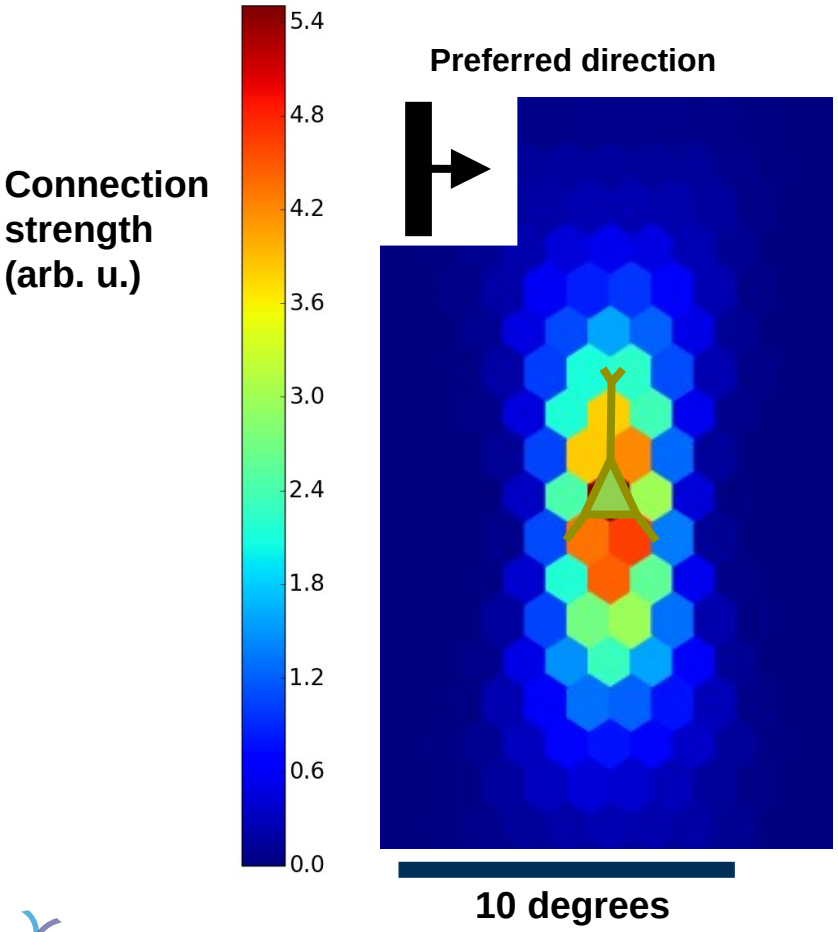
Comparison with Recordings *in Vivo* Example: Direction Selectivity

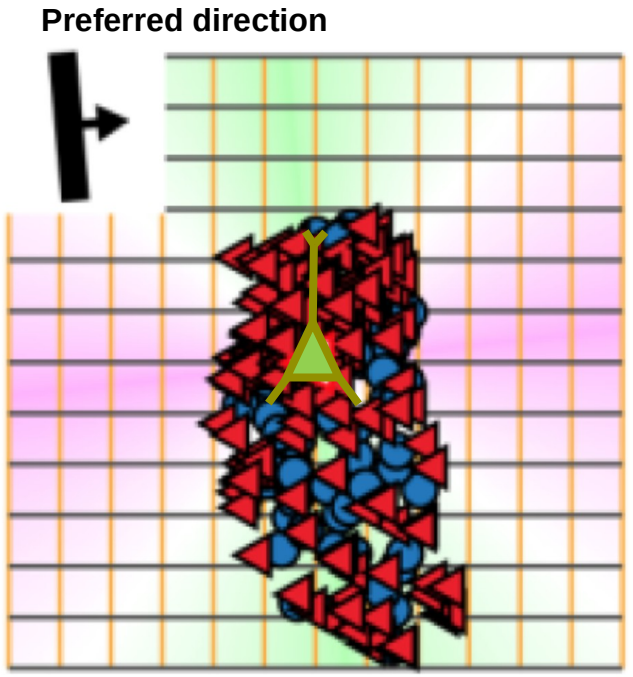
DSI: Direction Selectivity Index



Predicting the Logics of Neural Connectivity

Distribution of connections in the Visual Space



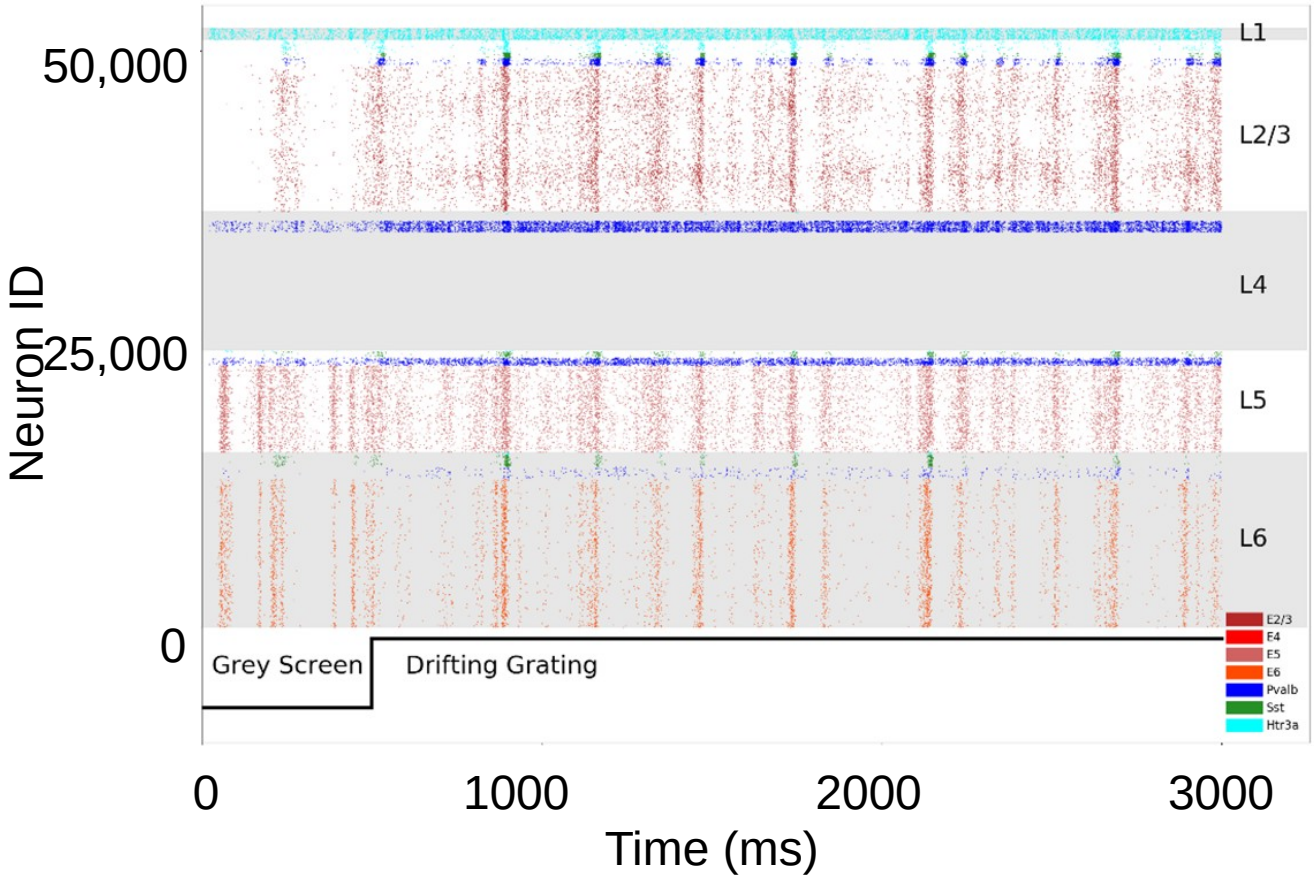


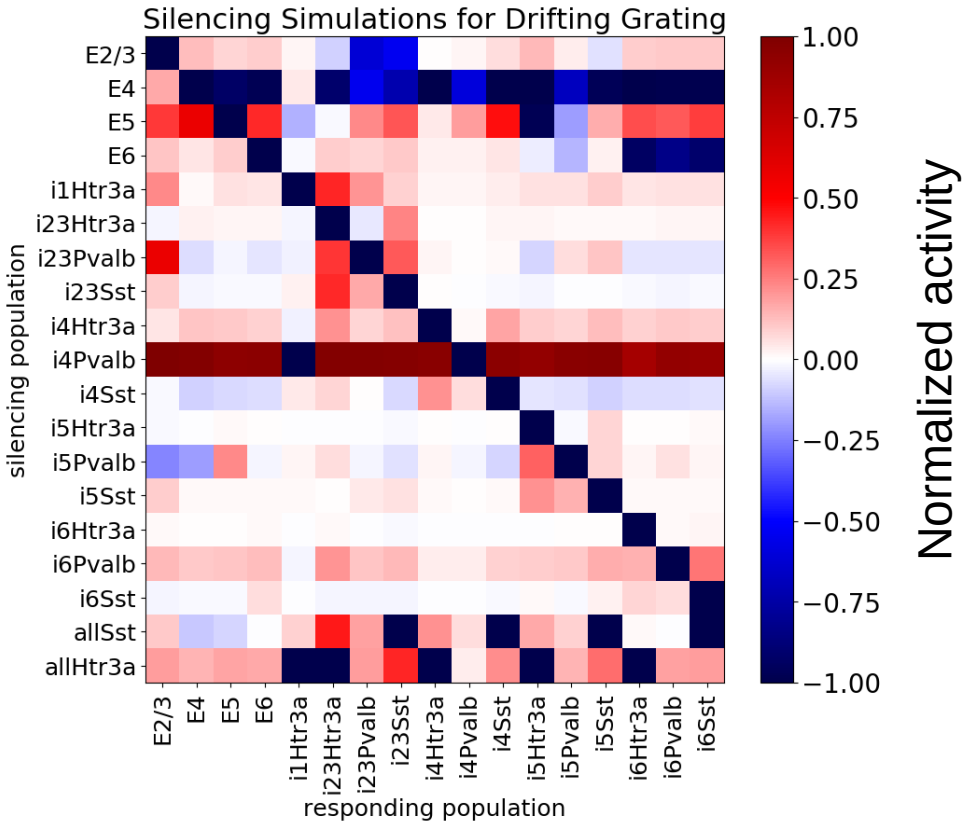
Rossi et al., *BioRxiv*, 2019

Billeh et al., *BioRxiv*, 2019

Predicting Cell-Type Specific Effects of Optogenetic Perturbations

Perturbation: Silence Layer 4 Excitatory Neurons

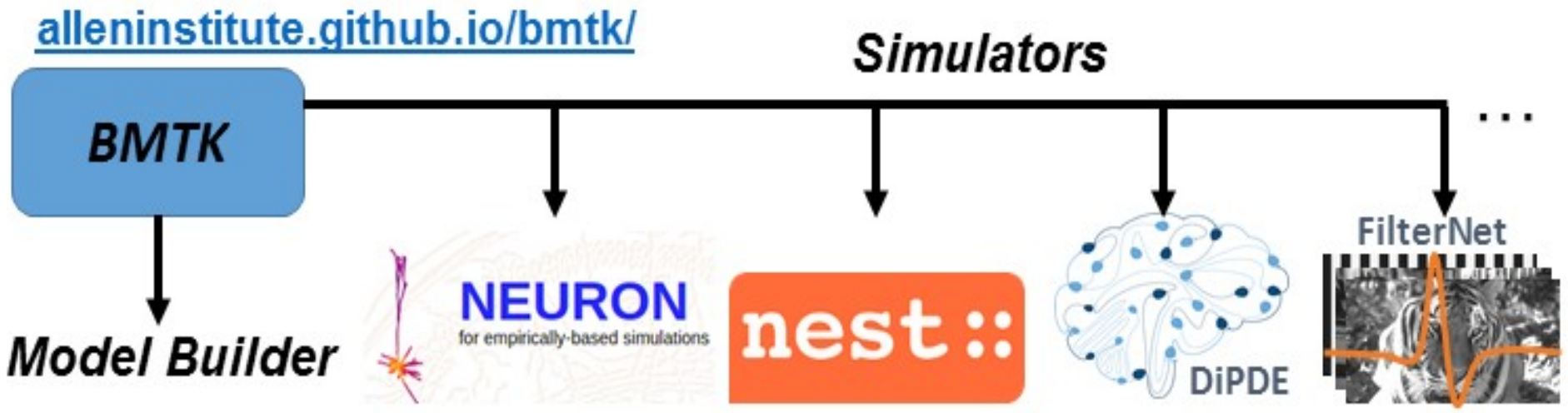




Collaboration with the team of S. Mihalas

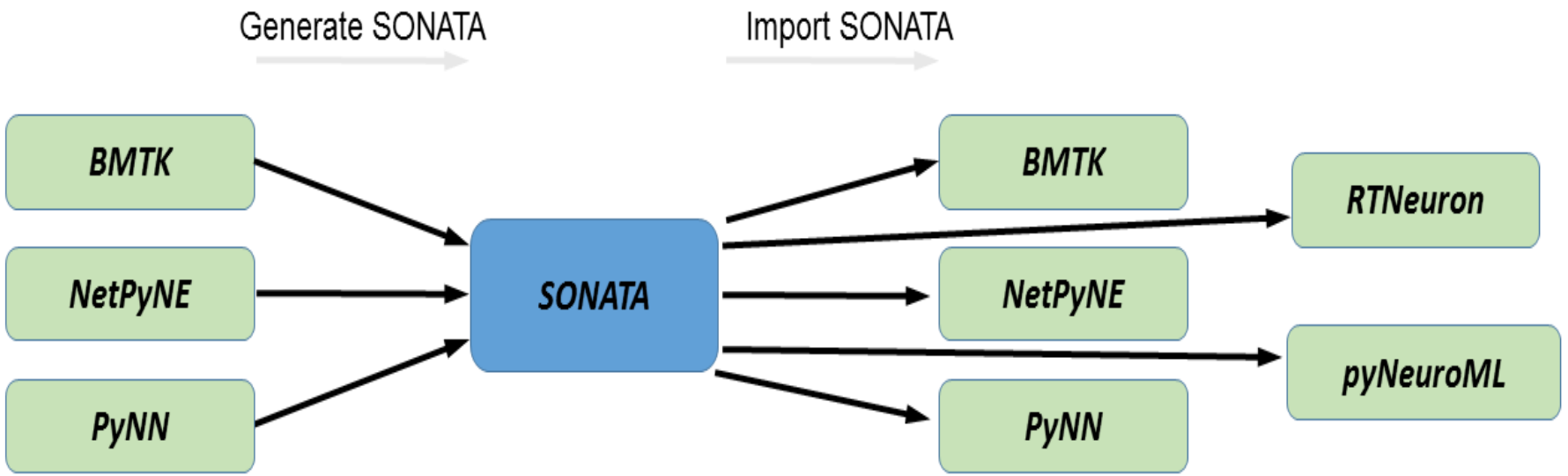
Our Models and Modeling Software Are Freely Available to the Community

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

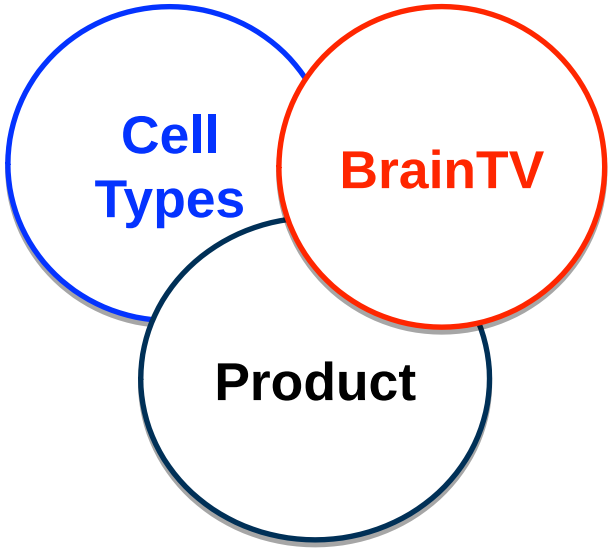


Our Models and Modeling Software Are Freely Available to the Community

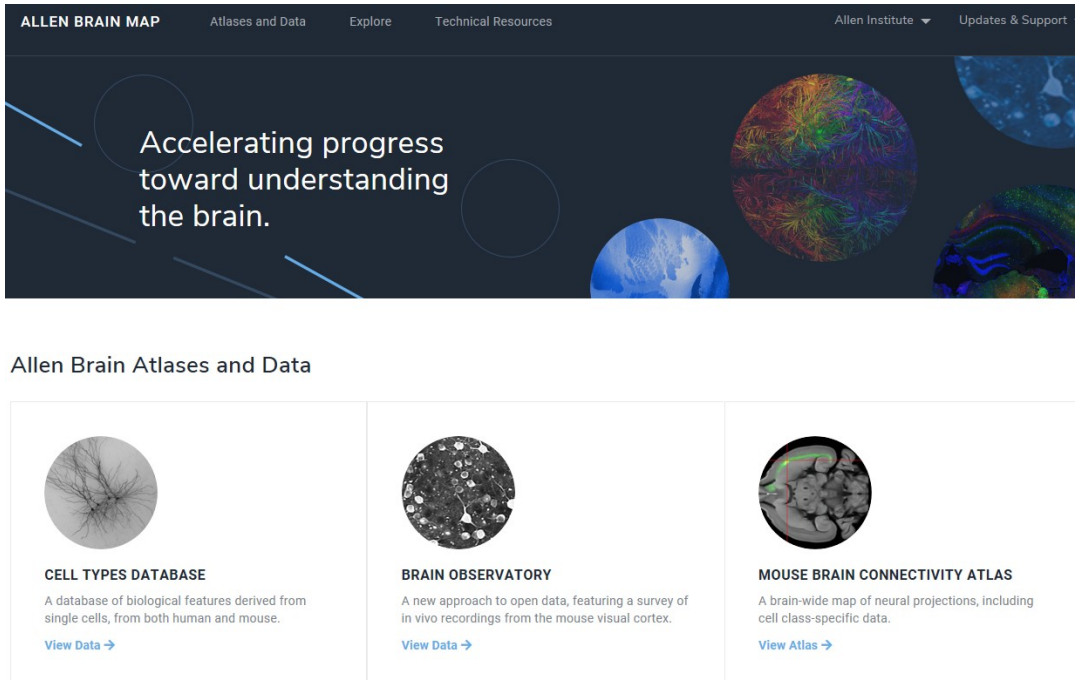
Scalable Open Network Architecture TemplAte (SONATA):
https://github.com/AllenInstitute/sonata
An interface between SONATA and the NWB format has been developed as well



Product Program



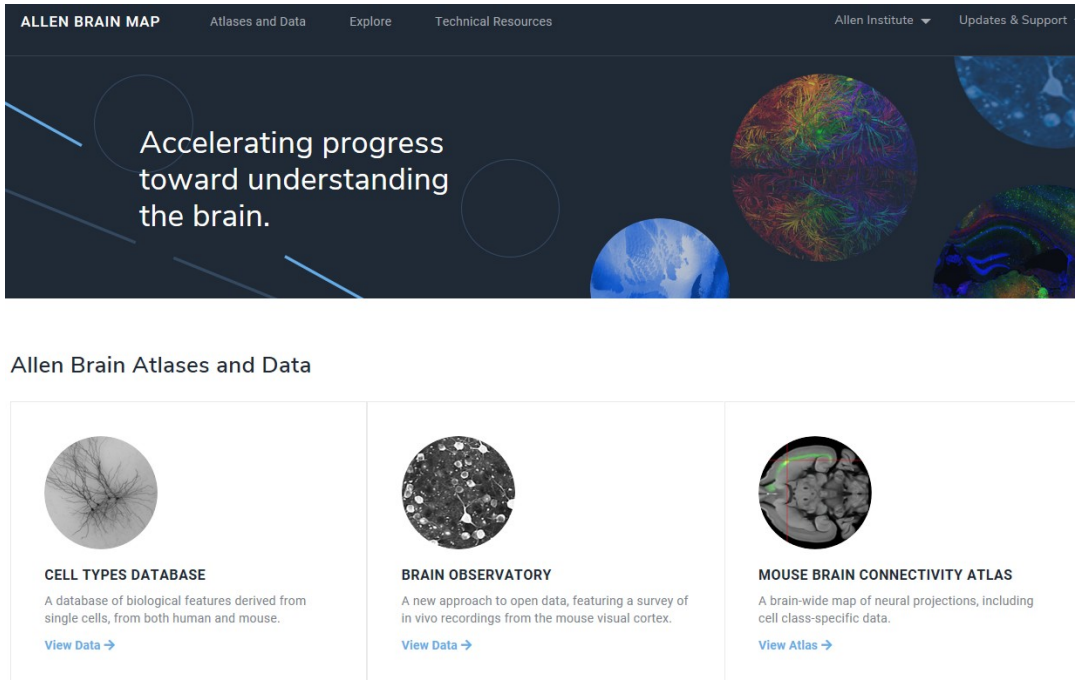
http://brain-map.org/

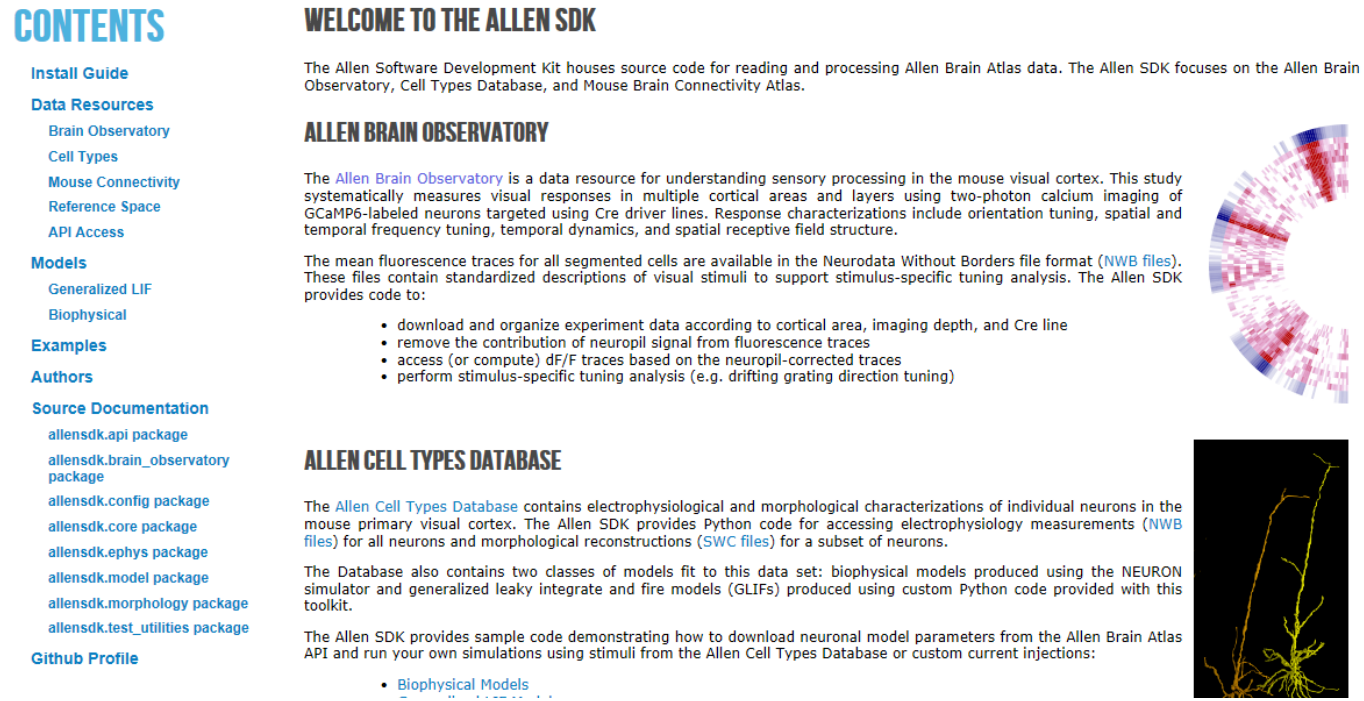


Allen Institute's Databases and Allen Software Development Kit (Allen SDK)

http://brain-map.org/

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





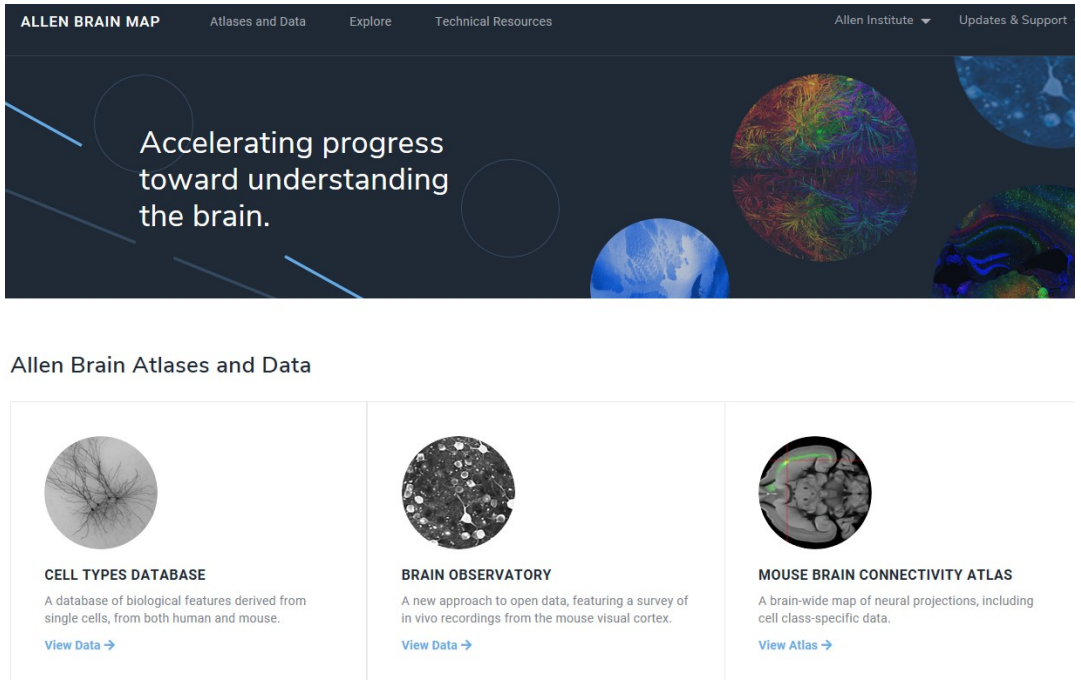
Our Data, Models, and Software Are Freely Available

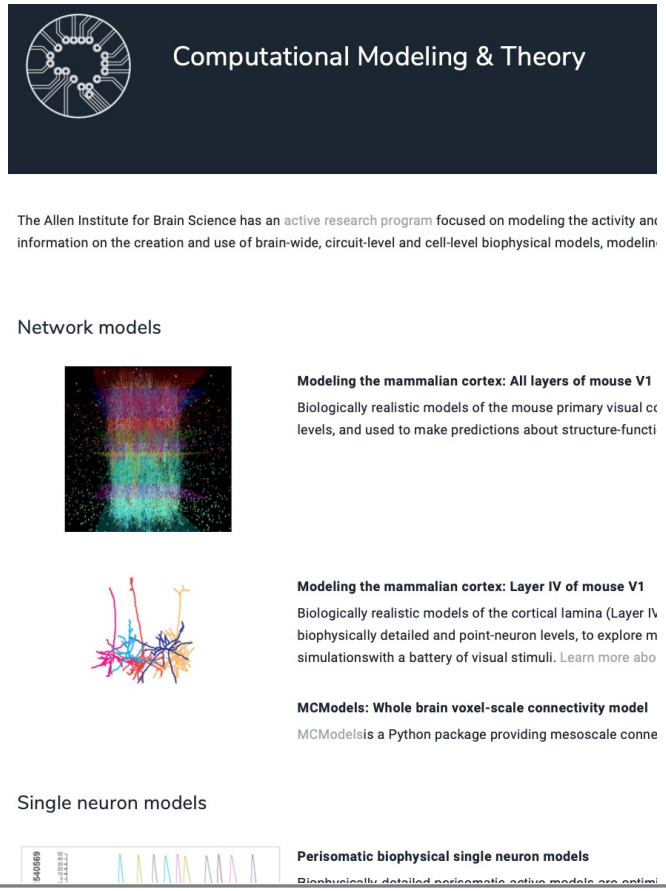
Models: http://portal.brain-map.org/explore/models

Brain Modeling ToolKit: https://alleninstitute.github.io/bmtk/

http://brain-map.org/

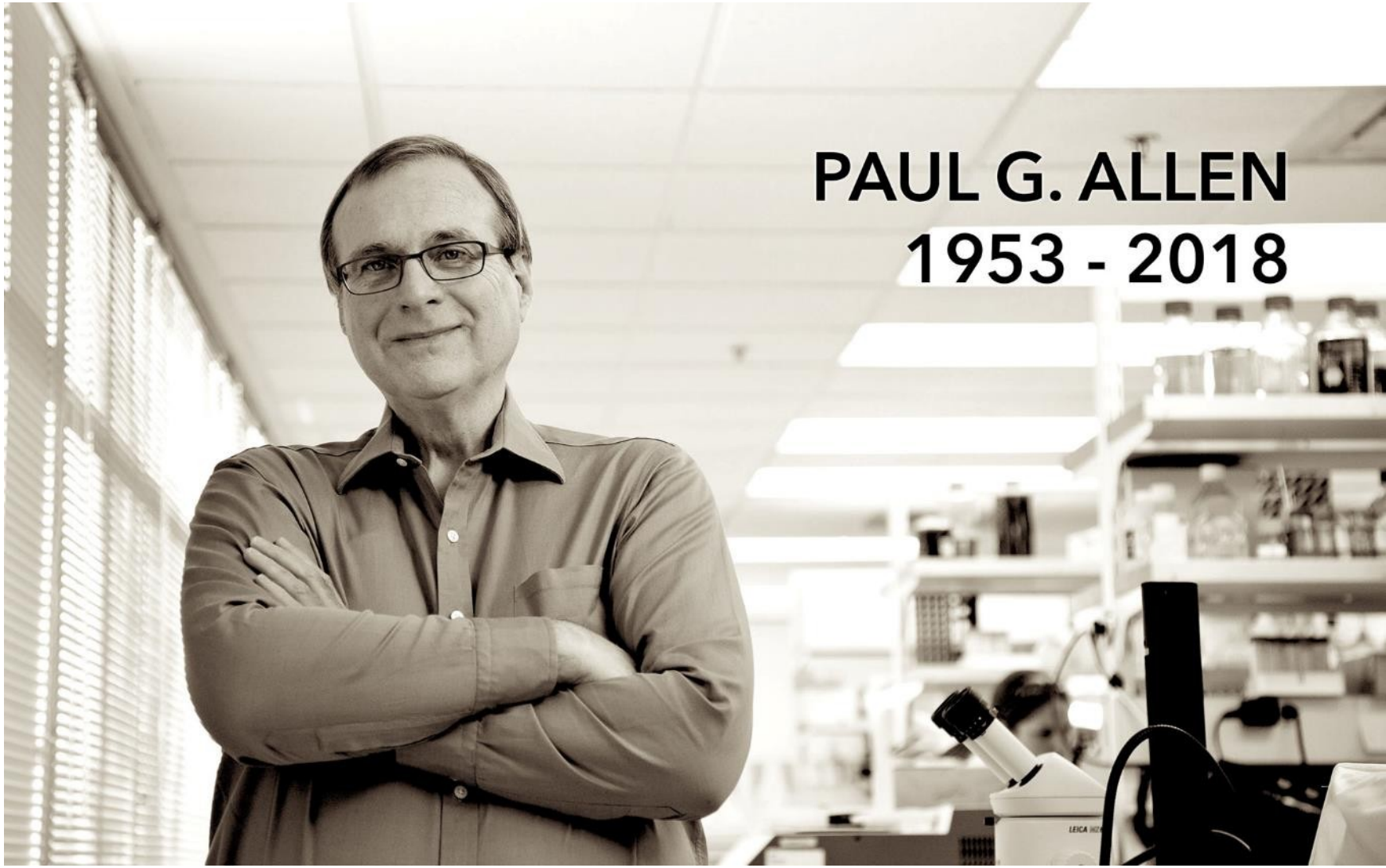
Modeling file format SONATA: https://github.com/AllenInstitute/sonata





THANK YOU

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



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