

# **Brain Observatories -**

## **Exploring Cortex in an Open Access and High Throughput Manner**

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**Chief Scientific Officer**

**Allen Institute for Brain Science**

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# The Allen Institute for Brain Science

- An independent, non-profit medical research organization, founded in 2003, supporting basic research in the brain sciences
- 160 staff in 2011, 310 in 2015, 500 by 2021
- Culture between an university and a biotech startup, focussed on 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
- 2015 Budget ca \$80M/year
- We are moving into a new 27,000 m<sup>2</sup> building on September 2015
- All of it made possible by the unprecedented generosity of Paul Allen

# We Are About

- Big Science
- Team Science
- Open Science
- Since 2004, all data are publicly accessible via API once they pass QC
- All data are freely available without any commercial restrictions
- All data are accessible several years prior to publications

# The Allen Institute is Creating Community Standards

## Neurodata Without Borders:

Standardizing Cellular Physiology Data

## Imec Neuropix:

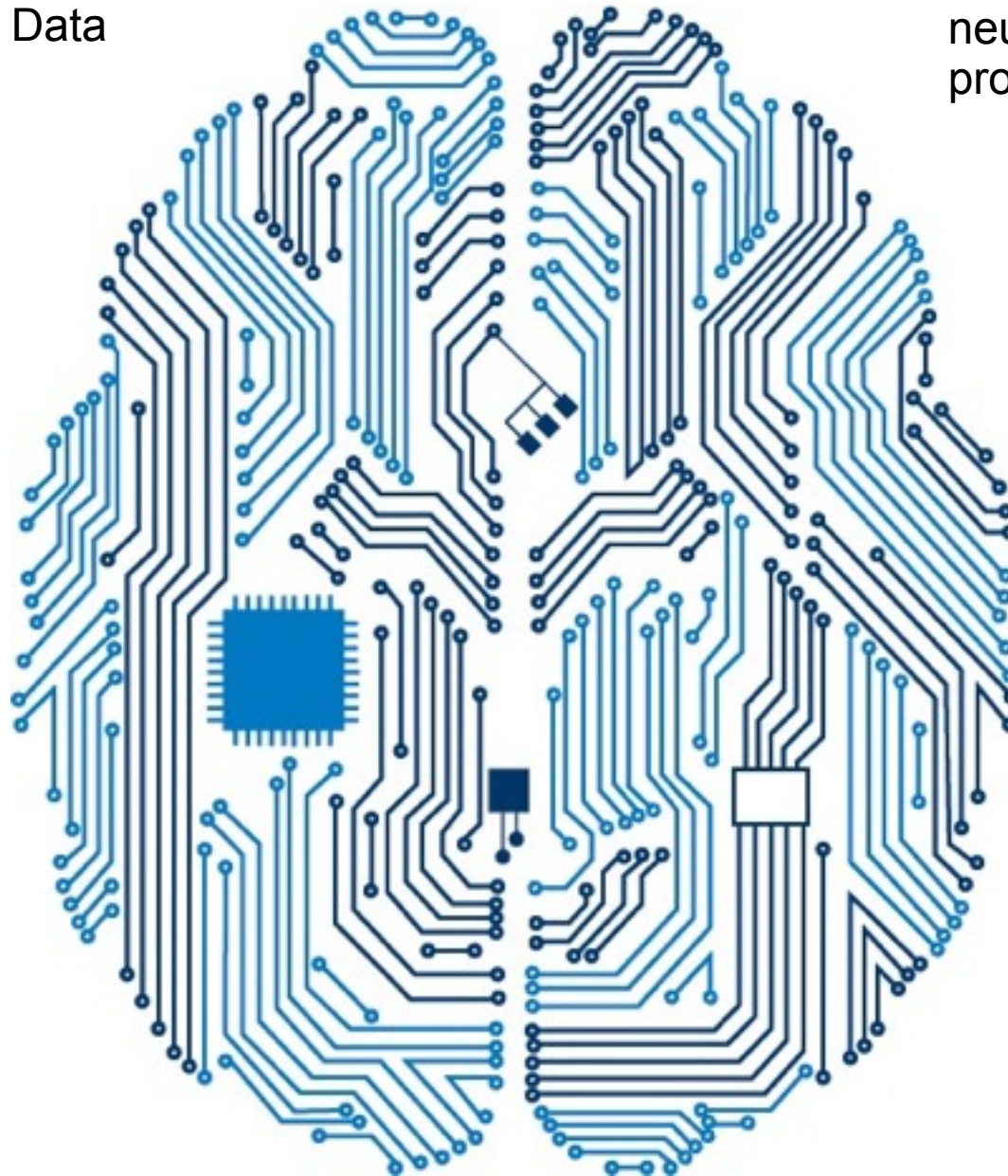
state-of-the-art sensor array for ultra-dense recording neural activity

## Transgenic mice:

>12,000 Cre-driver (cell classes/types) and responder lines

## SimVis:

Modeling markup language for visualization of models



**Big Neuron:** Community effort, determine the state-of-the-art of single neuron reconstruction standardize the protocols, and establish a data resource

**Dynamic Brain:** Summer course at Friday Harbor Laboratories

**Common Coordinate Framework:** High resolution standard atlas framework for mouse

**BRAIN Initiative Grant:** Create a prototype database of cell types in the mouse brain

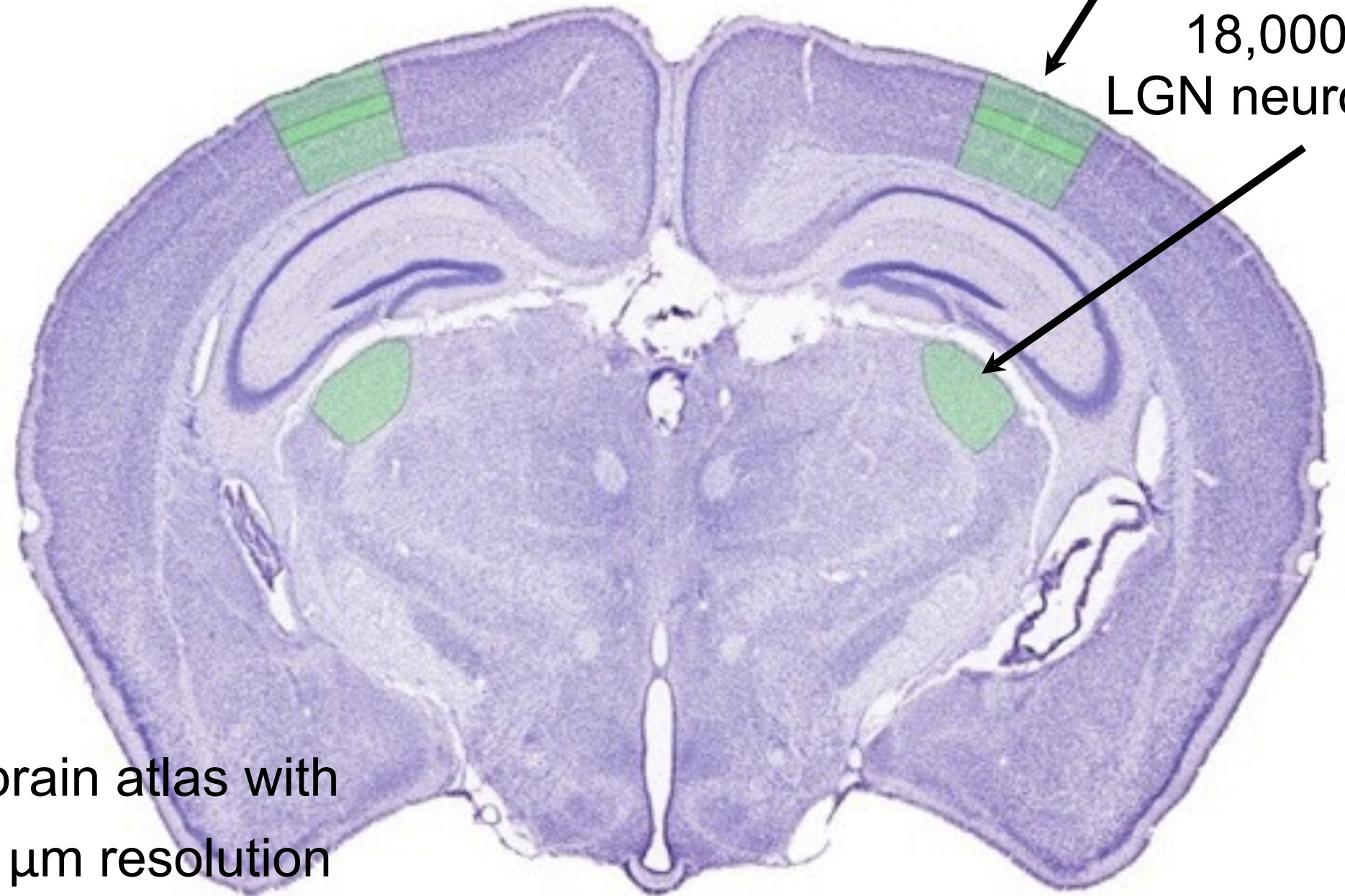
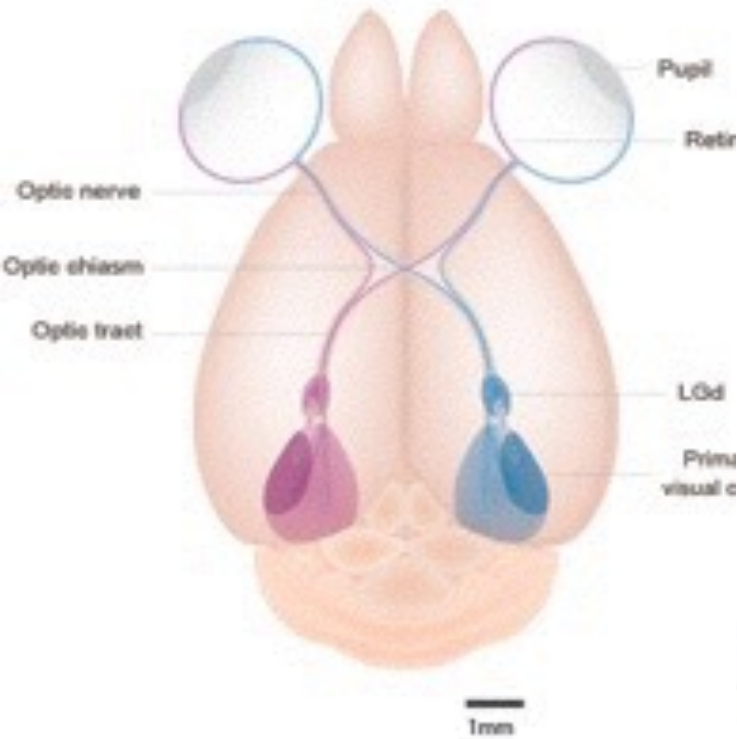


# Project MindScope

14 million  
cortical neurons

360,000  
V1 neurons

18,000  
LGN neurons



CCF - A 3-D mouse brain atlas with  
10  $\mu\text{m}$  pixels and 50  $\mu\text{m}$  resolution

45,000 retinal ganglion cells



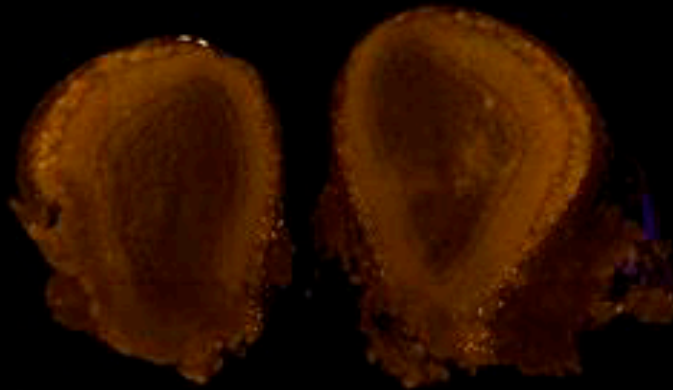
# Data Production Pipelines

- Next Generation Connectivity Atlas
- *In Vitro* Single Cell Characterization
- Cortical Activity Map (CAM)

These all use:

- Left cortex of young adult C57BL/6J male mice
- Mapped to the Common Coordinate Framework, a true 3-D atlas with 10 um pixel resolution and 320 million voxels for the entire mouse brain
- Common Cre lines
- Centralized & standardized database

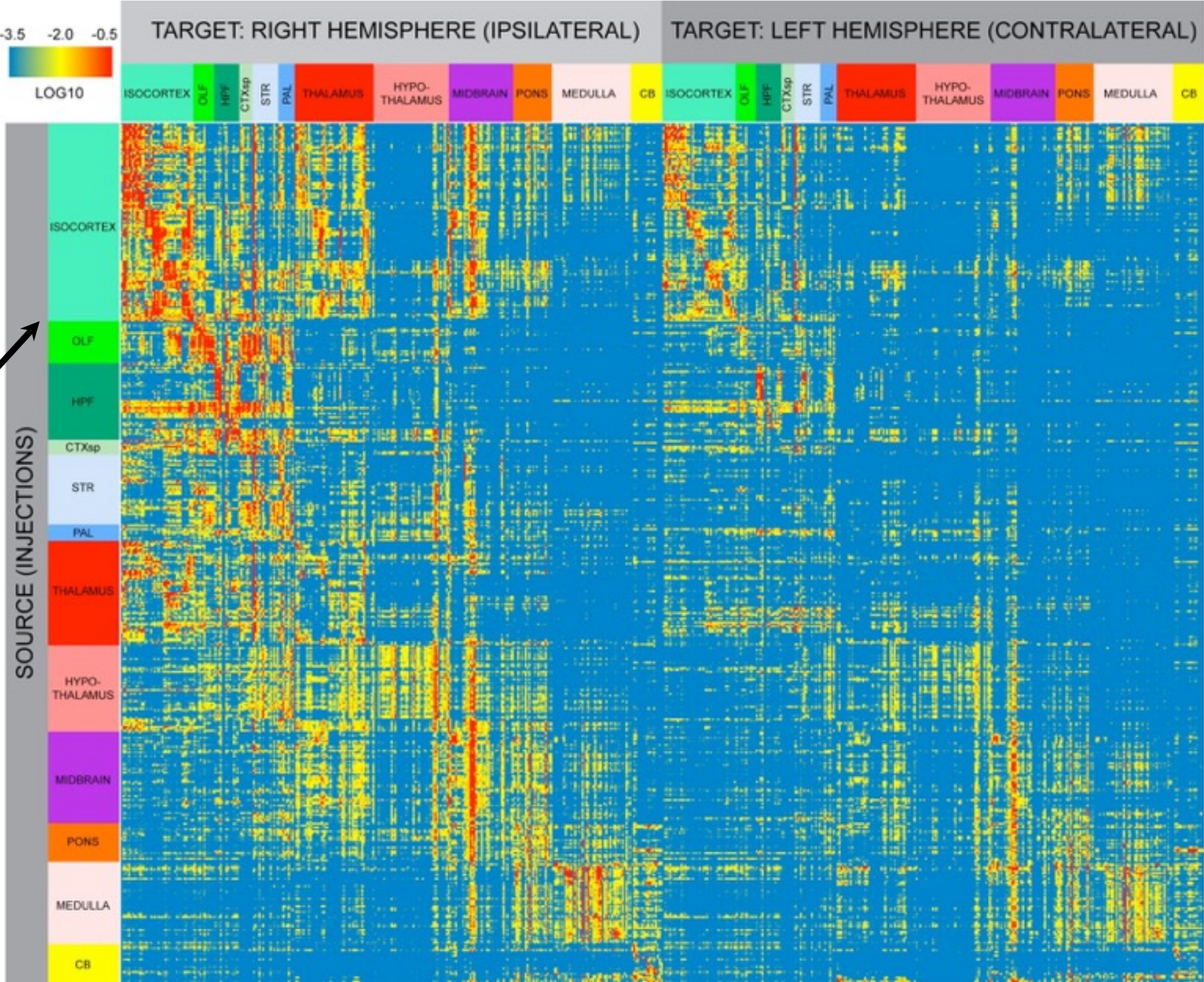
# Primary Visual Cortex Injection





# Connectivity Matrix for the Entire Mouse Brain

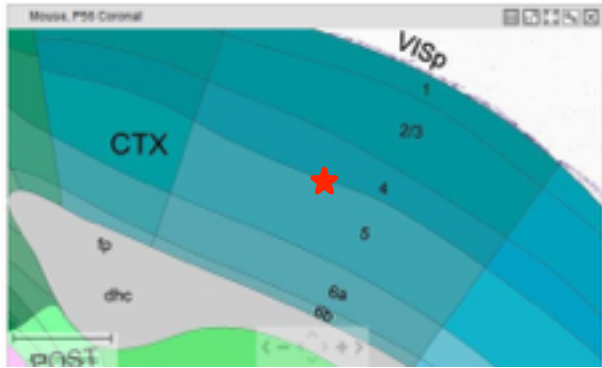
An injected brain region in one of 495 mice



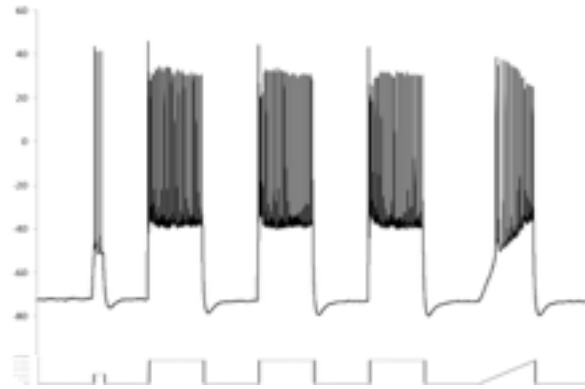
One of 295 brain regions



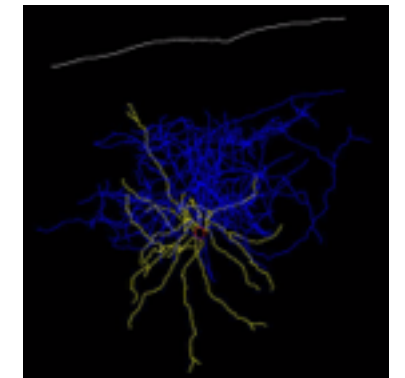
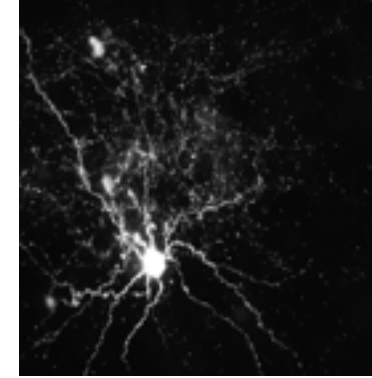
# In vitro Single Cell Characterization



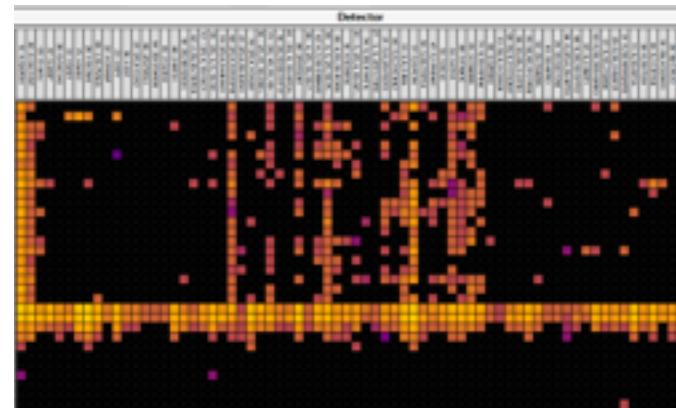
**Metadata**  
(Common Coordinate System)



**Electrophysiology**



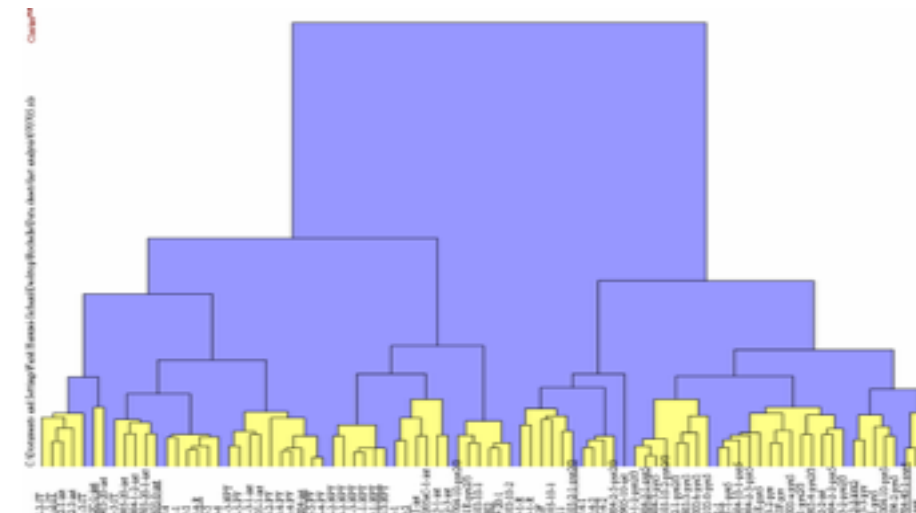
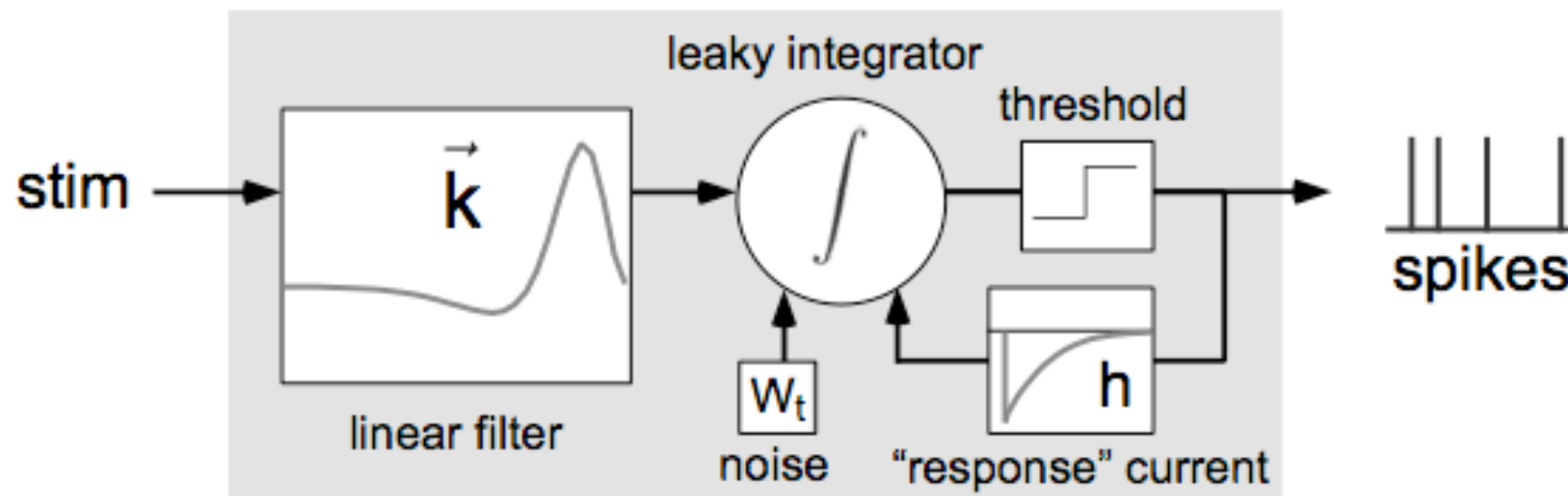
**Morphology**



**Fitting GLIF/GLM Models**

**mRNA transcripts**

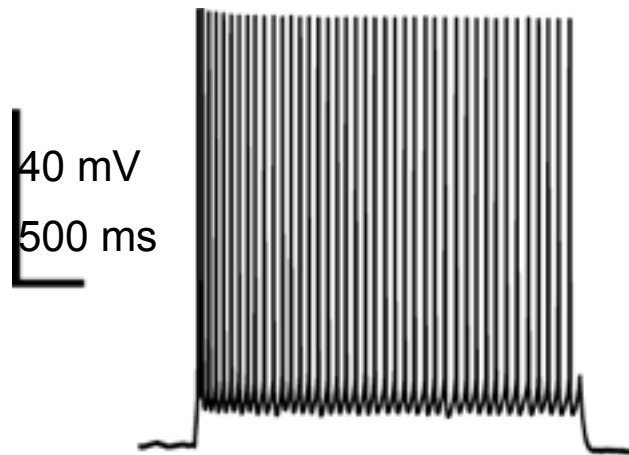
**Data-driven taxonomy of cell types**



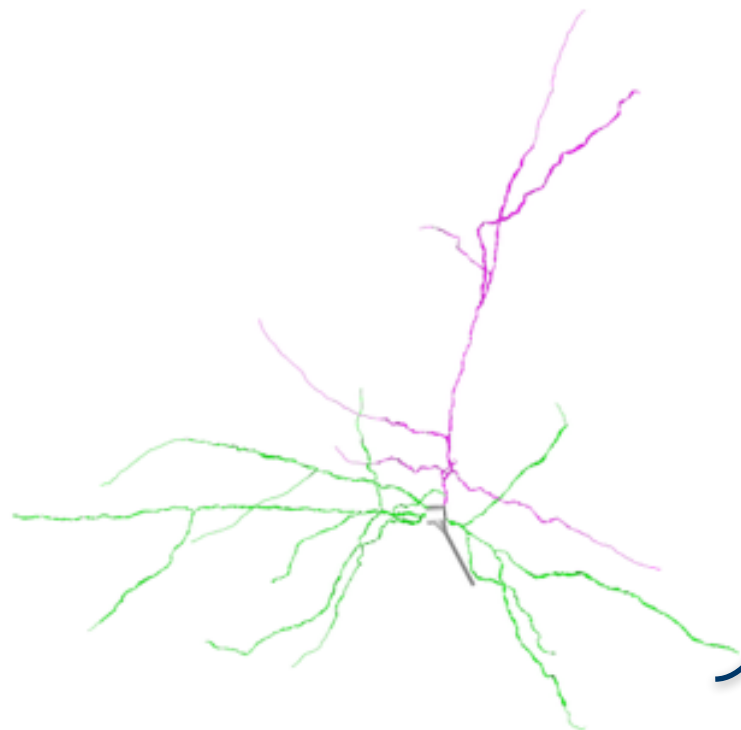
# From *in vitro* Data to Neuronal Models

## IVSCC

### Electrophysiology



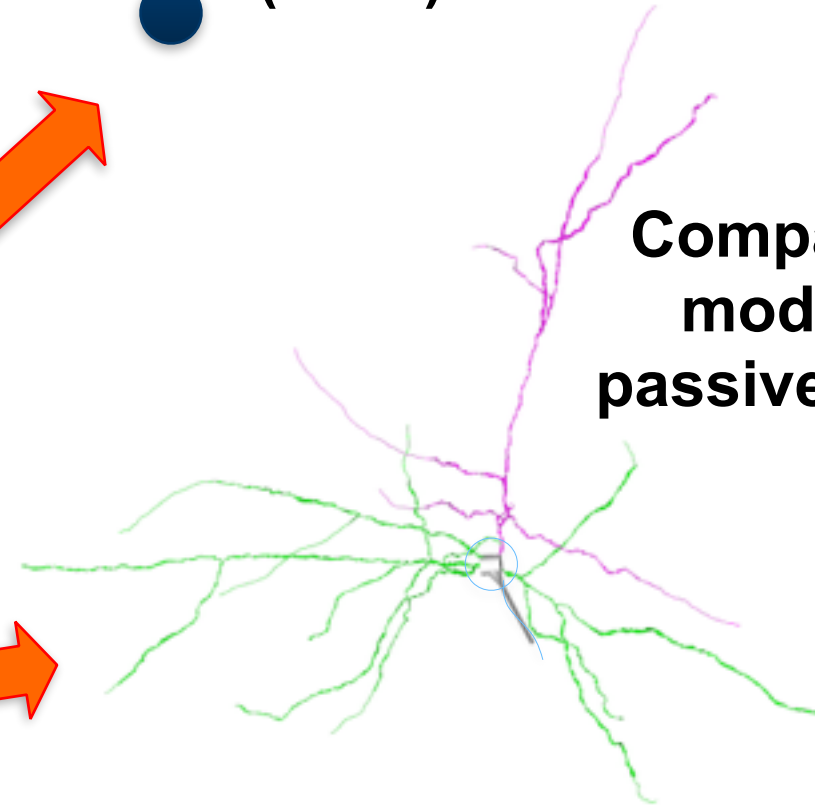
### Morphology



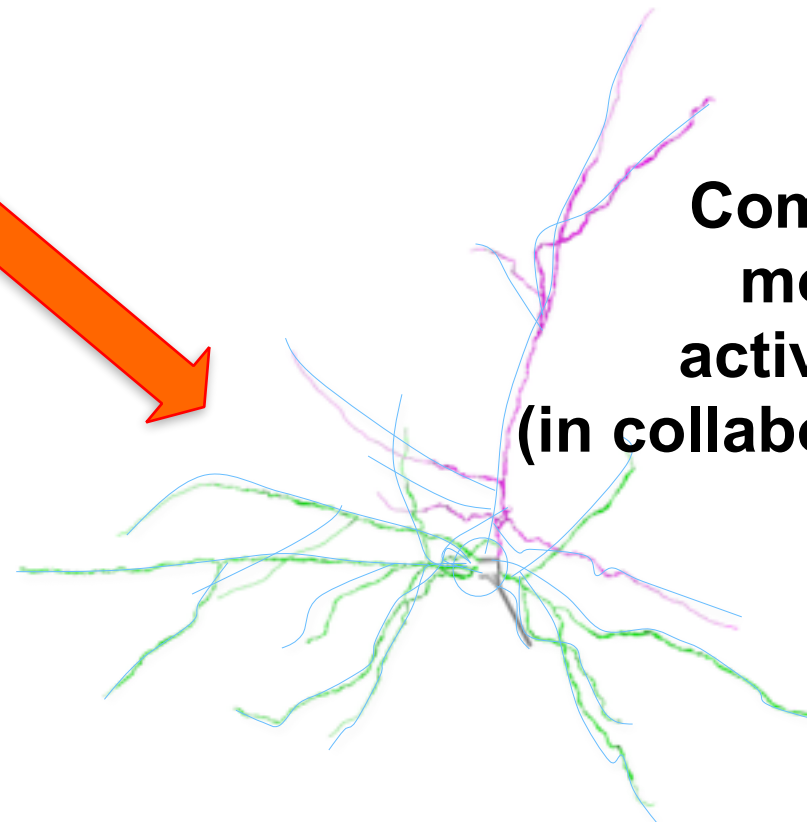
### Point models (GLIF)



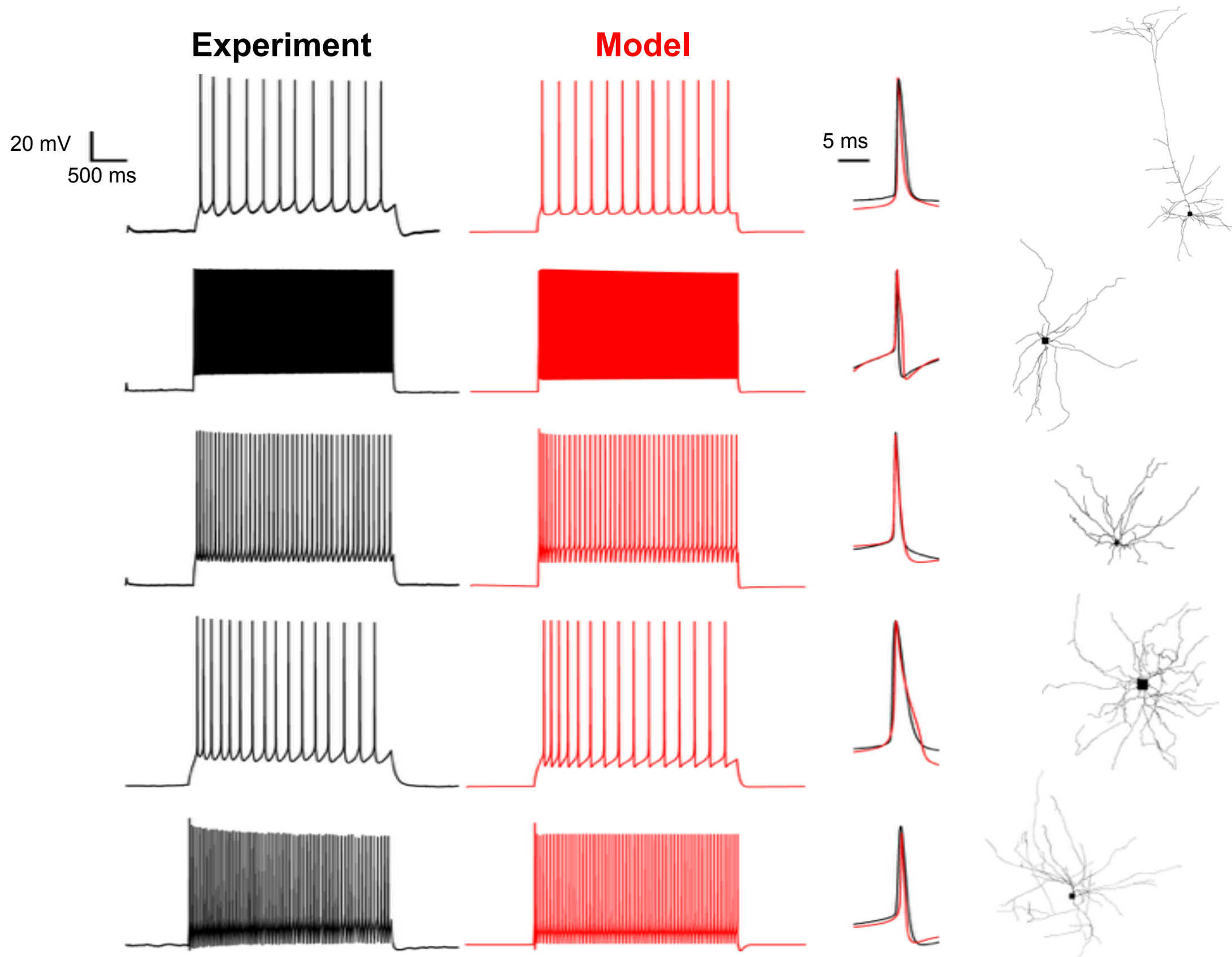
### Compartmental models with passive dendrites



### Compartmental models with active dendrites (in collaboration with BBP)



# Variety of Mouse Neurons





# Brain Observatories

- We have built highly reproducible instruments to observe the brain in action at the cellular level
- We call this the 'Cortical Activity Map' (CAM) and kicked off our first two last week!



# Allen Behavior Training Facility

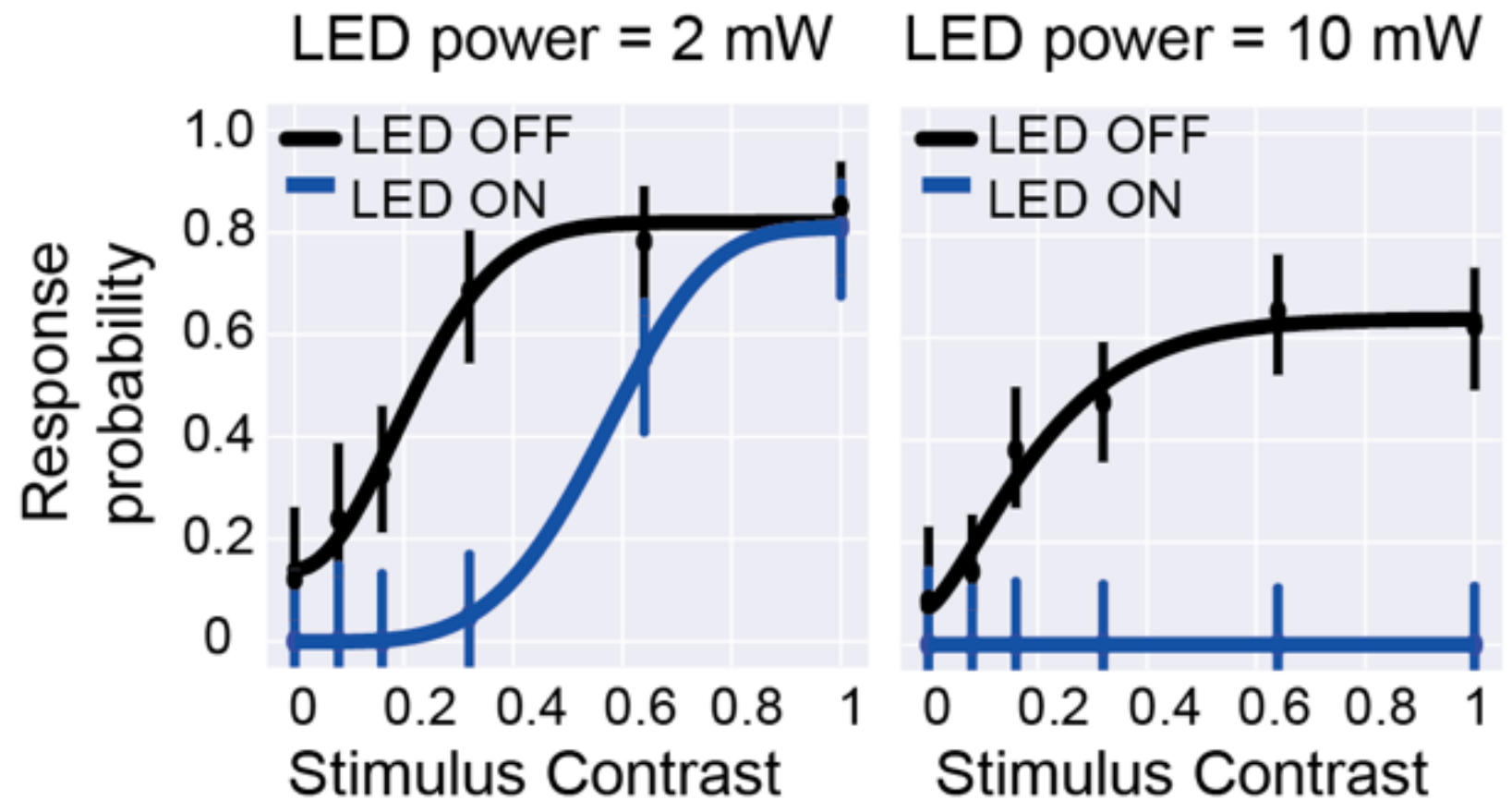
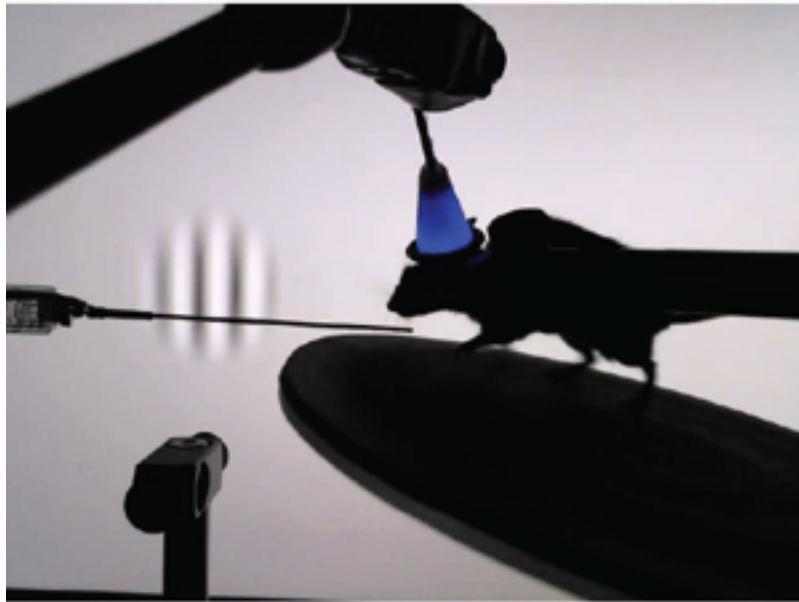


24 behavioral boxes  
2 hours per session, 4 sessions/box/day  
96 behavioral sessions/day  
3-4 weeks of training for psychophysical behavior





# Optogenetic Silencing of V1 Impairs Stimulus Detection



VGAT-ChR2

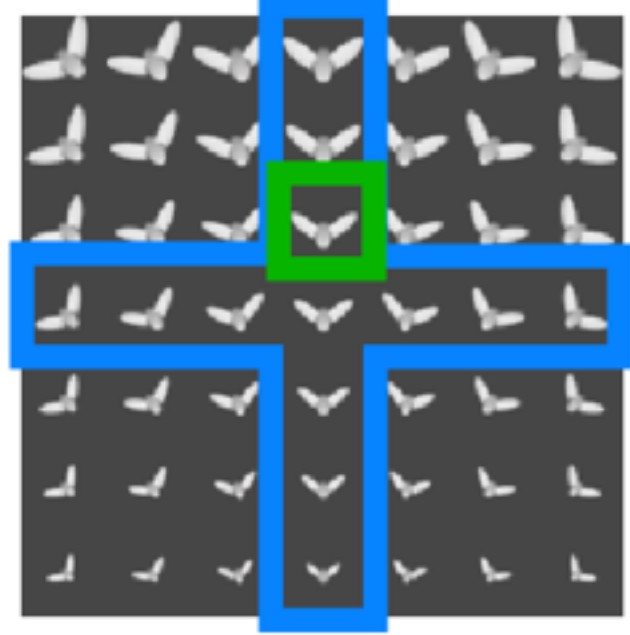
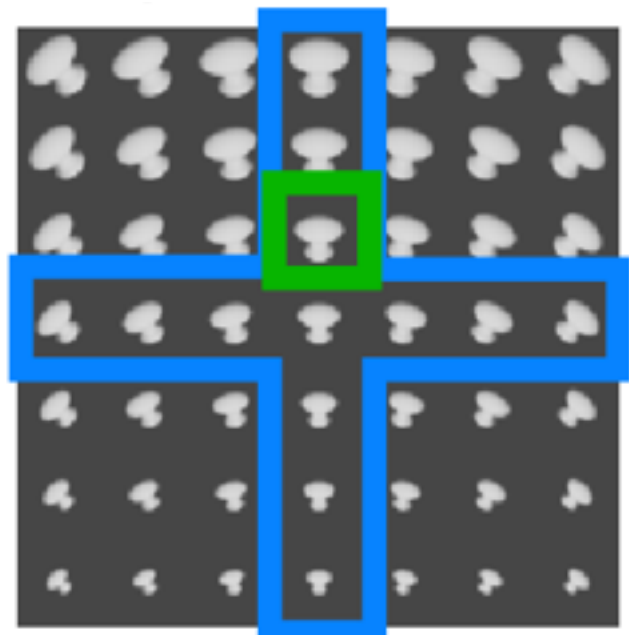
Inhibitory neurons express channelrhodopsin

Photostimulation with LED suppresses cortical activity

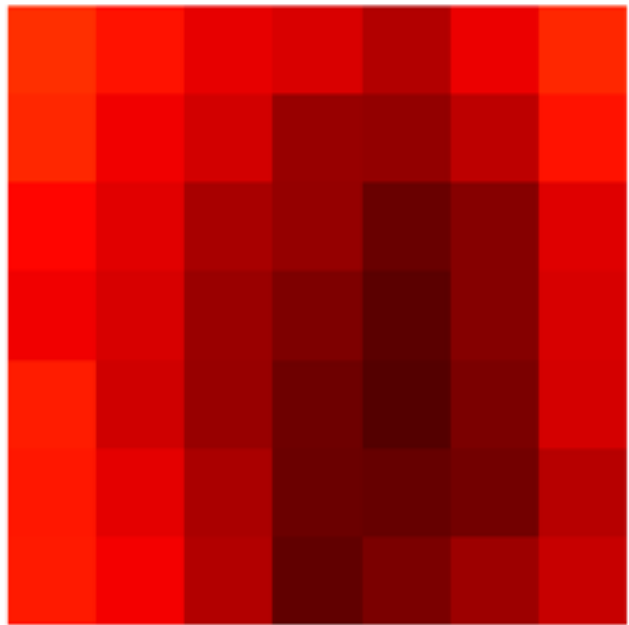




# Generalization to Untrained Views of Objects

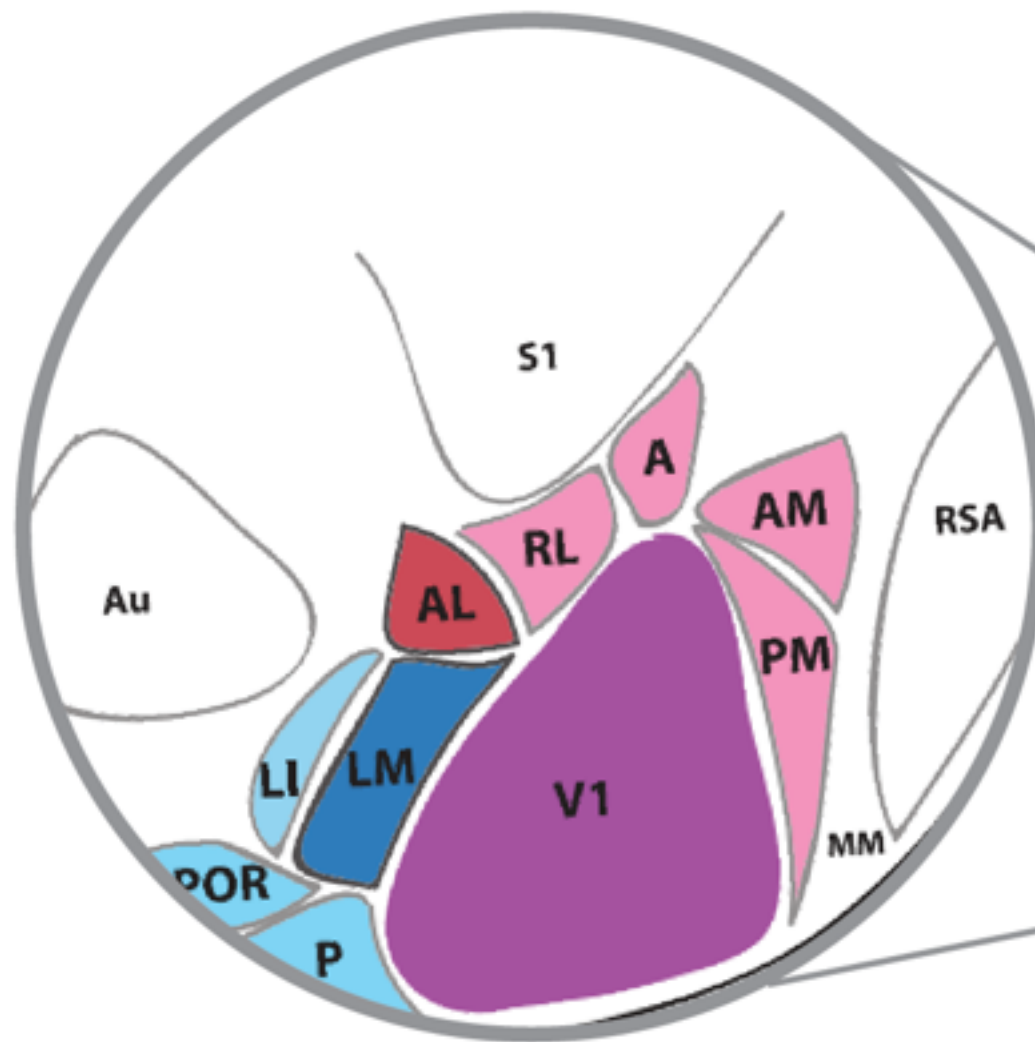


Response rate  $^1$   
 $0$

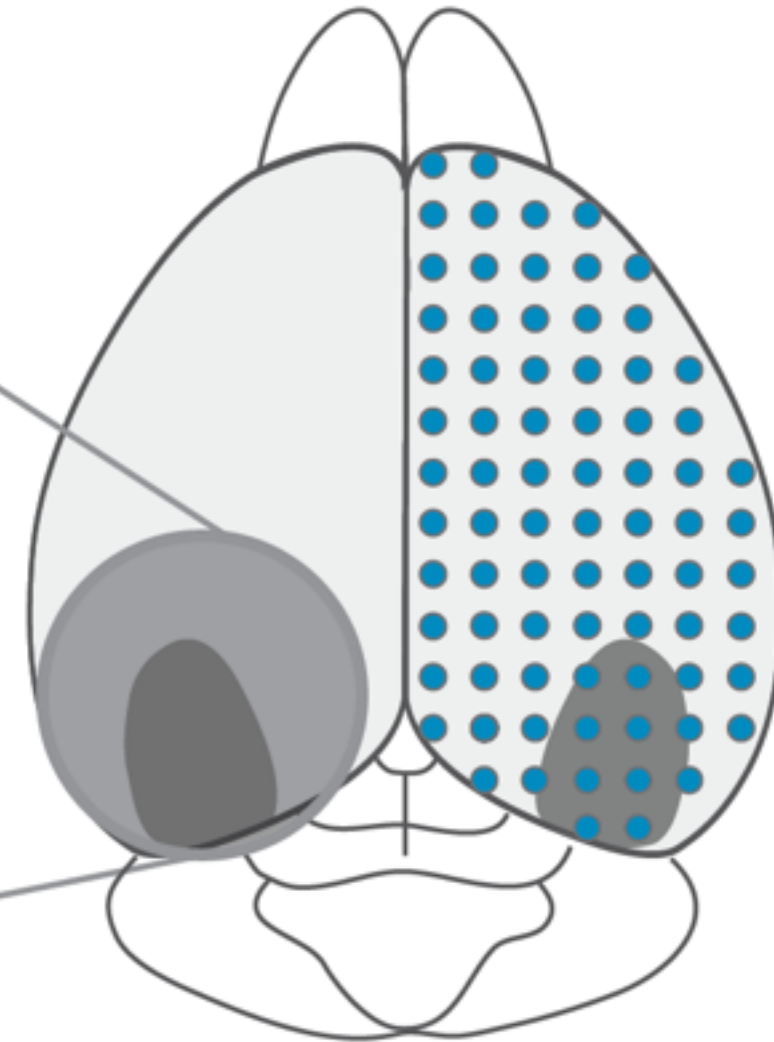


# Identifying Brain Regions Engaged During Behavior Via Intrinsic Signal Imaging

Widefield imaging

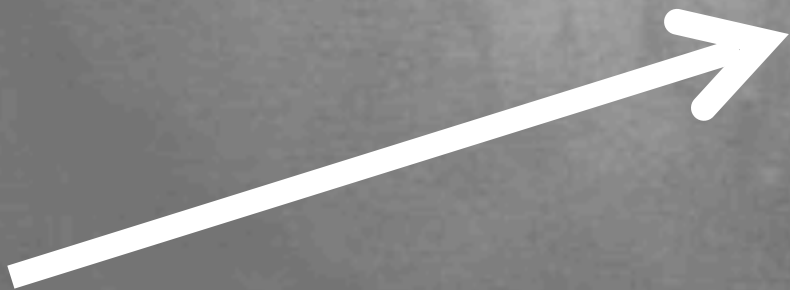


Optogenetic screen

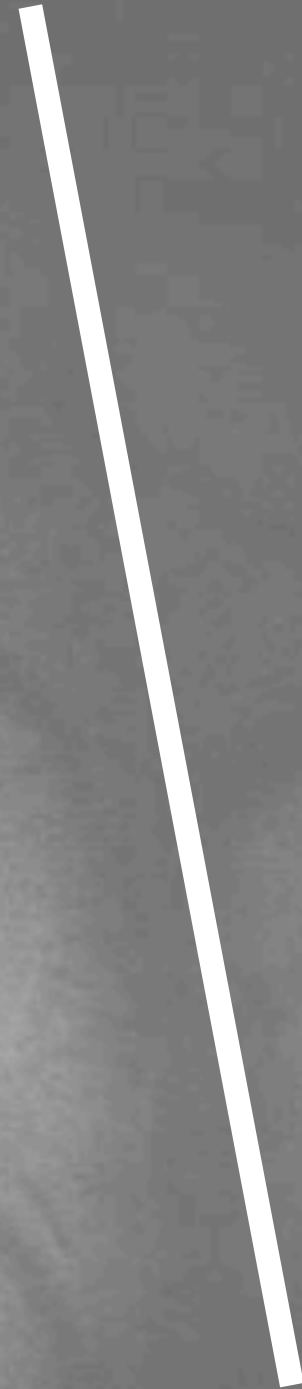


# Widefield imaging of GCaMP6

Visual  
cortex

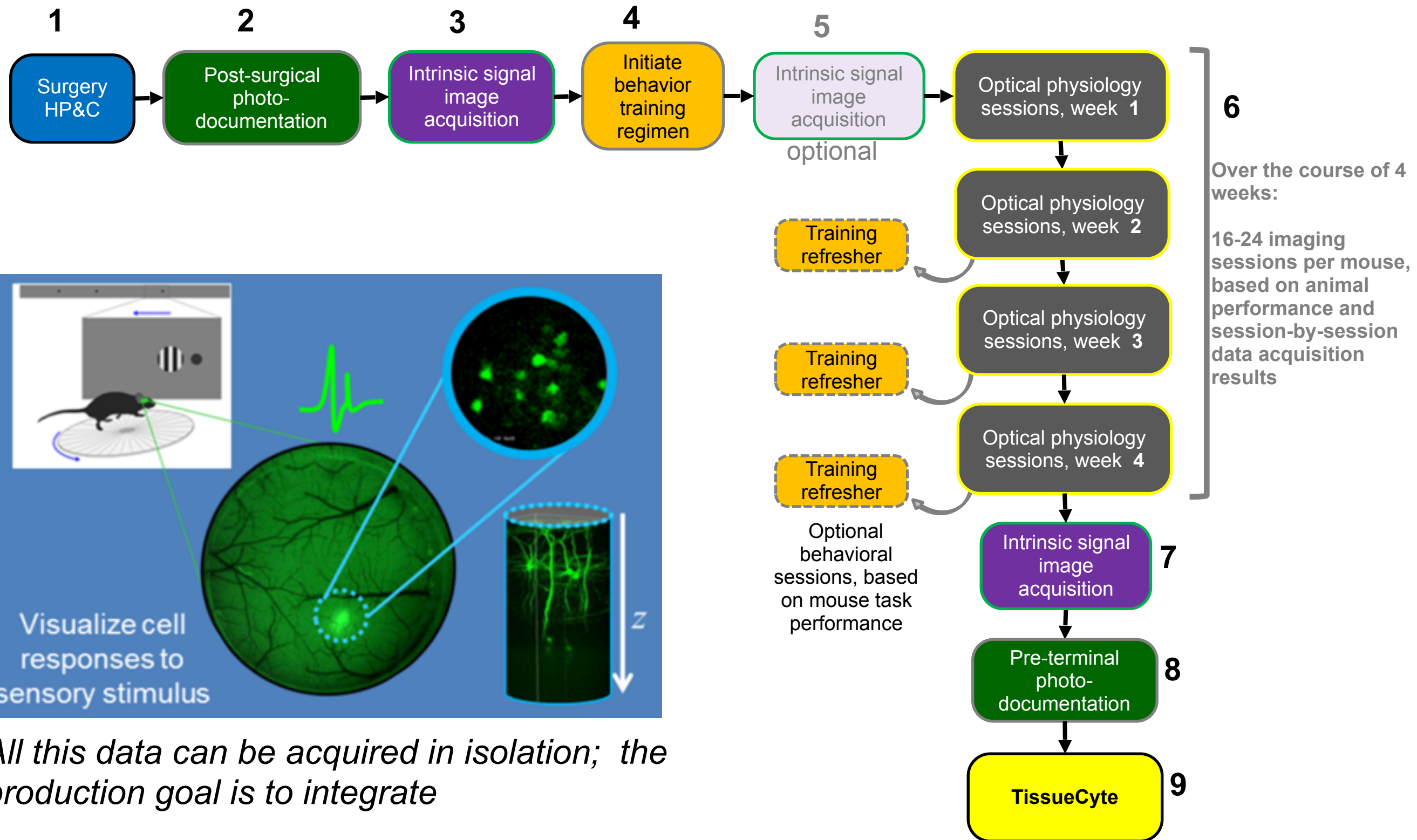


Midline





# Workflow Overview



*All this data can be acquired in isolation; the production goal is to integrate*

# Experimental Methods

- Wild-type mice injected with AAV-GCaMP6s in V1
- 2-Photon imaging in layers 2/3 and 4
- Awake, untrained mouse on running disc



# Analysis

## Single Cell Data

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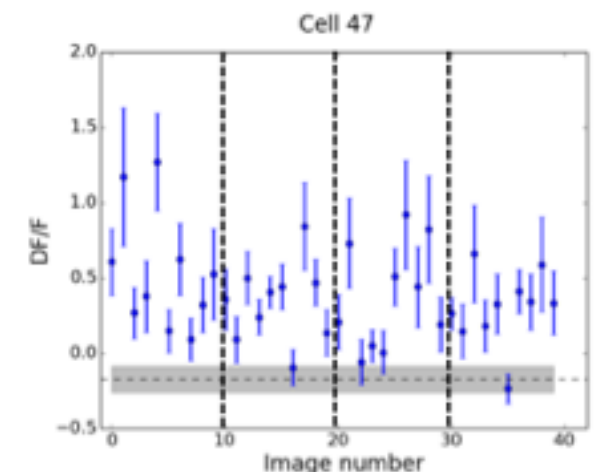
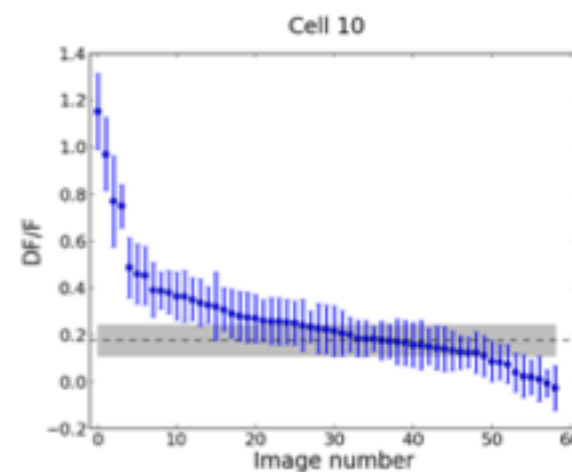
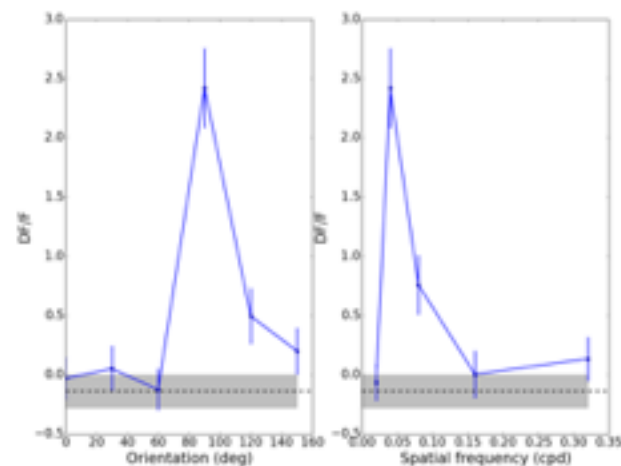
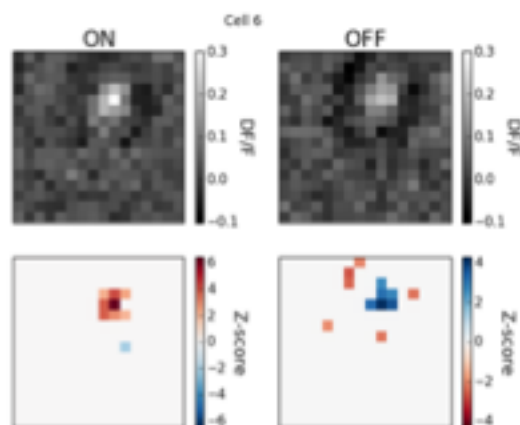
Spatial Receptive Fields

Orientation Tuning Curves

Rank Order Response to Natural Images and Simple Objects

Temporal Filters

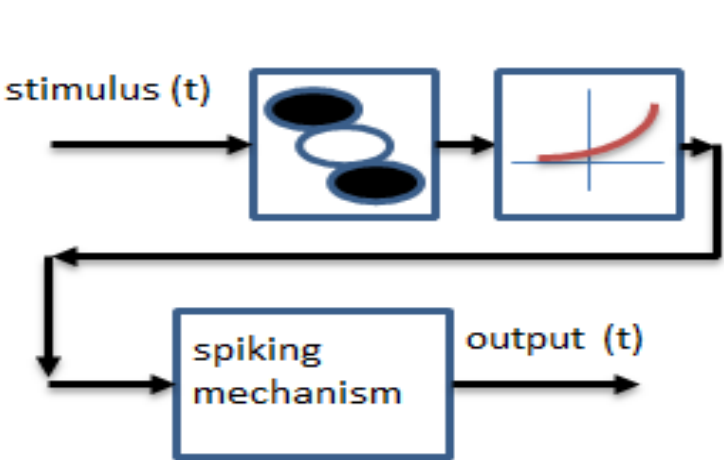
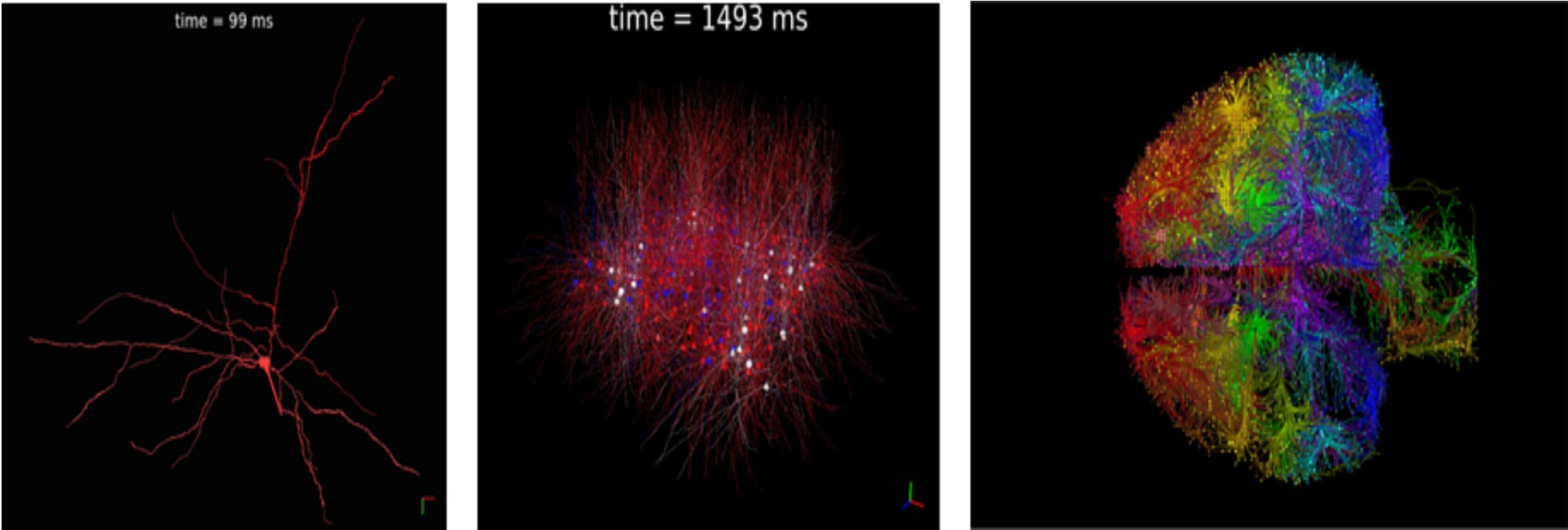
Extra Classical Receptive Fields



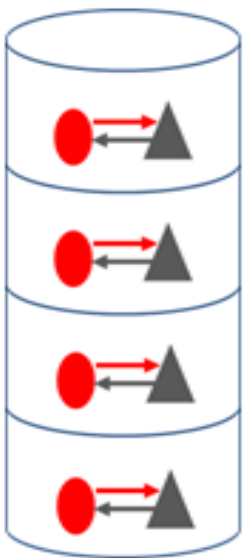


# Computer Modeling

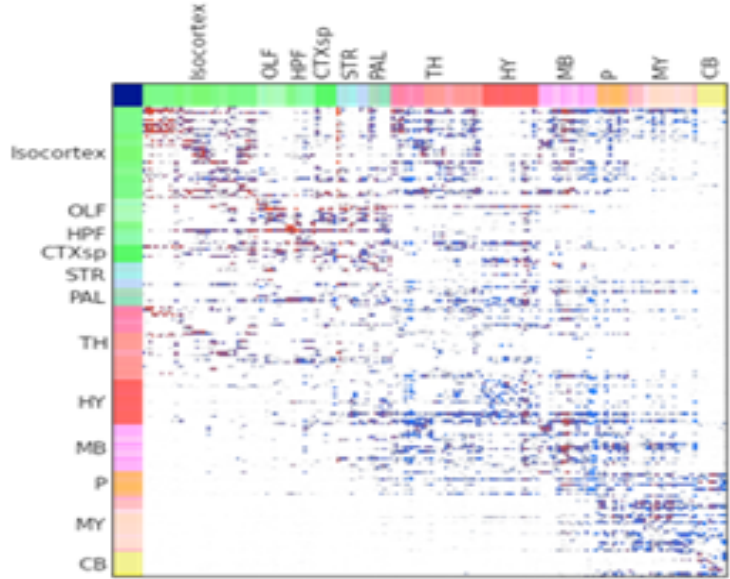
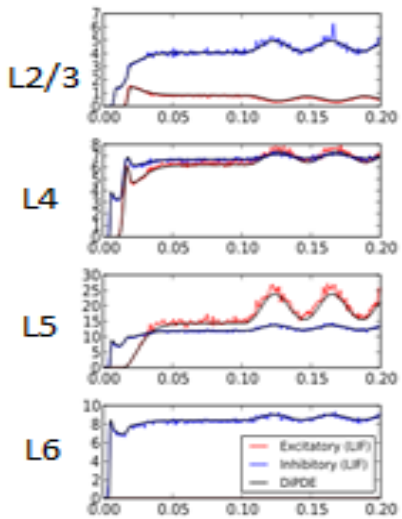
Construct minimalistic models which reproduce a desired function



Single neuron activity



Activity in local circuits



Mesoscopic models



# Acknowledgements - Paul G. Allen and Jody Allen

