Delivering data, tools and knowledge on brain cell types, connections and activity

March 30, 2017

Lydia Ng
Sr. Director, Technology

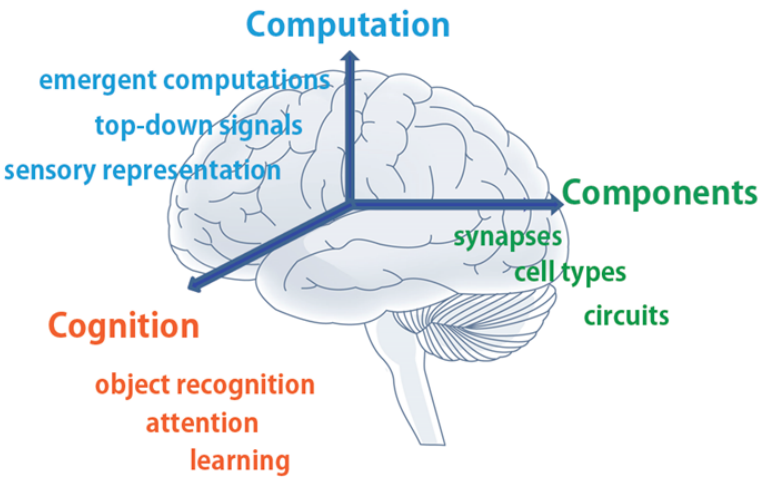
ALLEN INSTITUTE *for*
BRAIN SCIENCE

Allen Institute for Brain Science

Mission:

To accelerate the understanding of how the human brain works in health and disease.

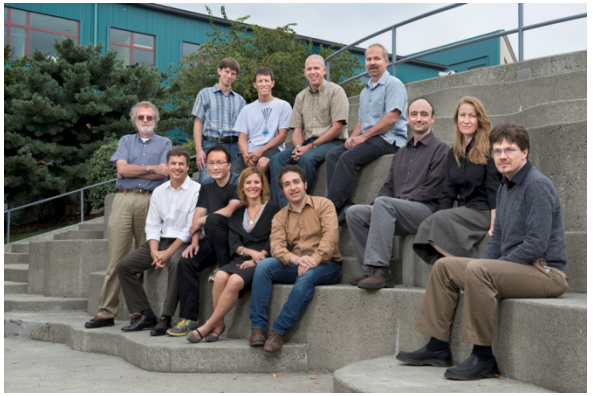
Using a big science approach, we generate useful public resources, drive technological and analytical advances, and discover fundamental brain properties through integration of experiments, modeling, and theory.



- **What are the parts?**
  - Genes, proteins, synapses, cells, functional areas
- **How are the parts connected?**
  - Synapses, neurotransmitters, circuits, relay centers
- **How do the parts receive, store, and respond to information?**
  - Circuit function, neural codes; behavior
- **What goes wrong in disease?**
  - Mechanism, pathways, interventions

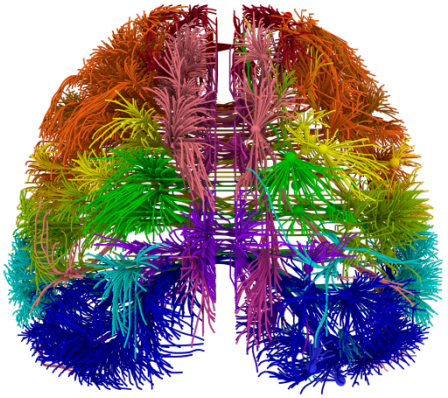
Allen Institute Guiding Principles

Team Science: Multi-disciplinary teams working towards common goal



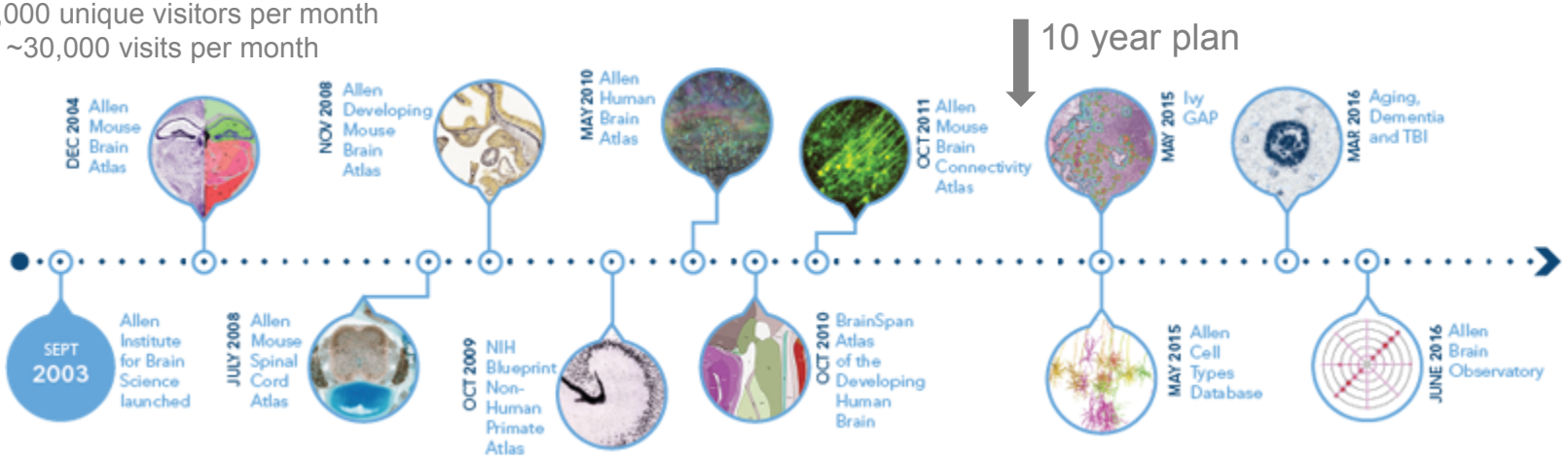
Big Science: Clear goals or milestones for large-scale projects

Open Science: All of our data, knowledge and tools are publicly available on brain-map.org.



Allen Institute for Brain Science Resources

~13,000 unique visitors per month
~30,000 visits per month



Data

Gene Expression
Connectivity
Single Cell Characterization
Visual Coding
Physiology
Transcriptomics
Visual Behavior
Morphology

Specimen

Mouse
NHP
Human
Brain
Spinal Cord
Cells
Development
Disease

Making a resource: from data to insight

Data Generation | Data Processing | Data Integration | Data Presentation | Data Access | Community Usage

Large scale data generation using standard operating procedure (SOP) to ensure quality and uniformity

Experimental design optimized for automated downstream processing

Collect additional metadata and channel to enable integration and data interoperability

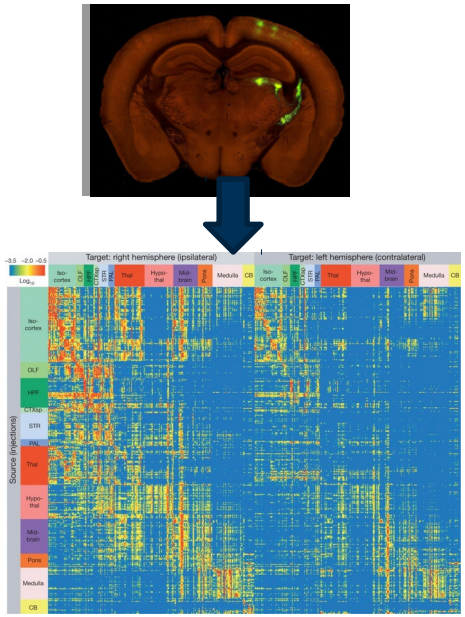
The purpose of computing is insight, not numbers - Richard Hamming

Making a resource: from data to insight

Data Generation | **Data Processing** | Data Integration | Data Presentation | Data Access | Community Usage

Processing and annotation of data to extract quantitative features for analysis

Systematic application of standardized informatics pipeline to work at scale



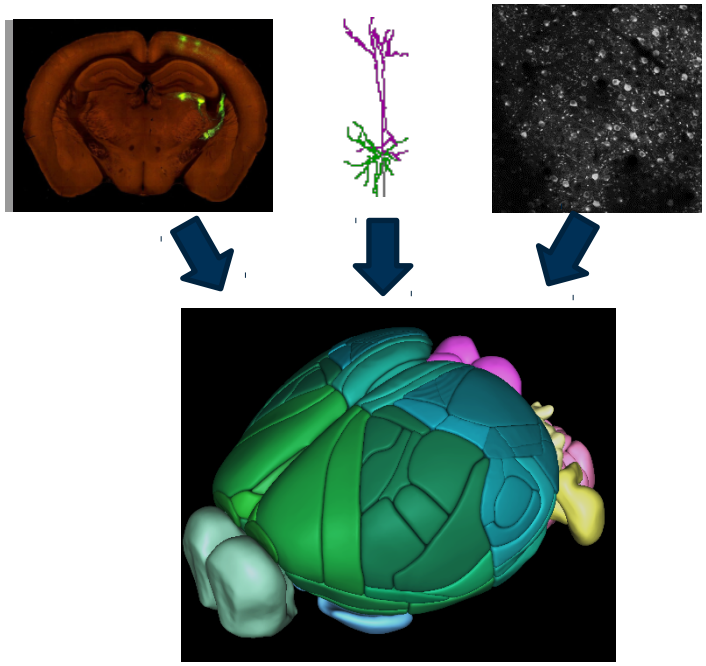
The purpose of computing is insight, not numbers - Richard Hamming

Making a resource: from data to insight

Data Generation | Data Processing | **Data Integration** | Data Presentation | Data Access | Community Usage

Enable computational comparison and interoperability of datasets within and across resources

- Unified database with common metadata
- Common coordinate framework
- Common mouse line across resources
- Standard file format (NWB)



The purpose of computing is insight, not numbers - Richard Hamming

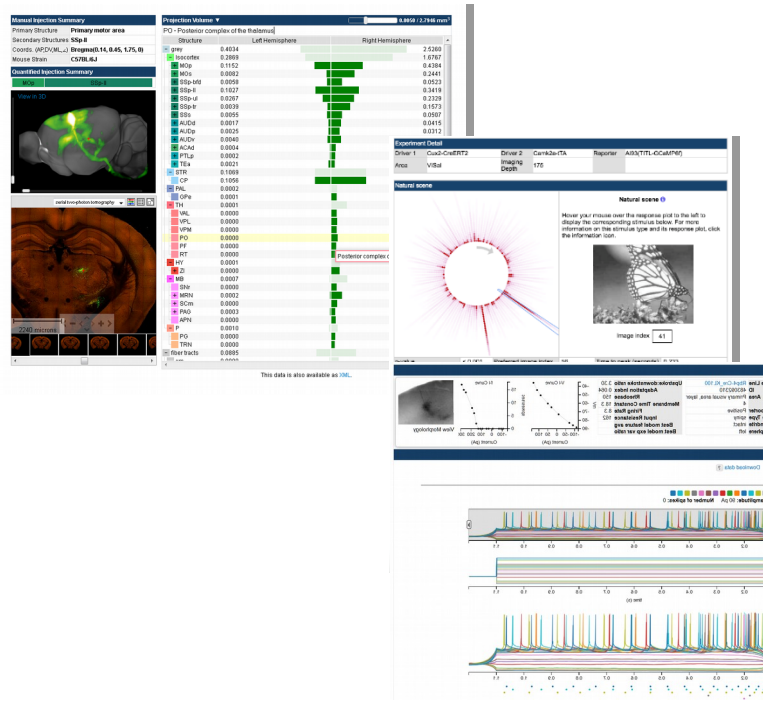
Making a resource: from data to insight

Data Generation | Data Processing | Data Integration | **Data Presentation** | Data Access | Community

Online browsing to provide insight into data content and meaning

Summary views to capture key biological features of data

Search, browse and explore data of interest



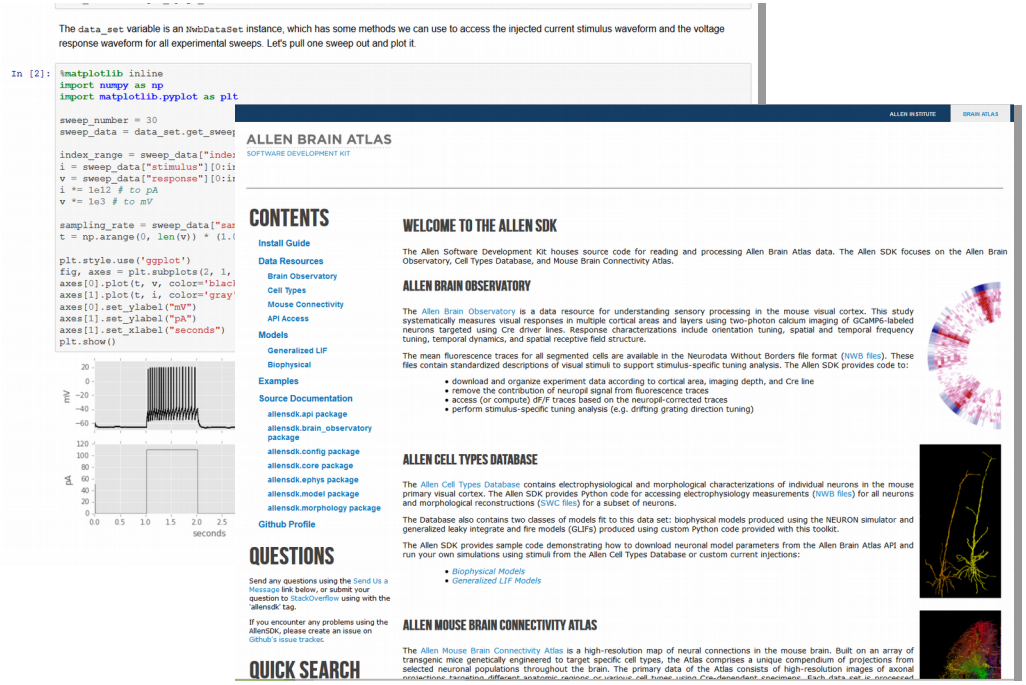
The purpose of computing is insight, not numbers - Richard Hamming

Making a resource: from data to insight

Data Generation | Data Processing | Data Integration | Data Presentation | **Data Access** | Community

Data access through application programming interface (API)

Software library of functions and scripts to get started on data analysis (SDK)



The purpose of computing is insight, not numbers - Richard Hamming

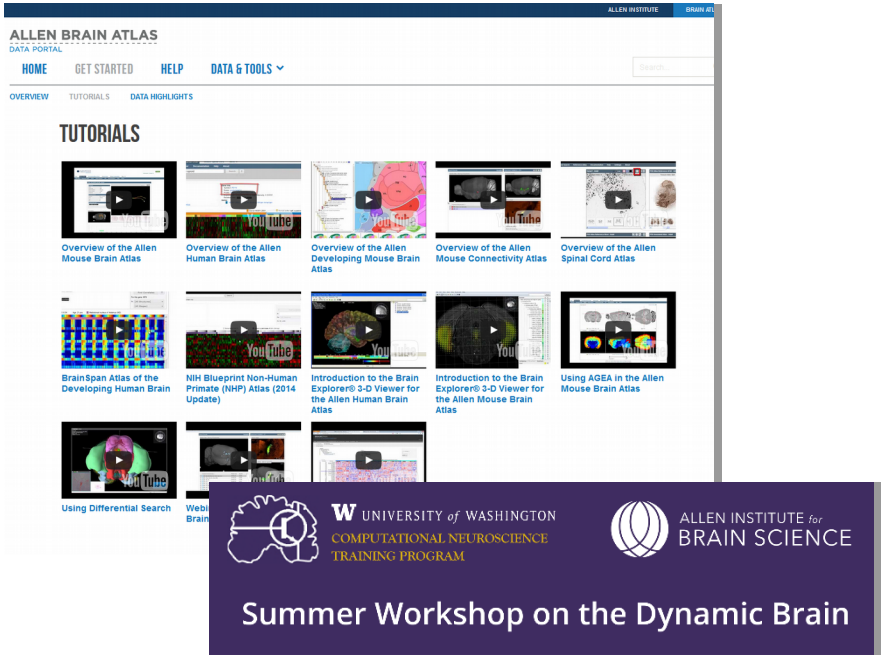
Making a resource: from data to insight

Data Generation | Data Processing | Data Integration | Data Presentation | Data Access | **Community Usage**

User training and tutorial

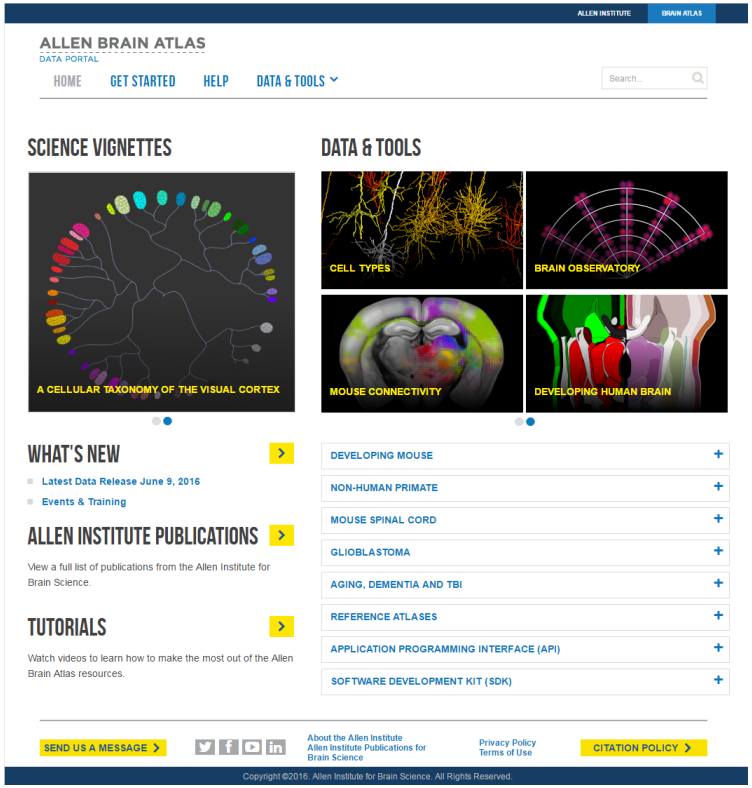
Collaboration

Summer workshop on the dynamic brain



The purpose of computing is insight, not numbers - Richard Hamming

Allen Brain Atlas: Data Portal
http://brain-map.org



Web: online browse and search
API: data download
SDK: tutorial and use cases

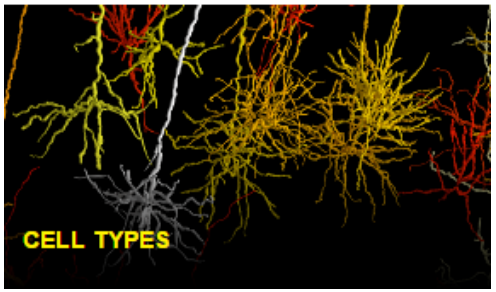
http://alleninstitute.github.io/AllenSDK/

Allen Mouse Brain Connectivity Atlas

Axonal projection from selected neuronal populations

Mesoscale Connectome

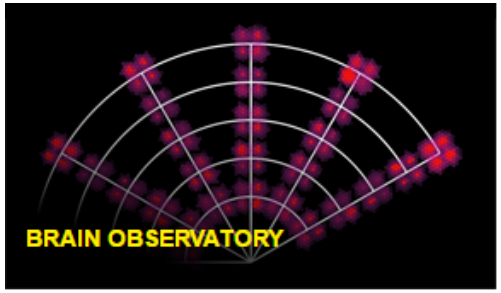
Allen Cell Types Database



Multimodal characterization of single cells

Cell Types Taxonomy

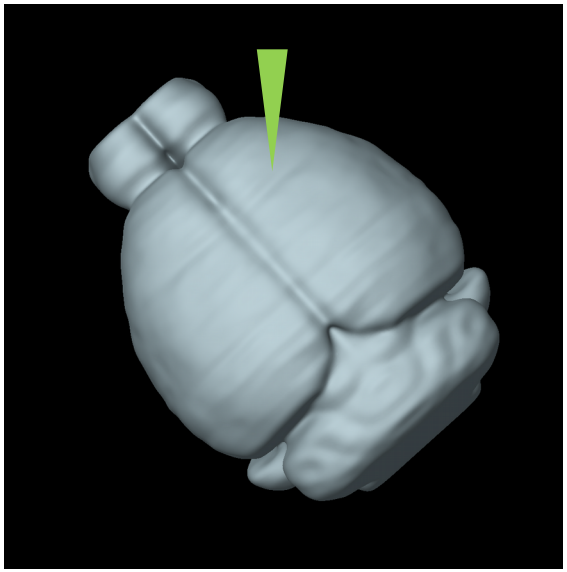
Allen Brain Observatory

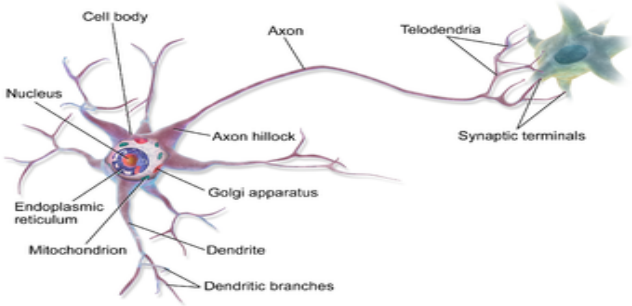


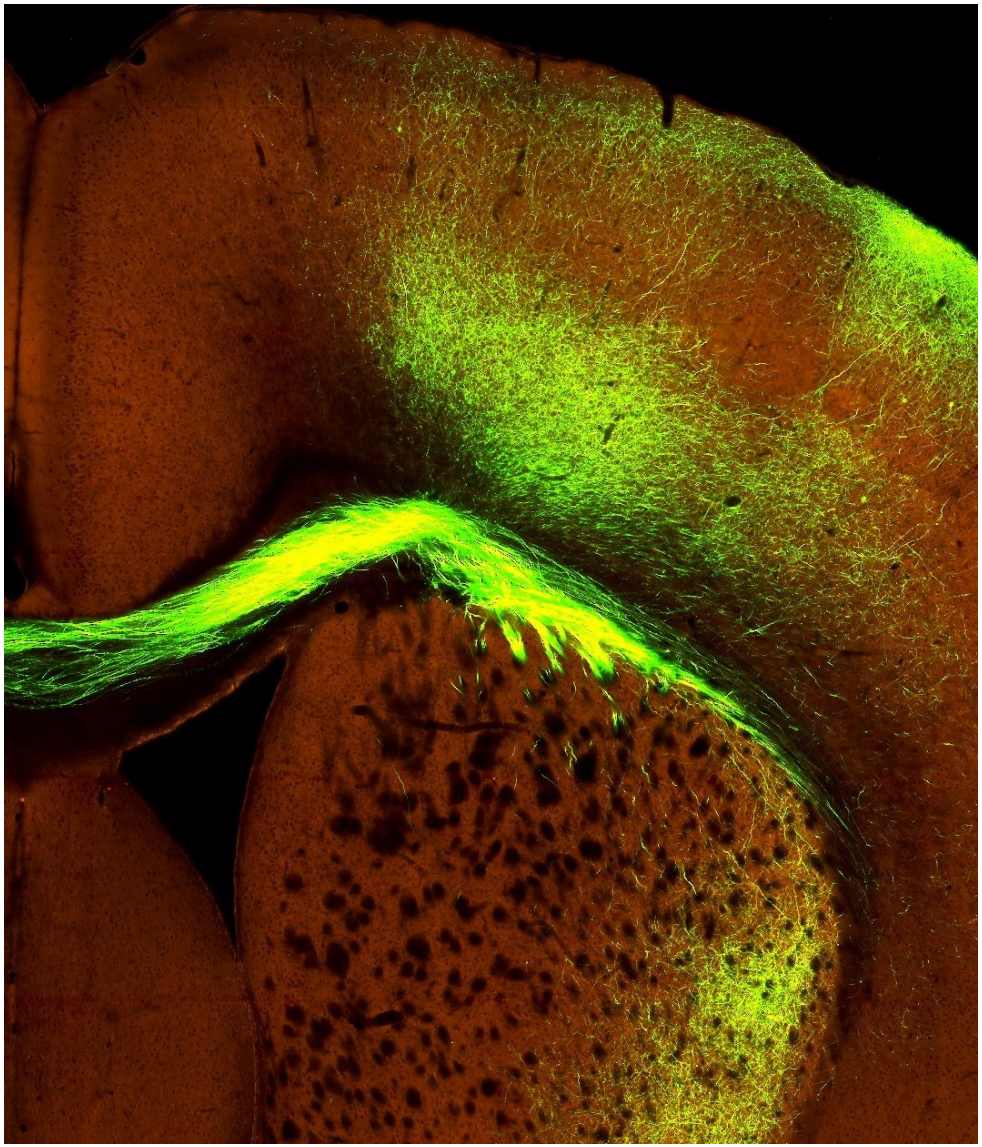
Physiological activity of cells in awake behaving mouse

Visual Coding
Visual Behavior

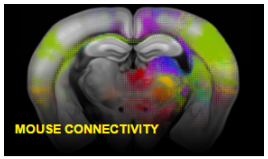
ALLEN **Mouse Brain Connectivity Atlas**



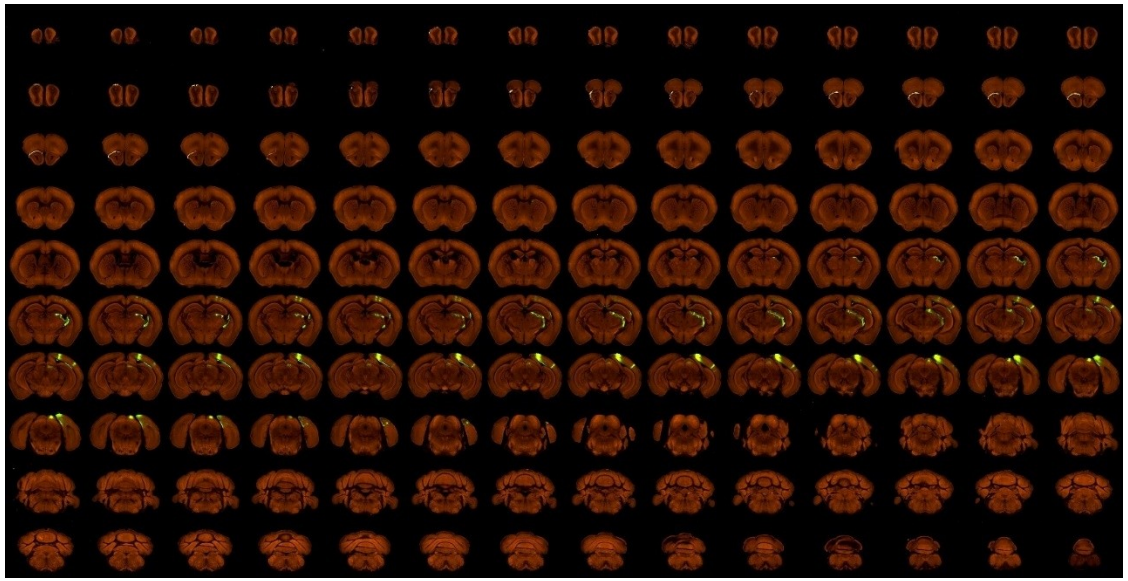


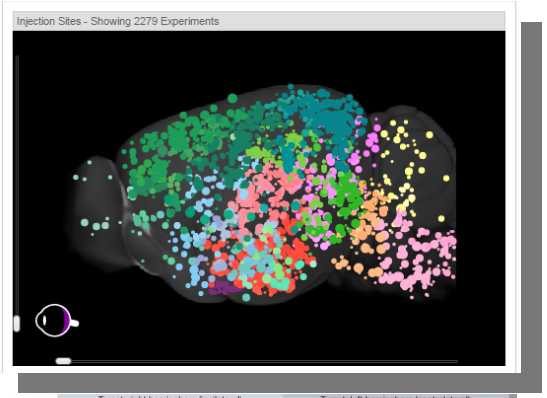


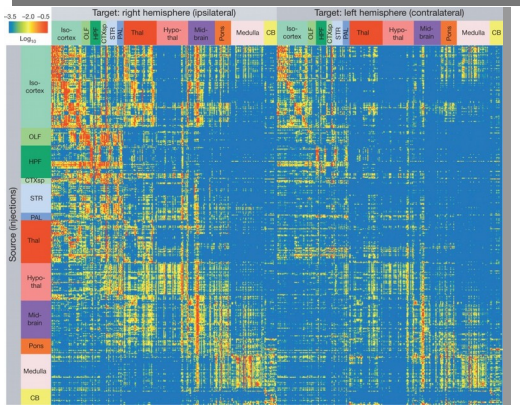
0.35µm pixels

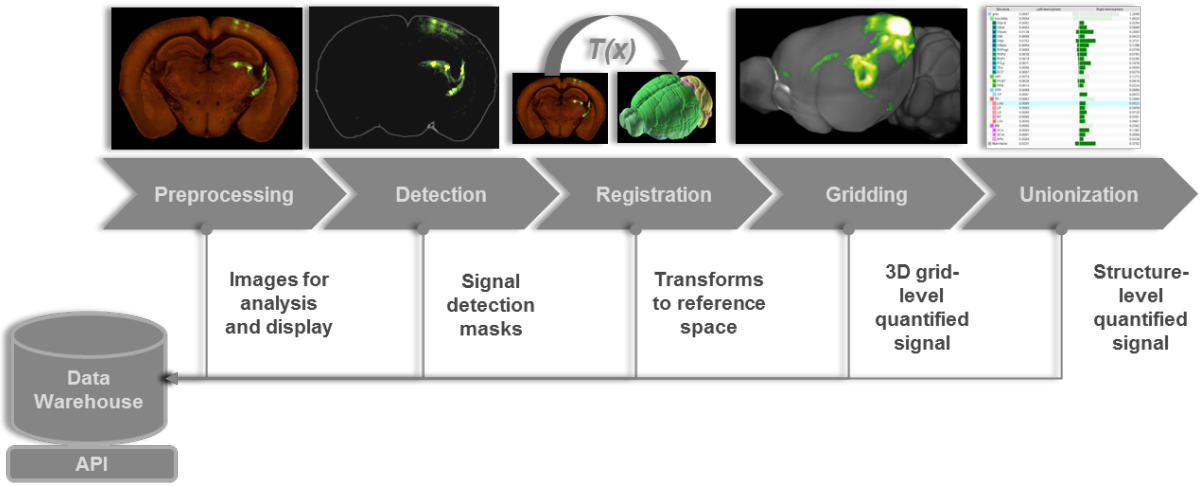


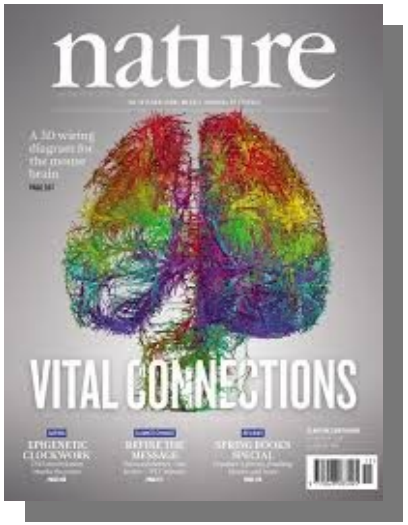
Allen Mouse Connectivity Atlas
http://connectivity.brain-map.org





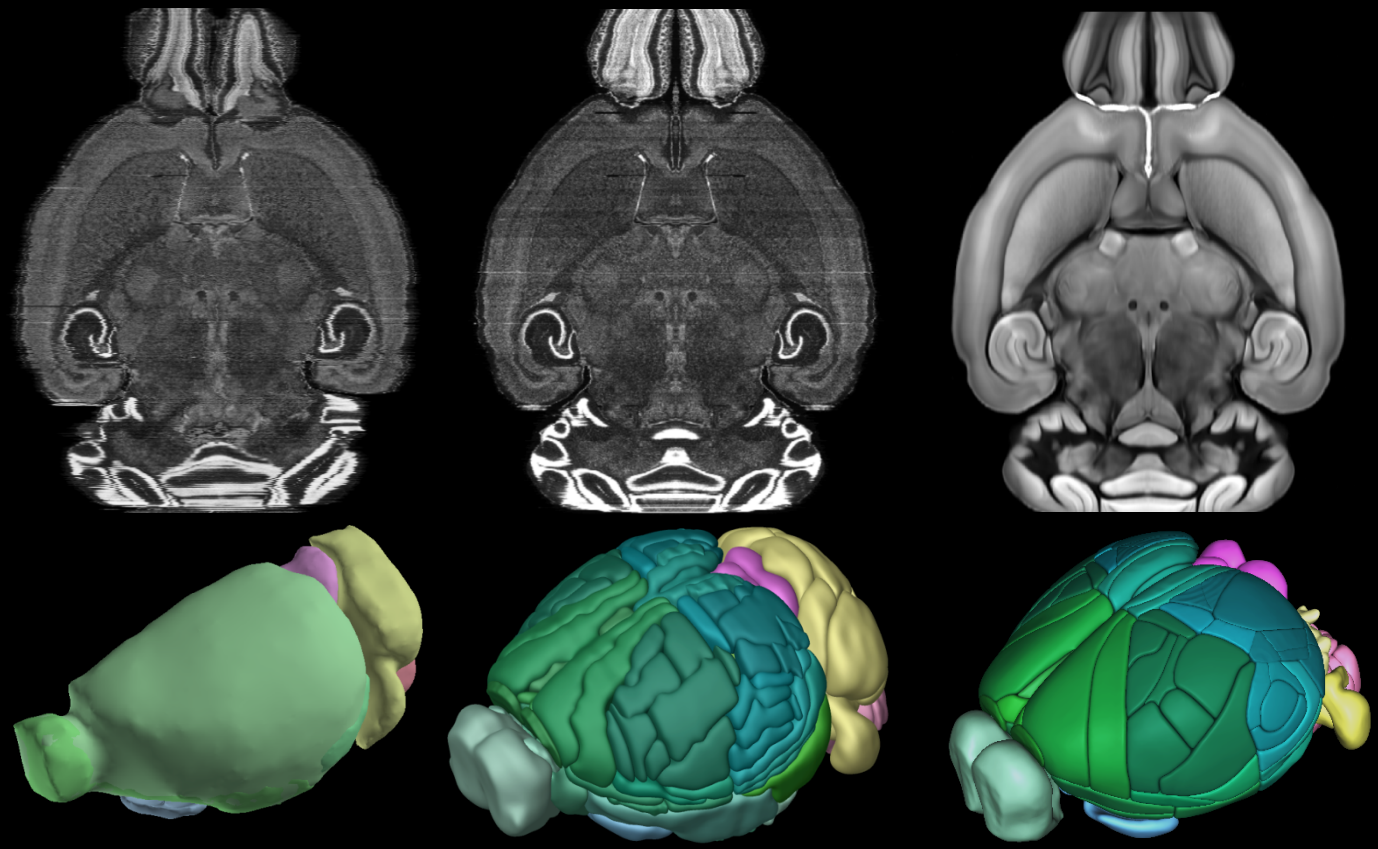






Allen Mouse Common Coordinate Framework

Version 1 (2005) | **Version 2 (2011)** | **Version 3 (2015, 2016)**

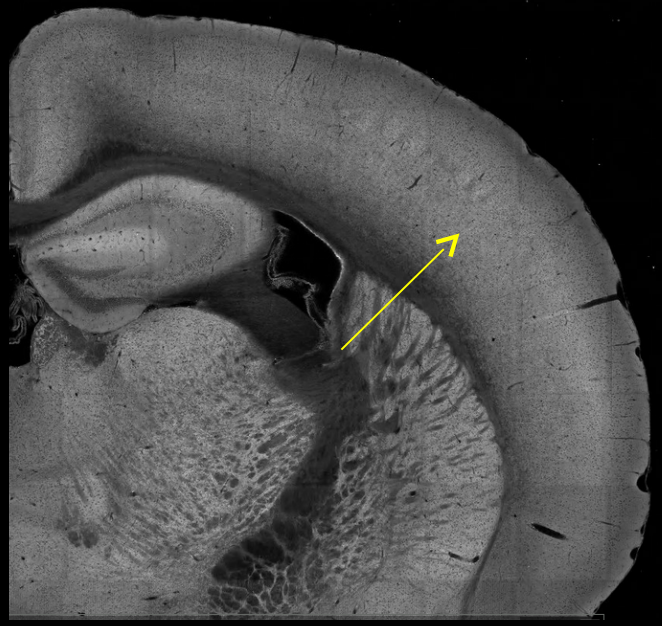


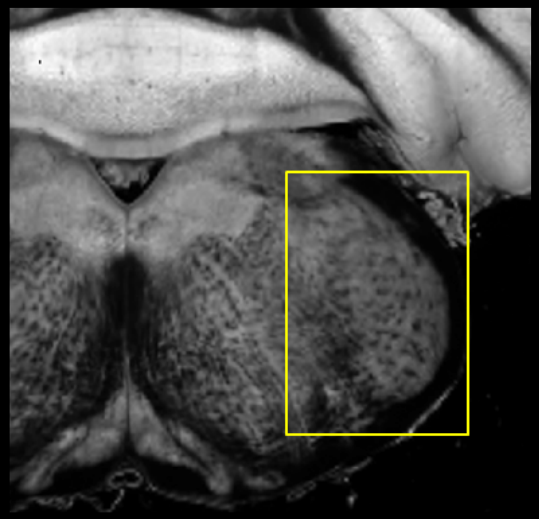
Single specimen
One-sided annotation
~200 structures

Symmetric
Double-sided annotation
860 structures

Shape and intensity average
of 1675 specimens
200+ newly drawn structures

Average Template: Construction





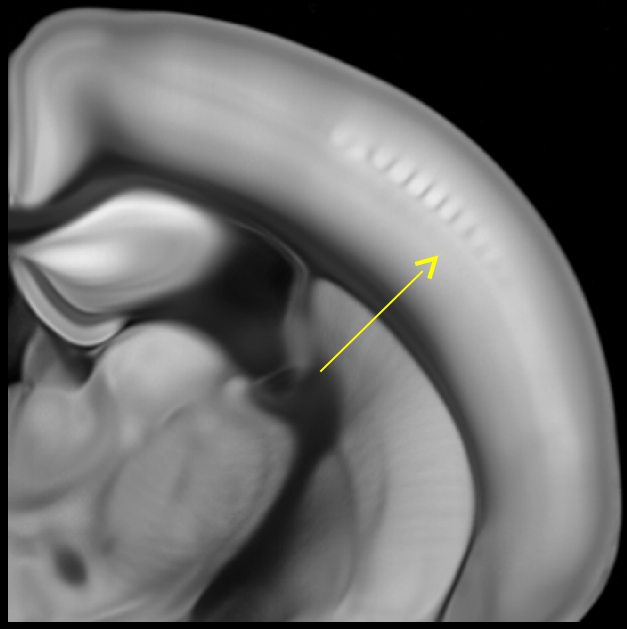
Specimen Images

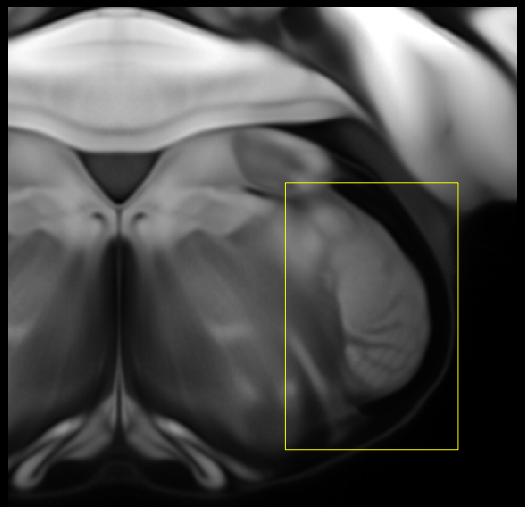
Iteration **N** Template

Registration and Warp

Average

Iteration **N+1** Template

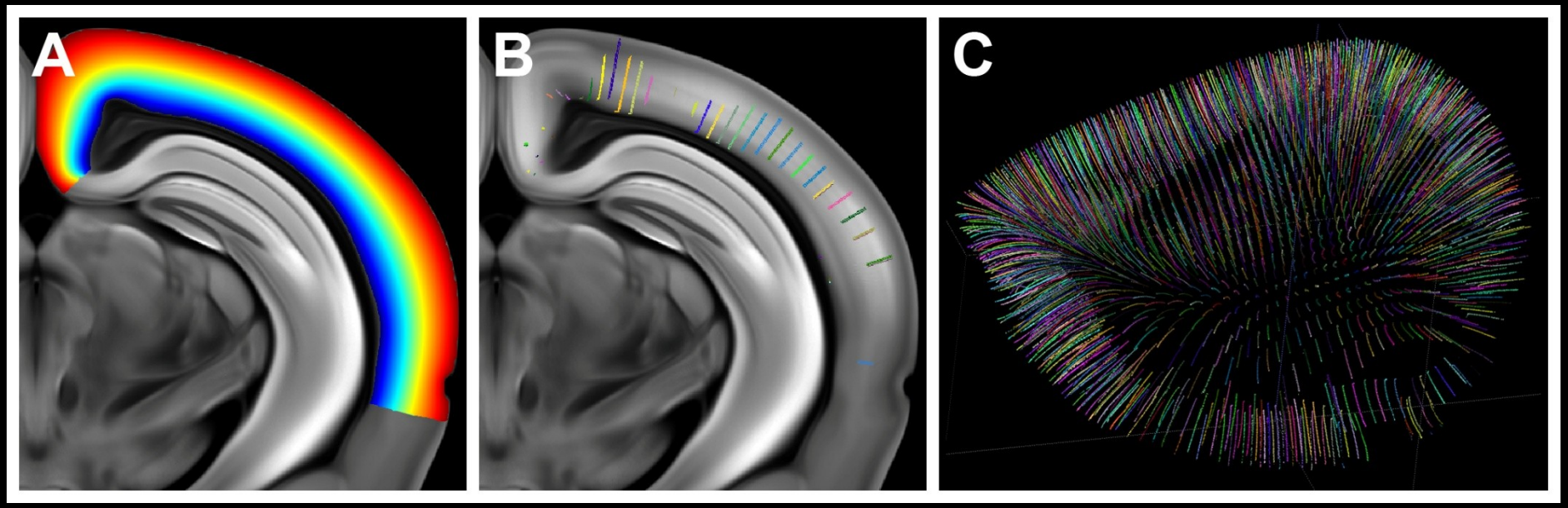




Single Specimen

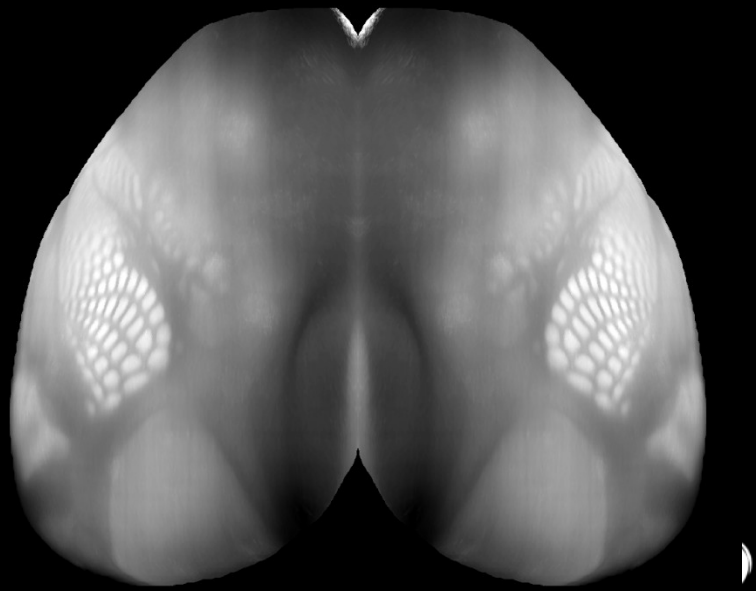
Shape and Intensity Average
1675 Specimens

Cortical Coordinates



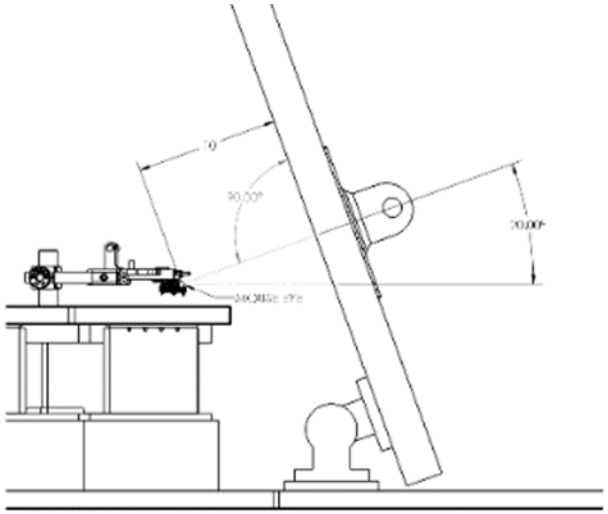
A curved cortical coordinate system for integrating information at different cortical depths

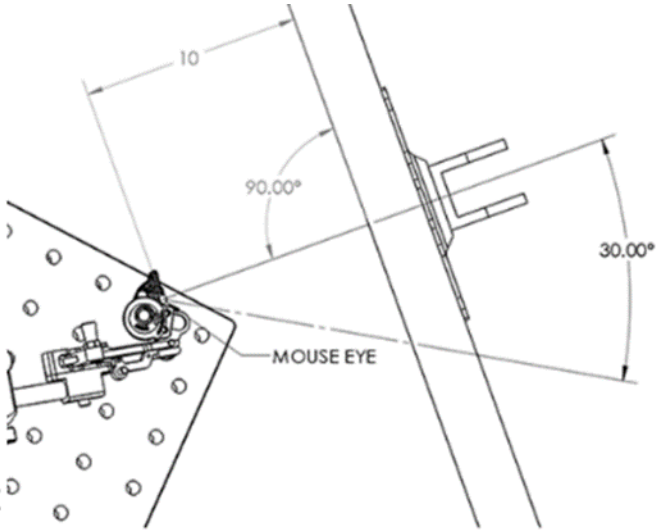
Use Laplace's equation to generate equi-potential surfaces. Streamlines are shortest path through equi-potential field.

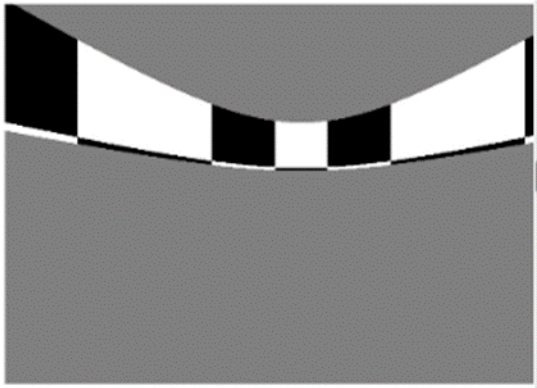


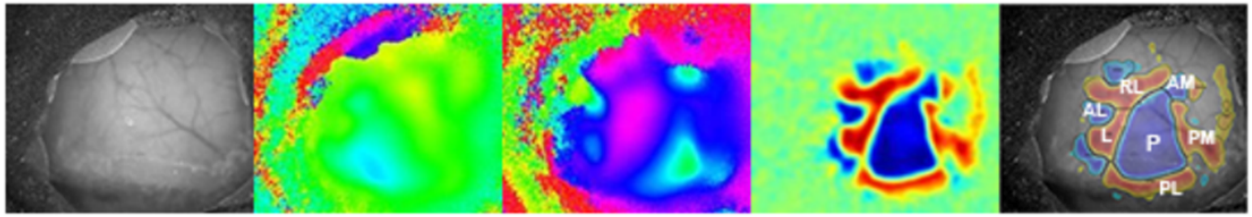
Maximum density projection along streamlines

Integrating functional information: Mapping visual areas by intrinsic signal imaging (ISI)





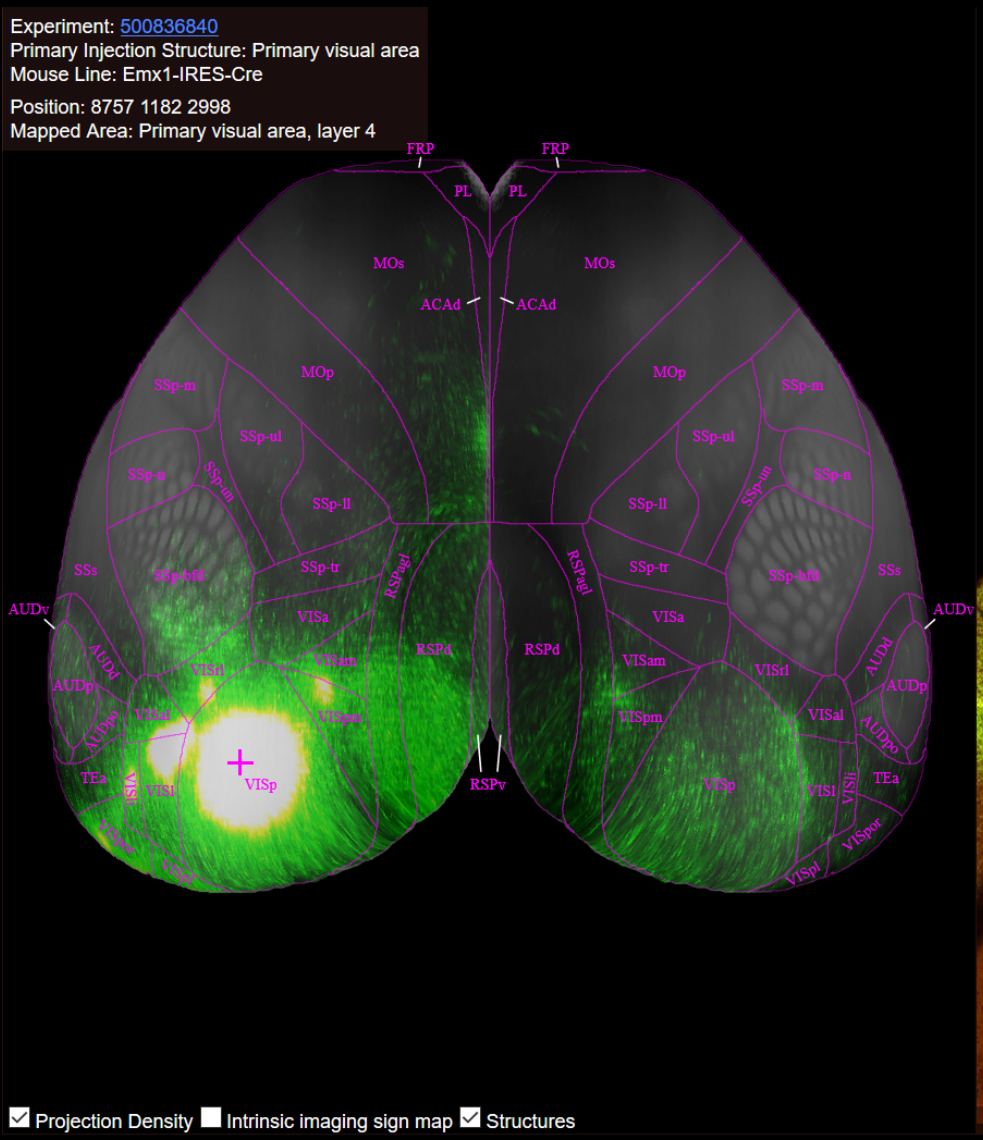


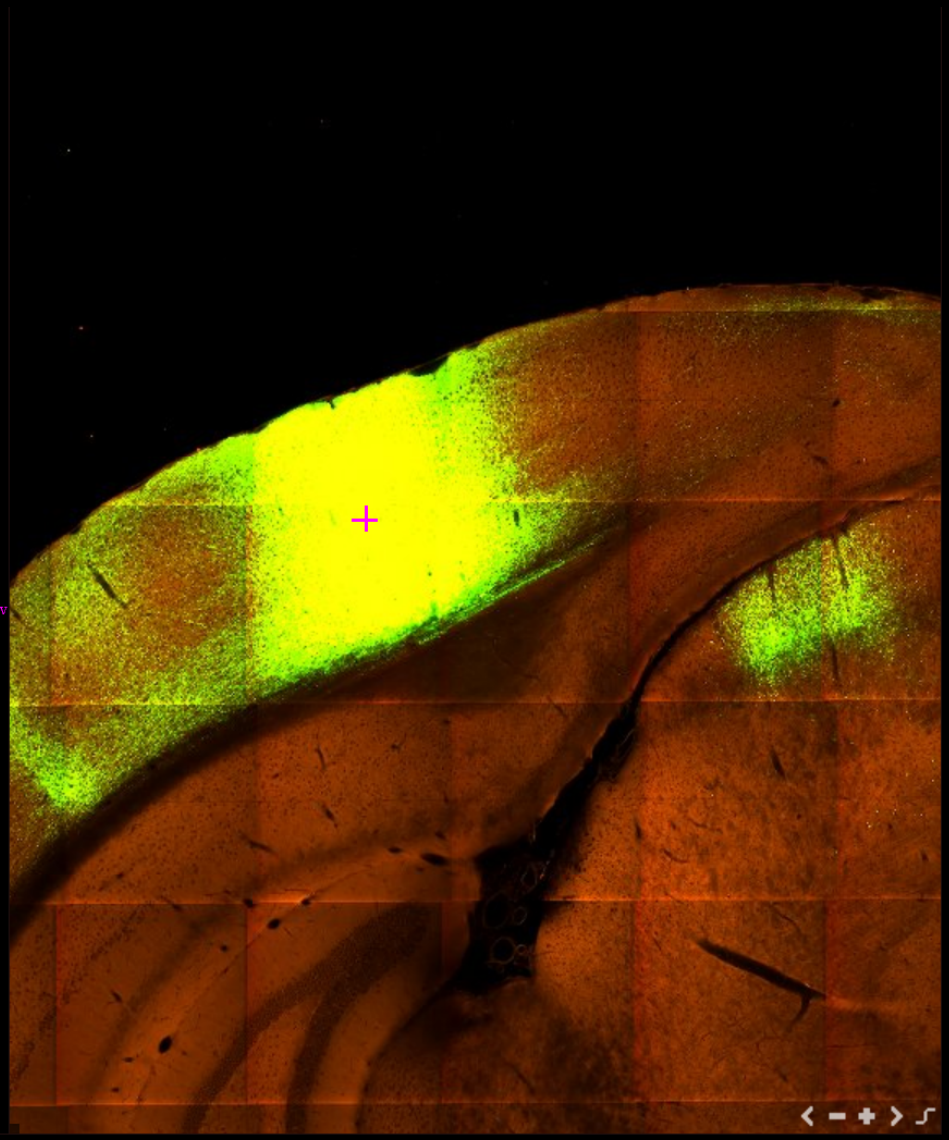


Surface Vasculature → ISI-derived Phase Maps → Sign Map → Overlay & Segmentation of Visual Areas

- **Stereotaxic injections can also be targeted to functionally known areas**

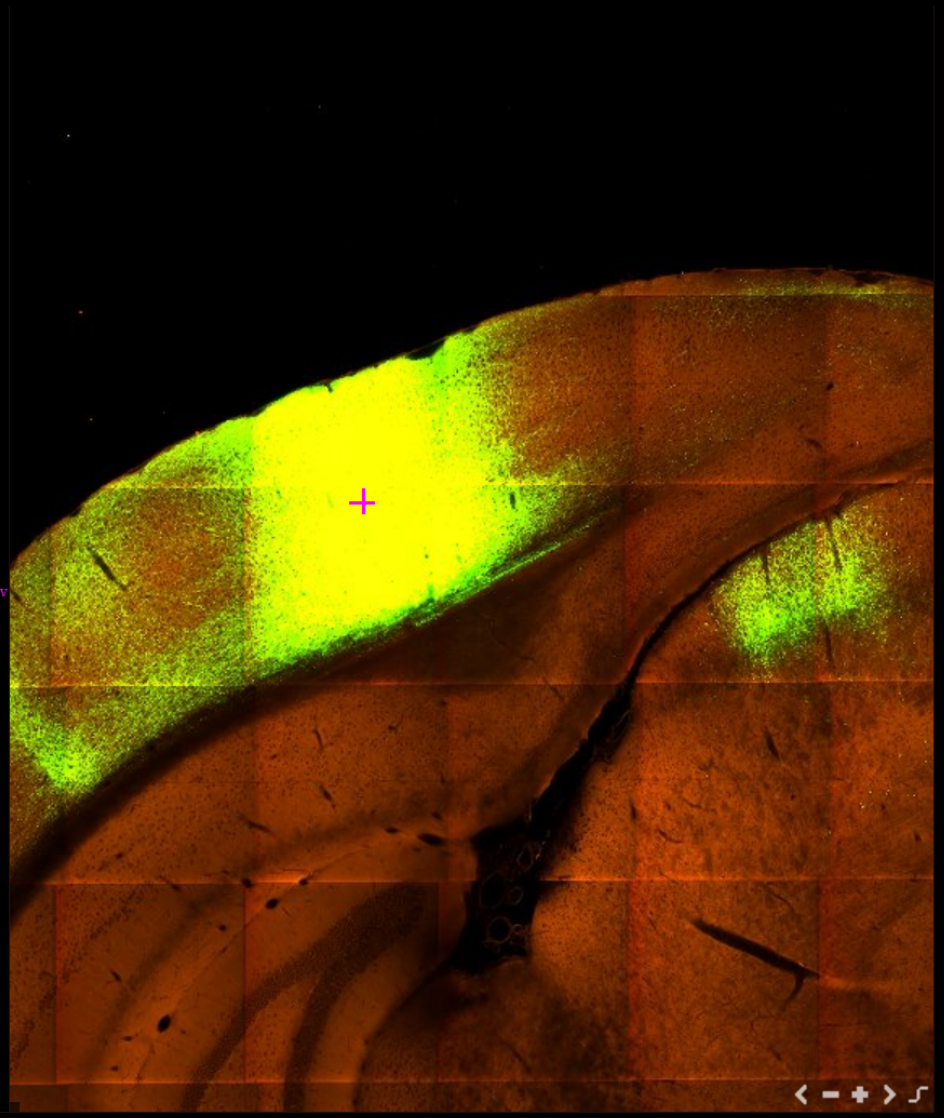
Cortical Flat maps: Projection



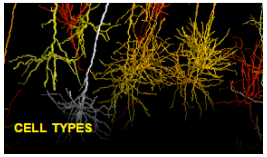


connectivity.brain-map.org

Cortical Flat maps: ISI sign map

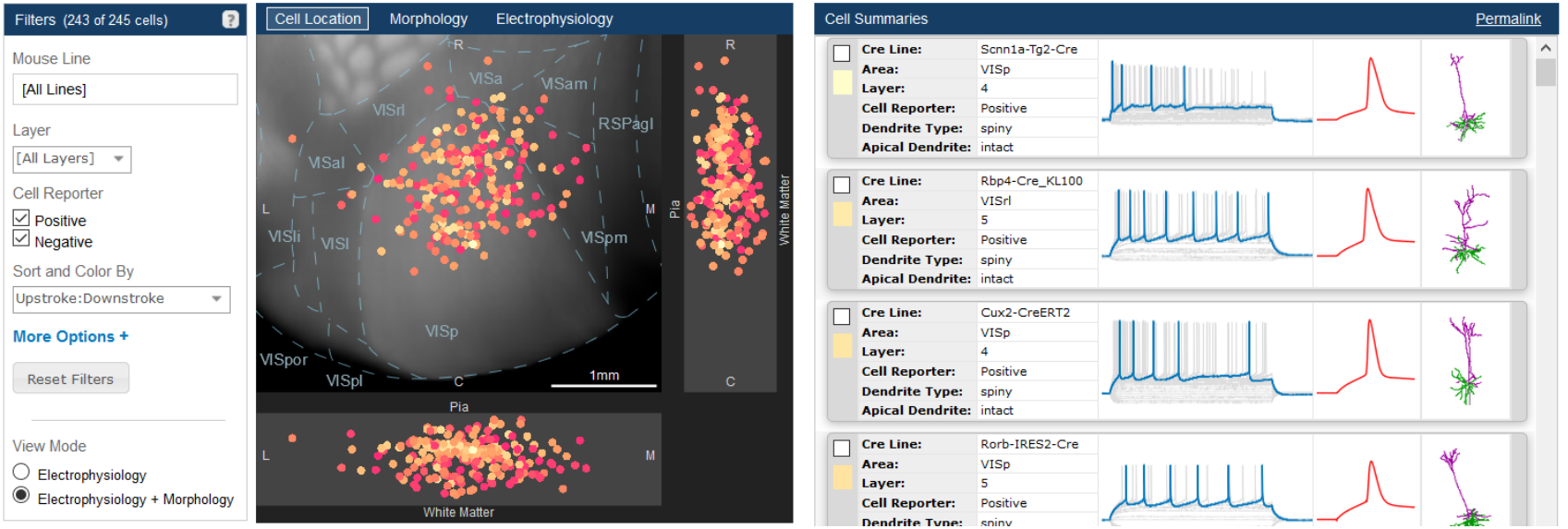


connectivity.brain-map.org



Allen Cell Types Database

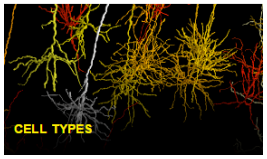
http://celltypes.brain-map.org



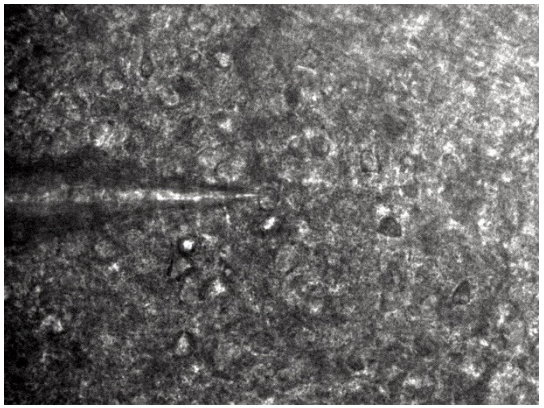
Search and Filter Options

Cell Positions in Common Coordinate Framework

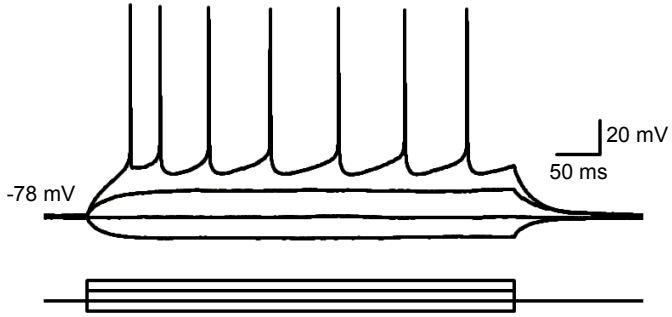
Summary of Cell Characteristics (*Click for additional details*)



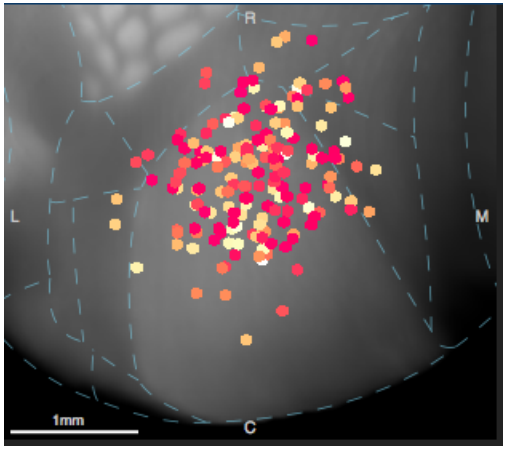
Data Processing Pipeline



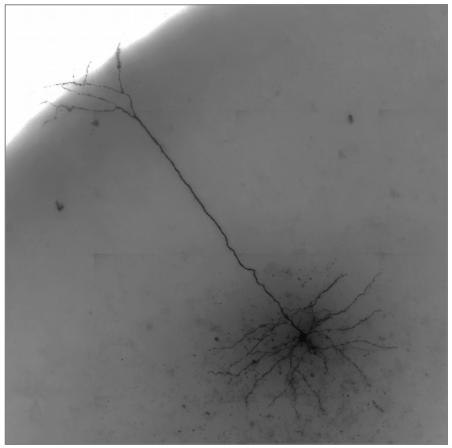
1. Record from Cre-labeled cell in slices



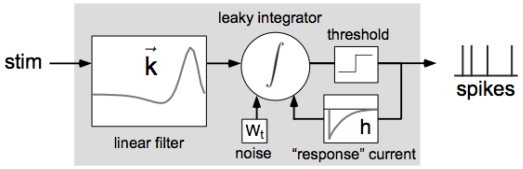
2. Collect standardized electrophysiology data and calculate relevant features

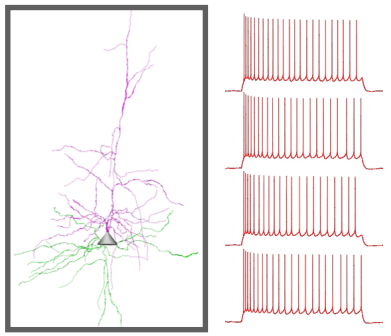


3. Place cell in CCF



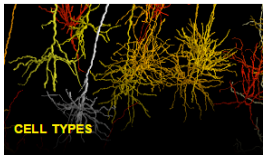
4. Fill, stain, and reconstruct morphology





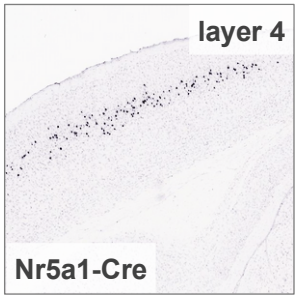
5. Build single-cell models

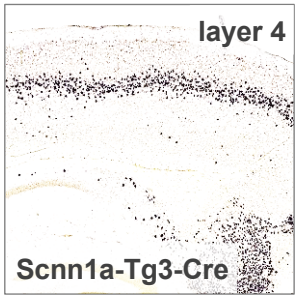
0.1 µm pixels

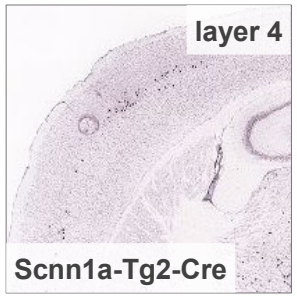


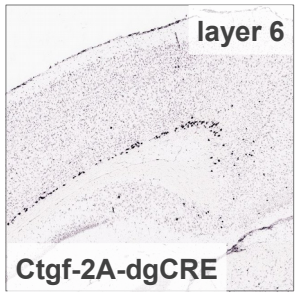
Genetic Markers via Cre Lines

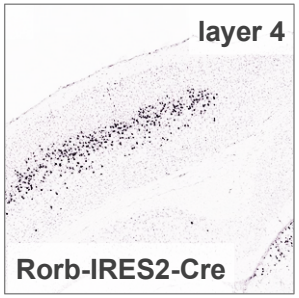
Excitatory neurons

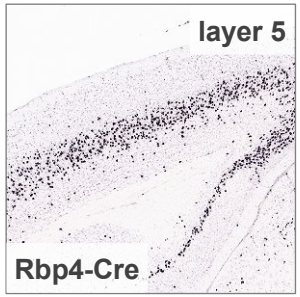


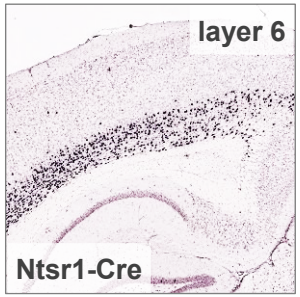


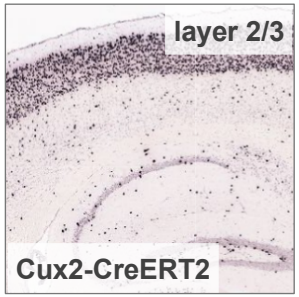




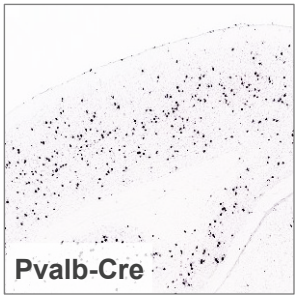


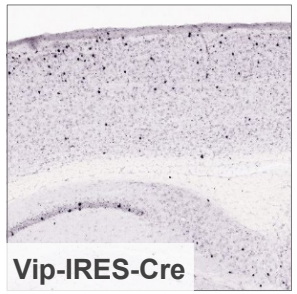


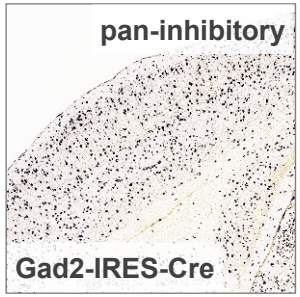




Inhibitory neurons



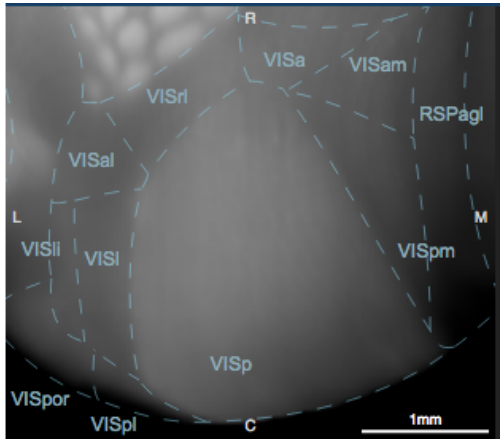




ALLEN Brain Observatory: Visual Coding

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

Cortical Visual Areas



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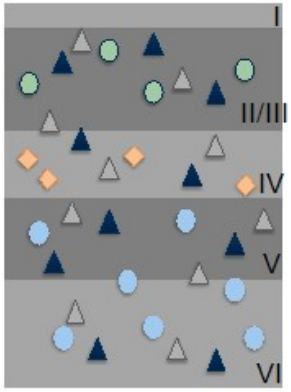
Cortical Layers
Cre Lines



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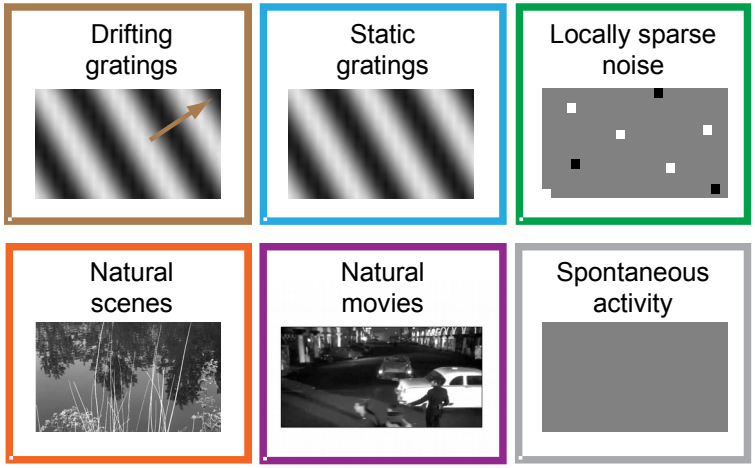
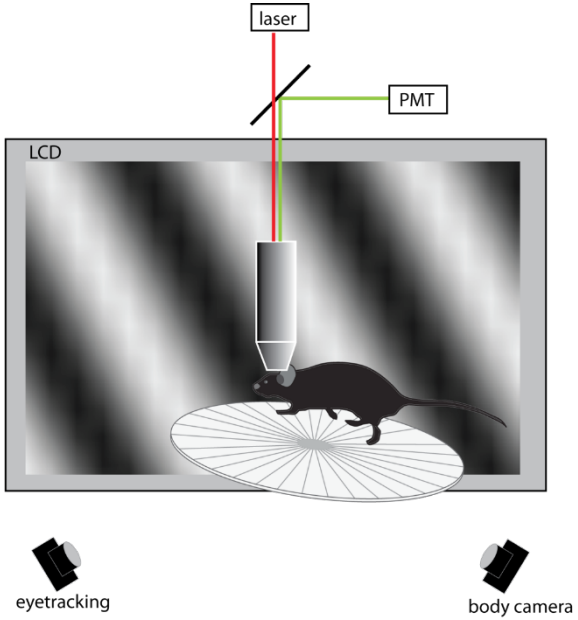
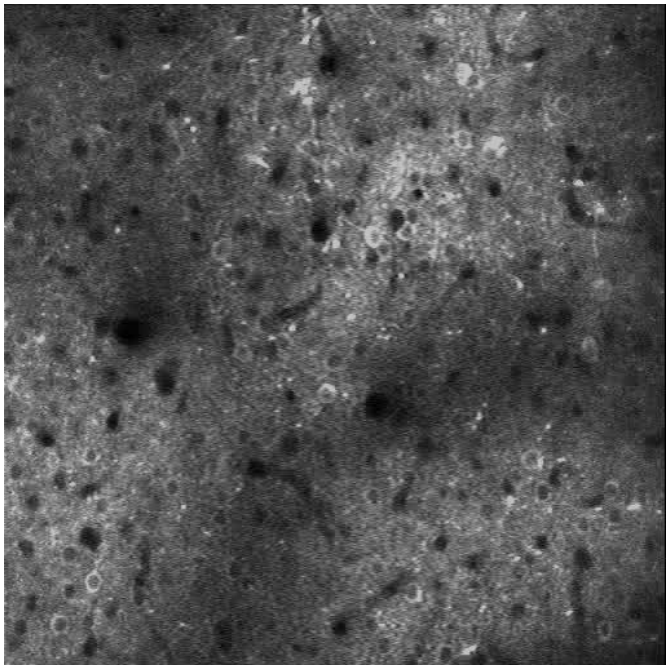
Visual Stimuli



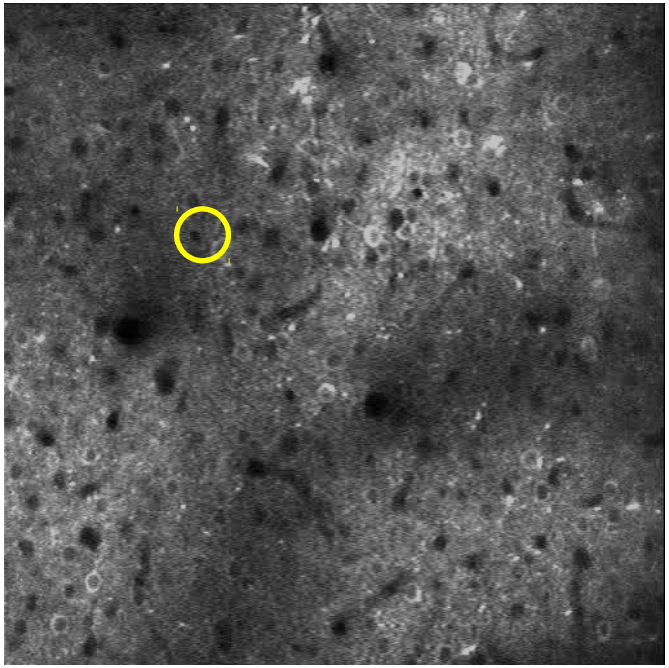
Two-photon imaging of visual responses in mouse cortex

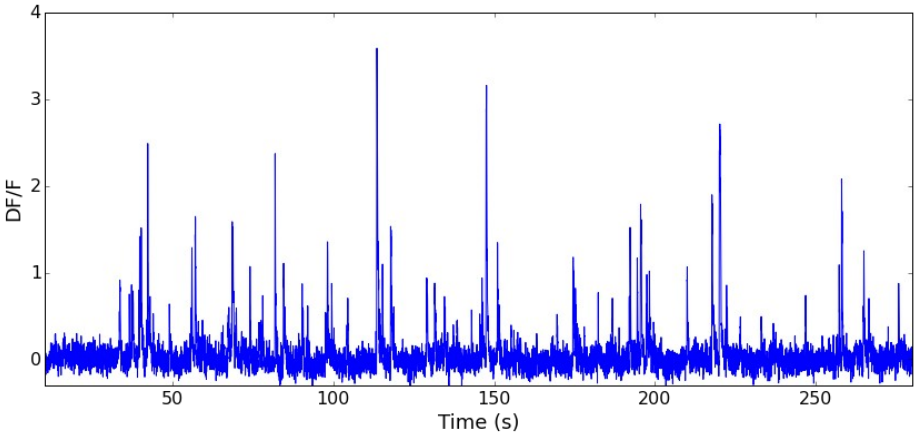


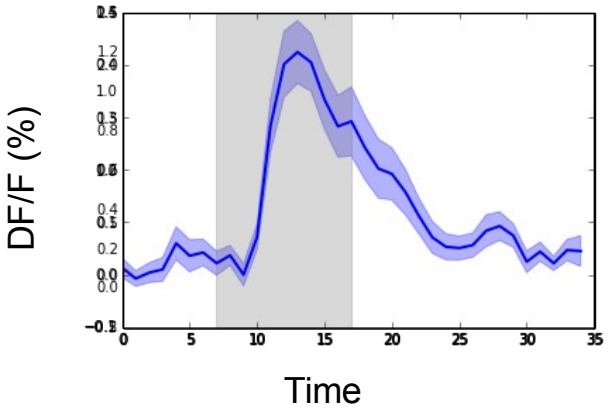


512 x 512 pixels
400 x 400 µm

Visual responses of individual cells

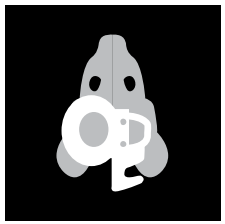


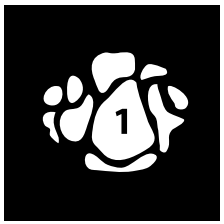


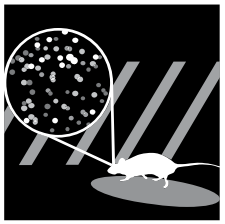


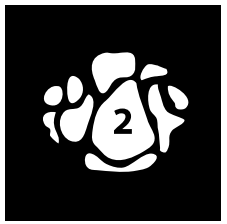
Data Production

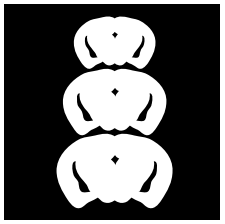
Surgery → Intrinsic Imaging 1 → Habituation → *In vivo* Two-photon Imaging → Intrinsic Imaging 2 → Serial Two-photon Imaging





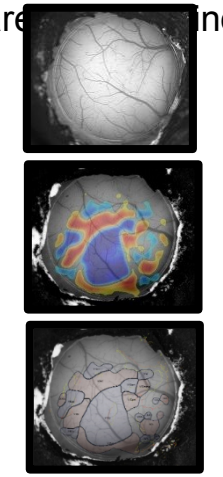






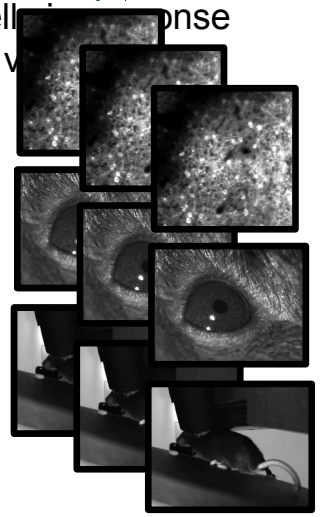
Create window

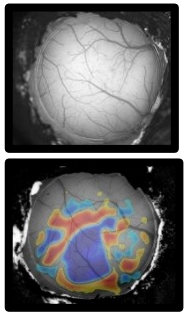
Map co al visual are notopy



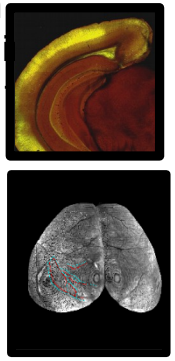
Acclimate mice to imaging experiment

Image ivity of cell nse to v

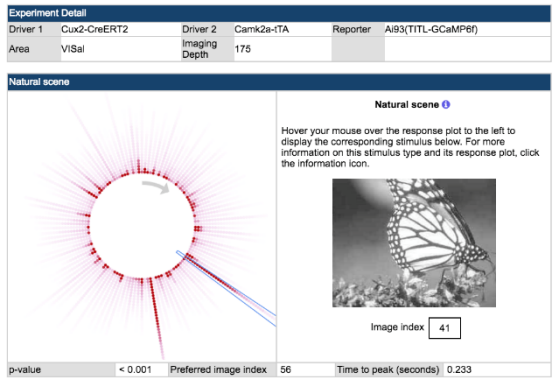


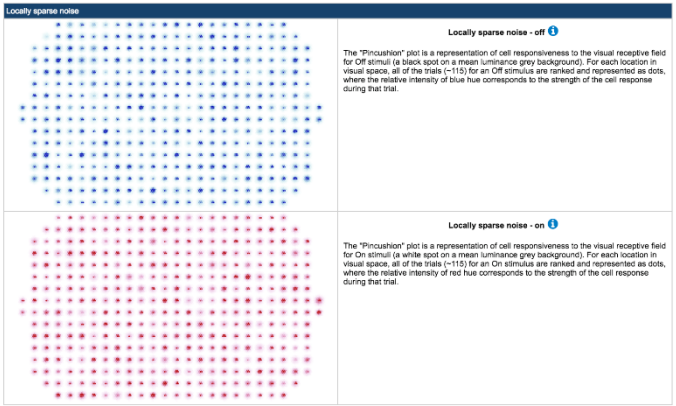


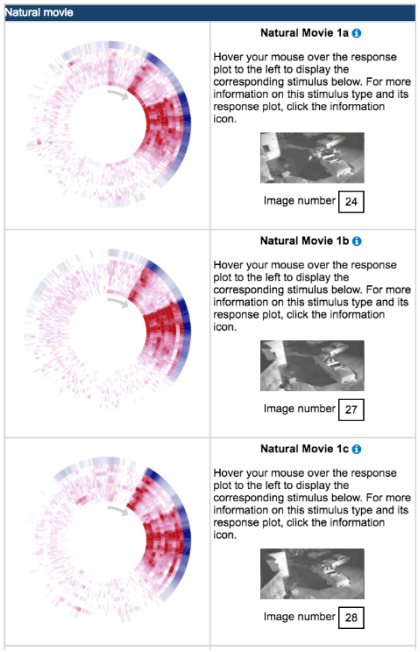
Reconstr t brain Map cells

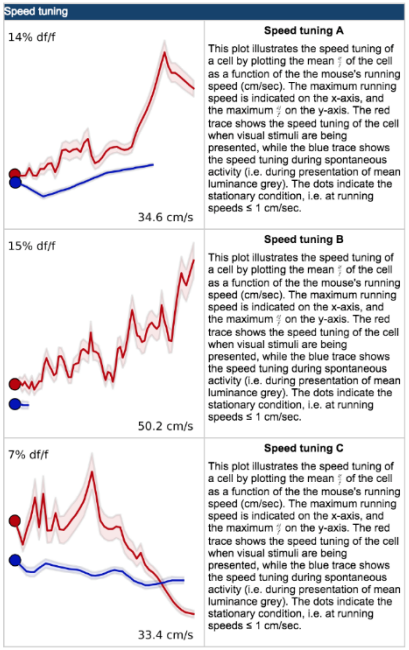


Dynamic Visualization of Cell Tuning



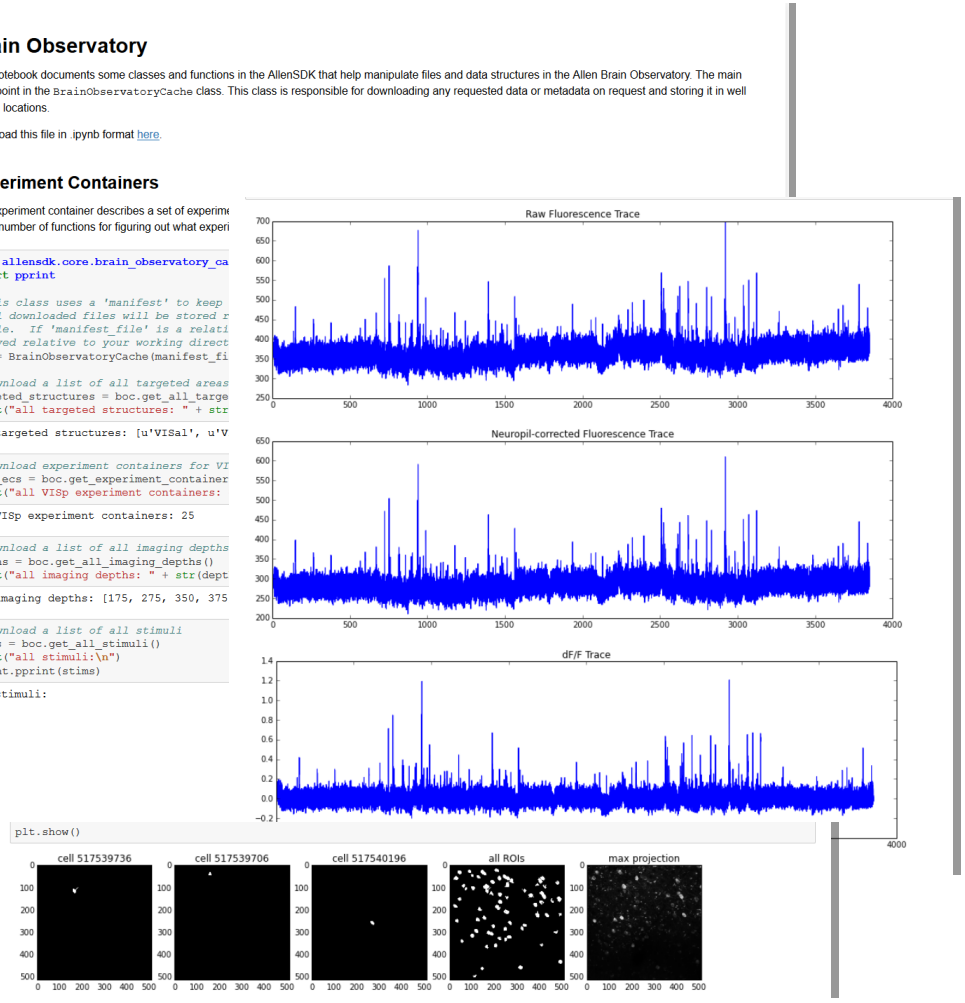






Data from each experiment session contained in a NWB file

- Max projection
- ROI masks
- Raw fluorescence for each ROI
- Surrounding neuropil trace and r value
- ∆F/F for each ROI
- Stimulus table
- Stimulus template
- Mouse's running speed
- Motion correction (x & y pixels)
- Meta data (cre line, visual area, imaging depth, experiment container, mouse ID, age, sex, etc)



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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BRAIN SCIENCE

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