Brain Observatories -
Exploring Cortex in an Open Access and High Throughput Manner

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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 m² 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 μm pixels and 50 μm 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

Experiment

Model

Note: morphologies not shown on same scale
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

1

0
Identifying Brain Regions Engaged During Behavior Via Intrinsic Signal Imaging
Widefield imaging of GCaMP6

Visual cortex

Midline
Workflow Overview

1. Surgery HP&C
2. Post-surgical photodocumentation
3. Intrinsic signal image acquisition
4. Initiate behavior training regimen
5. Intrinsic signal image acquisition
6. Optical physiology sessions, week 1 (optional)
7. Optical physiology sessions, week 2
8. Optical physiology sessions, week 3
9. Optical physiology sessions, week 4
10. Intrinsic signal image acquisition
11. Pre-terminal photodocumentation
12. TissueCyte

Over the course of 4 weeks:
16-24 imaging sessions per mouse, based on animal performance and session-by-session data acquisition results.

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

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
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