The next frontier in Open Neuroscience
Large-scale, standardized, brain observatories

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Illustration: B. Rossi
CONTENT

1. Rationale

2. Building a standardized observatory in Systems Neuroscience

3. Scientific outcomes

4. Future of the observatory and OpenScope
How is sensory information represented and processed in the cortex?
Allen Institute databases

- Anatomic locations
  - Connectivity
- Single cell electrophysiology, morphology, …
- Cell type classifications
- Genetic expression atlases
Working hypothesis for an observatory in Neuroscience

**Hypothesis 1:** A large number of *in vivo* experiments are required to understand how the brain works, causing data integration issues.

**Hypothesis 2:** A large number of experiments are duplicated across experimental labs and rarely integrated.

**Hypothesis 3:** An observatory model will synergize the 3 main communities: Experimental, technological and theoretical neuroscientists and incentivizes a market place of ideas.
Success of the observatory model in Astronomy

Keck telescopes in Hawaii

The Role of the W. M. Keck Observatory in U.S. Astronomy by Taft Armandroff
1. Rationale

2. **Building a standardized observatory in Systems Neuroscience**

3. Scientific outcomes

4. Future of the observatory and OpenScope
Reminder: Our goal

How is sensory information represented and processed in the cortex?
At scale!

How is sensory information represented and processed in the cortex?
A simplification to start

How is sensory information represented and processed in the cortex?
Data timeline

Transgenic mice → Surgery → Intrinsic Imaging 1 → Habituation → In vivo Two-photon imaging → Intrinsic Imaging 2 → Serial Two-photon imaging

Cux2
Rorb
Rbp4
Scnn1a
A pipeline in system neuroscience

- Surgery
- Intrinsic imaging
- In vivo Two photon imaging
- Serial two-photon tomography
An integrated coordinate and hardware system
Careful data curation, standardization at high throughput
CONTENT

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3 hours worth of visual stimuli broken in 3 sessions

- **Stim A**: Drifting gratings
- **Stim B**: Static gratings
- **Stim C**: Locally sparse noise

- **Natural scenes**
- **Natural movies**
- **Spontaneous activity**
### Current experimental count

<table>
<thead>
<tr>
<th>Cre line</th>
<th>Layers</th>
<th>E/I</th>
<th>V1</th>
<th>LM</th>
<th>AL</th>
<th>PM</th>
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<td>E</td>
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<td>E</td>
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4 data releases: June 2016, September 2016, June 2017, October 2018
## Brain-map.org: Functional database of cells

### Allen Brain Atlas

#### DATA PORTAL
- **HOME**
- **GET STARTED**
- **BRAIN OBSERVATORY**
- **TOOLS**

#### FILTERS
- **Show filters**
- **Clear filters**

#### Current Filters
- Brain area: VISp

#### Sorting Options
- **Sort by:** P value, static gratings, drilling gratings

#### Data Table

<table>
<thead>
<tr>
<th>Brain area</th>
<th>Cre driver</th>
<th>Imaging depth</th>
<th>P value</th>
<th>OS</th>
<th>PS</th>
<th>PTF</th>
<th>TTP</th>
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<th>Drifting gratings</th>
<th>Natural scenes</th>
<th>Locally sparse noise</th>
<th>Locally sparse noise</th>
<th>Natural movie 1 A</th>
<th>Natural movie 1 B</th>
<th>Natural movie 1 C</th>
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<td>Rorb-IRES2.</td>
<td>275</td>
<td>&lt;= 0.001</td>
<td>1.02</td>
<td>0.25</td>
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</table>

**Images:**
- ![Static gratings](image1)
- ![Drifting gratings](image2)
- ![Static gratings](image3)
- ![Drifting gratings](image4)
- ![Static gratings](image5)
- ![Drifting gratings](image6)
- ![Static gratings](image7)
- ![Drifting gratings](image8)
- ![Static gratings](image9)
- ![Drifting gratings](image10)
Responsiveness across stimuli

A large-scale, standardized physiological survey reveals higher order coding throughout the mouse visual cortex, 71 authors, bioRxiv, 2018
A large-scale, standardized physiological survey reveals higher order coding throughout the mouse visual cortex, 71 authors, bioRxiv, 2018
The Allen SDK

```python
import matplotlib.pyplot as plt
import numpy as np

cmap = 'hot'
interpolation='nearest'

def direction_selectivity()
    im = ax1.imshow(ds, clim=[0, max_count], cmap=cmap, interpolation=interpolation)
    ax1.set_xlabel('temporal frequency')
    ax1.set_ylabel('direction')
    ax1.set_xticks(np.arange(len(dg.tvals)) - 1)
    ax1.set_yticklabels(dg.tvals[1:])
    ax1.set_title('direction selective cells')

def orientation_selectivity()
    im = ax2.imshow(os, clim=[0, max_count], cmap=cmap, interpolation=interpolation)
    ax2.set_xlabel('temporal frequency')
    ax2.set_ylabel('orientation')
    ax2.set_xticks(np.arange(len(dg.tvals)) - 1)
    ax2.set_yticklabels(dg.tvals[1:])
    ax2.set_title('orientation selective cells')

def colorbars()
    fig.subplots_adjust(right=0.8)
    cbar_ax = fig.add_axes([0.55, 0.20, 0.07, 0.25])
    cbar = fig.colorbar(im, cax=cbar_ax)
    cbar.set_ticks(np.arange(0, max_count, 2) + 0.5)
    cbar.set_ticklabels(np.arange(0, max_count, 2, dtype=int))

plt.show()
```
External Publications using the Allen Brain Observatory

- Tracking the same neurons across multiple days in Ca²⁺ imaging data. Sheintuch et al. https://www.sciencedirect.com/science/article/pii/S2211124717314304
- Running reduces firing but improves coding in rodent higher-order visual cortex. Christensen & Pillow. https://www.biorxiv.org/content/early/2017/11/04/214007
- Organization of neural population code in mouse visual system. Esfahany et al. https://www.biorxiv.org/content/early/2017/12/04/220558
- Population coupling predicts the plasticity of stimulus in cortical circuits. Sweeney & Clopath. https://www.biorxiv.org/content/early/2018/02/14/265041
- High-accuracy Decoding of Complex Visual Scenes from Neuronal Calcium Responses. Ellis, et al. https://www.biorxiv.org/content/early/2018/03/26/271296
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Future 1: Detection of change

How is sensory information represented and processed in the cortex?
Future 1: Detection of change

Events Relative to Trial Start

Pre-change

Post-change

GO

GO

GO

GO

Events Relative to Stimulus Change

Time from trial start (s)

Time from stimulus change (s)

Groblewski

Ollerenshaw

Garrett

Olsen
Future 2: Multi-area imaging

Layer I
Layer II/III
Layer IV
Layer V
Future 3: Electrophysiology

A

B

C

D

E

mouse brain

<table>
<thead>
<tr>
<th>TARGET</th>
<th>AM</th>
<th>PM</th>
<th>V1</th>
<th>LM</th>
<th>AL</th>
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<td>4259</td>
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<td>2800</td>
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<td>816</td>
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<tr>
<td>TH/SC</td>
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<td>2907</td>
<td>532</td>
<td>3870</td>
<td>1822</td>
<td>13,850</td>
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</table>
Future 4: OpenScope

Illustration: B. Rossi
Each project: a 2 year process
PILOT:
Over 2 calls, we received 33 projects from a group of internal and external scientists

Selected projects in 2018:

1. **Searching for signatures of “credit assignment” in the mouse visual cortex** (T. Lillicrap, Y. Bengio, B. Richards, J. Zylberberg).
2. **Meaningfulness of naturalistic stimuli and differentiation of neurophysiological responses** (G. Tononi, W. Mayner, W. Marshall, Y. Billeh, A. Arkhipov).

Scientific review ongoing for projects in 2019
2018: Results are starting to come out
1. We have built a high-throughput system neuroscience pipeline for reproducible, standardized and efficient data generation.

2. A standardized map of functional responses is now freely available for researchers around the world to explore.

3. OpenScope: a market place of ideas leveraging this platform to accelerate scientific discoveries and hypothesis testing.
THANK YOU
We wish to thank the Allen Institute founder, Paul G. Allen, for his vision, encouragement and support.

We honor his legacy today, and every day into the long future of the Allen Institute, by carrying out our mission of tackling the hard problems in bioscience and making a significant difference in our respective fields.

alleninstitute.org
brain-map.org
THANK YOU

ALLEN INSTITUTE (>100 persons so far!)

Alexander Henry
Allison Kriedberg
Alyse Doperalski
Amy Bernard
Andrew Sodt
Anh Ho
Anthony Siuda
Anton Arkhipov
Ashley Brochwicz Donimirski
Brandon Rogers
Carol Thompson
Caroline Habel
Cassandra White
Chihchau Kuan
Chinh Dang
Chris Barber
Chris Mochizuki
Christine Cuhaciyan
Christof Koch
Christopher Mochizuki
Christopher Hill
Christopher Lau
Clay Reid
Clifford Slaughterbeck
Colin Farrell
David Feng
David Sullivan
David Waters
Derric Williams
Doug Ollerenshaw
Eric Lee
Felix Lee
Fiona Griffin
Florence Lai
Fuhi Long
Gabriel Ocker
Hongkui Zeng
Jaclyn Huffman
James Harrington
Jedediah Perkins
Jennifer Luviano
Jerome Lecoq
John Phillips
Jose Melchor Gonzalez
Joshua Larkin
Julie Pendergraft
Julie Nyhus
Justin Johal
Katie Roll
Keith Godfrey
Kristina Brouner
Laura Pearson
Lindsey Ballsmider
Lindsey Casal
Lydia Ng
Lydia Potekhina
Mahdi Ramadan
Marina Garrett
Marissa Garwood
Martin Schroedter
Melaine Sarreal
Melissa Reding
Michael Tieu
Michael Buice
Michael Chapin
Michael Hawrylycz
Michelle Stoecklin
Miranda Robertson
Nadia Dotson
Natalia Orlova
Natalie Wong
Nathalie Gaudreault
Nathan Sjoquist
Naveed Mastan
Nicholas Bowles
Nicholas Dee
Nicole Blesie
Nika Hejazinia
Perry Hargrave
Peter Groblewski
Rachael Larsen
Roald Dietzman
Rodolfo Tiburcio
Samantha Whiteside
Sam Seid
Saskia de Vries
Shawn Olsen
Shiella Caldejon
Shu Shi
Stefan Mihalas
Stephanie Cross
Suvro Datta
Thomas Keenan
Thuyanh Nguyen
Timothy Dolbeare
Timothy Fliss
Veronica Maldonado
Vonn Racel De Guzman Wright
Wayne Wakeman
Yang Li
Zebulon Haradon