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

Illustration: B. Rossi

Jerome Lecoq

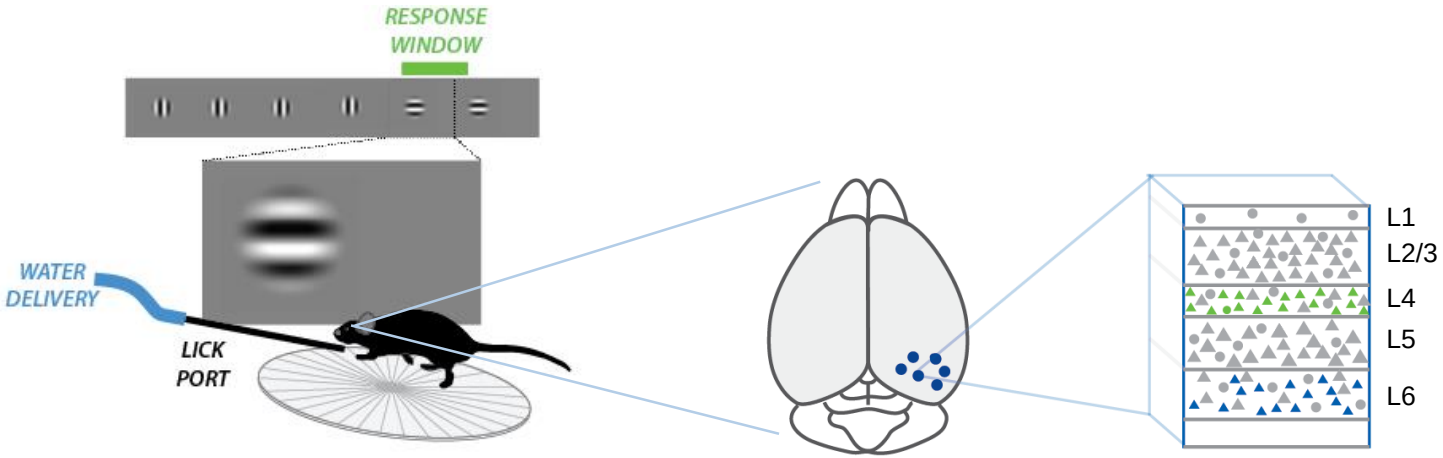
Senior Manager, Optical Physiology

Allen Institute for Brain Science

CONTENT

1. **Rationale**
2. Building a standardized observatory in Systems Neuroscience
3. Scientific outcomes
4. Future of the observatory and OpenScope

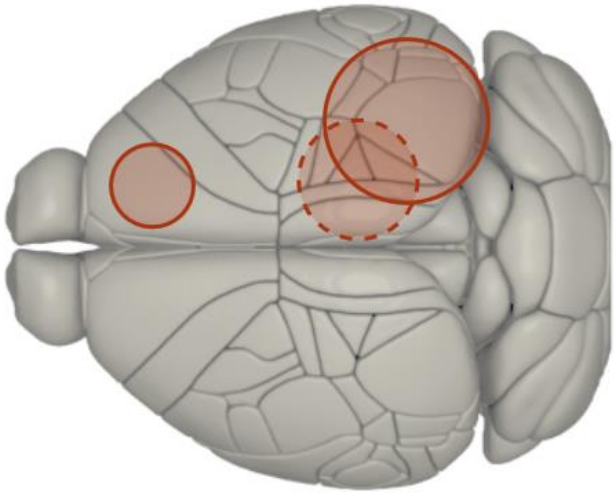
Our goal

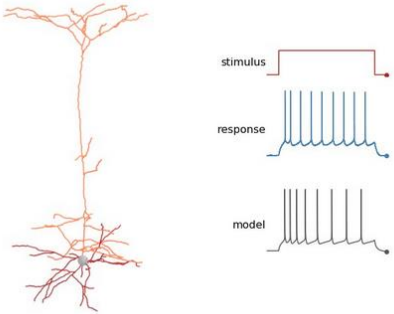


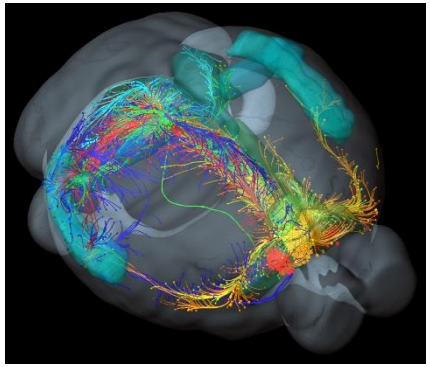
How is sensory information represented and processed in the cortex?

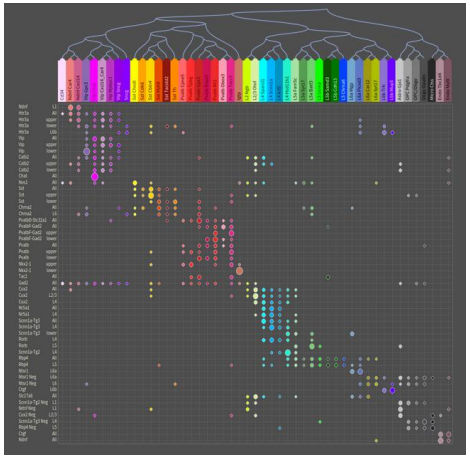
Allen Institute databases

- Anatomic locations
  - Connectivity
- Single cell electrophysiology, morphology, …
  - Cell type classifications
- Genetic expression atlases









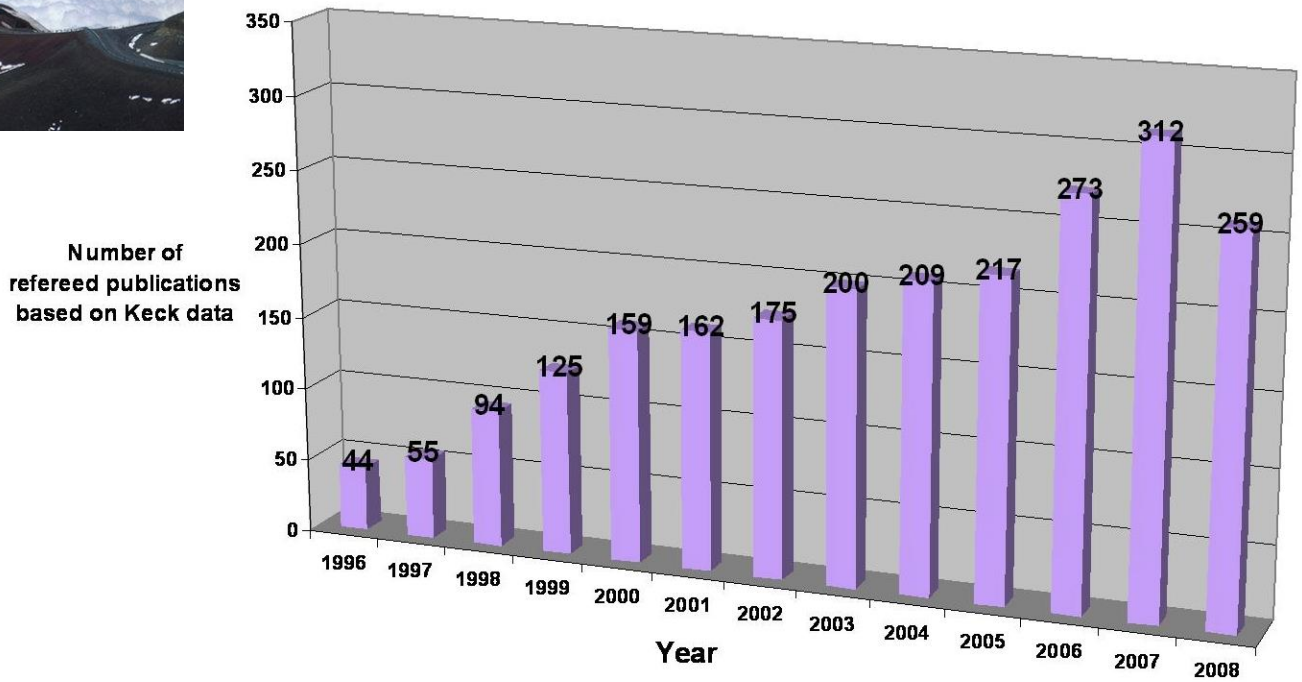
Working hypothesis for an observatory in Neuroscience

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



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

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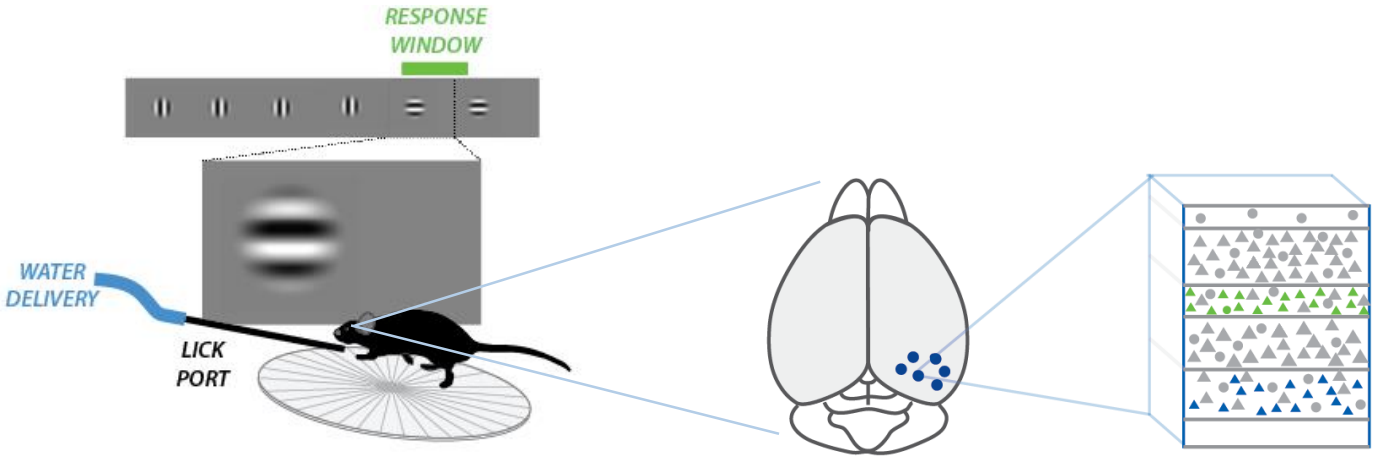
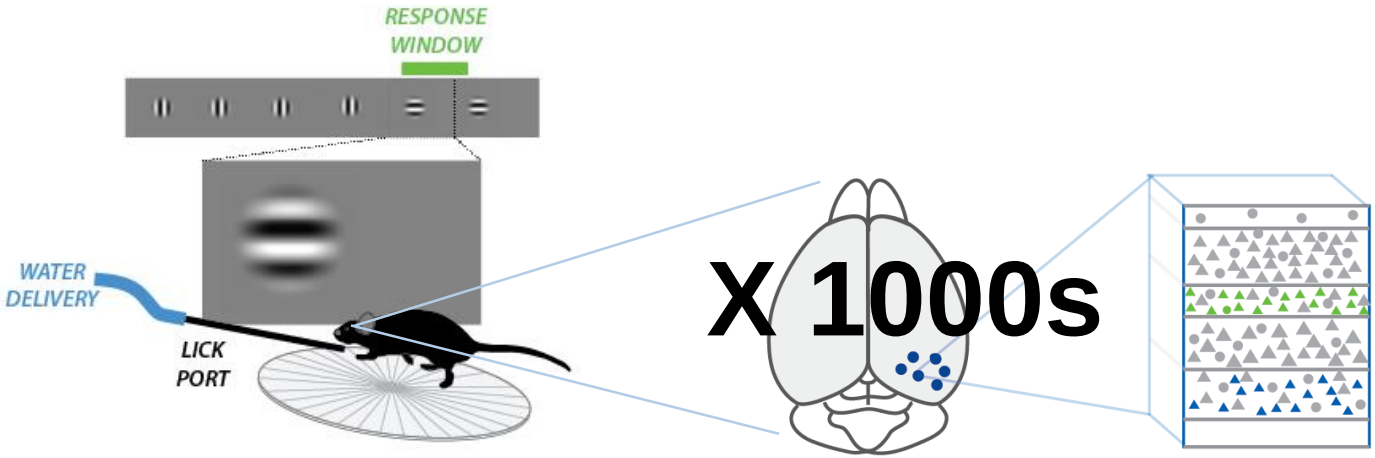
2. **Building a standardized observatory in Systems Neuroscience**
3. Scientific outcomes
4. Future of the observatory and OpenScope

Reminder : Our goal



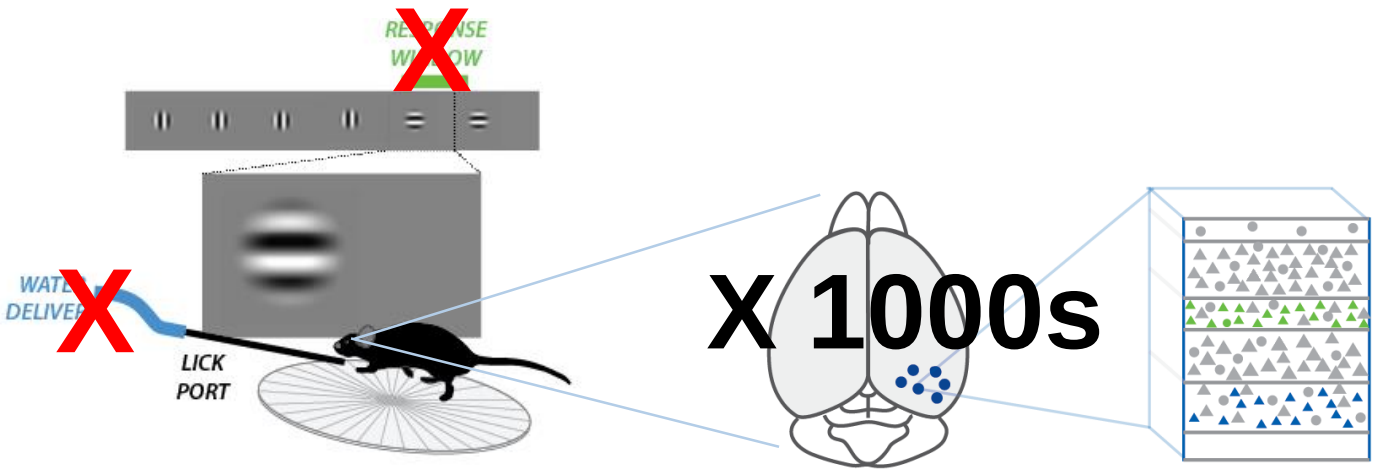
How is sensory information represented and processed in the cortex?

At scale!



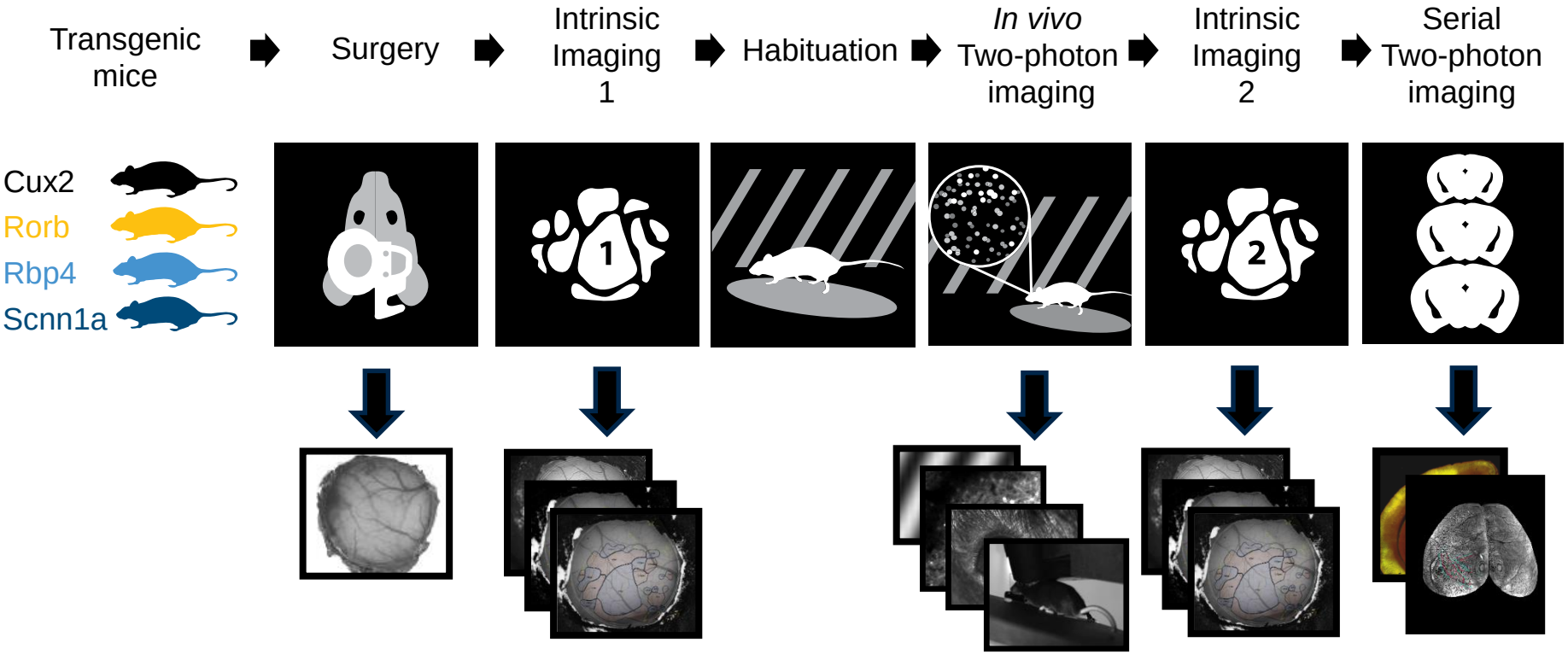
How is sensory information represented and processed in the cortex?

A simplification to start



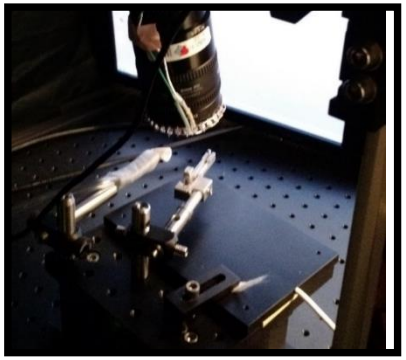
How is sensory information represented and processed in the cortex?

Data timeline



A pipeline in system neuroscience

Surgery

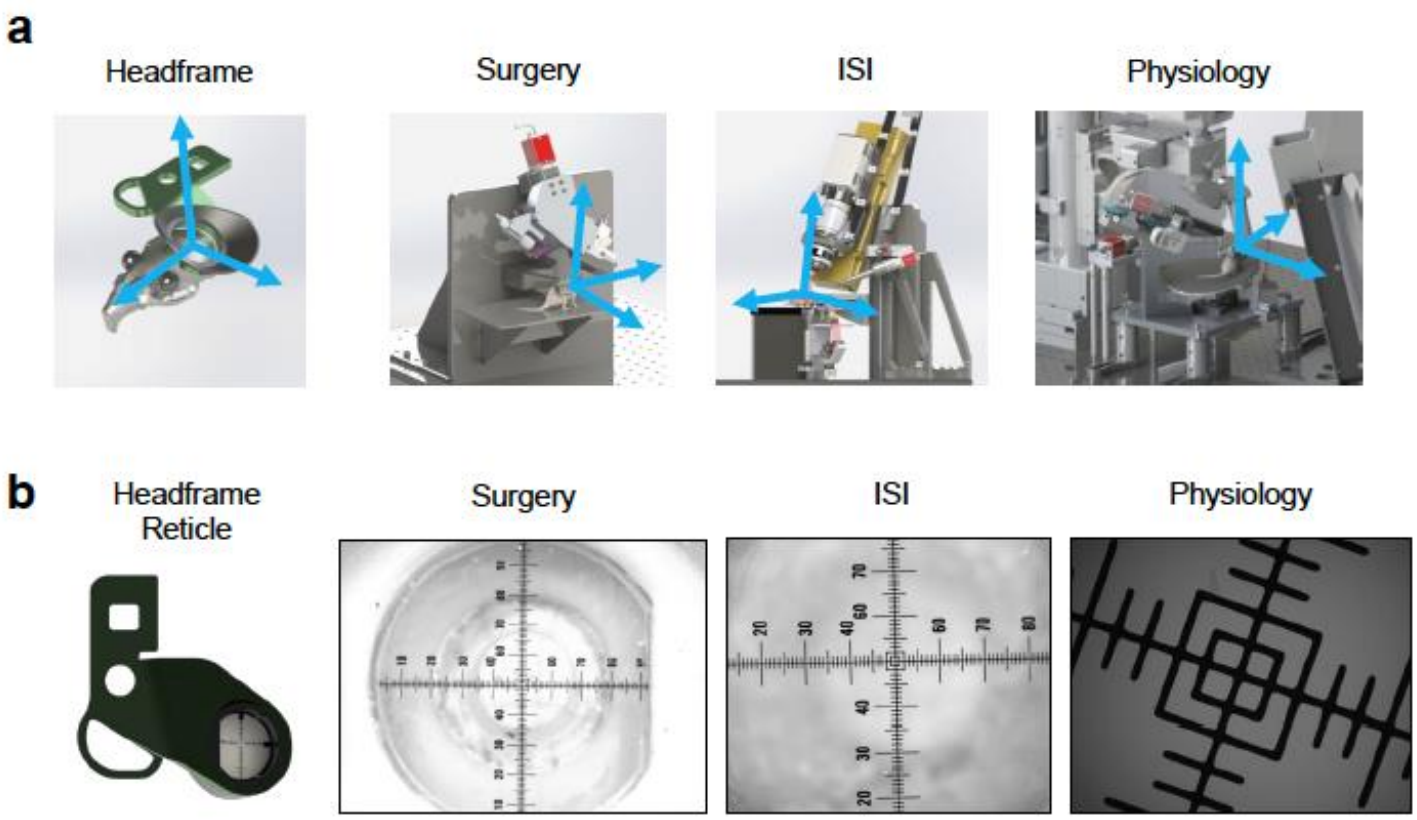


Intrinsic imaging

In vivo Two photon imaging

Serial two-photon tomography

An integrated coordinate and hardware system

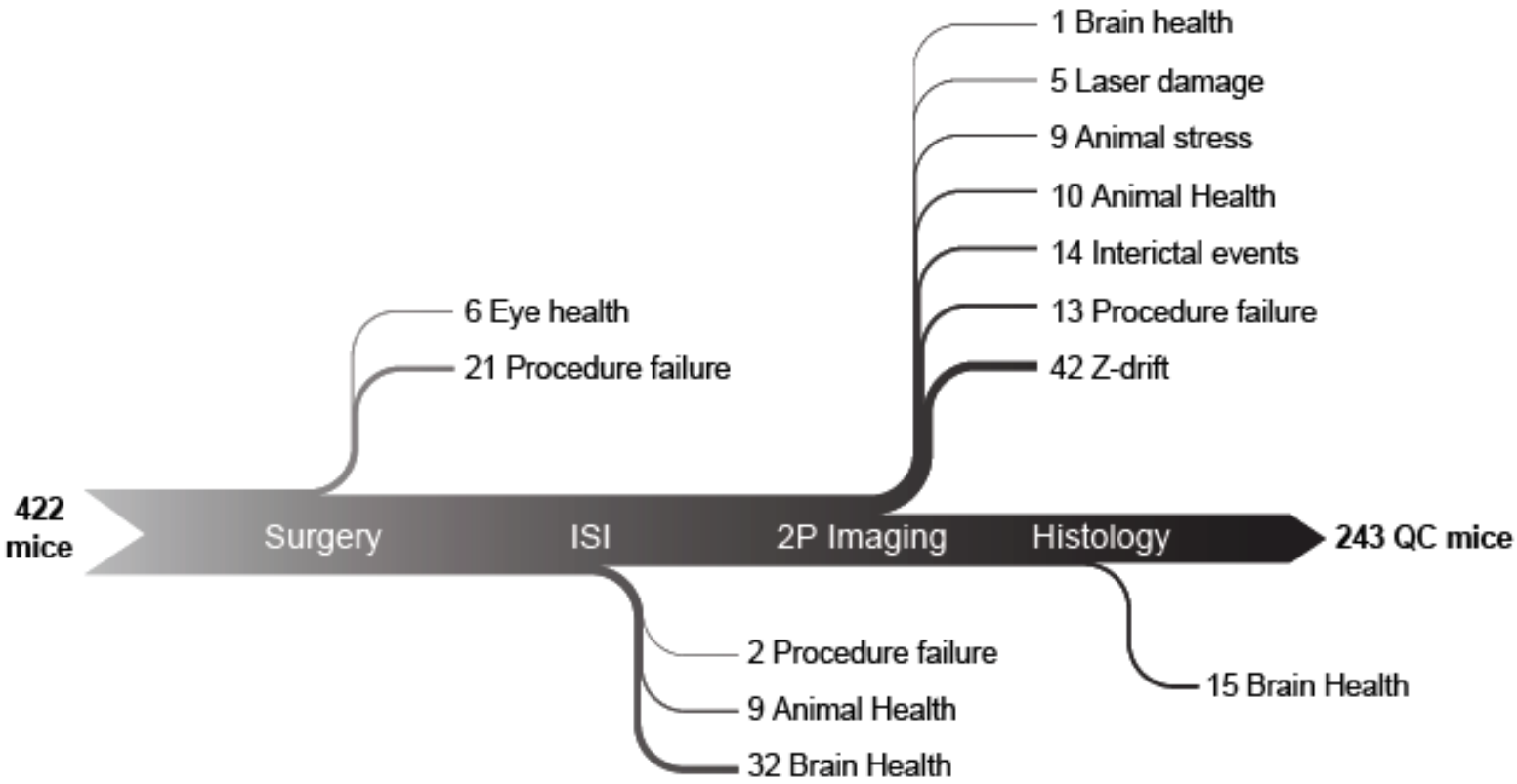


Slaughterbeck

Sullivan

Farrell

Careful data curation, standardization at high throughput



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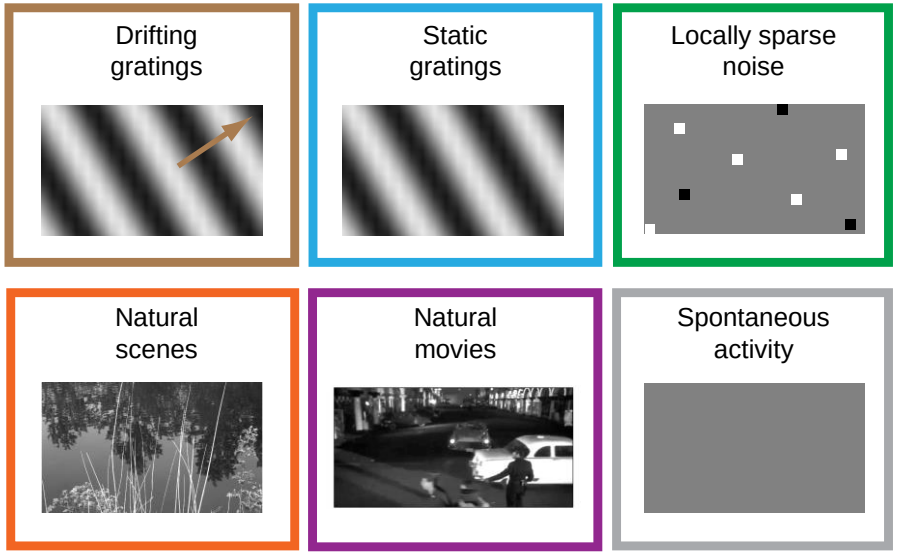
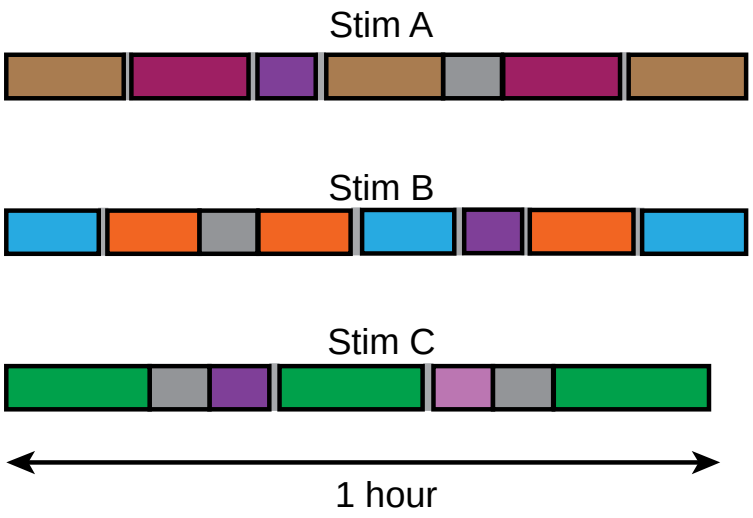
3 hours worth of visual stimuli broken in 3 sessions





De Vries

Buice

Current experimental count

Cre line	Layers	E/I	V1	LM	AL	PM	AM	RL
Emx1-IRES-Cre; Camk2a-tTA; Ai93	2/3,4,5	E	3073 (10)	2098 (8)	1787 (7)	835 (4)	457 (3)	2152 (9)
Slc17a7-IRES2-Cre; Camk2a-tTA; Ai93	2/3,4,5	E	4840 (17)	3230 (16)	374 (2)	1970 (15)	235 (2)	137 (2)
Cux2-CreERT2; Camk2-tTA; Ai93	2/3, 4	E	5081 (16)	2792 (11)	3103 (13)	2361 (13)	1616 (11)	1578 (12)
Rorb-IRES2-Cre; Camk2a-tTA; Ai93	4	E	2218 (8)	1191 (6)	1242 (6)	764 (7)	735 (8)	1126 (5)
Scnn1a-Tg3-Cre; Camk2a-tTA; Ai93	4	E	1873 (9)					
Nr5a1-Cre; Camk2a-tTA; Ai93	4	E	578 (8)	421 (6)	220 (6)	331 (7)	171 (6)	1354 (6)
Rbp4-Cre_KL100; Camk2a-tTA; Ai93	5	E	458 (7)	485 (7)	441 (6)	509 (6)	355 (8)	93 (4)
Fezf2-CreER;Ai148 (cortico-thalamic)	5	E	407 (4)	981 (5)				
Tlx3-Cre_PL56;Ai148 (cortico-cortical)	5	E	1181 (6)	946 (3)				
Ntsr1-Cre_GN220;Ai148	6	E	573 (6)	719 (7)		581 (5)		
Sst-IRES-Cre;Ai148	4, 5	I	266 (17)	301 (15)	24 (1)	247 (14)		46 (2)
Vip-IRES-Cre;Ai148	2/3, 4	I	352 (17)	315 (17)		387 (16)		

4 data releases : June 2016, September 2016, June 2017, October 2018

Brain-map.org : Functional database of cells

ALLEN BRAIN ATLAS
DATA PORTAL

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Show filters | Clear filters

Current Filters: Brain area in VISp

Sort: P value - static gratings

Add/Remove Columns: Showing 16 of 19

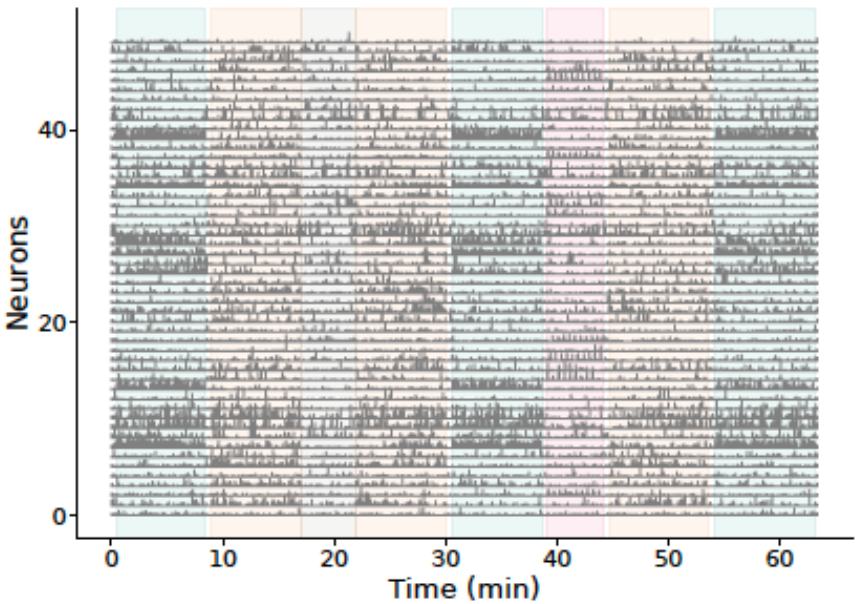
Showing rows 1 through 6 of 16031

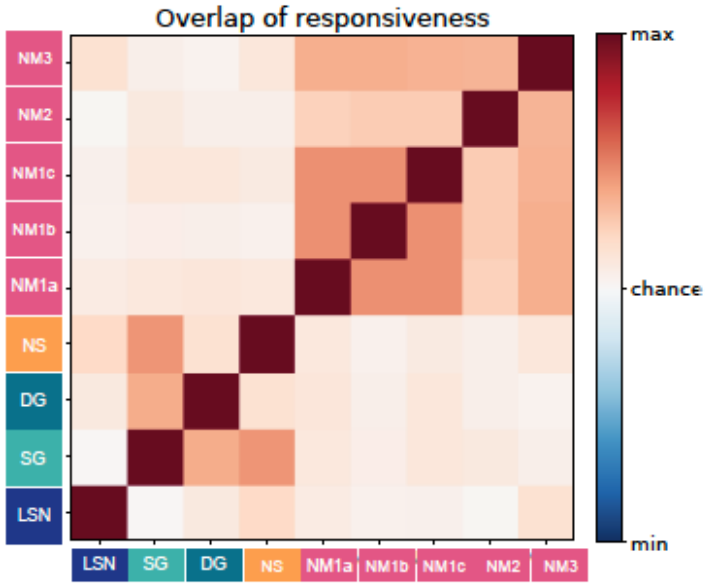
Brain area	Cre driver	Imaging depth	Static gratings	Drifting gratings	Natural scenes	Locally sparse noise -	Locally sparse noise -	Natural movie 1 A	Natural movie 1 B	Natural movie 1 C	Natural movie 3
VISp	Rorb-IRES2...	275	p: <= 0.001 osi: 1.02 po: 90 pp: 0.25 psf: 0.02 ttp: 0.20	NA	p: <= 0.001 pii 43 ttp 0.17			NA			NA
VISp	Cux2-CreER...	275	p: <= 0.001 osi: 1.12 po: 60 pp: 0.25 psf: 0.04 ttp: 0.20	p: <= 0.001 osi: 0.88 pd: 270 dsi: 0.79 ptf 2	p: <= 0.001 pii 12 ttp 0.20						
VISp	Emx1-IRES-...	175	p: <= 0.001 osi: 0.23 po: 150 pp: 0.75 psf: 0.32 ttp: 0.20	NA	p: <= 0.001 pii 17 ttp 0.20	NA	NA	NA		NA	NA
VISp	Emx1-IRES-...	175	p: <= 0.001 osi: 1.06 po: 90 pp: 0.75 psf: 0.04 ttp: 0.20	p: <= 0.001 osi: 1.08 pd: 90 dsi: 0.38 ptf 1	p: <= 0.001 pii 81 ttp 0.20						
VISp	Rorb-IRES2...	275	p: <= 0.001 osi: 1.00 po: 150 pp: 0.50 psf: 0.02 ttp: 0.30	p: <= 0.001 osi: 1.11 pd: 225 dsi: 0.71 ptf 15	p: <= 0.001 pii 76 ttp 0.30	NA	NA			NA	

Ng

Feng

Responsiveness across stimuli

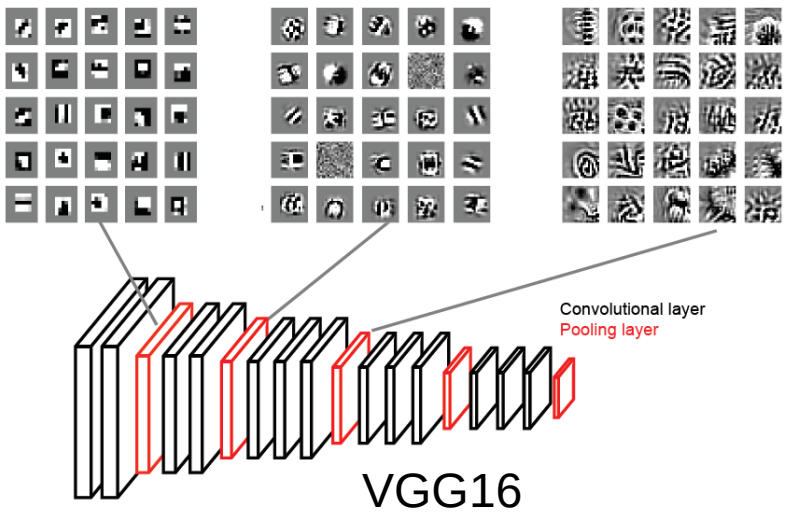


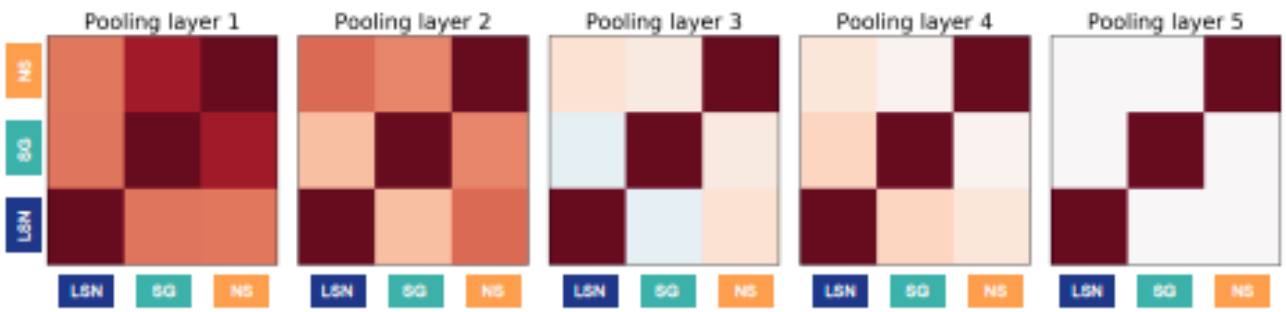


A large-scale, standardized physiological survey reveals higher order coding throughout the mouse visual cortex, *71 authors*, bioRxiv, 2018

De Vries

Comparison to feed-forward network





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

Buice

The Allen SDK

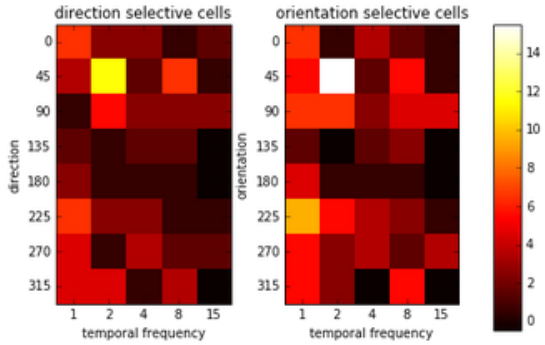
jupyter brain_observatory (unsaved changes)

File Edit View Insert Cell Kernel Help Python [Root]

In [16]:

```
import matplotlib.pyplot as plt
import numpy as np
%matplotlib inline
fig, (ax1, ax2) = plt.subplots(1,2)

# plot direction selectivity
im = ax1.imshow(ds, clim=[0,max_count], cmap='hot', interpolation='nearest')
ax1.set_xlabel('temporal frequency')
ax1.set_ylabel('direction')
ax1.set_xticks(np.arange(len(dg.tfvals)-1))
ax1.set_xticklabels(dg.tfvals[1:])
ax1.set_yticks(np.arange(len(dg.orivals)))
ax1.set_yticklabels(dg.orivals)
ax1.set_title('direction selective cells')

# plot orientation selectivity
im = ax2.imshow(os, clim=[0,max_count], cmap='hot', interpolation='nearest')
ax2.set_xlabel('temporal frequency')
ax2.set_ylabel('orientation')
ax2.set_xticks(np.arange(len(dg.tfvals)-1))
ax2.set_xticklabels(dg.tfvals[1:])
ax2.set_yticks(np.arange(len(dg.orivals)))
ax2.set_yticklabels(dg.orivals)
ax2.set_title('orientation selective cells')

# plot a colorbar
fig.subplots_adjust(right=0.9)
cbar_ax = fig.add_axes([0.95, 0.05, 0.05, 0.85])
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()
```

In [1]:



Feng

External Publications using the Allen Brain Observatory

- Network reconstruction from high dimensional ordinary differential equations. Chen *et al.* https://arxiv.org/abs/1610.03177
- Tracking the same neurons across multiple days in Ca^{2+} imaging data. Sheintuch *et al.* https://www.sciencedirect.com/science/article/pii/S2211124717314304
- SCALPEL: Extracting neurons from calcium imaging data. Petersen *et al.* https://arxiv.org/abs/1703.06946
- Exact spike train inference via L0 optimization. Jewell & Witten. https://arxiv.org/abs/1703.08644
- Untuned but not irrelevant: the role of untuned neurons in sensory information coding. Zylberberg. https://www.biorxiv.org/content/early/2017/09/21/134379
- Running reduces firing but improves coding in rodent higher-order visual cortex. Christensen & Pillow. https://www.biorxiv.org/content/early/2017/11/04/214007
- Identification and targeting of cortical ensembles. Carrillo-Reid *et al.* https://www.biorxiv.org/content/early/2017/11/29/226514
- 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
- Neuronal activities in the mouse visual cortex predict patterns of sensory stimuli. Cai *et al.* https://link.springer.com/article/10.1007%2Fs12021-018-9357-1
- High-accuracy Decoding of Complex Visual Scenes from Neuronal Calcium Responses. Ellis, et *al*. https://www.biorxiv.org/content/early/2018/03/26/271296
- Weighted Network Density Predicts Range of Latent Variable Model Accuracy. Palmerston, et *al*. https://www.biorxiv.org/content/early/2018/06/11/343285

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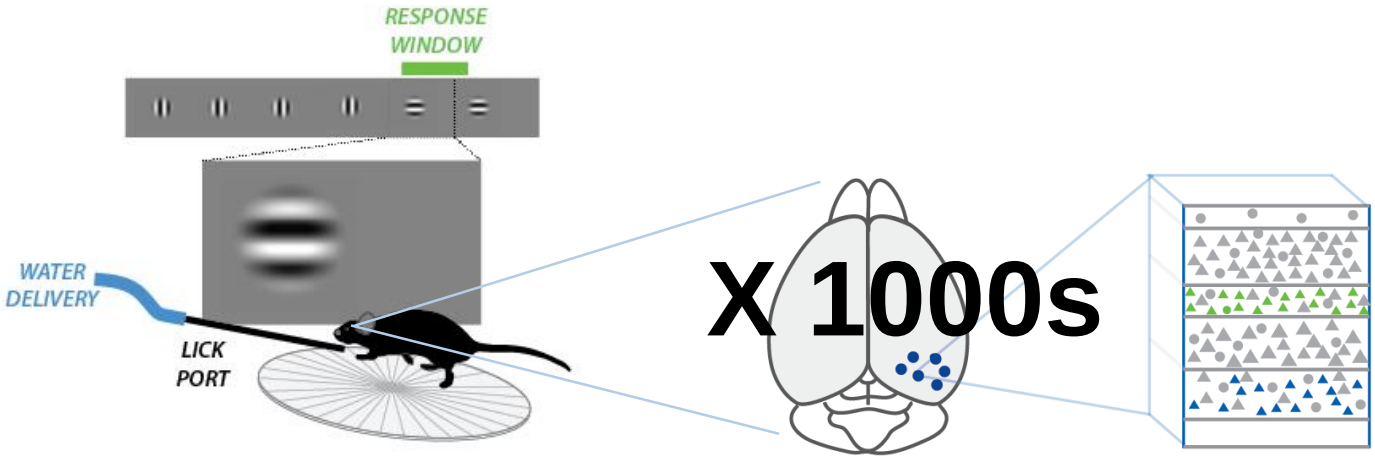
Future 1 : Detection of change



How is sensory information represented and processed in the cortex?

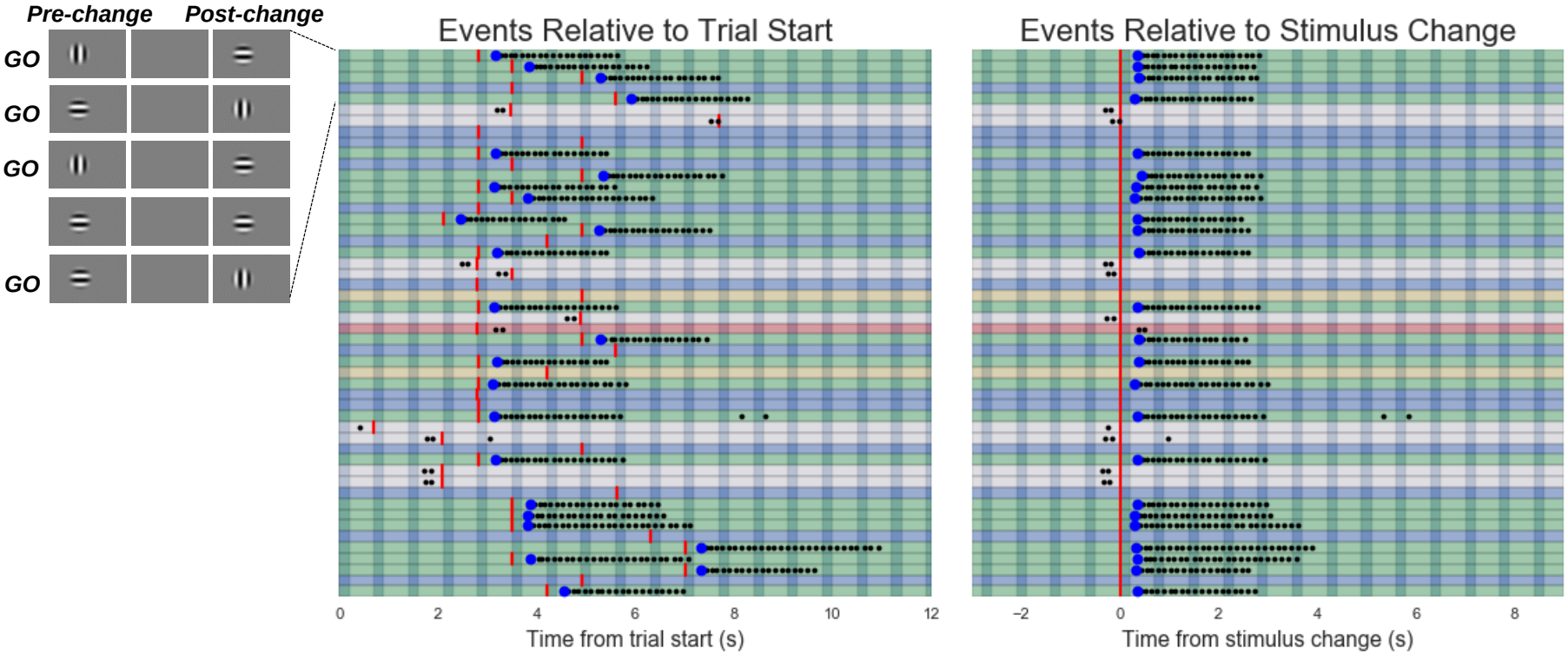
Groblewski

Ollerenshaw

Garrett

Olsen

Future 1 : Detection of change



Groblewski

Ollerenshaw

Garrett

Olsen

Future 2: Multi-area imaging

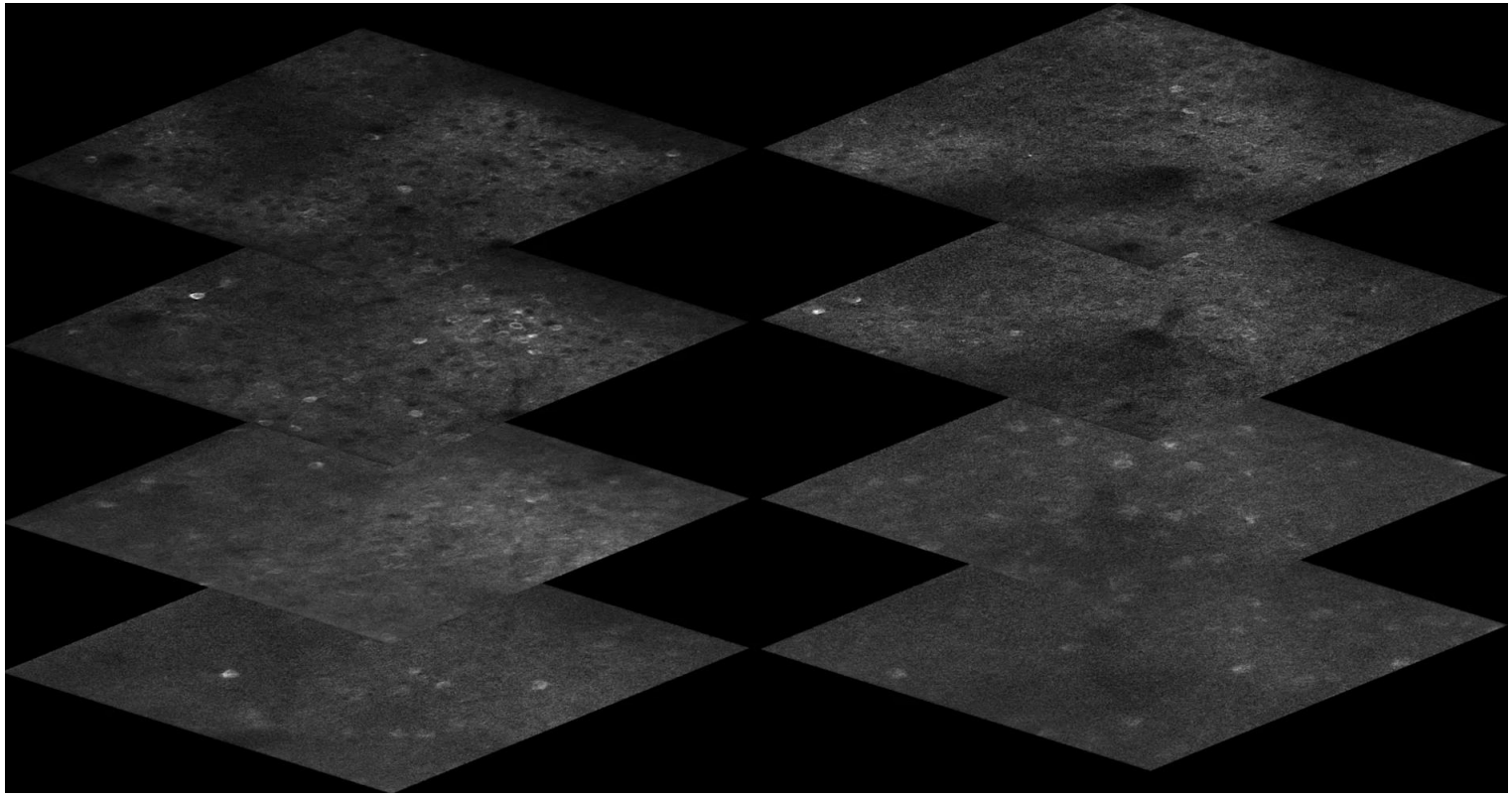
V1 LM

Layer I

Layer II/III

Layer IV

Layer V

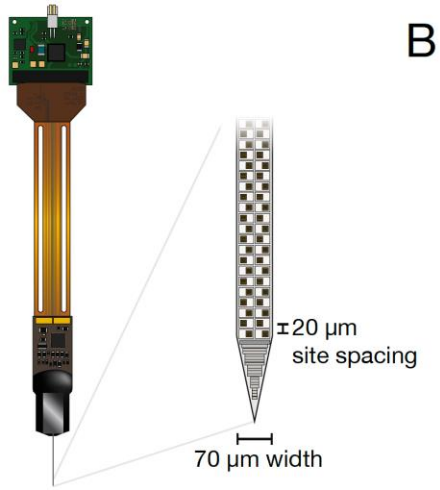


Tsyboulski

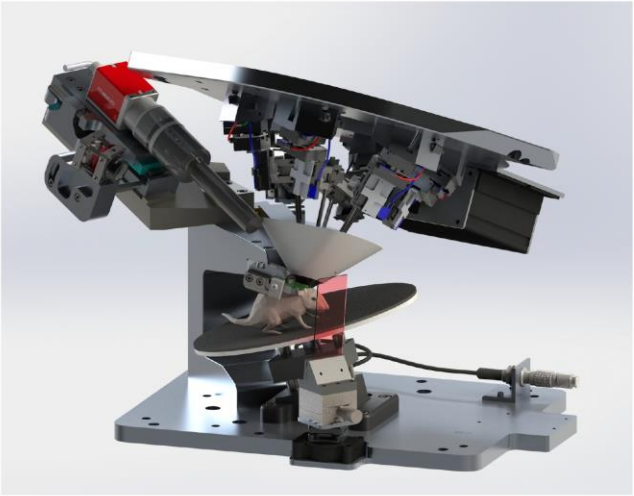
Orlova

Future 3: Electrophysiology

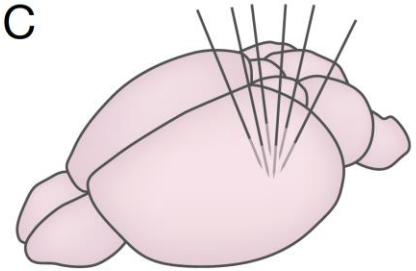
A



B

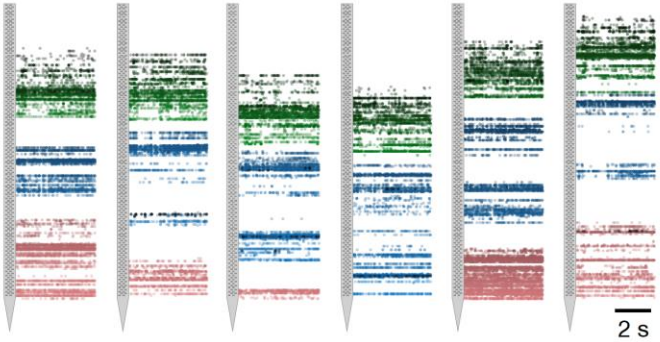


C



mouse brain

D



E

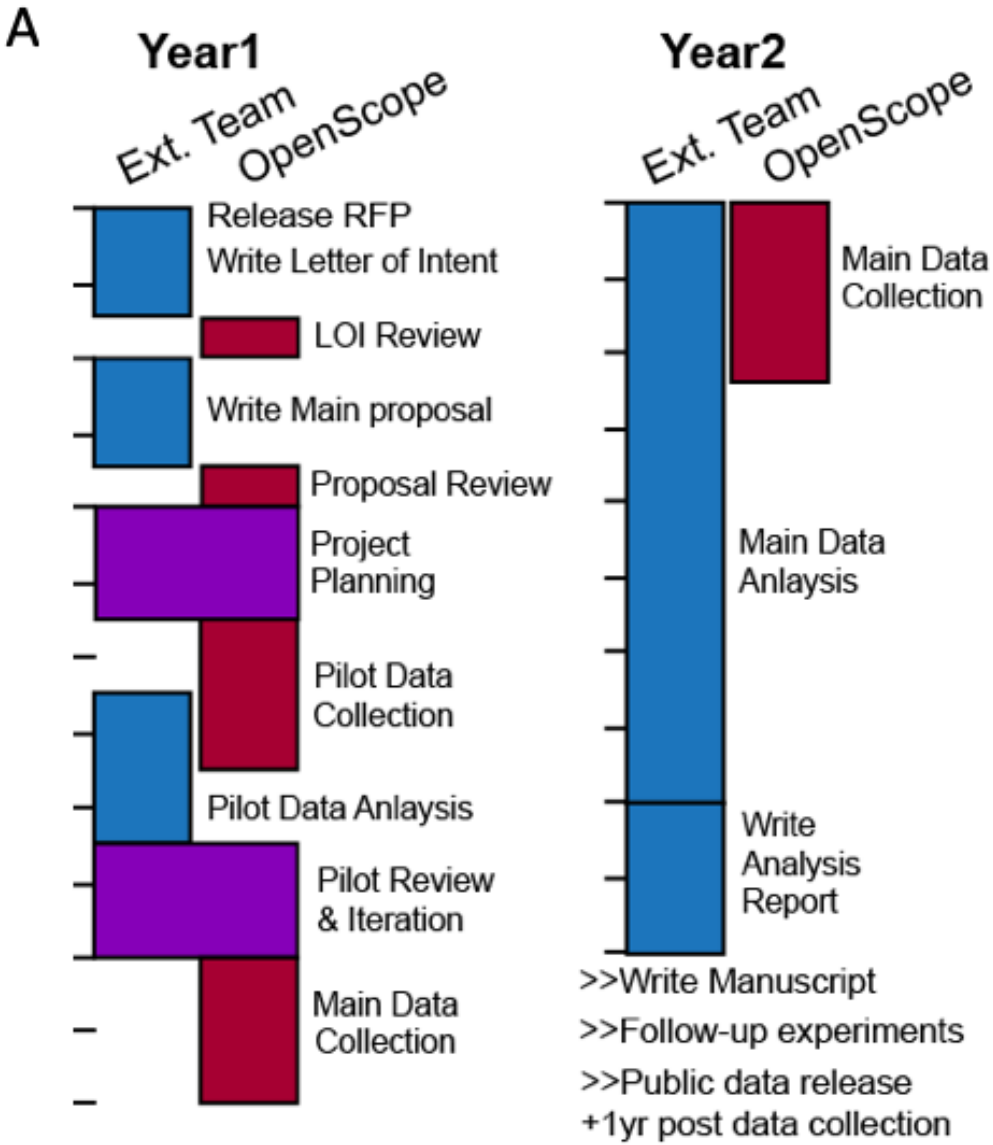
TARGET	AM	PM	V1	LM	AL	RL	TOTAL
CTX	4153	3813	5283	3678	4259	3625	24,811
CA1/CA3	2537	1896	2800	1796	1677	1736	12,442
DG	279	430	907	1465	1412	816	5309
TH/SC	2133	2586	2907	532	3870	1822	13,850

Siegle

Future 4: OpenScope

Illustration: B. Rossi

Each project : a 2 year process



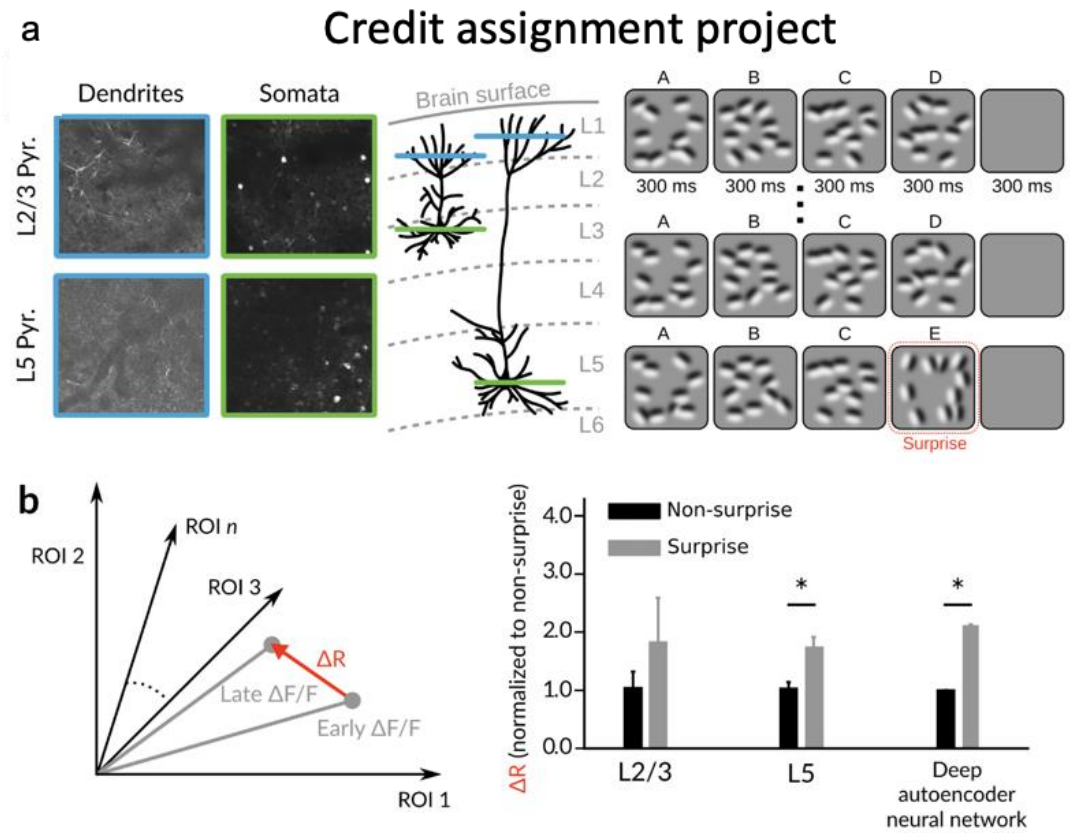
PILOT :
Over 2 calls, we received 33 projects from a group of internal and external scientists

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).
3. **Testing models of predictive coding in mouse visual cortex** (N. Cain, M. Garrett, H. Choi, R. Larsen).

Scientific review ongoing for projects in 2019

2018: Results are starting to come out

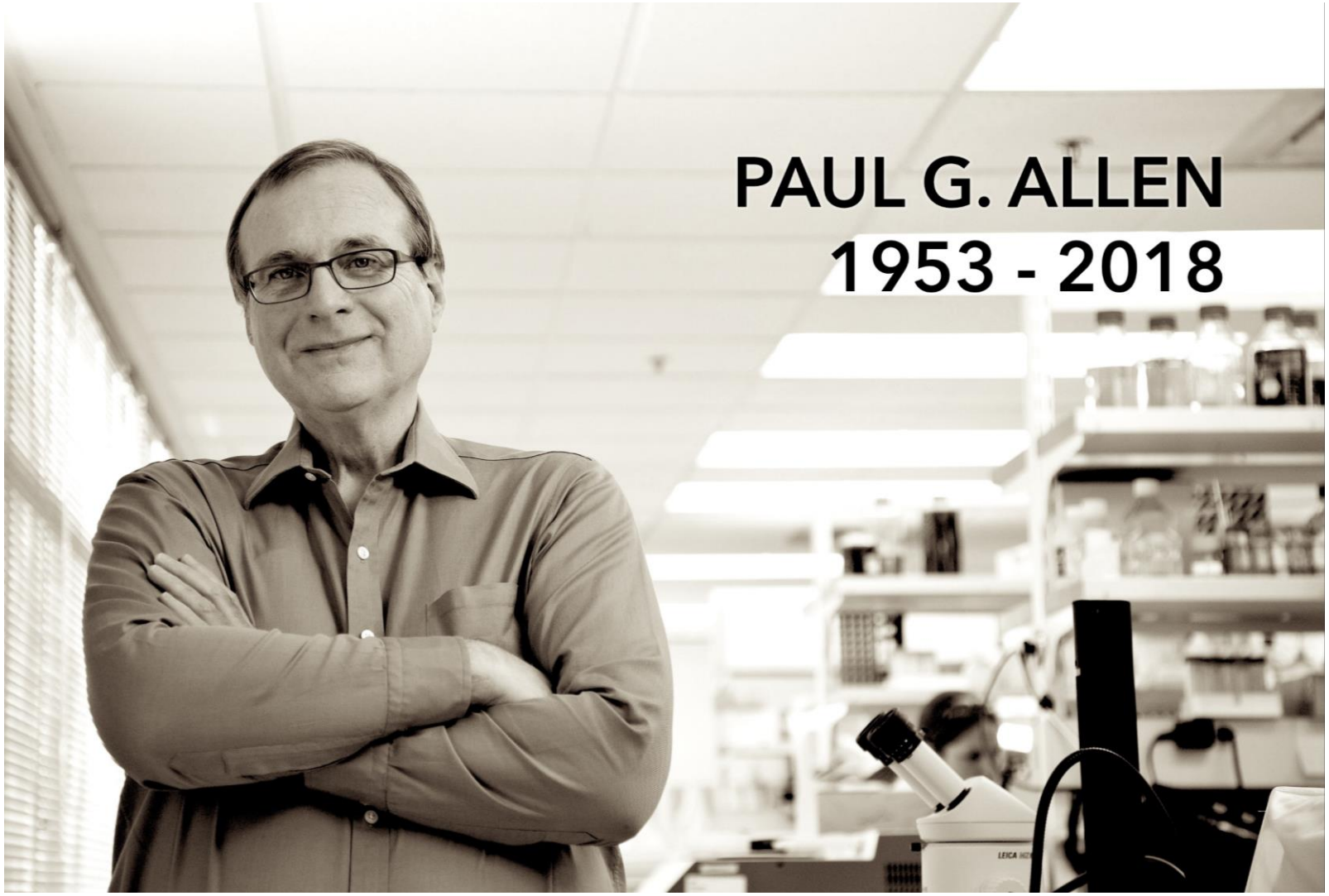


SUMMARY

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
Fuhui Long
Gabriel Ocker
Hongkui Zeng
Jaclyn Huffman
James Harrington
Jedediah Perkins
Jennifer Luviano
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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