# Big Science, Team Science & Open Science to Understand Mouse Cortex

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May 27. 2016



# The Allen Institute for Brain Science

- Independent, non-profit medical research organization, founded in 2003, supporting basic research in the brain sciences
- 310 staff
- Culture between an university and a biotech handful of large projects that can be done at s interactions across disciplines
- Ten year program initiated in 2012
- \$75 M budget for 2016





## 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
- Data are accessible several years prior to publications



# **All our Data Production Pipelines Use**

- Visual cortex of young adult C57BL/6J mice
- Mapped to the Common Coordinate Framework, a 3-D atlas based on a template established by averaging 1675 specimen, with (10 μm)<sup>3</sup> pixels and 320 million voxels for the whole brain
- Common Cre lines
- Centralized & standardized database







# In vitro Single Cell Characterization





Electrophysiology





Morphology



Metadata (Common Coordinate System)

Fueling Discovery

Fitting Models for Electrical Behavior mRNA transcripts

Data-driven taxonomy of cell types





# Allen Cell Type Data Base

### www.brain-map.org





### www.brain-map.org





# **Cell Type Clustering via Transcriptional Analysis**





Tasic et al. Nature Neurosci. 2016

## **Allen Brain Observatory**



- Record cellular level brain activity
- Doing so in a routine, reliable and high-throughput manner in behaving animals has never previously been attempted
- Three modalities

# Observatories of the mind

An ambitious project to map the mouse brain at the Allen Institute for Brain Science is a huge undertaking that may unify neuroscience, argue **Christof Koch** and **R. Clay Reid**.

Reuroscience is a splintered field. Some 10,000 laboratories worldwide are pursuing distinct questions about the brain across a panoply of spatio-temporal scales and in a dizzying variety of animal species, behaviours and developmental time-points. At any large neuroscience meeting, one is struck by the pace of discovery, with 50,000 or more practitioners heading away from each other in all directions, in a sort of scientific Big Bang.

Although this independence is necessary, it has prevented neuroscience from entering a more mature phase, which we developing common standards and collaborative projects. Neurophysiologists are more likely to use each other's toothbrushes than each other's data and software; physiological results are hoarded and rarely made accessible online; molecular compounds and transgenic animals are shared only after publication. All of this has made comparisons across laboratories difficult and has slowed progress.

At the Allen Institute for Brain Science in Seattle, Washington, we and our colleagues are initiating an experiment in the sociol-

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that will involve several hundred scientists, engineers and technicians at the institute. Philanthropist Paul G. Allen, who founded the institute in 2003, has pledged US\$300 million for the first four years of an ambitious ten-year plan that will accelerate progress in neuroscience, bringing his total commitment so far to \$500 million. Our goal is to attract the best young scientists and build a series of 'brain observatories', with the aim of identifying, recording and intervening in the mouse cerebral cortex, the outermost layer of the brain. Unlike the tele-



#### Koch & Reid Nature 2012

# Setting up 2pCI Pipeline



### **Animal Timeline**



# **A High Throughput Pipeline**



Surgery



Intrinsic imaging



In vivo Two photon imaging



Serial two-photon tomography



# **An Integrated Coordinate System**



*In vivo* two-photon imaging

Serial two-photon tomography



## **Reliable Visual Area Mapping Platform**







Cux2

Rorb

Rbp4

Scnn1a

Intrinsic Signal Imaging for Every Experiment



# 3 hours stimuli over 3 sessions













1 hour

## Watching the Brain of a Mouse Watching A Touch of Evil



One experiment in a transgenic mouse (AL – Cux2 – Layer 2/3)



## **Allen Brain Observatory - First Release**



- 25 mice, 53 surgeries, 133 imaging & 353 recording sessions
- 100 staff



## Acknowledgements - Paul G. Allen and Jody Allen





