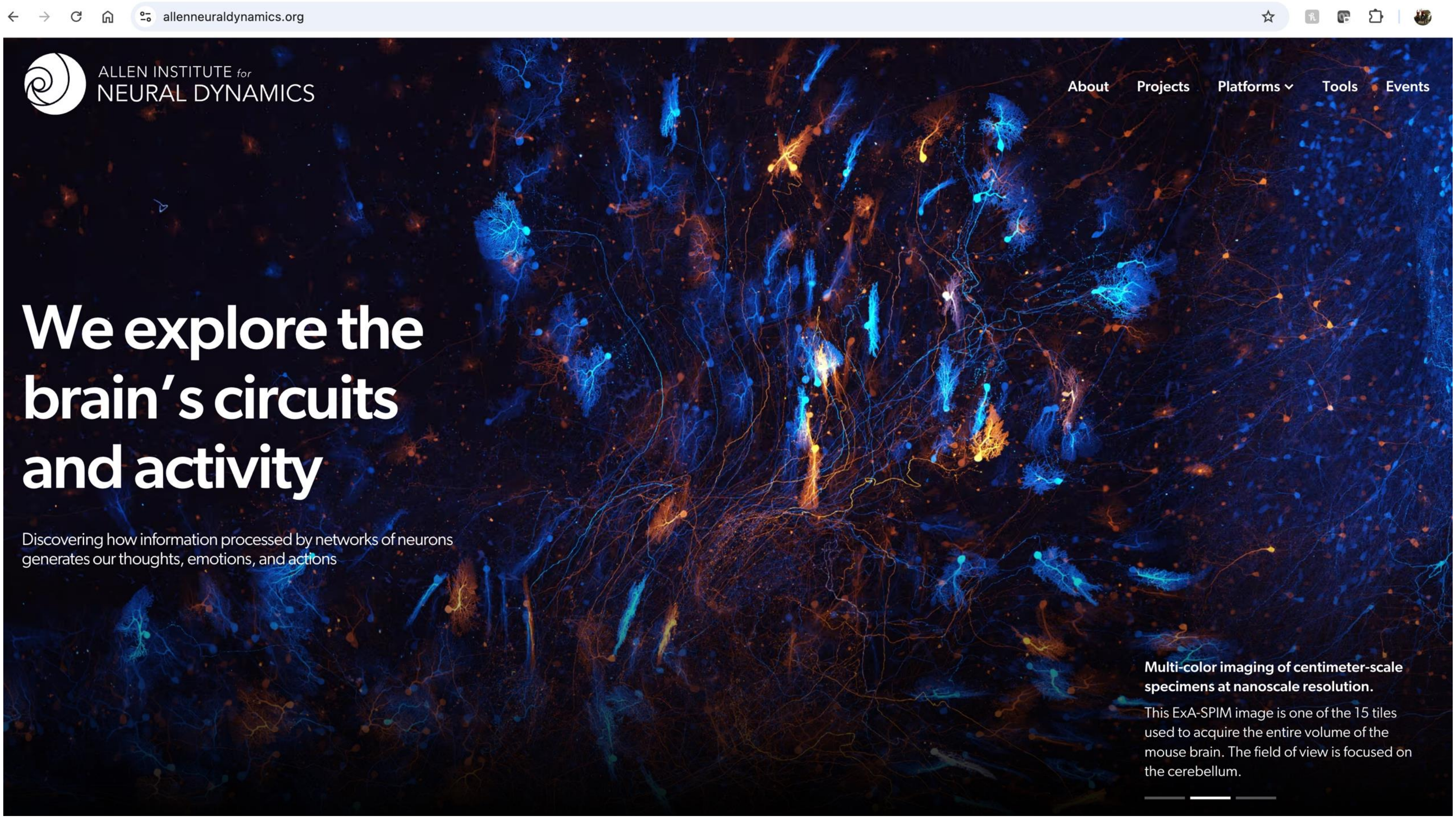
ALLEN INSTITUTE for NEURAL DYNAMICS

EXPLORING CREDIT ASSIGNMENT WITH A BRAIN COMPUTER INTERFACE EXPERIMENT

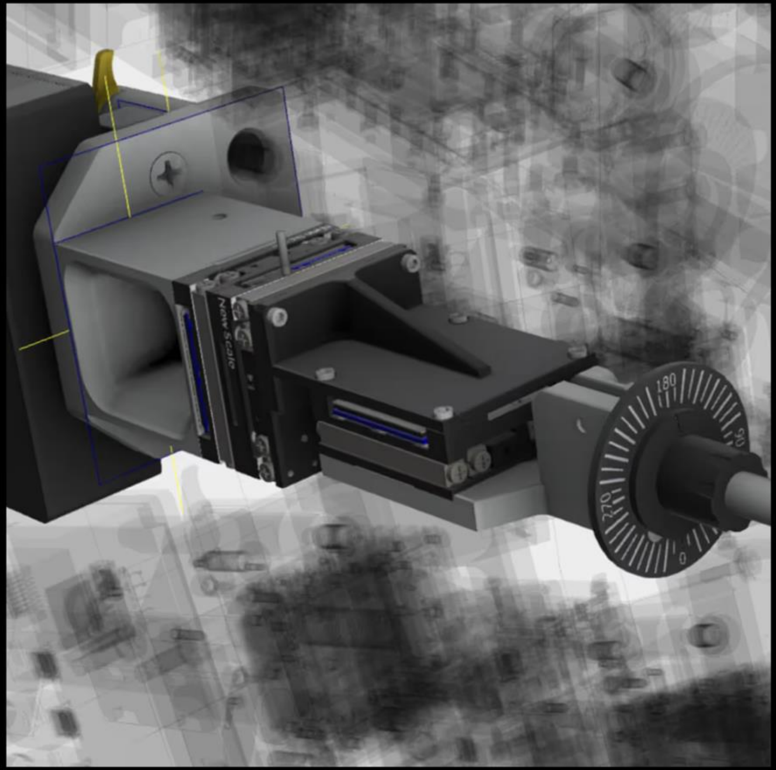
SASKIA DE VRIES AND SU-YEE LEE

SEPTEMBER 24, 2025



allenneuraldynamics.org

Data platforms accelerate our work



Neuropixels Electrophysiology

The Neuropixels platform uses pioneering technology for highly reproducible, targeted, brain-wide, cell-type-specific electrophysiology to record neural activity from defined neuron types across the brain.

Brain-Wide Anatomy At Cellular Resolution

The Molecular Anatomy platform combines innovative histology, imaging, and analysis techniques to map the morphology and molecular identity of neuron types across the whole brain.

Fiber Photometry

The Fiber Photometry platform enables optical measurement of neural activity in live animals to study neural circuits' function and dynamics in behaving animals.

Behavior

The Behavior platform uses advanced technology to implement a standardized, modular, multi-task virtual reality gymnasium for mice, with the goal to study brain function across different behaviors at scale.

ALLEN INSTITUTE for NEURAL DYNAMICS

About | Projects | Platforms | Tools | Events

Cell Types & Learning

We are combining longitudinal in vivo calcium imaging with spatial transcriptomics to investigate how specific cell types restructure their activity during novelty processing and task learning.

Explore Project

Dynamic Routing

We are studying task-switching behaviors in mice to determine how the brain controls the flow of its own activity and how neuronal circuits are reconfigured to dynamically route information for different tasks.

Explore Project

OpenScope

OpenScope provides access to cutting-edge neurophysiological methods to scientists across the world. Similar to astronomical observatories, scientists propose experiments that are then executed at the Allen Institute.

Explore Project

Single-Cell Computation

Our goal is to investigate the computations performed by individual neurons, based on measuring synaptic input and firing output. We are developing technologies with single synapse resolution in the living brain. New microscopes allow tracking synaptic activity across the entire dendritic arbor.

Explore Project

Brain-Wide Neuromodulation

We are studying the molecular and anatomical subclasses of neuromodulator neurons and exploring how networks use neuromodulators to drive learning and decision making.

Explore Project

Credit Assignment During Learning

We are using optical connection-mapping techniques and brain computer interface (BCI) in the context of a learning task to ask how the brain updates its synapses to support behavioral learning without interfering with existing skills or memories.

Explore Project

ALLEN INSTITUTE for NEURAL DYNAMICS

About Projects Platforms Tools Events

Credit Assignment During Learning

PROJECT

Overview

The human brain contains trillions of synapses. Through their patterns and strengths, these synapses are thought to encode our memories and acquired skills. How does the brain update its synapses to support behavioral learning without interfering with existing skills or memories? To study this question, we have developed i) optical connection-mapping techniques that leverage cellular-resolution two-photon (2P) optogenetics and calcium imaging in mouse motor cortex (MC) to track changes in the causal influence of each neuron in a recorded population; alongside ii) optical brain computer interface (BCI) learning tasks that explicitly define the causal relationship between imaged MC activity and behavior.

Optical Brain Computer Interface

To simplify the study of learning, we developed an optical BCI task in which mice control the position of a motorized reward port with a single neuron in layer 2/3 of primary motor cortex (Figure 1). Mice quickly learn to increase the activity of this conditioned neuron (CN), resulting in increased reward rates in approximately 30 trials

Data Platforms Utilized

Surgery

Project Team

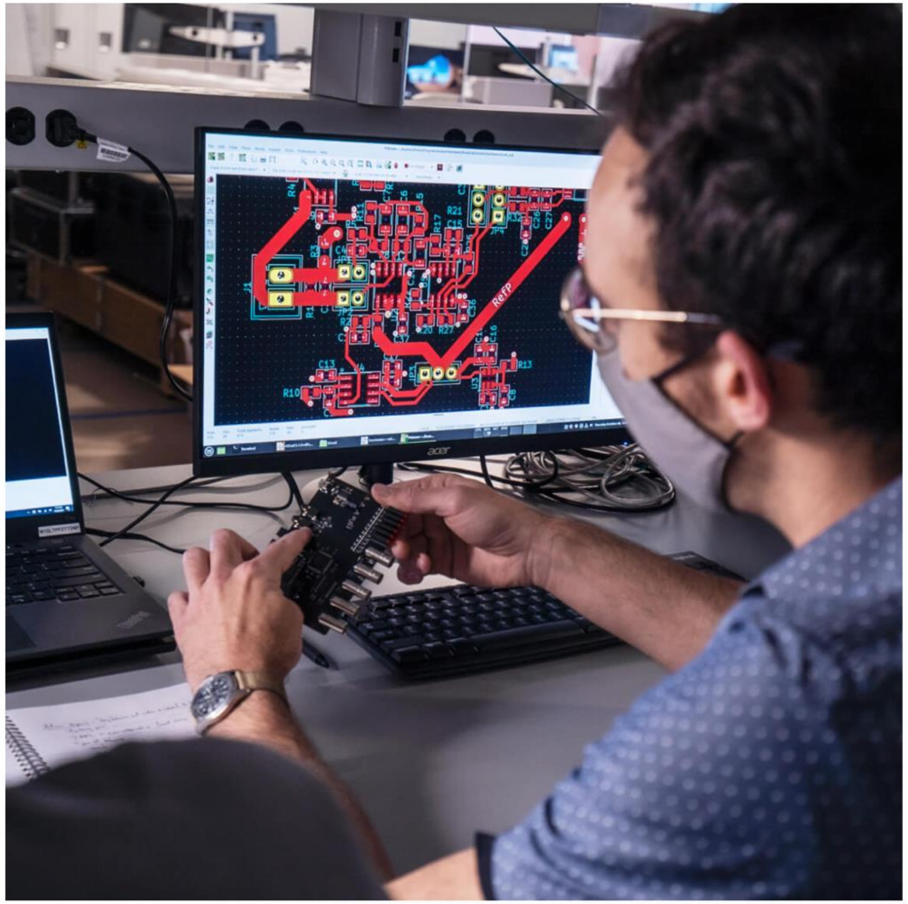
Kayvon Daie, Sr. Scientist

Márton Rózsa, Scientist I

Karel Svoboda, Executive Vice President, Director of AIND

Kenta Hagihara, Scientist I

Kanghoon Jung, Scientist II - Neurophysiology of Dynamic Decision



WHAT WE STAND FOR

Open Science

We share and distribute data, tools, and knowledge as soon as is practical and useful. We share the generosity of our founder and other sponsors to accelerate scientific discovery elsewhere. Sharing is necessary to maximize scientific progress. One measure of our success is the value the larger scientific community derives from the scientific and technical resources we produce. Sharing data, tools, and resources also facilitates reproducible science.

- **Share in a community.** Actively engage with collaborators and colleagues in the field. Trust and seek community feedback. We want to do science together.
- **Share intentionally.** Include metadata, documentation, and tutorials to facilitate use and re-use.
- **Share freely.** Prioritize freedom of use over free cost but reduce cost when possible.
- **Share rapidly.** Even if imperfect.
- **Share fairly.** Adhere to FAIR standards. Engage with community standards and domain-specific data repositories when possible.

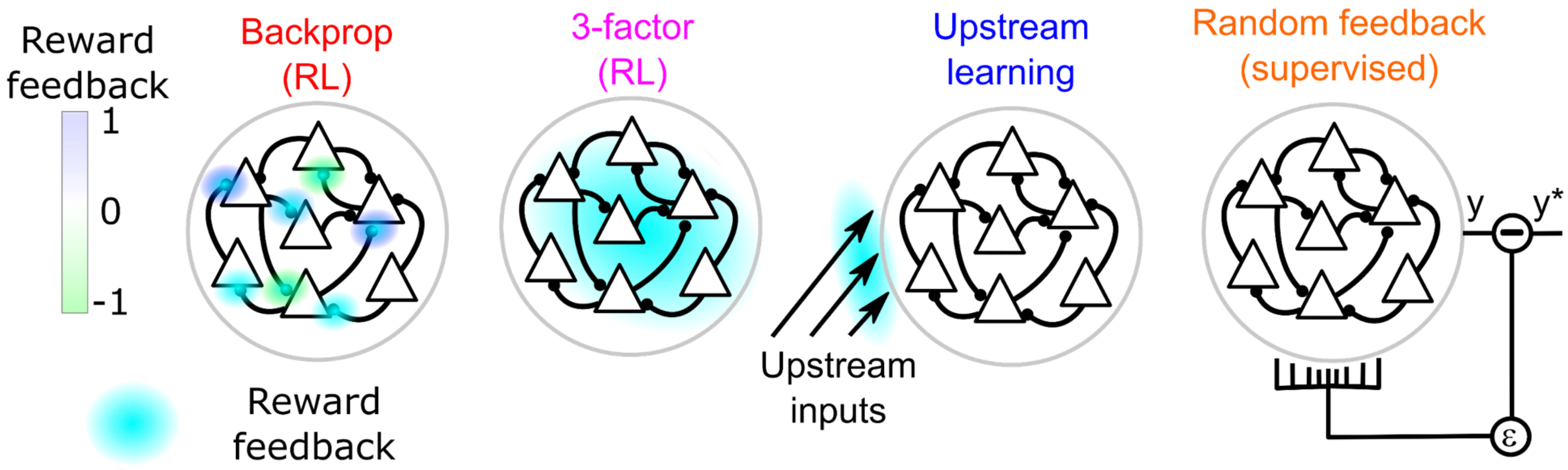
→ Read Open Science Policy

How does learning impact neural circuits?

Specifically:

How do the connections between neurons change with learning?

Neural circuit learning rules



Rumelhart & Hinton, 1986
Williams & Zipser, 1990

Williams 1992
Fiete & Seung 2006
Miconi, 2017

Legenstein et al, 2010
Engelhard et al, 2019

Lillicrap et al, 2016
Murray, 2019

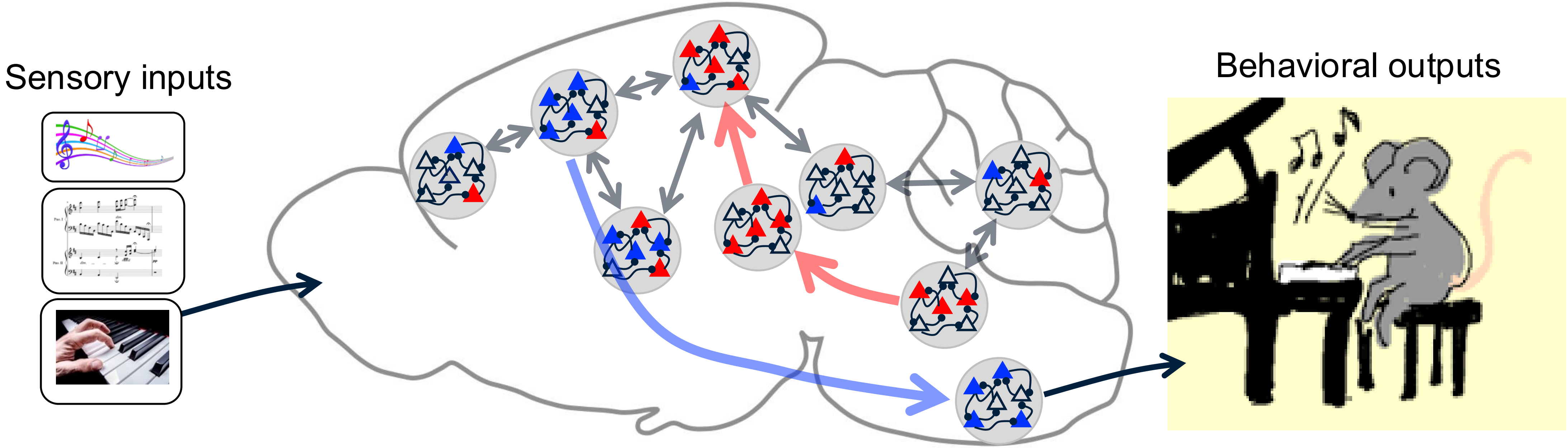
How does learning impact neural circuits?

Specifically:

How do the connections between neurons change with learning?

1. Measure connections
2. Learn a task
3. Re-measure connections

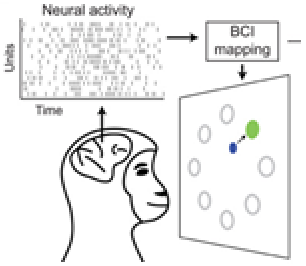
Challenge 1: complexity of neural circuits



Challenge 1: complexity of neural circuits

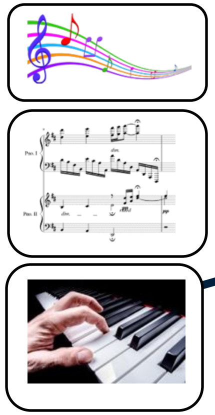
Solution: Brain computer interfaces

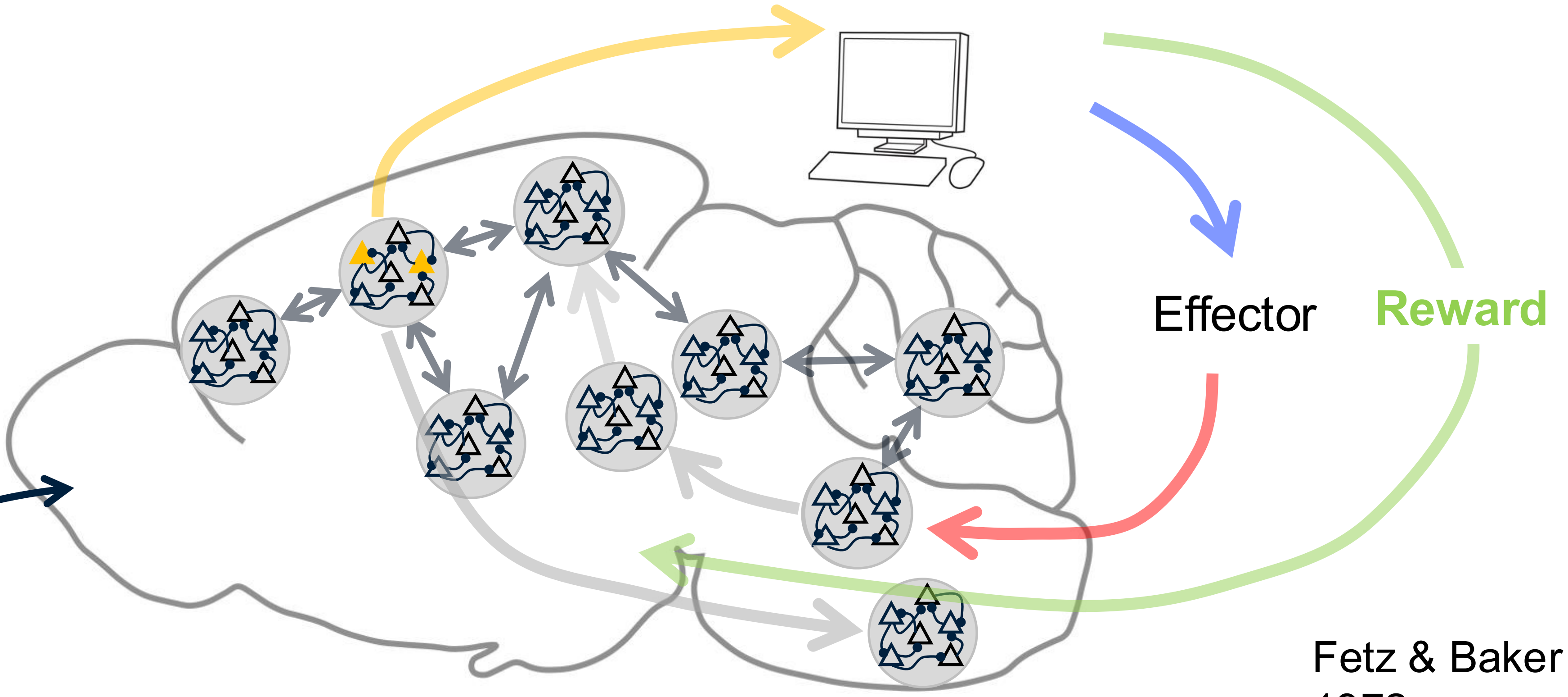
Example BCI



Sadtler et al, 2014

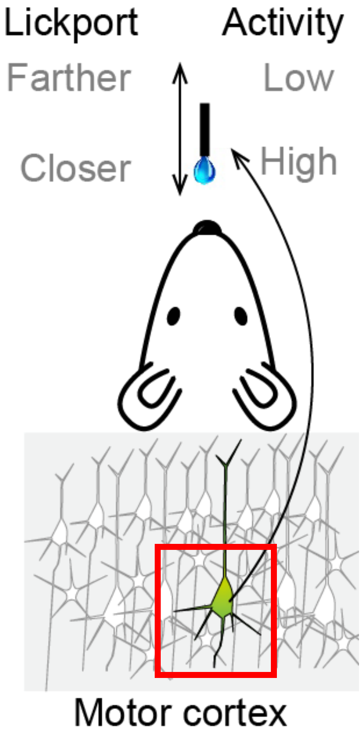
Sensory inputs

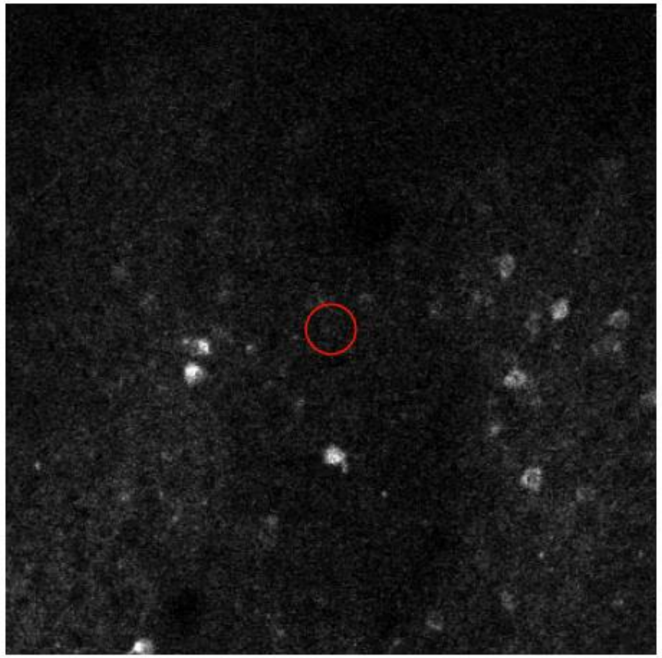


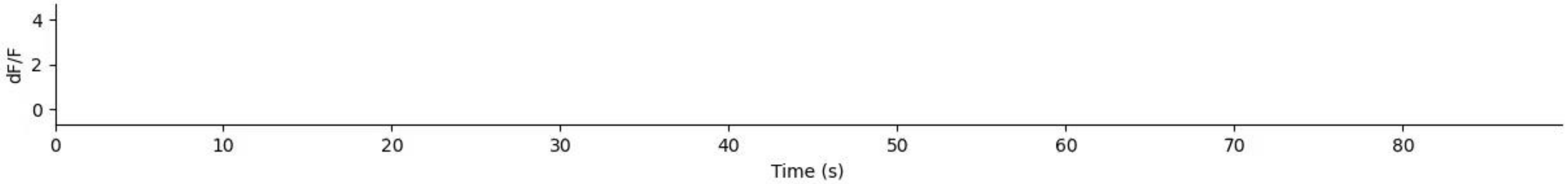


Fetz & Baker 1969; 1972; many others

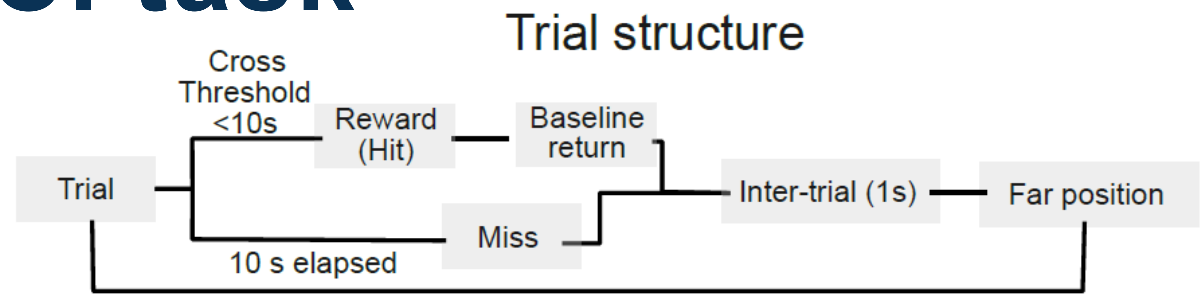
Optical BCI task

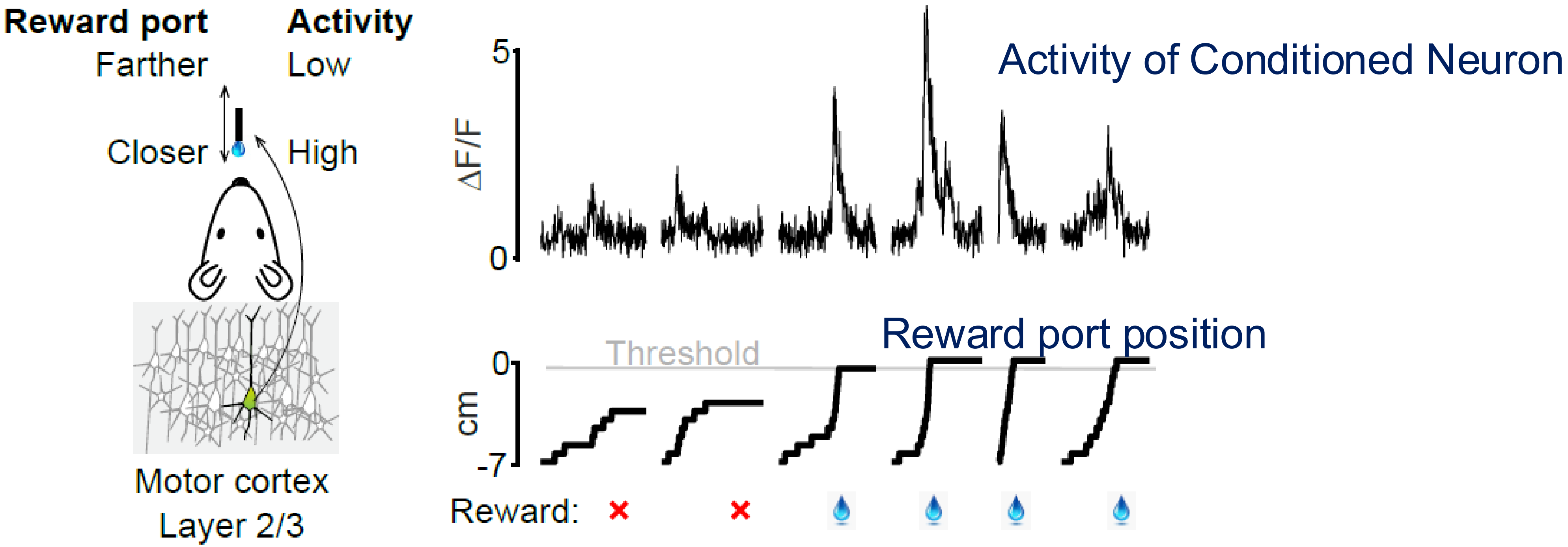






Optical BCI task





Challenge 2: Measuring connection between neurons ($\Delta W_{i,j}$)

1. Measuring activity from a population of neurons in a circuit

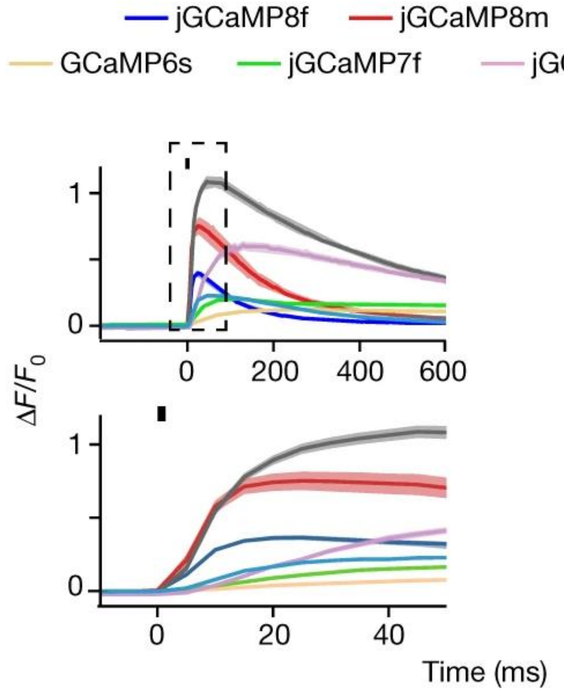
2. Measuring the strength of the connections between those neurons

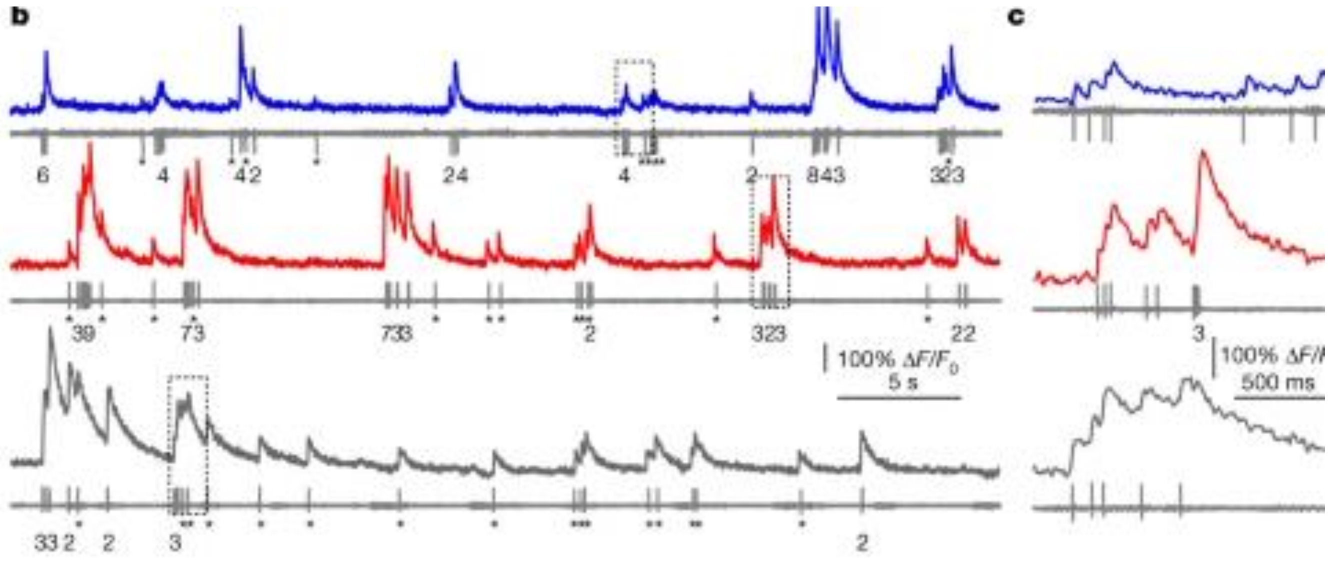
2-photon calcium imaging

GCaMP6

Chen et al, 2013

Calcium indicators





Zhang, Rozsa et al, 2023

Strategies for expressing calcium indicators

Transgenic approaches

Viral approaches

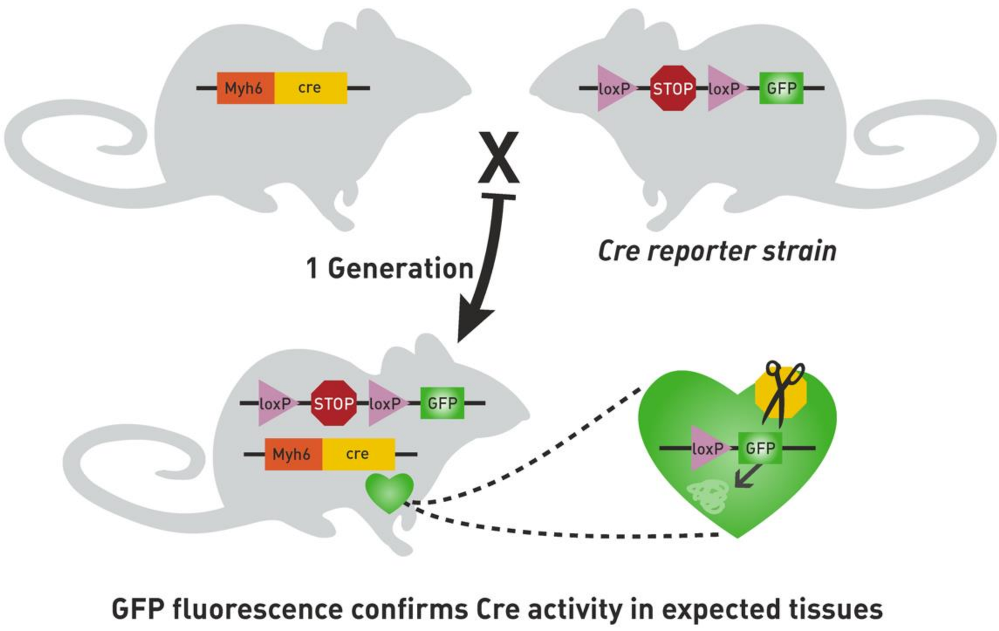
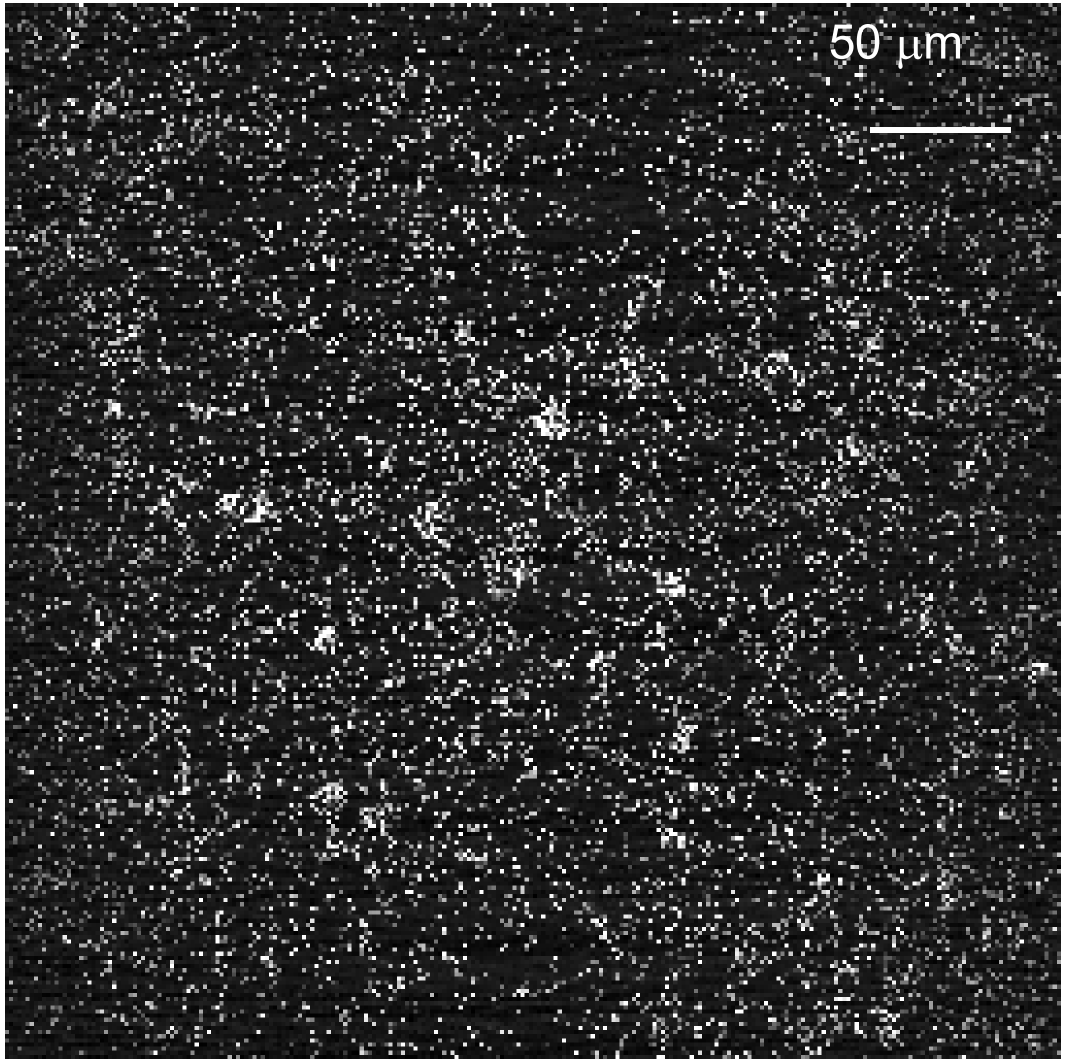
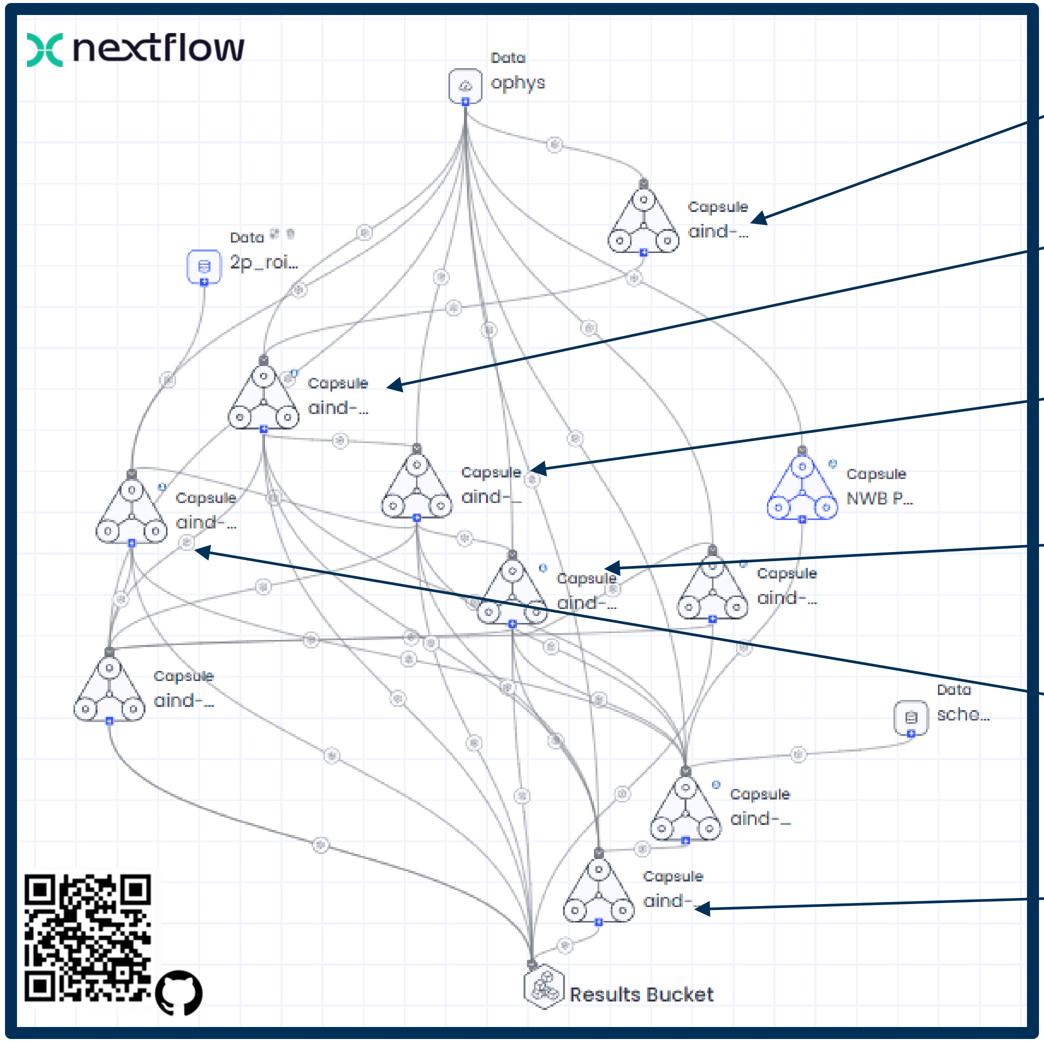


Image taken from The Jackson Laboratory.

Population imaging

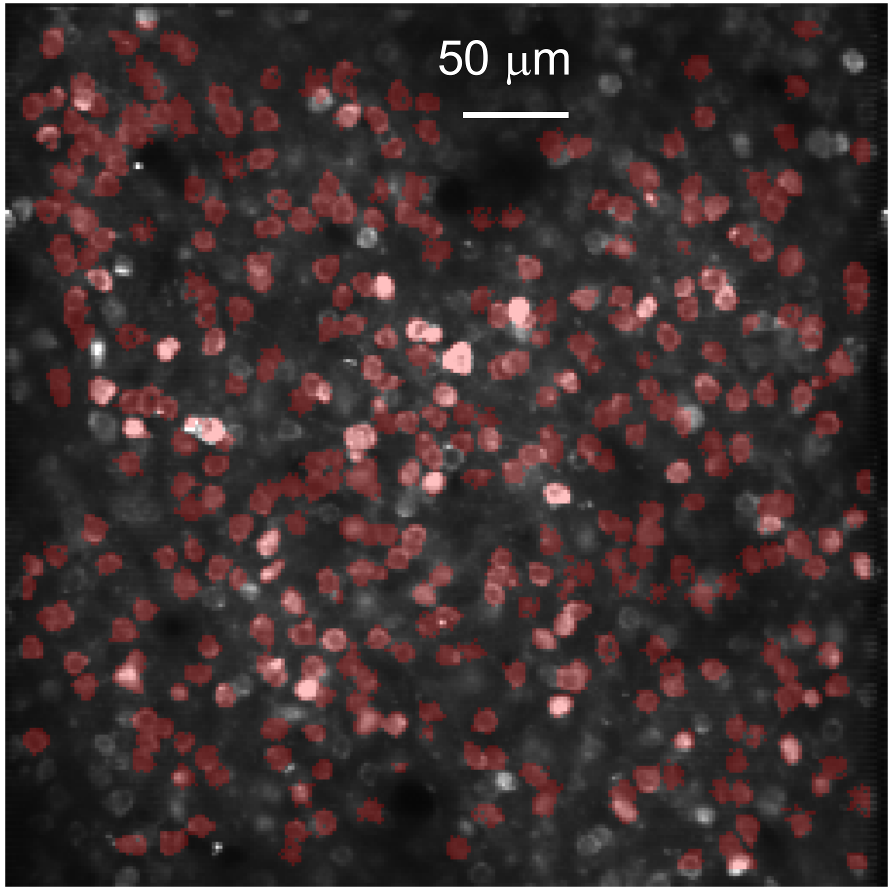


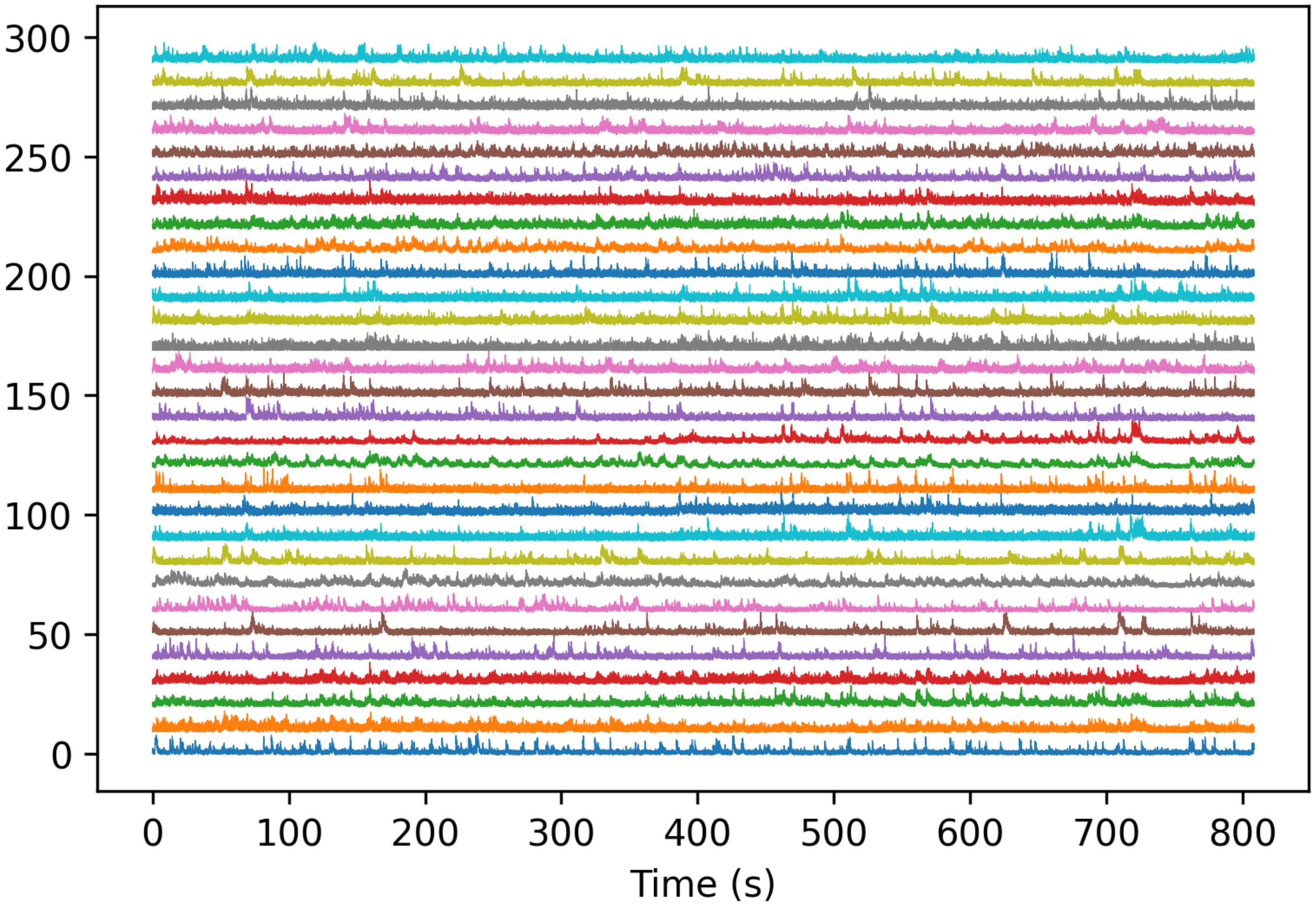
A modular pipeline for calcium imaging



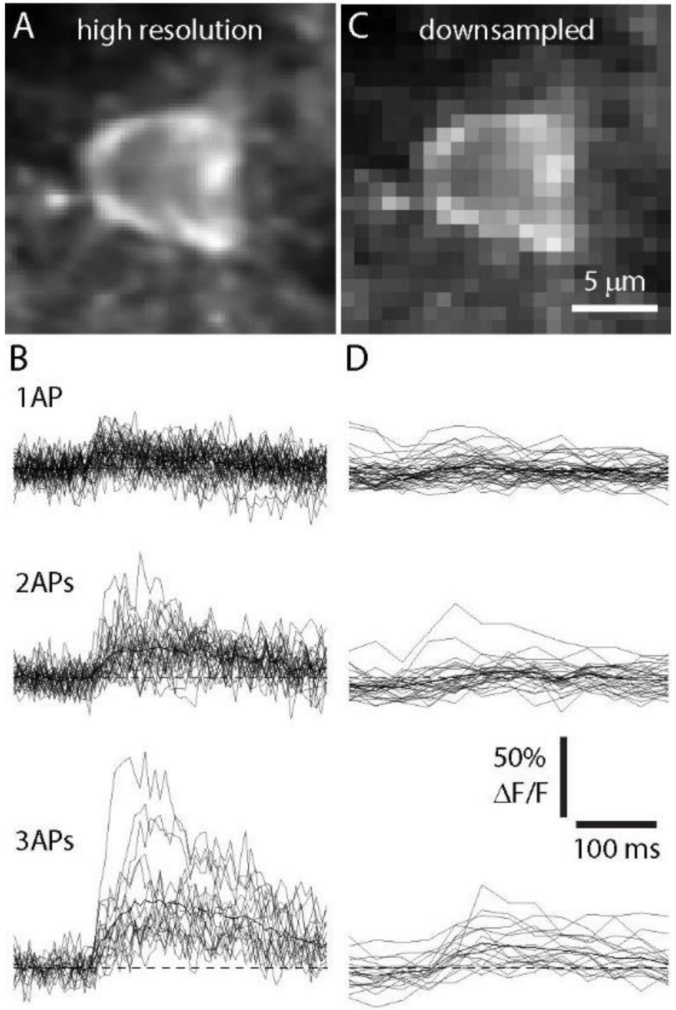
Data Conversion	Standardize incoming file formats
Motion Correction	Account for brain movement
Signal Extraction	Detect ROIs and extract their signals
DF/F	Normalize fluorescent signals
Classification	Soma, dendrite, …
NWB Packaging	Release to the public

Population imaging





Population imaging has lower spatial and temporal resolution than validation data



Huang, Ledochowitsch *et al.* eLife 2021

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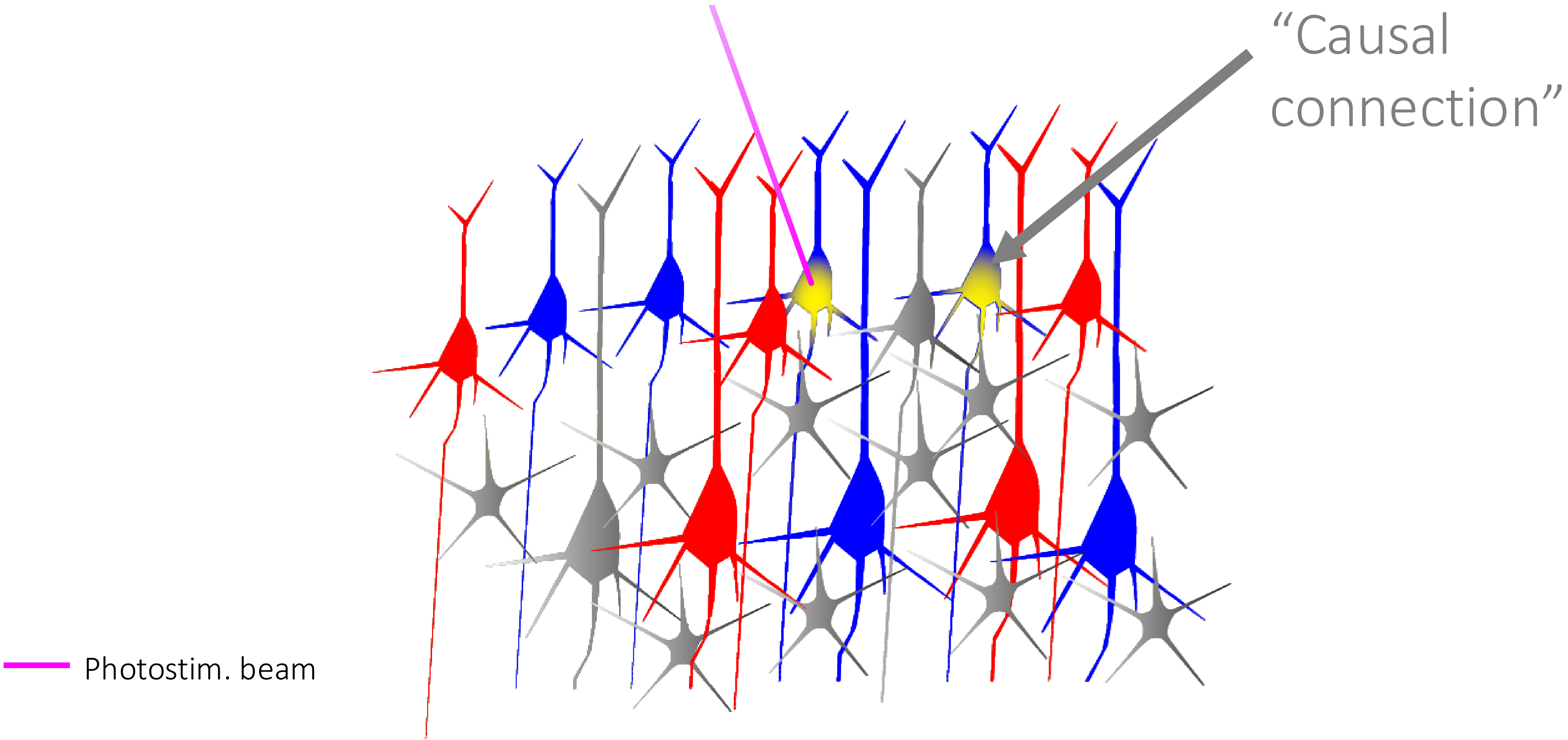
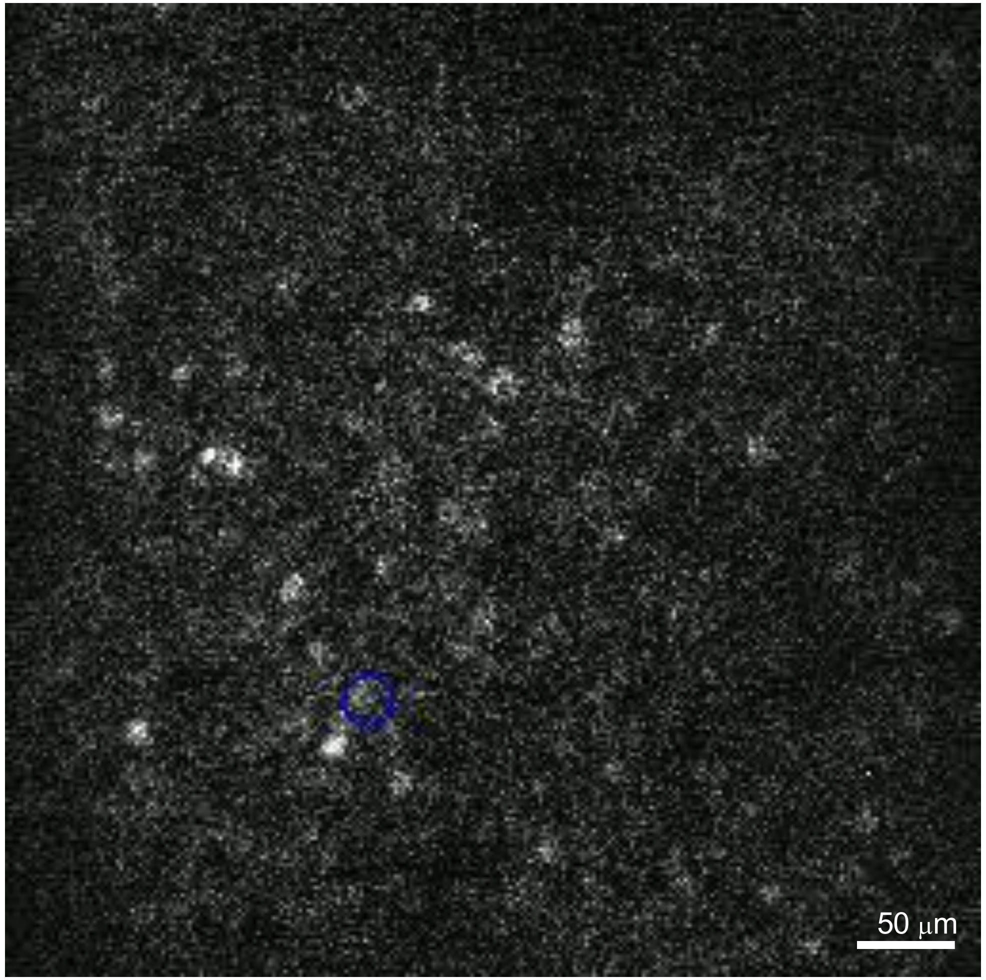
Challenge 2: Measuring connection between neurons ($\Delta W_{i,j}$)

1. Measuring activity from a population of neurons in a circuit
2. Measuring the strength of the connections between those neurons
    1. Spontaneous activity (today's workshop!)
    2. Photostimulation

Two-photon optogenetics

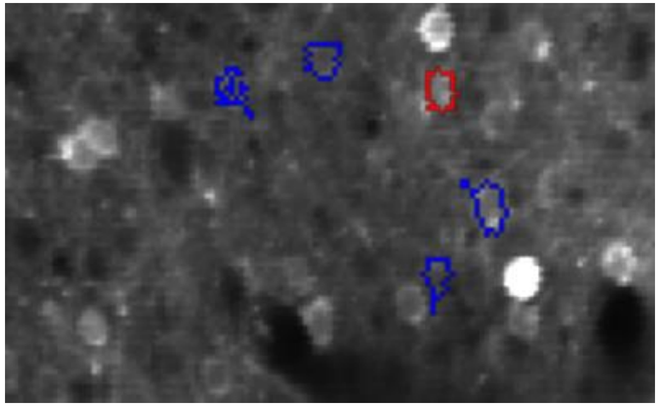


Network responses to photostimulation

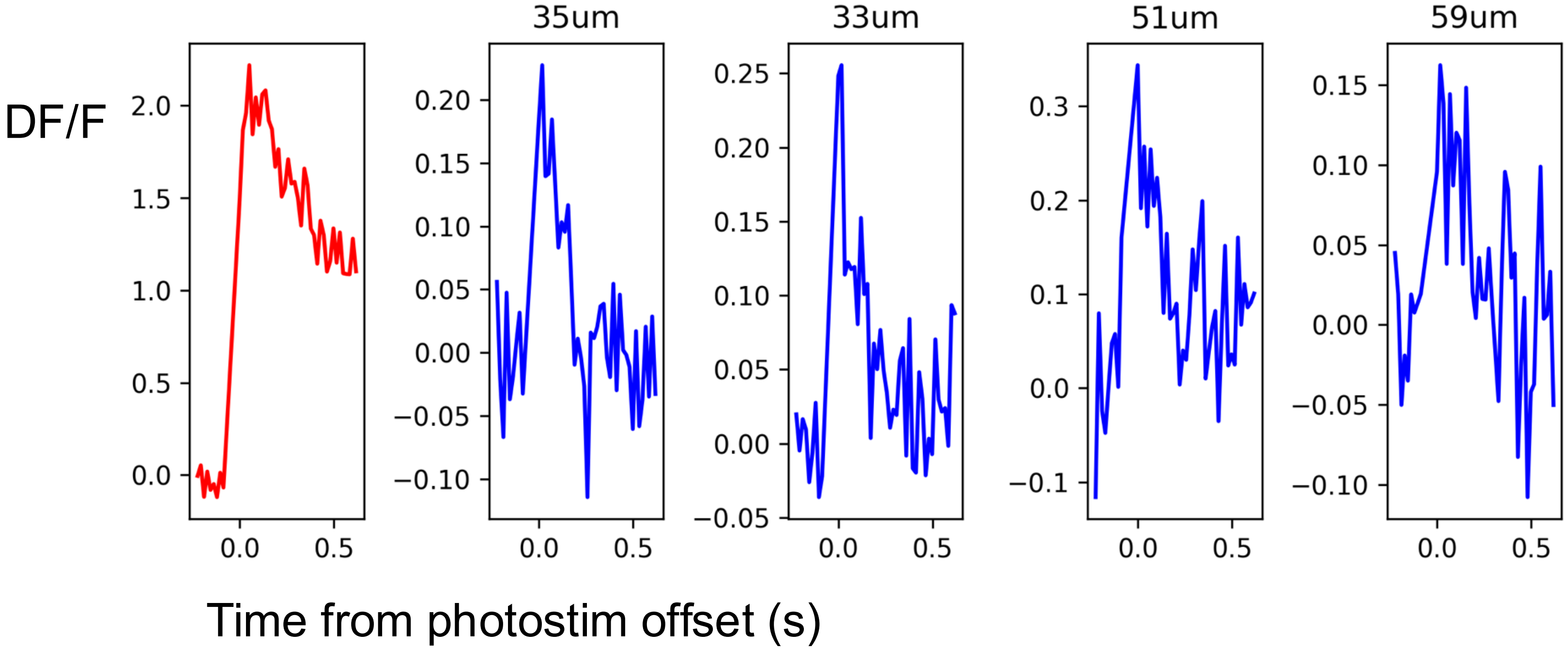


- 1 neuron stimulated at a time
- 50-100 neurons stimulated in the FOV
- Each neuron stimulated ~20 trials (randomized).

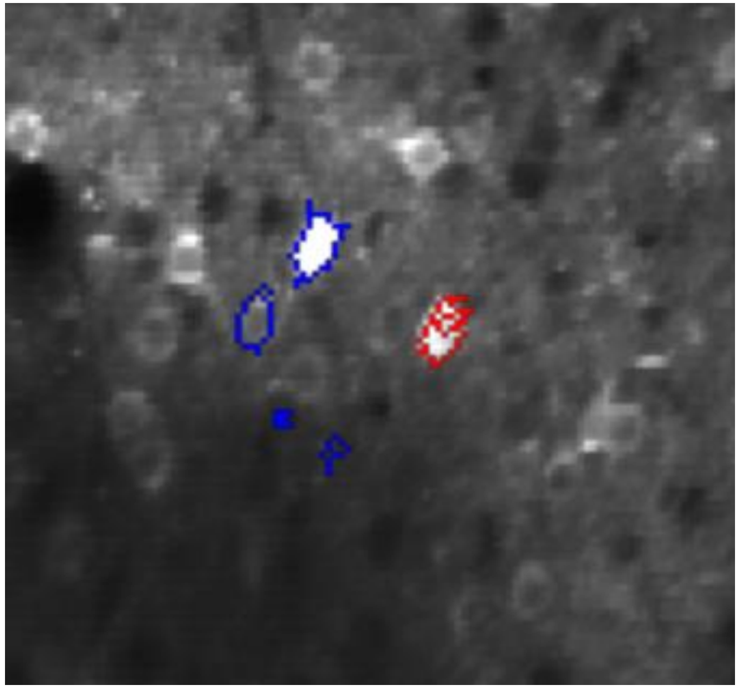
Examples of connected neurons



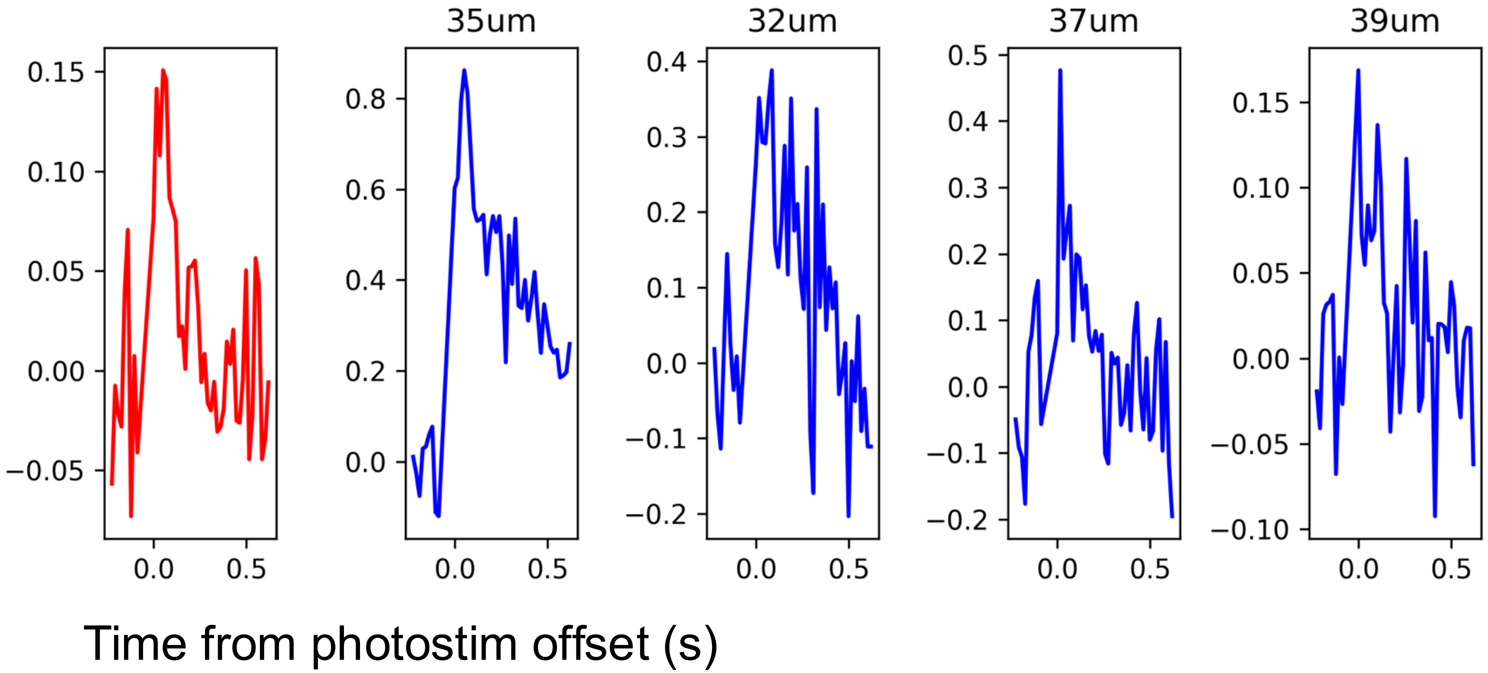
Target cell
Non-photostim



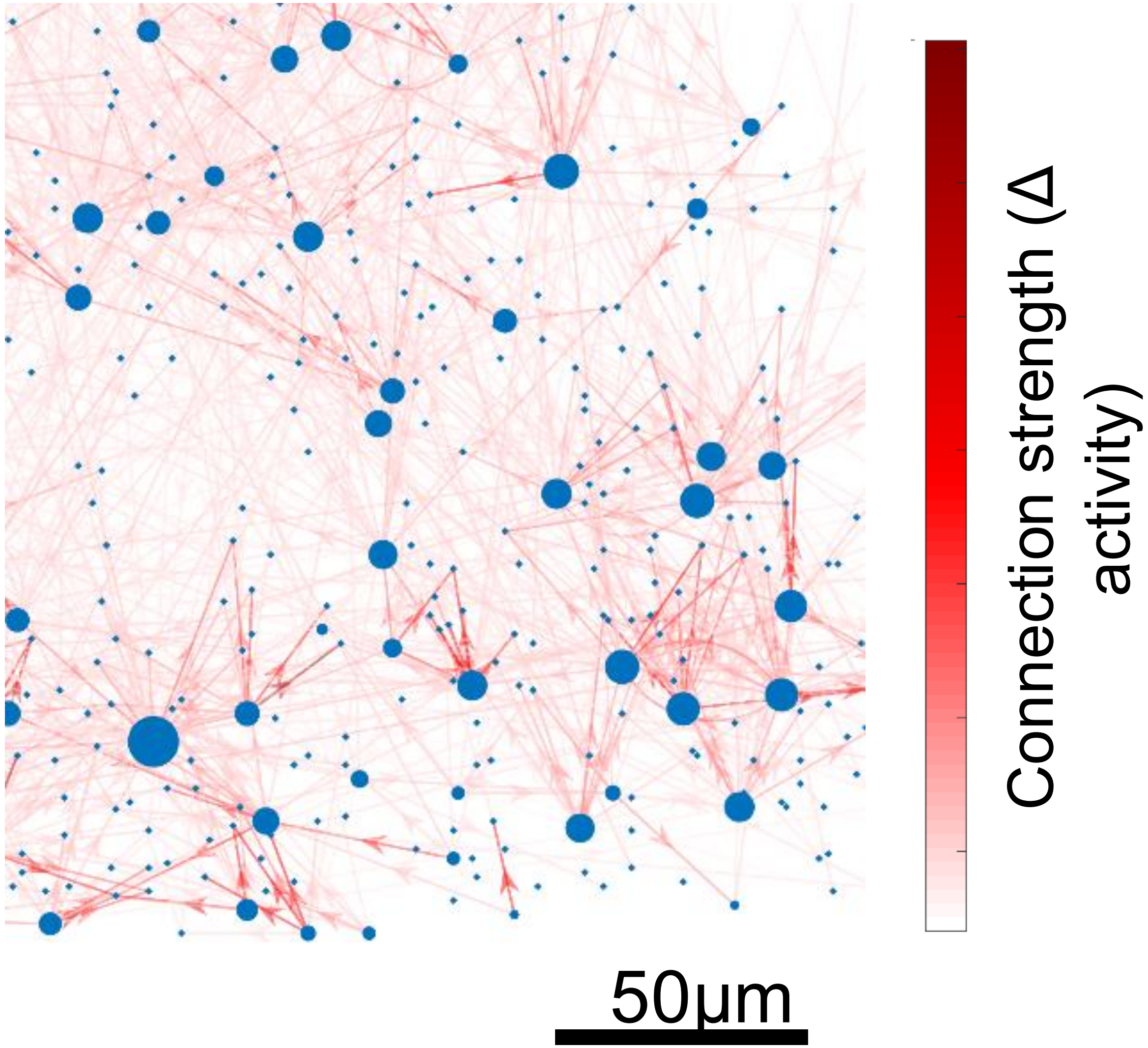
Examples of connected neurons



Target cell
Non-photostim

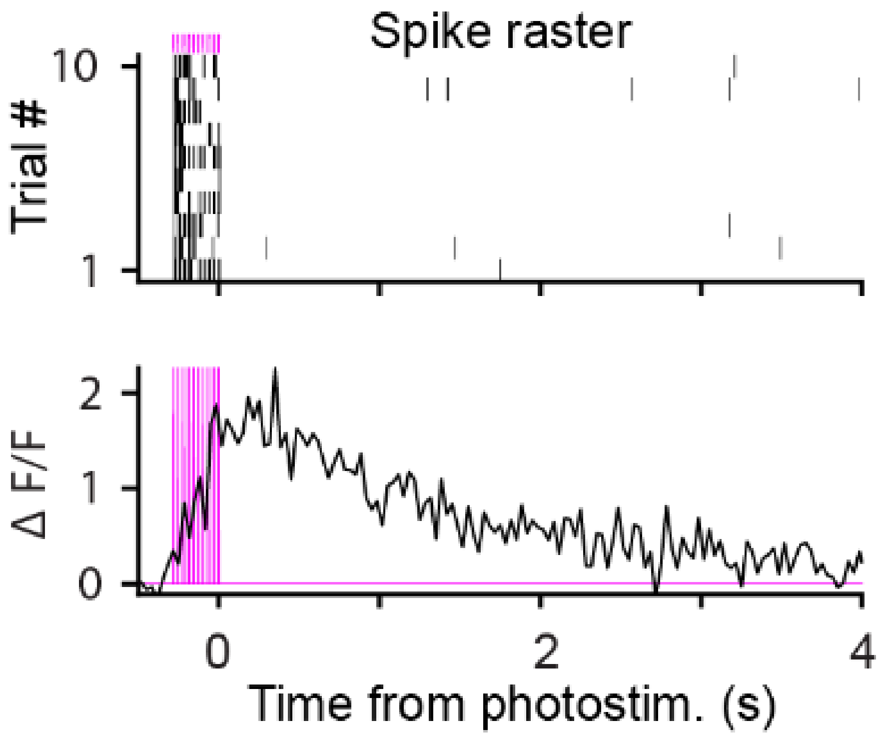


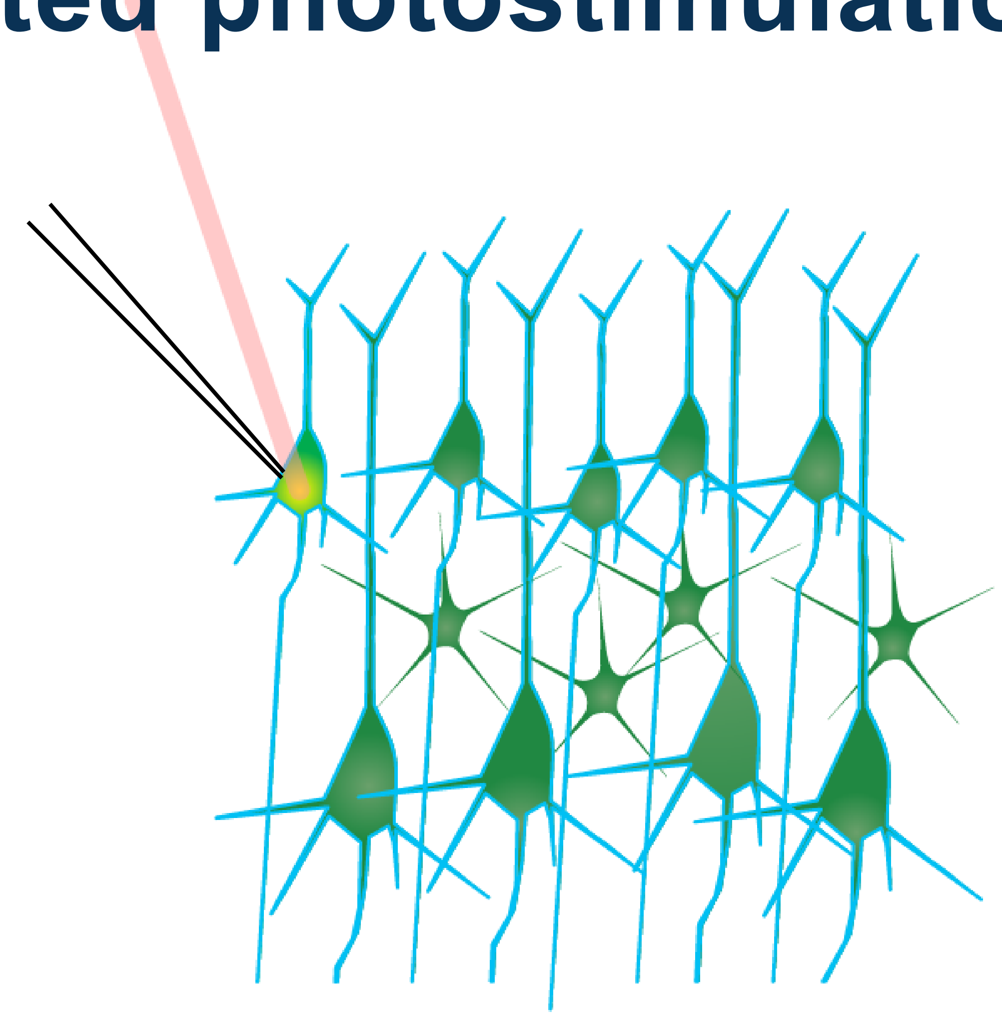
All optical mapping ‘causal connectivity’ *in vivo*



Finkelstein, Daie, Rozsa, Darshan, Svoboda 2023

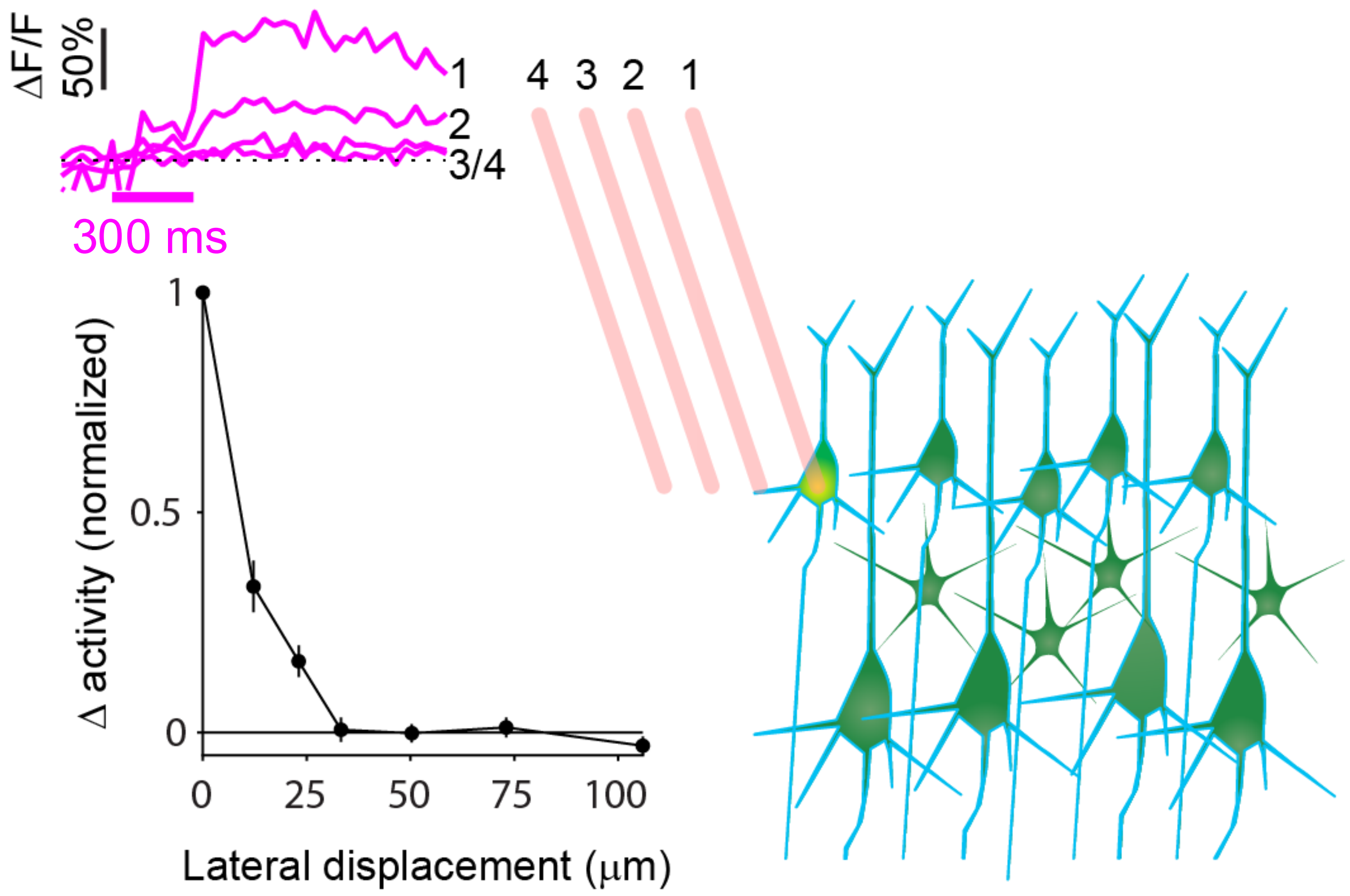
Validation of targeted photostimulation





Daie et al, 2021

Spatial resolution of photostimulation



Daie et al, 2021

Strategies for expressing ~~calcium indicators~~ channelrhodopsin

Transgenic approaches

Viral approaches

Transgenic approaches

Viral approaches

Strategies for expressing channelrhodopsin AND calcium indicators

Camk2a-tTA/wt;TetO-**jGCaMP8s**-01/wt

OR

Camk2a-tTA/wt;tetO-**GCaMP6s**/wt

(GCaMP in excitatory cells)

+

pAAV-CaMKIIa-**ChRmine**-oScarlet-Kv2.1-WPRE

(ChRmine in excitatory cells)

Slc17a6-IRES-Cre/wt;Ai230(TIT2L-XCaMPG-WPRE-ICL-**ChRmine**-oScarlet-IRES2-tTA2-WPRE)-hyg/wt

(ChRmine in excitatory cells)

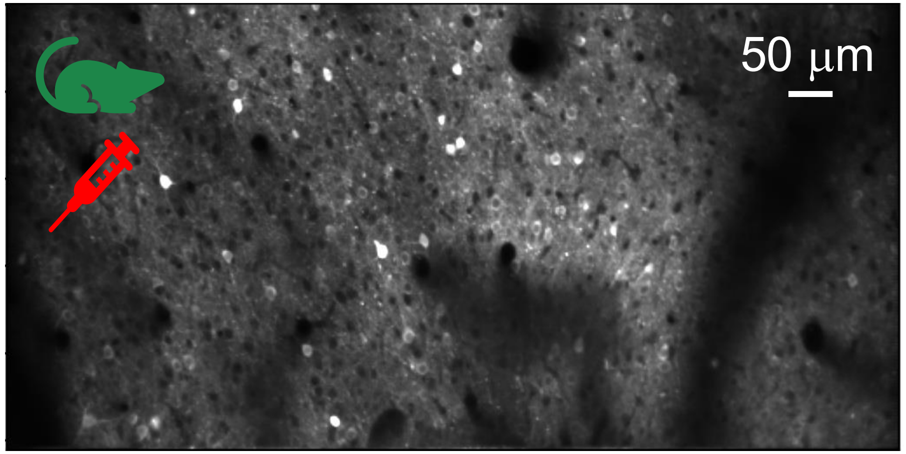
+

pAAV-hSyn1-RiboL1-**GCaMP8s**-WPRE

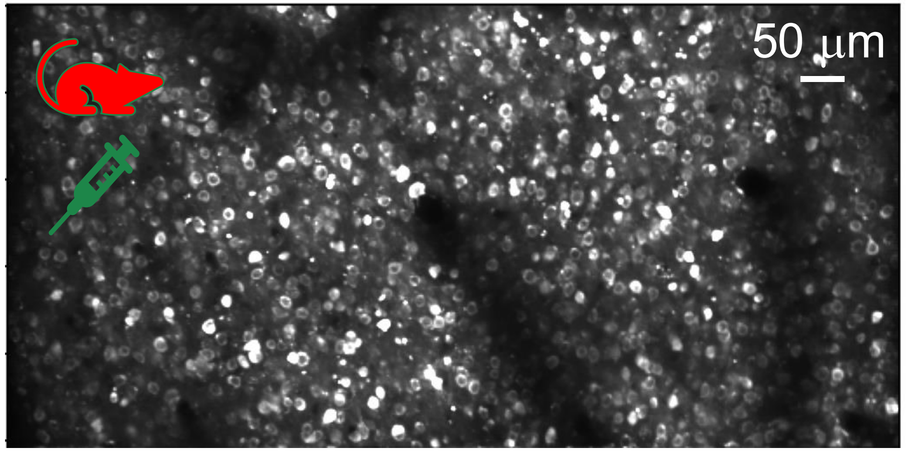
(GCaMP in all cells)

Calcium indicators / expression strategies in our dataset

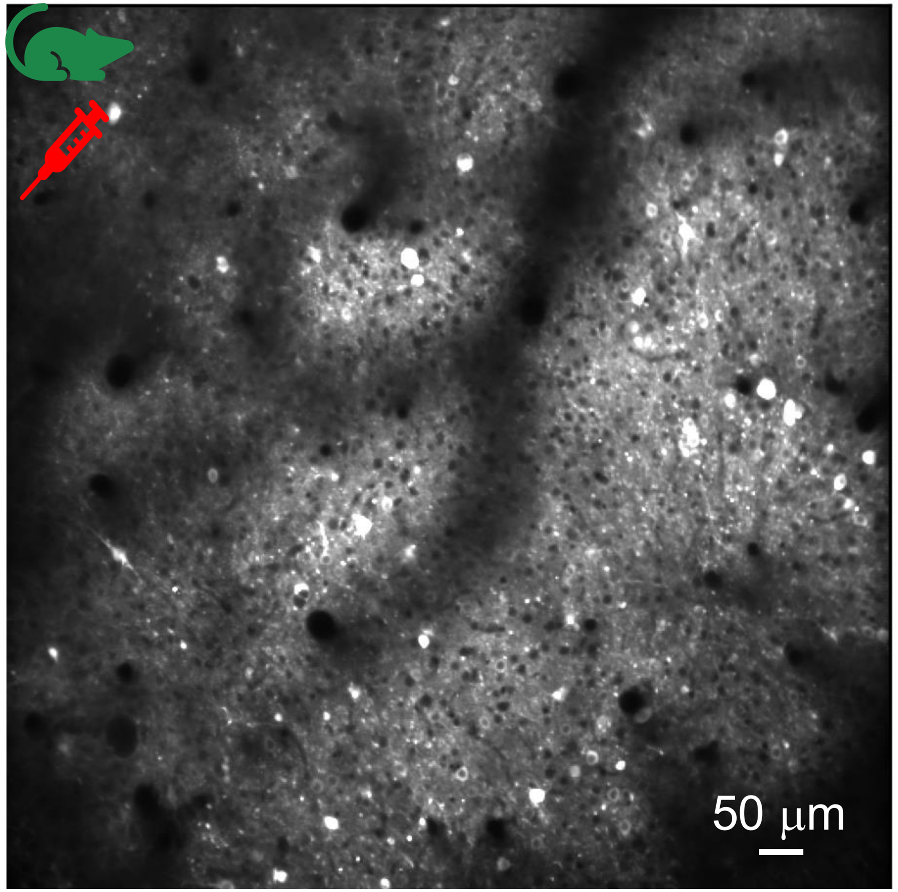
Camk2a-tTA x TetO-jGCaMP8s-01(ND) + CaMKIIa-ChRMine-oScarlet 10x dilution



Ai230 x slc17a6-Cre + hSyn-RiboL1-GCaMP8s

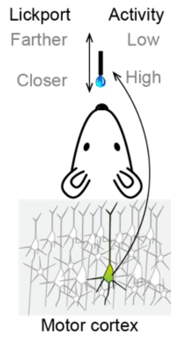


TetO-GCaMP6s x Camk2a-tTA + CaMKIIa-ChRMine-oScarlet

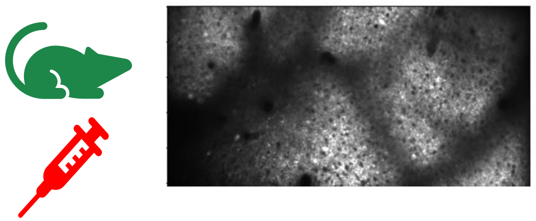


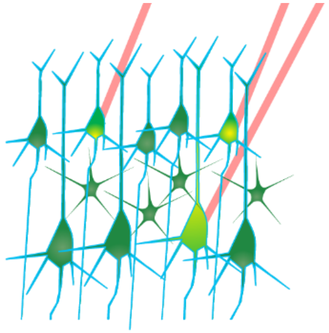
How does learning impact neural circuits?

Challenge 1: complexity of neural circuits



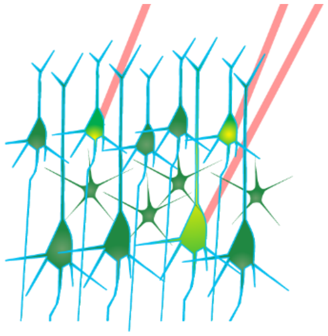
Challenge 2: Measuring connection between neurons ($\Delta W_{i,j}$)

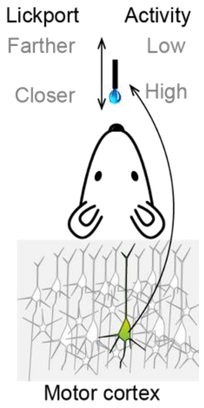


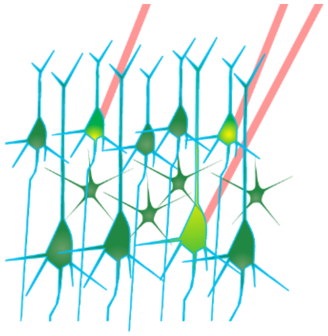


Experimental timeline:

Spont → Photostim → BCI → spont → Photostim.



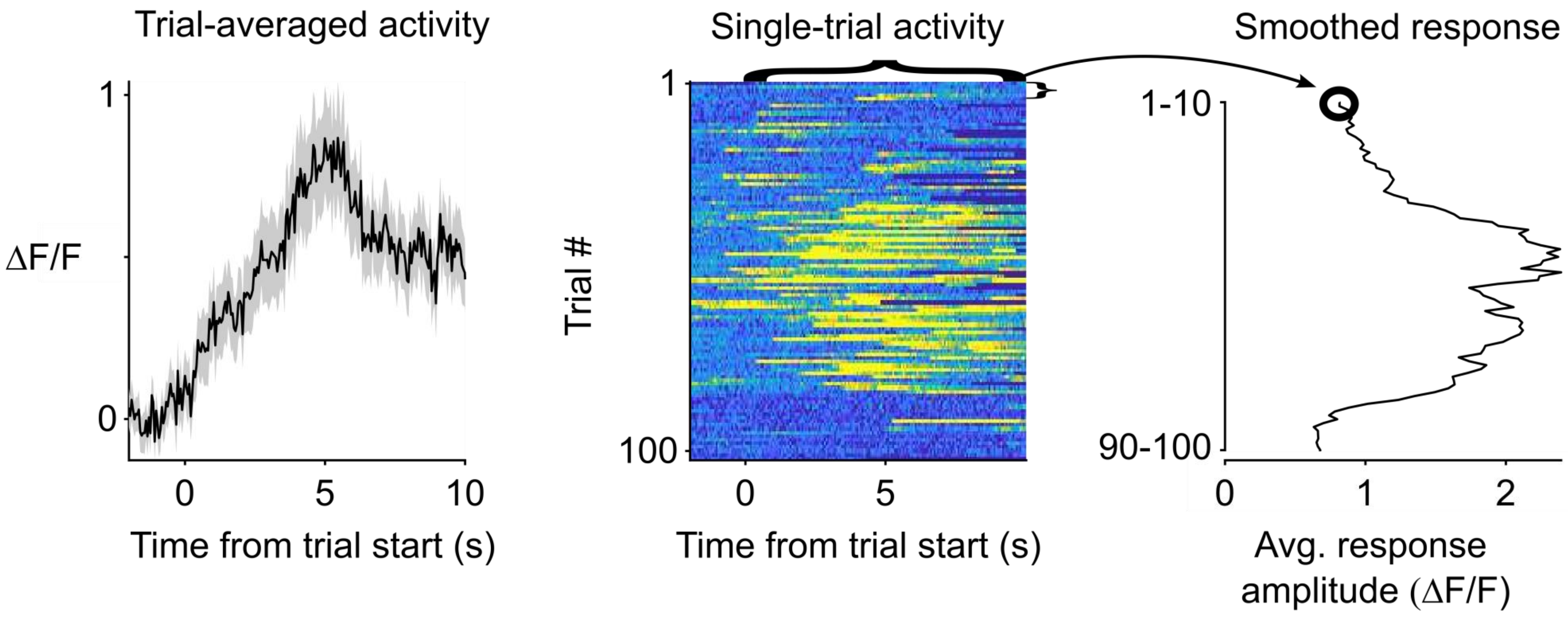




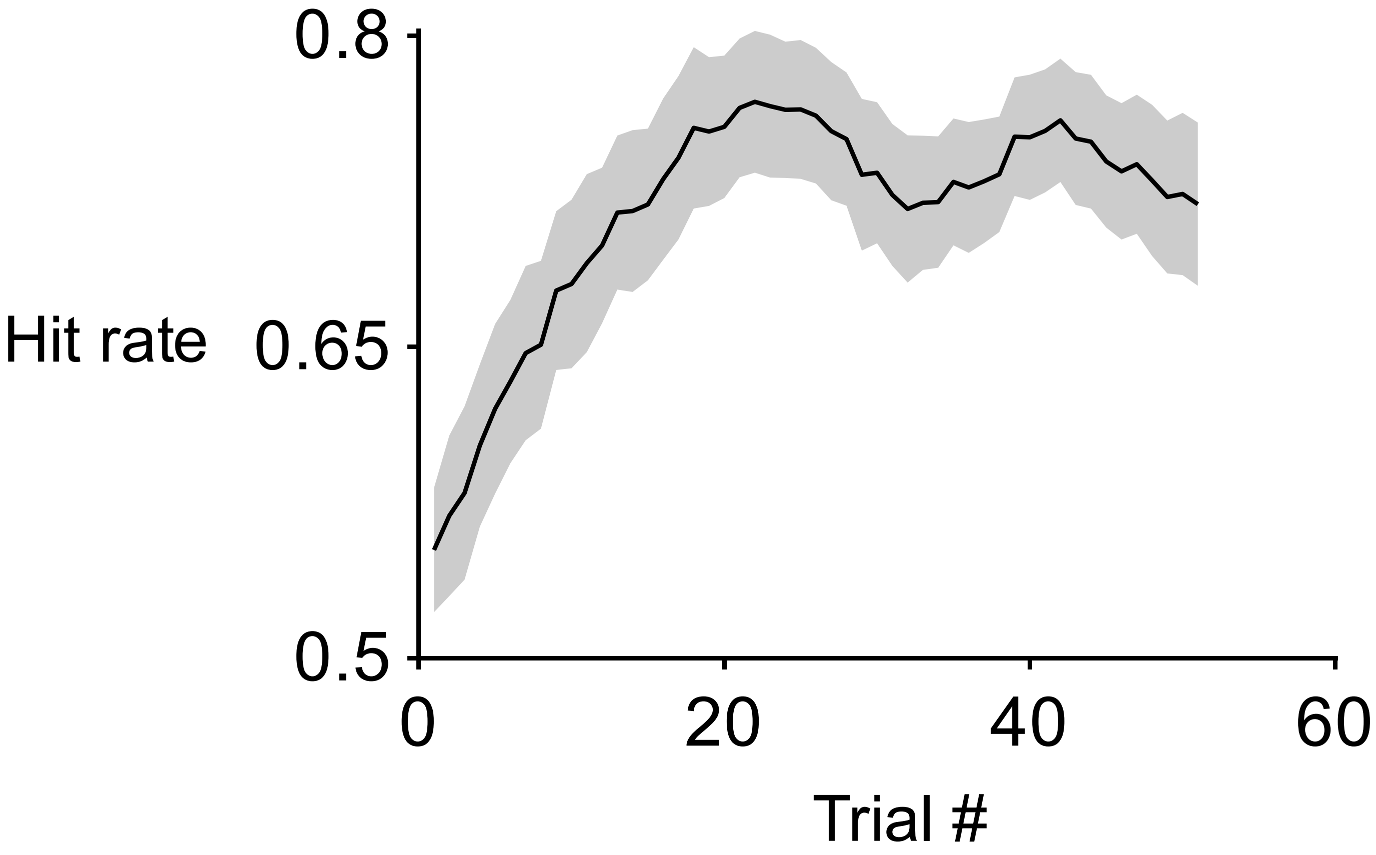
Experiment notes

- The same mouse is imaged across many days
- Experimenters image the same group of neurons (“field of view” or FOV) for many days. They sometimes then move to a different field of view in the same mouse.
    - While the same FOV was imaged across days, individual cells have not (yet) been tracked from session to session
- Each day, a different neuron is chosen to be the “conditioned neuron” (CN) for the BCI task.
- The conditioned neuron may or may not be stimulated during photostim. (photostim targets are chosen randomly, so it can happen, but it doesn’t necessarily happen)
- This data is fresh!

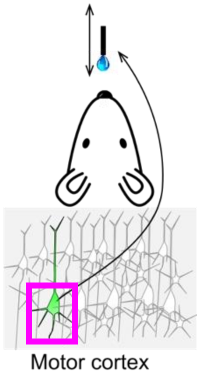
Conditioned neuron becomes ‘tuned’ to trial start

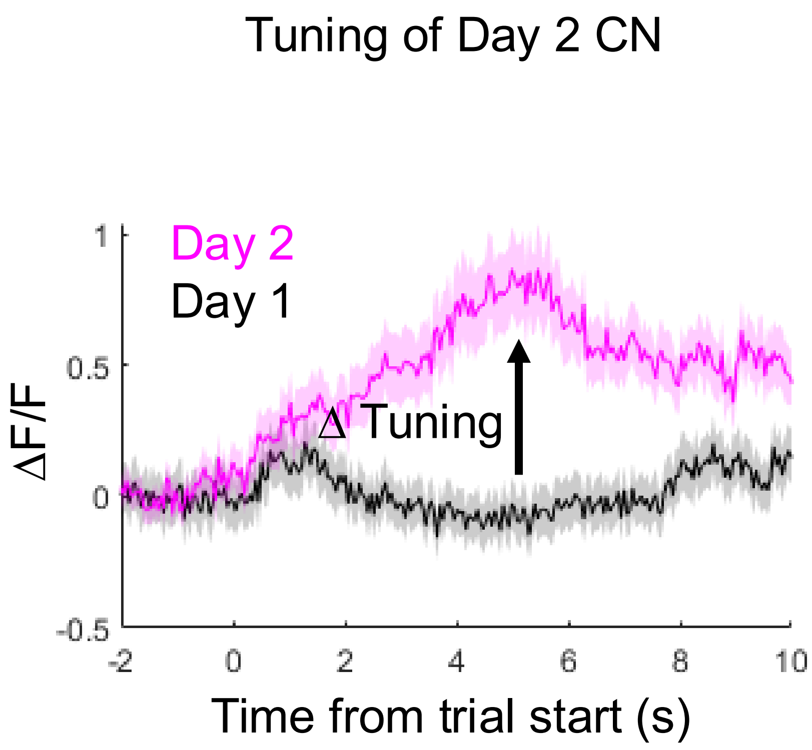


Learning is fast

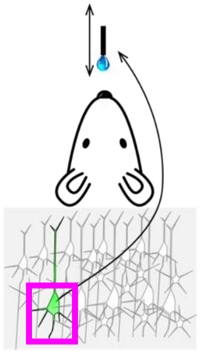


Tuning changes are sparse

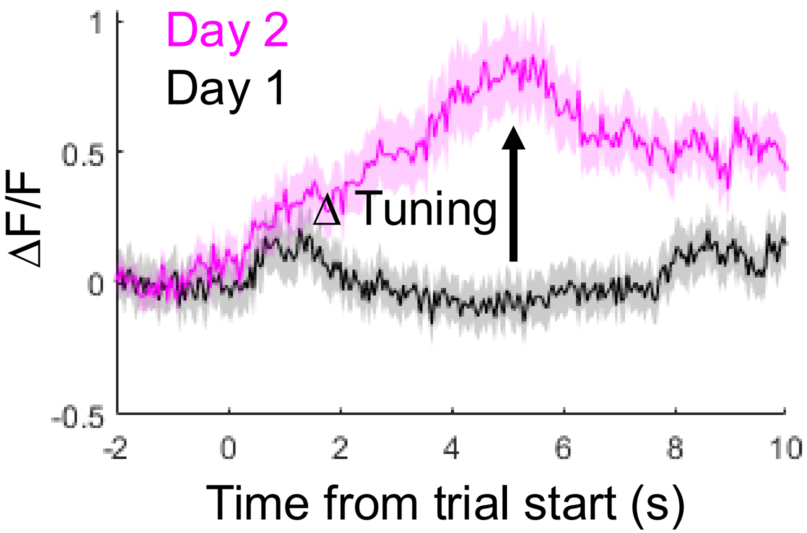




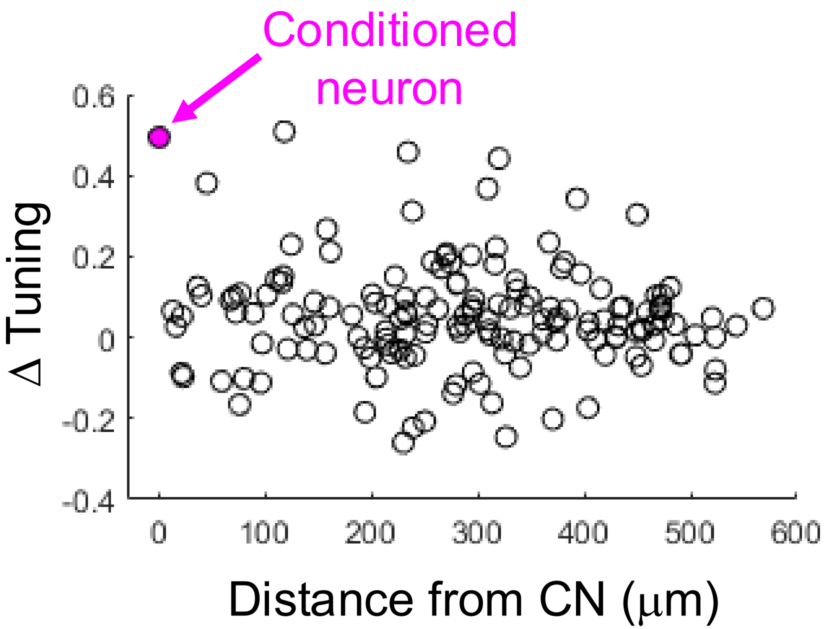
Tuning changes are sparse



Tuning of Day 2 CN



Population change



THANK YOU

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Kayvon Daie
Marton Rosza
Christina Wang
Arielle Leon
Ahad Bawany
Karel Svoboda

Data Demo

Su-Yee Lee