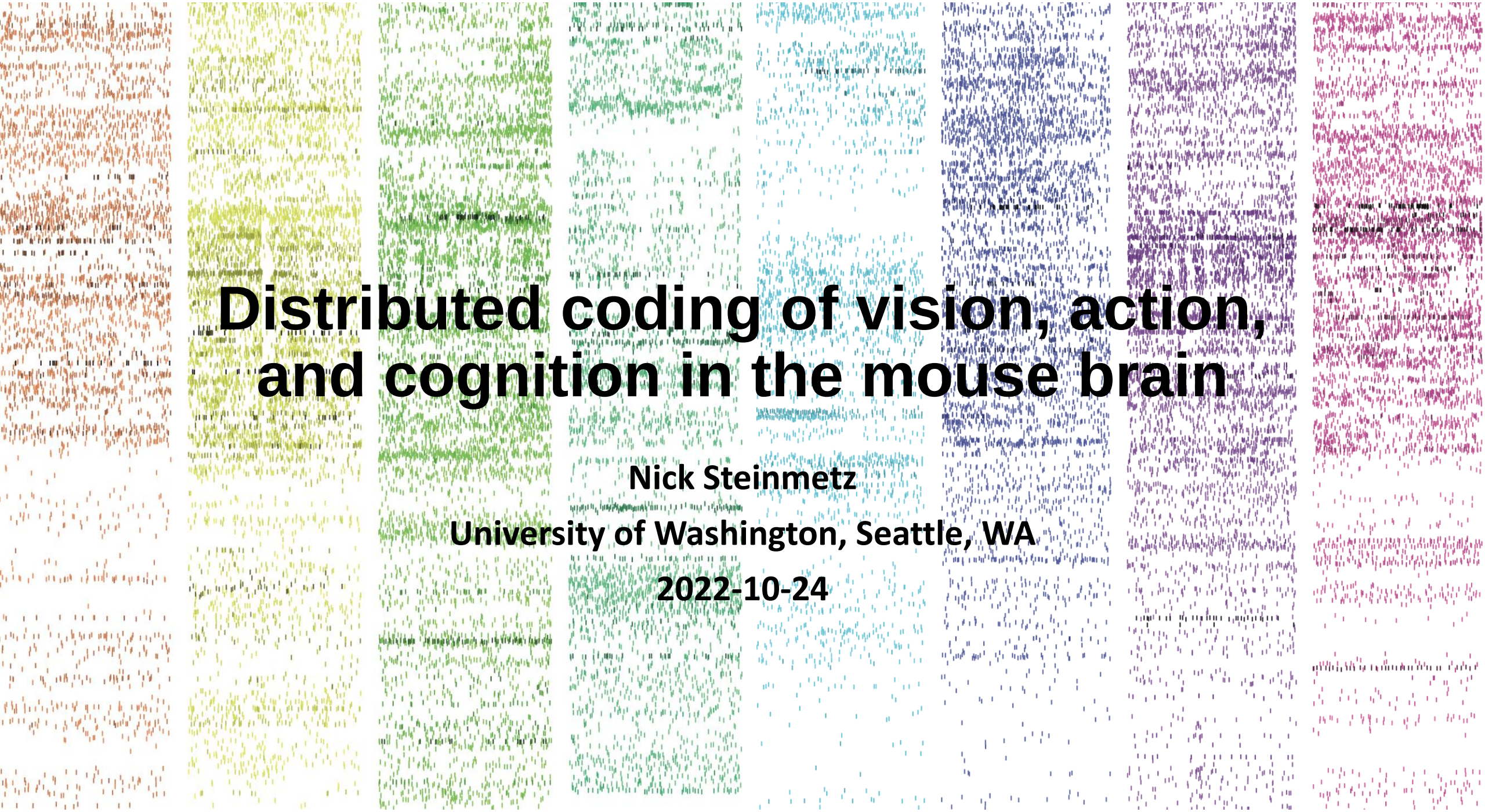


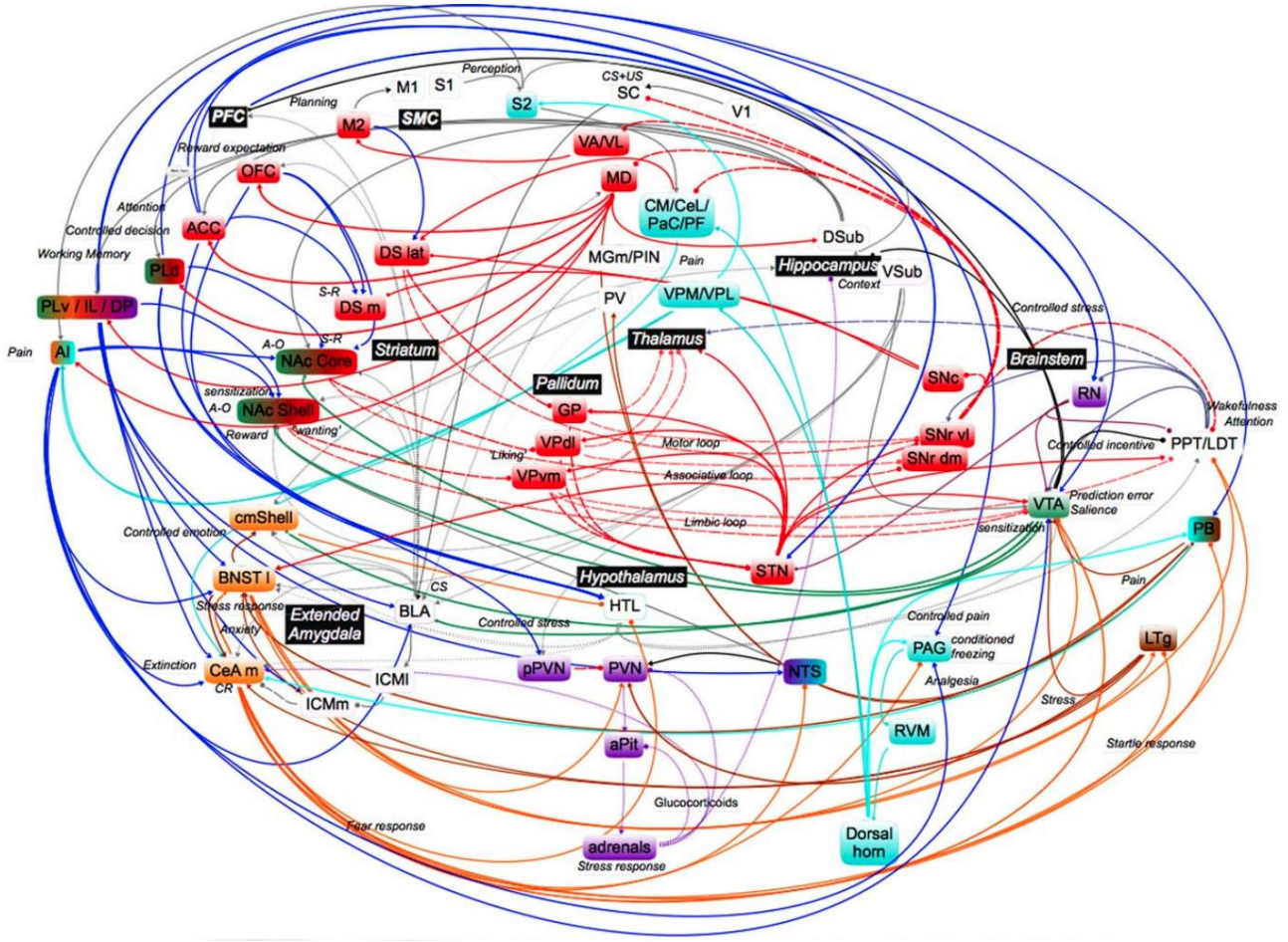
Distributed coding of vision, action, and cognition in the mouse brain

Nick Steinmetz

University of Washington, Seattle, WA

2022-10-24

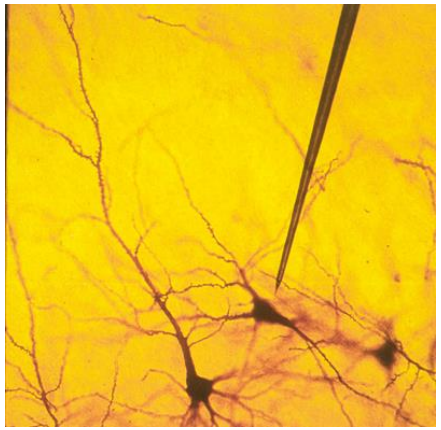
Recurrent loops between structures can mix signals and create complex dynamics



George & Koob 2010

What we need

- ***Extensive*** recording of neuronal activity
- With access to both ***deep and superficial*** structures
- At ***single neuron*** spatial resolution
- And ***millisecond*** temporal resolution



Dowben & Rose, 1953

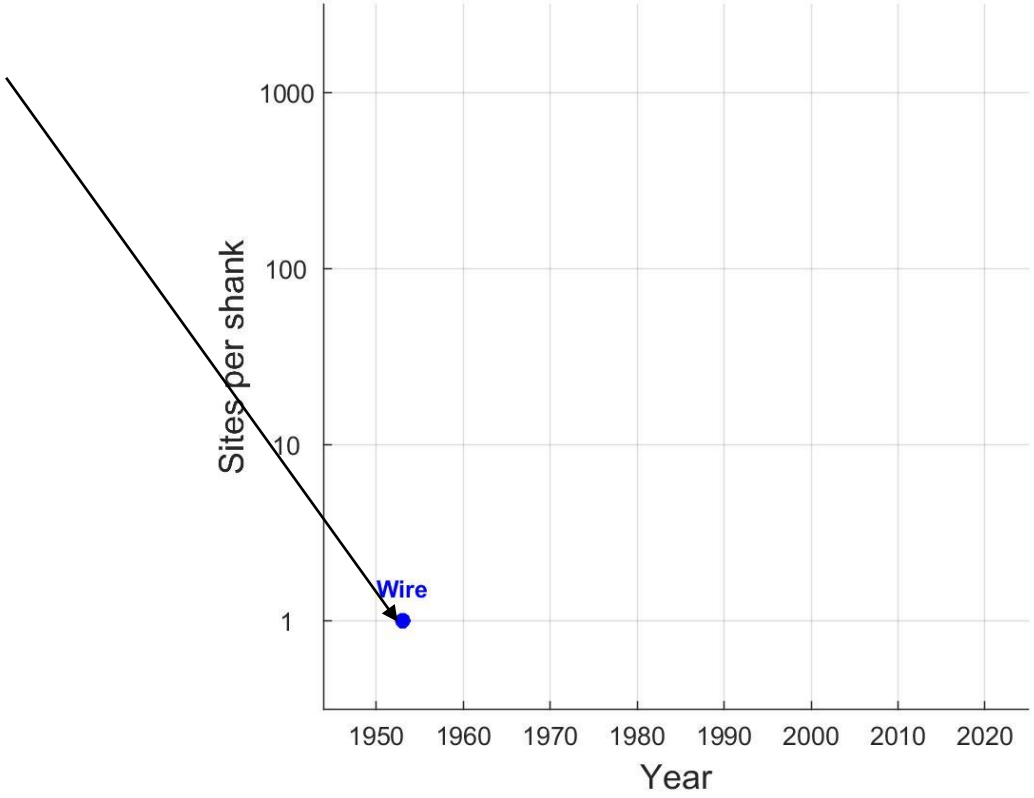
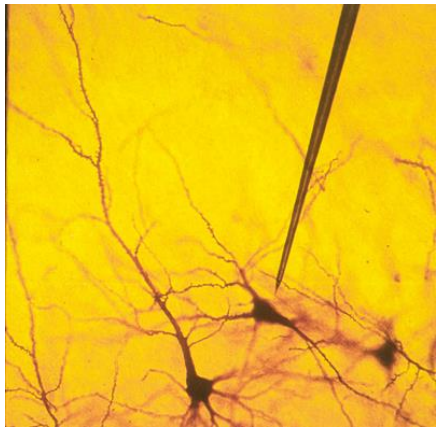
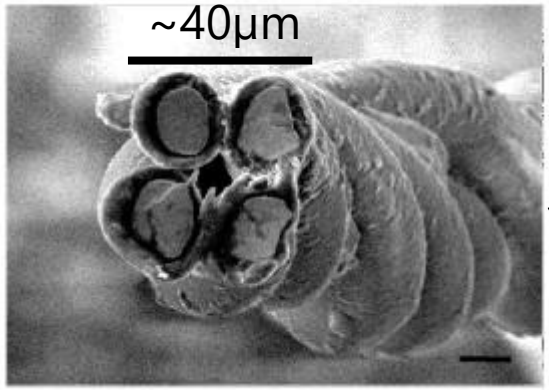


Figure by Matteo Carandini



Dowben & Rose, 1953



Recce & O'Keefe, 1989

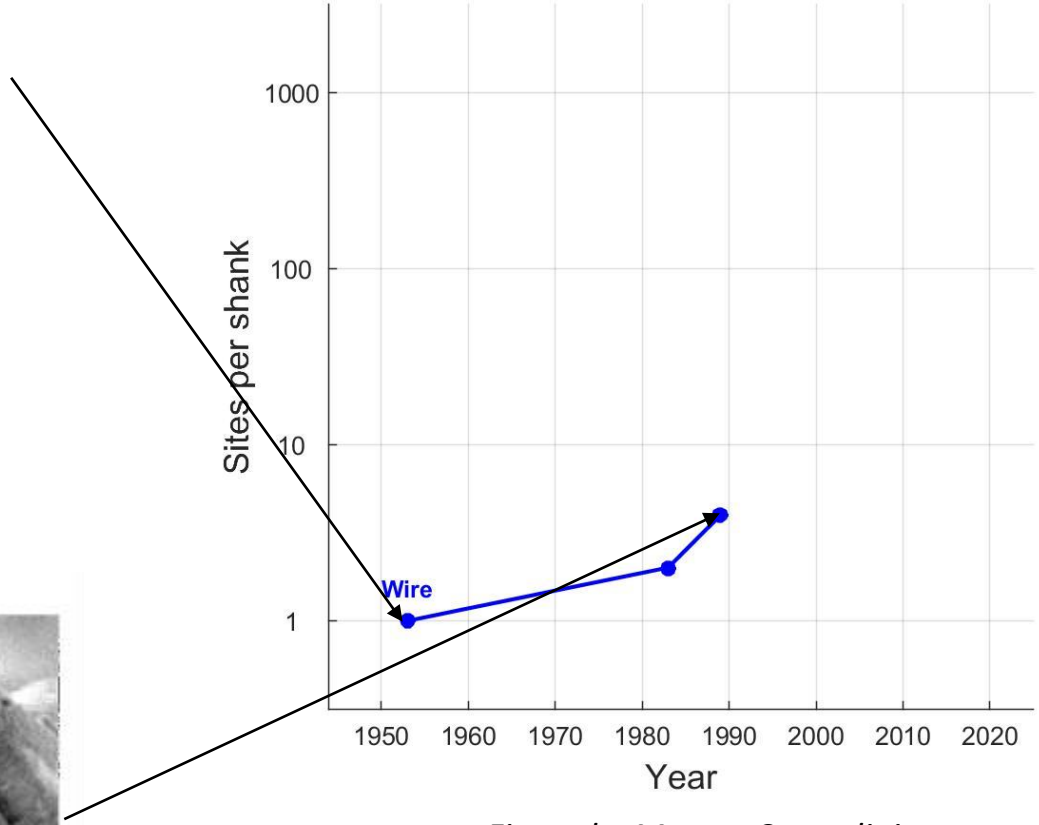
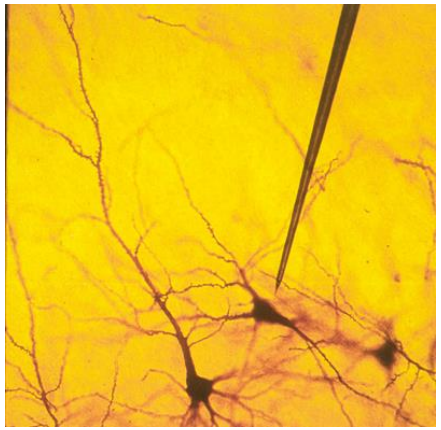


Figure by Matteo Carandini



Dowben & Rose, 1953

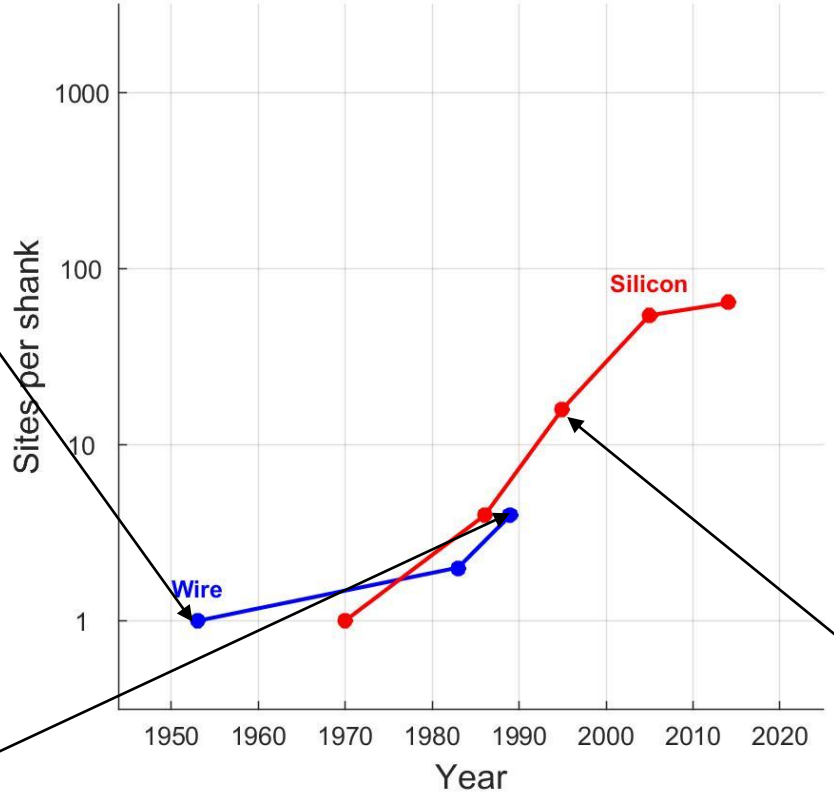
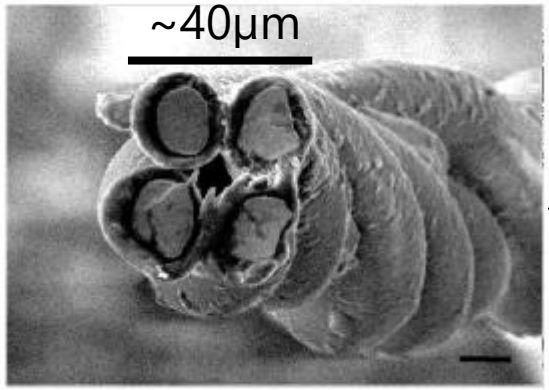
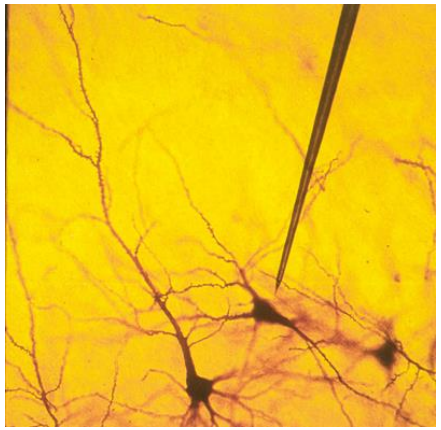


Figure by Matteo Carandini



Recce & O'Keefe, 1989

Ylinen et al. 1995



Dowben & Rose, 1953

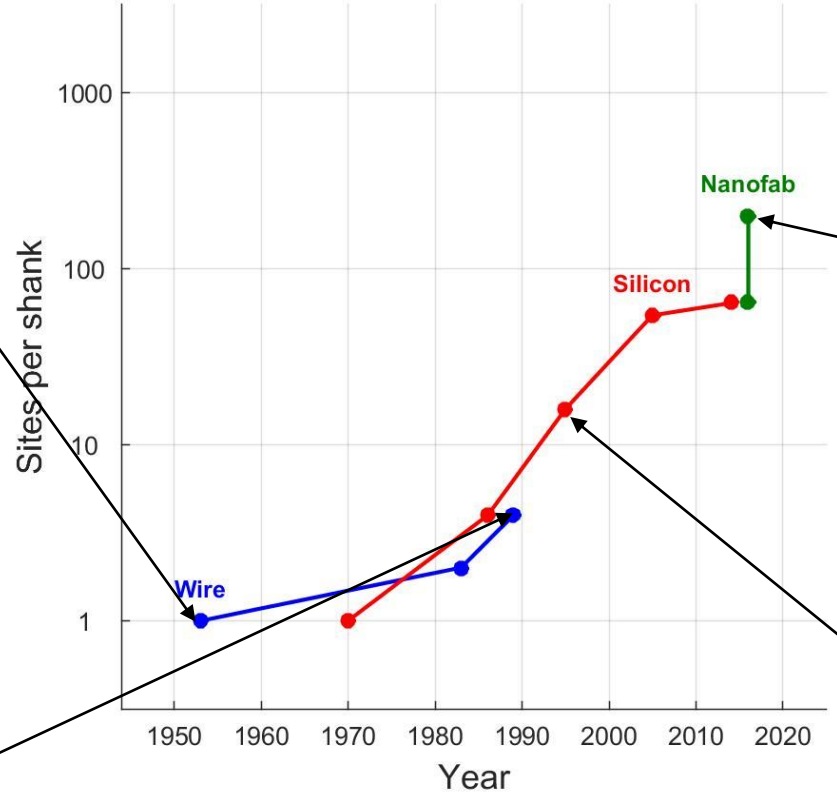
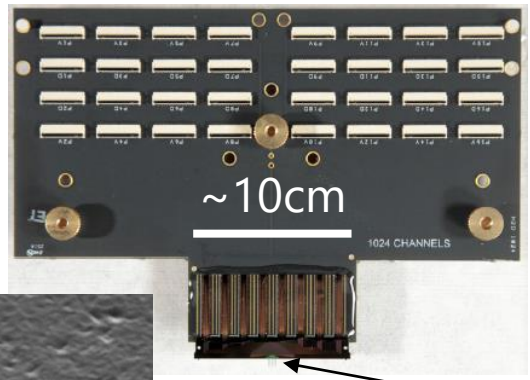
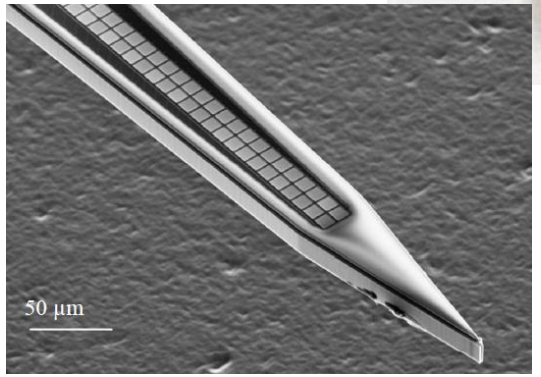


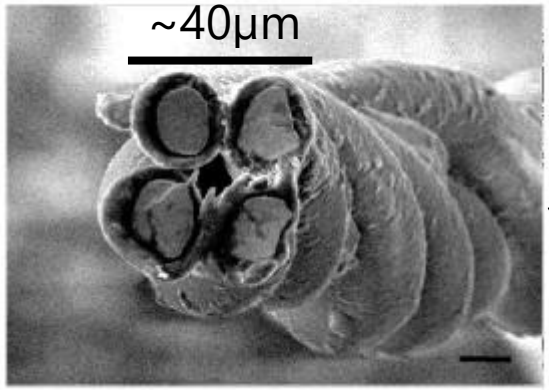
Figure by Matteo Carandini



Probe here!

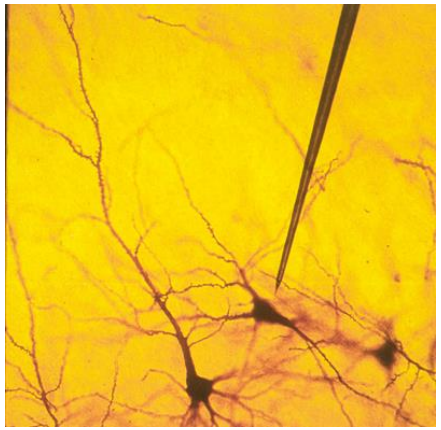


Scholvin et al 2016



Recce & O'Keefe, 1989

Ylinen et al. 1995



Dowben & Rose, 1953

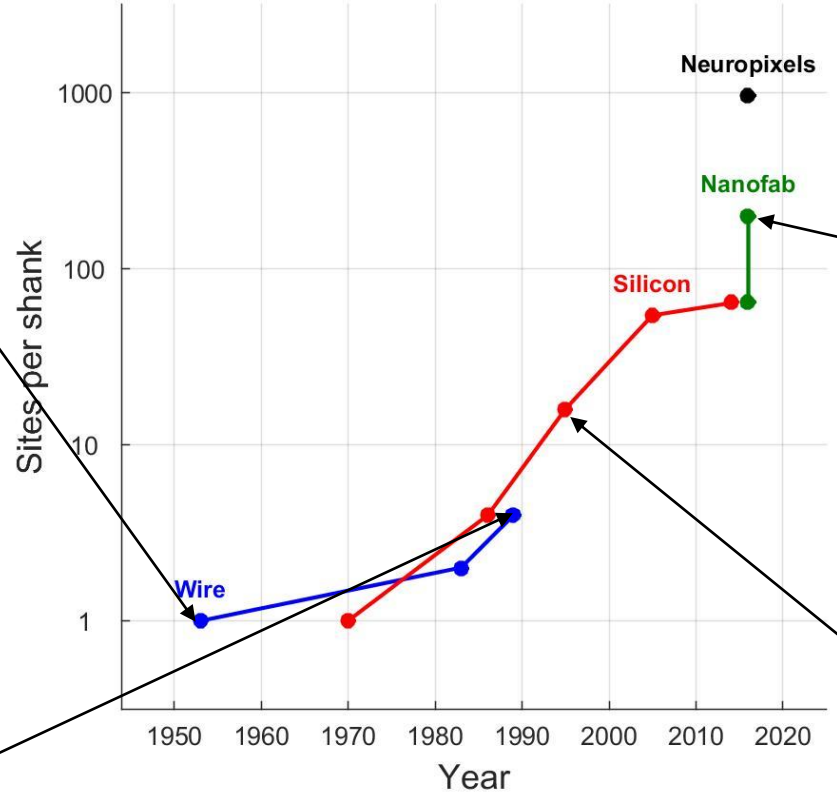
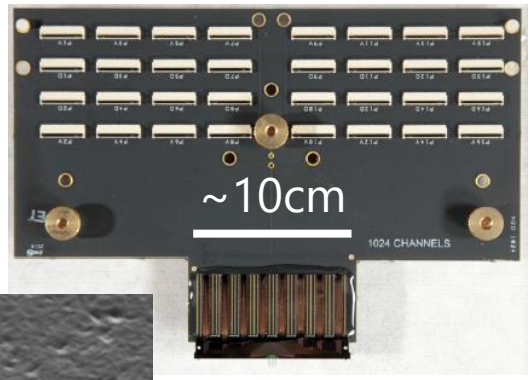
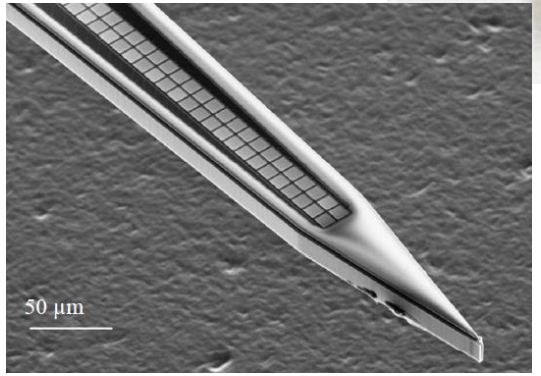
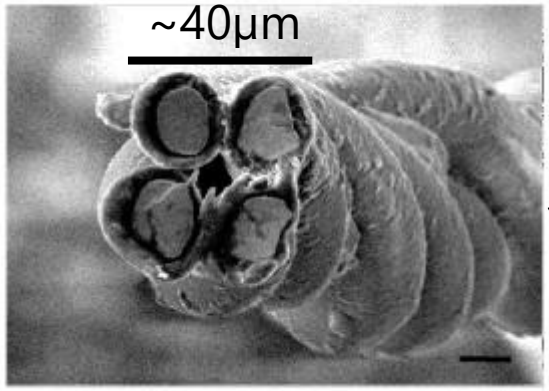


Figure by Matteo Carandini





Scholvin et al 2016

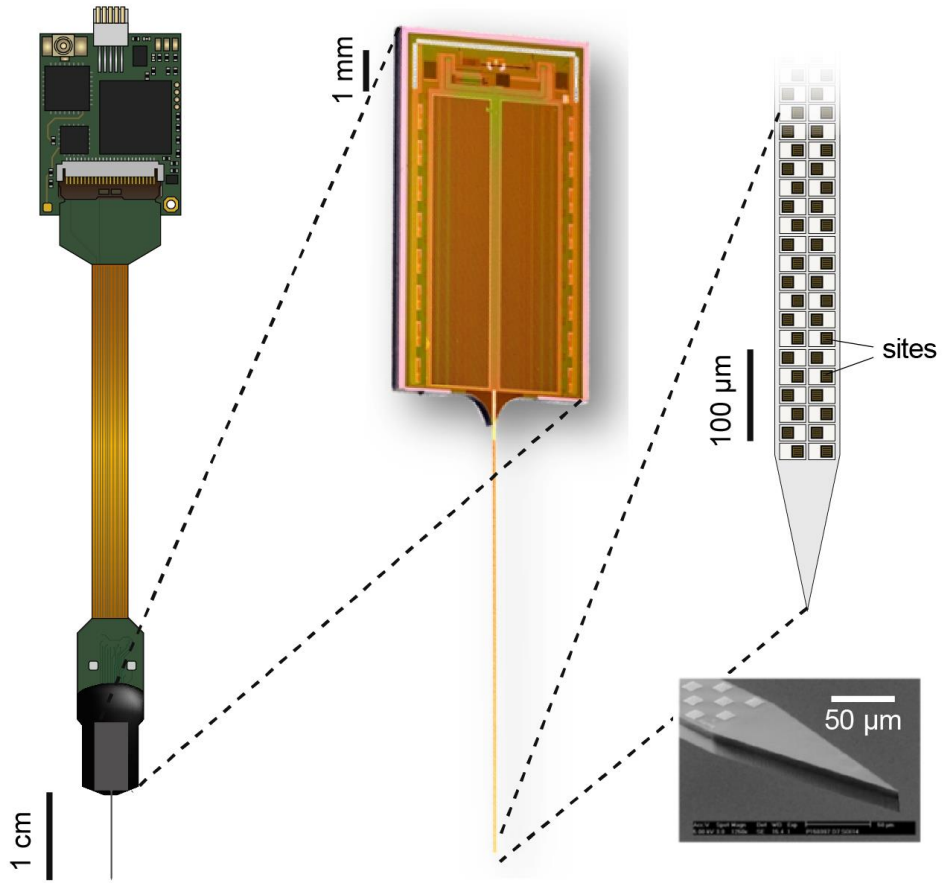


Recce & O'Keefe, 1989

Ylinen et al. 1995

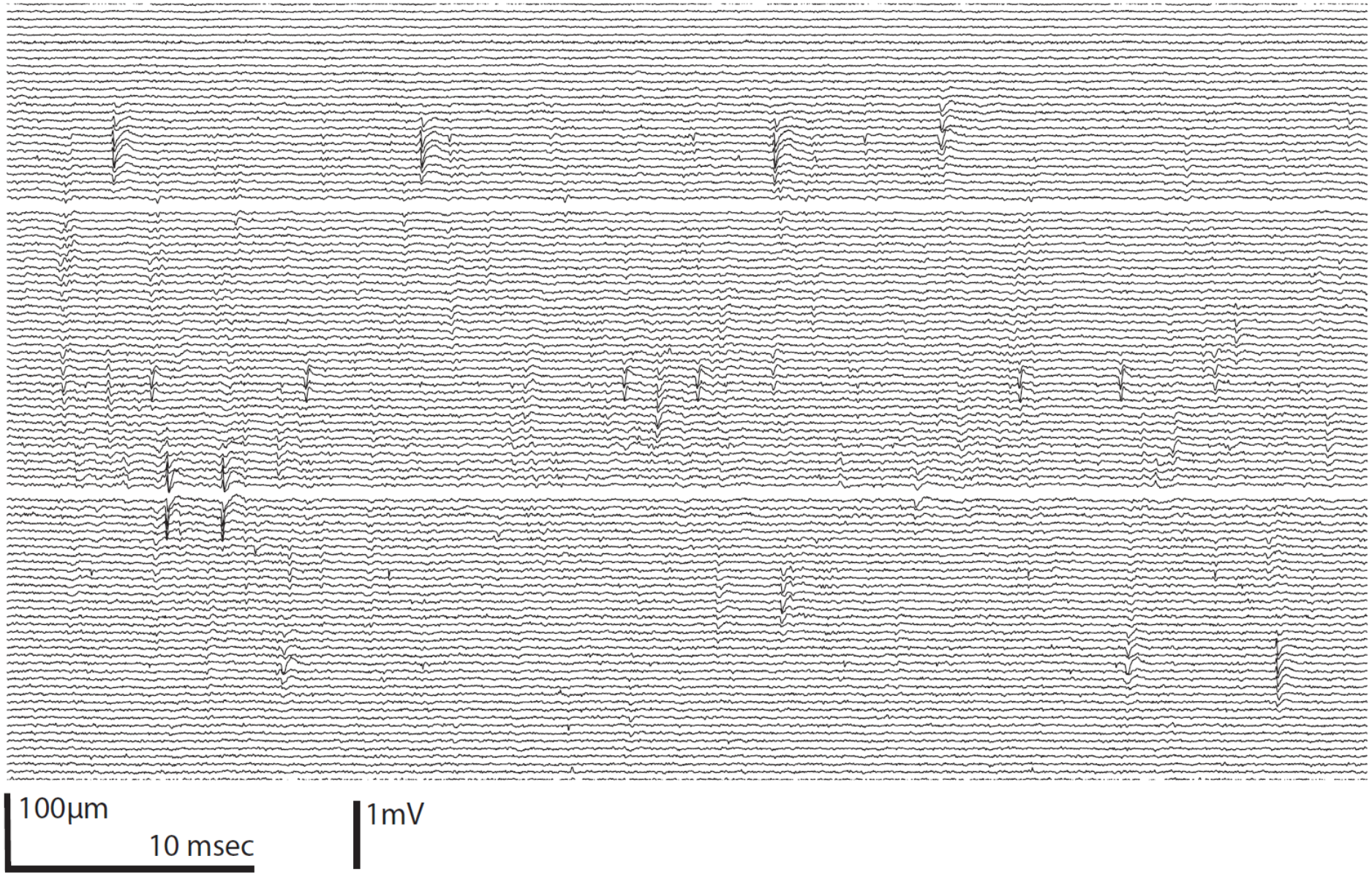
Neuropixels 1.0 probes enabled large-scale recording

Led by Tim Harris, Janelia Research Campus

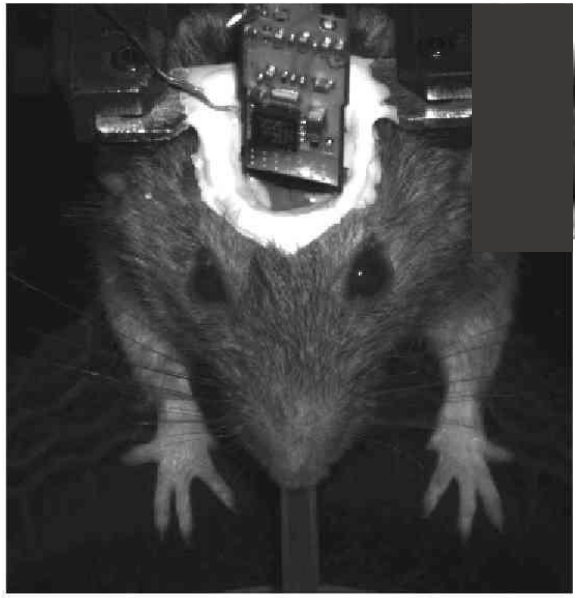


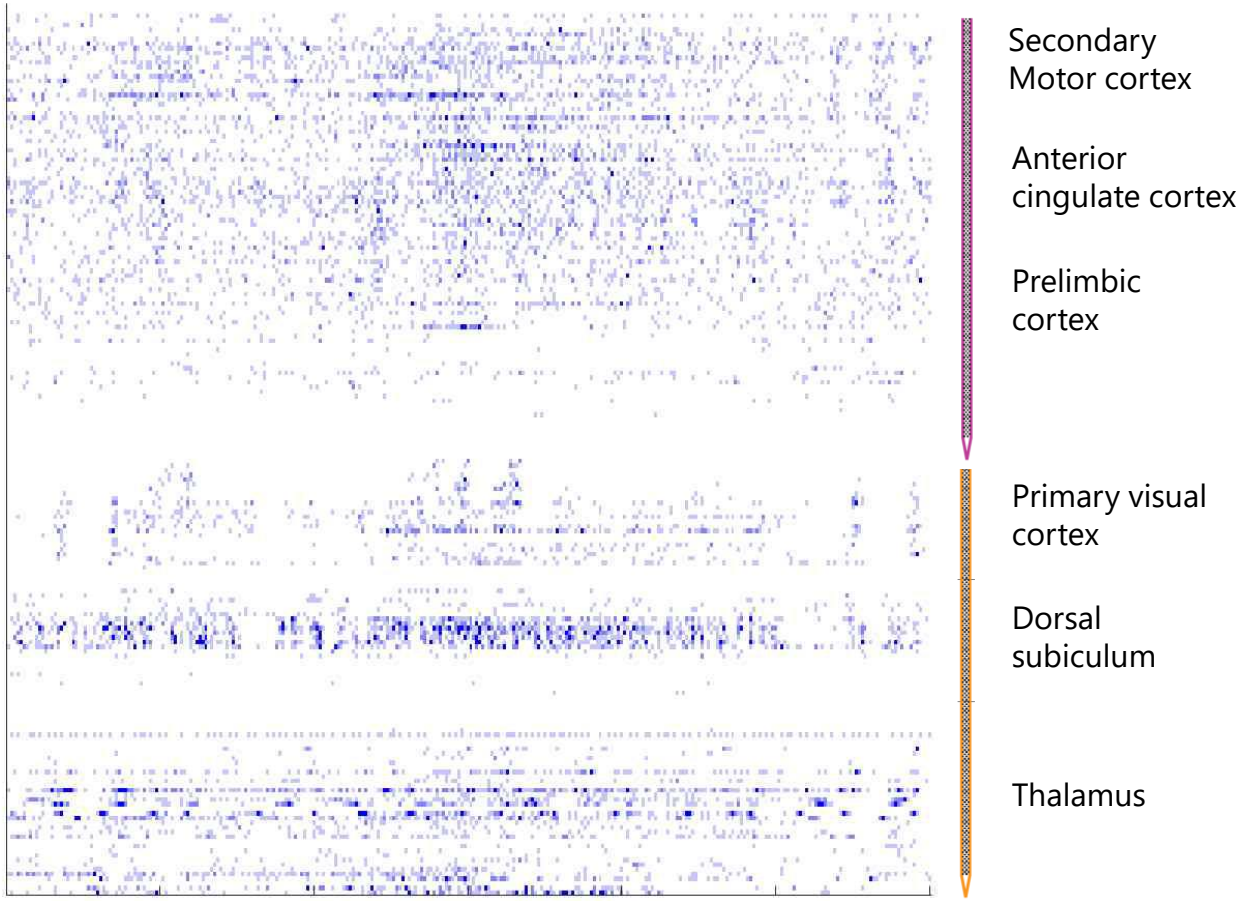
Jun*, Steinmetz*, Siegle*, Denman*, Bauza*, Barbarits*, Lee*, et al. *Nature* 2017

Raw data is very high quality



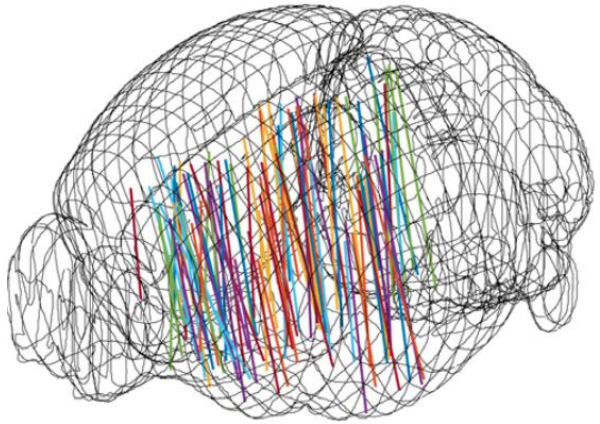
Neuropixels recordings during a visual detection and discrimination task



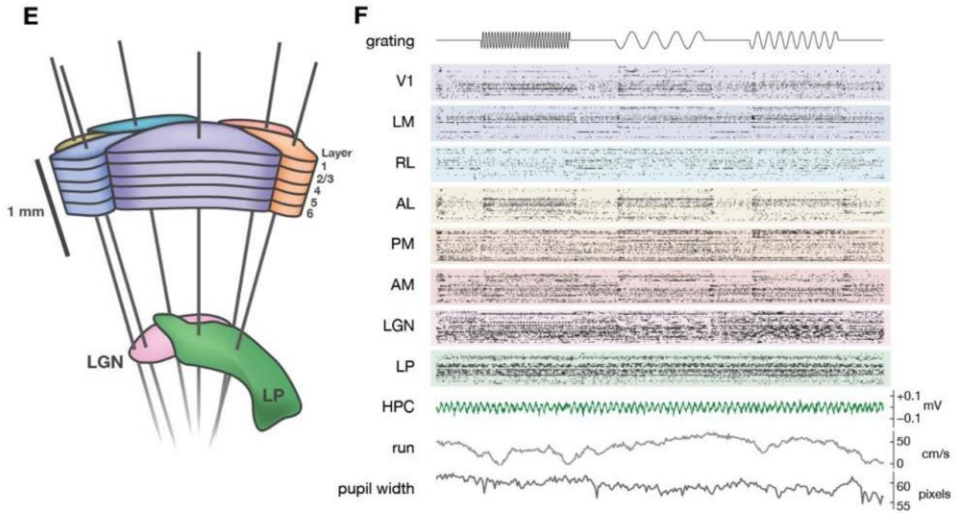


Steinmetz, Zatka-Haas, Carandini, Harris *Nature* 2019
Data freely available, see www.steinmetzlab.net/shared

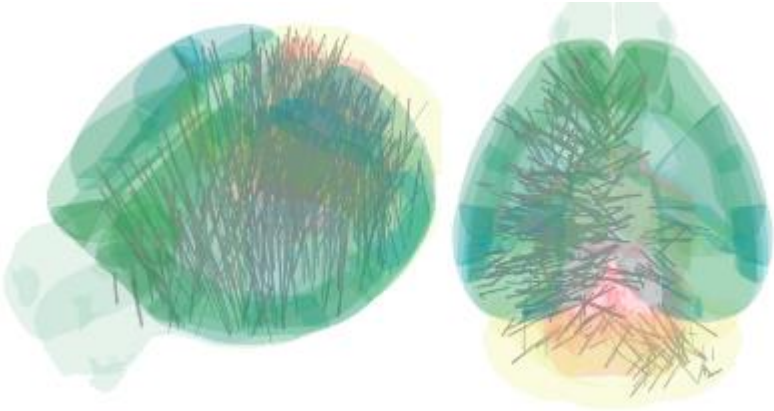
Other successful applications



Allen et al. *Science* 2019

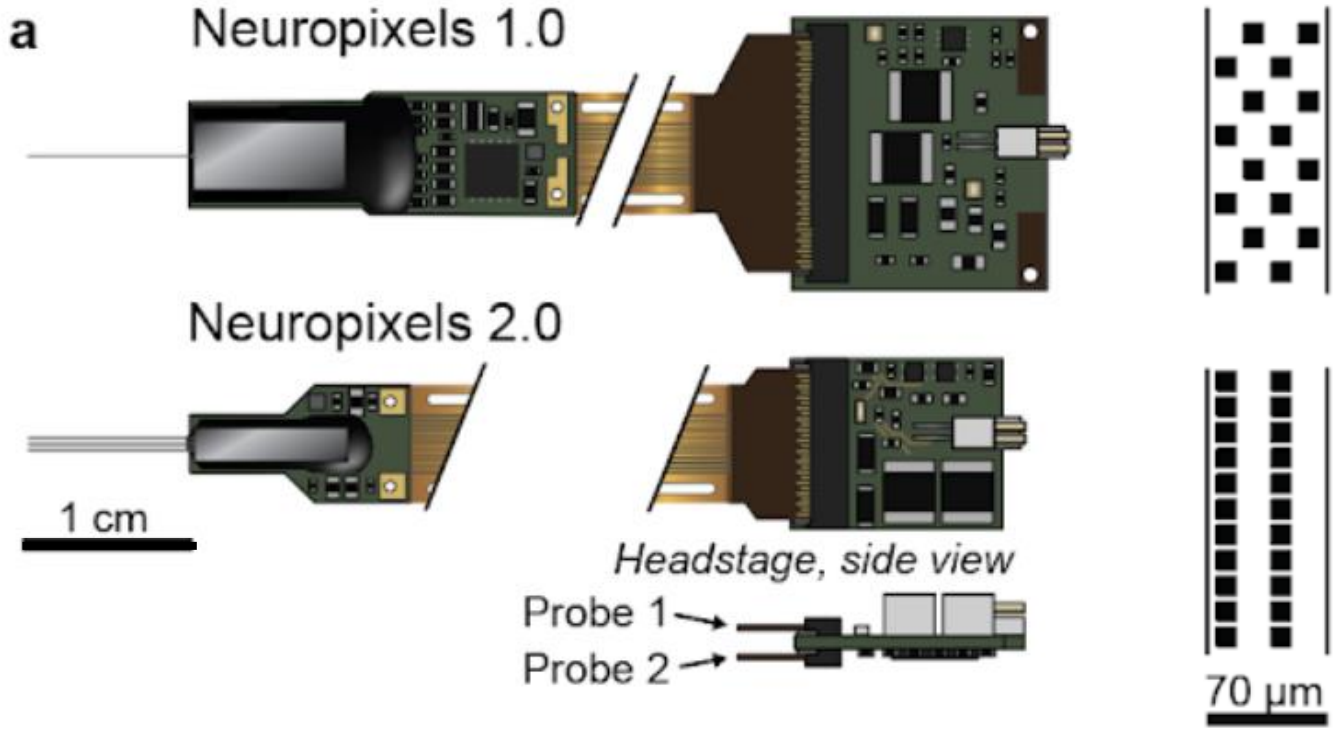


Siegle, Jia, et al. *Nature* 2020

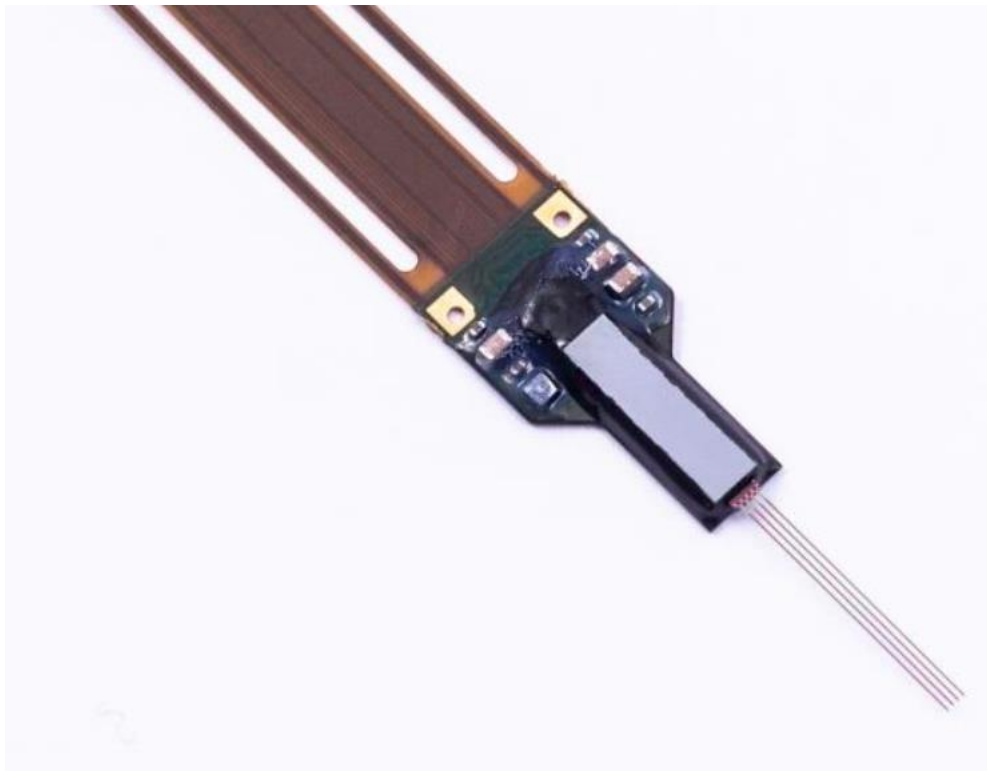


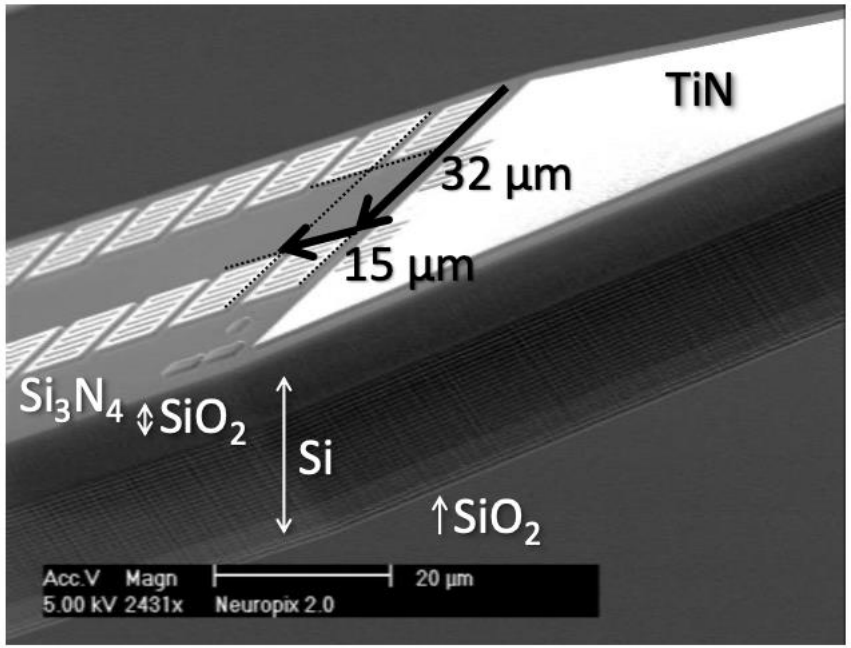
The International Brain Lab

Neuropixels 2.0 probes are designed for long-term, stable recordings in mice (still large-scale)

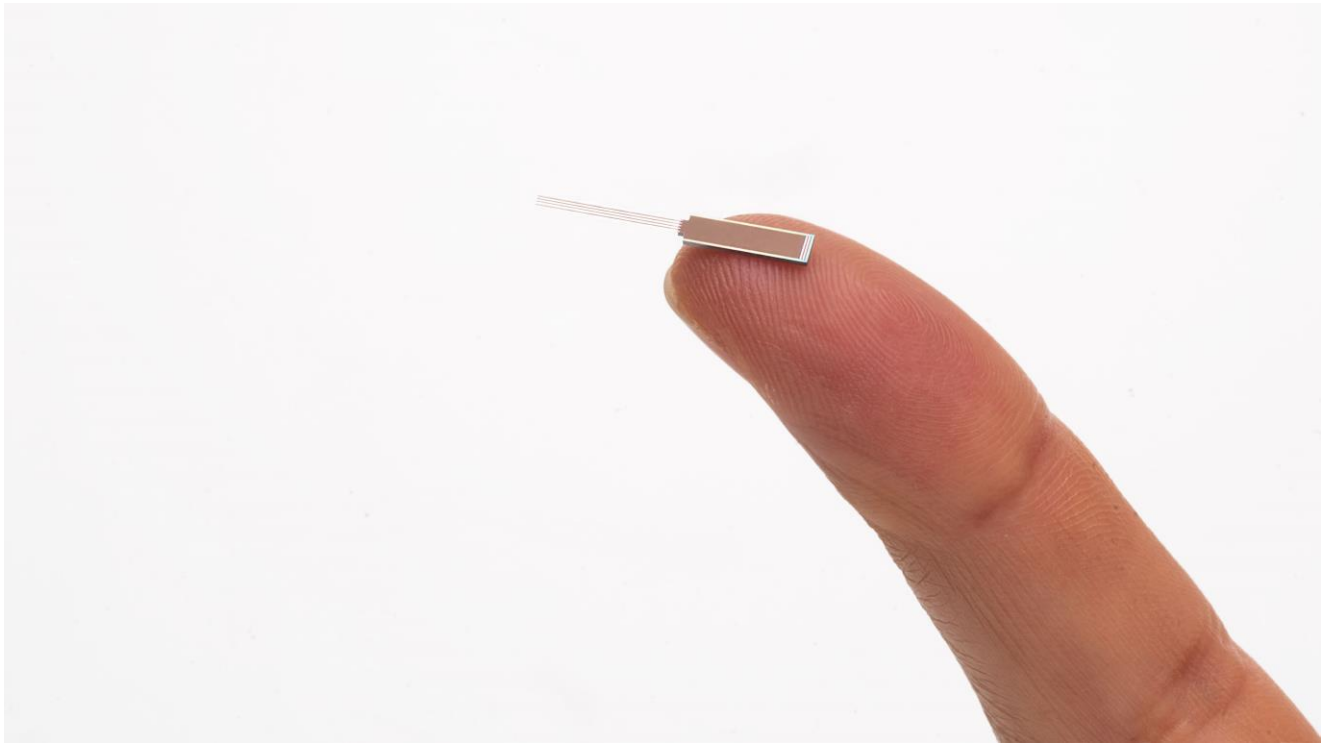


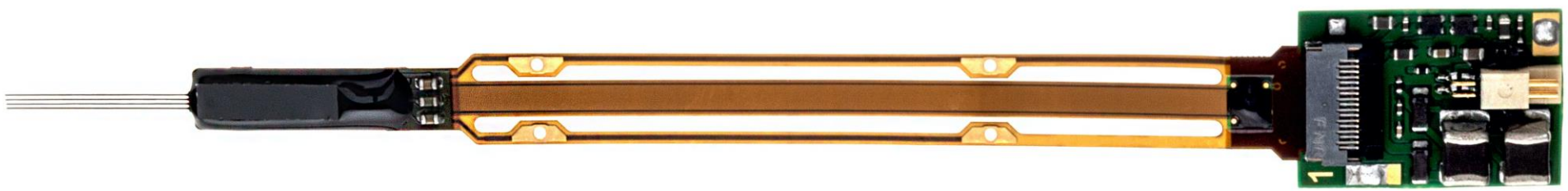
Steinmetz*, Aydin*, Lebedeva*, Okun*, Pachitariu*, et al.
Science 2021




TiN
32 µm
15 µm
Si_3N_4
SiO_2
Si
SiO_2
Acc.V Magn
5.00 kV 2431x
Neuropix 2.0
20 µm

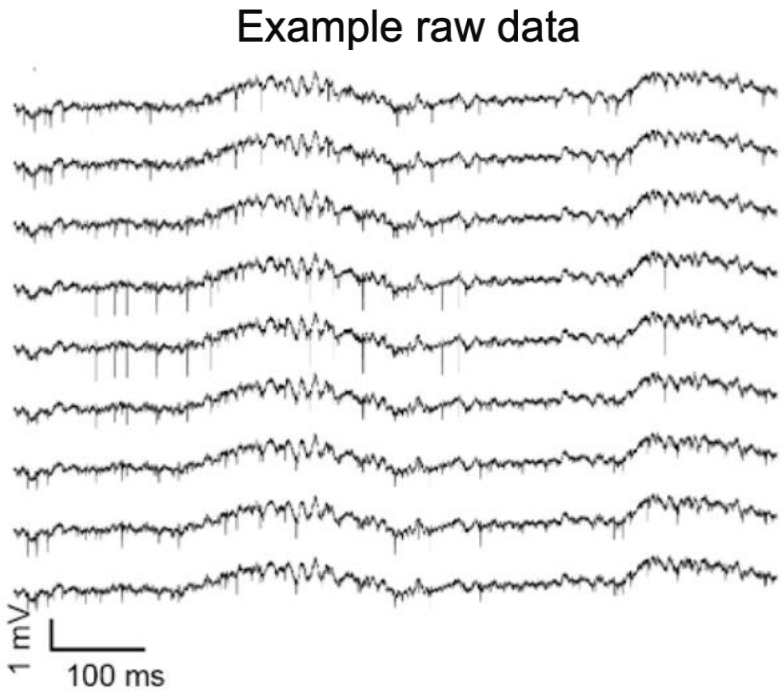
imec

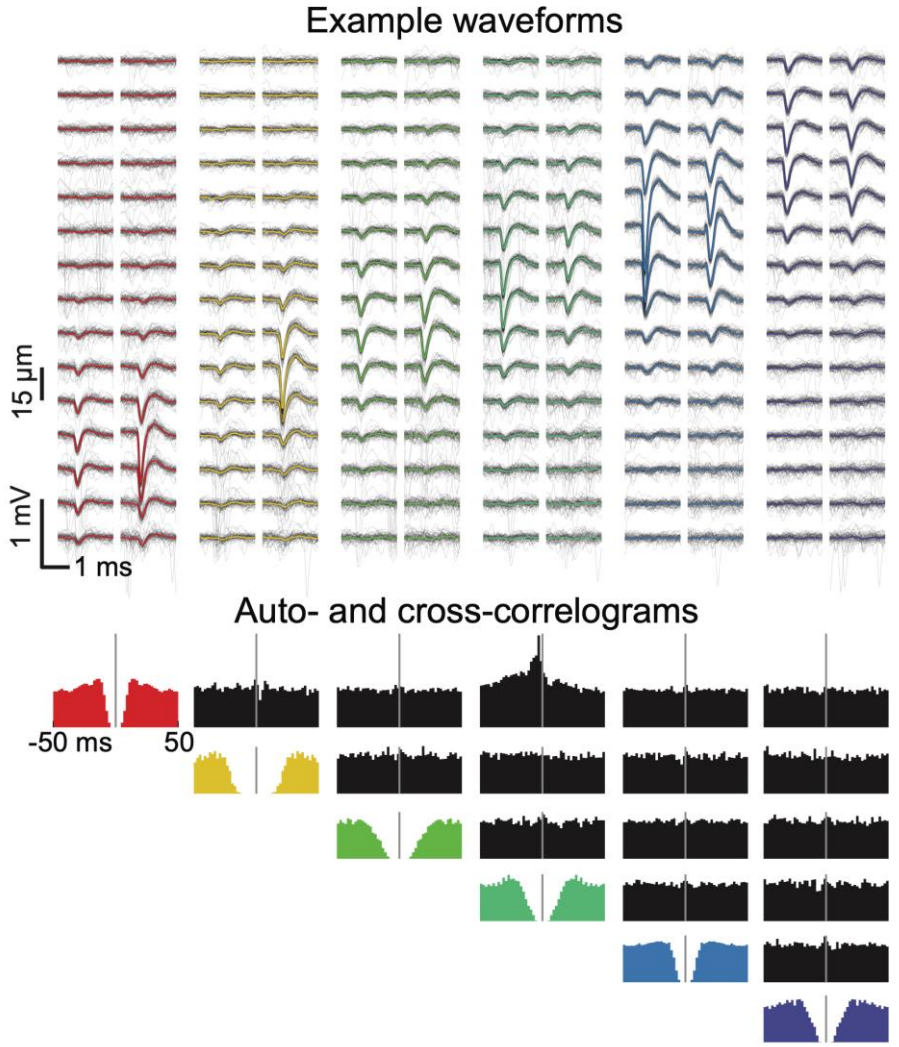




imec

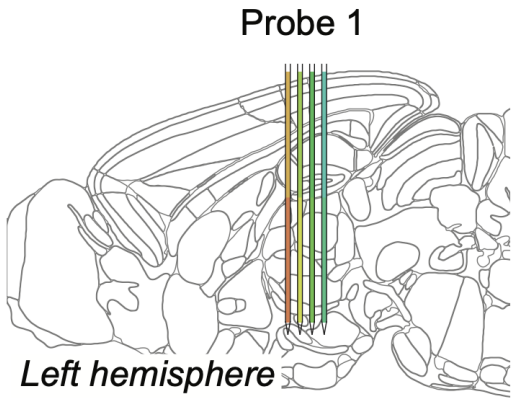
NP 2.0 data quality is still high

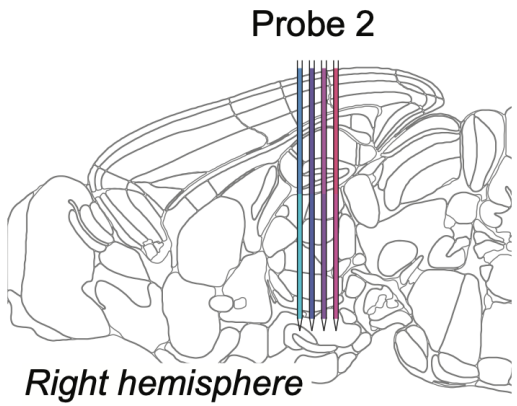


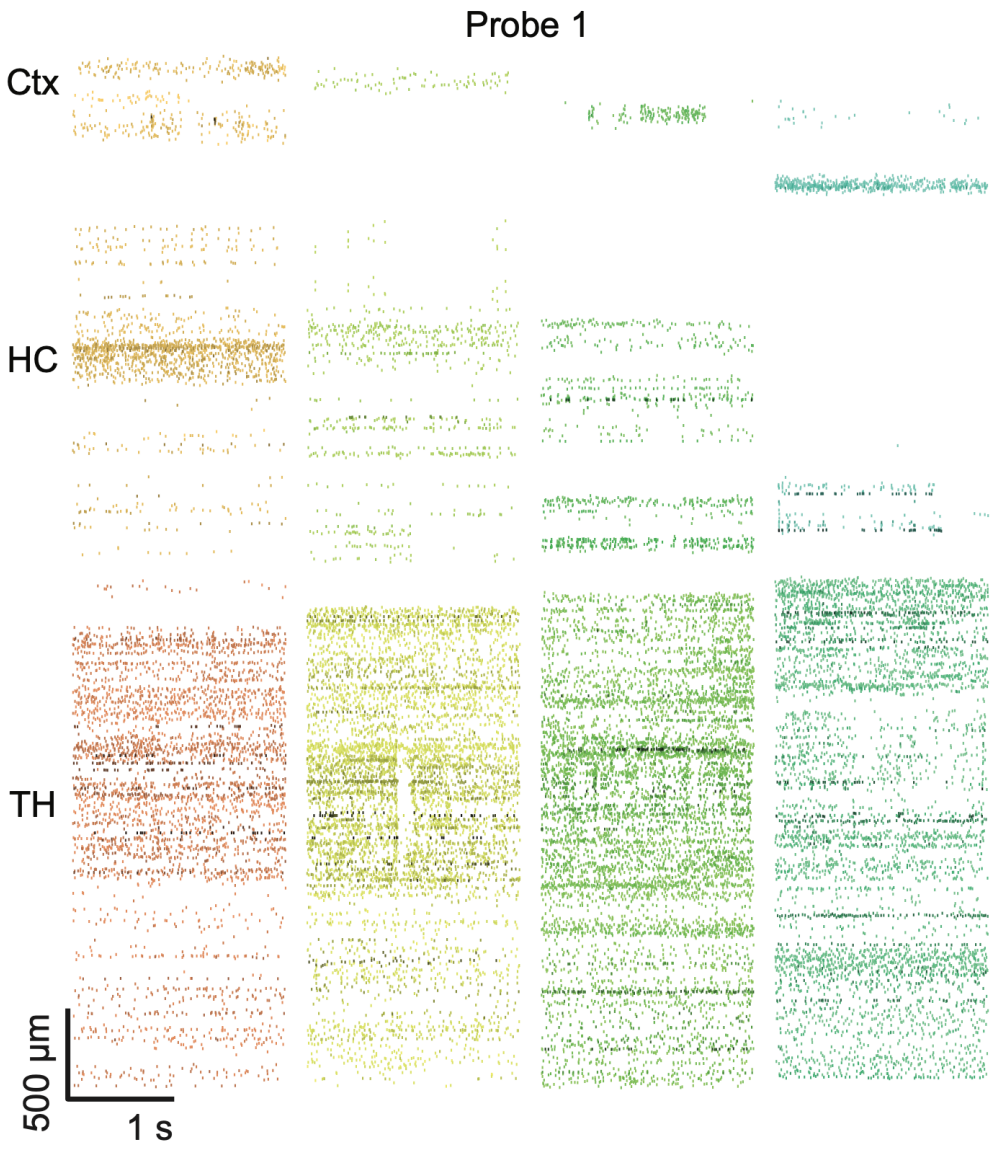


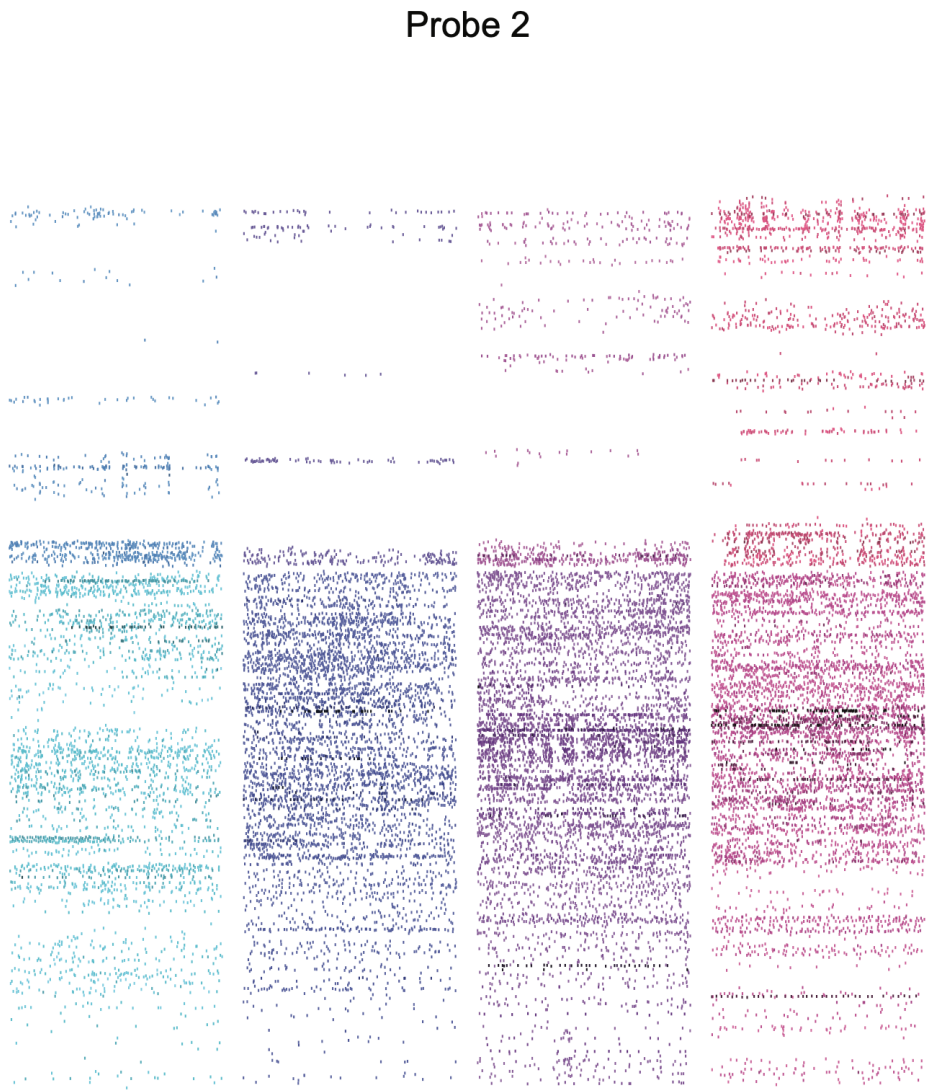
Neuronal spiking from 6144 sites (of 10,240 available) in a freely-moving mouse

Recorded 768 sites at a time over 8 sequential recordings



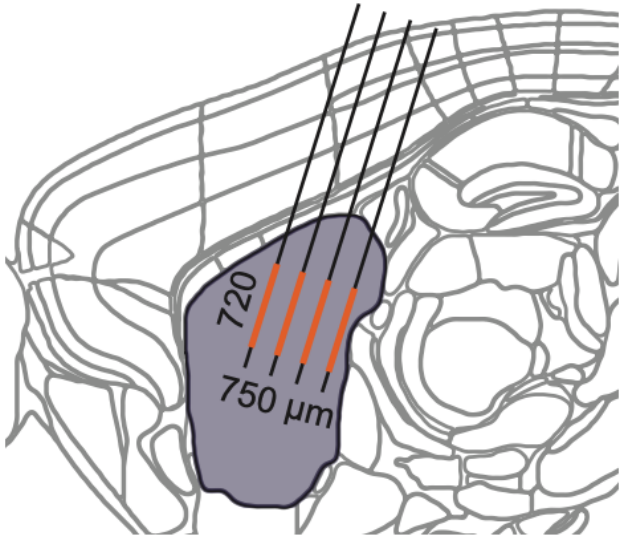


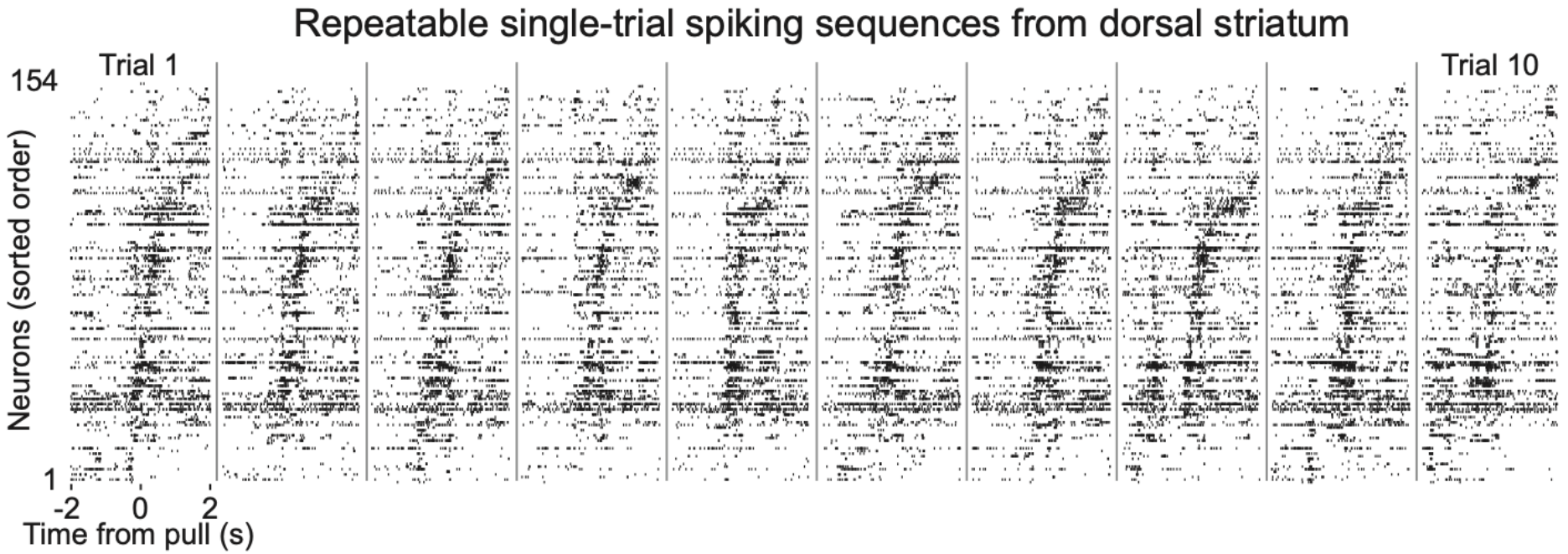




Data from Cagatay Aydin

NP 2.0 densely samples a 2D plane





Data from Junchol Park and Josh Dudman

Neuropixels 2.0 summary

- Neuropixels CMOS probes enable large-scale electrophysiology
- Neuropixels 2.0 are miniaturized with 5,000 sites on four shanks
- They are optimized for stable, long-term recordings
- With new algorithms, we can correct for brain movement on short and long timescales

Detection

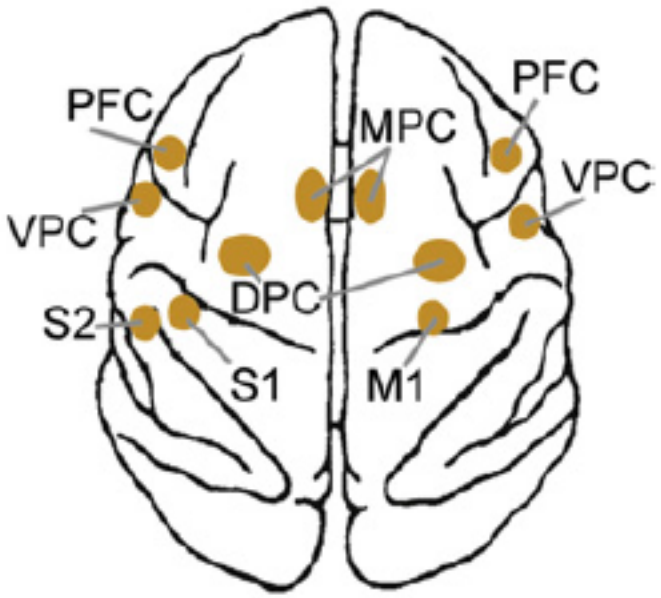
- Why are some stimuli perceived and others are not?

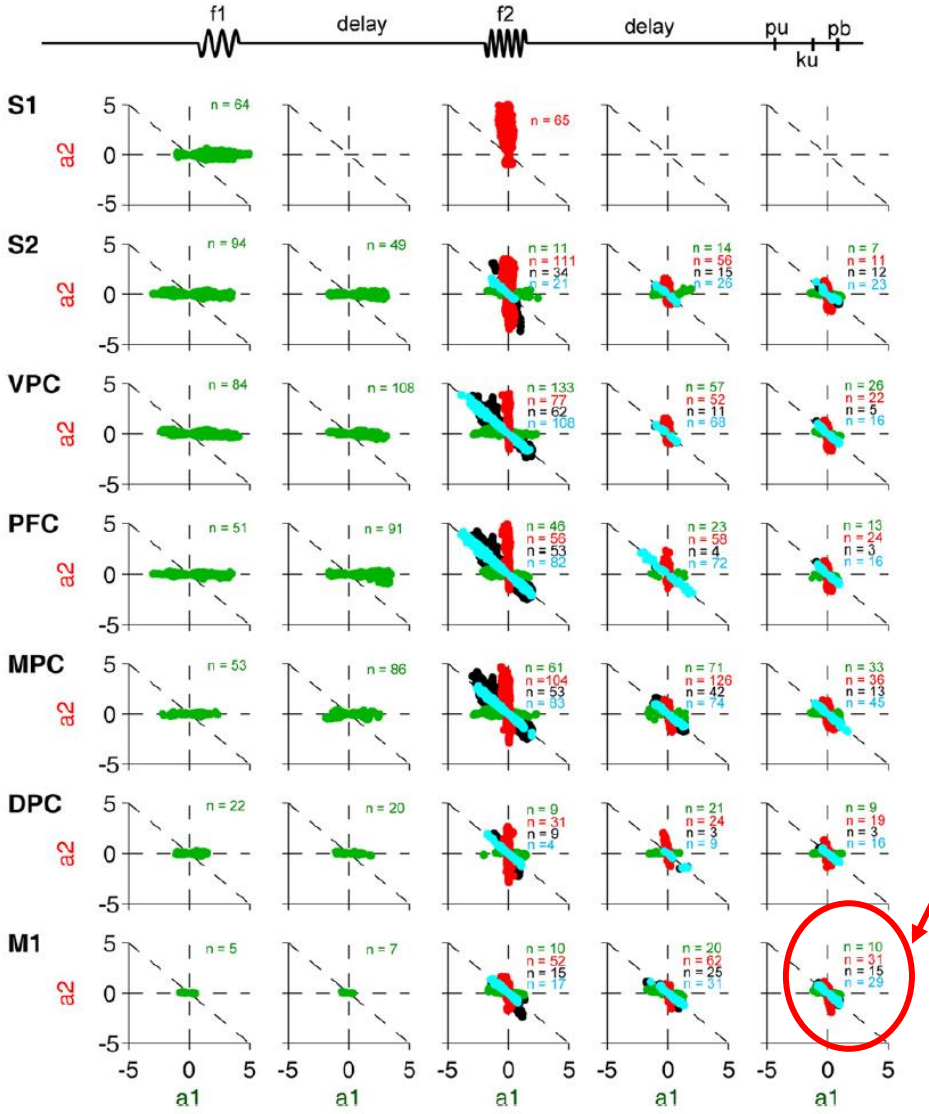
Discrimination

- How are multiple pieces of sensory evidence combined to make a choice?

Are the correlates of these processes distributed or localized?

Classic work showed diverse responses across cortical areas





Even M1 has many neurons that continue to code each individual stimulus!

Hernandez … Romo 2010

A visual contrast detection and discrimination task for mice

Peter Zatka-Haas

Matteo Carandini

Kenneth Harris

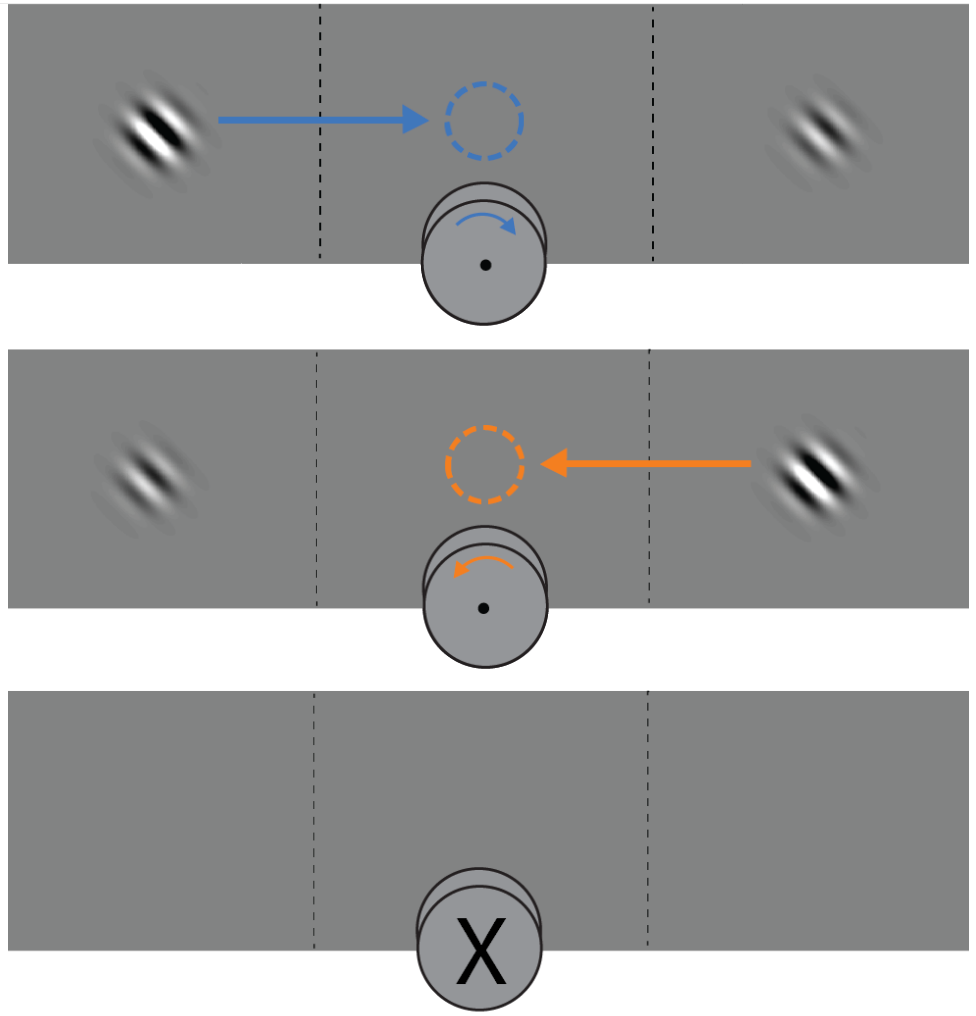
Burgess*, Lak*, Steinmetz*, Zatka-Haas* et al,
Cell Reports 2017

A visual contrast detection and discrimination task for mice

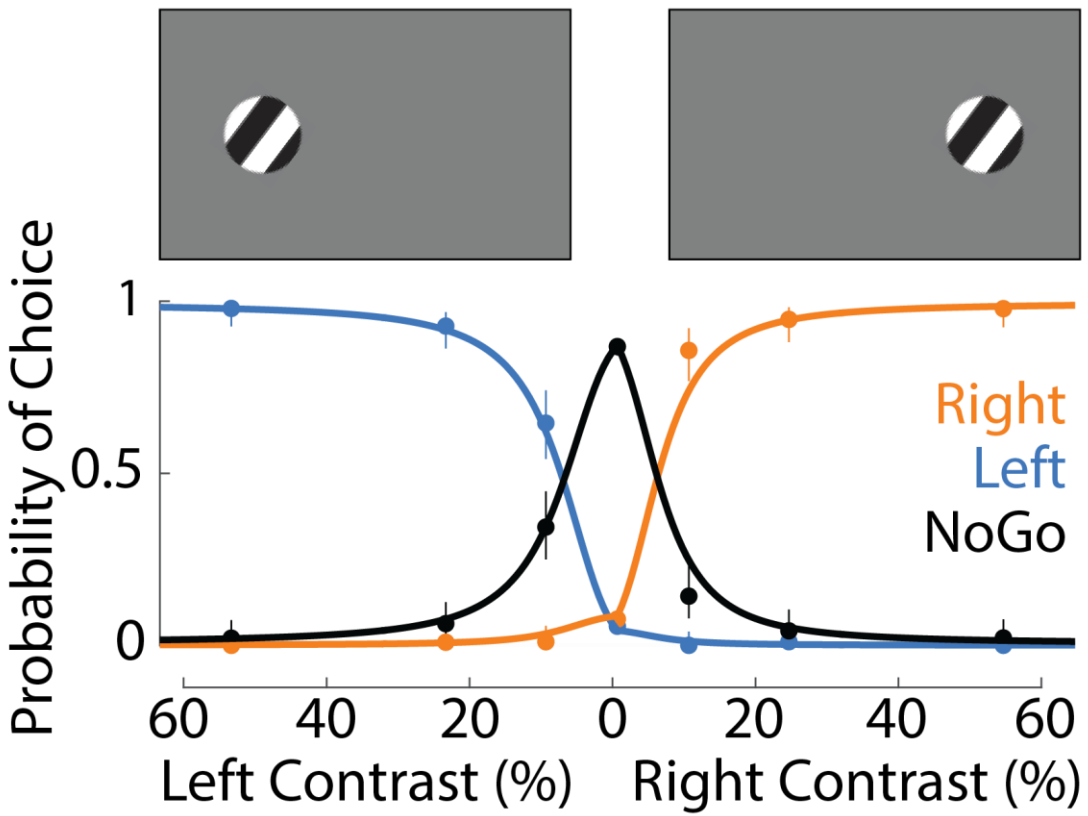
Choose left

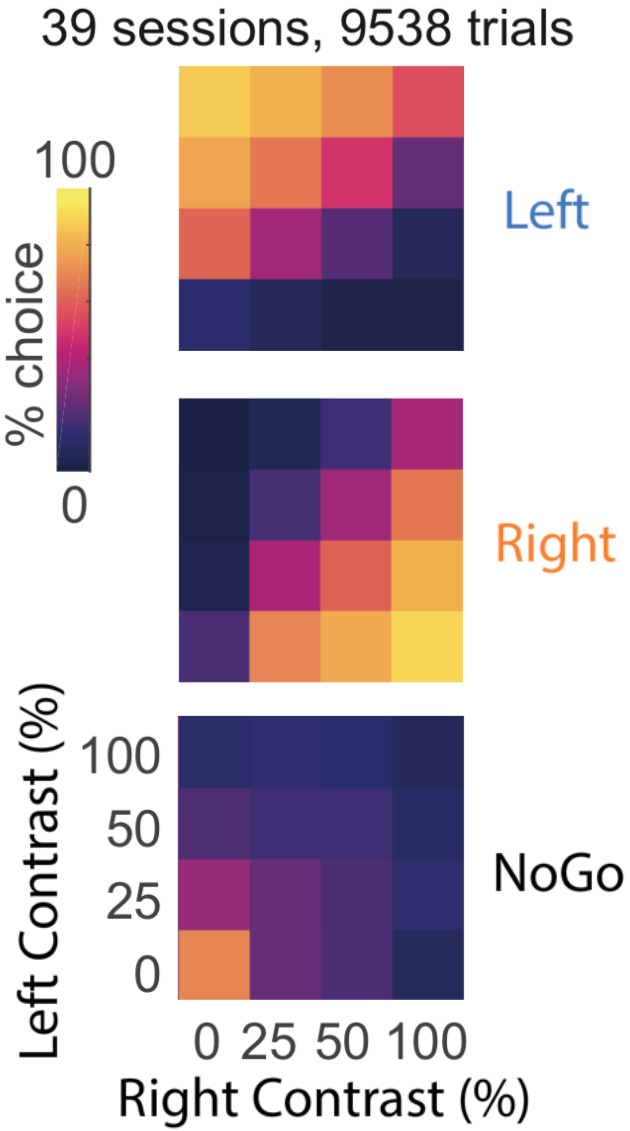
Choose right

Choose nogo

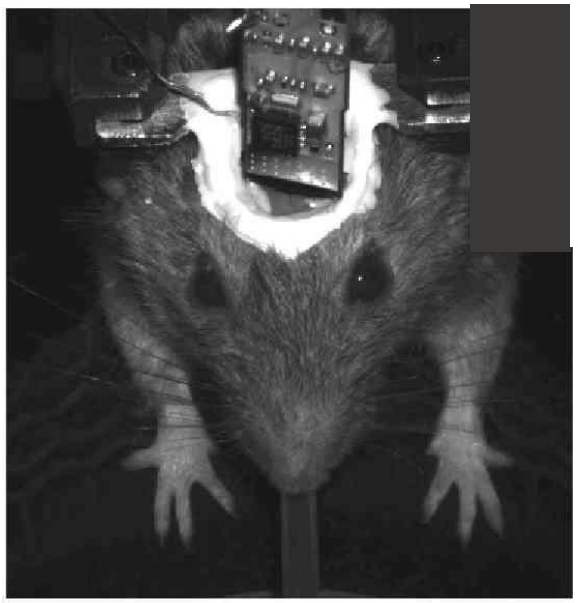


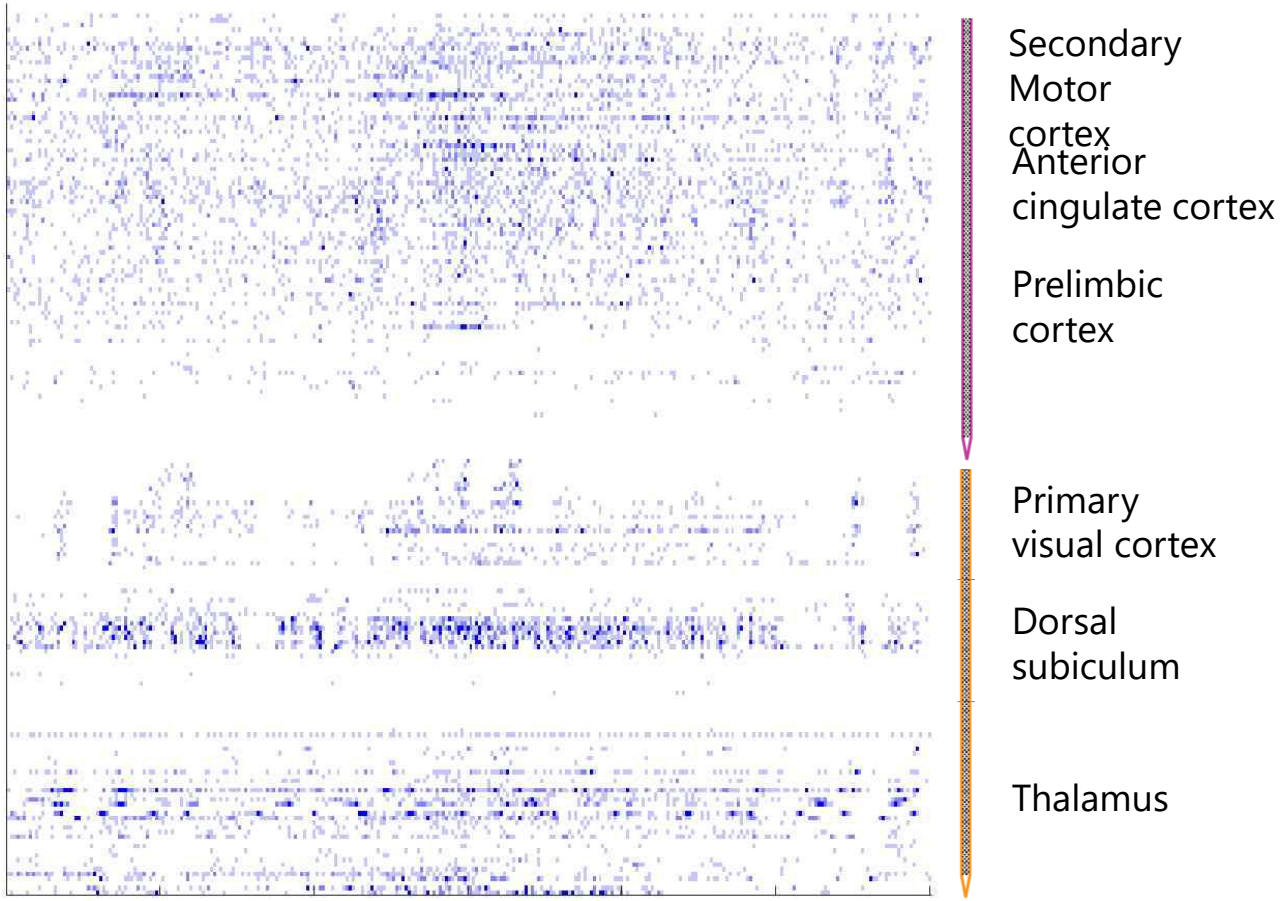
Choices depend strongly on contrast





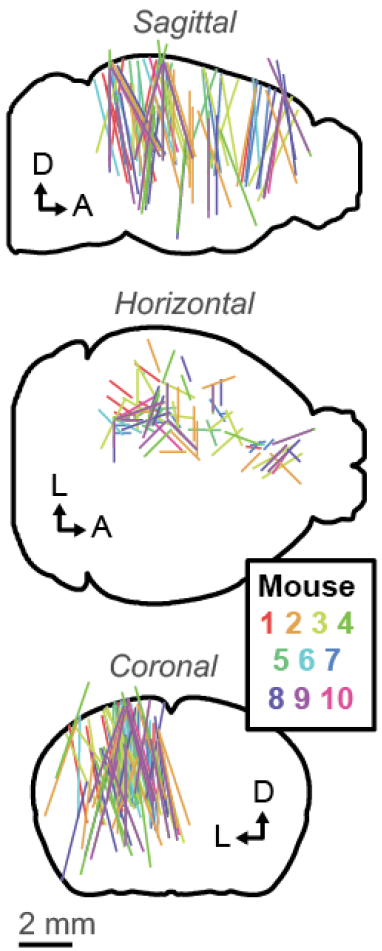
Neuropixels recordings during a visual detection and discrimination task

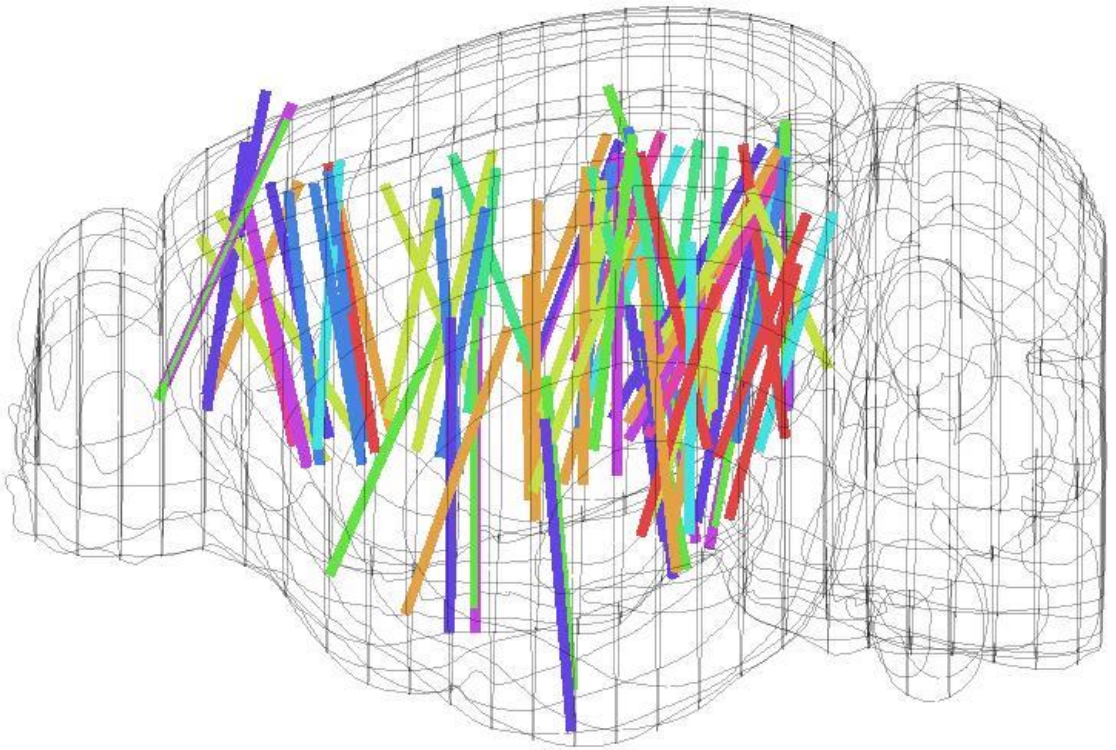




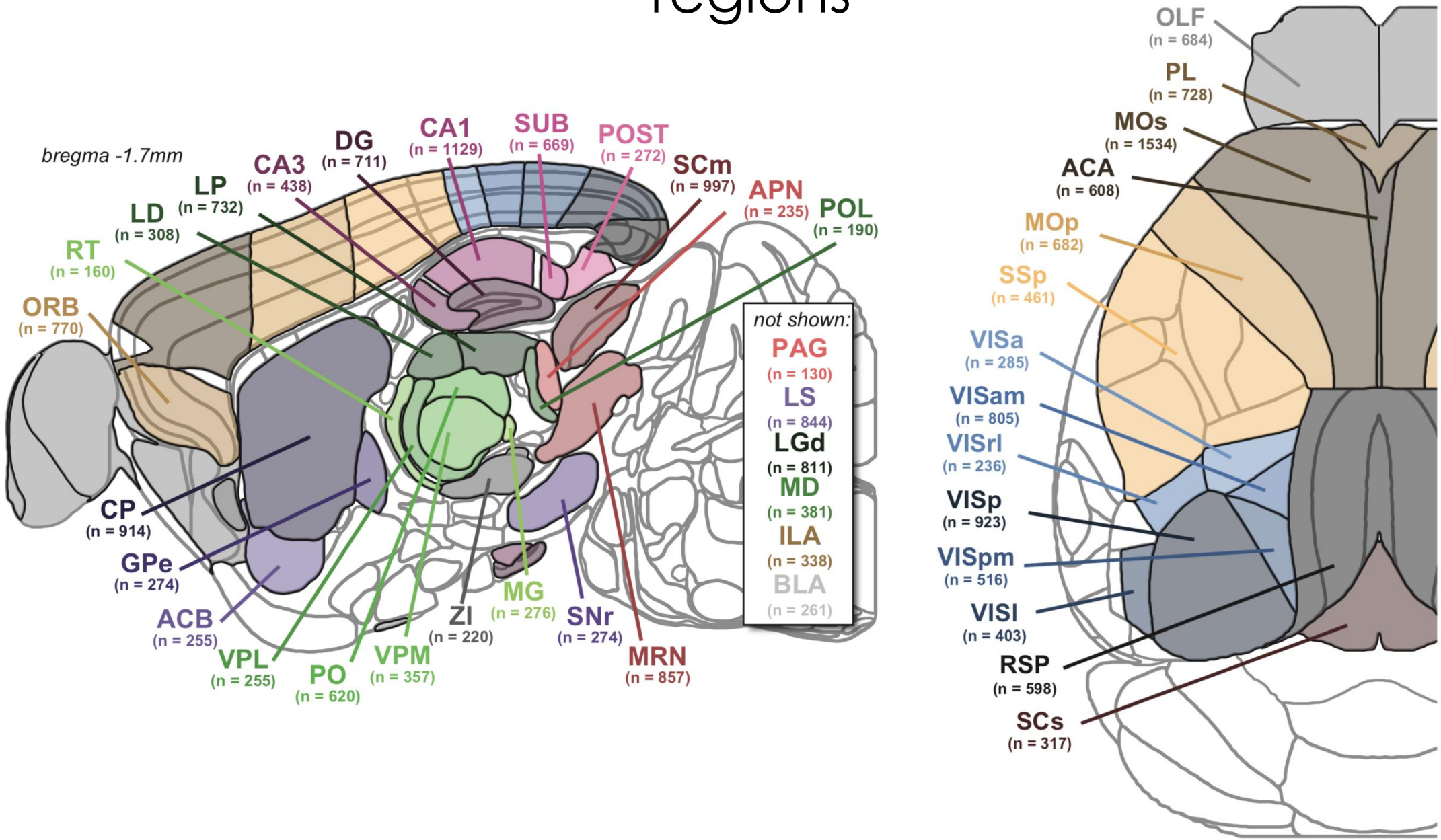
Steinmetz, Zatka-Haas, Carandini, Harris *Nature* 2019
Data freely available, see www.steinmetzlab.net/shared

Recordings were made of 29134 neurons across 39 sessions in 10 mice



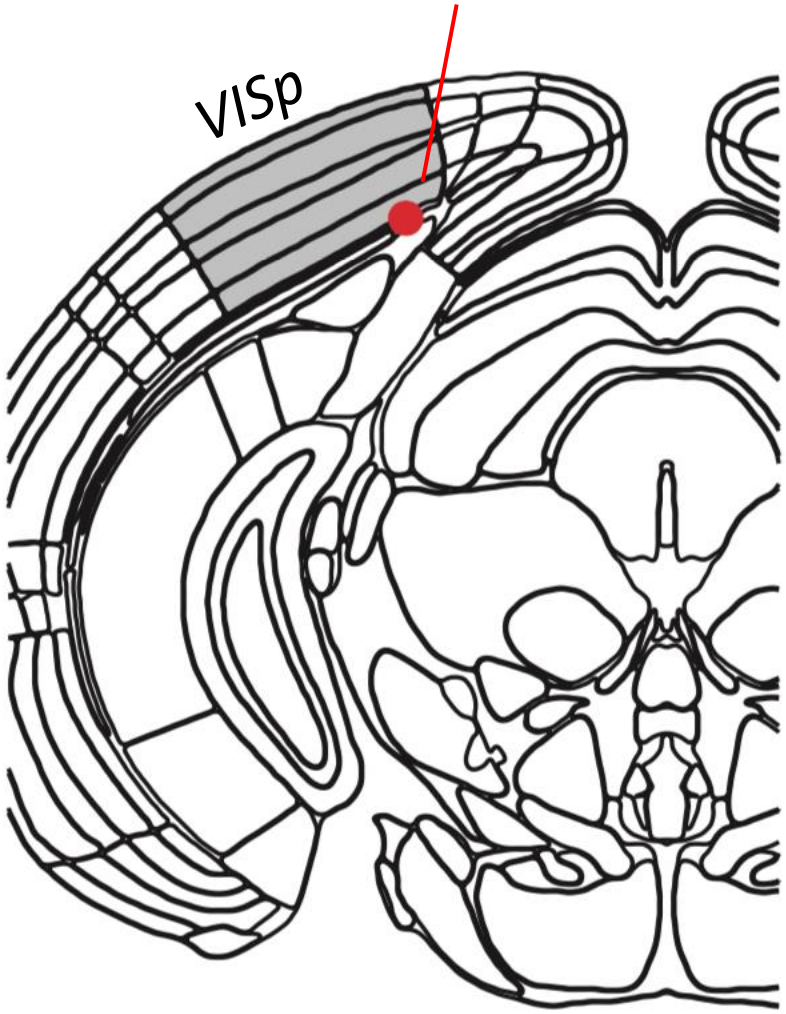


Neurons were recorded in each of 42 brain regions



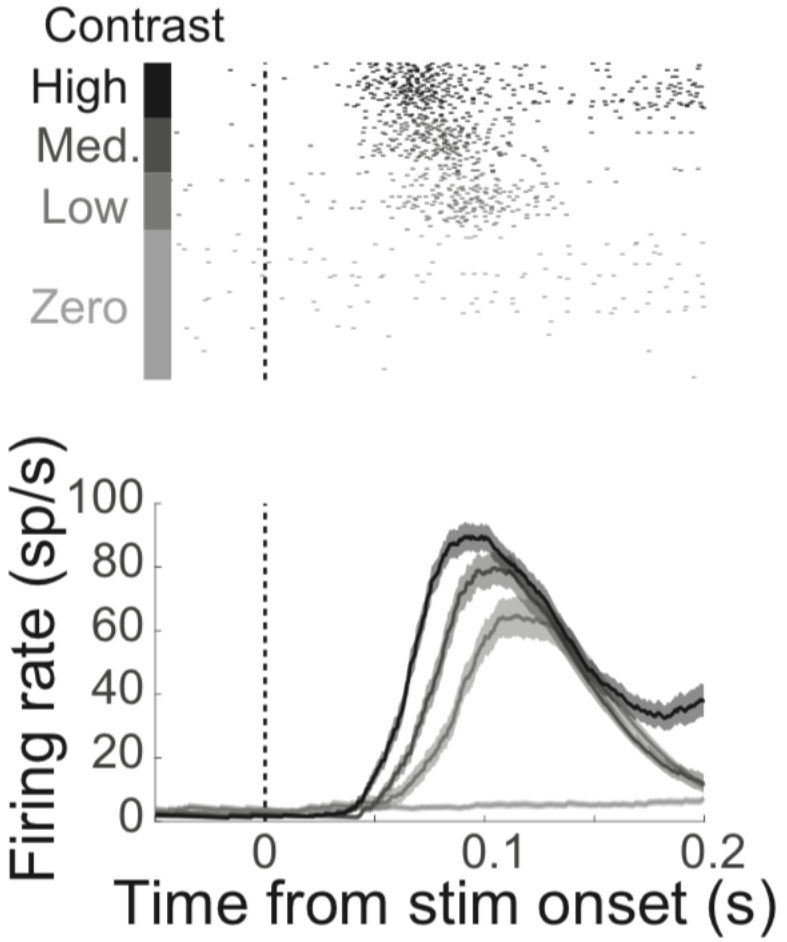
Example neuron: Primary Visual Cortex

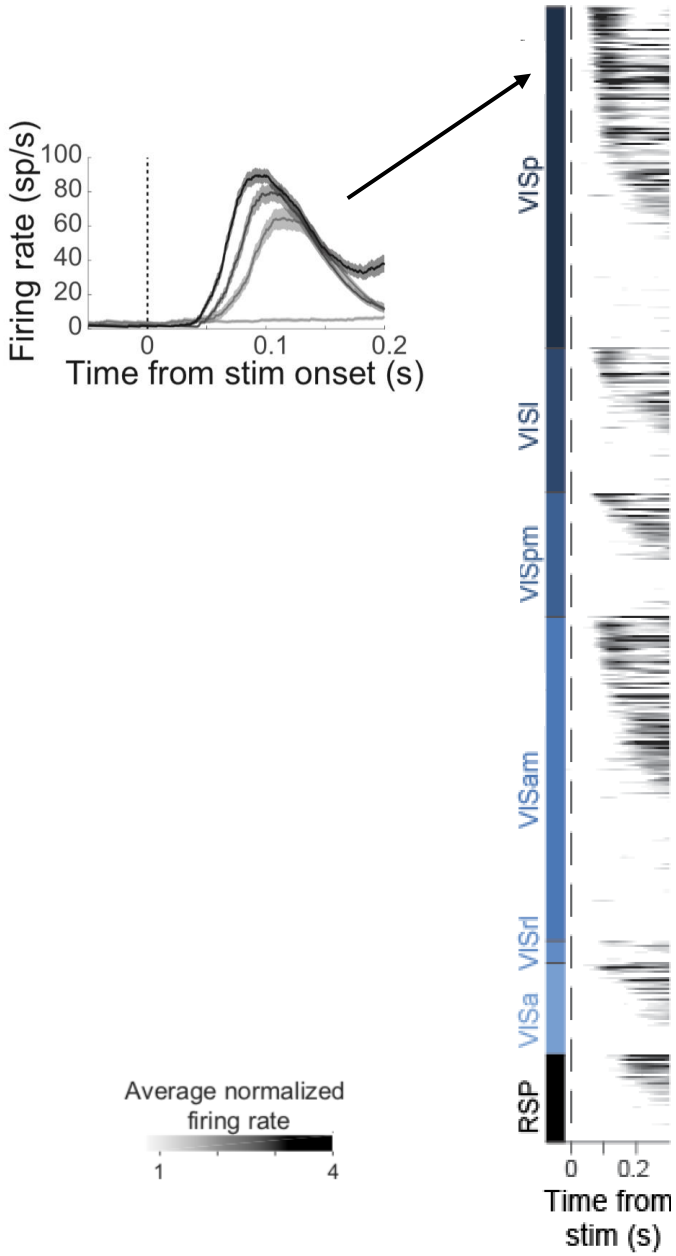
Neuron location



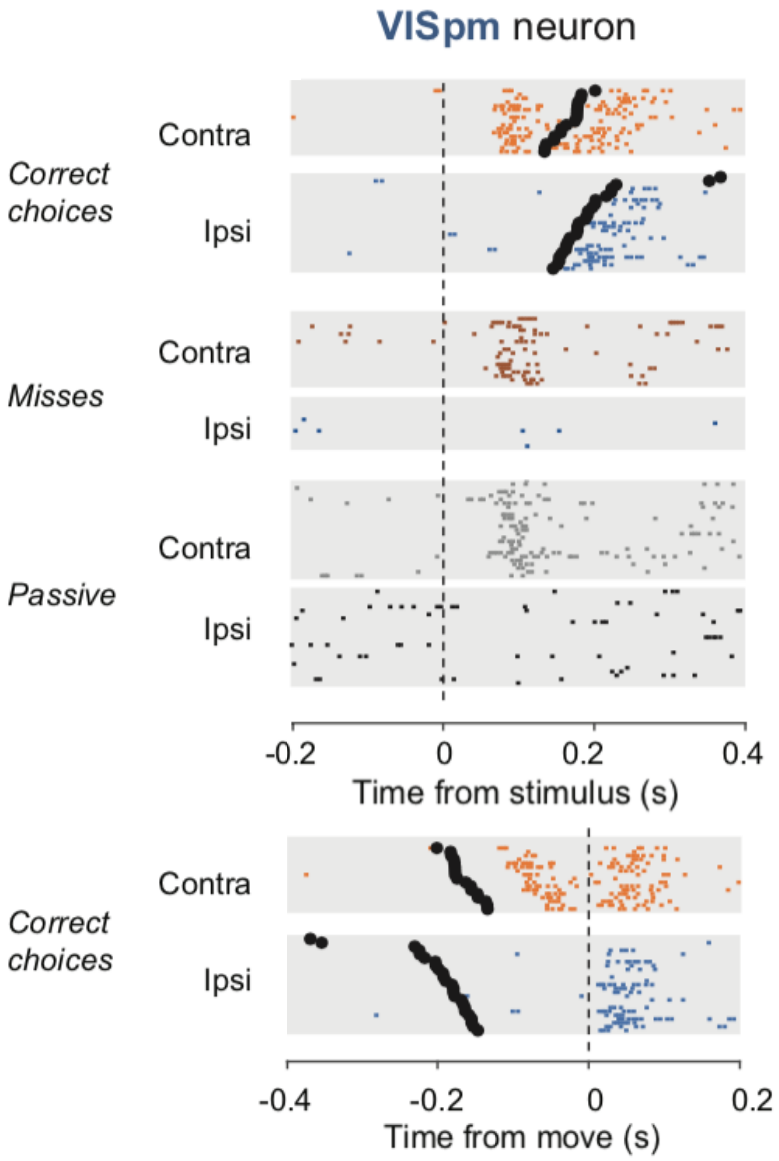
Waveform

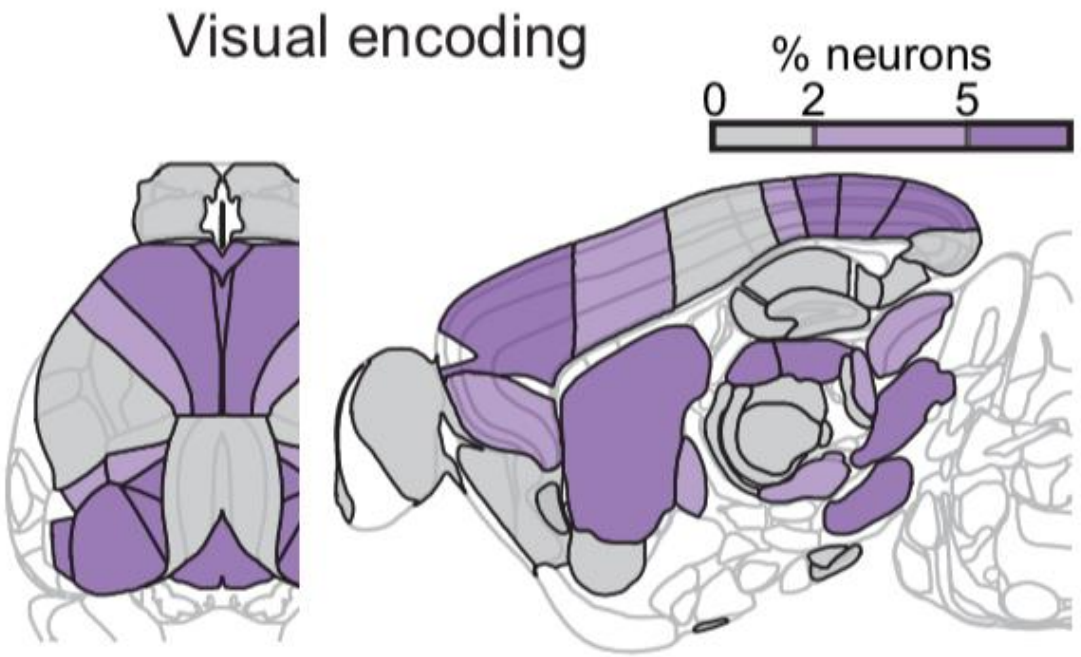
Task activity



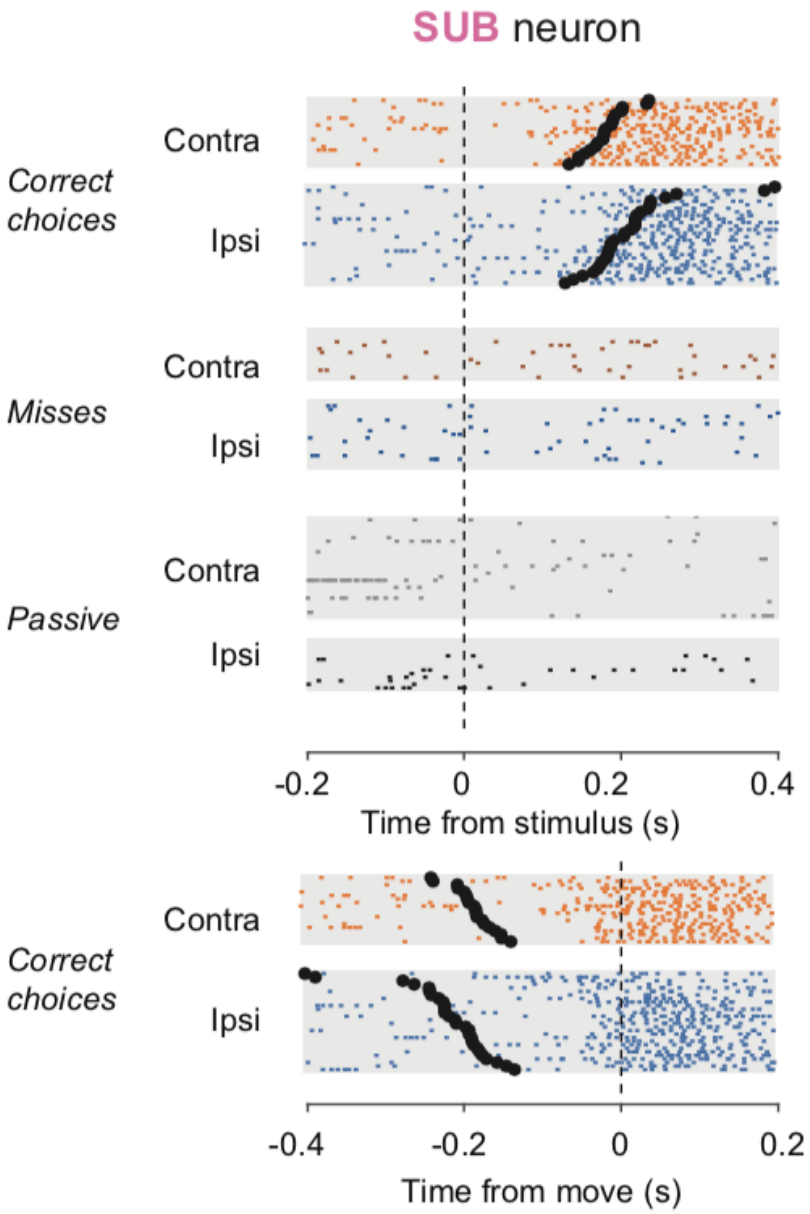

Firing rate (sp/s)
100
80
60
40
20
0
0
0.1
0.2
Time from stim onset (s)
VISp
VISl
VISpm
VISam
VISrl
VISa
RSP
Average normalized firing rate
1
4
0
0.2
Time from stim (s)

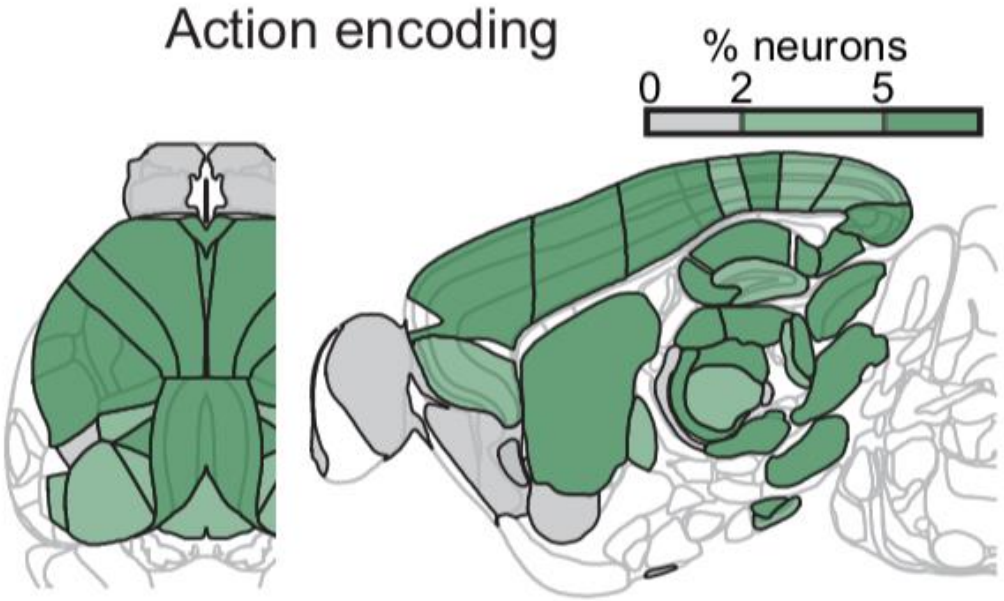
Visual encoding is largely in the classic visual pathway



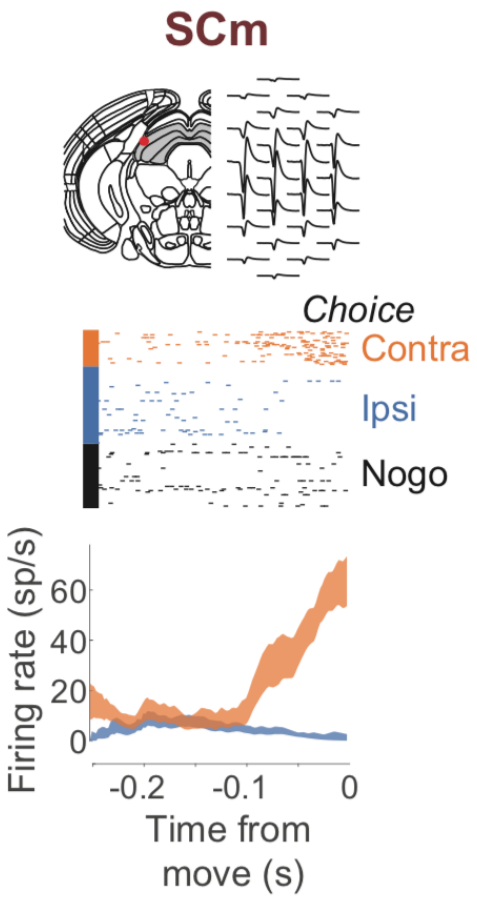


Goal-directed actions are encoded globally

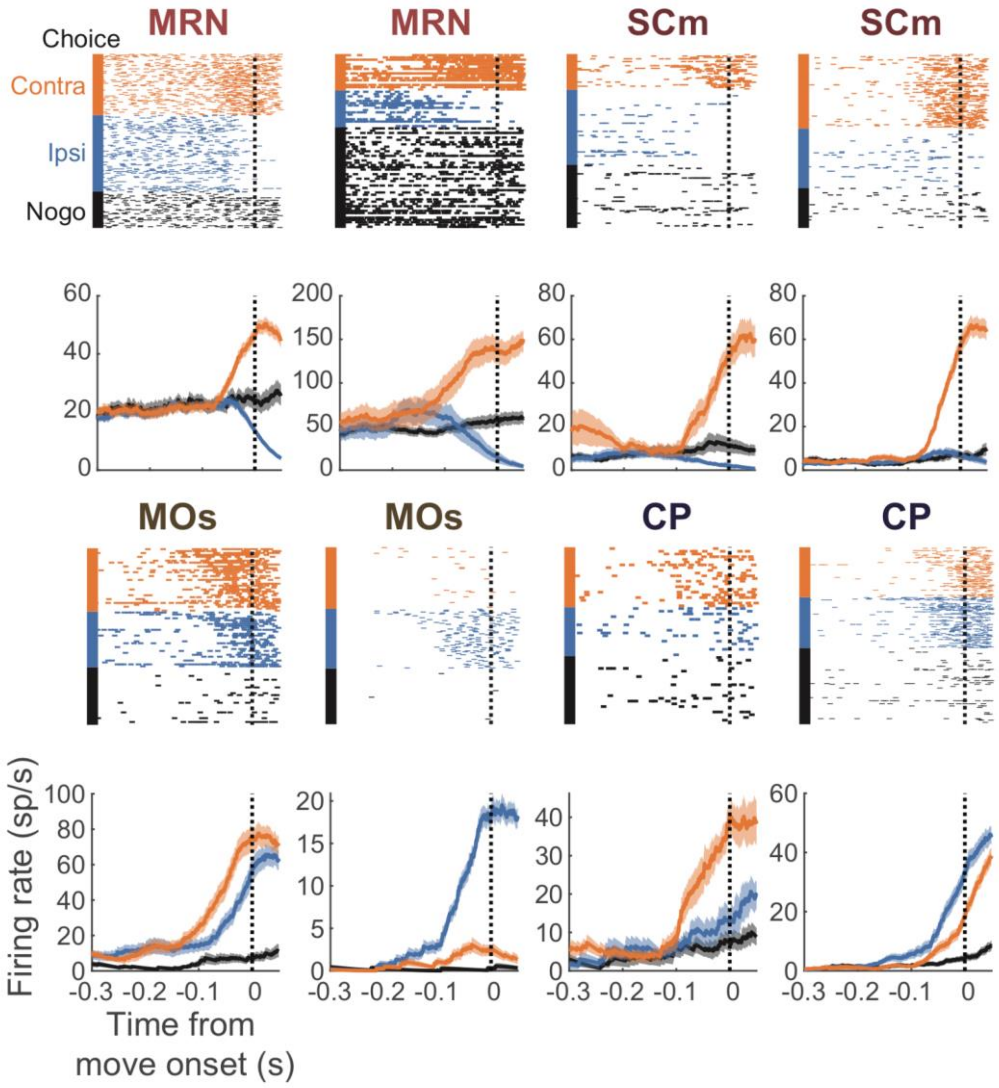


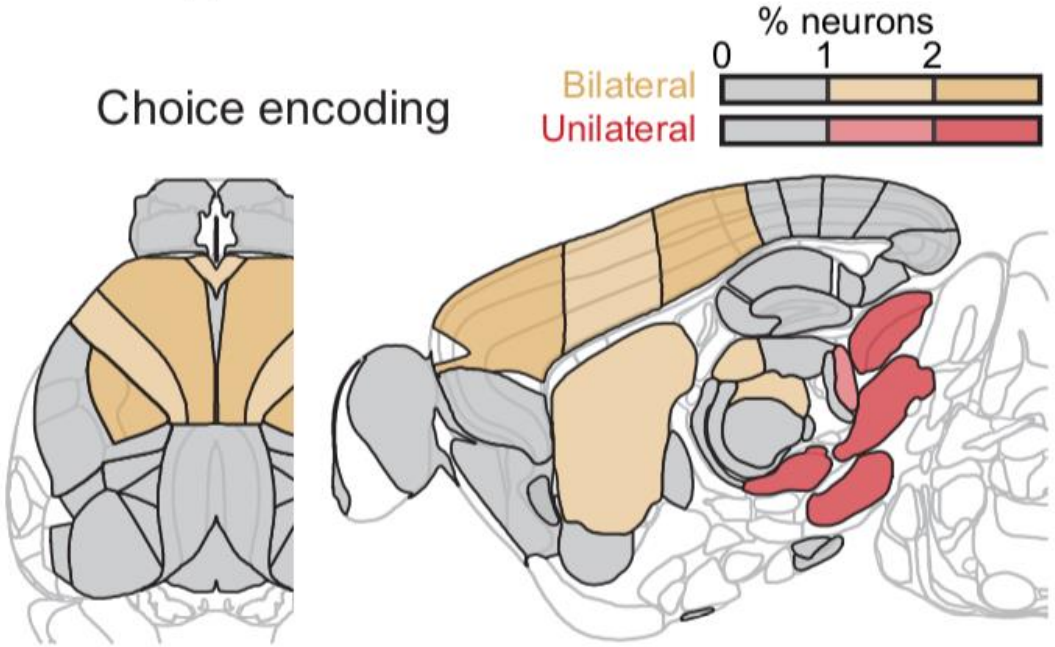


Rare cortical and subcortical neurons encode the upcoming decision



Choice is encoded bilaterally in the forebrain and unilaterally in the midbrain





Are the correlates of detection and discrimination distributed or localized?

- Distributed: choice and action are represented broadly across the brain
- What about abstract representations?

Distributed coding of value

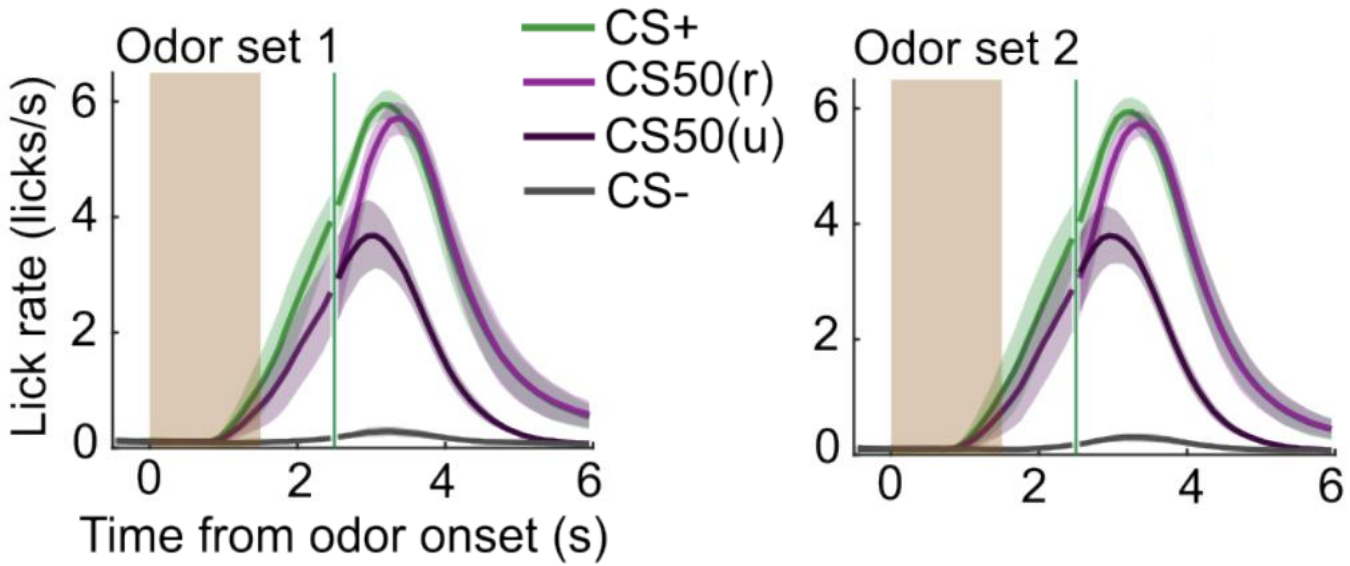
David Ottenheimer

Anna Bowen

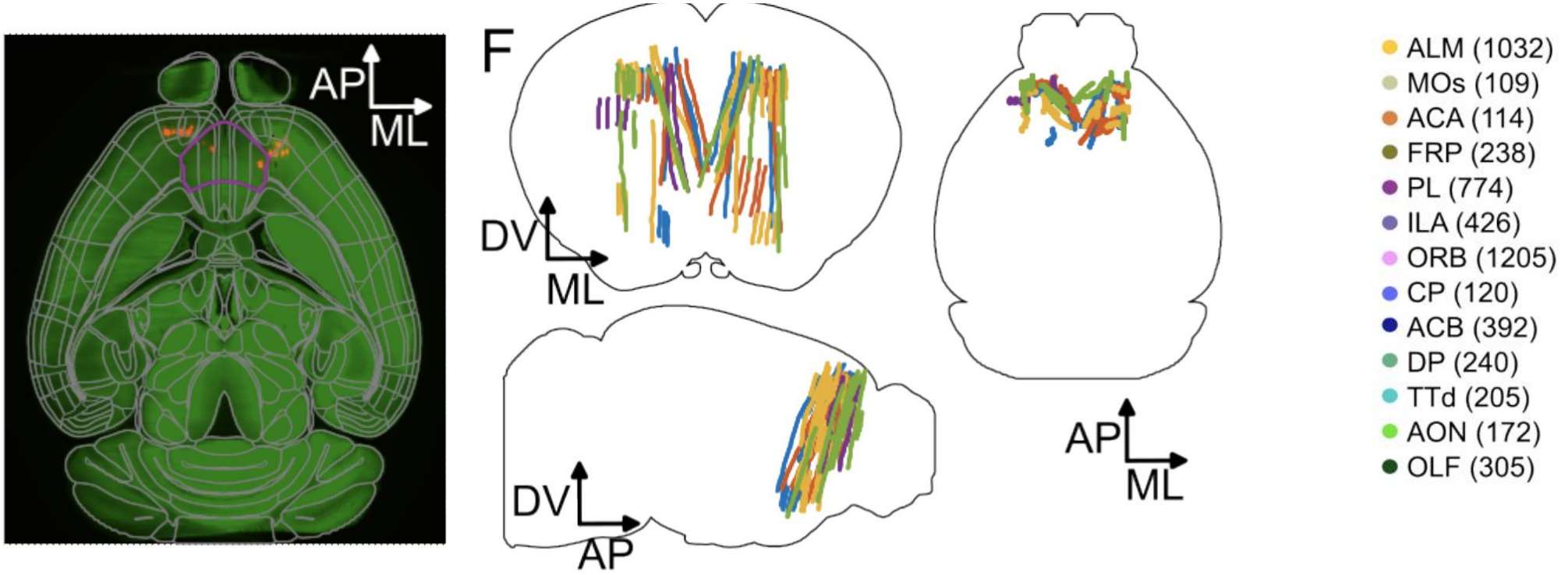
Madelyn Hjort

Garret Stuber

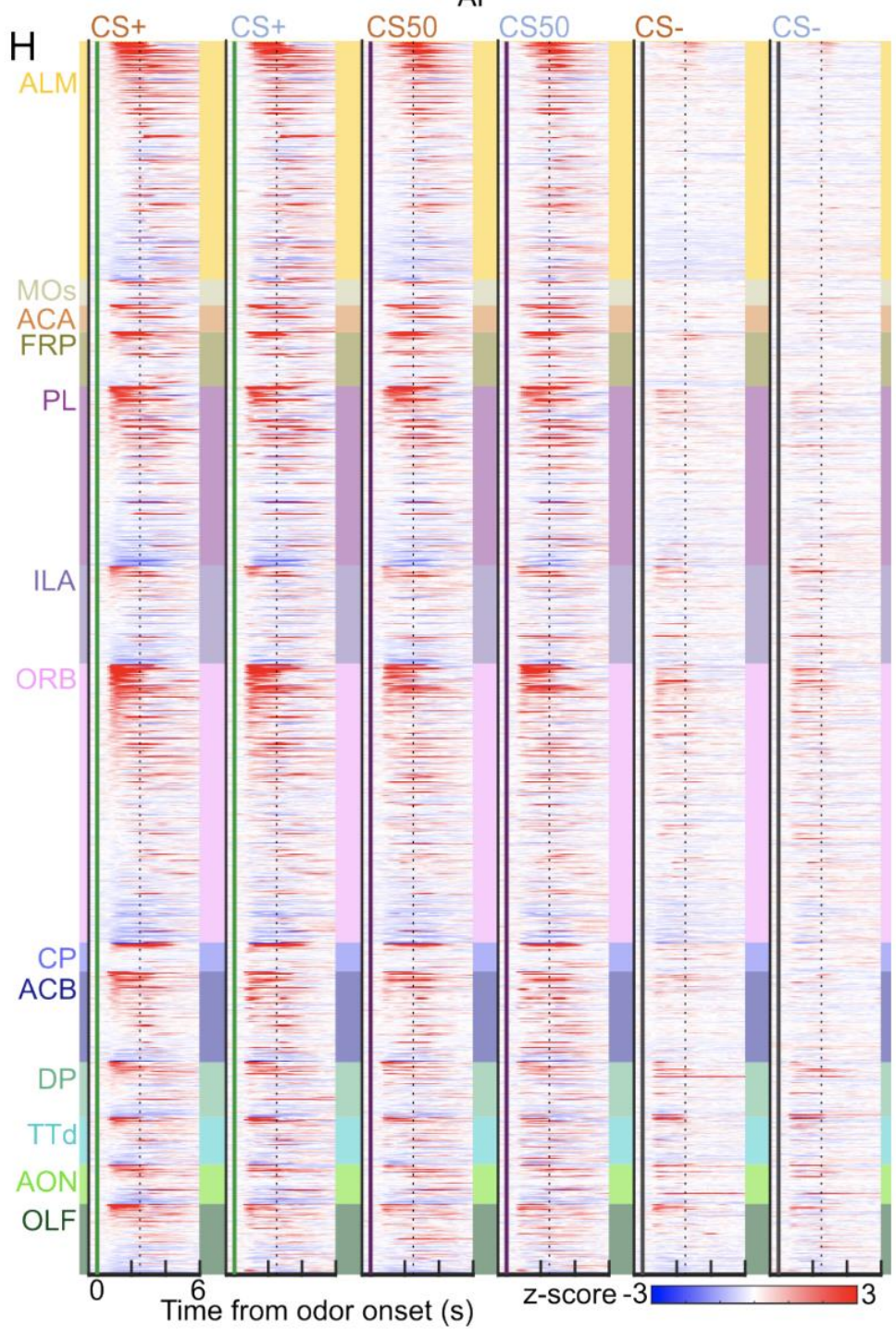
How to measure a mouse's "valuation" of a stimulus?



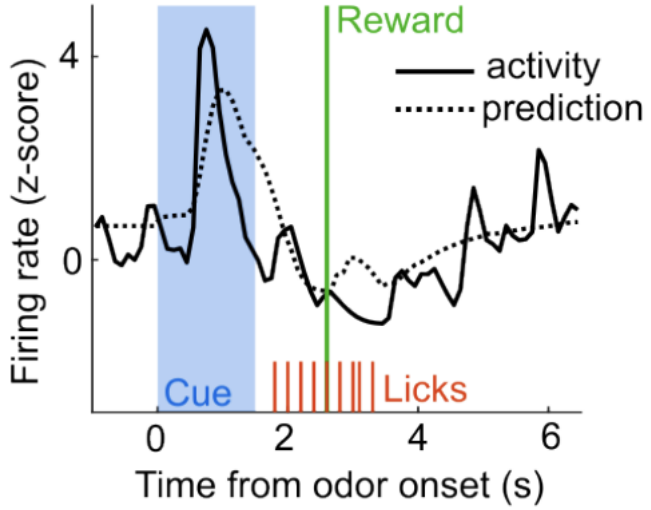
Recordings made across diverse parts of cortex and basal ganglia

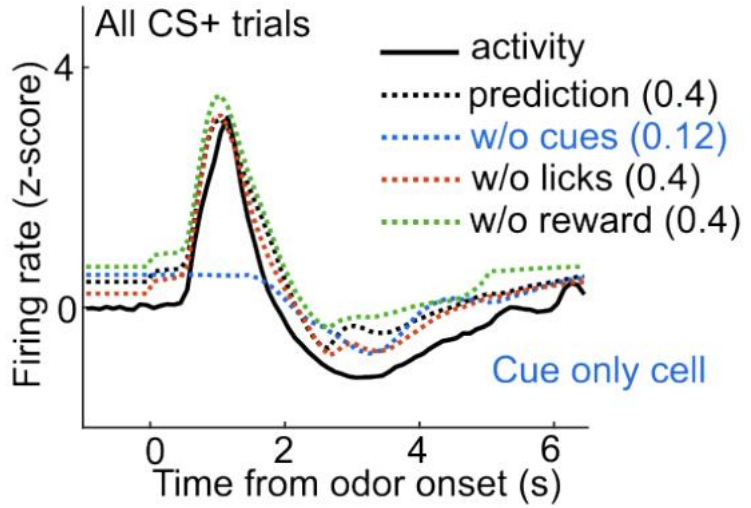


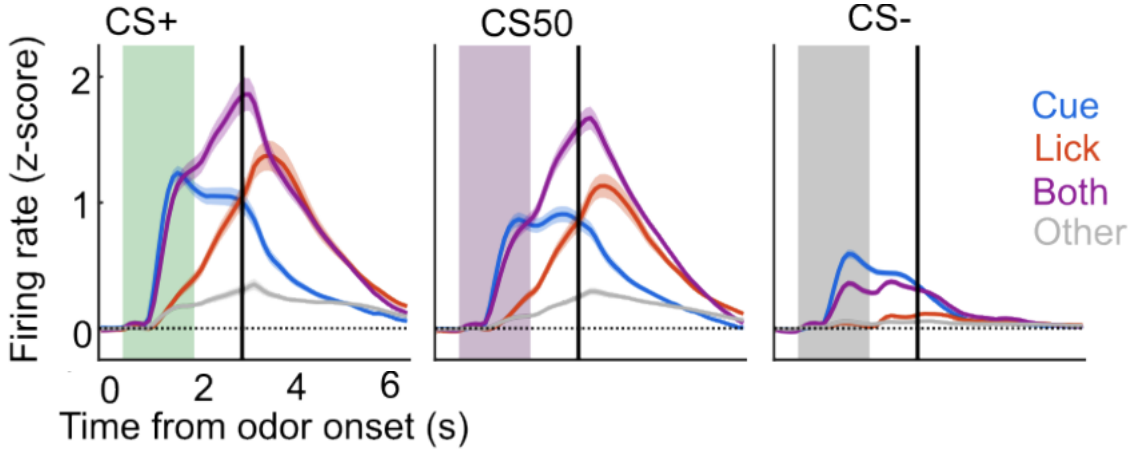
Responsive neurons found in each area

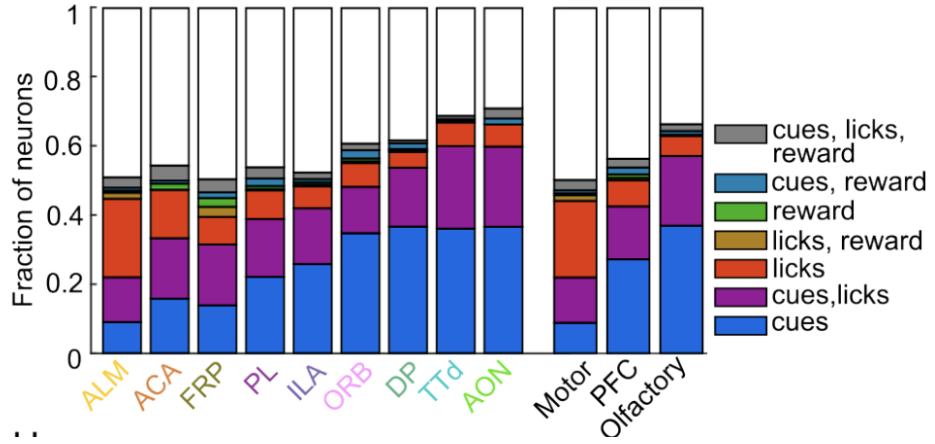


Neurons responding only to the cue (not licks) were selected

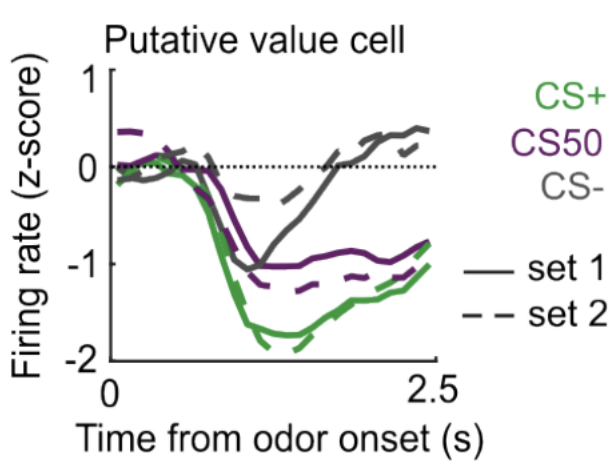


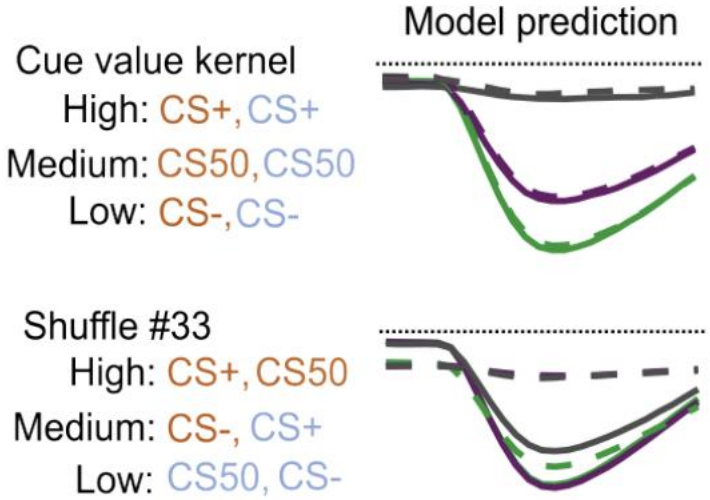


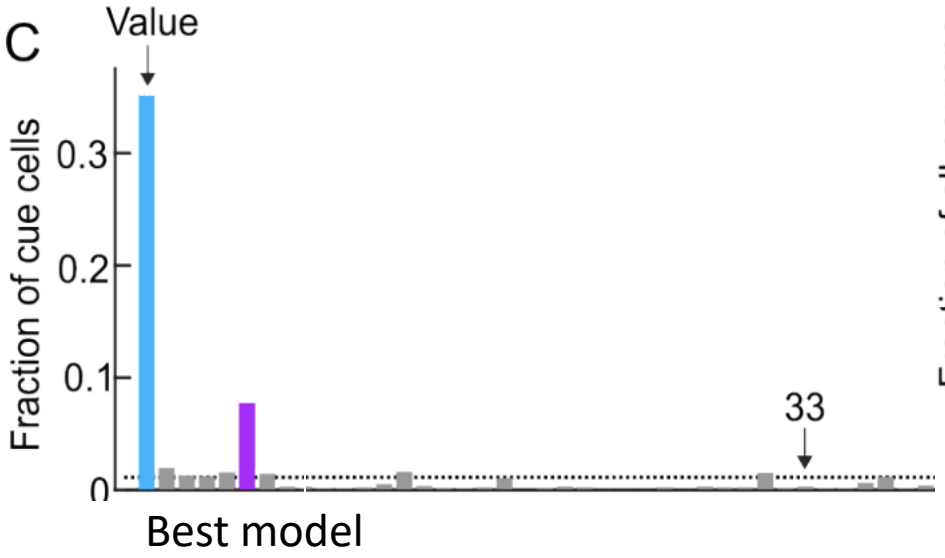


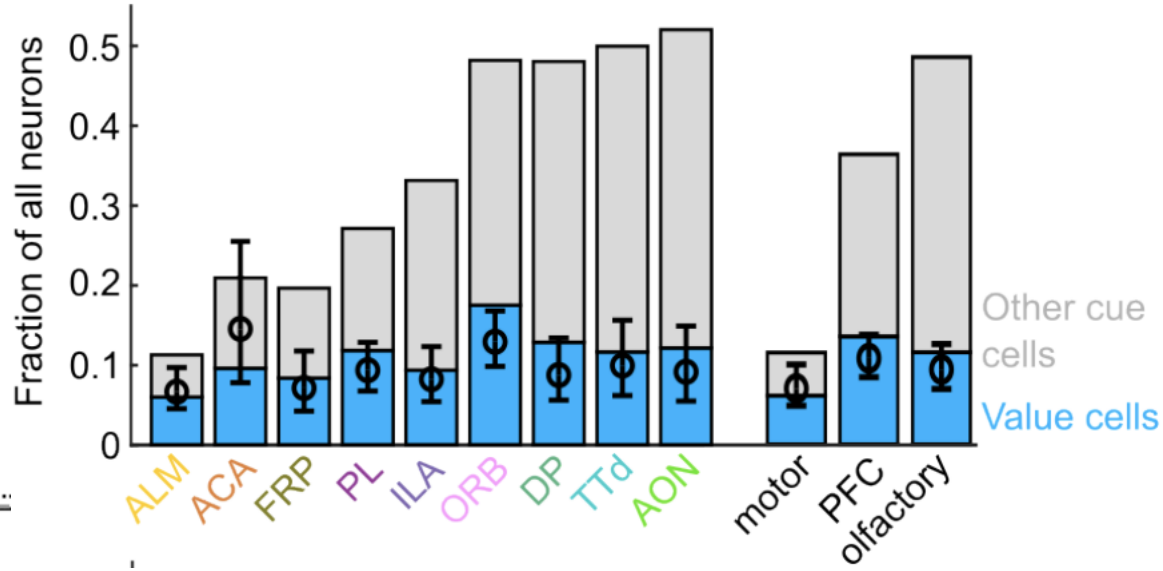


Value-encoding neurons are widely distributed



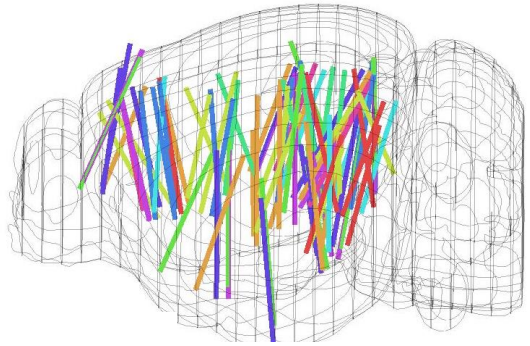


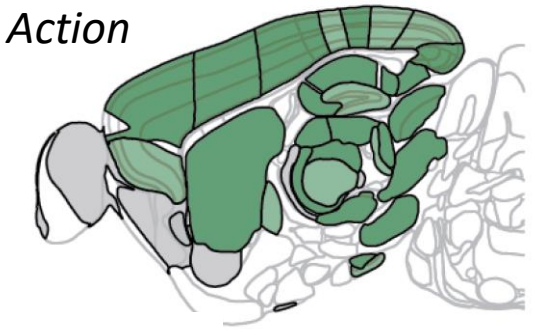


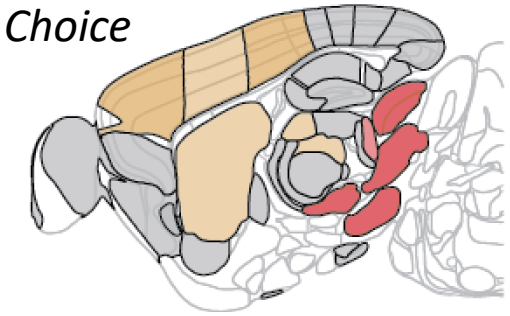


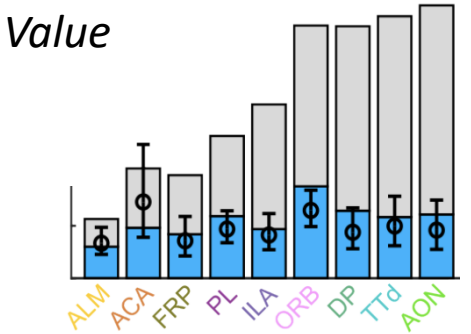
Conclusions

- Neuropixels CMOS probes have enabled unprecedented scale across the entire brain without loss of resolution
- Principles organizing behavioral coding across the brain:
  - Motor processes including action initiation and action selection are encoded broadly across the brain
  - Choice encoded in midbrain unilaterally, and in forebrain bilaterally
  - Abstract value is encoded equivalently across diverse cortical and basal ganglia regions









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