

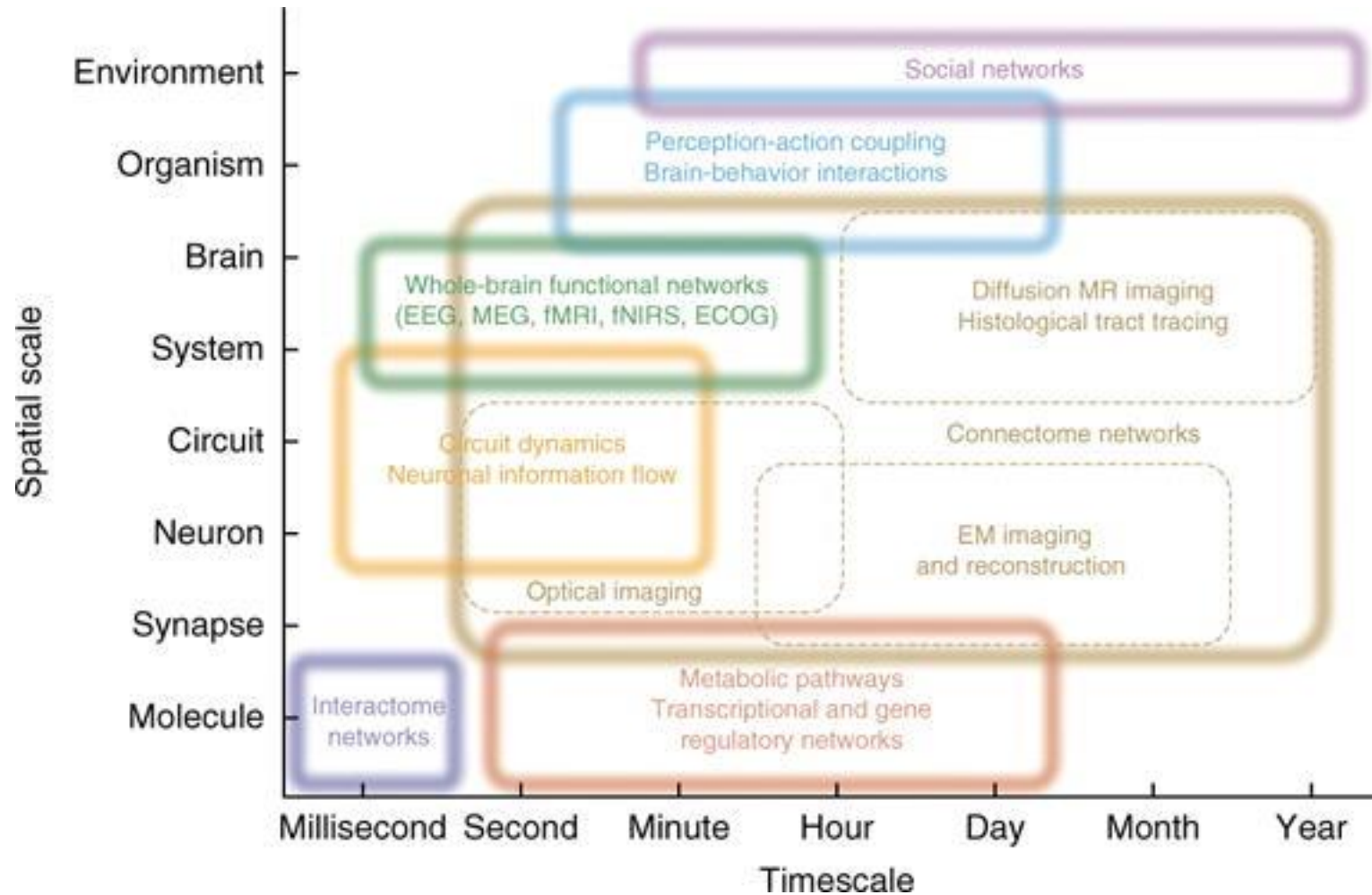
# BIO-311 - Neuroscience

Tools & Technology to study neuroscience

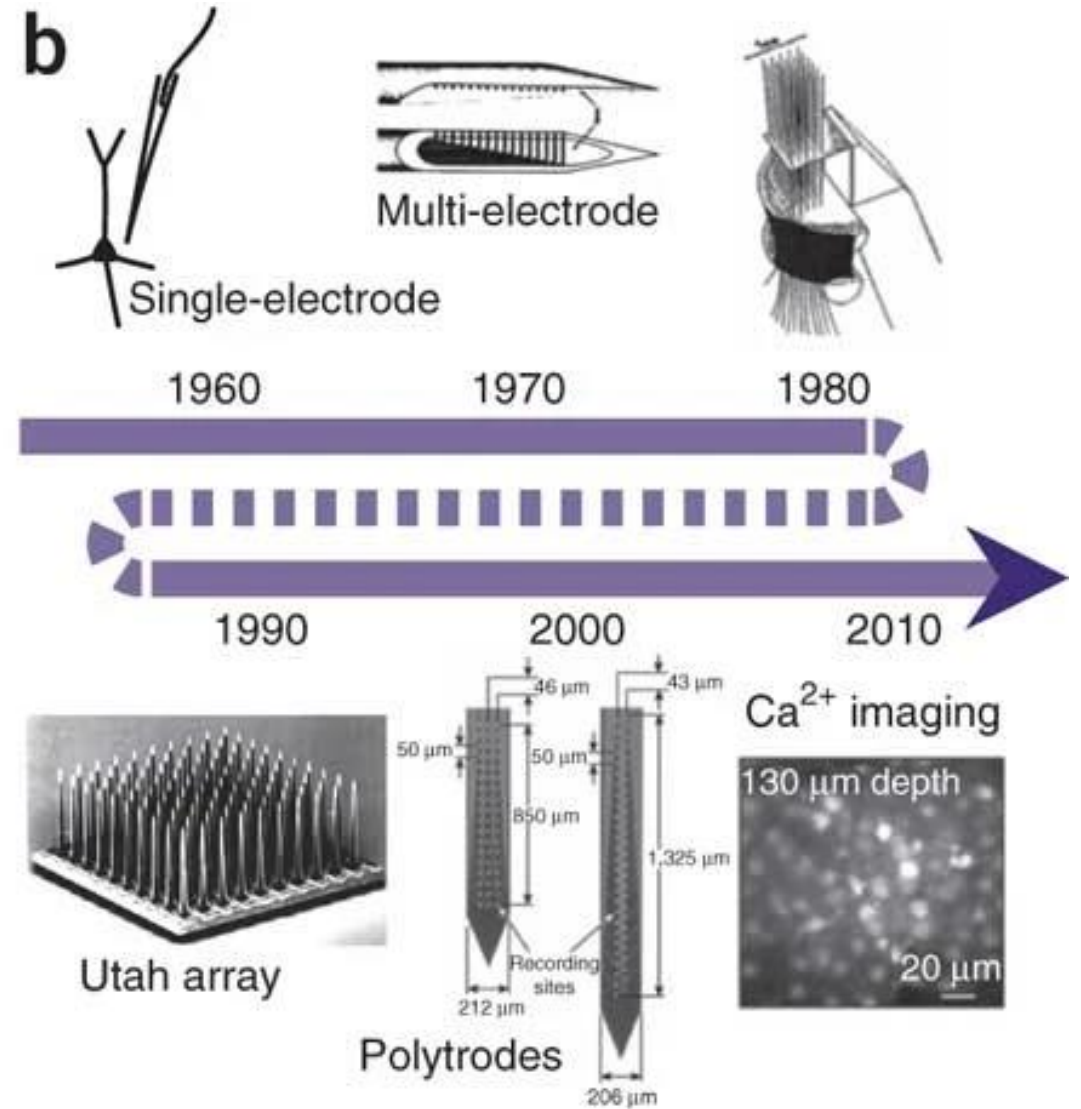
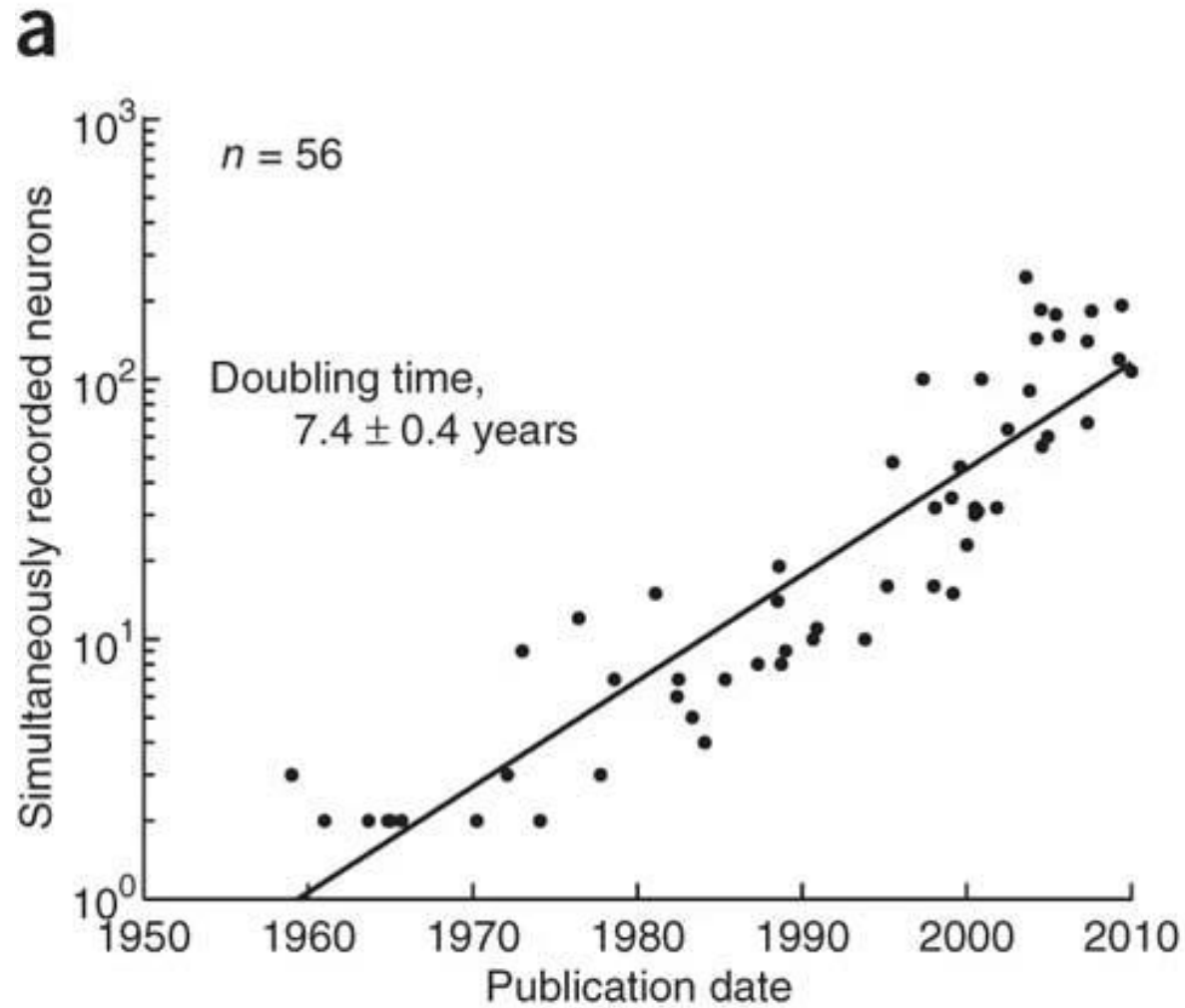
# Summary

- Calcium Imaging
- Electrical stimulation of neurons
- Optogenetics
- TMS
- Extracellular electrophysiology & Neuropixels
- Behavioral tracking
- Neural dynamics modeling

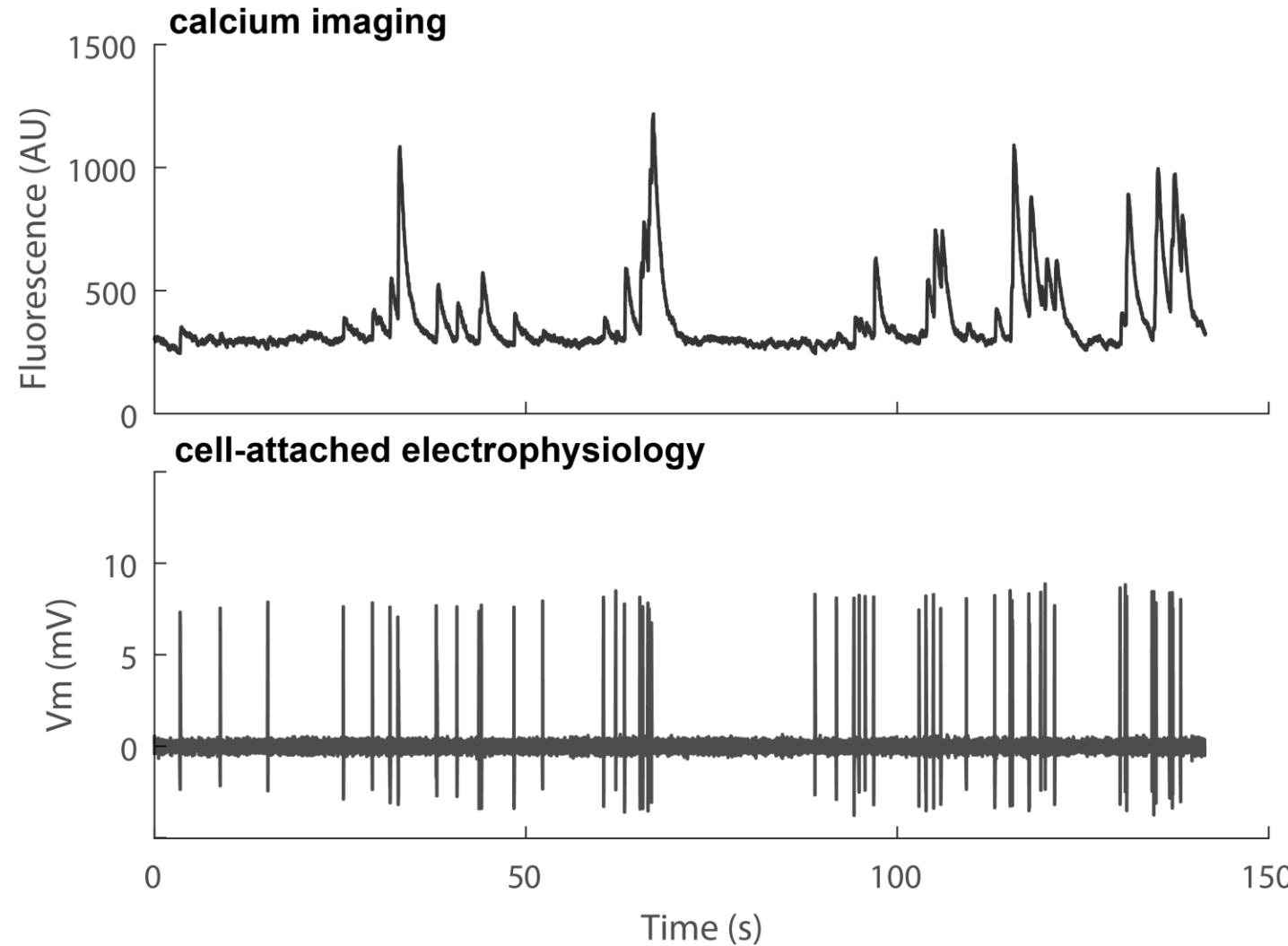
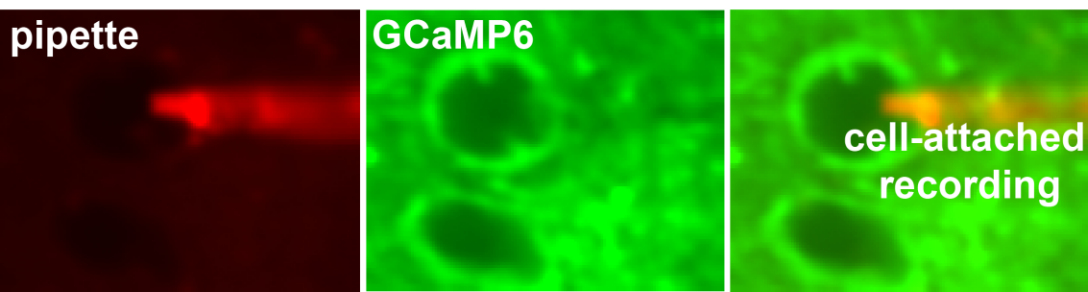
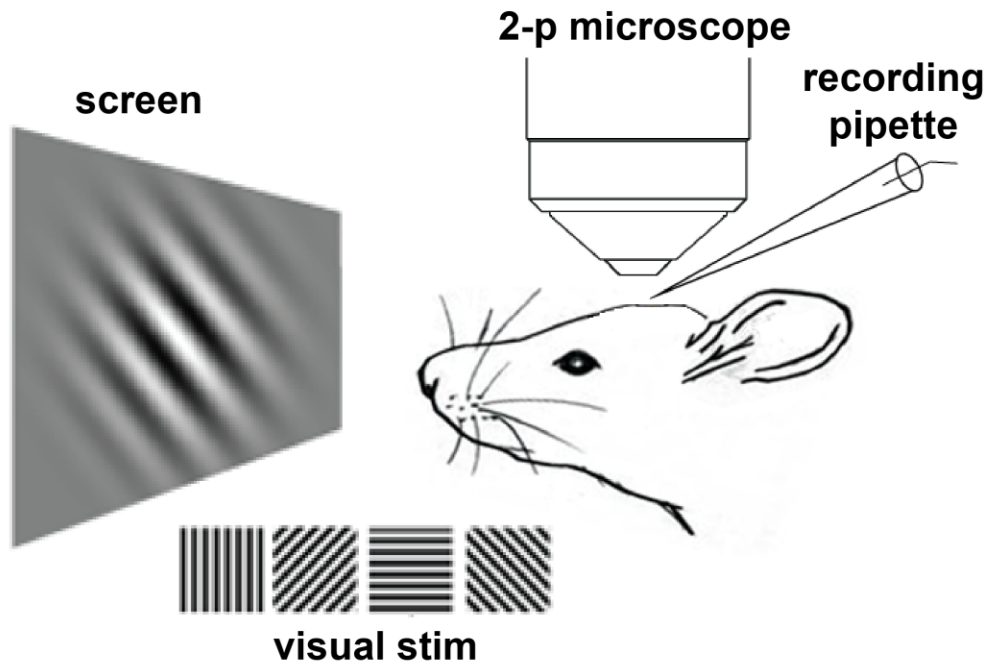
# Methods for measuring brain function



# Single unit recoding: “Moore’s law”



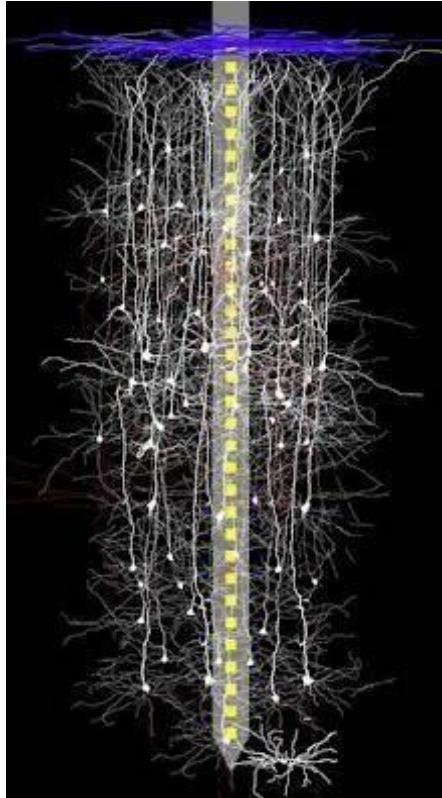
# GCaMP imaging in mice



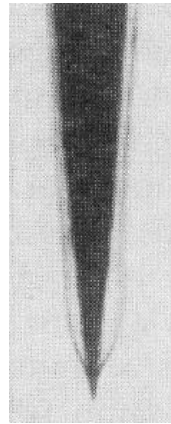
## JOINTLY RECORDED NEURONS AT MULTIPLE LEVELS OF MAGNIFICATION.

The dataset consists of 91 neurons from 4 transgenic mouse lines for which calcium imaging was performed at high optical zoom focused on individual cells. A subset (37) of these neurons were additionally imaged at a lower zoom factor, i.e. one at which the responses of many neurons can be characterized in parallel. The dataset is described in Huang, Knoblich et al., *Relationship between spiking activity and simultaneously recorded fluorescence signals in transgenic mice expressing GCaMP6*.

# Extracellular Electrophysiology: a brief history



Microelectrode  
(1953)  
5  $\mu\text{m}$  wires



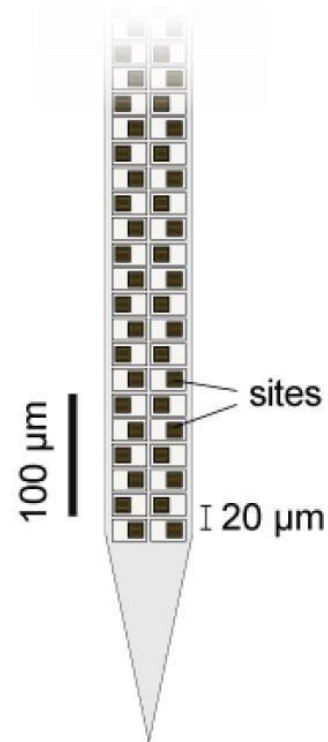
Hubel  
*Science* 1953

Polytrode  
(2005)  
1.5  $\mu\text{m}$  wires

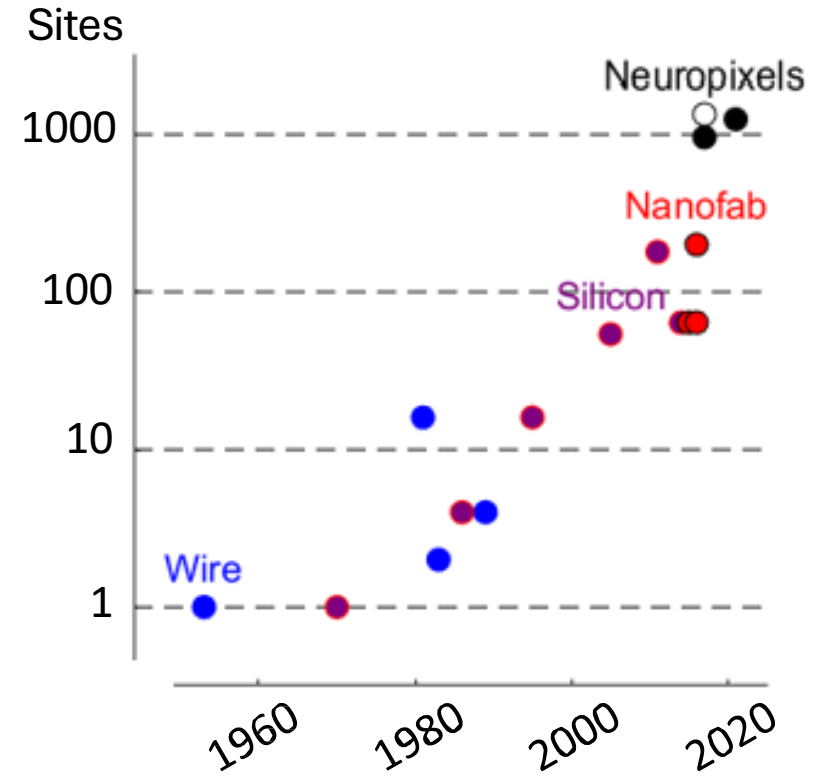


Blanche et al  
*J Neurophys* 2005

Neuropixels  
(2018)  
0.2  $\mu\text{m}$  "wires"



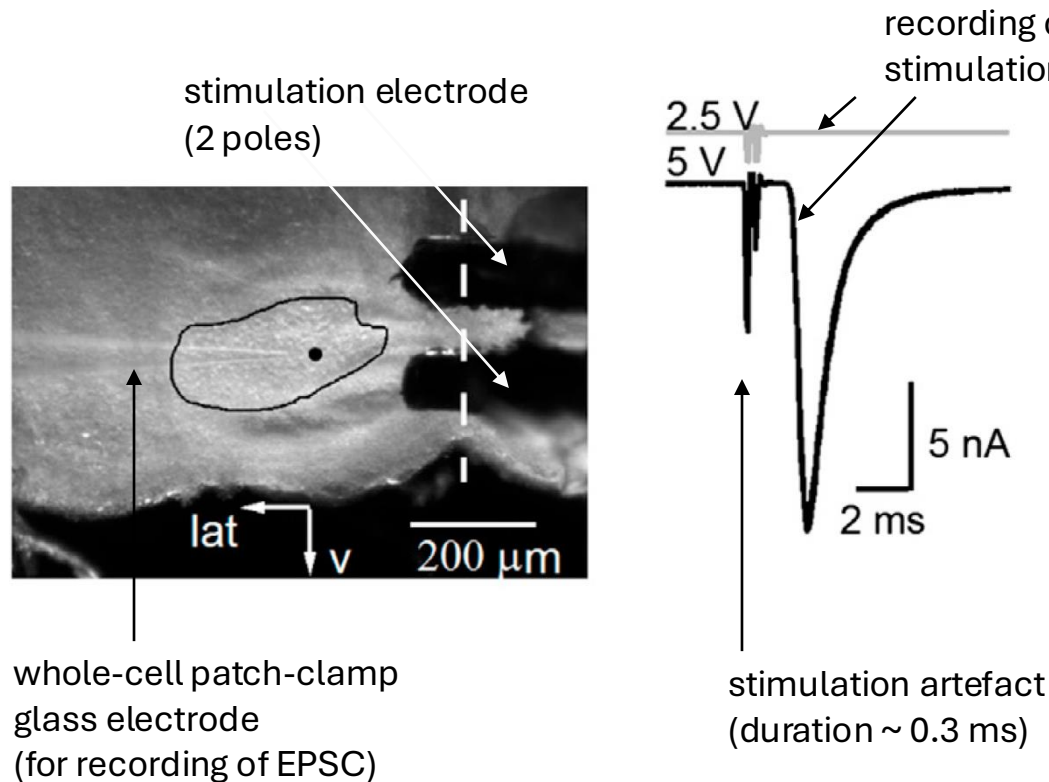
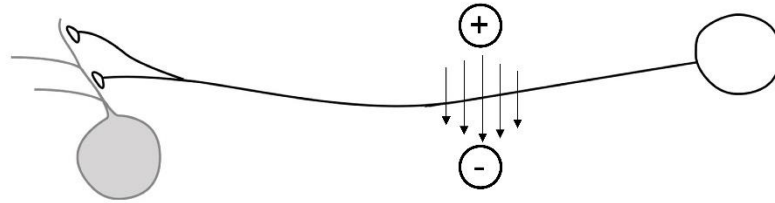
[Steinmetz et al,](#)  
*Cur.Op.Neurobiol* 2018  
[Jun et al,](#) *Nature* 2017



[Steinmetz et al,](#) *Curr Op Neurobiol* 2018

# Stimulation by extracellular (stimulation) electrode

Example: "bipolar" stimulation of axons in a brain slice preparation

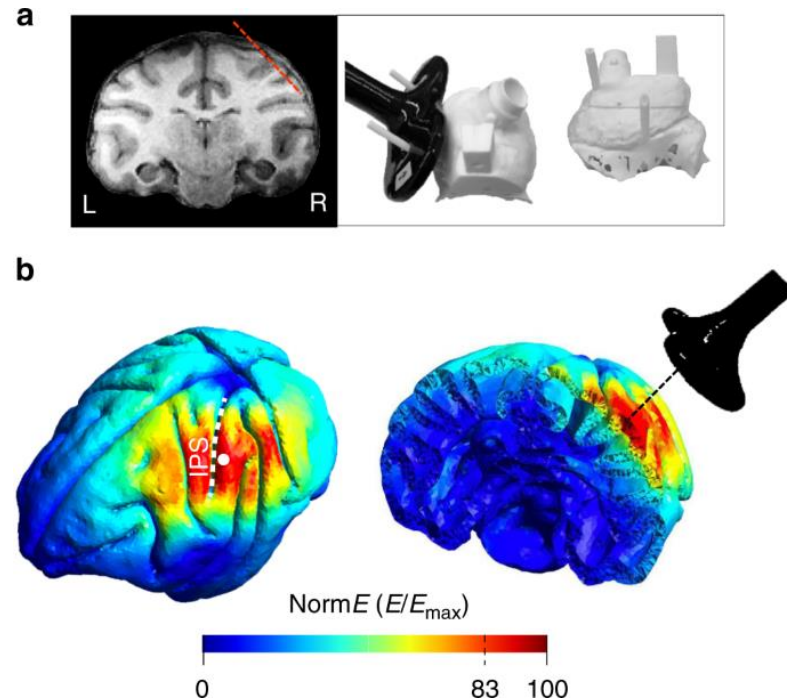


Advantage: high timing precision

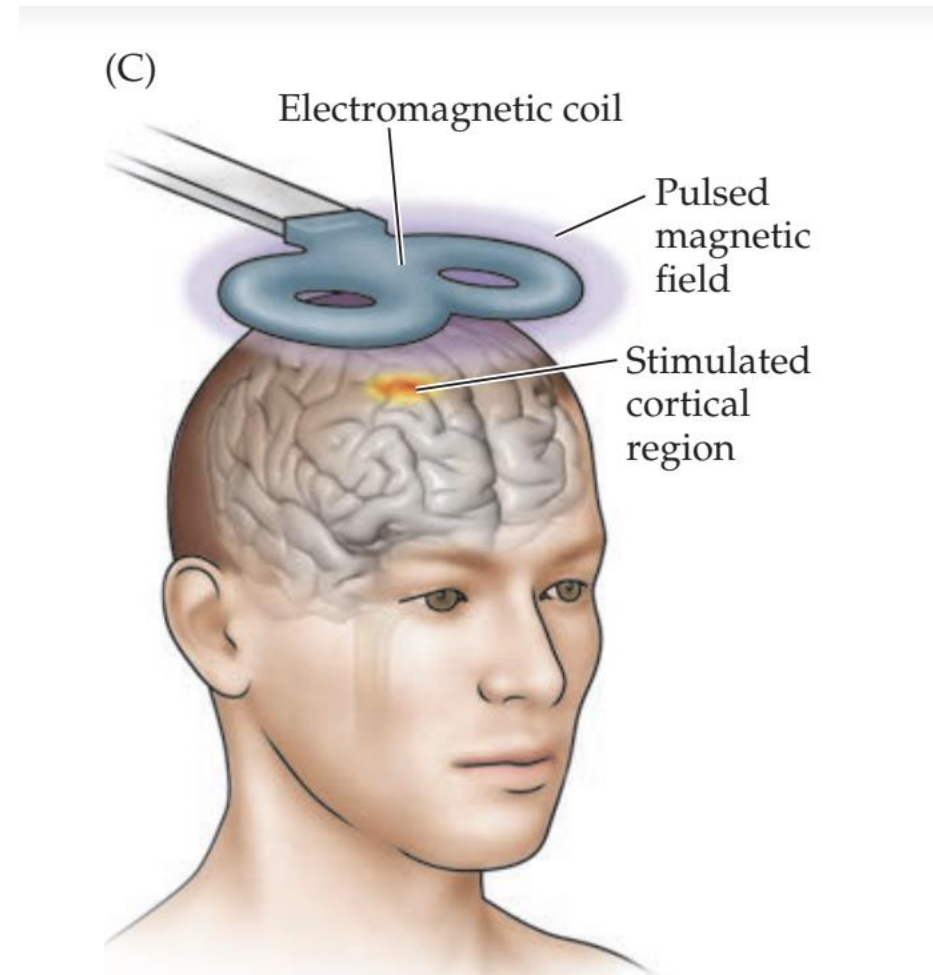
Disadvantage:

- no control over *which* (molecularly defined) presynaptic neuron gets stimulated

# TMS is used as a non-invasive method in humans to modulate neuron activity



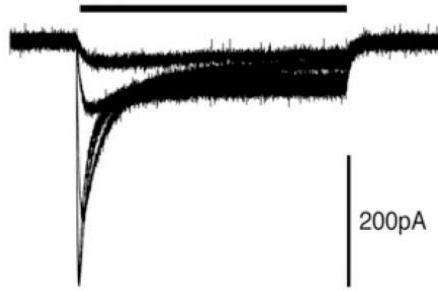
- **Transcranial magnetic stimulation (TMS)** is a noninvasive form of brain stimulation in which a changing magnetic field is used to cause electric current at a specific area of the brain through electromagnetic induction.



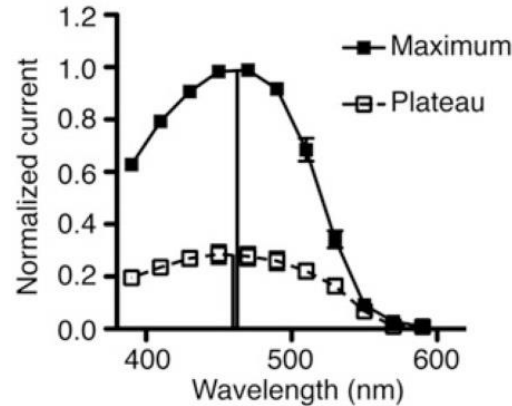
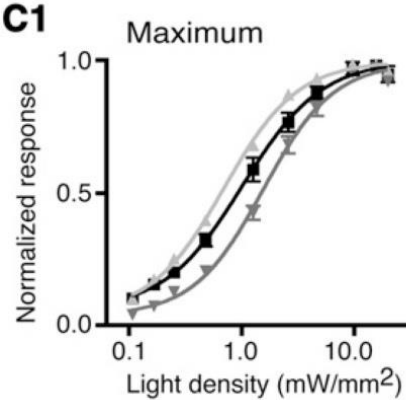
# Channelrhodopsin-2 (ChR2) is a light-activated cation channel

- blue light  $\lambda$  470 nm, 500 ms
- different intensities

B1



C1



## Take Homes:


- absorption maximum  $\sim$  470 nm
- inward currents (**nonselective cation channel**)
- channel activates fast  $\sim$  2 ms
- channel *inactivates* with prolonged light

Nagel et al., 2003 *PNAS*; Lin et al. 2009 *Biophysical J.*

- From green alga, *Chlamydomonas reinhardtii*
  - ChR2 expressed in HEK293 cells
  - Whole-cell voltage clamp recording
  - Light exposure with LED / monochromator

# Deep learning for measuring behavior

**A Traditional Methods**



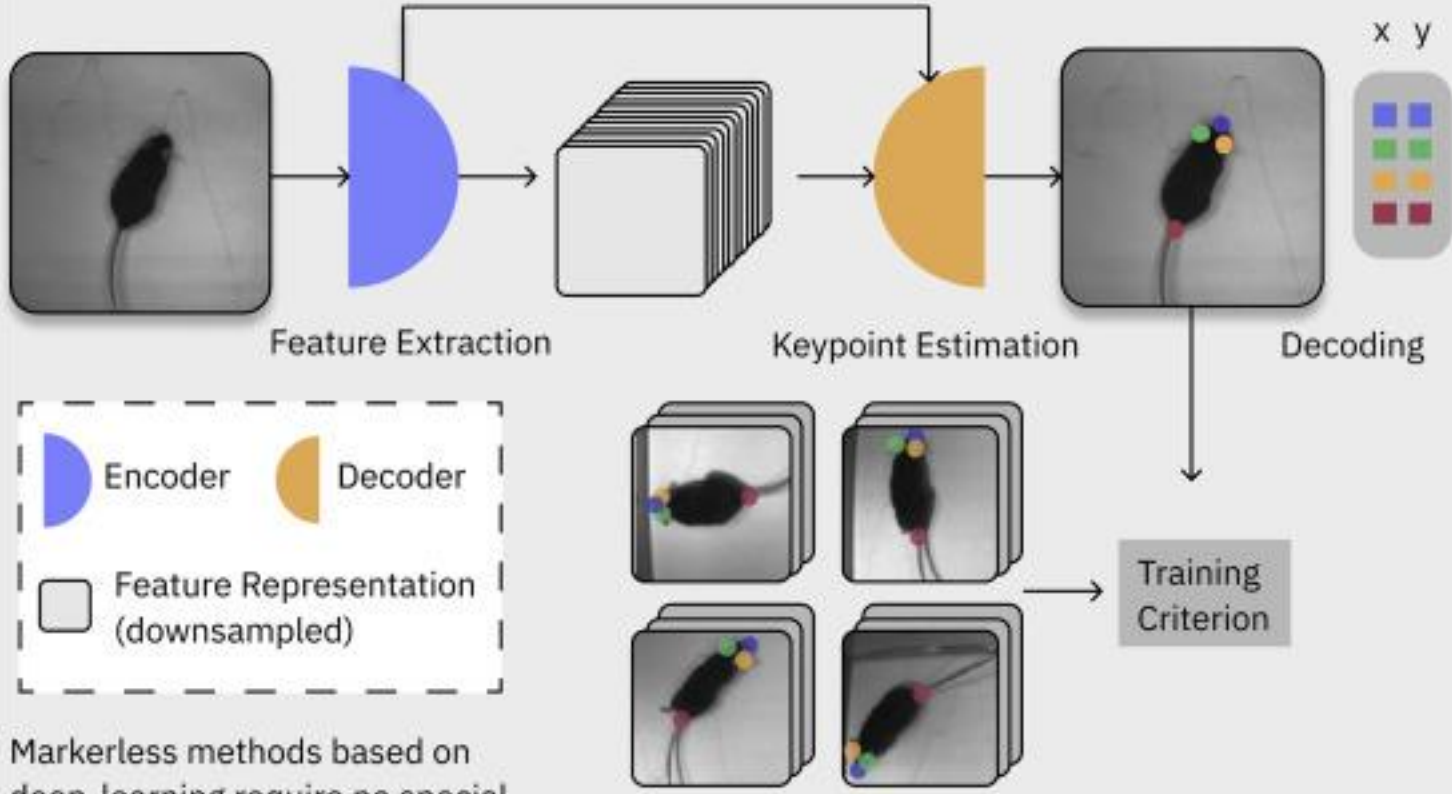
Lighthouse Tracking

IMU-based Tracking

Color-based Tracking

Traditional methods work *ad-hoc*: subjects need to be prepared, but no annotation is needed.

**B Markerless Pose Estimation**



Feature Extraction

Keypoint Estimation

Decoding

x y

Encoder

Decoder

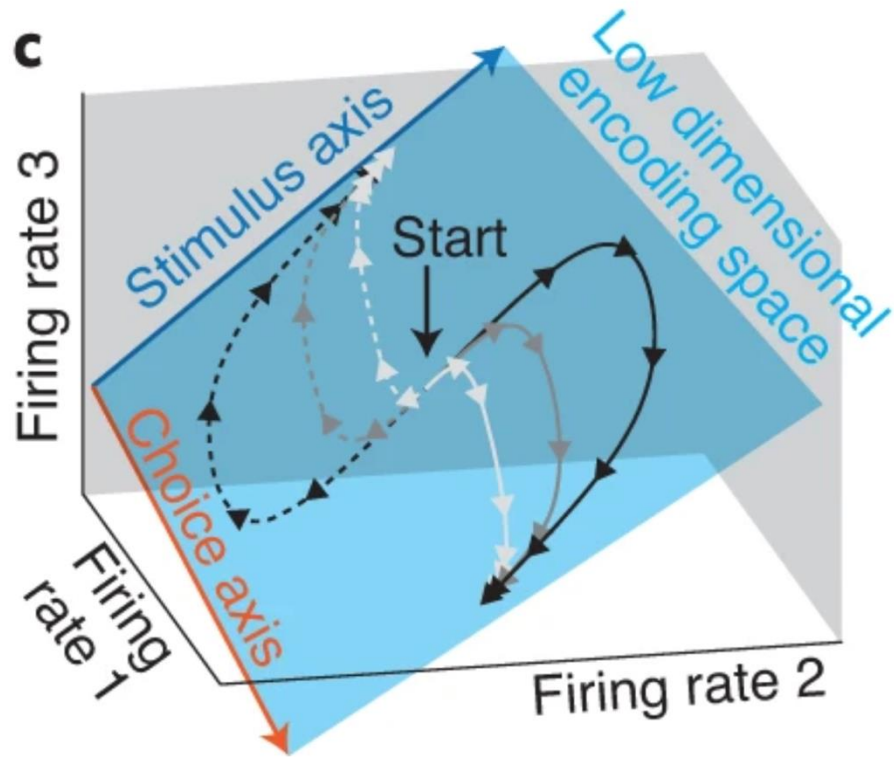
Feature Representation (downsampled)

Database with human annotations

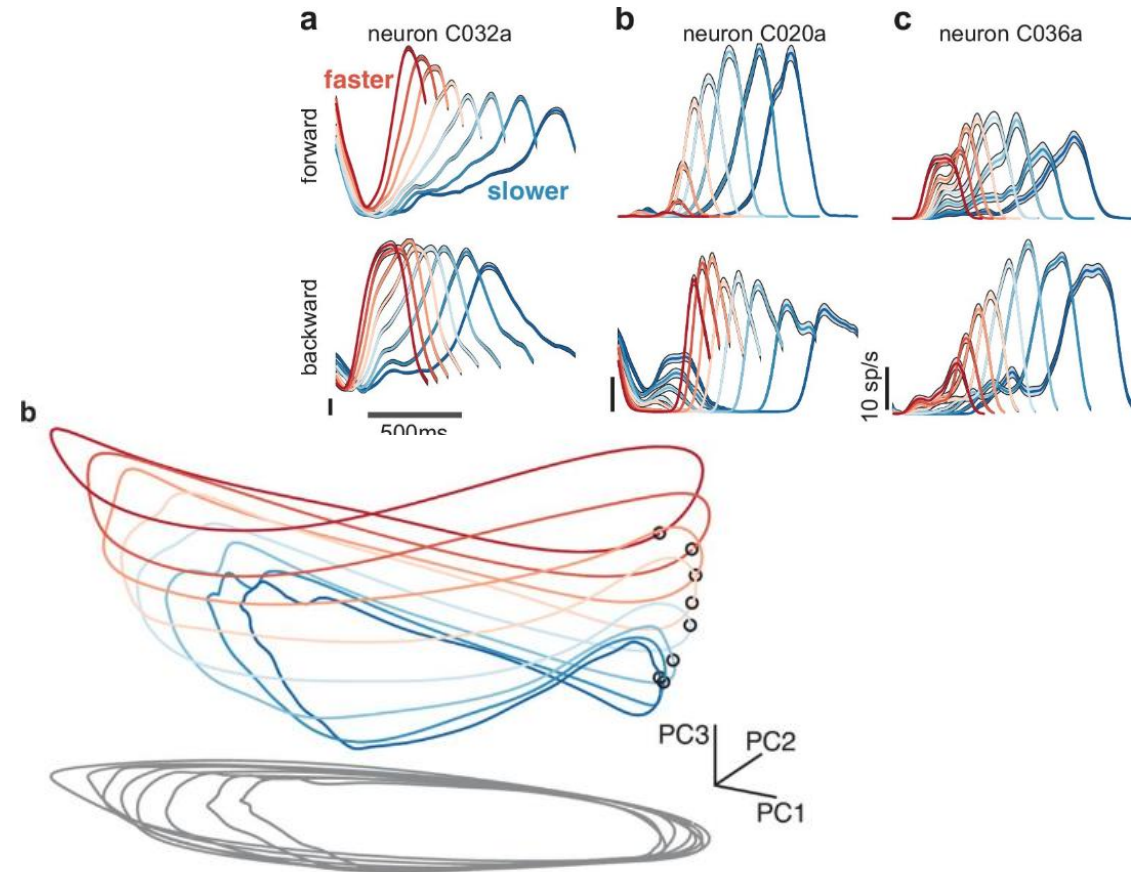
Training Criterion

Markerless methods based on deep-learning require no special preparation, but manually annotated example images.

# Population analysis can reveal core principles of neural coding



Behaviorally relevant neural variance explained by a **small number of dimensions**.



Neural computations at population dynamics in a **latent space**, but not in single-neuron firing rates.