Outline

1) Ephys – principle methods and how they can be used
2) Imaging – principle methods and how they can be used
3) Manipulating activity – stimulation and inactivation

4) Manipulating circuits - network tracing, and specificity

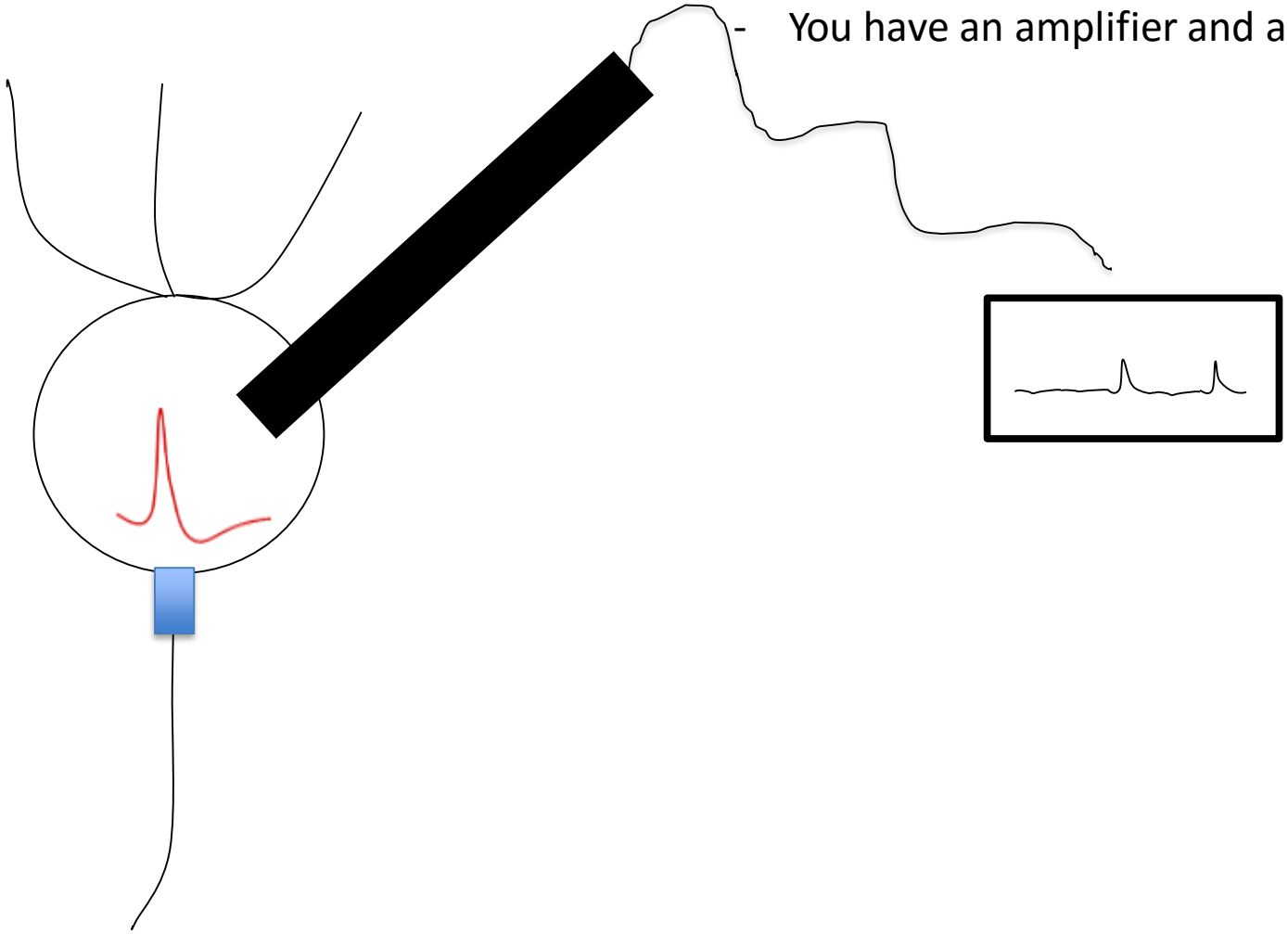
A jumble of other things:

Immediate early genes
Behaviour
Freely moving experiments

The point is to discuss things and ask all kinds of "basic" questions

Electrophysiology – a brief summary

- You want to know what neurons are doing
- You have an amplifier and an electrode



Buszaki 2000

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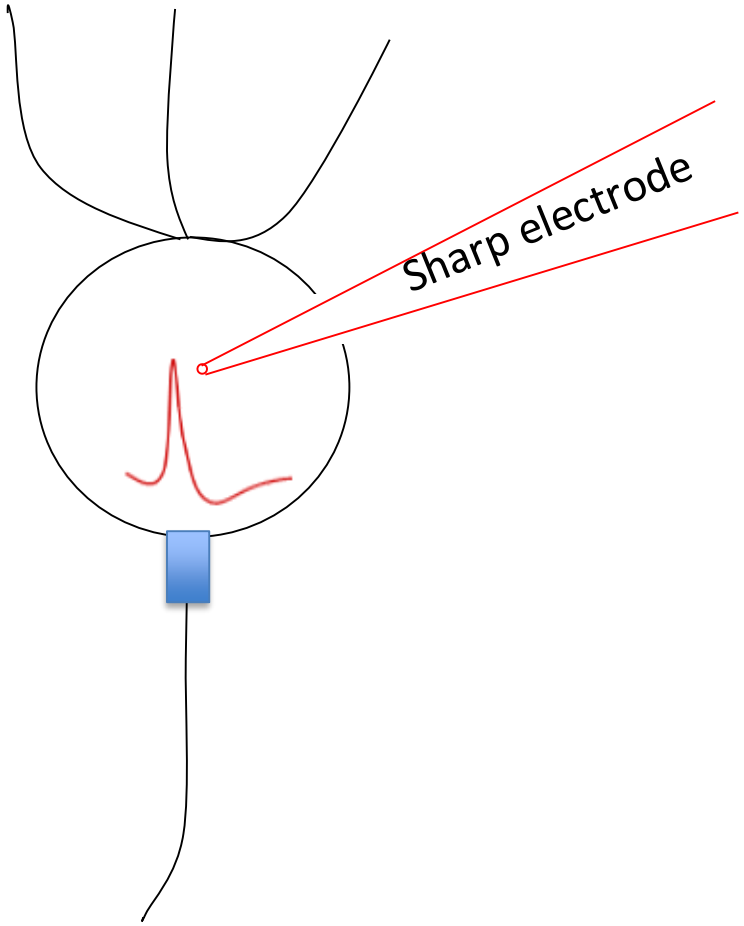
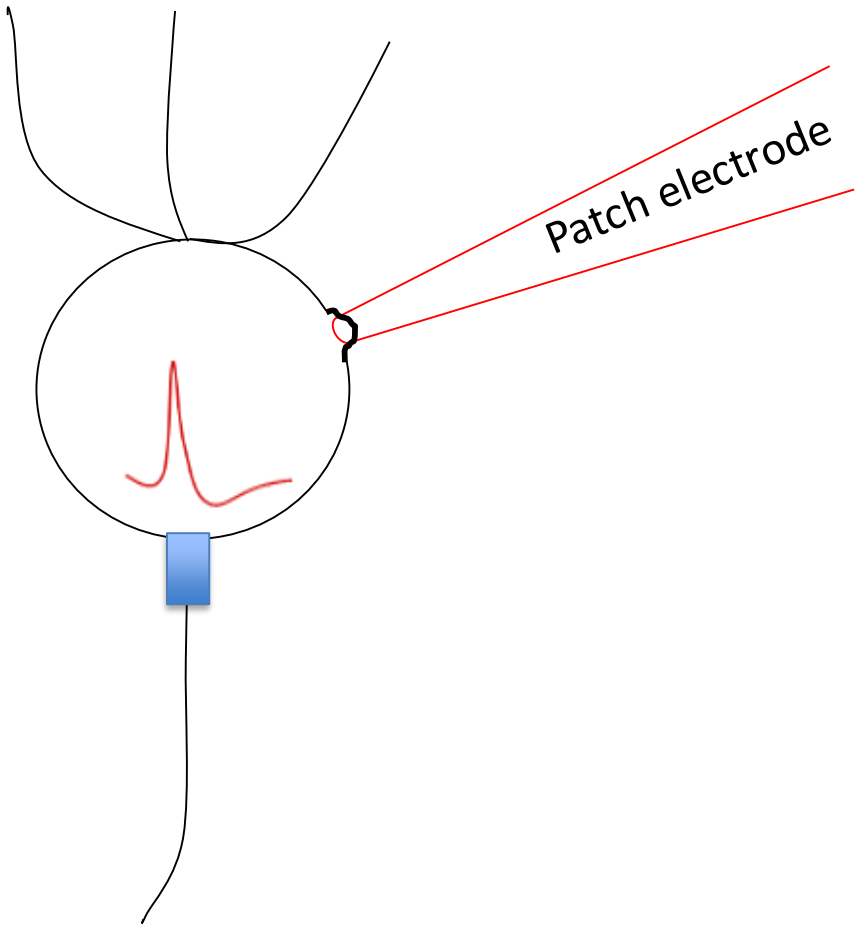


Buszaki 2000

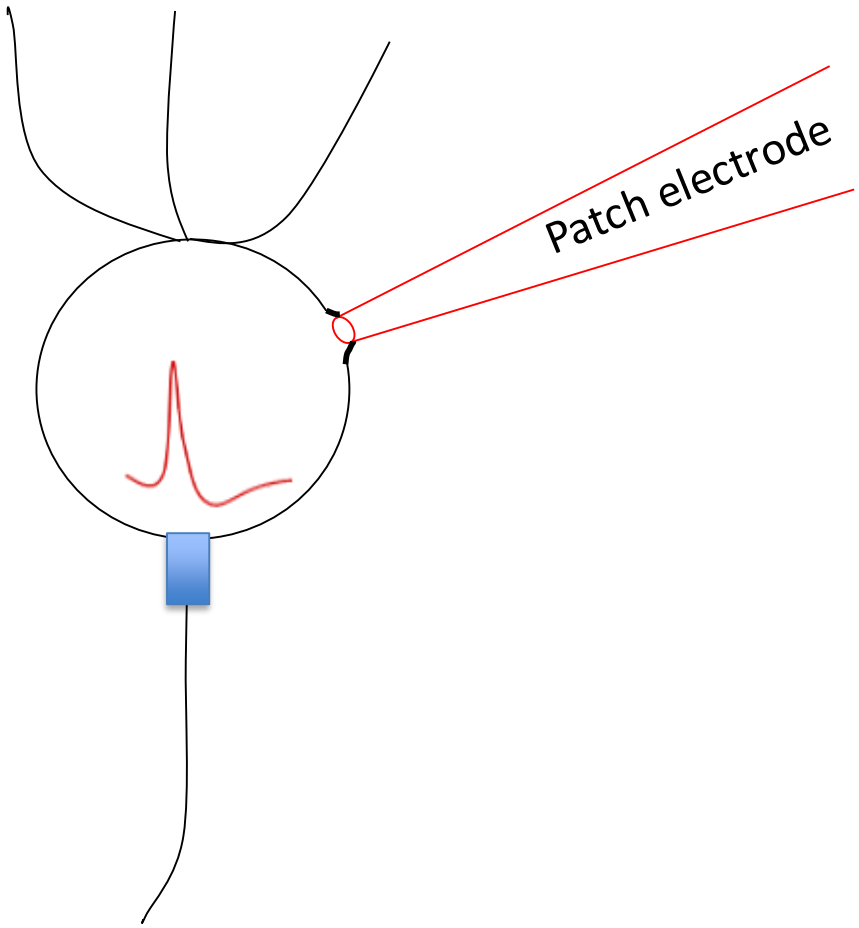
Electrophysiology – intracellular vs extracellular recordings



- Full electrical control of a cell
- Control of intracellular contents (i.e. dyes, drugs, and ions)

Buszaki 2000

Electrophysiology – intracellular vs extracellular recordings



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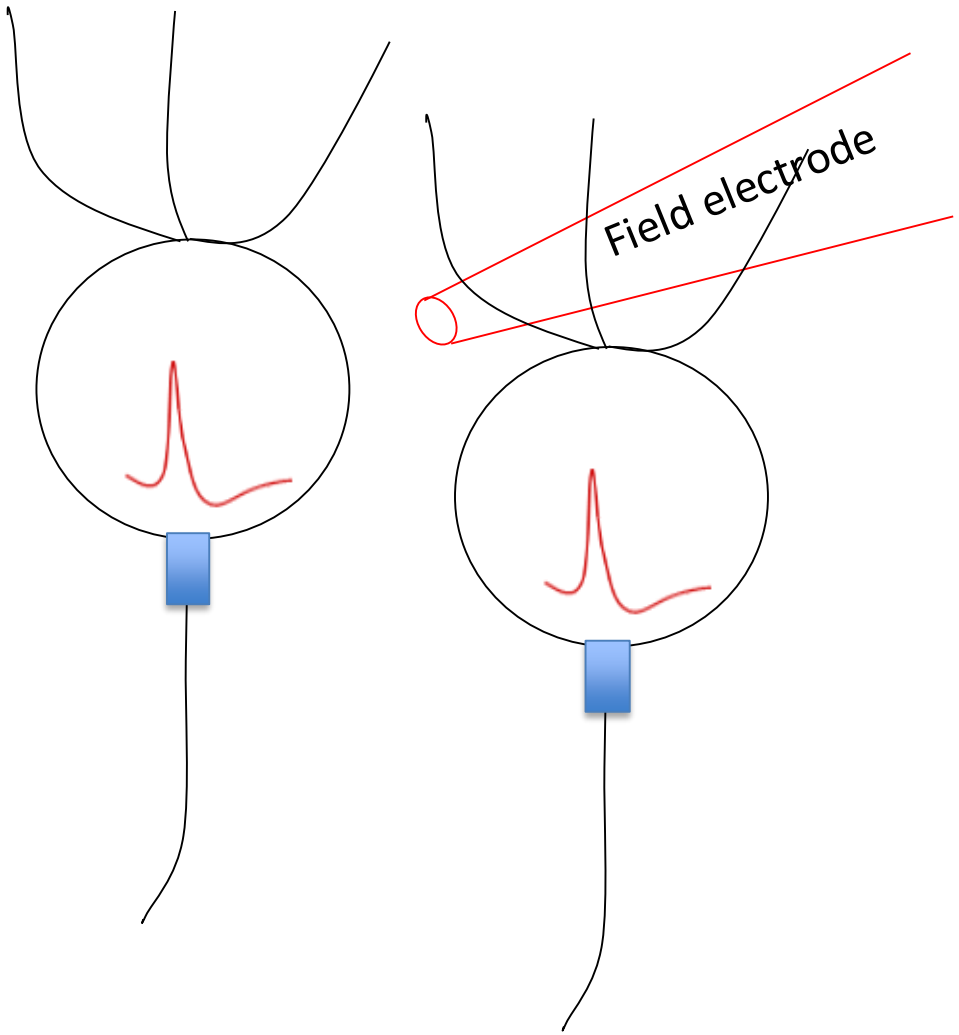

Buszaki 2000

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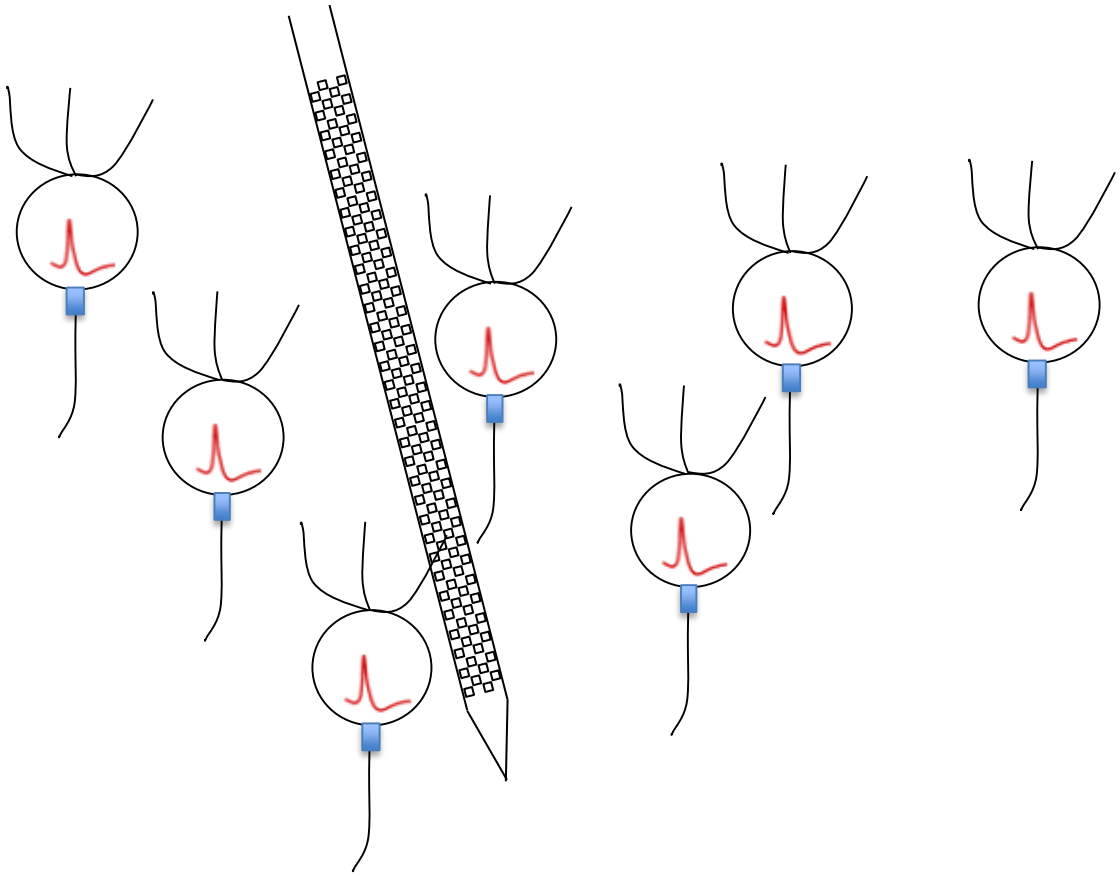
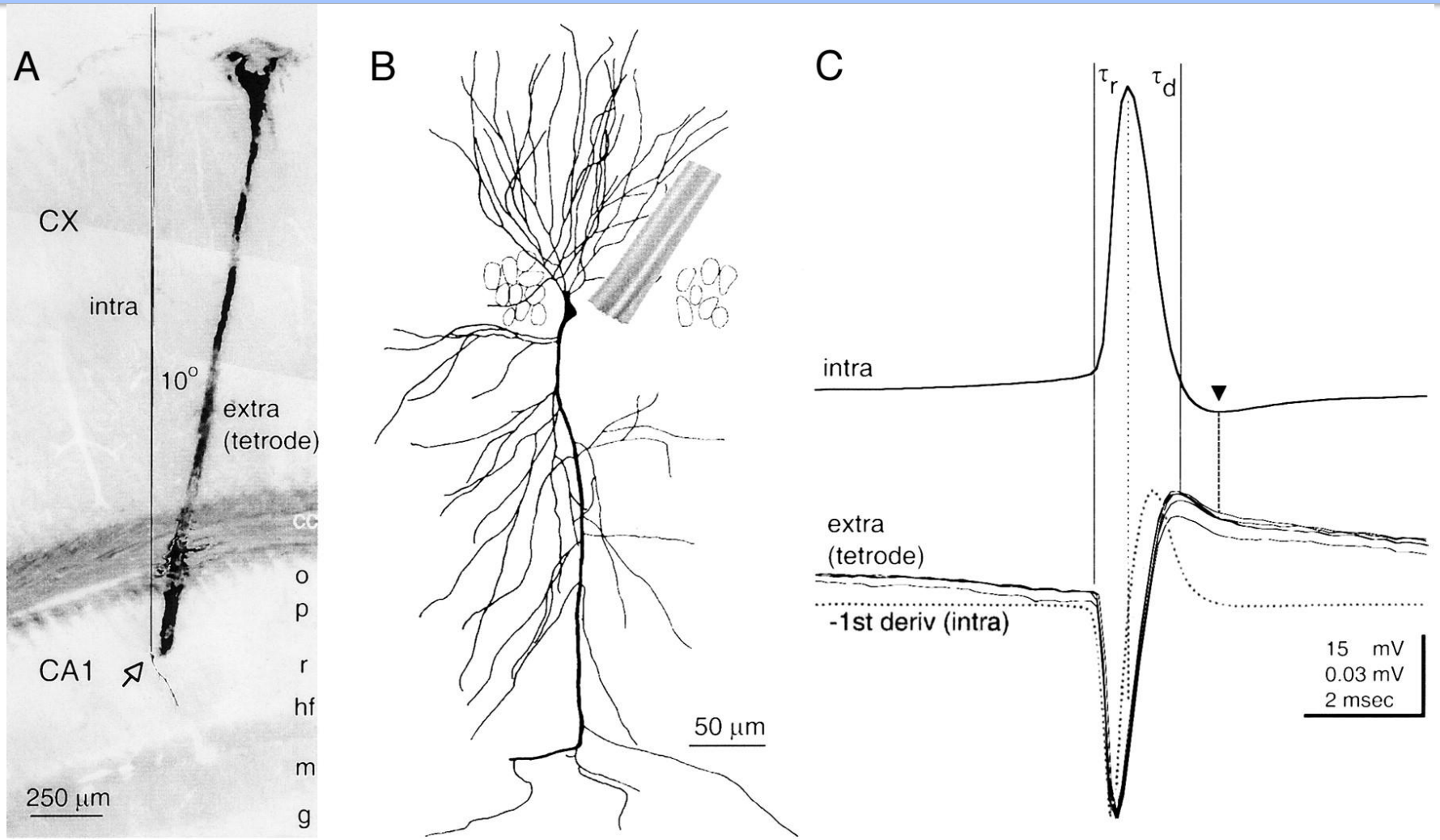


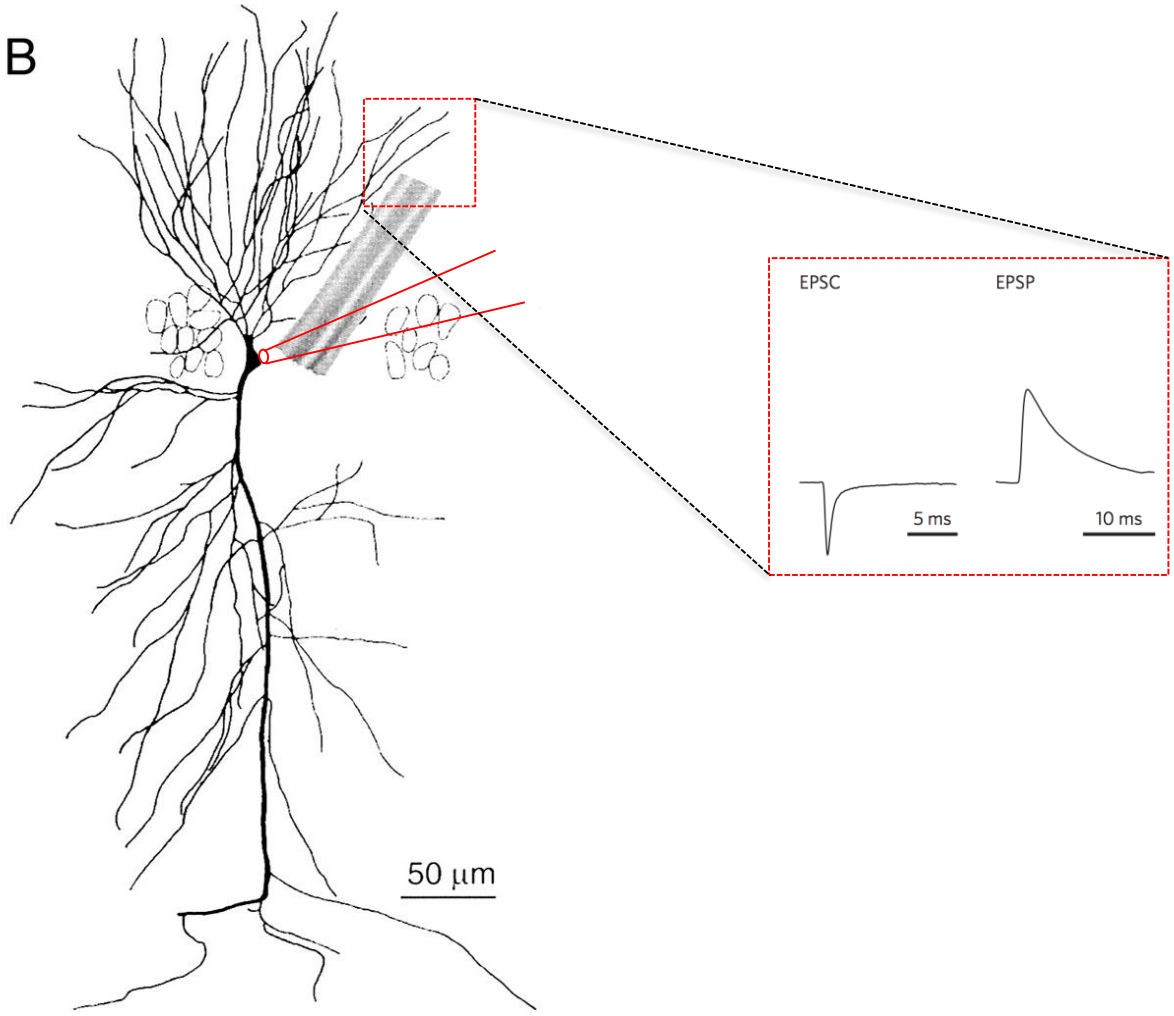
Buszaki 2000

Electrophysiology – intracellular vs extracellular recordings



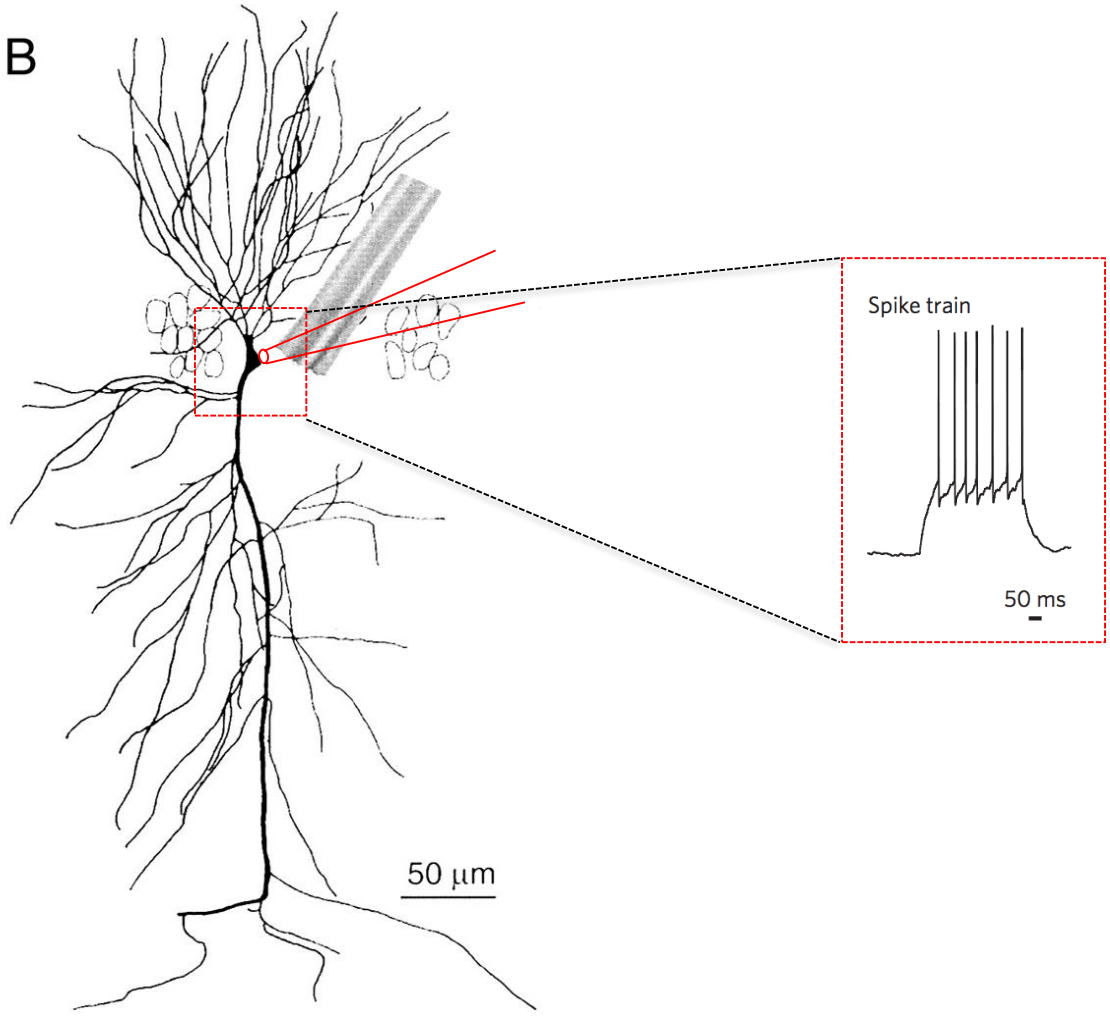
Buszaki 2000

Electrophysiology – intracellular vs extracellular recordings



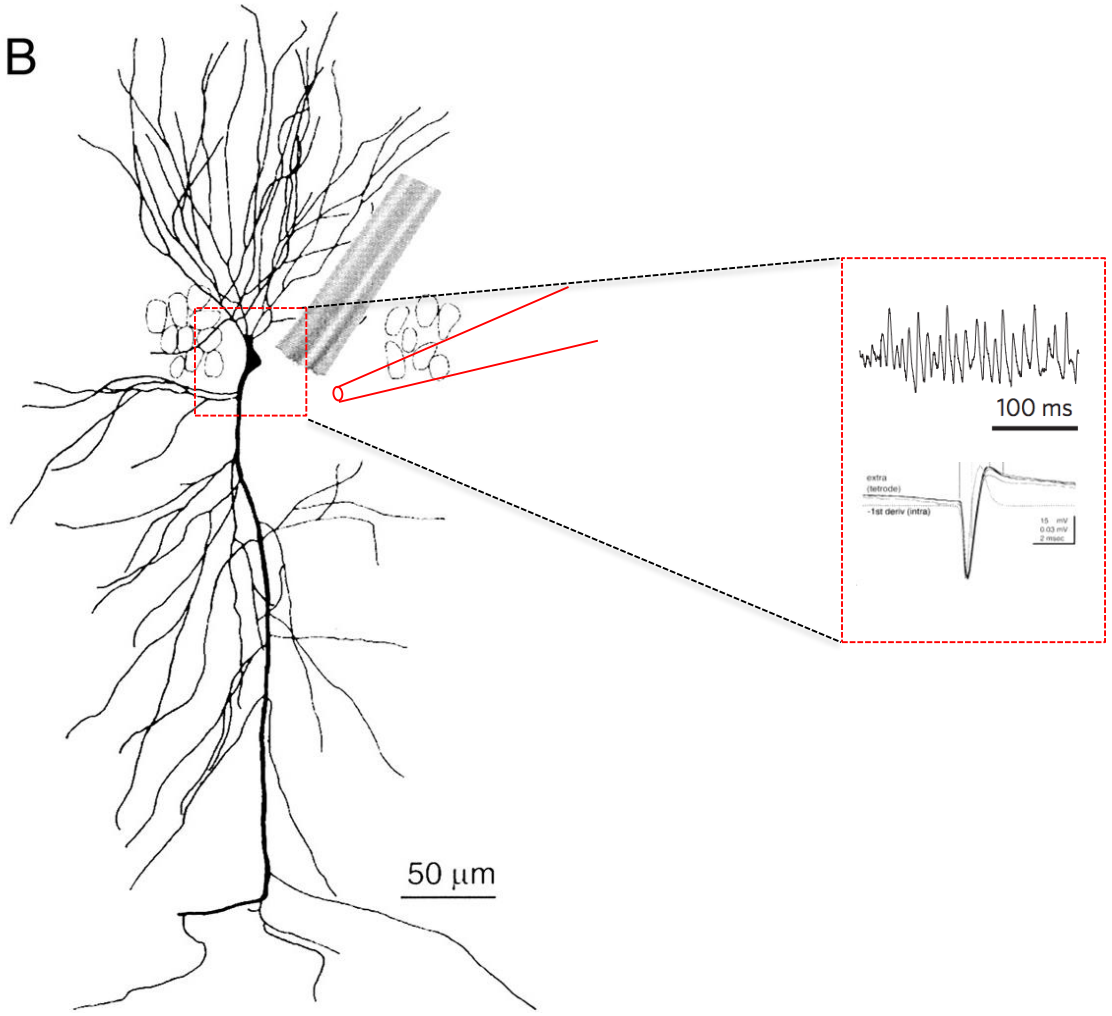
Buszaki 2000

Electrophysiology – intracellular vs extracellular recordings



Buszaki 2000

Electrophysiology – intracellular vs extracellular recordings

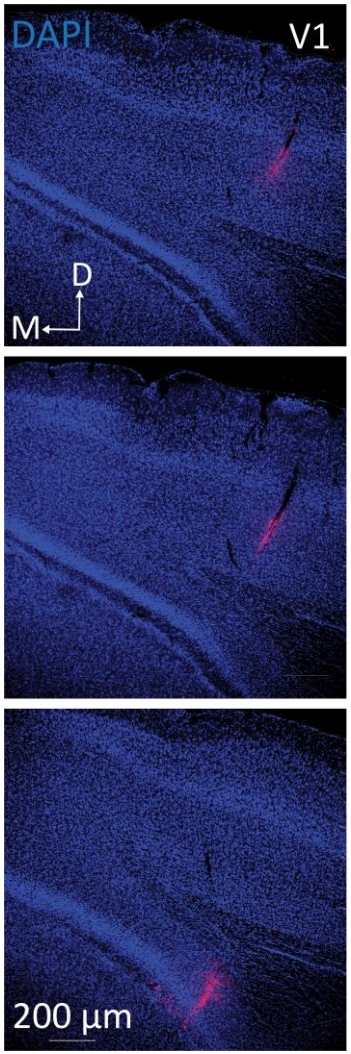


LFP

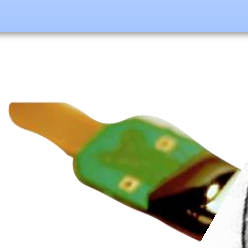
Extracellular spike

Buszaki 2000

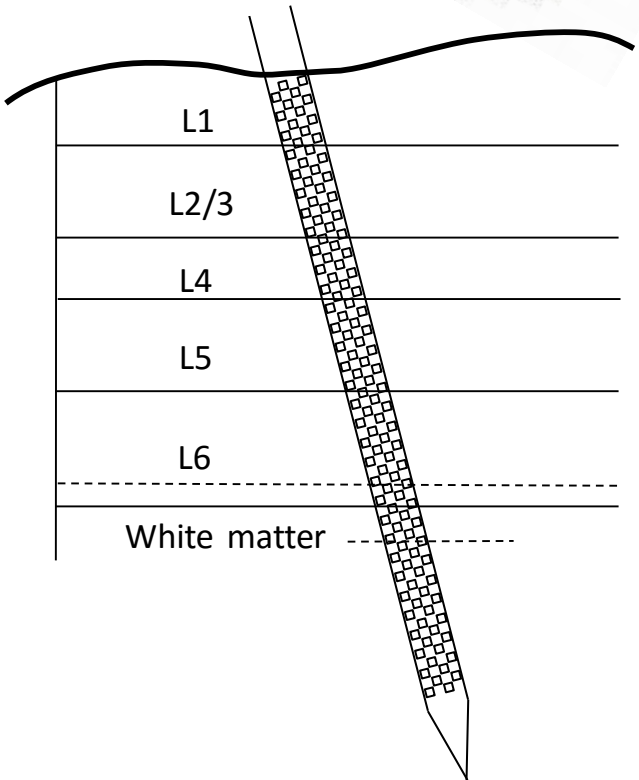
Population recordings with a high density probe

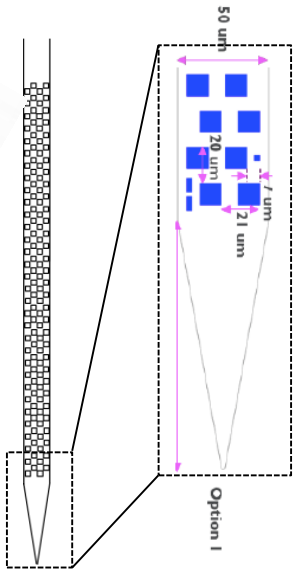


Velez-fort



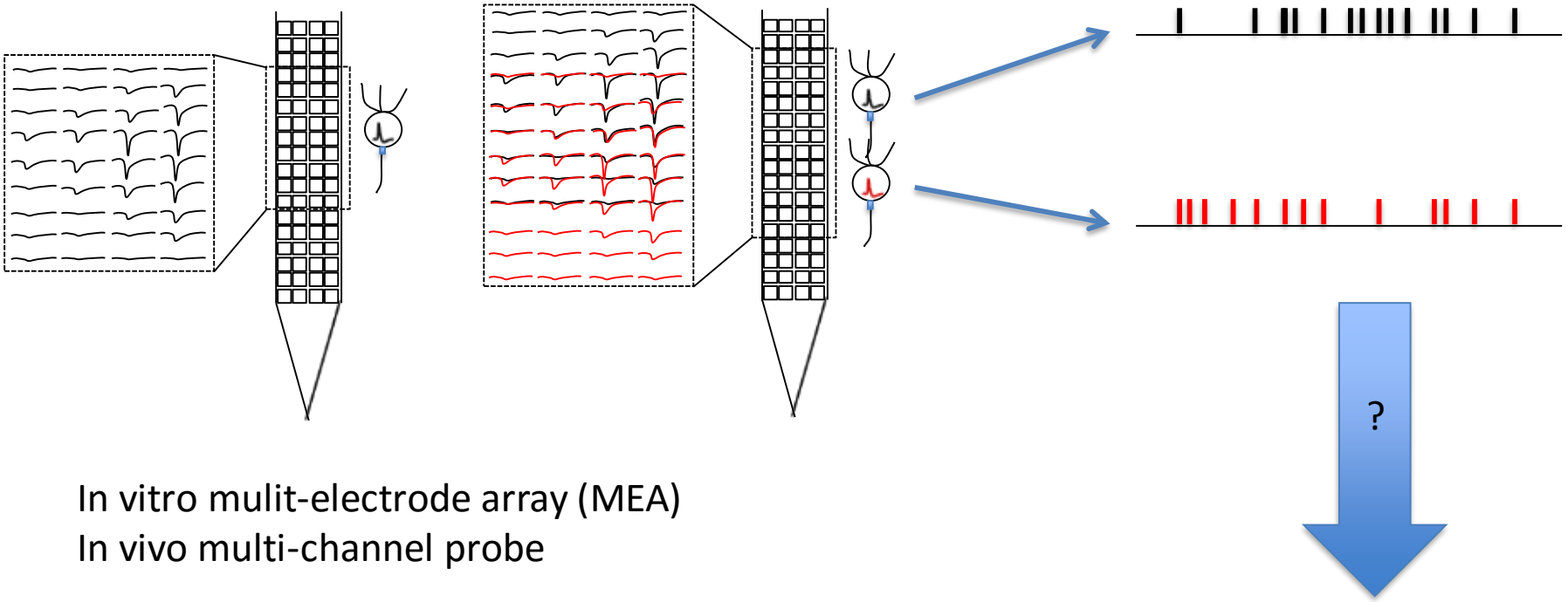
NeuroPixels Project
HHMI Gatsby Foundation
Wellcome Trust
Nerf (Belgium)





- 960 electrodes
- 384 available for recording

Analytical challenge – spike sorting

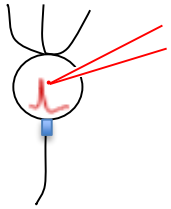


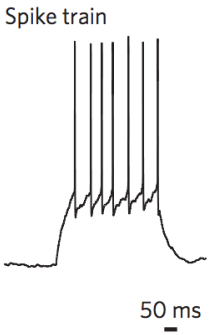
In vitro mulit-electrode array (MEA)
In vivo multi-channel probe

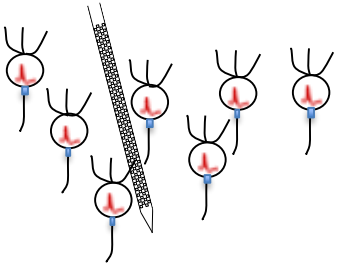
Population code

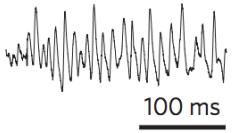
Key challenge is how to make sense of huge datasets of hundreds/thousands of neurons

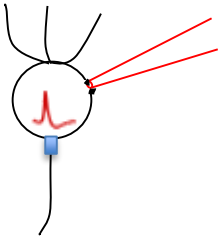
Electrophysiology – intracellular vs extracellular recordings

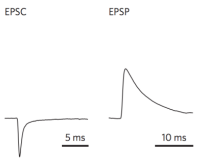


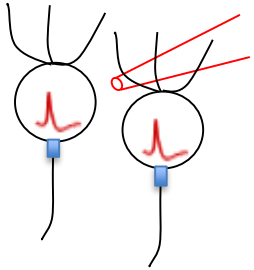


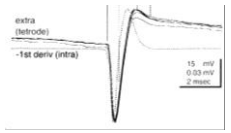




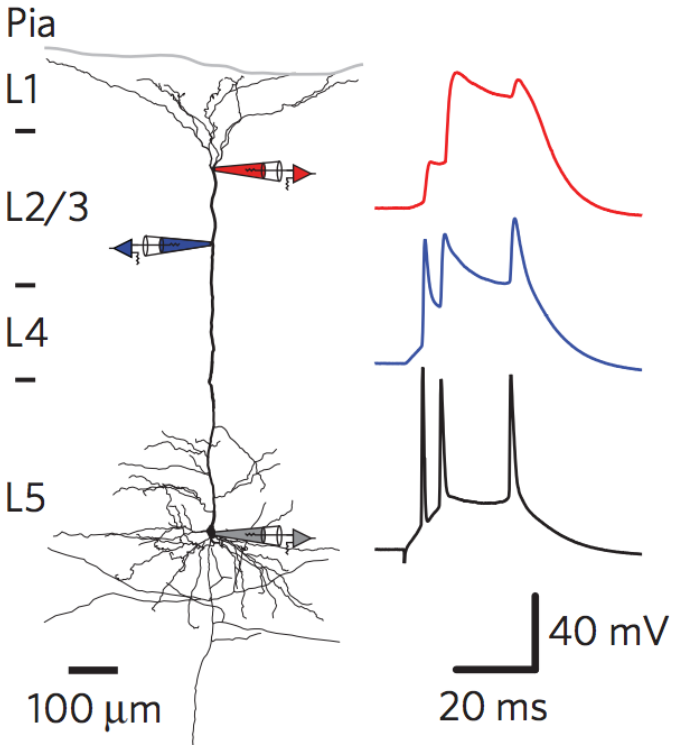






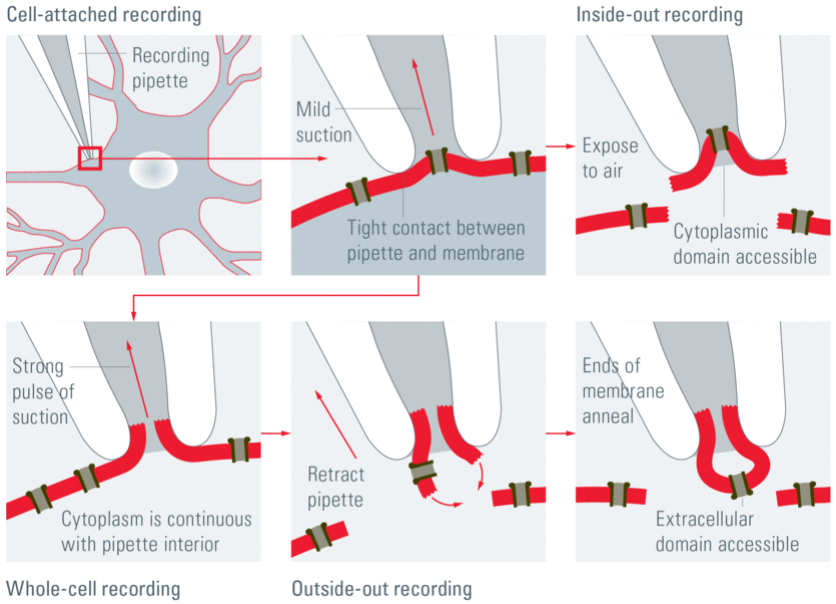


Buszaki 2000

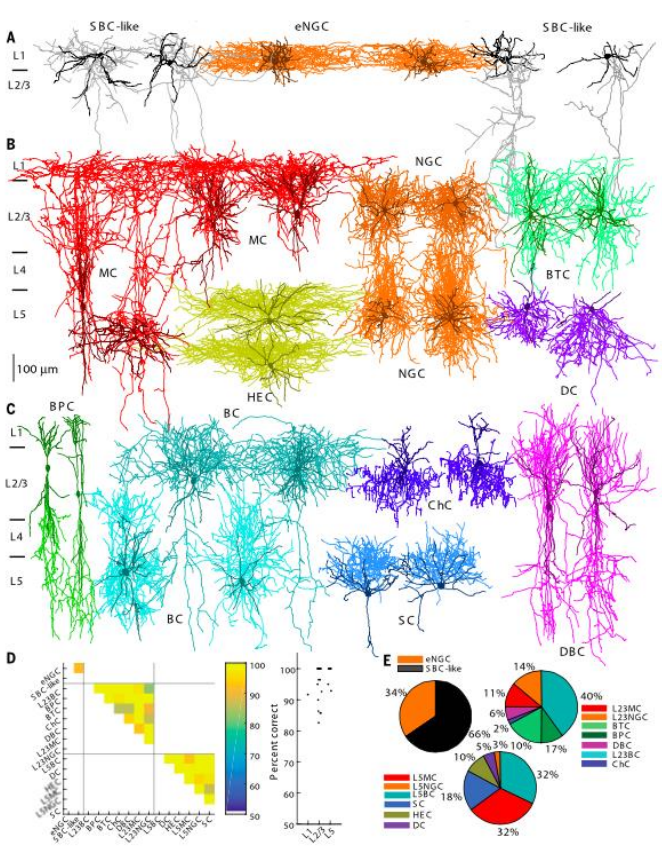


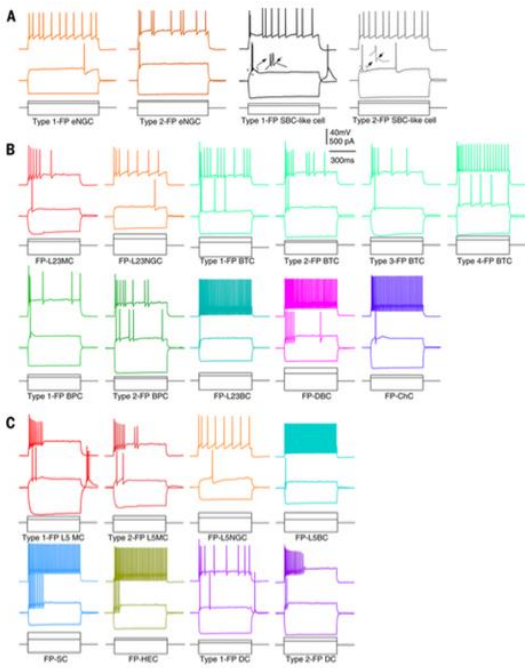
Smart use of holding potential in V-clamp to see contribution of some channel types to some response (e.g. drug)

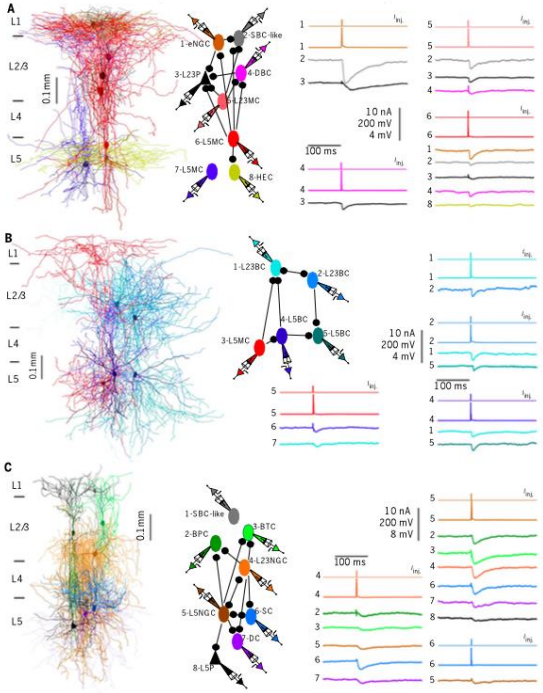
Specific study of channels themselves



Applications of patching – multiple patch clamp connectivity studies

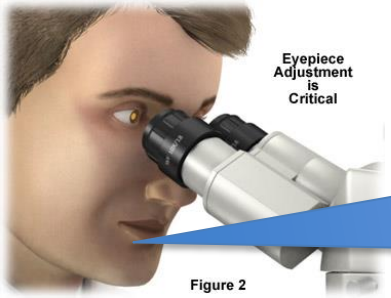






Jiang 2015

Imaging – core principles



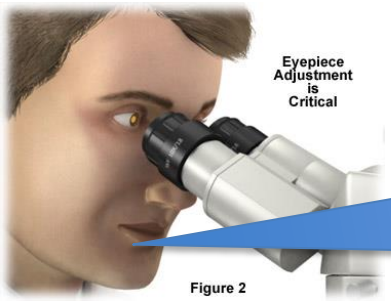
I CAN NOT SEE MUCH

Introduce dye e.g. Ca2+ indicator

LASER

Dye molecule

Imaging – core principles



I CAN SEE MUCH MORE NOW

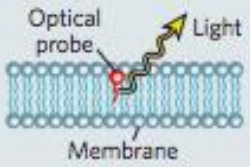
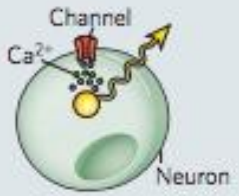
LASER

molecule

Ca2+

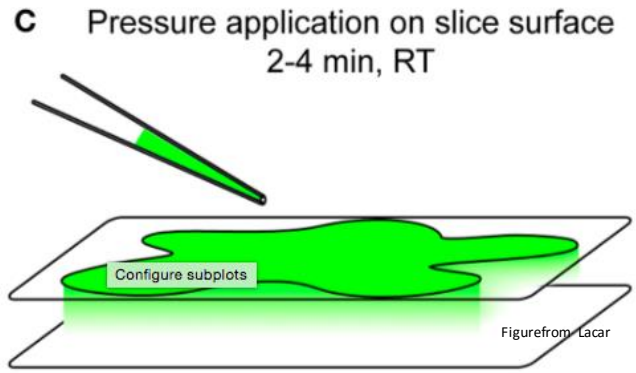
Different types of optical sensor

Table 1 | Classes of optical probes and reporters

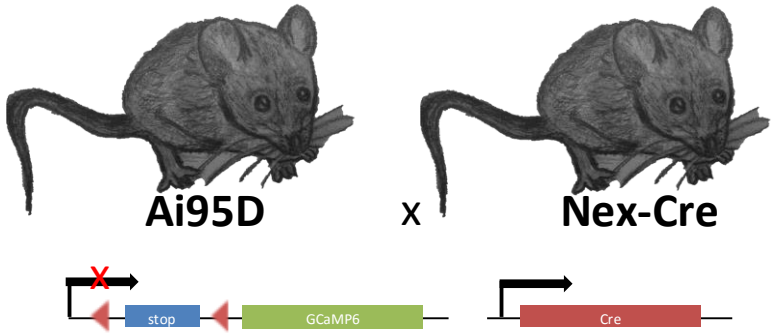
Type of molecule	Illustration
Measuring	
Voltage sensors	
Calcium sensors	
Receptor/channel reporters	
Synaptic release reporters	

Dye loading and field recordings

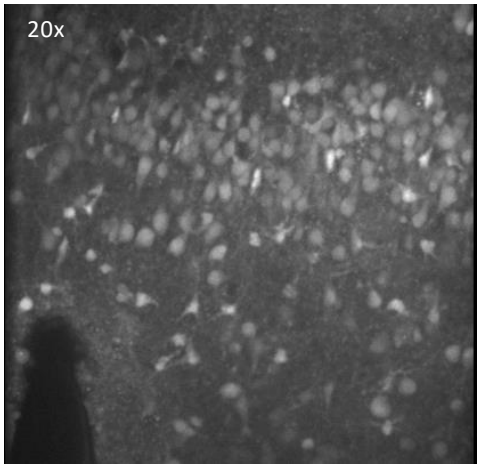
Acute dye loading (Bolus OGB-1AM)

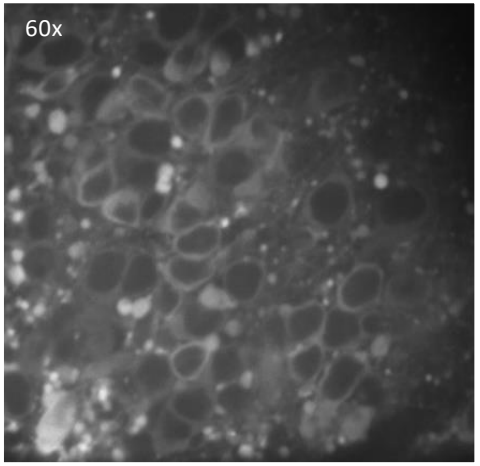


Constitutive GCaMP6f expression

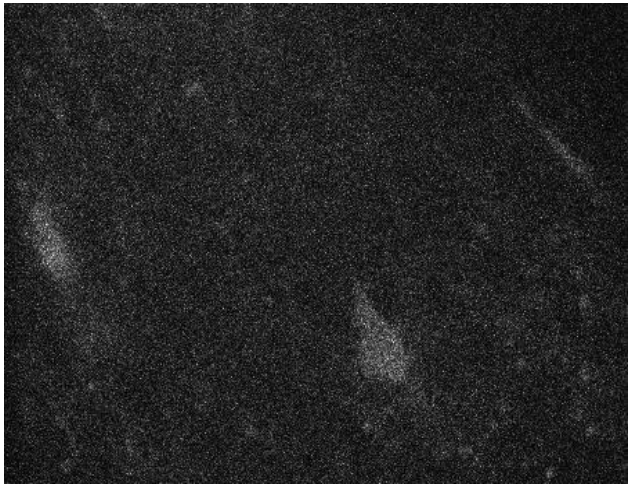


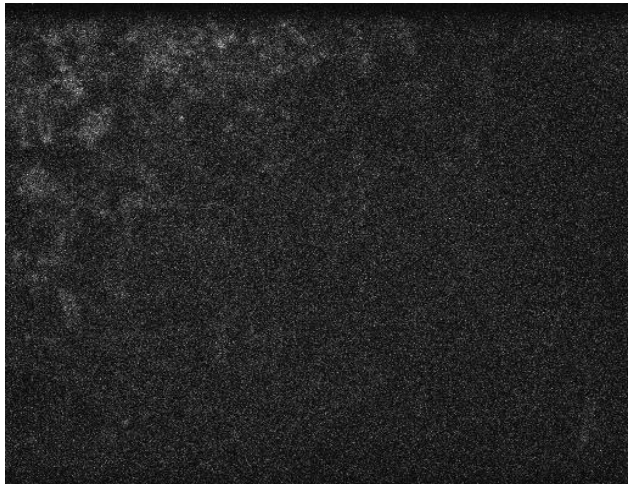
Spinning disc, 10Hz/40Hz

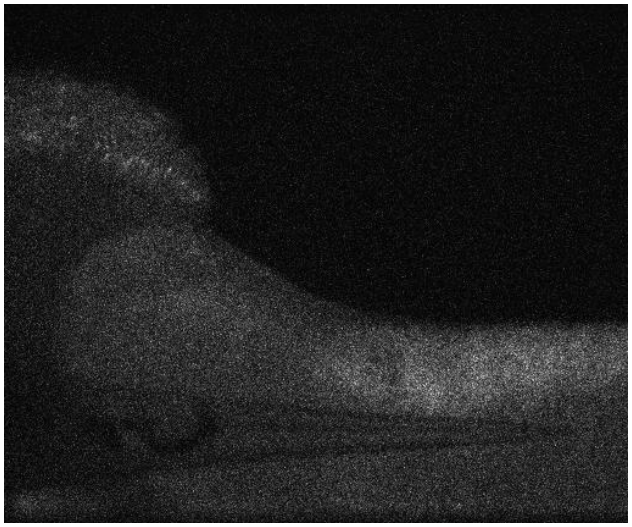




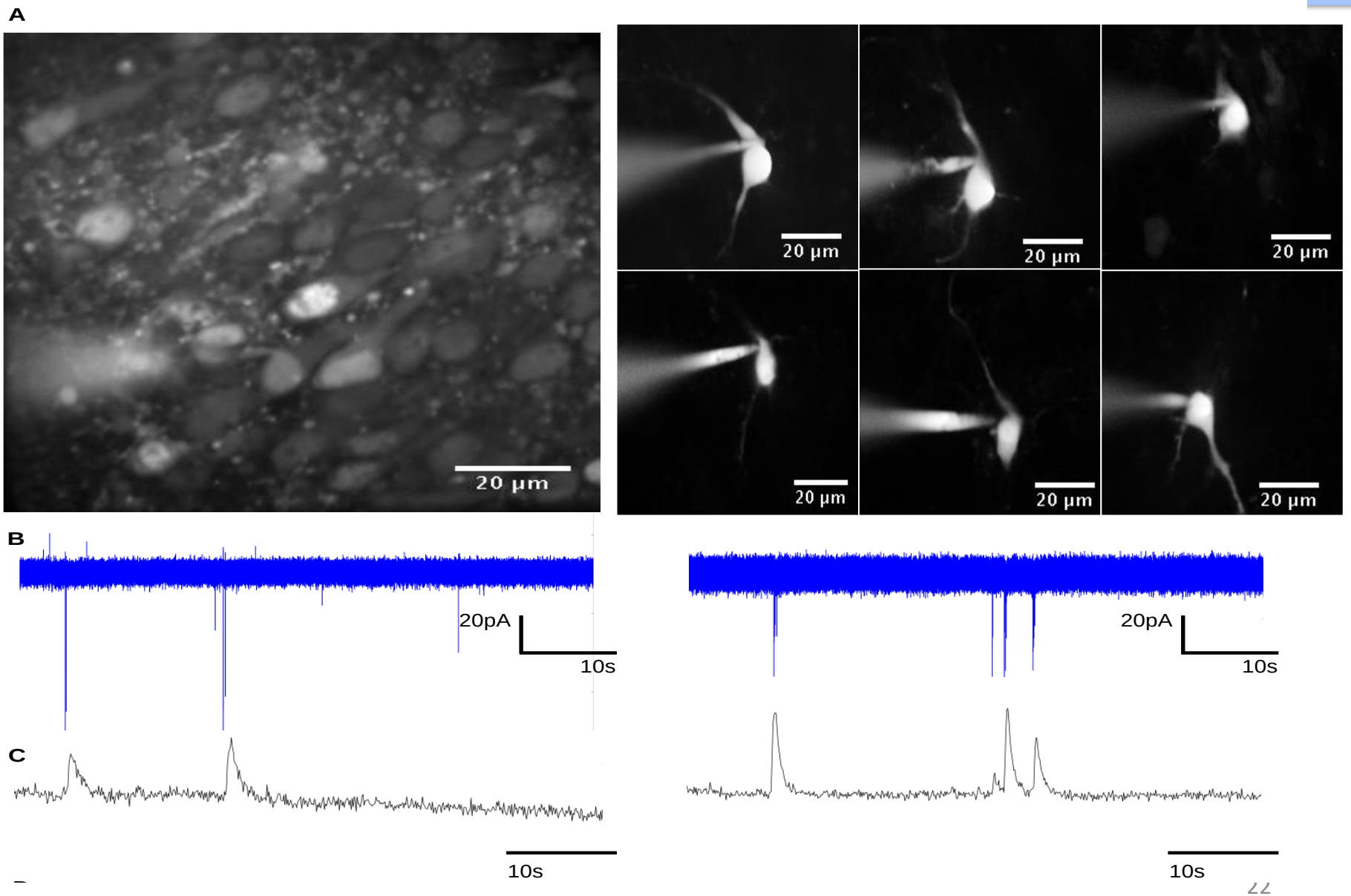
Ca2+ imaging - examples



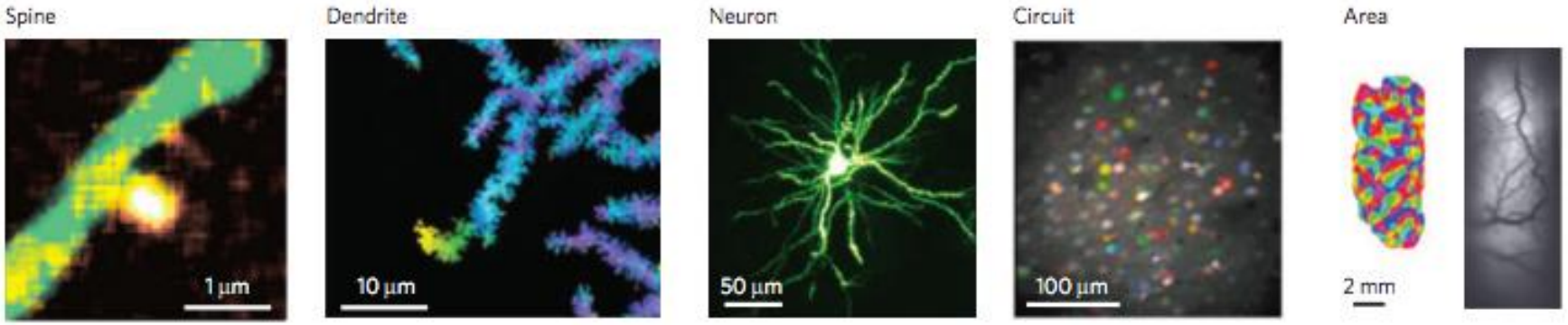


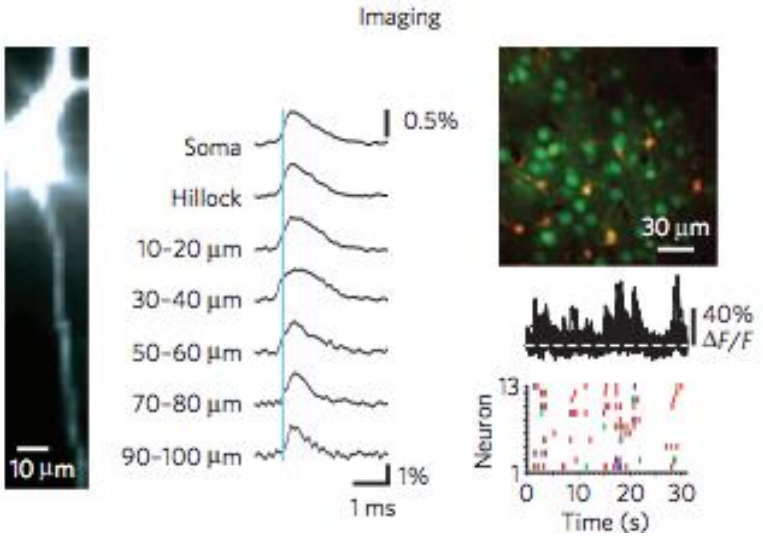


Combined ephys and imaging



Imaging different structures

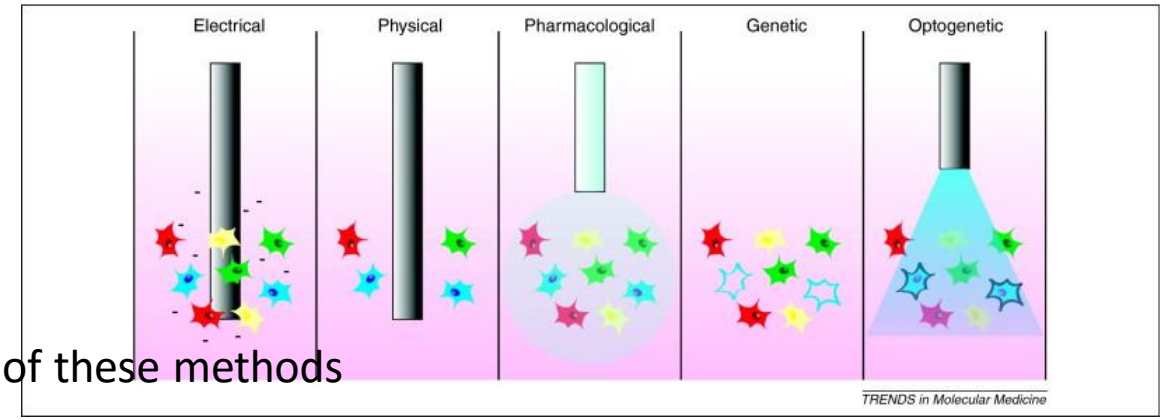




Hausser and Scanziani 2009

Manipulating neuronal activity

- Causality
- testing sufficiency/necessity of activity
- i.e. if I remove activity I think is important, what happens, if I introduce activity, what happens

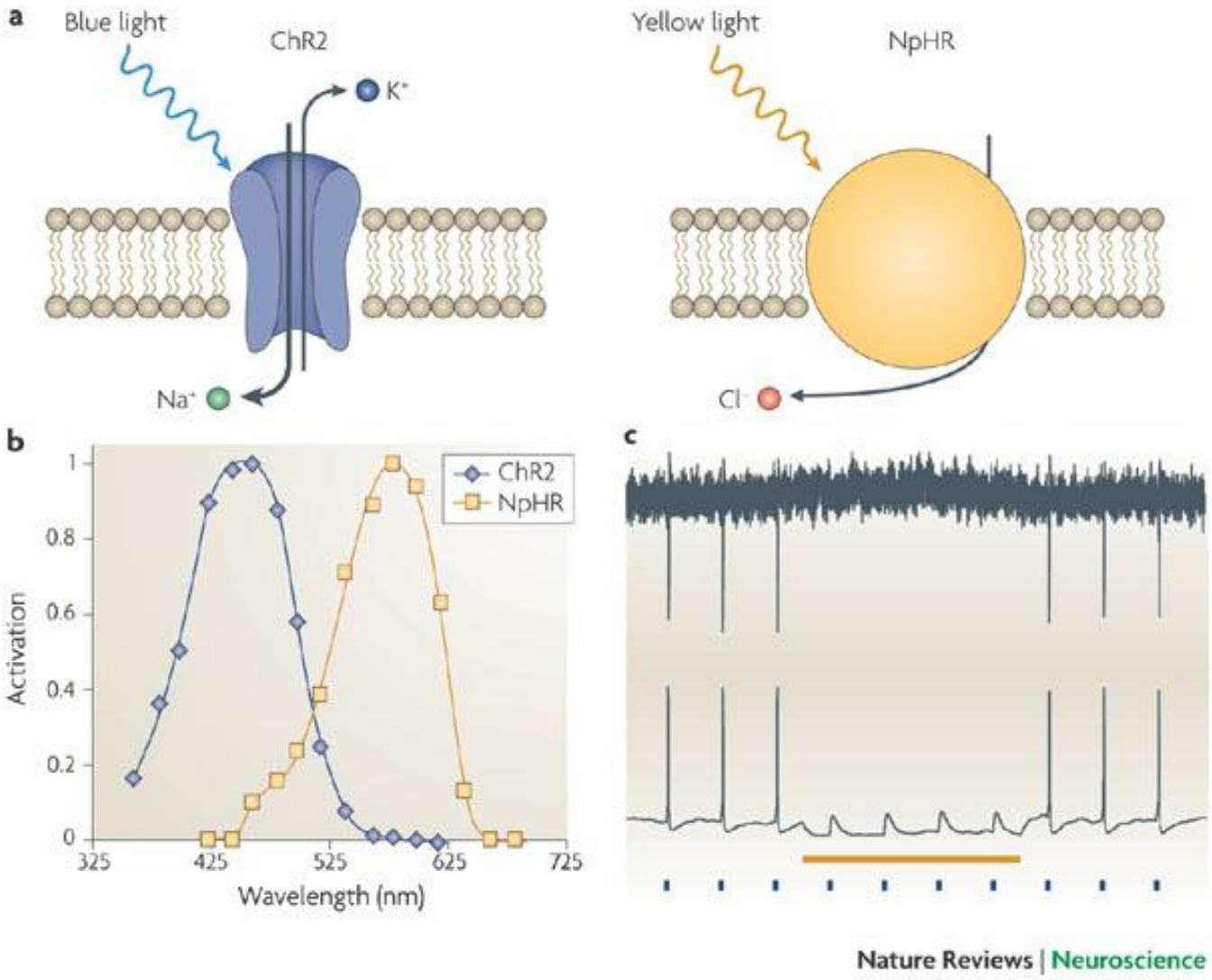


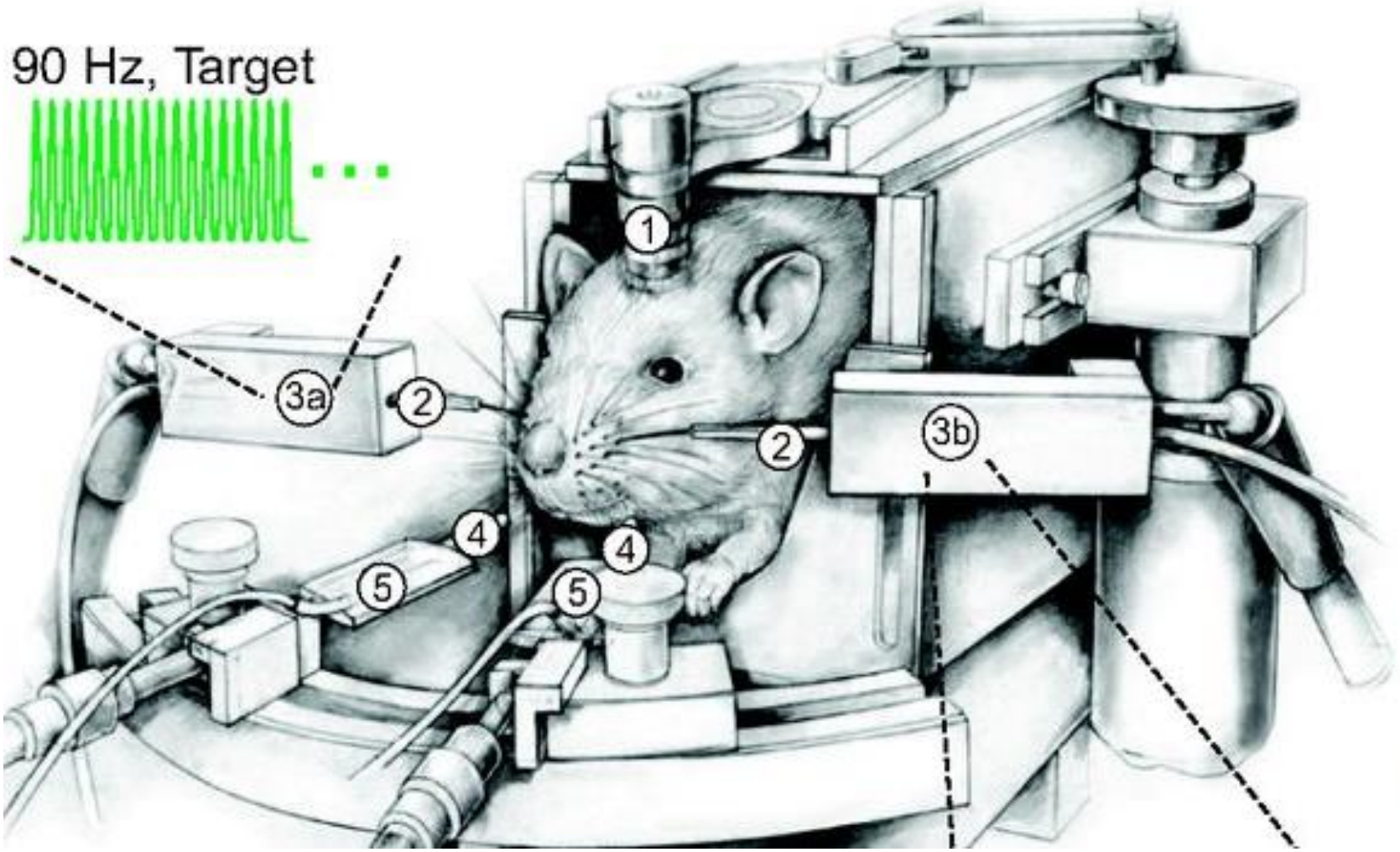
Oldschool methods

- Lesions
- Electrical stimulation

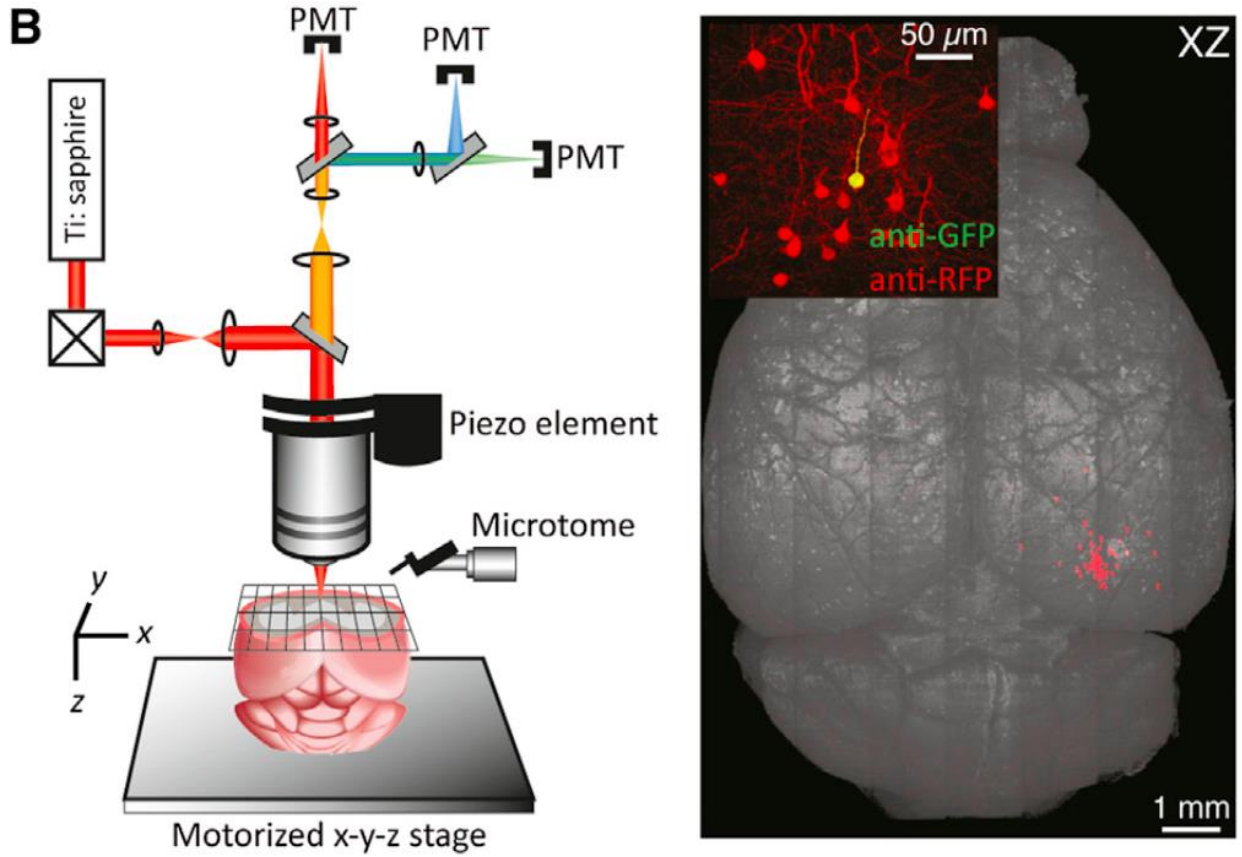
- Loads of problems with both of these methods

Manipulating neuronal activity - optogenetics

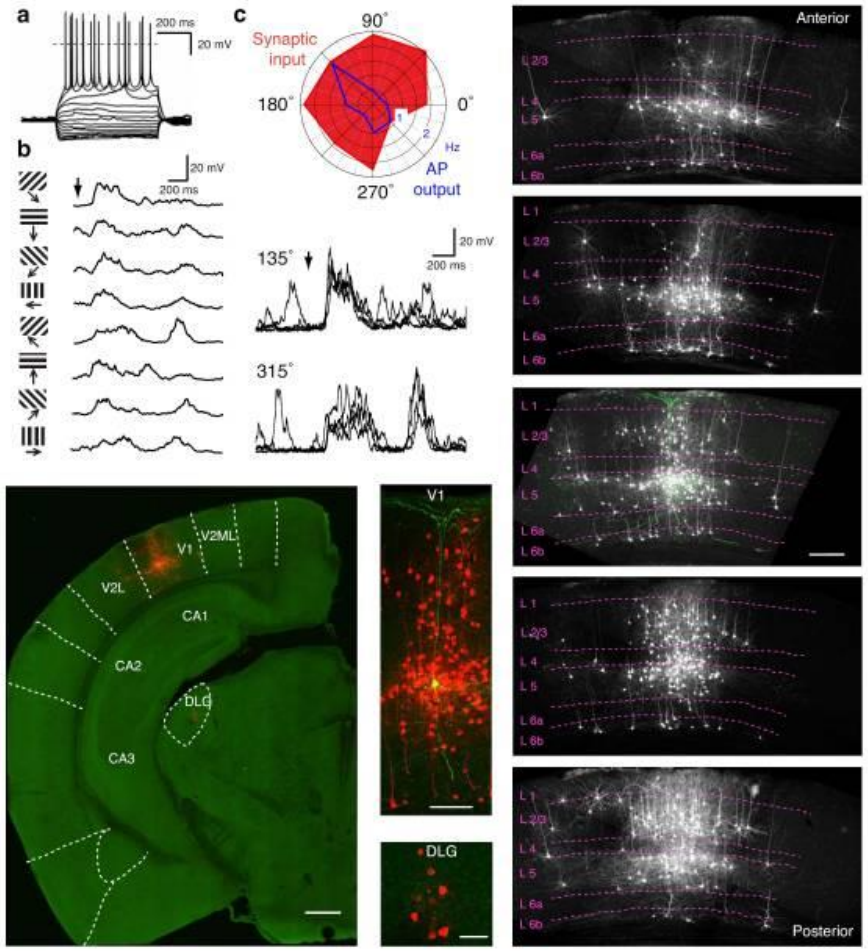



90 Hz, Target
1
2
2
3a
3b
4
4
5
5

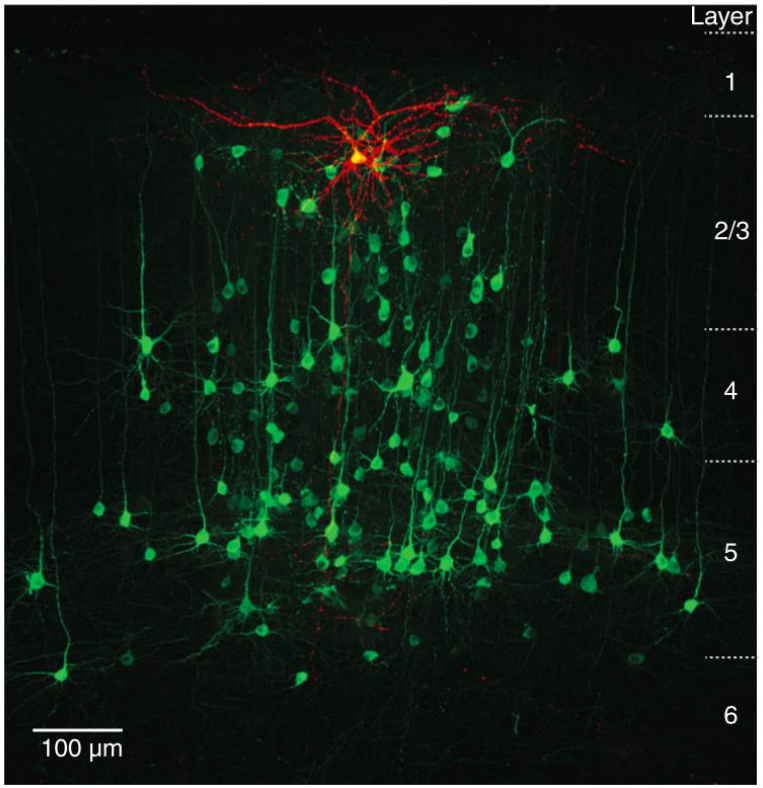
Whole brain reconstruction with tracing



Circuit tracing before/after electrical recording



Rancz, margrie 2011



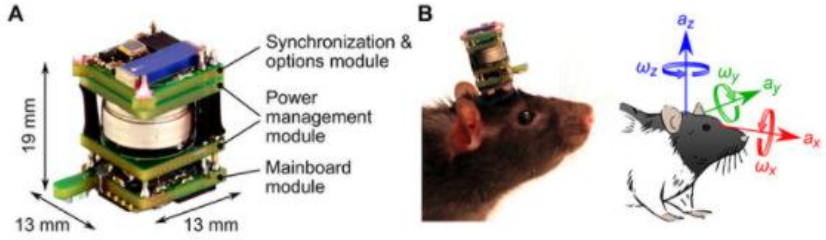
Wertz, Roska 2015

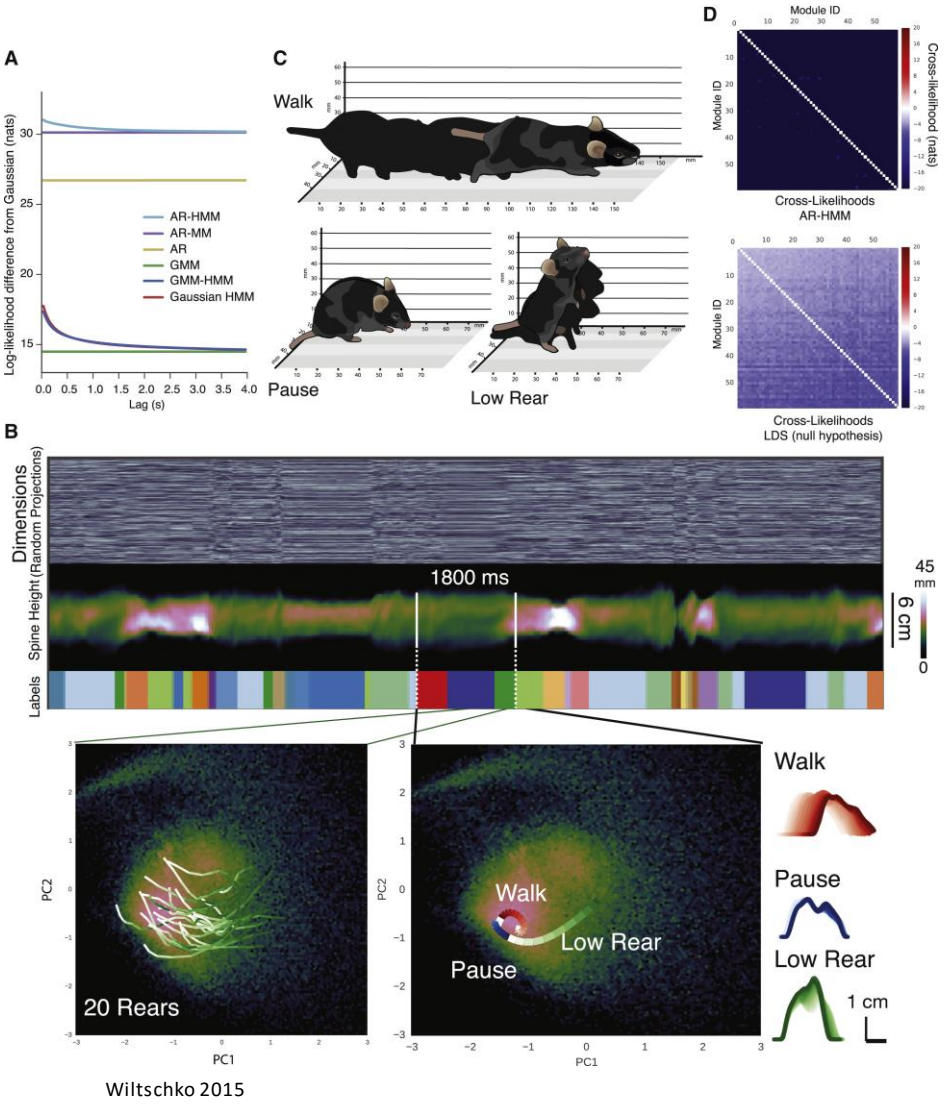
- record from a neuron
- Anatomical and synaptic receptive field
- See all direct inputs to that neuron
- Inducible GCaMP6

Behaviour

https://www.youtube.com/watch?v=t8XZ-_EgWB8

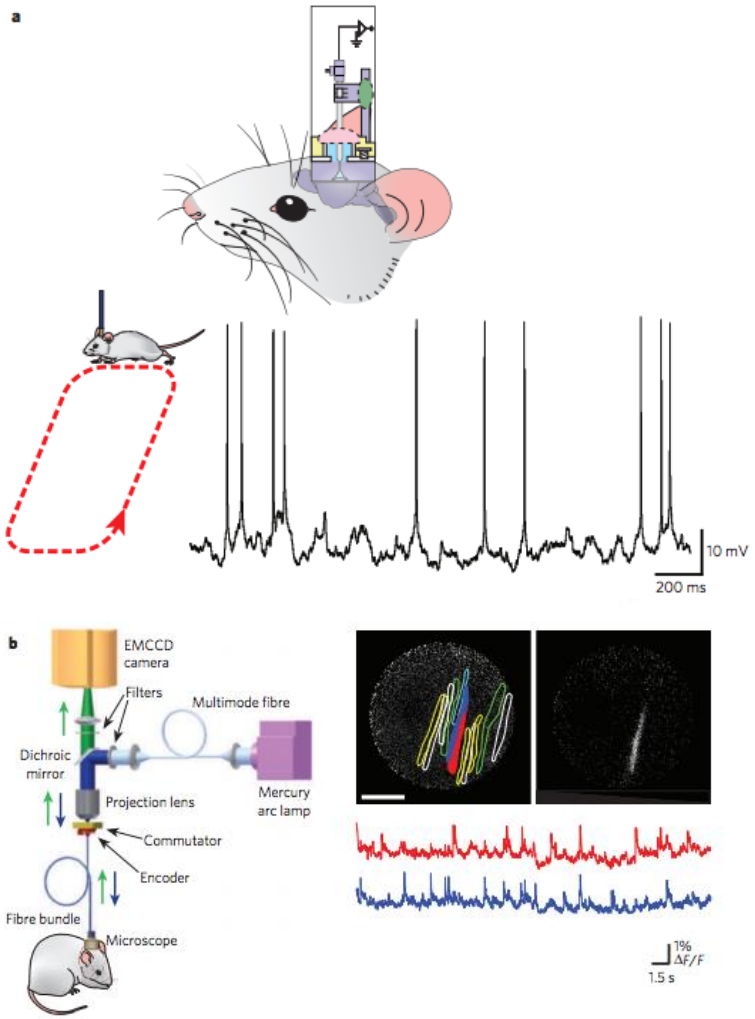
Extracting behavioural variables

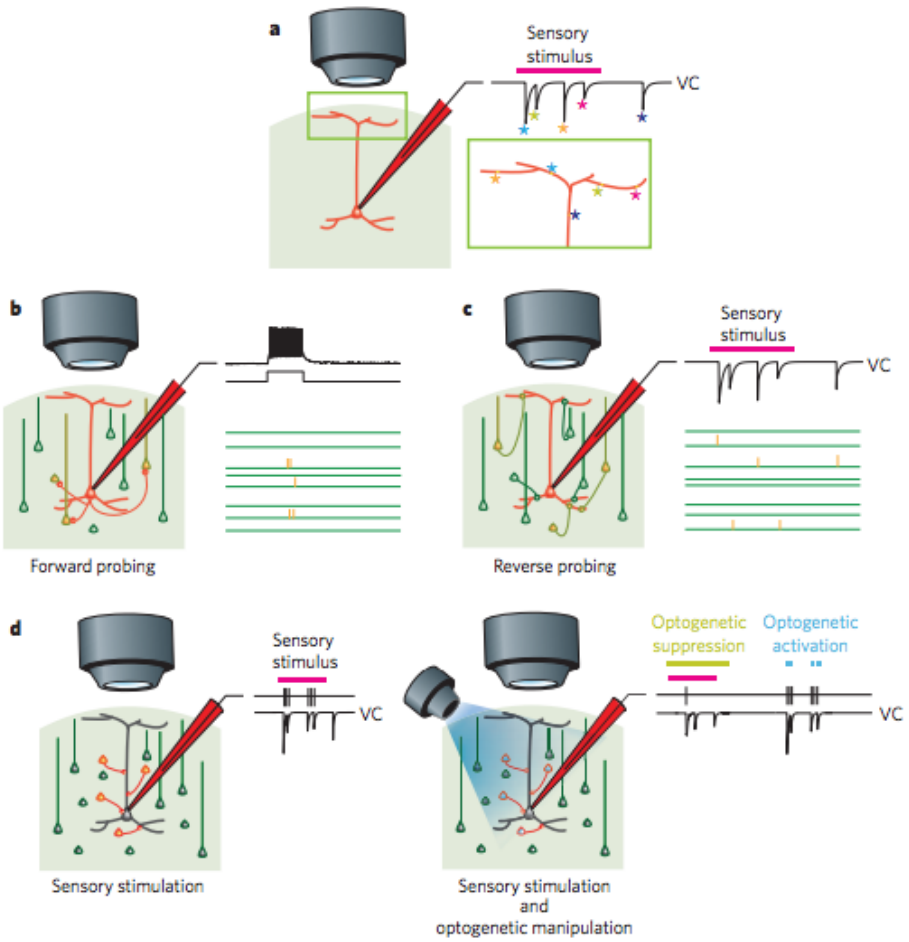




Wiltschko 2015

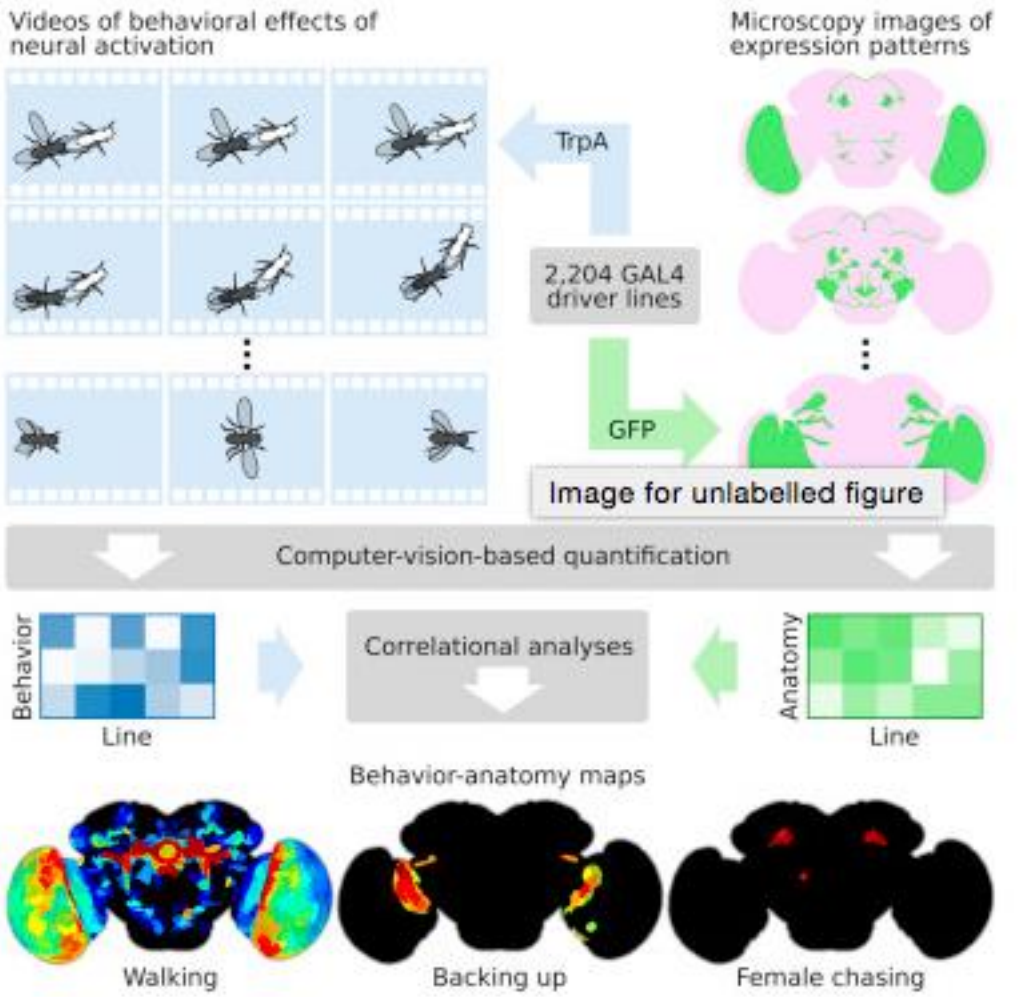
Recording during free behaviour





Hausser and scanziani 2009

Mapping behaviour onto neuronal activity



Robie 2017