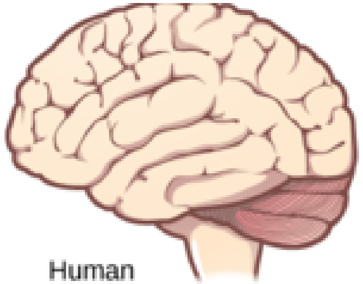
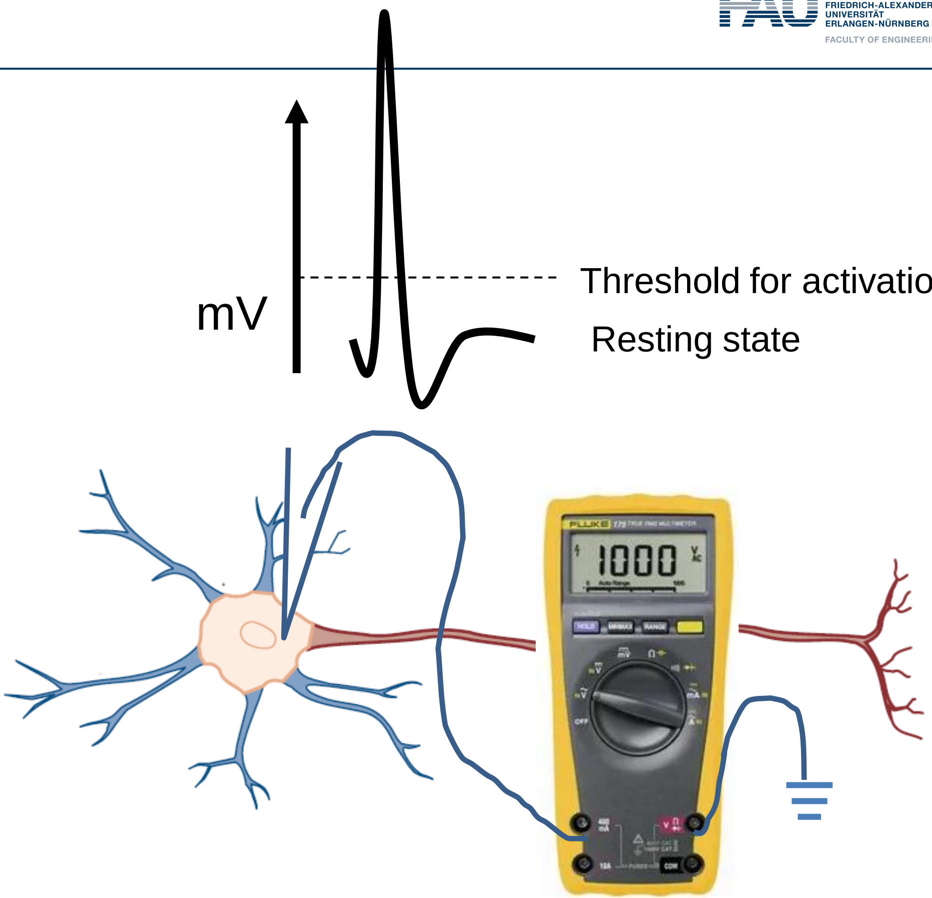
FRIEDRICH-ALEXANDER
UNIVERSITÄT
ERLANGEN-NÜRNBERG
FACULTY OF ENGINEERING

Cognitive Neuroscience for AI Developers

Week 07 – Measuring neural activity and connectivity

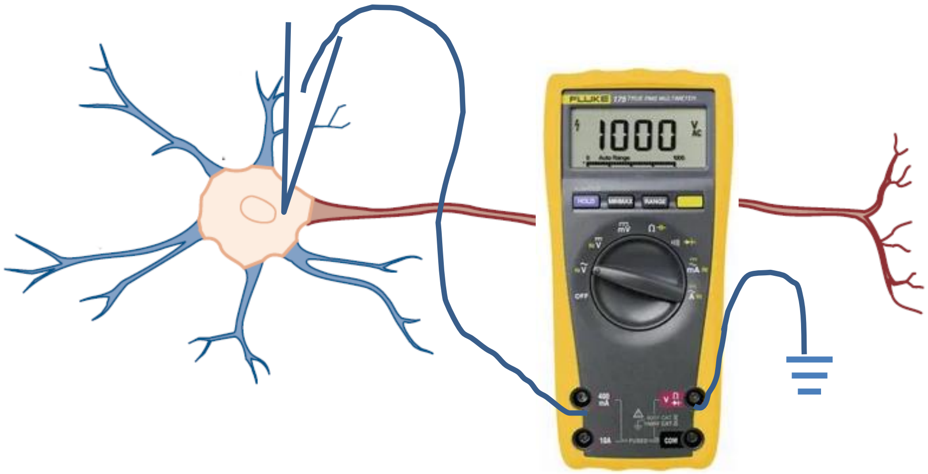
How do we actually know…?

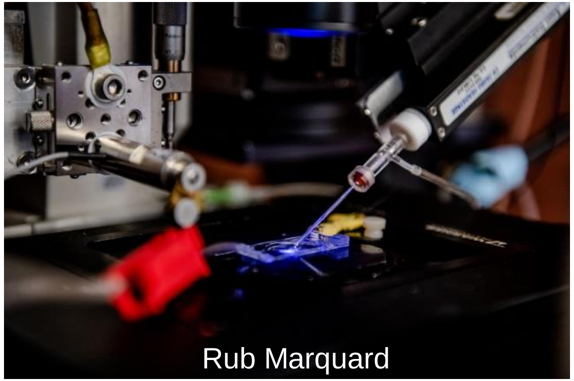


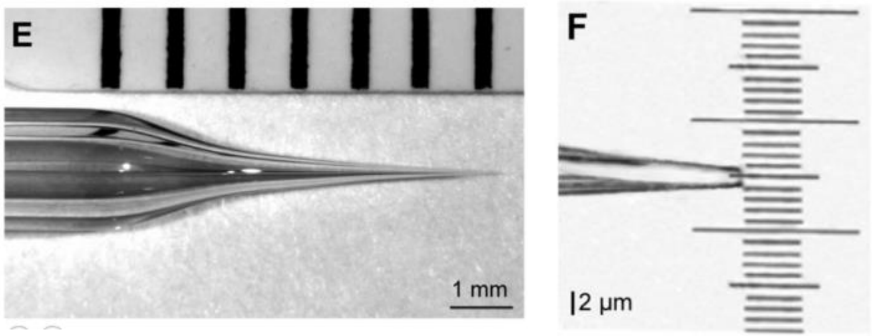


Voltage change → Electrical signal!

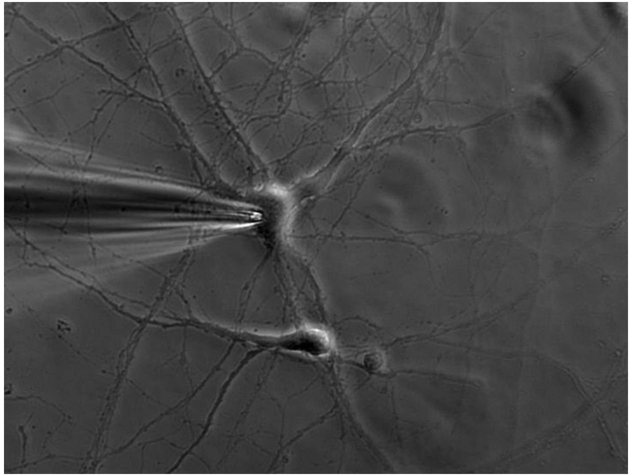
Measuring a potential across a cell





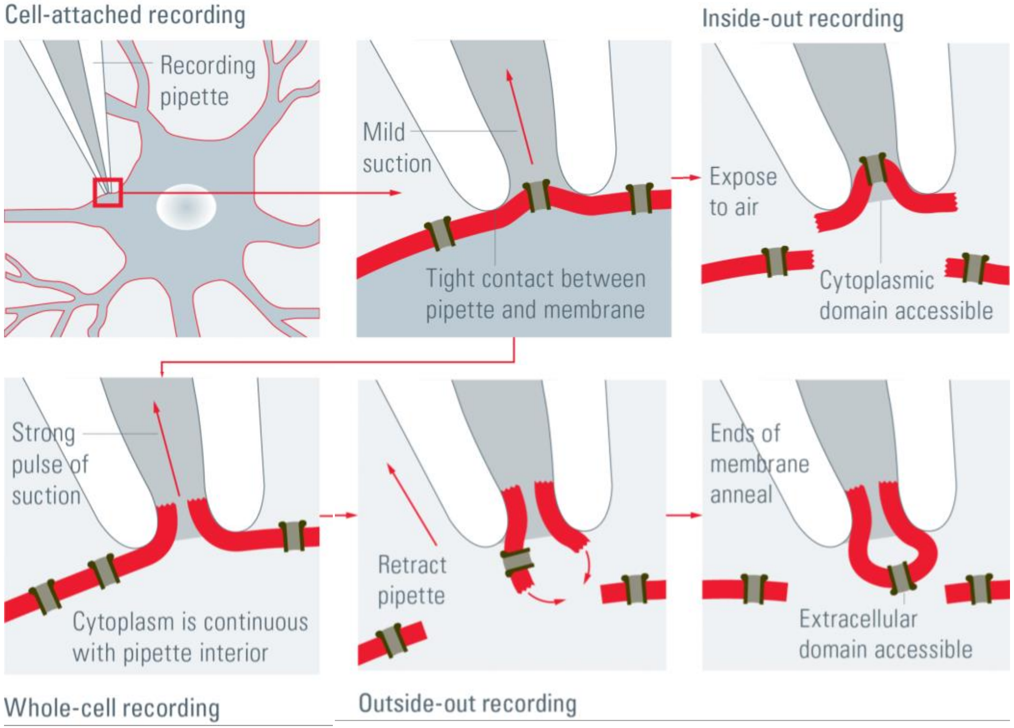


Jouhanneau, Poulet 2019

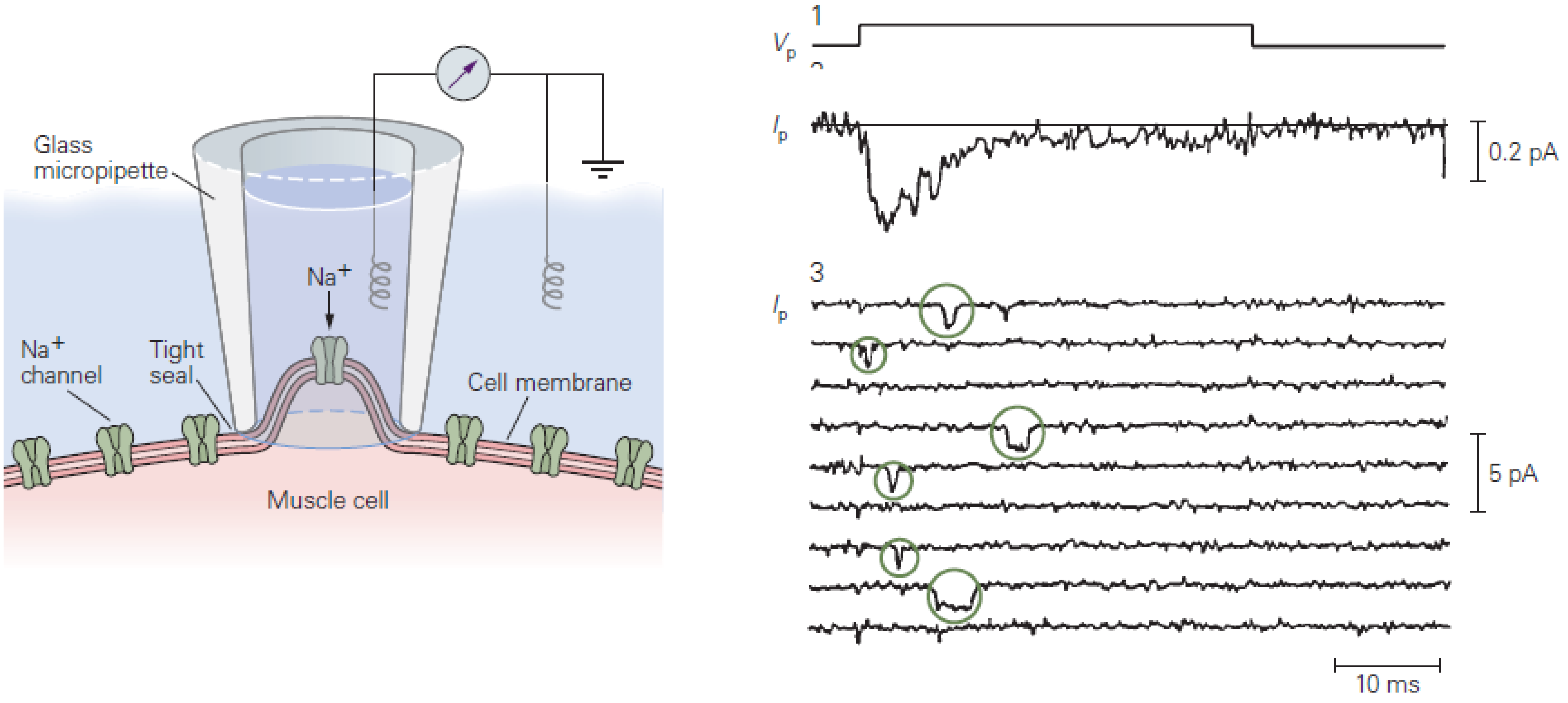


https://www.leica-microsystems.com/science-lab/the-patch-clamp-technique/

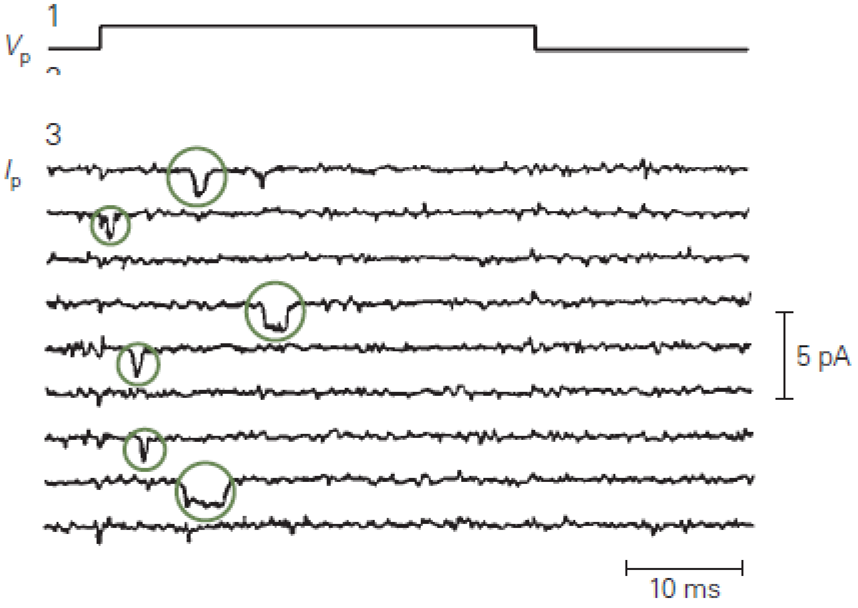
Accessing the cell

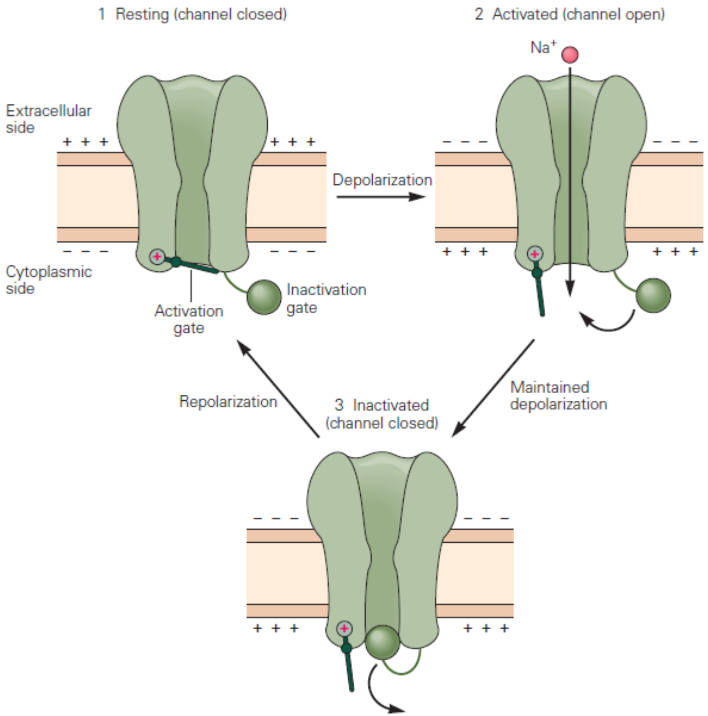


Measuring a single channel

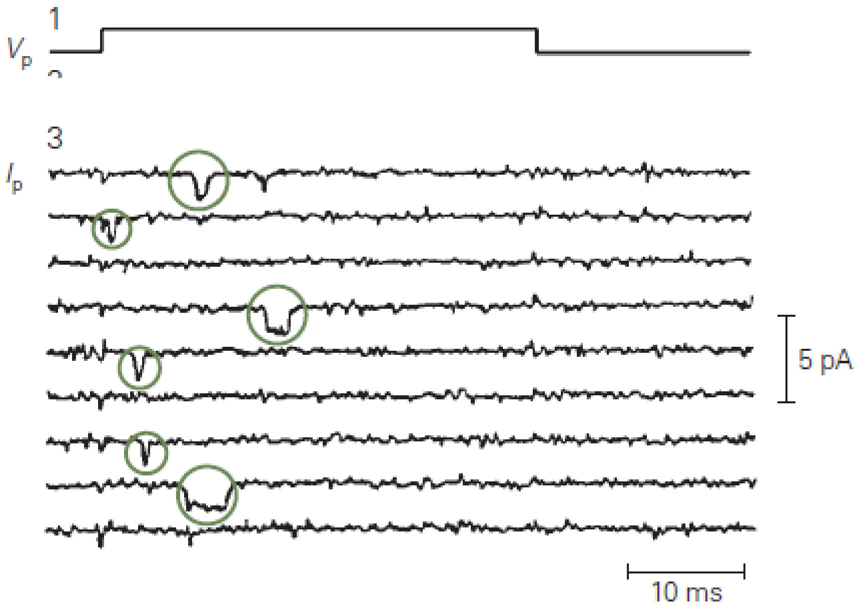


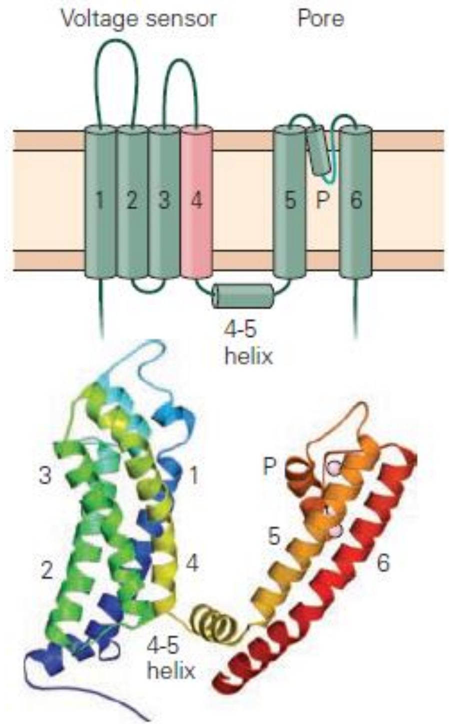
Ion channels

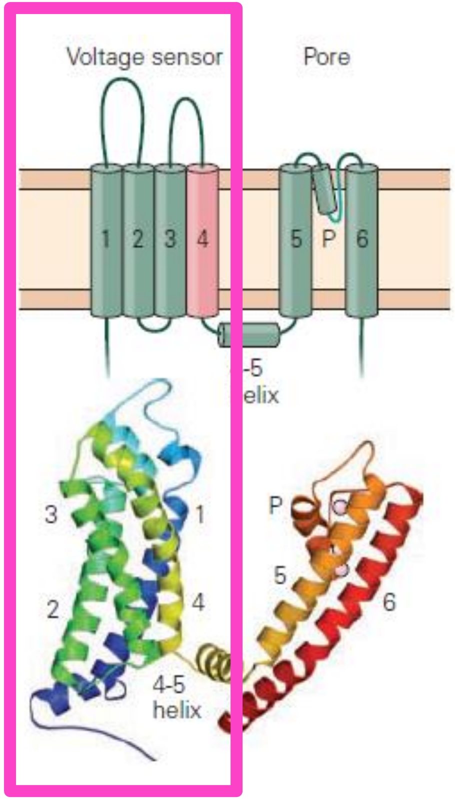


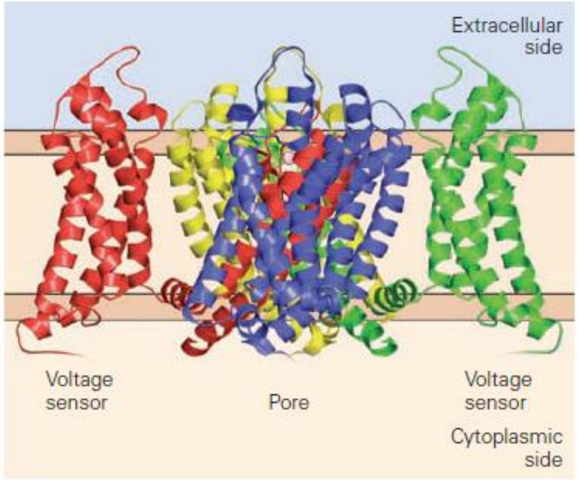


Sensing voltage

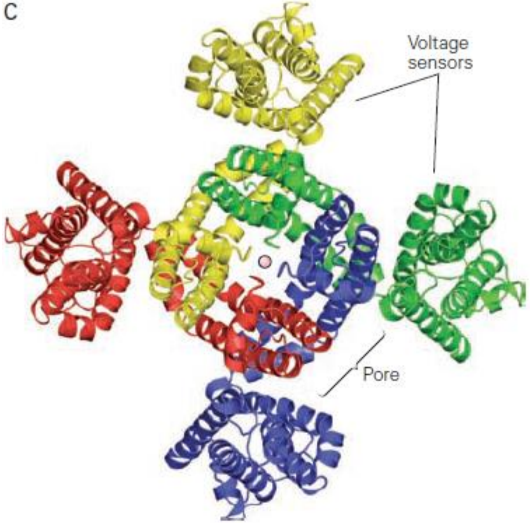




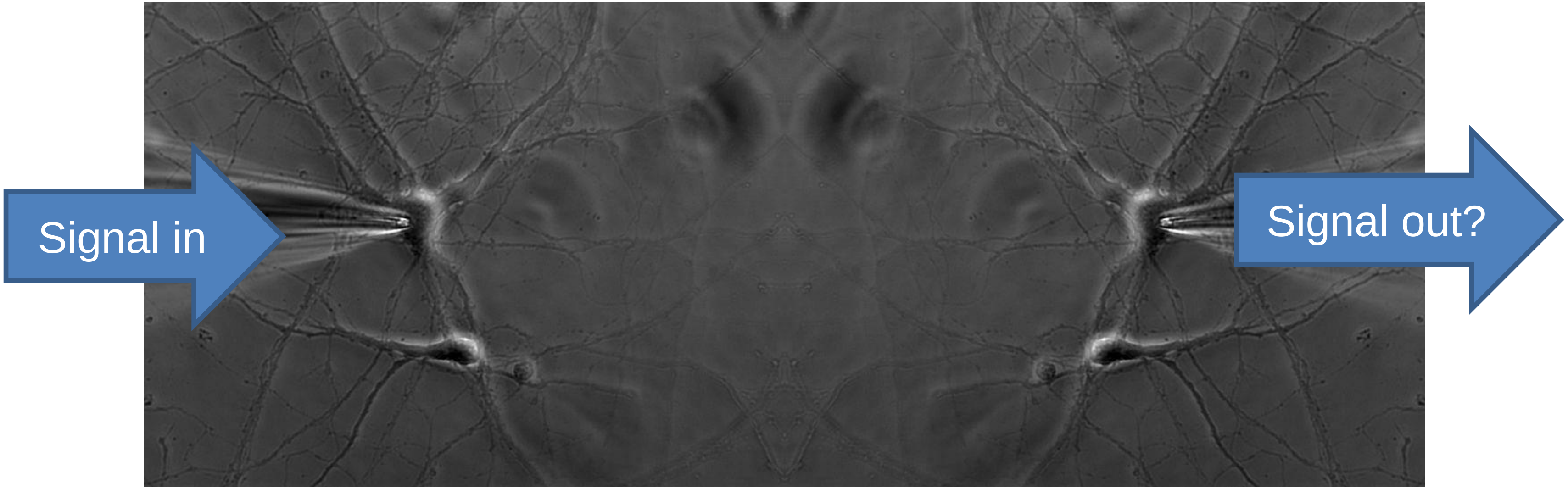

Voltage sensor
Pore
1
2
3
4
5
P
6
4-5 helix
3
1
2
4
4-5 helix
P
5
6


Extracellular side
Voltage sensor
Pore
Voltage sensor
Cytoplasmic side

C


Voltage sensors
Pore

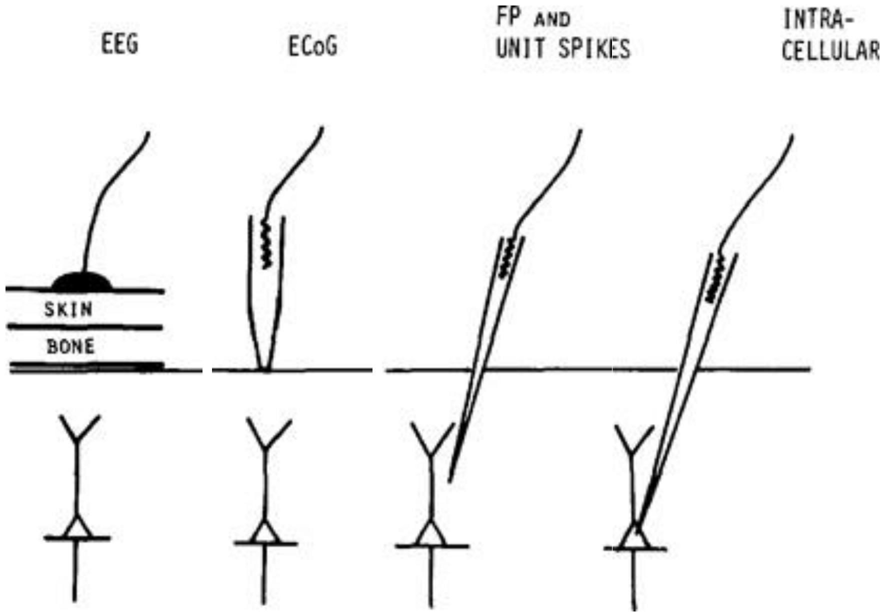
Measuring single neurons…?



Paired recordings → identification of functional circuitry

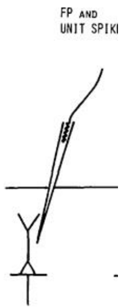
Electrophysiology methods

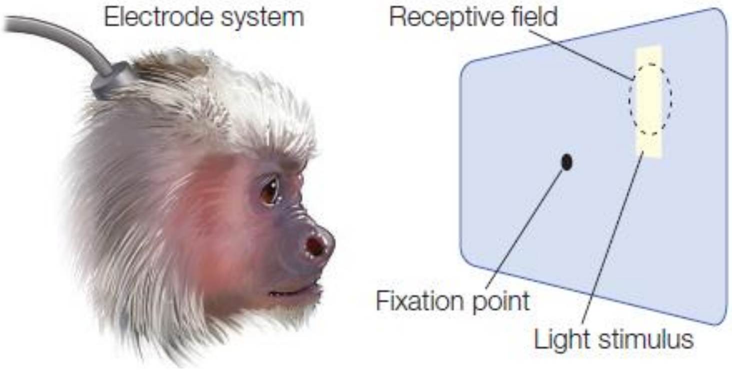
Localization

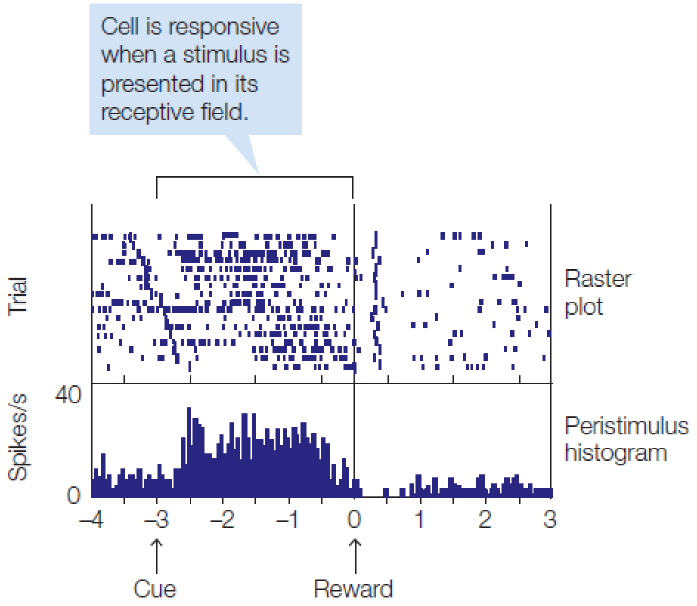


invasiveness

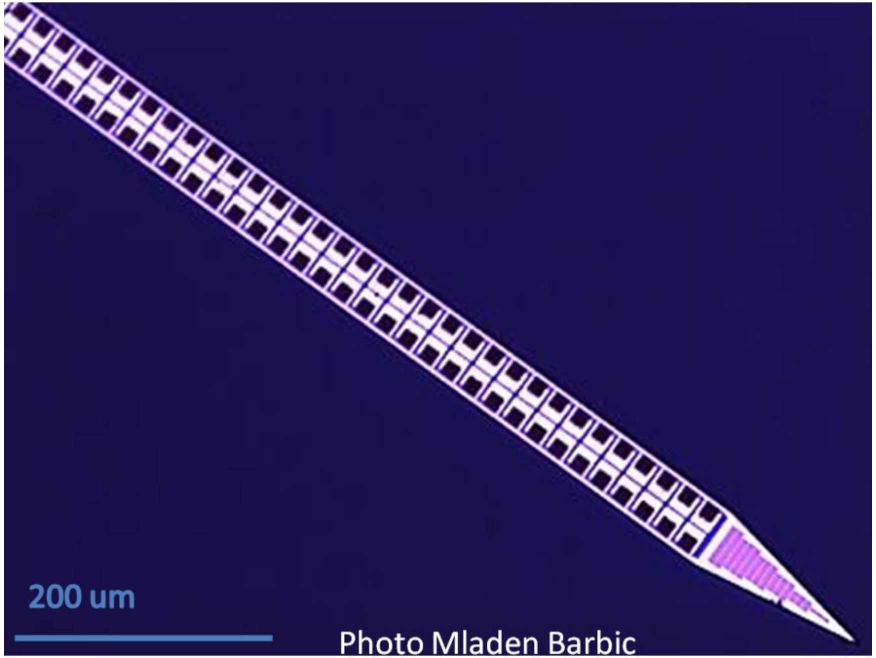
Local Field Potentials

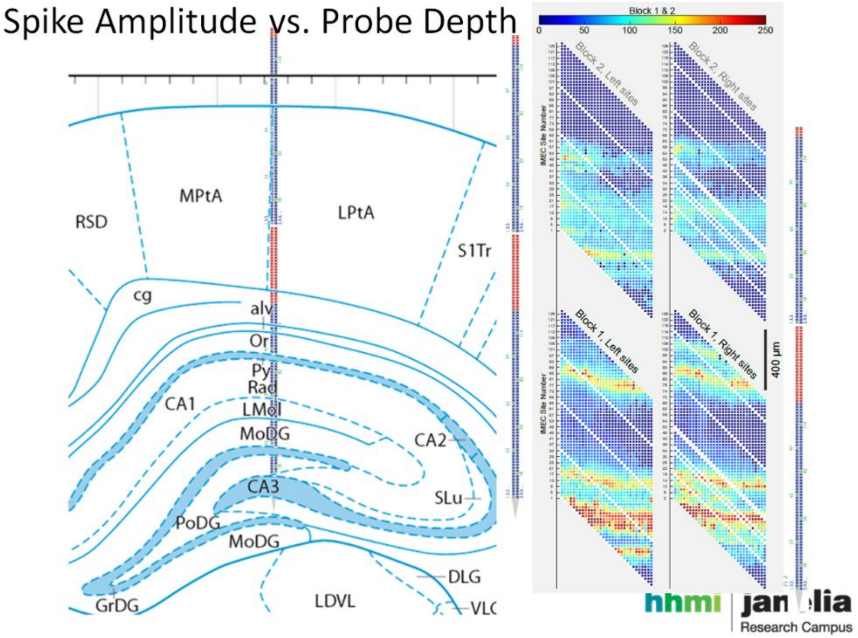






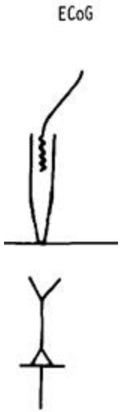
Multielectrodes



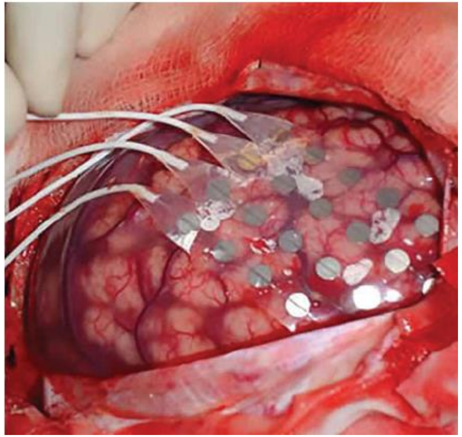


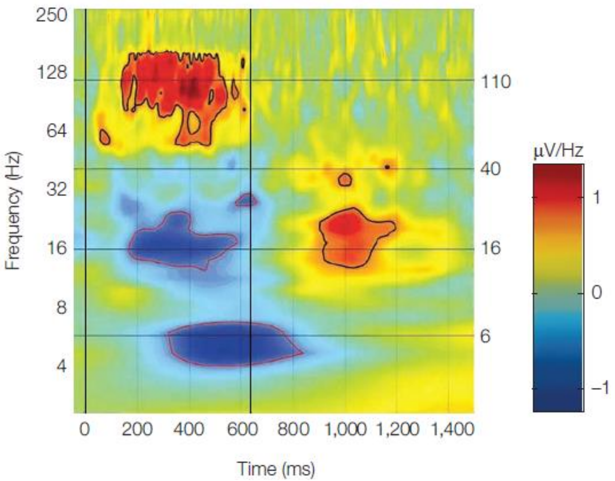
ECoG/iEEG

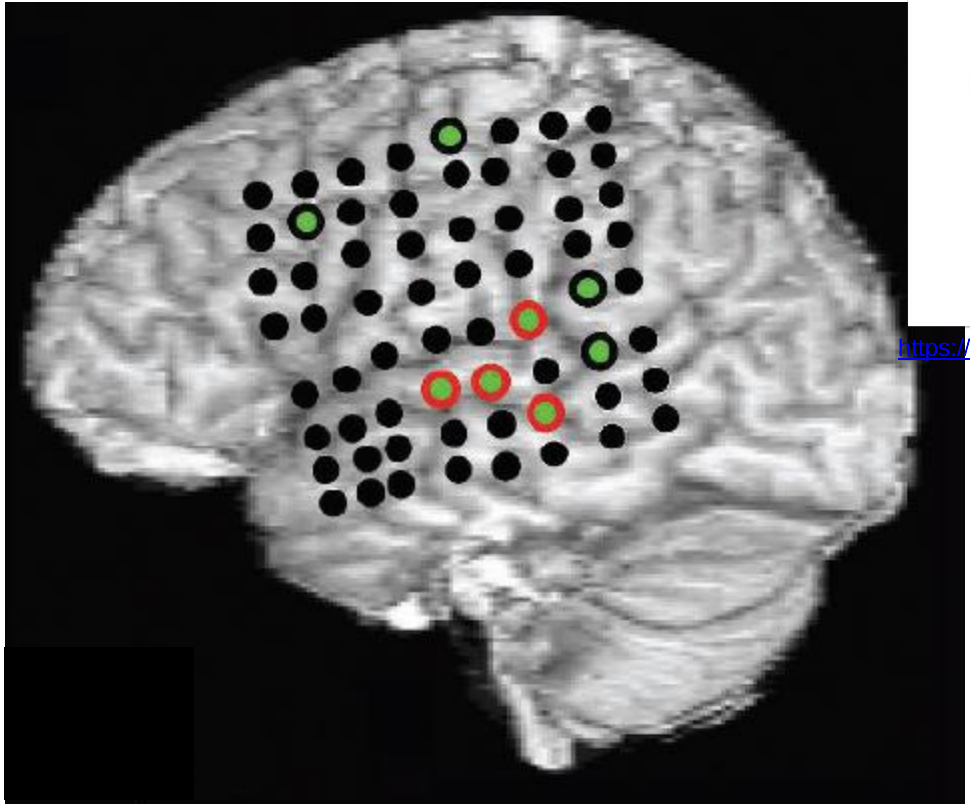
Electrocorticography and **intracranial electroencephalography**

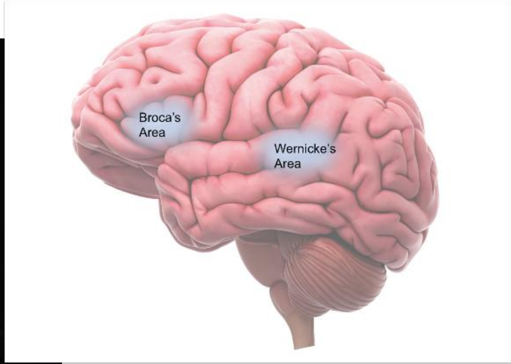


https://www.eurekalert.org/pub_releases/2016-10/uow-ftf102616.php



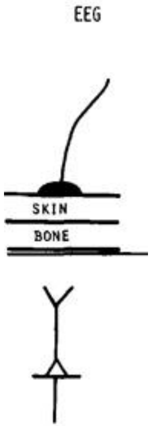


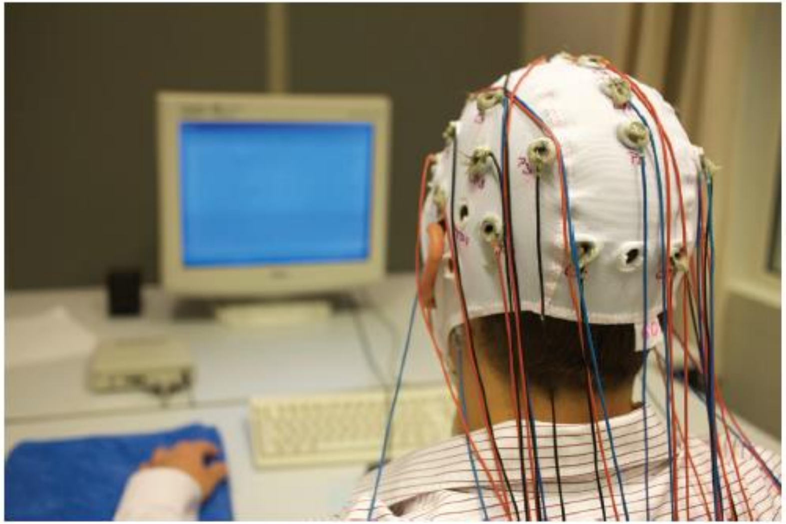




https://sapienlabs.org/searching-the-brain-for-lan

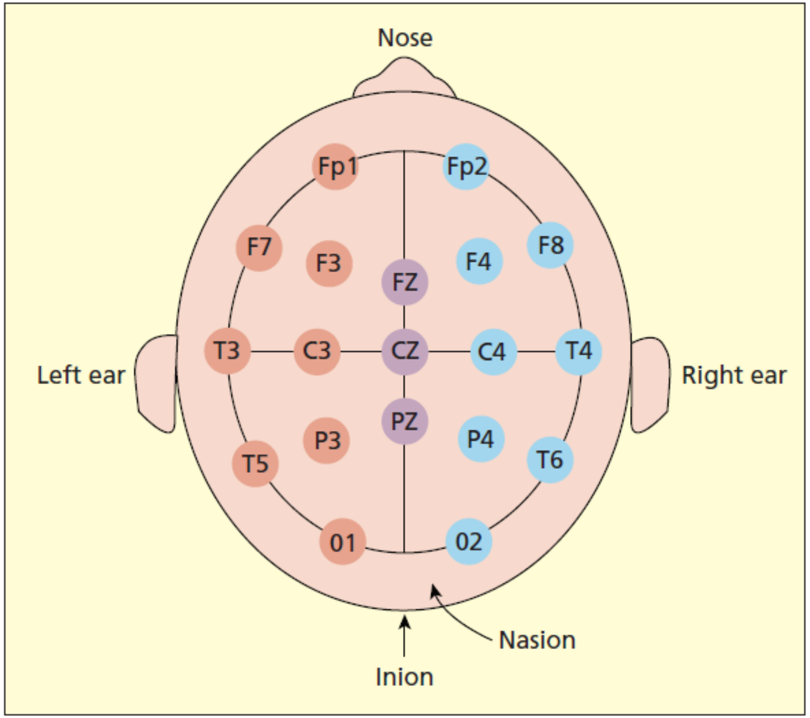
EEG



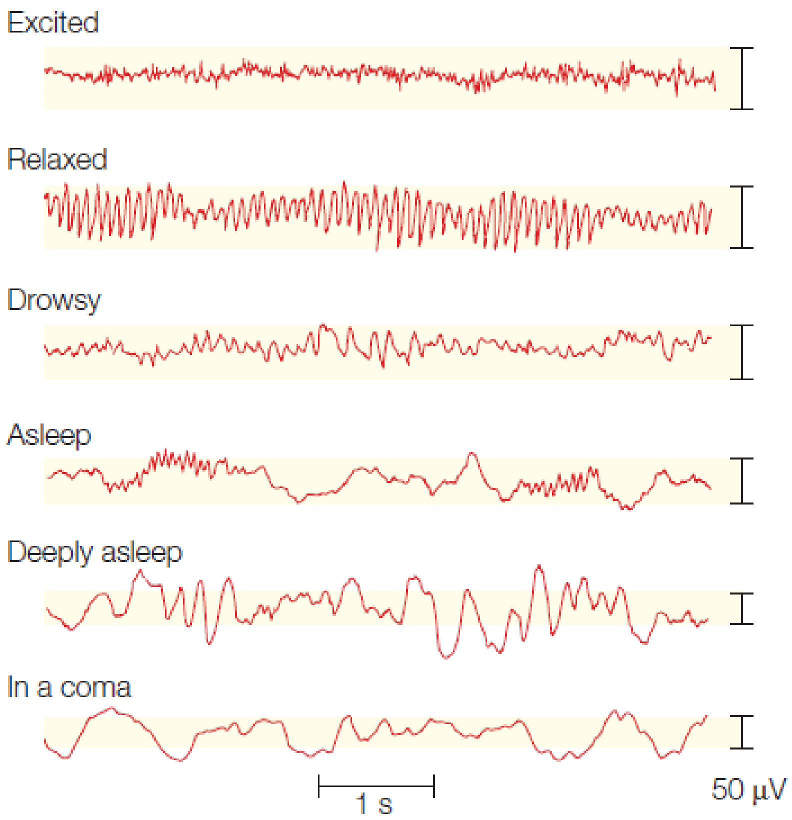


fotografixx/iStock

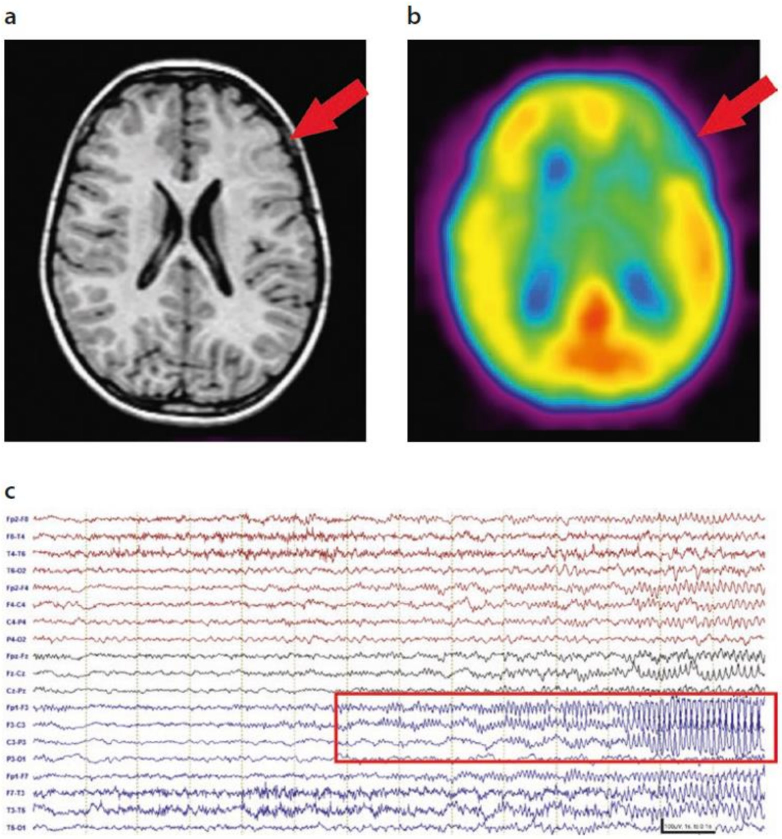
The 10-20 System



EEG signals

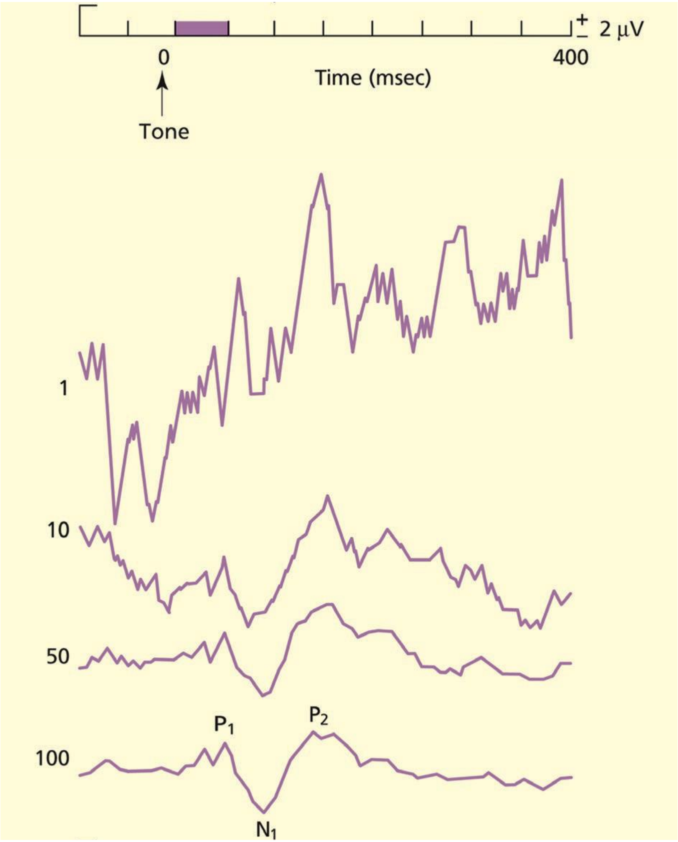


Excited
Relaxed
Drowsy
Asleep
Deeply asleep
In a coma
1 s
50 µV



a
b
c

Event-related potentials



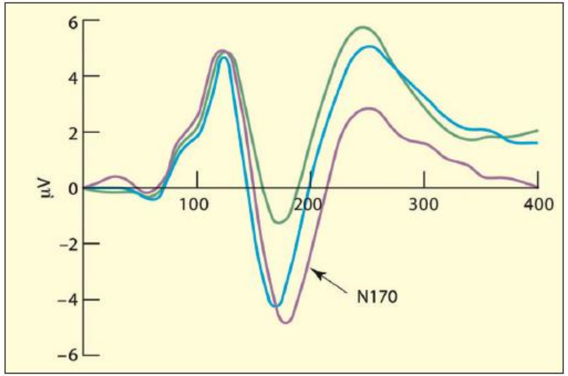


FIGURE 3.14: The N170 is observed for both human faces (purple) and animal faces (blue), but not other objects (green). From Rousselet *et al.*, 2004. With permission of ARVO.

A single recording has a low signal-to-noise ratio.

Averaging over hundreds of trails reveals the tiny signal, as noise is canceling.

White noise averaging

Other EEG signals are treated as being non-correlated to the stimulus

→ Serially uncorrelated random variable

→ 0 mean (!) and finite variance

→ No prior distrubtion is assumed

AVERAGING REMOVES THE NOISE

Python example

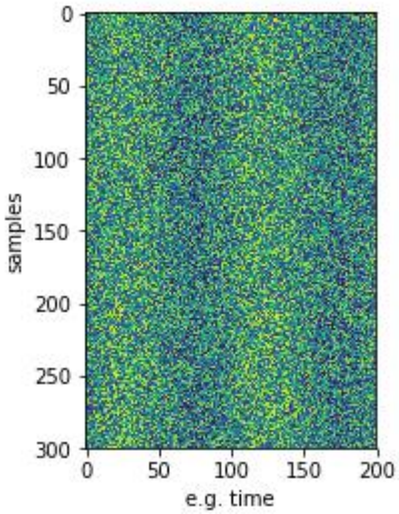
In [2]:
```python
import numpy as np
import matplotlib.pyplot as plt
```

Generate true signal

In [3]:
```python
x = np.linspace(0, 4*np.pi, 200)
y = np.sin(x)
```

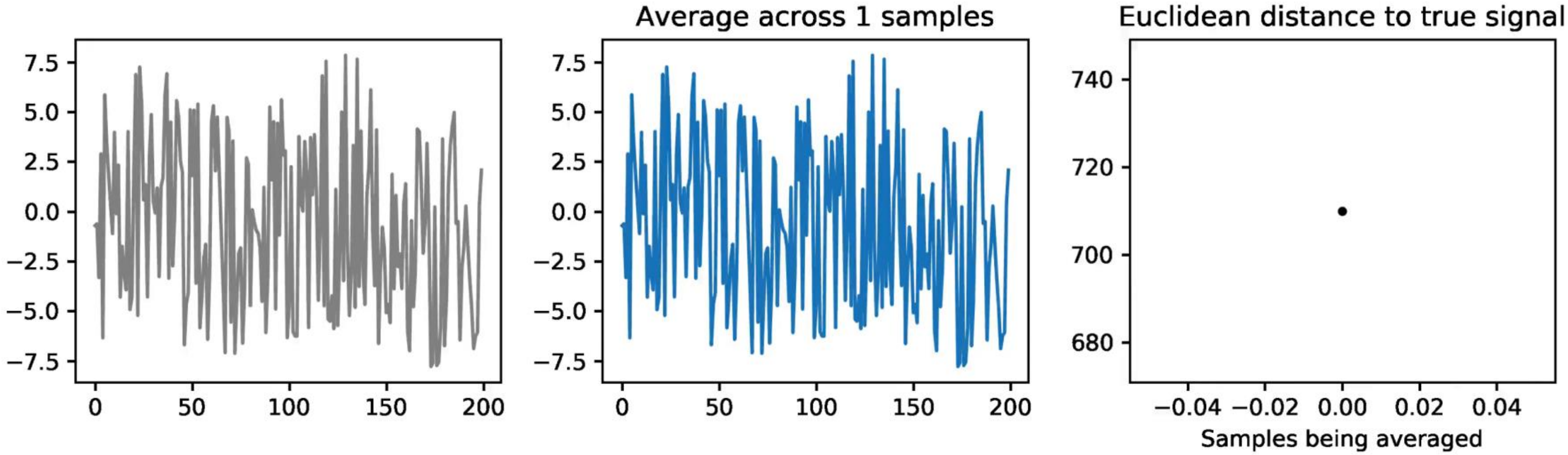
Generate samples from the true signal with added noise.

```python
s = []
factor=7

for _ in range(300):
    s.append(y + np.random.uniform(-factor, factor, y.size))

plt.imshow(s)
plt.ylabel("samples")
plt.xlabel("e.g. time")
```



Averaging over multiple samples

Sine signal with plenty of white noise (drawn from uniform distribution)



Noise2Noise and Noise2Void

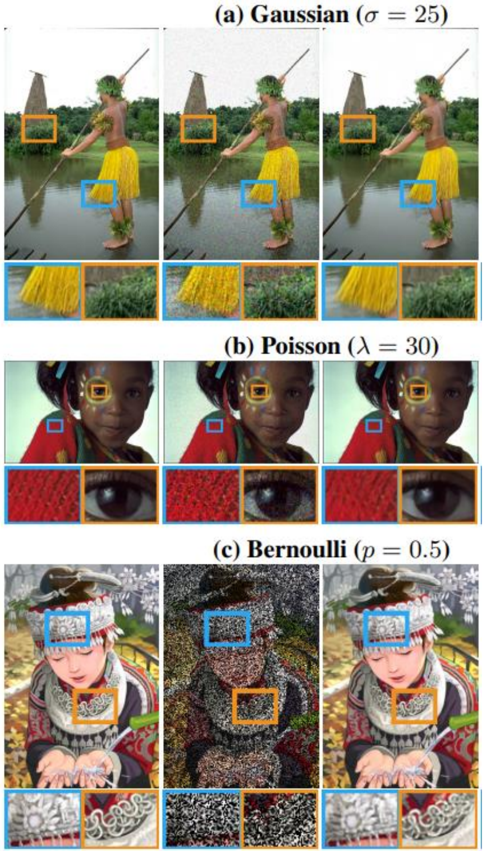
For the L_2 loss $L(z, y) = (z - y)^2$, this minimum is found at the arithmetic mean of the observations:

$$z = \mathbb{E}_y\{y\}. \qquad (3)$$

The L_1 loss, the sum of absolute deviations $L(z, y) = |z - y|$, in turn, has its optimum at the median of the observations.

conditional expected values. *This implies that we can, in principle, corrupt the training targets of a neural network with zero-mean noise without changing what the network learns.* Combining this with the corrupted inputs from Equa-

Example training pairs | Input ($p \approx 0.25$) 17.12 dB | L_2 26.89 dB | L_1 35.75 dB | Clean targets 35.82 dB | Ground truth PSNR

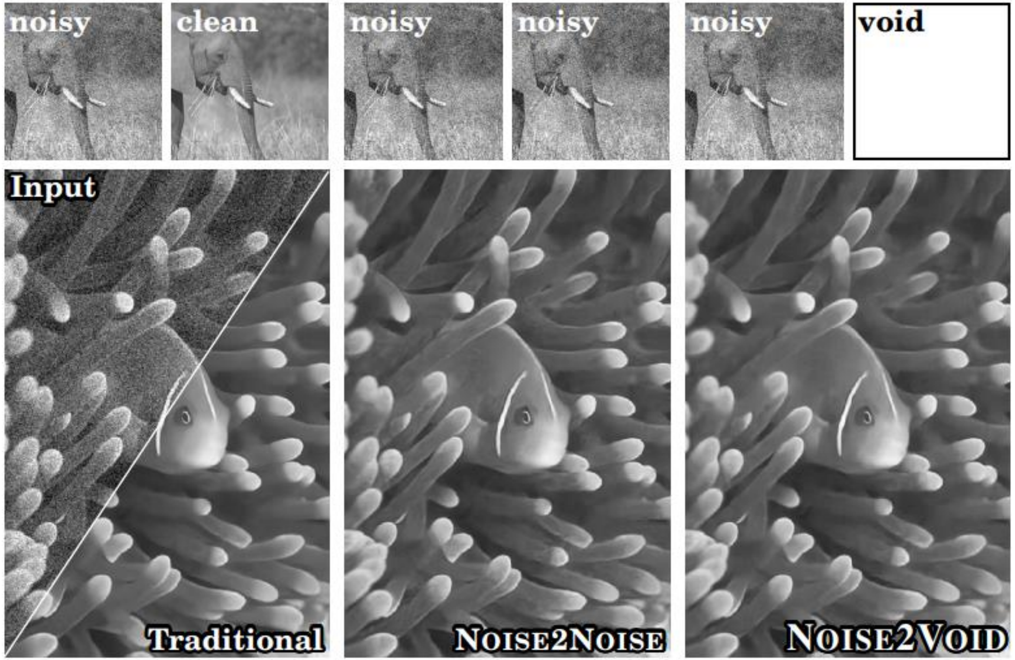


Ground truth Input Our

Lehtinen et al., 2018

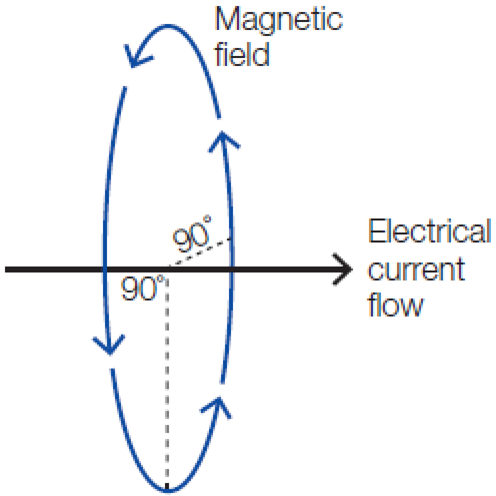
Noise2Noise and Noise2Void

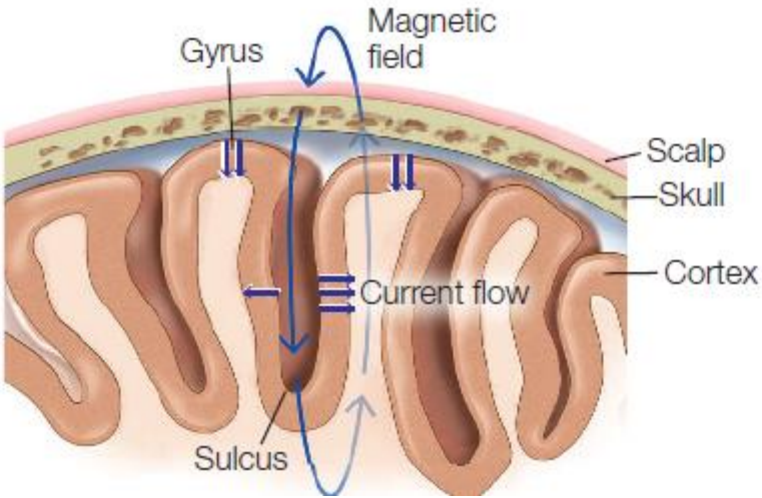
Example training pairs



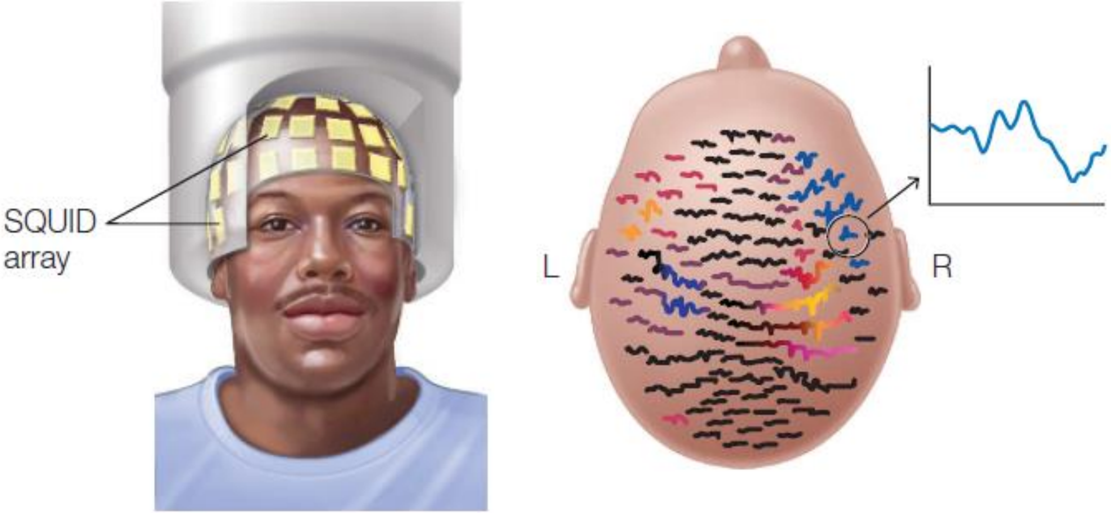
Krull et al., 2019

Magnetoencephalography (MEG)

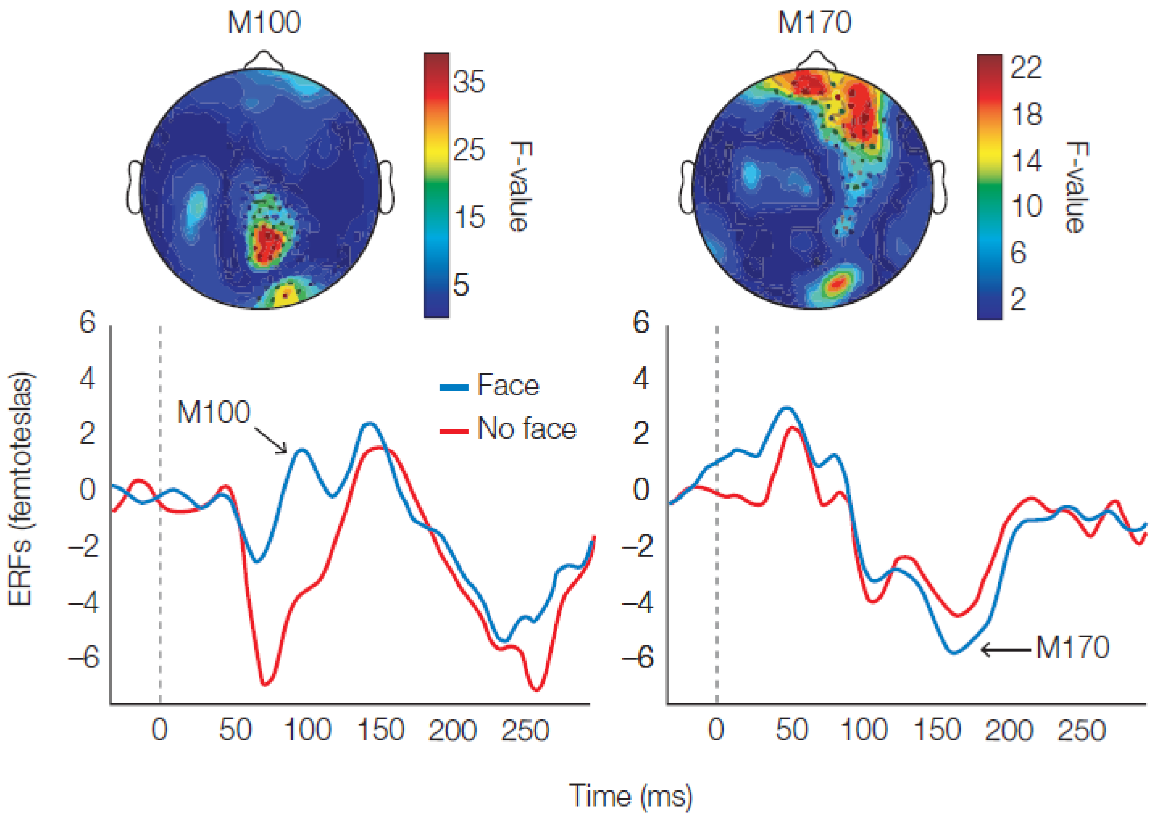




MEG recording setting



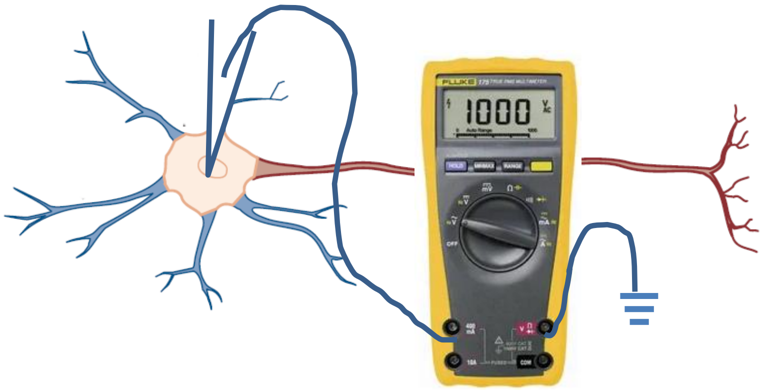
Topoplots

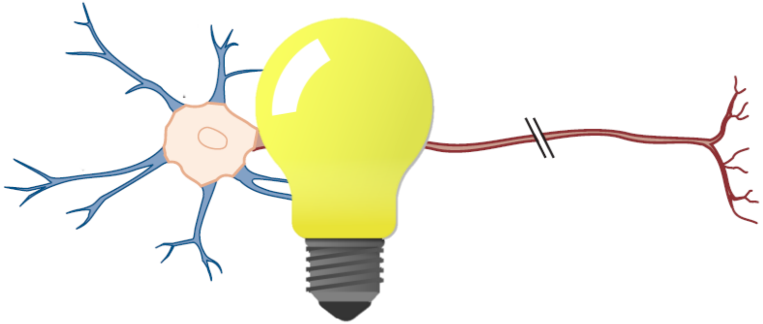


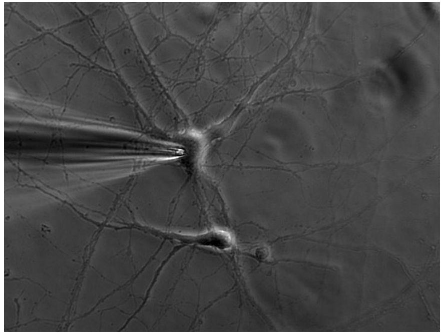
M100
M170
35
25
15
5
F-value
22
18
14
10
6
2
F-value
ERFs (femtoteslas)
6
4
2
0
–2
–4
–6
M100
Face
No face
M170
0
50
100
150
200
250
Time (ms)

Optical approaches

Measuring neural activity

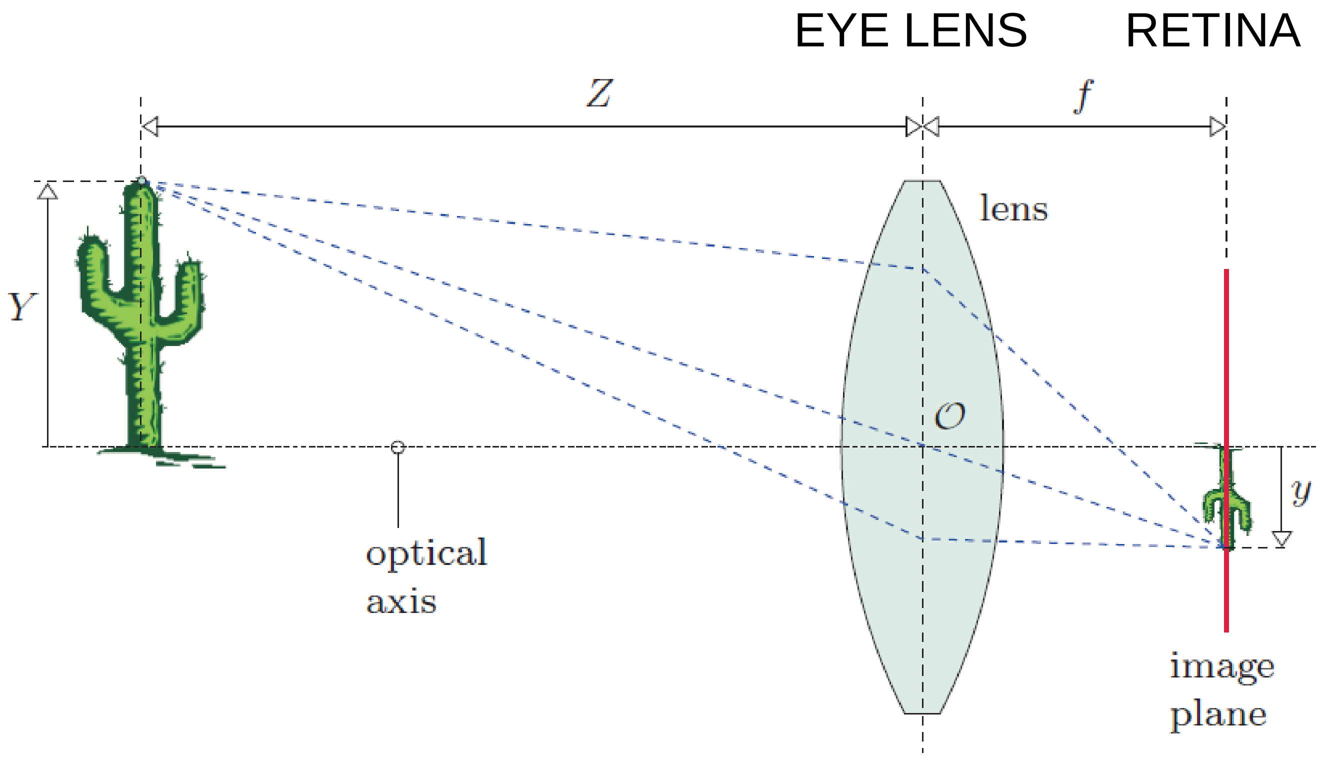




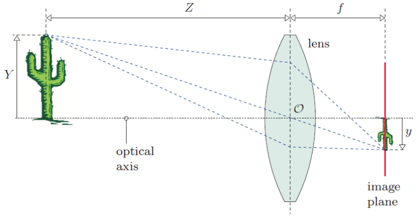


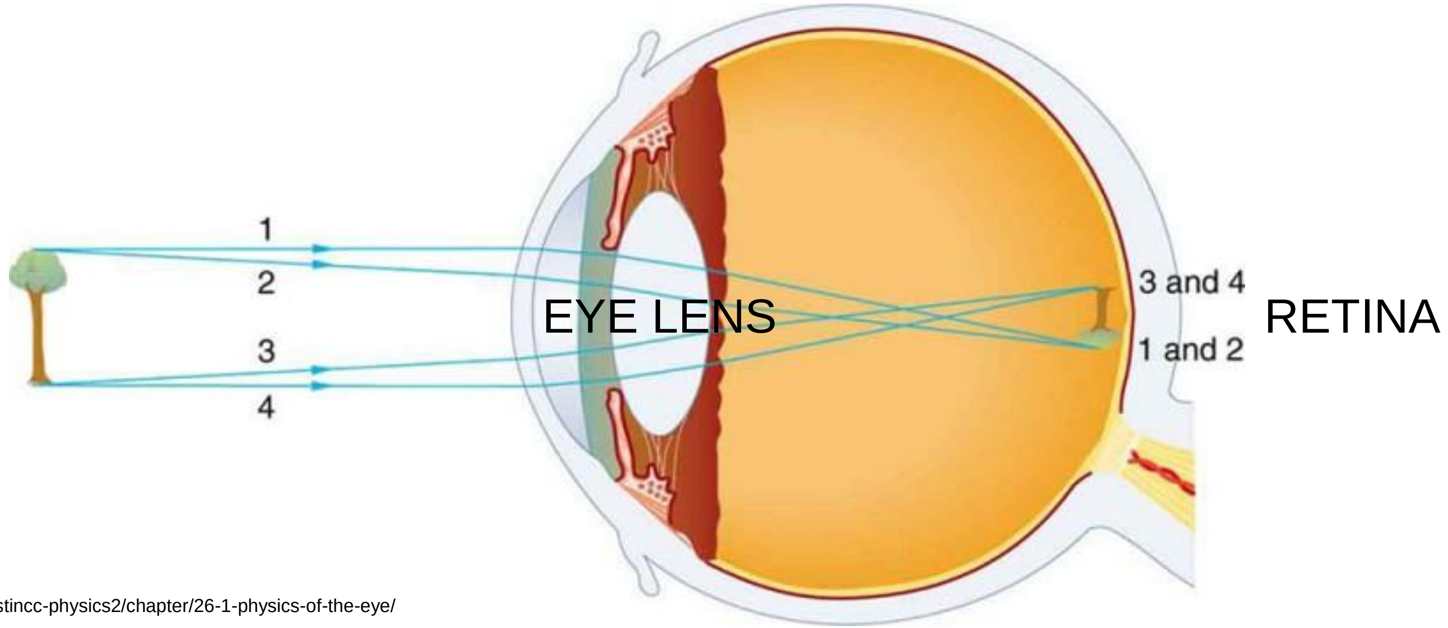
Optical approaches to measure neural activity

How does imaging work?



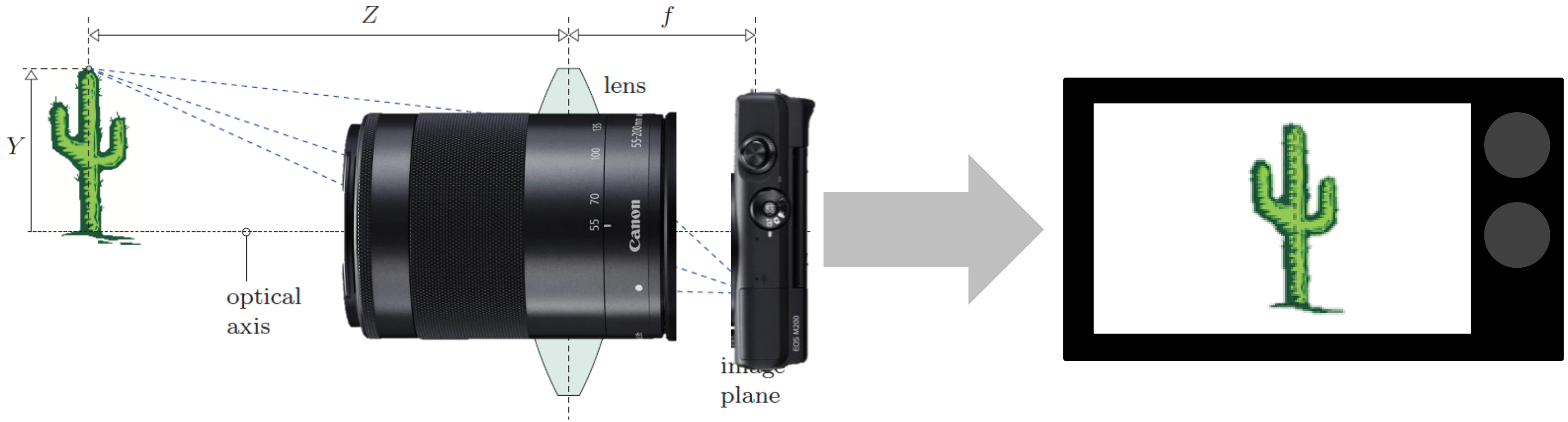
How does imaging work?

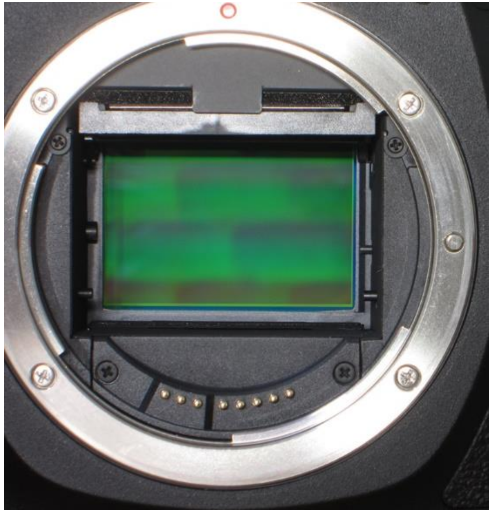


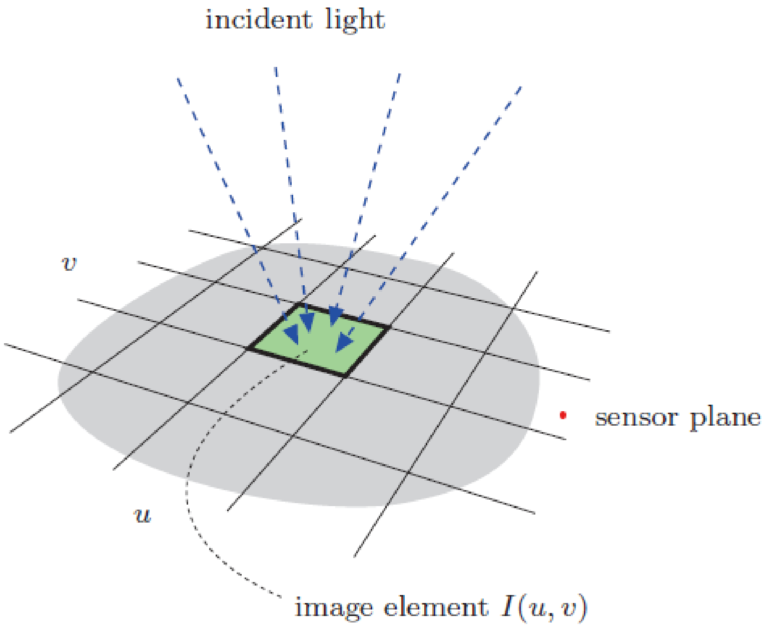


https://courses.lumenlearning.com/austincc-physics2/chapter/26-1-physics-of-the-eye/

How does imaging work?

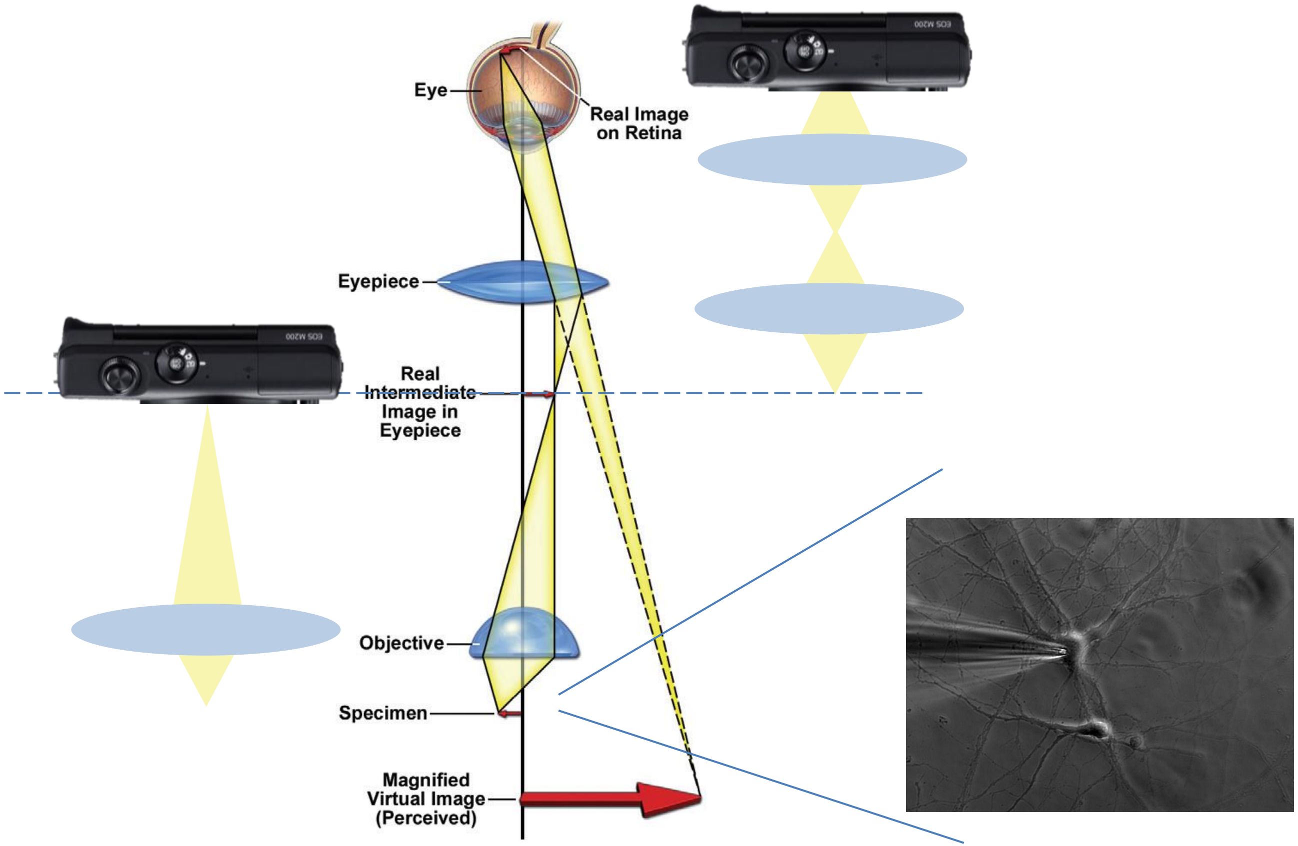




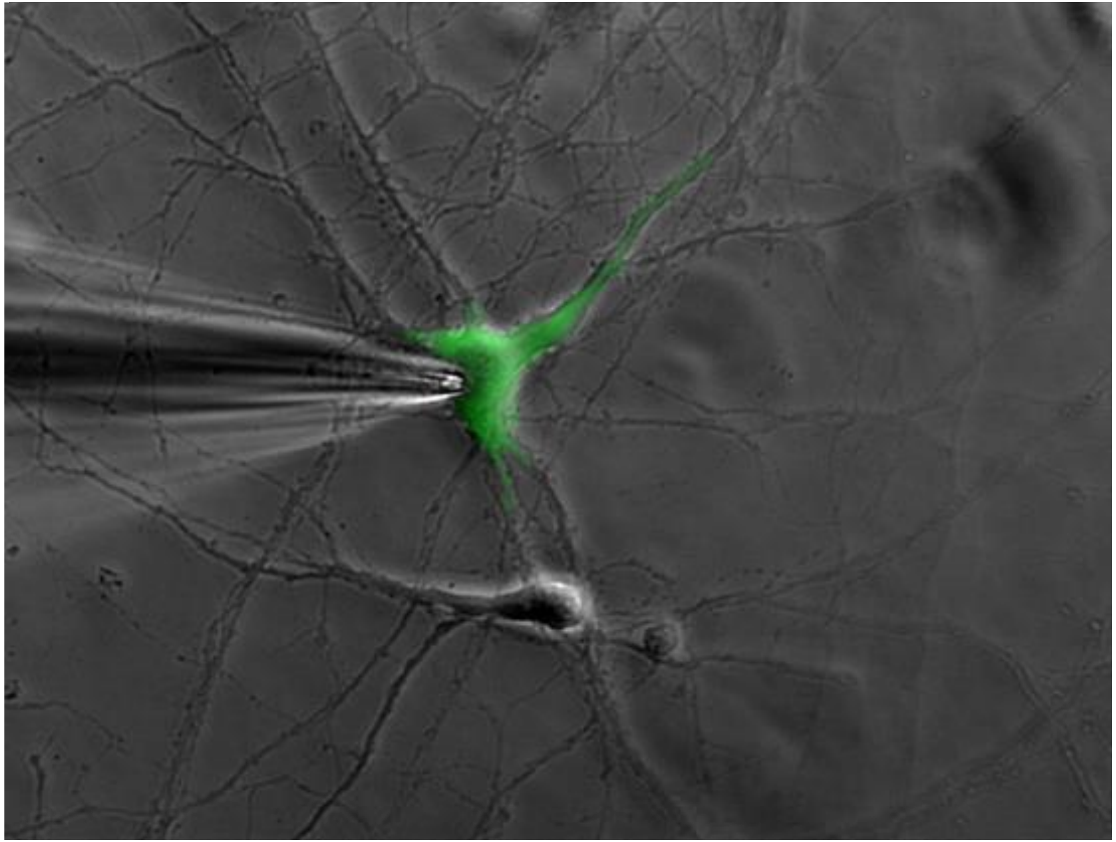


https://commons.wikimedia.org/wiki/File:CMOS_Image_Sensor_Big_and_Small.jpg

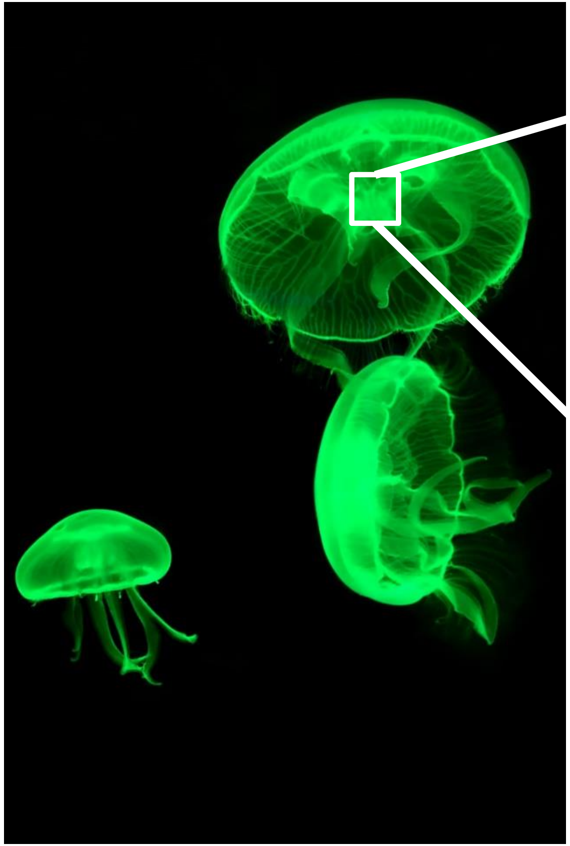
A basic microscopy setup



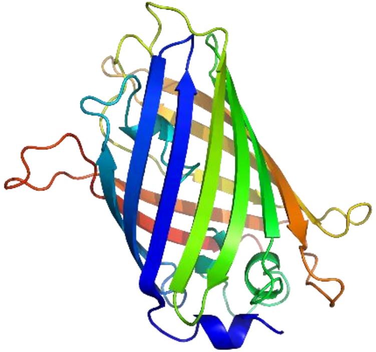
Making cells shine

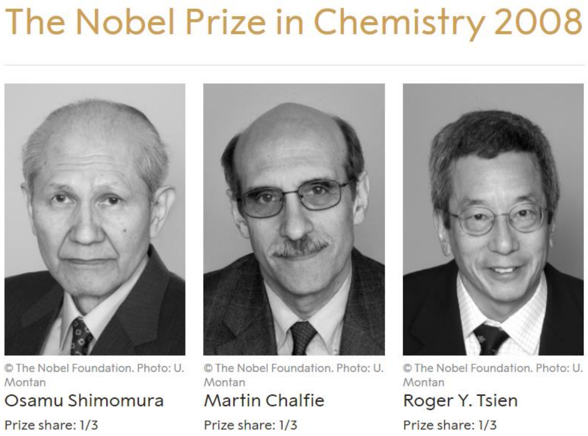


Glowing jellyfish



Green fluorescent protein (GFP)





The Nobel Prize in Chemistry 2008 was awarded jointly to Osamu Shimomura, Martin Chalfie and Roger Y. Tsien "for the discovery and development of the green fluorescent protein, GFP."

https://blog.microbiologics.com/green-fluorescent-proteins-shining-new-light-on-food-qc/

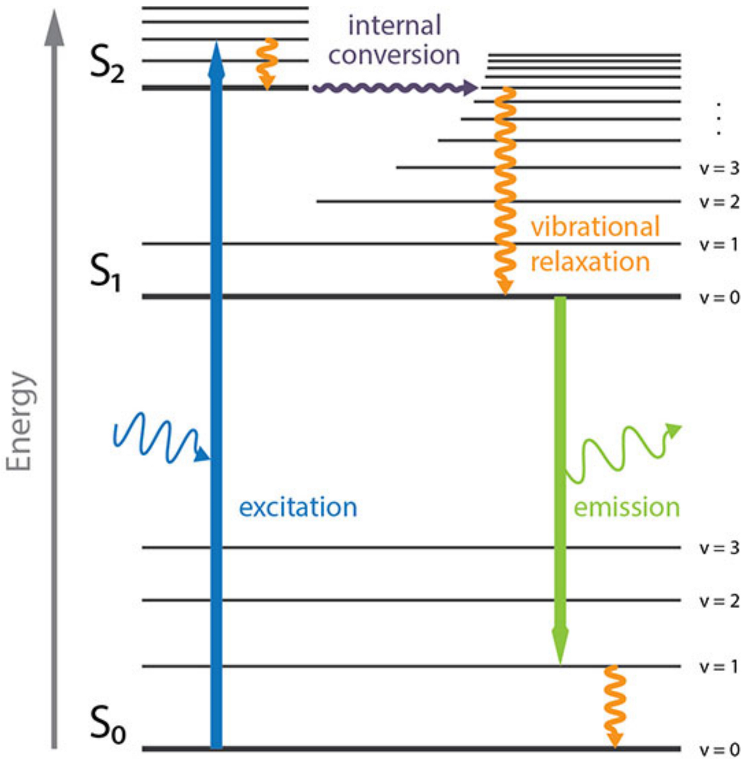
A protein that fluoresces

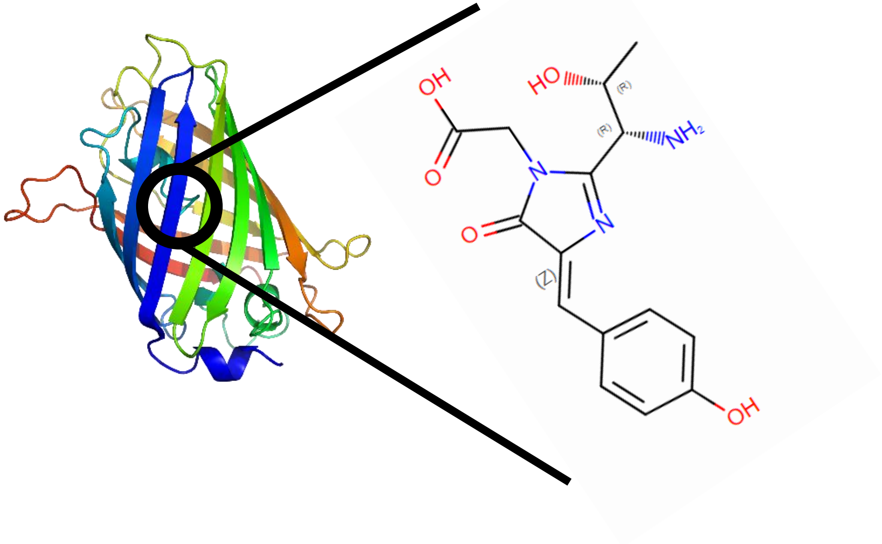
Bacteria expressing GFP

What is fluorescence?

Why is it useful?

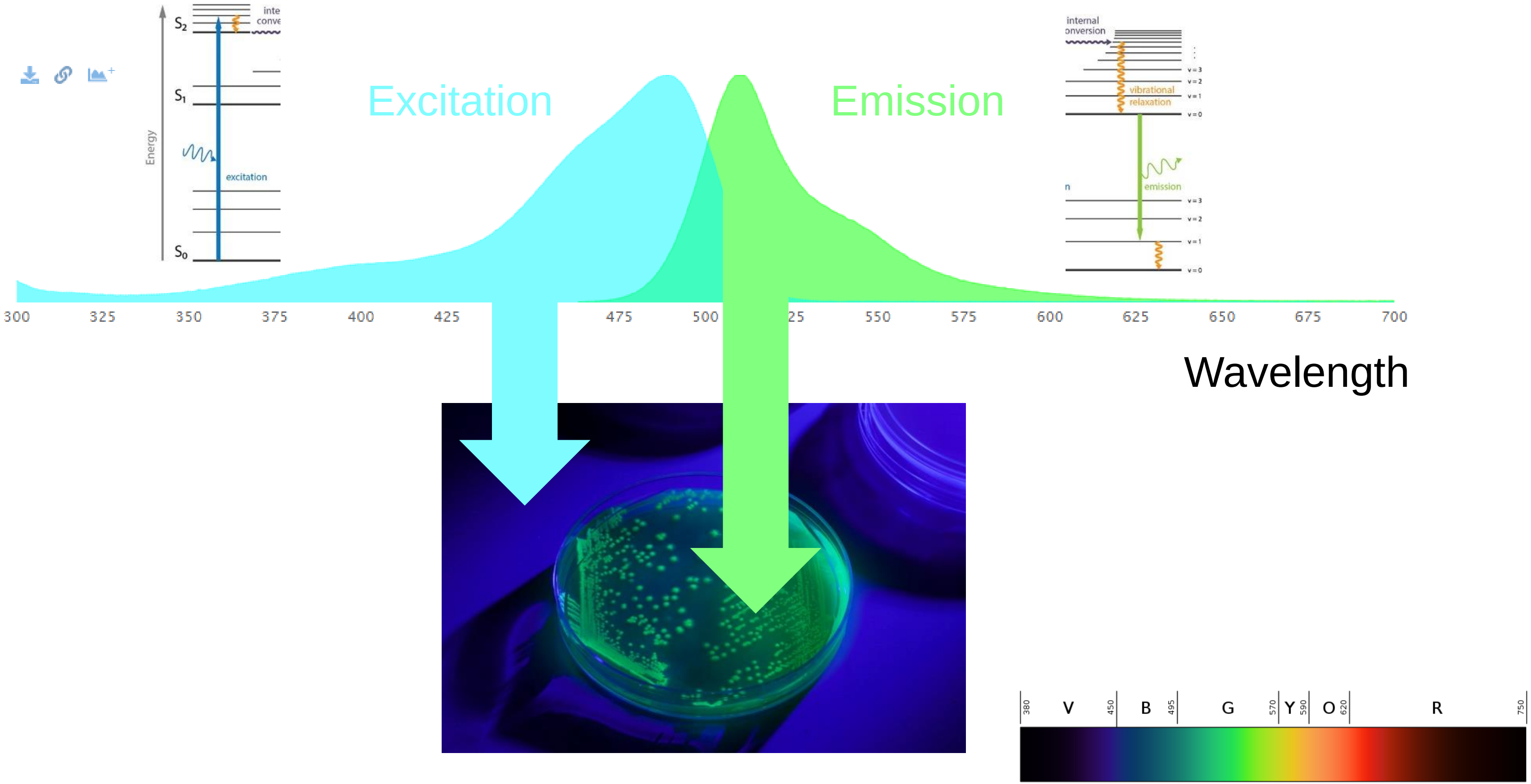
Fluorescence in essence



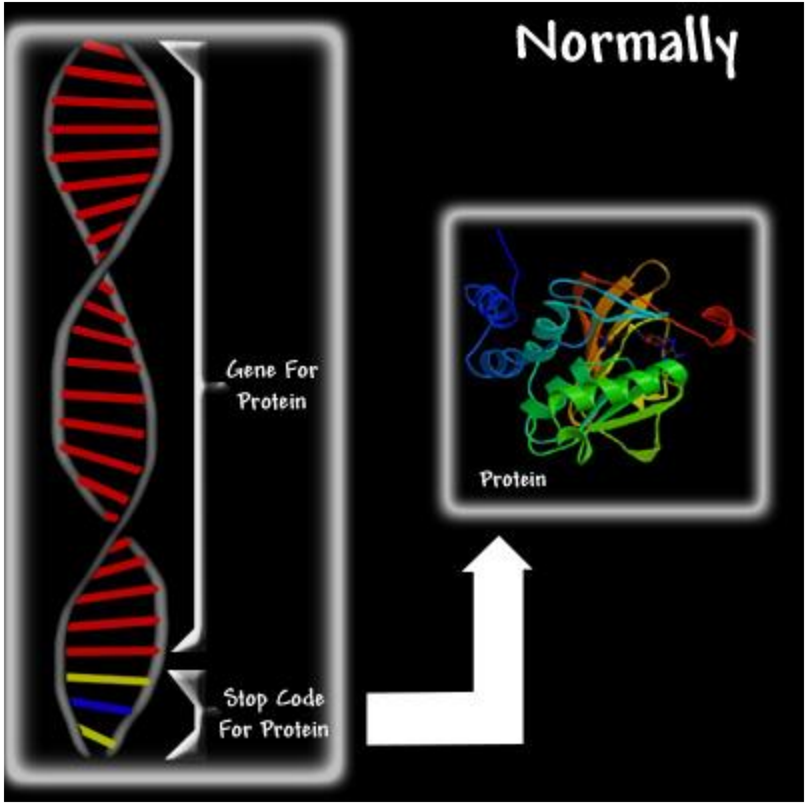


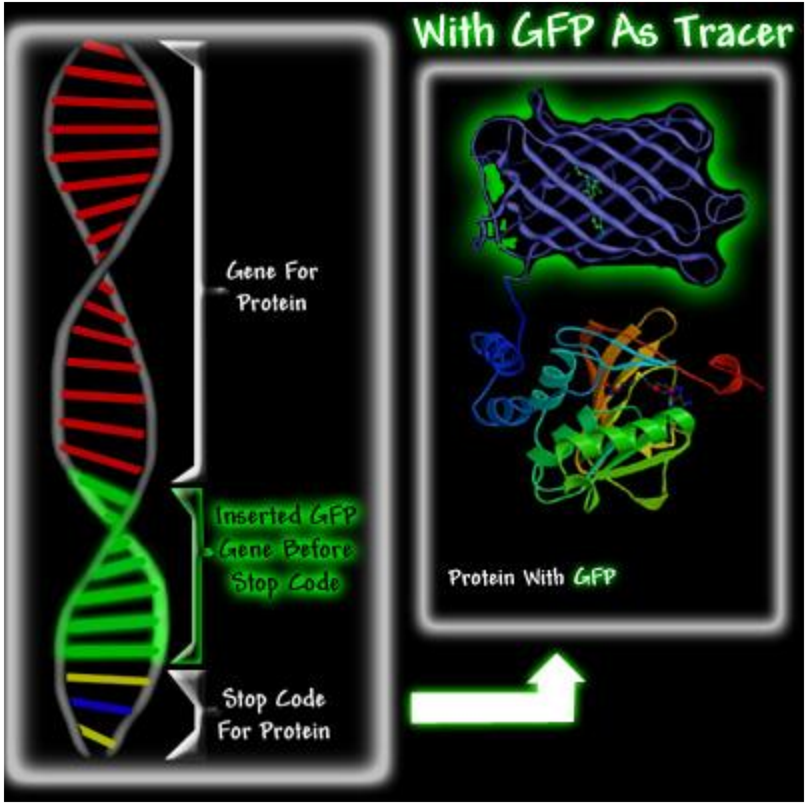
https://www.enzolifesciences.com/science-center/technotes/2019/december/what-is-the-difference-between-fluorescence-phosphorescence-and-luminescence?/

Spectral properties of GFP



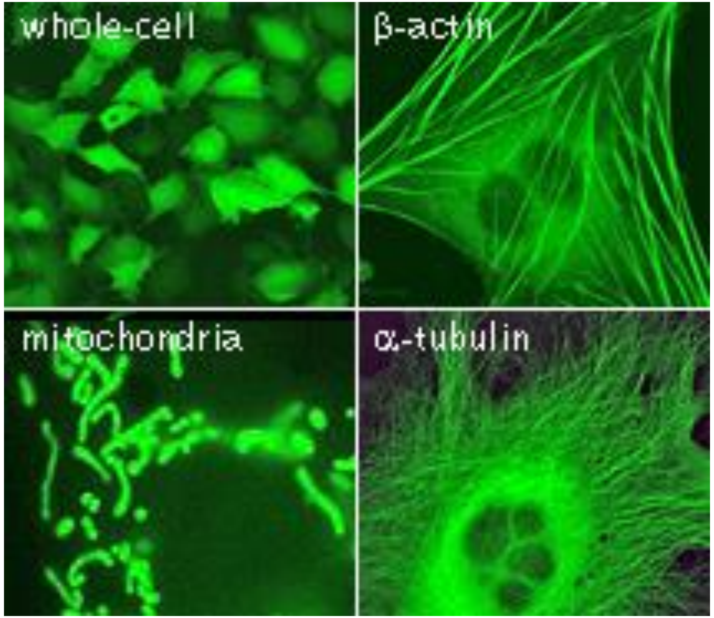
Why is it useful



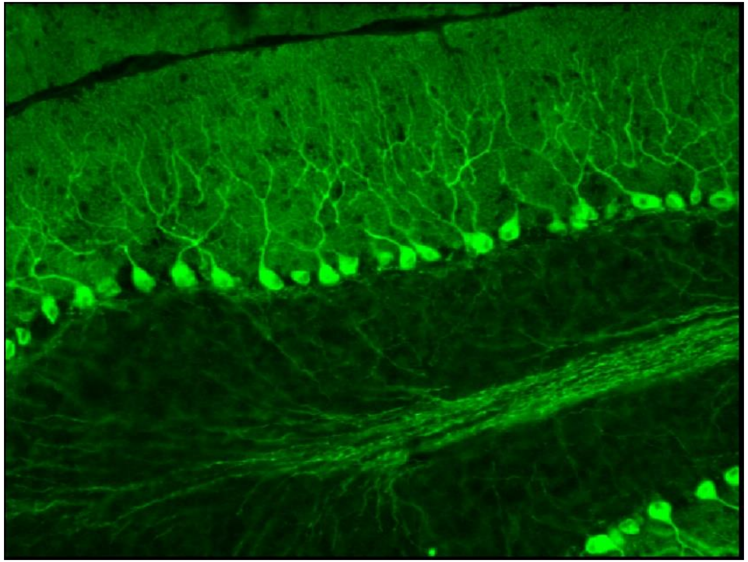


GFP tagging

GFP allows the visualization of cell structures,
when CELLS ARE ALIVE!



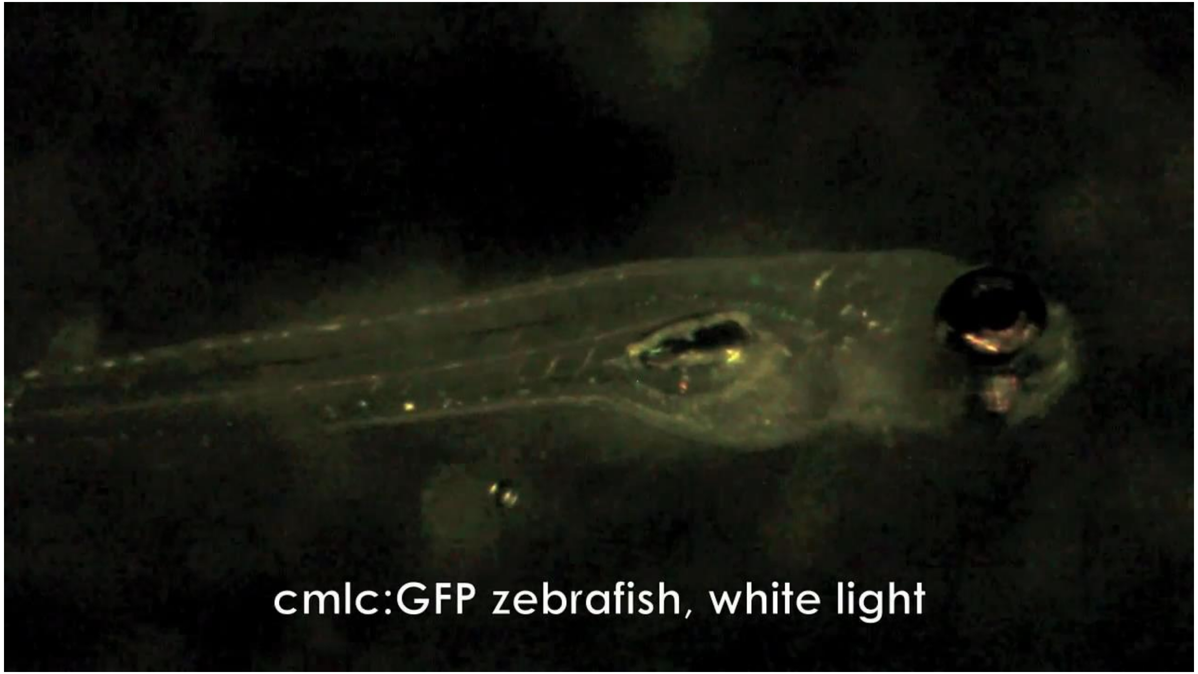
https://www.biocat.com/proteomics/green-fluorescent-proteins-gfp-s



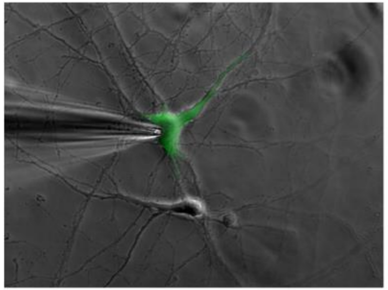
https://www2.tmig.or.jp/Mn_B/English/GFP_in_Purkinje_cell.html

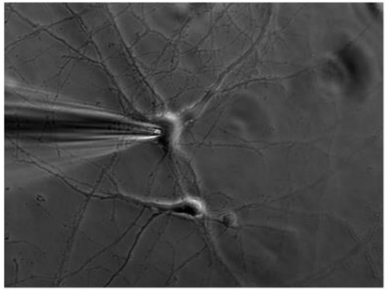
GFP in alive animals

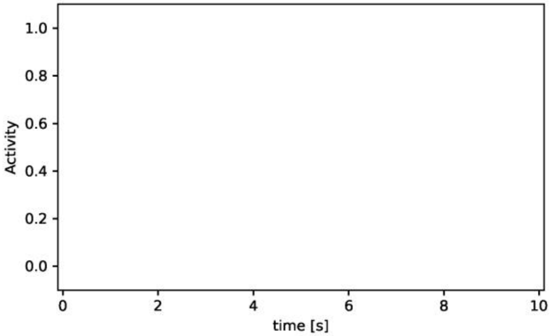
Larval zebrafish (ca. 5 days old)

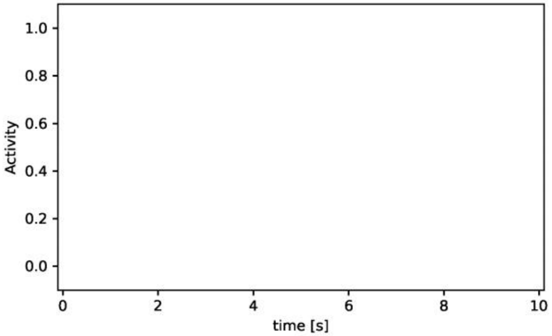


How to track neural activity?



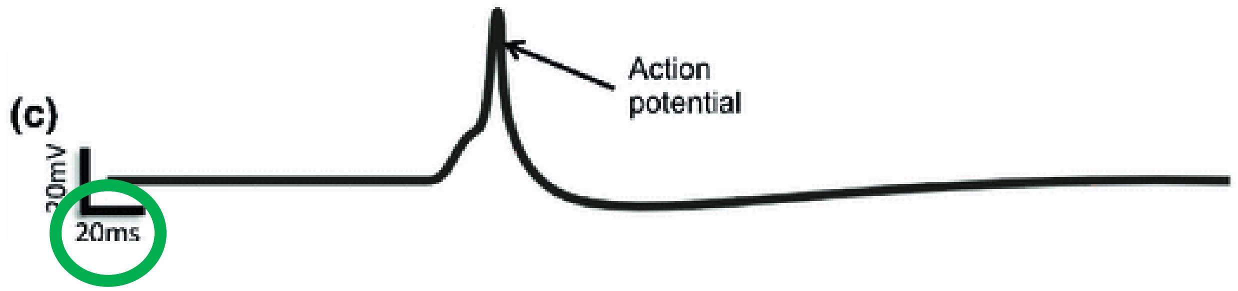






Activity-dependent fluorescence!

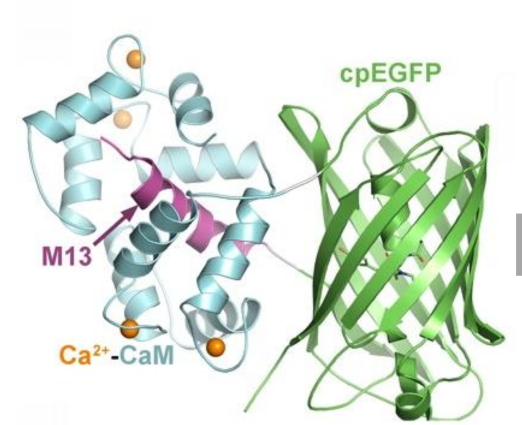
Activity dependent fluorescence



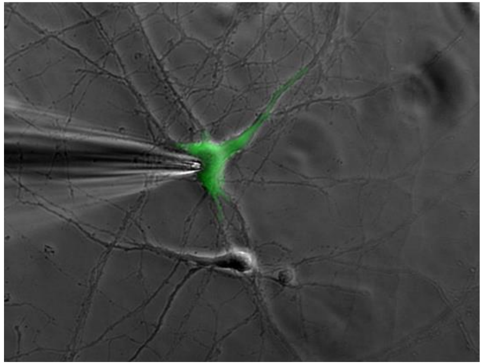
Measuring Calcium

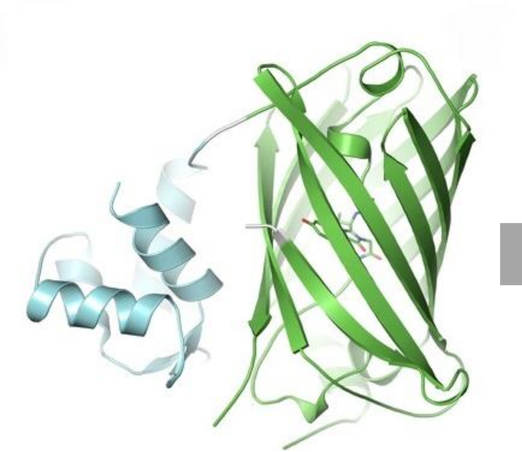
Measuring voltage

Calcium imaging

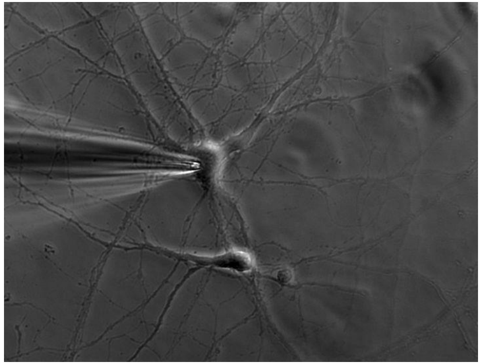


with Ca^{2+}

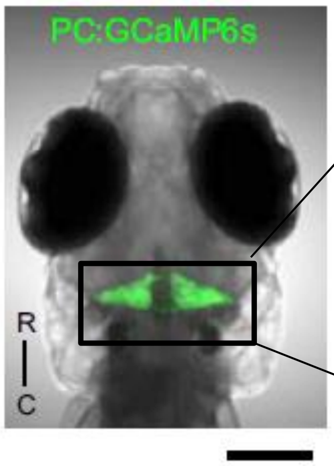


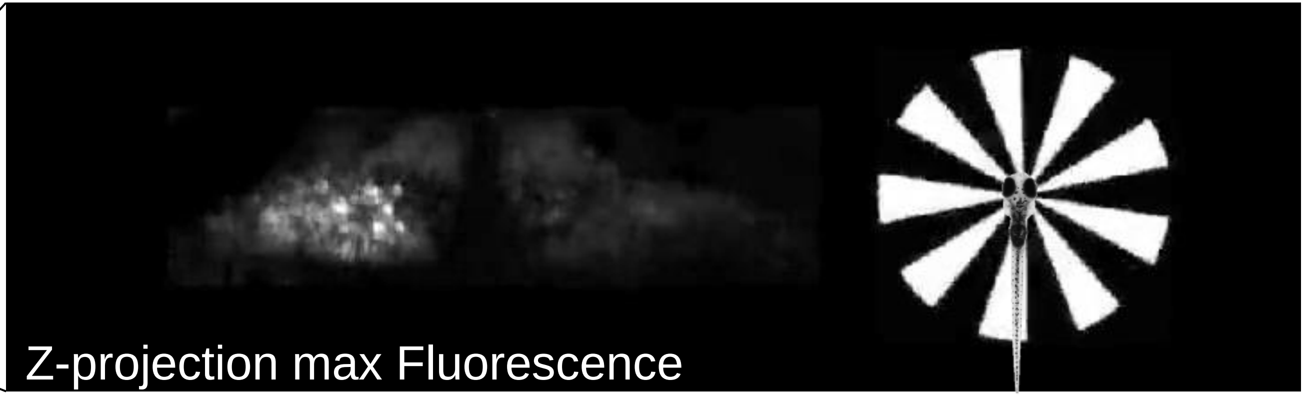


w/o Ca^{2+}

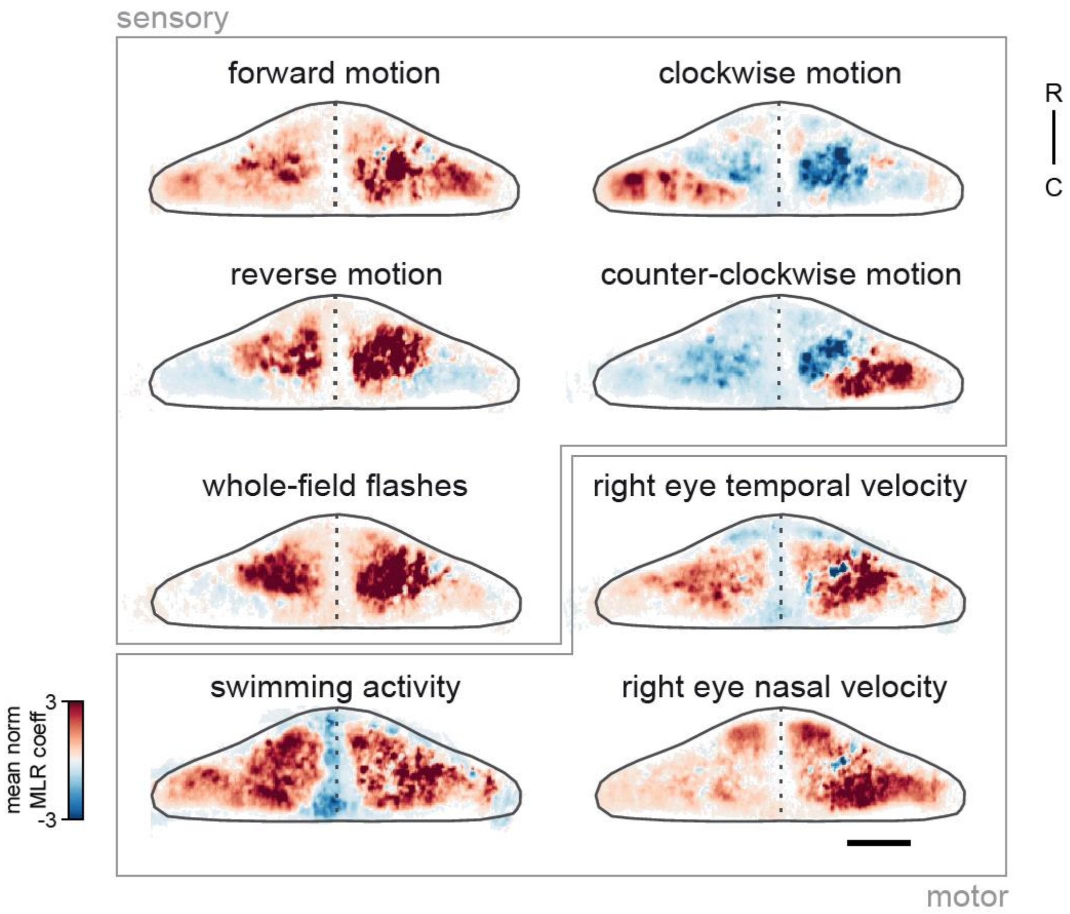


Imaging Purkinje cells in larval zebrafish

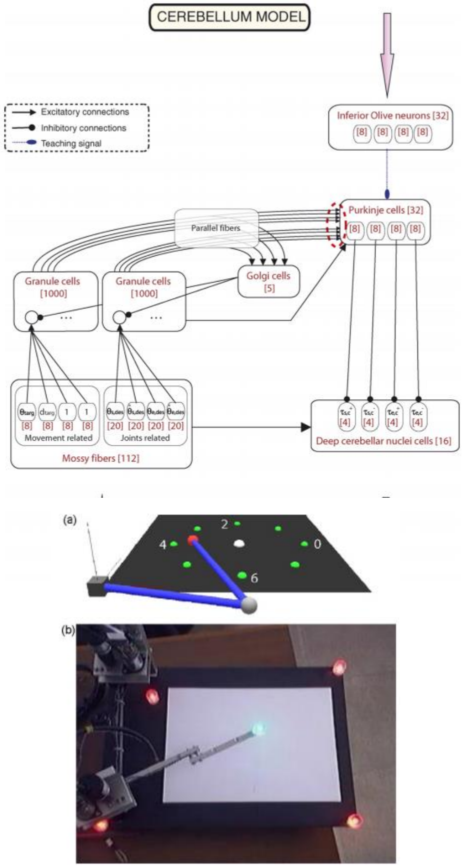


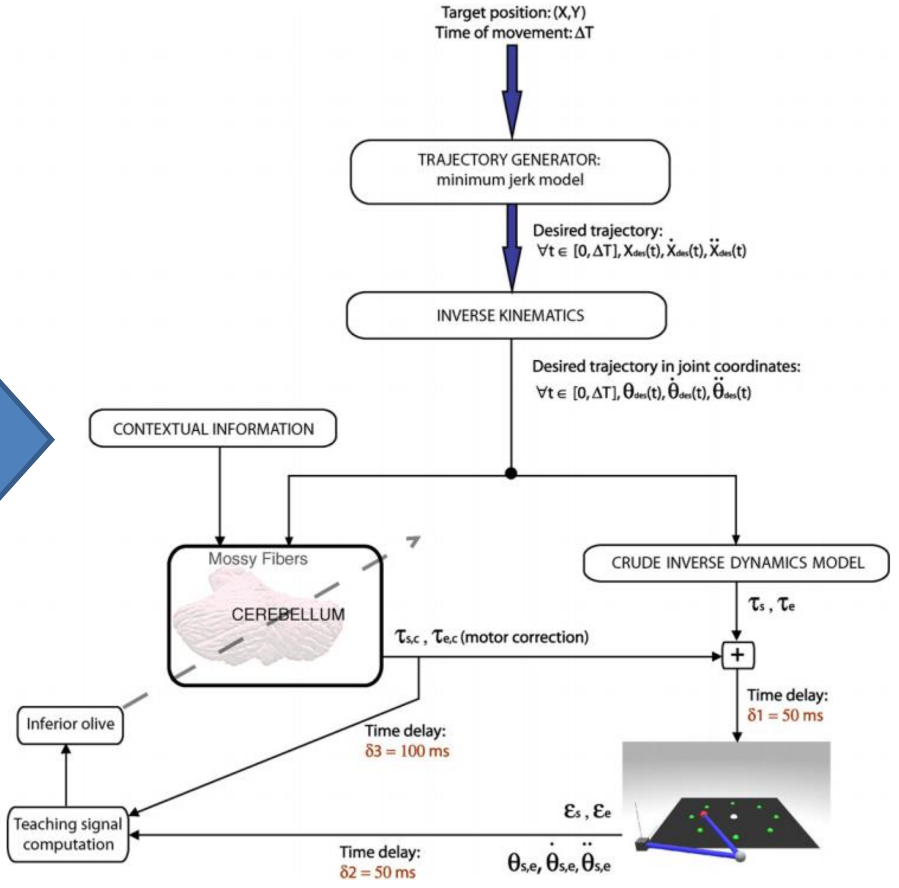


Calcium imaging reveals activity dependent on sensory stimuli



Why is this important to AI Developers?





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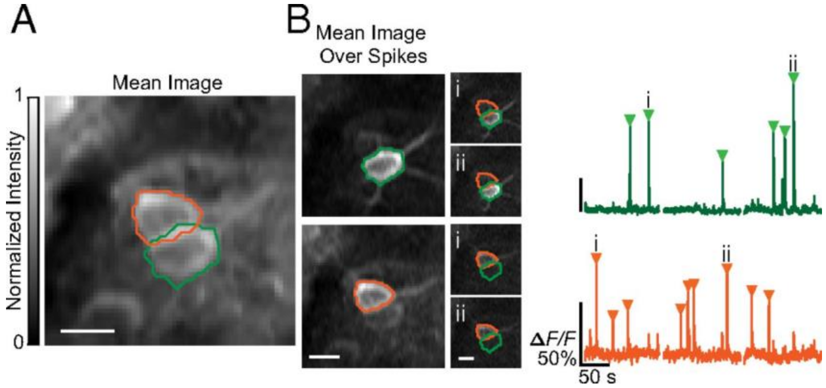

CalciumGAN: A Generative Adversarial Network Model for Synthesising Realistic Calcium Imaging Data of Neuronal Populations

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Theoklitos Amvrosiadis[2] t.amvrosiadis@ed.ac.uk
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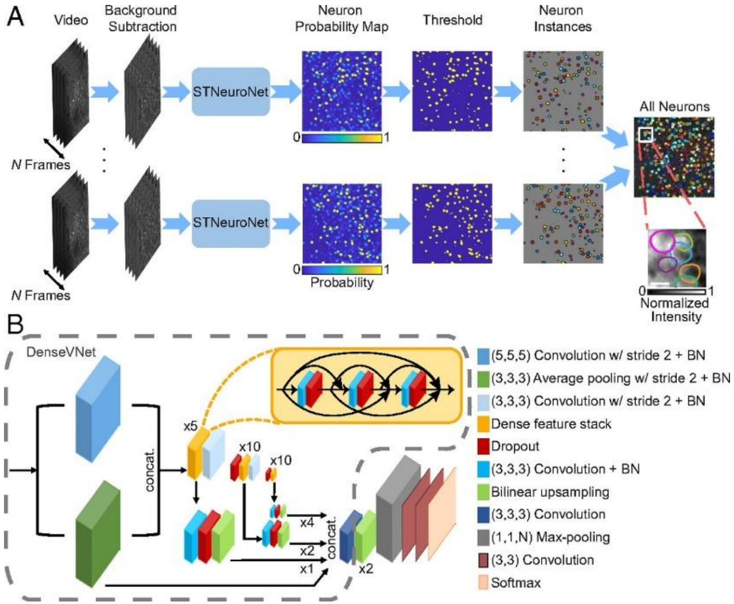
Fast and robust active neuron segmentation in two-photon calcium imaging using spatiotemporal deep learning

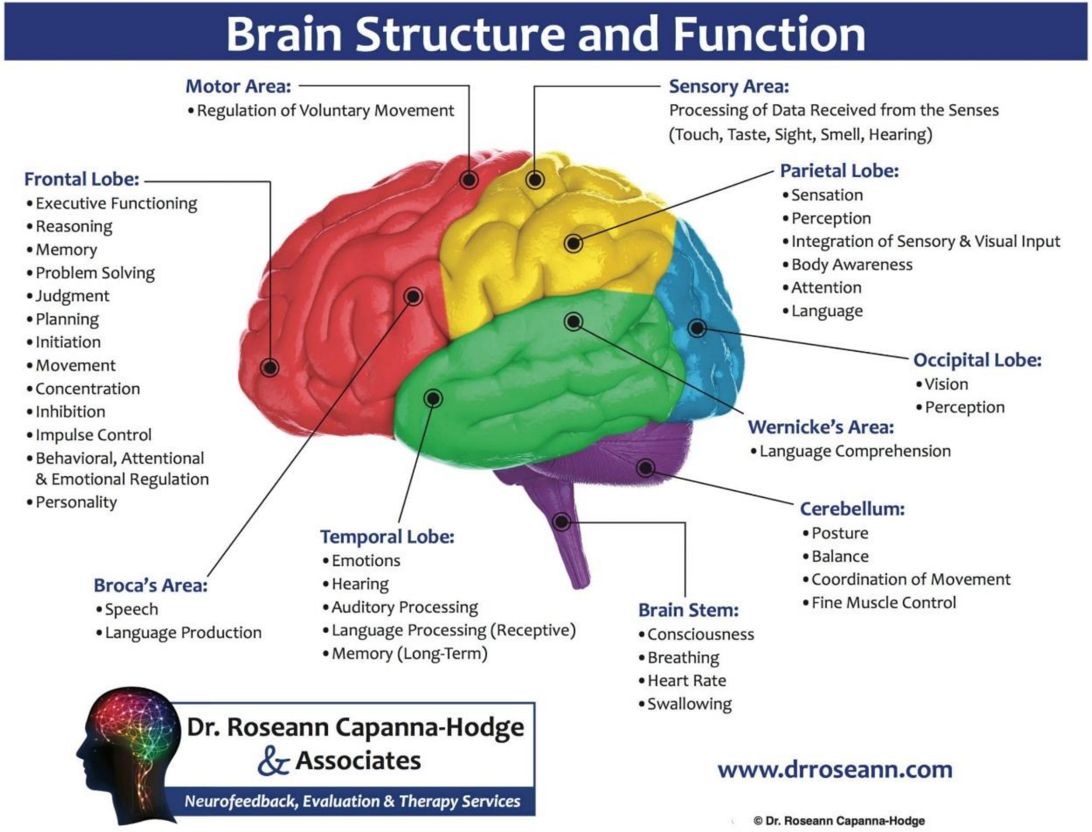
Somayyeh Soltanian-Zadeh, Kaan Sahingur, Sarah Blau, Yiyang Gong, and Sina Farsiu
+ See all authors and affiliations

PNAS April 23, 2019 116 (17) 8554-8563; first published April 11, 2019; https://doi.org/10.1073/pnas.1812995116



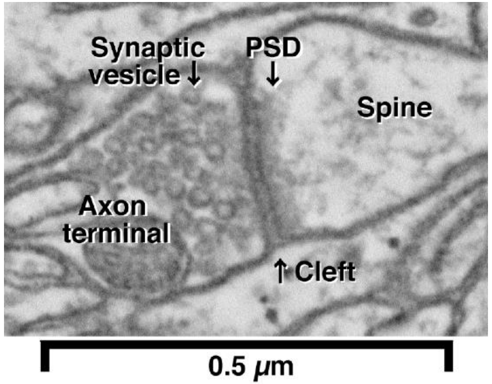
Connectivity

The brain does it, but … where?



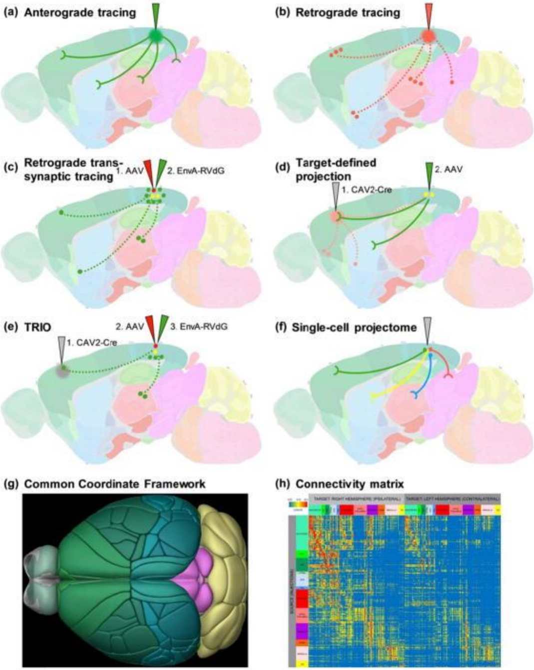
Connectivity analysis

Micro [µms]



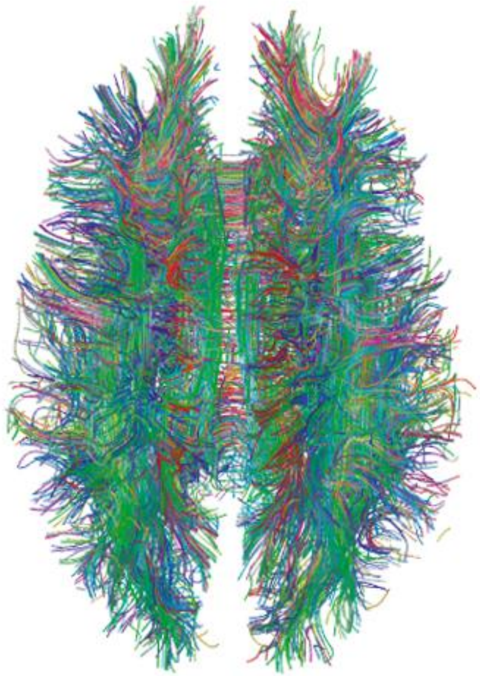
https://blogs.zeiss.com/microscopy/en/brain-circuits/

Meso [100 µms]



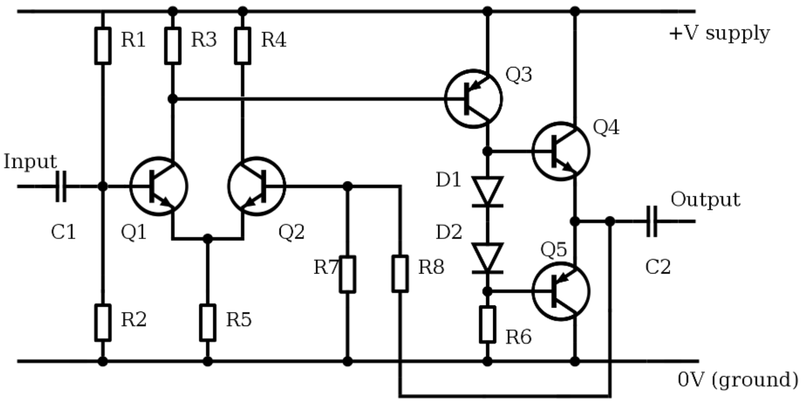
Zeng, Curr Opin Neurobiol 2018

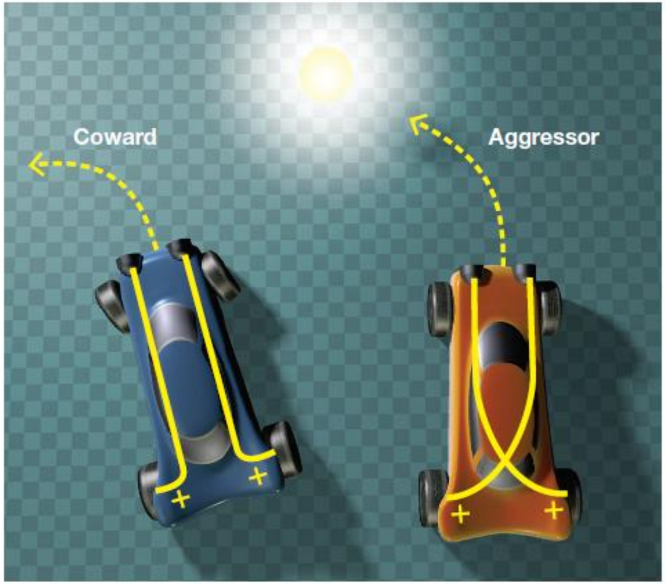
Macro [mms]



Xavier Gigandet et al., 2008

Why is it important?

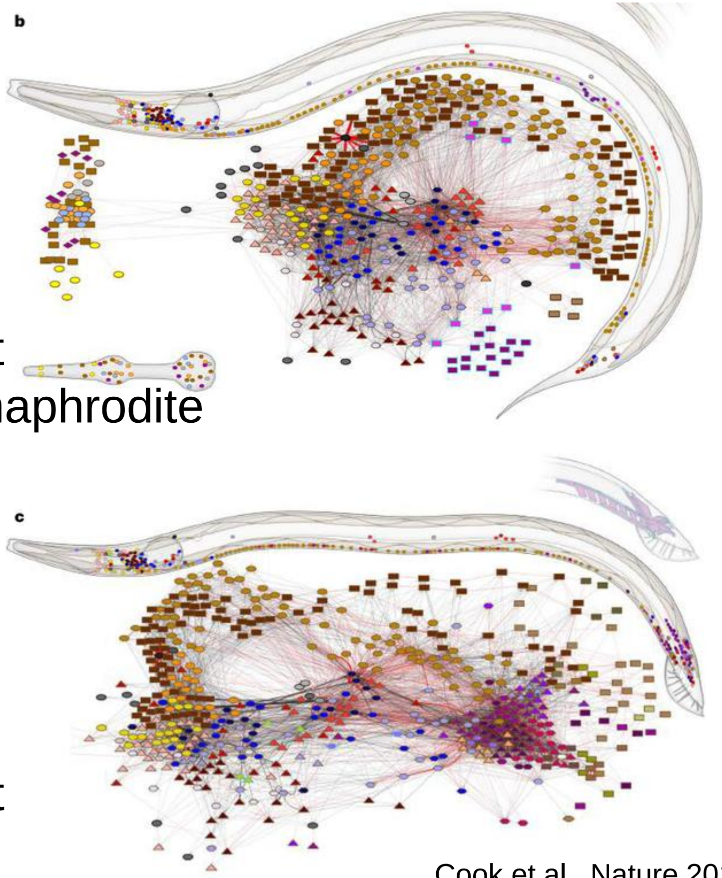




Knowing the circuitry helps in identifying the purpose

https://en.wikipedia.org/wiki/Amplifier#/media/File:Amplifier_Circuit_Small.svg

C. elegans connectome

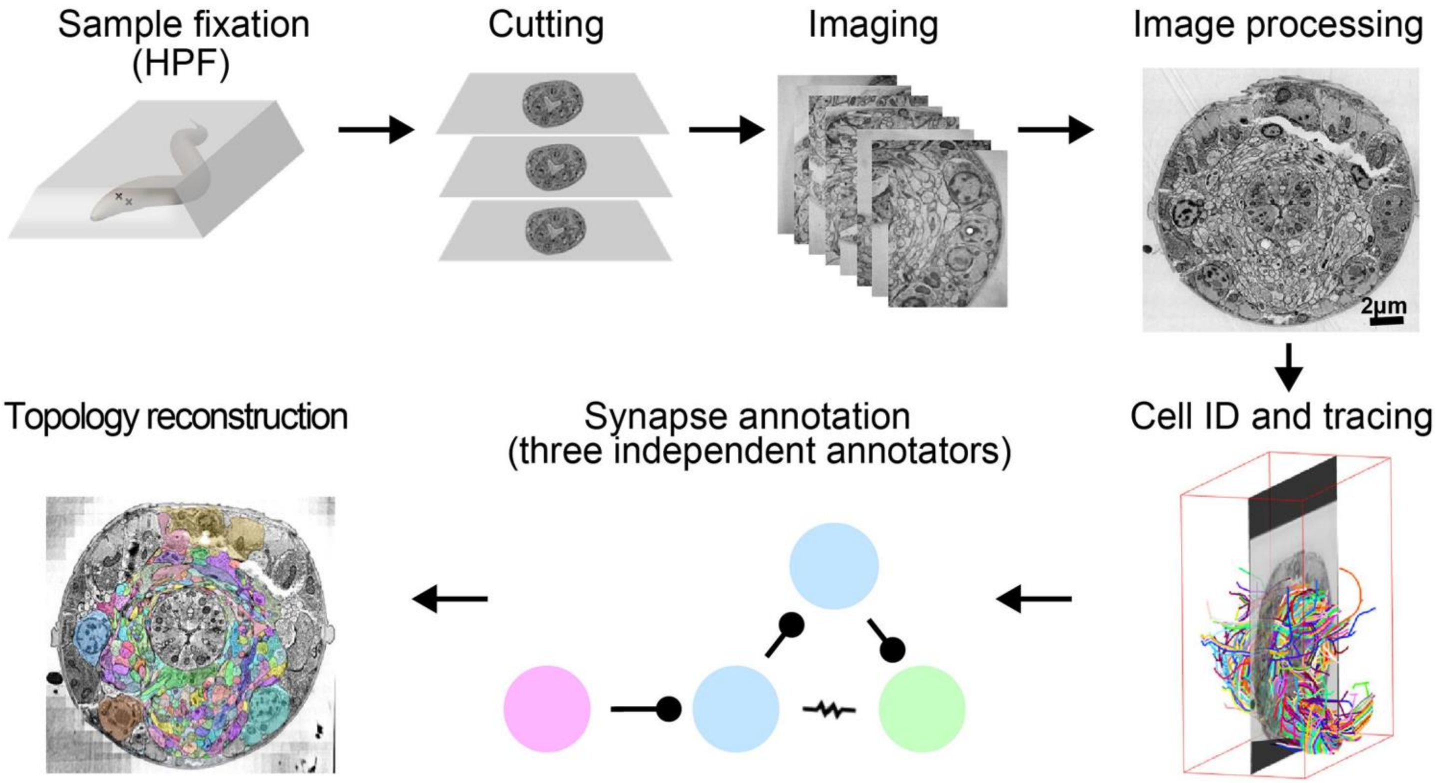


Adult hermaphrodite

Adult male

Cook et al., Nature 2019

Electron microscopy



Mulcahy et al., Front. Neural Circuits 2018

Brainflight

Gamification of tasks

Using AI for connectomics analysis

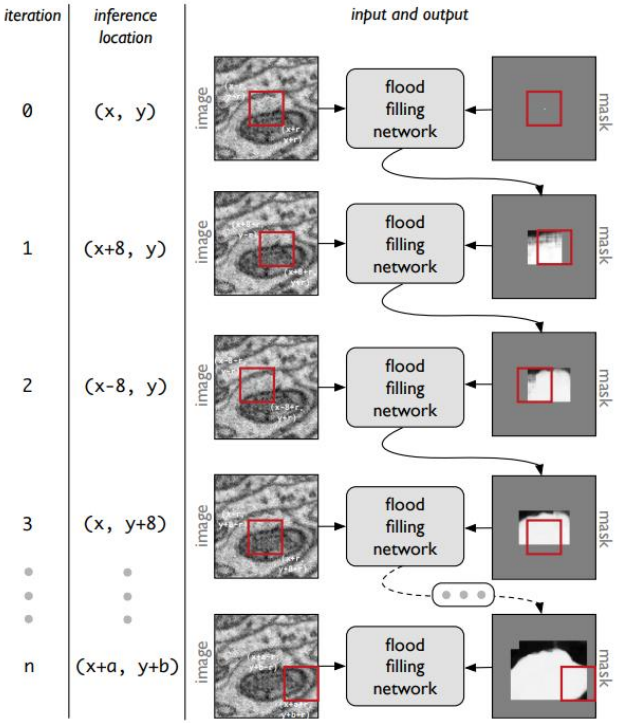


Figure 2: Schematic of multiple-field-of-view inference of a flood-filling network.

Januszewski et al., arxiv 2016

Connectivity analysis

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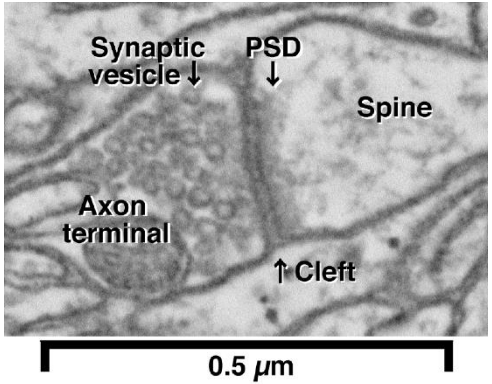
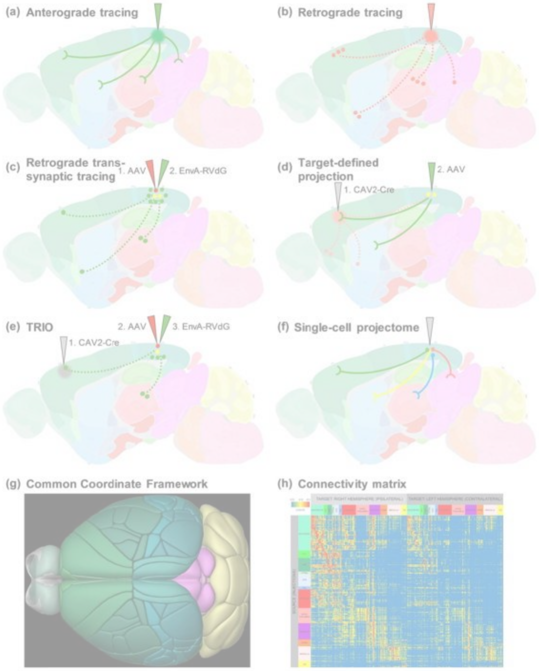
Micro [µms]



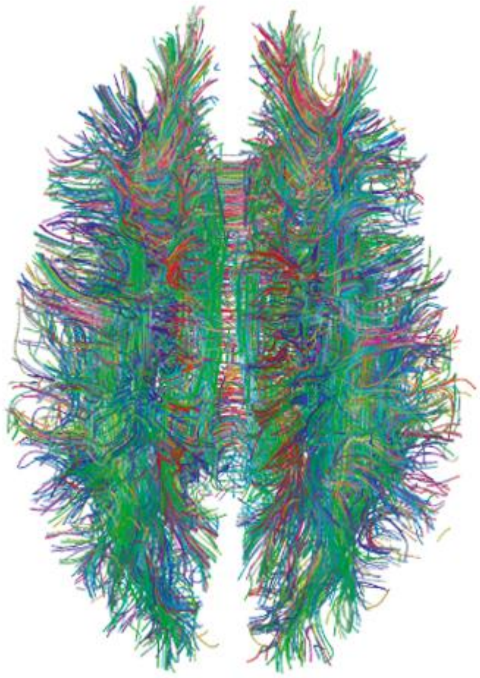
https://blogs.zeiss.com/microscopy/en/brain-circuits/

Meso [100 µms]



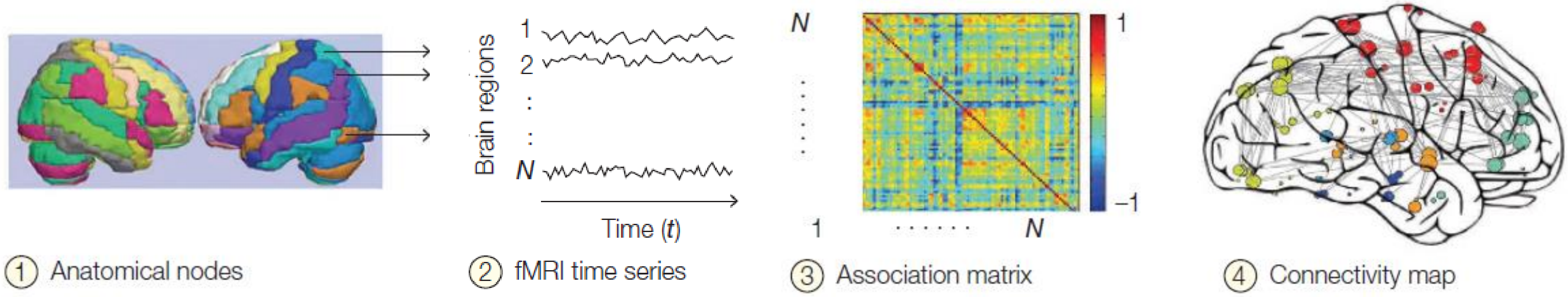
Zeng, Curr Opin Neurobiol 2018

Macro [mms]



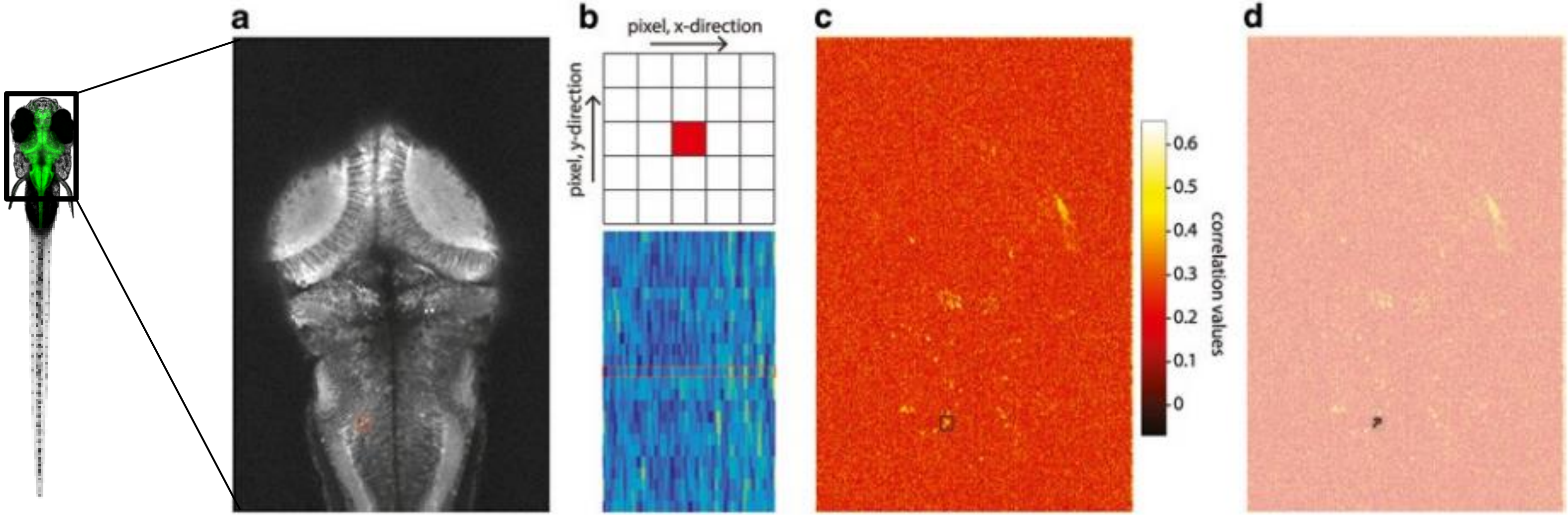
Xavier Gigandet et al., 2008

Construction a human brain network

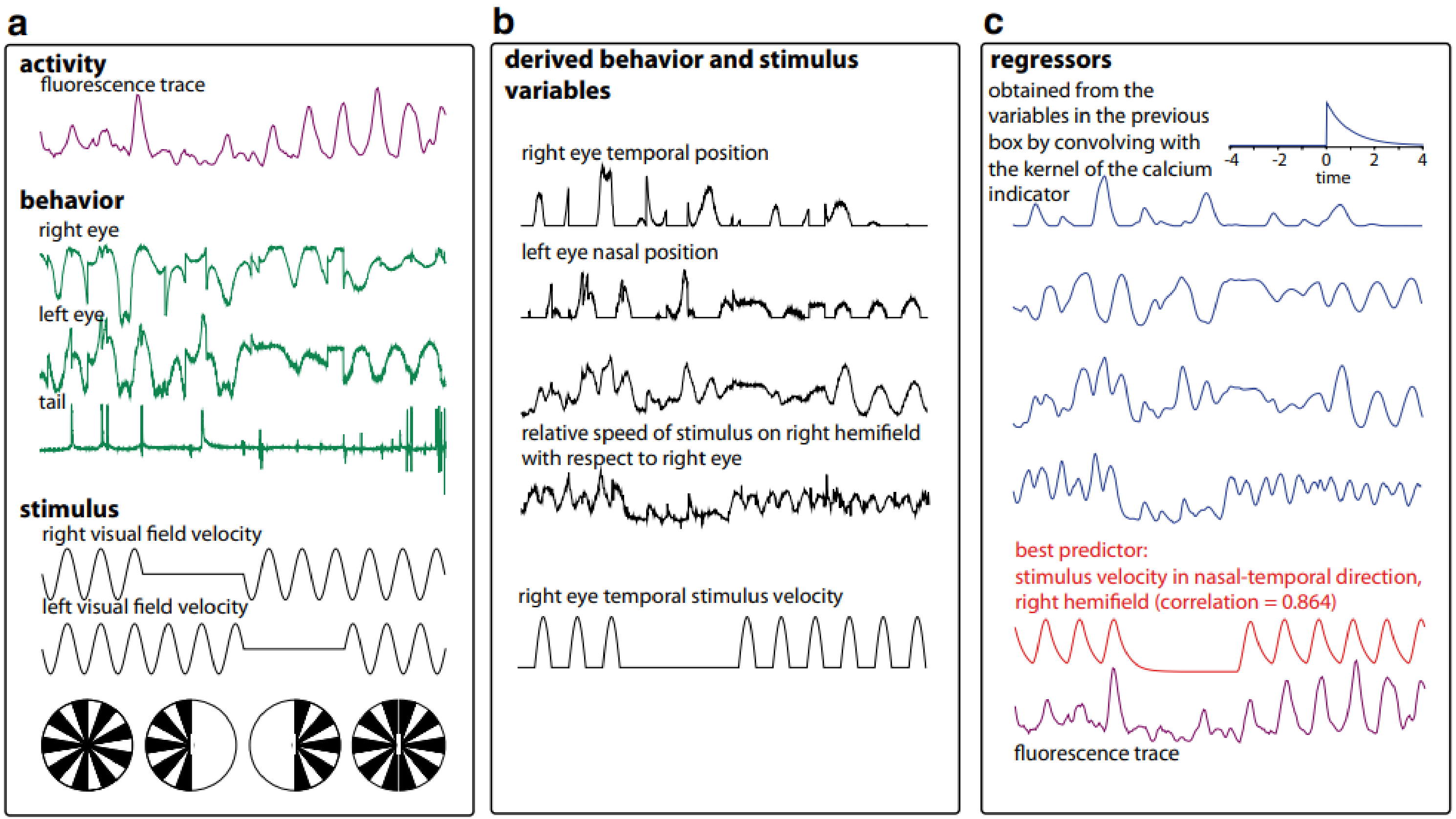


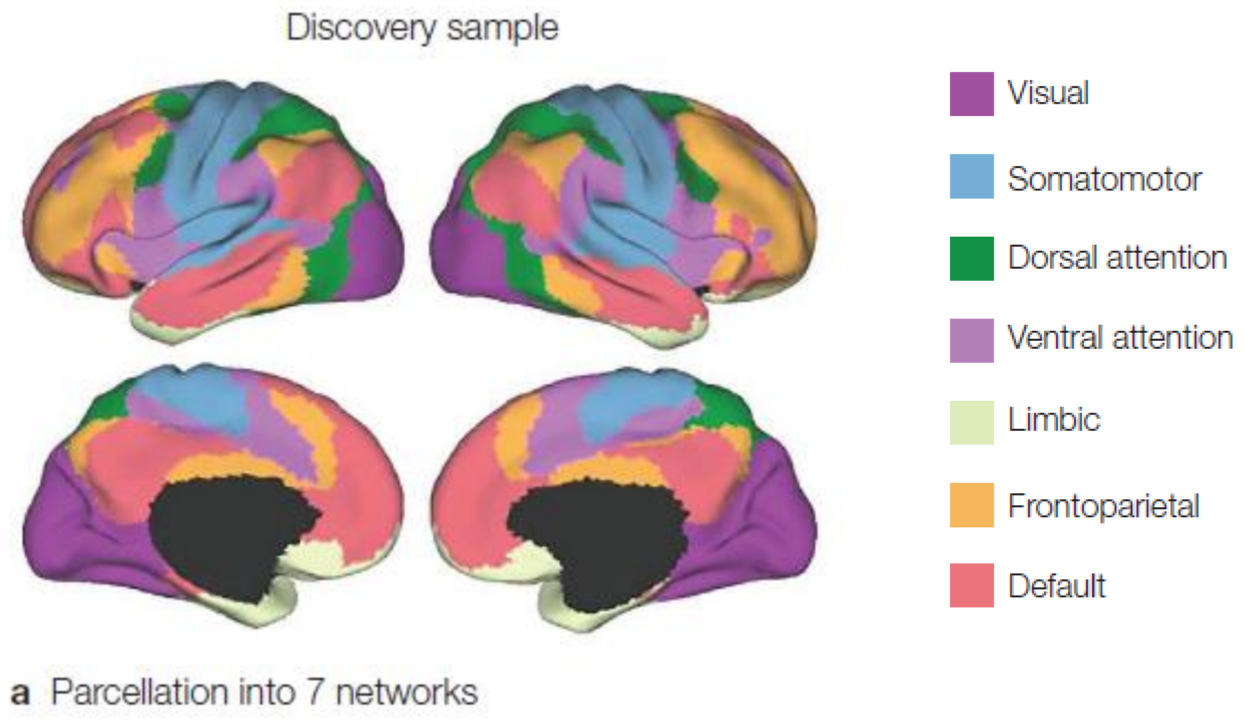
Voxel-based correlation map

Unbiased voxel-based self-correlation



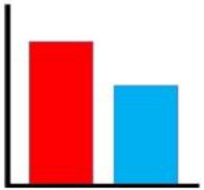
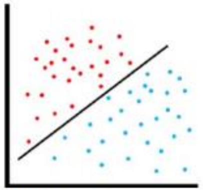
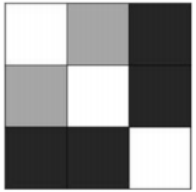
Voxel-based correlation maps



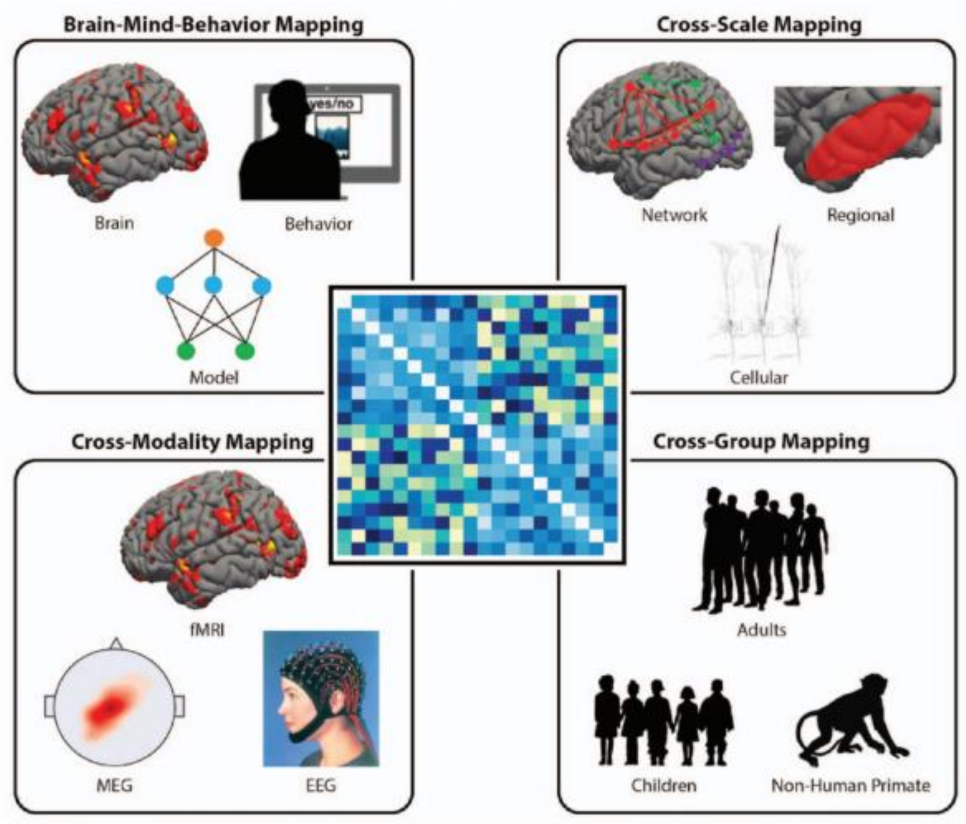

Discovery sample
Visual
Somatomotor
Dorsal attention
Ventral attention
Limbic
Frontoparietal
Default
a Parcellation into 7 networks

Analytic approaches

Table 1. Comparison between different fMRI analytic approaches

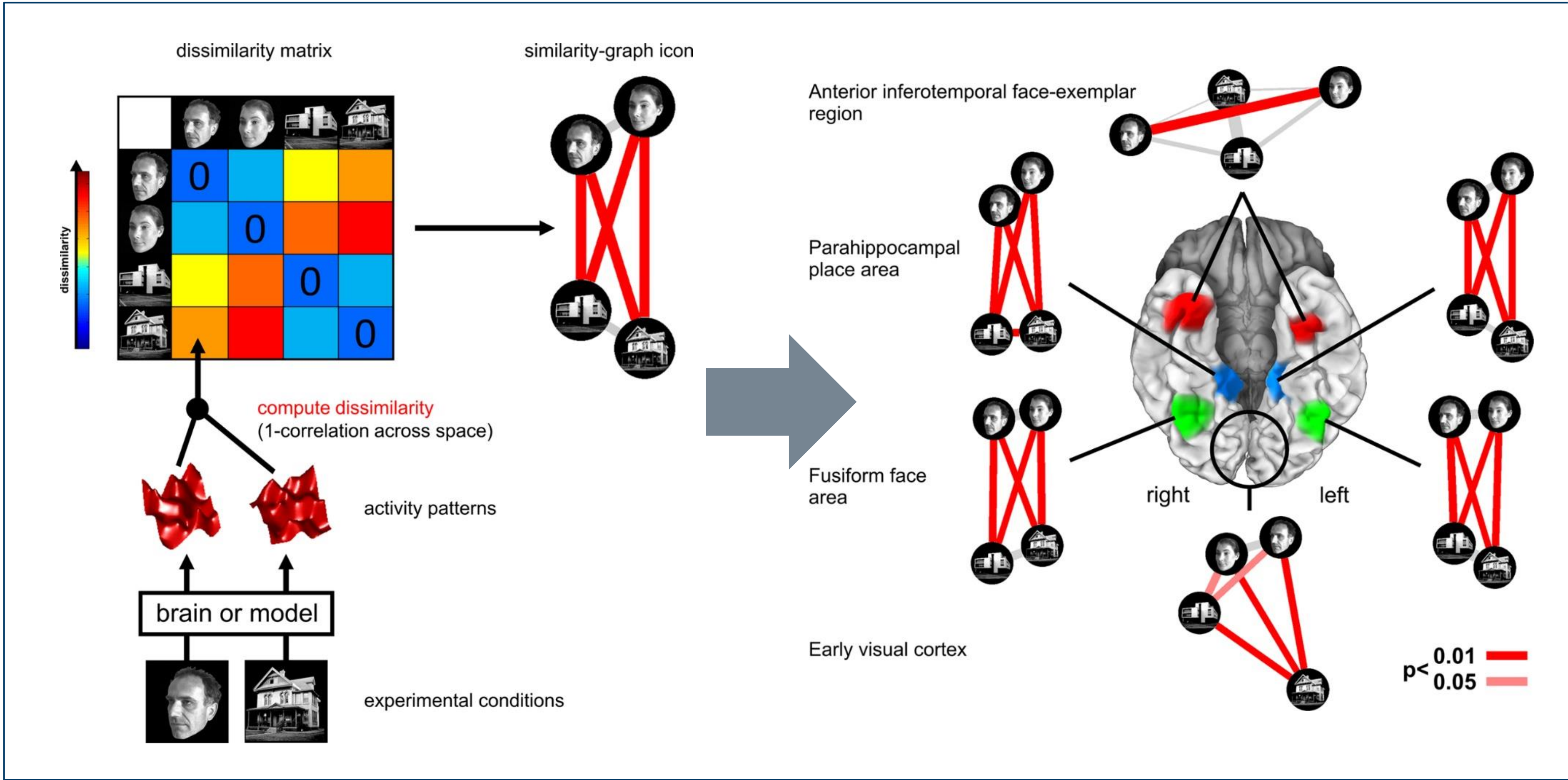
			
	Mass-Univariate	**MVPA Decoding**	**RSA**
Granularity of representational inference	Task/state level of information	Category and item level of information	Item level of information
Handling multivoxel data	Averaged across voxels	Jointly analyze across voxels	No requirement
Inferred format of representation	Discrete categories	Classification for discrete categories, regression for continuous dimensions	Discrete categories and continuous dimensions
Implementation	Contrast subtraction	Train-test learning phase	Representational dissimilarity matrix
Algorithm	Linear	Both linear and non-linear classifier	Mostly linear
Data modelling in GLM	Single-category modelling and aggregated across runs	Single-category modelling and then cross-validate across runs	Single-trial modelling, within- or between-runs
Optimal study design	Factorial design	Only few numbers of stimulus categories (<5), each with many repetitions for train-test learning	No limits on number of categories, stimuli with many features
Testing computational models	Easy (but univariate encoding models have to fit a model first using separate data)	Difficult (due to its decoding nature)	Easy (due to its encoding nature)
Linking multimodal data	Difficult	Difficult	Easy

RSA

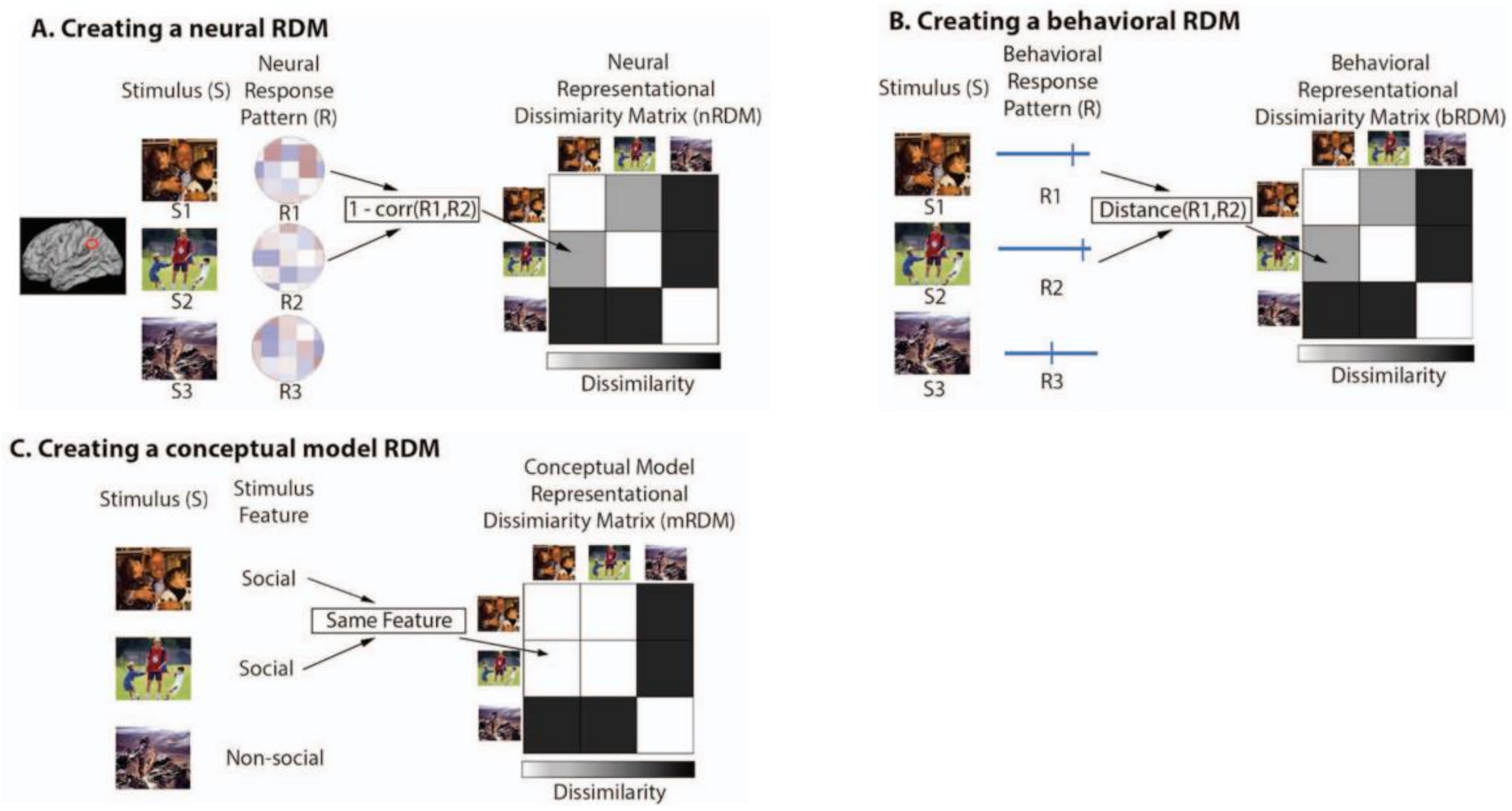


Brain-Mind-Behavior Mapping
yes/no
Brain
Behavior
Model
Cross-Scale Mapping
Network
Regional
Cellular
Cross-Modality Mapping
fMRI
MEG
EEG
Cross-Group Mapping
Adults
Children
Non-Human Primate

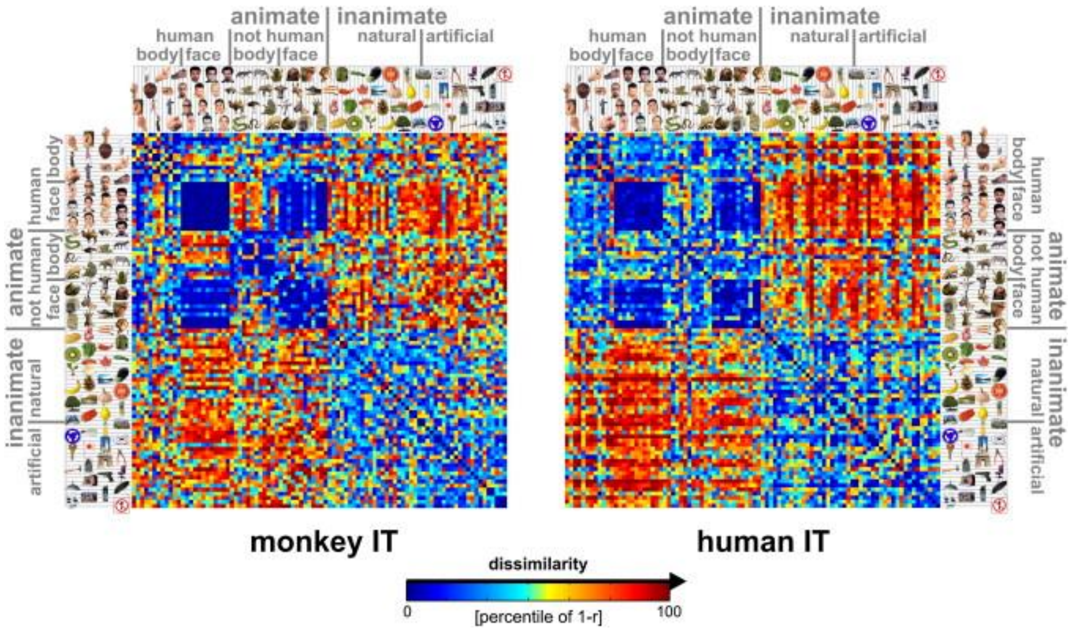
Representational Dissimilarity Matrices (RDMs)

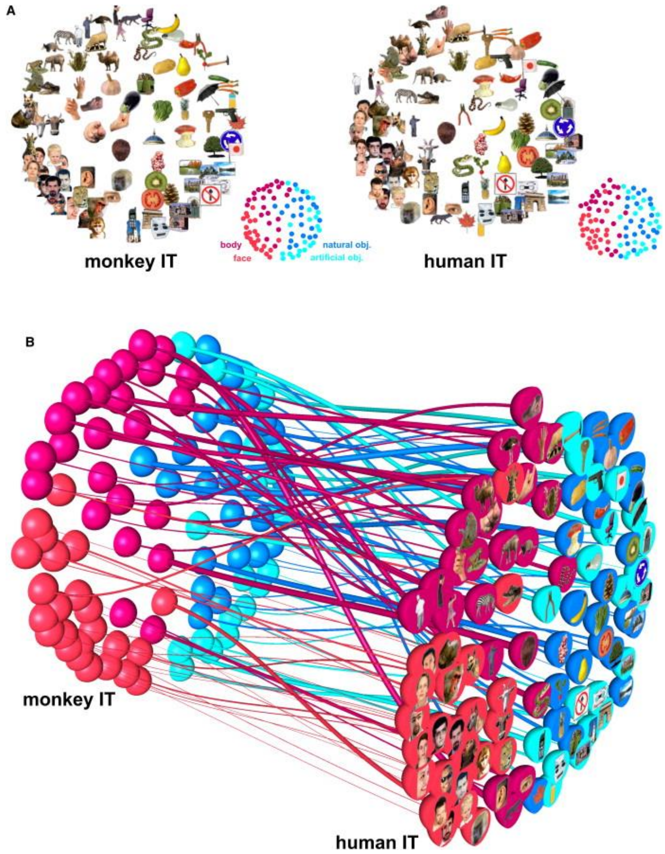


Creating RDMs



RSA to uncover brain coding in humans and monkeys





Kriegeskorte et al., Neuron 2008