CBMM Summer School 2018

Neuroscience Methods Tutorial

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Purpose of Tutorial

- Provide understanding of the principles underlying neural signals and some of the most used methods to record them, enabling basic comprehension of Neuroscience data and results.
- Develop a critical perspective of different Neuroscience methodological tools, their capabilities and limitations. – Which questions can/can’t be answered with each technique?

Goals of Neuroscience

- 1. Understand the mechanisms by which the brain/nervous system carries out all functions (e.g. sensory processing, cognition, motor functions, etc.).
- 2. Understand what failures in those mechanisms lead to particular disorders of the brain.
- 3. Develop treatments for those disorders in order to restore function.

Psychophysics: the “black box” method

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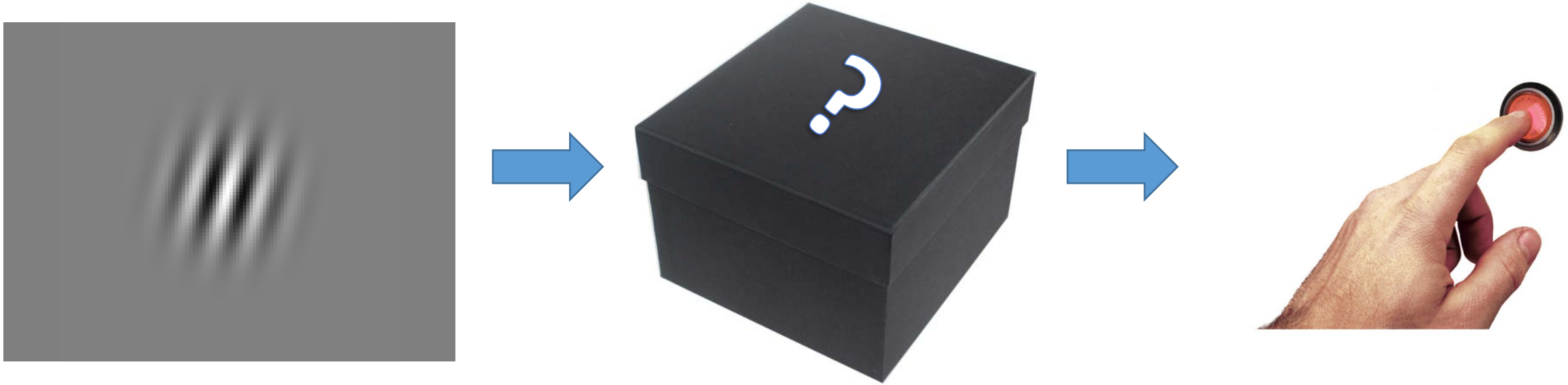


Interrogating the brain: neural signals

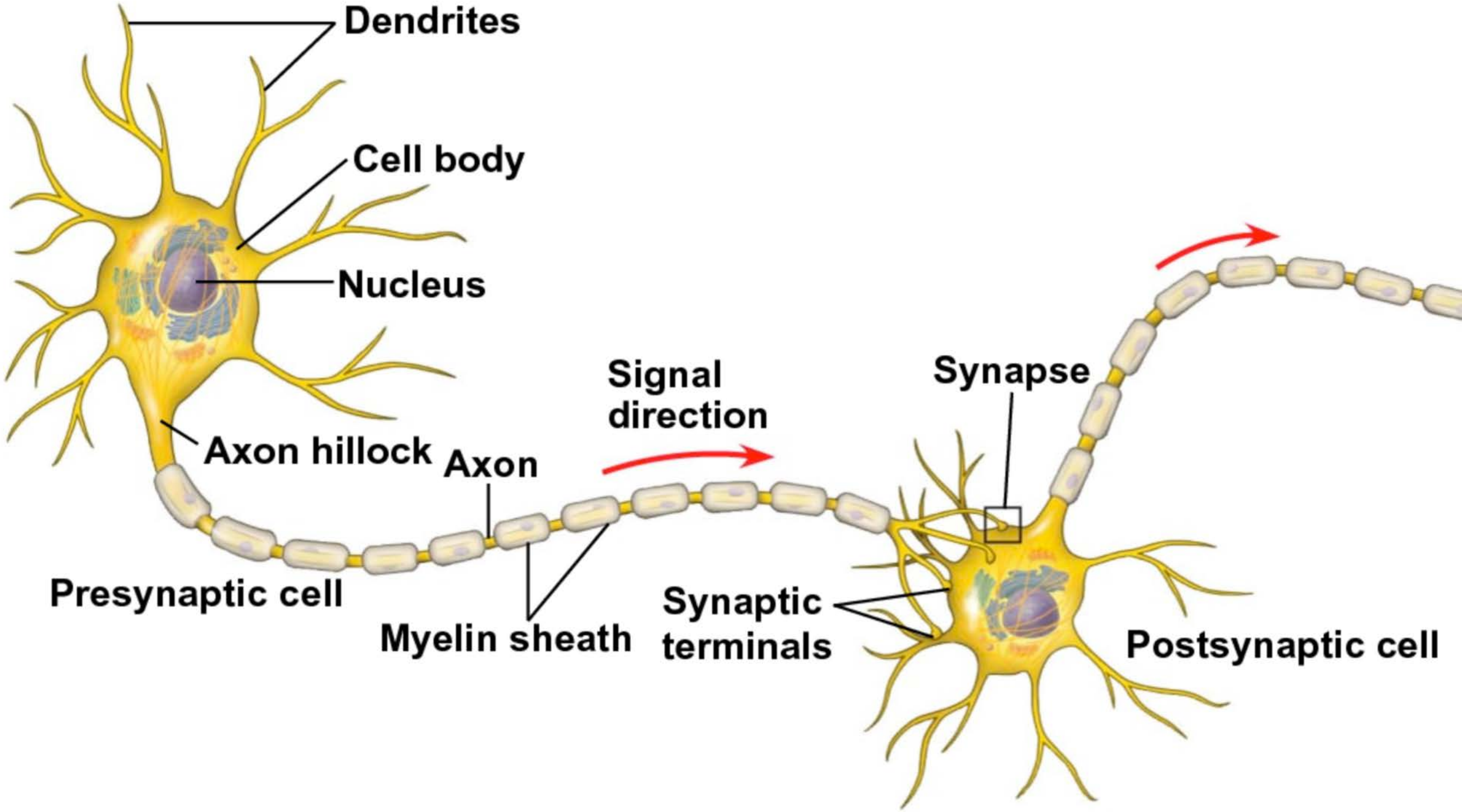
Signal: A fluctuating quantity in a medium whose variations represent information.

Examples of signal media:

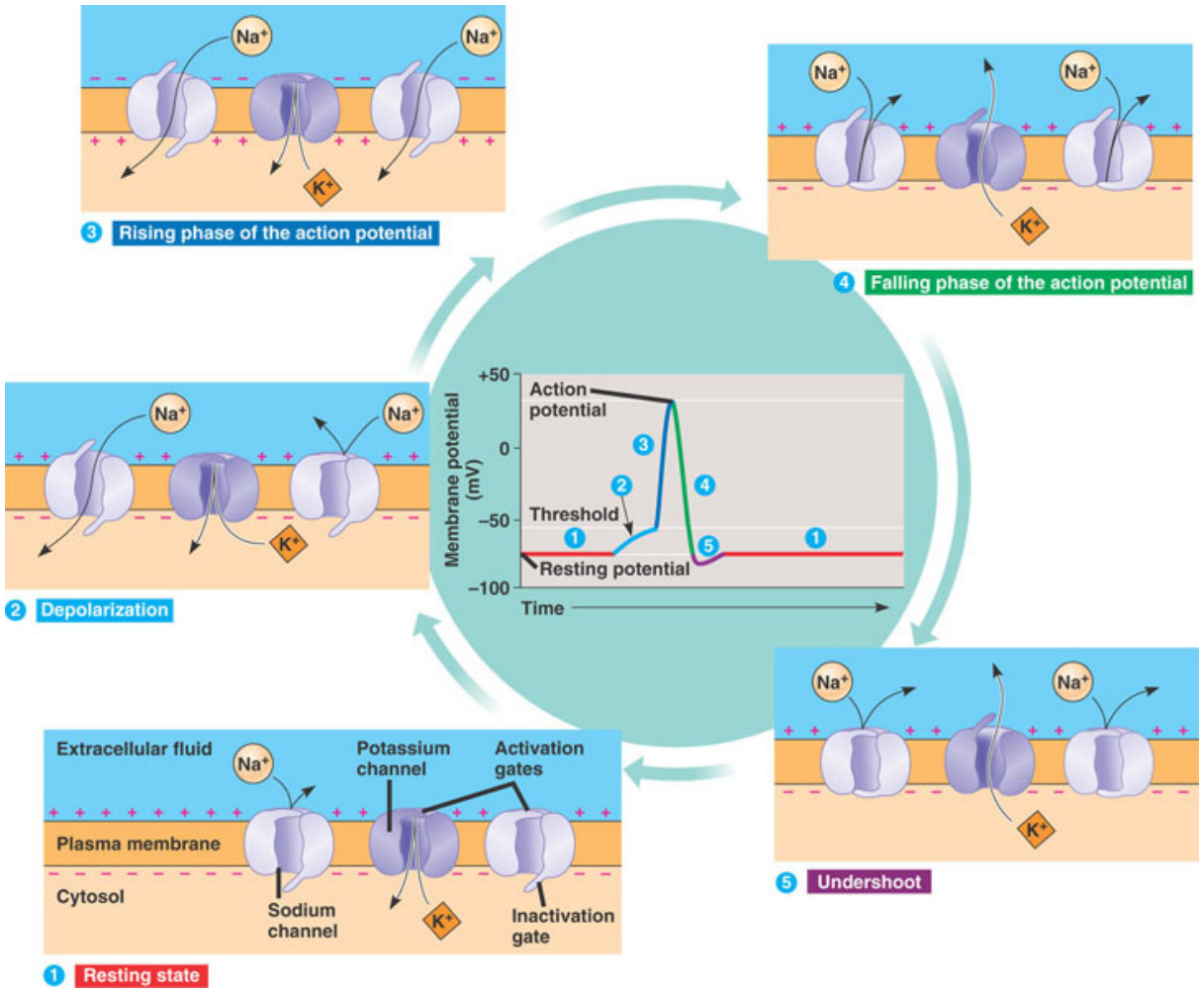
Light, sound, electricity, magnetism, heat, material (e.g. chemical).

SIGNAL in neural function vs. SIGNAL in experimental acquisition

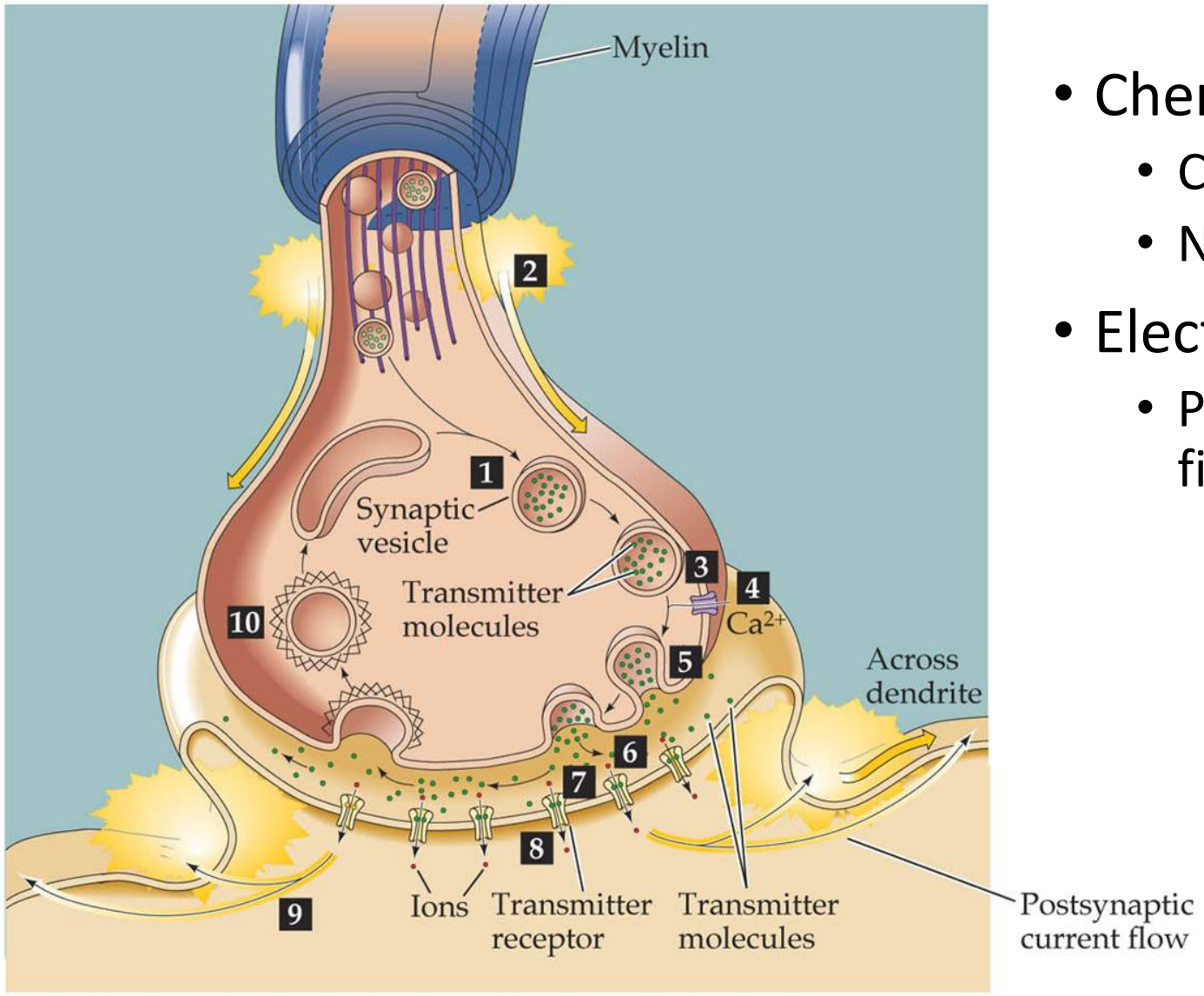
e.g. Neuromagnetic and BOLD signals


Dendrites
Cell body
Nucleus
Axon hillock
Axon
Signal direction
Synapse
Presynaptic cell
Myelin sheath
Synaptic terminals
Postsynaptic cell

Action potentials

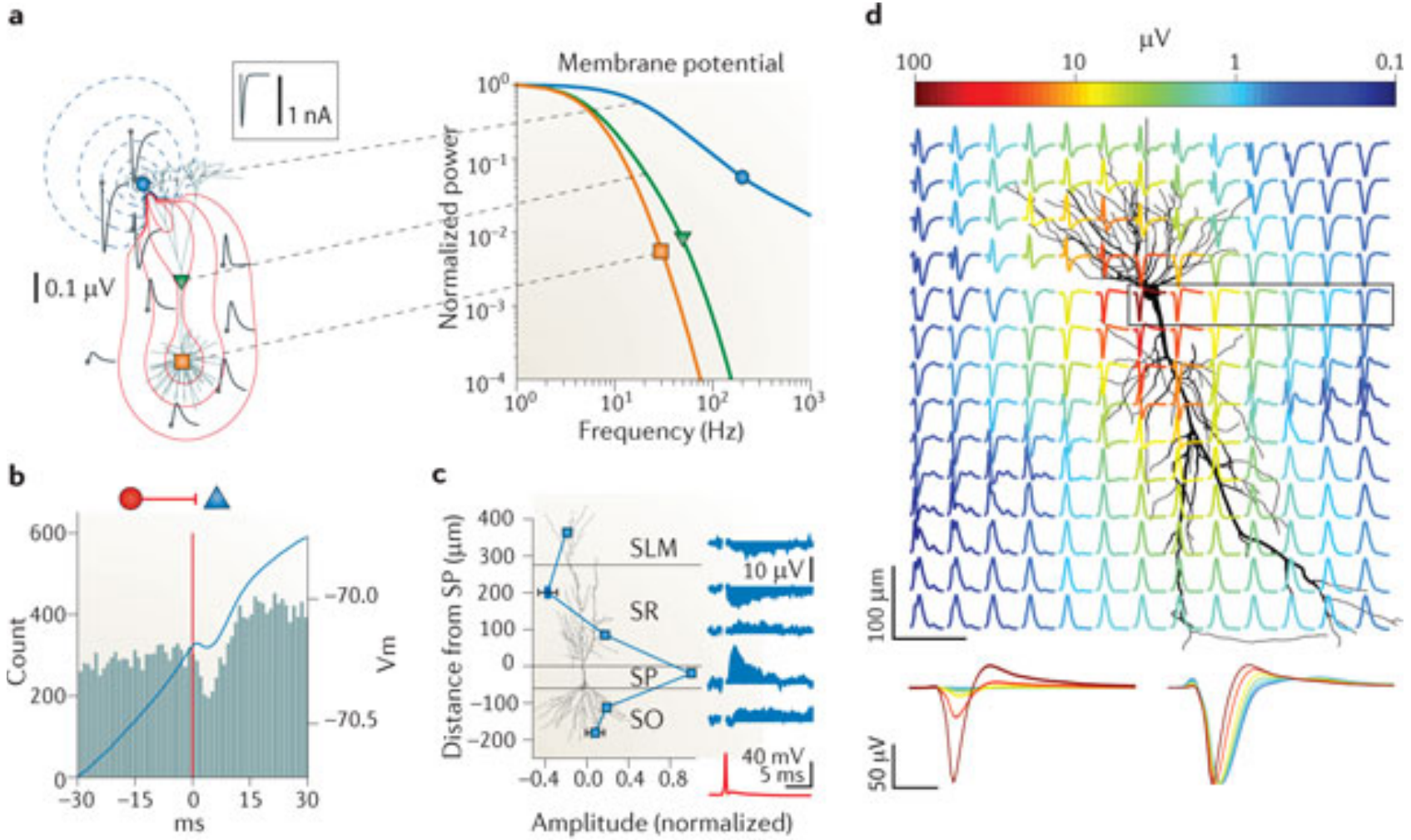


Synaptic transmission



- Chemical signals:
  - Ca++ influx
  - Neurotransmitter release
- Electrical signals:
  - Postsynaptic currents – Local field potentials

Local Field Potentials (LFP): perisynaptic currents



Nature Reviews | Neuroscience

Buszaki et al., 2012

Neural signals summary

- Electrical signals:
  - Action potentials
  - Local field potentials

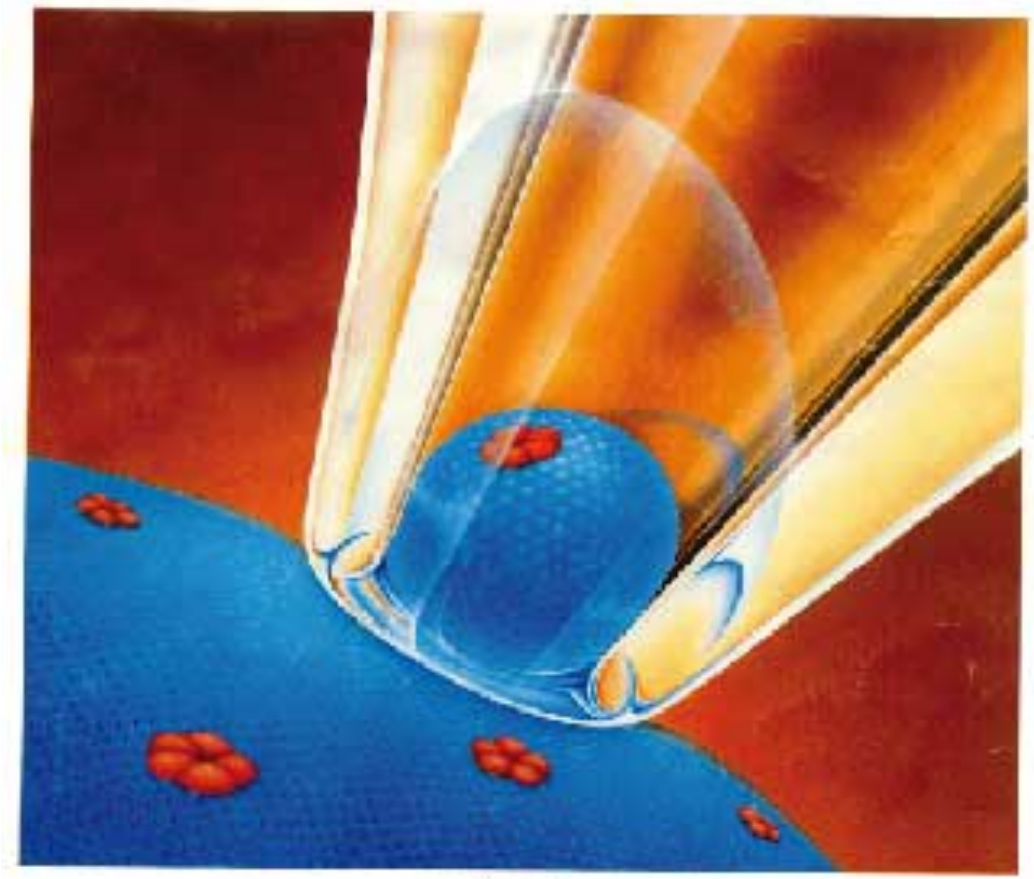
- Chemical signals:
  - Ca++ influx
  - Neurotransmitter release

Neural acquisition methods: Electrophysiology

- Acquisition of electrical signals of biological origin over time
- Various spatial scales:
  - Patch clamp
  - Intracellular electrode recordings
  - Extracellular electrode recordings
  - Electrocorticography (ECoG)
  - Electroencephalography (EEG)

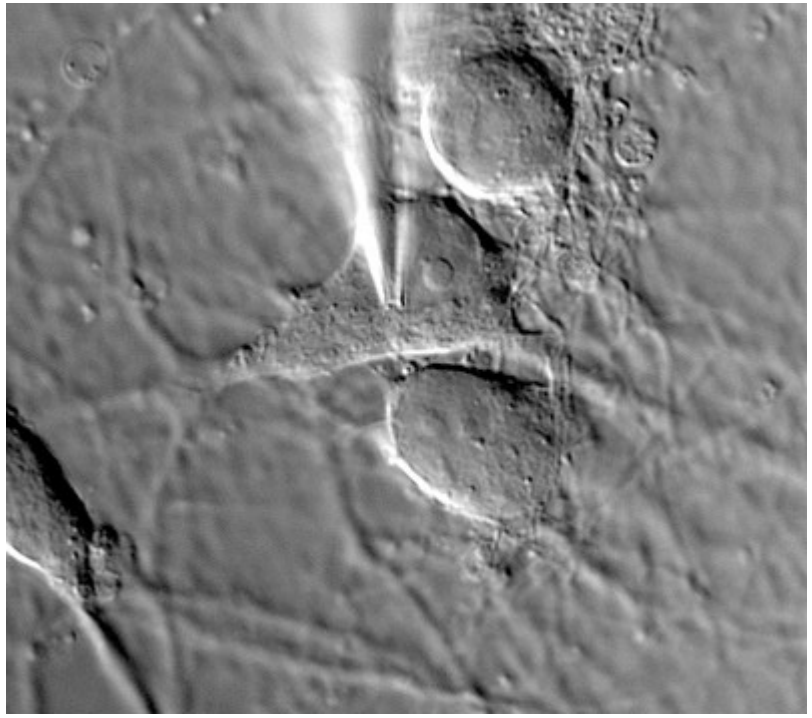
Electrophysiology: Patch-clamp

- Glass pipette seals membrane patch by suction.
- Measures voltage changes in solution inside pipette (electrolyte)
- Used to study properties of a small patch of membrane, even individual ion channels!



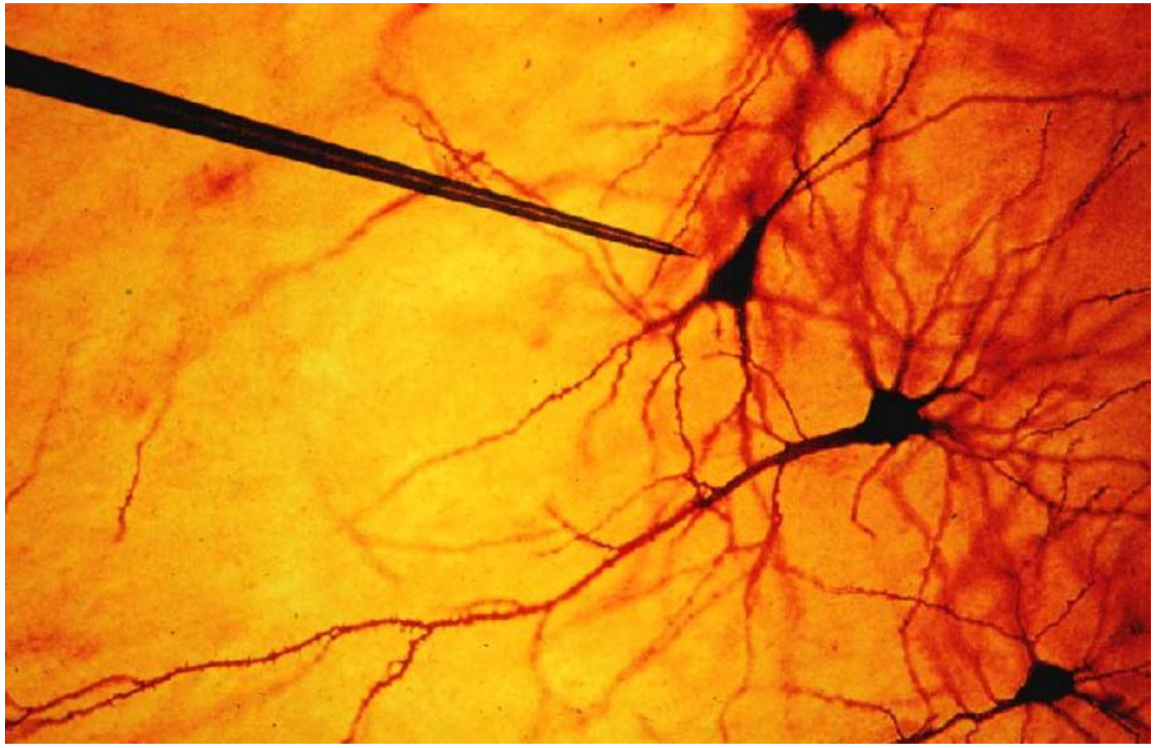
Electrophysiology: Intracellular recordings

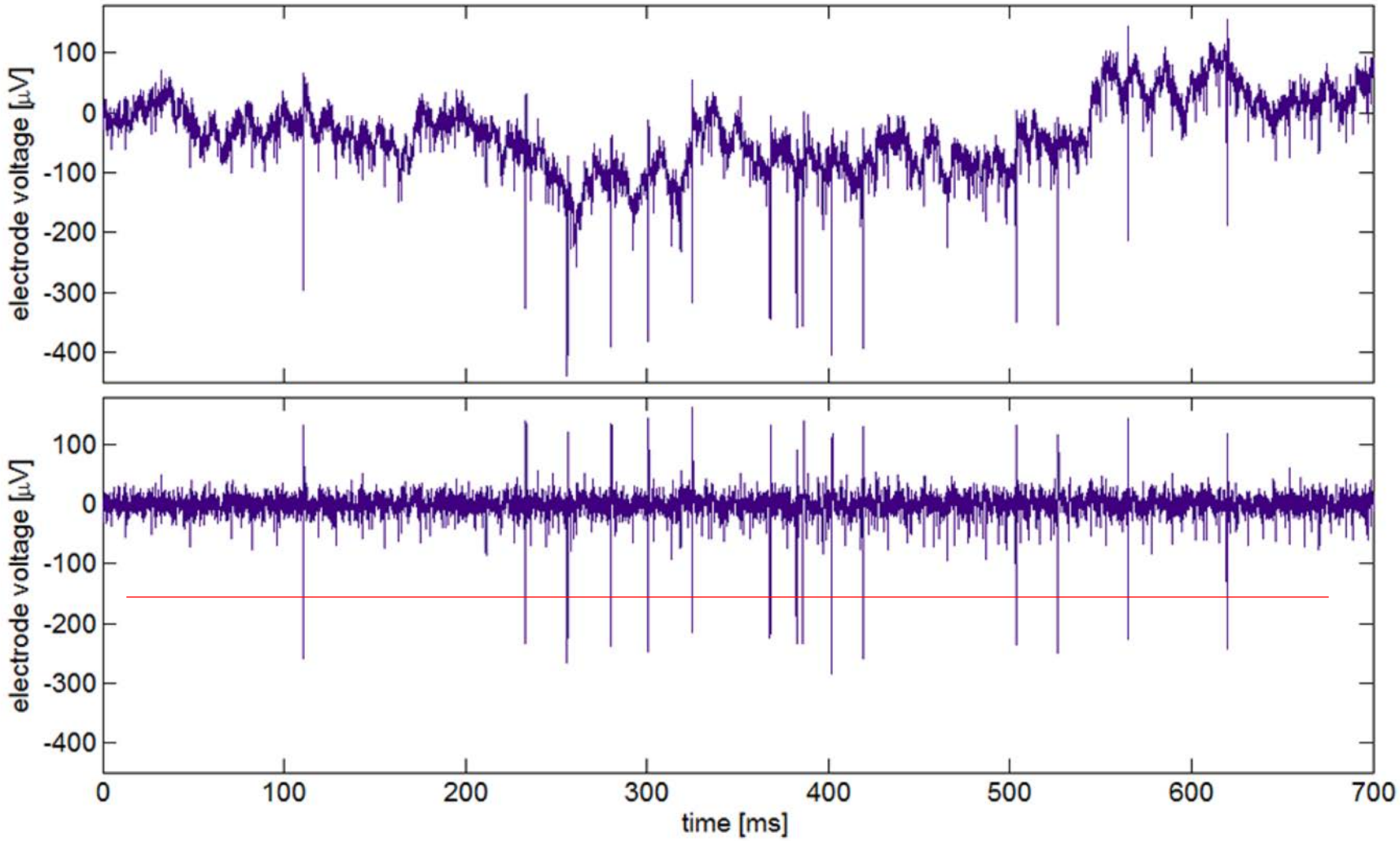
- Sharp glass pipette filled with electrolyte solution
- Pipette tip penetrates cell membrane of a single neuron
- Acquires voltage readings from intracellular space



Electrophysiology: Extracellular recordings

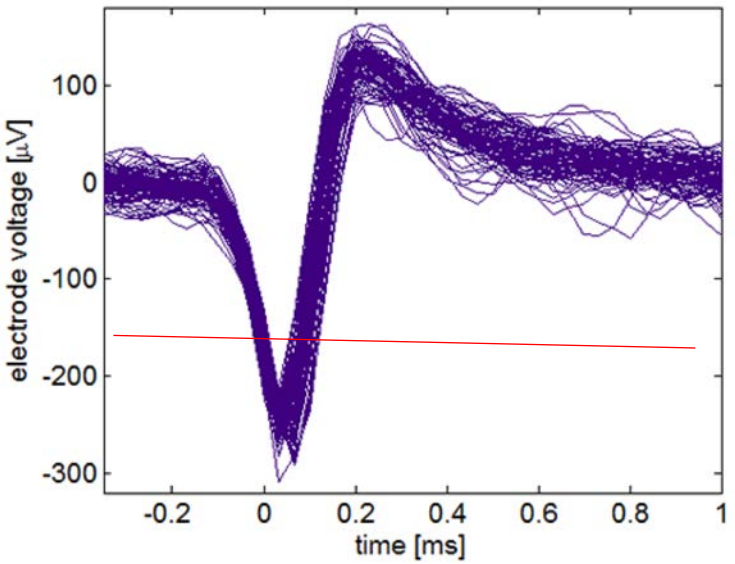
- Microelectrode made of metal (e.g. tungsten) coated with insulating material but with an exposed tip
- Acquires voltage readings in extracellular space
- Voltage signal has several components:
  - Noise
  - LFP
  - Single-unit spiking activity
  - Multi-unit spiking activity

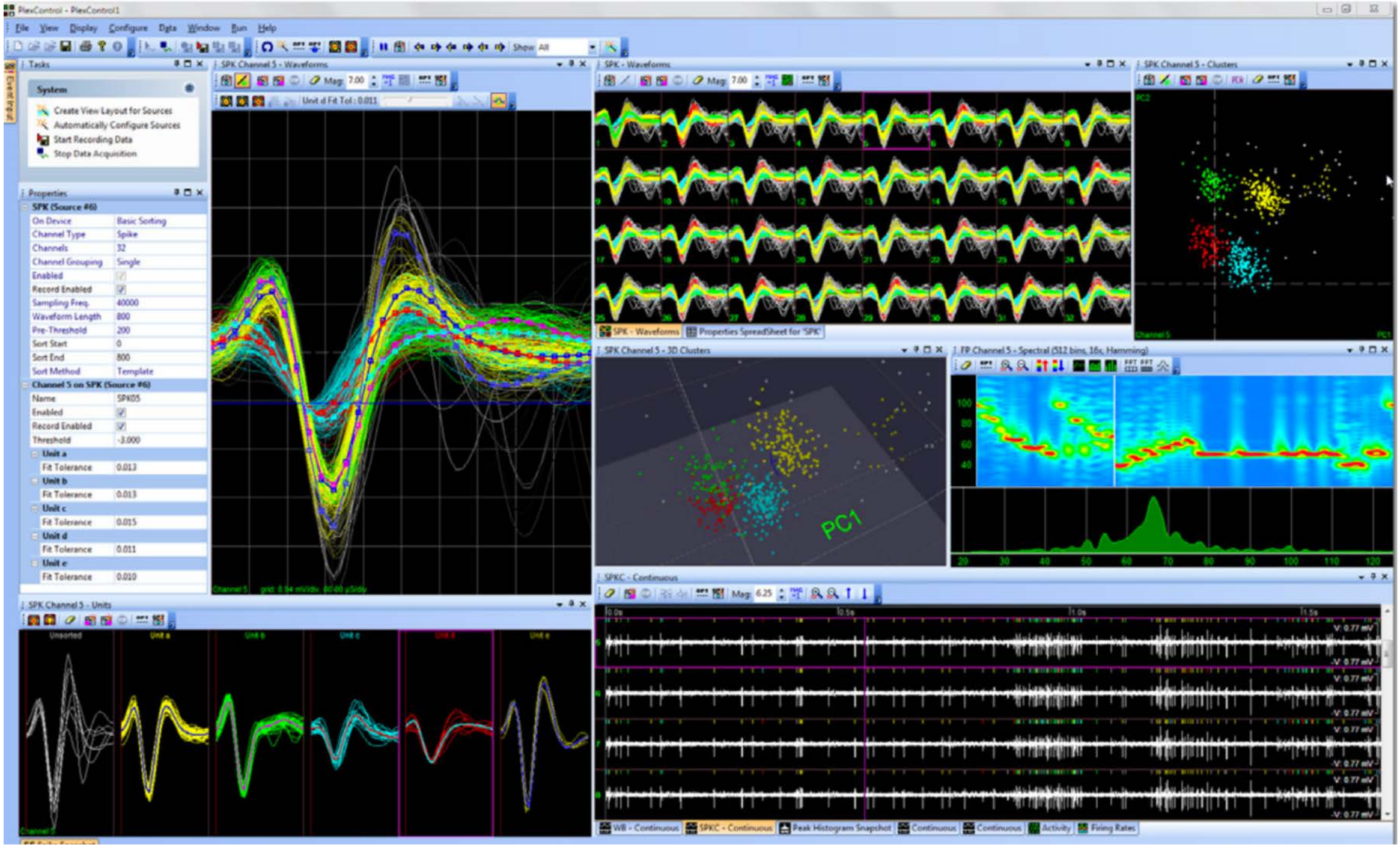




Filtered between 1 and 9000 Hz
- LFP + spikes

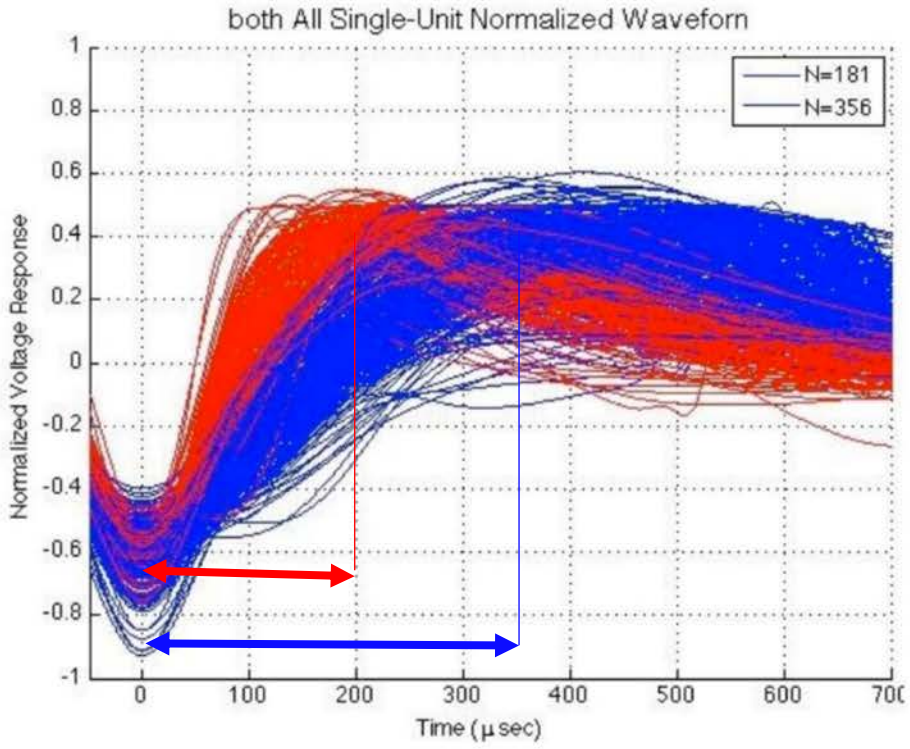
High-pass filter at 300 Hz
- Spikes

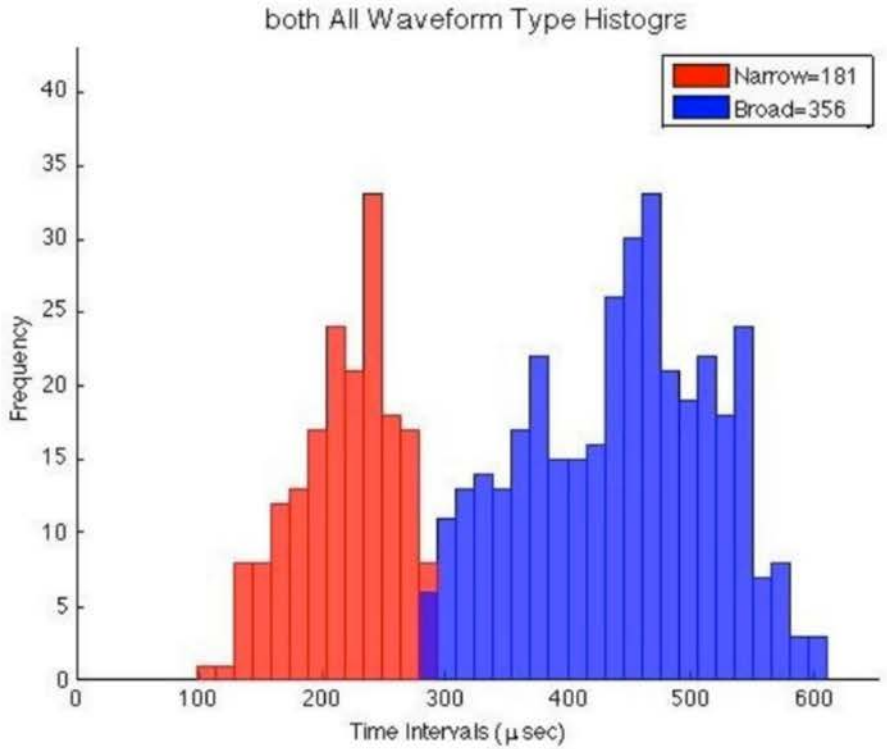



PlexControl - PlexControl1
File View Display Configure Data Window Run Help
Tasks
System
Create View Layout for Sources
Automatically Configure Sources
Start Recording Data
Stop Data Acquisition
Properties
SPK (Source #6)
On Device Basic Sorting
Channel Type Spike
Channels 32
Channel Grouping Single
Enabled
Record Enabled
Sampling Freq. 40000
Waveform Length 800
Pre-Threshold 200
Sort Start 0
Sort End 800
Sort Method Template
Channel 5 on SPK (Source #6)
Name SPK05
Enabled
Record Enabled
Threshold -3.000
Unit a
Fit Tolerance 0.013
Unit b
Fit Tolerance 0.013
Unit c
Fit Tolerance 0.015
Unit d
Fit Tolerance 0.011
Unit e
Fit Tolerance 0.010
SPK Channel 5 - Waveforms
SPK - Waveforms
SPK Channel 5 - Clusters
SPK Channel 5 - 3D Clusters
PC1
FP Channel 5 - Spectral (512 bins, 16s, Hamming)
SPK Channel 5 - Units
Unsorted
Unit a
Unit b
Unit c
Unit d
Unit e
SPKC - Continuous
WB - Continuous
SPKC - Continuous
Peak Histogram Snapshot
Activity
Firing Rates

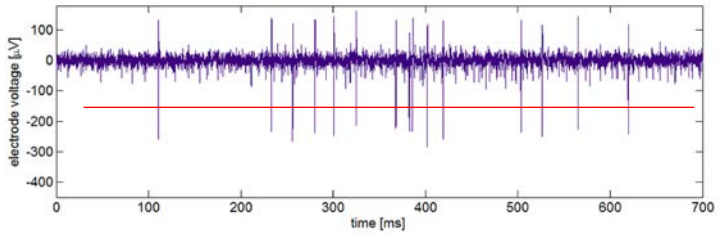
Spike waveform analyses

- Excitatory neurons: broad-spiking
- Inhibitory interneurons: narrow-spiking

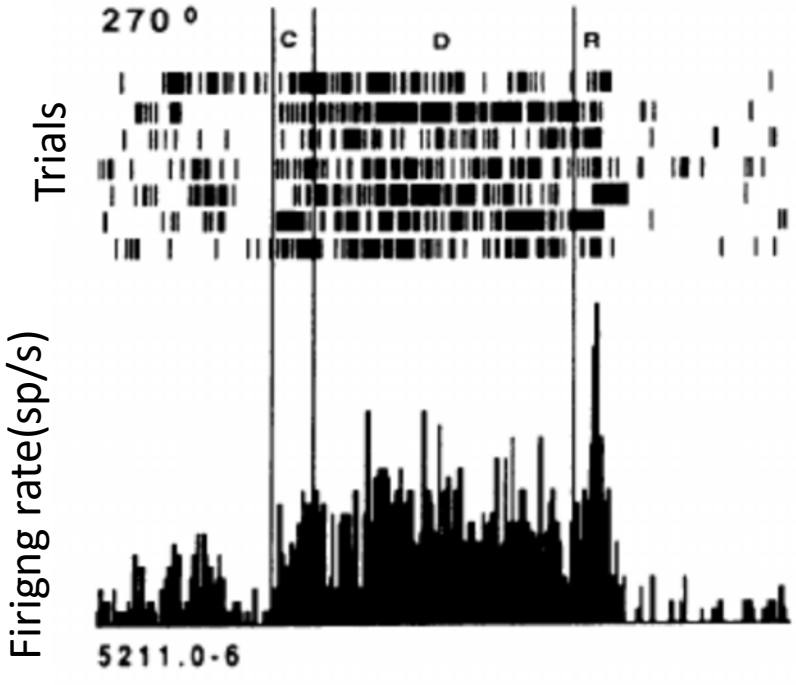




Plotting spiking data



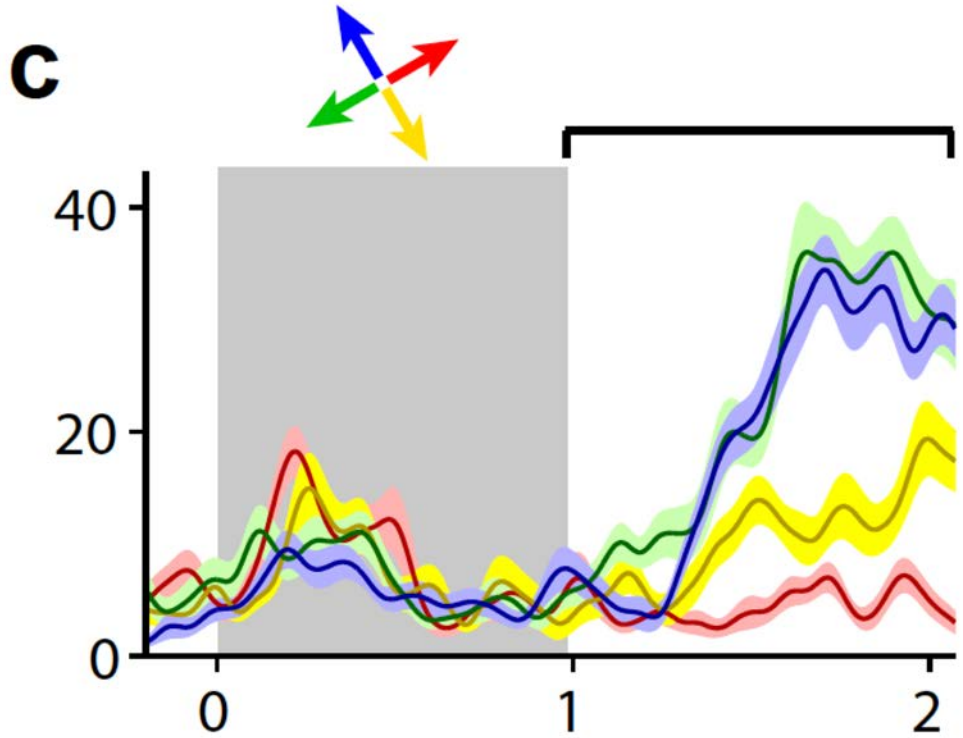
RASTER PLOT



Time (s)

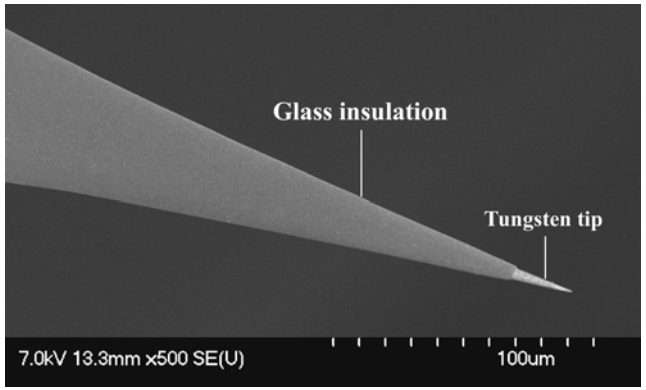
PERISTIMULUS TIME HISTOGRAM (PSTH)

SPIKE DENSITY FUNCTION

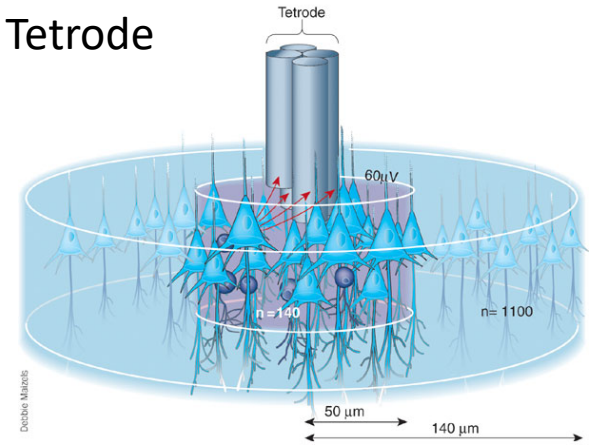


Types of microelectrodes

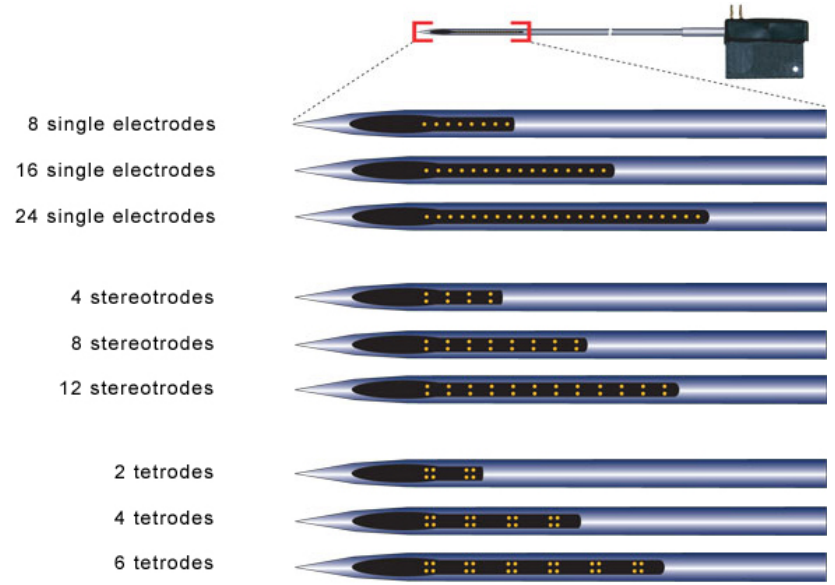
Single microelectrode



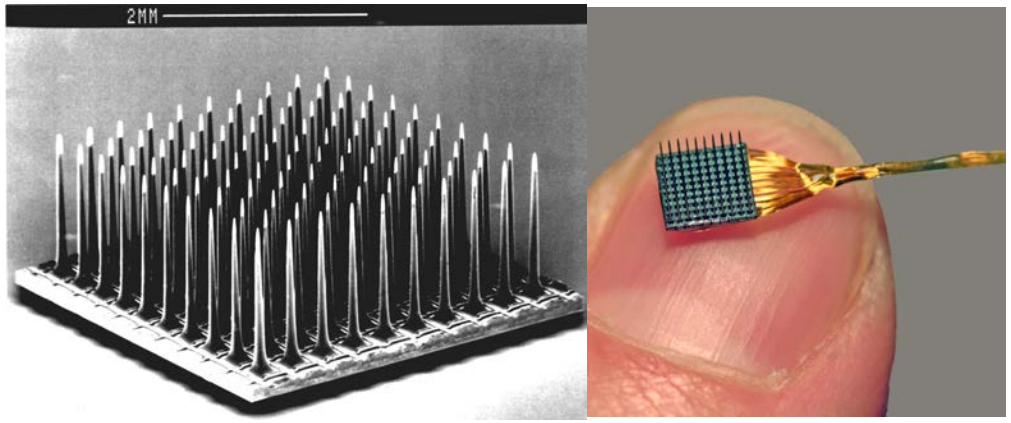
Tetrode



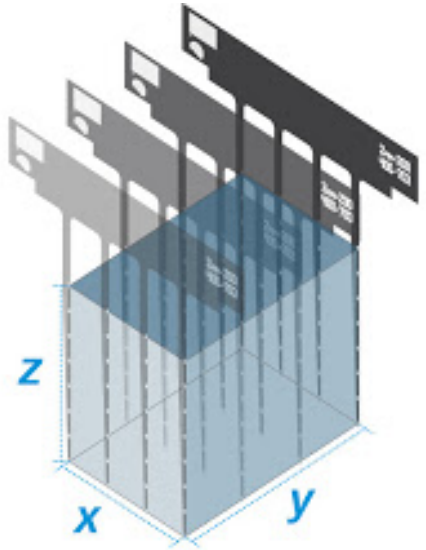
Linear electrode array

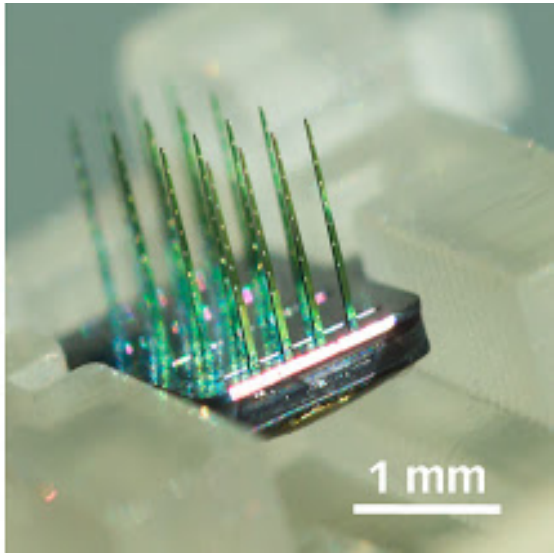


2D matrix electrode array

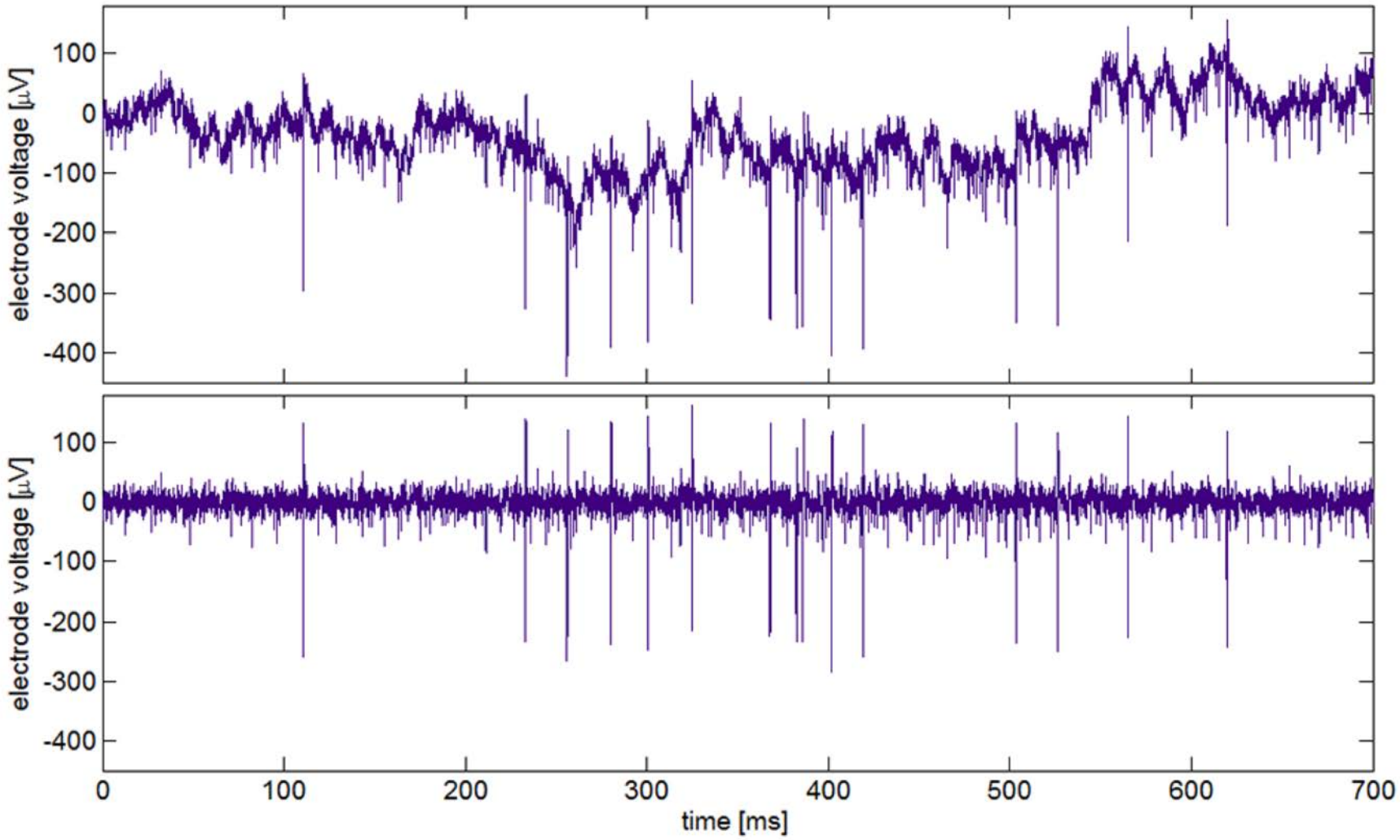


3D matrix electrode array





Local Field Potentials (LFP)

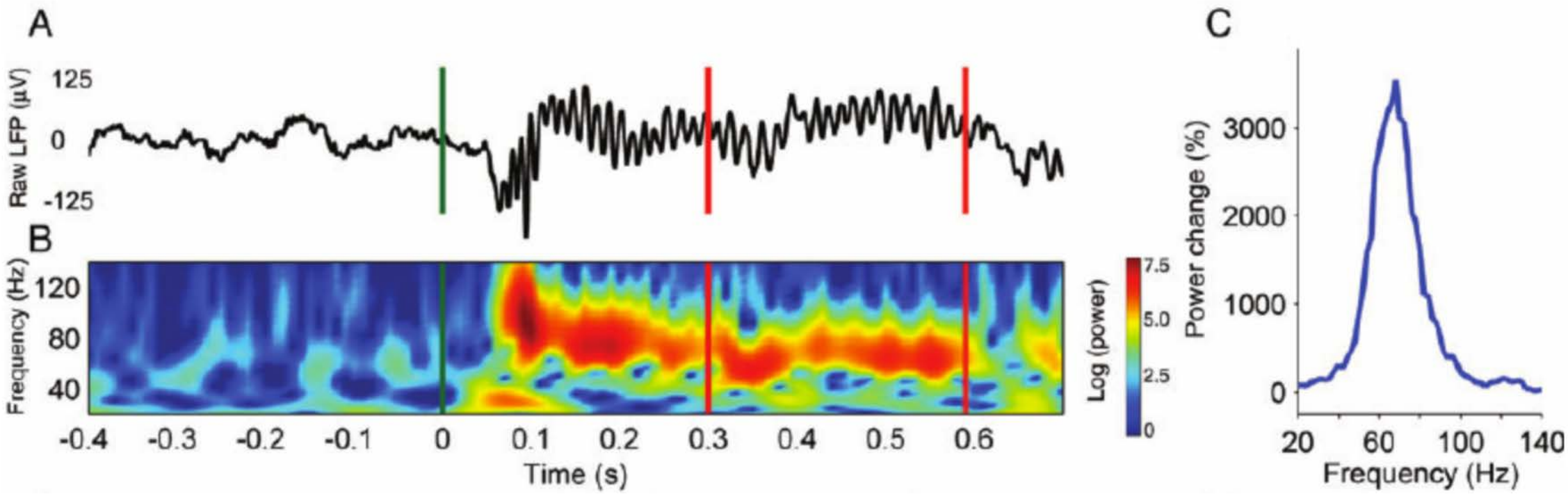


Filtered between 1 and 9000 Hz
- LFP + spikes

High-pass filter at 300 Hz
- Spikes

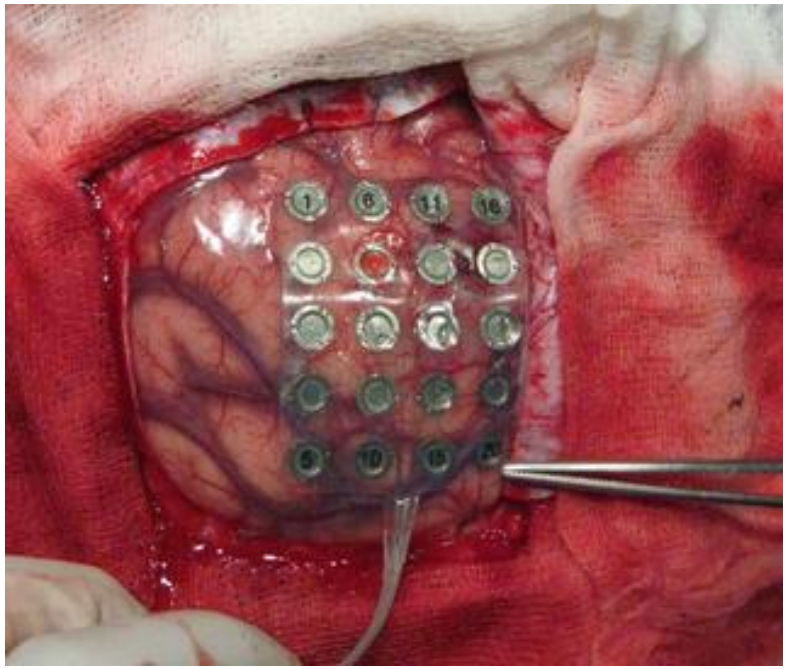
Local Field Potentials (LFP)

- Spectral analysis (Fourier transform)



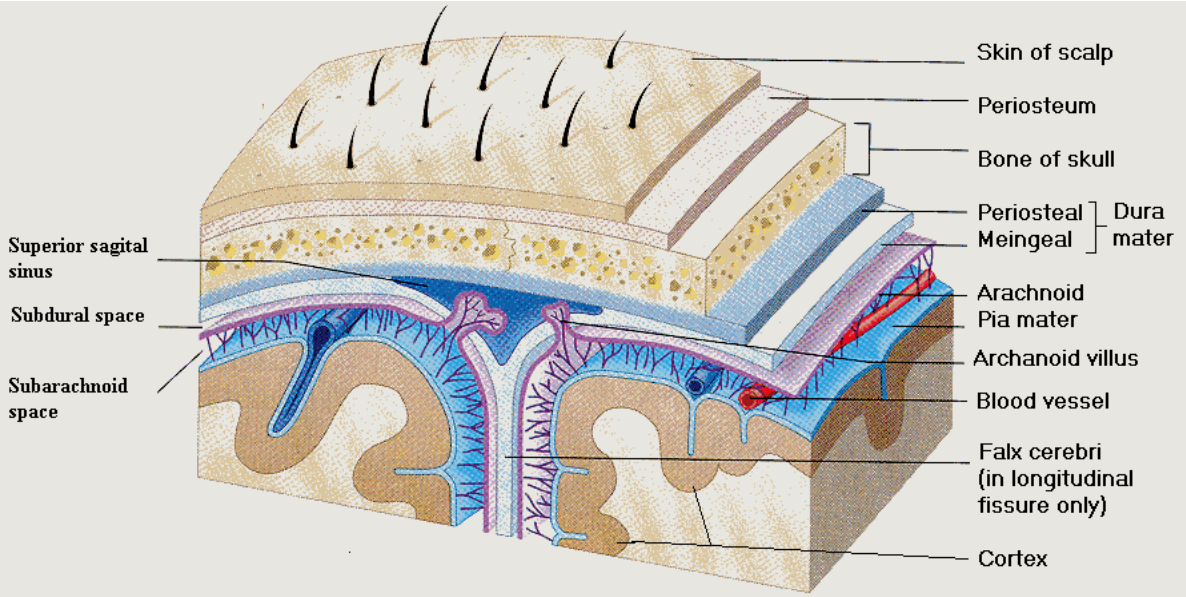
Electrocorticogram (ECoG)

- Electrophysiological recordings from cortical surface
- Advantage: Human (patient) electrophysiological data
- Records field potentials (not so local anymore…)



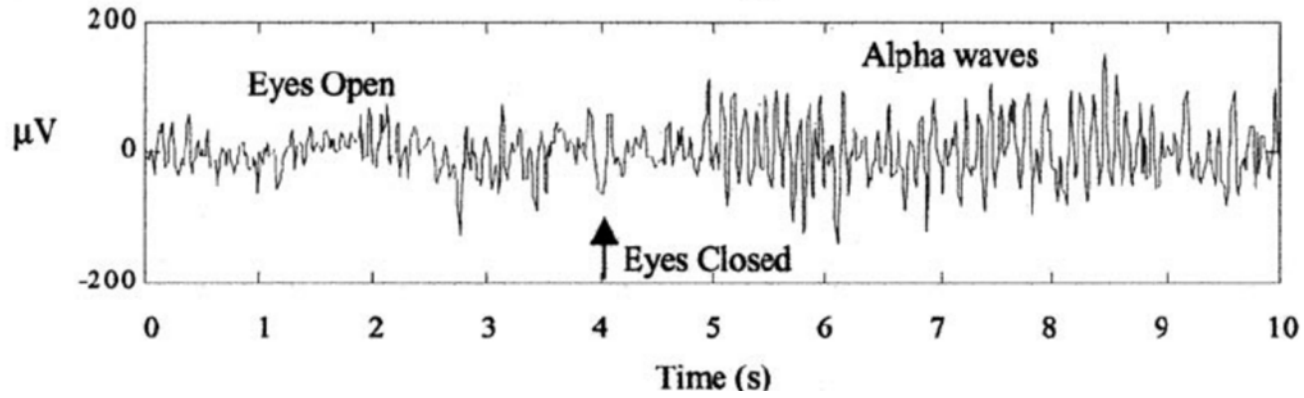
Electroencephalogram (EEG)

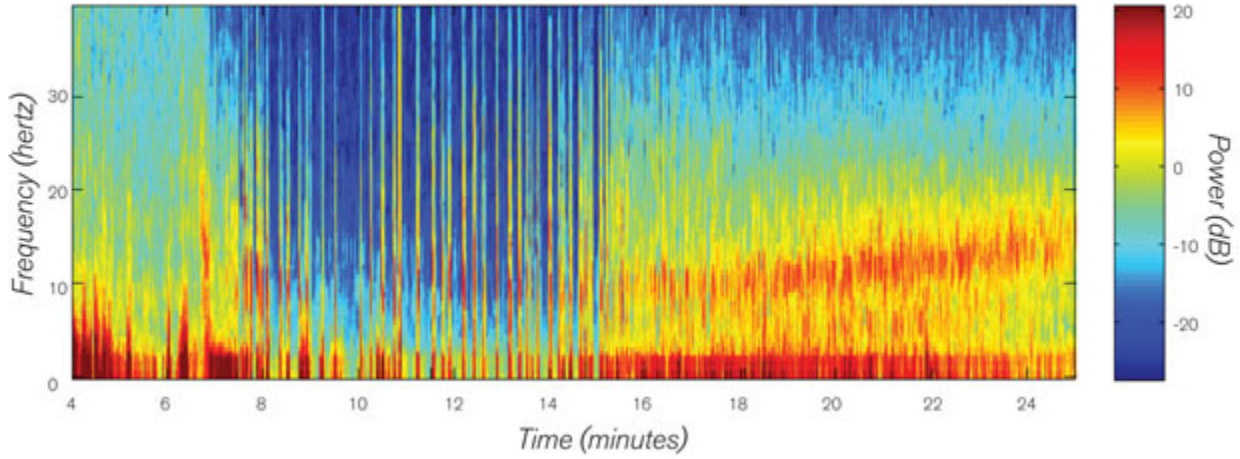
- Electrophysiological recordings from scalp surface
- High temporal resolution but low spatial resolution

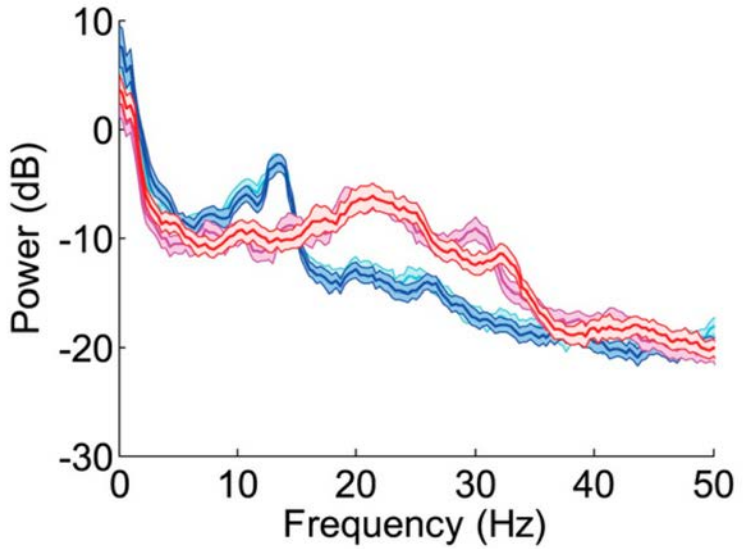


Electroencephalogram (EEG)

- Records cortical oscillatory activity (e.g. alpha waves)

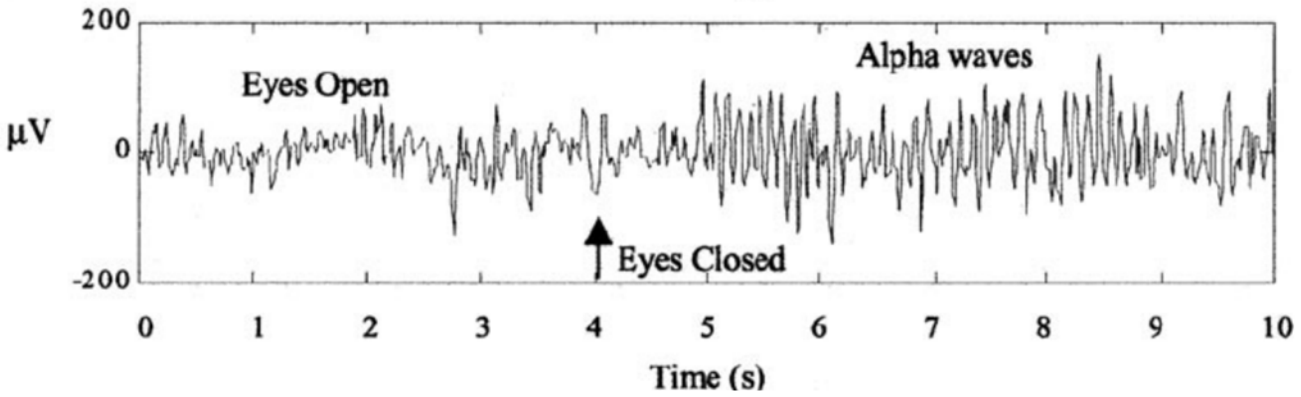


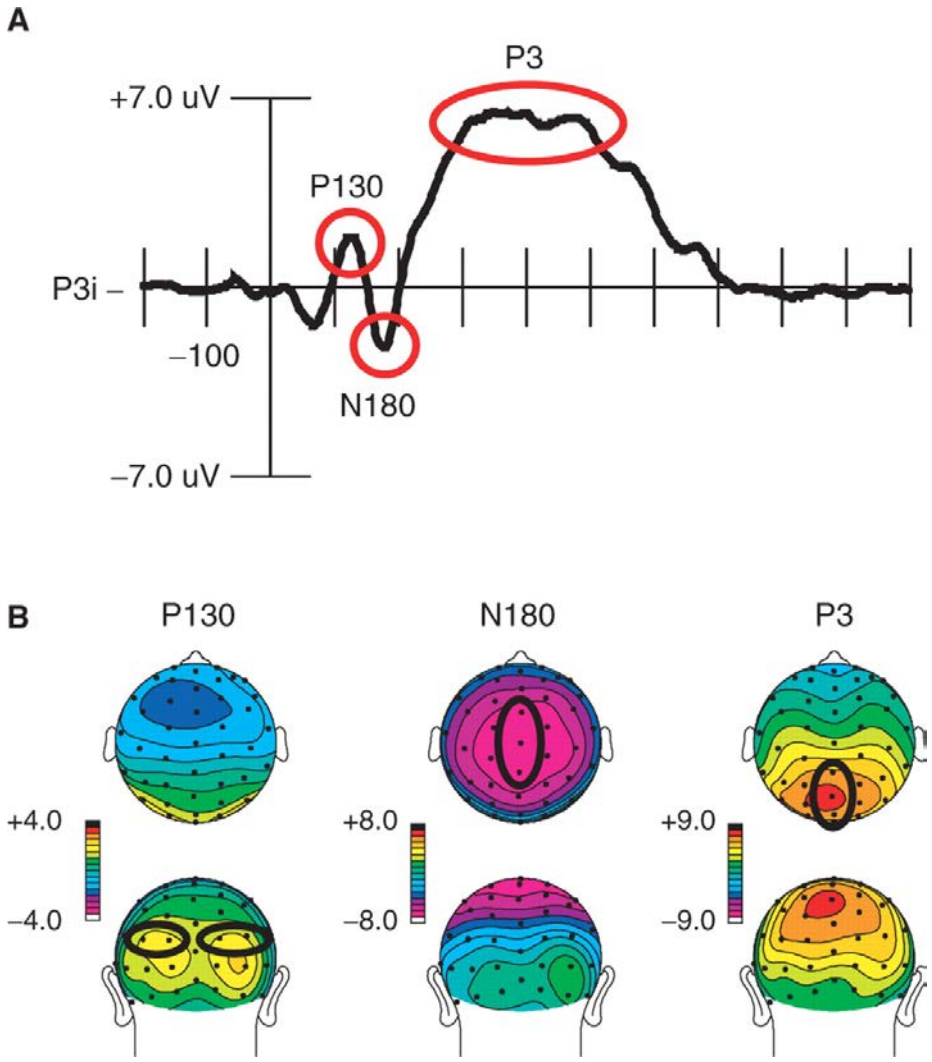




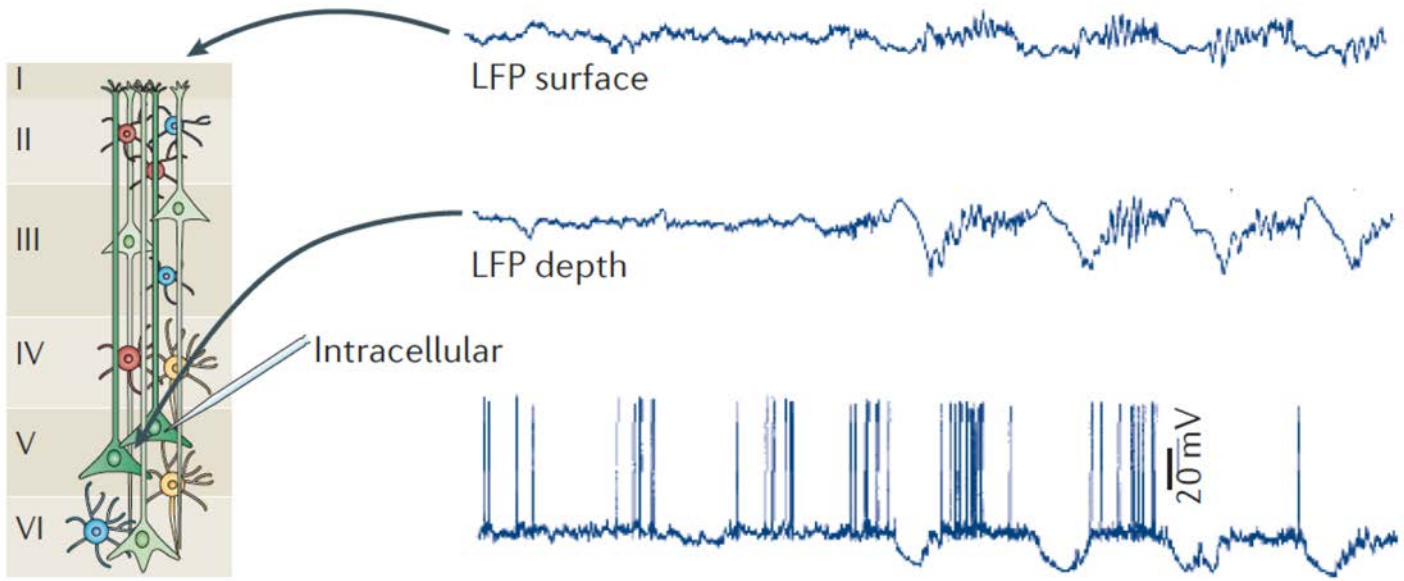
Electroencephalogram (EEG)

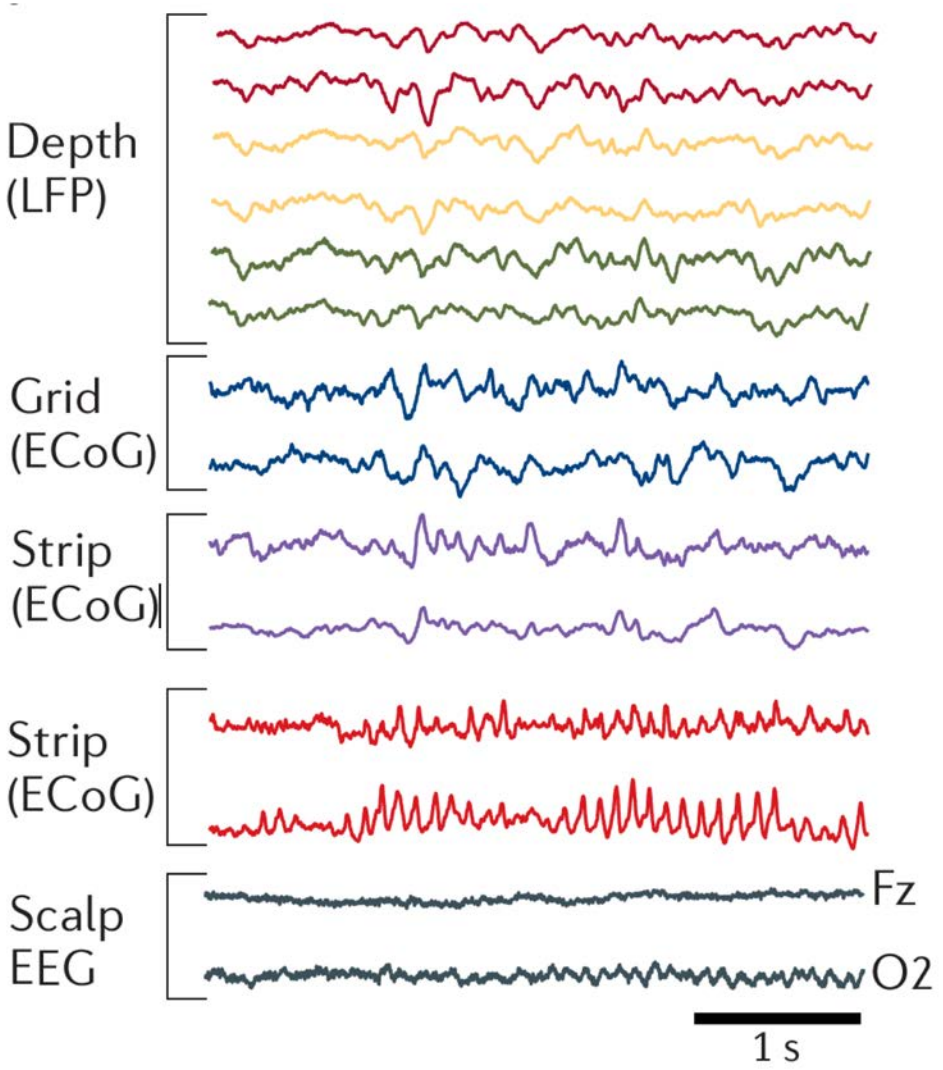
- Event-related potentials (ERP)
  - Measures positive and negative potentials (e.g. N180, P3)
    - Neural function signatures
  - Requires multiple-trial averaging
  - Potential amplitudes compared between conditions





Comparing electrophysiological methods





Buszaki et al., 2012

Neural signals summary

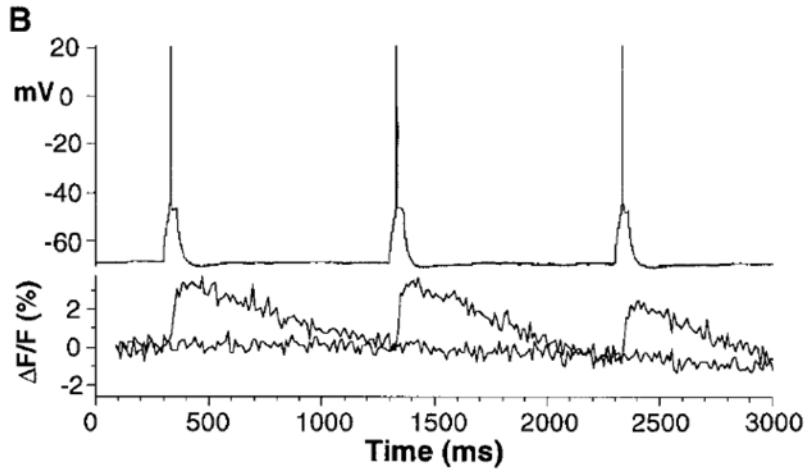
- Electrical signals:
  - Action potentials
  - Local field potentials

- Chemical signals:
  - Ca++ influx
  - Neurotransmitter release

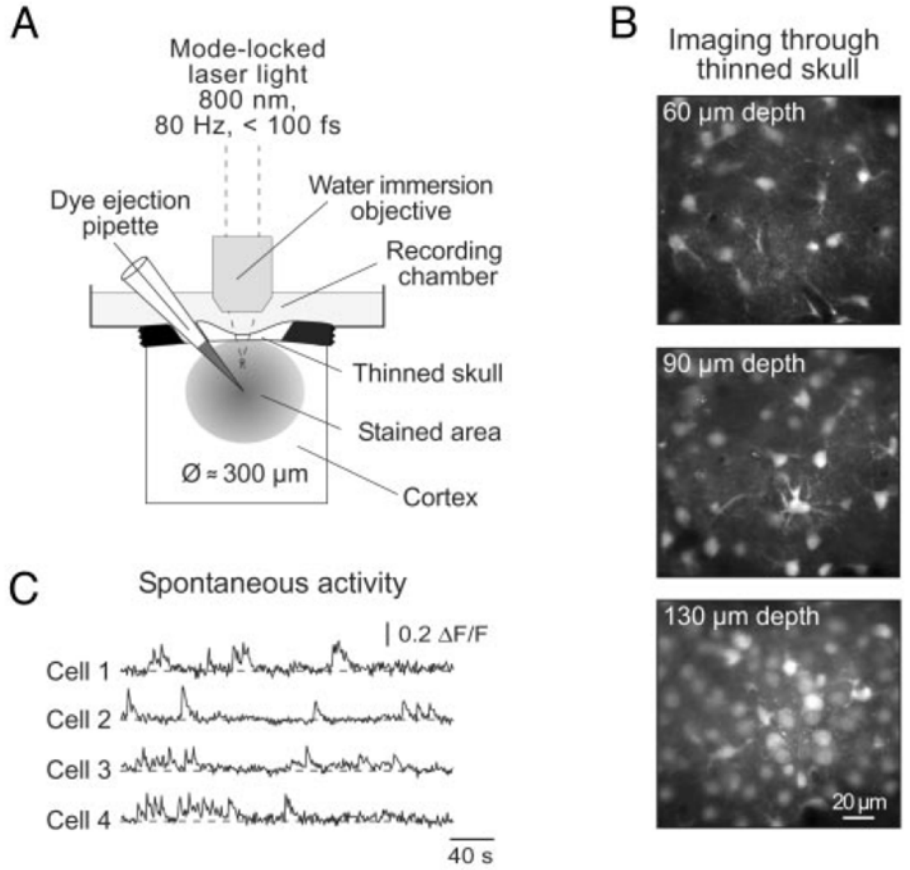
Calcium imaging

Calcium imaging:

- Calcium-indicator dyes: Fluorescence dependent on Ca++ concentration
- Becomes optical signal



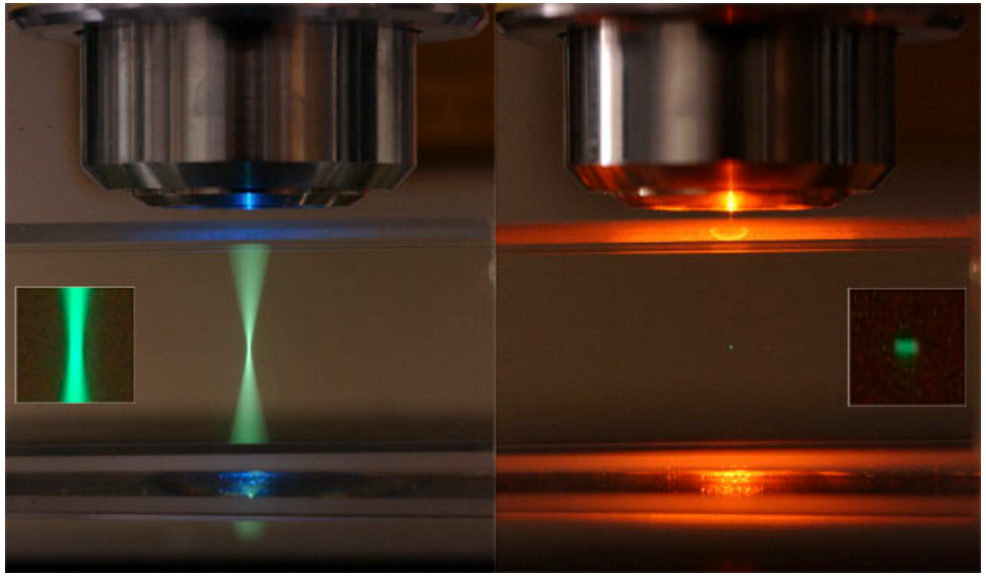
Smetters et al., 1999

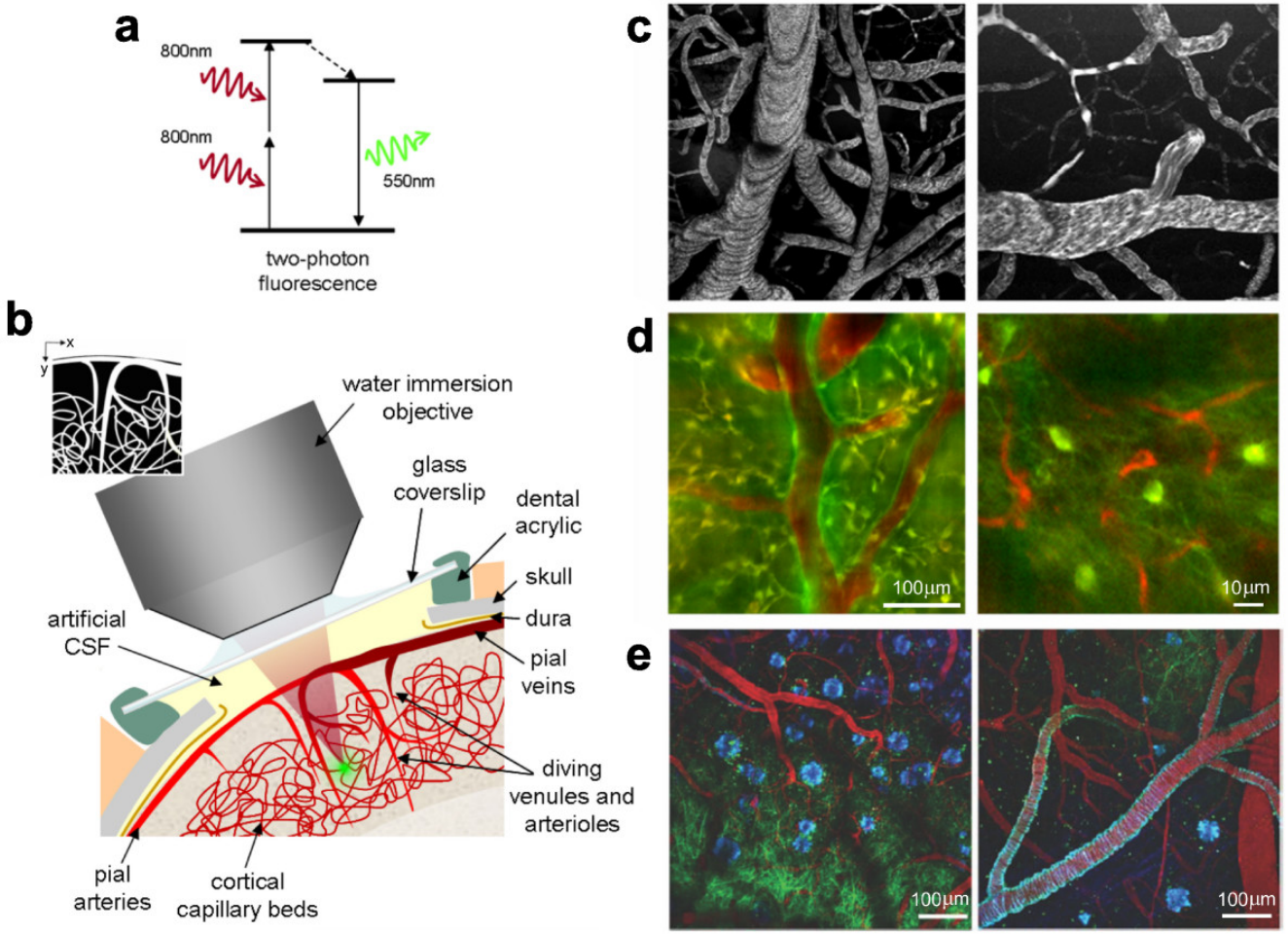


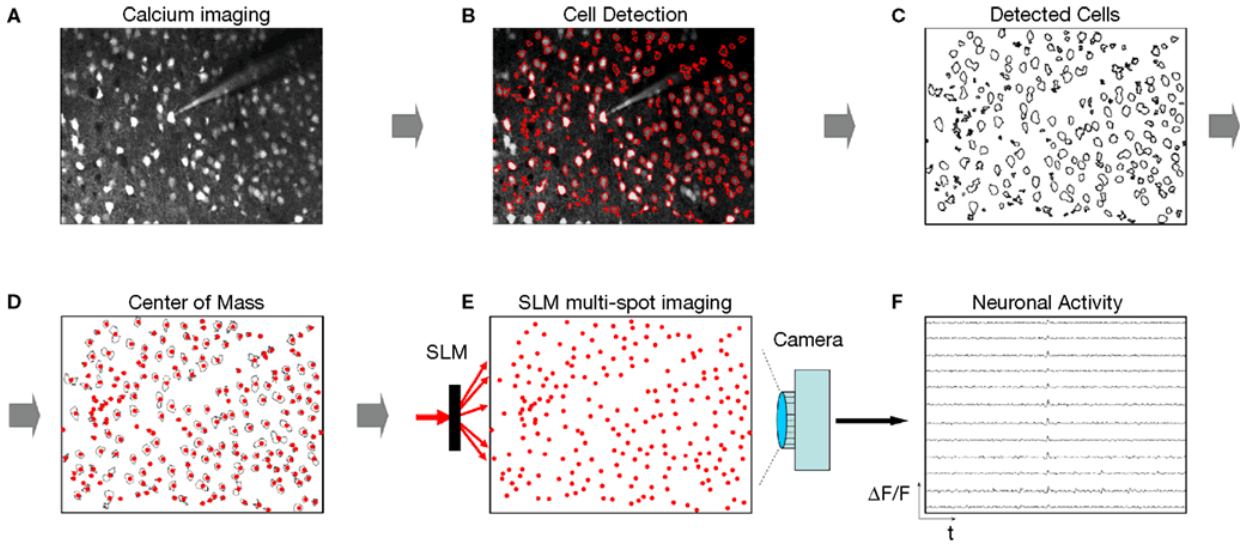
Stosiek et al., 2003

Two-photon calcium imaging

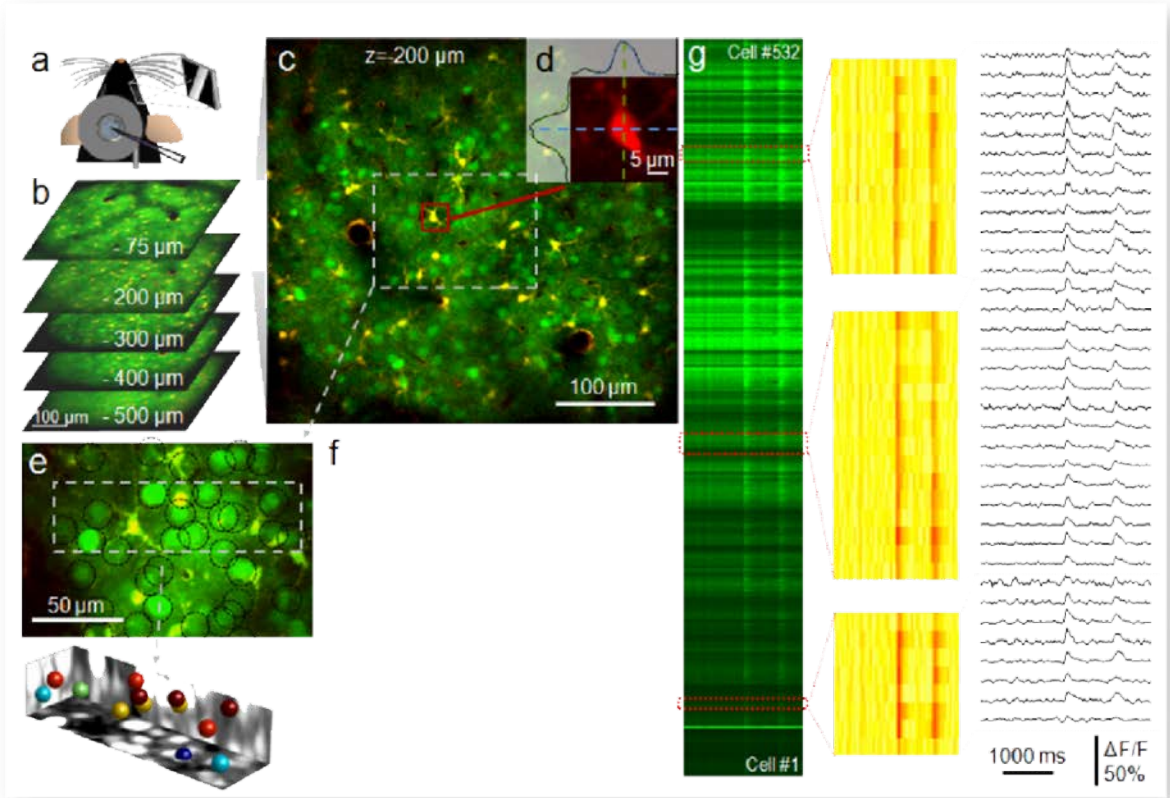
Two-photon microscopy







Nikolenko et al., 2008



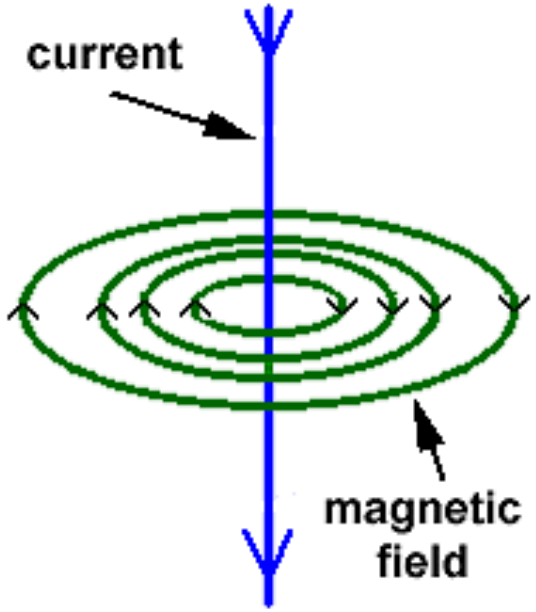
Katona et al., 2012

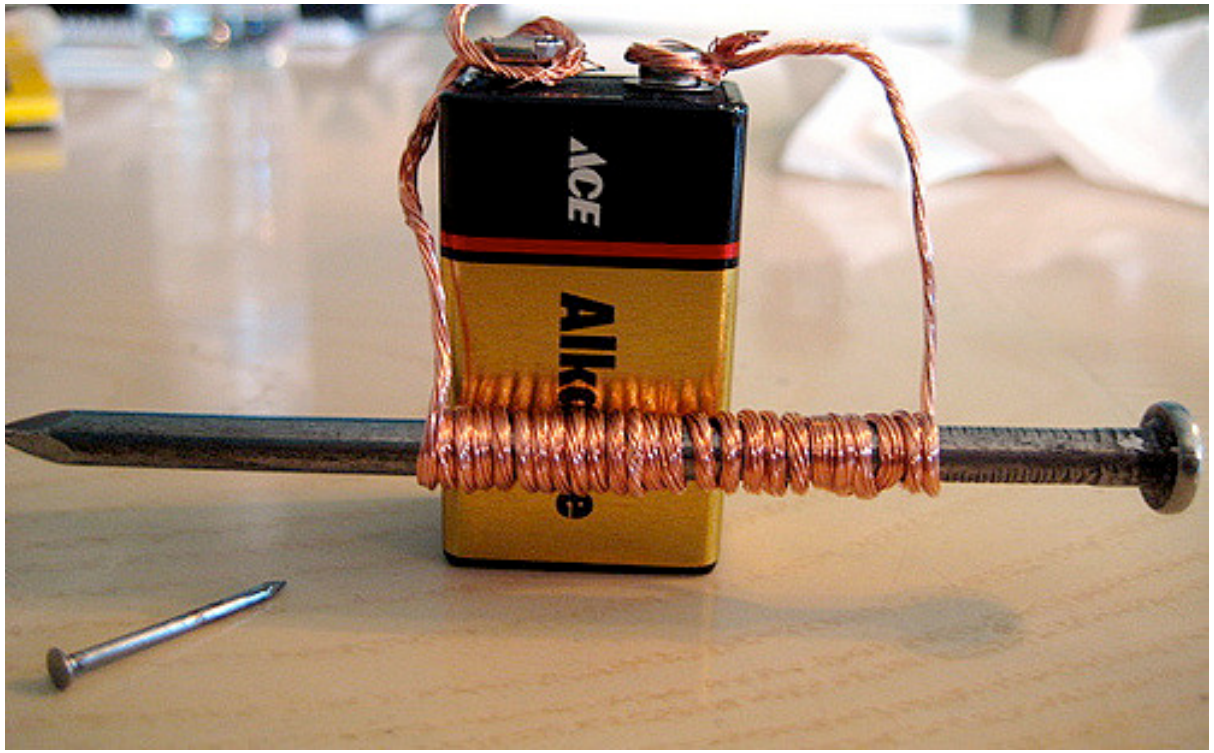
Indirect signals linked to neuronal activity

- Neuromagnetic signals
- Neurovascular coupling

Indirect signals linked to neuronal activity

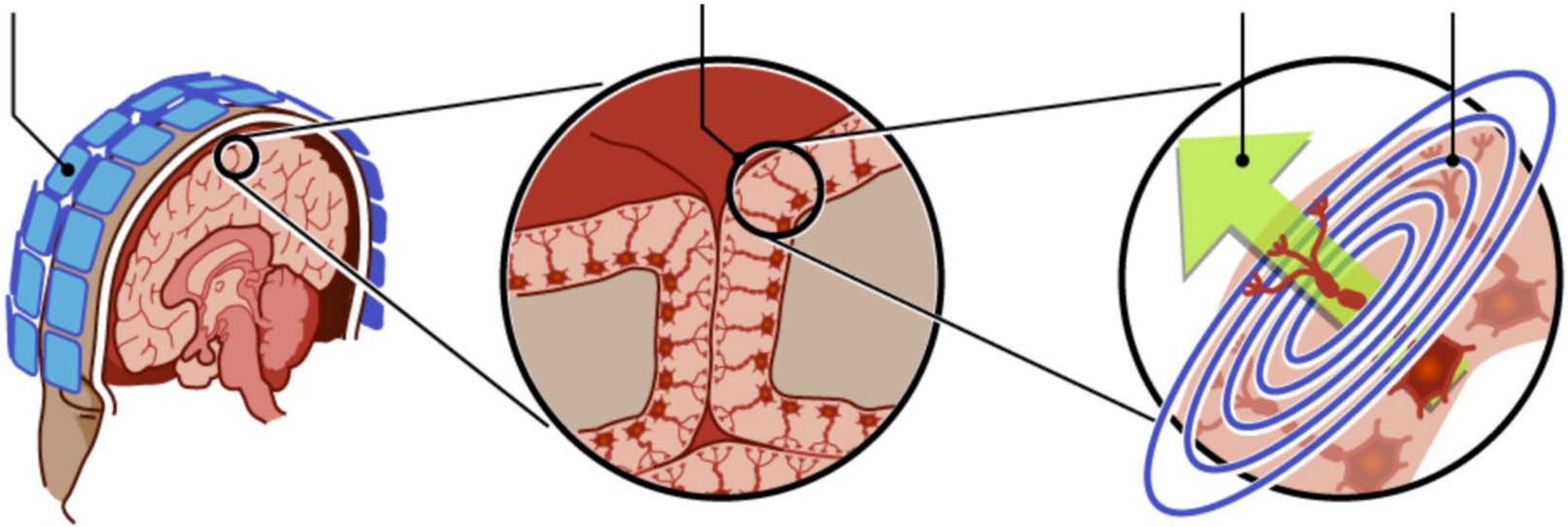
Neuromagnetic signals





Indirect signals linked to neuronal activity

Neuromagnetic signals

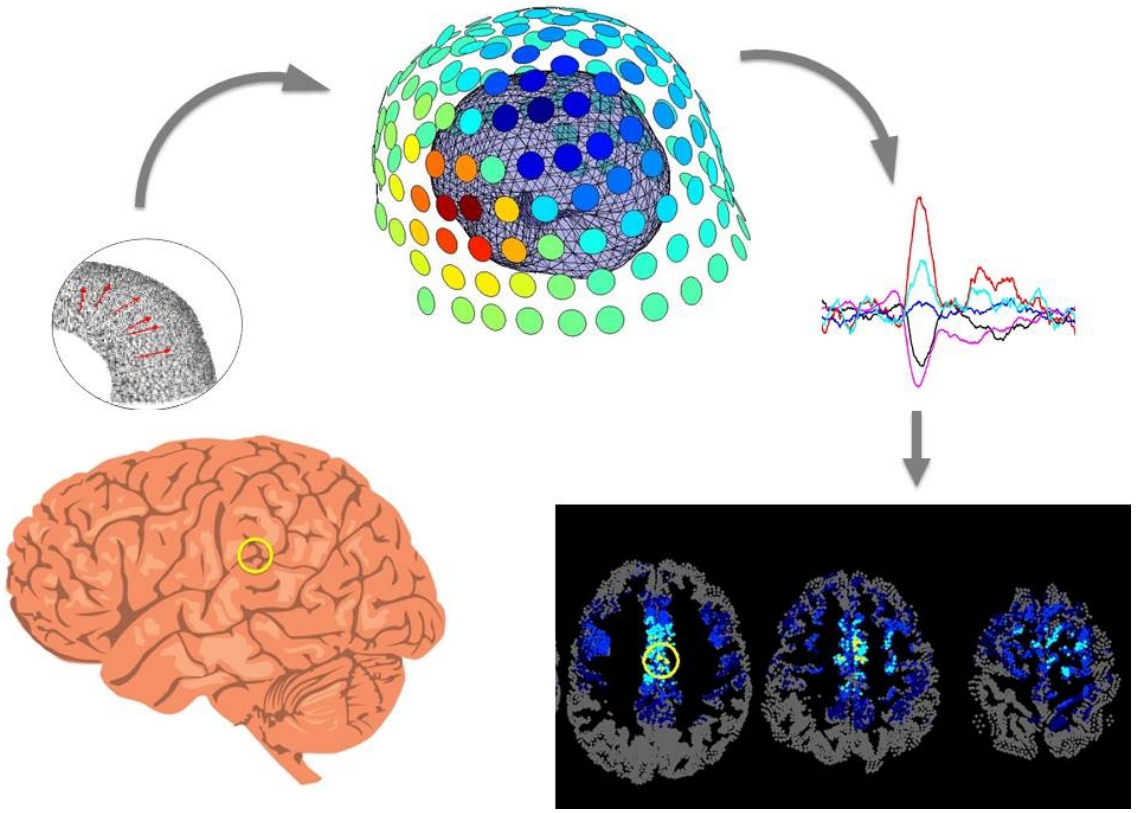


Magnetoencephalography (MEG)

Superconducting sensors

Magnetoencephalography (MEG)

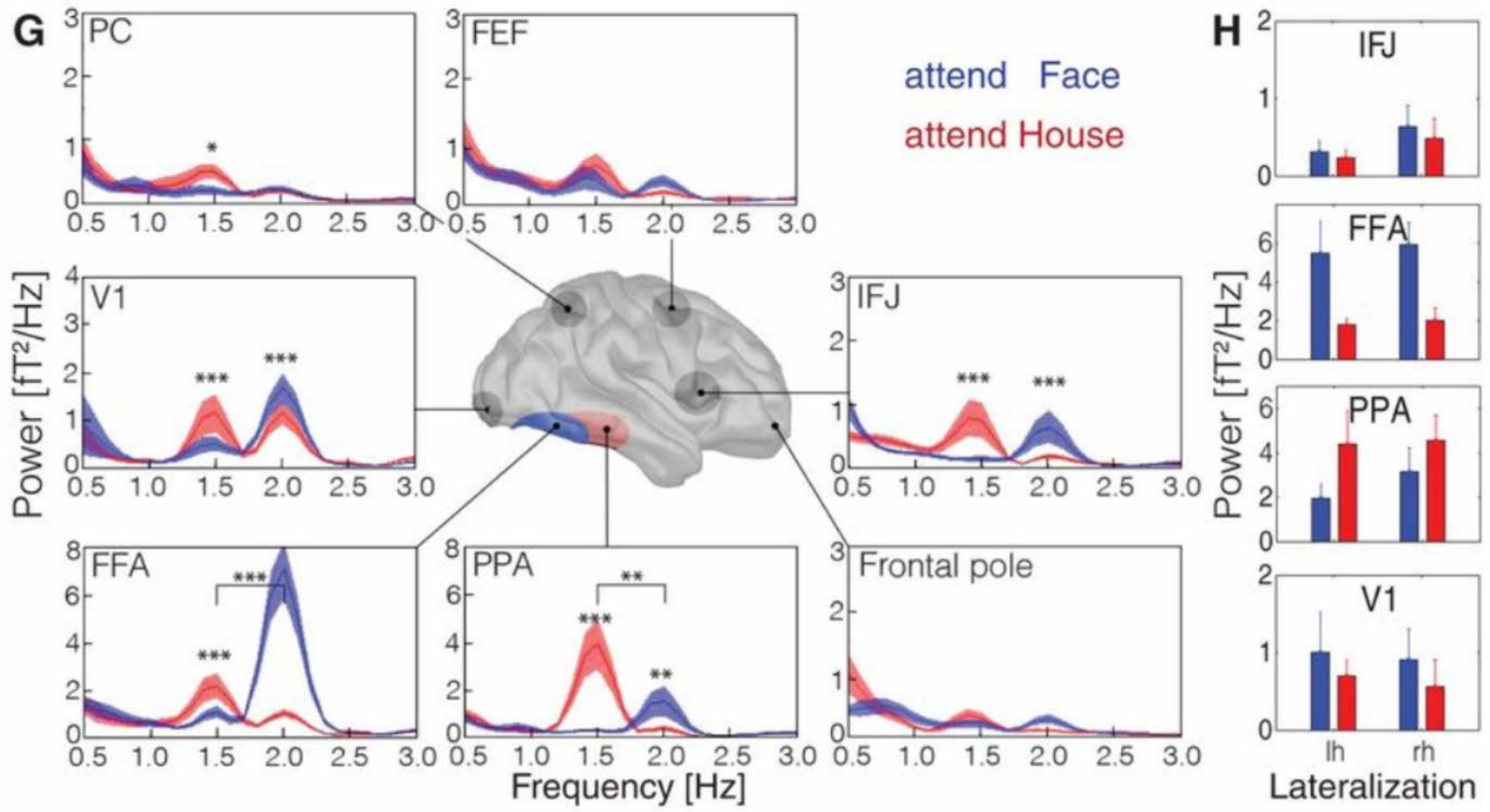
- Inverse problem of signal localization



Superconducting sensors

Magnetoencephalography (MEG)

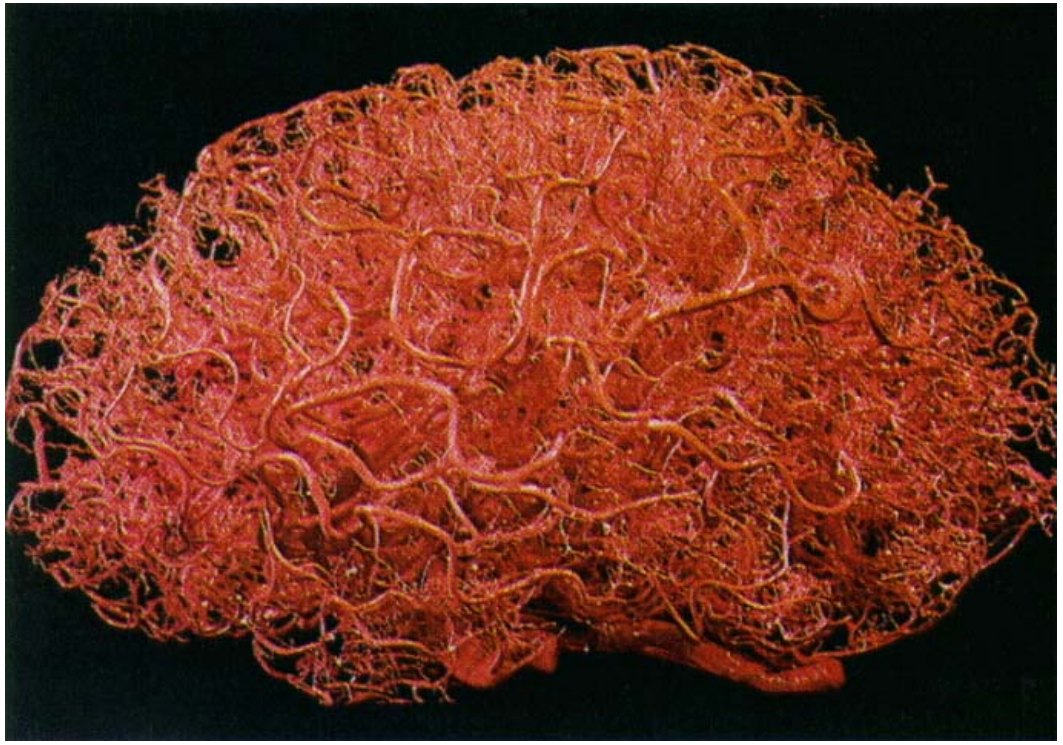
- MEG data



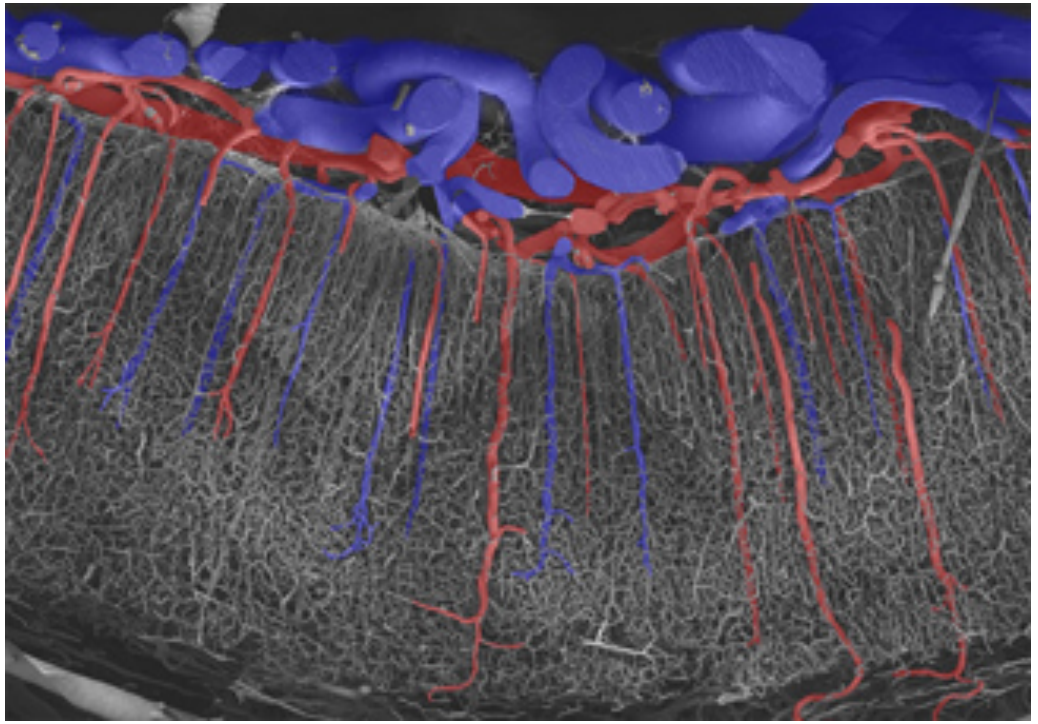
Baldauf and Desimone, 2014

Indirect signals of neuronal activity: Neurovascular coupling

Whole brain vasculature

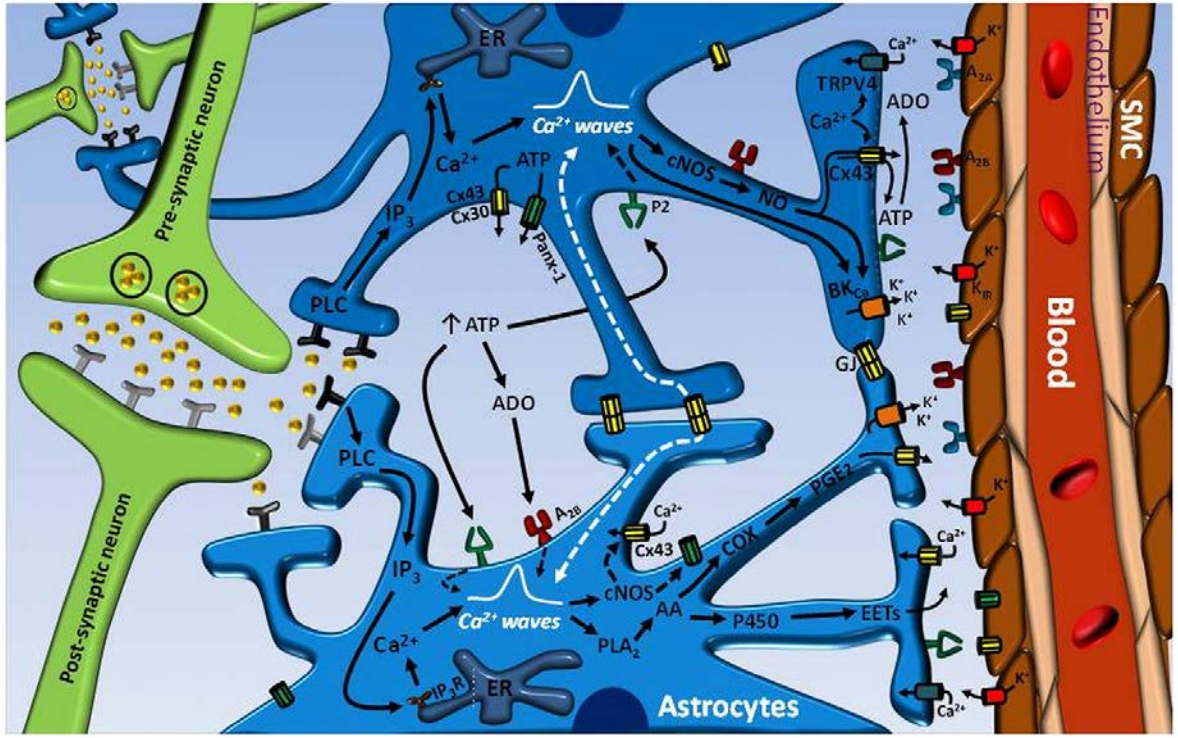


Macaque V1 microvasculature

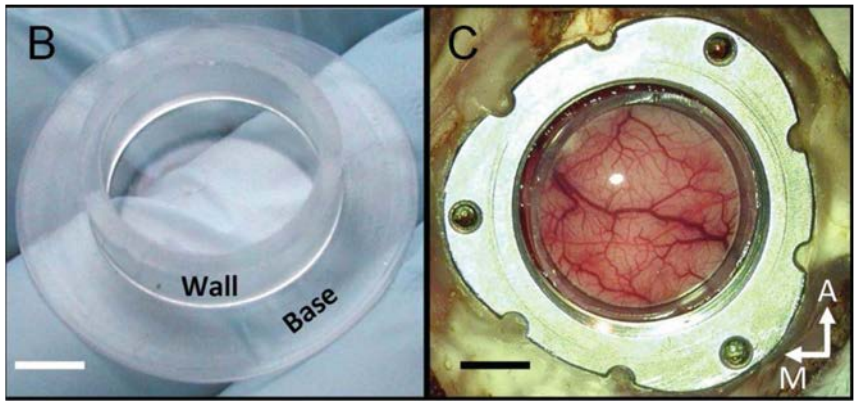


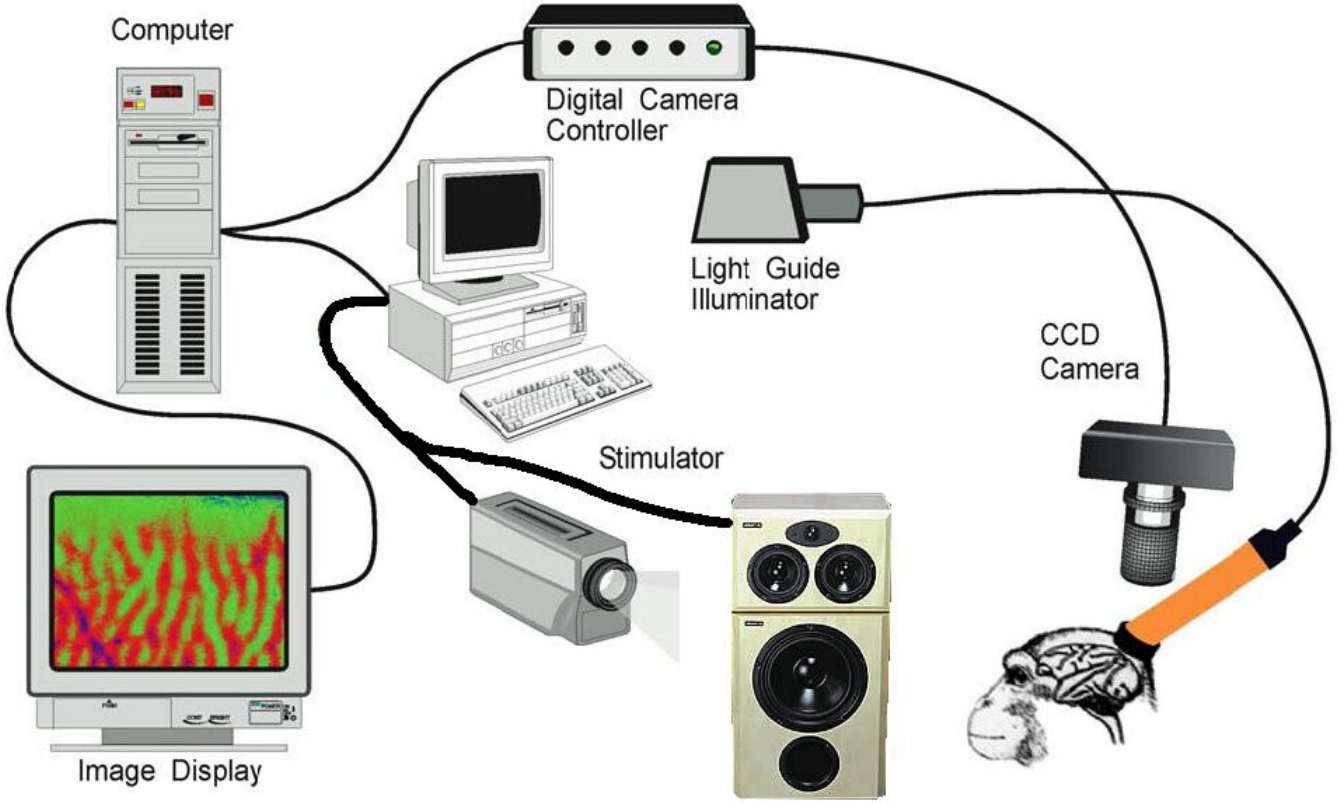
Neurovascular coupling:
Blood Oxygenation-Level Dependent (BOLD) signal

- Synaptic transmission activates a signaling cascade in neighboring astrocytes, which in turn signal vascular smooth muscle cells to cause vasodilation, resulting in a local increase in cerebral blood flow.
- Increased CBF causes an increase in blood oxygenation that overcompensates for the decrease due to neuronal activity.



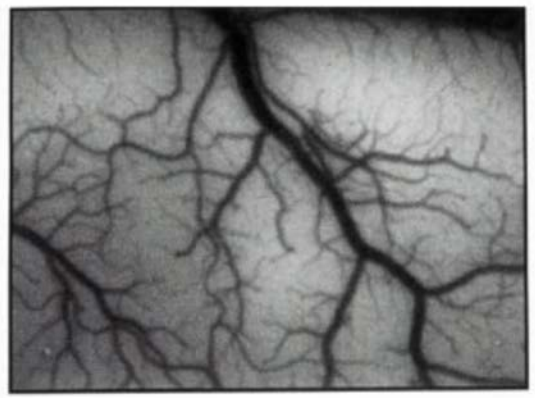
Optical imaging (intrinsic signals)

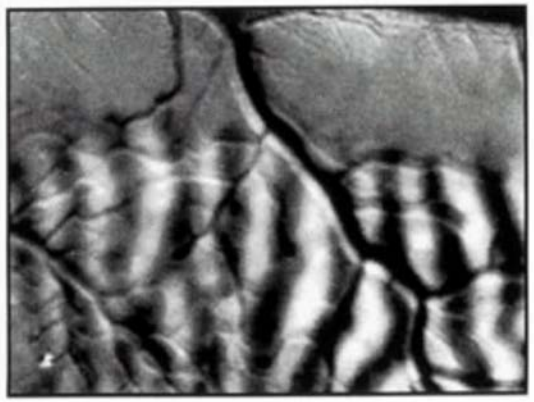


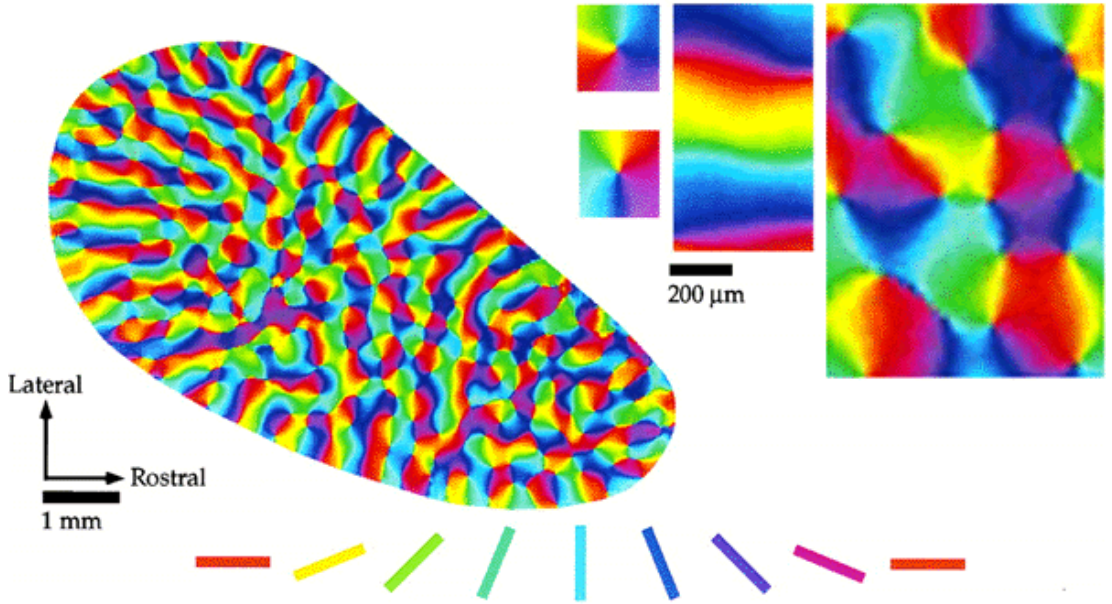


Optical imaging (intrinsic signals)

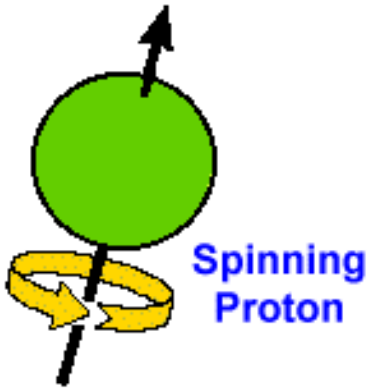
- Functional maps across cortical surface
- Ocular dominance columns
- Orientation columns

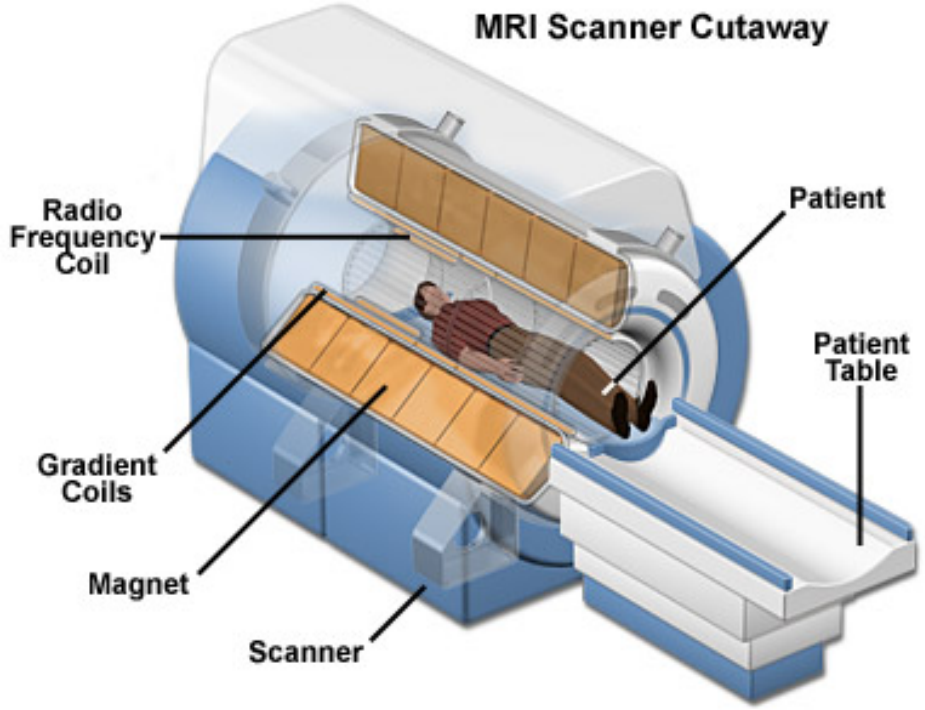


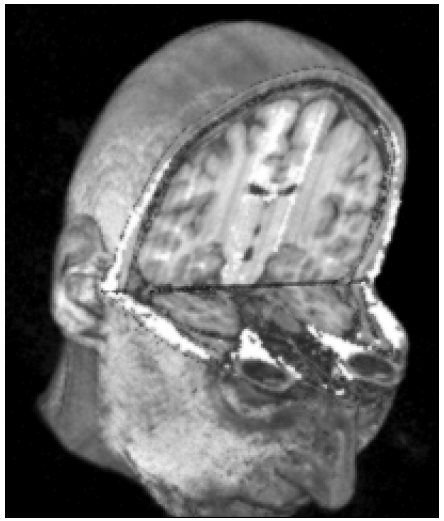


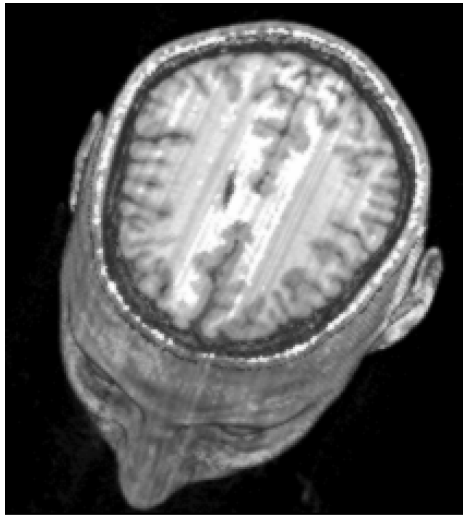


Functional Magnetic Resonance Imaging (fMRI)

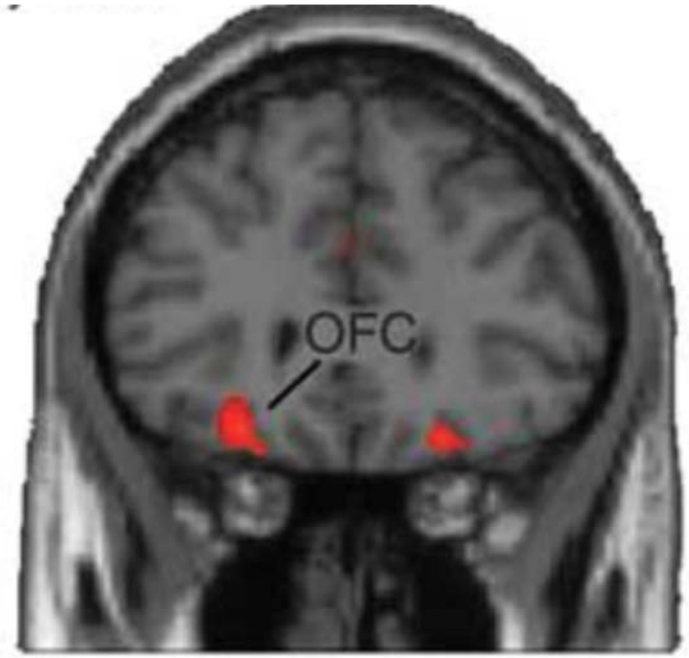




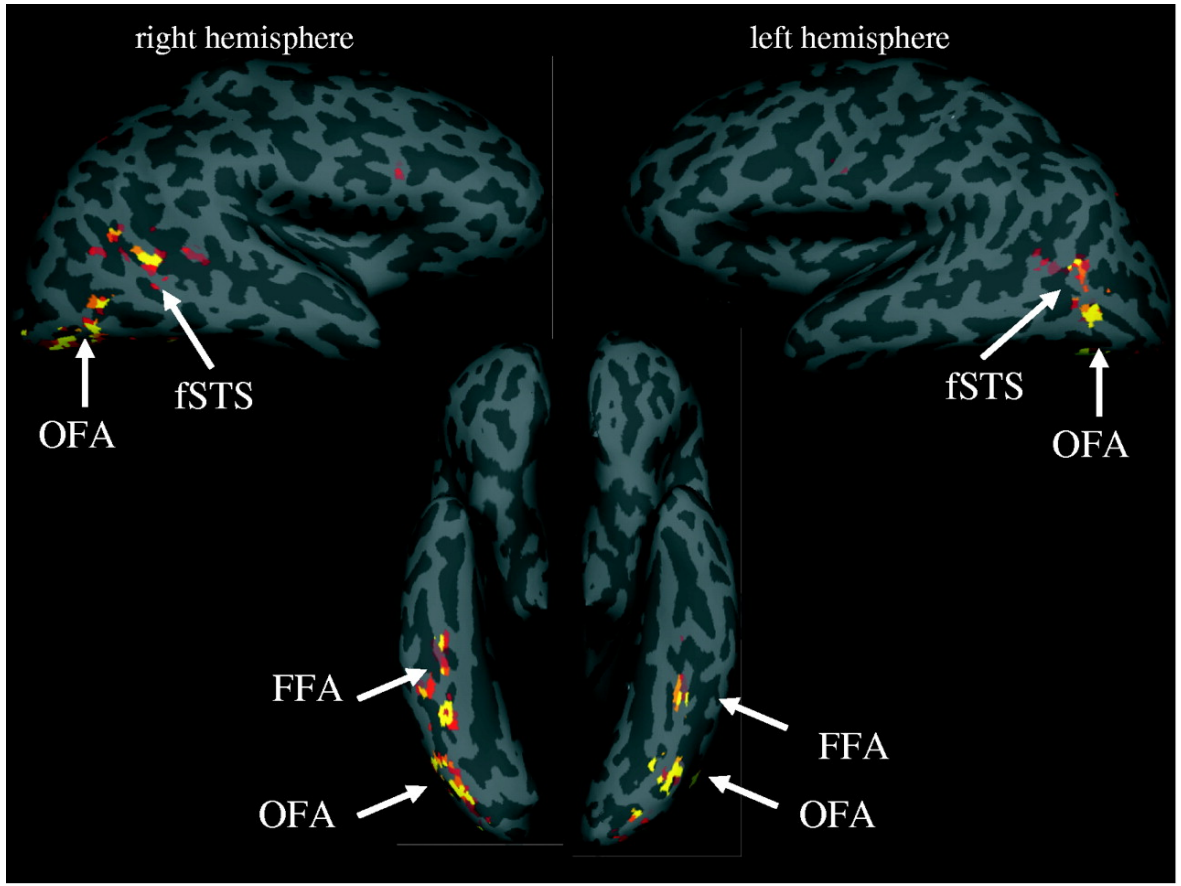




Functional Magnetic Resonance Imaging (fMRI) Univariate method



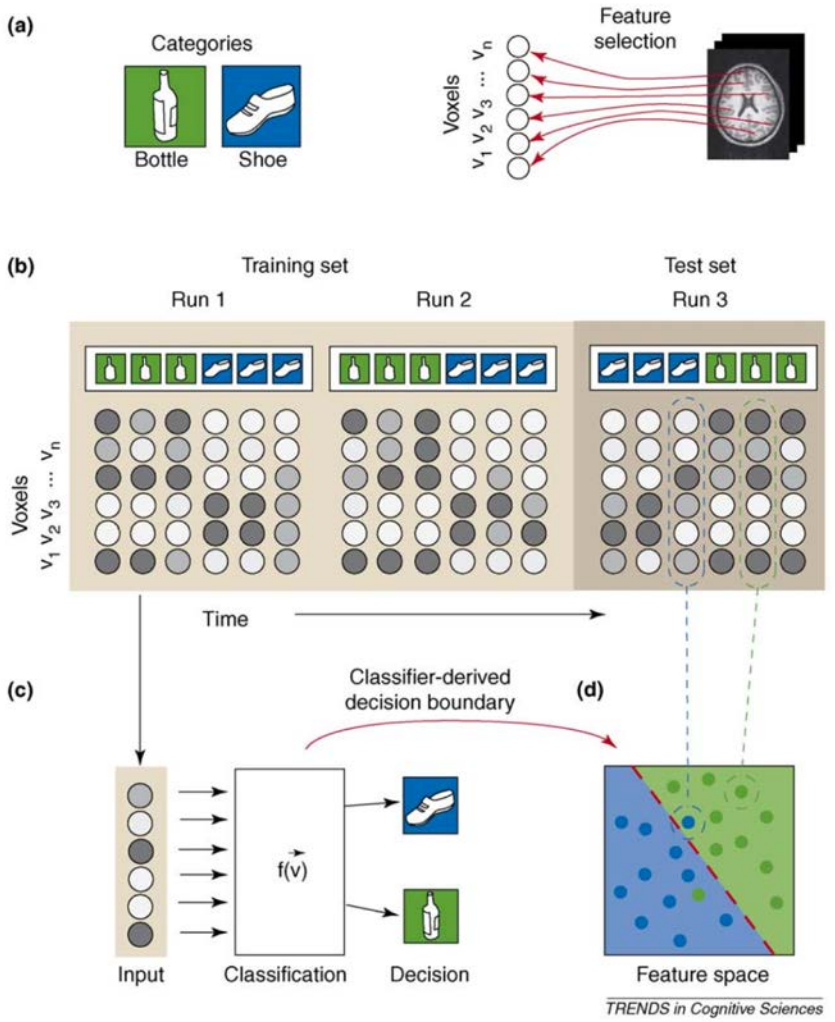
Face-selective activation (faces > objects, $p<0.0001$)



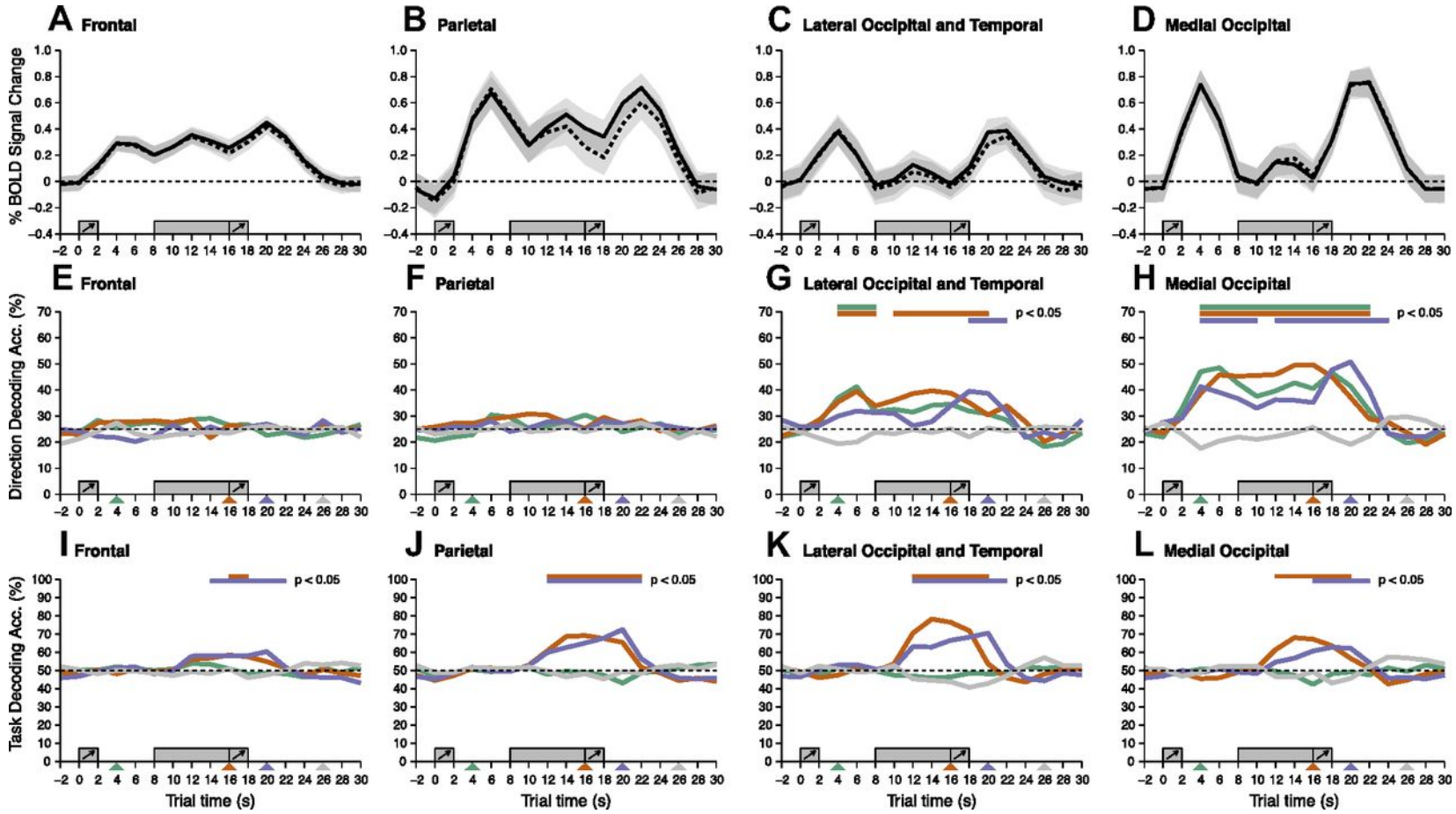
Kanwisher et al., 1997

Functional Magnetic Resonance Imaging (fMRI) Multivariate method

Multivoxel Pattern Classification Analysis (MVPA)



ROI BOLD and decoding time courses.



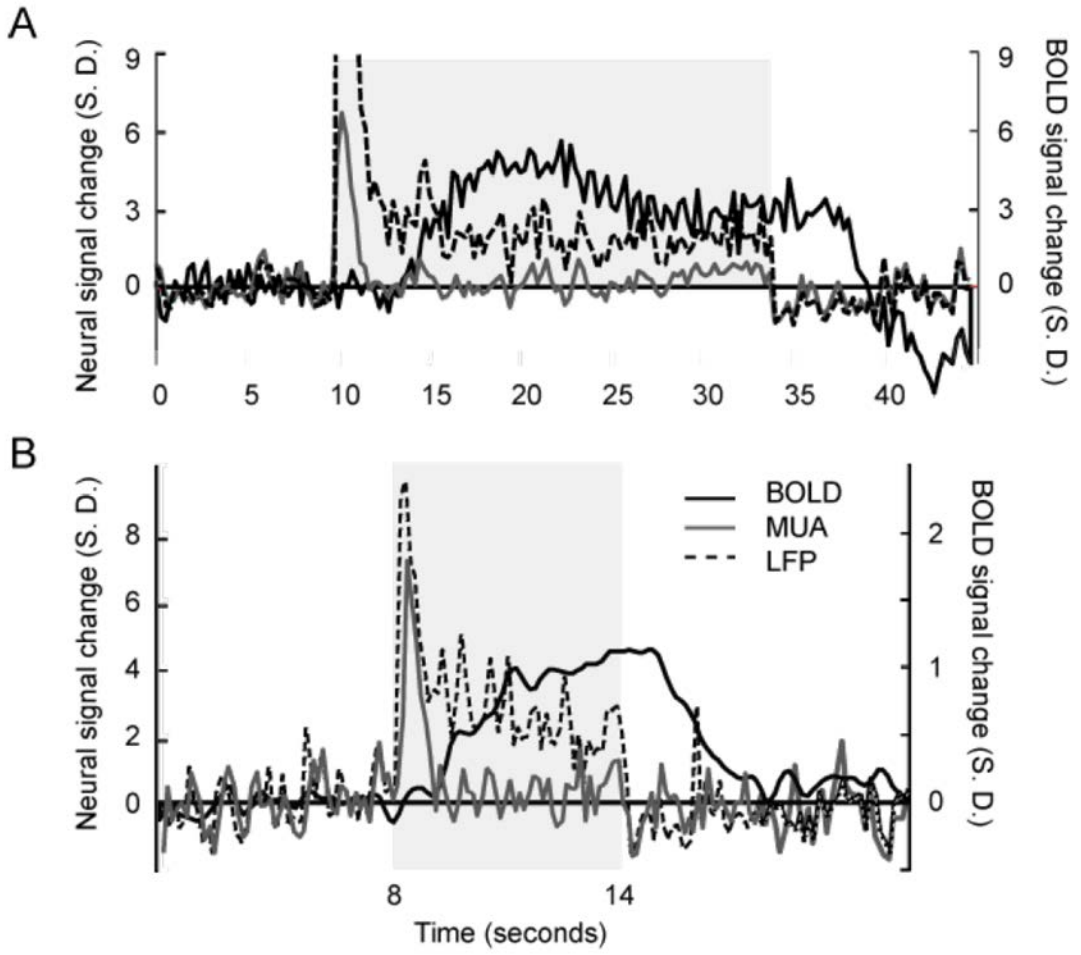
Adam C. Riggall, and Bradley R. Postle J. Neurosci. 2012;32:12990-12998

Relationship between spikes, LFPs and BOLD

- Spikes, LFP power and BOLD usually correlate, but not always.

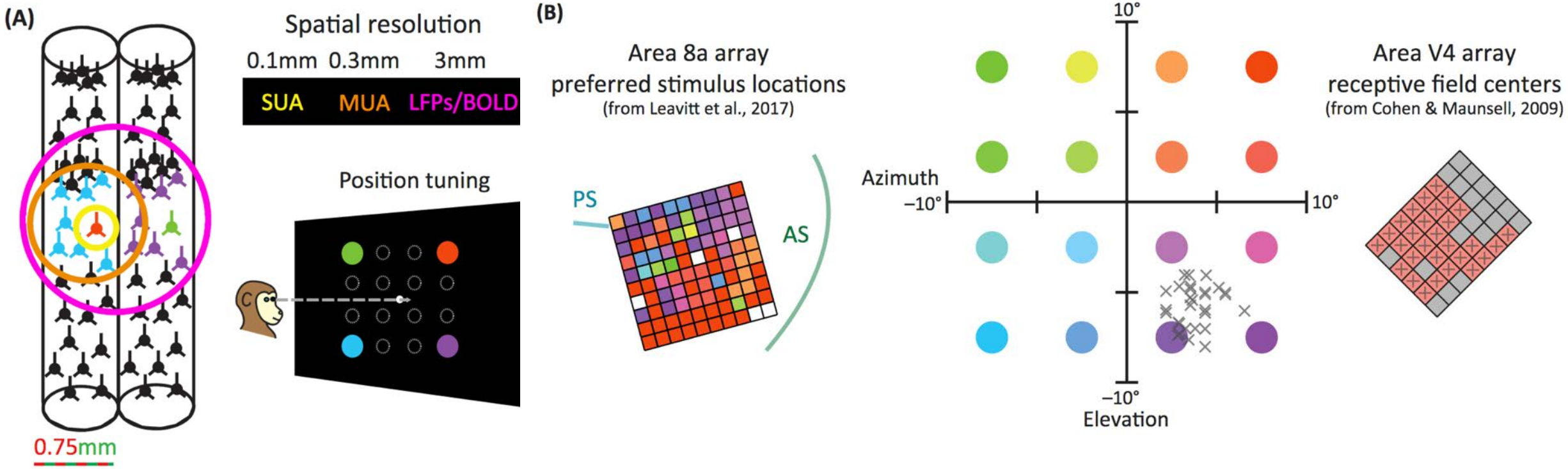
- BOLD correlates more with LFPs than with spikes.

- WARNING!

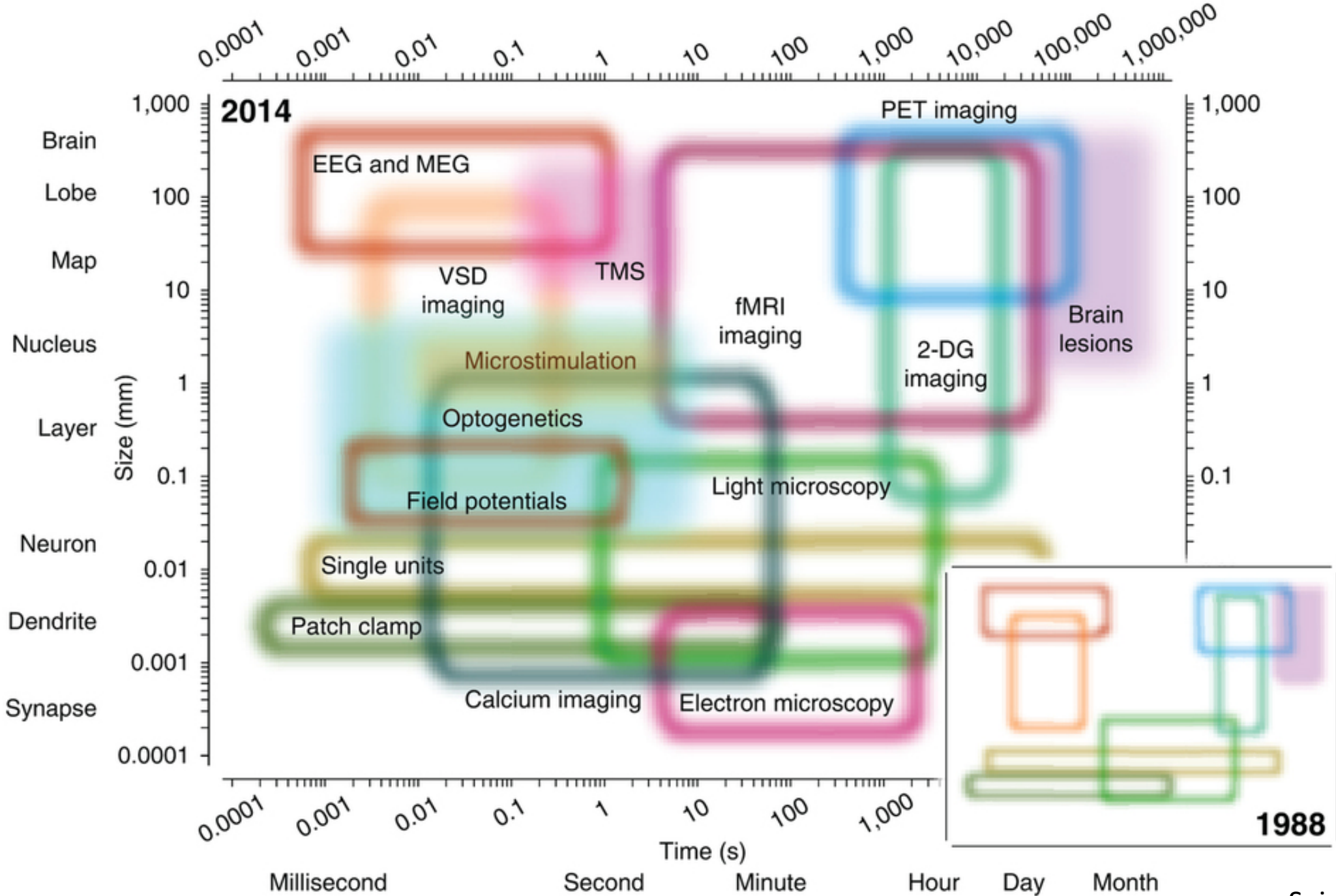


Berens et al., 2010

Spatial extent of SUA, MUA, LFPs and BOLD



Leavitt, Mendoza-Halliday & Martinez-Trujillo, 2017



Sejnowski et al., 2014

QUESTIONS?