CBMM Summer School 2019

# Neuroscience Methods Tutorial

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Postdoctoral Fellow

Desimone Lab

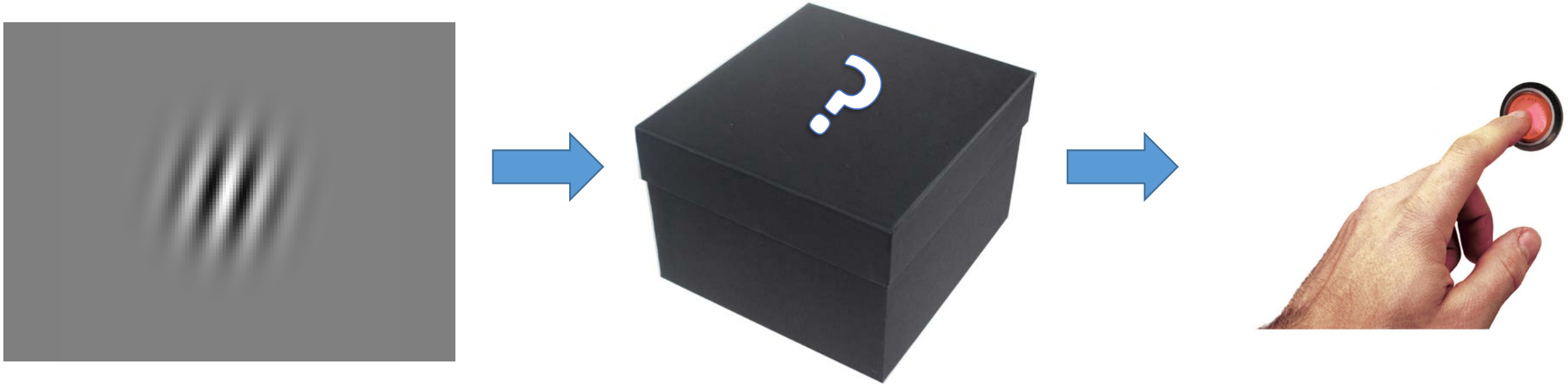
McGovern Institute at MIT

# 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?

Why Neuroscience Methods Tutorial at CBMM Summer School?

# Psychophysics: the “black box” method



# Interrogating the brain: neural signals

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

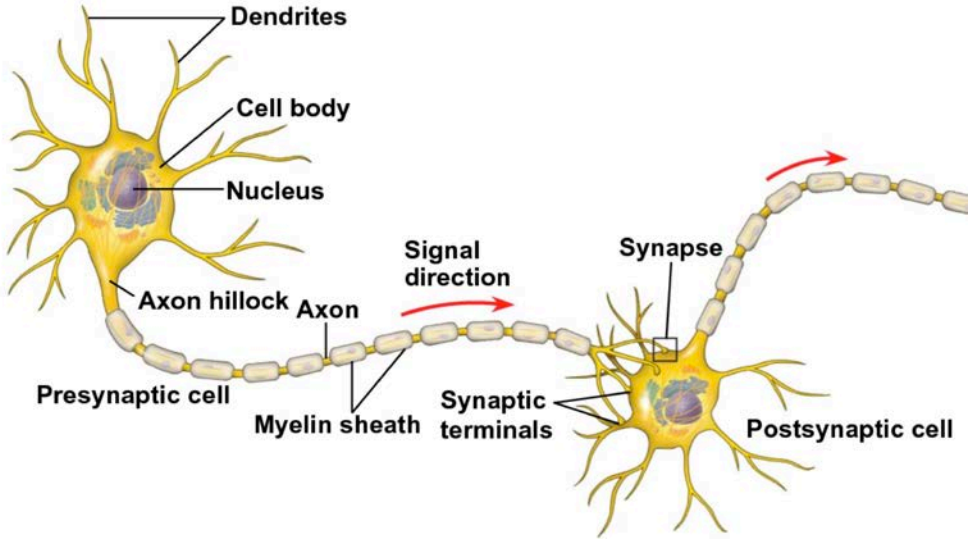
Examples of signal media:

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

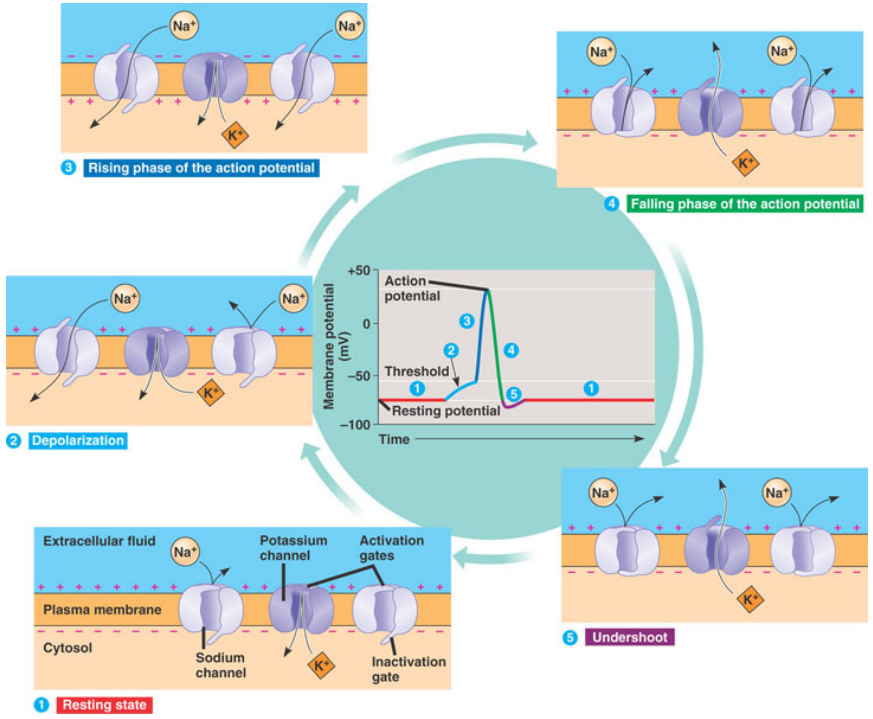
SIGNAL in neural function vs. SIGNAL in experimental acquisition

e.g. Neuromagnetic and BOLD signals

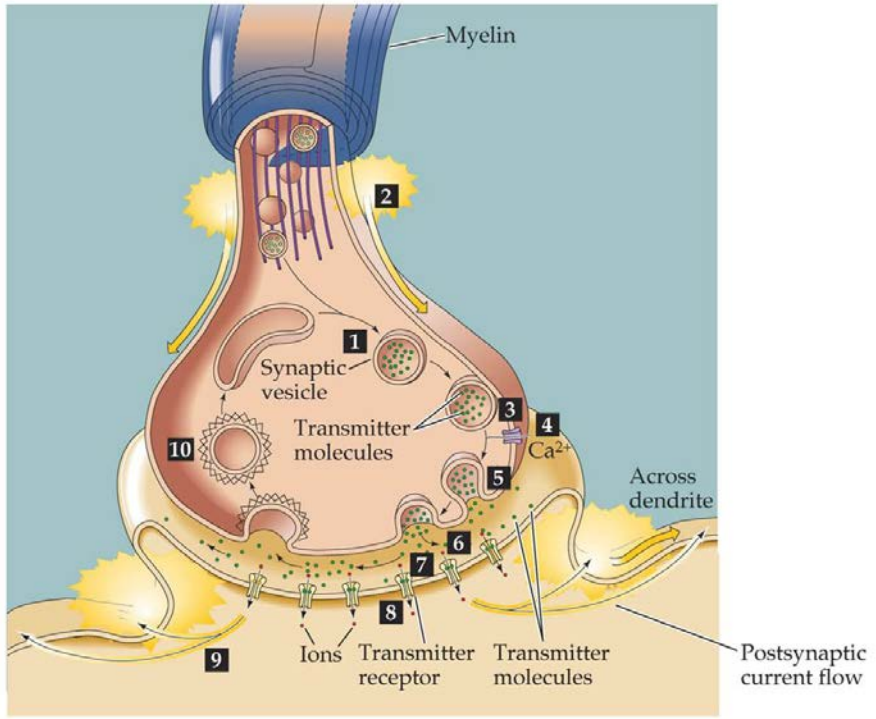
# Neural signals




## Action potentials

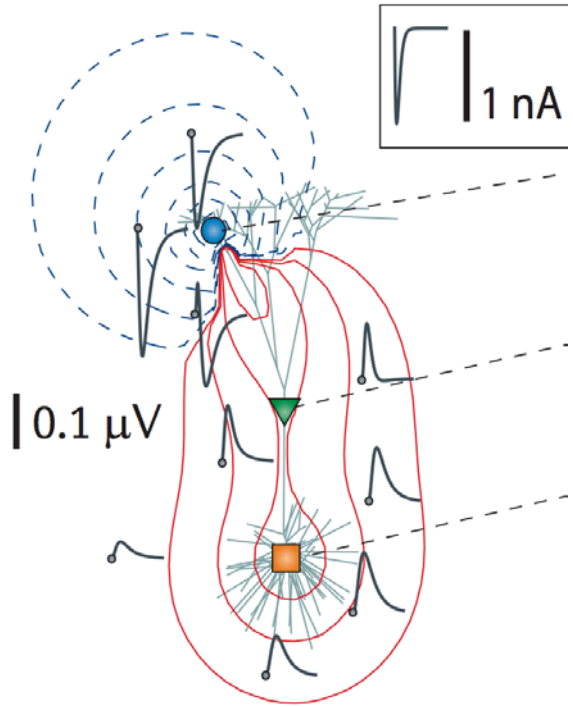



## Synaptic transmission




NEUROSCIENCE, Third Edition, Figure 5.3 © 2004 Sinauer Associates, Inc.

## Local field potentials (LFP)



# Neural signals summary

- Electrical signals:
  - Action potentials
  - Local field potentials

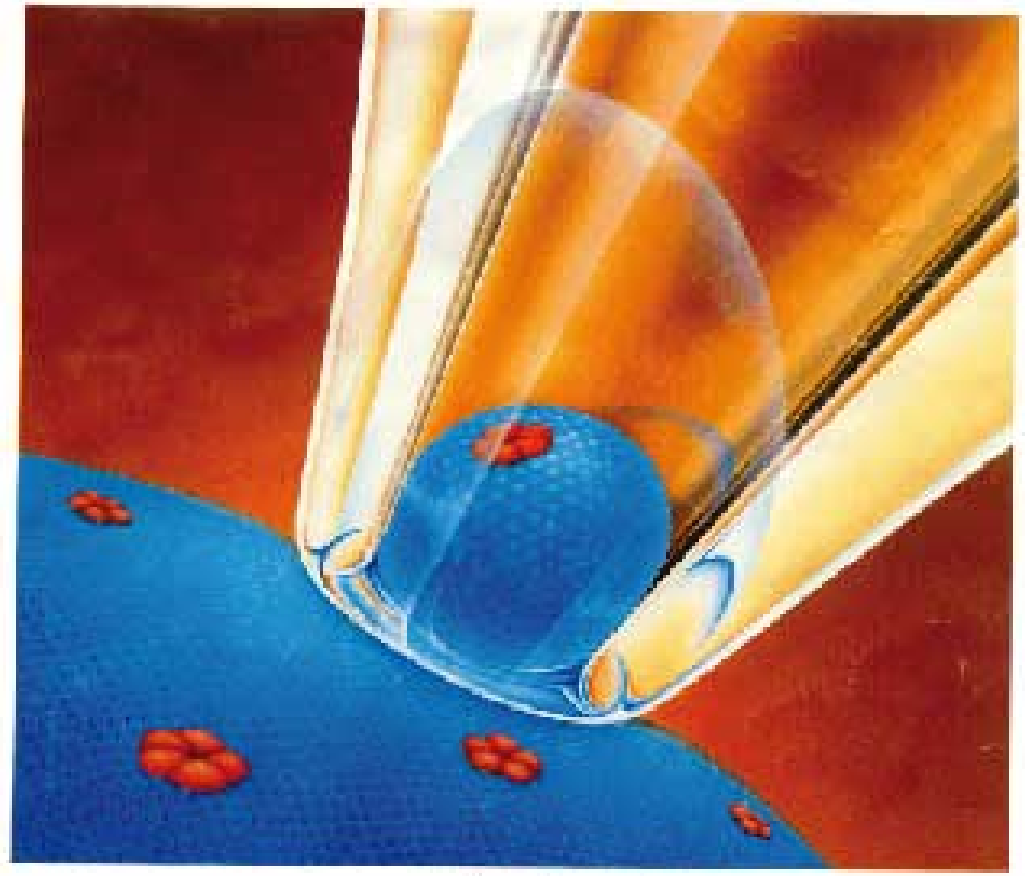
- Chemical signals:
  - Ca++ influx
  - Neurotransmitter release

# Neural acquisition methods: Electrophysiology

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

# Electrophysiology: Patch-clamp

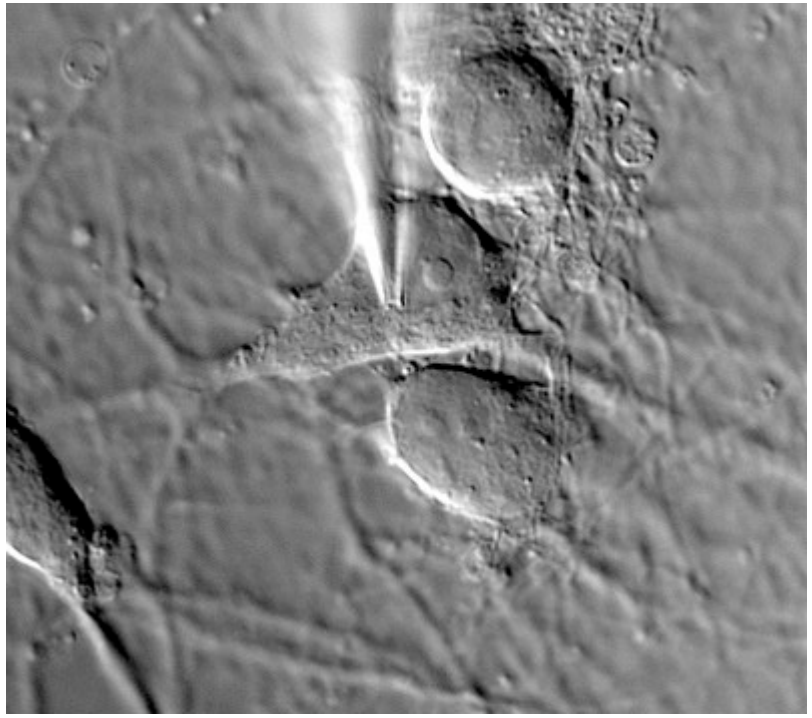
- Glass pipette seals membrane patch by suction.
- Measures voltage changes in solution inside pipette (electrolyte)
- Used to study properties of a small patch of membrane, even individual ion channels!



# 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

* Difficult to perform in large behaving animals



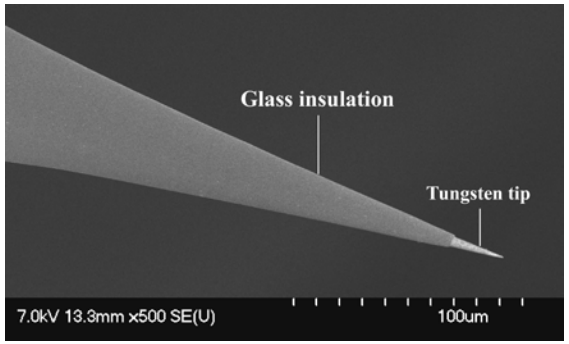
# Electrophysiology: Extracellular recordings

- 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
  - Local Field Potentials (LFP)
  - Single neuron spiking activity
  - Multi-unit spiking activity
- Can be performed in behaving animals

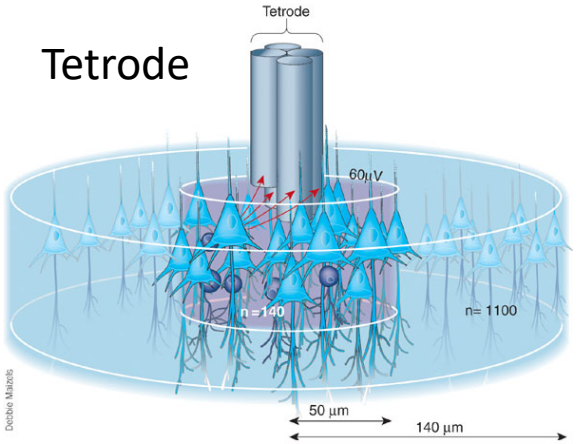


# Types of microelectrodes

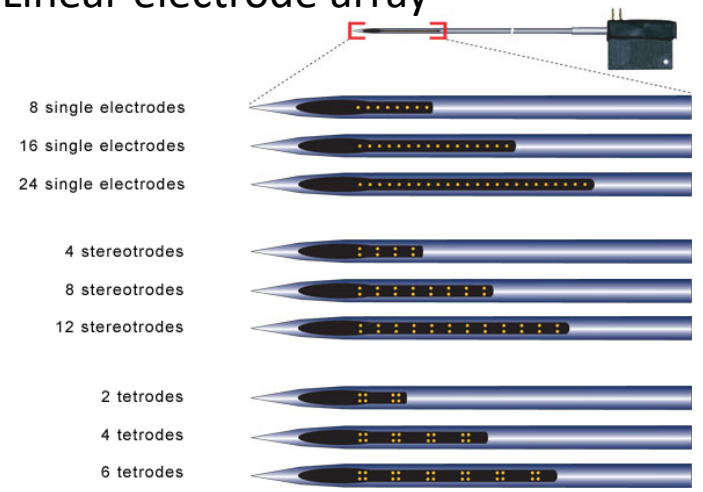
Single microelectrode



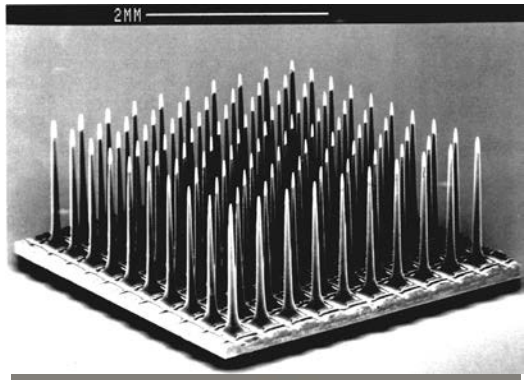

Tetrode

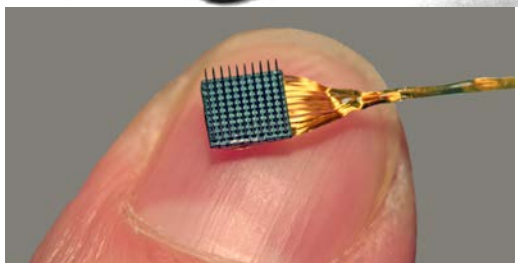



Linear electrode array

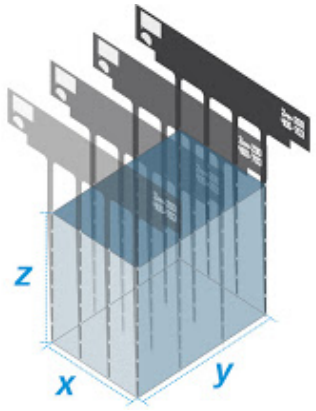


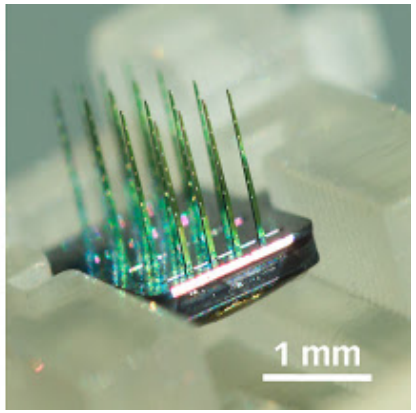

2D matrix electrode array



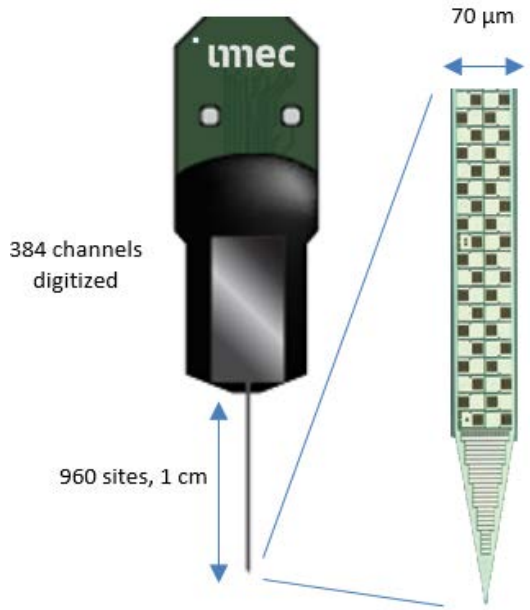



3D matrix electrode array

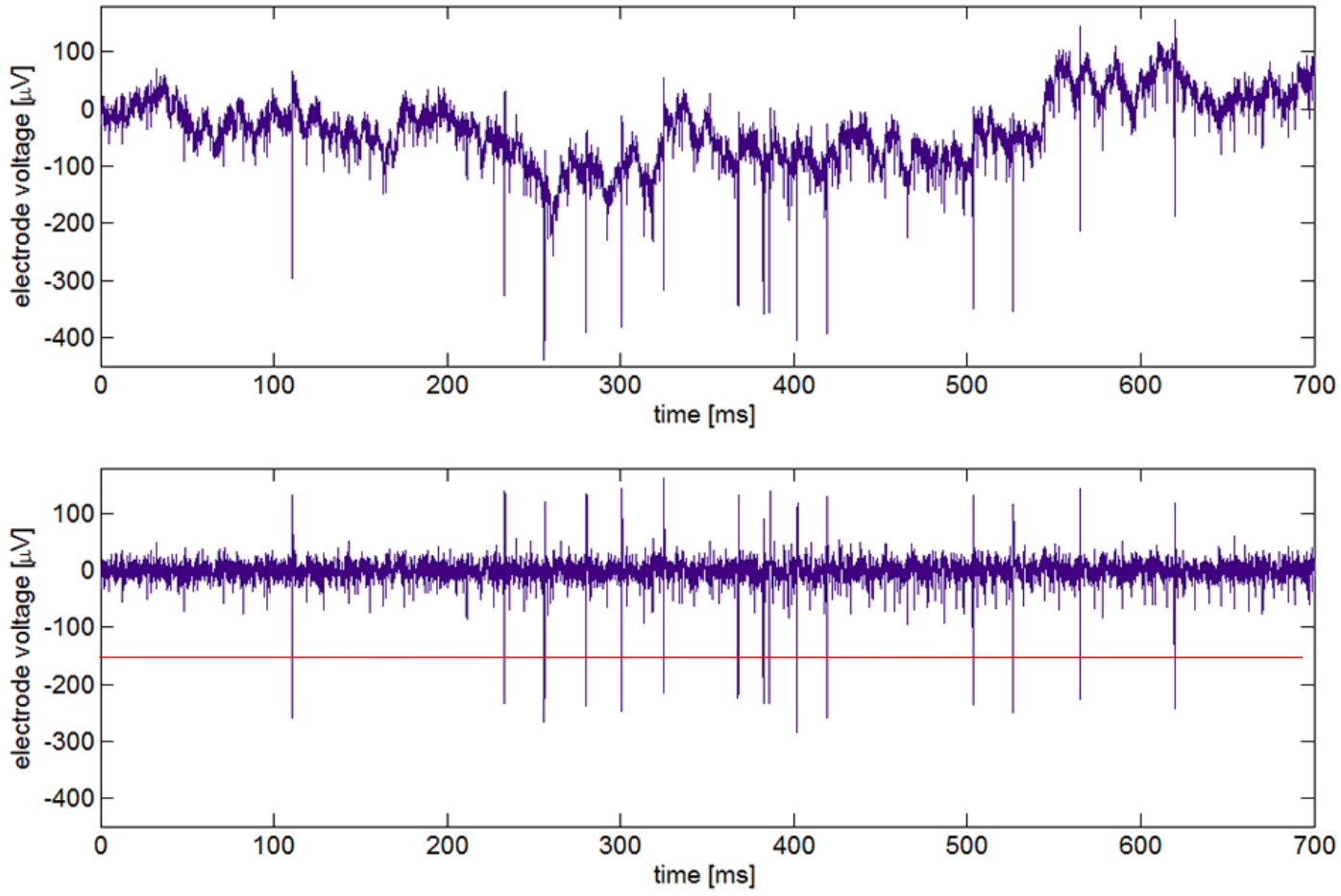



High density probes



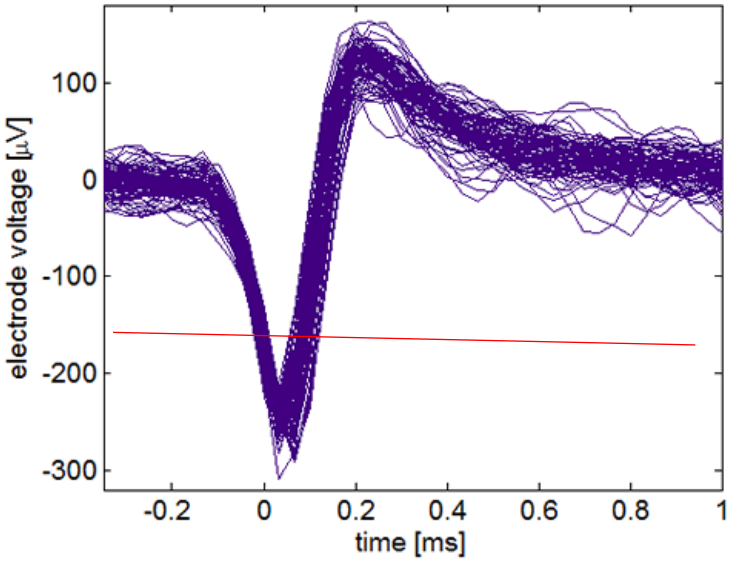
# Electrophysiological signal processing



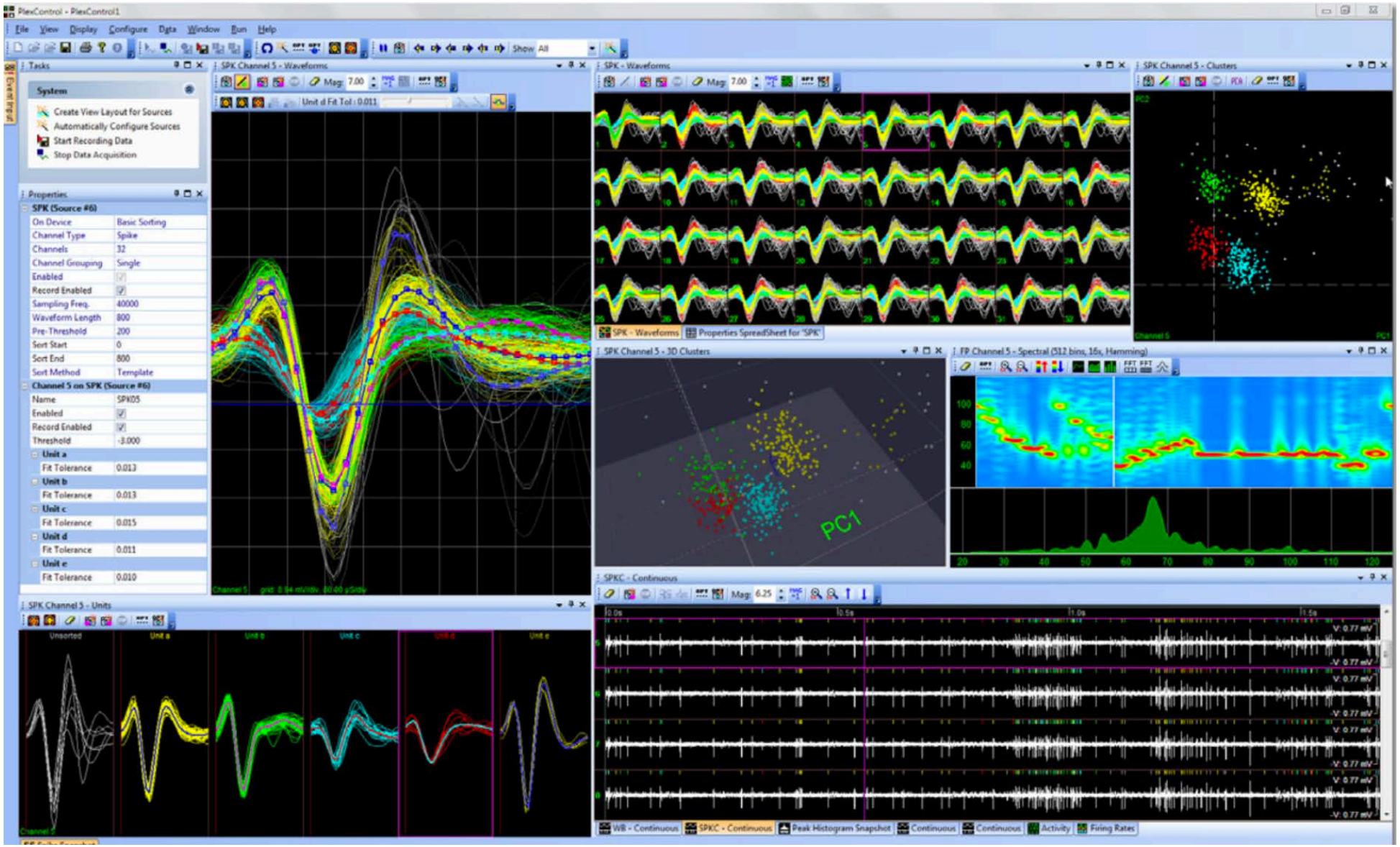

Filter between 1 and 9000 Hz = LFP + spikes

Low-pass filter at ~250 Hz = LFP

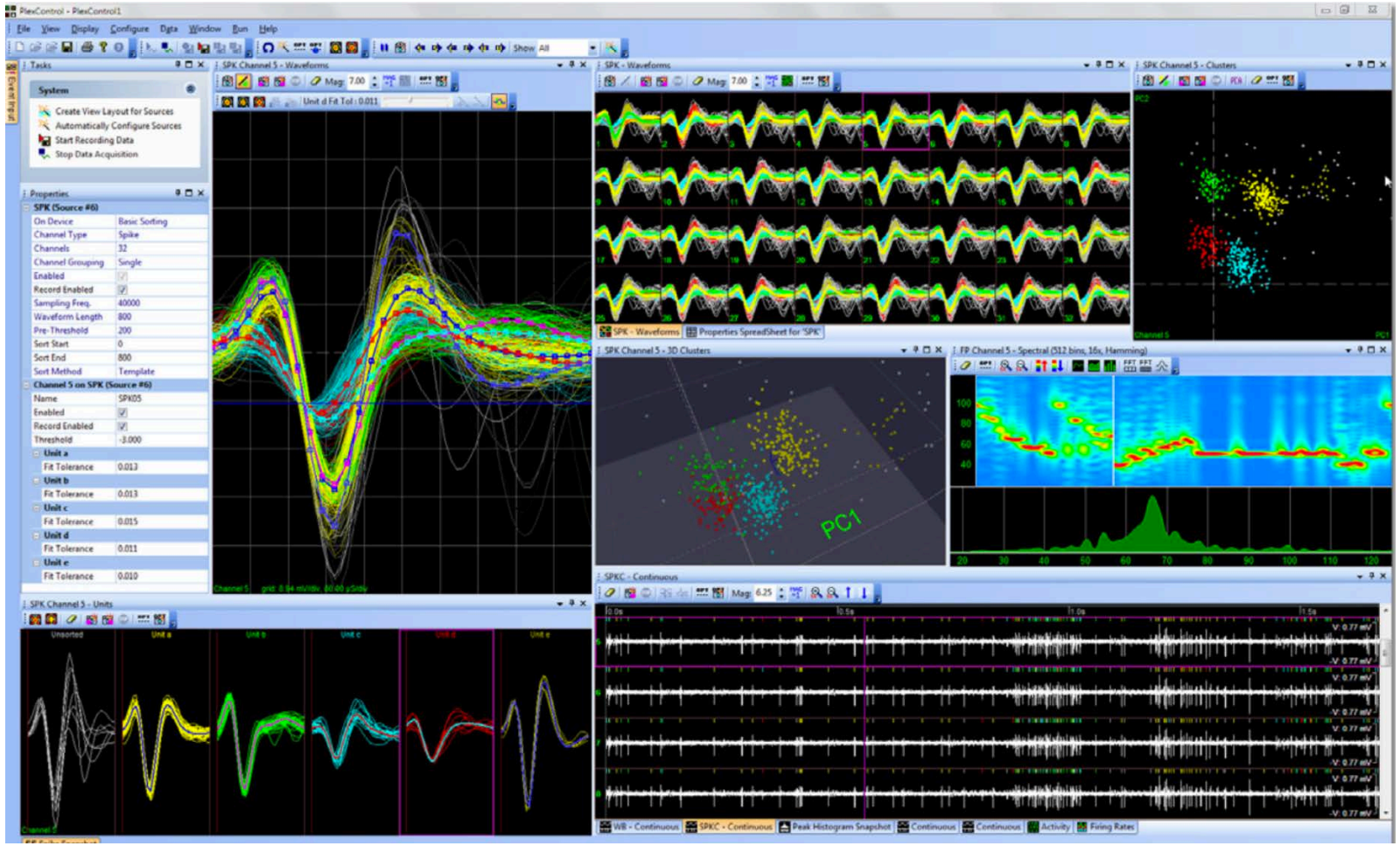
High-pass filter at ~300 Hz = Spikes

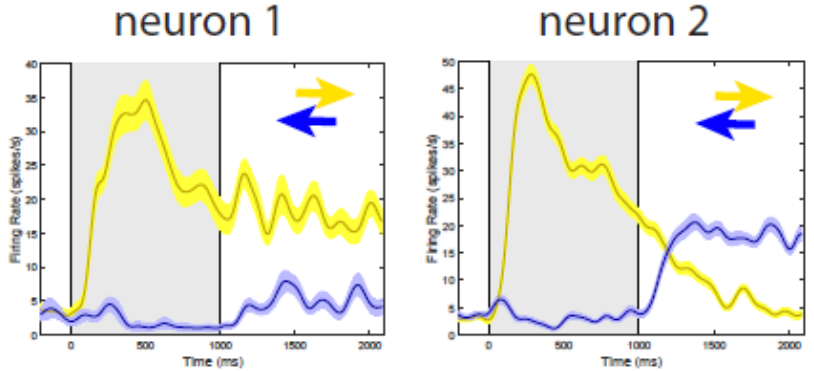


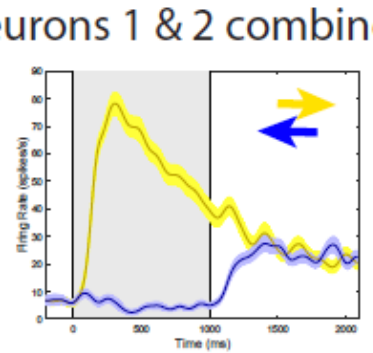
# Spike sorting



# Spike sorting: Single units vs. multiunits

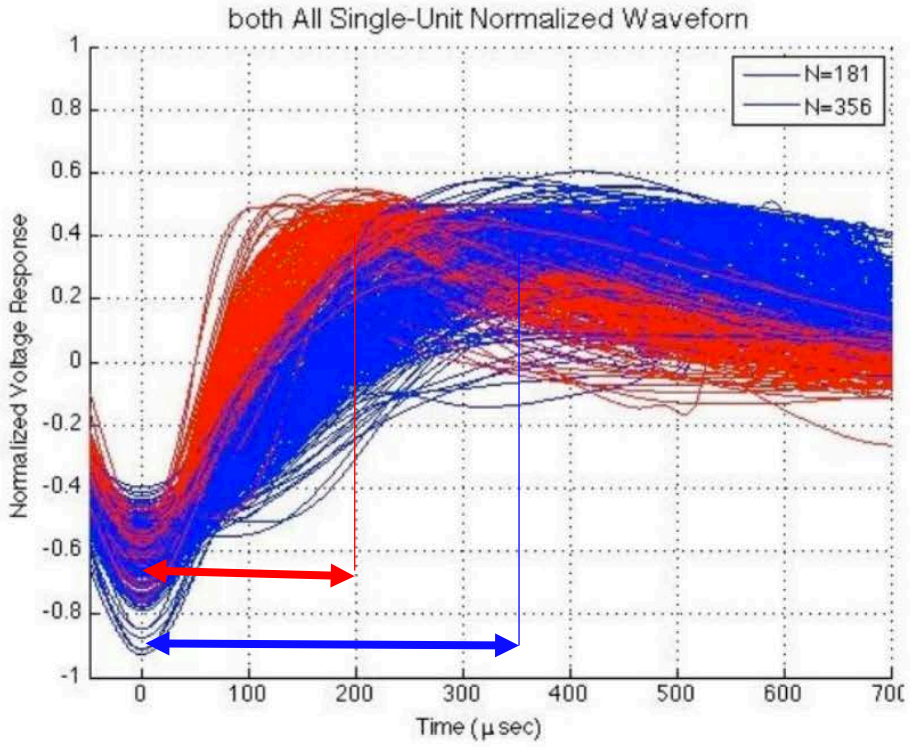


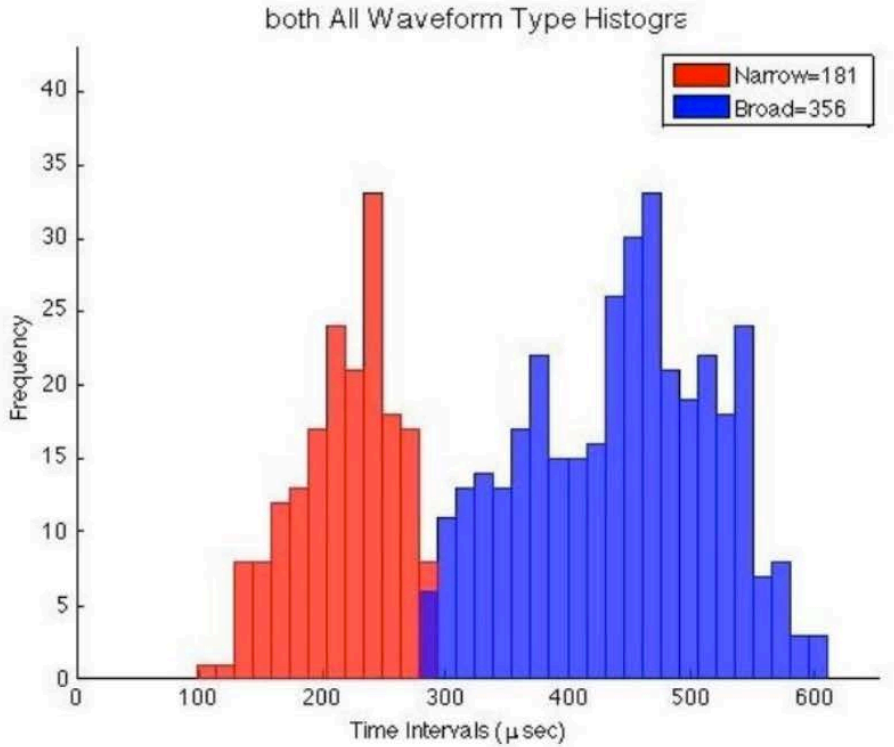



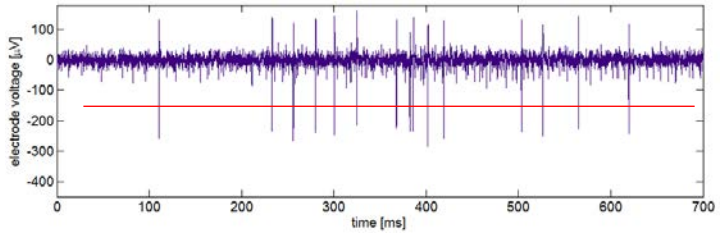
# Spike waveform analyses

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

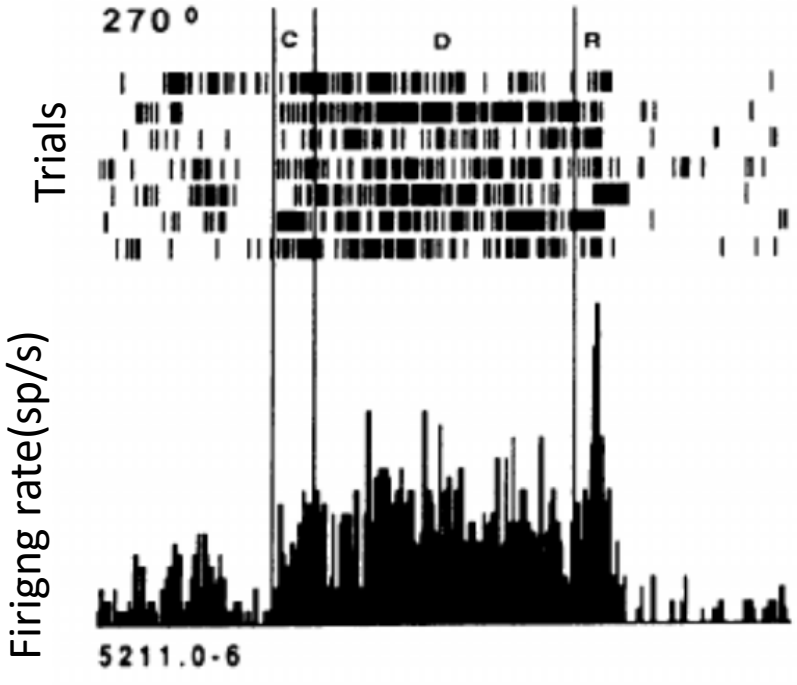


# Graphical representations of spiking activity



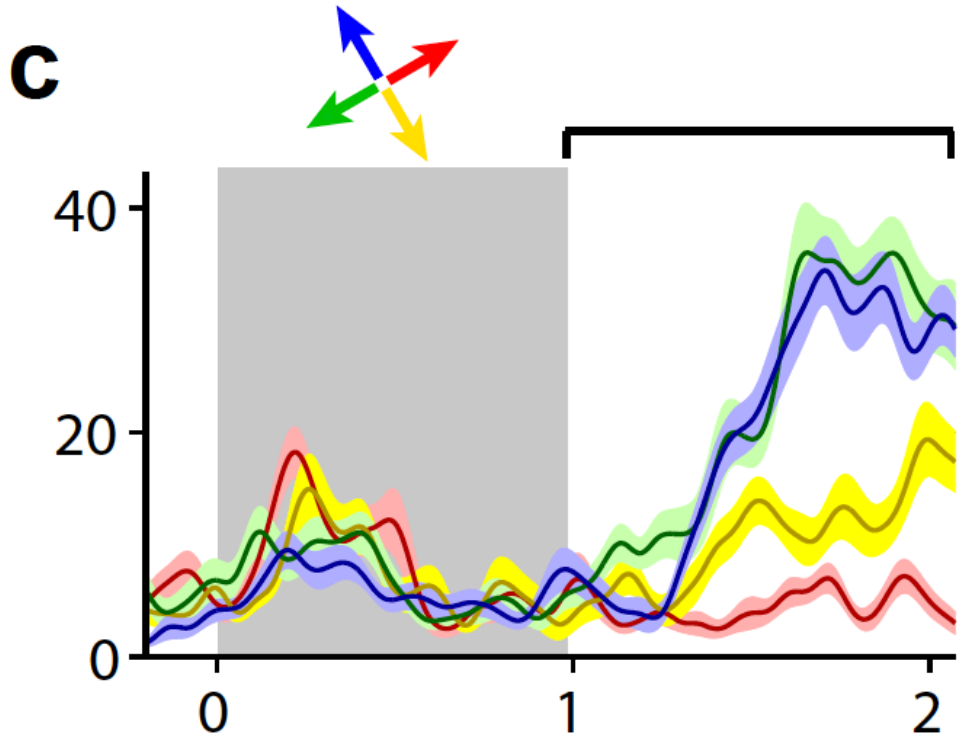

RASTER PLOT



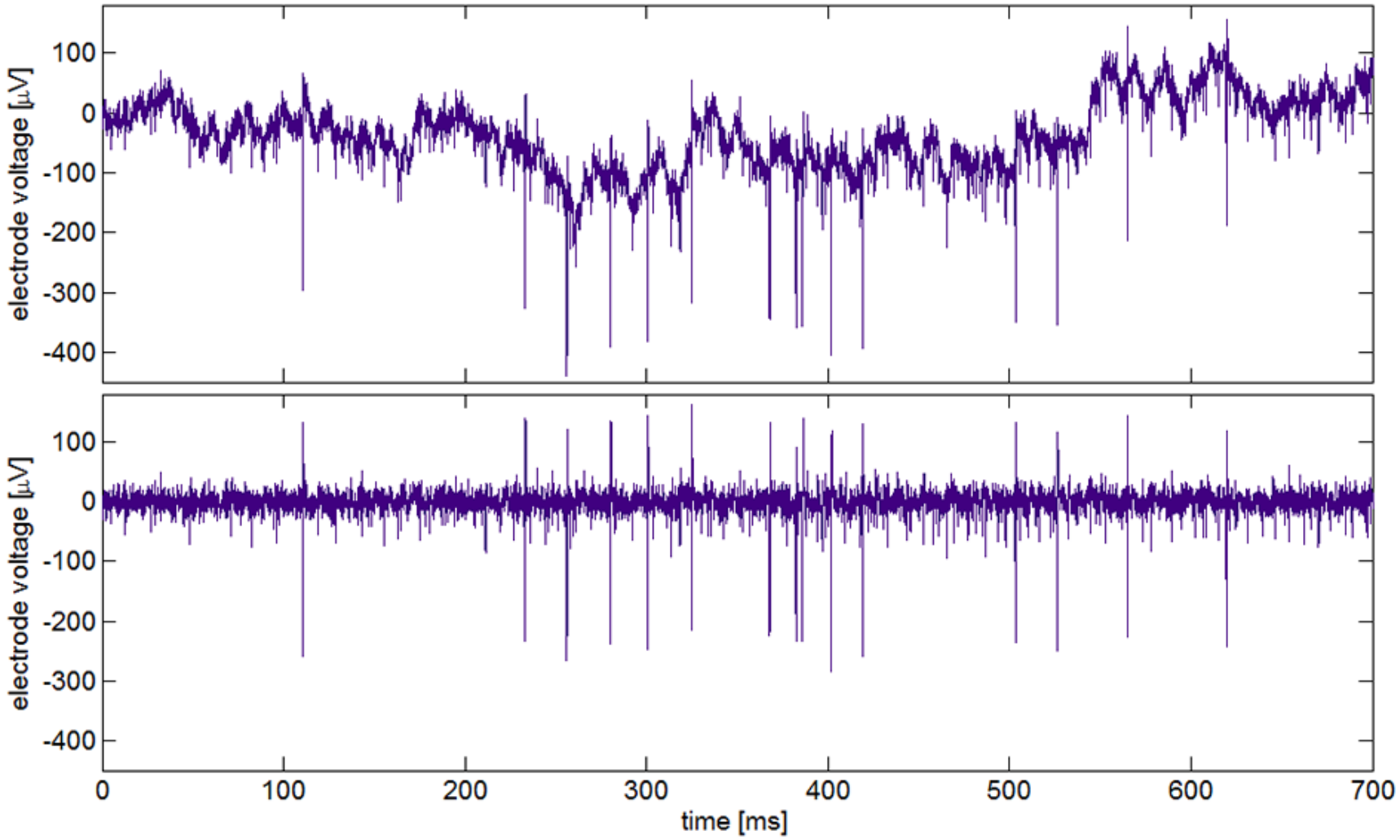

Time (s)

PERISTIMULUS TIME HISTOGRAM (PSTH)

SPIKE DENSITY FUNCTION



# Local Field Potentials (LFP)

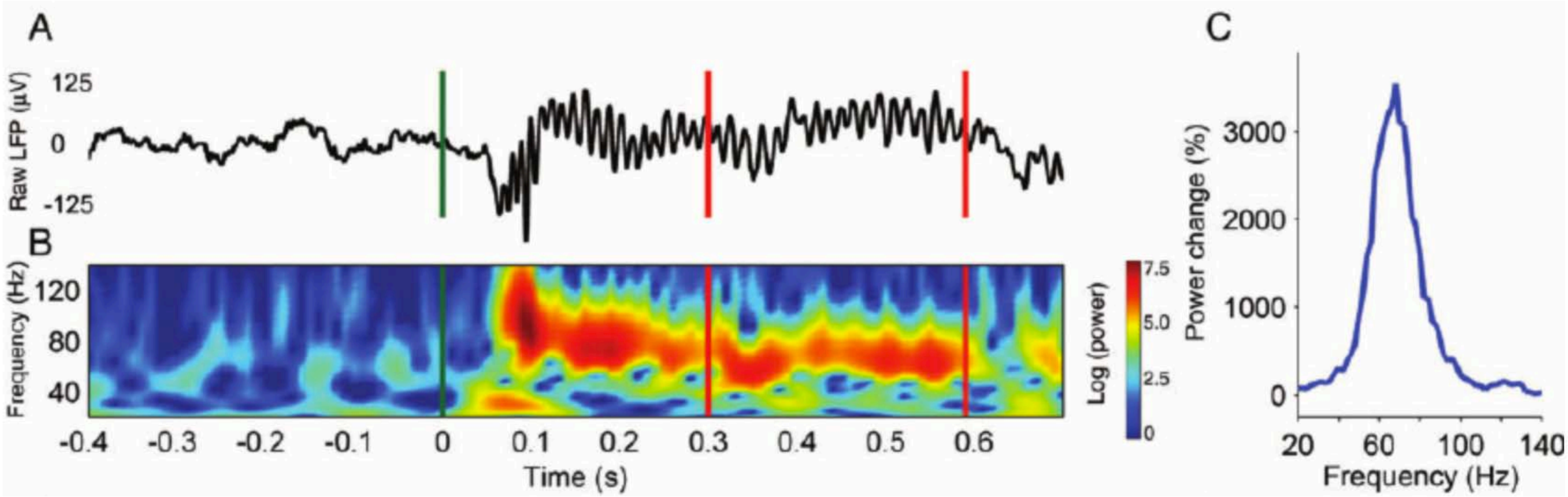



Filtered between 1 and 9000 Hz
- LFP + spikes

High-pass filter at 300 Hz
- Spikes

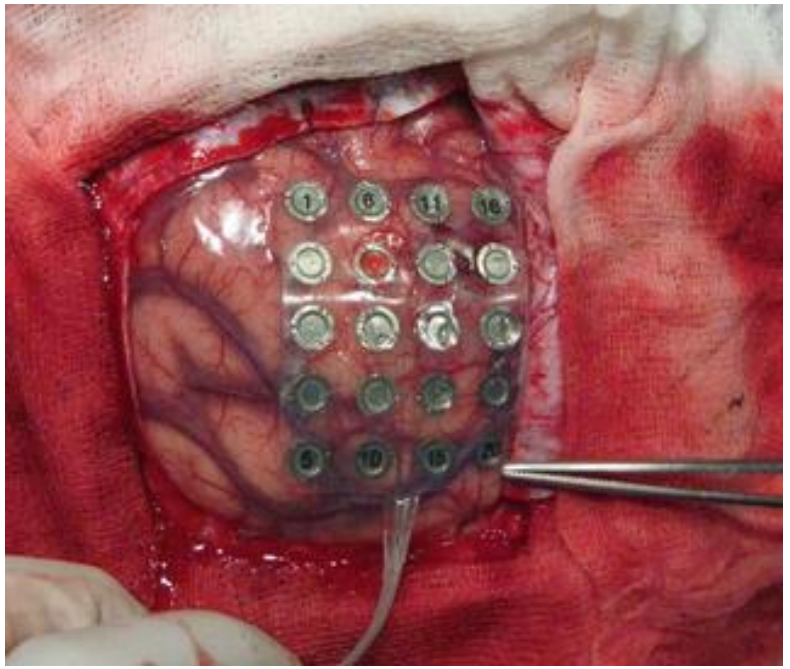
# Local Field Potentials (LFP)

- Spectral analysis (Fourier transform)
- Oscillatory activity – neuronal synchronization



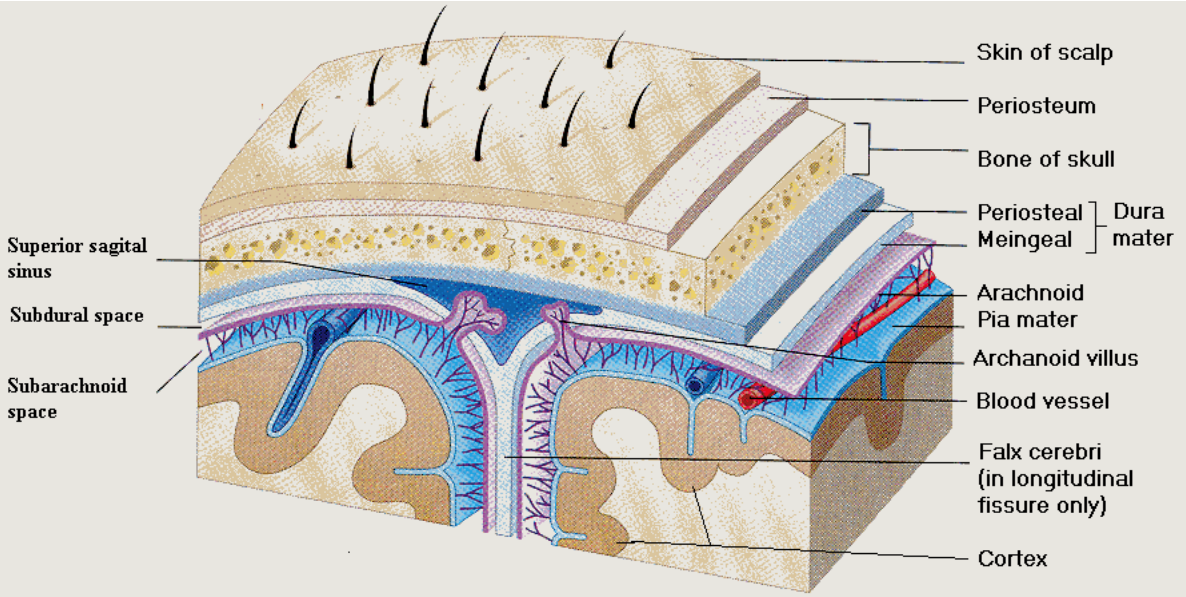
# Electrocorticogram (ECoG)

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



# Electroencephalogram (EEG)

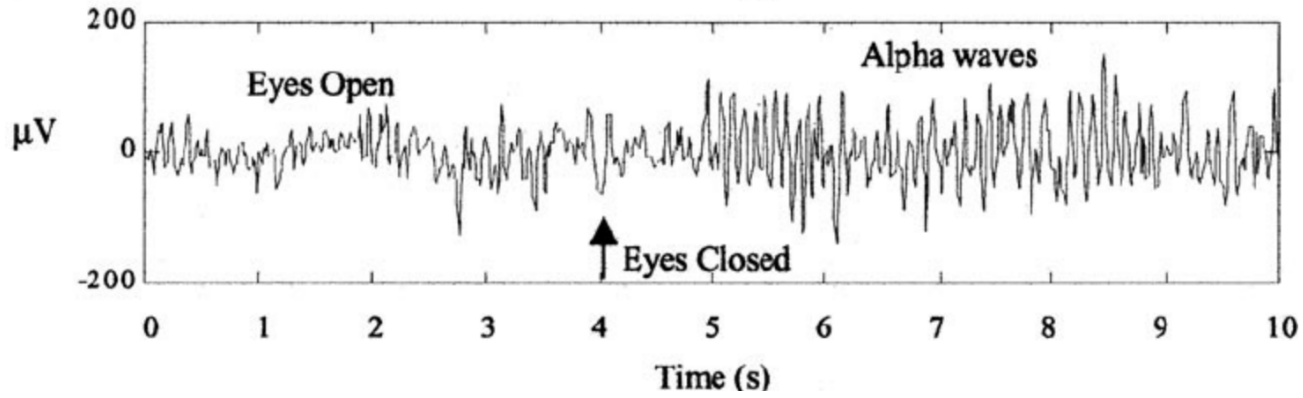
- Electrophysiological recordings from scalp surface (non-invasive!)
- High temporal resolution but low spatial resolution

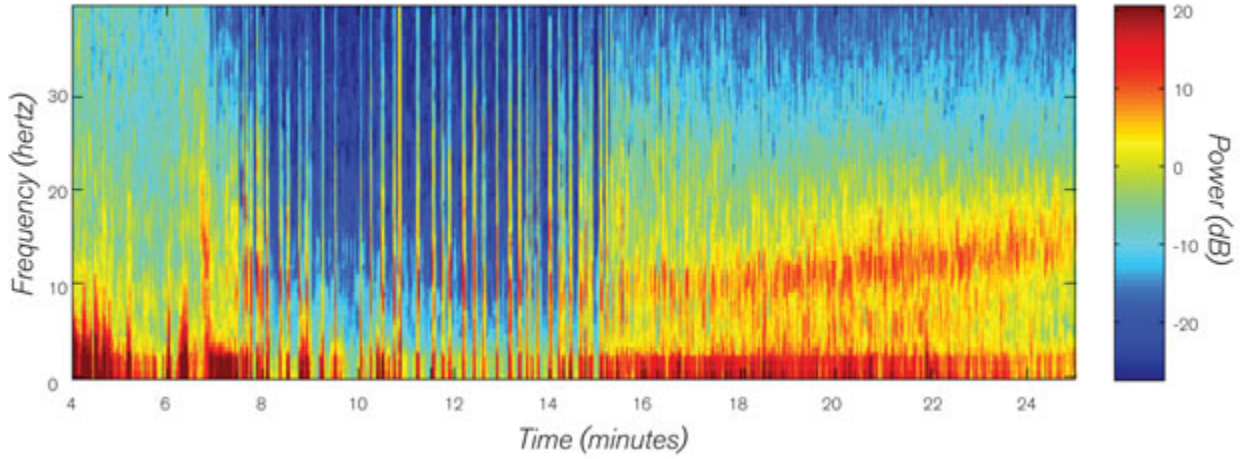


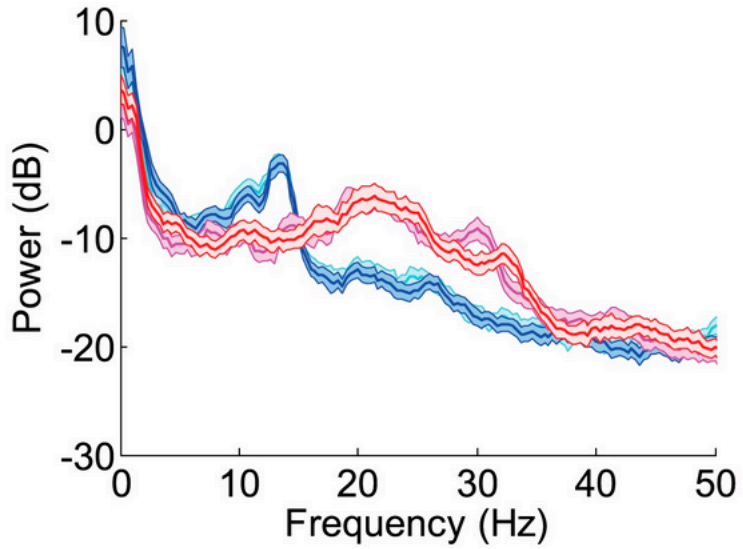



# Electroencephalogram (EEG)

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

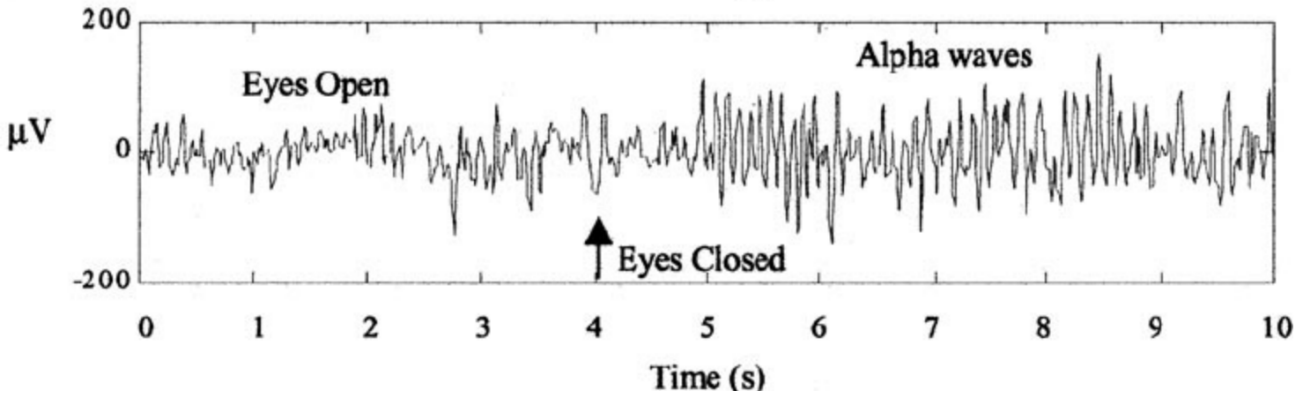


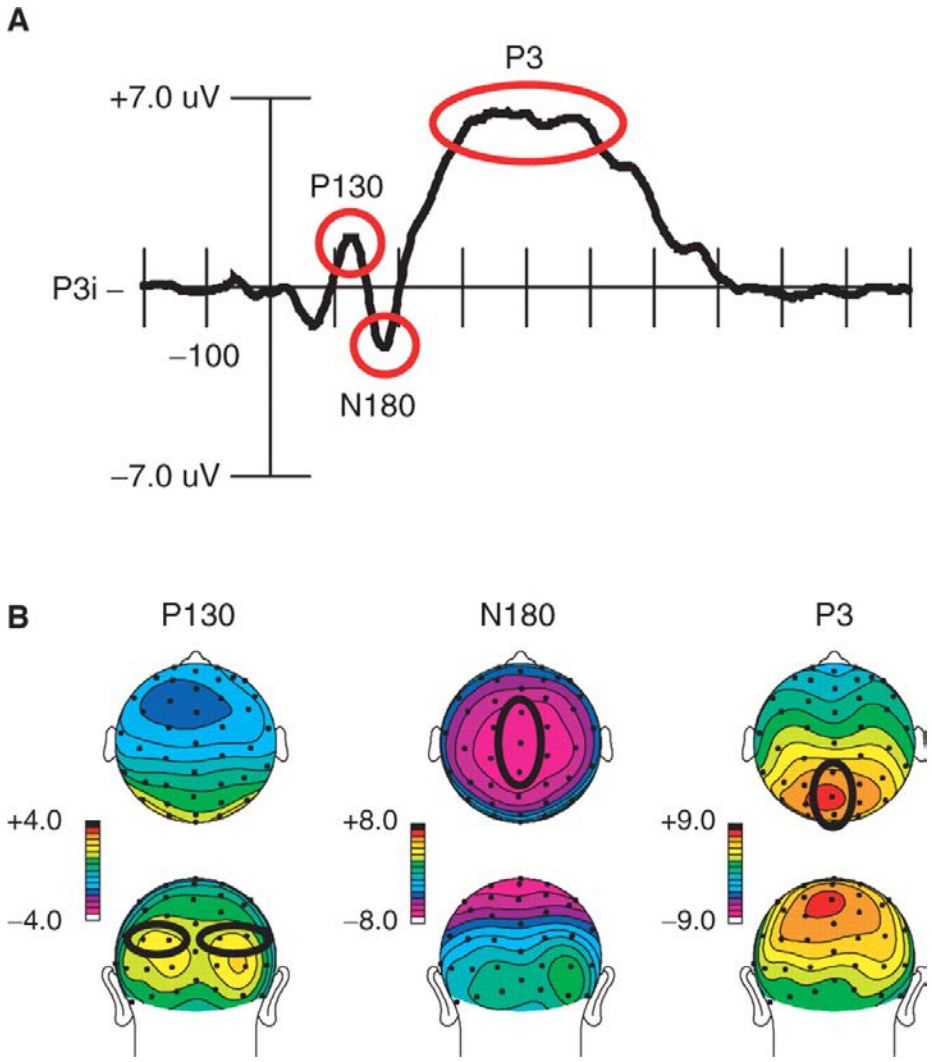



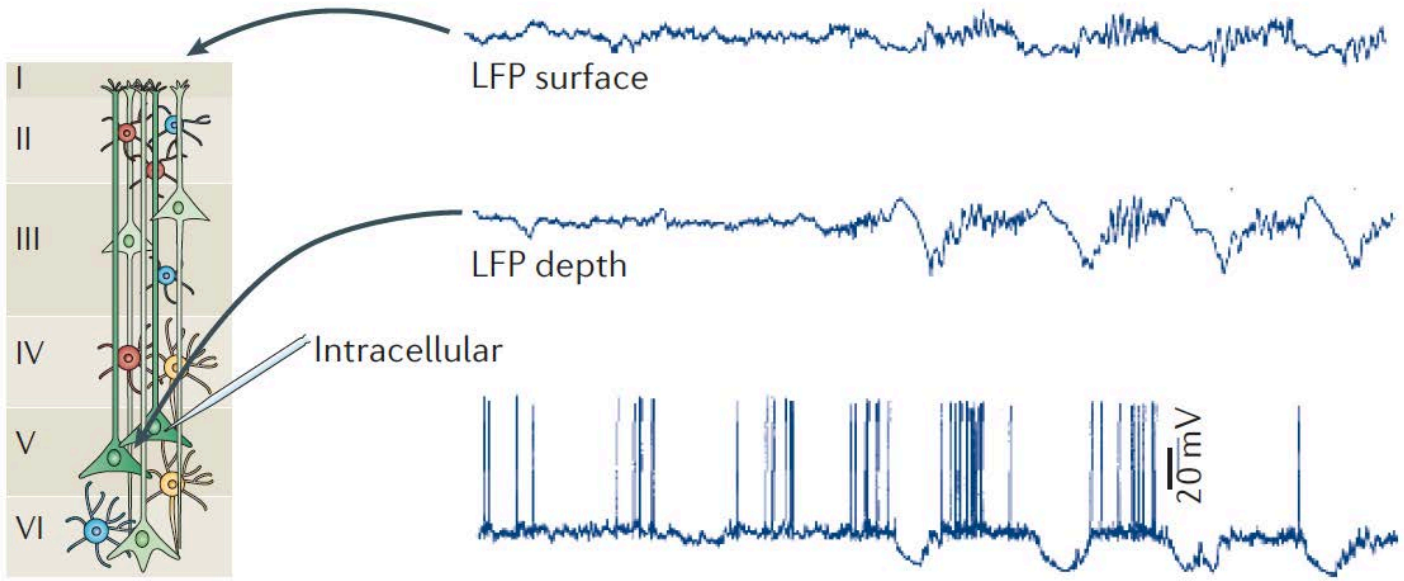
# Electroencephalogram (EEG)

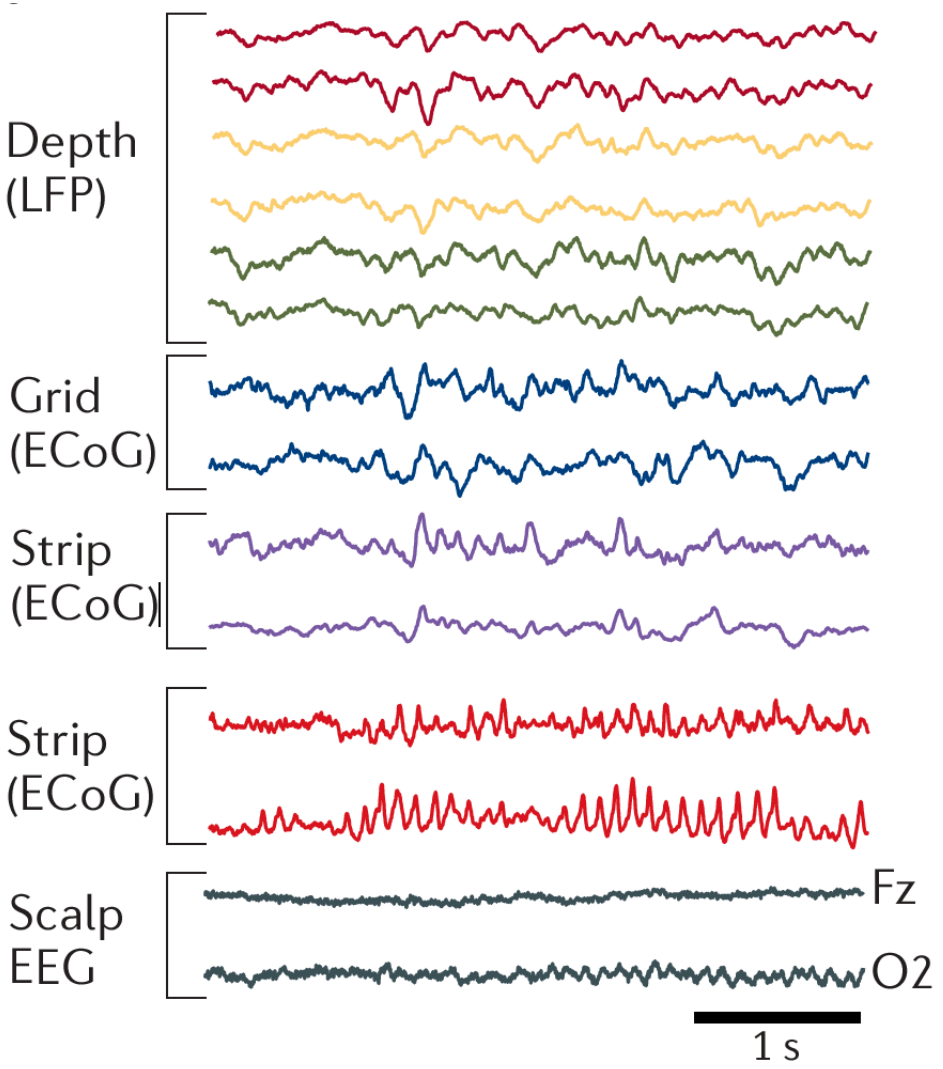
- Event-related potentials (ERP)
  - Measures positive and negative potentials (e.g. N180, P3)
    - Neural function signatures
  - Requires multiple-trial averaging
  - Potential amplitudes compared between conditions



# Comparing electrophysiological methods




**Buszaki et al., 2012**

# Neural signals summary

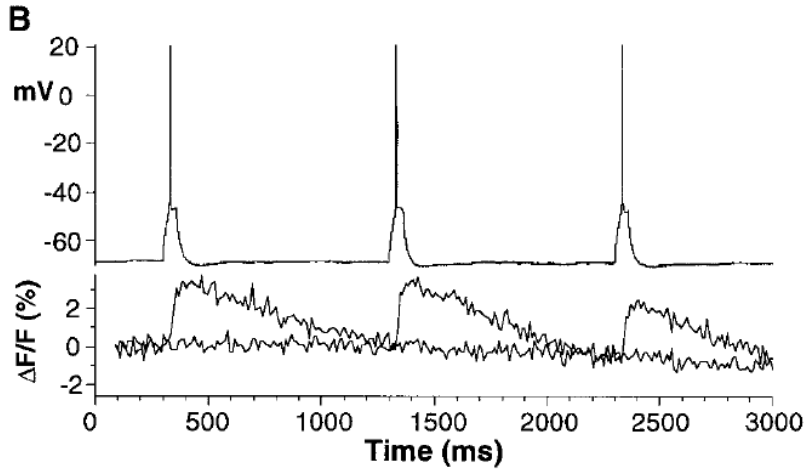
- Electrical signals:
  - Action potentials
  - Local field potentials

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

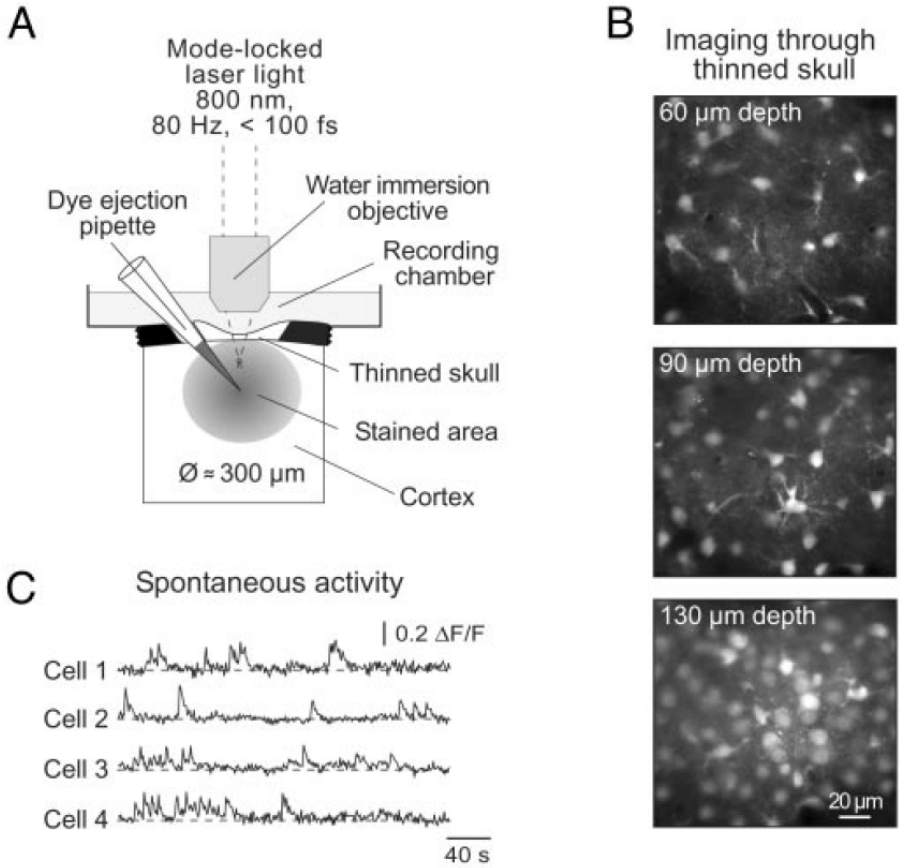
# Calcium imaging

Calcium imaging:

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



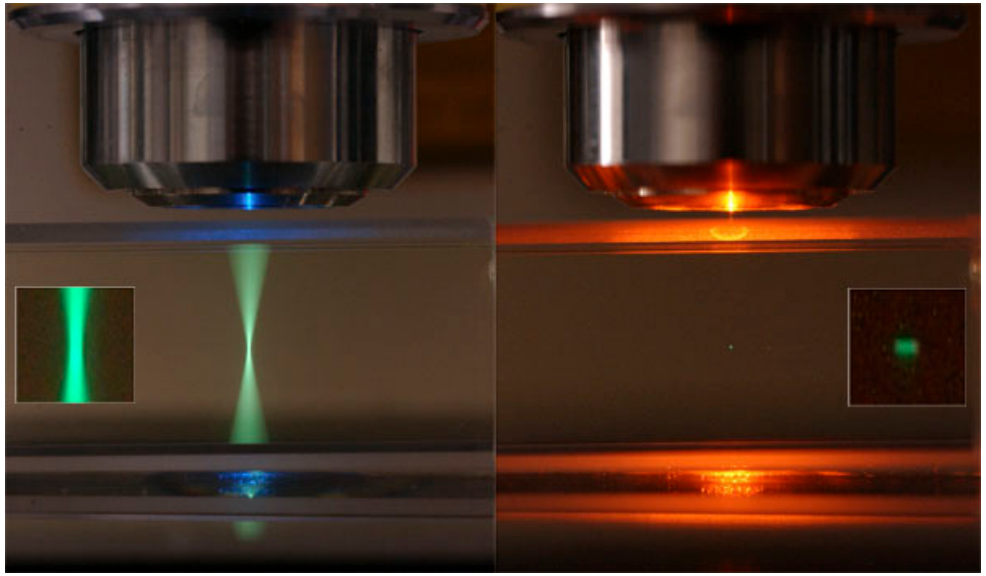

Smetters et al., 1999

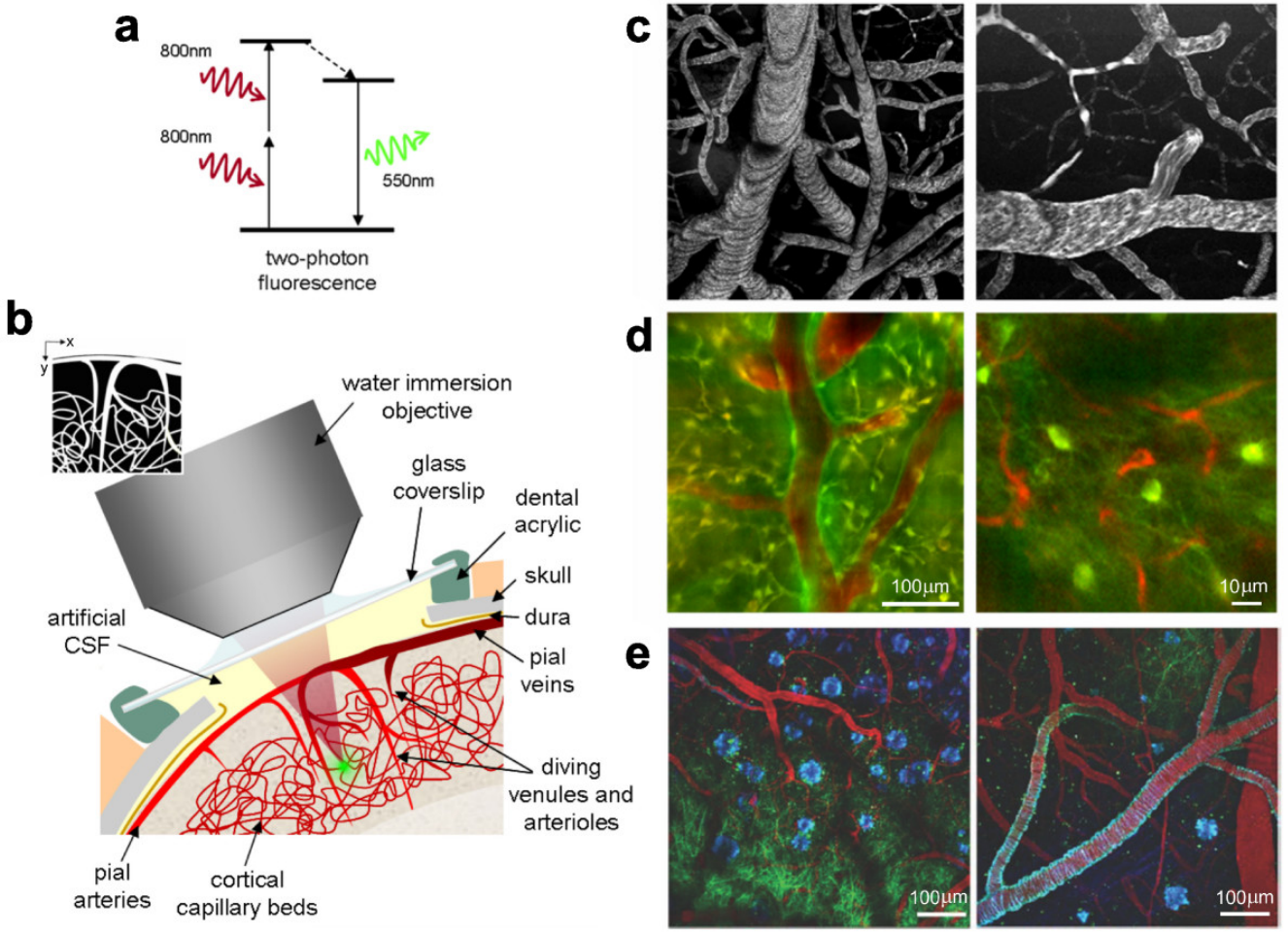


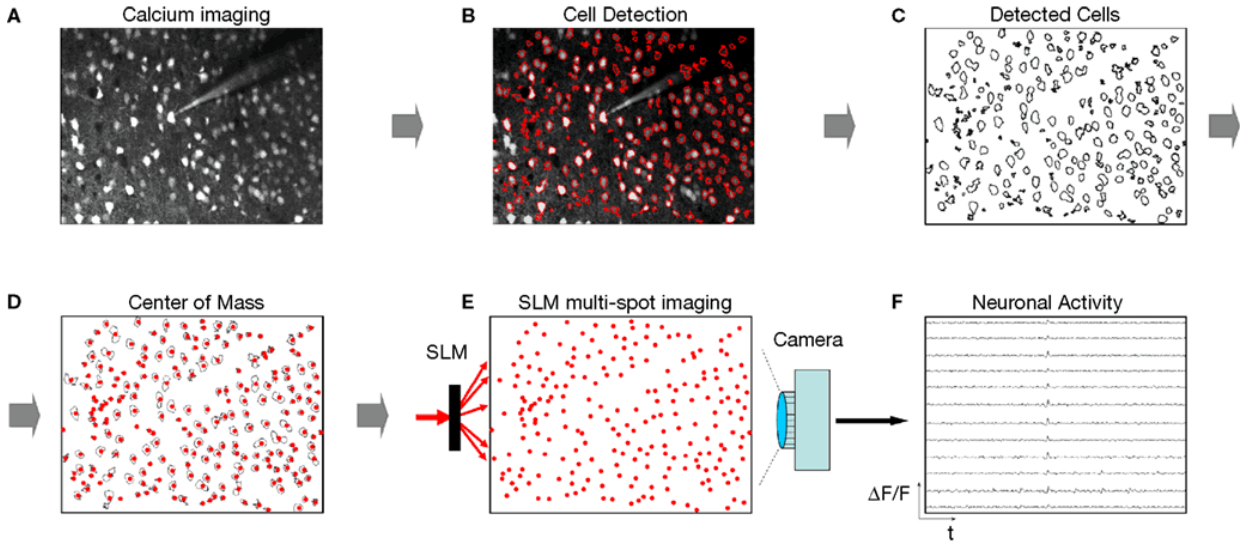

Stosiek et al., 2003

# Two-photon calcium imaging

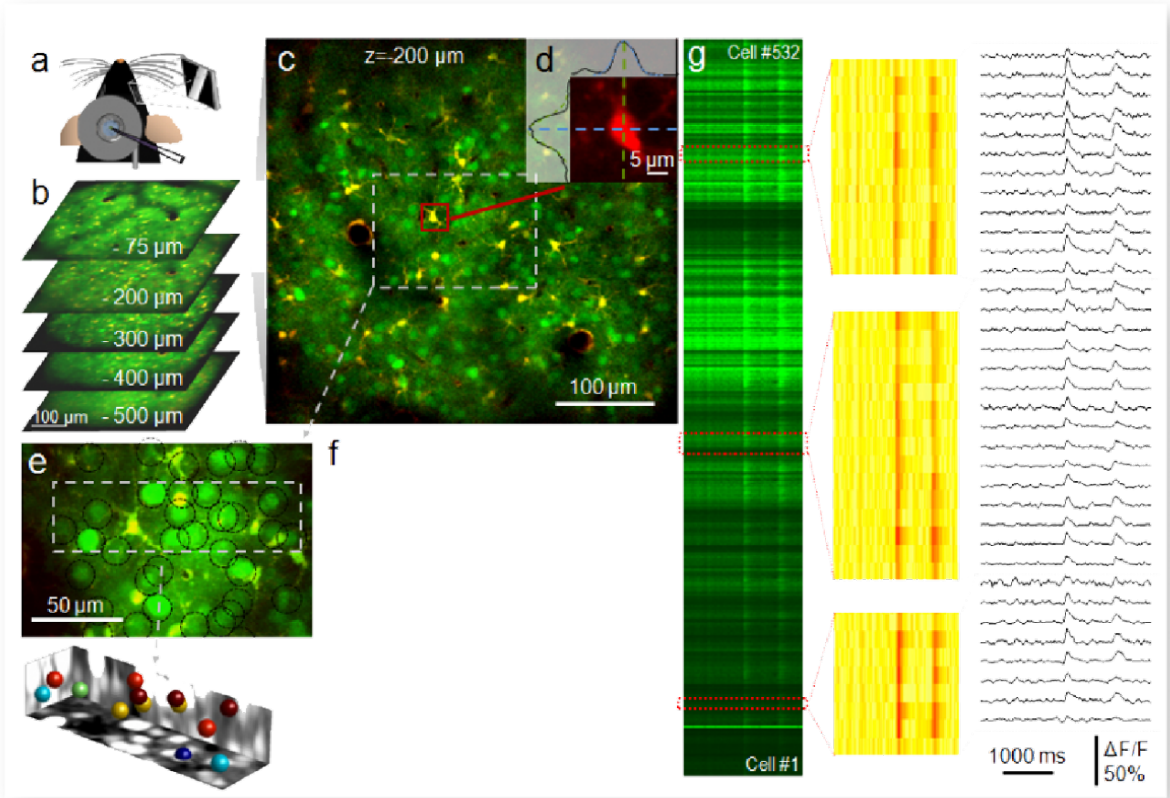
Two-photon microscopy








Nikolenko et al., 2008



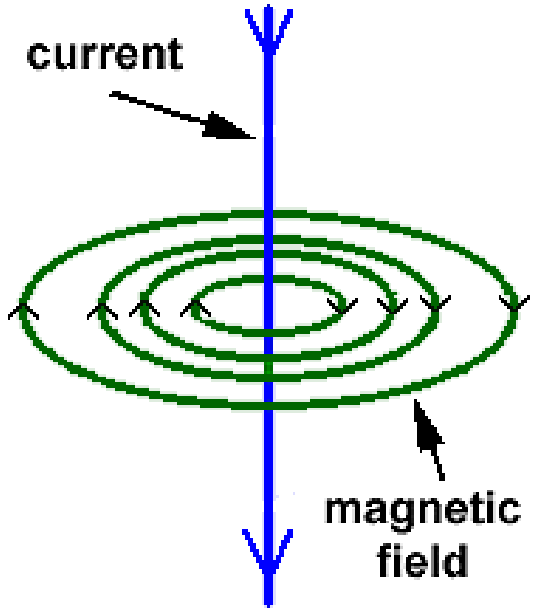

Katona et al., 2012

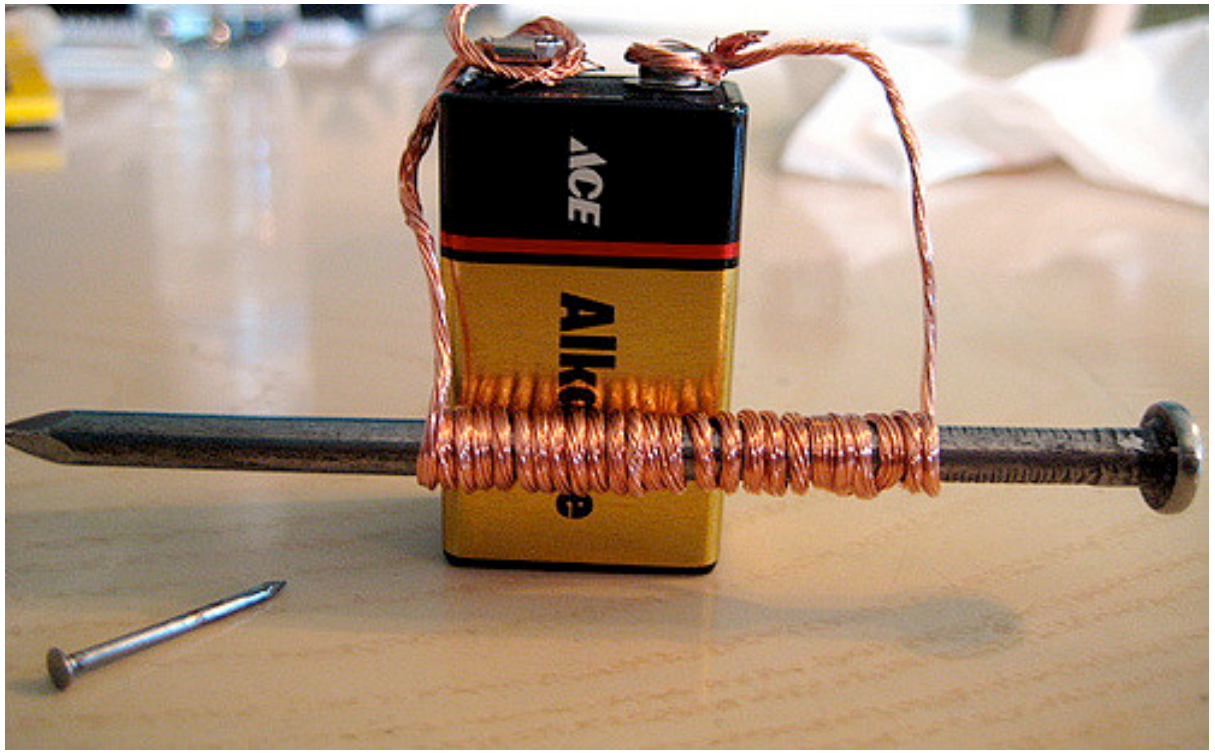
# Indirect signals linked to neuronal activity

- Neuromagnetic signals
- Neurovascular coupling

# Indirect signals linked to neuronal activity

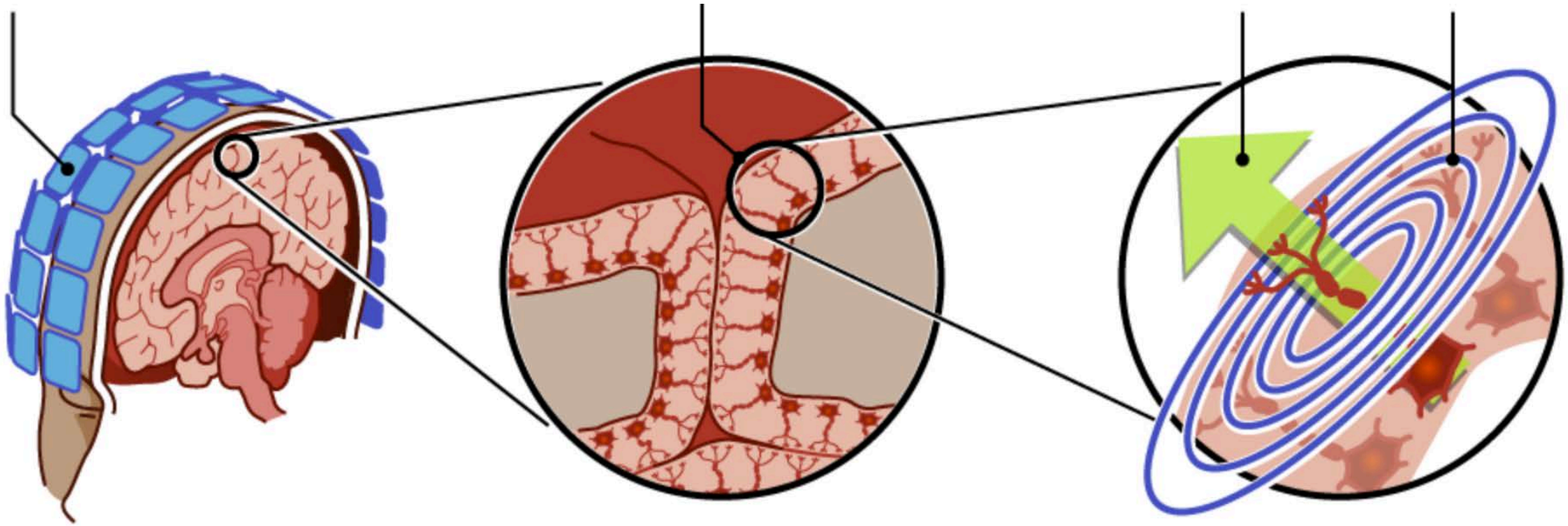
Neuromagnetic signals



# Indirect signals linked to neuronal activity

Neuromagnetic signals



# Magnetoencephalography (MEG)

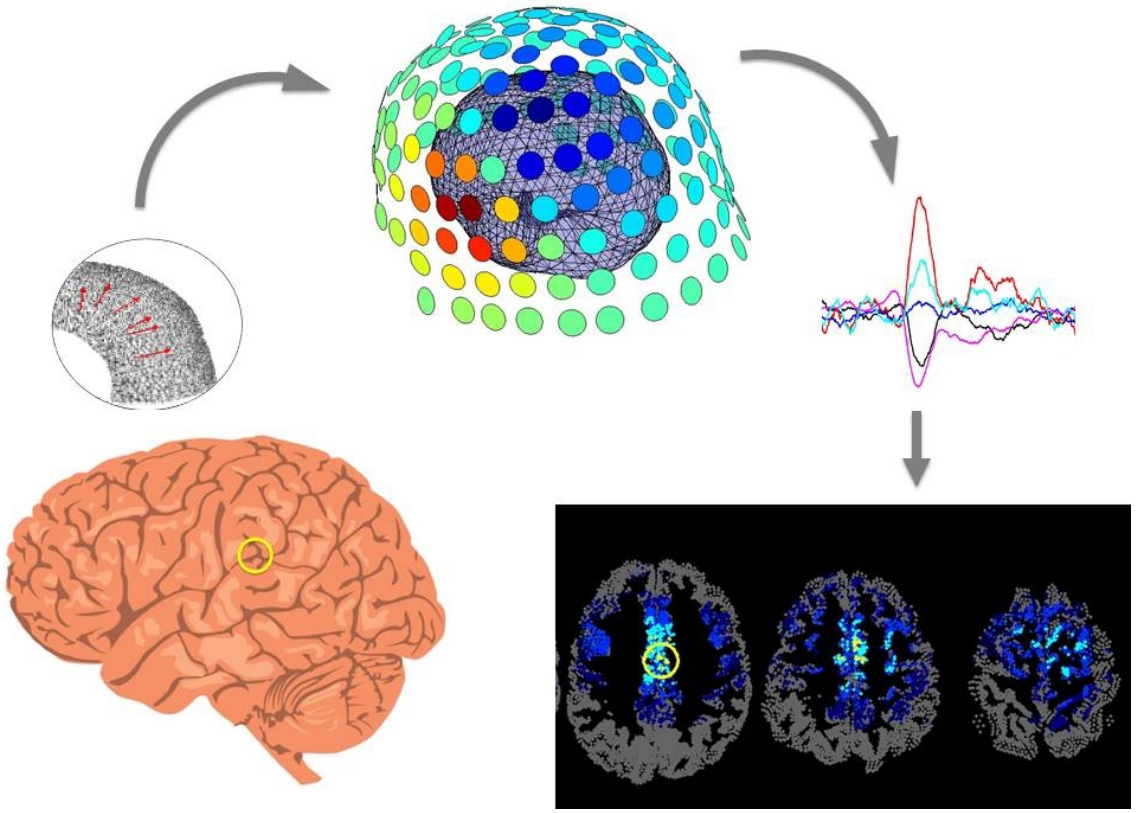



Superconducting sensors



# Magnetoencephalography (MEG)

- Inverse problem of signal localization

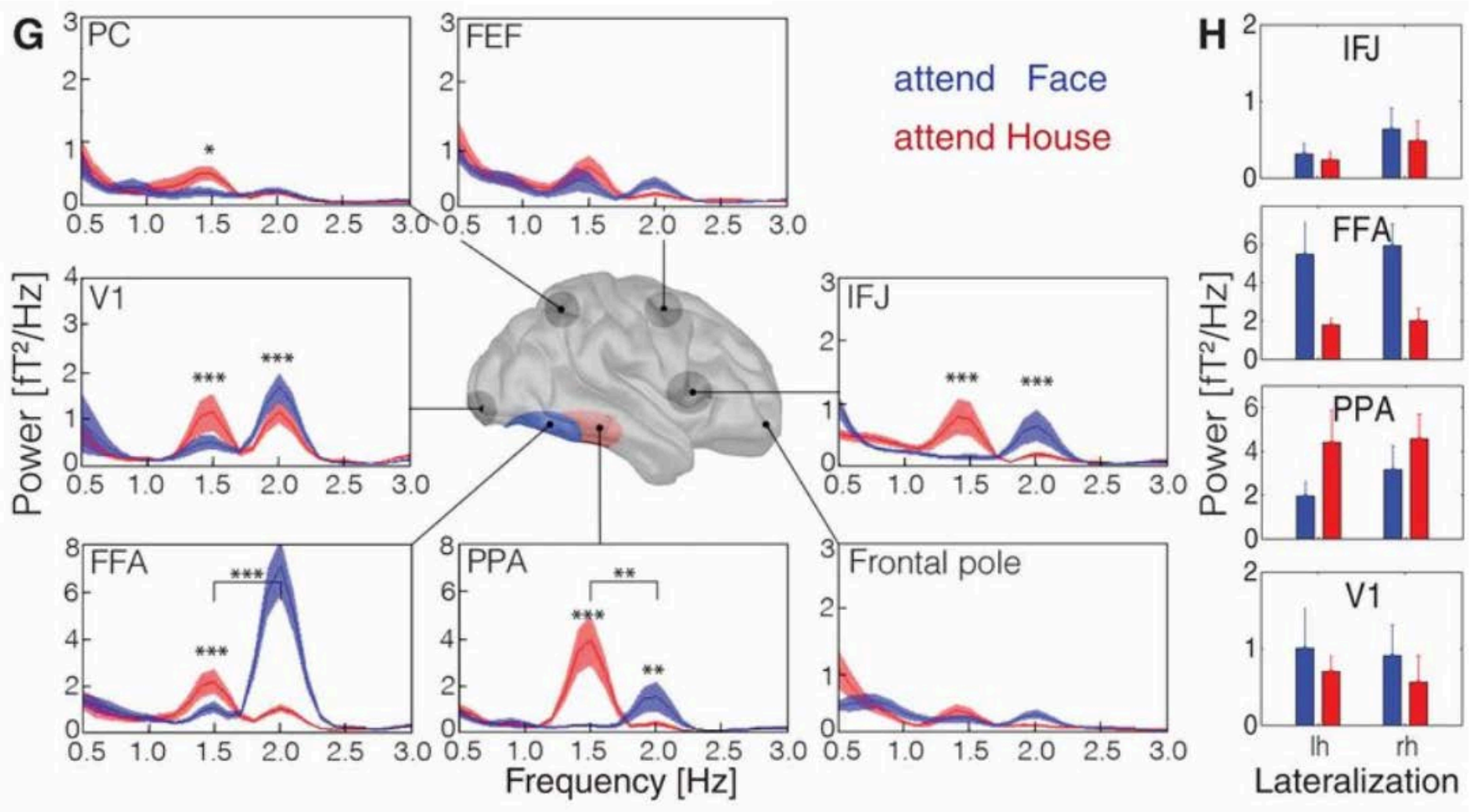


Superconducting sensors



# Magnetoencephalography (MEG)

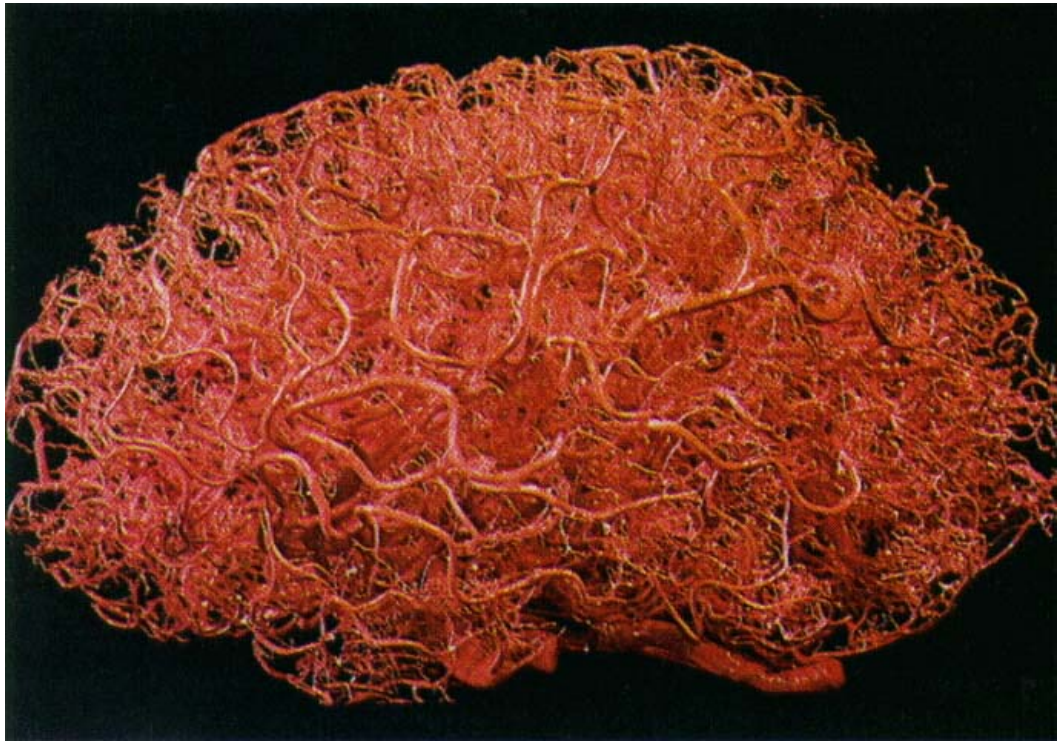
- MEG data



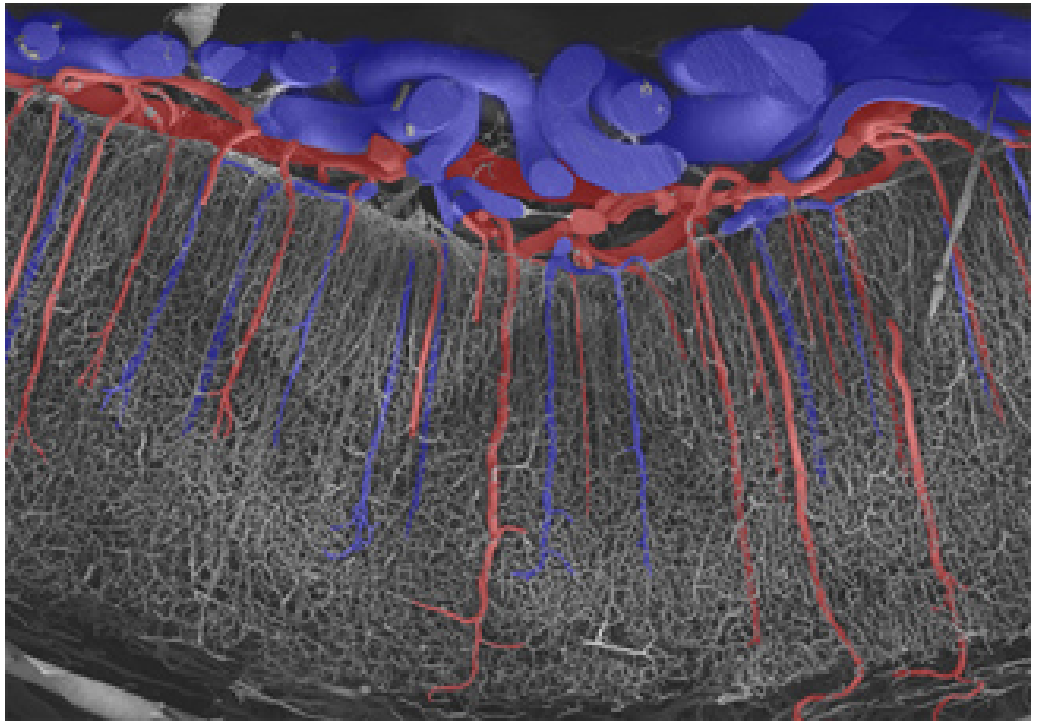

Baldauf and Desimone, 2014

# Indirect signals of neuronal activity: Neurovascular coupling

Whole brain vasculature

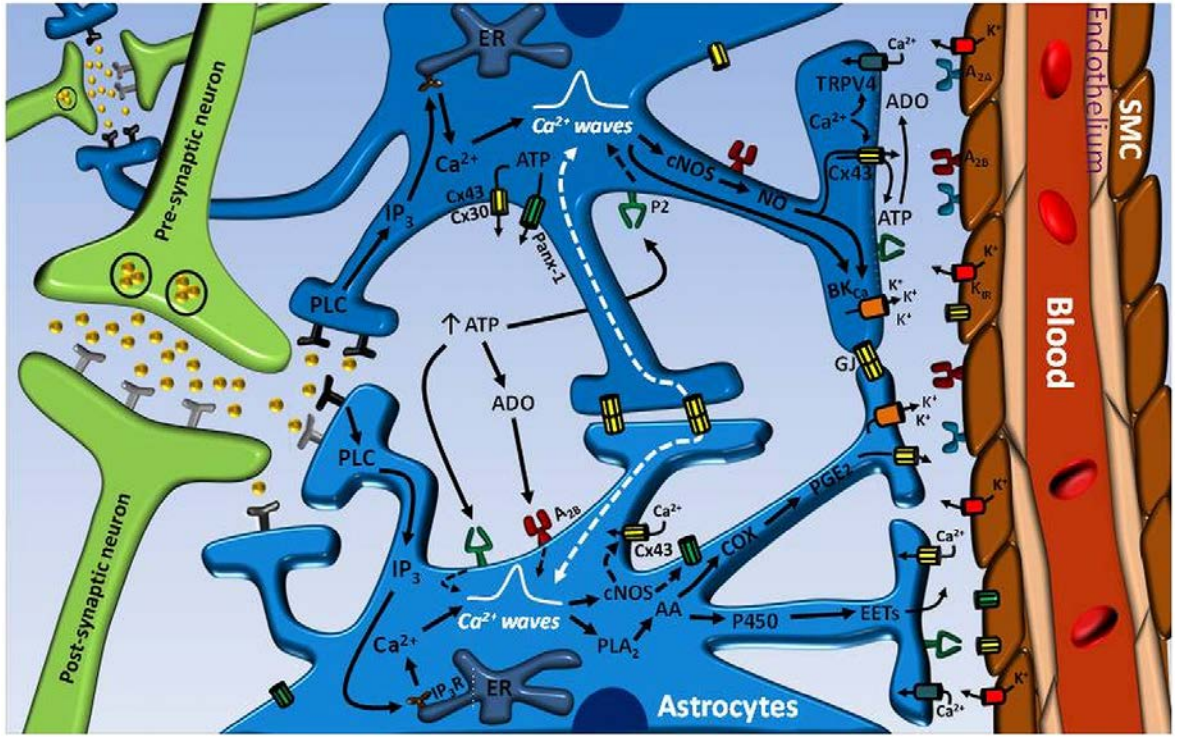


Macaque V1 microvasculature

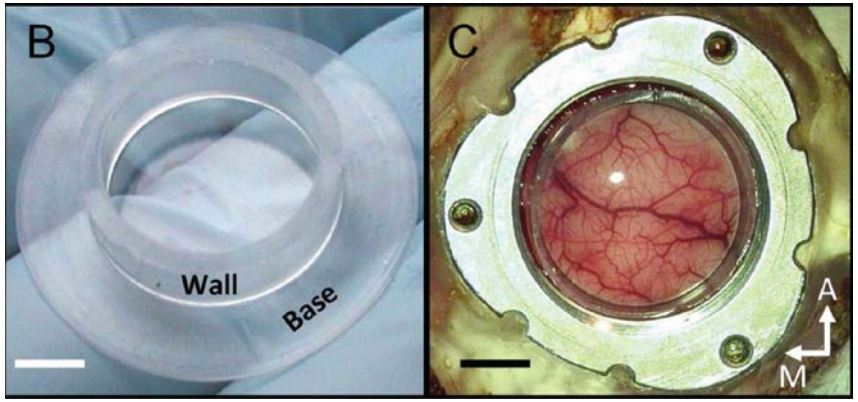


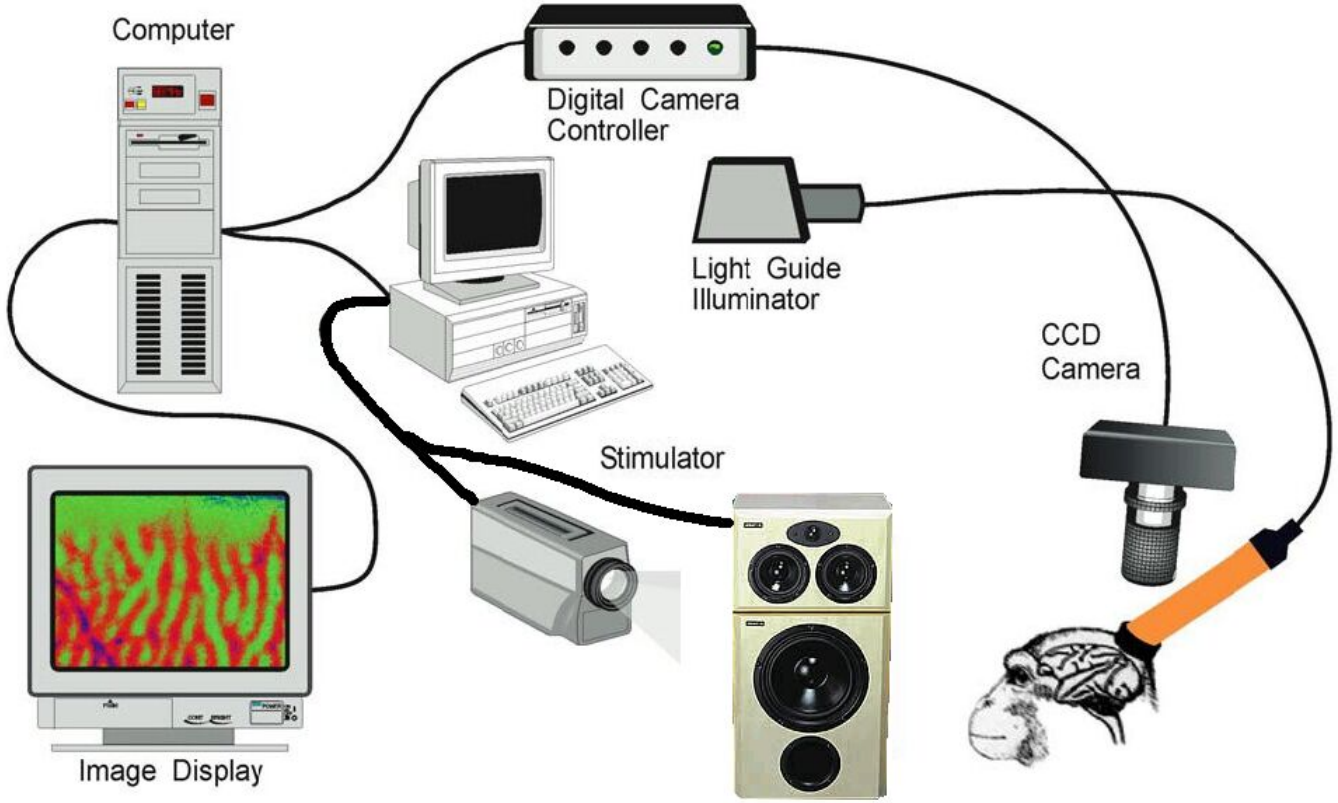
# Neurovascular coupling:
# Blood Oxygenation-Level Dependent (BOLD) signal

- 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.



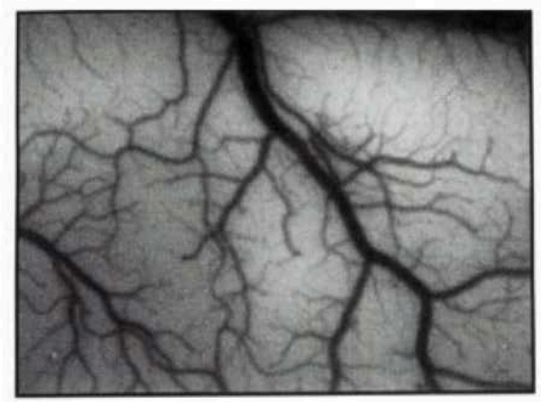
# Optical imaging (intrinsic signals)

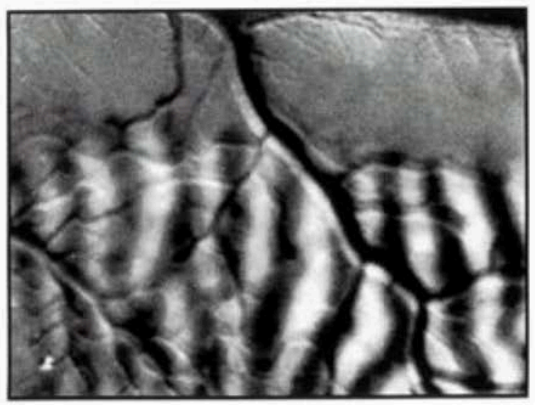


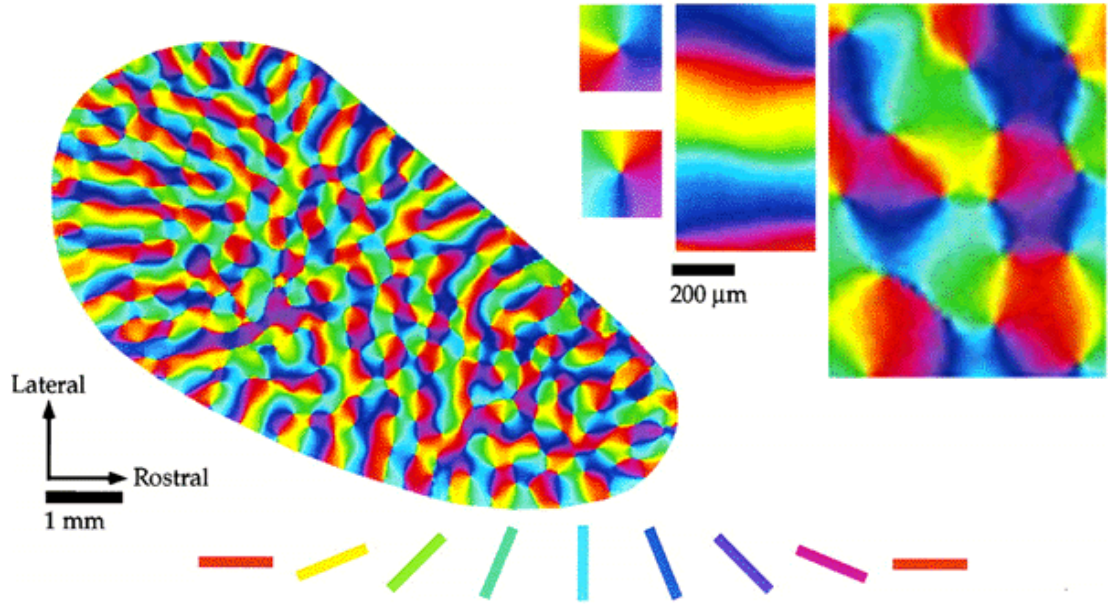



# Optical imaging (intrinsic signals)

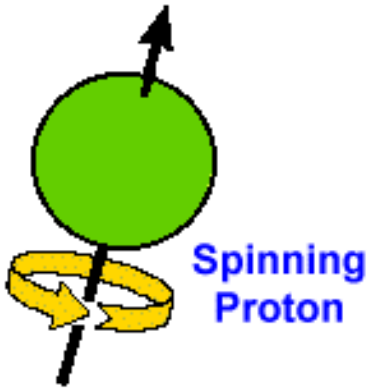
- Functional maps across cortical surface
- Ocular dominance columns
- Orientation columns

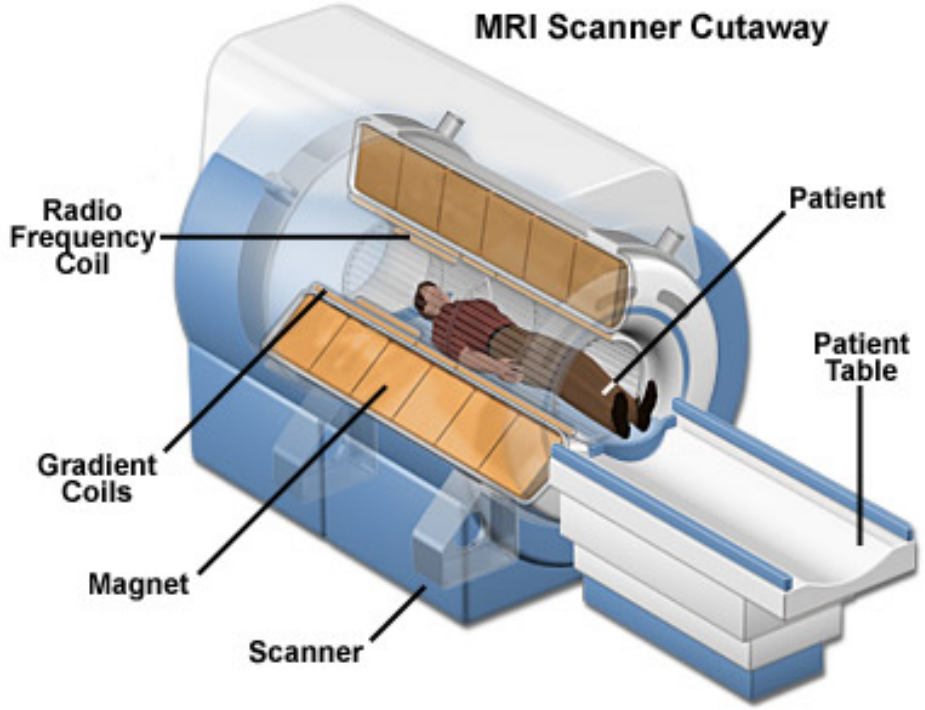


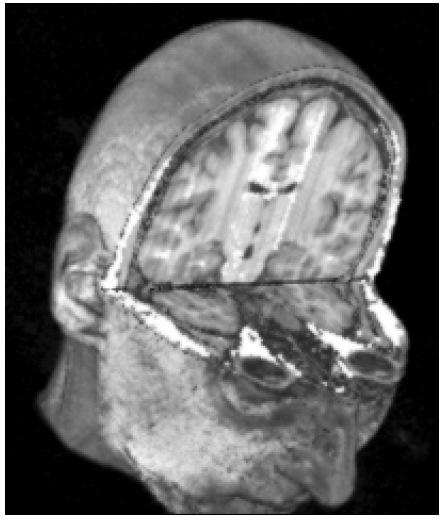


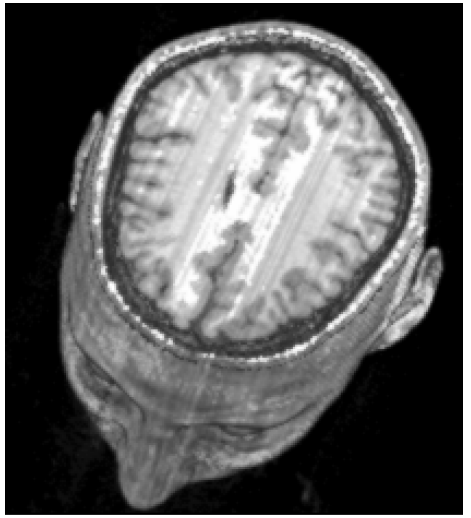


# Functional Magnetic Resonance Imaging (fMRI)

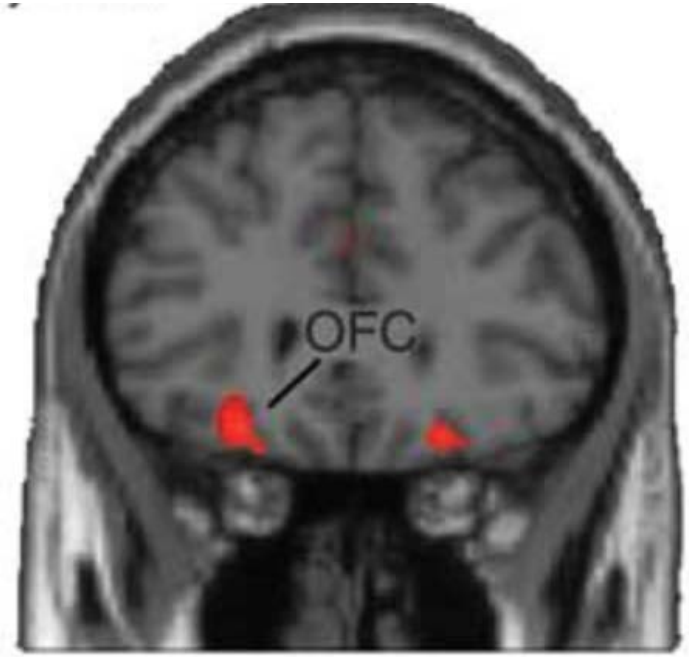


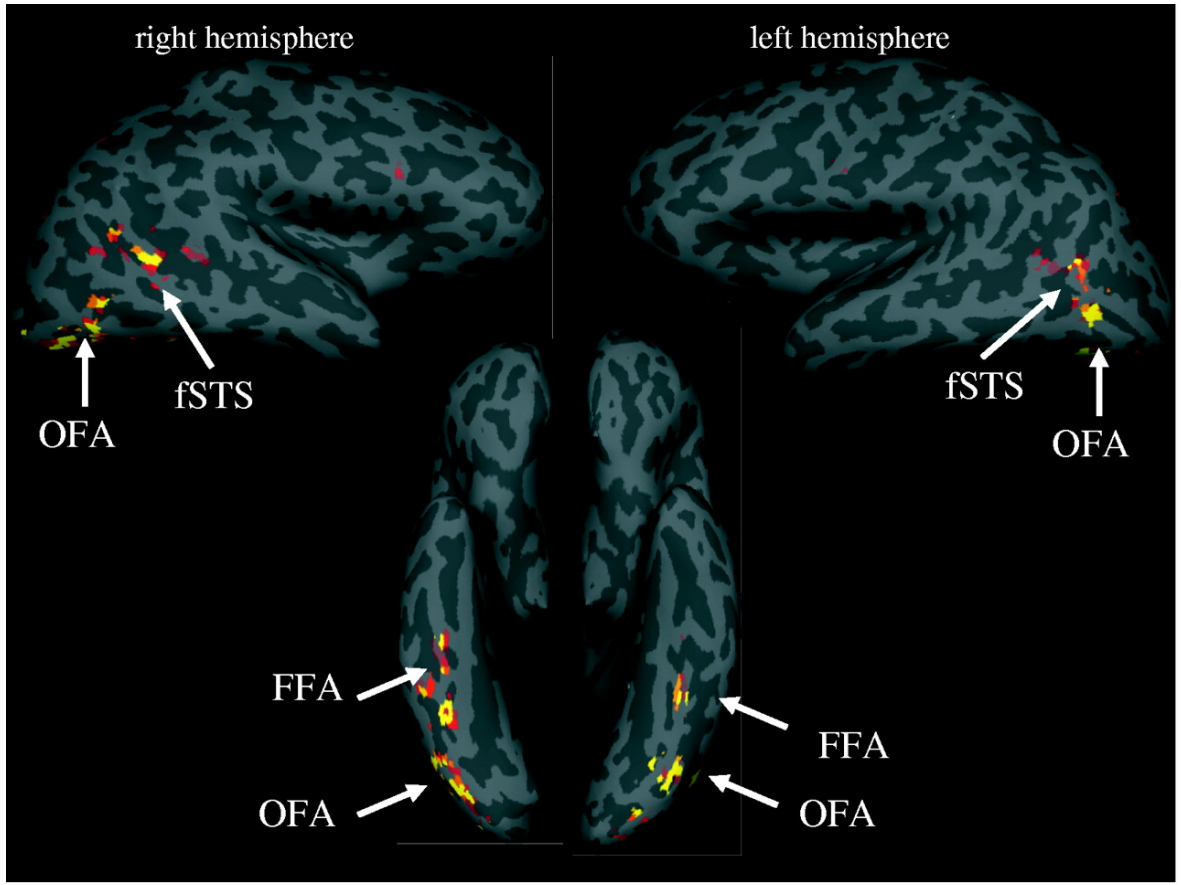





# Functional Magnetic Resonance Imaging (fMRI) Univariate method



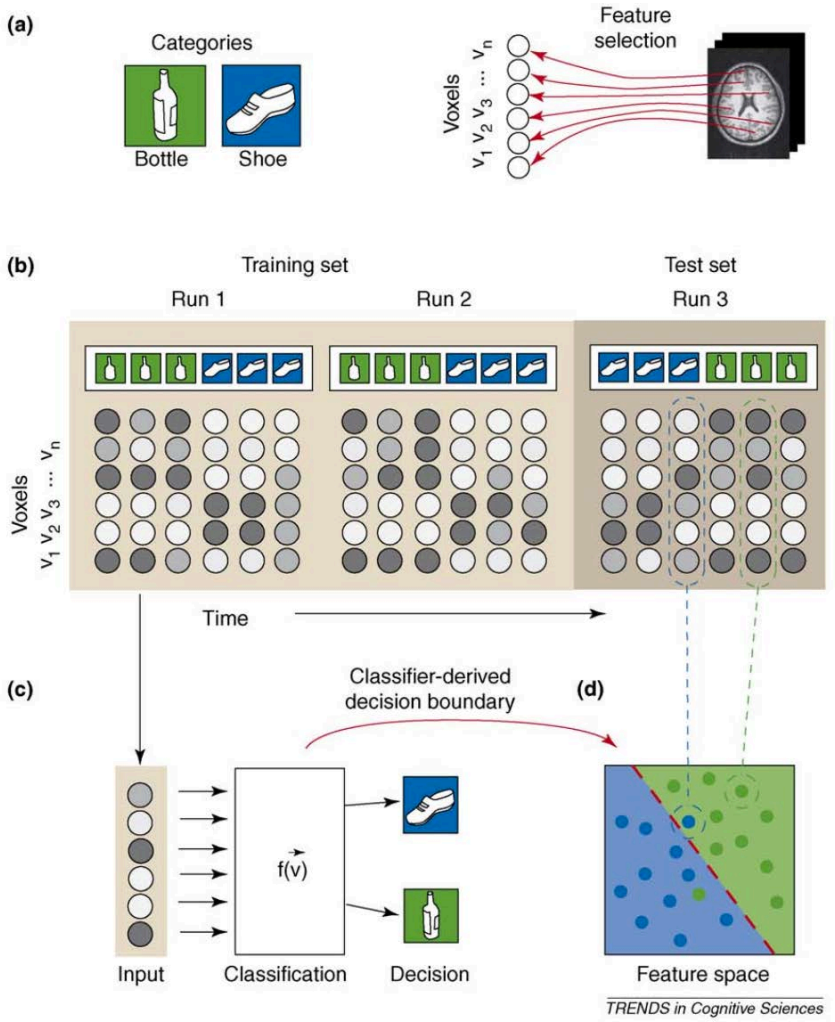

Face-selective activation (faces > objects, $p<0.0001$)



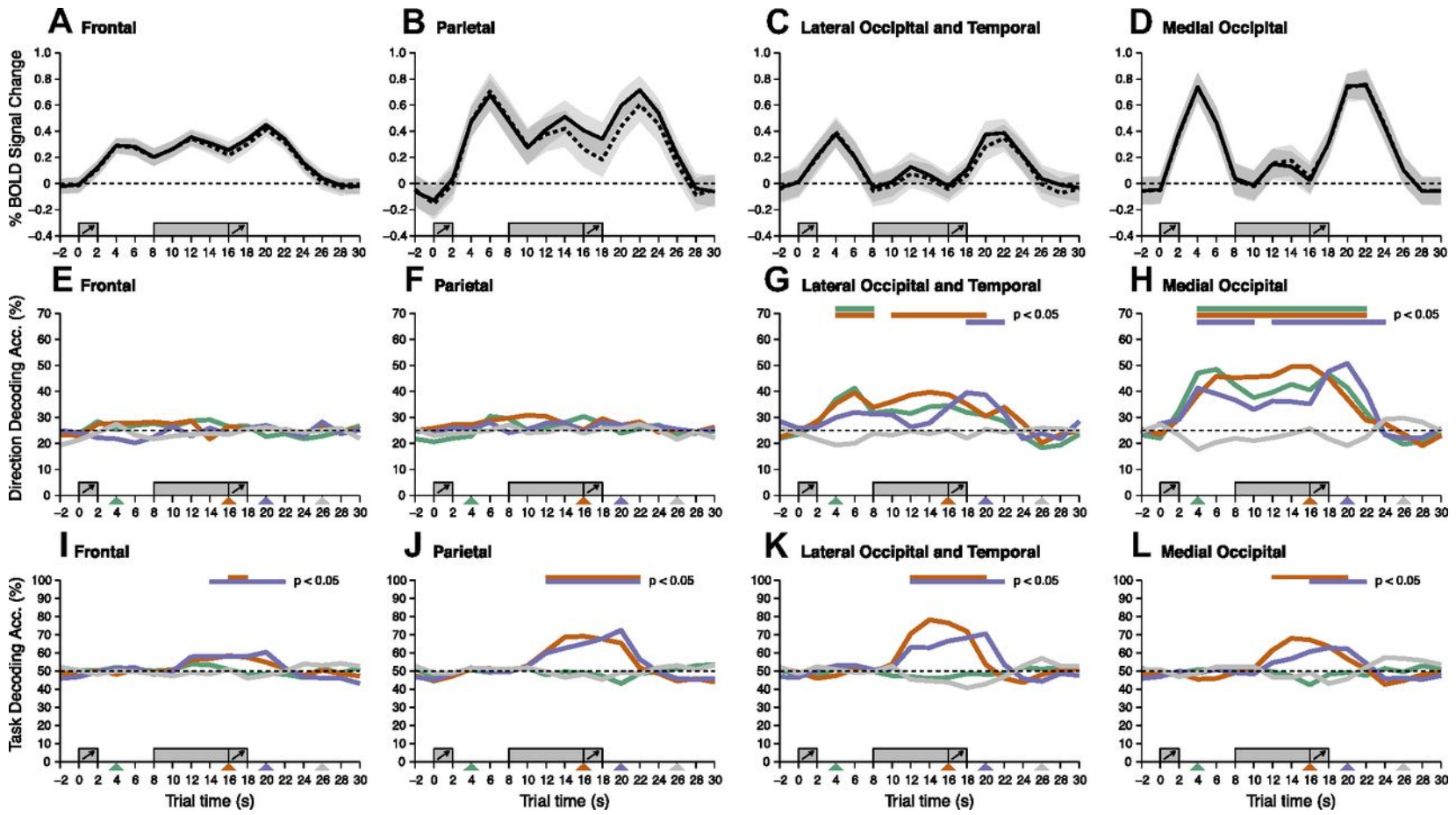

Kanwisher et al., 1997

# Functional Magnetic Resonance Imaging (fMRI) Multivariate method

Multivoxel Pattern Classification Analysis (MVPA)



# ROI BOLD and decoding time courses.



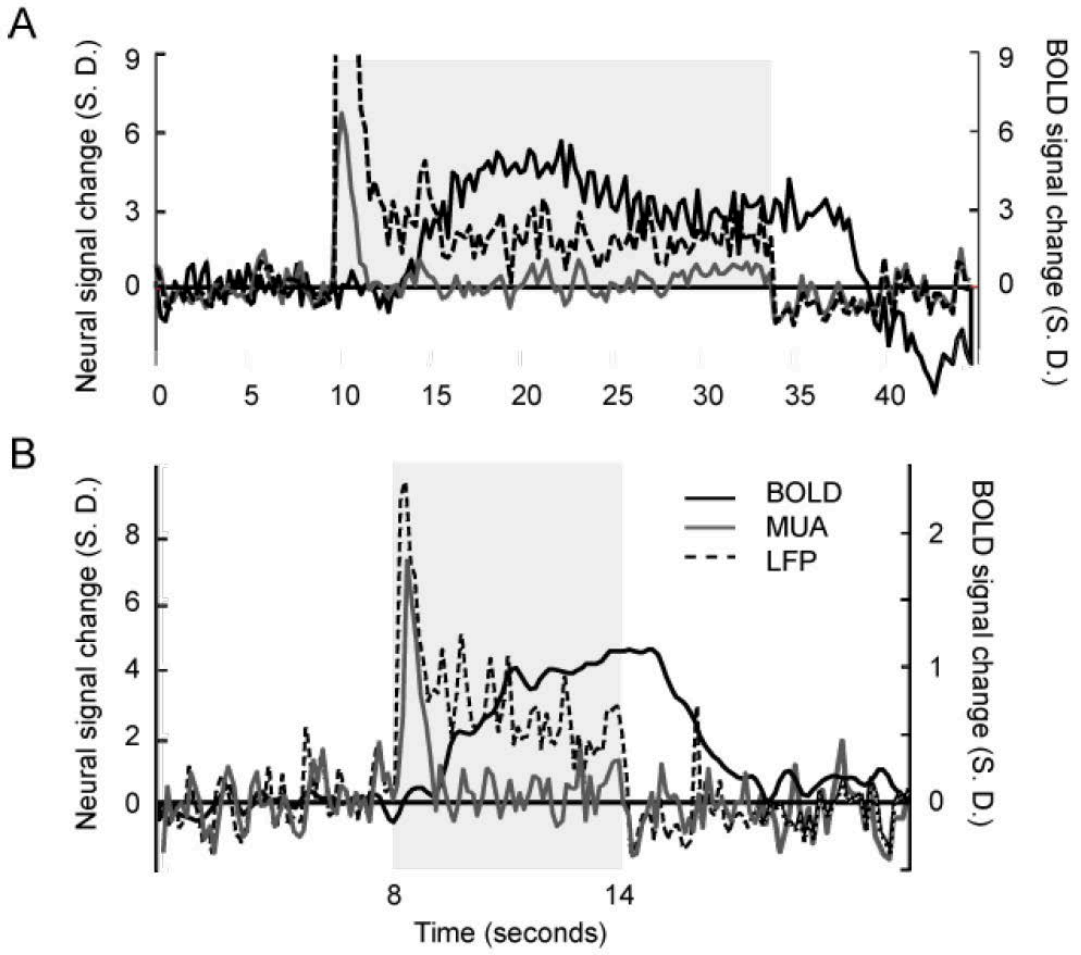

Adam C. Riggall, and Bradley R. Postle J. Neurosci. 2012;32:12990-12998

# Relationship between spikes, LFPs and BOLD

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

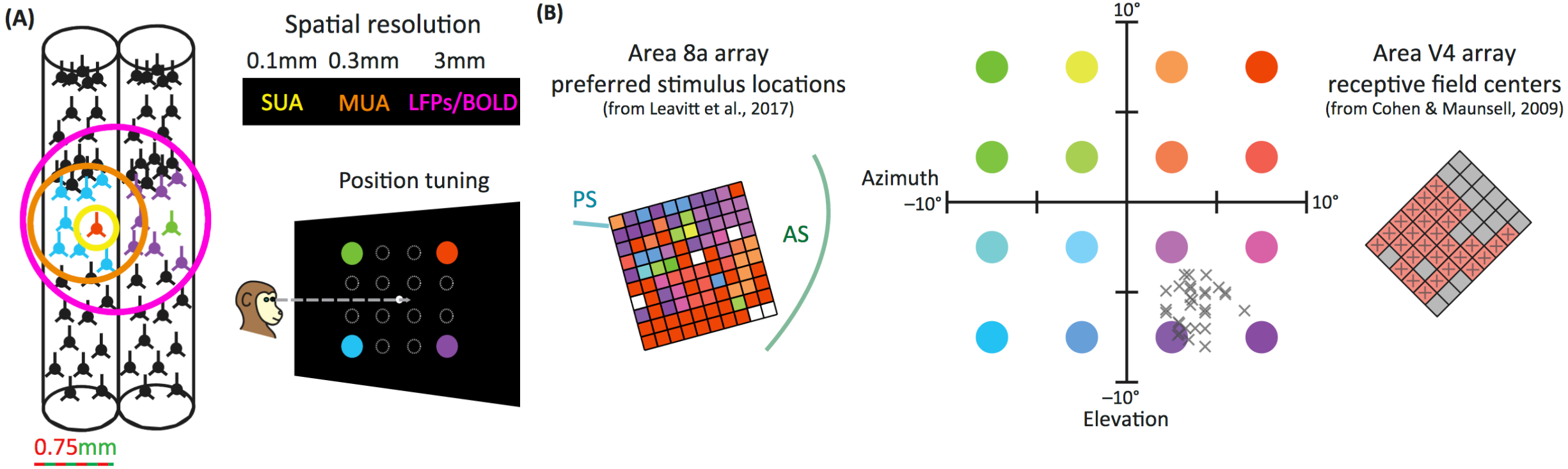
- BOLD correlates more with LFPs than with spikes.

- WARNING!

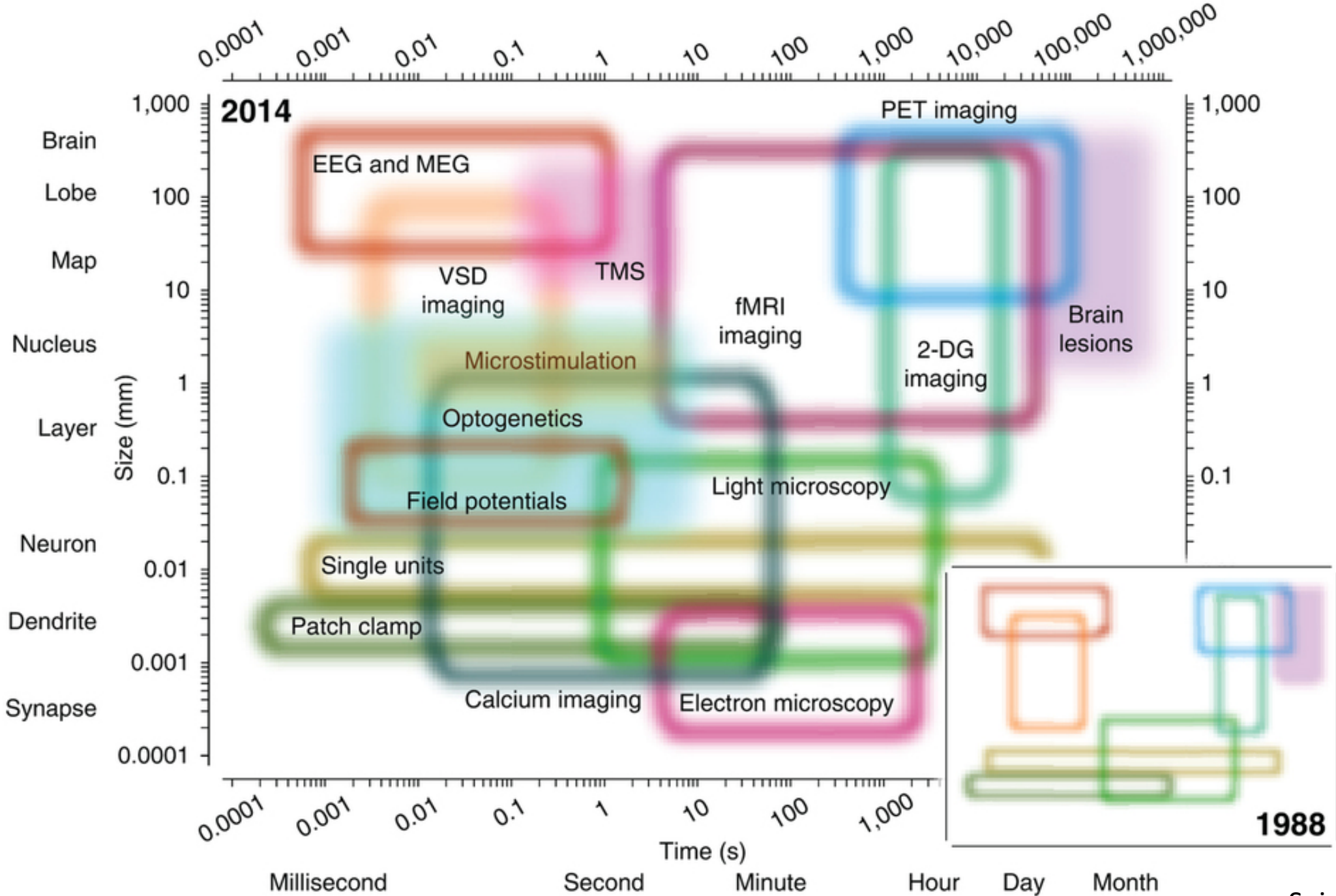



Berens et al., 2010

# Spatial extent of SUA, MUA, LFPs and BOLD




Leavitt, Mendoza-Halliday & Martinez-Trujillo, 2017




Sejnowski et al., 2014

# QUESTIONS?