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?

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

- Rising phase of the action potential
- Falling phase of the action potential
- Depolarization
- Extrinsic cellular fluid
- Plasma membrane
- Sodium channel
- Ion channel
- Undeveloped
- Resting state

Synaptic transmission

- Myelin
- Synaptic vesicle
- Transmitter molecules
- Synaptic receptor
- Transmitter molecules
- Postsynaptic current flow

Local field potentials (LFP)

- 1 nA
- 0.1 μV
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

2D matrix electrode array

3D matrix electrode array

Tetrode

Linear 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

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

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  - Local field potentials

- Chemical signals:
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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.

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!
Spatial extent of SUA, MUA, LFPs and BOLD

Leavitt, Mendoza-Halliday & Martinez-Trujillo, 2017
QUESTIONS?