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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
Action potentials
Synaptic transmission

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

- Electrical signals:
  - Postsynaptic currents – Local field potentials
Local Field Potentials (LFP): perisynaptic currents

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
Spike waveform analyses

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

**RASTER PLOT**

- Trials
- Firing rate (sp/s)
- Time (s)

**PERISTIMULUS TIME HISTOGRAM (PSTH)**

**SPIKE DENSITY FUNCTION**
Types of microelectrodes

- Single microelectrode
- Tetrode
- Linear electrode array
  - 8 single electrodes
  - 19 single electrodes
  - 24 single electrodes
  - 4 stereotrodes
  - 8 stereotrodes
  - 12 stereotrodes
  - 2 tetrodes
  - 4 tetrodes
  - 6 tetrodes
- 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:
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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)
Magnetoencephalography (MEG)

- Inverse problem of signal localization
Magnetoencephalography (MEG)

- MEG data
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!

Berens et al., 2010
Spatial extent of SUA, MUA, LFPs and BOLD

Leavitt, Mendoza-Halliday & Martinez-Trujillo, 2017
Sejnowski et al., 2014
QUESTIONS?