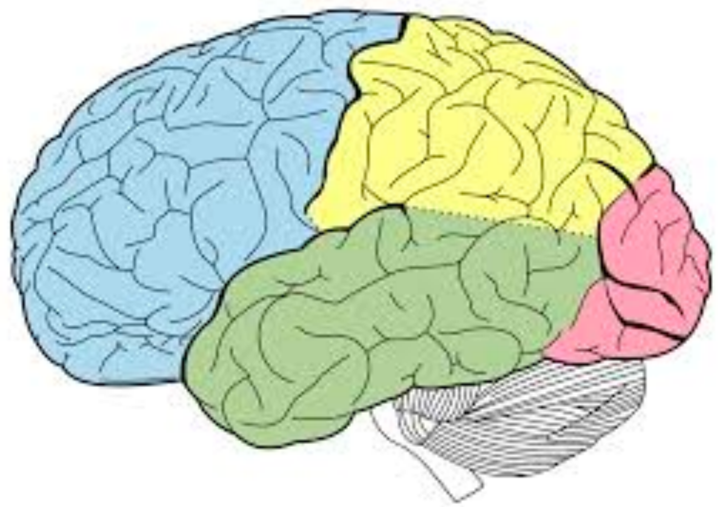
Question of the Day

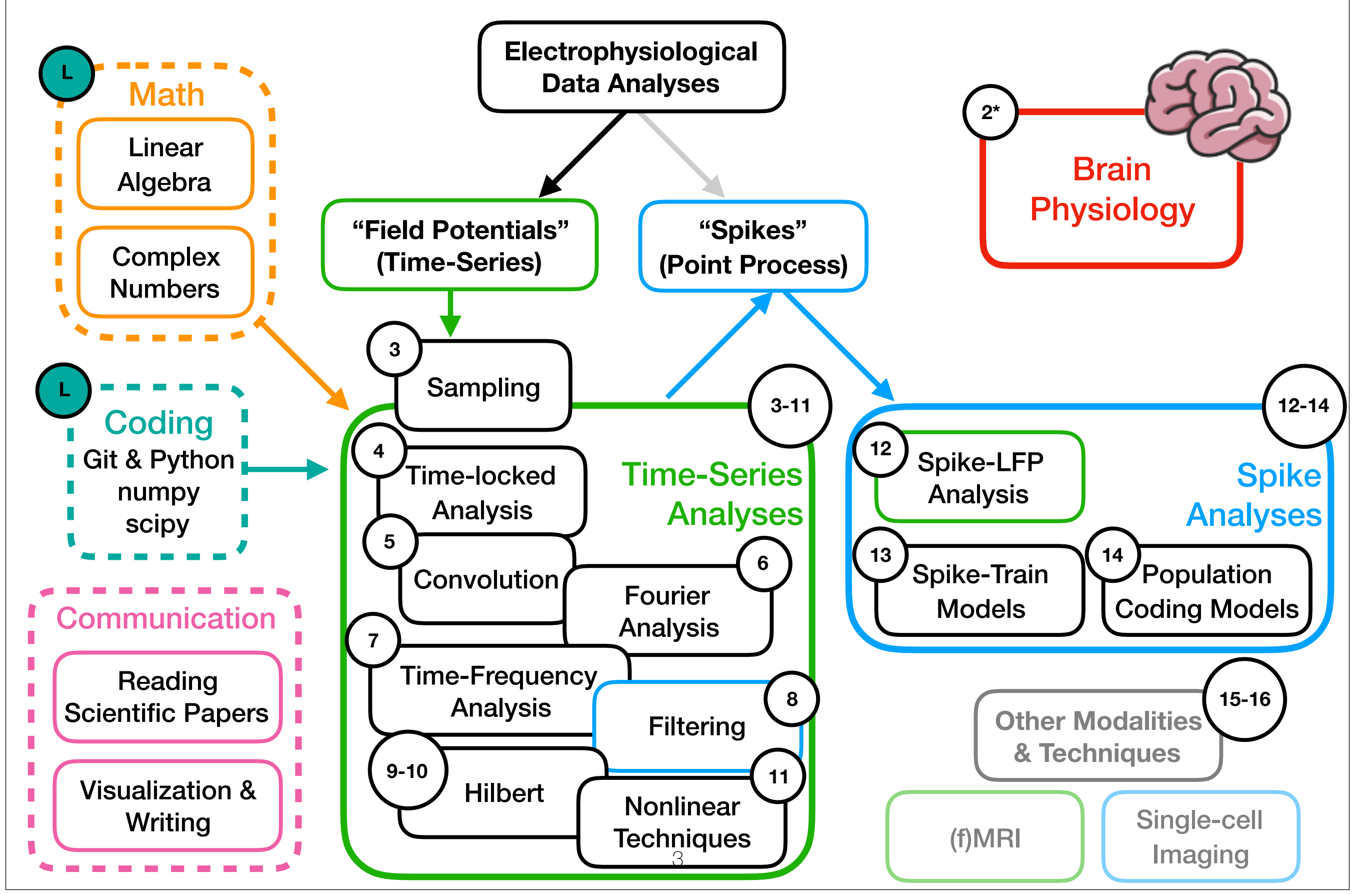


Which part of the human brain shown here has the highest number of neurons?

Crash Course
Neurophysiology

Lecture 2
July 2, 2019

Course Outline: Road Map



Goals for Today

1. Review the cellular and anatomical components of the brain.

2. Map out the different neural signal modalities.

3. Understand the detailed mechanism behind electrical signals in the brain.

Disclaimer: there is still a LOT we don't know about the brain.

The Nervous System

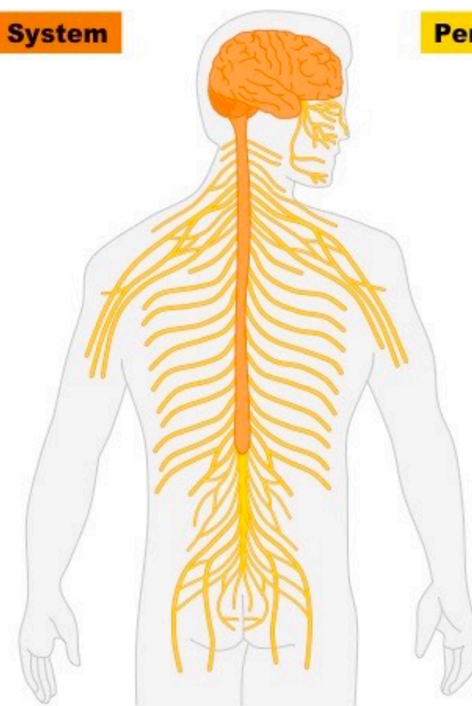
Central Nervous System

Composed of:

- Brain
- Spinal cord

Contains:

- Relay neurons (interneurons)



Peripheral Nervous System

Composed of:

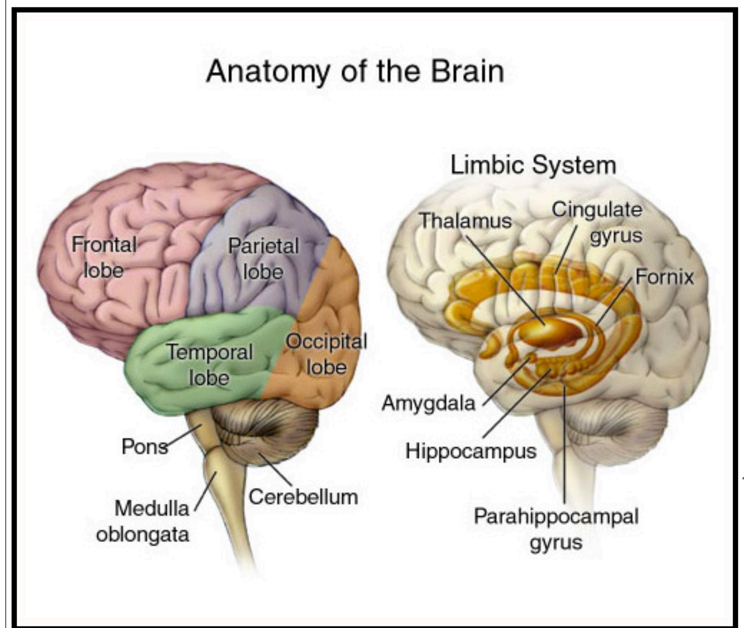
- Cranial nerves
- Spinal nerves
- Peripheral nerves

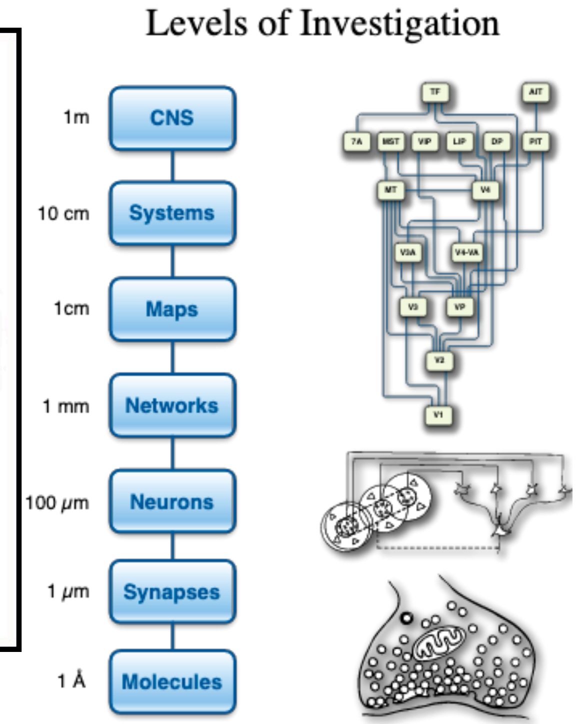
Contains:

- Sensory neurons
- Motor neurons

Our brains are embedded inside a body, connected to a vast network of peripheral nerves. Never forget that!

Components of the Brain





Sejnowski Lab, Salk Institute

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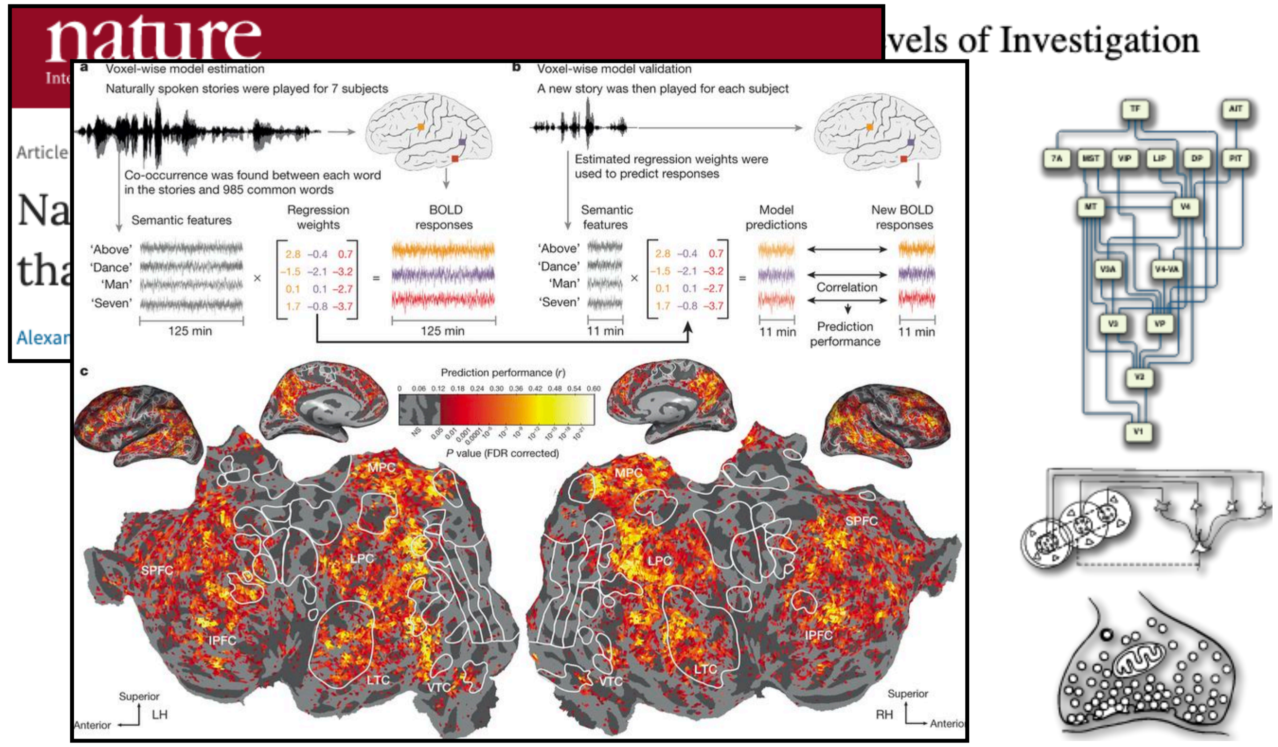
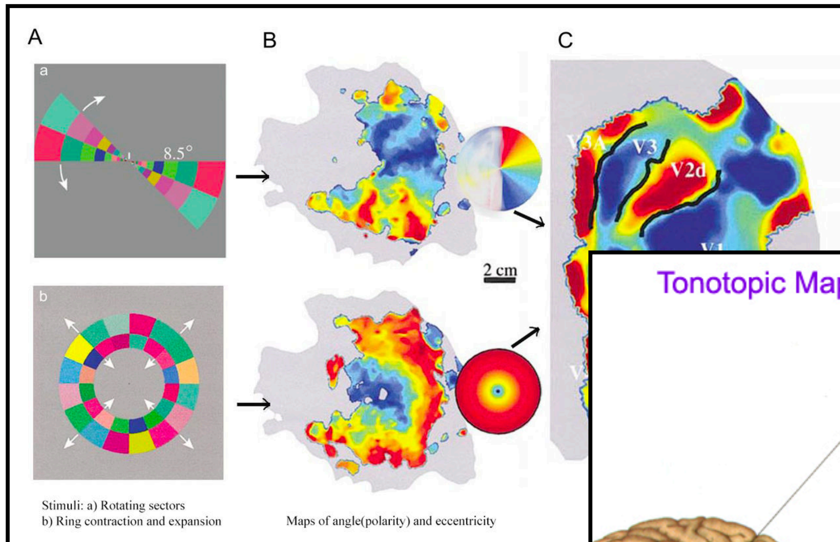
Macro regions of the brain - at least know where these things are, and their rough function:
Occipital lobe: visual processing
Temporal lobe: auditory/speech processing
Parietal lobe: bodily sensation (see sensory homunculus)
Frontal lobe: initiating movement of limbs (see motor homunculus), higher order cognitive processes (e.g., self control, working memory)
Cerebellum: fine motor coordination
Hippocampus: long-term memory, spatial memory
Thalamus: sensory relay, know which sense does **not** enter the thalamus
Amygdala: emotion activation, fear

Components of the Brain



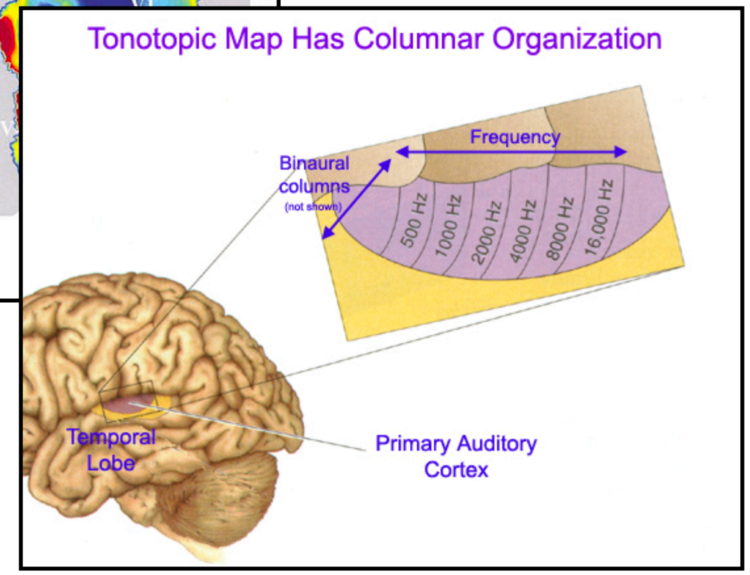
Functional organization (maps) across the cortical surface

Functional Organization



V1: “Retinotopic” Map

A1: “Tonotopic” Map



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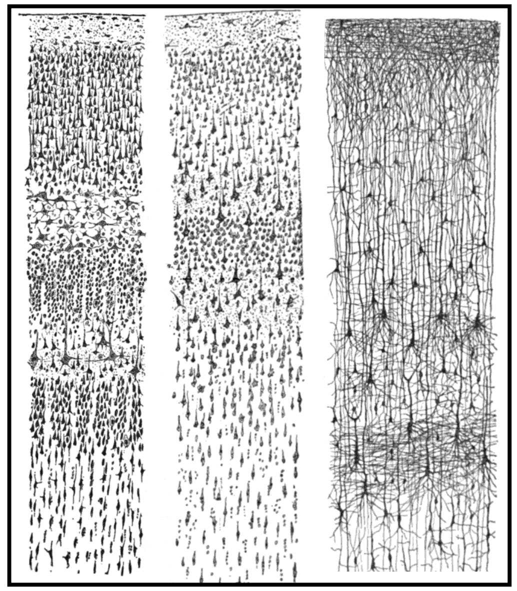
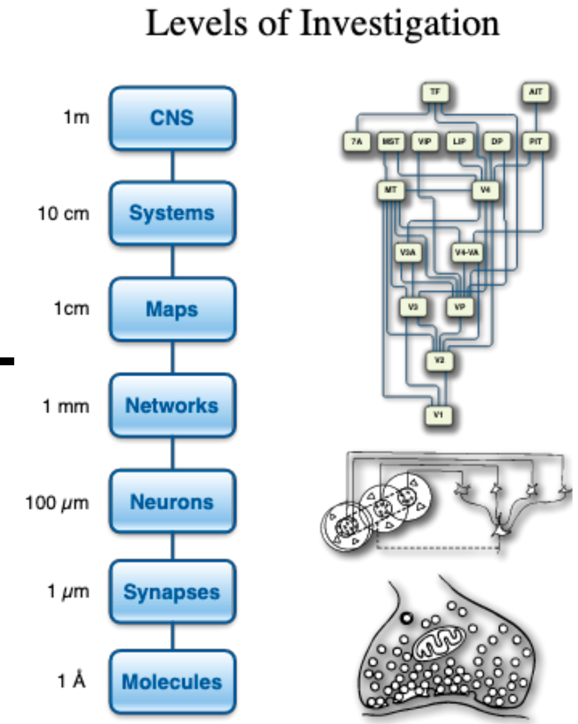
Brain circuits, columns, and layers.
Know what retinotopic and tonotopic mean

Components of the Brain



Cortical Columns
Ramon y Cajal

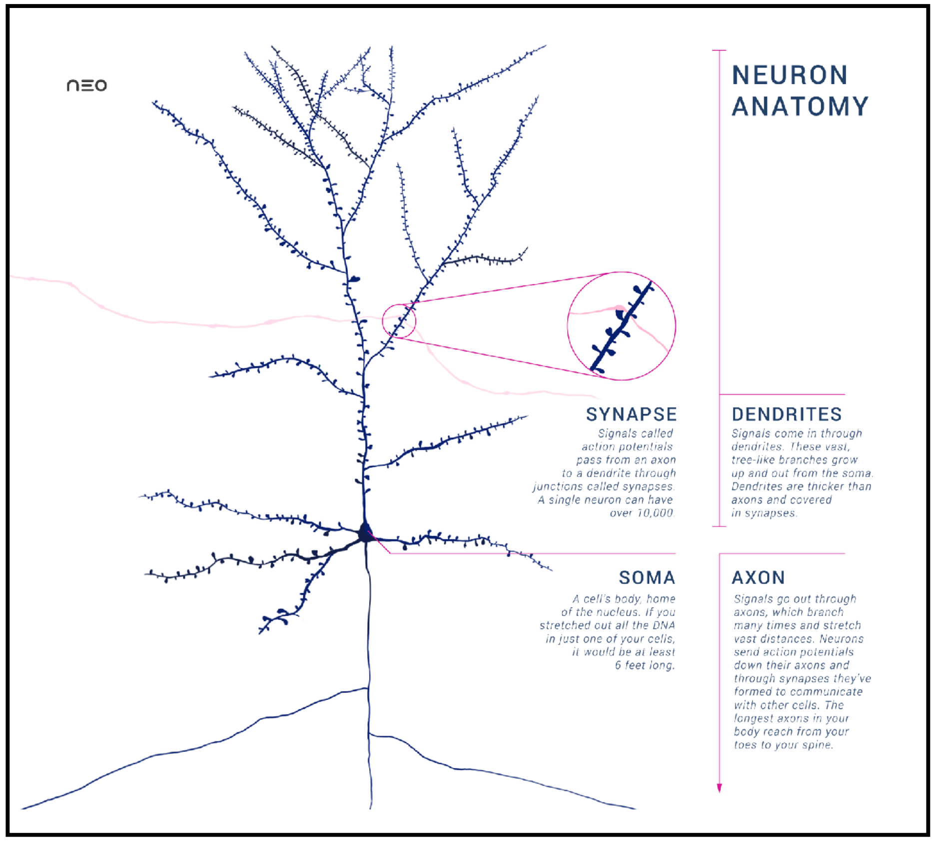


Cortical columns, layers, and neurons.

Brain Cells

Receive inputs

Send outputs



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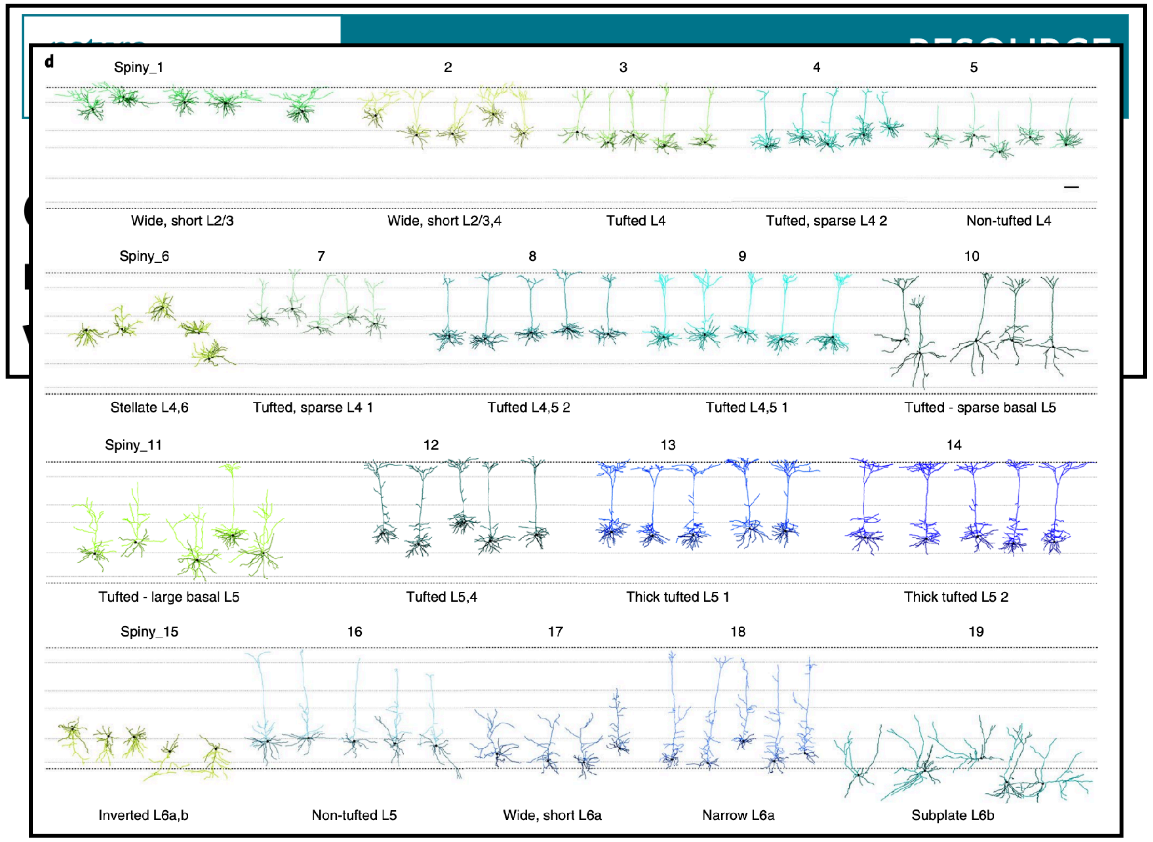
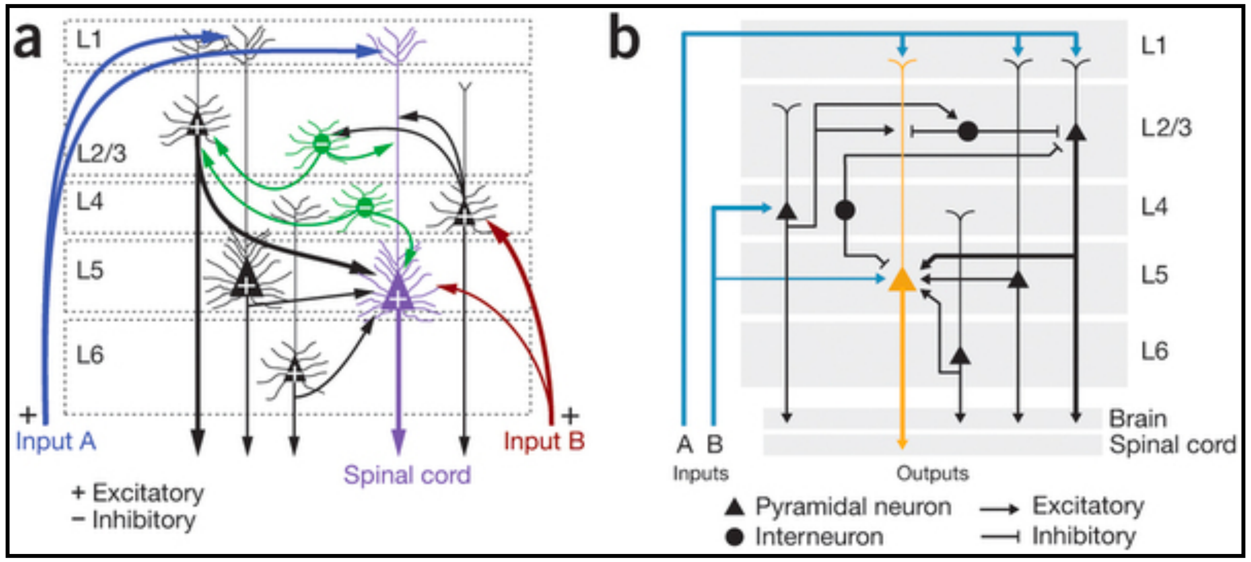
This is what a single neuron looks like.
Know the components of a pyramidal neuron (shown here), and their function.

Neurons



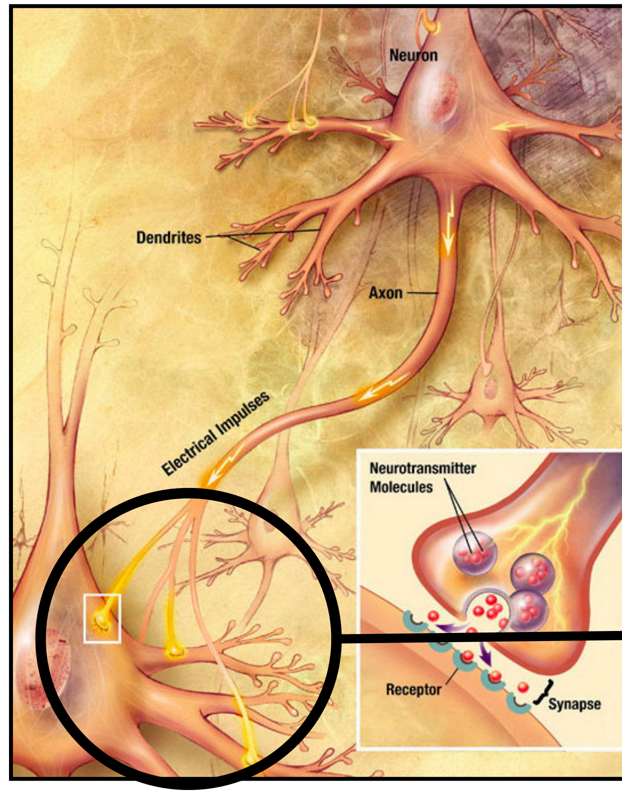
We’re still cataloguing and discovering more types of cells, even neurons. This is an unsolved problem.

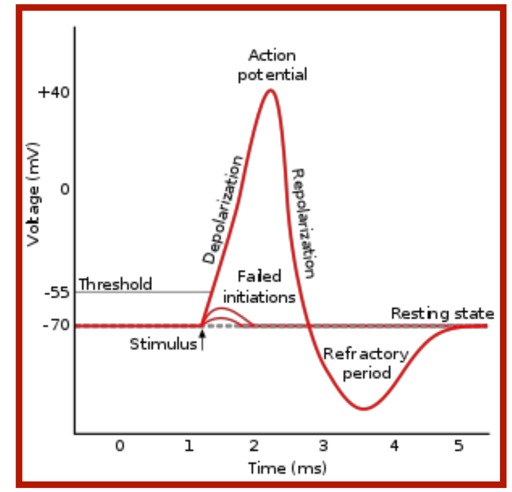
Neuronal Networks



Neurons and other types of brain cells connect together to form neural circuits.

Neurons & Synapses

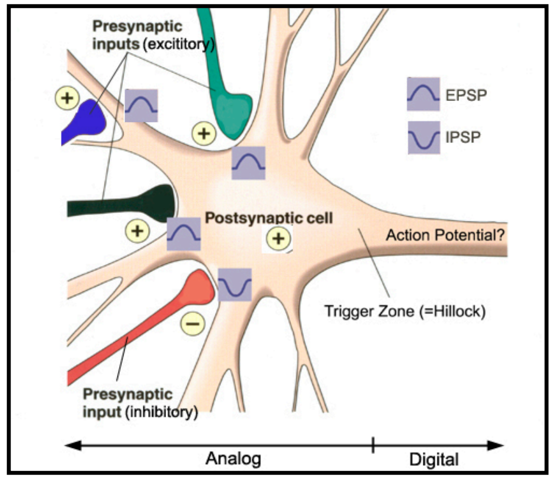


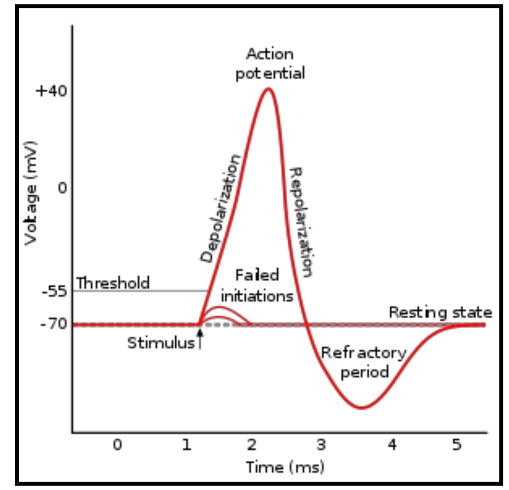


This is, for the most part, what generates the signals we will be studying.

Neurons communicate through action potentials, which trigger neurotransmitter release at synaptic terminals, changing the downstream neuron’s membrane potential.

(Very) Brief Intro on Neuronal Dynamics





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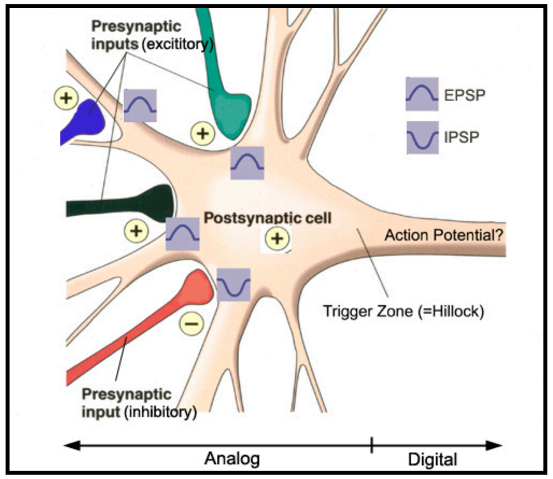
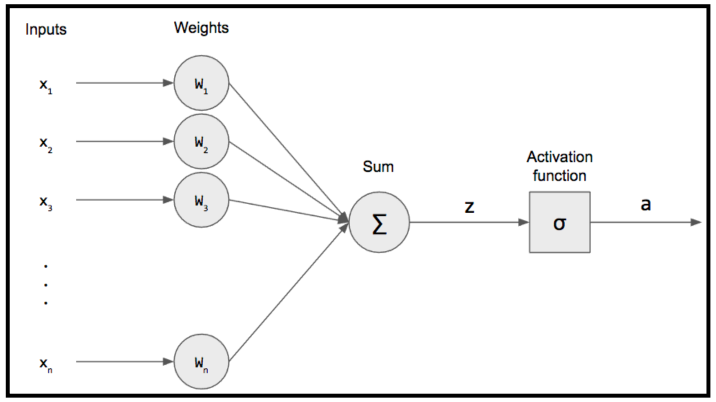
The neuron integrates its upstream excitatory and inhibitory inputs, until it crosses an AP threshold and fires an action potential
Know the different kinds of synapses (excitatory vs. inhibitory), and their effect on membrane potential of downstream neuron (depolarizing vs. hyperpolarizing). Know the phases of the action potential generation, as well as AP threshold.

Aside: Neuronal Computation

Synaptic Integration



Perceptron (Artificial Neural Network)



The perceptron in an ANN is a heavy abstraction of the synaptic integration that neurons perform.

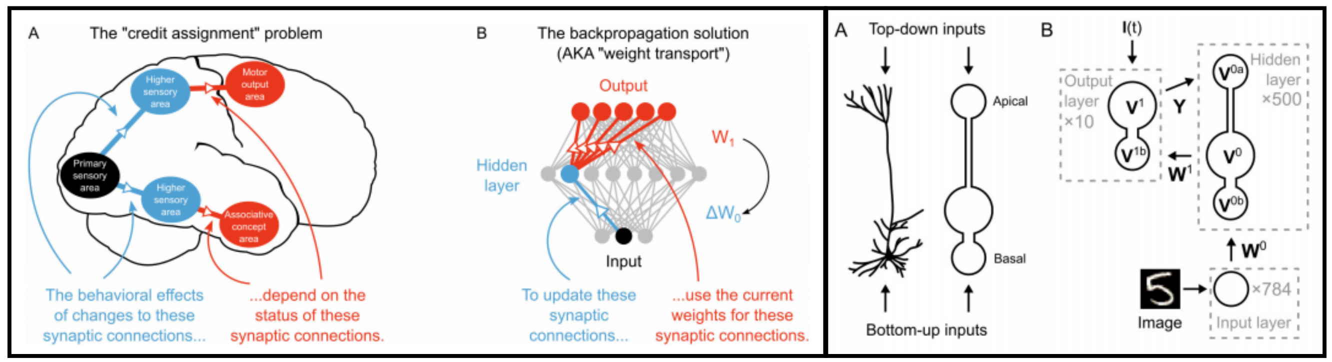
Aside: Neuronal Computation

Towards deep learning with segregated dendrites

Jordan Guerguiev[1,2], Timothy P Lillicrap[3], Blake A Richards[1,2,4*]

[1]Department of Biological Sciences, University of Toronto Scarborough, Toronto, Canada; [2]Department of Cell and Systems Biology, University of Toronto, Toronto, Canada; [3]DeepMind, London, United Kingdom; [4]Learning in Machines and Brains Program, Canadian Institute for Advanced Research, Toronto, Canada

Credit assignment and Backpropagation



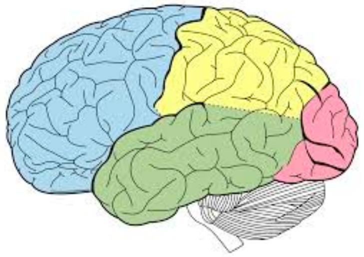
Better approximation of the physical neuron can do more sophisticated computations.

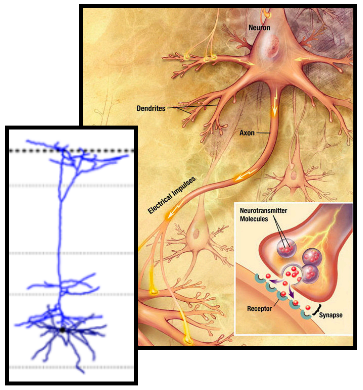
Goals for Today

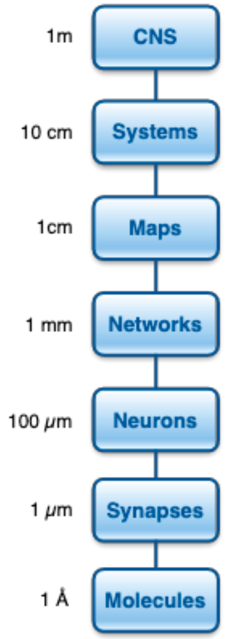
1. Review the cellular and anatomical components of the brain.
2. Map out the different neural signal modalities.
3. Understand the detailed mechanism behind electrical signals in the brain.

Exploring Brain Space

~ 80 billion neurons in the brain, along with billions of other cells

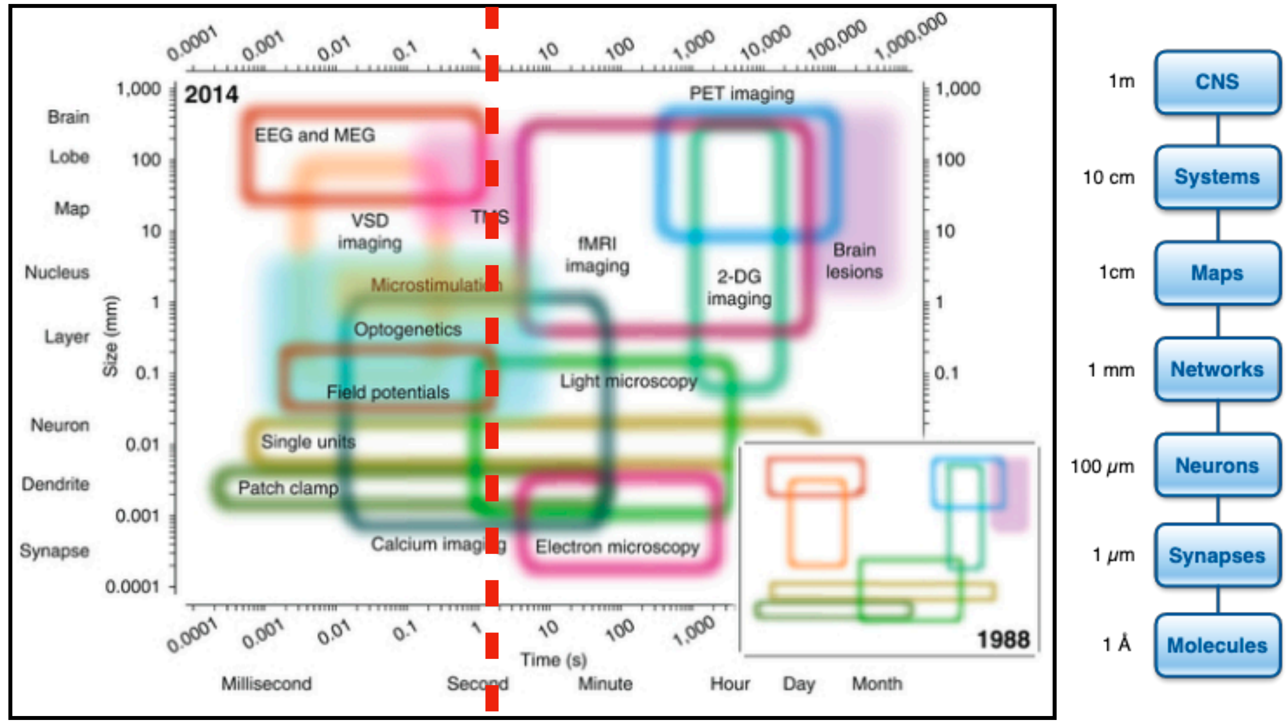






Mapping out different types of neural signals, across many scales. It's like exploring the frontiers of space, kinda?

Exploring Brain Space



~ Electrophysiology ~ Imaging

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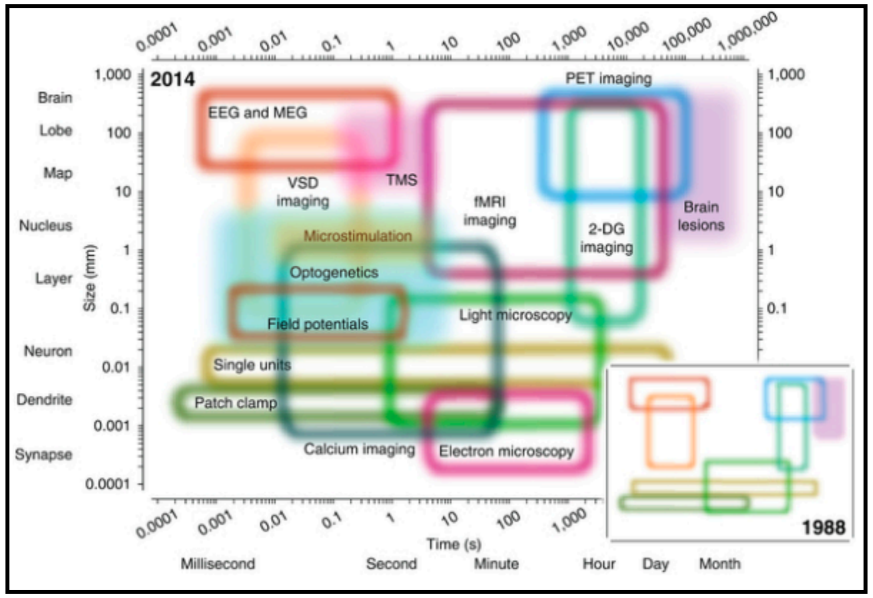
Studying the brain requires recording data spanning several orders of magnitude in both space and time
Know the different modalities, especially the ones we highlighted in electrophysiology, and their spatial and temporal scale.

Exploring Brain Space



Know the approximate spatial & temporal scales!

3 min: List 3 examples of behaviors/changes that occur to you along the spectrum of timescales.

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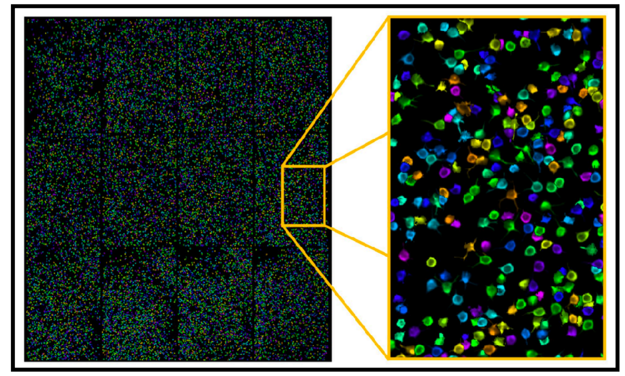
Studying the brain requires recording data spanning several orders of magnitude in both space and time

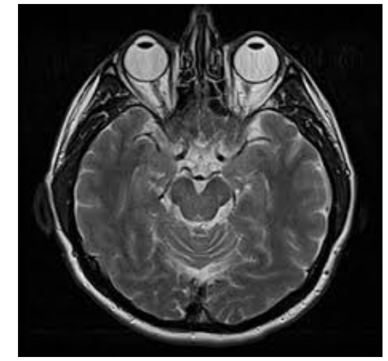
Imaging

Cellular

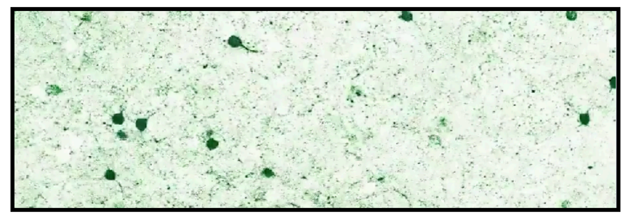
Regional

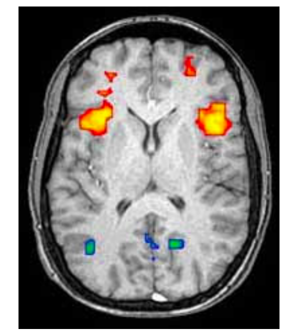
Anatomical





“Functional”



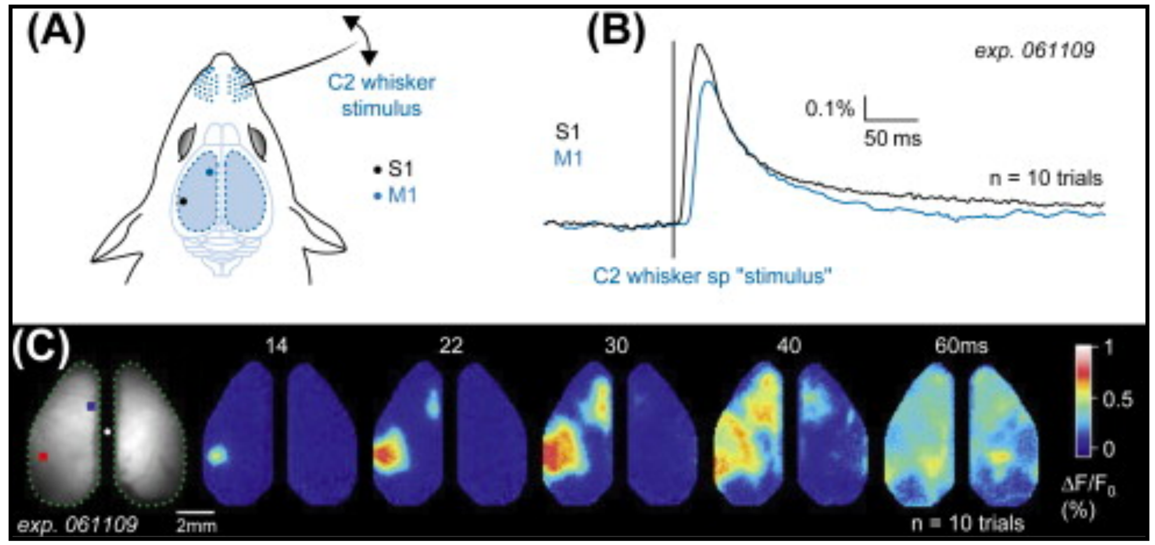


“Imaging” (loosely defined) typically requires taking some kind of literal image of an underlying metabolic/slower process.

left: Intracellular dye, calcium fluctuations; right: magnetic resonance (MR), BOLD (blood oxygenation)

Whole-Brain (Wide-Field) Imaging

Voltage Sensitive Dye



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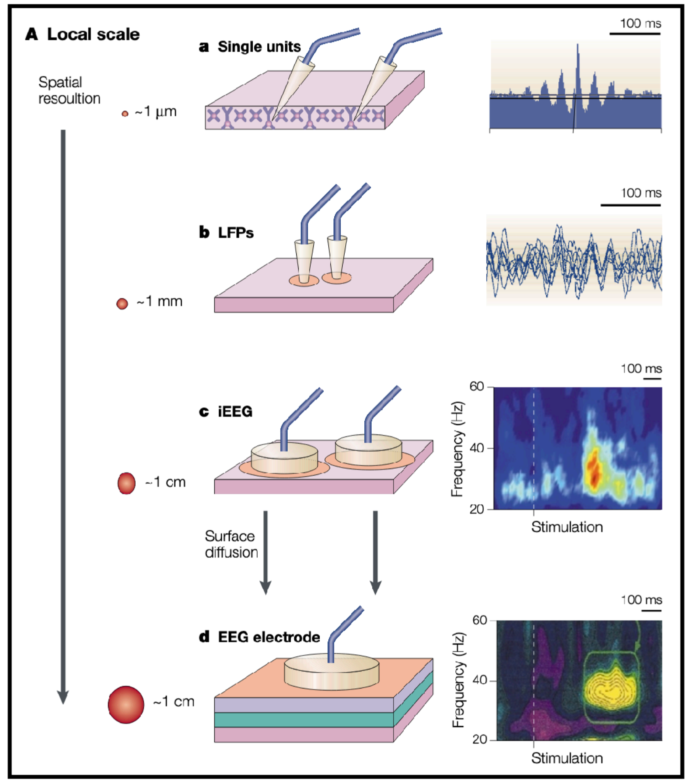
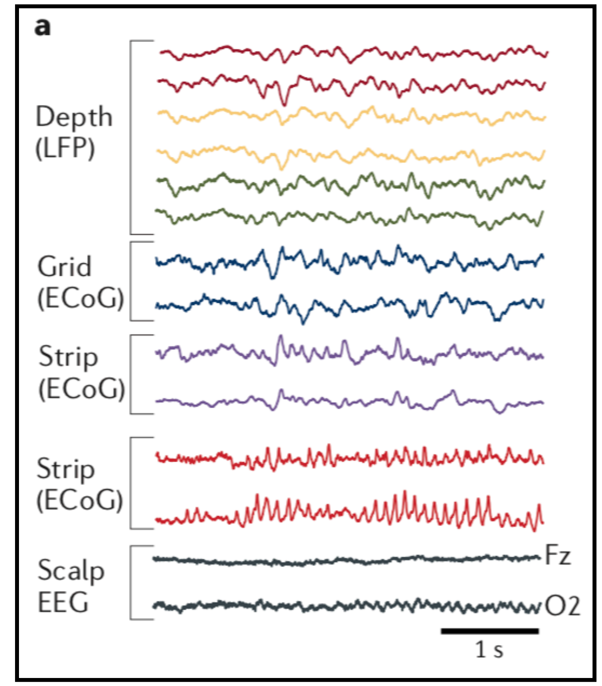
VSD (voltage sensitive dye) imaging, for example, is a fast functional imaging technique that relies on voltage sensitive dyes that change light color or intensity when binding to ions inside the neuron (or any cell).

Electrophysiology



Varela et al., 2001. Nat Rev Neurosci



Buzsaki et al. 2012 Nat Rev Neurosci

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Electrophysiological measurements can also occur at multiple spatial resolutions, but they're almost always fast (note that the spatial axis is inverted from previously)

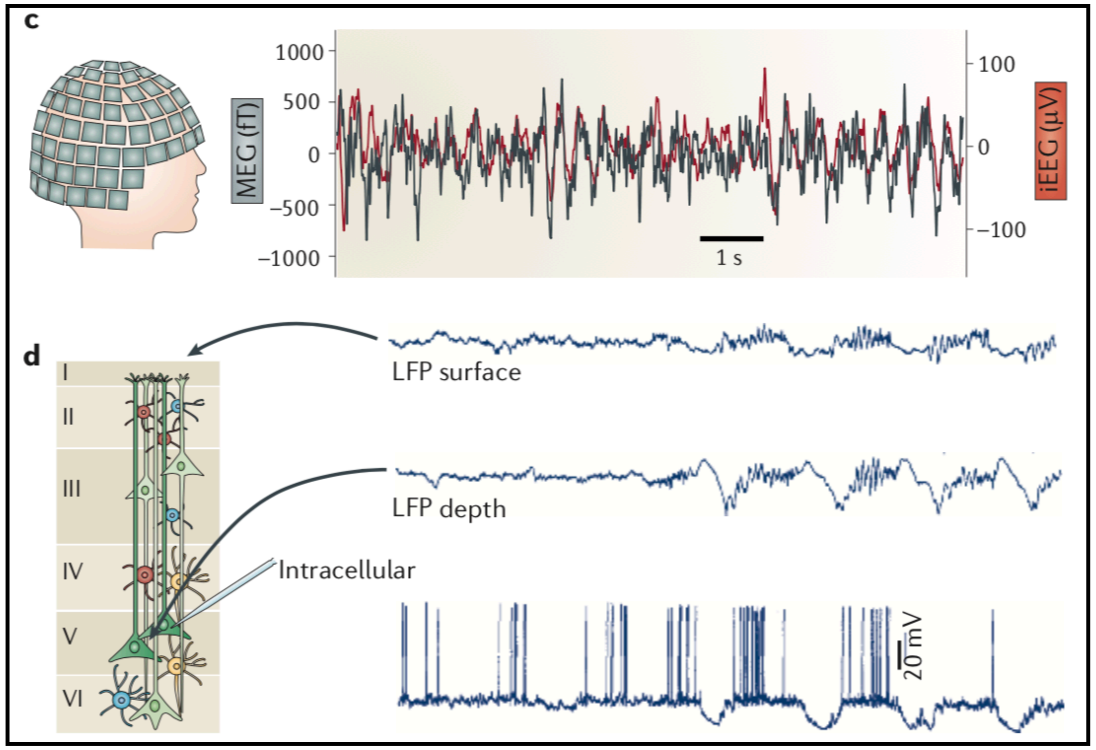
Know the different measurements and their characteristic spatial scales.

LFP = local field potential

iEEG = intracranial EEG, but more commonly referred to as ECoG (electrocorticography). Know why this is performed.

EEG = electroencephalography

Electrophysiology



Buzsaki et al. 2012 Nat Rev Neurosci

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Electrophysiological measurements can also occur at multiple spatial resolutions, but they're almost always fast (note that the spatial axis is inverted from previously)
MEG = magnetoencephalography. Know the difference between MEG and the signals from the last slide.

1. Review the cellular and anatomical components of the brain

2. Map out the different neural signal modalities

3. Understand the detailed mechanism behind electrical signals in the brain

Disclaimer: there is still a LOT we don't know about the brain.

This is something **we** are actively working on.

Electrophysiology Biophysics

Rule of Thumb:

Electrophysiological recordings measure **changes in voltage** (potential) across space,

usually caused by **electrical currents** (moving charged particles)…

…with a lot of complicating factors.

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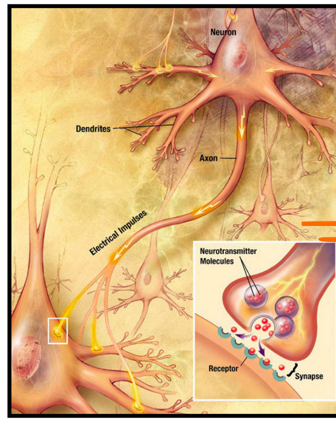
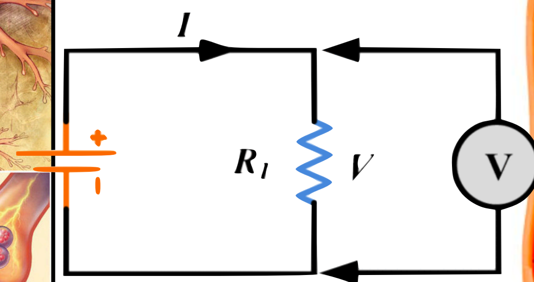
MEG is the one special case where we are measuring magnetic changes caused by current, not voltage changes.

Measuring Voltage

Difference in Potential





Voltmeter

across:
- membranes
- extracellular space
- cortical surface
- scalp

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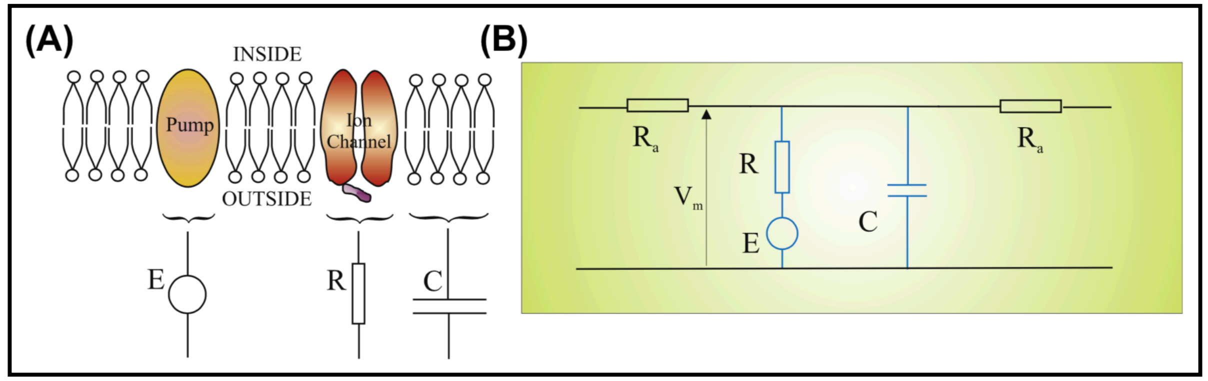
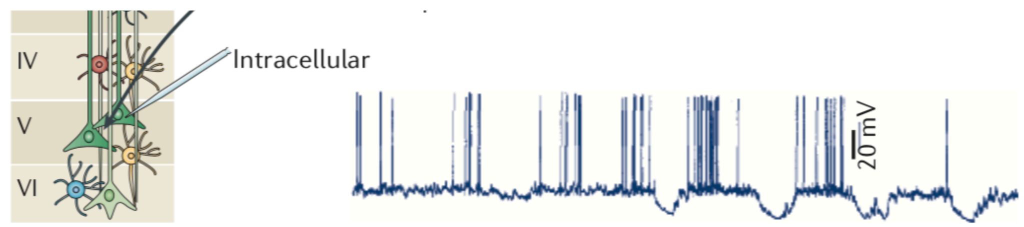
Membrane Potential

Cell Membrane as Electrical Circuit

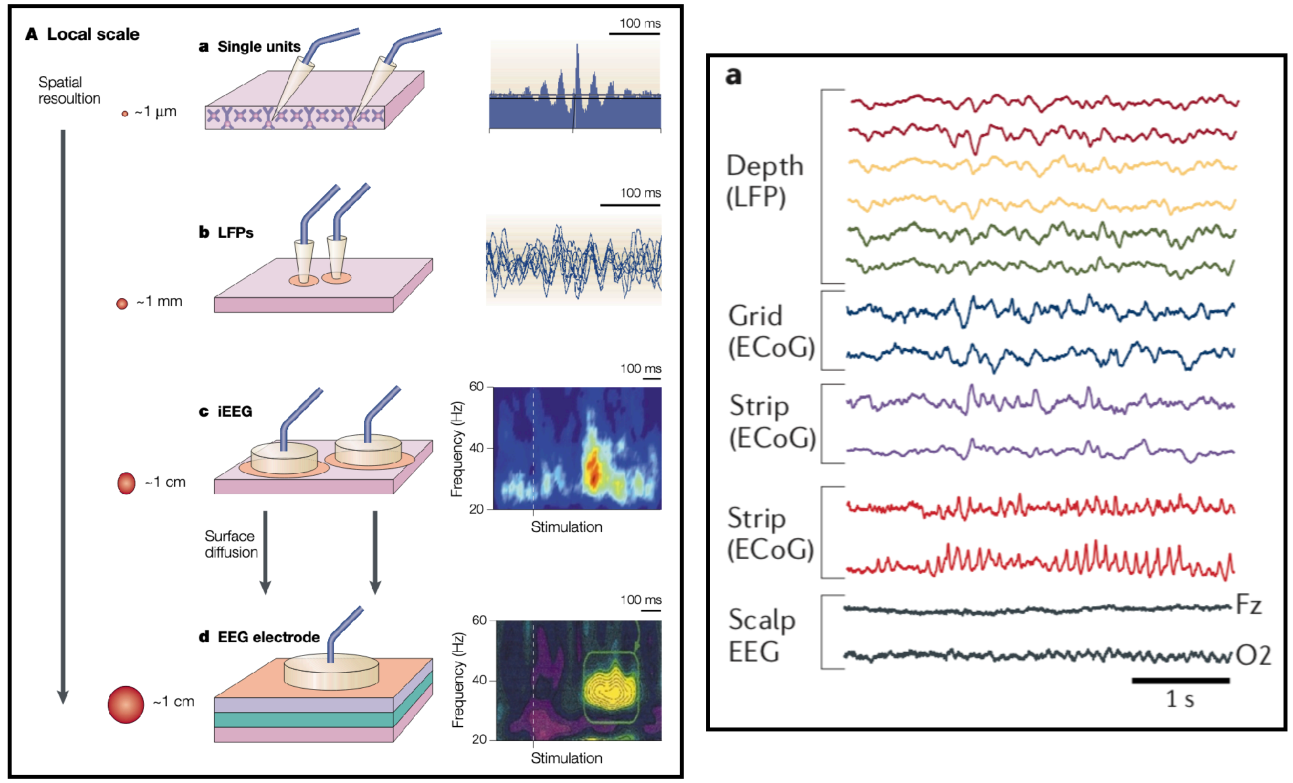


WvD Ch.1



This is how we measure action potentials and membrane (and synaptic) potentials and currents.

Extracellular Potential



Varela et al., 2001. Nat Rev Neurosci

Buzsaki et al. 2012 Nat Rev Neurosci

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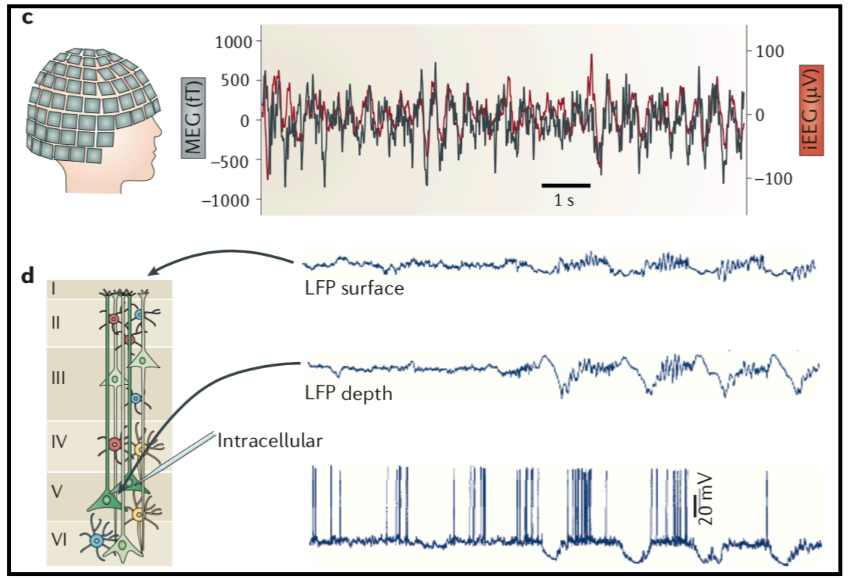
Extracellularly, we are usually measuring a voltage difference across space, between a point of interest and a “null” reference, or just between two locations, depending on how the signal is referenced.

Know the difference between intracellular (membrane potential, last slide) recording vs. extracellular recording

Extracellular Potential



- Synaptic activity
- Action potentials
- Calcium spikes
- Intrinsic currents
- Afterpolarizations
- Gap junctions & Glial Interactions
- Ephaptic effects

5 min: What are the main contributors of extracellular potential?
(*hint: see Buzsaki et al., 2012 Nat Rev Neurosci*)

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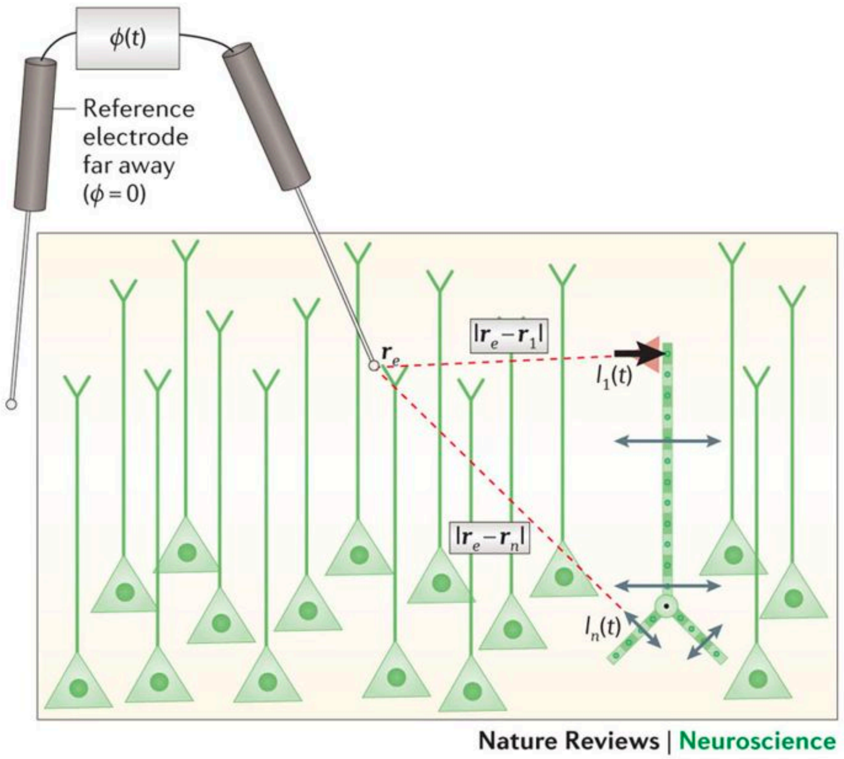
Extracellular Potential



Einevoll et al. 2013 Nat Rev Neurosci

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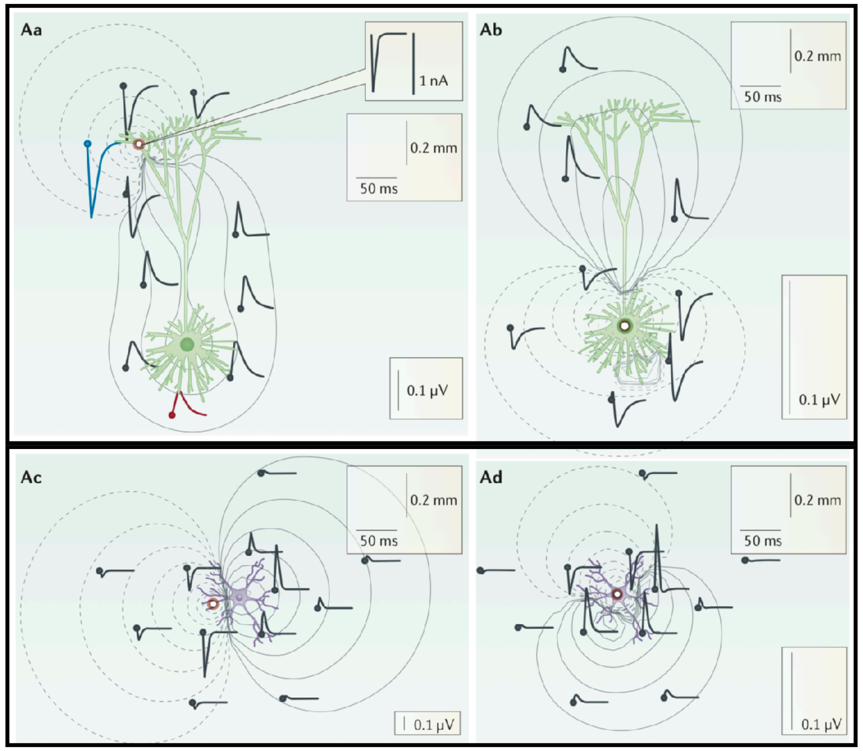
LFPs depend heavily on the spatial arrangement of the neuron and where the electrodes are relative to the cell bodies.

Spatial Arrangement & Morphology Matter

Pyramidal (Excitatory) Neurons

Stellate (Inhibitory) Interneurons



Einevoll et al. 2013 Nat Rev Neurosci

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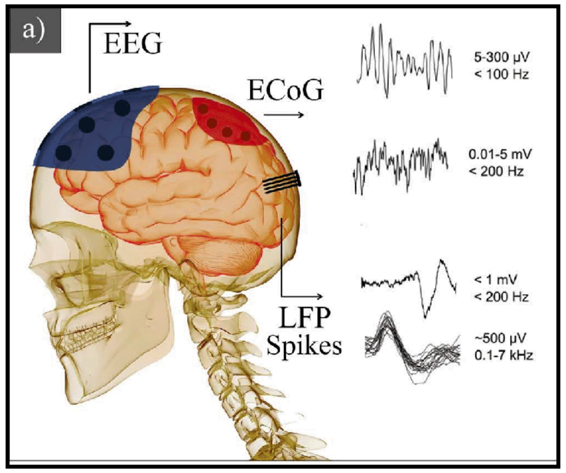
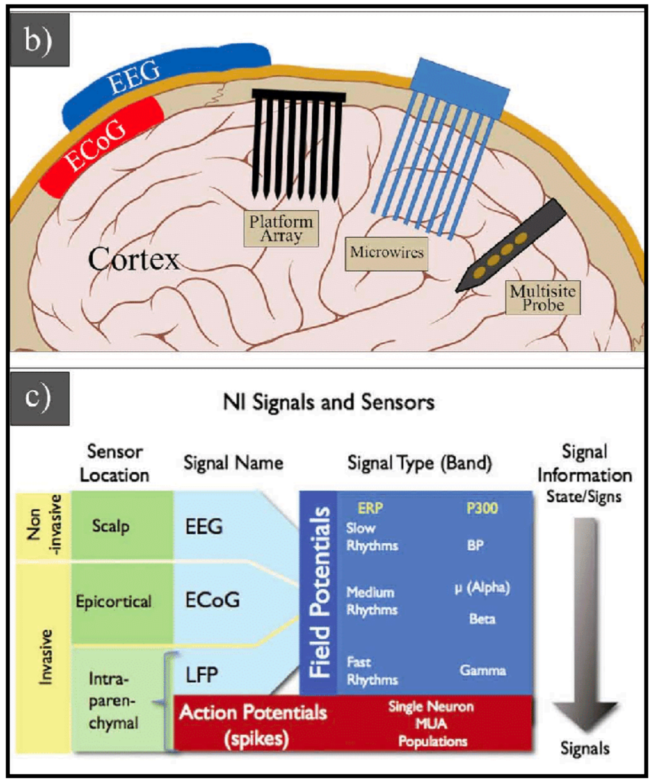
Because we're measuring a relative difference in voltage, the signal amplitude and even polarity can differ depending on where the measurement is taken and what the cell looks like.

Know why signals recorded from the pyramidal cells are usually of greater amplitude

From Micro to Macro



Fattahi et al. 2014 Adv. Mater.



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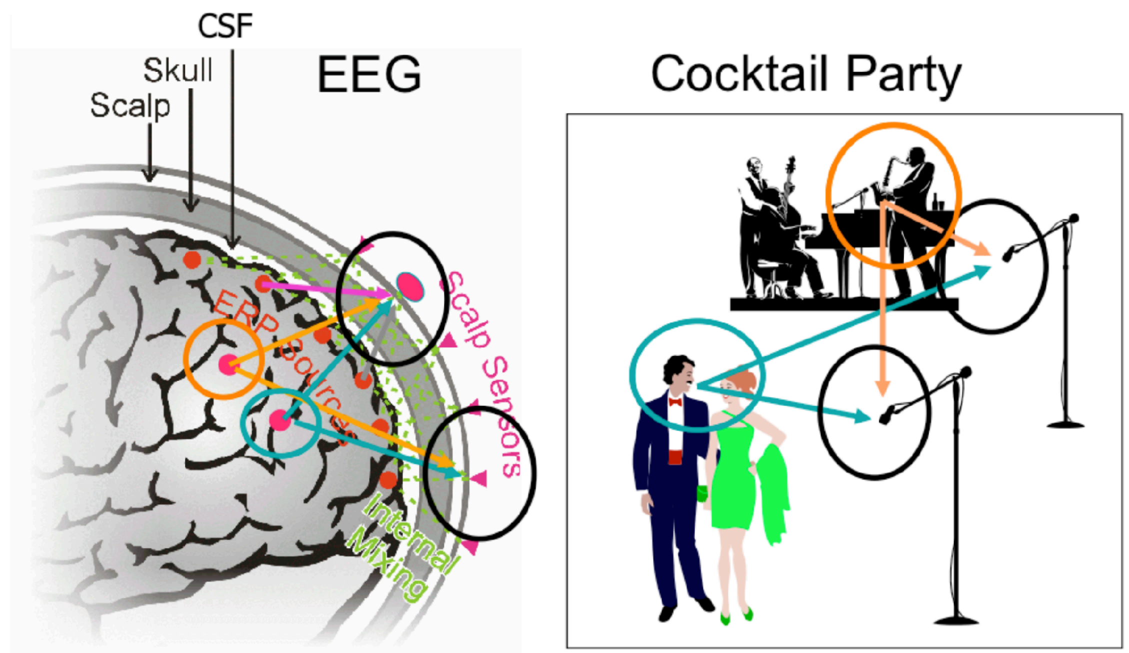
Scales of electrophysiological signals
Different graphic saying the same as slide 31

EEG & Signal Mixing



S. Makeig, SCCN

EEG recorded from the scalp goes through massive filtering

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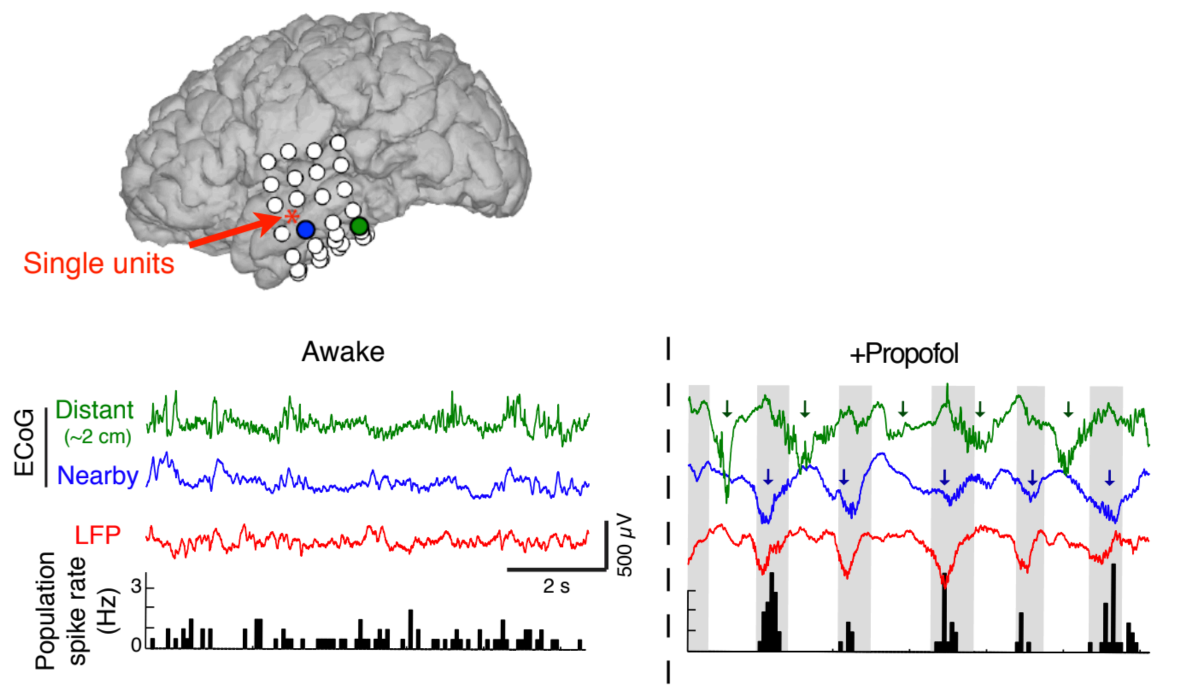
EEG recorded from the scalp goes through massive filtering. It's like listening to what people are saying in a party next door through 6ft. of concrete wall.

Know why EEG signal is dampened compared to ECoG, and what the cocktail party problem is.

Bridging Across Scales



Lewis et al., 2012 PNAS

Active area of research because we want to understand electrophysiology better across scales!

Summary

1. Review the cellular and anatomical components of the brain

2. Map out the different neural signal modalities

3. Understand the detailed mechanism behind electrical signals in the brain

https://tinyurl.com/cogs118c-l2

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Further Readings

- **Buzsáki, G., Anastassiou, C. A. & Koch, C. The origin of extracellular fields and currents--EEG, ECoG, LFP and spikes. *Nat. Rev. Neurosci.* 13, 407–420 (2012). *****

- Einevoll, G. T., Kayser, C., Logothetis, N. K. & Panzeri, S. Modelling and analysis of local field potentials for studying the function of cortical circuits. *Nat. Rev. Neurosci.* **14**, 770–785 (2013).

Further Readings

The origin of extracellular fields and currents — EEG, ECoG, LFP and spikes

György Buzsáki[1,2,3], Costas A. Anastassiou[4] and Christof Koch[4,5]