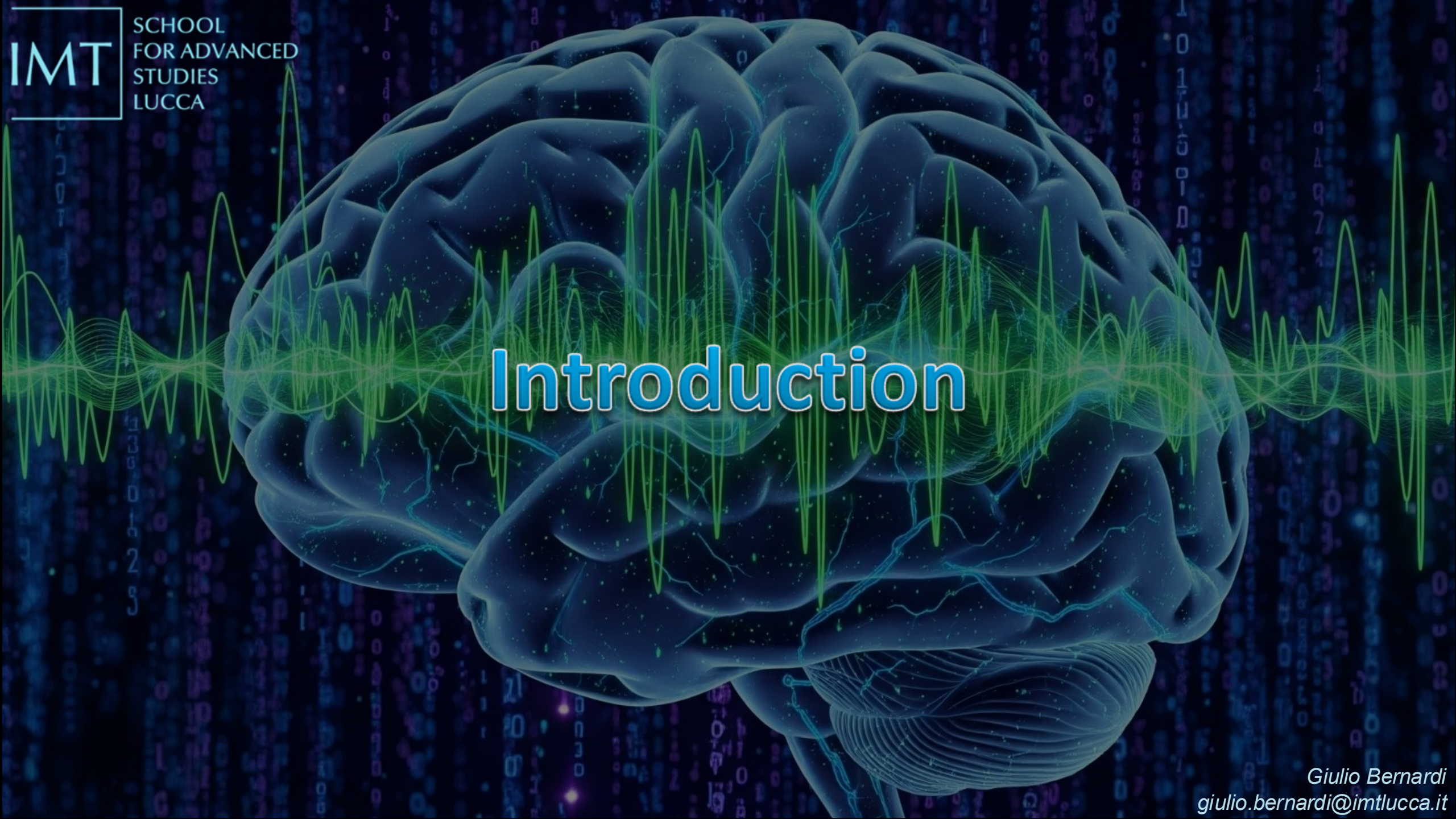
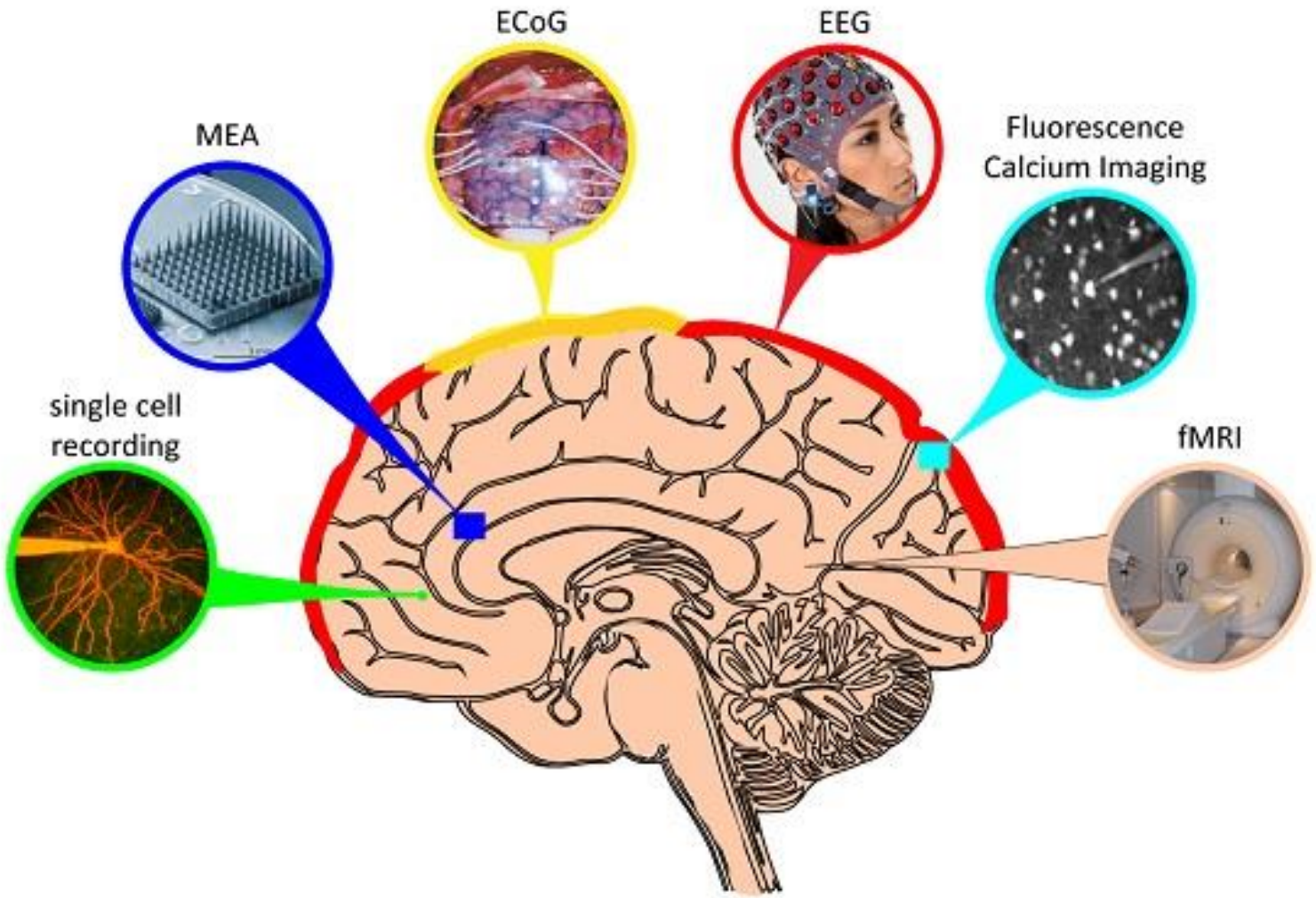
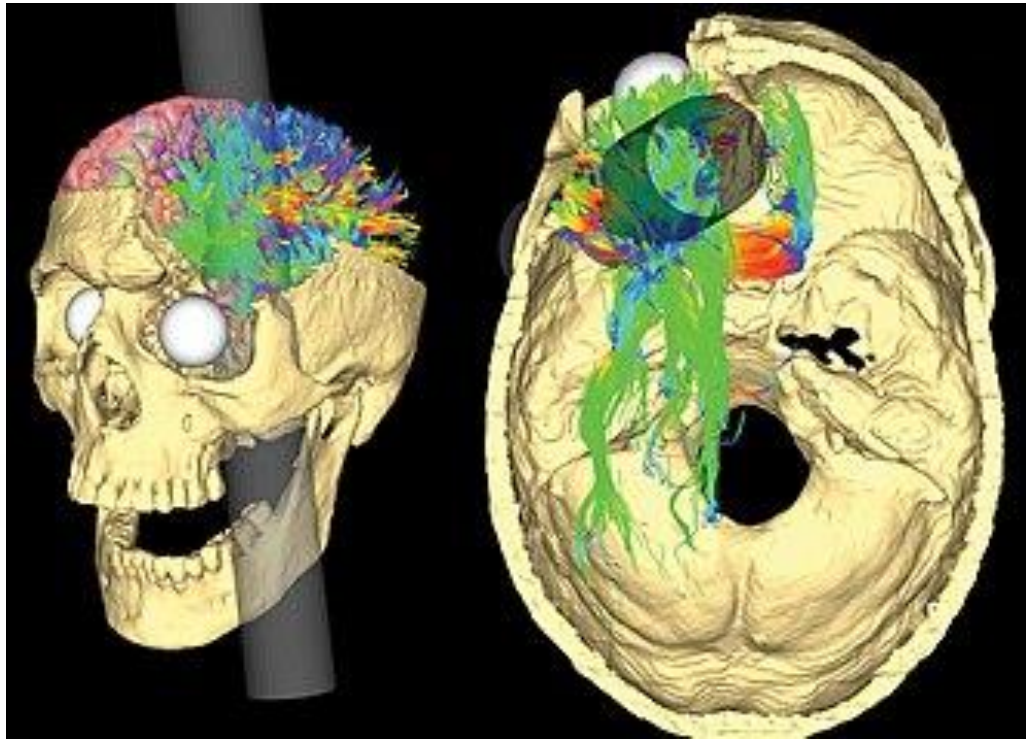


Giulio Bernardi
giulio.bernardi@imtlucca.it

The study of the brain and brain function



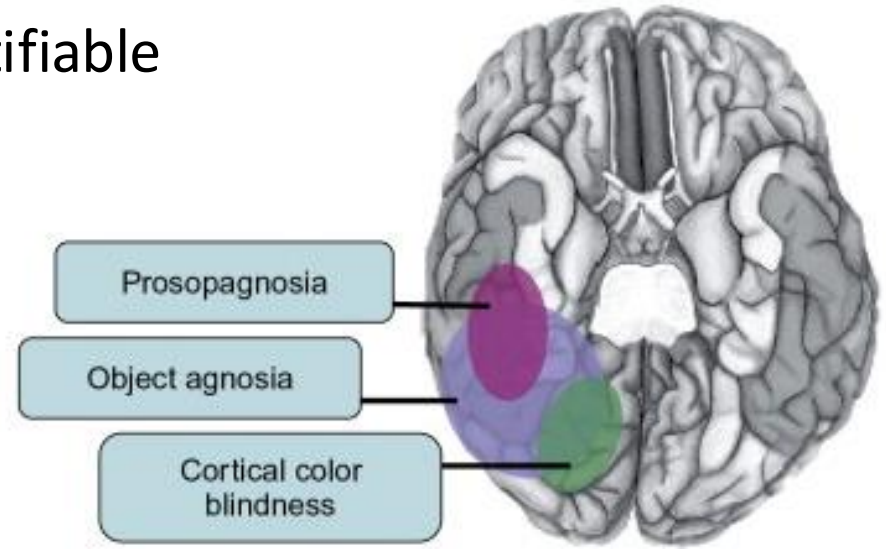
Lesion studies



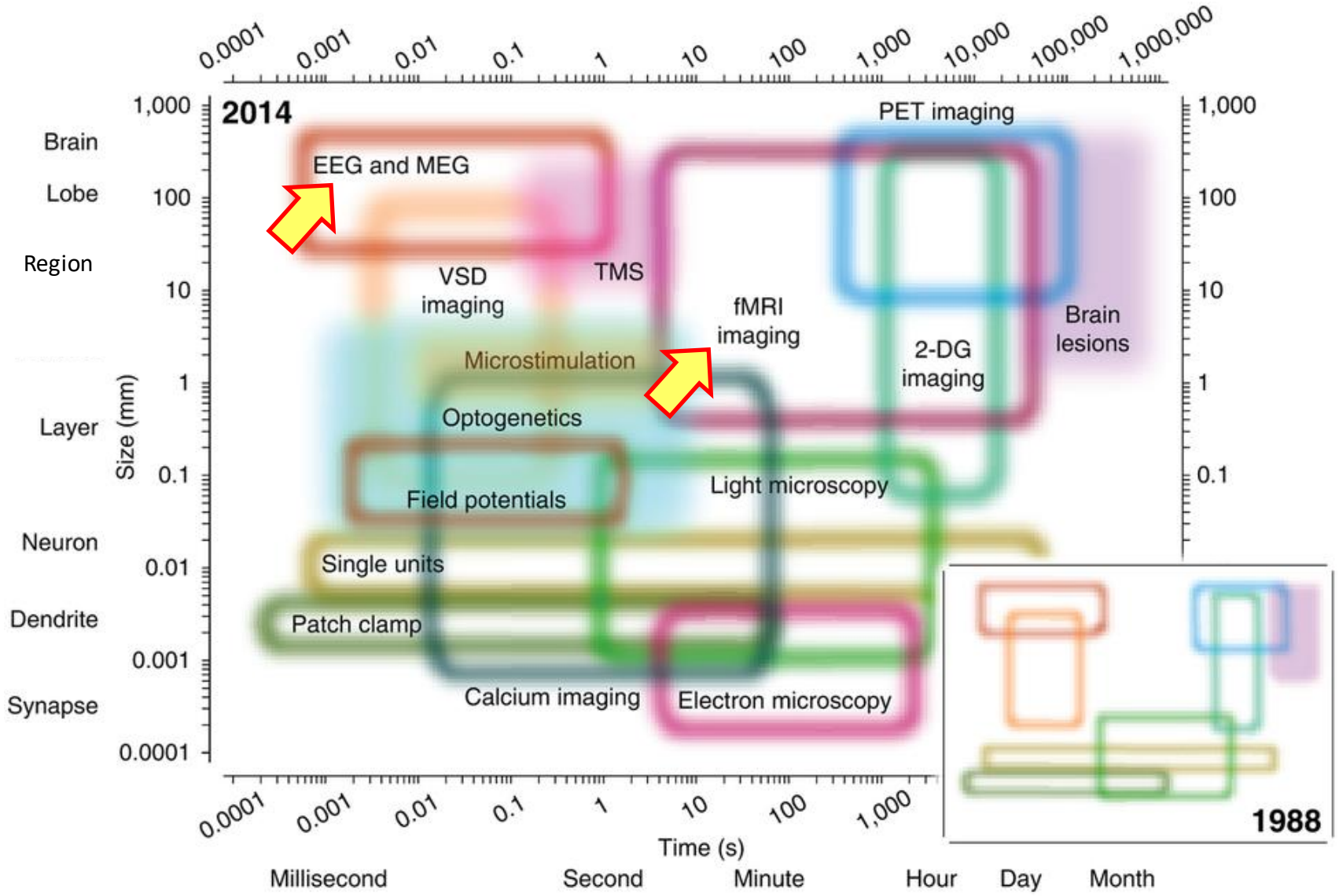
Lesion studies

Limitations:

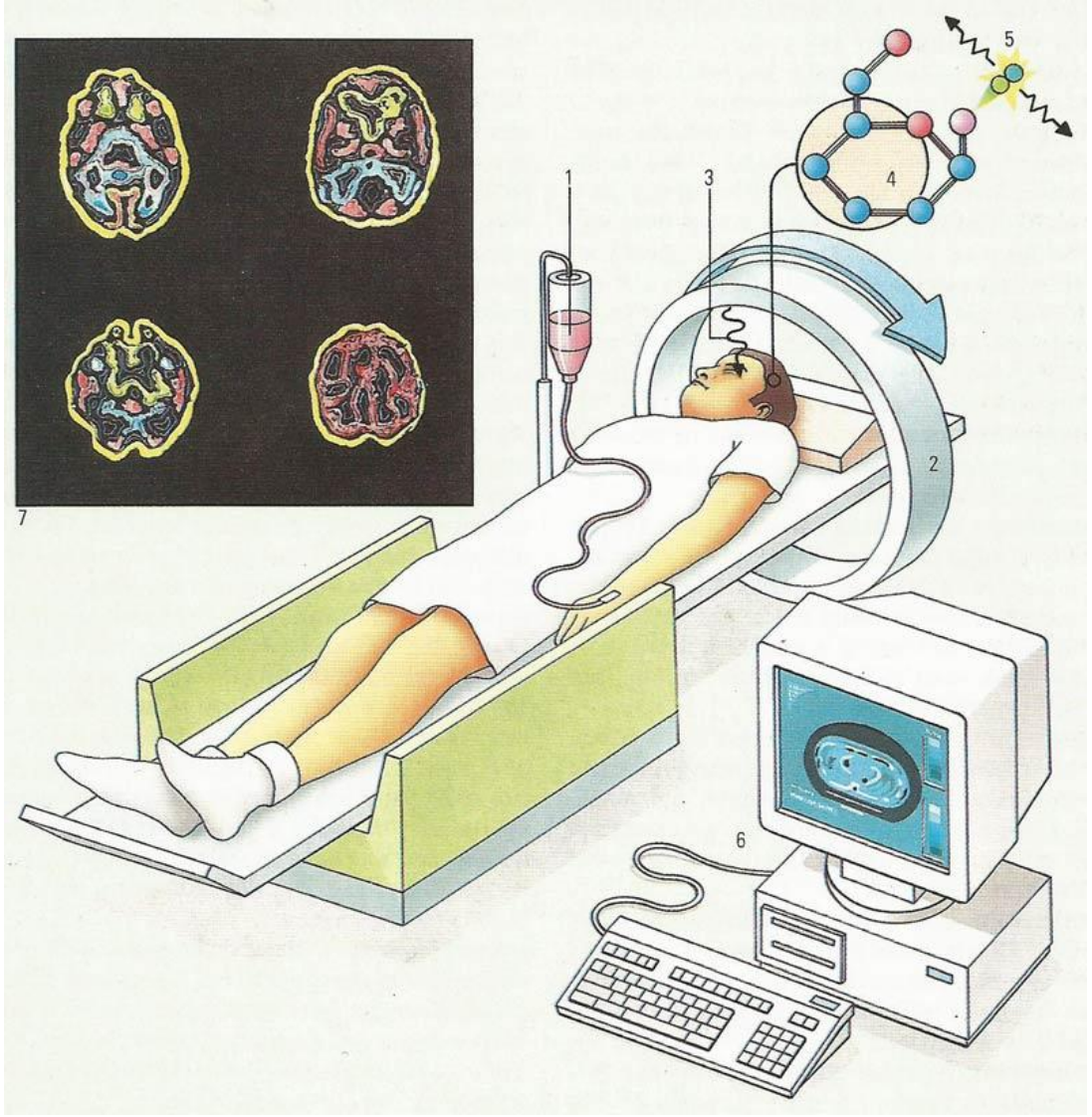
- Brain lesions are rarely selective
- Symptoms change with time
- The specific deficit is not easily identifiable



Modern neuroimaging techniques

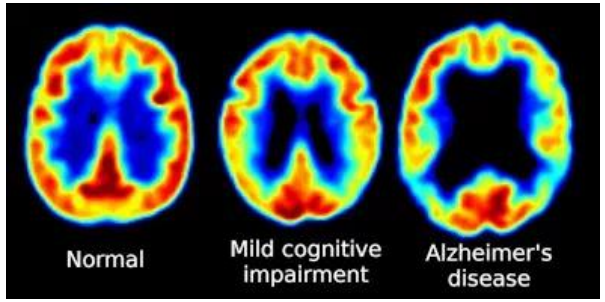


Positron Emission Tomography



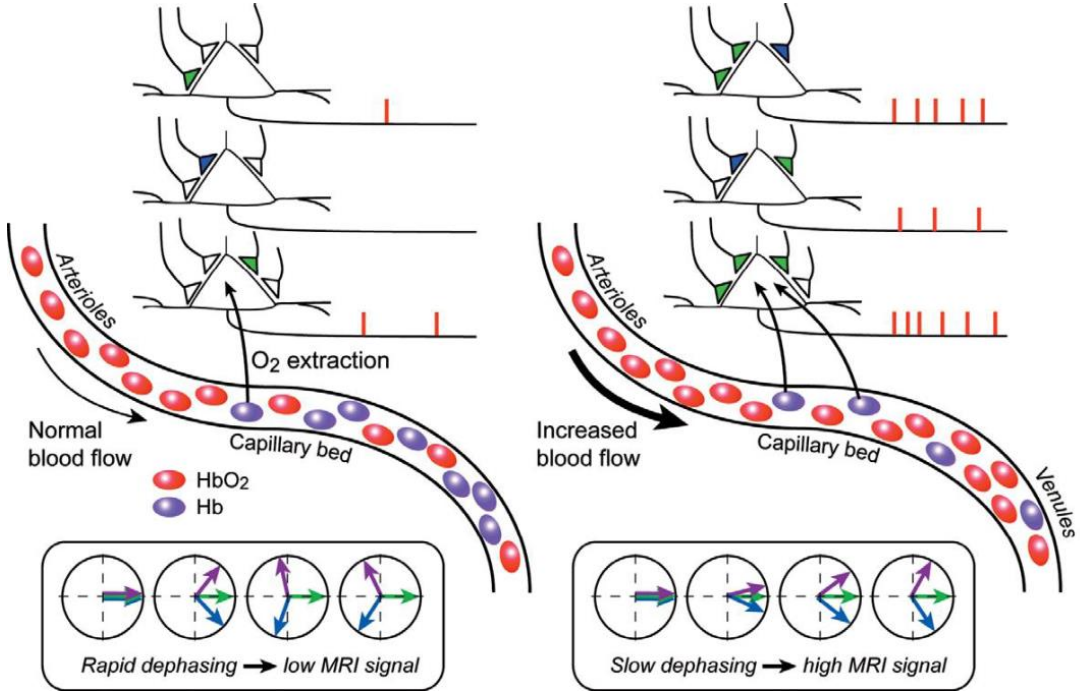
PET measures emissions from radioactively labeled metabolically active chemicals that have been injected into the bloodstream.

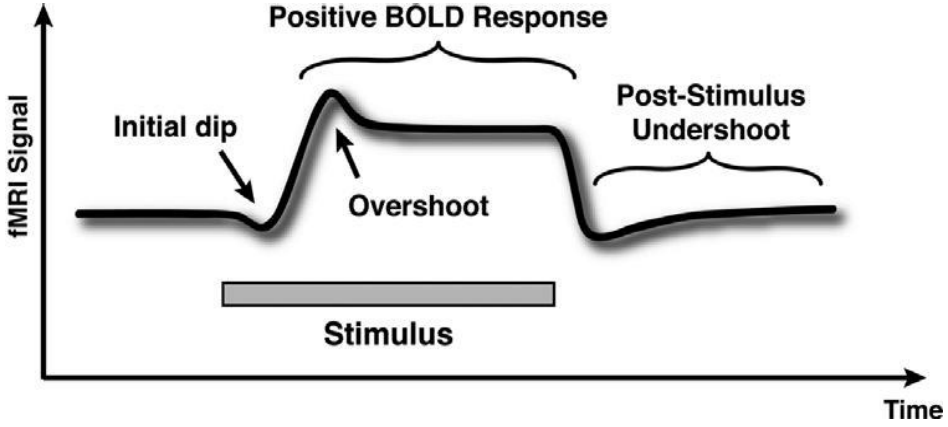
Fludeoxyglucose (18F) – FDG-PET



Functional Magnetic Resonance Imaging

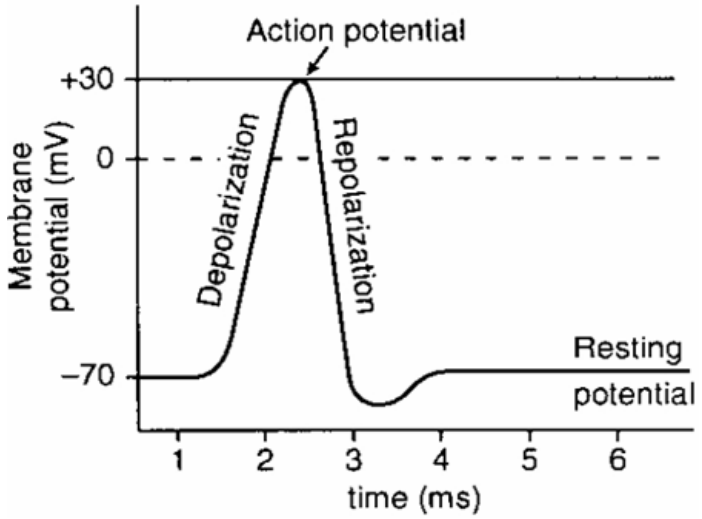
fMRI measures brain activity by detecting changes associated with blood flow. This technique relies on the fact that cerebral blood flow and neuronal activation are coupled. When an area of the brain is used, blood flow to that region also increases.





Functional Magnetic Resonance Imaging

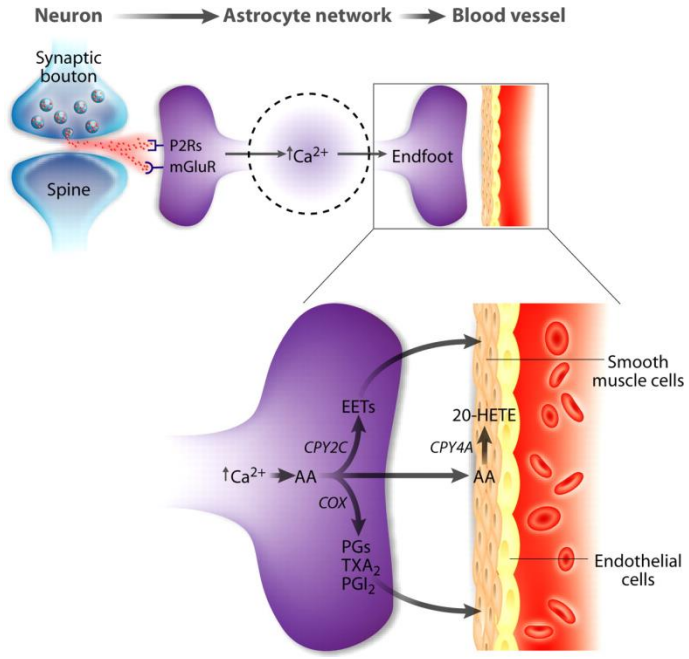
Neuronal Activation



Neurovascular Coupling

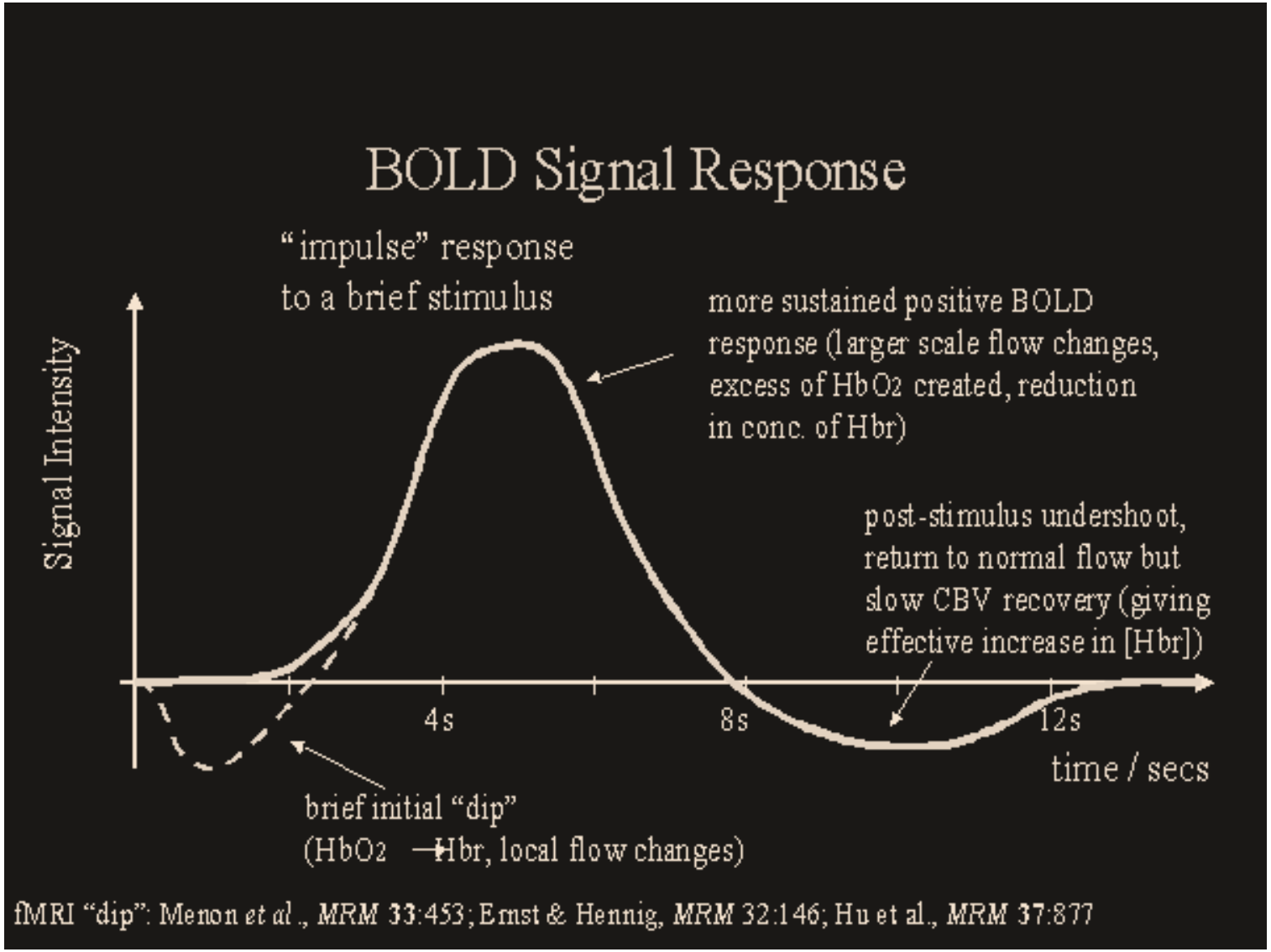
fMRI

Hemodynamic Response

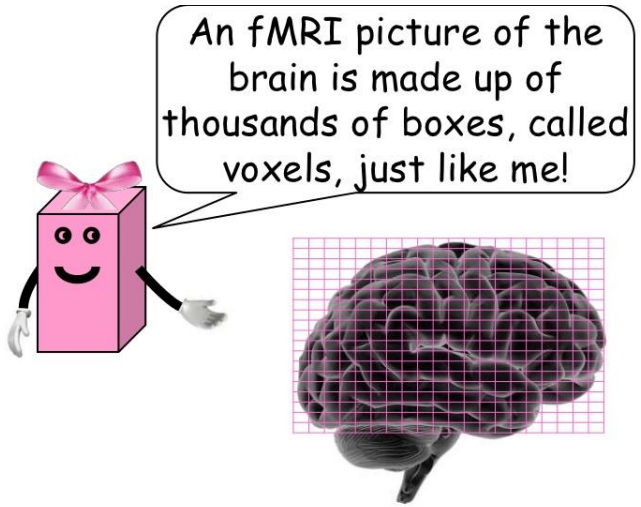


Neural Activation → Activity Na^+/K^+ pump → ATP Consumption → Oxygen Consumption → Cerebral Blood Flow → Oxidative Glucose Metabolism → ATP Consumption

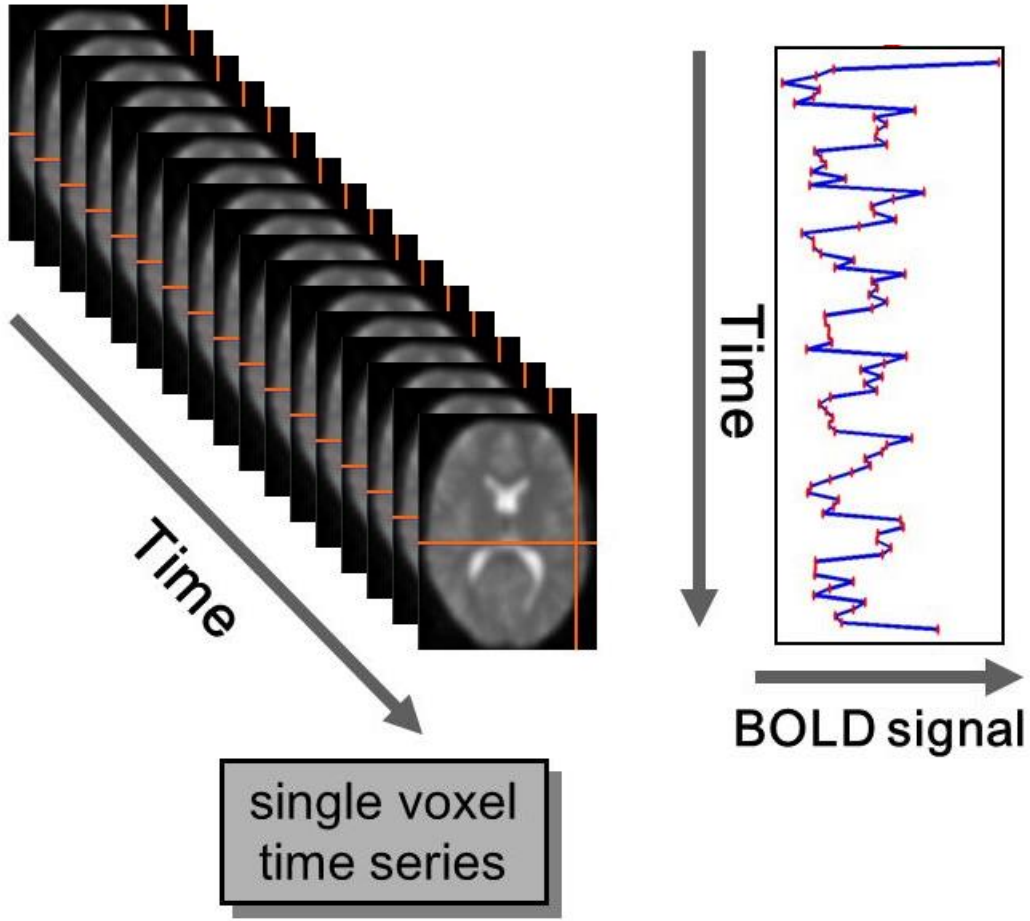
Functional Magnetic Resonance Imaging



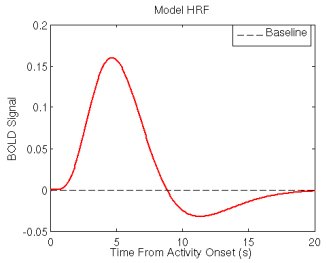
Functional Magnetic Resonance Imaging

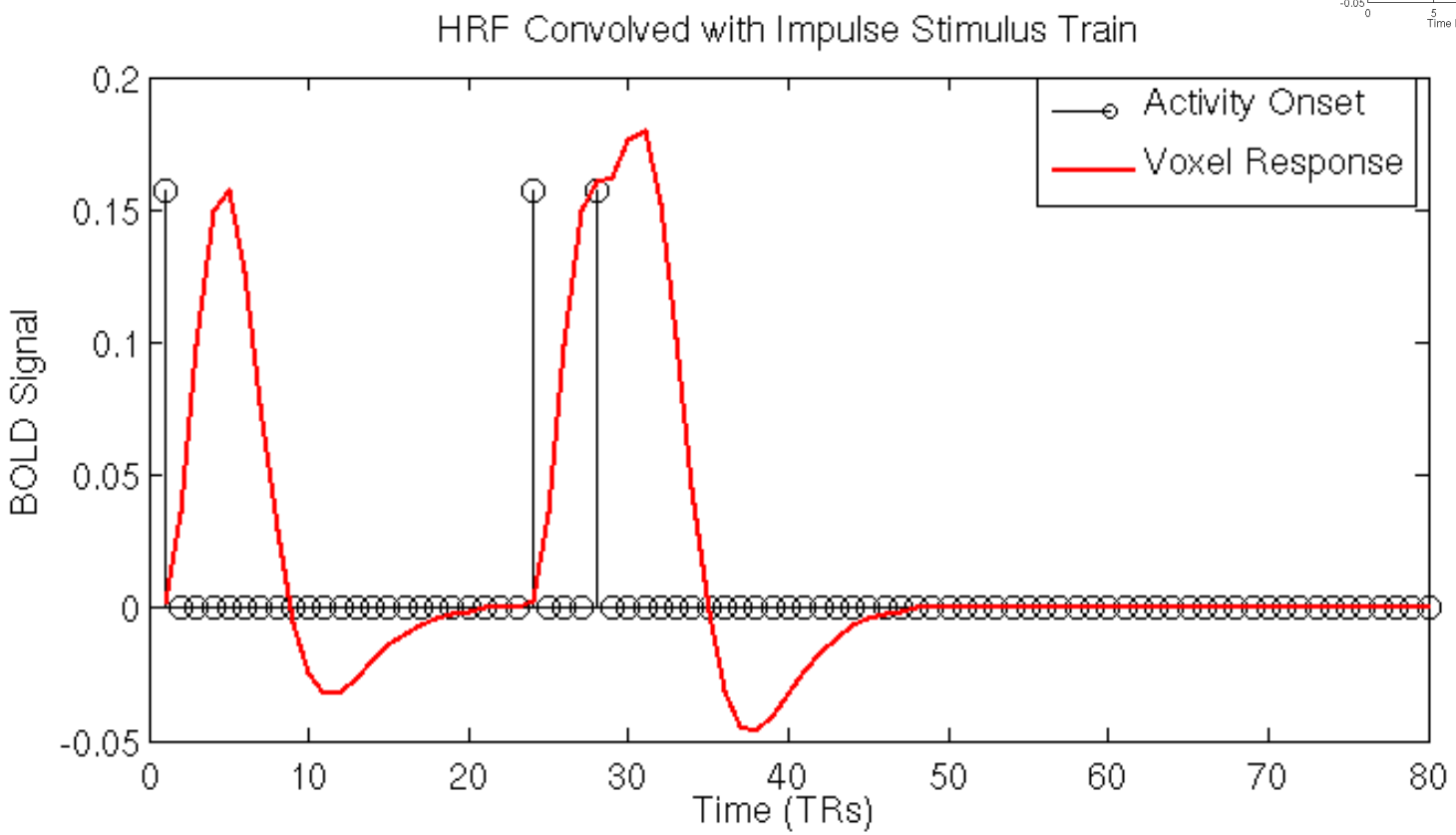


The goal of fMRI data analysis is to detect correlations between brain activation and a task the subject performs during the scan.

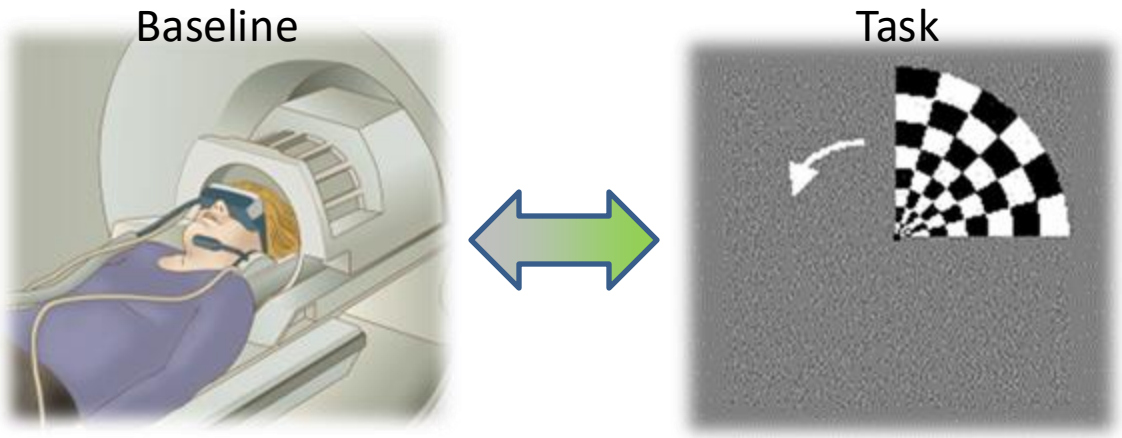


Functional Magnetic Resonance Imaging

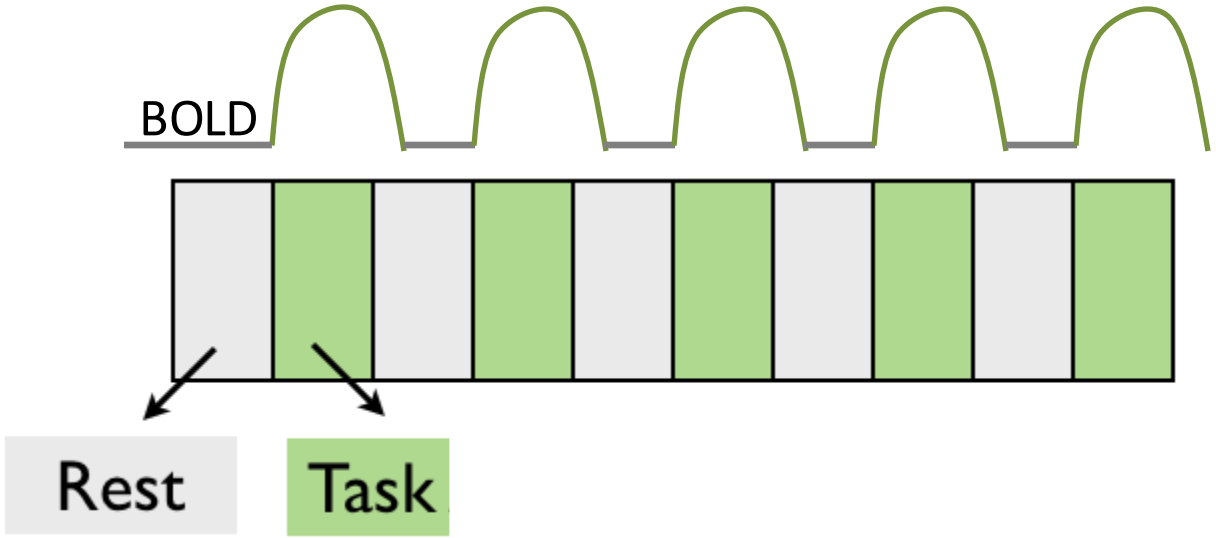




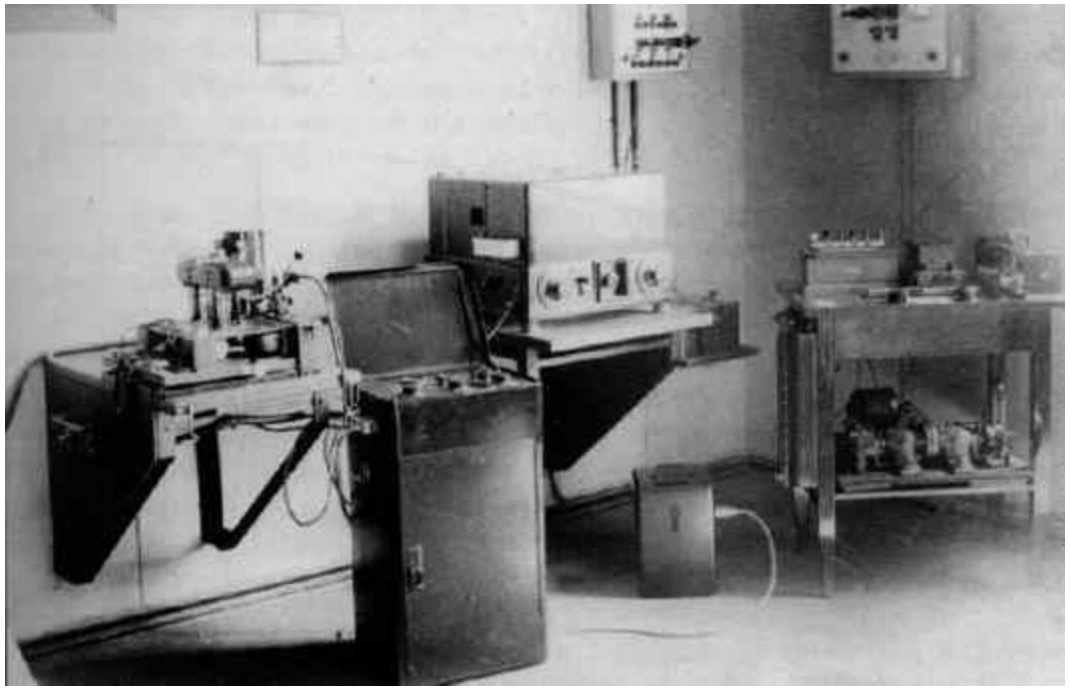
Functional Magnetic Resonance Imaging

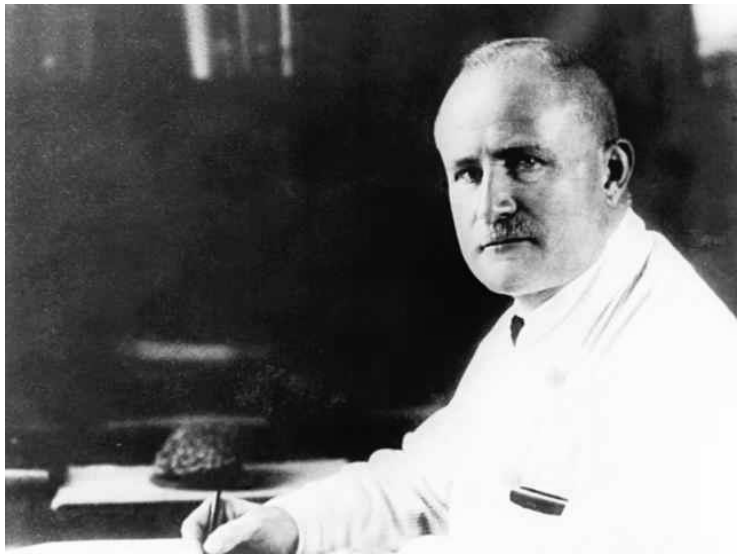


Experimental Paradigm – Block Design

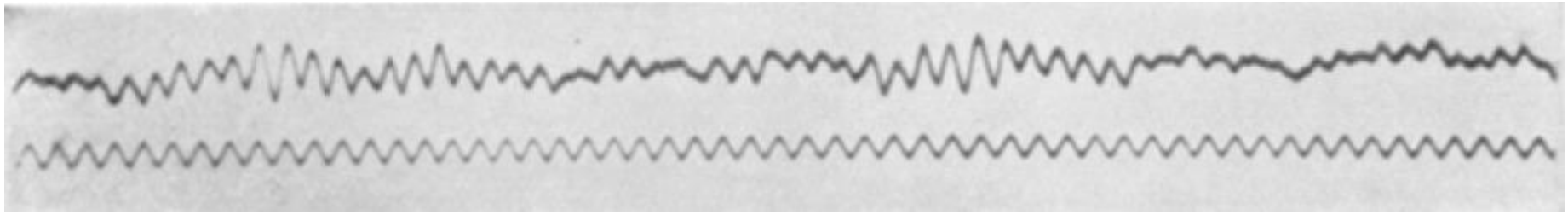


The First Electroencephalogram





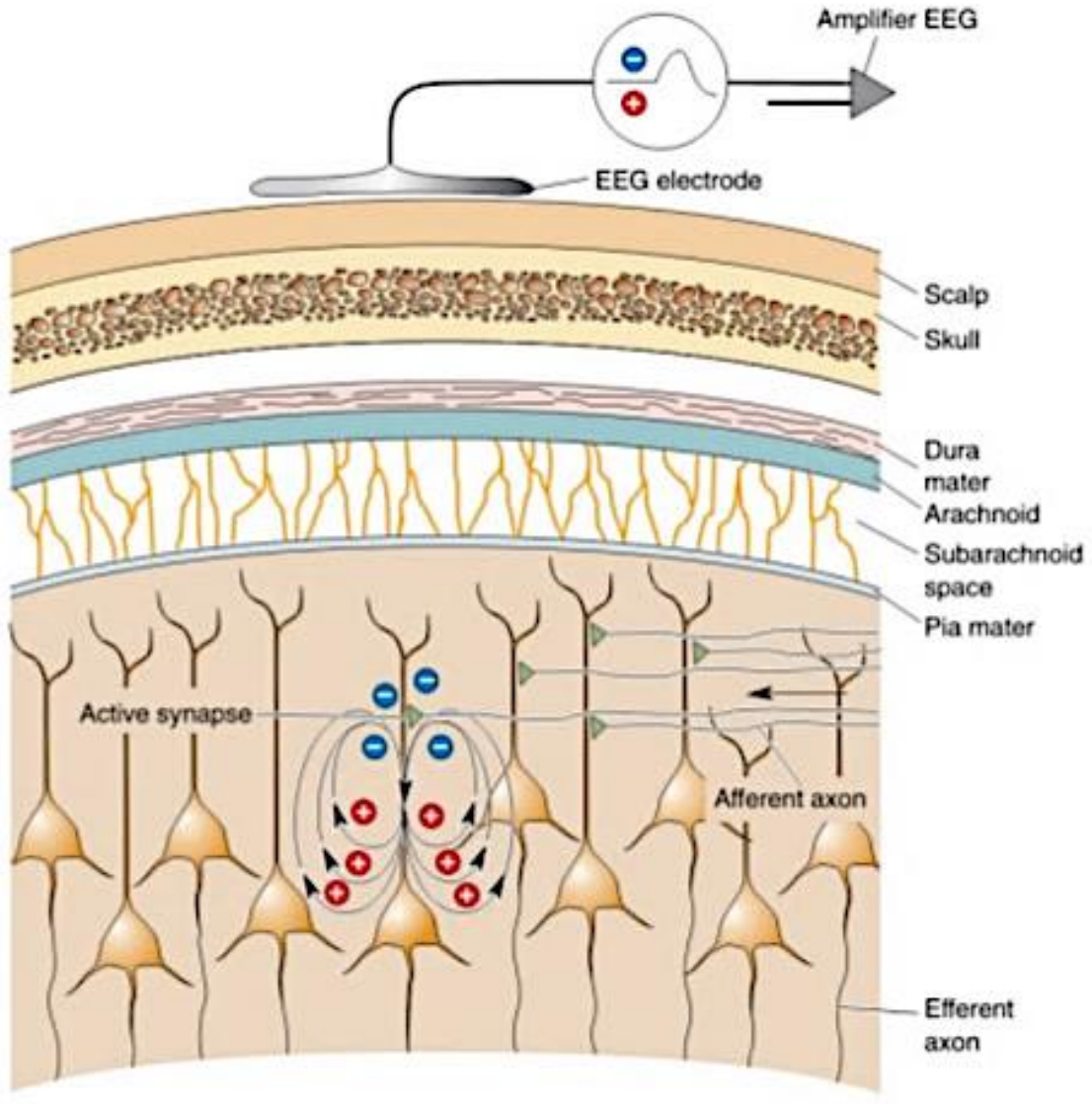
German physiologist and psychiatrist Hans Berger (1873–1941) recorded the first human EEG in 1924.



The EEG signal

The EEG signal reflects the generation of very small electrical fields by synaptic currents in ***pyramidal cells***.

Only if thousand of cells contribute their small voltage is the signal large enough to reach the scalp surface.

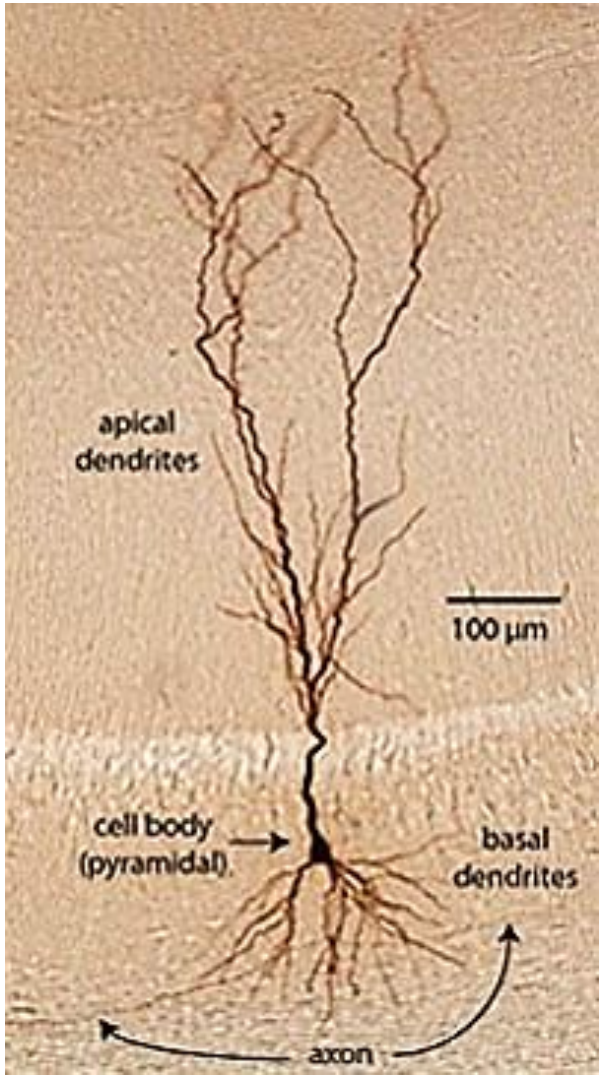


Pyramidal Neurons

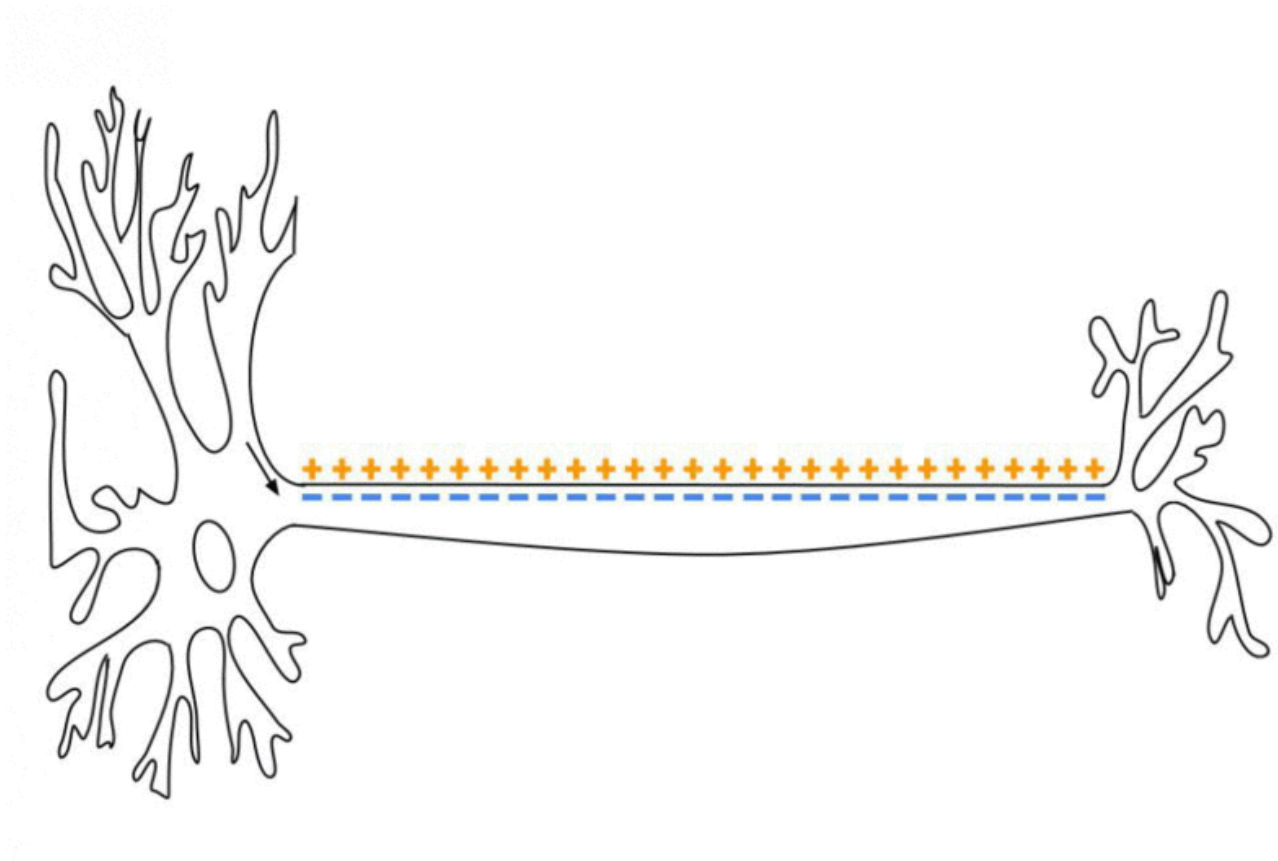
Pyramidal cells are found in ***forebrain structures*** such as the cerebral cortex, hippocampus, and amygdala, but not in the olfactory bulbs, striatum, midbrain, hindbrain, or spinal cord.

They are the most numerous ***excitatory cell type*** in mammalian cortical structures.

Pyramidal neurons have multiple dendrites (input) and a single axon (output), but both dendrites and axons branch extensively.

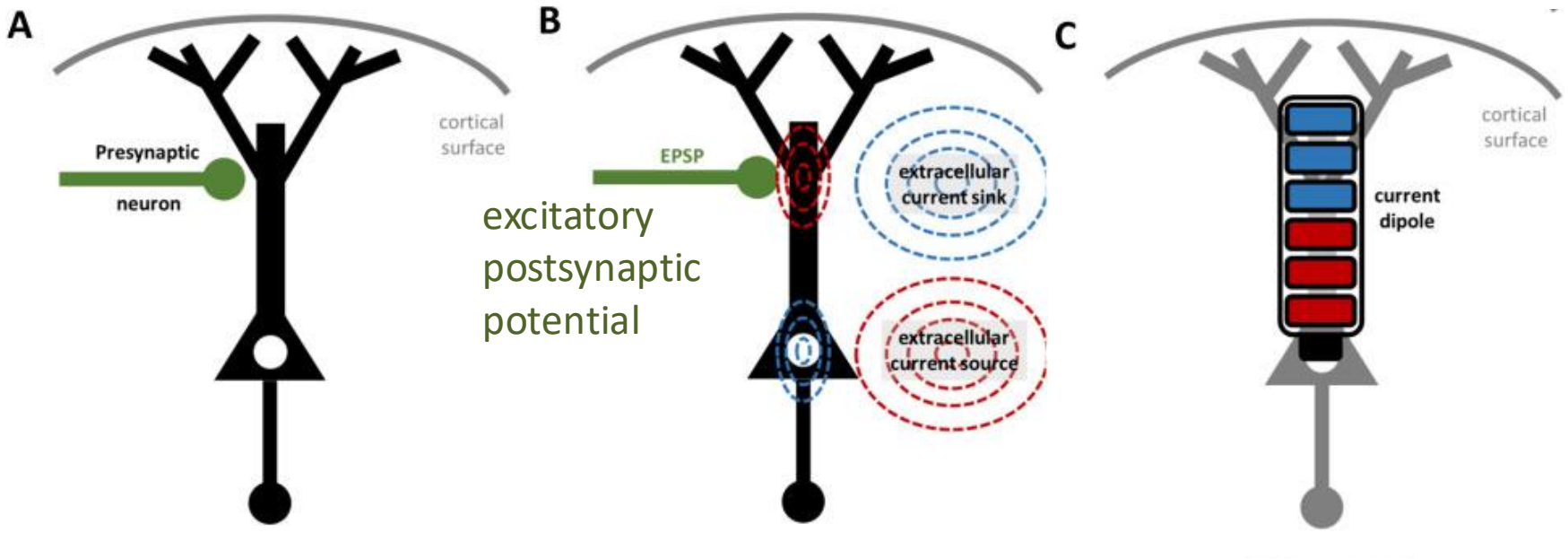


Action Potential



At the beginning of the action potential, the Na+ channels open and Na+ moves into the axon, causing depolarization. Repolarization occurs when the K+ channels open and K+ moves out of the axon. This creates a change in polarity between the outside of the cell and the inside. The impulse travels down the axon in one direction only.

Action Potential

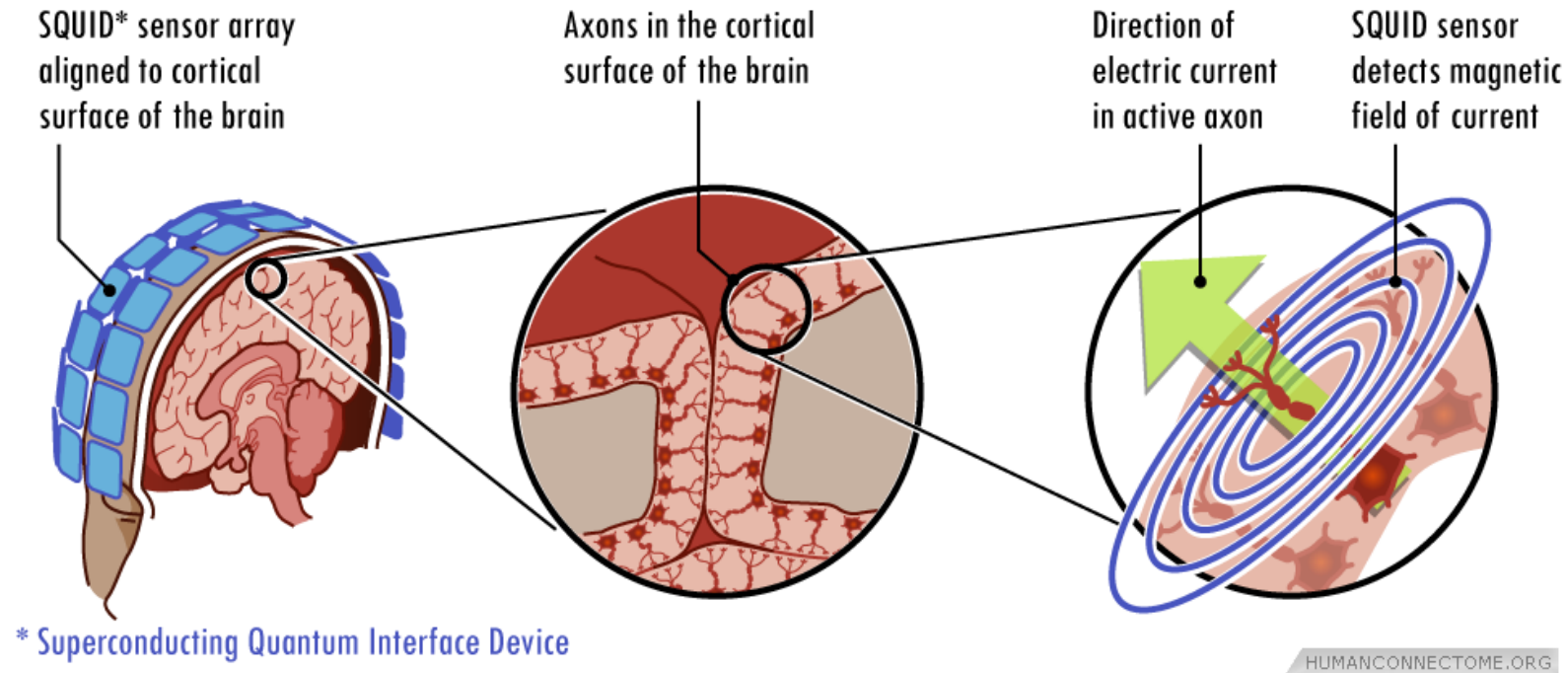


EEG measures postsynaptic currents in extracellular space.

EEG vs MEG

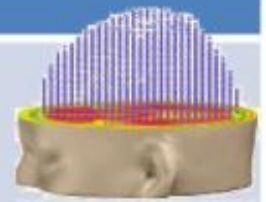
Both the MEG and EEG signals derive from the net effect of ionic currents flowing in the dendrites of neurons during synaptic transmission.

In accordance with ***Maxwell's Equations*** (*Electromagnetism*), any electrical current will produce a magnetic field.



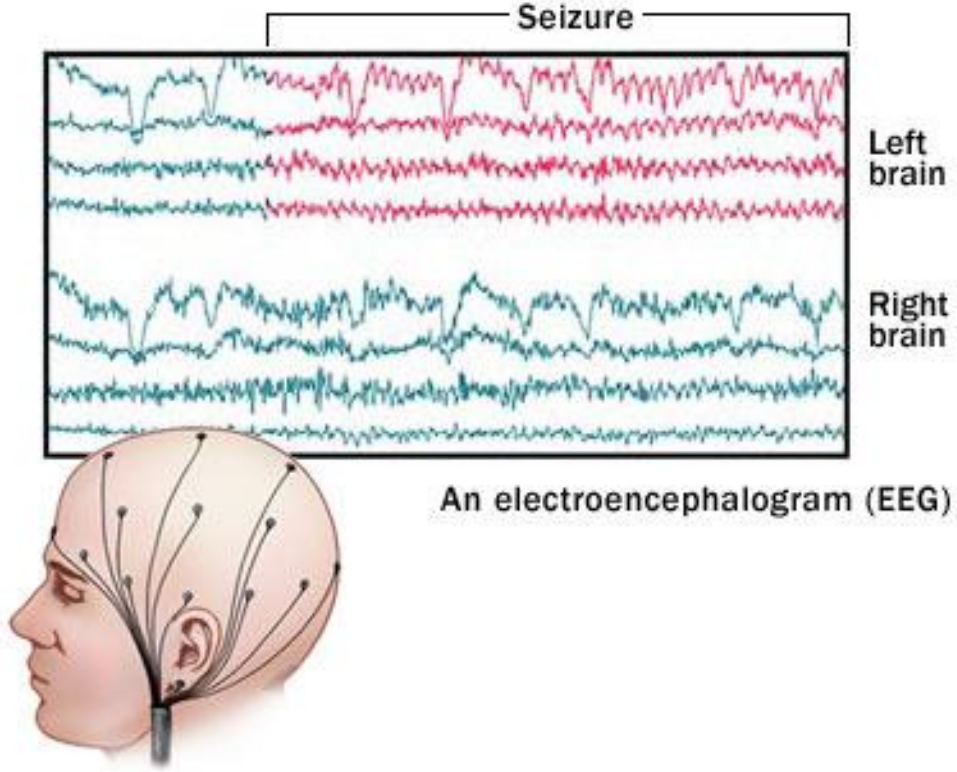
EEG vs Other Techniques

Weaknesses (and what's done about them)	
Low spatial resolution	• Undeniably, fMRI has a higher spatial resolution. • However, simulations and empirical work has demonstrated **localization error <1cm** (and methods are still improving) • Some have contended that MEG has a higher spatial resolution – **this is untrue** (discussed in Malmivuo, 2012 *Brain Topography*; Michel & Murray, 2012 *Neuroimage*). When the same number of sensors were compared, EEG was actually shown to have a higher resolution (Liu, Dale, & Belliveau, 2002). However, this point is admittedly still a subject of some debate and may depend on the specific distribution of active sources (e.g., Sharon et al., 2007). • **EEG is sensitive to both radial and tangential sources (MEG is sensitive only to radial sources)** • **EEG is sensitive to both superficial and deep sources**
Low SNR	• Evoked activity is visible in single trial data (e.g. De Lucia et al. 2007 *IEEE-ITAB*; Tzovara et al. 20012 *Neuroimage*)
Weak analysis pathway	• True. But, this is changing with open-source and freeware as well as general EEG renaissance. • Veritable alphabet soup of so-called components • Large and diverse profiles of users with different research agendas, lack of stringent guidelines
Weak understanding of neurophysiology and interpretability of data	• There has been a general "split" between approaches focusing on correlates of presumed brain processes and those focusing on neurophysiologic mechanisms. • The analyses themselves have often been a major impediment to interpretability. • Long history of comparative neurophysiology (works of Vaughan Jr et al., Schroeder et al.) • Biophysics can help disambiguate likely mechanisms.



Routine Clinical EEG

Typically based on scalp EEG recording from up to 21 electrodes (2-8 sensors are commonly used in polysomnographic [PSG] recordings).



An electroencephalogram (EEG)

Routine EEG is typically used for the diagnosis and evaluation of epilepsy and/or for the diagnosis and evaluation of sleep-related clinical conditions.

Number of Sensors in EEG Systems

Clinical EEG & PSG

1-21 Electrodes

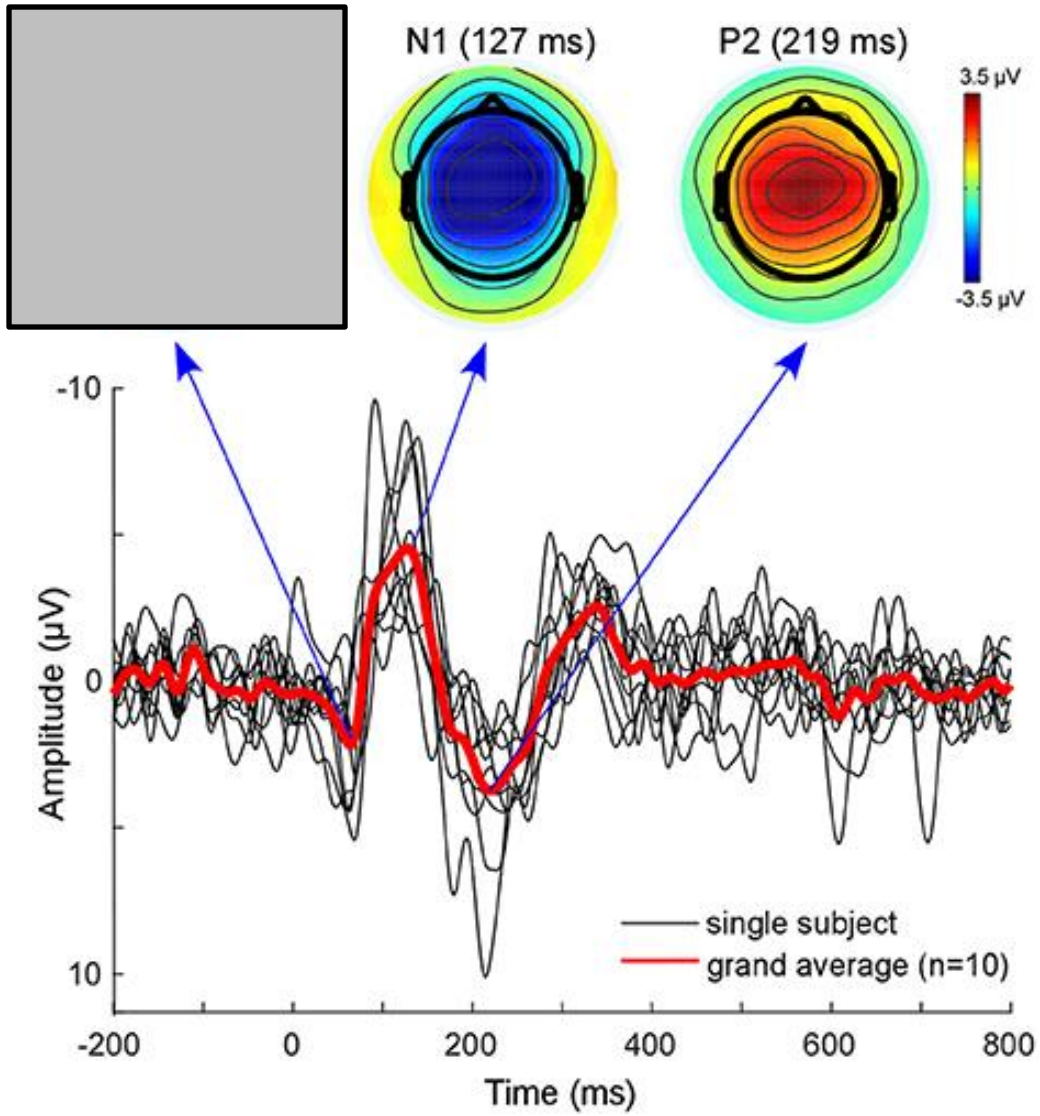
Standard Research EEG

32-64 Electrodes

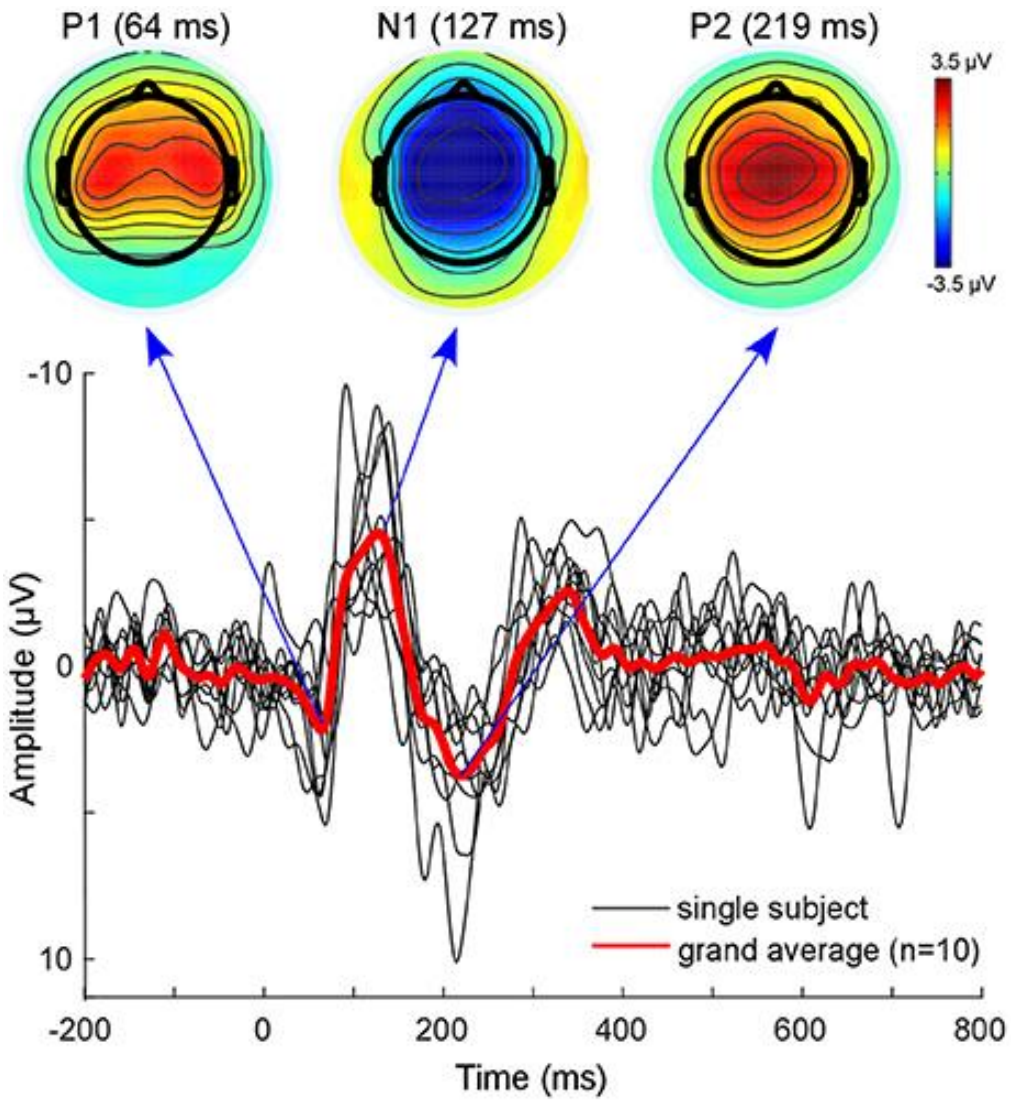
High-Density EEG

128-256 Electrodes

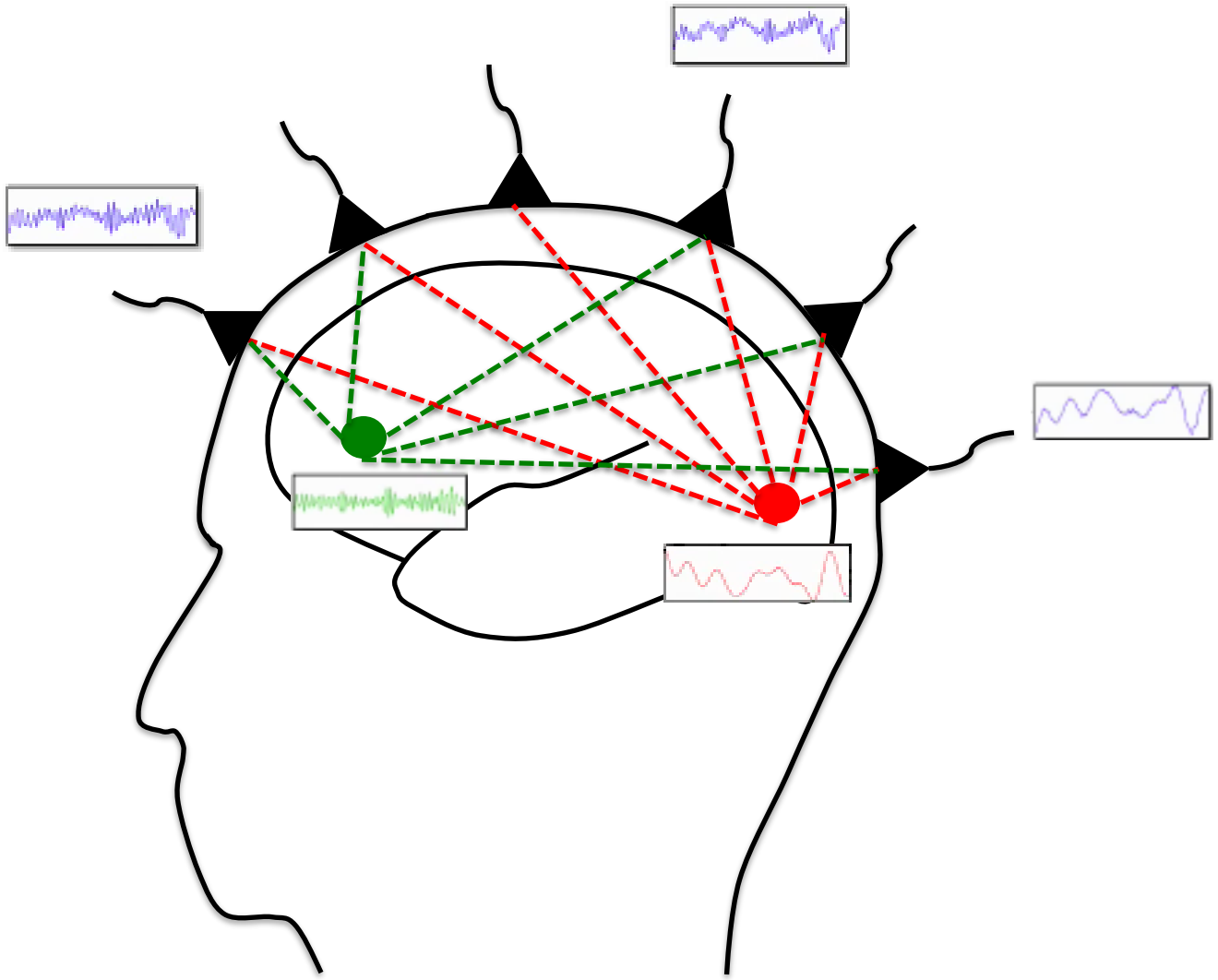
EEG Spatial Resolution



EEG Spatial Resolution

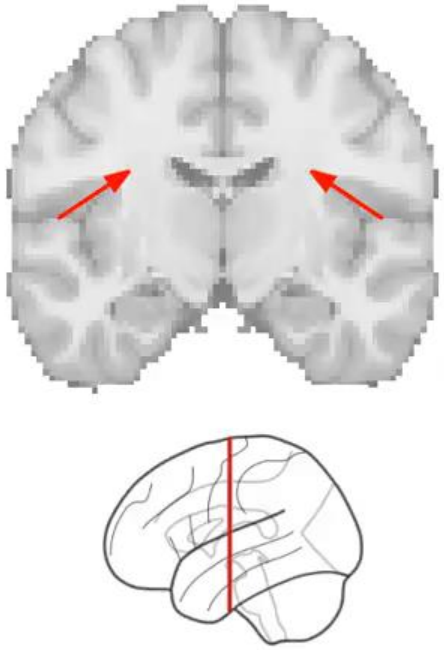


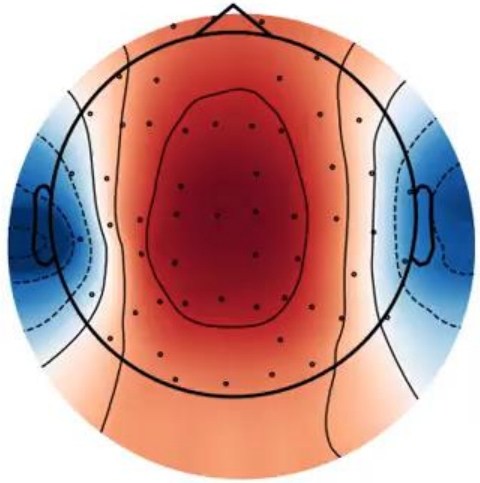
EEG Spatial Resolution



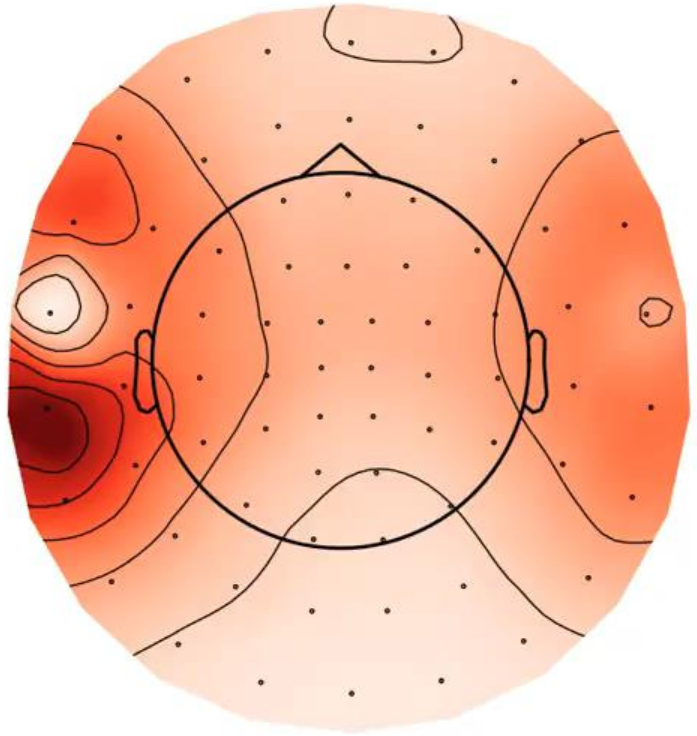
EEG Spatial Resolution

bilateral sources in auditory cortex EEG vs. MEG





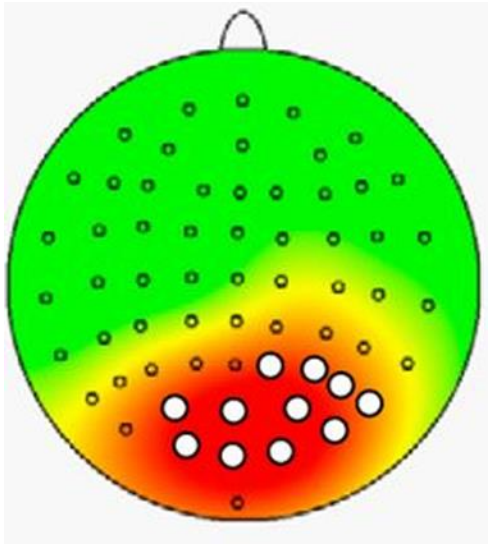
EEG electrodes



MEG gradiometers

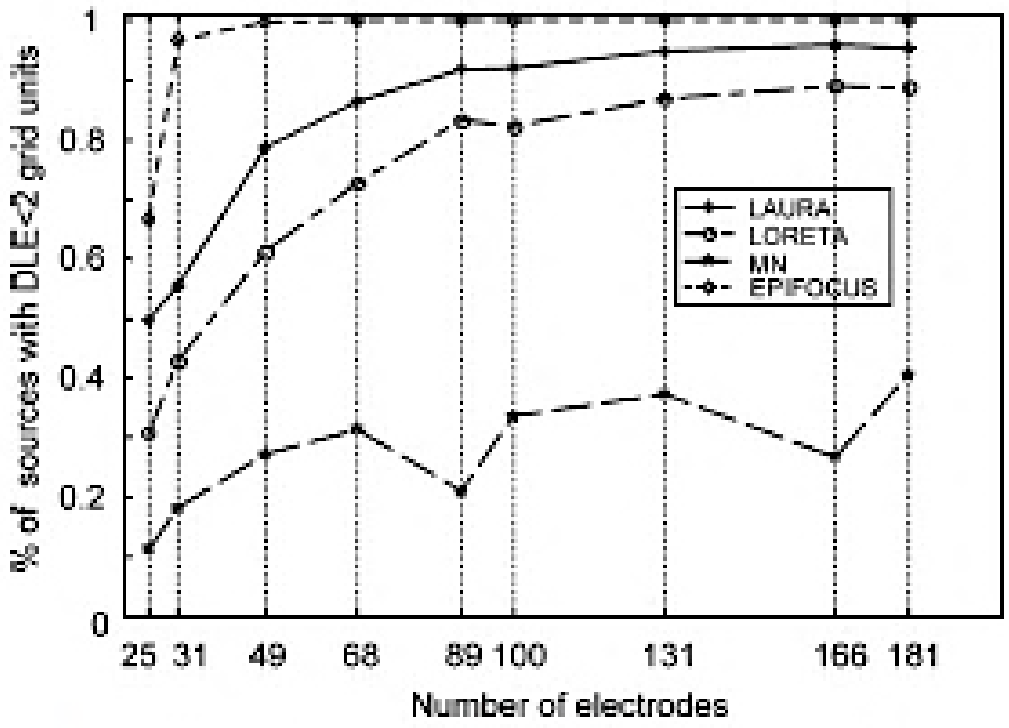
EEG Spatial Resolution

Scalp EEG



Source Localization

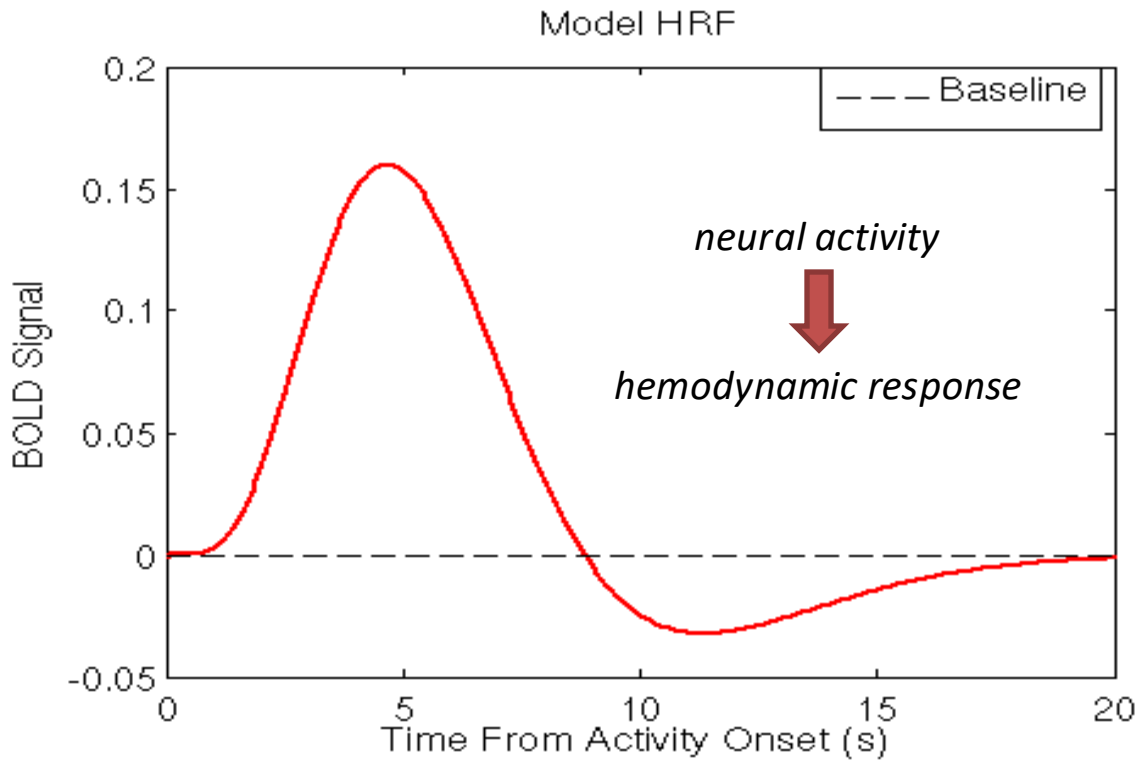
EEG Spatial Resolution



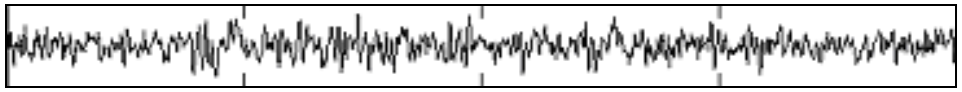
Accuracy of localization of a focus epilecticus (using source modelling)

Michel, Clin Neurophysiol, 2004

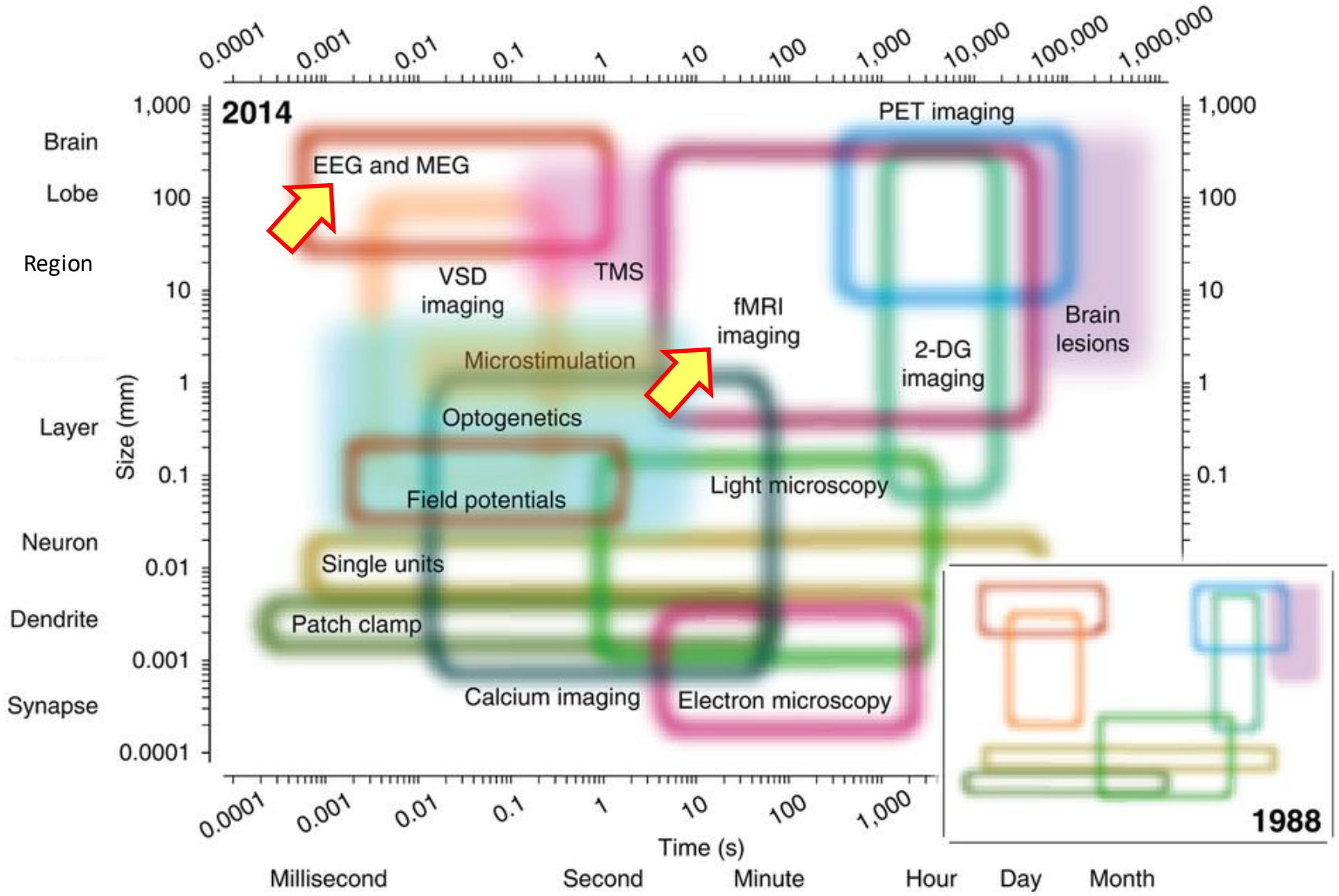
EEG vs fMRI: temporal resolution



EEG signal



Spatial and temporal resolution



fMRI, EEG and MEG

Selection of the technique

	EEG	MEG	fMRI
Signal Measured	Electrical activity from postsynaptic potentials in cortical neurons	Magnetic fields generated by neuronal electrical currents	Blood-oxygen-level-dependent (BOLD) signal, reflecting neural activity indirectly
Temporal Resolution	Excellent (~1 ms)	Excellent (~1 ms)	Poor (~1–2 s)
Spatial Resolution	Poor (~cm scale)	Similar to EEG (~mm–cm)	Excellent (~1–3 mm)
Invasiveness	Non-invasive, safe	Non-invasive, safe	Non-invasive, safe; but contraindicated with metal implants or pacemakers
Cost & Accessibility	Low-cost, widely available	Very expensive, less widely available	High-cost, moderately available
Portability	Highly portable	Limited portability	Not portable
Sensitivity to Brain Areas	Good for cortical surface; poor for deep structures	Mainly cortical sulci; limited for deep structures	Good for both cortical and subcortical regions
Susceptibility to Artifacts	High (muscle, eye movement)	Moderate (less sensitive to scalp/skull conductivity than EEG)	Moderate (motion-sensitive; physiological noise like heartbeat, respiration)

Number of Sensors in EEG Systems

M/EEG

1. Excellent temporal resolution
2. Portable & relatively cheap
3. Direct measure of neural activity

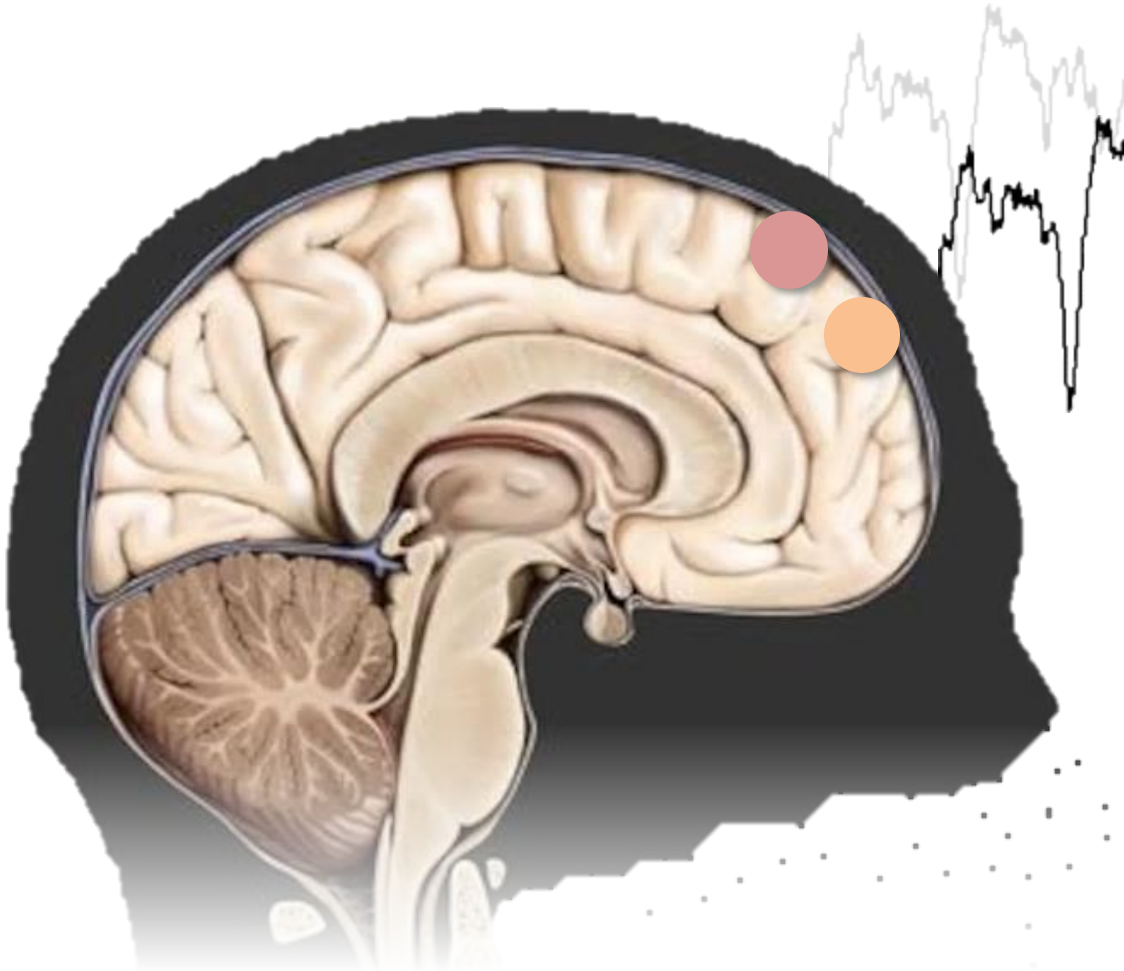
1. Poor spatial resolution
2. Mostly sensitive to cortical surface
3. Susceptible to artifacts

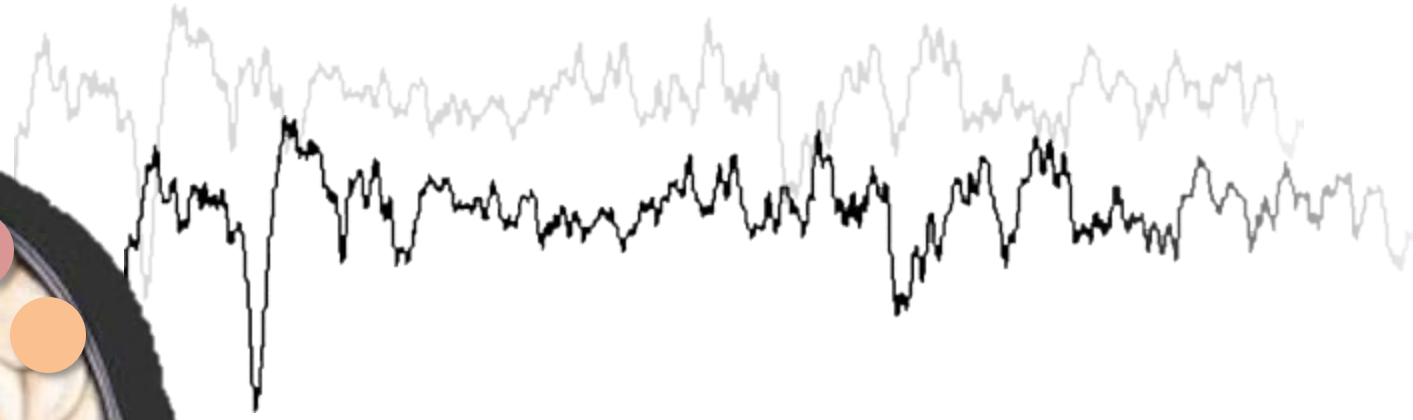
fMRI

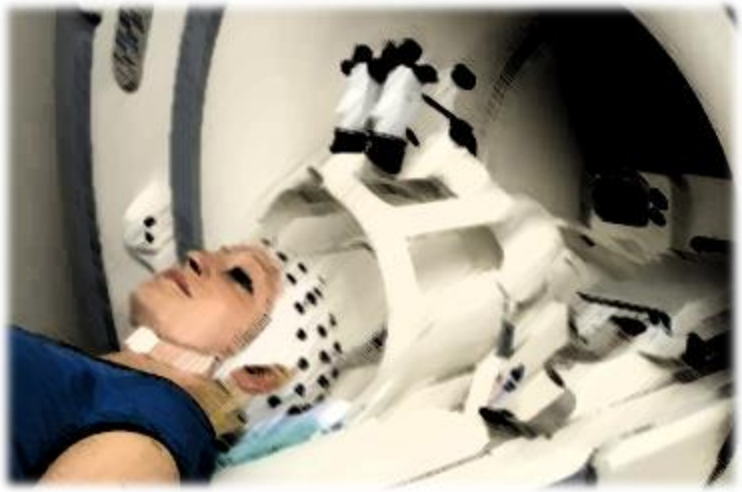
1. Excellent spatial resolution
2. Can image deep brain structures
3. Non-invasive and widely validated

1. Poor temporal resolution
2. Indirect measure of neural activity
3. Sensitive to motion and physiological noise

EEG + fMRI







EEG + TMS