Introduction to Neuroimaging Data

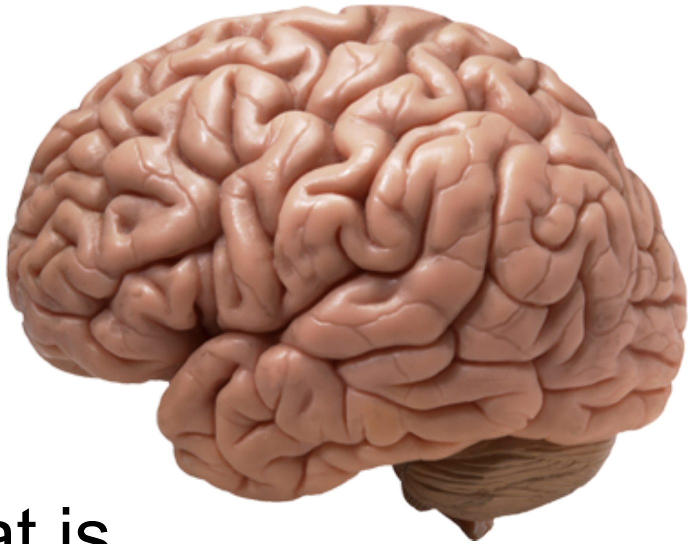
Phebe Kemmer

BIOS 516

Sept 17, 2015

The Human Brain

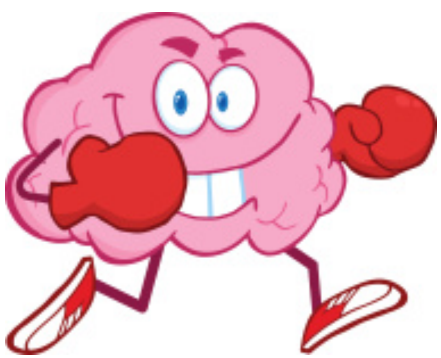
- Controls all body activities
  - Heart rate, breathing, sexual function
  - Motor activities and senses
  - Learning, memory, language
  - Emotion, mood, behavior
  - Consumes ~20% of energy



- Daunting task for an organ that is
  - 3 pounds of fatty tissue
  - Cortex thick as 4 sheets of paper

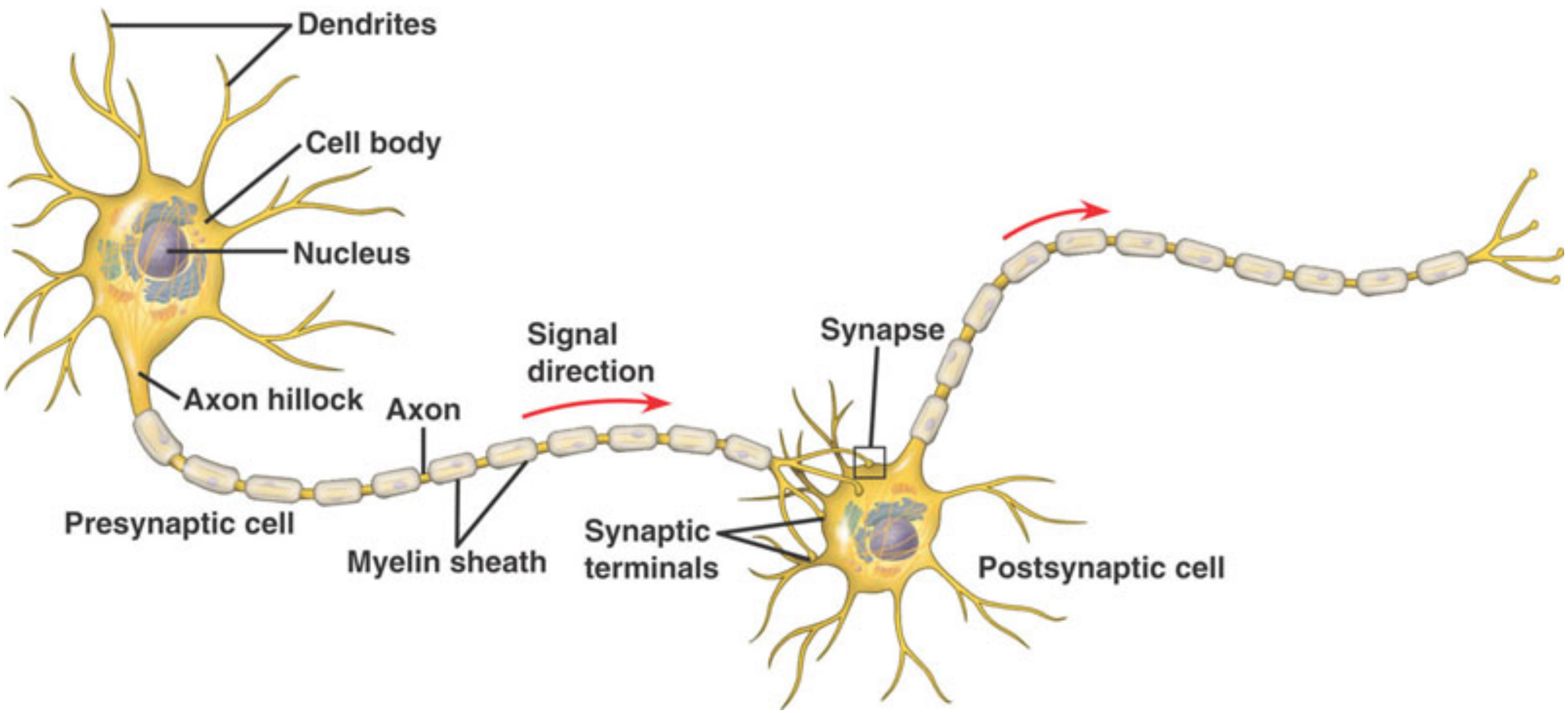
The Human Brain

- How does this small package provide such a powerful punch?
  - Contains a network of an estimated 100 billion neurons
  - Highly sophisticated organization and system of communication
  - Each neuron has an estimated 7,000 synaptic connections (on average), giving up to 700 trillion connections!



The Neuron

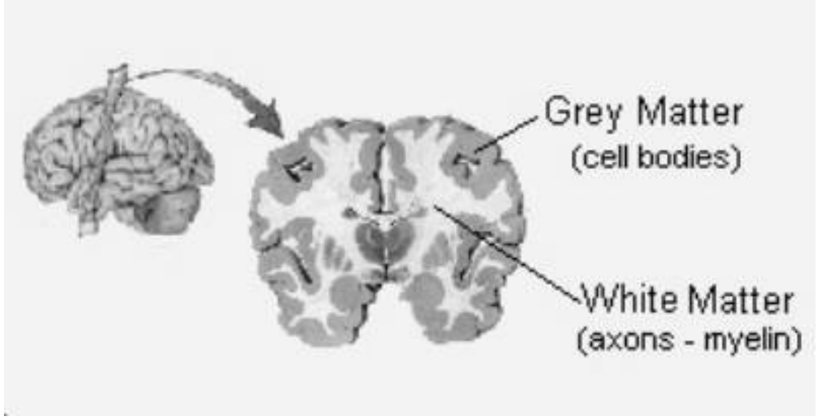
- The brain achieves amazing functionality via networks of interconnected neurons
- Basic neuron structure:



Gray vs. White Matter

Two main types of brain tissue:

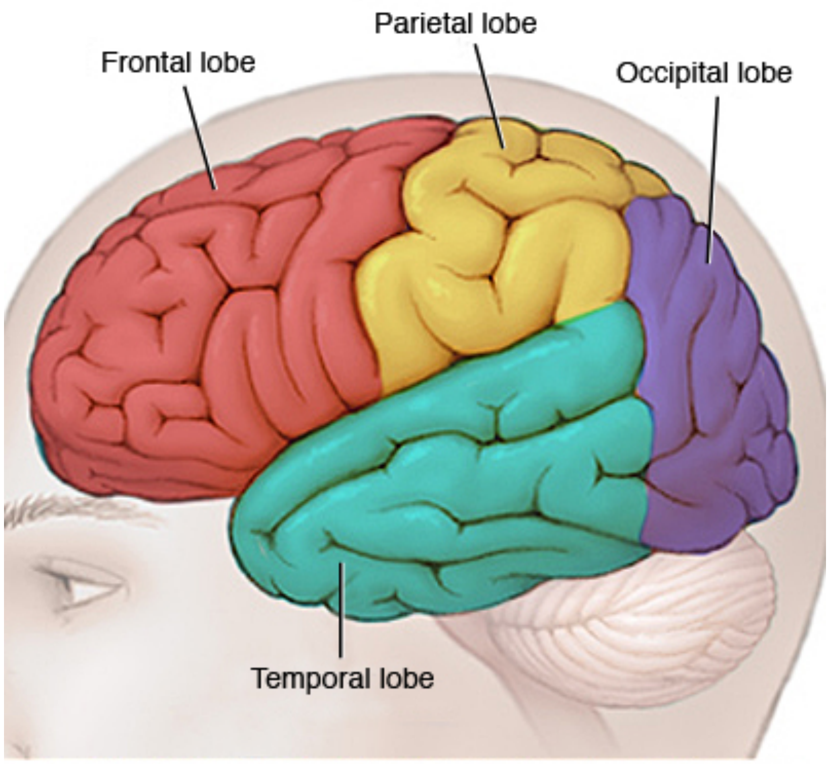
- **Gray Matter**
  - Makes up the surface of the cortex
  - Composed of neuron cell bodies
- **White Matter**
  - Lies beneath the cortex
  - Composed of fiber tracts that connect nerve cells
  - Enables communication between remote brain locations!



Some Brain Terminology

- Two Hemispheres (Left, Right)
  - connected by the **corpus callosum** (thick white matter fiber bundle)

- Four lobes:
  - Frontal (conscious thought)
  - Parietal (sensory info)
  - Temporal (auditory)
  - Occipital (vision)



Neuroimaging

- Neuroimaging methods allow us to understand interactions between the mind, brain, and body in a way we never have before.
- These interactions determine whether we are healthy or sick, energized or depressed, etc.
- Understanding these interactions is one of the most complex, important, and challenging issues in science today.

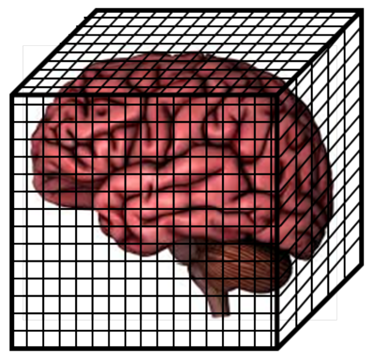
Neuroimaging

- Brain imaging can be separated into two major categories:
  - Structural neuroimaging
  - Functional neuroimaging

- There are a number of different modalities for performing each category

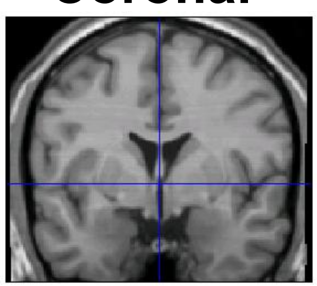
Brain Imaging Basics

- A brain image is represented by a 3D matrix of numbers that correspond to spatial locations
- Each location in the matrix is called a **voxel** (volumetric pixel)

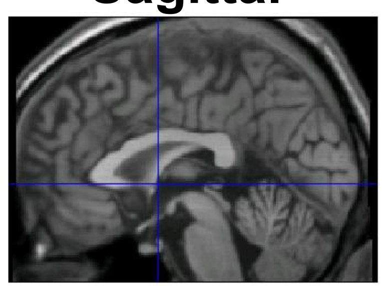


- Can be displayed in slices, in 3 orientations:

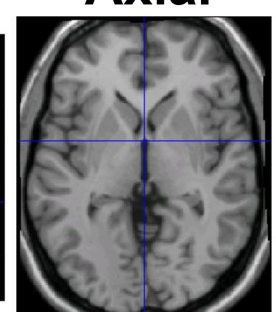
Coronal



Sagittal



Axial



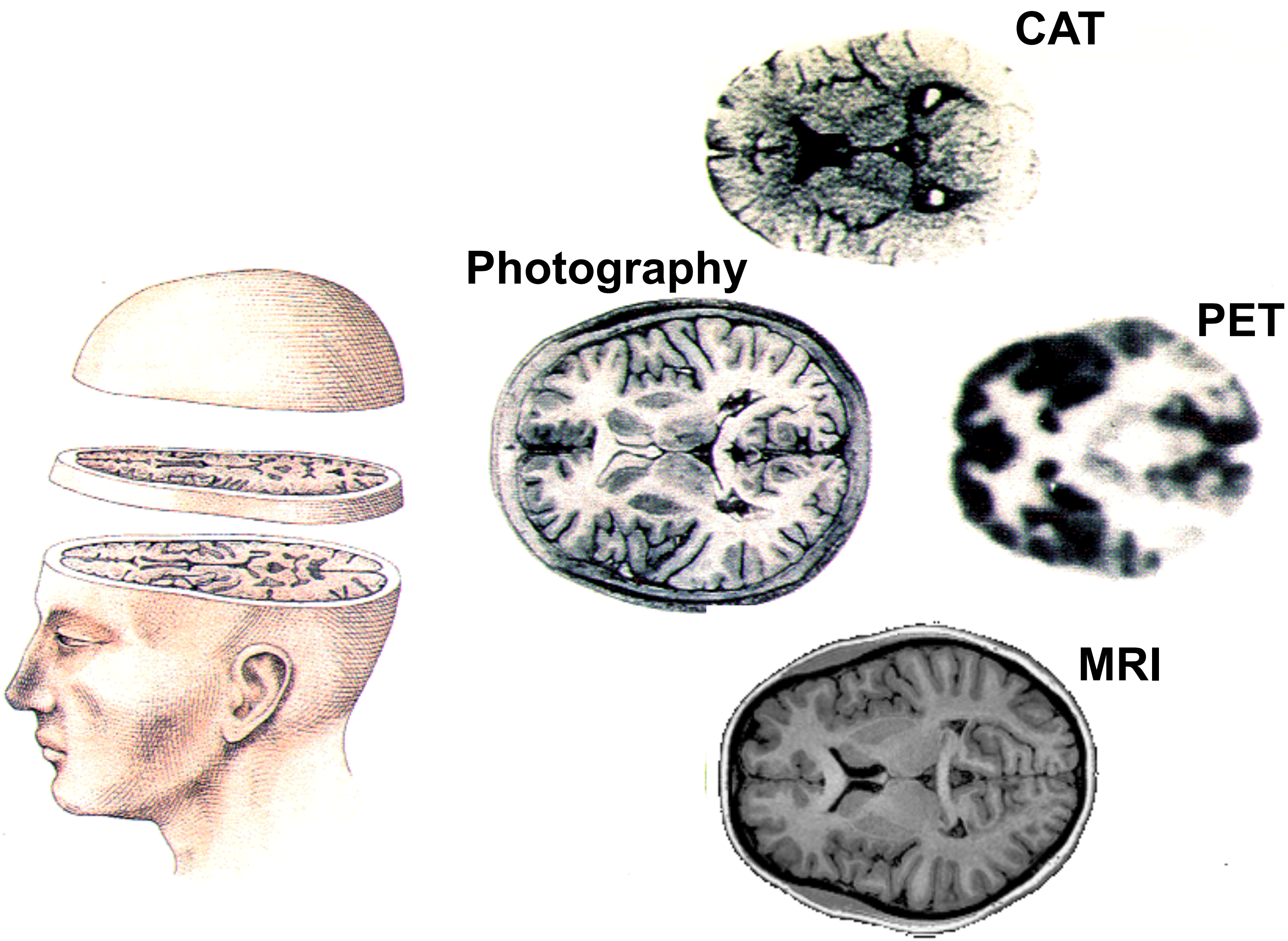
(MRI)

Structural Brain Imaging

- **Structural brain imaging** deals with the study of brain structure and the diagnosis of disease (e.g. tumors) and injury.

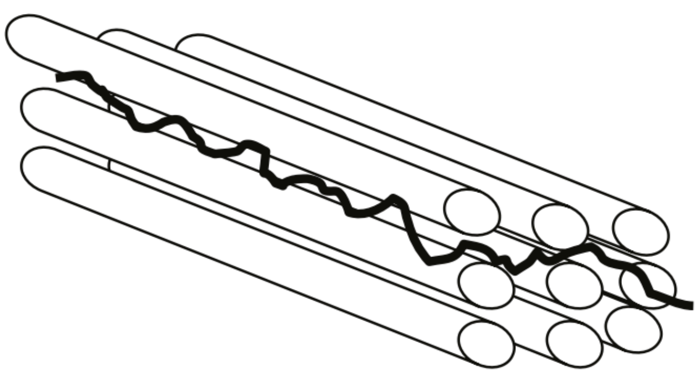
- Modalities include:
  - computed axial tomography (CAT),
  - magnetic resonance imaging (MRI), and
  - positron emission tomography (PET).

Structural Brain Imaging



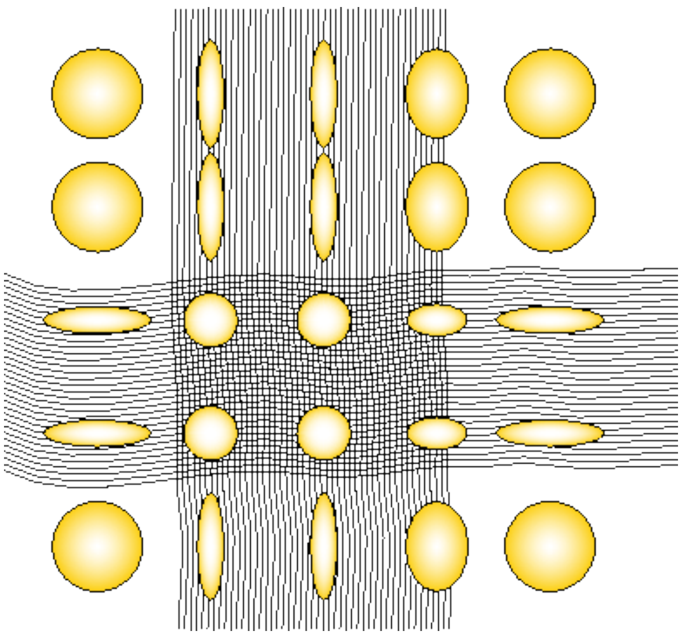
Diffusion Tensor Imaging

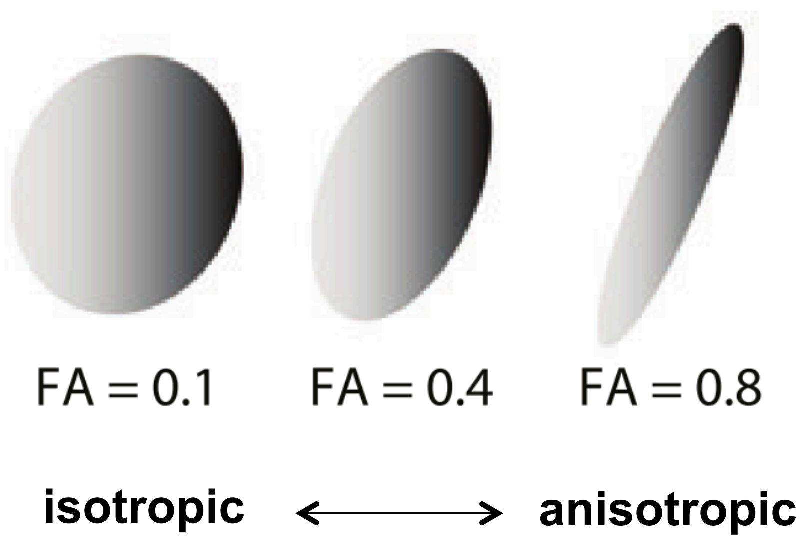
- An MRI technique that maps **white matter fiber tracts** in the brain by measuring the diffusion of water molecules.
- Water diffuses more quickly <u>along</u> axons than <u>across</u> them (water and fat don't mix!)



Diffusion Tensor Imaging

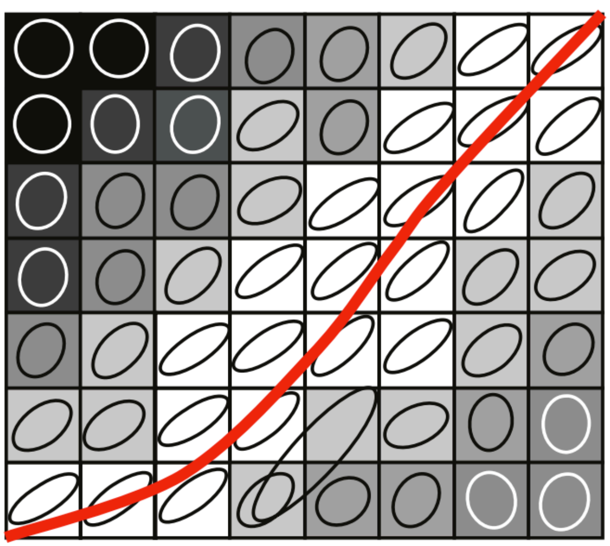
- Magnetic gradients are applied in different directions to calculate the **diffusion tensor** at each voxel location.
- **Fractional Anisotropy (FA)** – ranges from 0-1 and describes degree of diffusion restriction

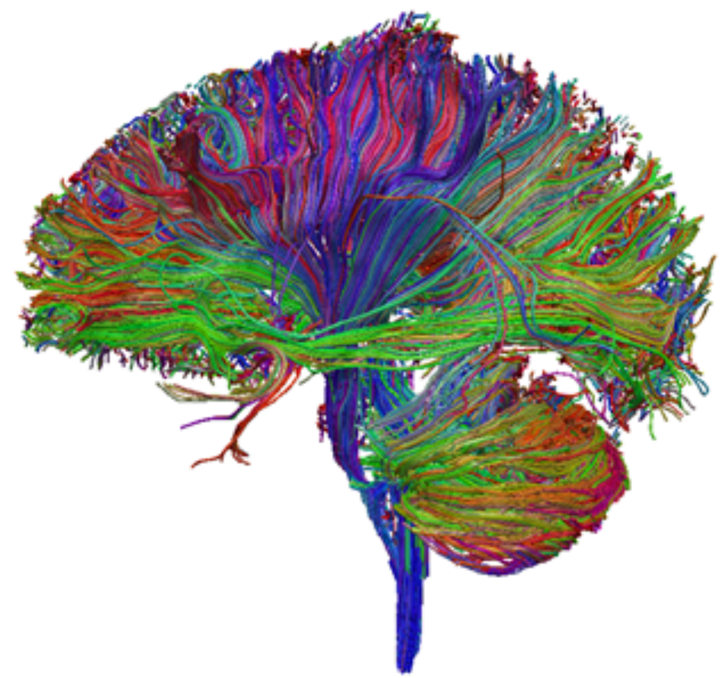




Tractography

- We can trace streams through the tensor field to reconstruct the structural connections in the brain!



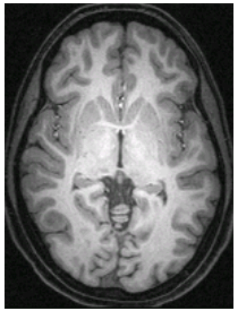


Functional Brain Imaging

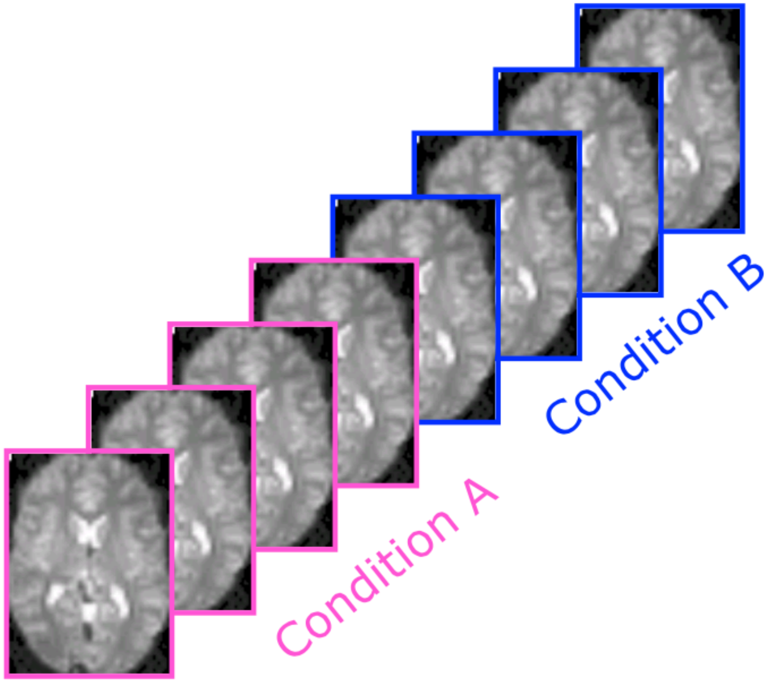
- The process of mapping brain activity *in vivo* over time
- Useful for studying cognitive and affective processes.
- Popular non-invasive modalities include:
  - positron emission tomography (PET),
  - functional magnetic resonance imaging (fMRI),
  - electroencephalography (EEG), and
  - magnetoencephalography (MEG).

fMRI vs MRI

- Structural image (MRI):
  - High spatial resolution
  - No temporal information



- Functional image (fMRI):
  - Lower spatial resolution
  - Higher temporal resolution
  - Can relate changes in signal to experimental task

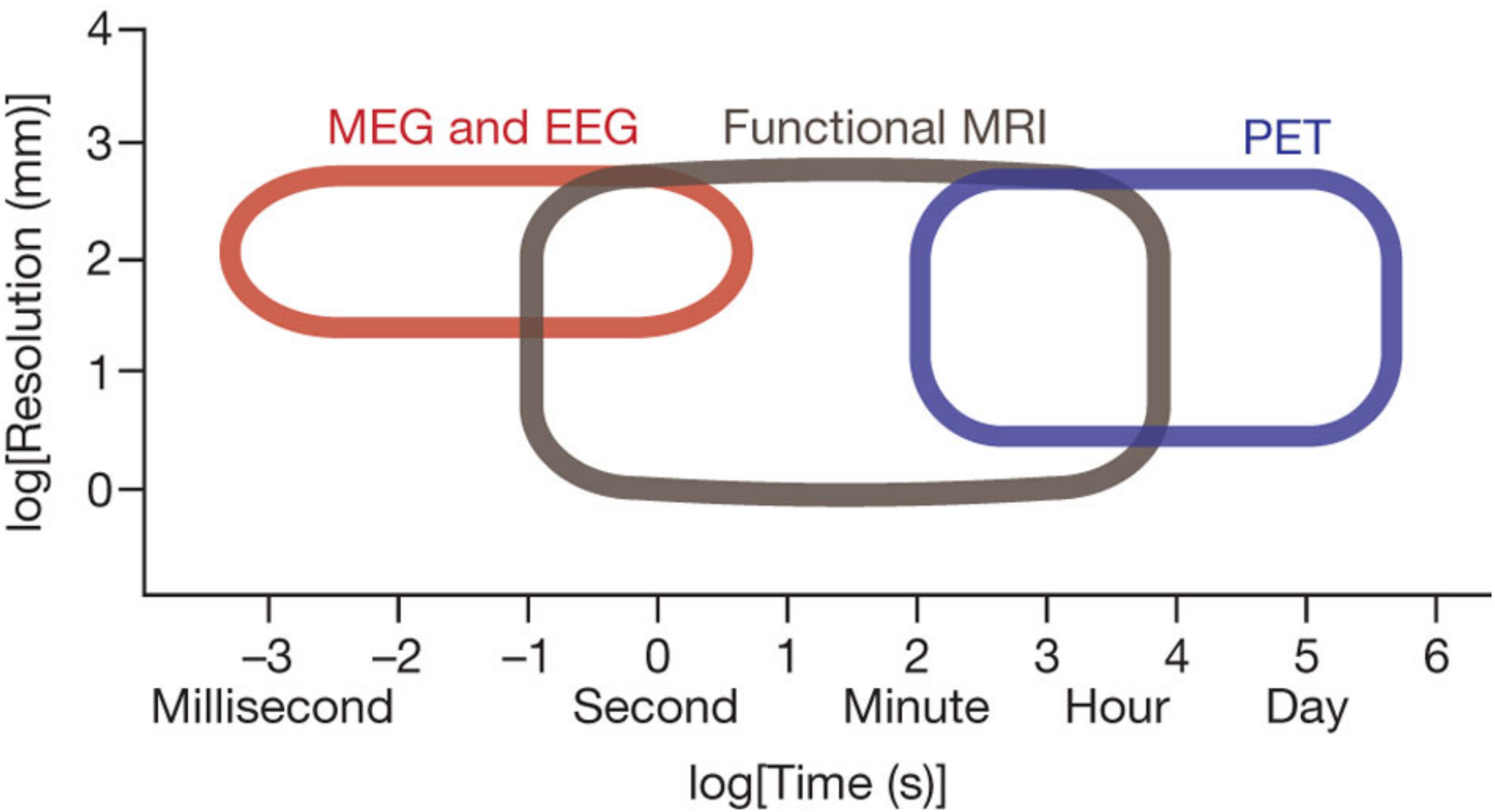


Functional Imaging Modalities

- Each functional modality provides a different type of measurement of brain activity.
  - **PET**: brain metabolism
  - **fMRI**: blood flow
  - **MEG/EEG**: electromagnetic signals generated by neural activity

- They also have their own pros and cons with regards to spatial resolution, temporal resolution, and invasiveness

Spatial & Temporal Properties



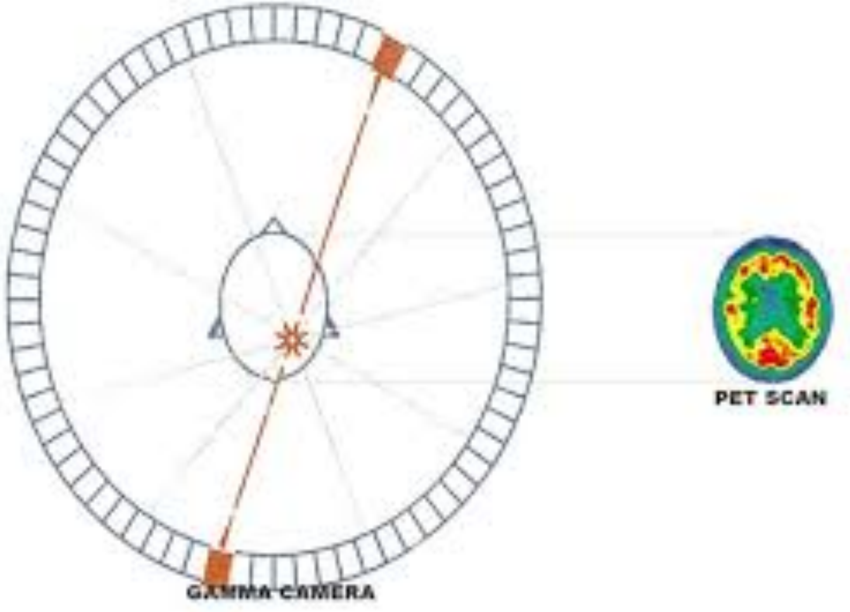
Meyer-Lindenberg, Nature, 2010

PET Overview

- PET is used to locate and quantify radioactivity emitted by radioactive tracers in the brain.
- Depending on the tracer, PET can be used to measure glucose metabolism, oxygen consumption, and regional cerebral blood flow – all correlates of neural activity.

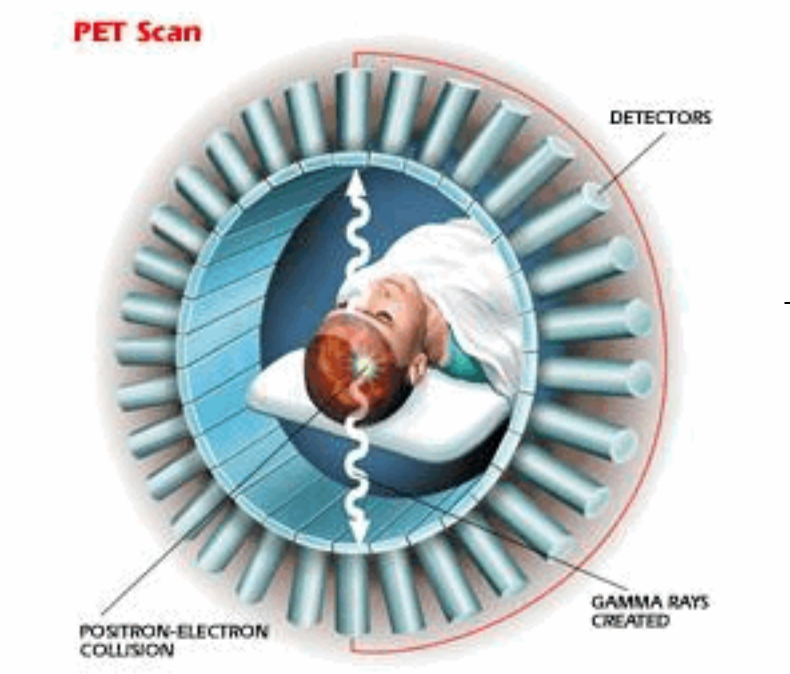
PET Overview

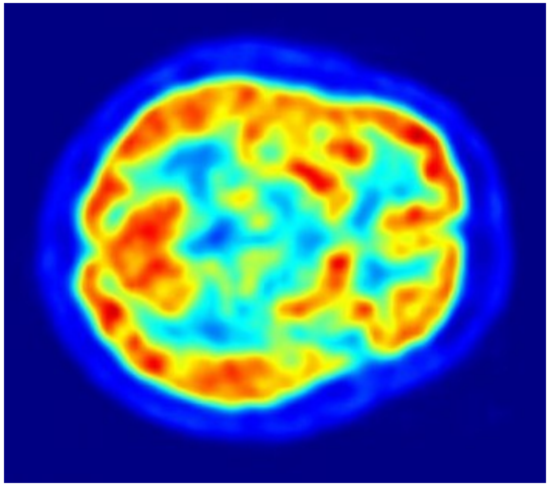
- The PET camera has several detector elements positioned on a circular array surrounding the patient.
- After the tracer is injected, the isotope emits a positron, which finds a nearby electron and annihilates, producing two gamma rays in opposite directions.



PET Overview

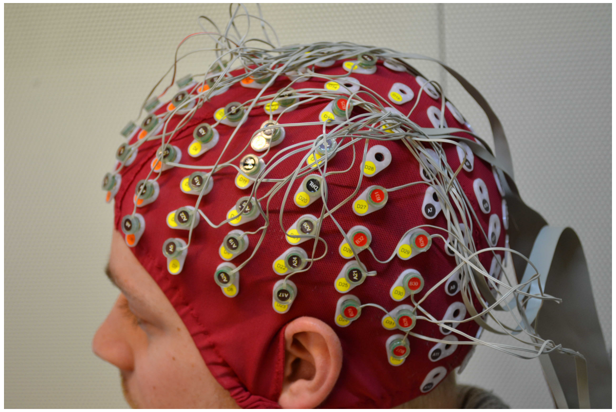
- Each gamma ray/photon “hits” one of the detectors. If a pair of photons are detected within a small time window, an event is recorded to have occurred along the line between the two detectors.
- A computer translates this information into an image





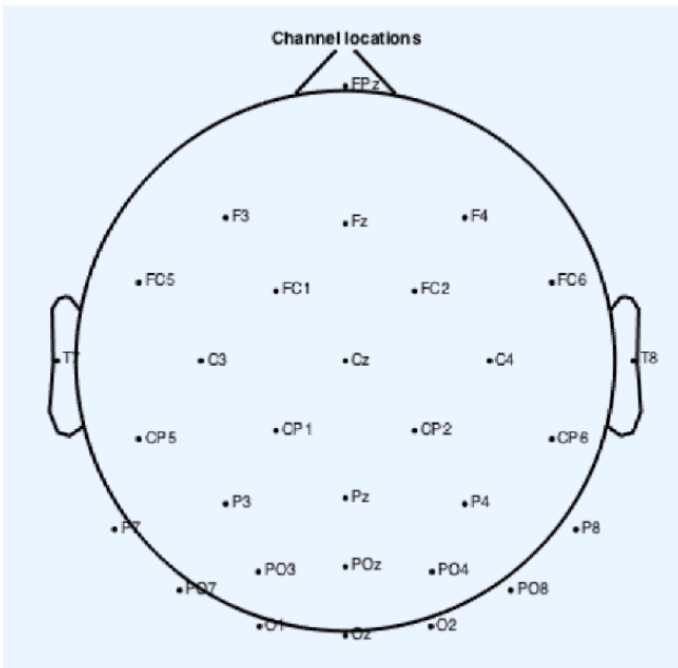
EEG/MEG Overview

- The electrical activity of neurons produces currents that spread through the brain
- When these currents reach the scalp, in the form of voltage changes and magnetic fields, they can be measured non-invasively.
- **EEG** measures voltage fluctuations sensed by an array of electrodes placed on the scalp.
- **MEG** measures the magnetic fields produced by the electrical currents using an array of sensitive magnetic field detectors.

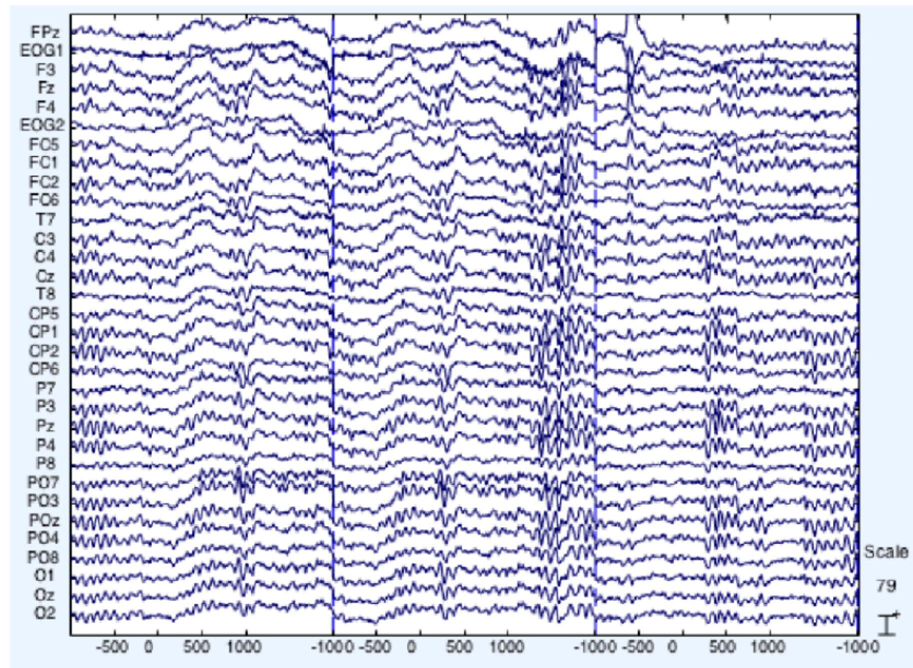


EEG Data

EEG channel locations



EEG signals at each location

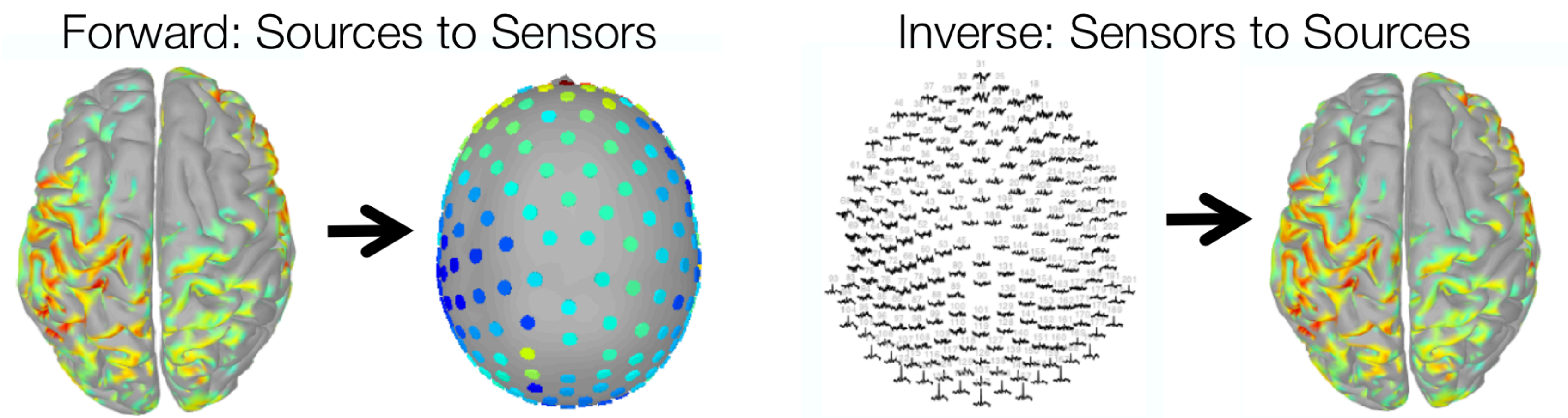


EEG/MEG Overview

- The signals recorded by EEG/MEG directly reflect current flows generated by neurons in the brain. (As opposed to PET & fMRI which measure correlated of neural activity).
- These signals are measured with millisecond temporal resolution, and provide the most direct measurement of brain processing available non-invasively.
- However, the spatial resolution of these methods is limited.

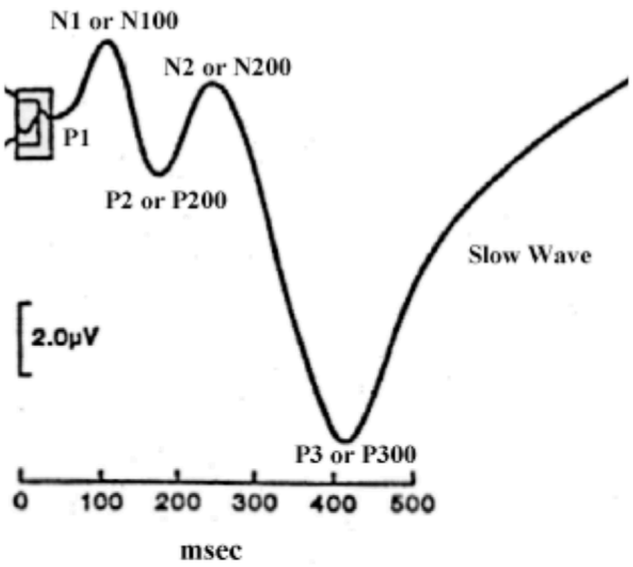
EEG/MEG Overview

- Building maps of brain activity from EEG/MEG signals requires the solution of an inverse source localization problem.



EEG/MEG Overview

- Typical EEG/MEG studies involve the presentation of repeated stimuli
- MEG and EEG data is often averaged over trials to form even-related fields (ERFs) and event-related potentials (ERPs), respectively.
- ERFs and ERPs are typically characterized by a series of deflections in their time course, which are pronounced at different recording sites on the scalp.



http://neurocog.psy.tufts.edu/images/ERP_components.gif

fMRI Overview

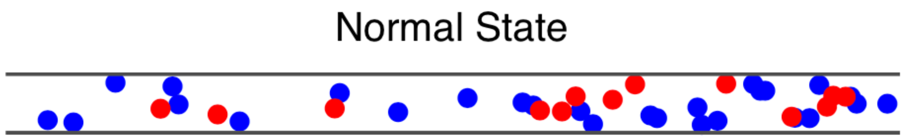
- Functional magnetic resonance imaging (fMRI) is a prominent non-invasive technique for studying brain activity.
- It provides an attractive balance of spatial and temporal resolution compared to alternative methods.

BOLD fMRI

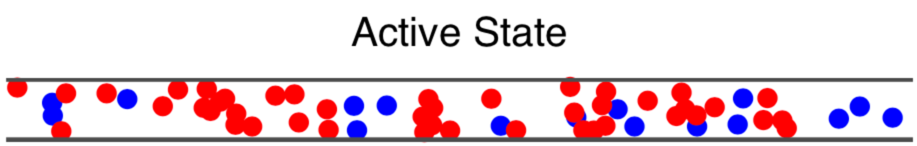
- fMRI measures the blood oxygenation level dependent **(BOLD) signal** as a correlate of neural activity
- Basis:
  - Neural activity causes localized increases in oxygen consumption
  - The body responds with an influx of oxygen-rich cerebral blood flow to fuel the increased metabolic activity
  - The increased oxygen supply actually outpaces the metabolic demand, resulting in an excess of oxygenated hemoglobin (oxyhemoglobin) in active brain tissue.
  - Therefore, there is relatively more oxyhemoglobin (OxyHb) than deoxyhemoglobin (deOxyHb) in these active areas

BOLD fMRI

- Normal State
  - Normal blood flow
  - deOxyHb is paramagnetic (small, positive susceptibility to magnetic fields)
  - Faster MRI signal decay, i.e. decreased MRI signal



- Active State
  - Increased blood flow
  - Increased oxygenation
  - OxyHb is diamagnetic (very weak, negative susceptibility to magnetic fields)
  - Slower MRI signal decay, i.e. increased MRI signal



MRI scanner

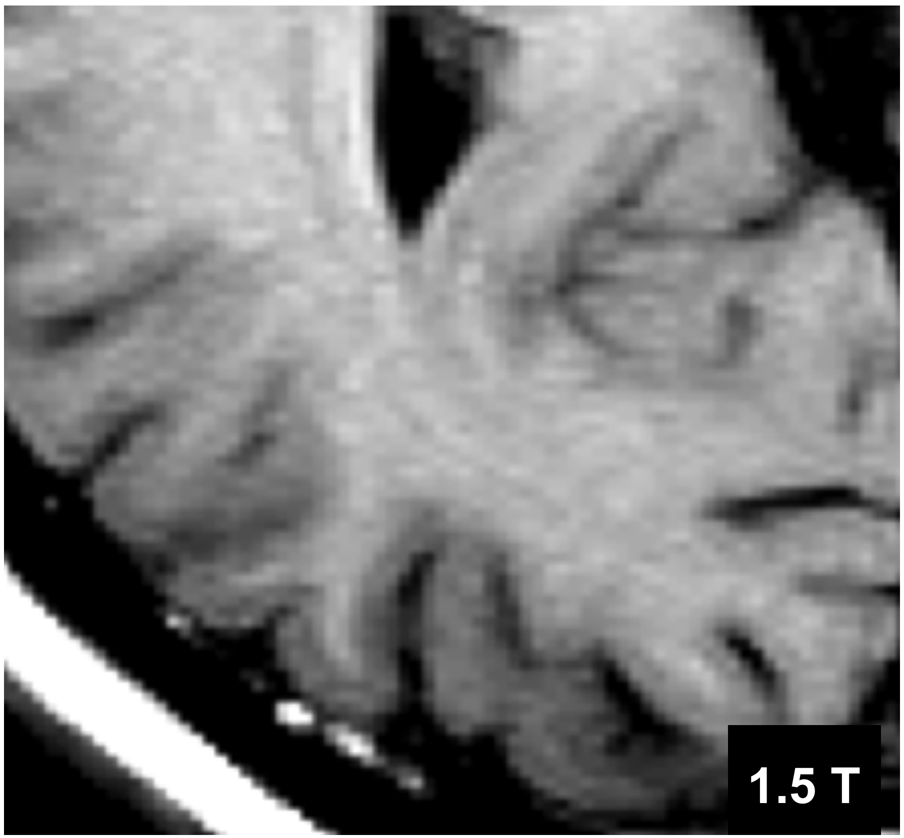
An MRI scanner consists of an electromagnet with a very strong magnetic field (1.5 - 7.0 Tesla)

Earth's magnetic field = 0.00005 T

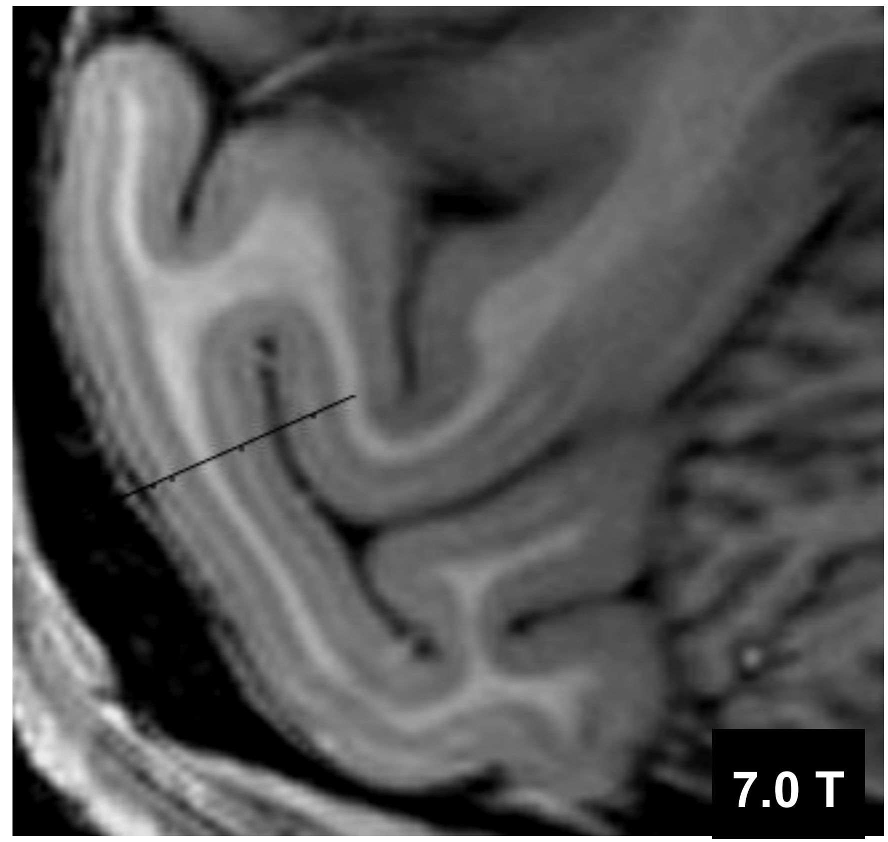
Be careful with metal objects……

Field Strength

Human V1 at 1.5 T vs. Monkey V1 at 7.0 T



2D T_1 images   780um x 780um x 5,000um



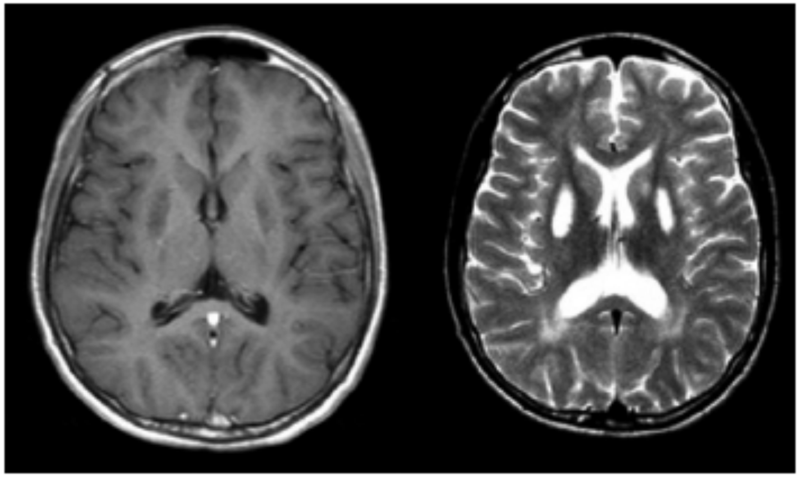
3D T_1 images   250um x 250um x 750um

Physiology of MRI

- The subject is placed in the MRI scanner which forms a strong magnetic field (B0)
- The nuclei of ^{1}H atoms align with B0
- A short radio frequency pulse is applied that knocks the ^{1}H nuclei out of alignment.
- After the pulse, the ^{1}H nuclei fall back into their original alignment (equlibrium), and as they do, release a signal that is picked up by the receiver coil in the scanner.
- A short video to illustrate... https://youtu.be/0YBUSOrH0lw

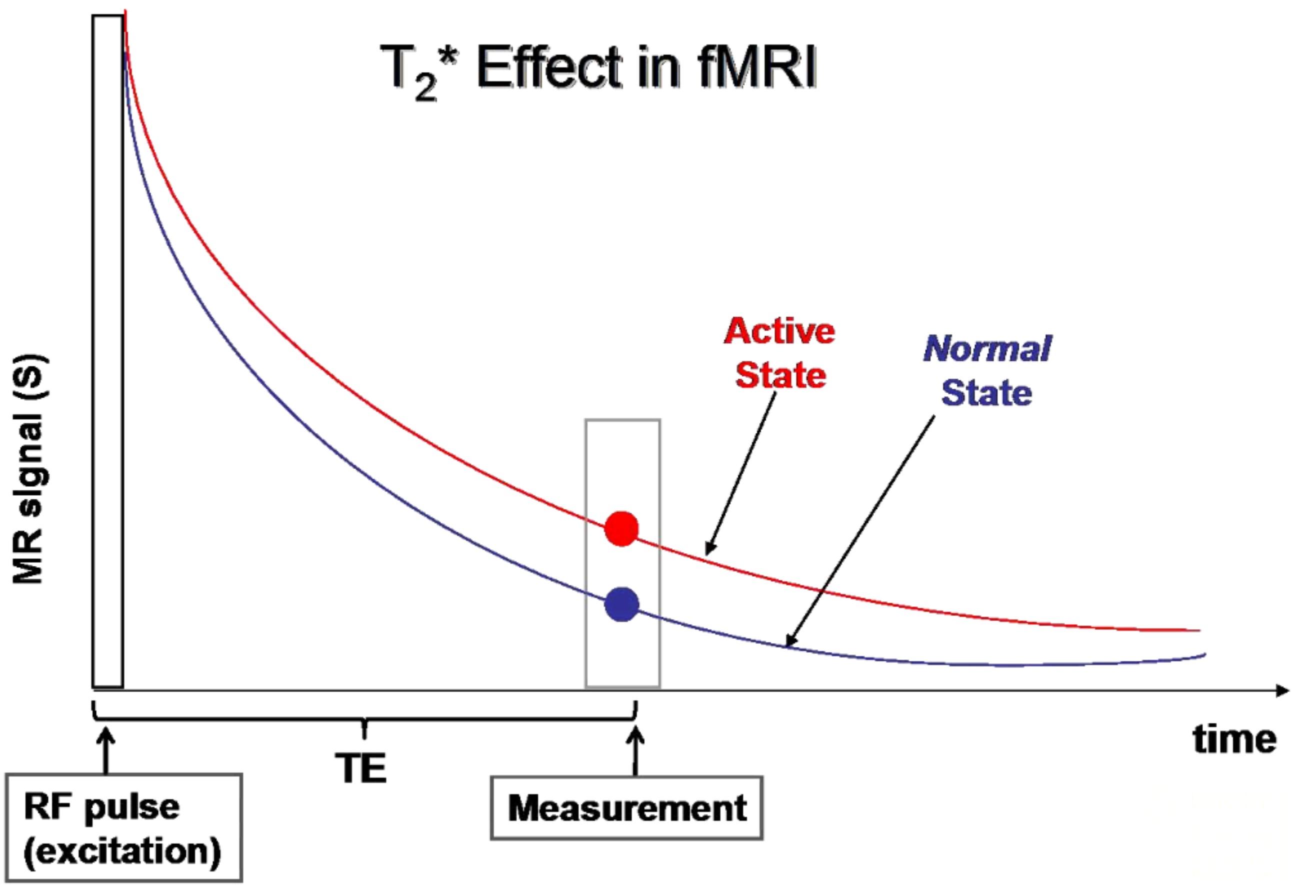
Physiology of MRI

- **Relaxation**: time to reach equilibrium after RF pulse
- Measured in 2 directions:
- Longitudinal (**T1**) – parallel to B0
  - Best for **anatomical MRI** – provides good contrast between tissue types. Fatty tissue (WM) is bright; CSF if dark.
- Transverse (**T2**) – perpendicular to B0
  - Best for **functional MRI** since T2 is much faster than T1. CSF appears bright and fatty tissue is dark.

T1  **T2**

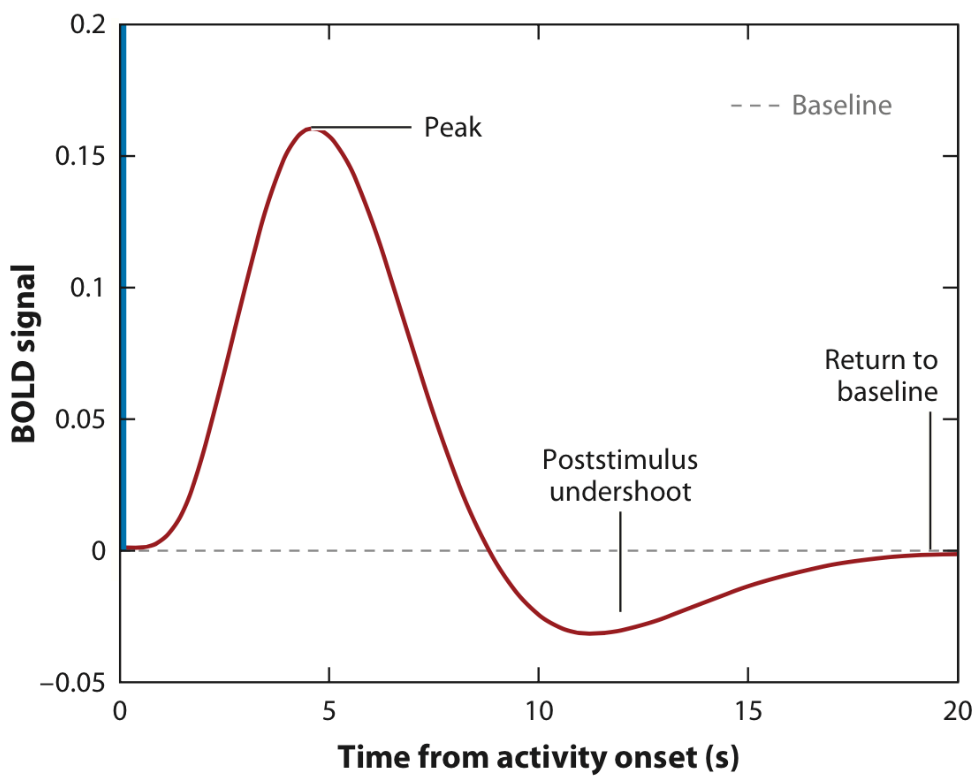
Physiology of fMRI

Deoxyhemoglobin suppresses the MRI signal. As the concentration of deoxyHb decreases (i.e. in active areas), the signal increases



HRF

The change in the MRI signal triggered by neural activity is known as the hemodynamic response function (HRF).



Bowman, 2014

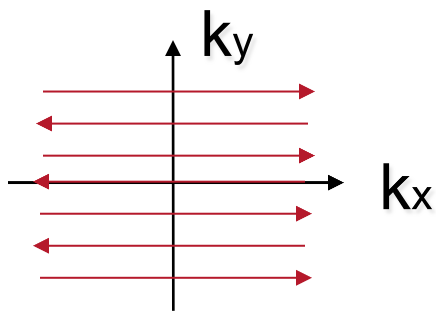
Properties of the HRF

- Magnitude of signal changes is quite small
  - 0.5 to 3% at 1.5 T
  - Hard to see in individual images

- Response is delayed and quite slow
  - Onset is ~2 sec after activity, and peaks 5-8 sec after the neural activity has peaked
  - Extracting temporal information is tricky, but possible
  - Even short events have a rather long response

Data Acquisition

k-space



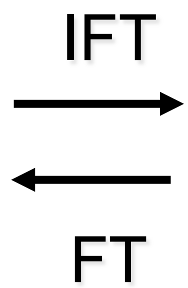
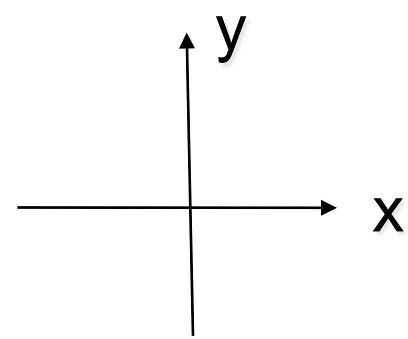
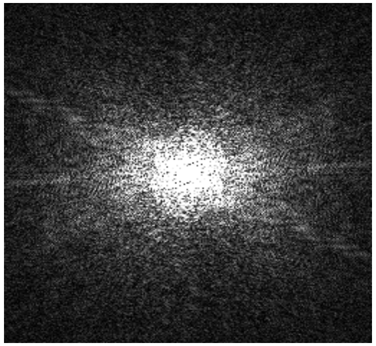
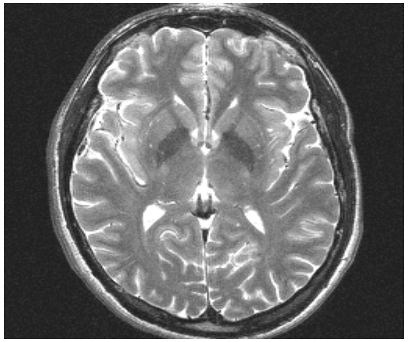


Image space

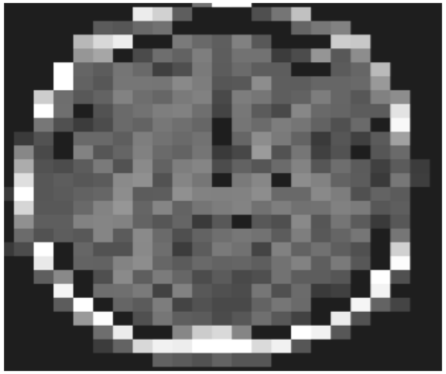




Data are acquired in k-space, and reconstructed in Image space

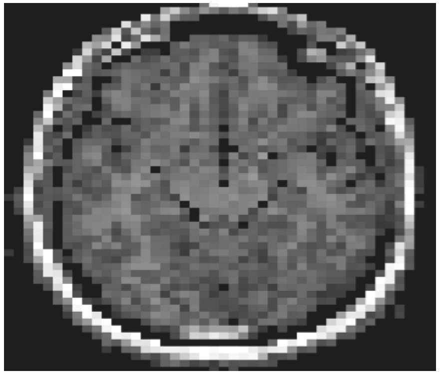


Spatial Resolution



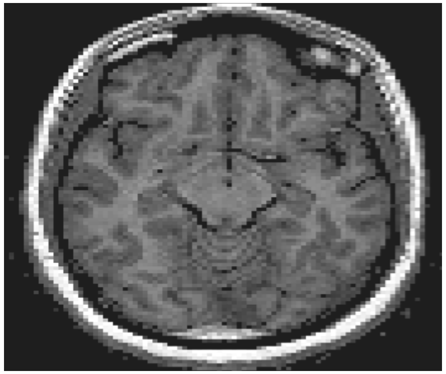
32x32 image

1024 points sampled in k-space



64x64 image

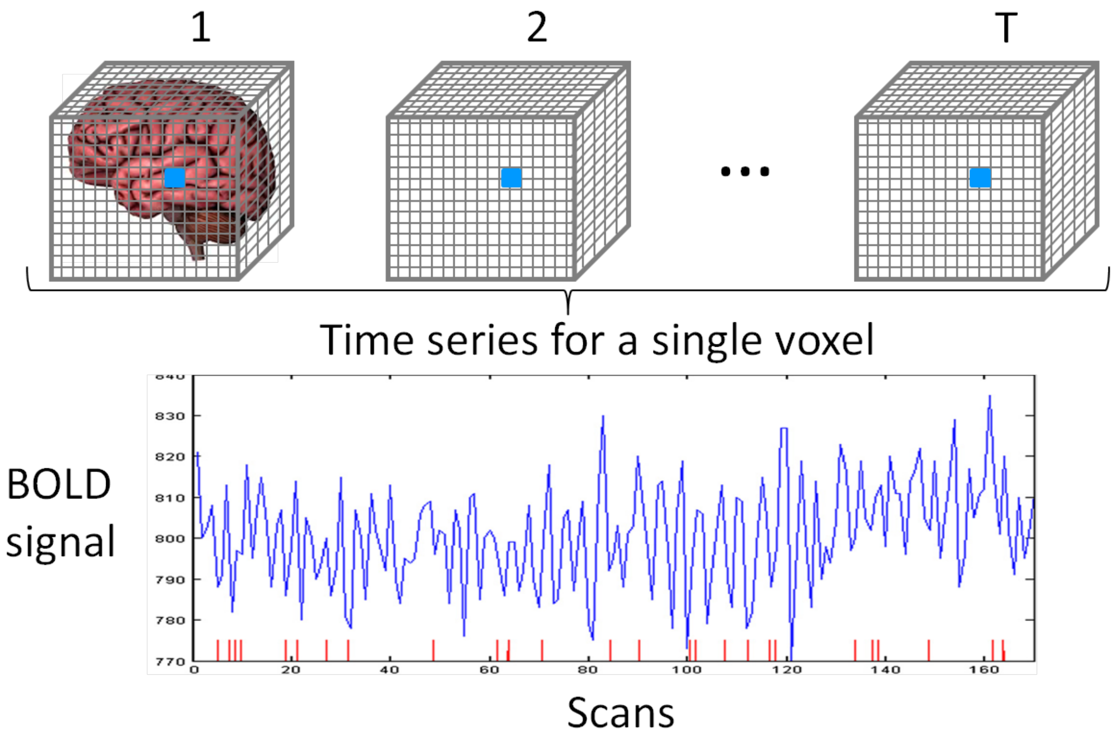
4096 points sampled in k-space



128x128 image

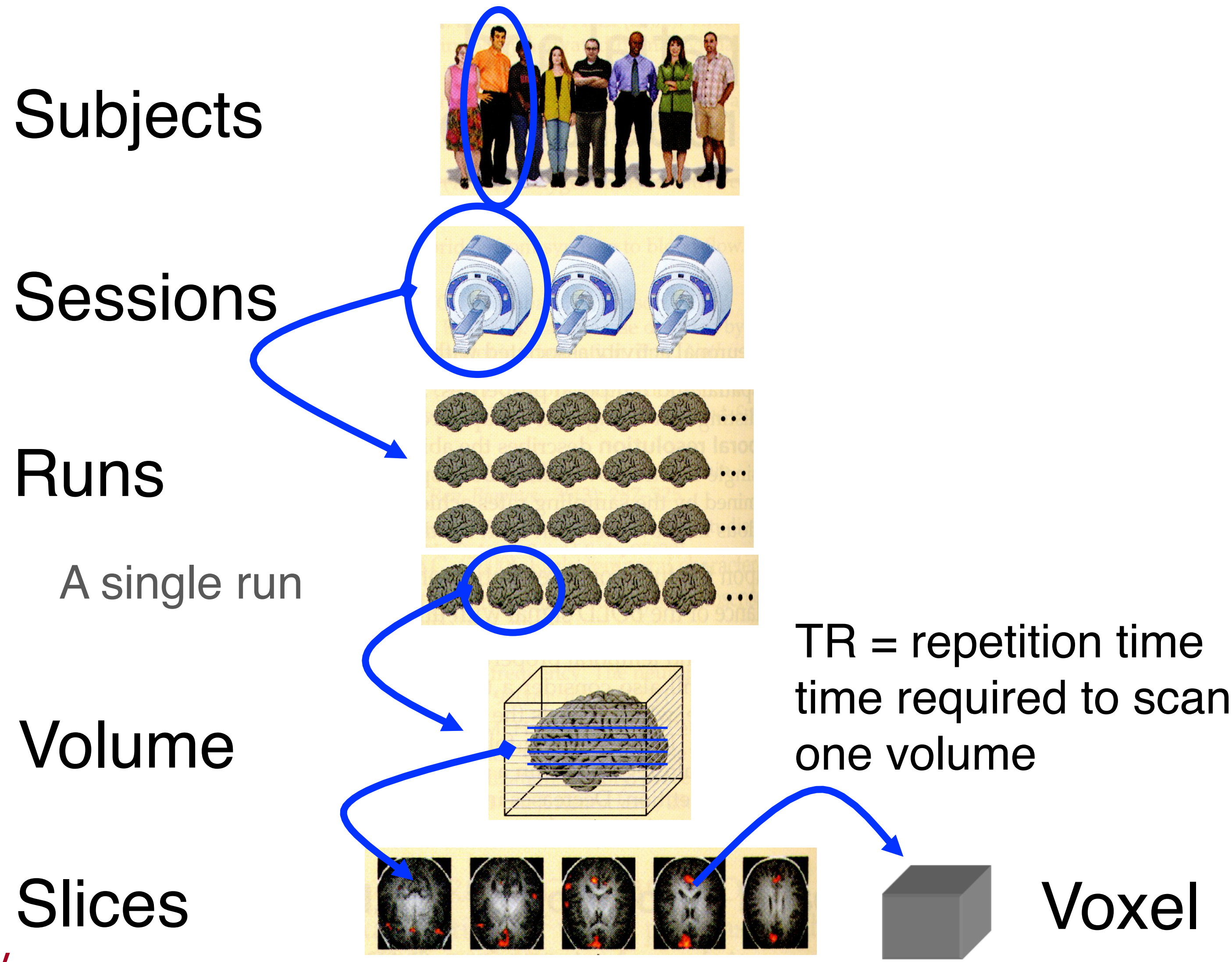
16,384 points sampled in k-space

fMRI data



- 3D brain scans captured over time – each with ~100K voxels
- Usually, T=100-2K, with scans every 2 sec
- Each voxel has a BOLD signal time course

fMRI hierarchy



Ged Ridgeway

Analysis of fMRI data

- The statistical analysis of fMRI data is challenging.

  - It is a massive data problem.
  - The signal of interest is relatively weak.
  - The data exhibits a complicated temporal and spatial noise structure.
  - We will discuss this more next week

Comparing Modalities

- Each functional neuroimaging modality provides a unique window into the brain
- PET and fMRI are the most widely used, and provide the most anatomically specific information across the entire brain.
- The relatively good spatial resolution of PET and fMRI complement the precise timing information provided by EEG/MEG.

PET vs fMRI

- Activation in both PET and fMRI reflect changes in neural activity measured indirectly, and they measure different biological processes related to brain activity, which may be broadly defined as the energy-consumption of neurons.

- The spatial resolution of PET is on the order of 1-1.5 cm^3 and fMRI is typically on the order of 27-36 mm^3 for human studies.

PET vs fMRI

- Because PET computes the amount of radioactivity emitted from a brain region, enough time must pass before a sufficient sample of radioactive counts can be collected.
  - Temporal resolution limited to blocks of at least 30 sec

- fMRI has its own temporal limitations due largely to the latency and duration of the hemodynamic response to neural events.
  - HRF doesn’t reach its peak until several seconds after local neuronal and metabolic activity has occurred.

PET vs fMRI

Table 2. Relative advantages of fMRI and PET

Advantages of fMRI	
Cost and availability	fMRI has lower cost, more facilities available
Spatial resolution	fMRI has higher resolution, but new PET scanners can have same functional resolution for group studies
Temporal resolution	fMRI is superior, permitting event-related designs
Brain connectivity analyses	fMRI permits time series connectivity analysis; PET and fMRI both permit individual differences analysis
Combination with other measures	Simultaneous time-series acquisition of fMRI and EEG provides most detailed mapping of relationships
Single-subject studies	fMRI permits detailed high-resolution studies of individuals
Repeatability	fMRI does not use radioactive substances, so frequent scans are considered safe

Advantages of PET	
Measuring neurochemistry	PET is superior; can be used to directly investigate neurochemistry
Transparency of activation measures	PET provides more direct measures of blood flow or metabolism
Artifacts	PET does not suffer from magnetic susceptibility artifacts and gradient- or RF-related artifacts
Combination with other measures	PET is not magnetic and can be combined with simultaneous EEG, MEG, and TMS
Studying baseline activity	PET provides quantitative measure of baseline state; ASL fMRI also can, but is less commonly available
Naturalness of environment	PET is quieter and has more open physical environment; advantage for auditory and emotion tasks

Wager et al, 2010

Comparing Modalities

- The signals recorded by EEG/MEG directly reflect current generated by neurons within the brain.
- The spatial resolution of EEG is around 6 cm^3. In addition, it only measures activity on the surface of the cortex, and not from deeper structures.
- However, it is less expensive and more convenient for using with patients compared to fMRI and PET.
- Due to its excellent temporal resolution, it is useful for monitoring online activity, and ideal for Brain-Computer Interface

MEG vs. EEG

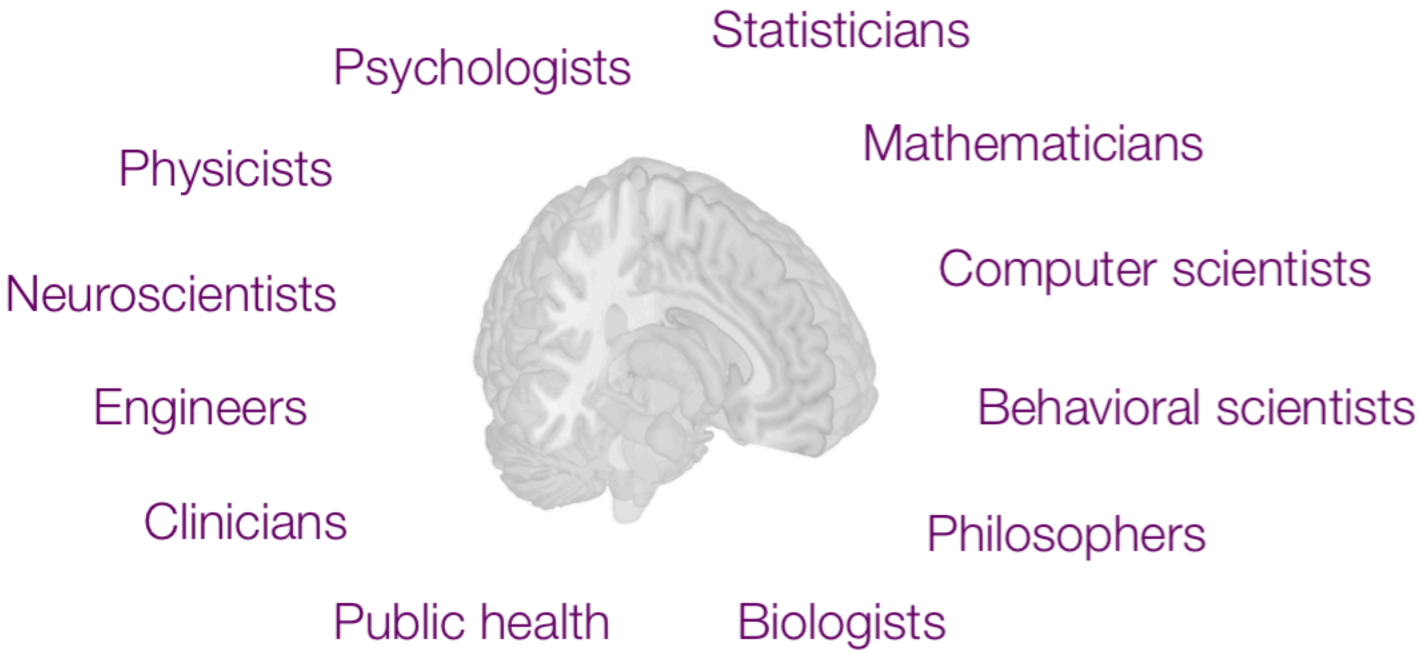
- MEG has relatively better spatial resolution than EEG
  - Magnetic fields are less distorted than electric fields by the skull and scalp.

- EEG tends to be sensitive to activity in more brain areas, but activity visible in MEG can also be localized with more accuracy

Combining modalities

- Recently, there is a trend towards using multiple imaging modalities to overcome some of the limitations of each method used in isolation.
  - EEG and fMRI: achieve best spatial and temporal resolution
  - fMRI and PET: requires a hybrid scanner
  - fMRI and DTI: study structure-function relationship
  - fMRI and Genetics (i.e. Imaging Genetics)

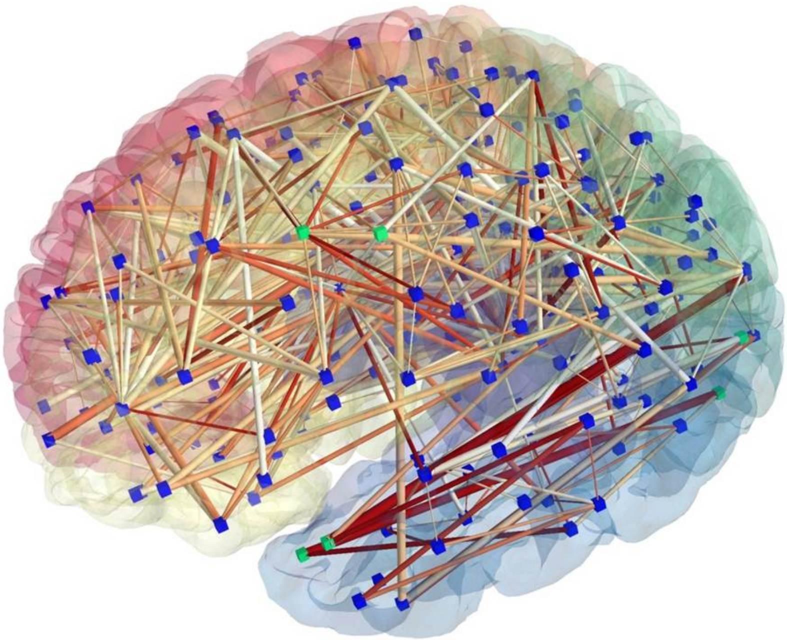
A multidisciplinary community



- Need experts in each discipline working together.
- Need individuals with multiple types of expertise.

Next week…

- Statistical Analysis of Neuroimaging Data
  - Preprocessing of fMRI data
  - Study Designs
  - Analysis Strategies:
    - Activation
    - Connectivity
    - Network Analysis
    - Prediction



Want to learn more?

- Join the Center for Biomedical Imaging Statistics (CBIS) group
  - led by Ying Guo
  - Weekly meetings on Fridays at 11am

- “Principles of fMRI” coursera course:
  - https://www.coursera.org/course/fmri1
  - Oct 12 - Nov 7