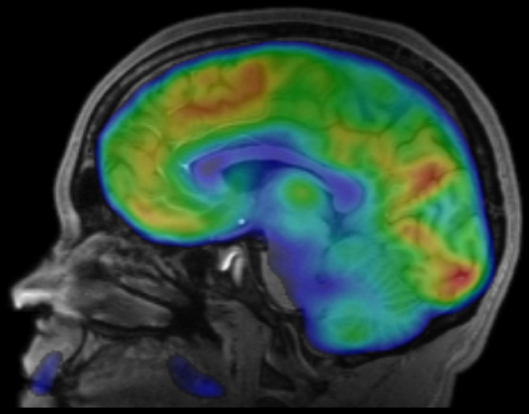
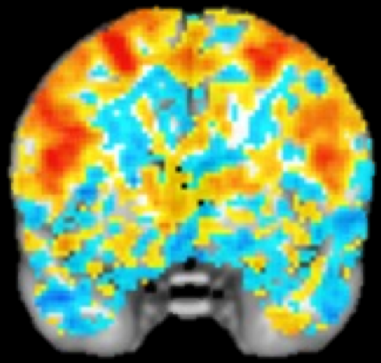
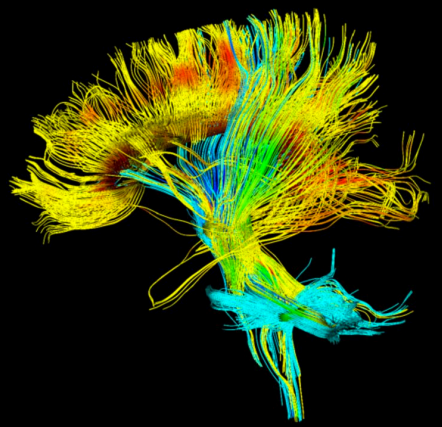
INTRO TO NEUROIMAGING:
PET, fMRI, and DWI

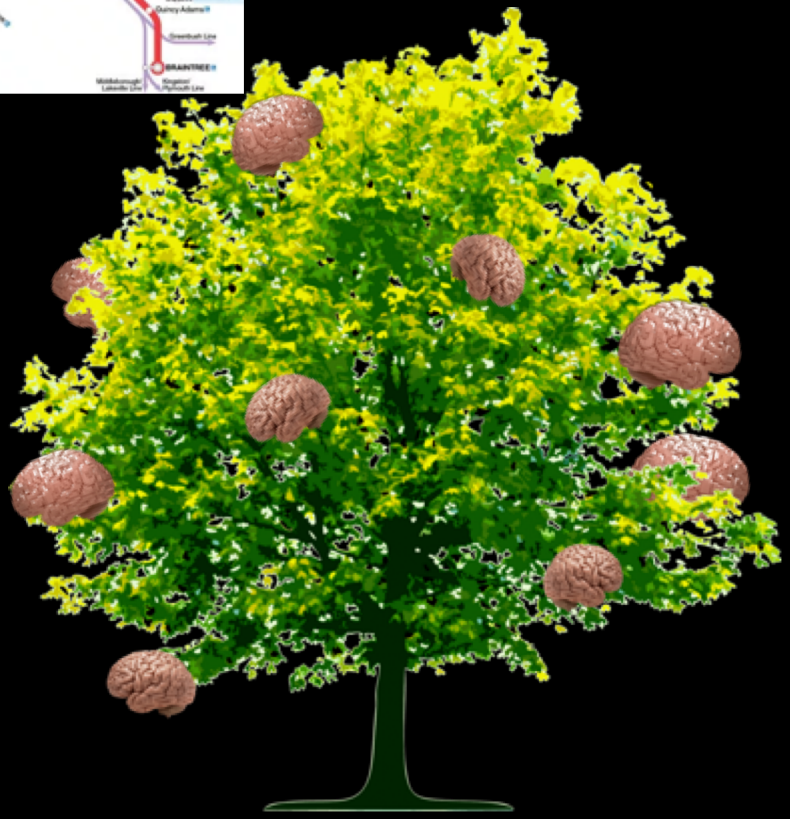
February 23, 2021

Tom Morin

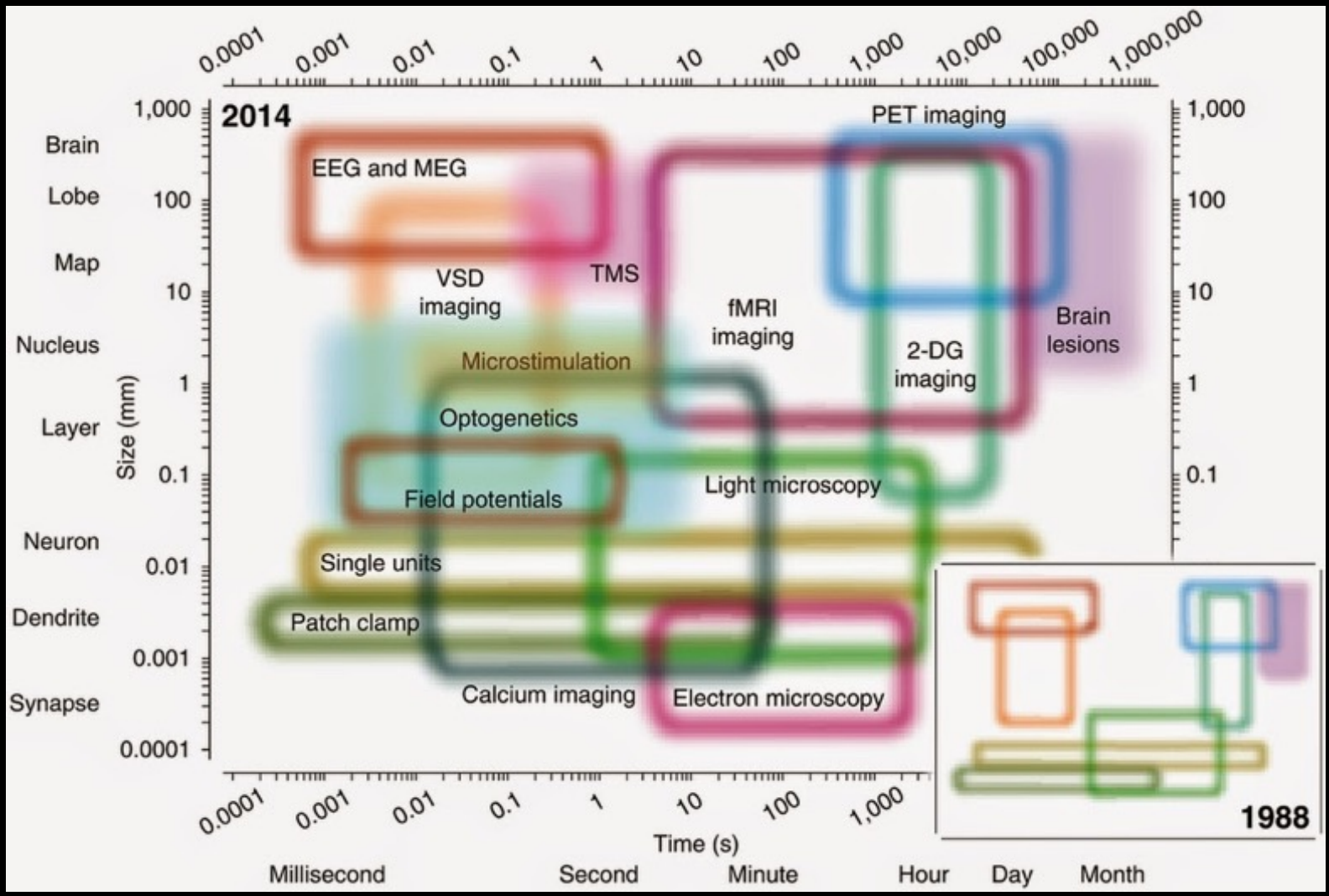

MASSACHUSETTS BAY
TRANSPORTATION AUTHORITY
RAPID TRANSIT/
KEY BUS ROUTES MAP
LEGEND


BRAINTREE
TO TRAINS


OLD BRAINTREE
1640
Welcome to
BRAINTREE



Temporal & Spatial Resolution



Sejnowski, et al. 2014

Agenda

- **How does MRI work?**
- Types of MRI Data
  - Structural MRI
    - Diffusion Weighted Imaging
  - Functional MRI
    - What is BOLD signal?
  - Three Ways to Look at fMRI Data
    - Activity Maps
    - Neural Decoding
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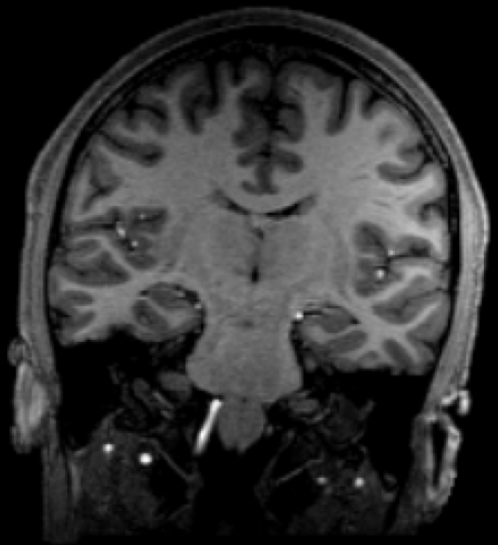
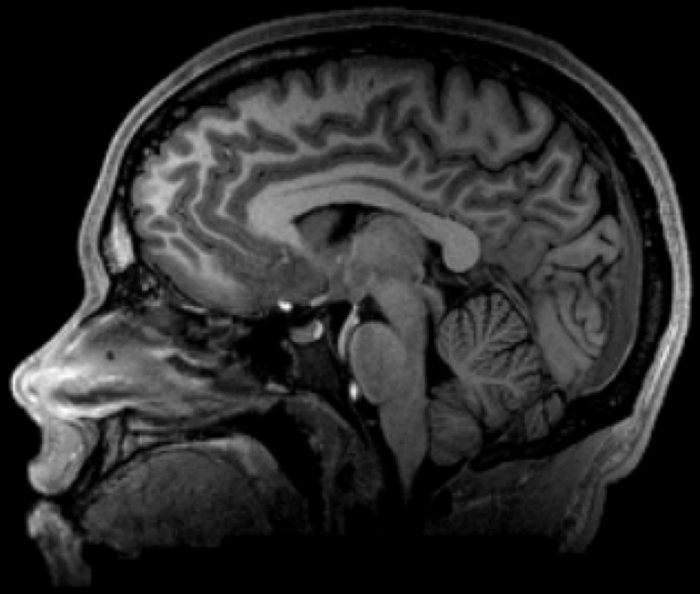
  - A Brief Overview of PET Imaging
- The future…

What am I Looking at?

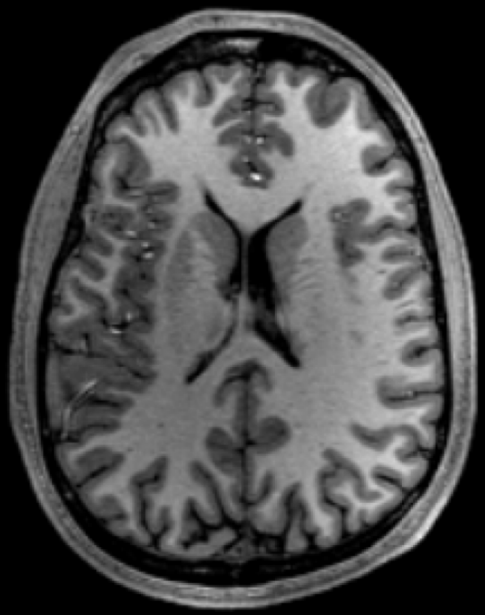
Coronal



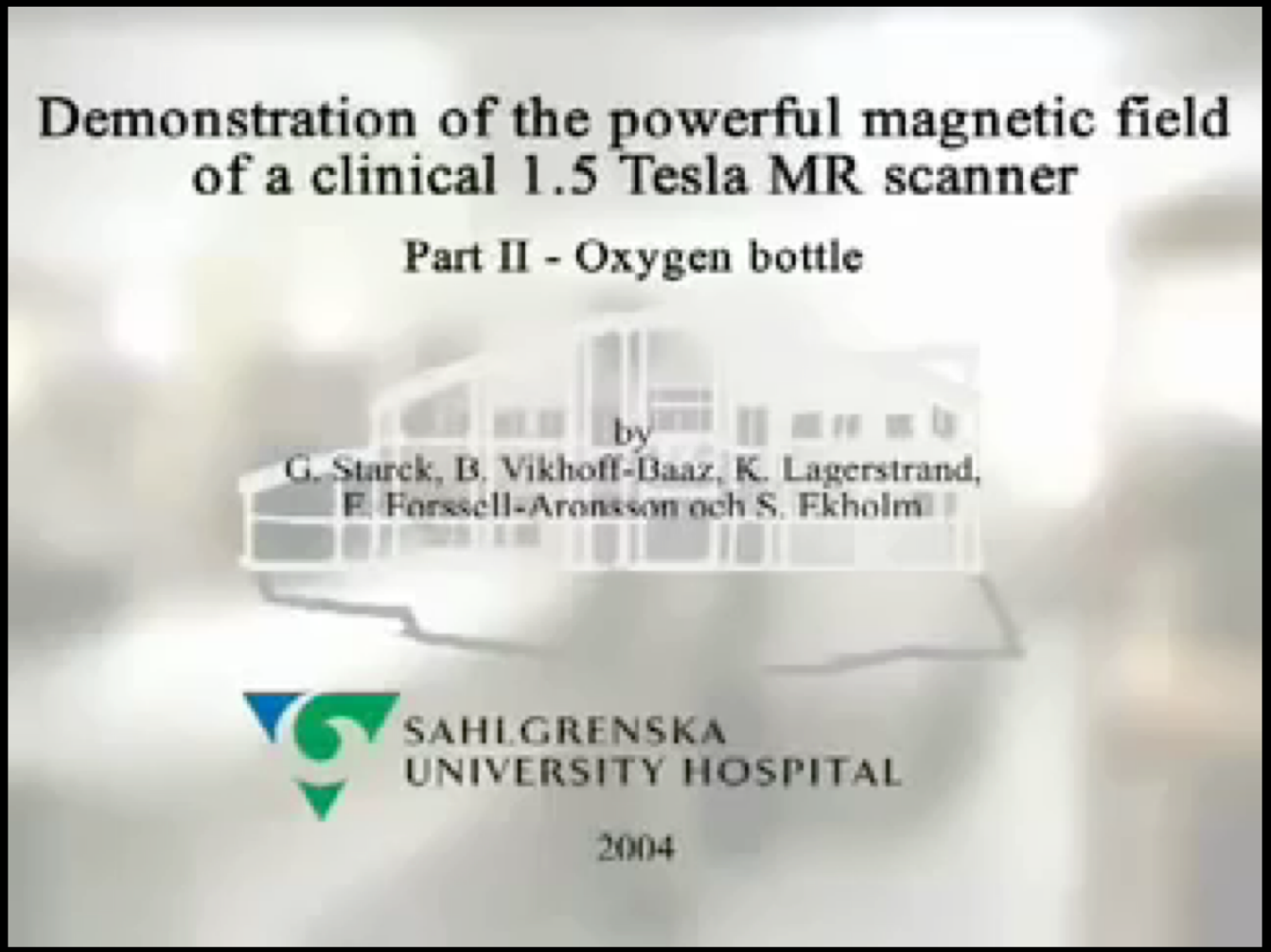
Sagittal



Axial



MR Safety

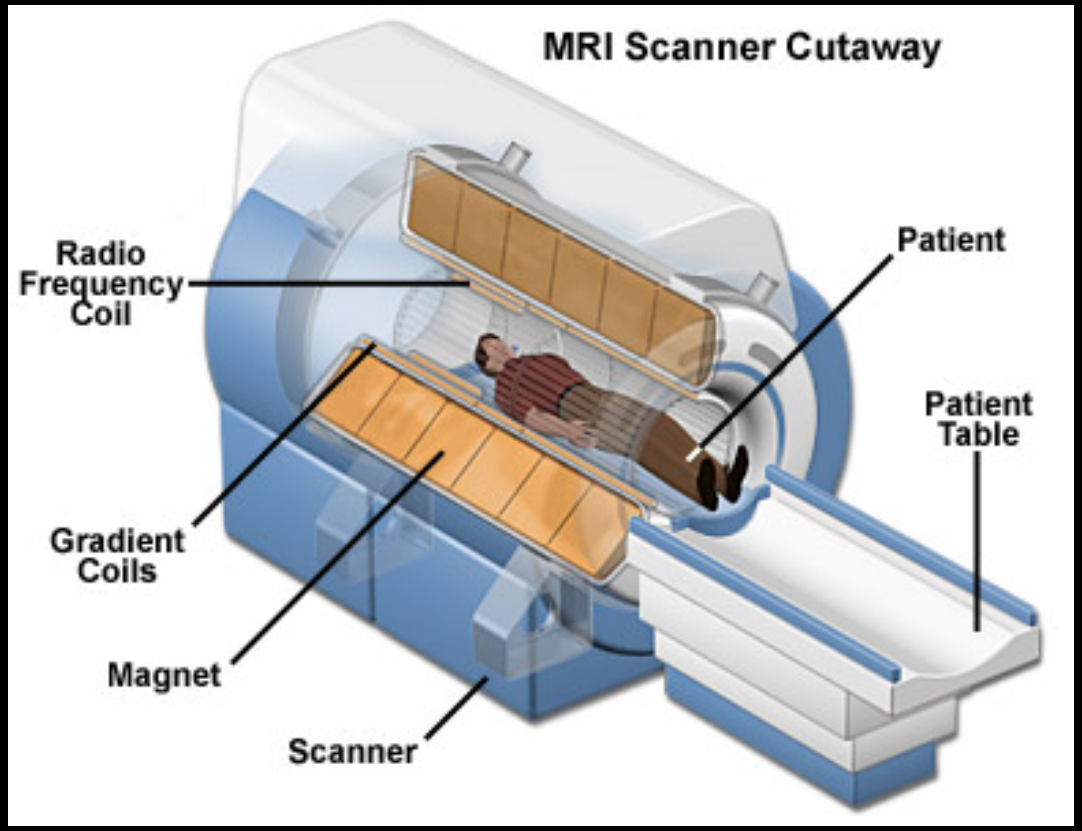


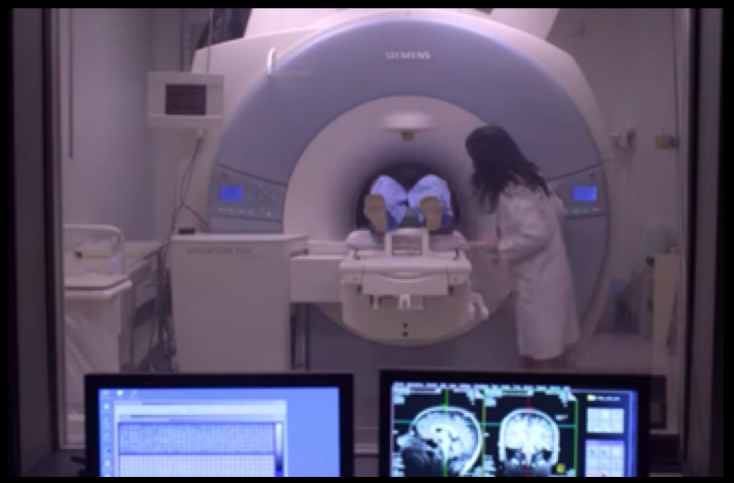
O_2 Tank vs. Watermelon:
https://www.youtube.com/watch?v=plvIEf7JsK

What Does MRI Sound Like?

MRI Sounds:
https://www.youtube.com/watch?v=xS_V_Oge

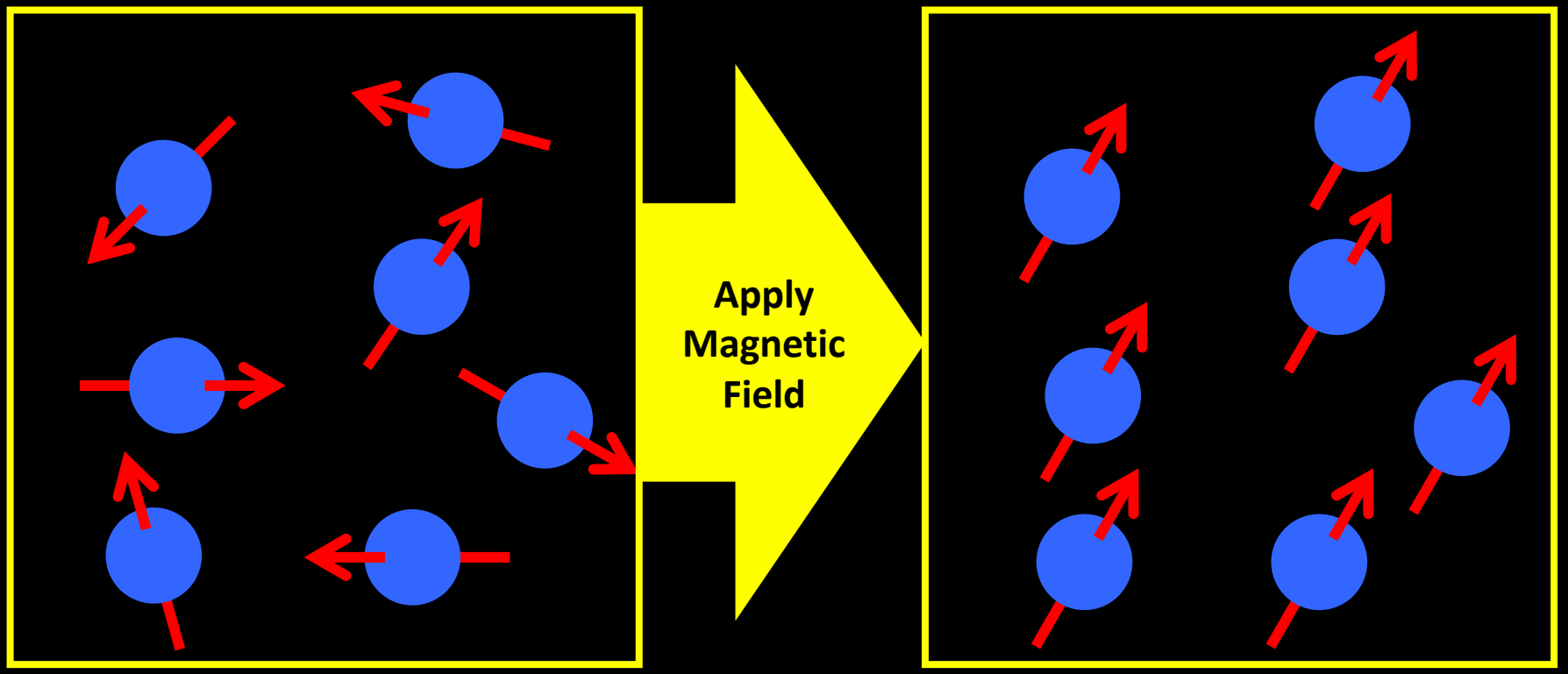
How Does MRI Work?





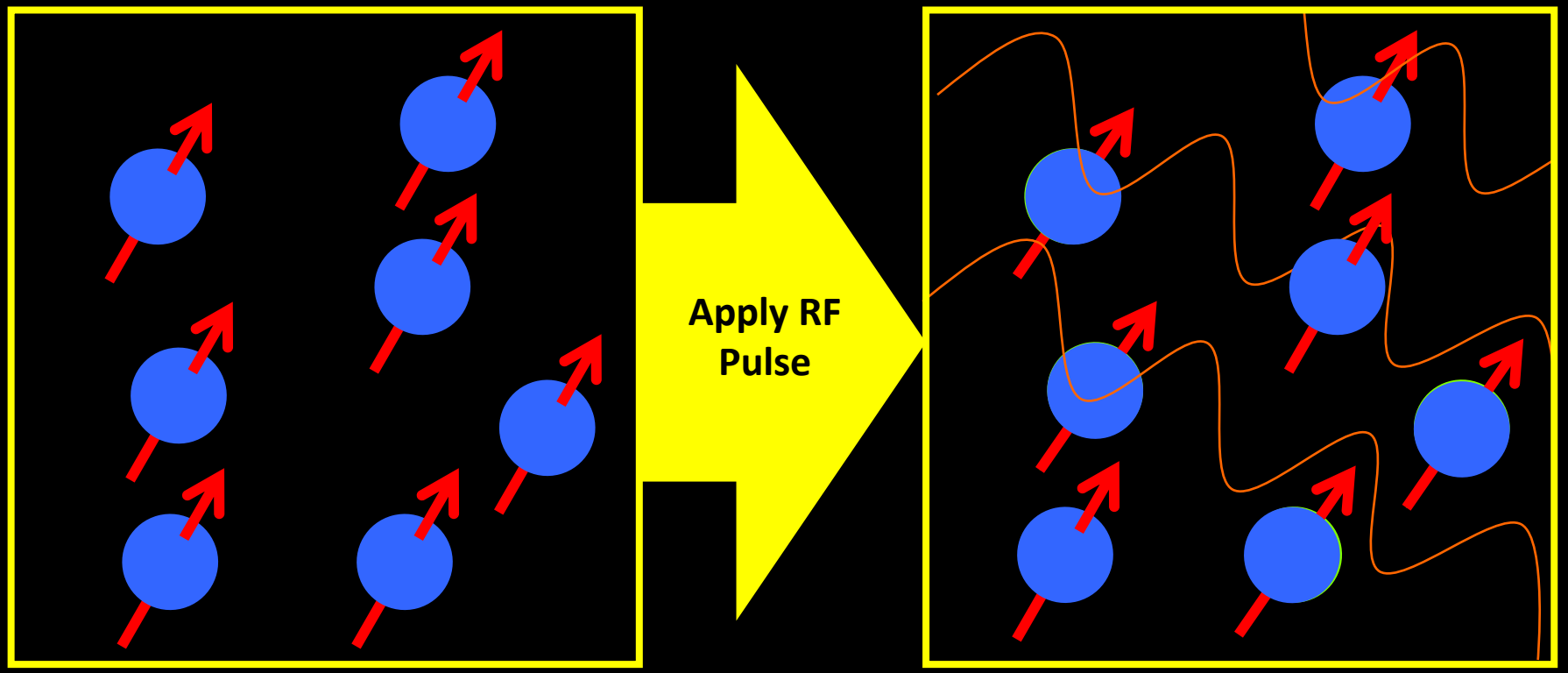
Magnetic Resonance Imaging

1. Place subject in a strong magnetic field
   - Protons align to the direction of the field



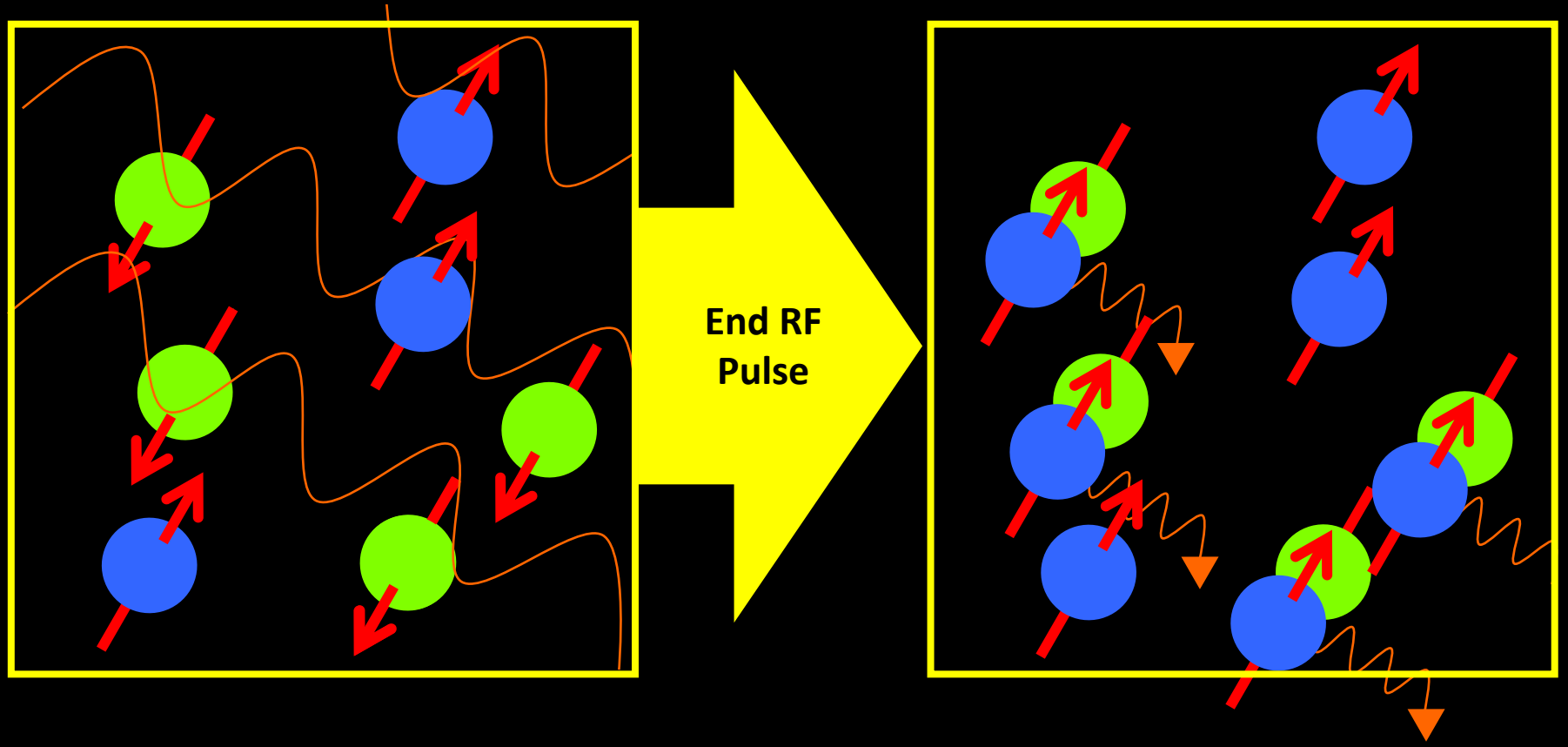
Magnetic Resonance Imaging

2. Apply a radiofrequency pulse, temporarily sending some protons into an excited state

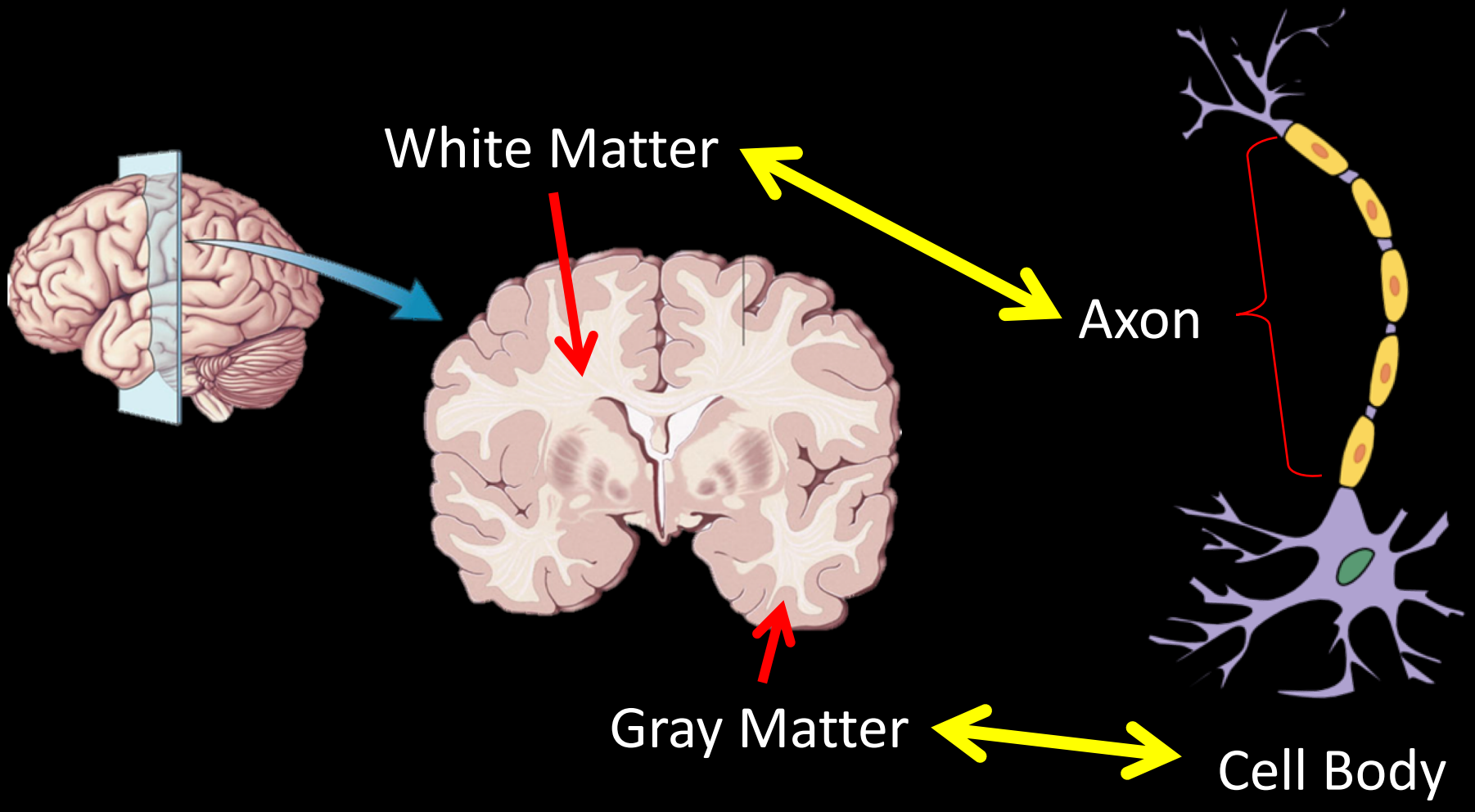


Magnetic Resonance Imaging

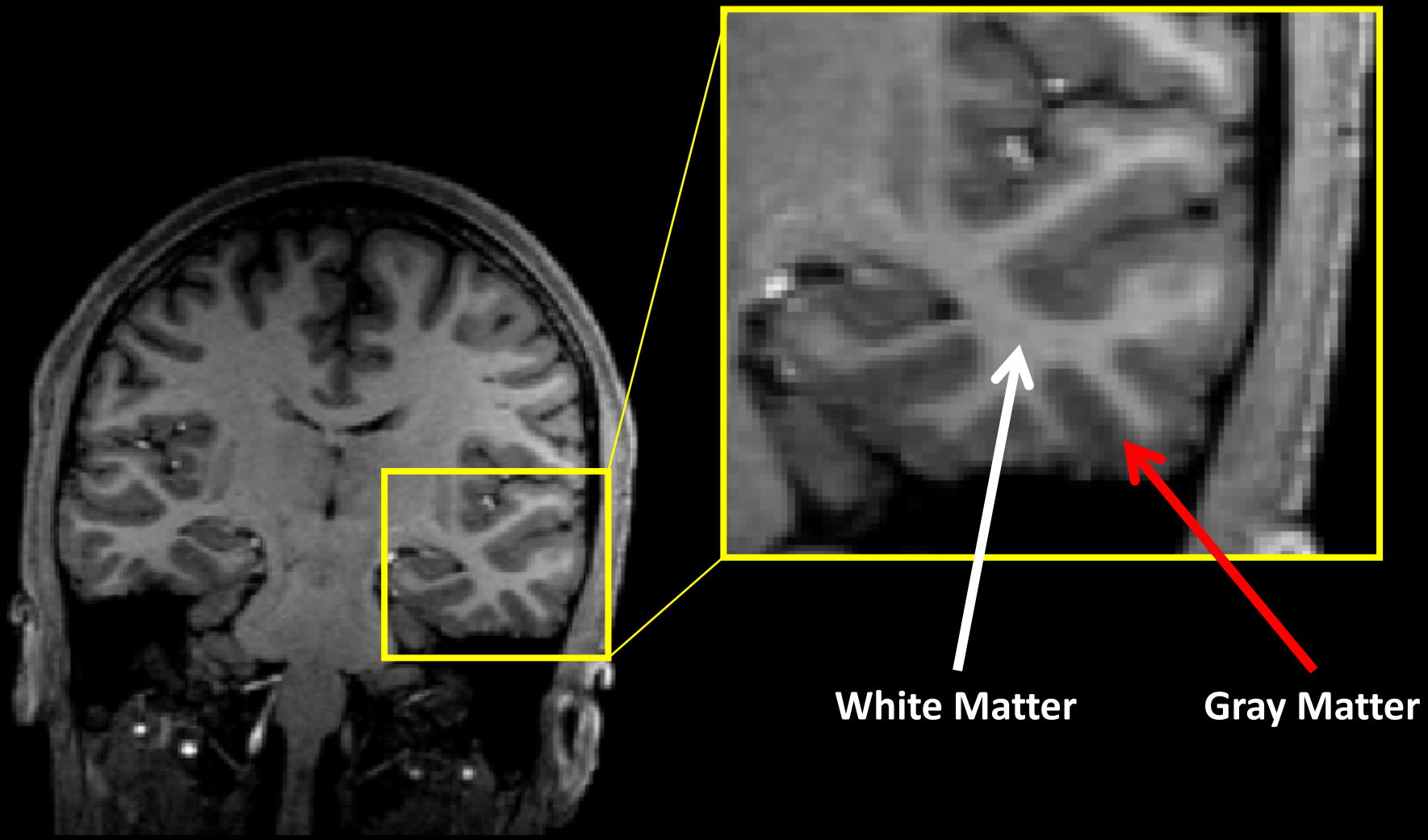
3. End the pulse, allowing protons to relax back
   - As they relax, the protons release energy in the form of radiowaves, that is detected by RF coils



Quick Brain Anatomy Review



MR Signal Differs for Each Tissue



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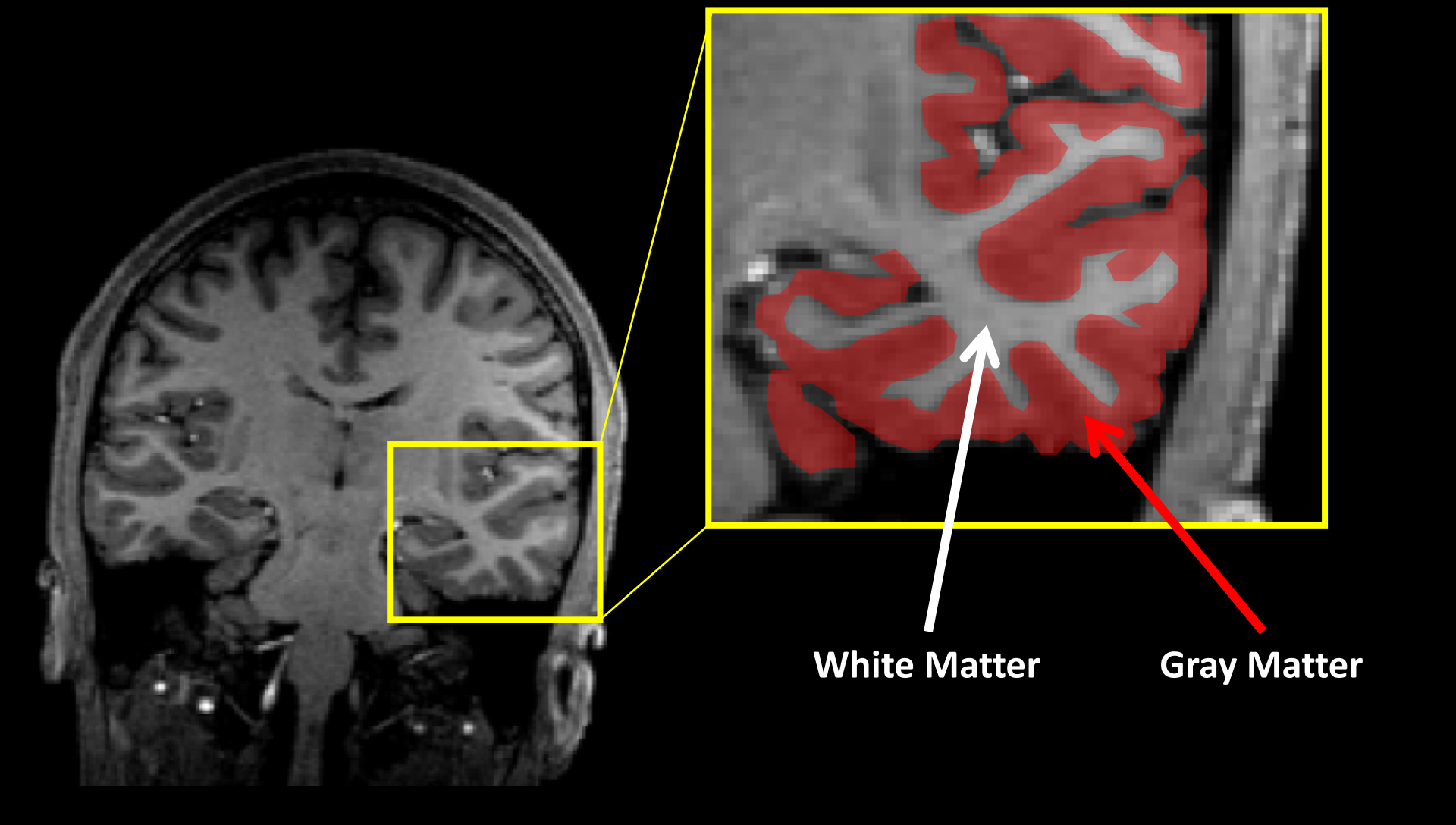

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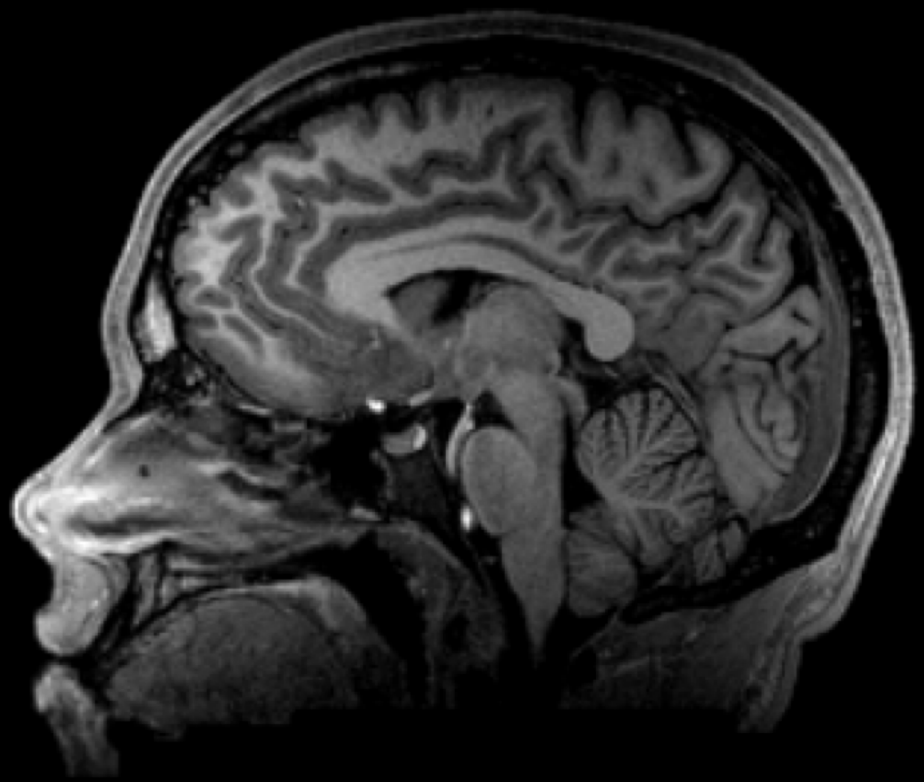
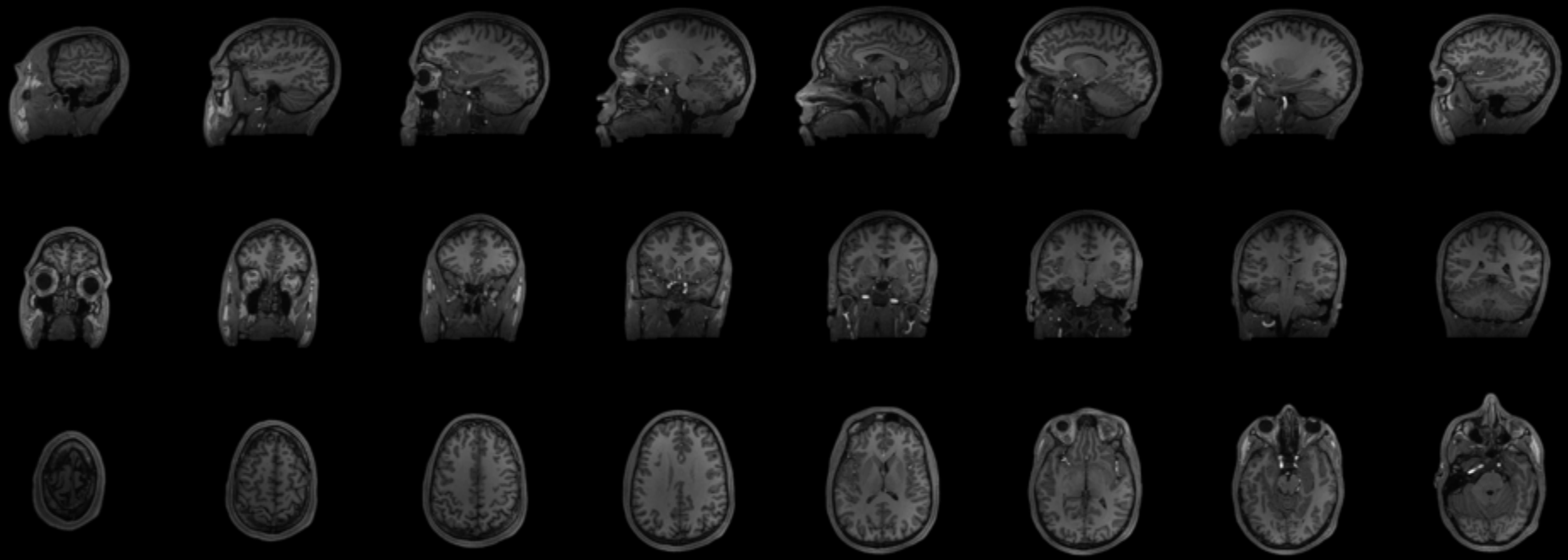
Structural MRI

- 5-10 minutes to acquire
- ~1mm resolution
- 3-Dimensional
  - Acquired in slices



We Acquire One Slice at a Time

- Online Example of Brain Slices:
  - http://www.tmmorin.com/brain_images/T1_june2016.html



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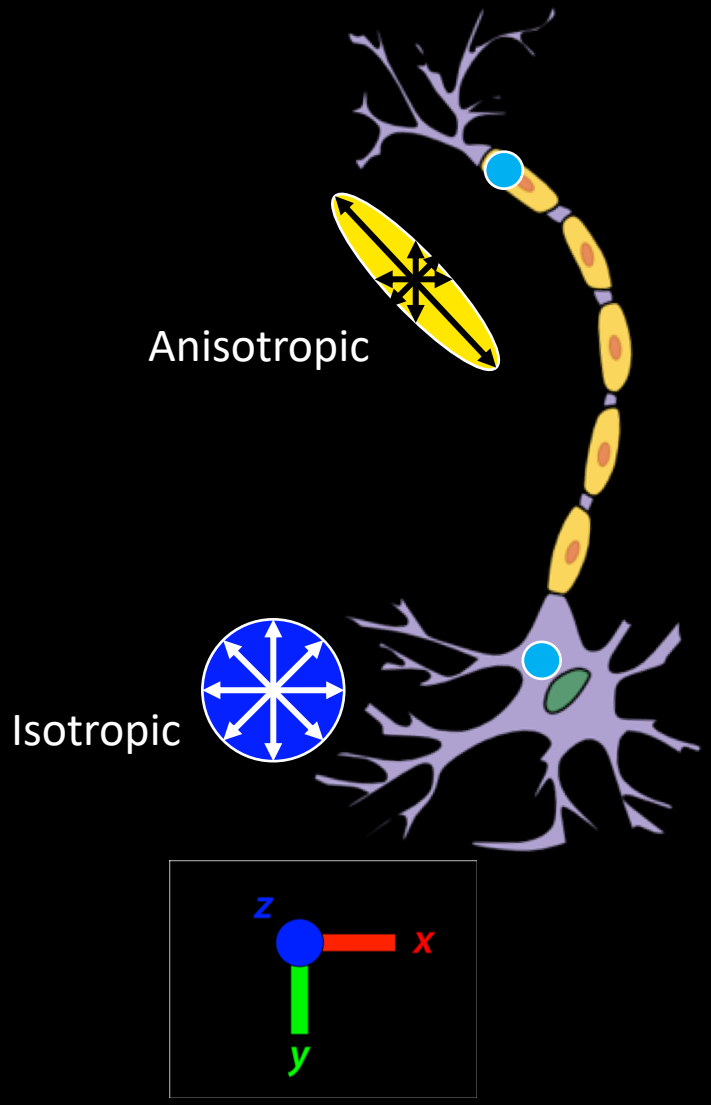
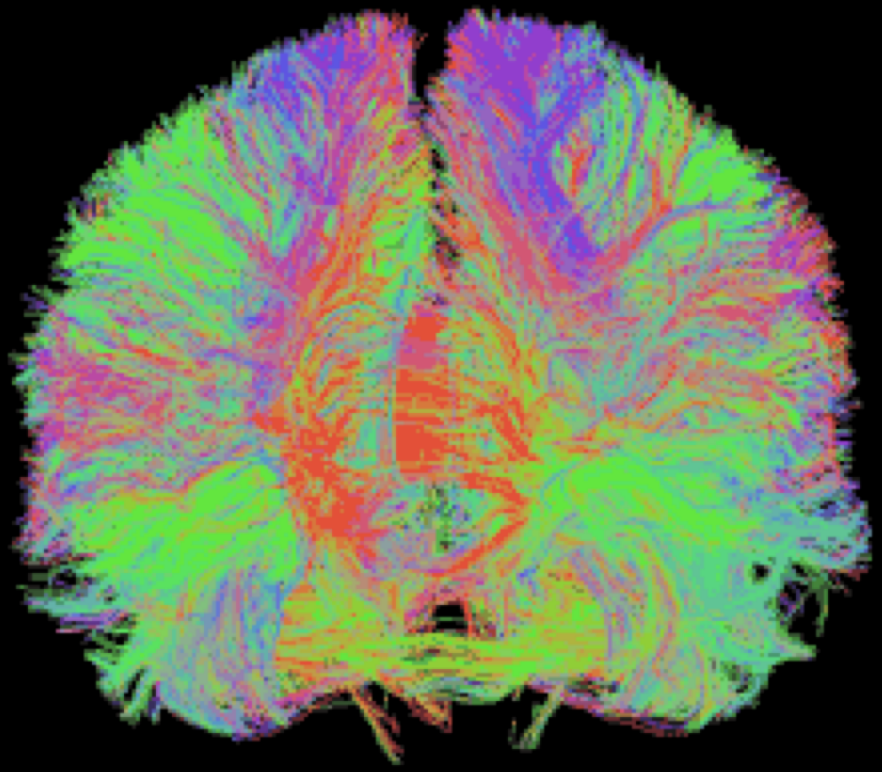
Diffusion Weighted Imaging (DWI)

- Measures tissue water diffusion rate
  - Which direction are water molecules moving within a certain tissue?
- **Diffusion Tensor Imaging (DTI):** A specific type of modelling of DWI datasets
  - Assumption: Water molecules diffuse differently depending on the type, integrity, architecture, and presence of barriers, in the observed tissue
  - Diffusion process is modelled by an ellipsoid, also known as a “tensor”
- For Physics Nerds: http://xrayphysics.com/dwi.html



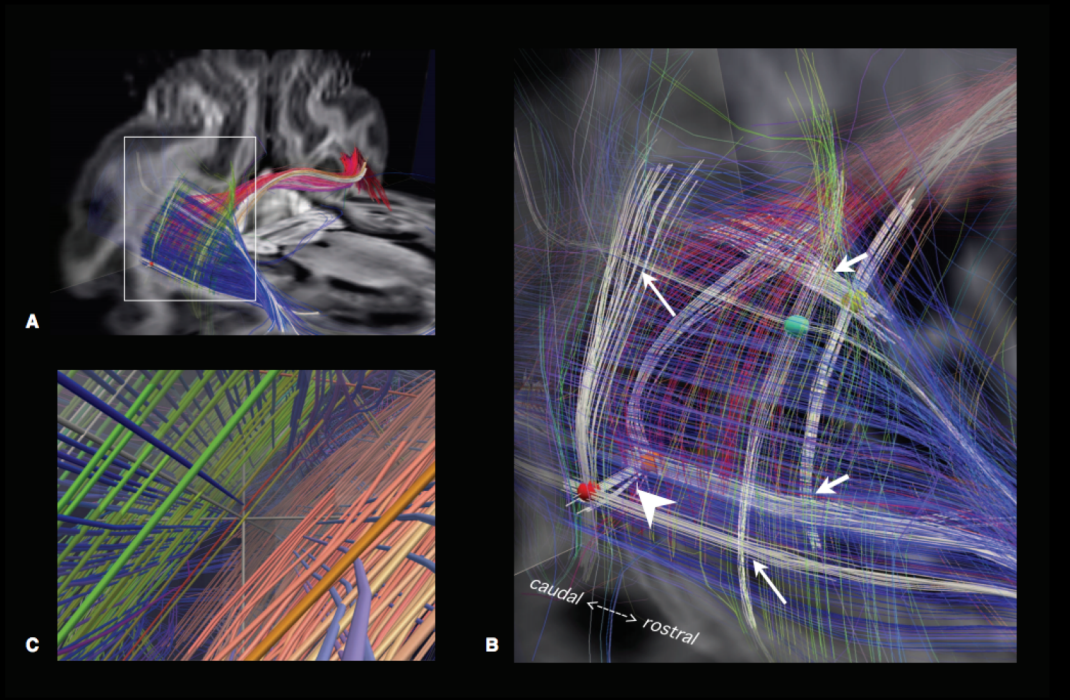
Diffusion Weighted Imaging (DWI)



Talvage et al. 2018

Diffusion Weighted Imaging: Case Study

- Image white matter fiber tracts of the brain
- Do these tracts follow a certain geometry?
- Wedeen et al. (MGH & BU) identified “grids” and “sheets” of fibers
- Catani et al. (London) refute the finding, saying it’s a side effect of their diffusion model…

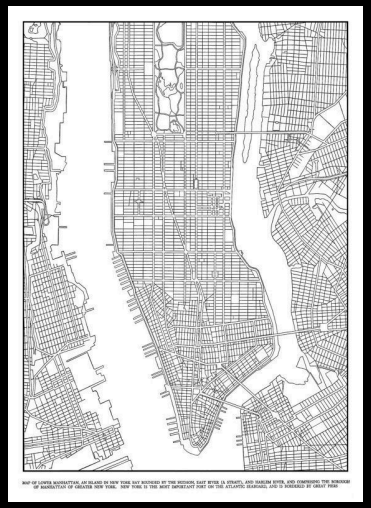


Wedeen et al. (2012)

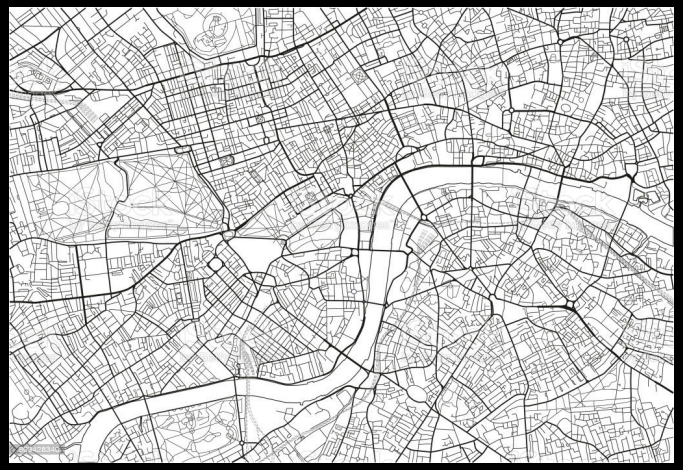
Diffusion Weighted Imaging: Case Study

“The thesis that brain pathways adhere to a simple geometric system best accounts for the available evidence—not like London, but Manhattan; not unfathomable, but unlimited.”

- Wedeen’s response to Catani’s critique



Manhattan



London

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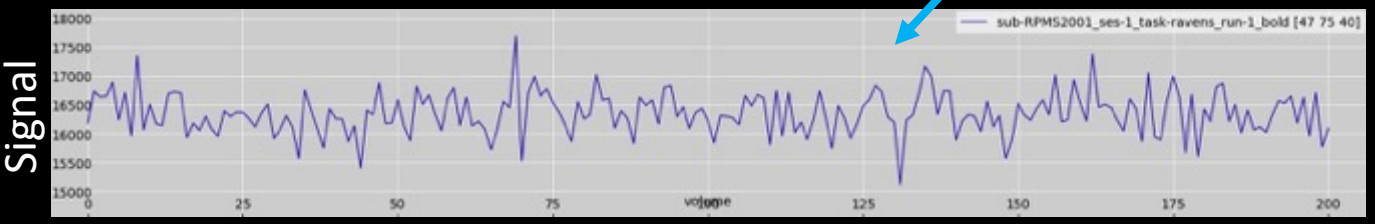
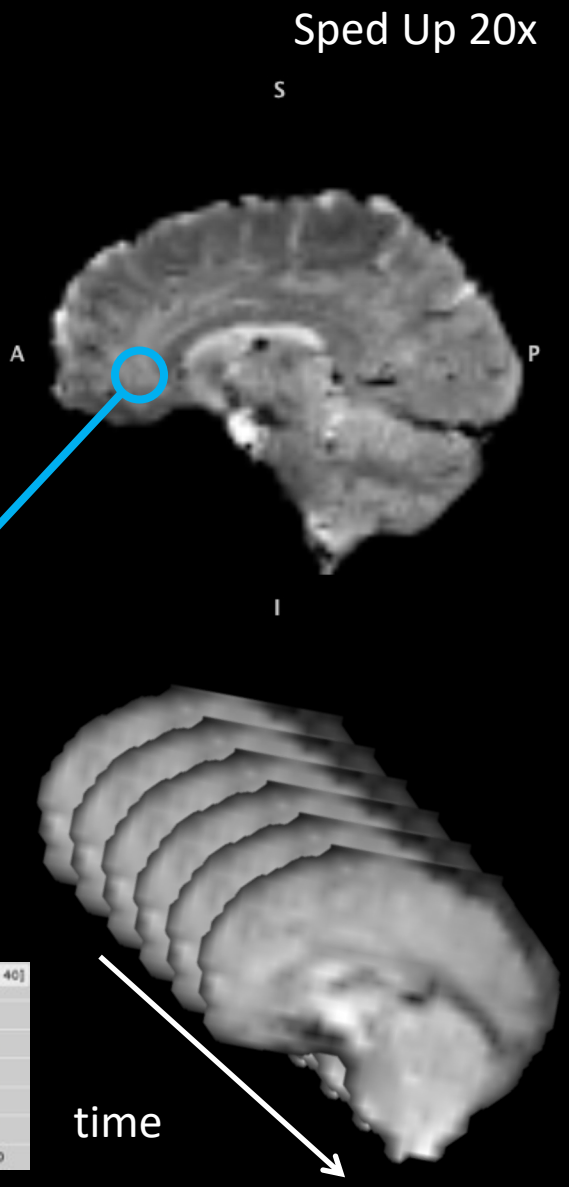
Functional MRI (fMRI)

- 4D “Video” of BOLD signal
  - An entire brain scan is acquired every 2-3 seconds (sometimes faster)
- Temporal Resolution:

  500 – 3000ms
- Spatial resolution:

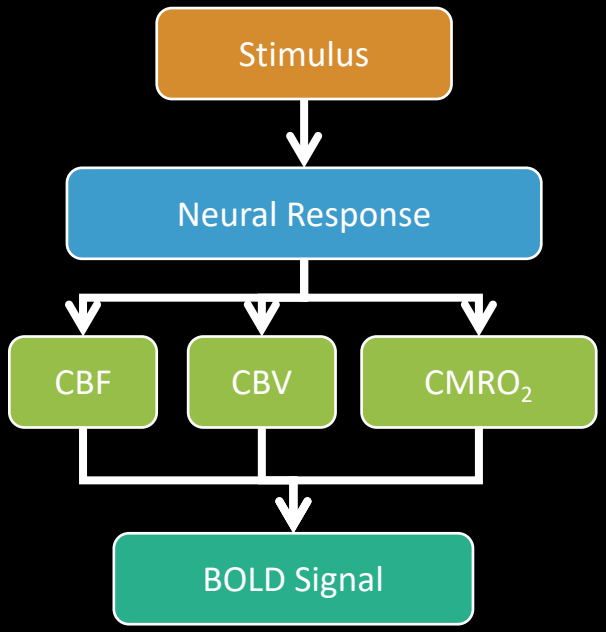
  ~2-3mm^3

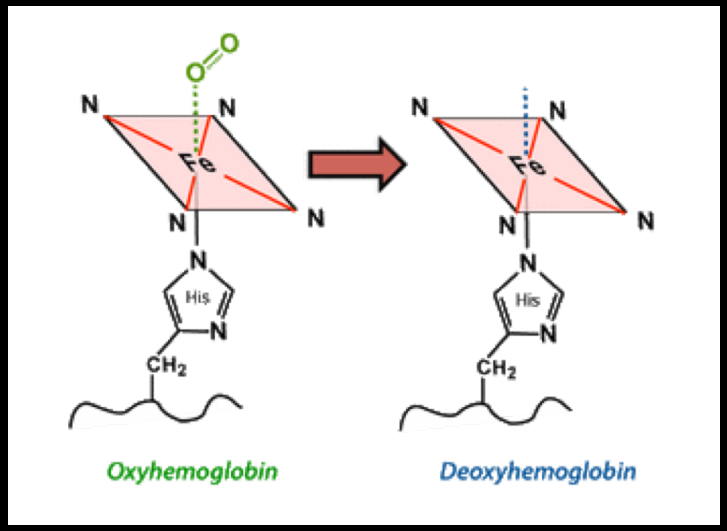




Blood Oxygen Level Dependent (BOLD) Signal

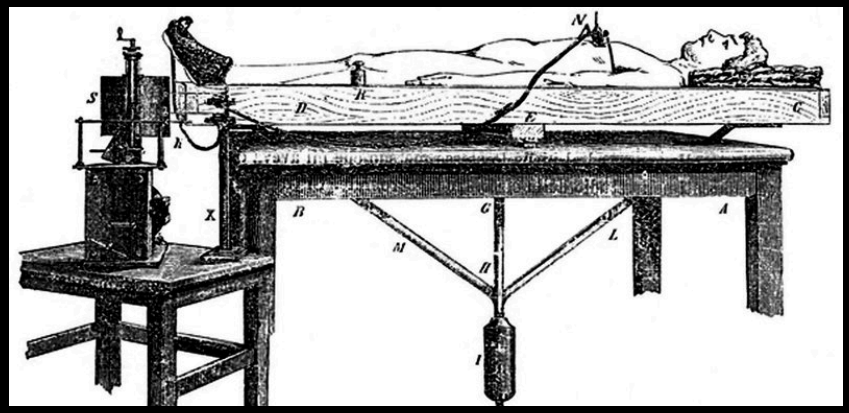
- Active neurons require oxygen as fuel.
- Brain regions with more oxyhemoglobin have increased BOLD signal and appear brighter.
- Oxyhemoglobin is diamagnetic (not affected by the magnetic field), deoxyhemoglobin is paramagnetic





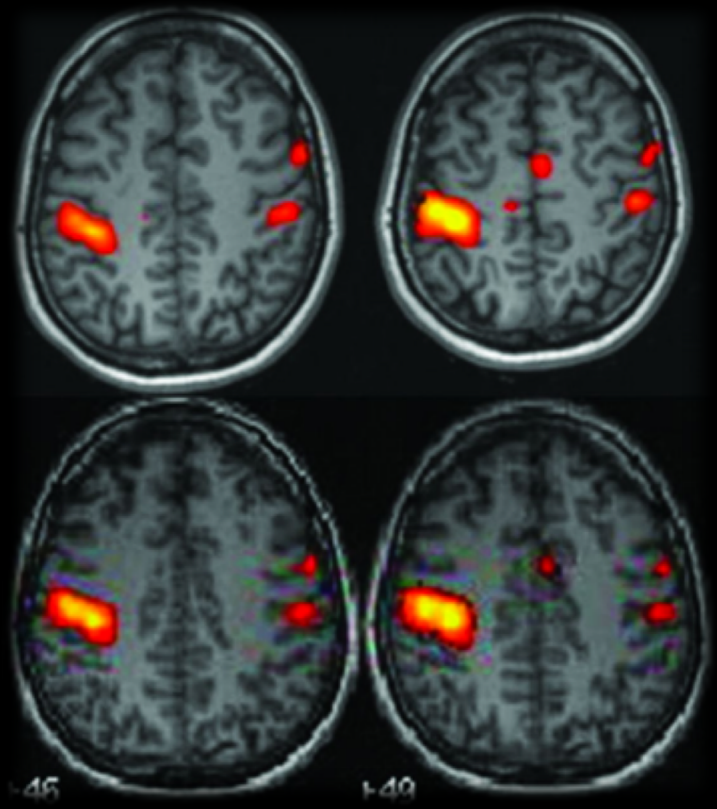
Historical Aside: Measuring Cerebral Blood Volume

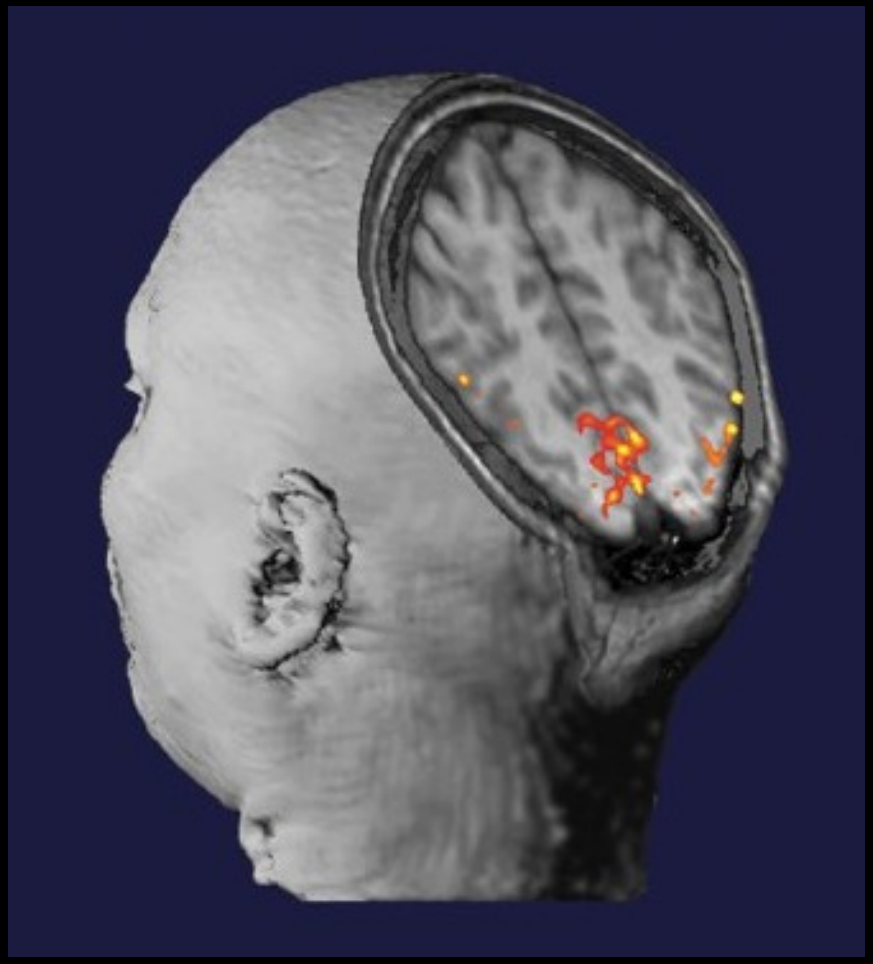
- Angelo Mosso's "Human Circulation Balance" (1882)
- What is the "weight" of a thought?
- Balance would "tilt" as the brain processed the sound of a bell. (Presumably increased blood-flow to auditory cortex)



Sandrone et al., 2014

Functional MRI (fMRI)





Aside: fMRI History

- Much of the pioneering research for fMRI was conducted here in Boston at MGH
- Published on the cover of *Science* in 1991

http://www.fmri25.org/behind-the-cover/

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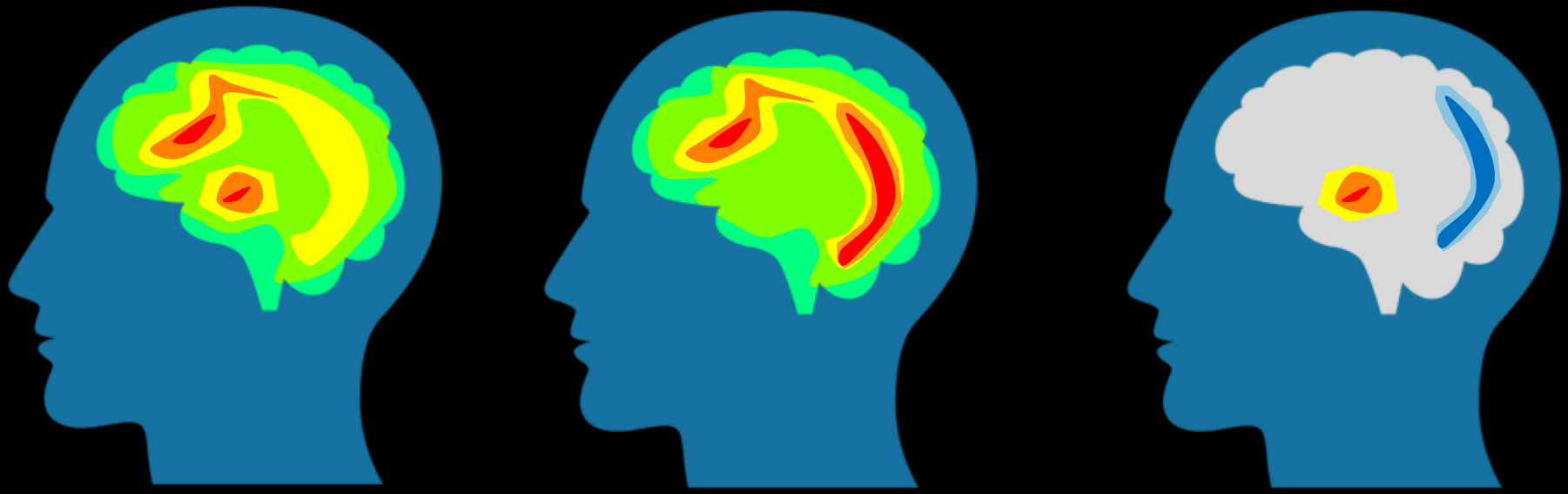
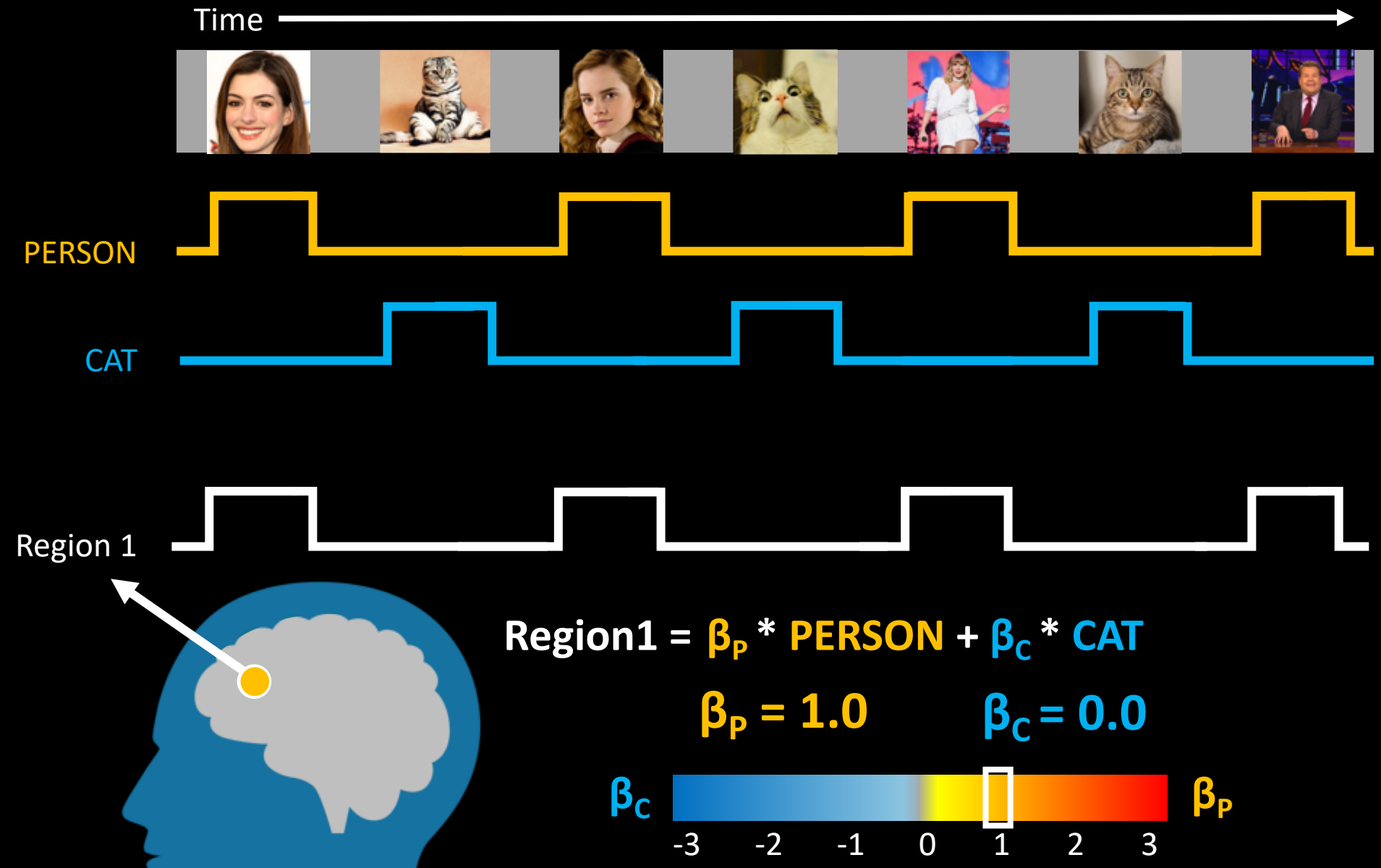
Image Subtraction



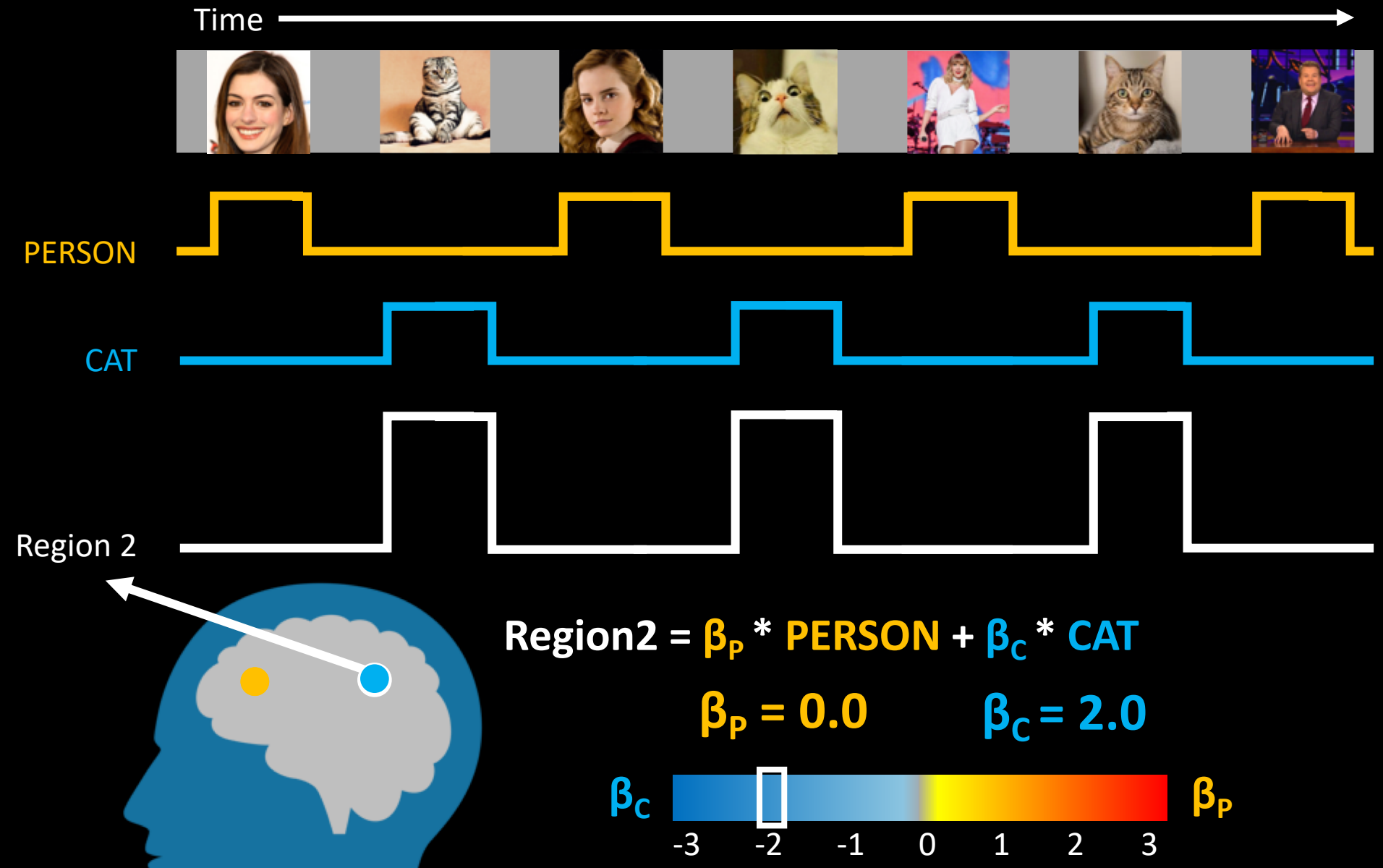
CONDITION A - CONDITION B = ACTIVATION MAP

A > B

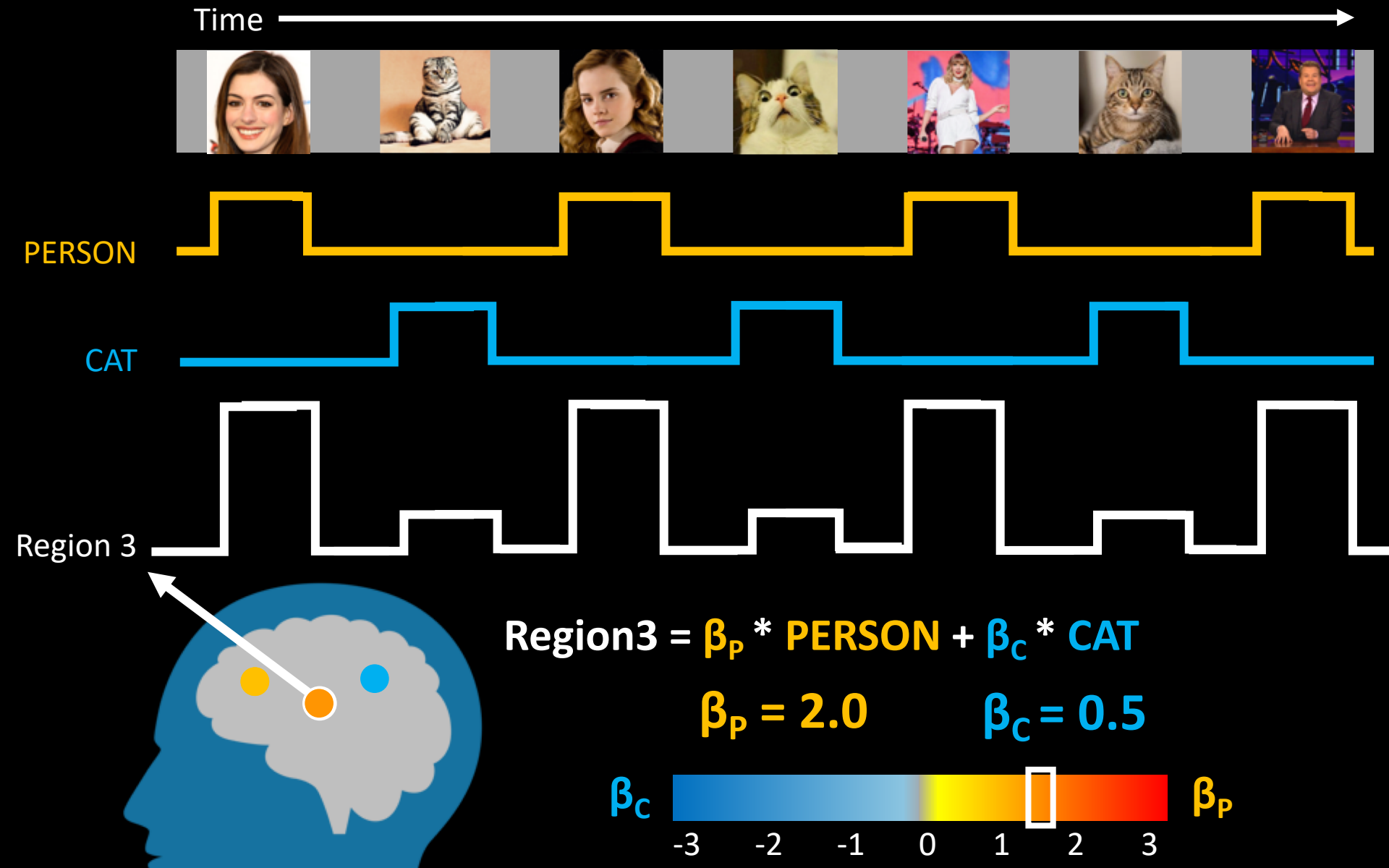
General Linear Model



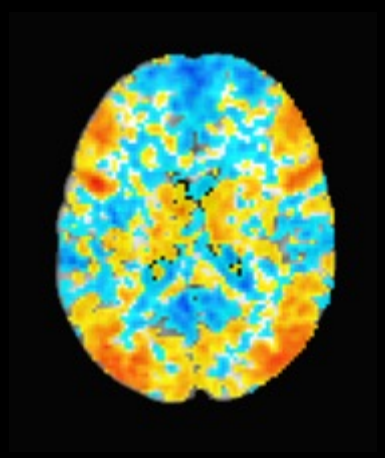
General Linear Model

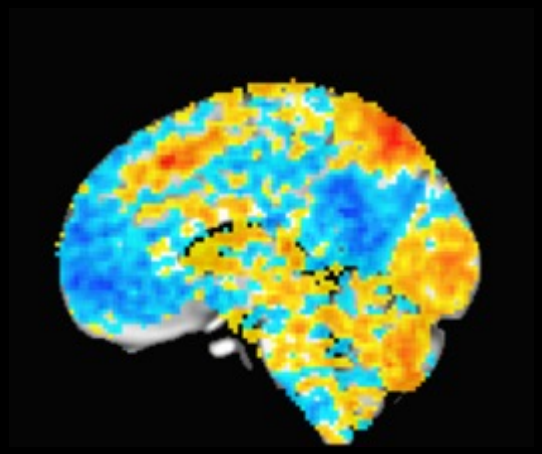


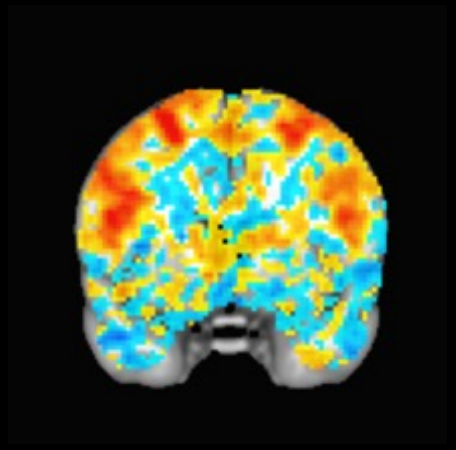
General Linear Model



Thresholding the Image

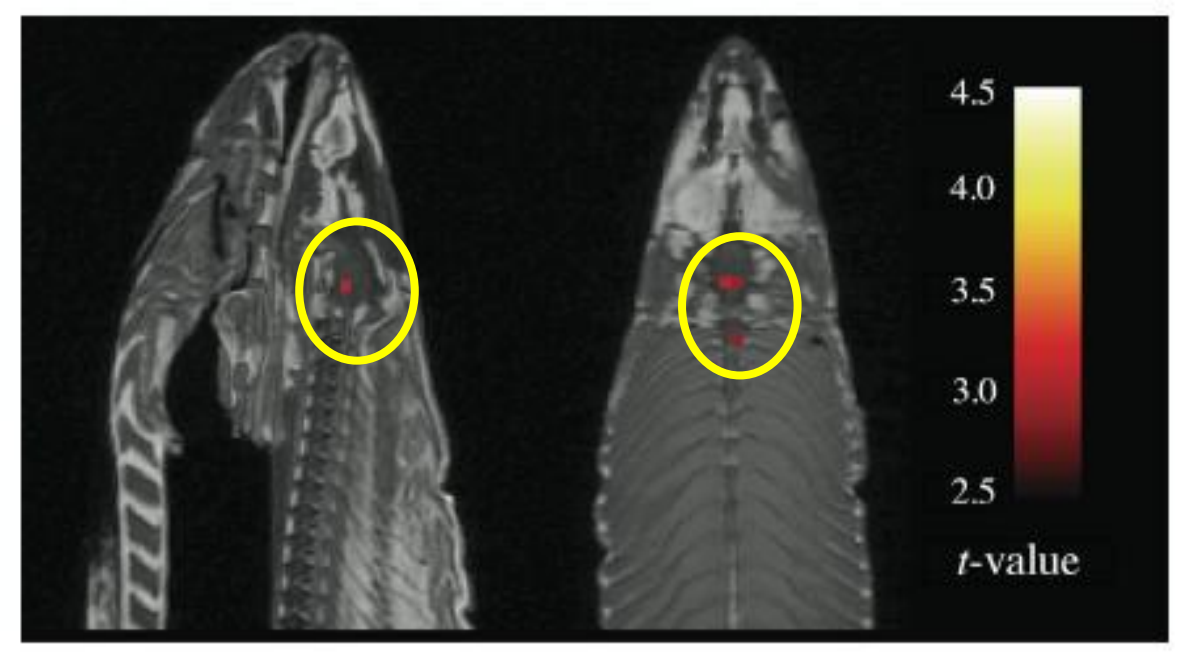






Limitations

- fMRI is noisy! (you can have **false positives**)
- Dead salmon shows “neural activity”



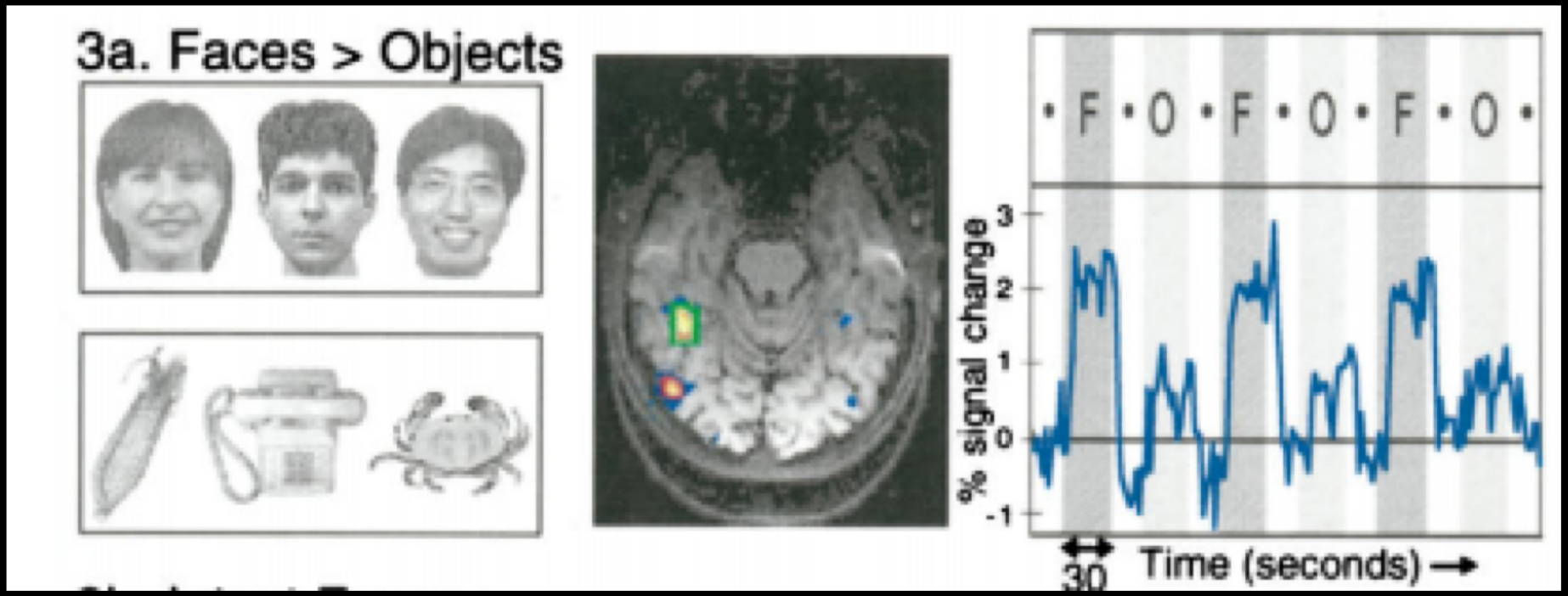
Bennett, et al. (2009)

Finding Functional Brain Regions

- Nancy Kanwisher, pioneering researcher in fMRI
- Demonstrated that we can localize brain regions that show increased activation associated with a cognitive task

Finding Functional Brain Regions

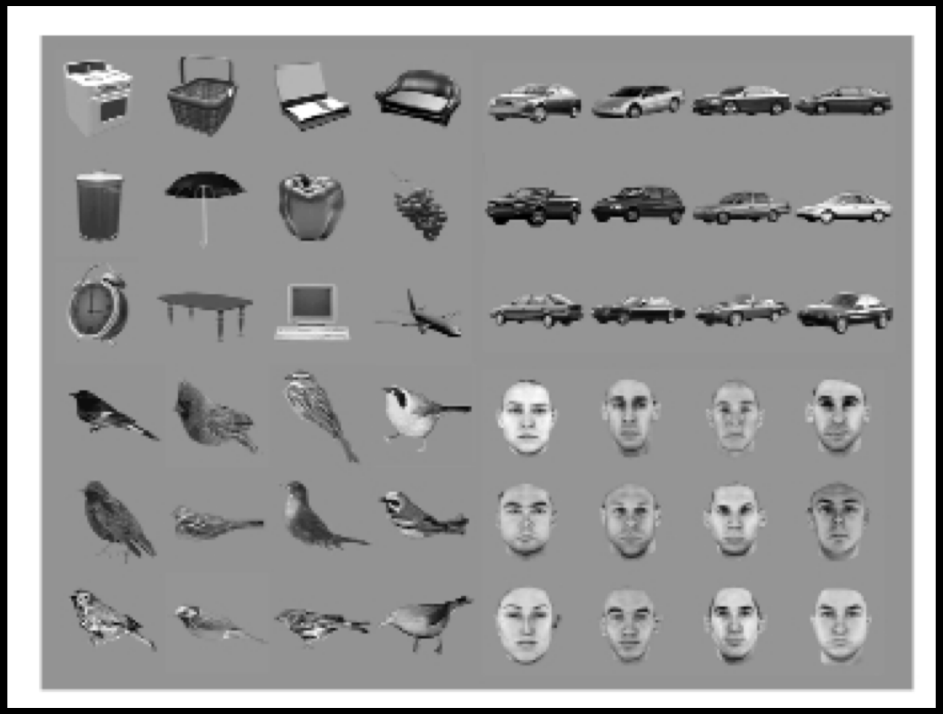
- Design a Task/Control Paradigm

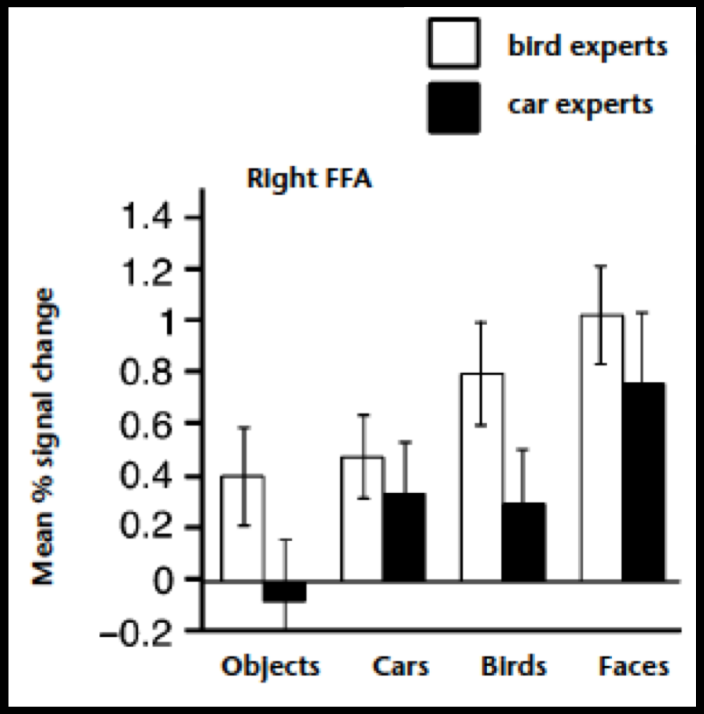


Kanwisher, et al. (1997)

Is the FFA Face-Specific?

- Car Experts & Bird Experts show increased FFA activation when viewing cars/birds compared to viewing objects

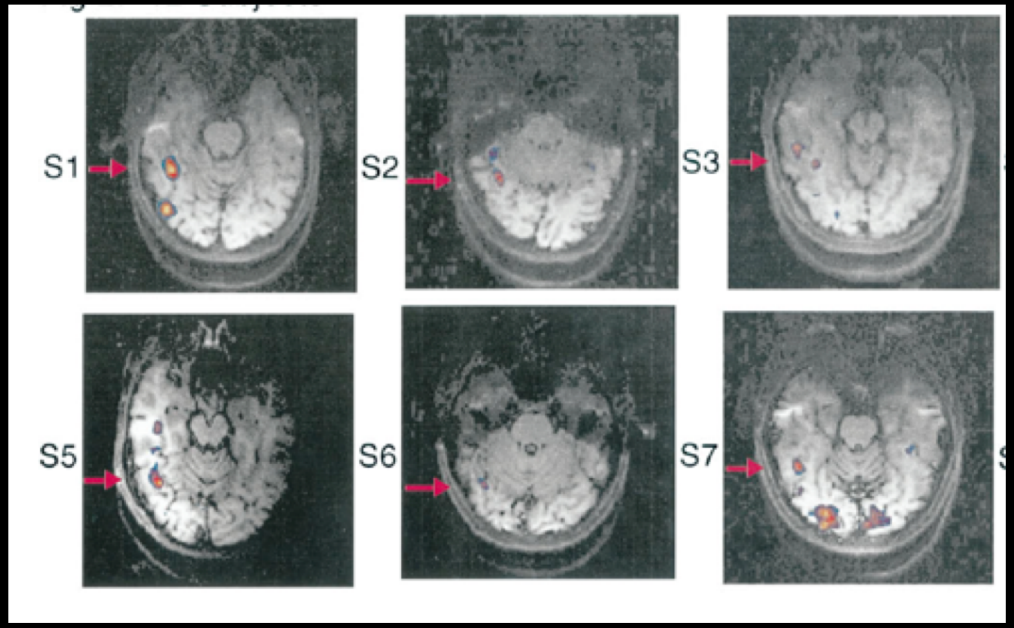




Gauthier, et al. (2000)

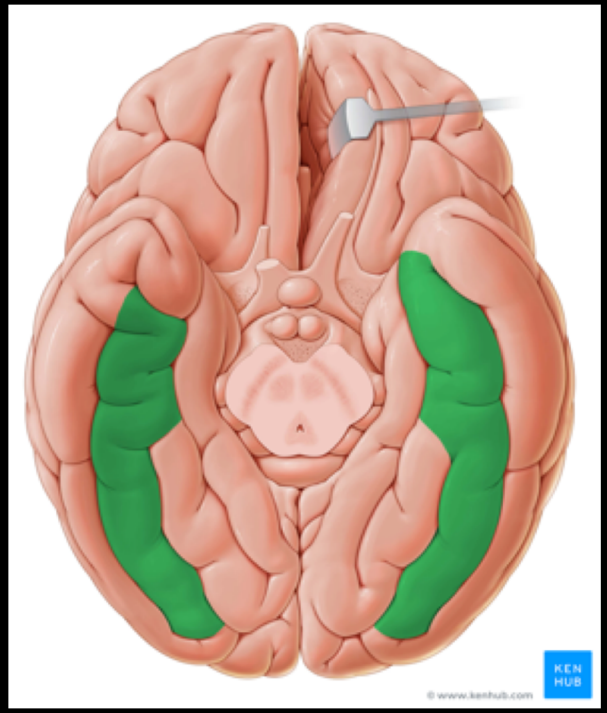
Functional vs. Anatomical Regions

Functional: Fusiform Face Area



Kanwisher, et al. (1997)

Anatomical:
Fusiform Gyrus



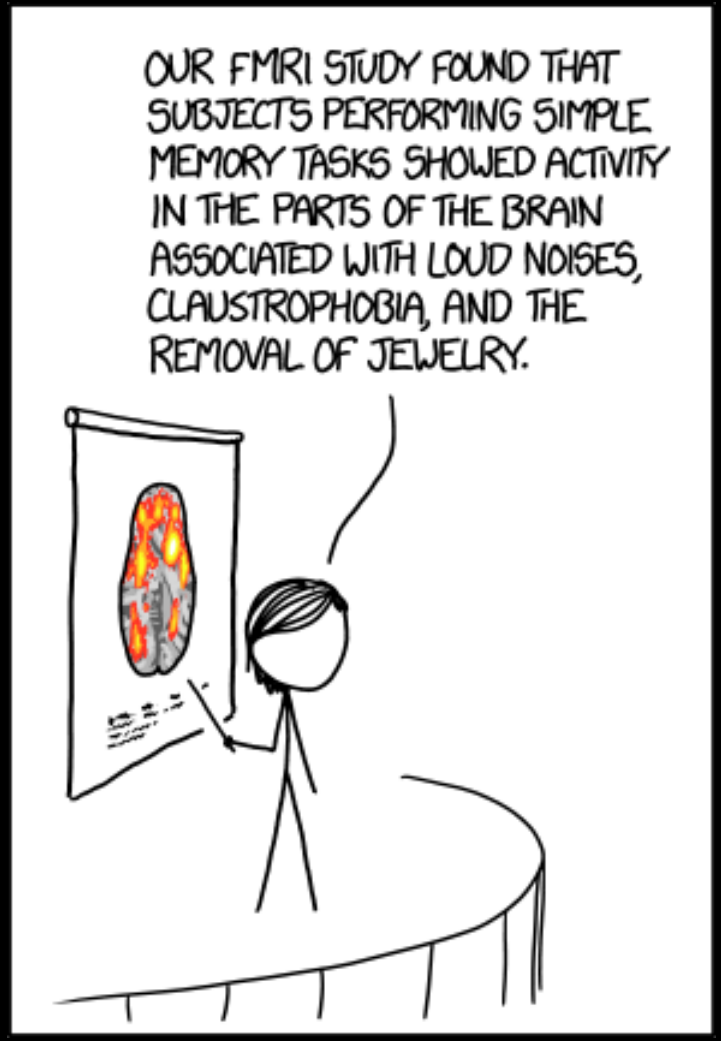
kenhub.com

Limitations

- This is “macro” imaging
  - Our best resolution is about $1mm^3$
  - About half a billion synapses per voxel
- The temporal resolution of fMRI is in seconds
  - EEG can measure brain activity in milliseconds
  - Neurons can fire hundreds of times per second
- Participants are lying down in a dark, loud, crammed tunnel

Forum Responses

- **<u>Student Response from 2018</u>**: “While I've never had a MRI before I've heard that they're both incredibly loud and time consuming. … I'm wondering if [Kanwisher’s] studies take into account the distractions of the noise of the MRI and the overall feeling of being in an MRI machine. These could possibly be confounding variables that affect her study.”



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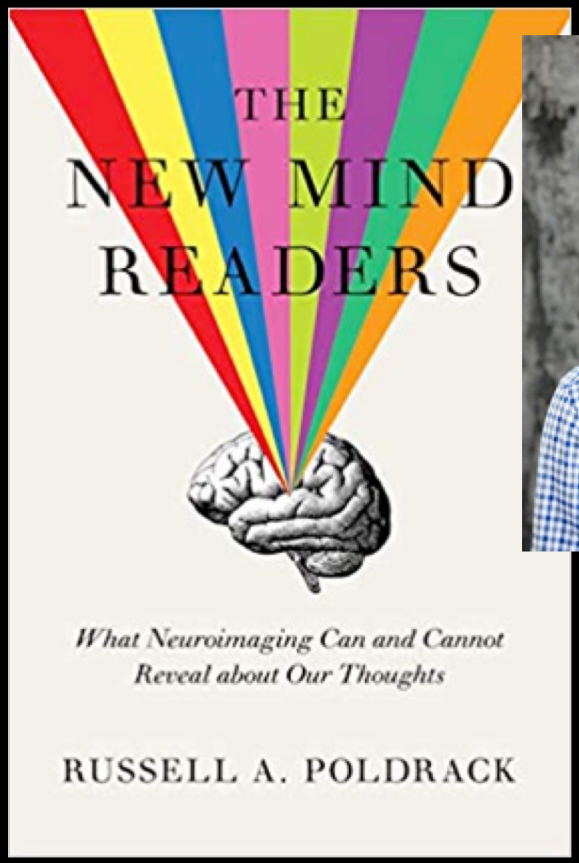
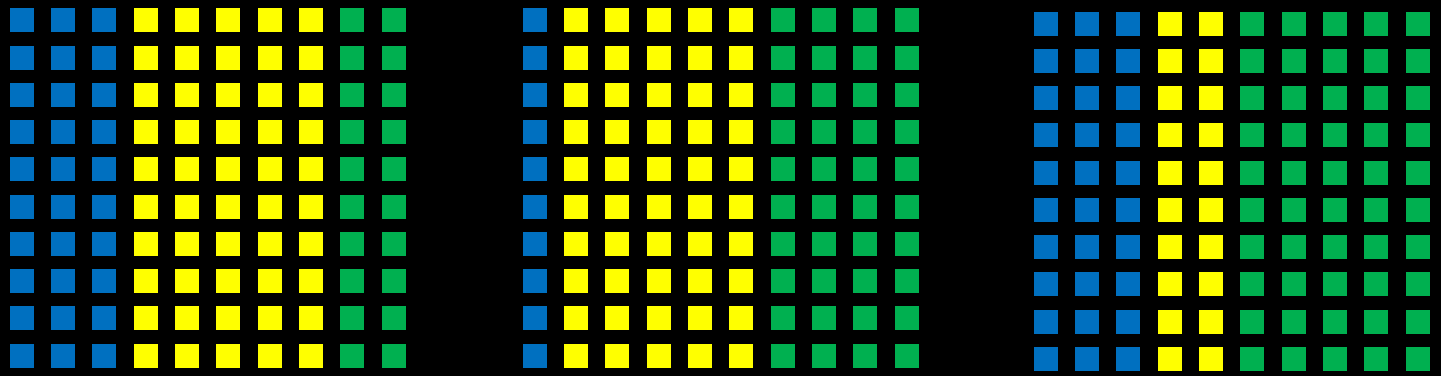
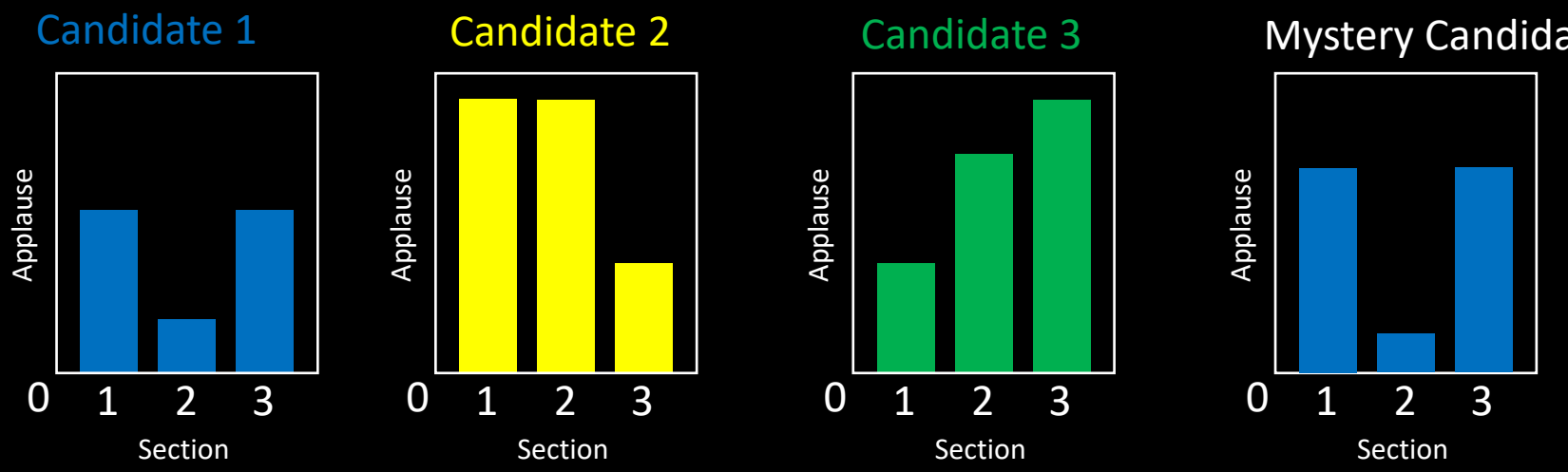
Neural Decoding



- Described in the homework reading
- Also known as: Multivoxel Pattern Analysis (MVPA)

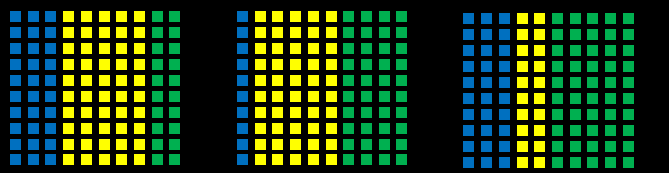
Neural Decoding Analogy: Audience Applause



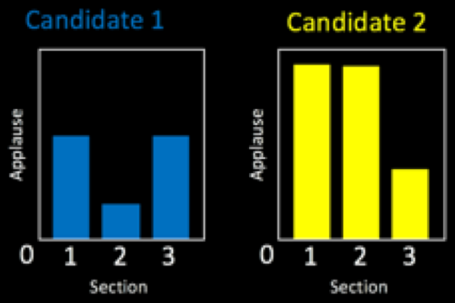


Neural Decoding Analogy

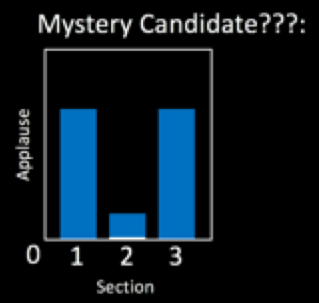
- Audience Sections = Brain Regions
- Candidates = Stimuli
- Applause Levels = Brain Activation (BOLD signal)
- Graphs = Activity Patterns



Training Set:

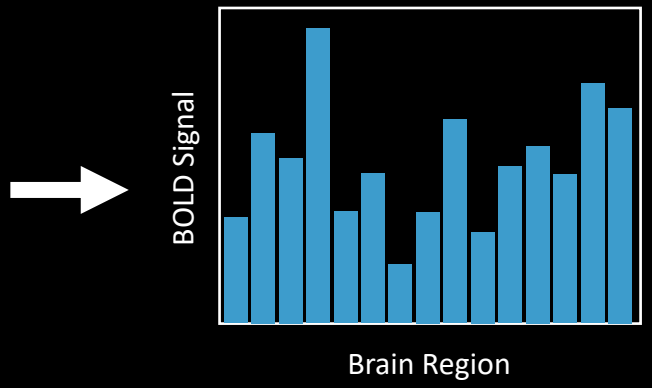


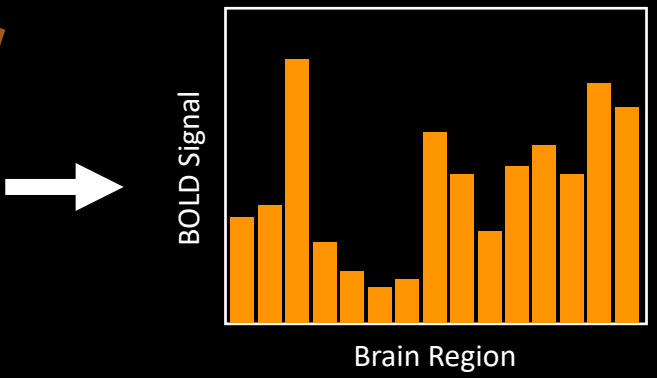
Test:



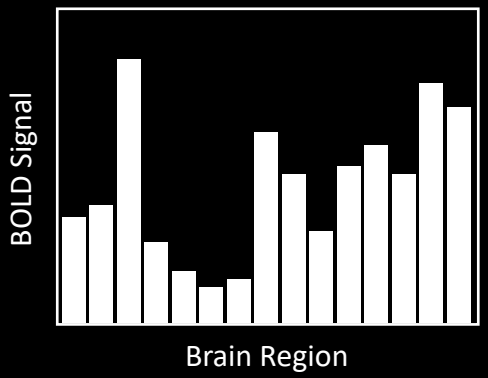
Neural Decoding

TRAINING SET:



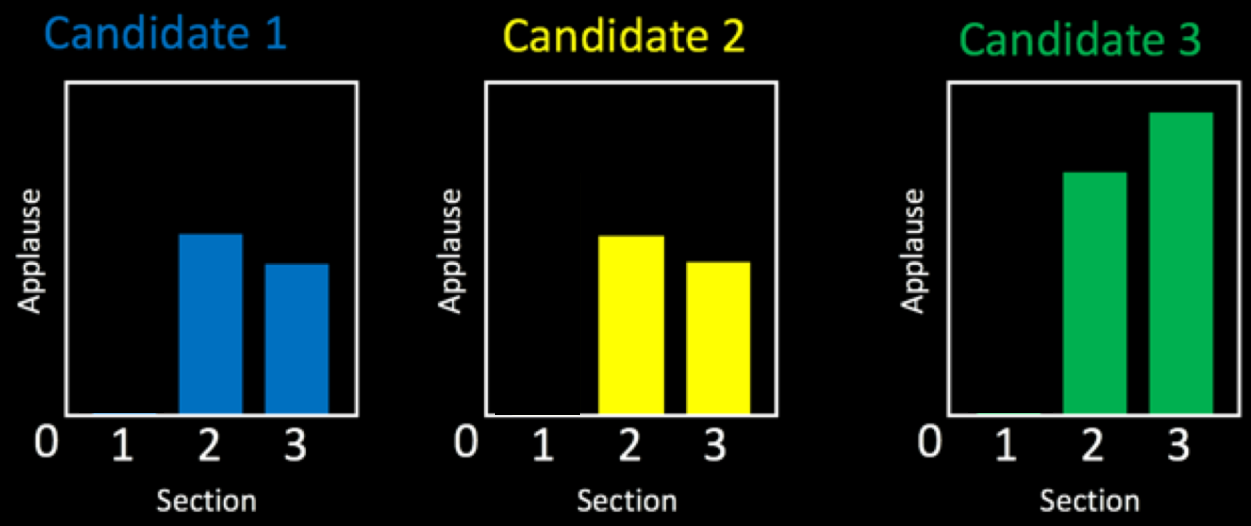


TEST ITEM:



Sensitivity Analysis

- Run the neural decoding analysis many times
- Each time, “perturb” activity in a different brain region, and see how it affects the results (drown out applause in one audience section)
- If this worsens the decoding, then this region is important for representing information about these stimuli
  - For example, removing section 1 in the plots below makes it difficult to differentiate Candidate 2 from Candidate 3.



Neural Decoding Example

- Hanson, et al. (2001) conducted a neural decoding analysis on faces, objects, houses, etc.
- Found that FFA activity contains information about these different categories

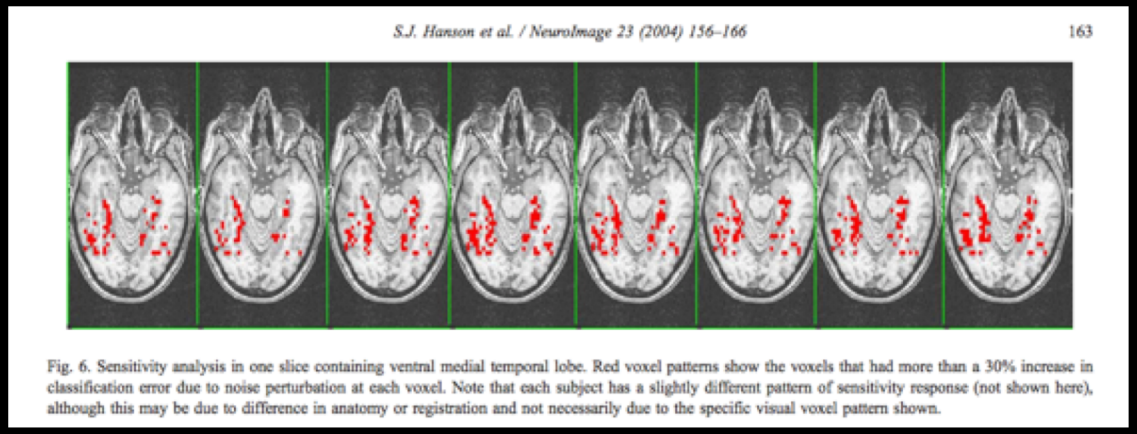
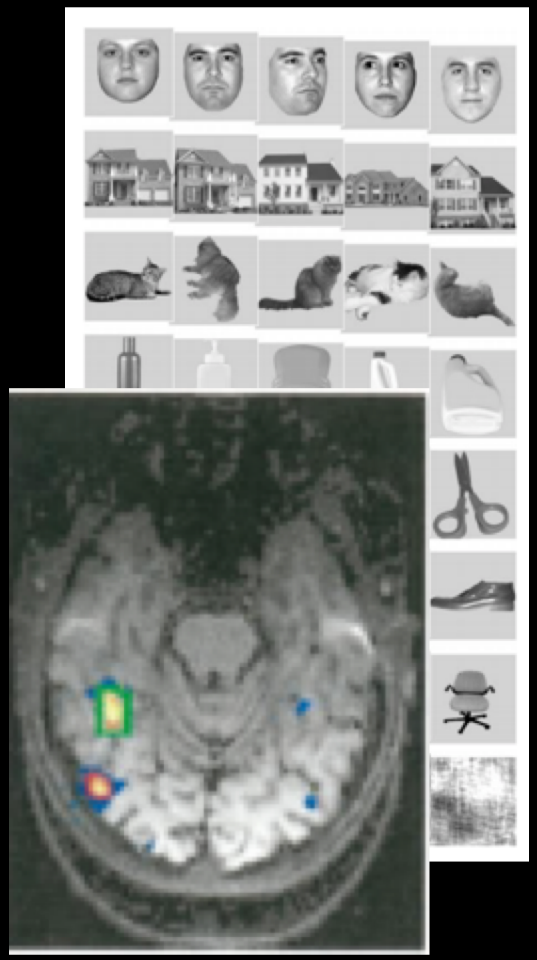


Fig. 6. Sensitivity analysis in one slice containing ventral medial temporal lobe. Red voxel patterns show the voxels that had more than a 30% increase in classification error due to noise perturbation at each voxel. Note that each subject has a slightly different pattern of sensitivity response (not shown here), although this may be due to difference in anatomy or registration and not necessarily due to the specific visual voxel pattern shown.



Kanwisher, et al. (1997)

Issues surrounding Neural Decoding & Machine Learning

- Are certain applications ethical (or even possible)?
  - Lie Detection?
  - Detection of “true” pain?
  - Detection of consciousness in coma patients?
- Training Data has a huge influence
  - Algorithms are as biased as the humans who create them
  - Like any machine-learning project, a diverse training dataset is essential

Agenda

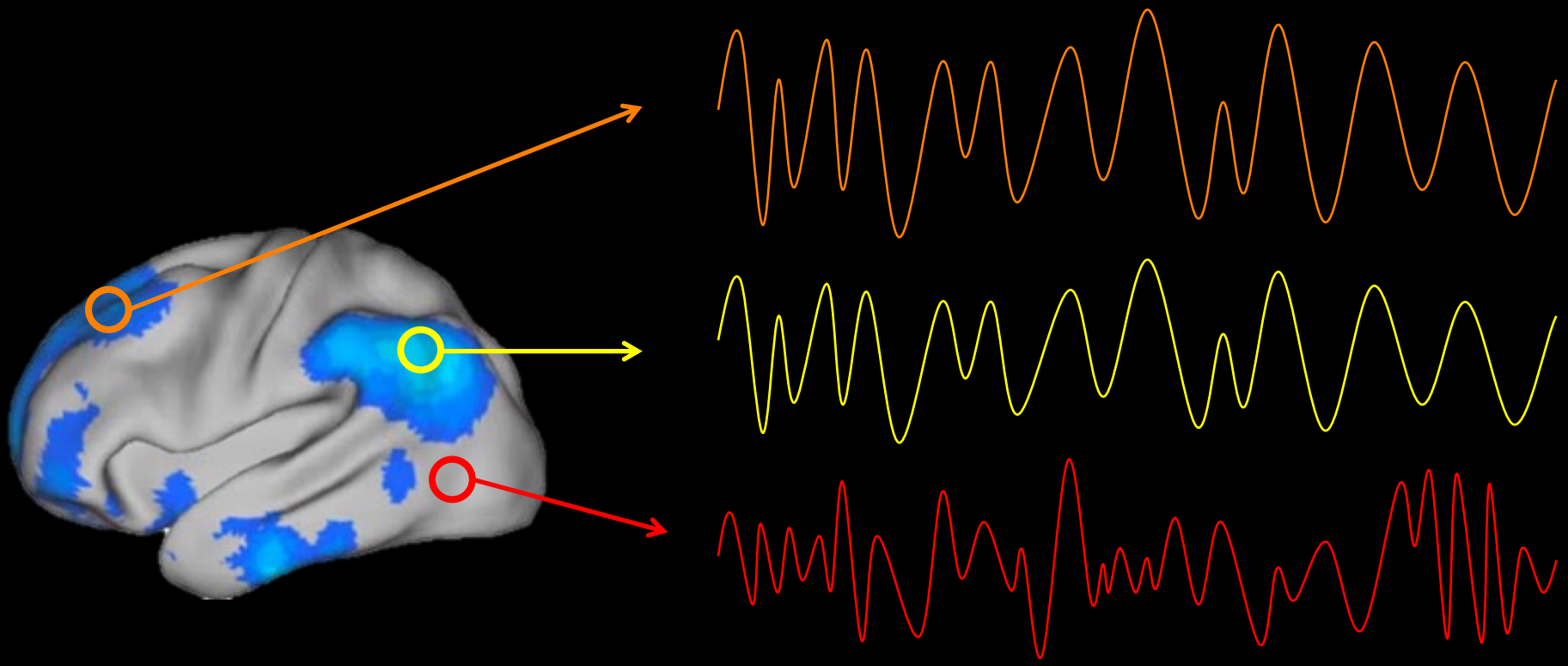
- How does MRI work?
- Types of MRI Data
  - Structural MRI
    - Diffusion Weighted Imaging
  - Functional MRI
    - What is BOLD signal?
  - Three Ways to Look at fMRI Data
    - Activity Maps
    - Neural Decoding
    - **Functional Connectivity Networks**
- A Brief Overview of PET Imaging
- The future…

Aside: Cortical Surface

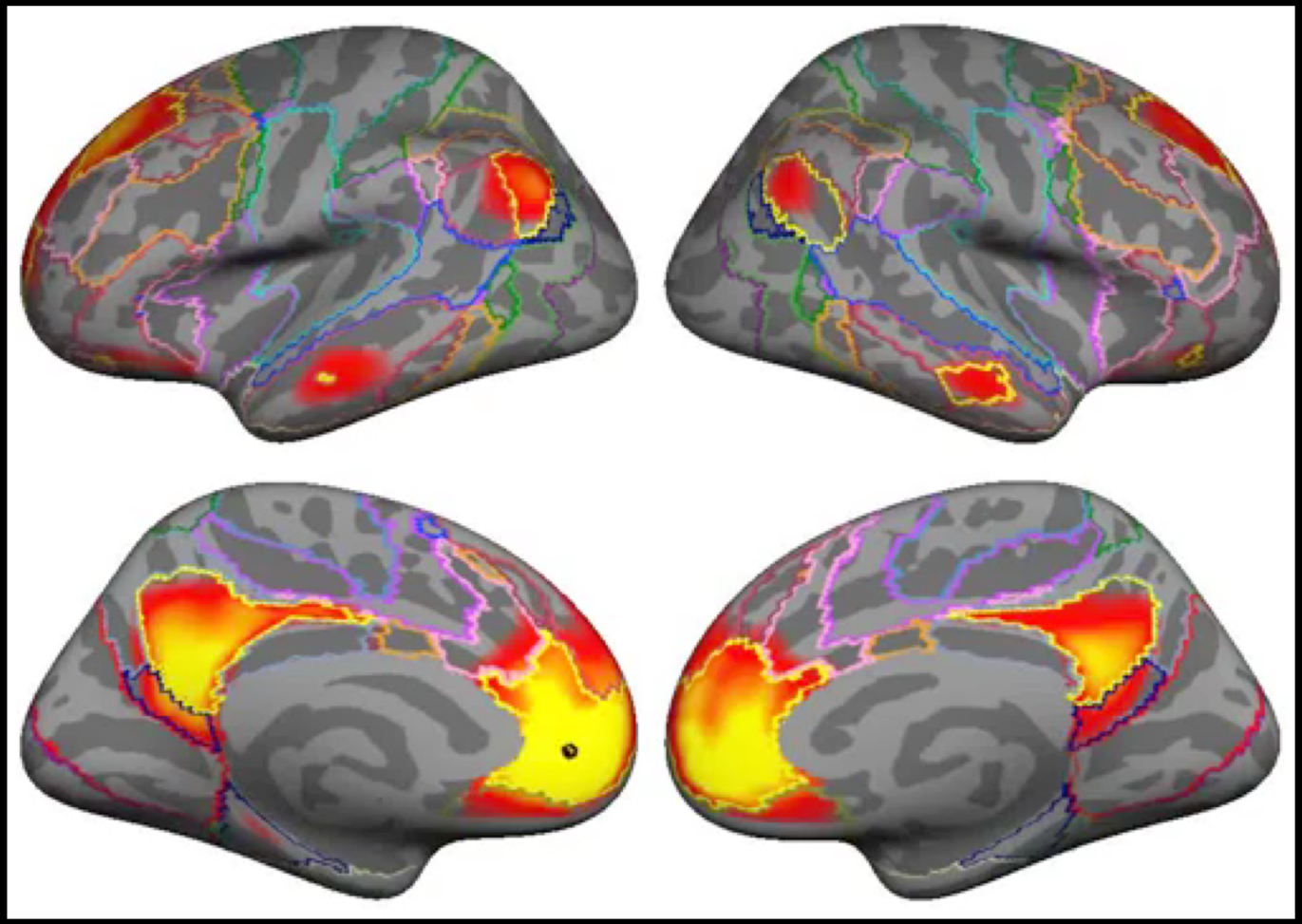
https://www.youtube.com/watch?v=aj-d8PZMXt8

Functional Connectivity

- How do spontaneous fluctuations in BOLD signal **correlate** between brain regions?



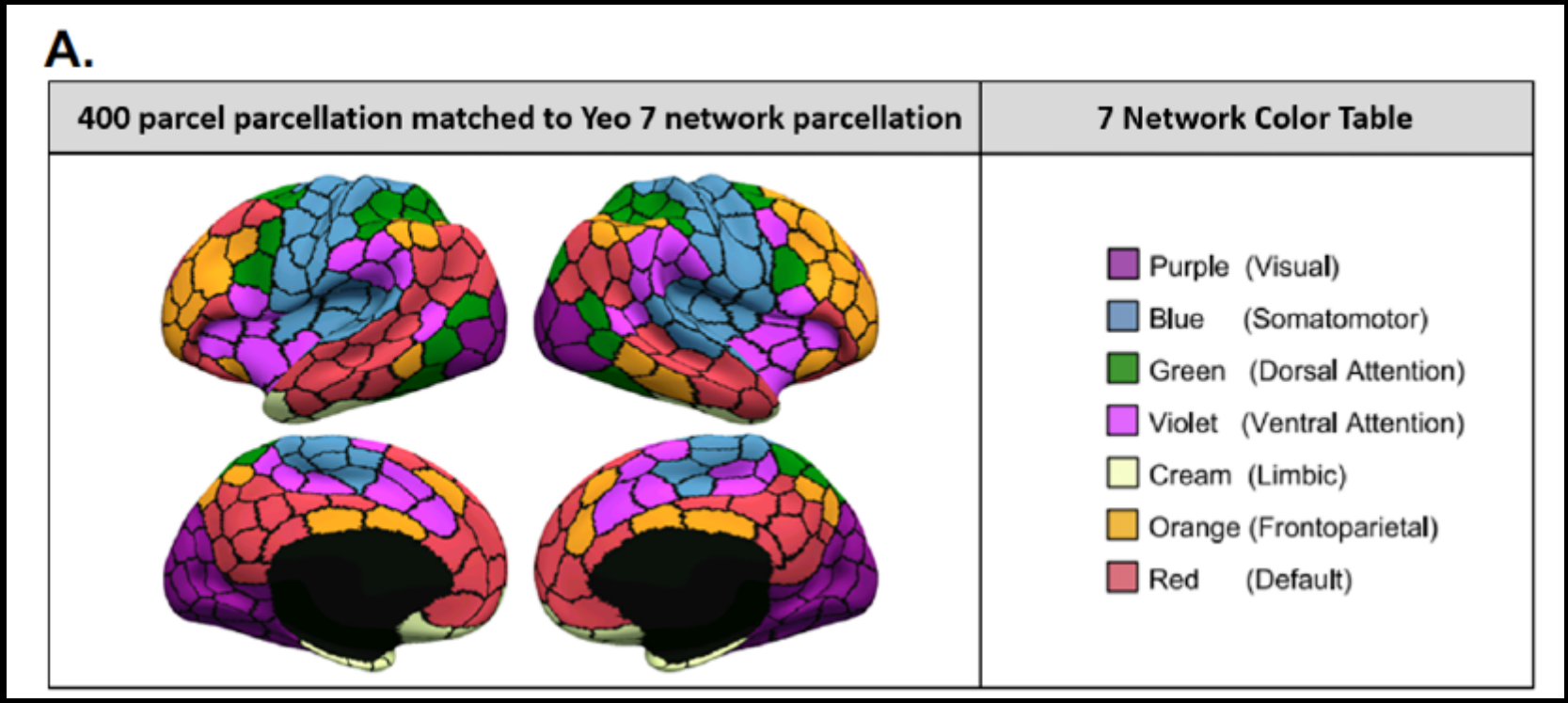
Functional Connectivity Networks



Yeo, et al. 2011

Functional Connectivity Networks

Yeo 7 Network Parcellation



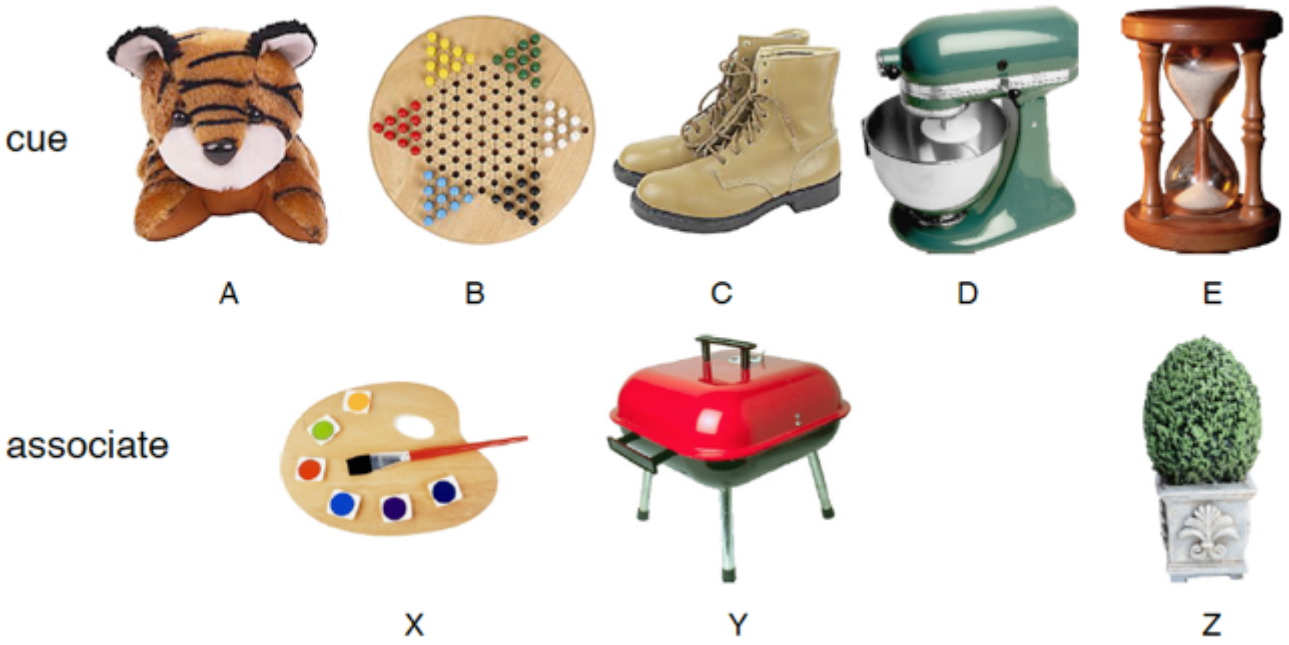
Schaefer, et al. 2018

Context Dependent Rules

Context Dependent Rule Learning Task

Research Question: How does the brain's functional network structure support rule-learning?

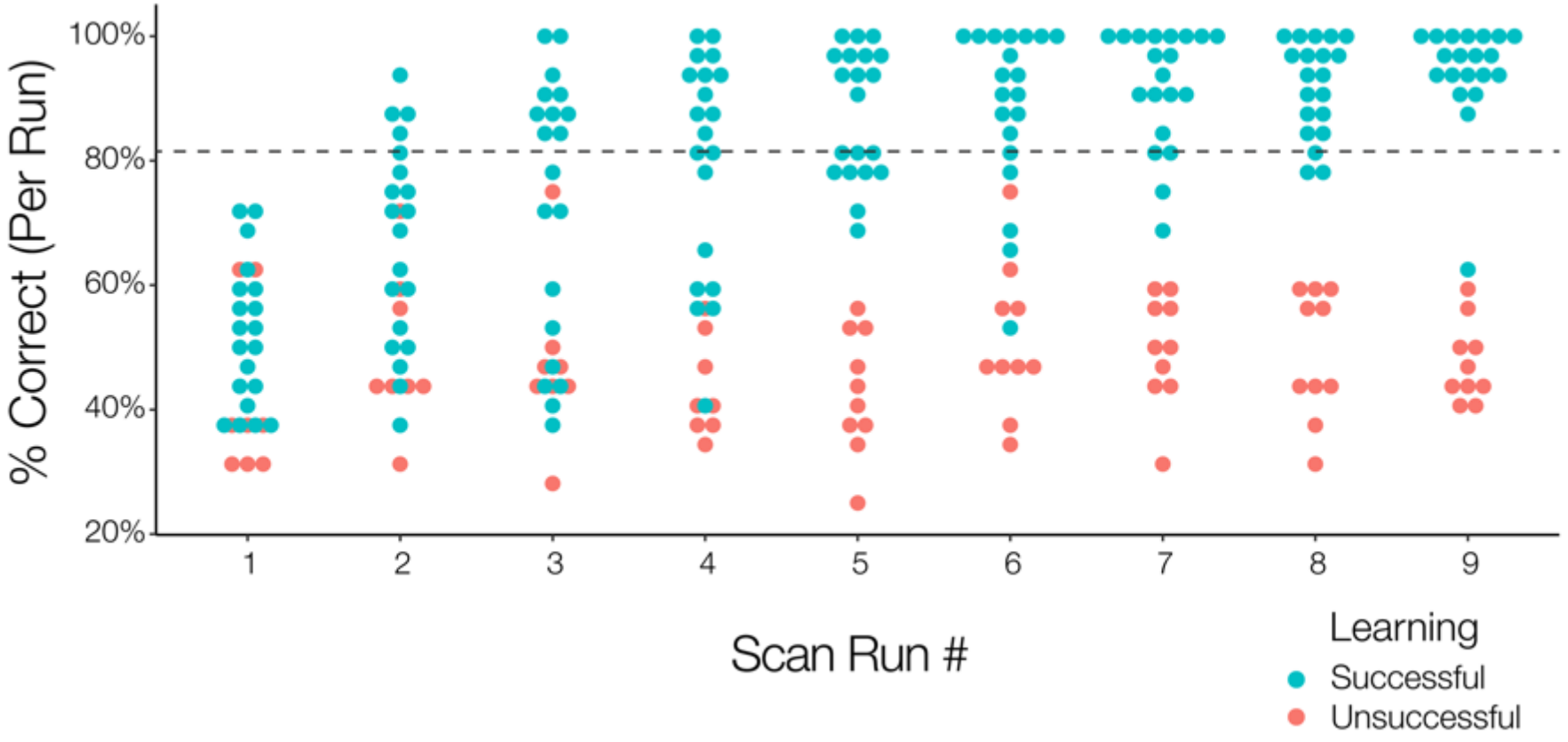
Task: Learn which pairs of objects go together during fMRI scanning.



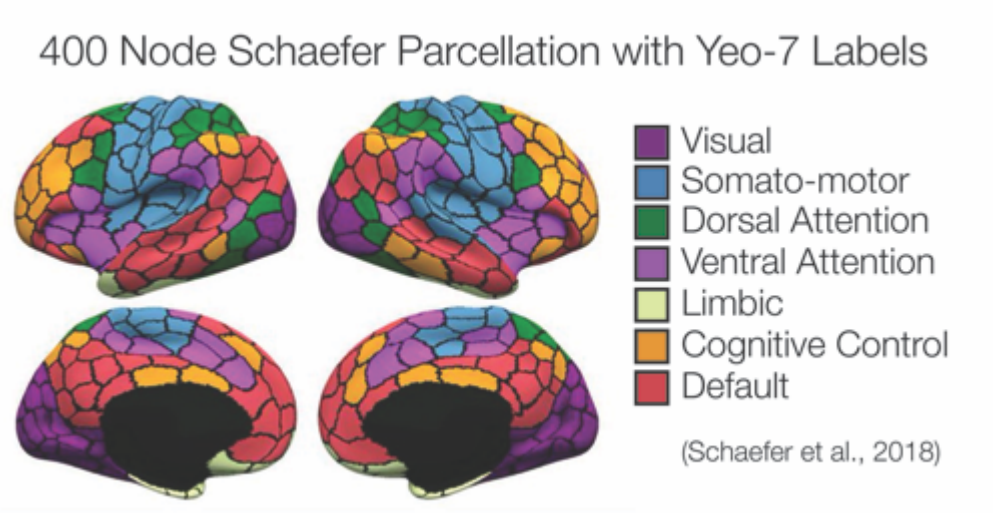
Morin et al. (*Under Review*)

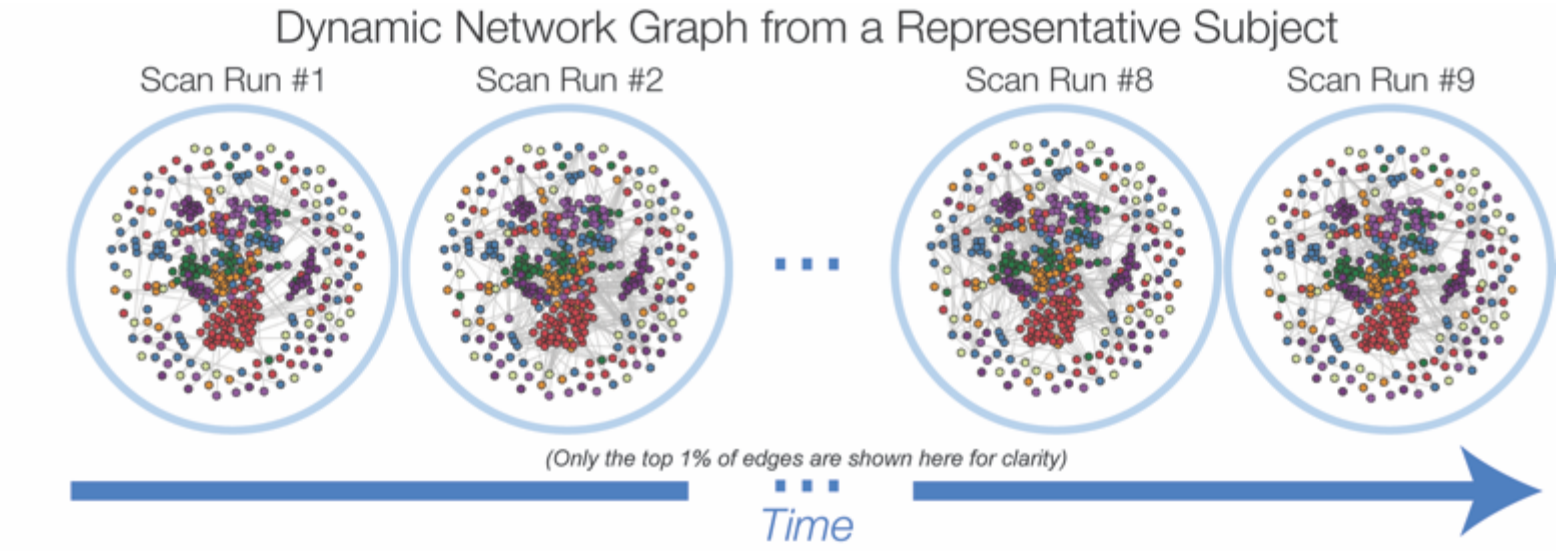
Incorrect

Learning Varies Across Subjects

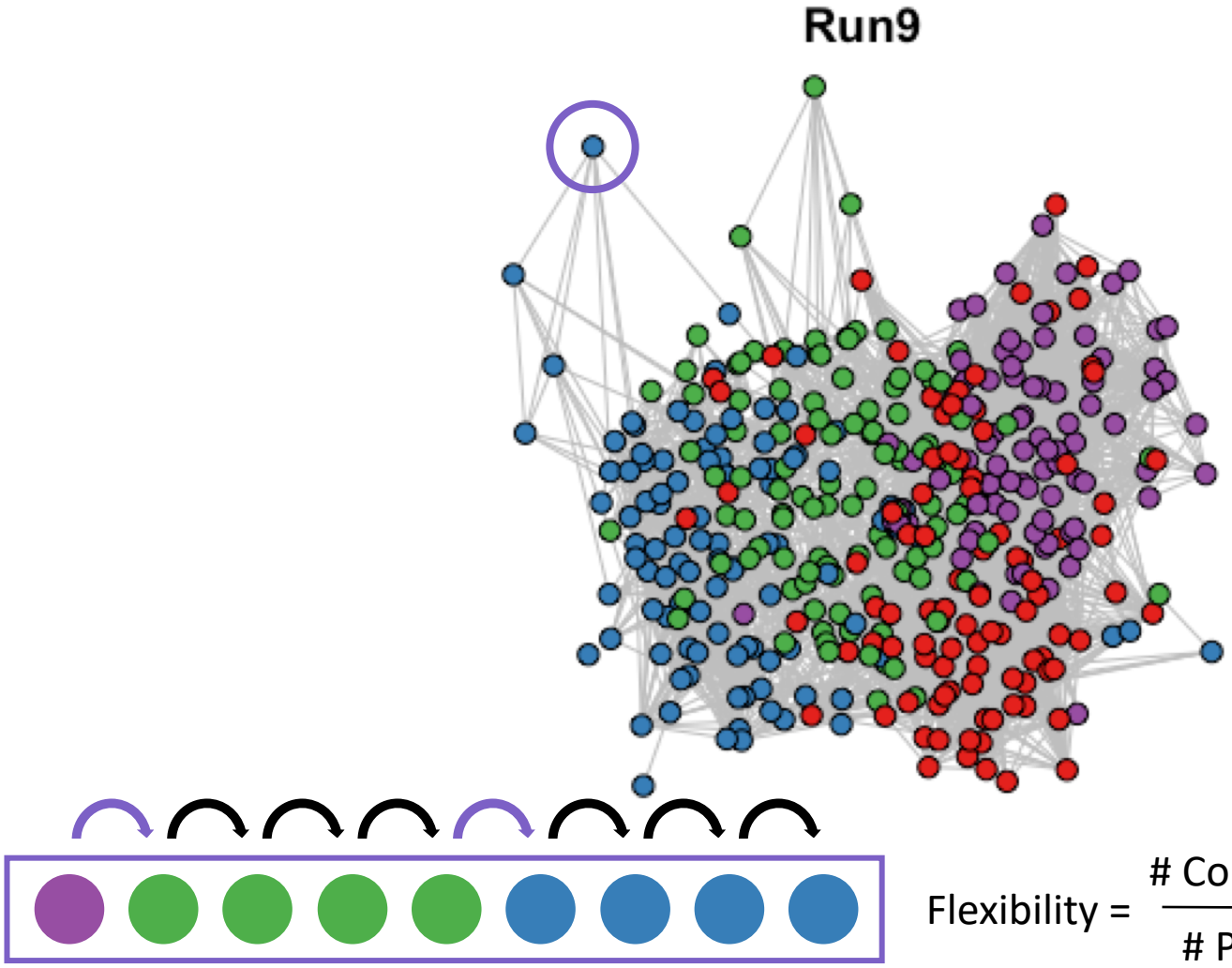


Dynamic Network Construction



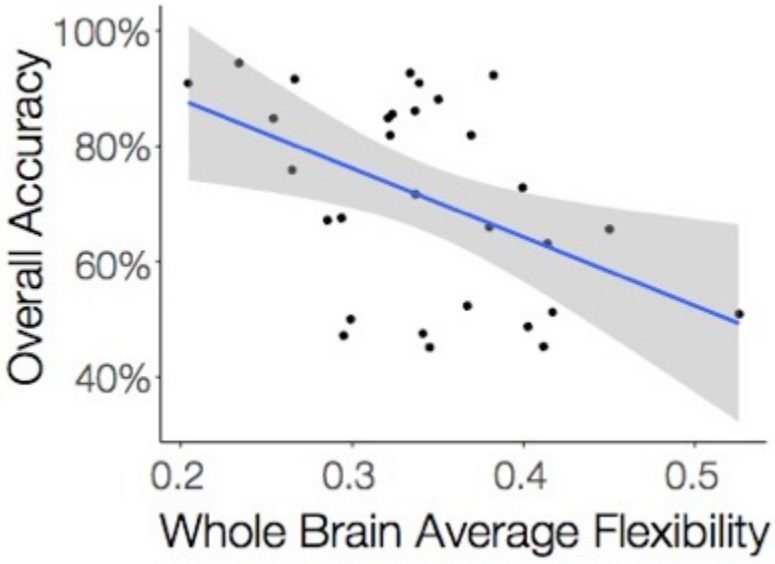


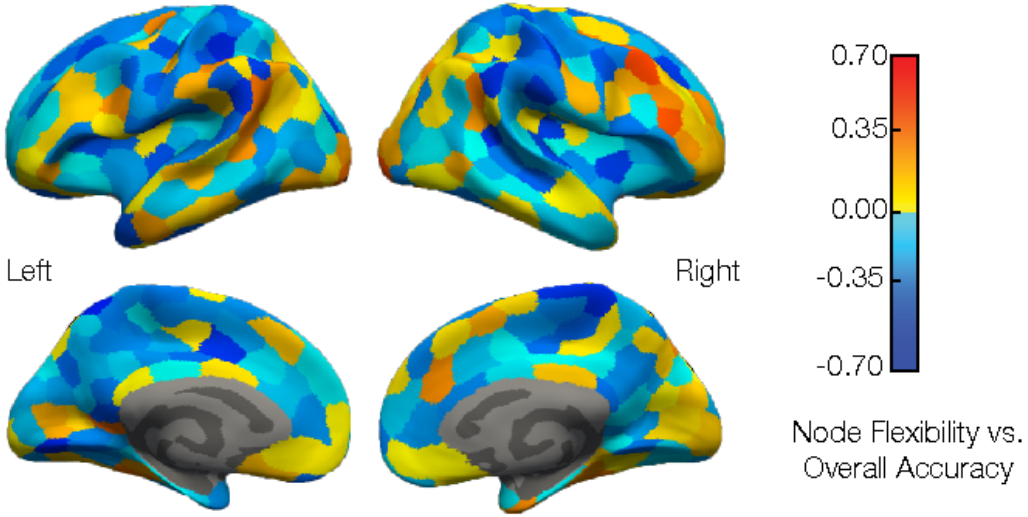
Calculating Node Flexibility



$$\text{Flexibility} = \frac{\text{\# Community Switches}}{\text{\# Possible Switches}} = 0.25$$

Flexibility and Accuracy

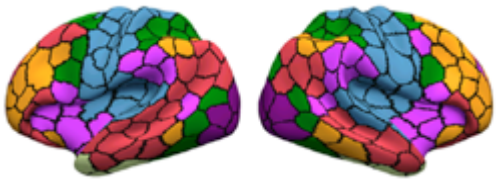


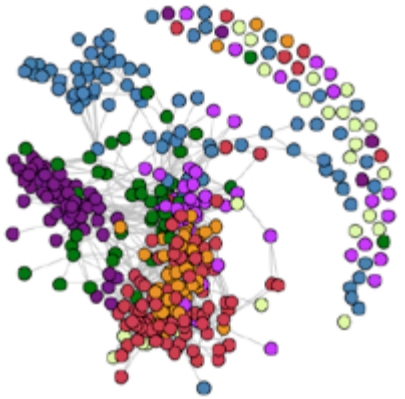


Morin et al. (*Under Review*)

Preliminary Takeaways

- Overall, successful learners have a more “rigid” brain network structure.
- Working Hypothesis: Successful learners latch onto an effective strategy quickly, and form stable representations of the rules.
  - This is represented in a stable brain network structure.





Limitations of Network Science Methods

- Network statistics is a new field and the “correct” mathematical methods are not quite settled
- These methods are computationally complex, requiring advanced computers for large datasets
- As a correlational measure, functional connectivity must be interpreted carefully (What does it mean for two regions to be “functionally connected”?)

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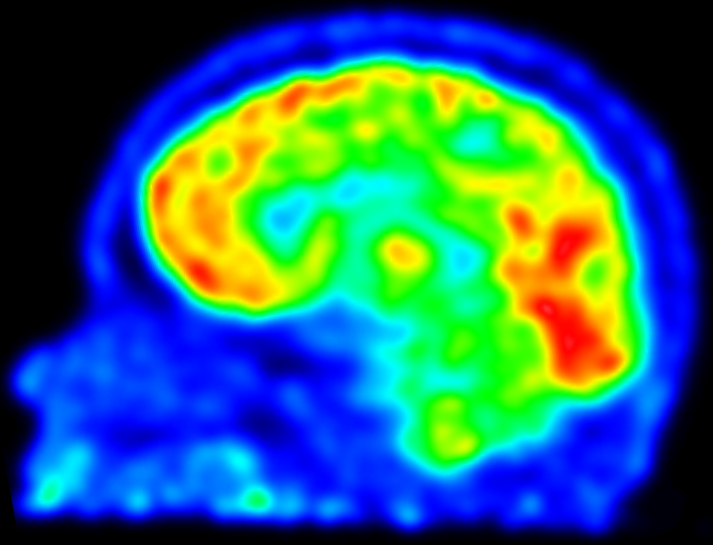
Positron Emission Tomography (PET)

- Temporal Resolution: Hours to Days (sometimes minutes)
- Spatial Resolution: ~2mm^3 (at best)



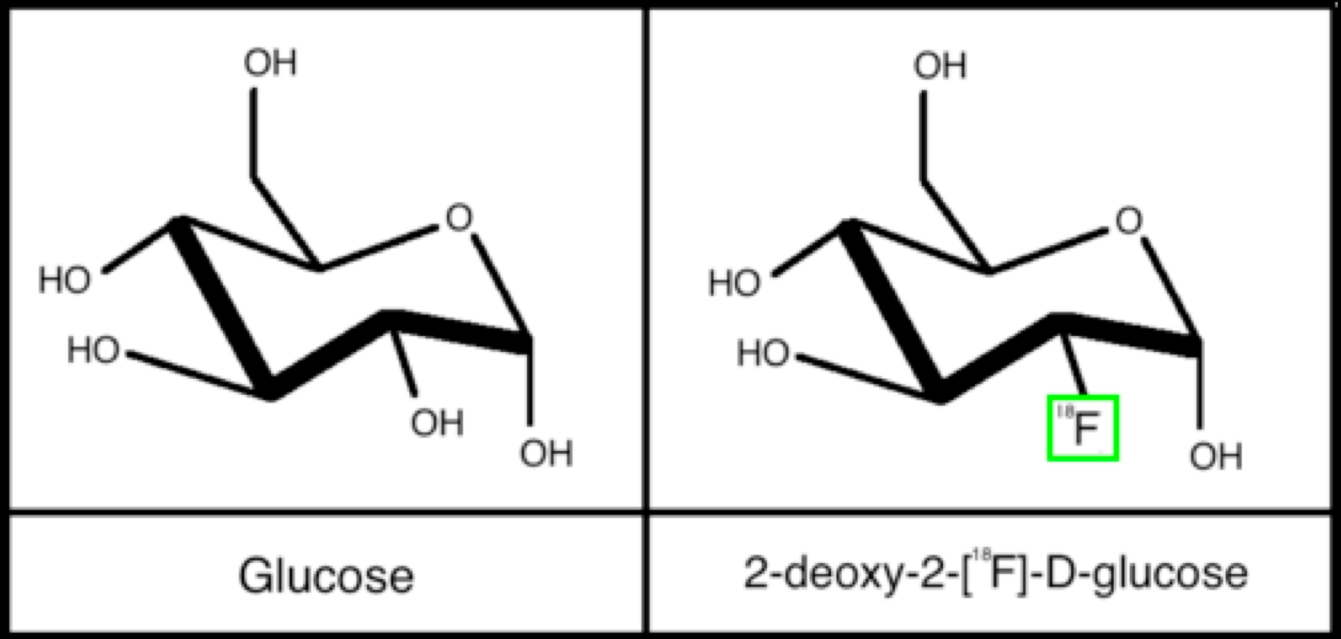
Positron Emission Tomography

https://www.youtube.com/watch?v=oySvkmezdo0 (1 min video – no sound)

https://www.youtube.com/watch?v=yrTy03O0gWw (4 min video - UCL)

Radiotracers

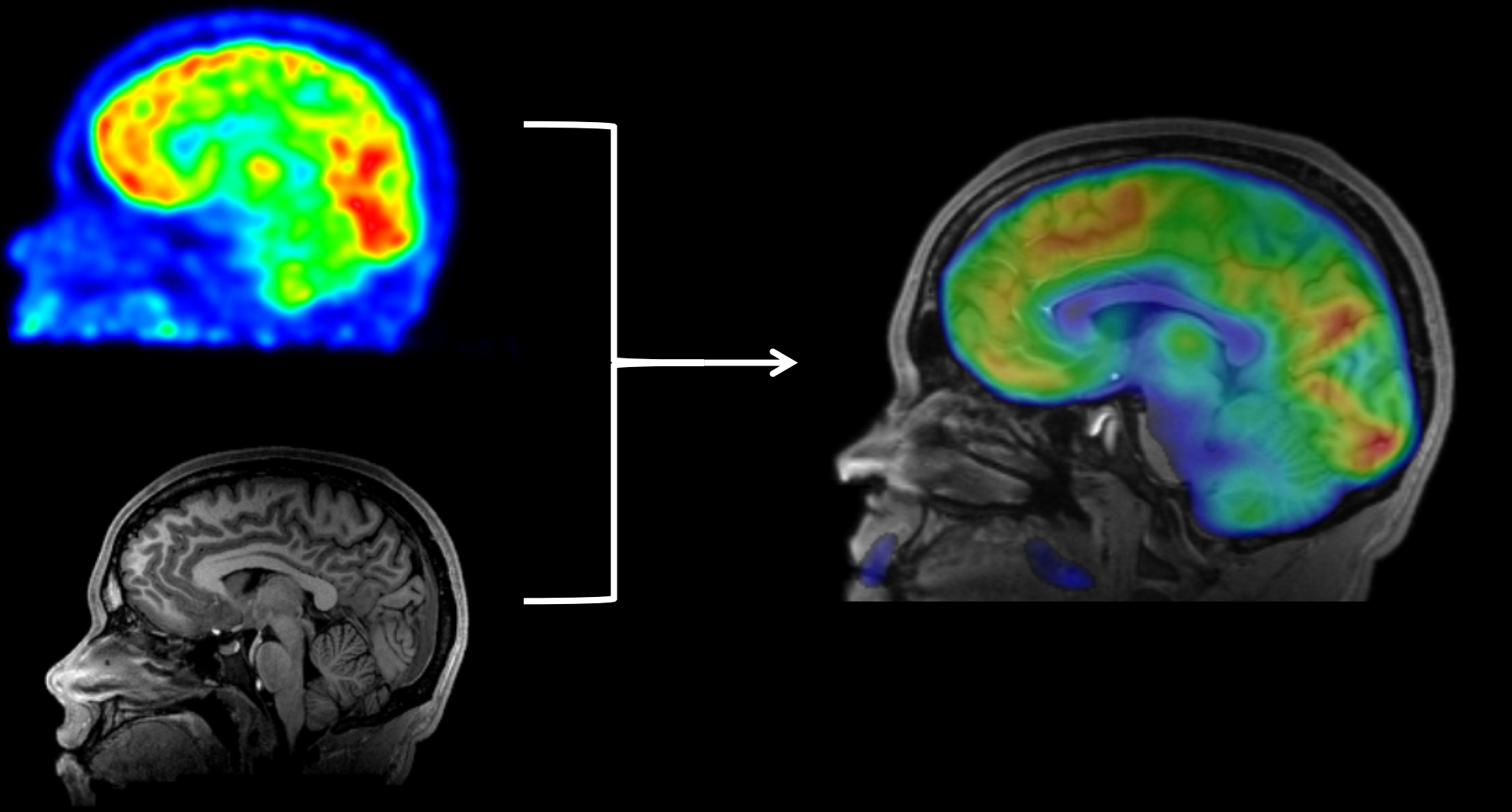
- “Tag” a chemical with a radioactive isotope
  For example, flourodeoxyglucose or FDG is just glucose (sugar) with an [^{18}F] tag



PET Applications

- FDG Imaging (Cancer & Neurology)
- Dopamine Imaging
- Opioid Imaging
- Amyloid & Tau Imaging (Alzheimer's)
- Imaging Neuroinflamation & Microglia
- HDAC (epigenetic) imaging
- And Many More!

Simultaneous MR/PET



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The Future is Now

- Dylan Williams, 21 year-old student at Tufts in 2012 when he was hit by a car
- Deemed “minimally conscious” by physicians at MGH
- Dr. Brian Edlow was conducting research at the time imaging unconscious individuals with fMRI
- Dylan responded to music and language sounds
- Dylan regained consciousness a few days later

https://giving.massgeneral.org/fmri-reveals-brains-secrets/

Acknowledgements

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Christine Wu
Baleigh Hightower

Tufts University
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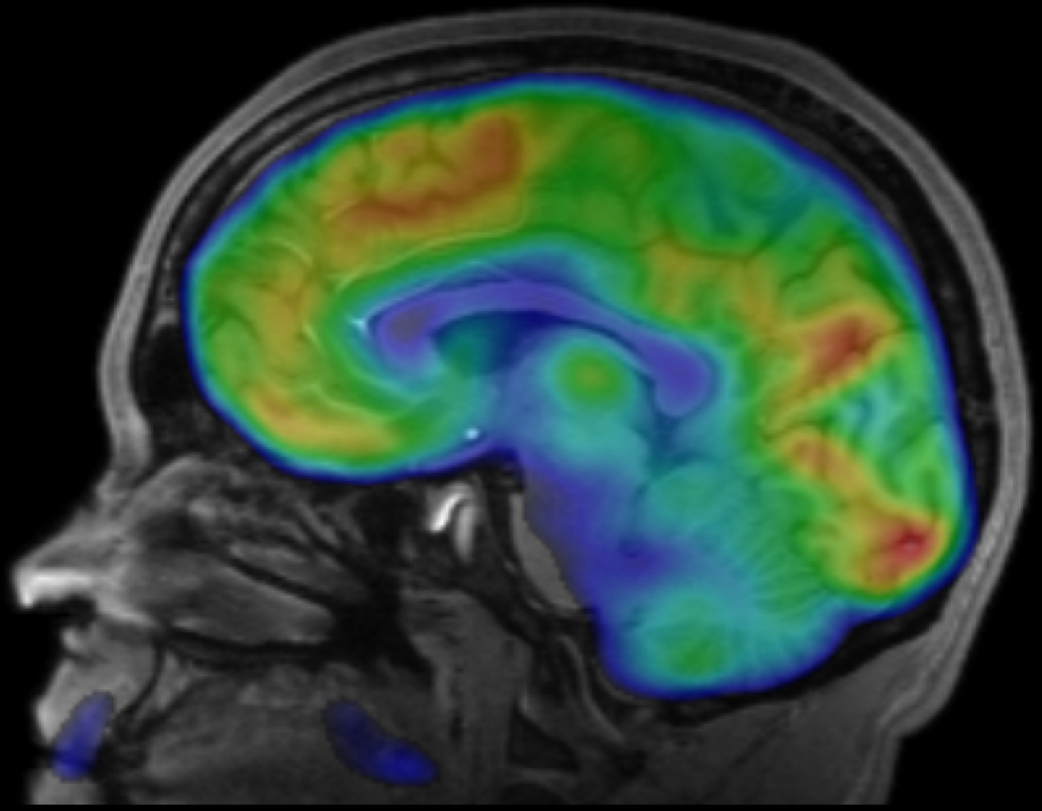
Dr. Ayanna Thomas
Dr. Ben Hescott
Dr. Elizabeth Race
Dr. Nathan Ward

Questions?



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