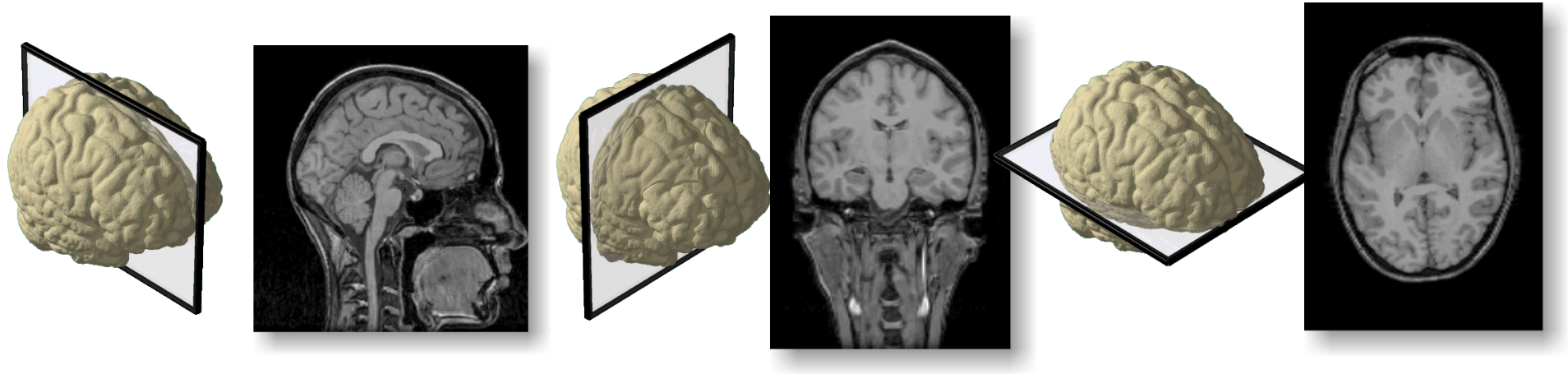
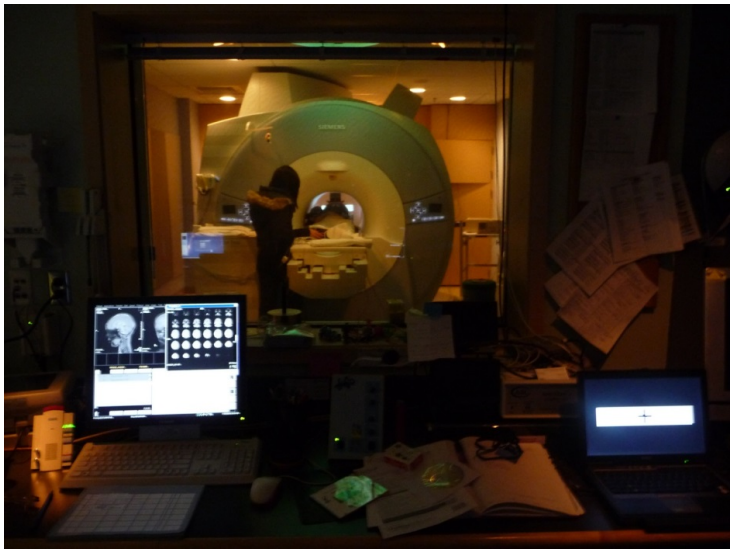
H-126 Recitation 2: Methods of Investigation

t  day's Section 

- Content review: ~40 mins
- Experimental Design activity: ~10 mins
- Questions: ~10 mins

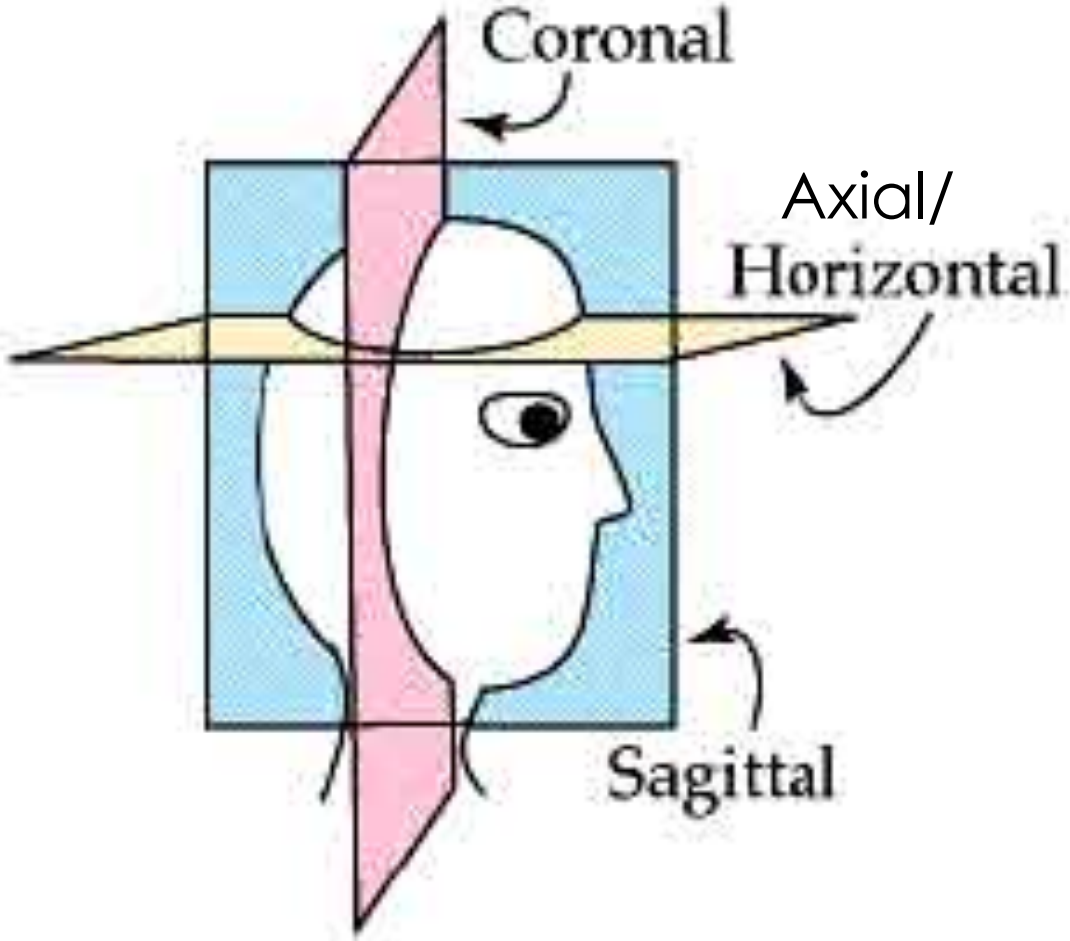
MRI Review



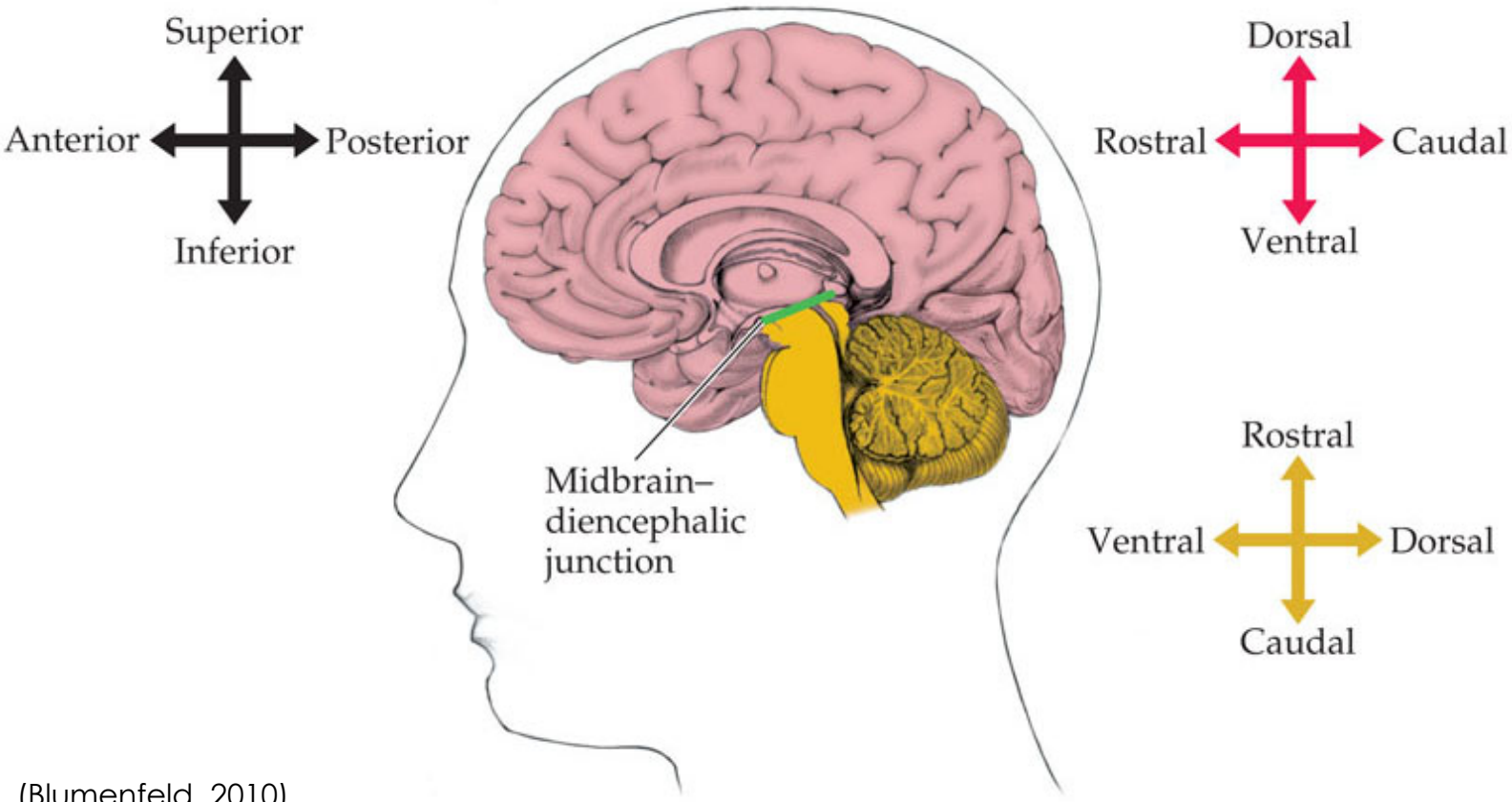


MRI Review: Orientations

(MIT OCW, 2006)



MRI Review: Directions



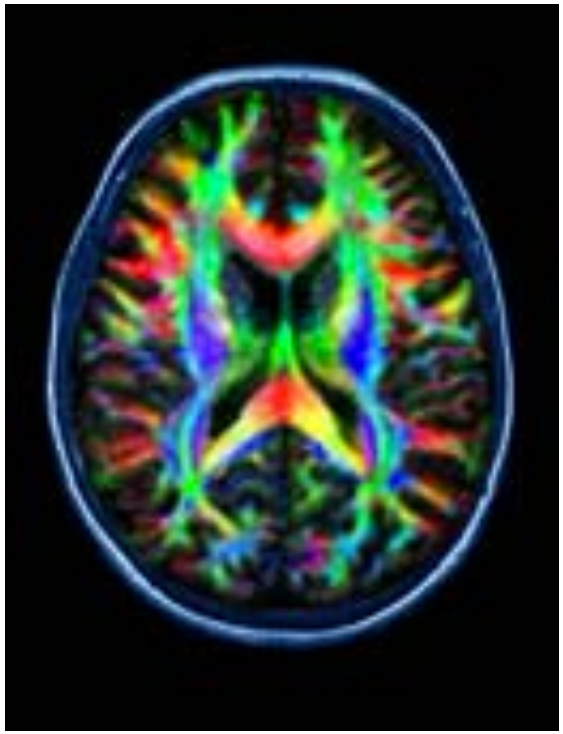
(Blumenfeld, 2010)

MRI Review

Structural MRI

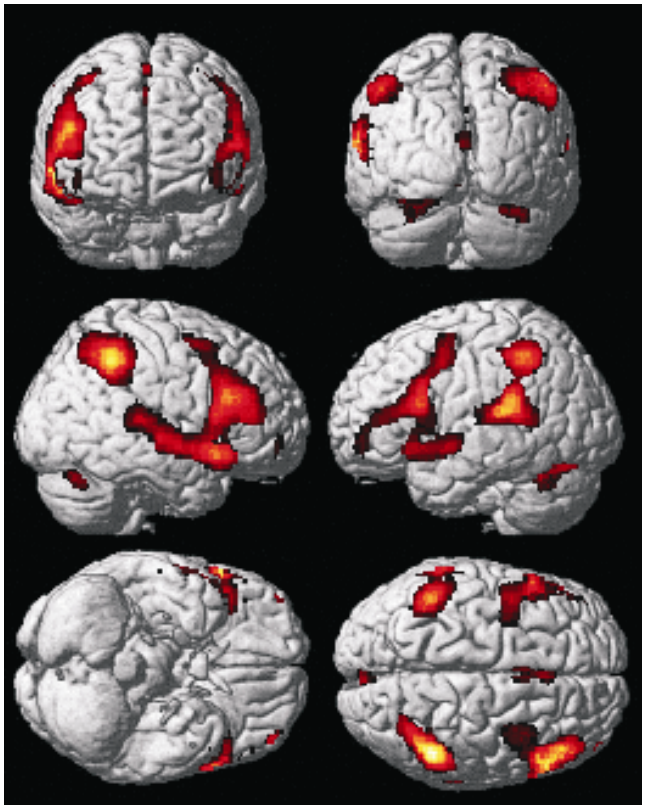
Gray matter properties (area, thickness, curvature)

Diffusion Tensor Imaging



White matter properties (structural connectivity)

Functional MRI (fMRI)



Task-based metabolic activity

MRI Review

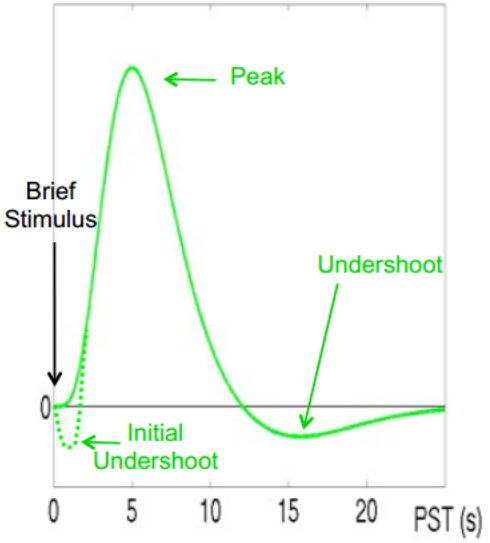
The BOLD Effect:

1. You **use a network of specific brain regions** to perform a task.

2. To perform the task, our brains use up the **oxygen** in our **blood** in those areas.

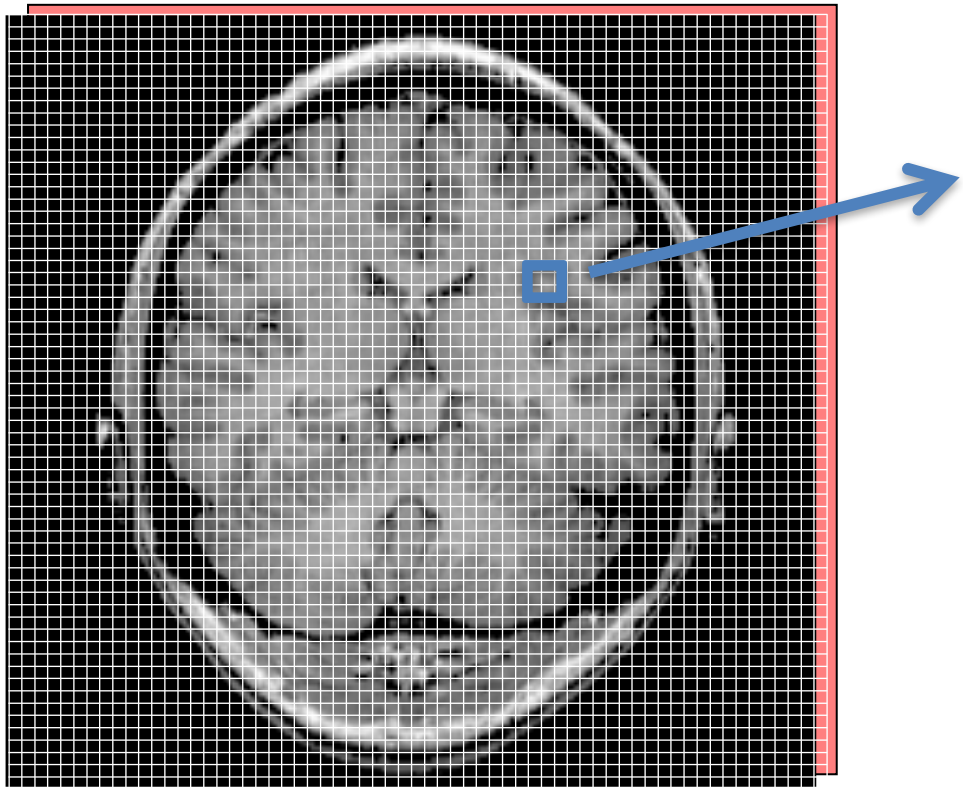
3. To get more oxygen, our bodies **send more blood** to those parts of the brain to overcompensate for the "use of oxygen."

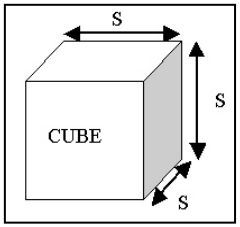
4. This **oxygen change** is what we measure to determine which brain regions are actively working to complete the task.

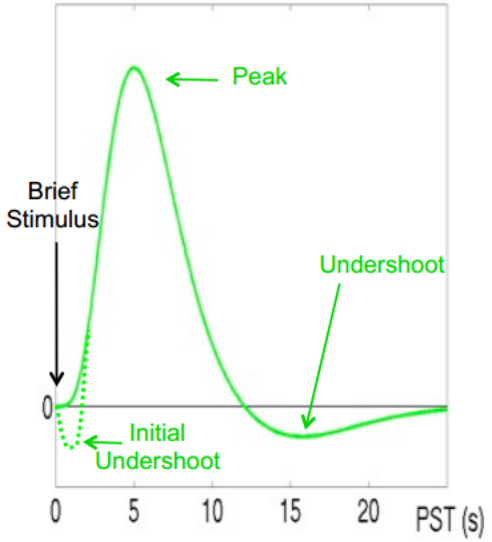


MRI Review

- The BOLD signal is measured and compared within small graphical units of the 3D brain images = Voxels







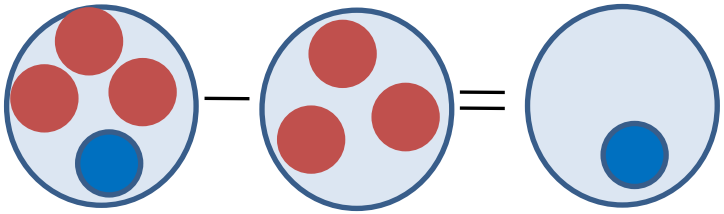
MRI Review

fMRI Task Localization

"Subtraction logic" is employed to localize BOLD signal associated with the task of interest:

Task A = our task of interest (e.g. motor task, perception task, memory task, etc.)

Task B = a less demanding control task with all the same properties *except* the task of interest

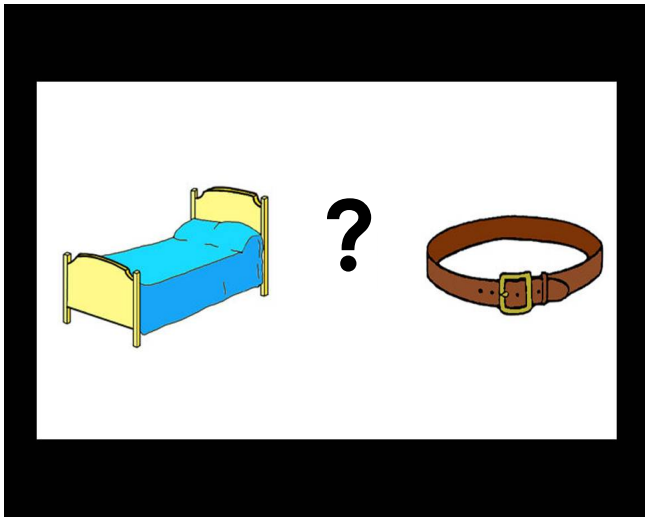


[BOLD signal during task A]
– [BOLD signal during task B]
= [BOLD signal associated with task A]

MRI Review

Raschle, Zuk, Gaab. (2012) PNAS

Stimuli: male / female voice, pictures corresponding with words



Experimental Task: indicate whether the first sounds of the words are the same
(First Sound Matching)

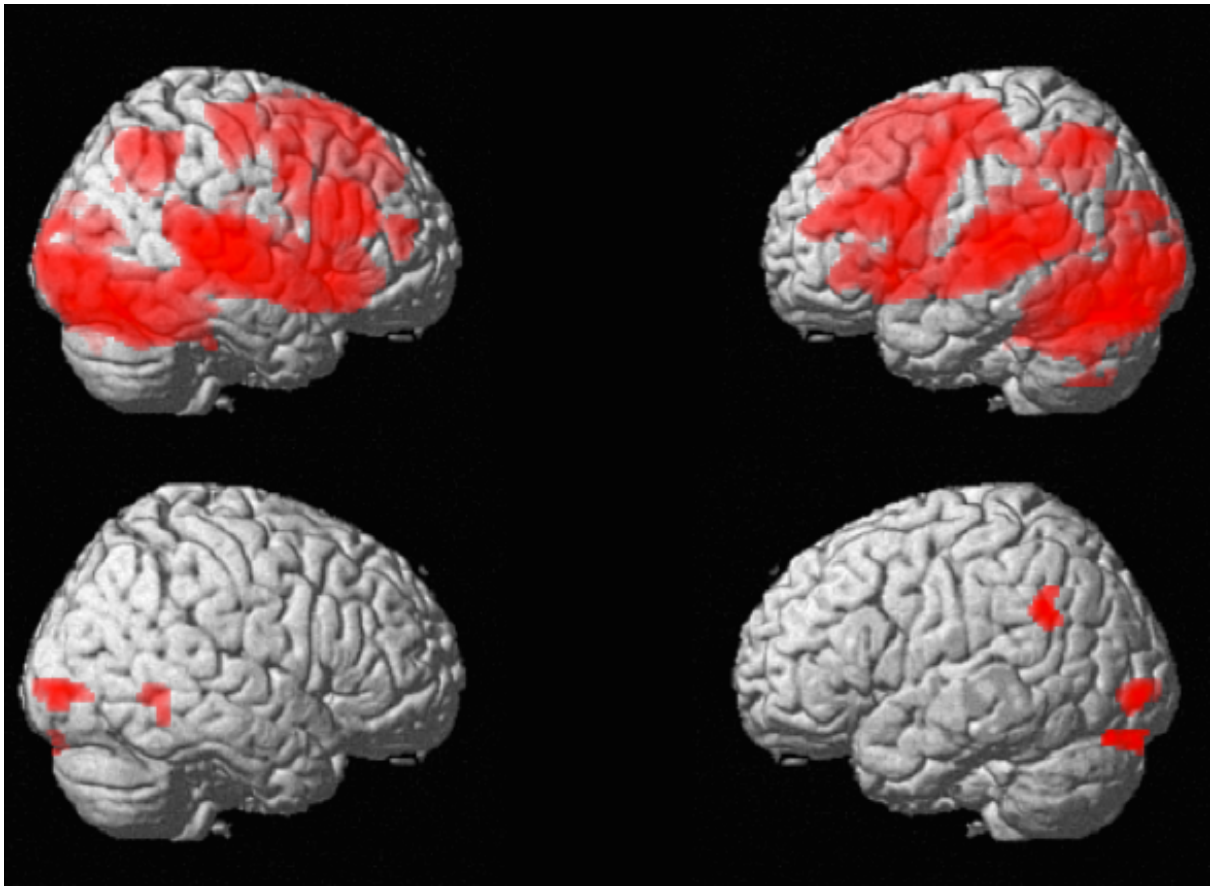
Control Task: indicate whether the voices of the speaker match
(Voice Matching) (SAME auditory stimuli, SAME visual stimuli)

Analysis: First Sound Matching - Voice Matching = **Phonological Processing ONLY**

MRI Review

Significance of experimental vs. control conditions in fMRI

Sample: *n*= 5, typically developing children ages 8-12 years old, completed FSM task



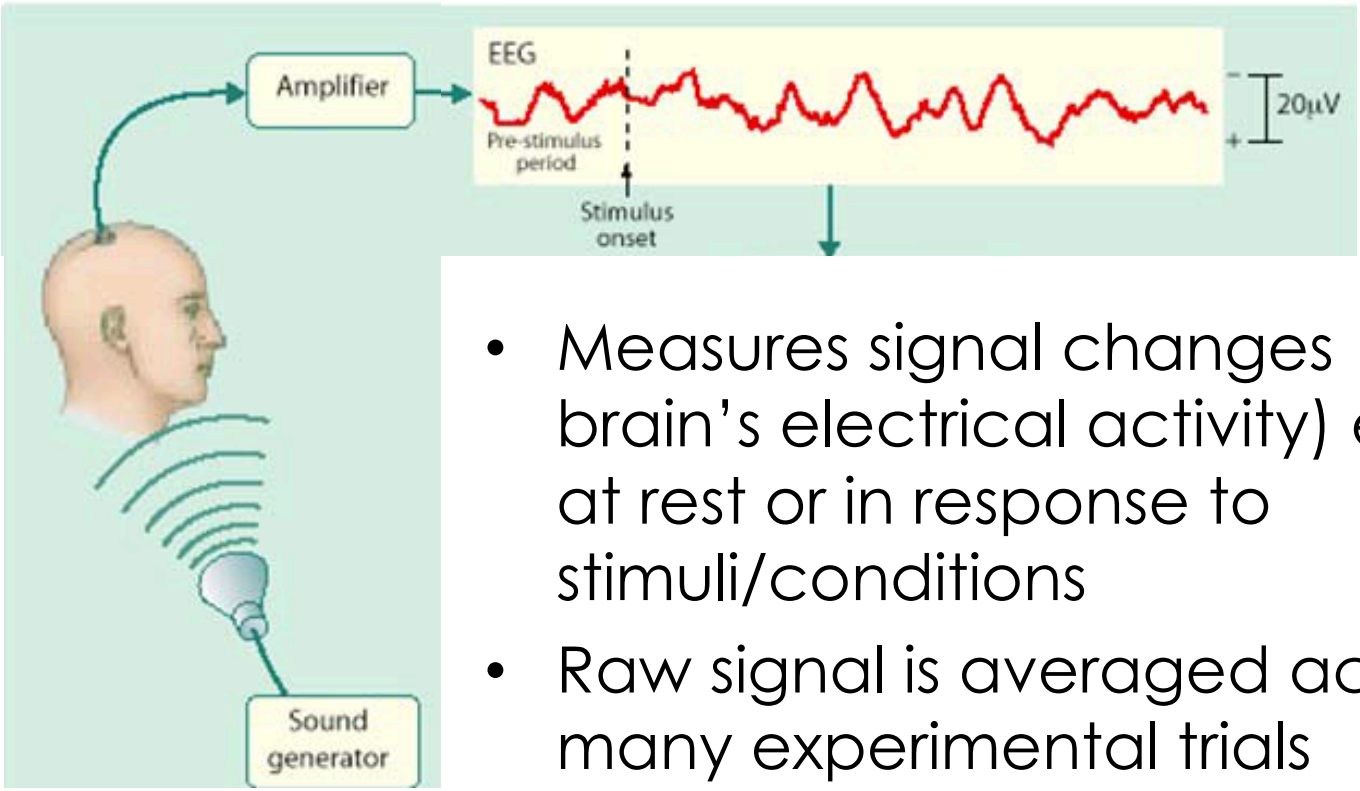
First Sound Matching > REST

First Sound Matching > Voice Matching

SAME threshold, p = 0.005 uncorrected

EEG/ERP Review

EEG

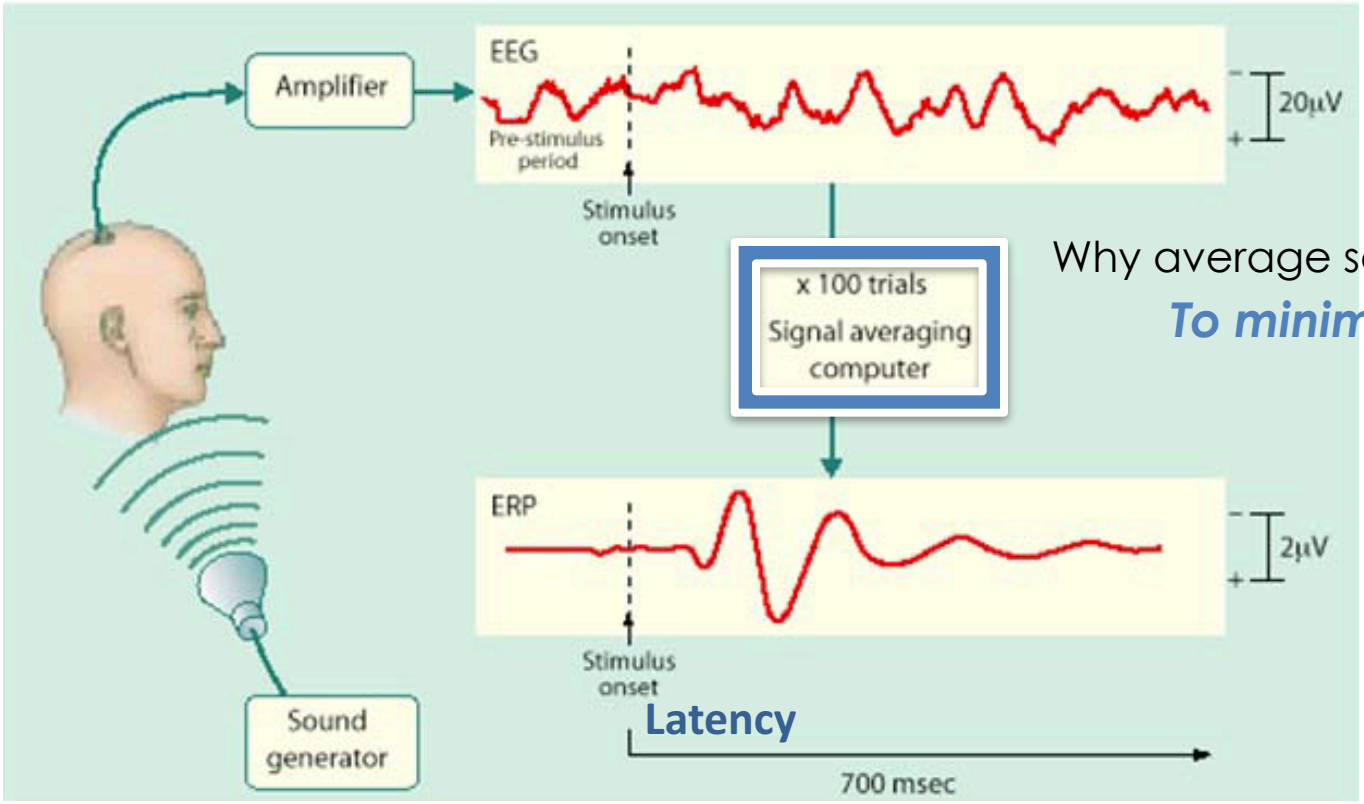


- Measures signal changes (of brain's electrical activity) either at rest or in response to stimuli/conditions
- Raw signal is averaged across many experimental trials
- represents several neural mechanisms acting in synchrony

Analysis:
Decompose raw signal into power spectrum,
Compare amplitudes across different frequency ranges.

EEG/ERP Review

ERP



Why average so many trials?

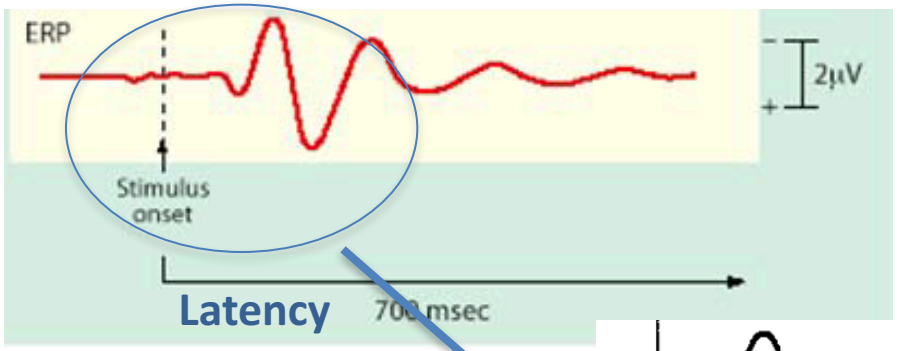
To minimize noise

Amplitude

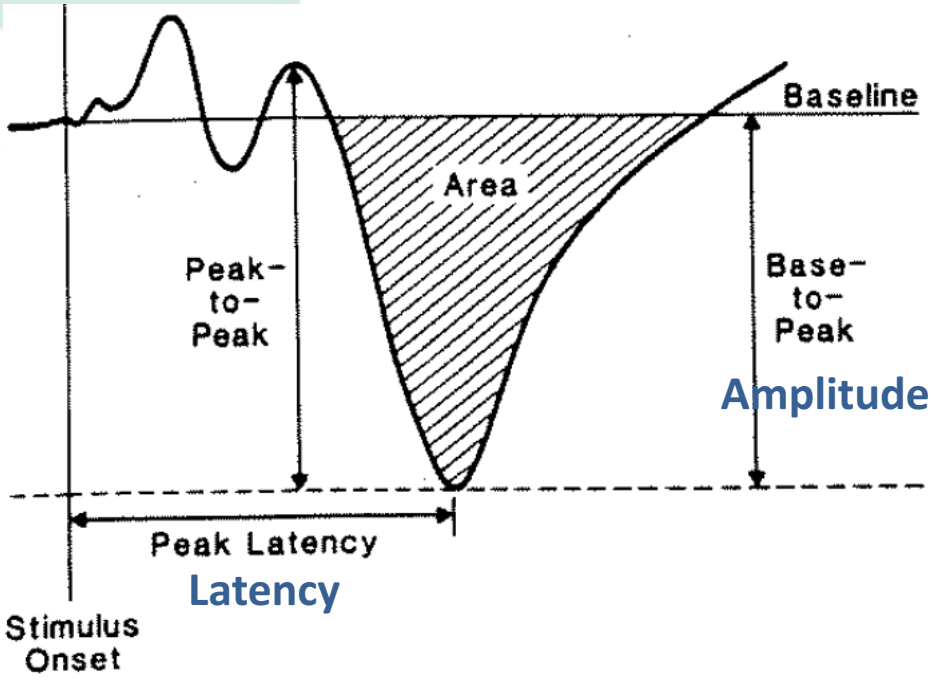
- **E**vent **R**elated **P**otential (ERP) technique
- Stimulus-specific responses from continuous EEG

EEG/ERP Review

ERP

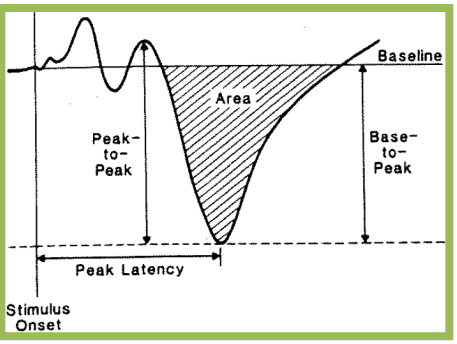


Amplitude



Analysis:

Comparing waveform or component amplitude & latency in response to the stimulus



EEG/ERP Review

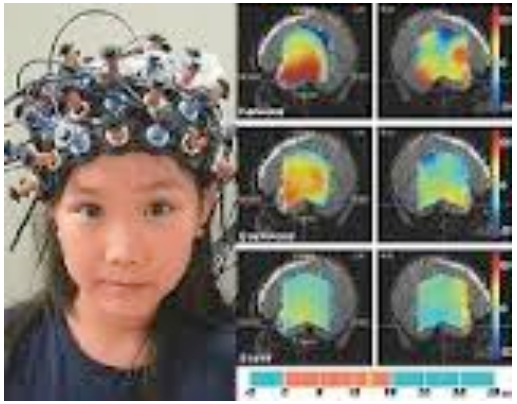
TABLE 1

Glossary of Some ERP Components Commonly Examined in Studies of Typical and/or Atypical Development and Some Relevant Adult Components

Process	Component	Ages Observed	Function	Scalp Distribution, Timing, ms	Notes
Auditory sensory	MMN	Birth onward	Obligatory auditory discrimination and/or sensory memory	Frontocentral, 100–250	Plotted as a difference wave (deviant stimulus–response minus standard stimulus–response)
	P50/P1 repetition suppression	Early adolescence onward	Reduction of amplitude after repetition, indexes sensory inhibition	Vertex, ~50 in adults	This function may be observable in neonates. This may also be observable in the visual domain.
	N2	Infancy onward	Stimulus complexity, tone processing, speech vs. nonspeech in children and adults	Frontocentral, 150–250 in adults; ~250–350 in children	
Visual sensory	P100	Birth/infancy	Visual pattern reversal, visual thresholds, visual discrimination thresholds	Occipital, ~100 in adults; 250–300 in neonates	
	C1	Adulthood	Initial cortical processing in V1 (~56 ms)	Occipital, ~60	
	P1	Infancy, adulthood	Under unique circumstances, may index magnocellular visual pathway functioning	Occipital, ~100	
	N1	Birth/infancy, adulthood	Under unique circumstances, may index parvocellular visual pathway functioning	Occipital, 65–85	
Face processing	N290	Infancy and early childhood	Sensory-perceptual processing of faces	Occipital-temporal, ~290	See also N170 and P400
	P400	Infancy and early childhood	Sensory-perceptual and early cognitive processing of faces	Occipital-temporal, ~400	See also N290 and N170
	P1/P100	Birth onward	Face processing during childhood, face inversion during childhood	Occipital-temporal, ~100 in adults	Significant developmental changes, sometimes indexing face processing
	N170/N1	Middle childhood onward	Sensory-perceptual processing of faces, perceptual experience	Occipital-temporal, ~170	See also VPP, P100, N290, and P400
	VPP	Adulthood	Sensory-perceptual processing of faces	Centrofrontal, ~170	Highly similar functionally to the N170

(Continued on next page)

Table in Nelson & McCleery (2008)
Great reference for future ERP literature

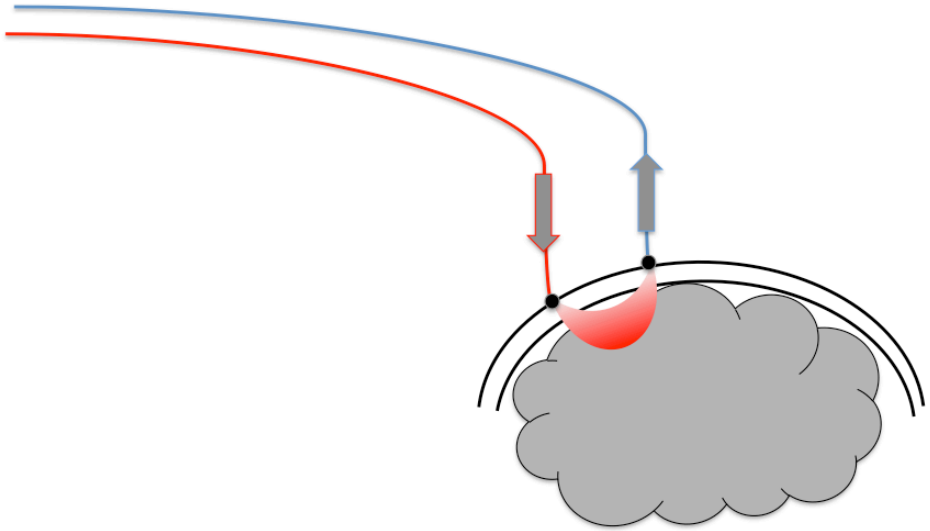


fNIRS

fNIRS uses light to see the brain

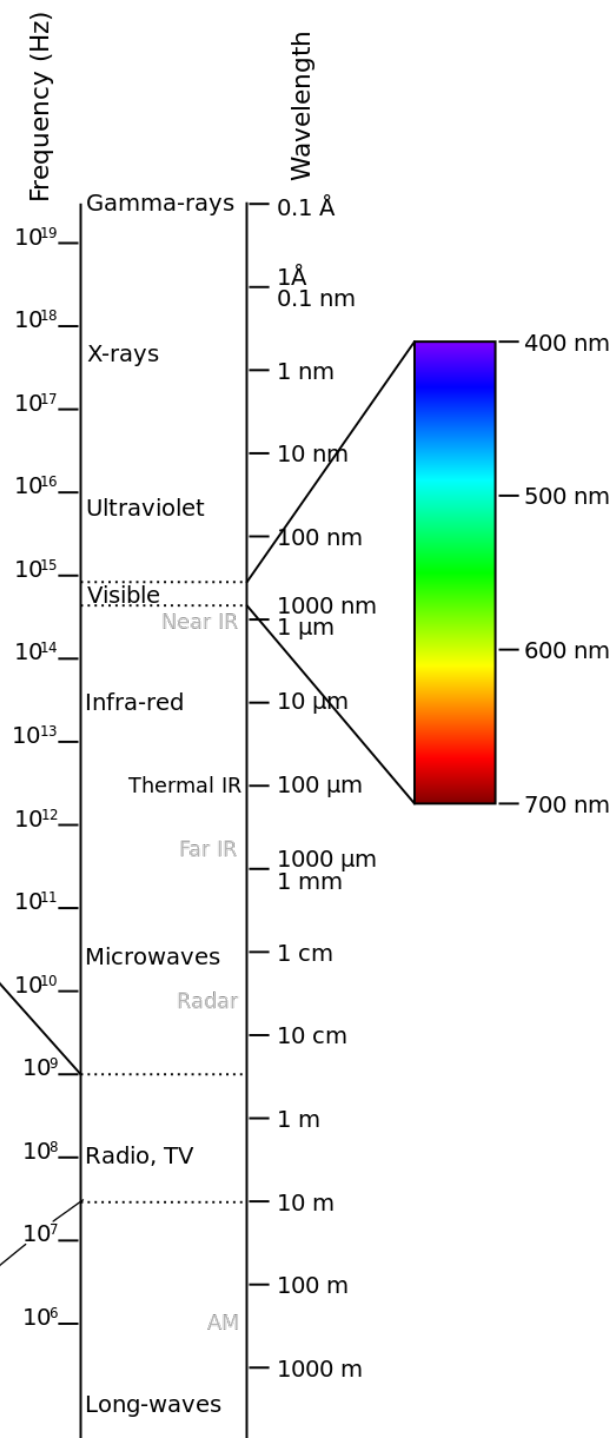
How does light interact with different tissues?

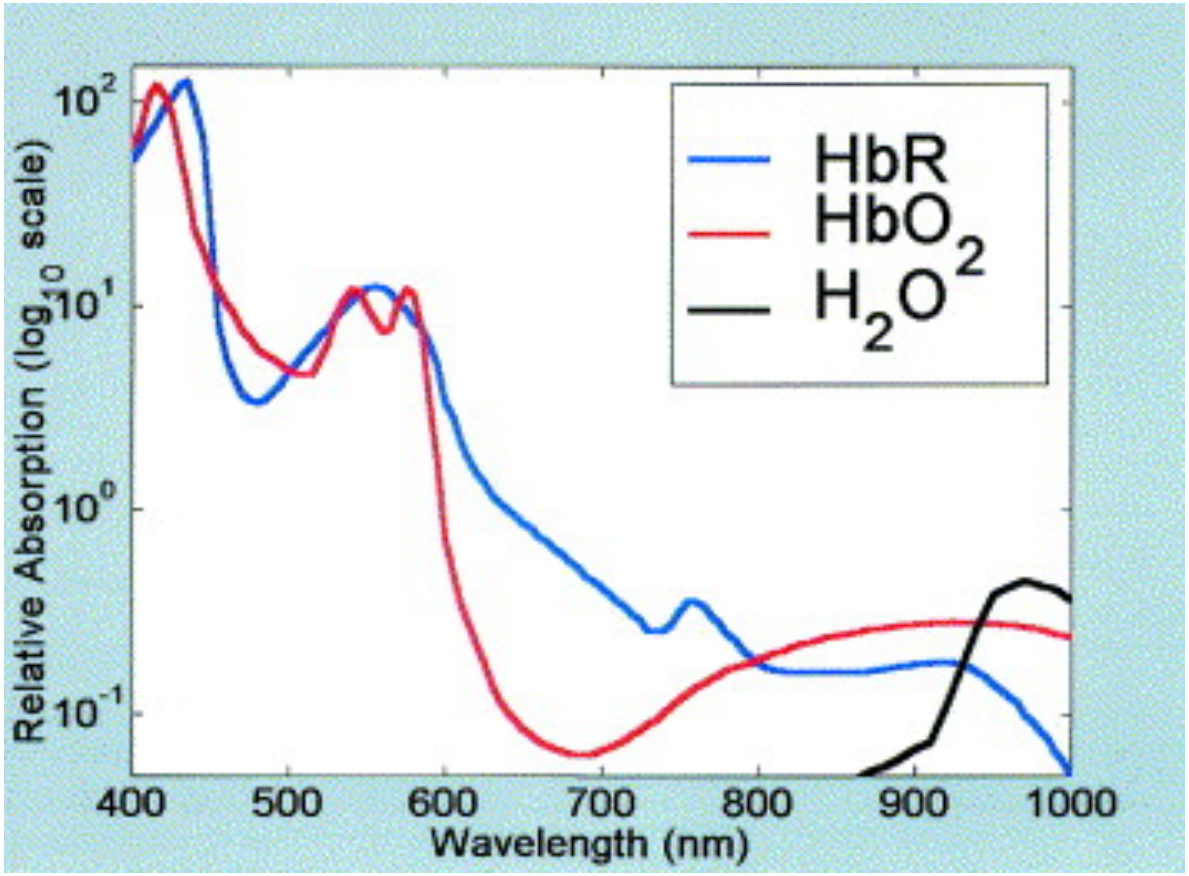
- **absorption**
- scattering
- reflection

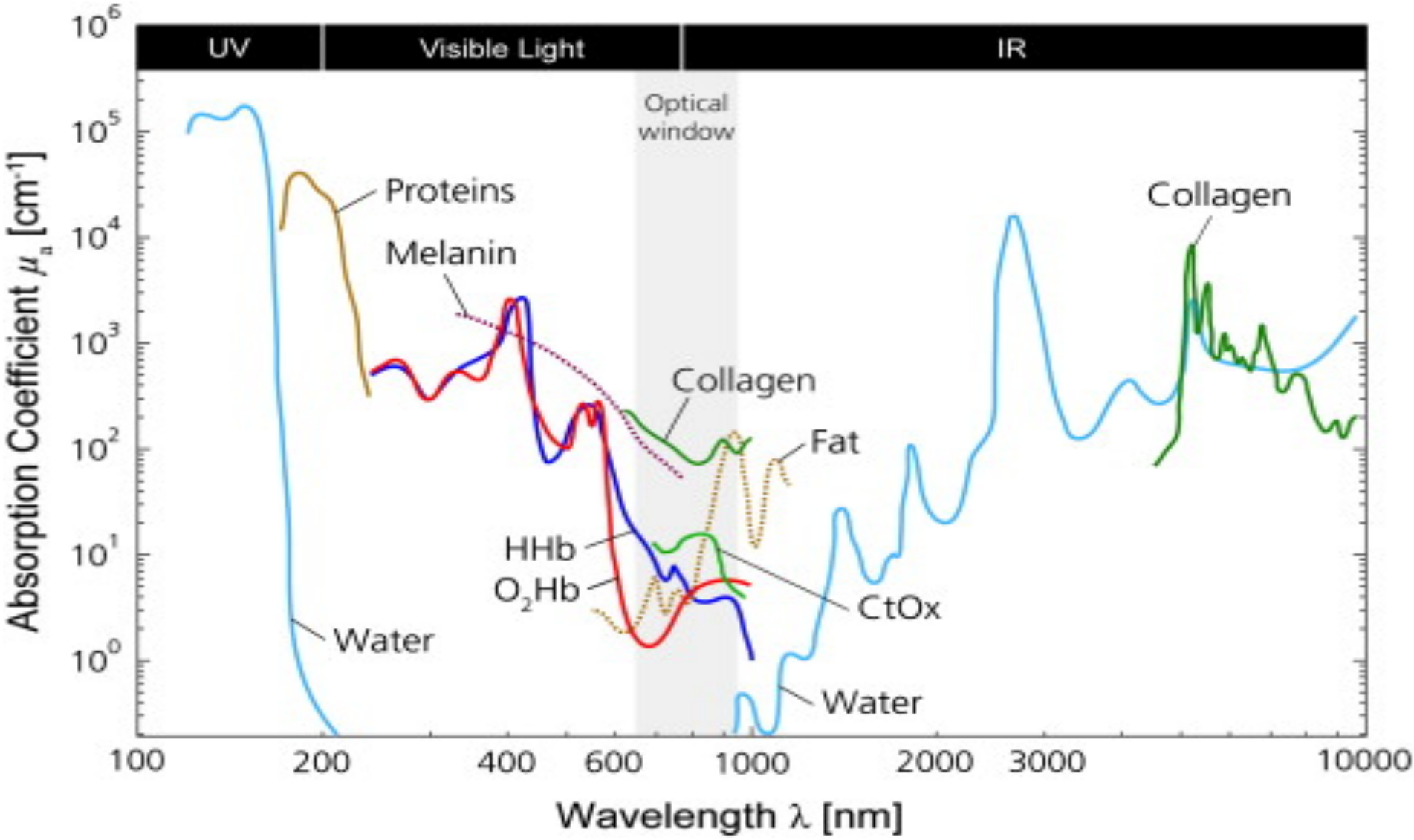


(Perdue, 2015)

fNIRS


Frequency (Hz)
Wavelength
Gamma-rays
X-rays
Ultraviolet
Visible
Near IR
Infra-red
Thermal IR
Far IR
Microwaves
Radar
Radio, TV
AM
Long-waves
0.1 Å
1Å
0.1 nm
1 nm
10 nm
100 nm
1000 nm
1 µm
10 µm
100 µm
1000 µm
1 mm
1 cm
10 cm
1 m
10 m
100 m
1000 m
400 nm
500 nm
600 nm
700 nm


HbR
HbO2
H2O
Relative Absorption (log10 scale)
Wavelength (nm)
400
500
600
700
800
900
1000



A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology

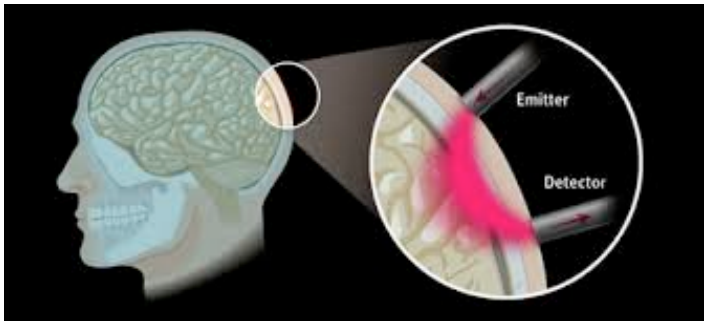
Felix Scholkmann, Stefan Kleiser, Andreas Jaakko Metz, Raphael Zimmermann, Juan Mata Pavia, Ursula Wolf, Martin Wolf

NeuroImage, Volume 85, Part 1, 2014, 6–27

fNIRS

- Pros:
  - inexpensive
  - not sensitive to motion
  - quiet
- Cons:
  - cortical surface only
  - depends on hair & skull
  - sensitive to optode placement

- What are some good research questions?



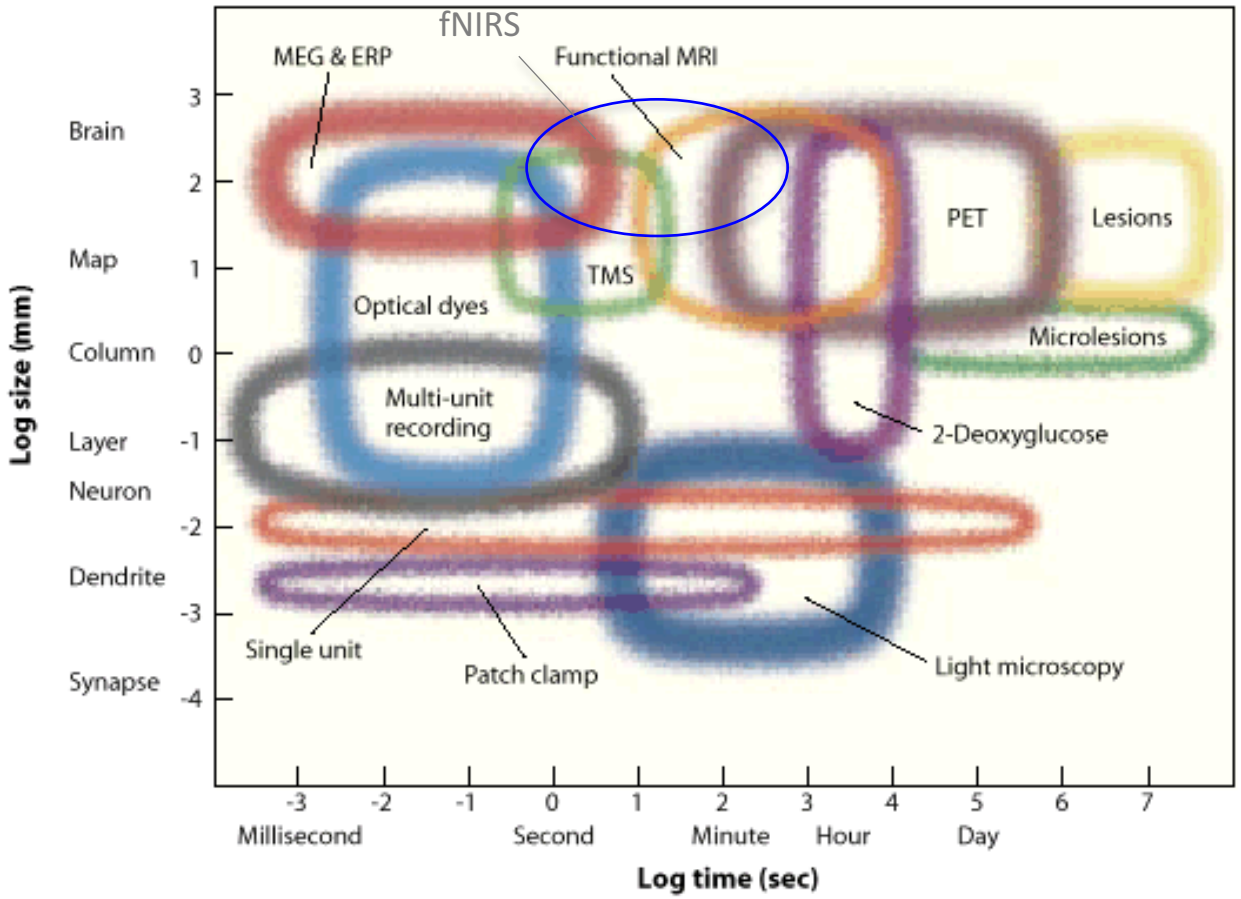
MEG

- Uses SQUIDs to detect small magnetic fields associated with electrical currents

- Pros:
  - Excellent spatial *and* temporal resolution
  - Quiet

- Cons:
  - Expensive
  - Sensitive to motion
  - Very sensitive to metal (especially dental metal)

Pros & Cons to Imaging Methods



fMRI

Good Spatial Resolution

EEG

Good Temporal resolution

fNIRS

Relatively Good Spatial Resolution (at the surface)

Experiment Design, part 1

Method	Measures	Tasks	Analysis	Examples	Considerations
Behavioral	Informational knowledge, Experimental RT, Accuracy	•Button press •Head turn •Pacifier sucking •Eye tracking •Standardized Assessments	• Comparison of accuracy between conditions and/or groups	•Stroop task •Infant testing of speech perception	•Understanding instructions •Infants can't press buttons •Counterbalancing
Structural MRI	Volume/ thickness/ surface area of gray and white matter	• None • Eyes open/closed • Watching movie	•Group comparison or correlation with behavior (usually a specific ROI)	Subcortical gray matter diffs in healthy children of people with bipolar disorder	•Hard to scan kids, but much shorter than the other scans, so easier to obtain (although can't motion correct)
DTI	Fractional Anisotropy (white matter connectivity/ integrity)	• None • Eyes open/closed • Watching movie	•Whole-brain FA comparison or comparison of specific tracts between groups	White matter differences in transgender people vs. cisgender controls	•Scanner shakes a bit, so might be frightening •Hard to correct for motion, so difficult to get good scans of kids
functional MRI (fMRI)	BOLD response (changes in blood oxygenation in response to activation)	•Looking at / watching / listening to various stimuli •Sometimes none (Resting state)	•Localization of a specific brain response by comparing target vs. control trials (through subtraction) •Group comparison	Emotional memory task	•Hard to scan children due to motion (although can be corrected/censored) •Cannot have metal in body (no pacemakers)

Experiment Design, part 2

Method	Measures	Tasks	Analysis	Examples	Considerations
Resting EEG	Electrical activity summed over groups of neurons	•Rest! •(May need to entertain young children)	Group/condition differences in power spectrum (how much energy in each frequency band)	•Infants at high risk of autism exhibit lower frontal gamma power	Highly related to ambient environment, so be mindful of any "stimulation"
Event Related EEG (ERP)	EEG response to a stimulus (event), averaged over many trials	•Looking at / watching / listening to various stimuli •May require some response (button press)	•Amplitude or latency of a specific component •Differences between conditions/groups	•N400 component has greater amplitude when a sentence has an unexpected semantic term	Difficult to determine exactly WHERE the measured activity comes from
fNIRS	Optical properties of blood flow	•Looking at / watching / listening to various stimuli •May require some response (button press)	•Comparison of regional brain activation on different stimulus conditions, and/or across different groups	•Infants at high risk of autism have abnormal functional connectivity during face processing	Can only measure activation that occurs at the surface of the brain (no deep structures)
MEG	Magnetic fields created by electrical activity from neural populations	•Looking at / watching / listening to various stimuli •May require some response (button press)	•Power spectrum •Amplitude or latency of a component •Differences between conditions/groups	•Males with autism show less phase coupling in the fusiform face area when viewing faces	Signal is extremely sensitive to metal, especially in the mouth

Small Group Activity

- Arrange yourselves into pairs.
- You will be given a multiple choice "quiz" in which you will read each scenario aloud and decide as a group which answer (or answers) best address the question.
- Please go through these fairly quickly so that we can discuss them as a class after 10 minutes or so.
- Good luck!

Questions?

Resources & References

References:

- Raschle, N.M., Lee, M., Buechler, R., Christodoulou, J.A., Chnag, M., Vakil, M., Stering, P.L., & Gaab, N., Journal of Visualized Experiments (2009) "Making MR imaging child's play- pediatric protocol, guidelines and procedures"
- Raschle, N., Zuk, J., Ortiz-Manilla, S., Sliva, D.D., Franceschi, A., Grant, E., Benasich, A. & Gaab, N., Annals of the New York Academy of Sciences (2012) "Pediatric Neuroimaging in Early Childhood and Infancy: Challenges and Practical Guidelines"
- Raschle. N.; Zuk, J. & Gaab, N., Proceedings of the National Academy of Sciences (2012) "Functional characteristics of developmental dyslexia in left-hemispheric posterior brain regions predate reading onset"

Resources for fun:

- Click here to see a detailed video about MRI
- See a neuropsychologist in action: NeuroExam
- Learn more about how MRI with infants works from Dr. Gaab's research study webpage: BabyMRI
- Check out this video about Prof Nelson's research in his lab: https://www.youtube.com/watch?v=-hfCV0lwJsg

MRI Review

Insight to the process of acquiring MRI/fMRI data & considerations with children:

Making MR Imaging Child's Play-Pediatric Neuroimaging Protocol, Guidelines and Procedure

Nora M. Raschle[1,2], Michelle Lee[1], Roman Buechler[1], Joanna A. Christodoulou[3], Maria Chang[1], Monica Vakil[1], Patrice L. Stering[1], Nadine Gaab[1,3,4]

[1] Developmental Medicine Center, Children's Hospital Boston
[2] Department of Neuropsychology, University of Zurich
[3] Graduate School of Education, Harvard University
[4] Harvard Medical School

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3148936/