Functional Magnetic Resonance Imaging

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Yesterday

- Brain Physiology
- Neuroanatomy
- BOLD response

Outline for Today

- Signal and Noise
- Data Analysis
  - Pre processing & Statistics
- Advanced Techniques
- Your Questions

1. Signal and Noise

What is signal? What is noise?

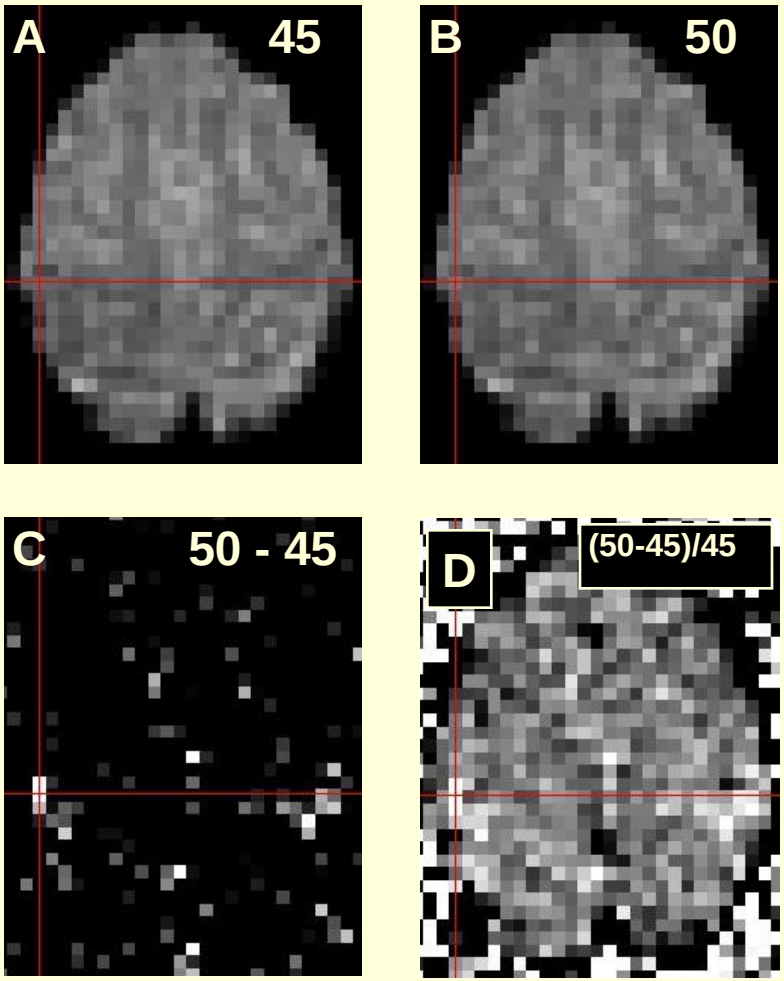
- Signal, literally: Amount of current in receiver coil
- Signal, practically: Task-related variability

- Noise, literally and practically: Non-task-related variability

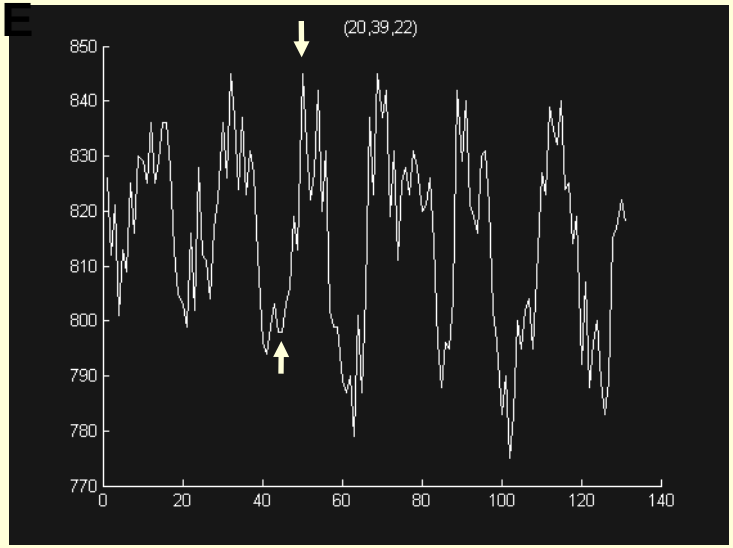
- How can we control the amount of signal?
  - Experimental task timing: efficient design
  - Scanner properties (e.g., field strength)
  - Subject compliance with task: through training

- How can we reduce the noise?
  - Choose good pulse sequences and have stable scanner
  - Minimize head motion, to some degree, with restrictors
  - Effectively *preprocess* our data

Signal Size in fMRI



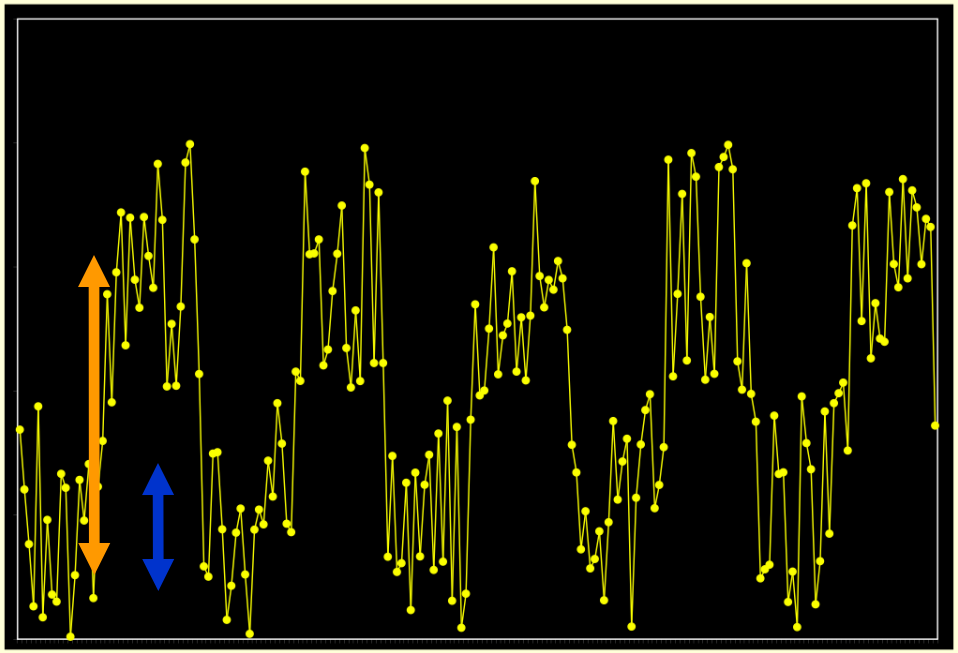
Let's look at two TRs (#s 45 and 50) of one dataset.

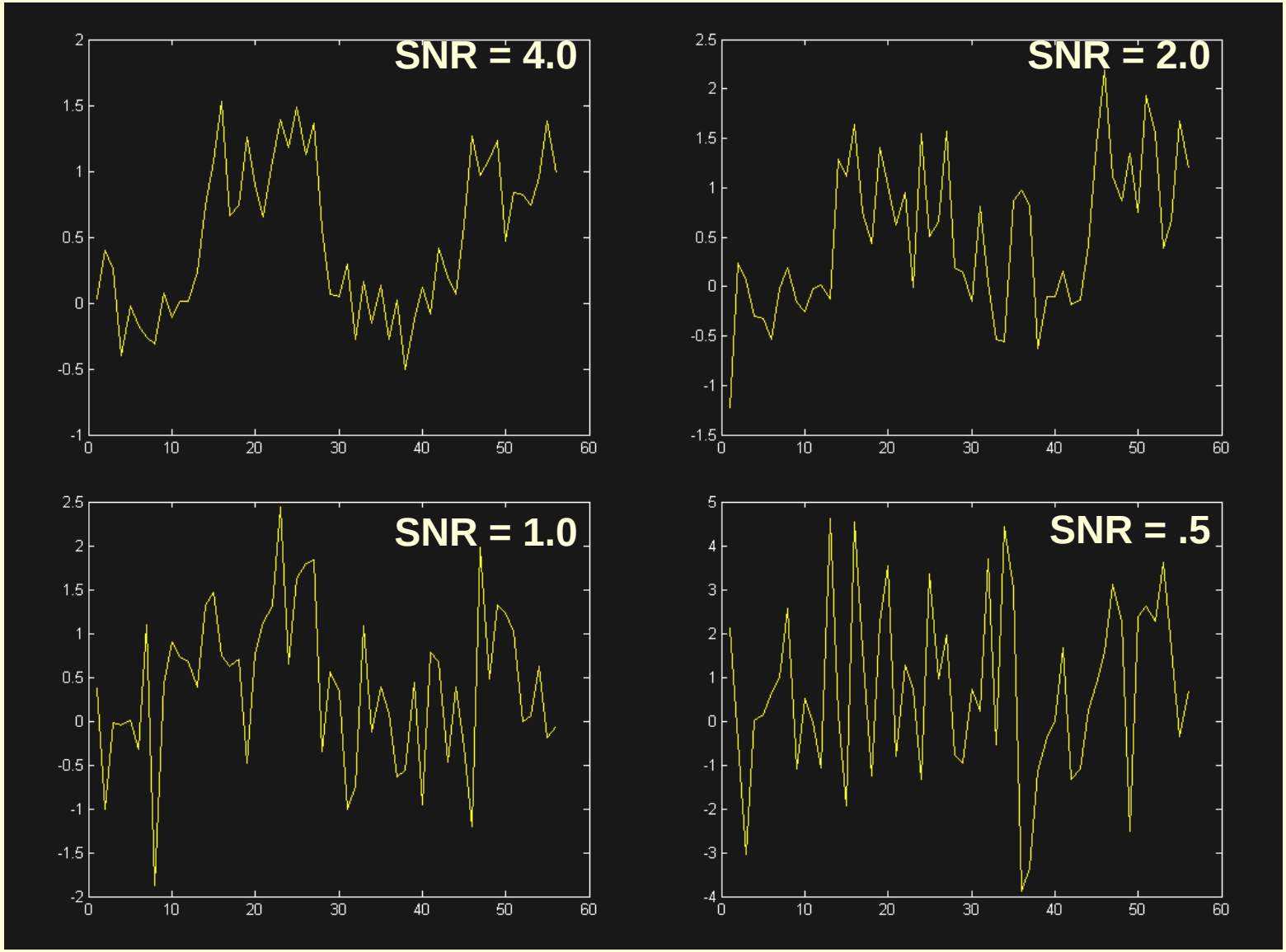


Signal-Noise-Ratio (SNR)

Task-Related Variability

Non-task-related Variability

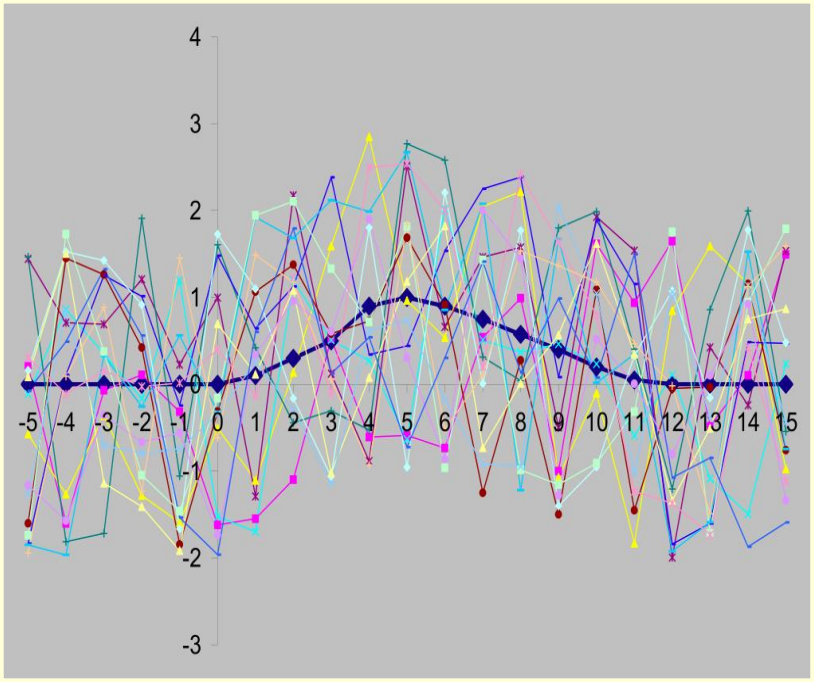



SNR = 4.0
SNR = 2.0
SNR = 1.0
SNR = .5

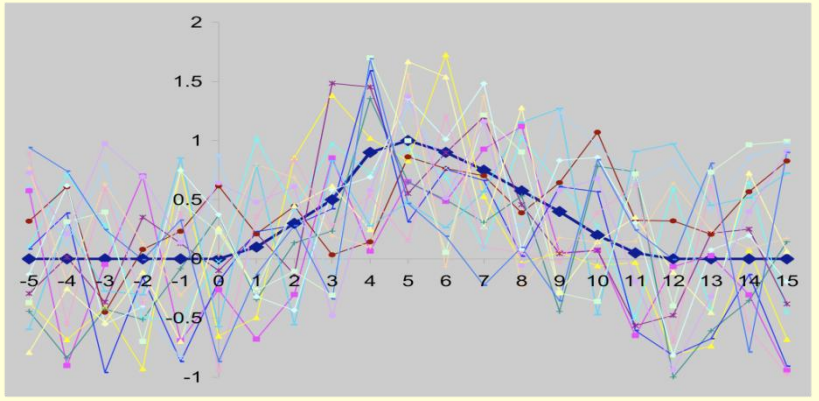
What are typical SNRs for fMRI data?

- Signal amplitude
  - Percent signal change: 0.2-2%
- Noise amplitude
  - Percent signal change: 0.5-5%
- SNR range
  - Total range: <0.1 to 4.0
  - Typical: 0.2 – 0.5

Typical SNRs for fMRI studies



SNR = 0.25



SNR = 0.5

Why do we see lower SNR values, smaller amplitudes for cognitive tasks?

- Increased individual variability in signal
  - V1 vs. FFA
- Increased variability in performance
- Increased complexity in cognitive processes
  - Press a button vs. name a picture

Types of Noise

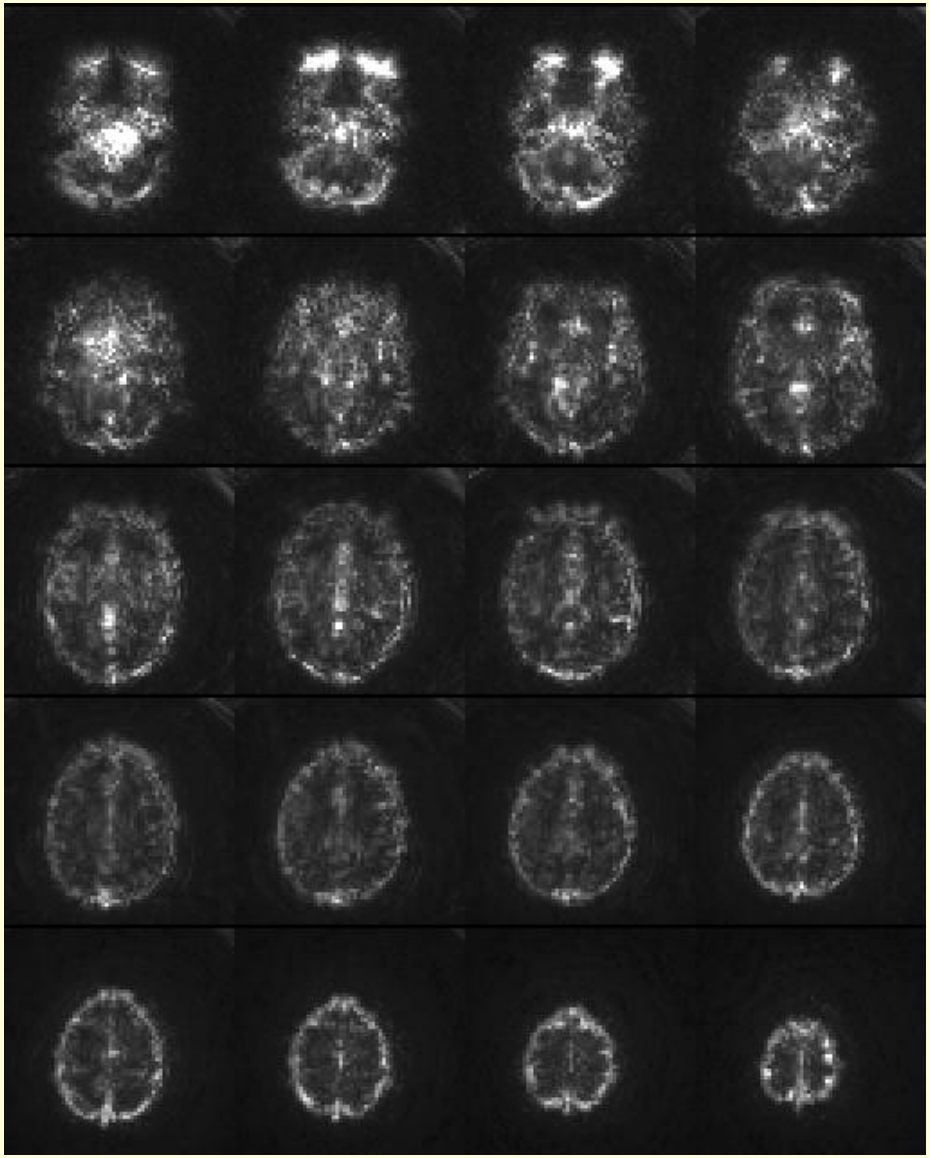
- Thermal noise
  - Responsible for variation in background of image
  - Eddy currents, scanner heating
- Power fluctuations
  - Typically caused by scanner problems
- Artifact-induced problems
- Variation in subject cognition
  - Timing of processes

- Head motion

- Physiological fluctuations
  - Respiration
  - Cardiac pulsation
- Differences across brain regions
  - Functional differences
  - Large vessel effects
  - Variability in gray and white matter

Is it a fair assumption that noise in fMRI is random?

Standard Deviation Image



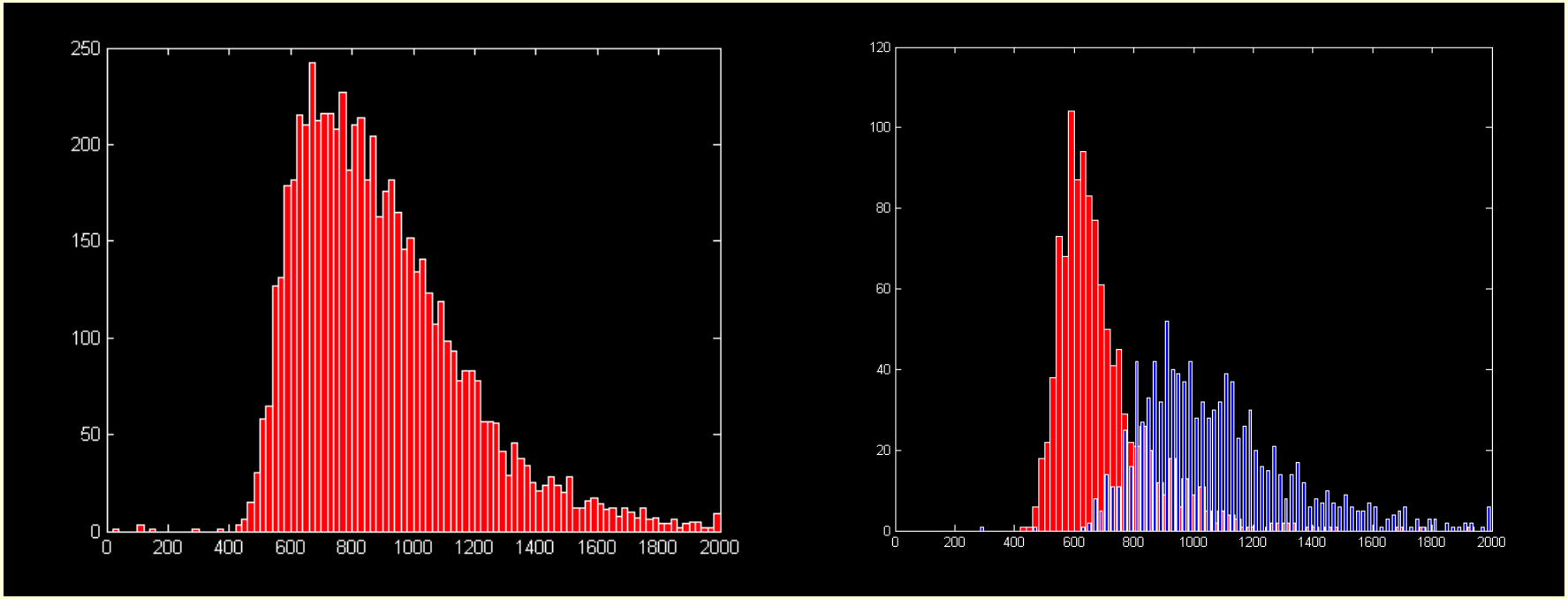
Noise vs. *Variability*

Variability in Subject Behavior: Issues

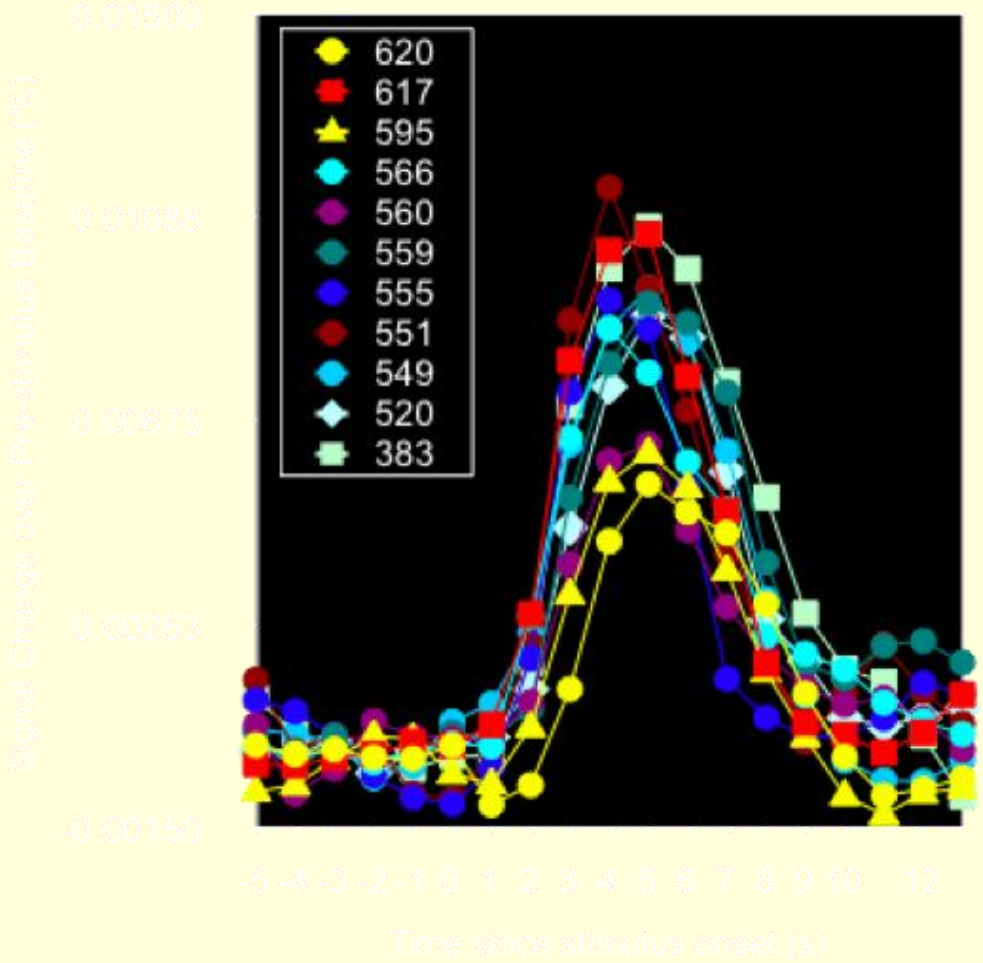
- Cognitive processes are not static
  - May take time to engage
  - Often variable across trials
  - Subjects' attention/arousal wax and wane
- Subjects adopt different strategies
  - Feedback- or sequence-based
  - Problem-solving methods
- Subjects engage in non-task cognition
  - Non-task periods do not have the absence of thinking

What can we do about these problems?

Response Time Variability



Consistency in the HDR



Spatial Variability?

Visual Paradigm

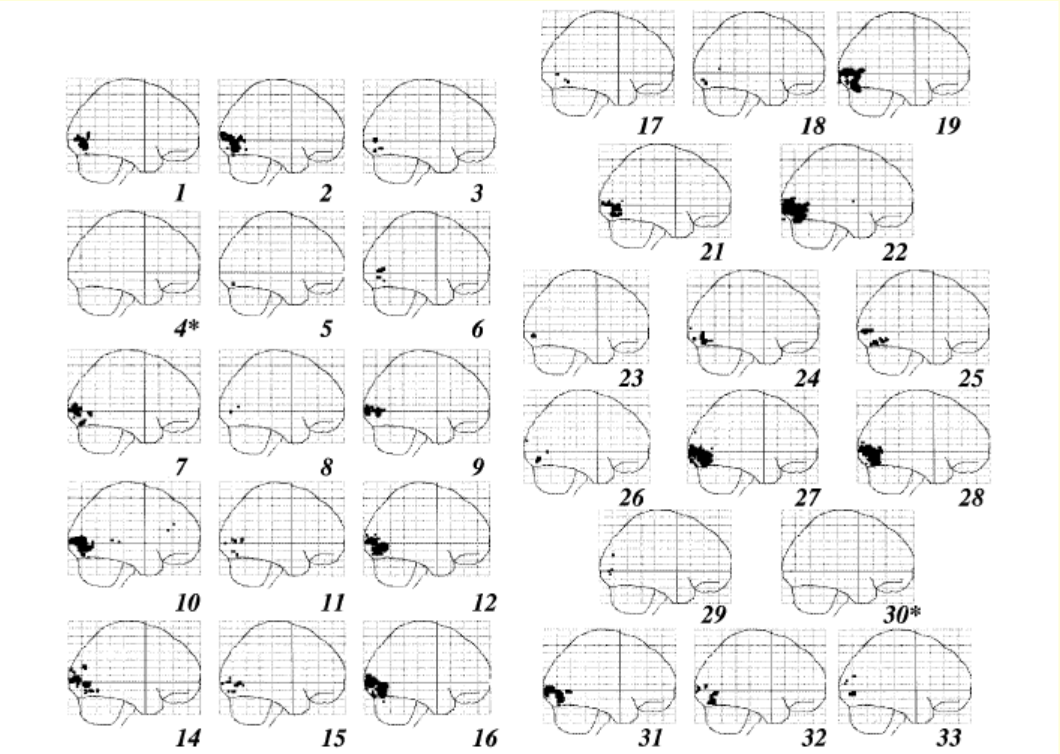
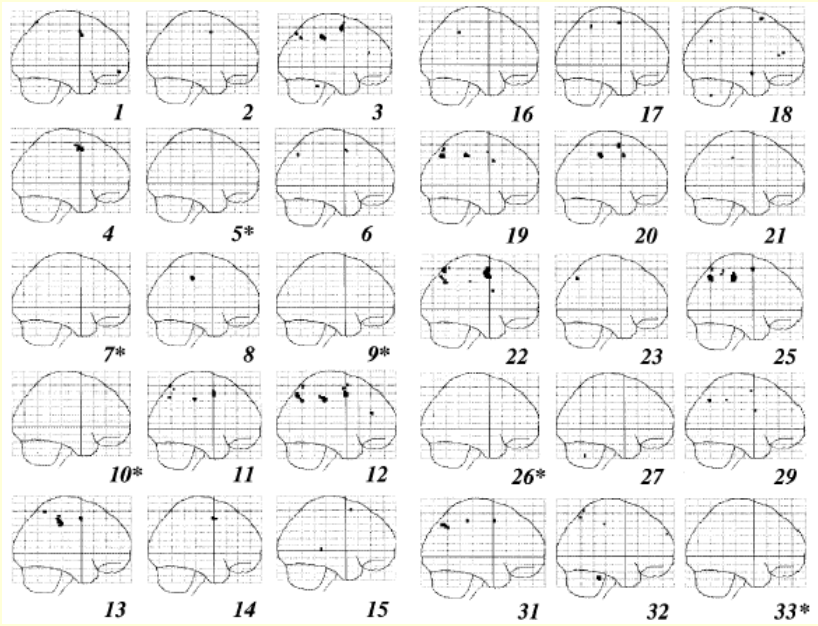


FIG. 4. Single-session sagittal MIPs for the visual paradigm. Similar to Figs. 2 and 3, only 31 sessions are displayed. Sessions marked with "*" contain no significant voxels.

Cognitive Paradigm

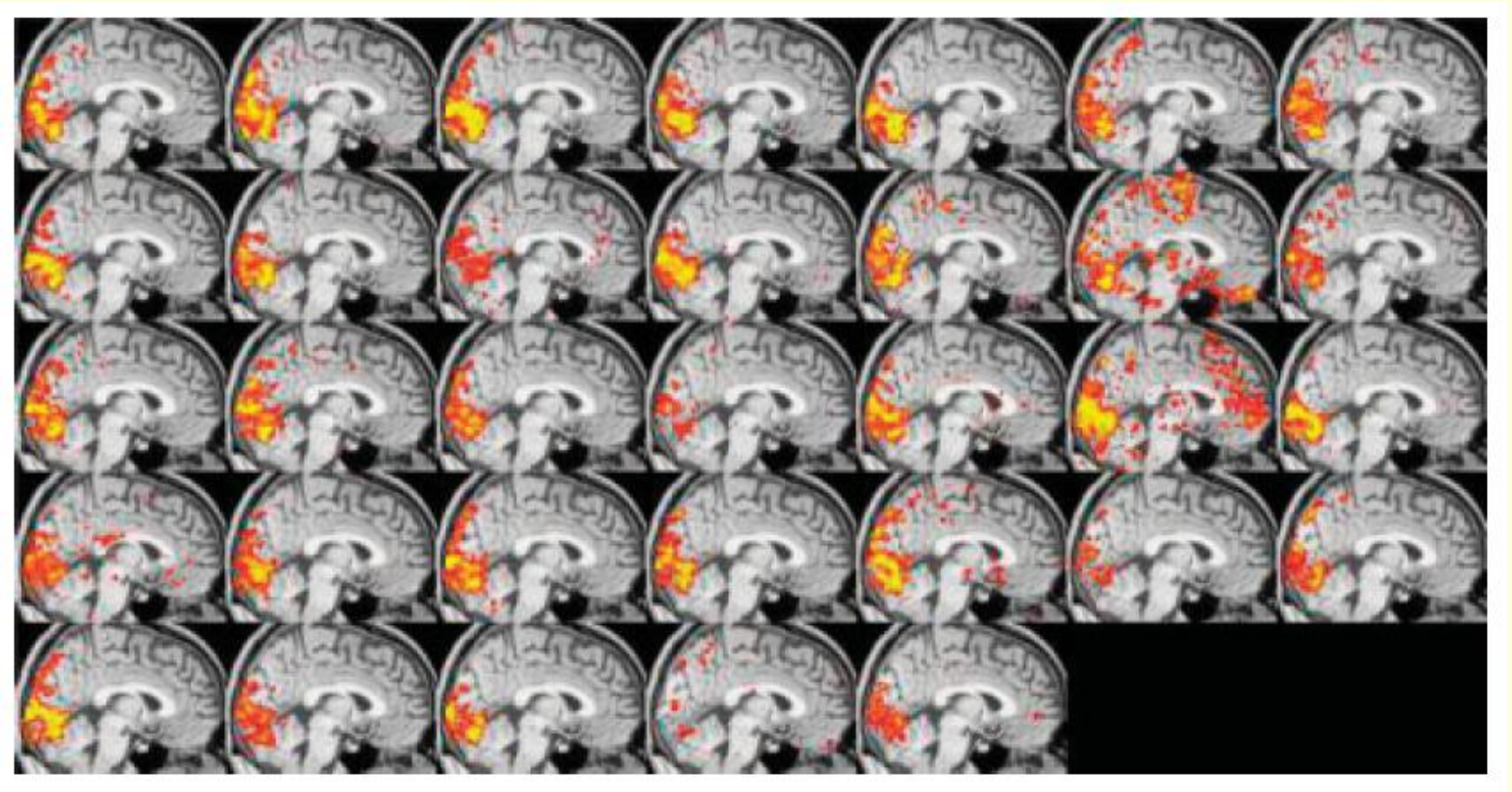


McGonigle et al., 2000

"The following precautions were taken: the same operators always controlled the scanner, ambient light and sound levels were similar between sessions, and spoken instructions to the subject were always exactly the same.

One obvious factor that we could not control was that our subject was always aware that he had performed the task before in the scanner, only under slightly different circumstances. We called this the "Groundhog Day" effect."

“A reanalysis…”

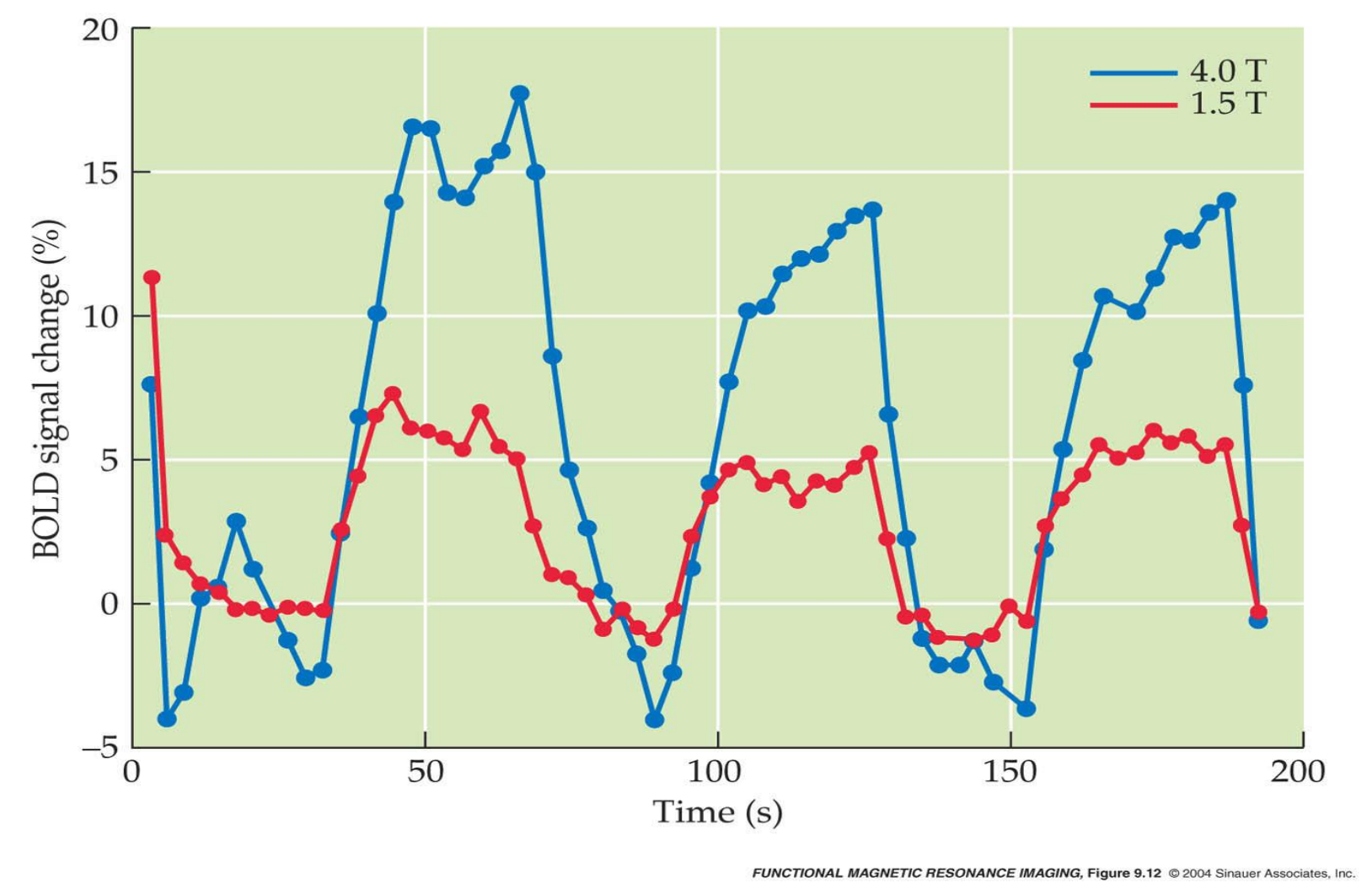


Smith et al., 2005

Reducing the threshold gives much less apparent variability.

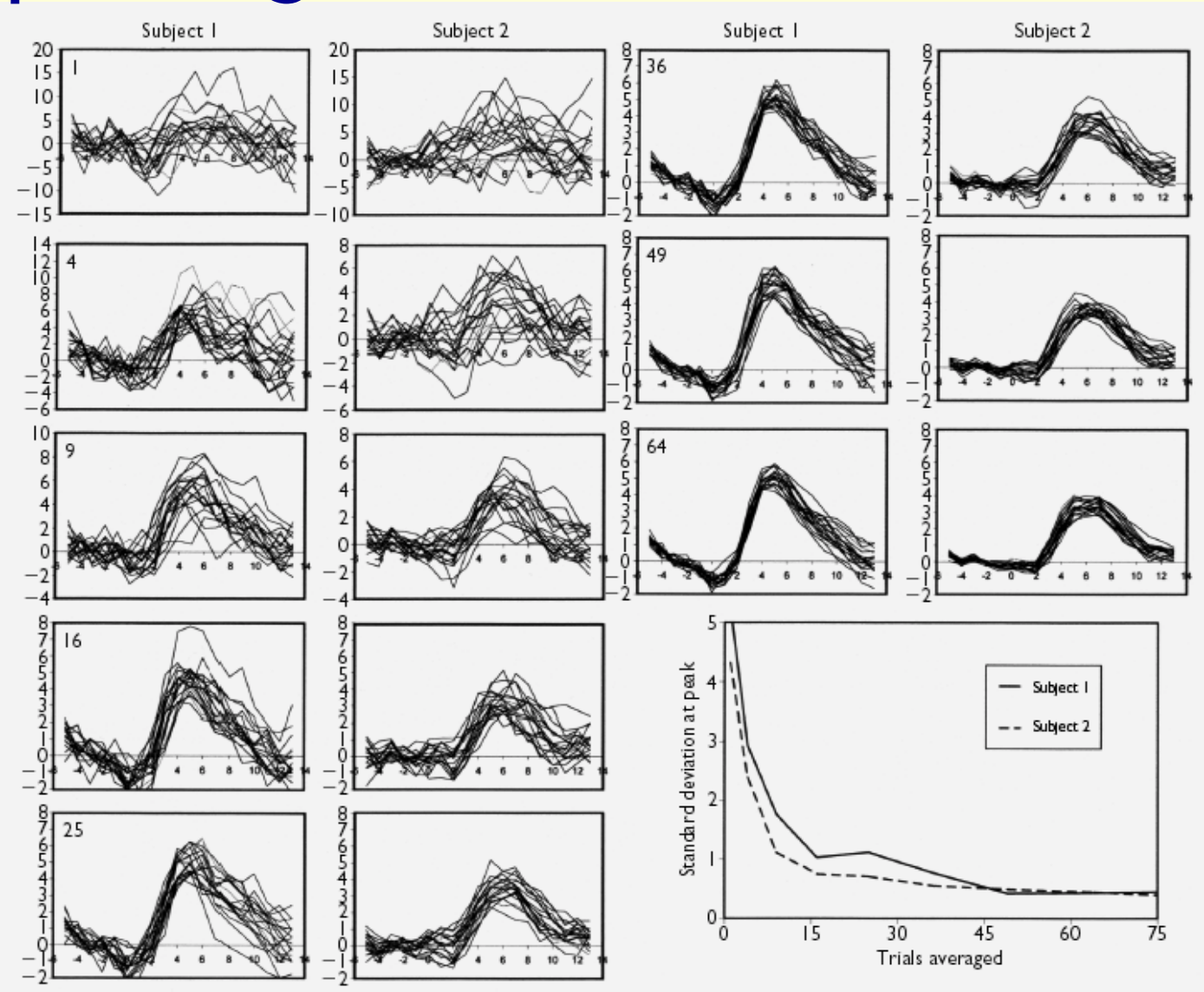
How can we Improve SNR?

Improving SNR: Increasing field strength?



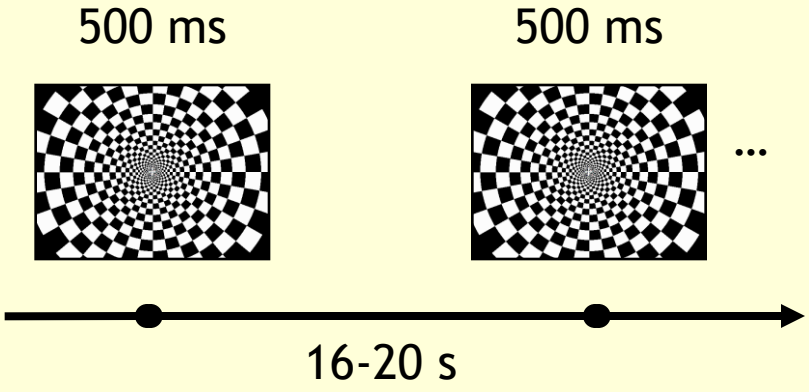
FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 9.12** © 2004 Sinauer Associates, Inc.

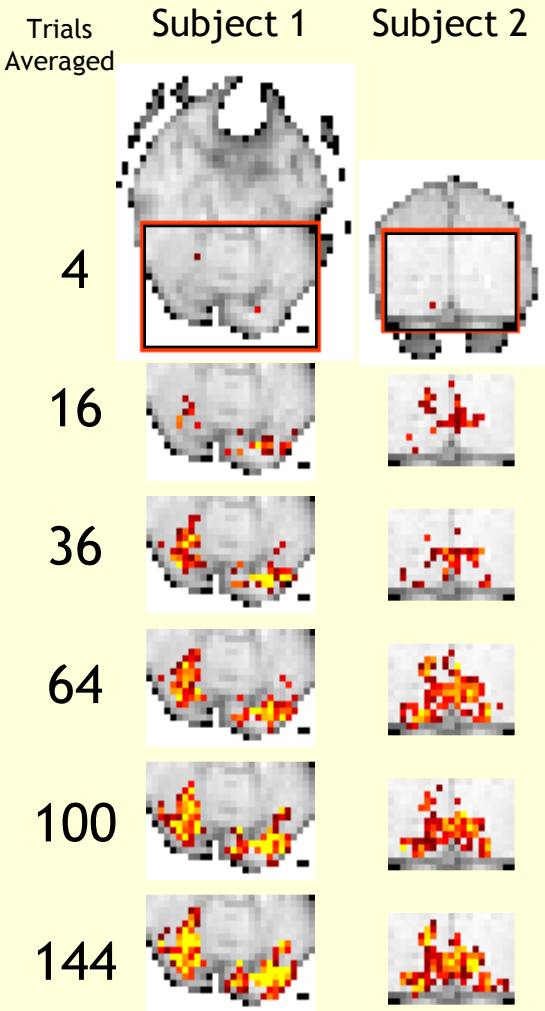
Improving SNR: Collect more data?



Huettel & McCarthy, 2000

Improving SNR: Increasing Power Increases Spatial Extent





Caveats

- Signal averaging is based on assumptions
  - Data = signal + temporally invariant noise
  - Noise is uncorrelated over time
- If assumptions are violated, then *pure averaging* ignores potentially valuable information
  - Amount of noise varies over time
  - Some noise is temporally correlated (physiology)
  - Some noise is task correlated
- Same principle holds for more complex analyses: increasing the quantity of data improves SNR

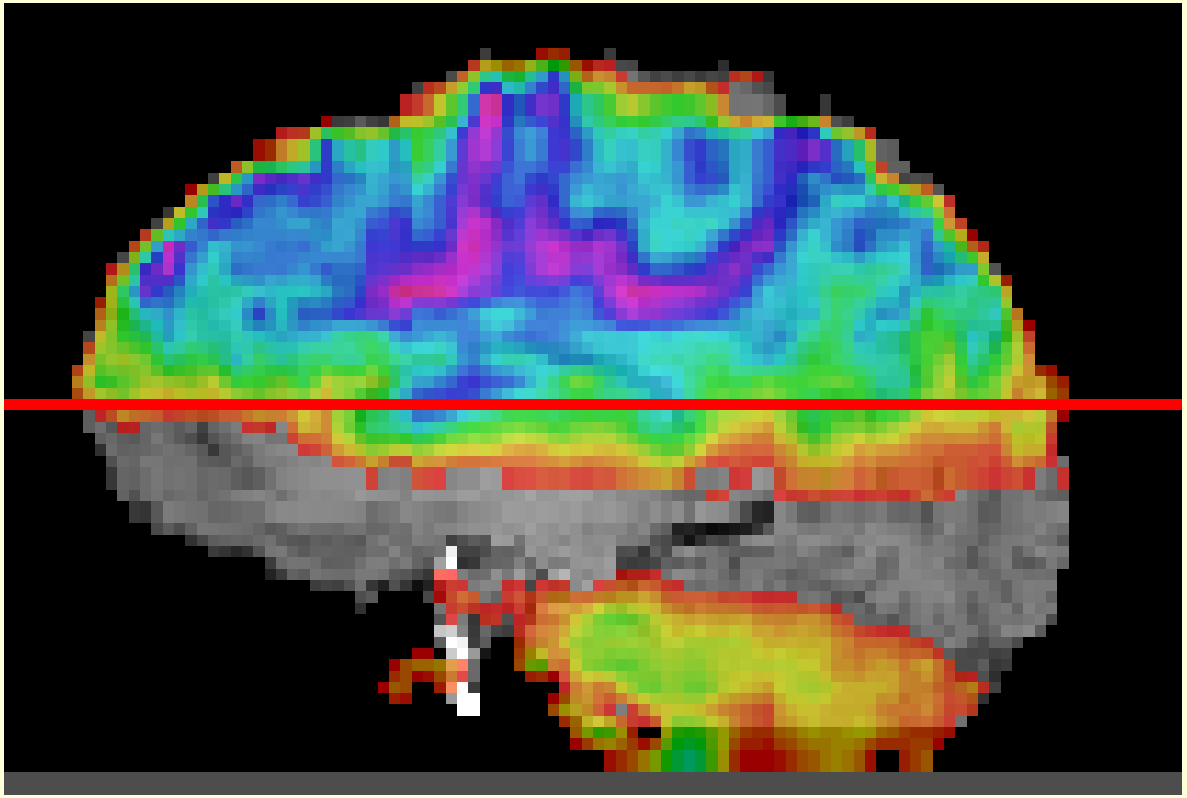
2. Data Analysis: Pre-processing & Statistics

What is preprocessing?

- Correcting for non-task-related variability in experimental data
  - Usually done without consideration of experimental design; thus, pre-analysis
  - Occasionally called *post-processing*, in reference to being after acquisition

- Attempts to remove, rather than model, data variability

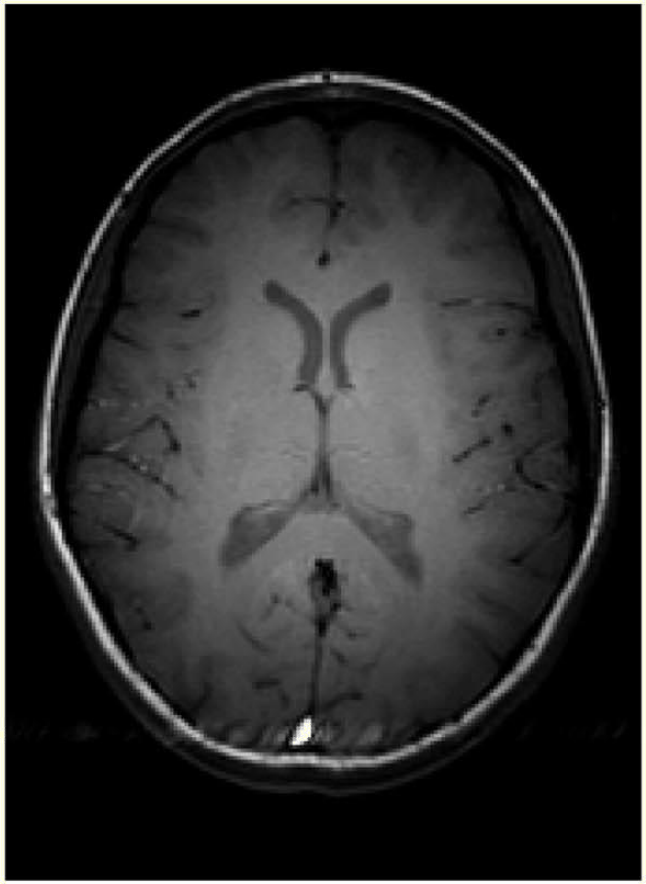
Why you always look at your data!



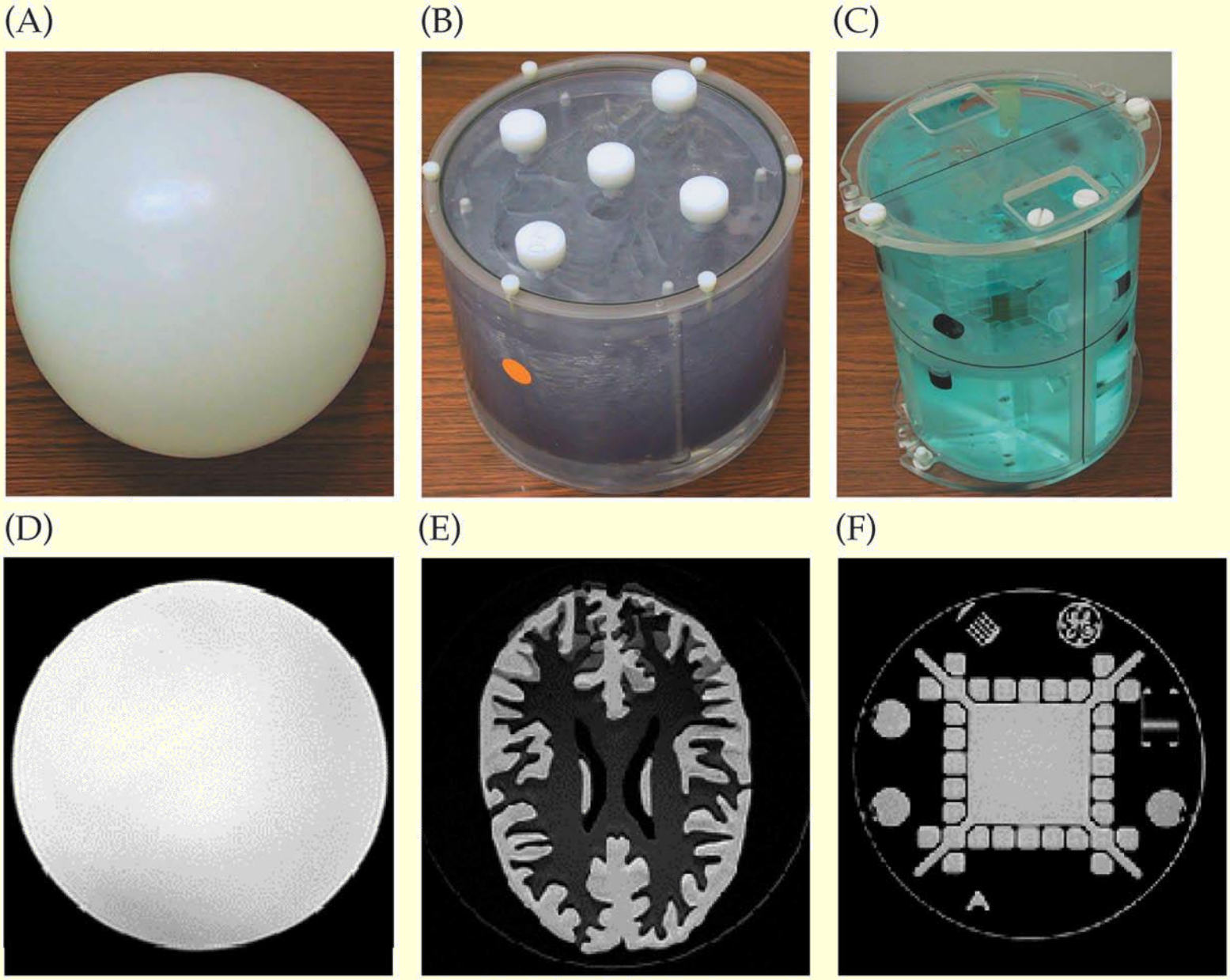
A. Quality Assurance

(A)

(B)

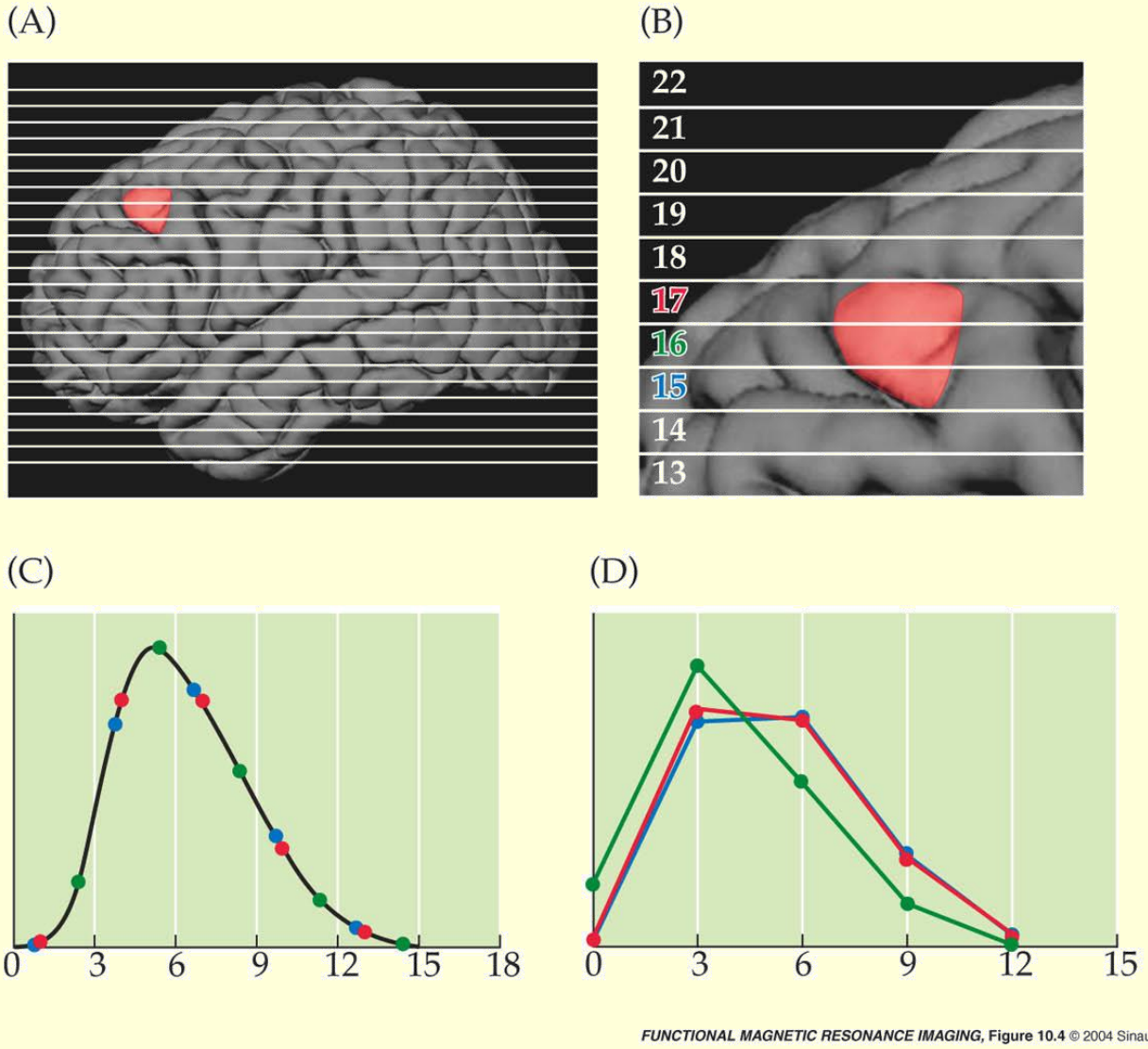


FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 10.2**



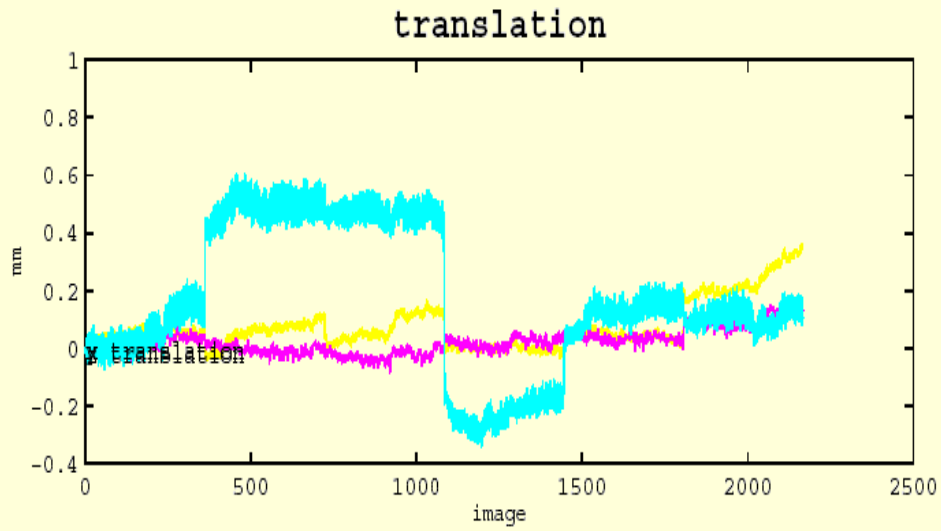
FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 10.3**

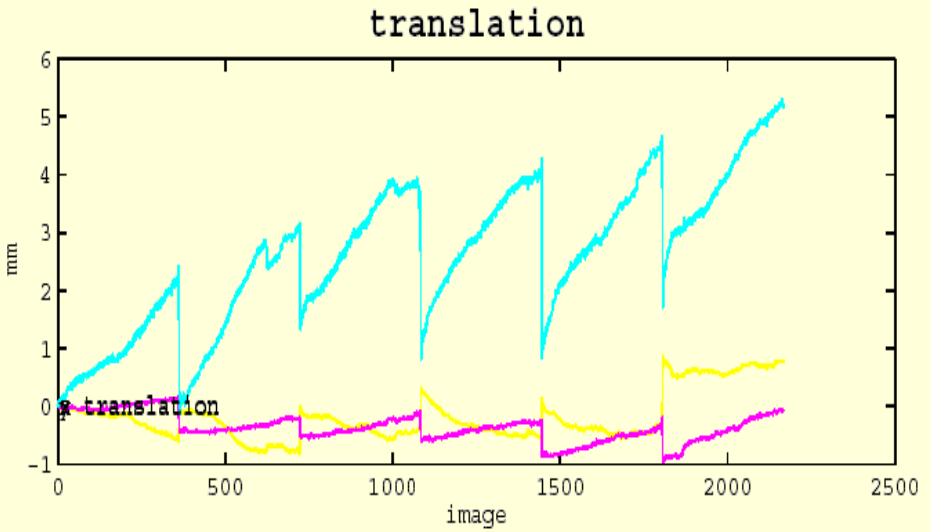
B. Slice Timing Correction

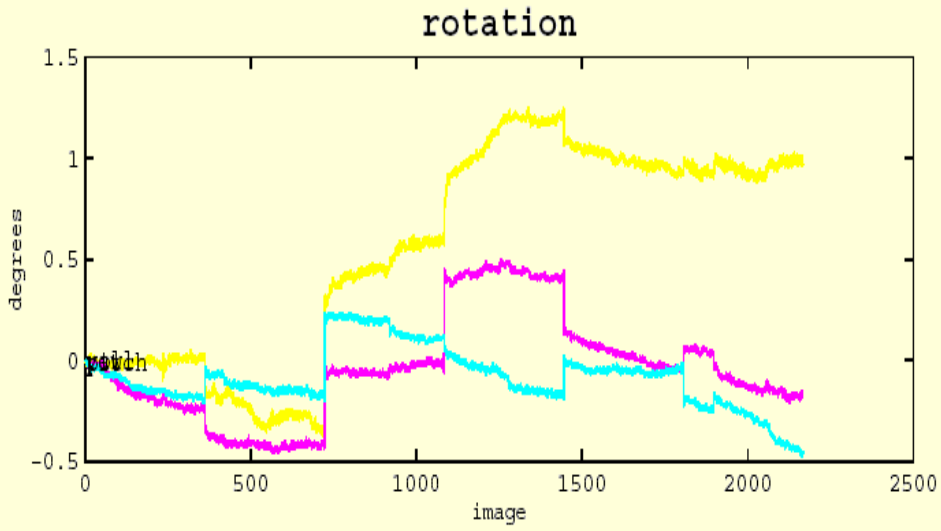


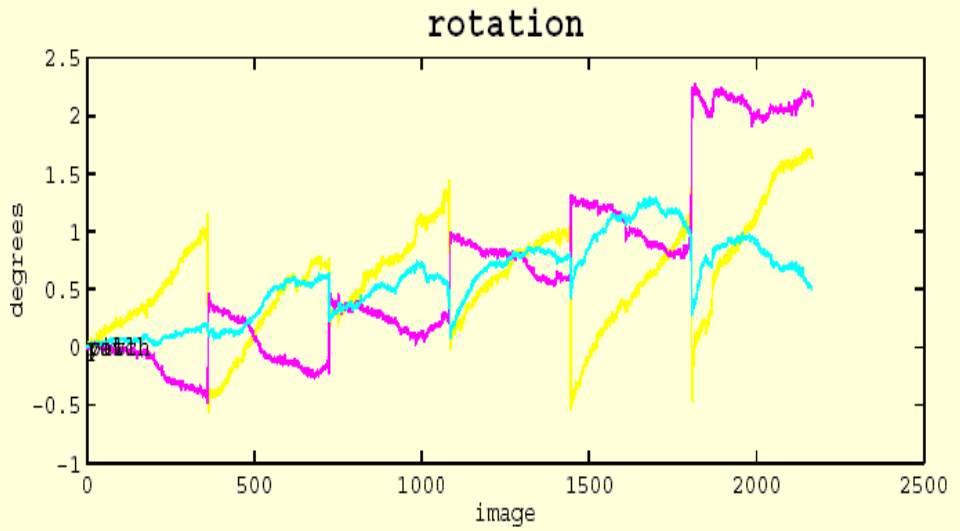
FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 10.4** © 2004 Sinauer Associates, Inc.

C. Motion Correction: Good, Bad,…

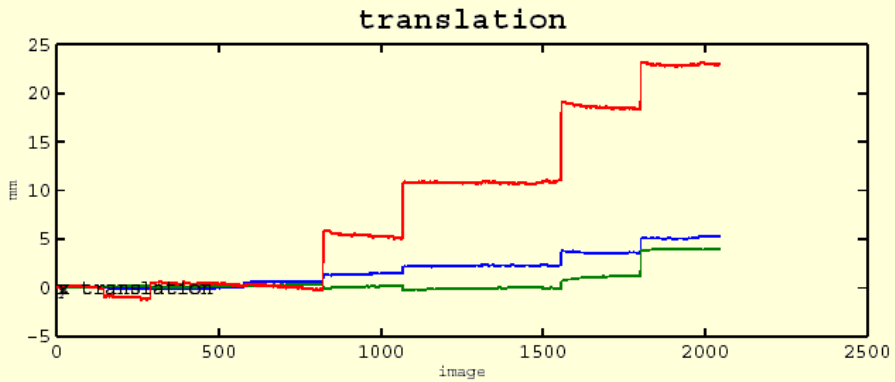


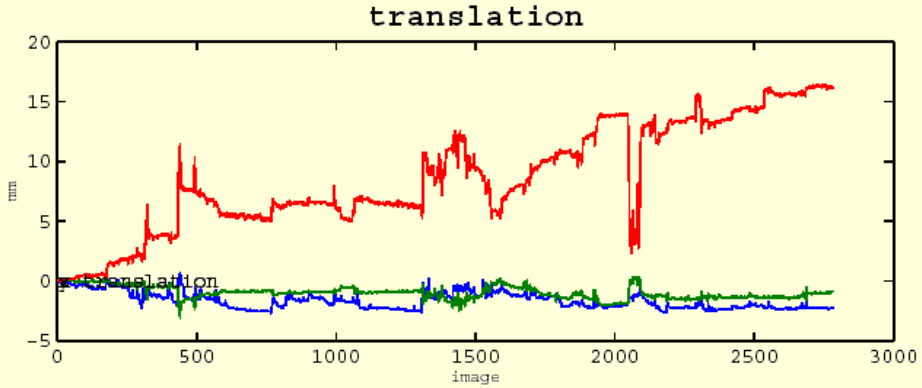


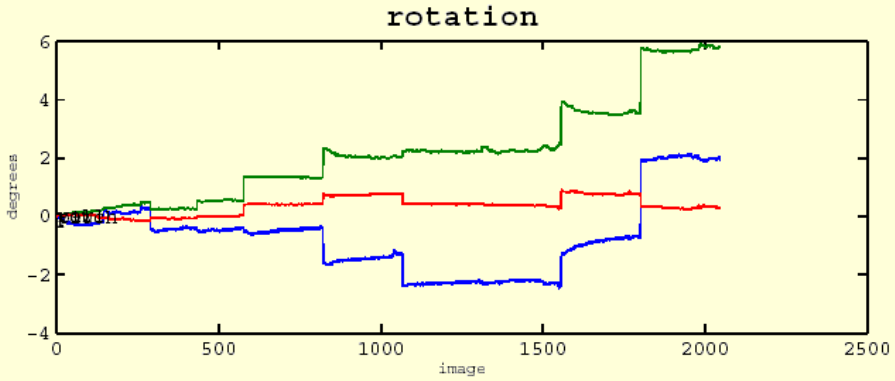


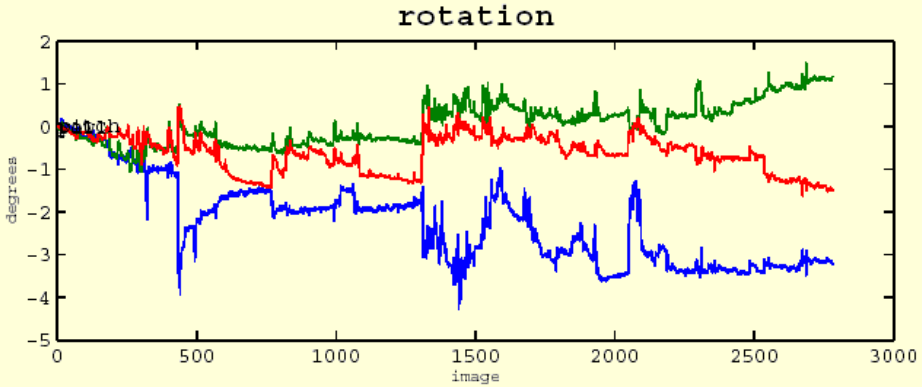


… and catastrophically bad



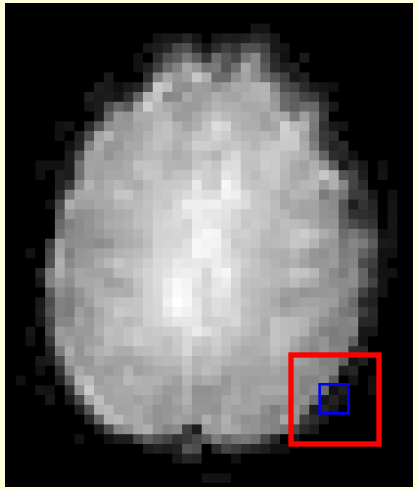




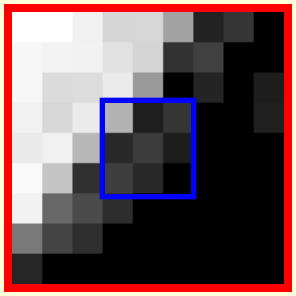


Why does head motion introduce problems?

A

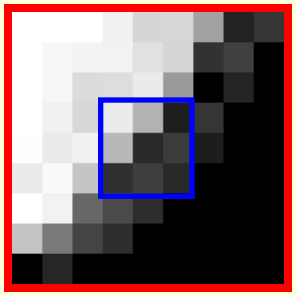


B



507	89	154
119	171	83
179	117	53

C



663	507	89
520	119	171
137	179	117

What are the best approaches for minimizing the influence of head motion?

(A)

(B)

(C)

(D)

Prevention…

FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 10.7** © 2004 Sinauer Associates, Inc.

(A)

(B)

… and training!

FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 10.8** © 2004 Sinauer Associates, Inc.

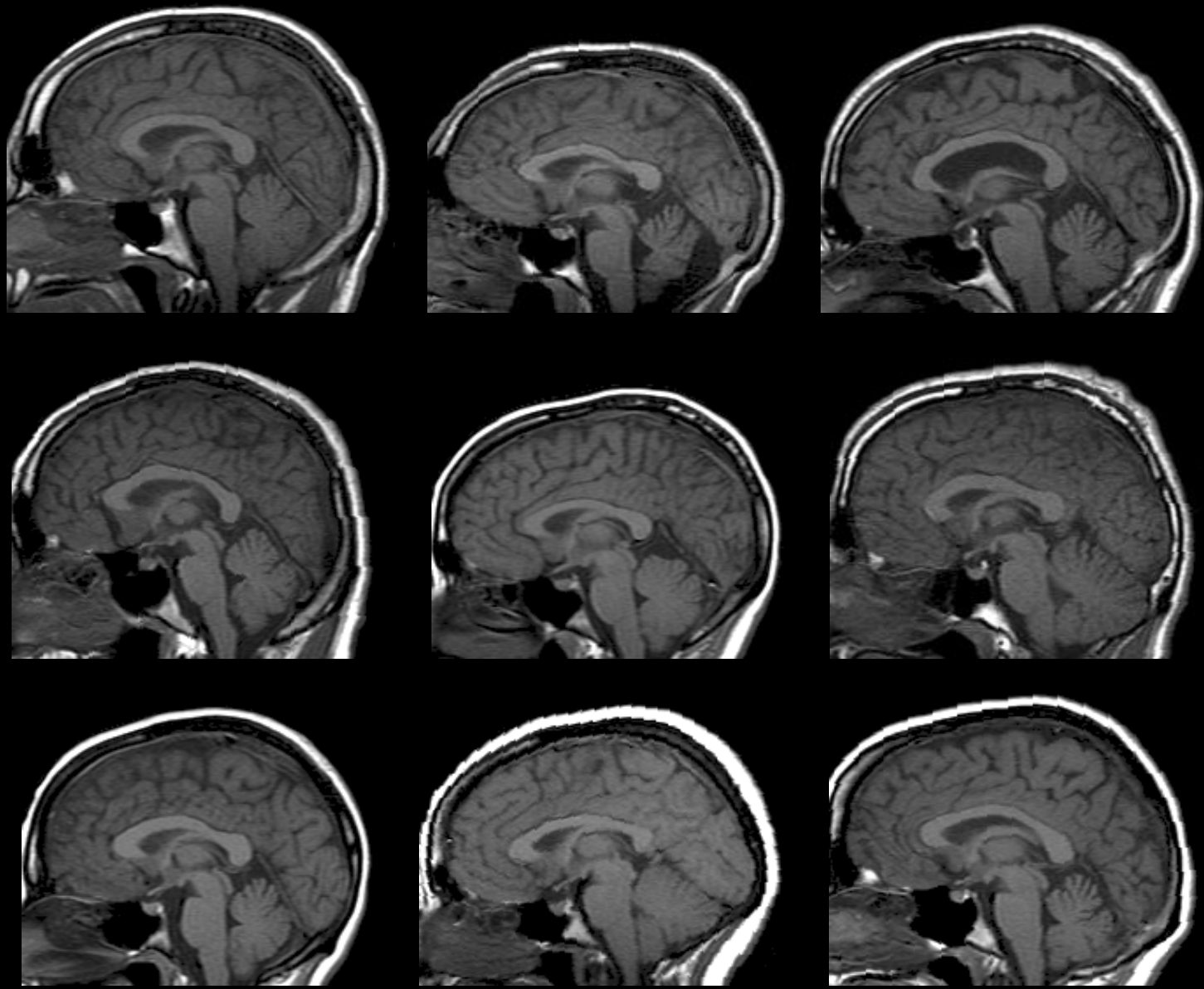
Head Motion: When is it ok for your subject to move?

- After the localizer, but before the anatomicals and functionals? We never use the localizer anyway.
- After the anatomicals, but before the functionals (when the real data is collected)?
- Between series, whenever the scanner isn't actively collecting data?
- Never, not at all, not ever

D. Co-Registration and Normalization

Matching two images of the same subject's brain collected using different pulse sequences.

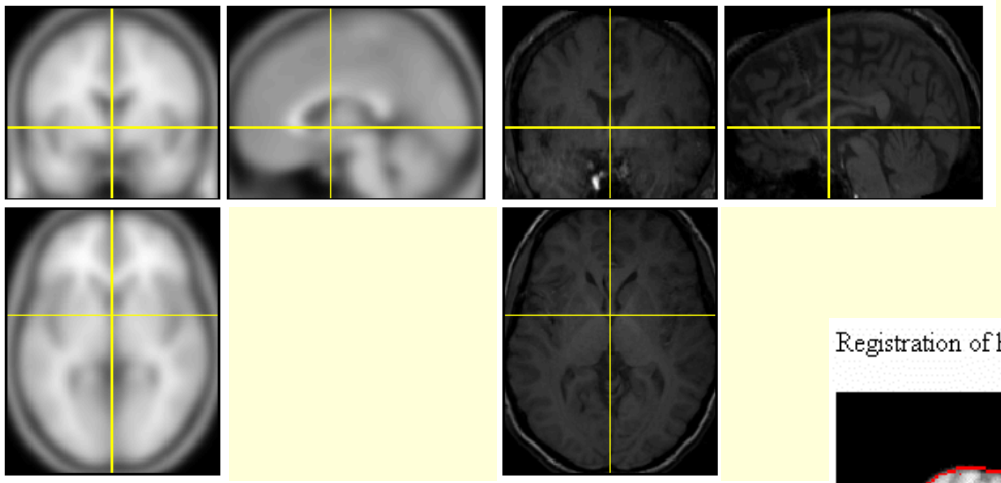
Matching an image from a single subject, typically a high-resolution anatomical, to a template in a standardized space.



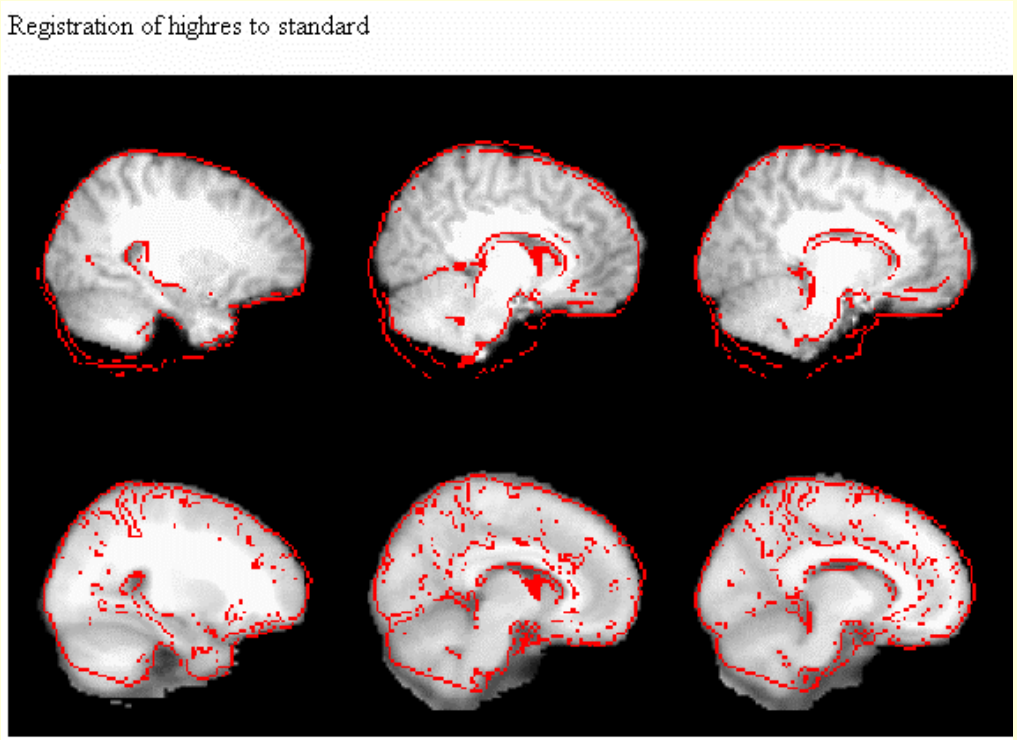
Normalization to Template

Normalization Template

Normalized Data



SPM

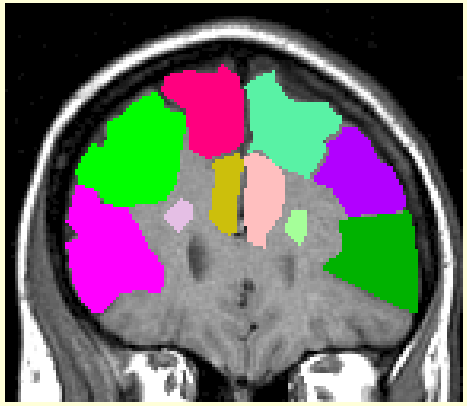


FSL

When wouldn't you normalize?

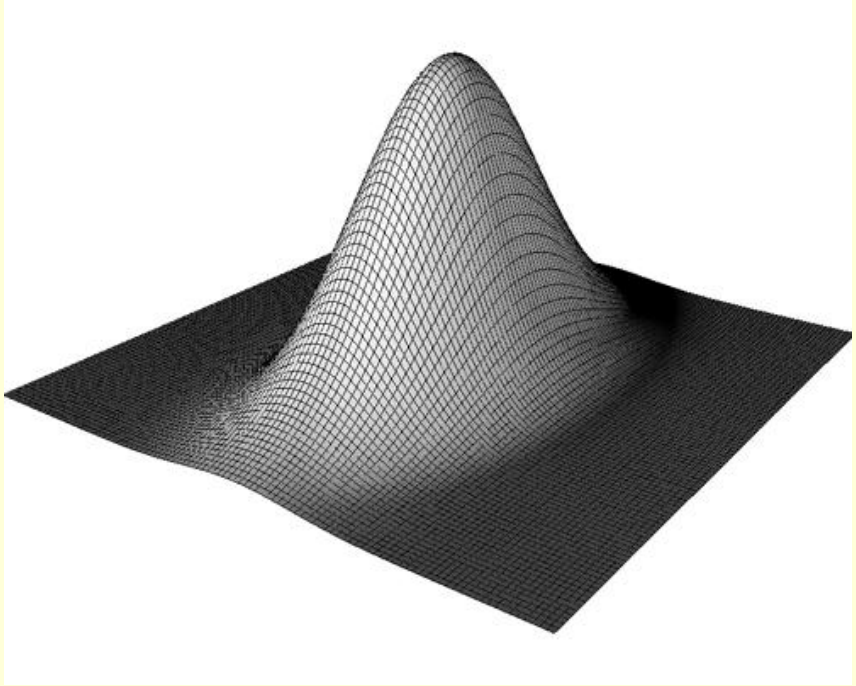
- Advantages
  - Allows generalization of results to larger population
  - Improves comparison with other studies
  - Provides coordinate space for reporting results
  - Enables averaging across subjects

- Other options?
  - Anatomical region-of-interest approach
  - Functional mapping within subjects



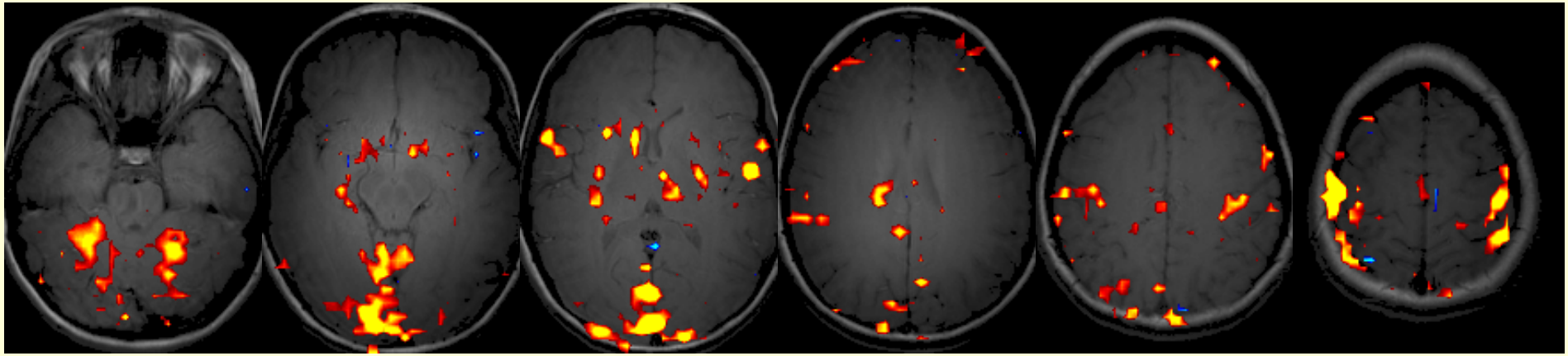
E. Spatial Smoothing

- Application of Gaussian kernel
  - Usually expressed in #mm FWHM
  - “Full Width – Half Maximum”
  - Typically ~2 times voxel size

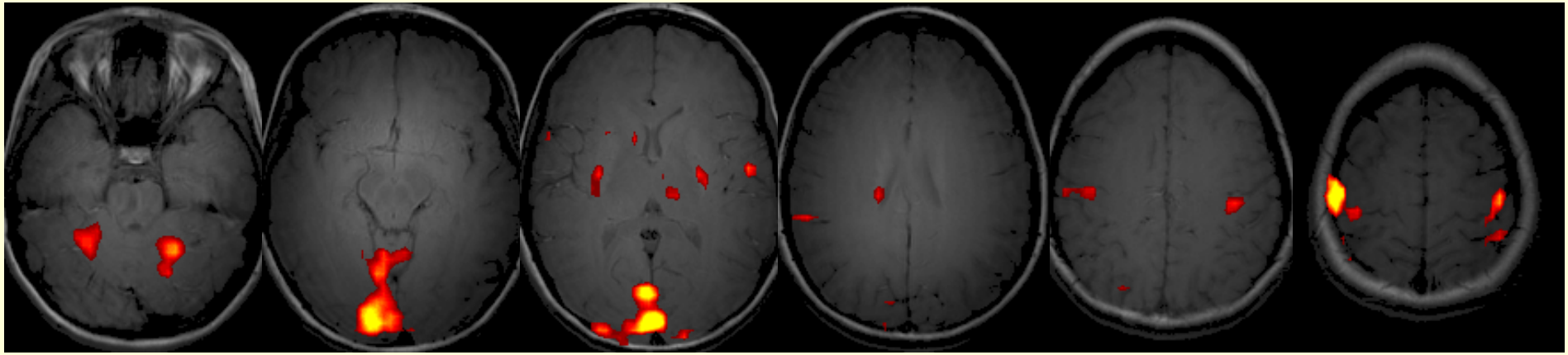


Effects of Smoothing on Activity

Unsmoothed Data



Smoothed Data (kernel width ~12mm)



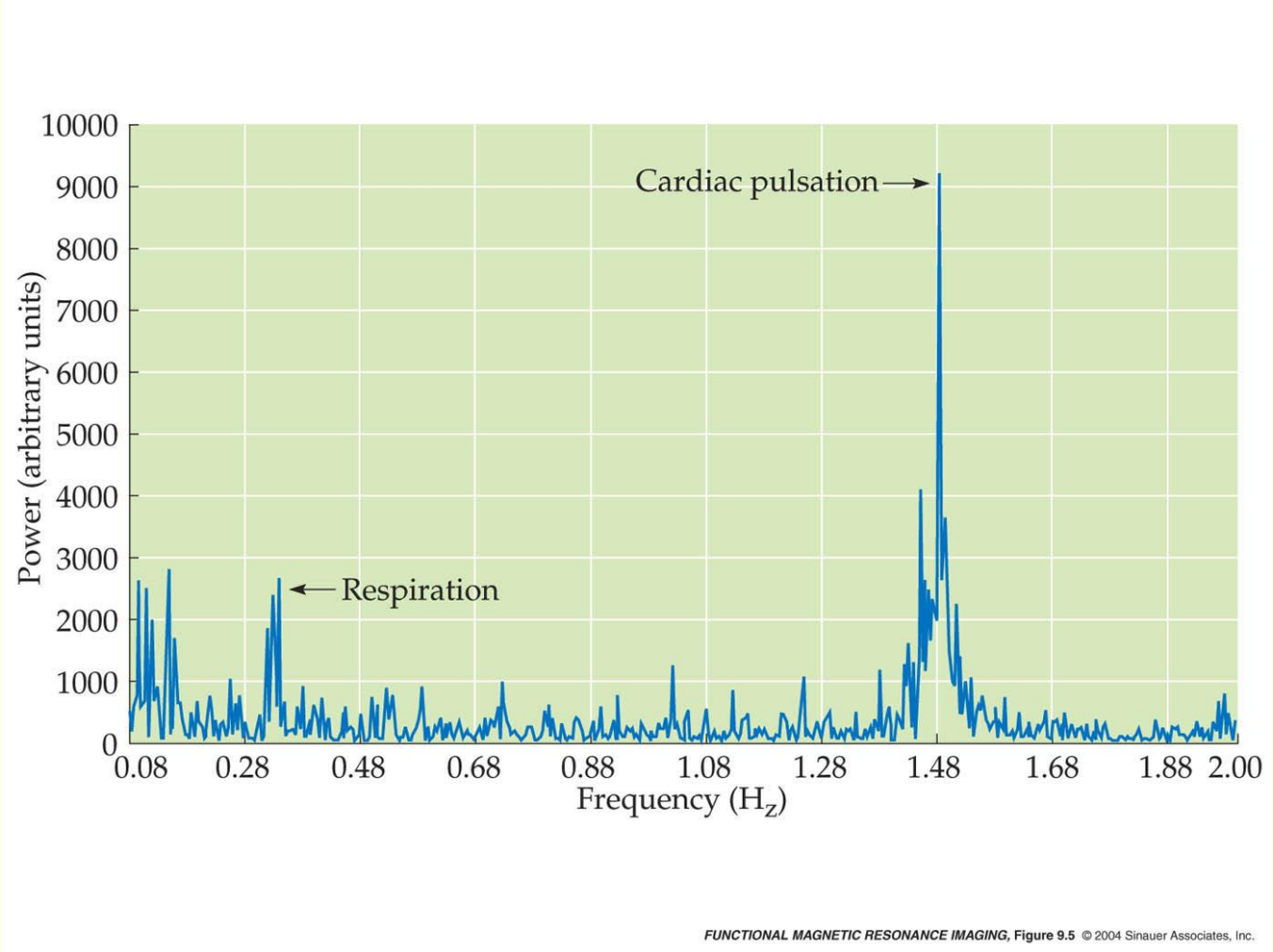
F. Temporal Filtering

- Identify unwanted frequency variation
  - Drift (low-frequency)
  - Physiology (high-frequency)

- Reduce power around those frequencies through application of filters

- Potential problem: removal of frequencies composing response of interest

Power Spectra: Frequencies to Eliminate



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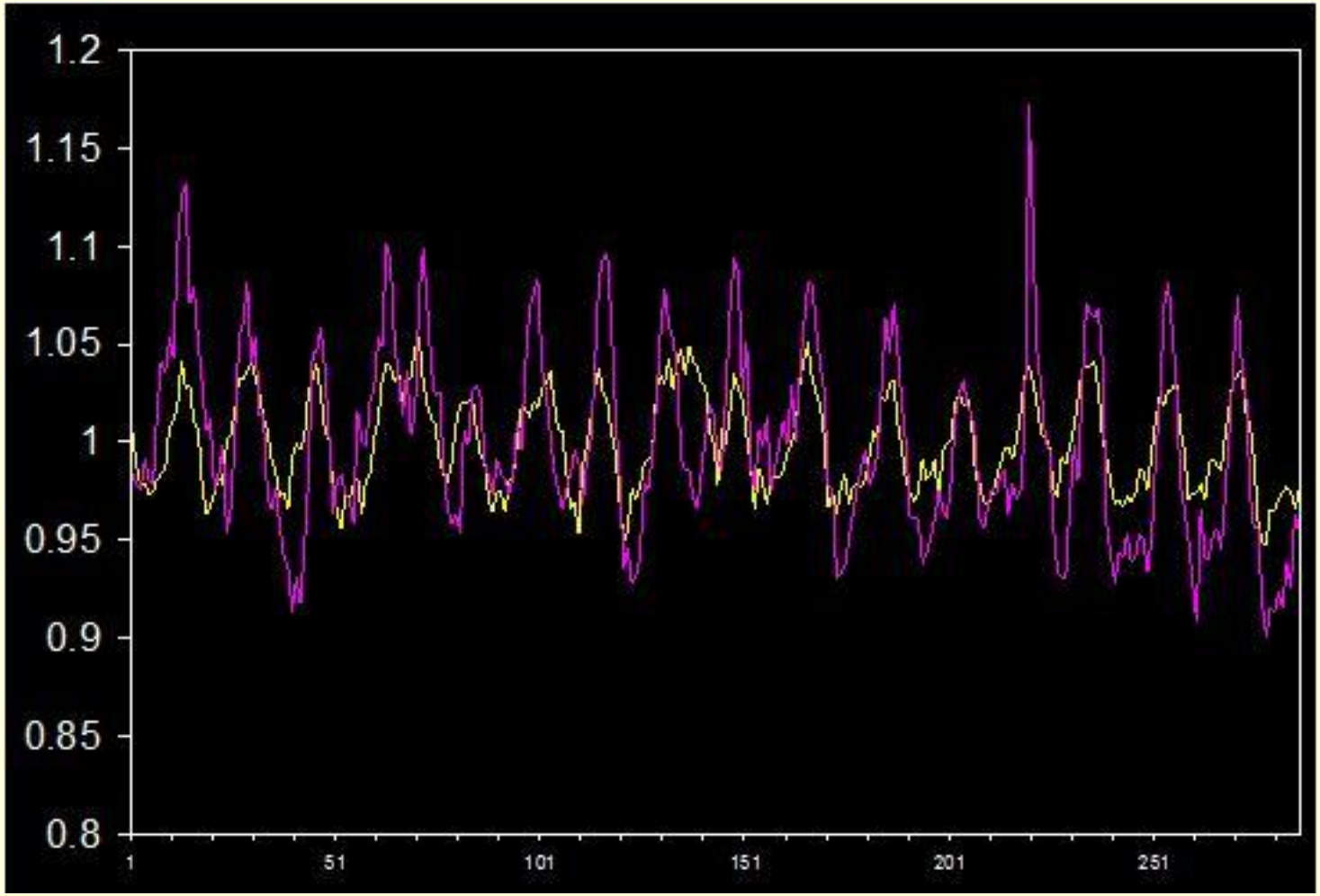
Statistics

When do we not need statistical analysis?



Why do we need statistics for fMRI?

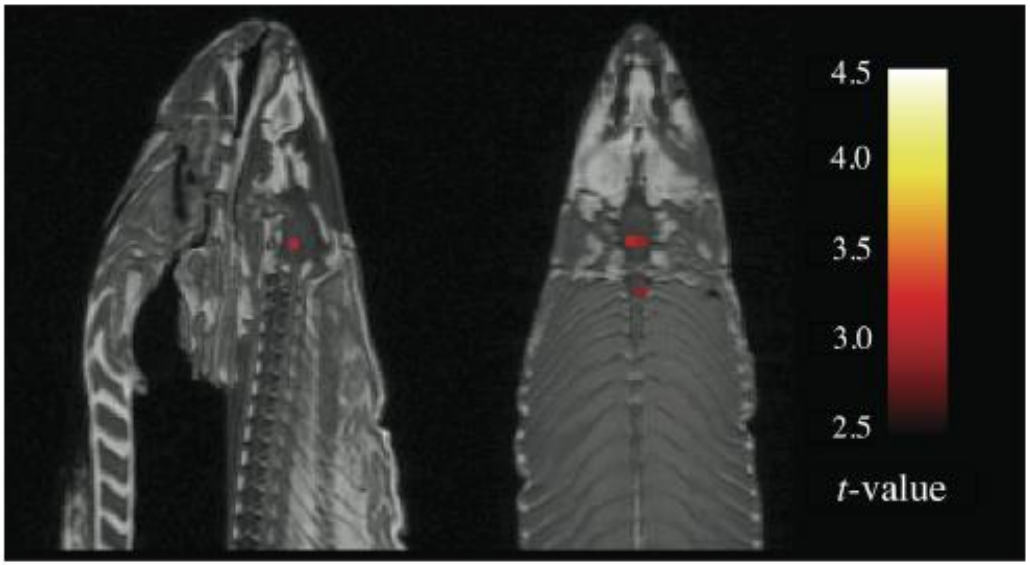
- What do we know about data from a single subject's single run?
  - it's abundant
    - 64 x 64 vxls x 32 slices x 200 trs = 26,214,400 vxls/run
  - it's noisy
  - it's highly correlated (spatially and temporally)

Why use statistical analyses?

- Replaces simple subtractive methods
  - Better handles sources of noise
    - Thermal variation (unstructured)
    - Physiological, task variability (structured)
- Assesses quality of data
  - How reliable is an effect?
  - Allows distinction of weak, true effects from strong, noisy effects

The functional Magnetic Resonance Imaging of Salmon

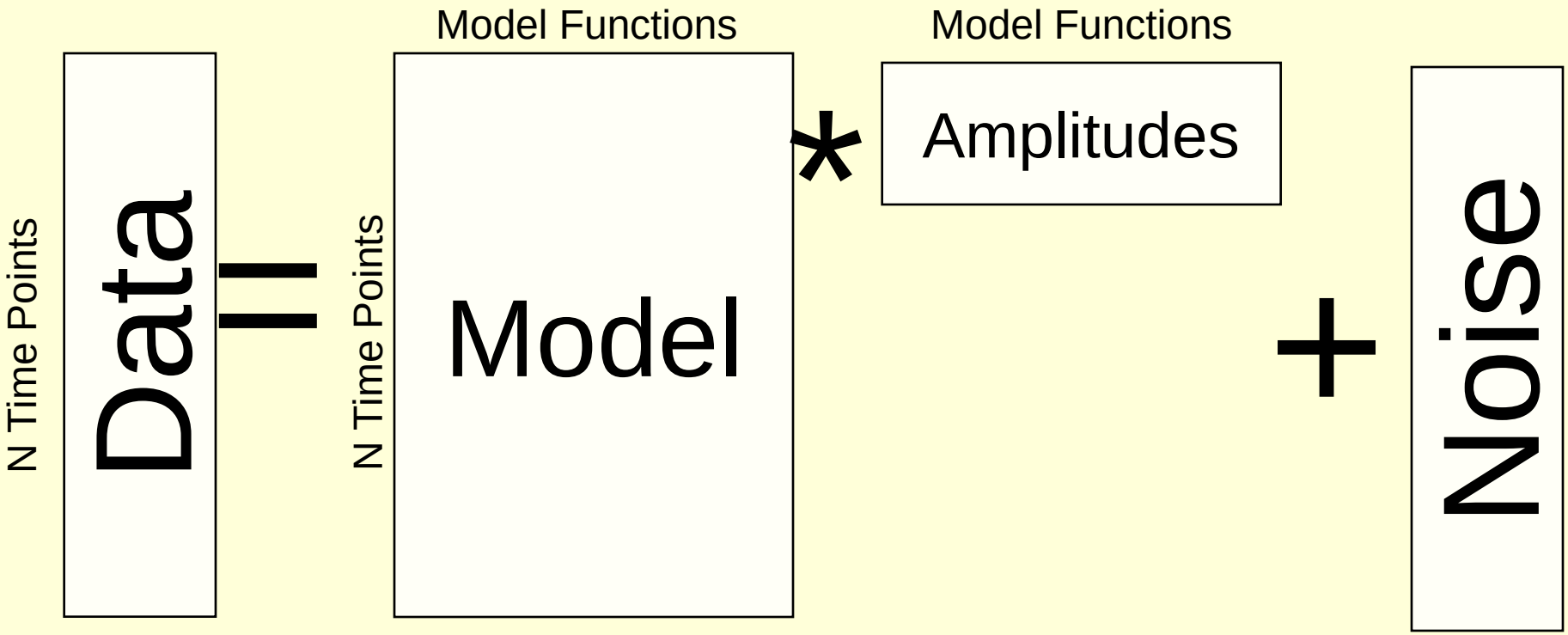
GLM RESULTS



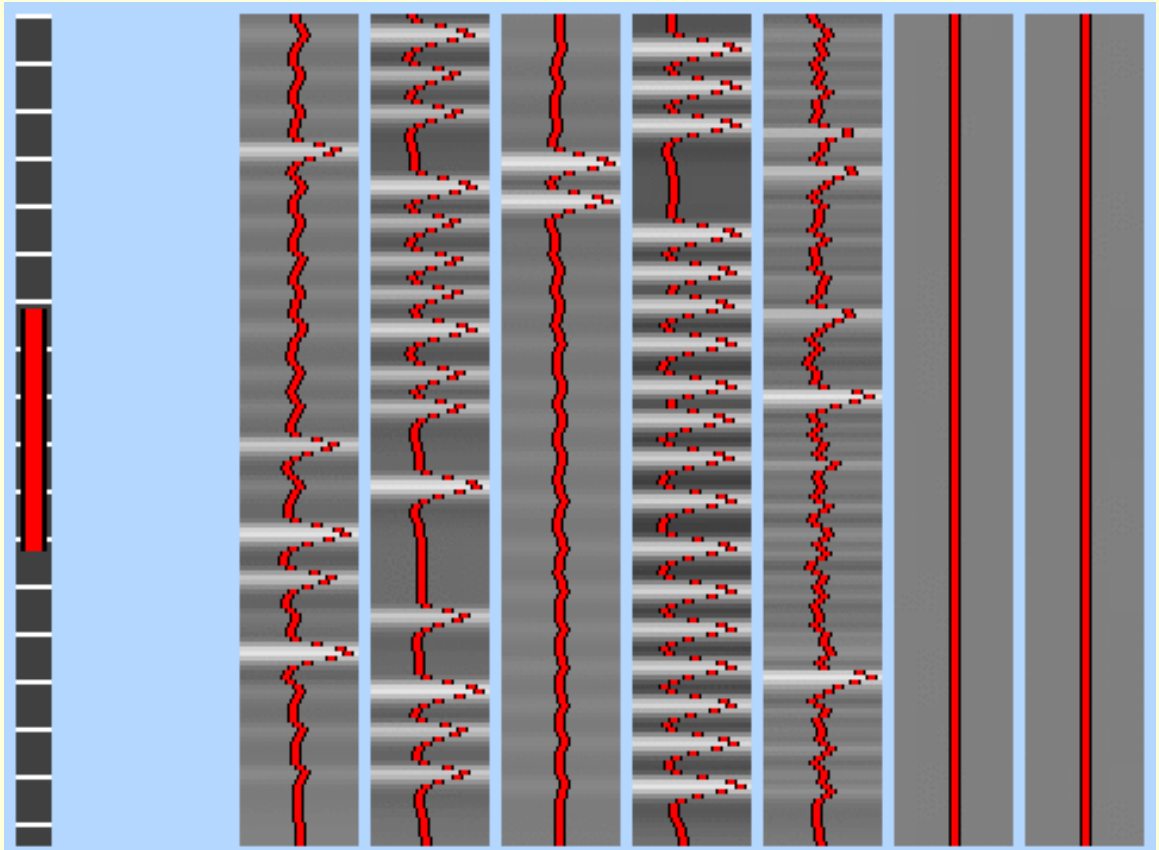
A *t*-contrast was used to test for regions with significant BOLD signal change during the photo condition compared to rest. The parameters for this comparison were $t(131) > 3.15$, p(uncorrected) < 0.001, 3 voxel extent threshold.

Bennet, et al., 2009

Form of the GLM



$$Y = \alpha M + \varepsilon$$



		good	bad	ev	ref	motor
C1	good-bad	1	-1	0	0	0
C2	bad-good	-1	1	0	0	0
C3	ev-ref	0	0	1	-1	0
C4	ref-ev	0	0	-1	1	0
C5	button	0	0	0	0	1
C6	good	1	0	0	0	0
C7	bad	0	1	0	0	0
C8	ev	0	0	1	0	0
C9	ref	0	0	0	1	0

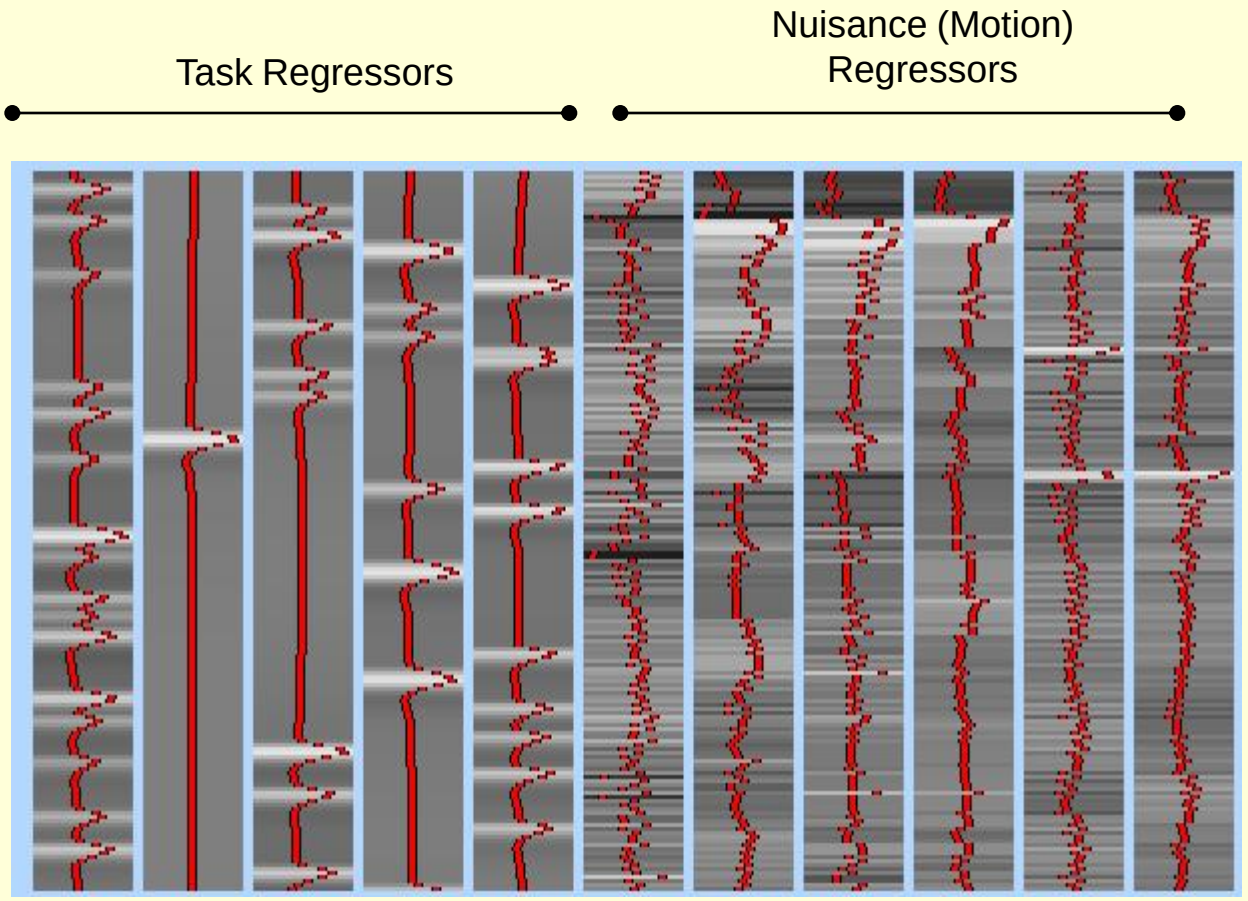
Regressors

(How much of the variance in the data does each explain?)

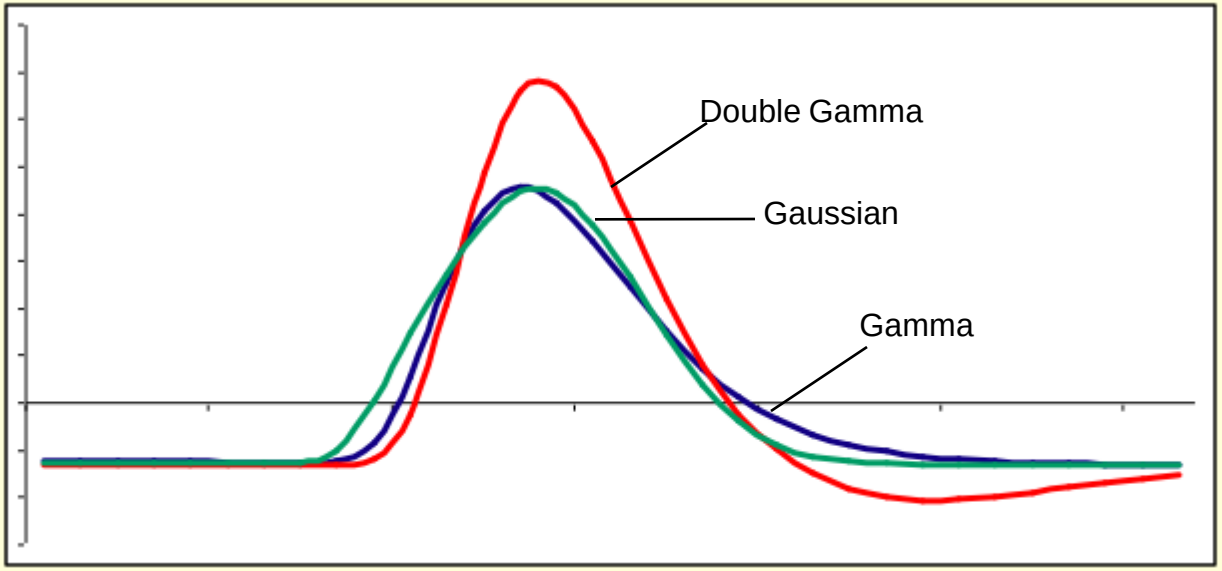
Contrasts

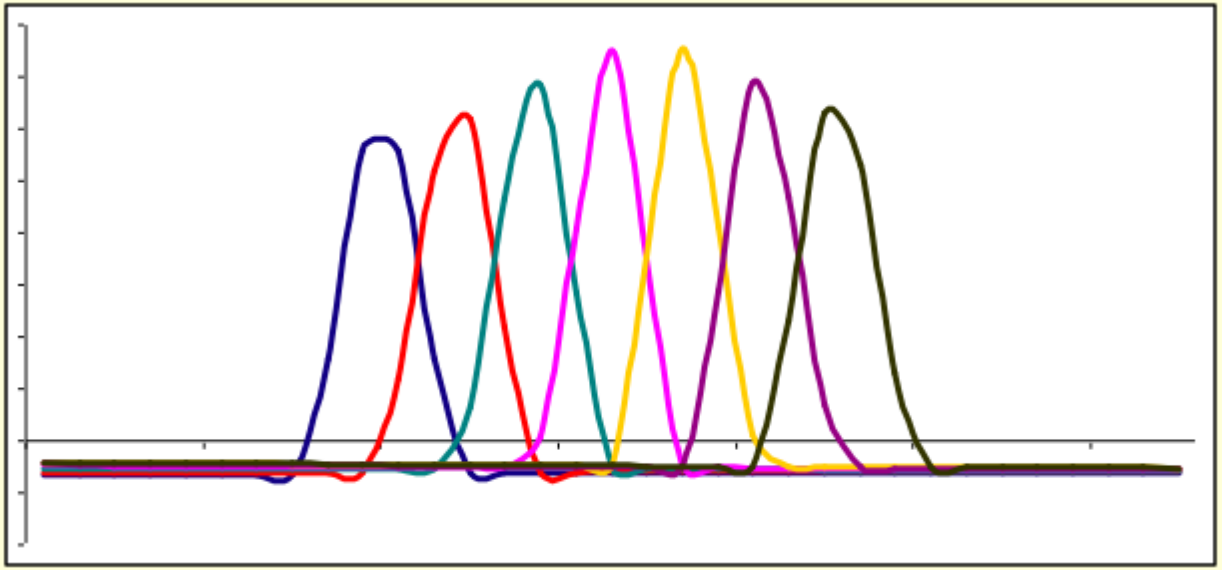
(Does one regressor explain more variance than another?)

Task and Nuisance Regressors



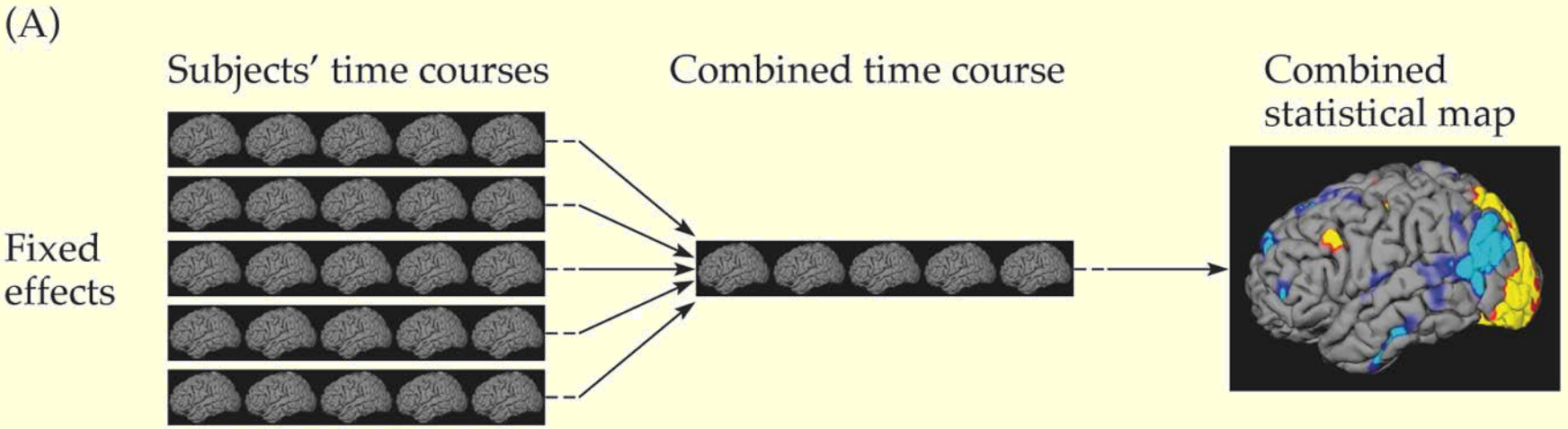
Hemodynamic and Basis Functions





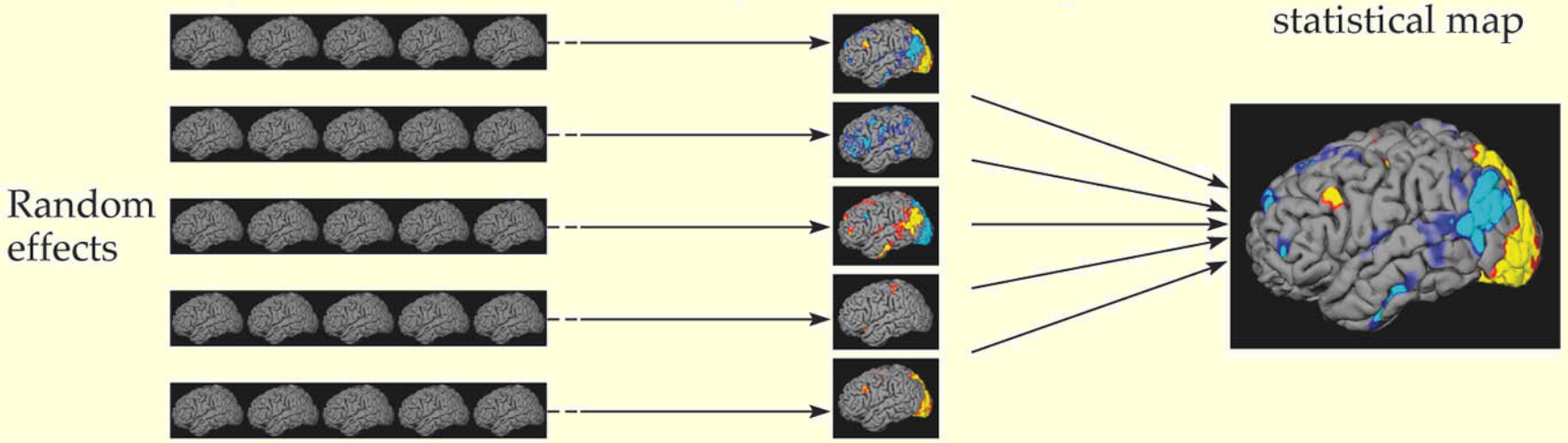
Fixed Effects

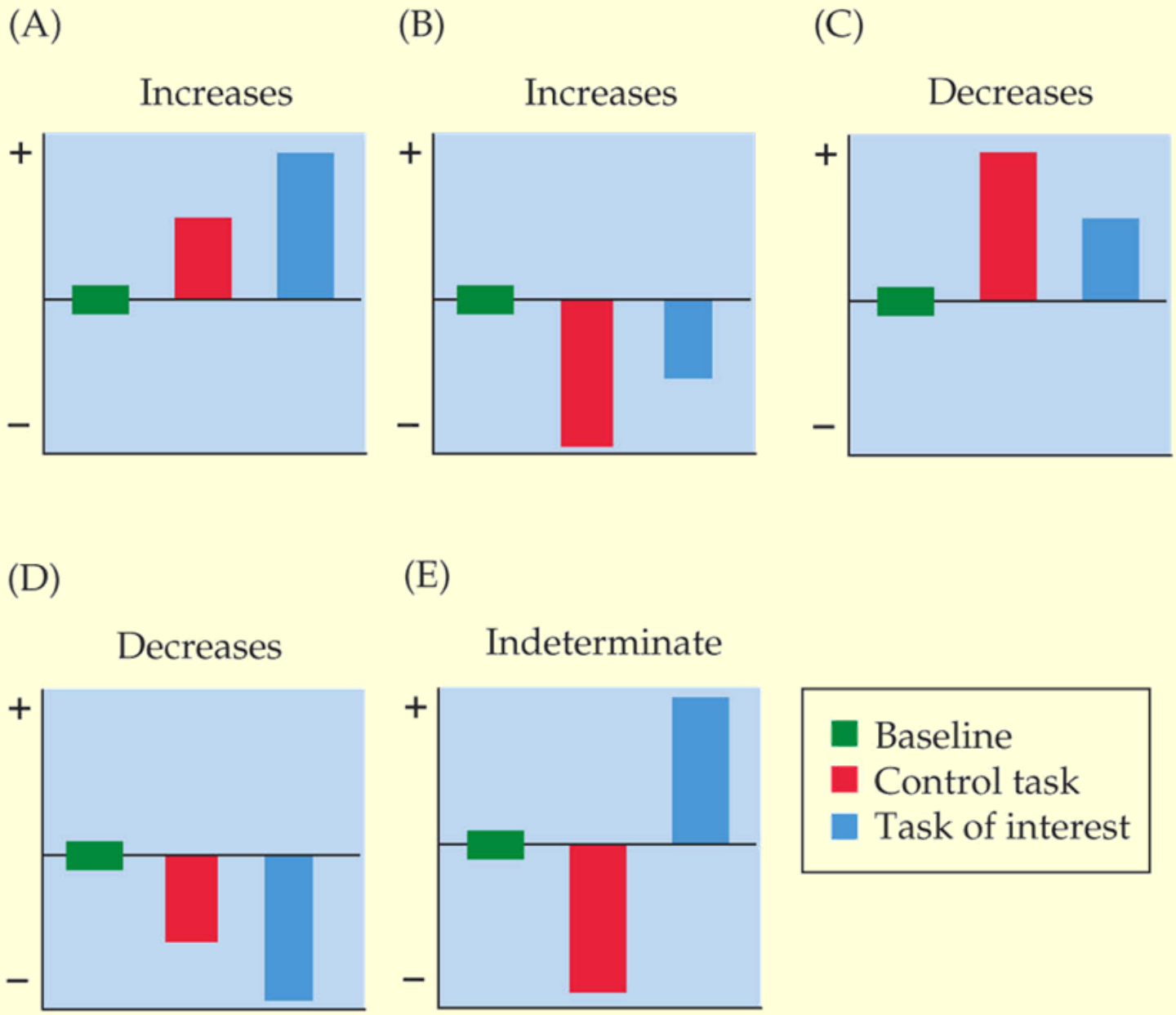
- Fixed-effects Model
  - Assumes that effect is constant ("fixed") in the population
  - Uses data from all subjects to construct statistical test
  - Examples
    - Averaging across subjects before a t-test
    - Taking all subjects' data and then doing an ANOVA
  - Allows inference to subject sample



Random Effects

- Random-effects Model
  - Assumes that effect varies across the population
  - Accounts for inter-subject variance in analyses
  - Allows inferences to population from which subjects are drawn
  - Especially important for group comparisons
  - Required by many reviewers/journals





Adapted from Gusnard & Raichle (2001)

How do we deal with this plethora of data (and statistical tests)?

Bonferroni Correction

- Very severe correction
  - Results in very strict significance values
  - Typical brain may have up to ~30,000 functional voxels
    - P(Type I error) ~ 1.0 ; Corrected alpha ~ 0.000003
- Greatly increases Type II error rate
- Not appropriate for correlated data
  - If data set contains correlated data points, then the effective number of statistical tests may be greatly reduced
  - Most fMRI data has significant correlation

Alternatives

- Gaussian Random Field Theory
  - Correct based on
    - cluster size
    - Number of clusters
- Permutation Analyses
- A priori ROI analyses
- Mask by lower level comparisons

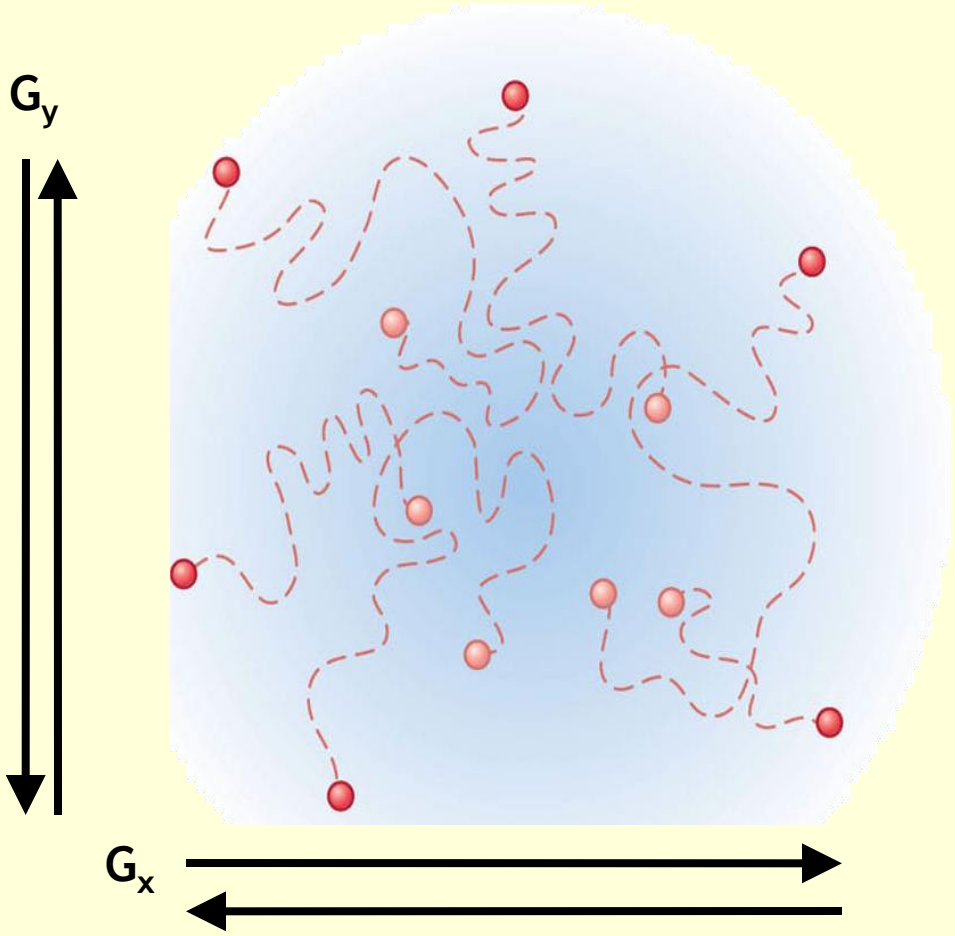
3. Advanced Techniques

Advanced Techniques

- DTI
- Incorporating Behavioral Data
  - Covariates of no interest
  - Psychometric Covariates
- Resting State Analyses
- Other approaches

Diffusion Tensor Imaging (DTI)

Core Approach of Diffusion Tensor Imaging (DTI)

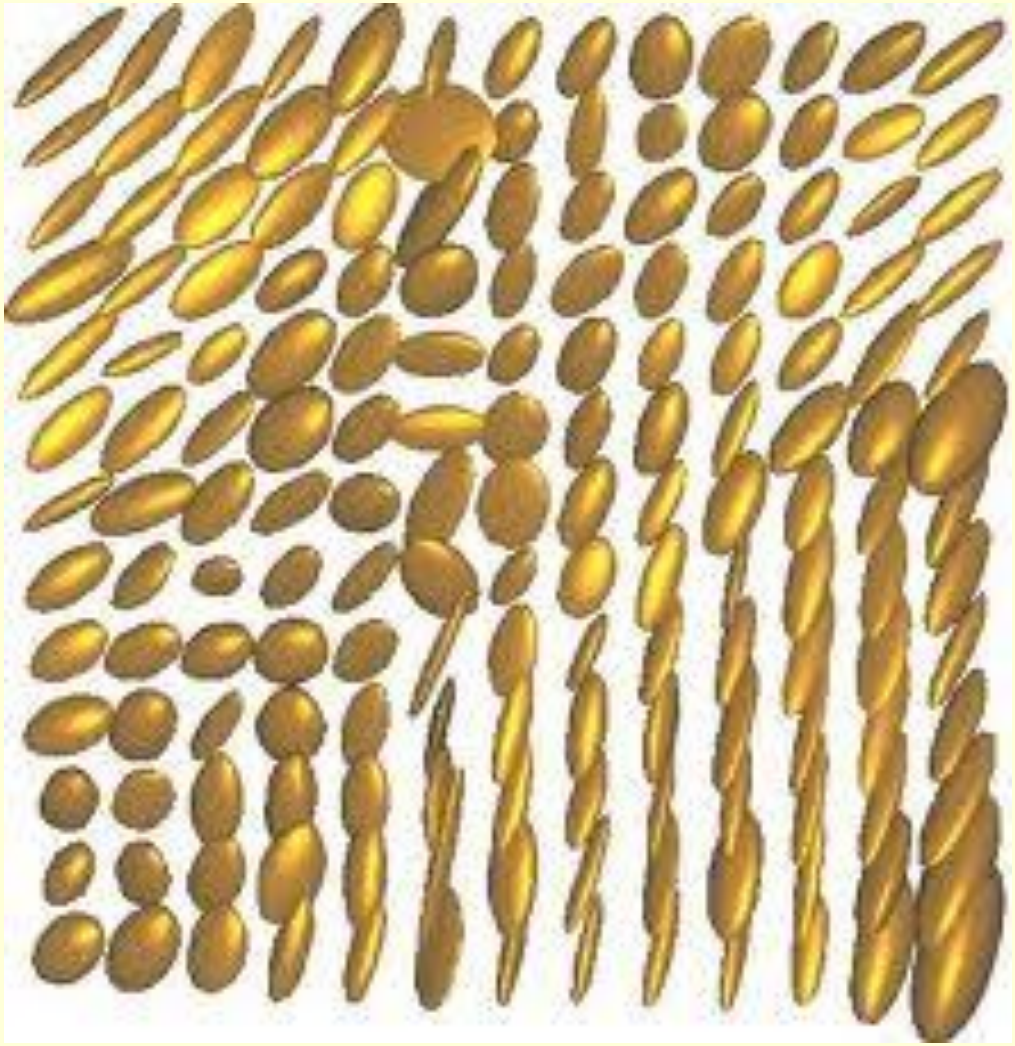


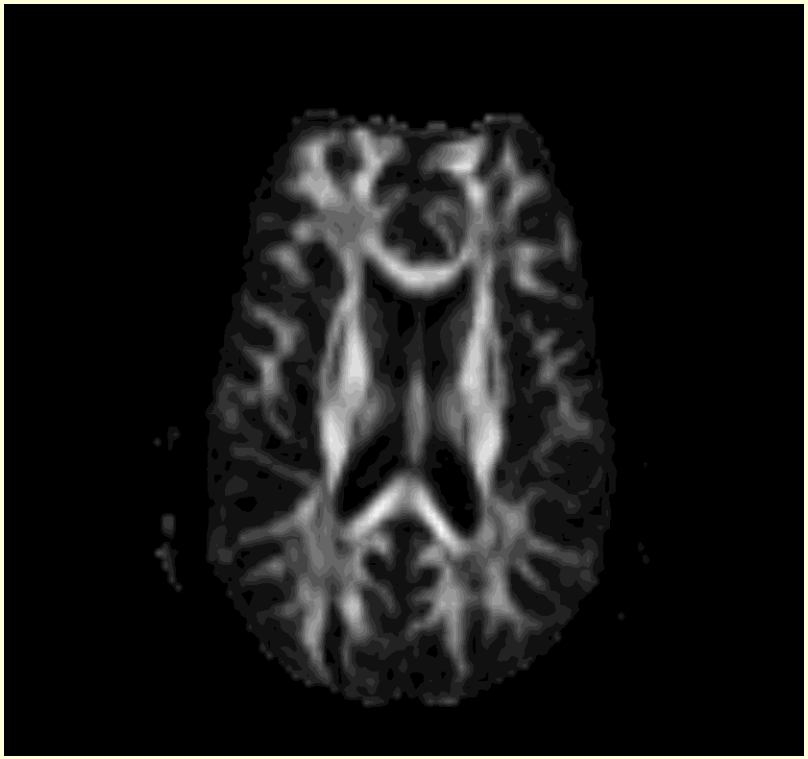
Apply alternating, opposite gradients along one direction. Measure signal.

Apply alternating, opposite gradients along a different direction. Measure signal.

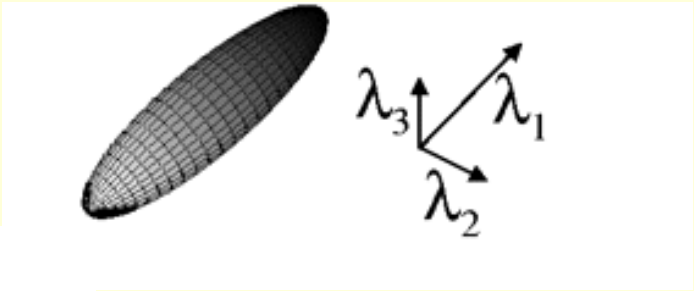
Repeat for a total of 6+ directions. The amplitude of the signal across these directions constitutes the diffusion tensor.

DTI – What do we measure





DTI – In Detail



$\lambda_{//}$

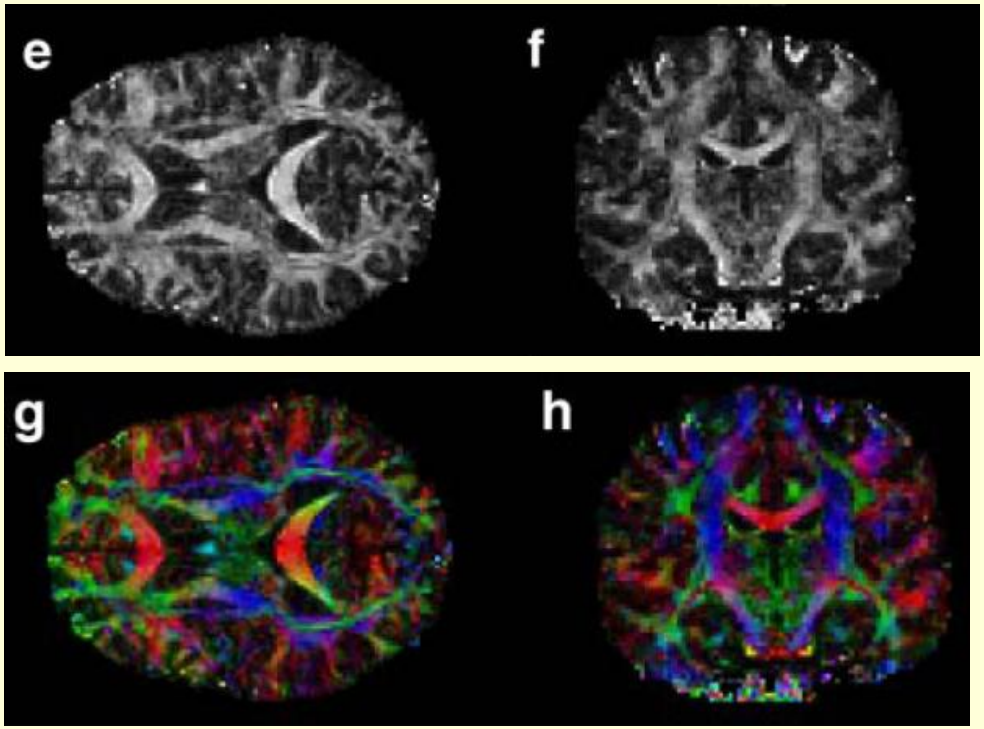
$\lambda_{\perp}$

- Longitudinal or Axial Diffusivity
  - Axonal integrity (λ_1)
- Transverse or Radial Diffusivity
  - Myelin integrity ($\lambda_{2\&3}$)
- Fractional Anisotropy

$$= \sqrt{\frac{1}{2}} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\sqrt{(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$

How do you use DTI data?

- FA values
  - Regional values
  - Does the FA value in the Genu influence fMRI activity, behavior



Left-right fibers

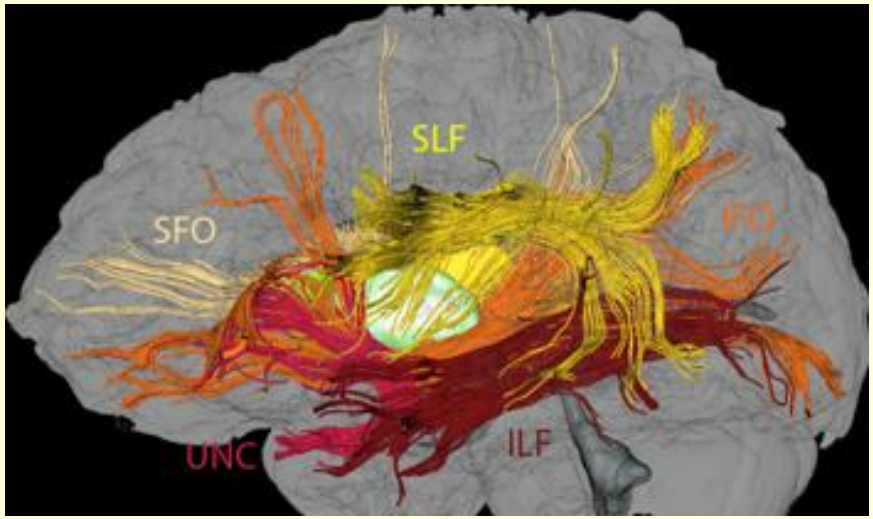
Inferior - superior fibers

Anterior -posterior fibers

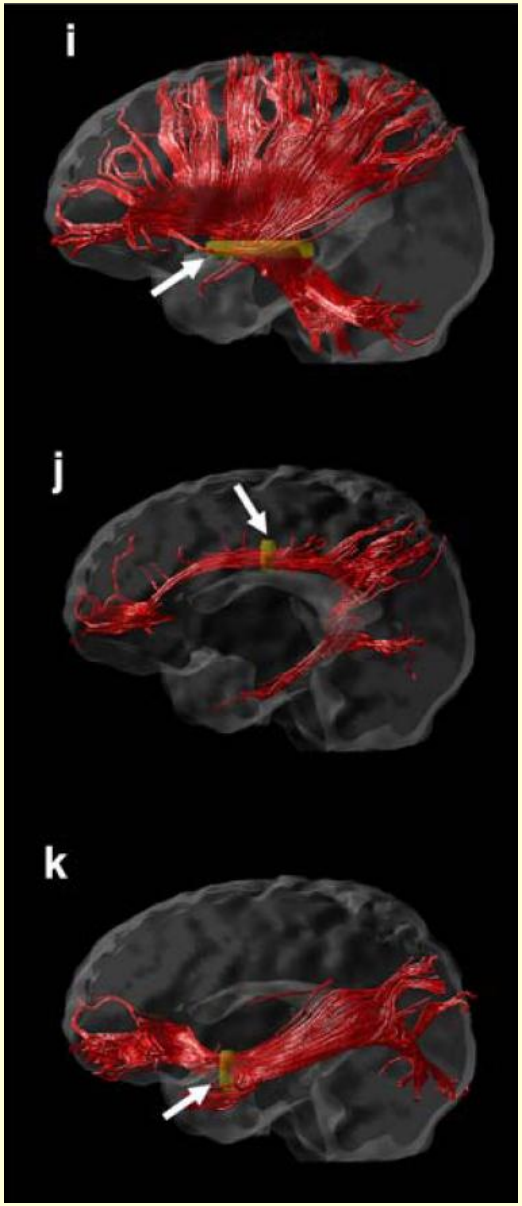
Assaf & Pasternak, 2008

How do you use DTI data?

- Tractography
  - How do tracts differ across a population or populations?



BIAC Data



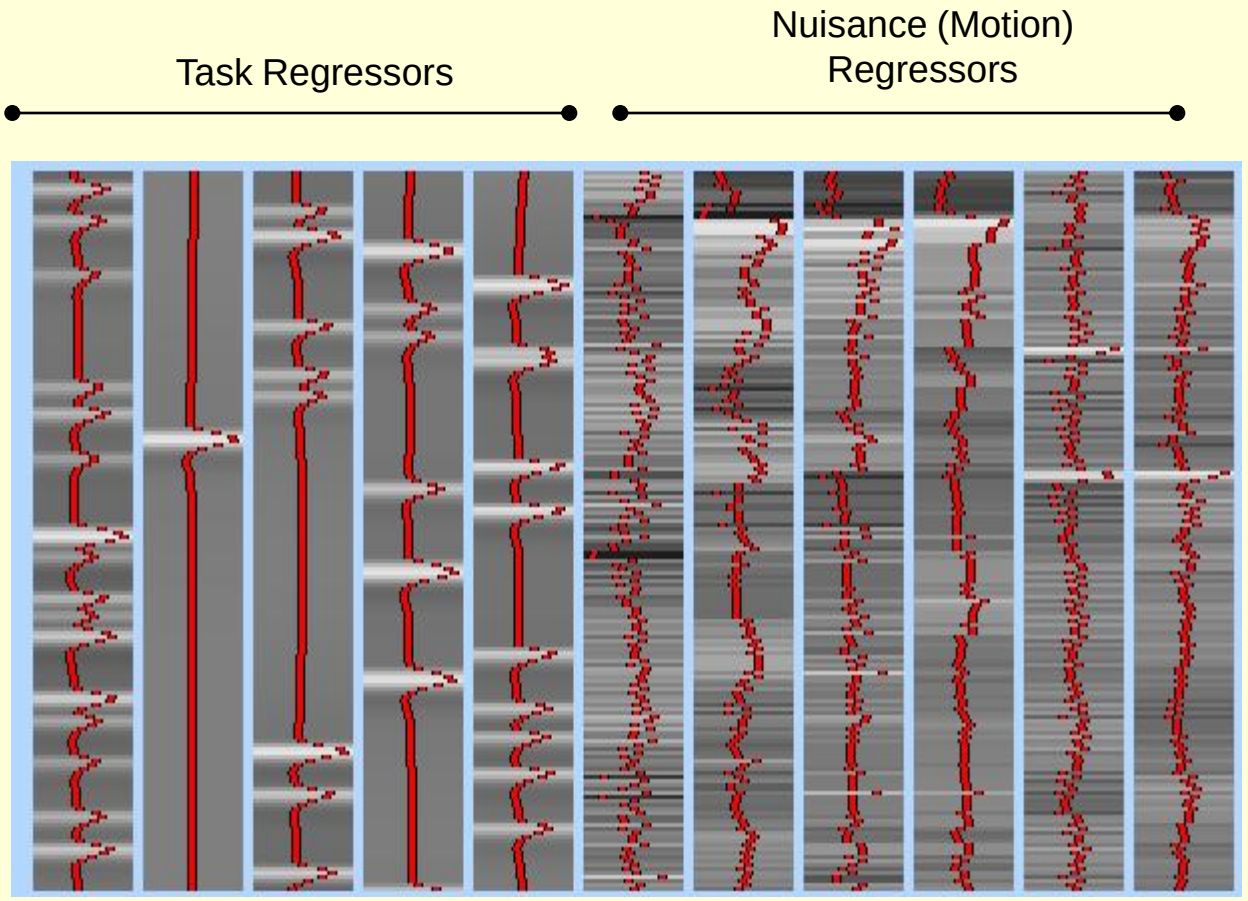
Assaf & Pasternak, 2008

Integrating Behavioral (and other) Data

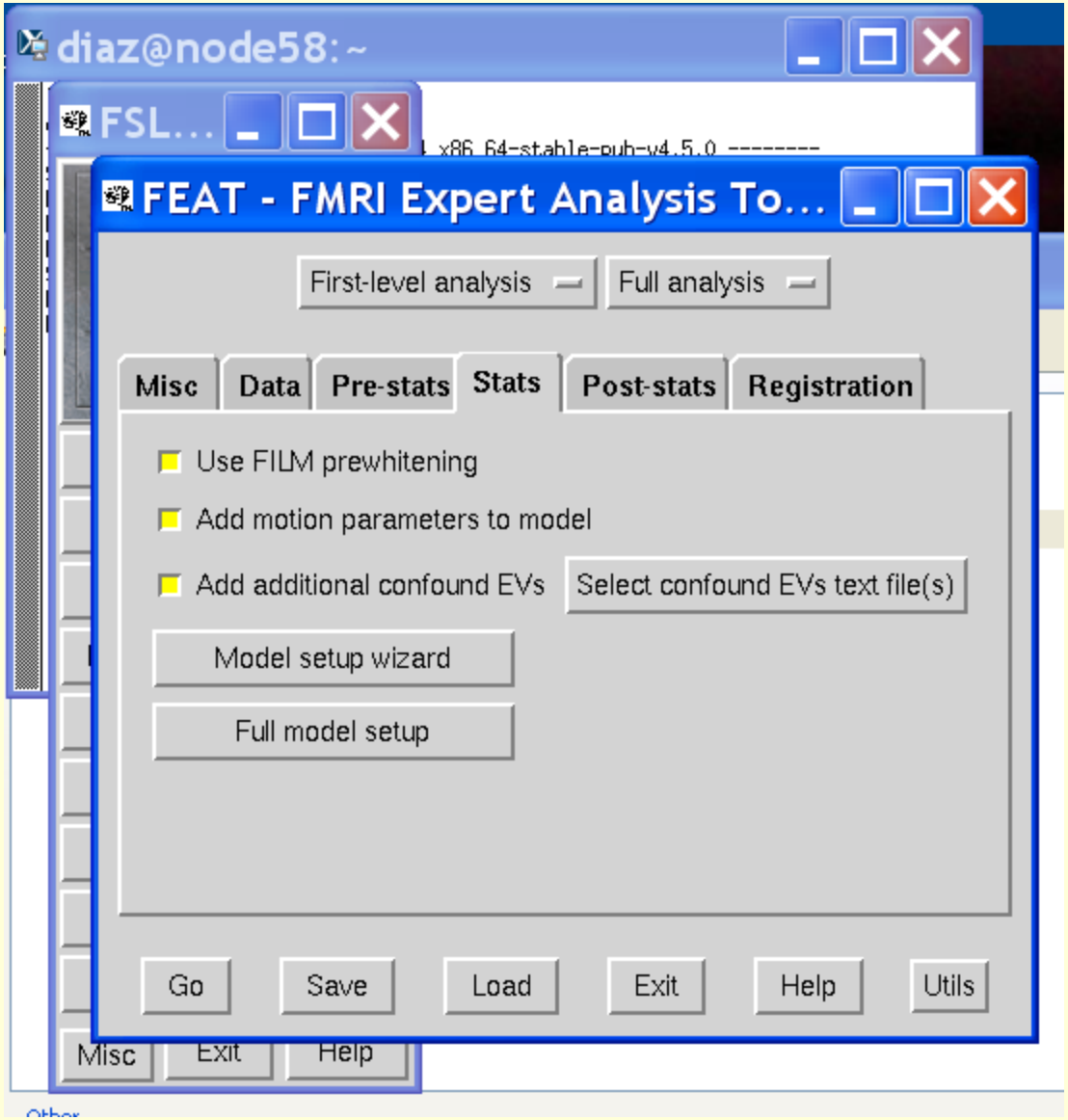
Integrating Other Types of Data

- Think about
  - What information is in the other data
  - How does it relate to your hypotheses (data of interest)

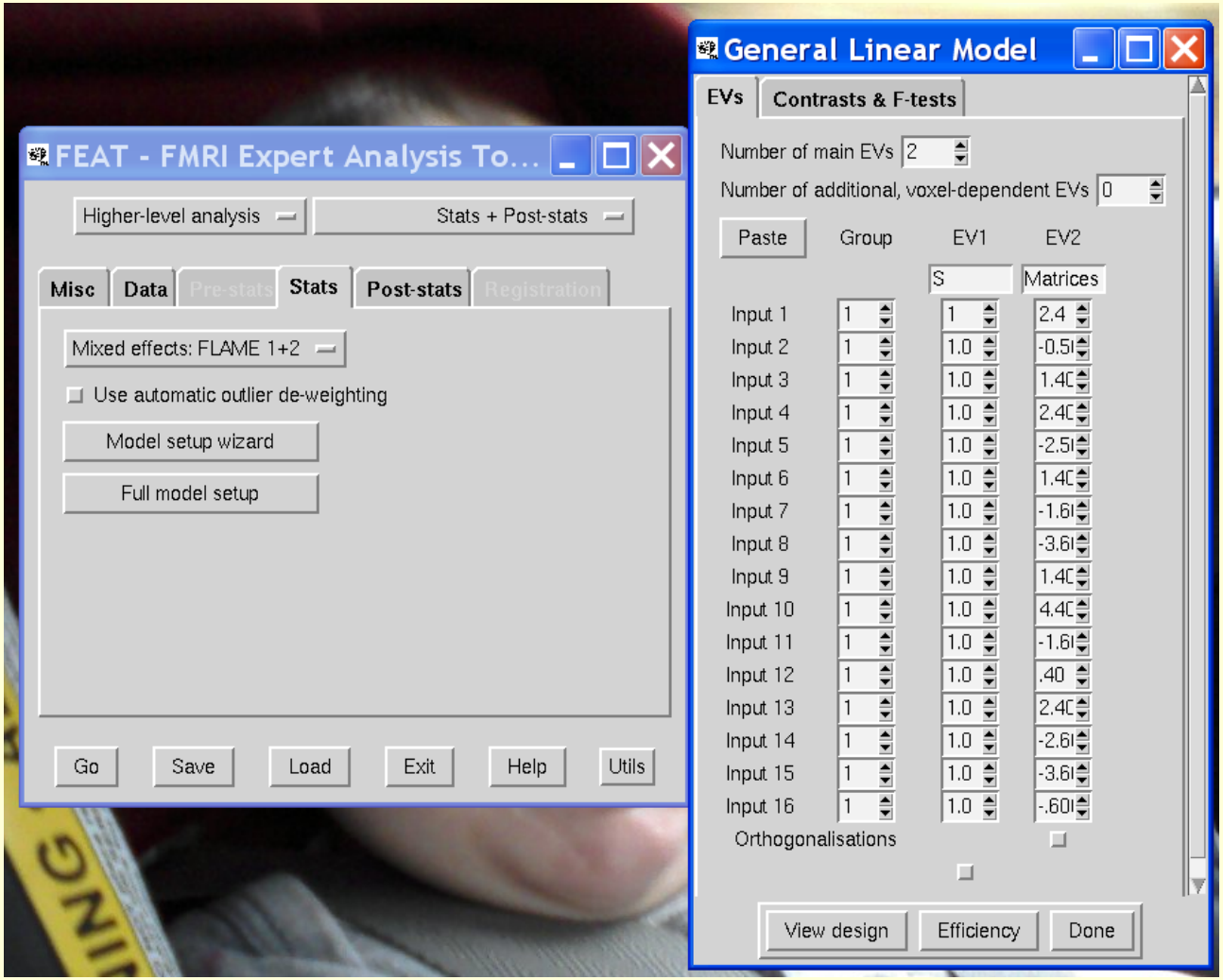
Potential Confounds: Motion



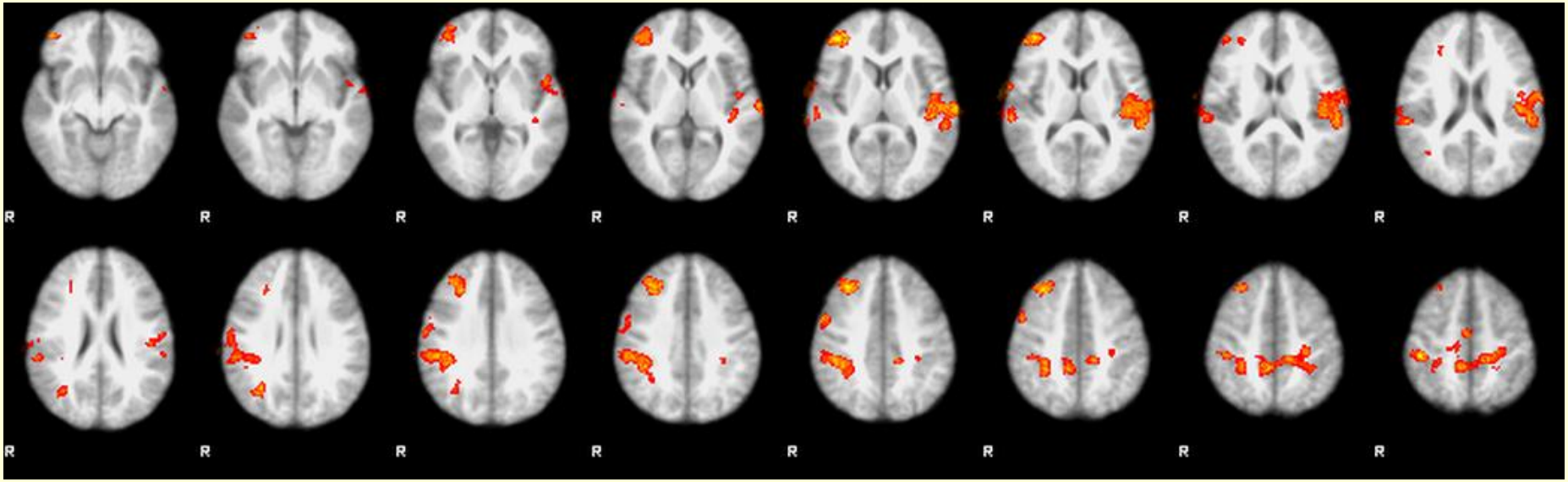
Integrating Potential Confounds



Integrating Variables of Interest



Integrating Variables of Interest: Matrices and Figurativeness

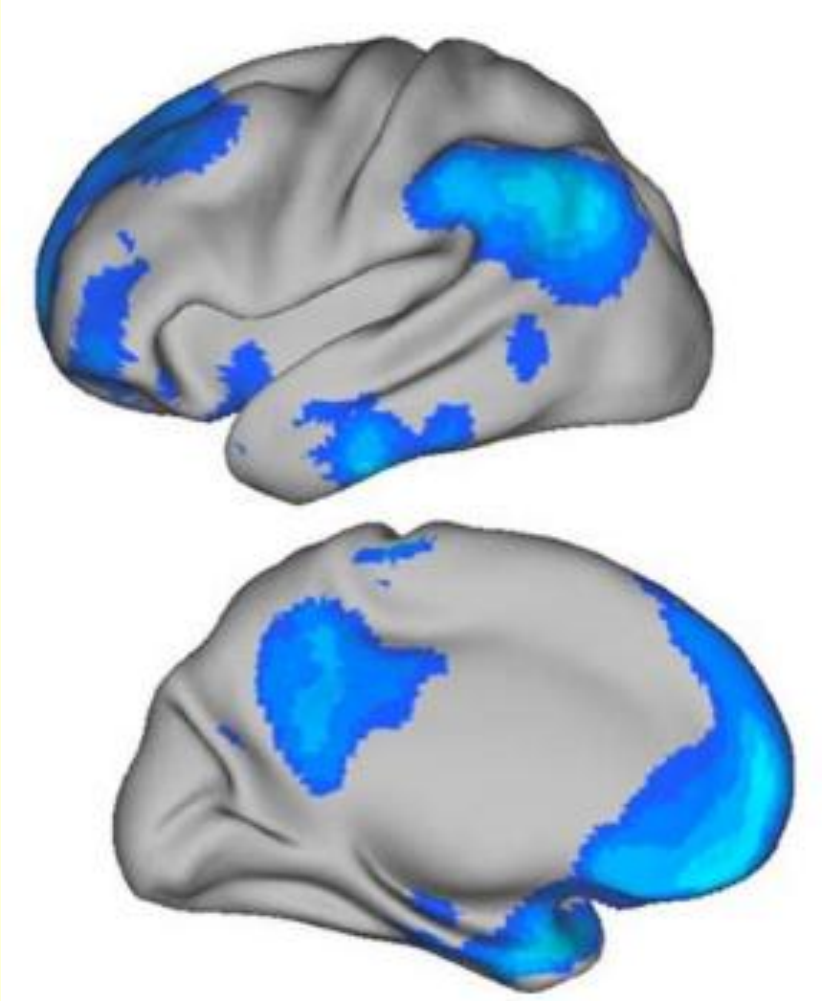


- Matrices negatively correlated with functional activation to metaphors (Met > Lit)

Resting State Analyses

Resting State Analyses

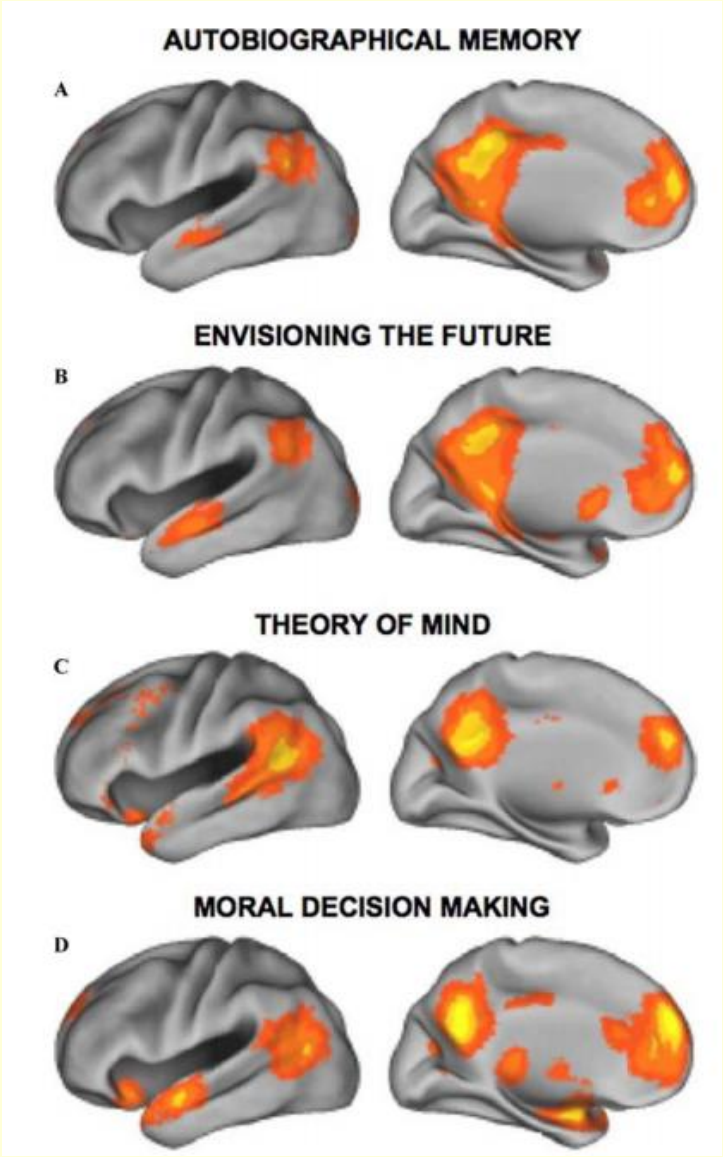
- Collect Data
  - While subject relaxes
  - Rest/Fixation blocks
- Areas more active at Rest than during task
- Terms
  - Default Network
  - Task Negative Network



Buckner, Andrews-Hanna, & Schacter, 2008

What does it mean

- Default Network Regions active during a variety of tasks.
  - Mental simulation
  - Perspective Taking
  - Planning
  - Internal dialogue



Buckner, Andrews-Hanna, & Schacter, 2008

How are Resting State Analyses used?

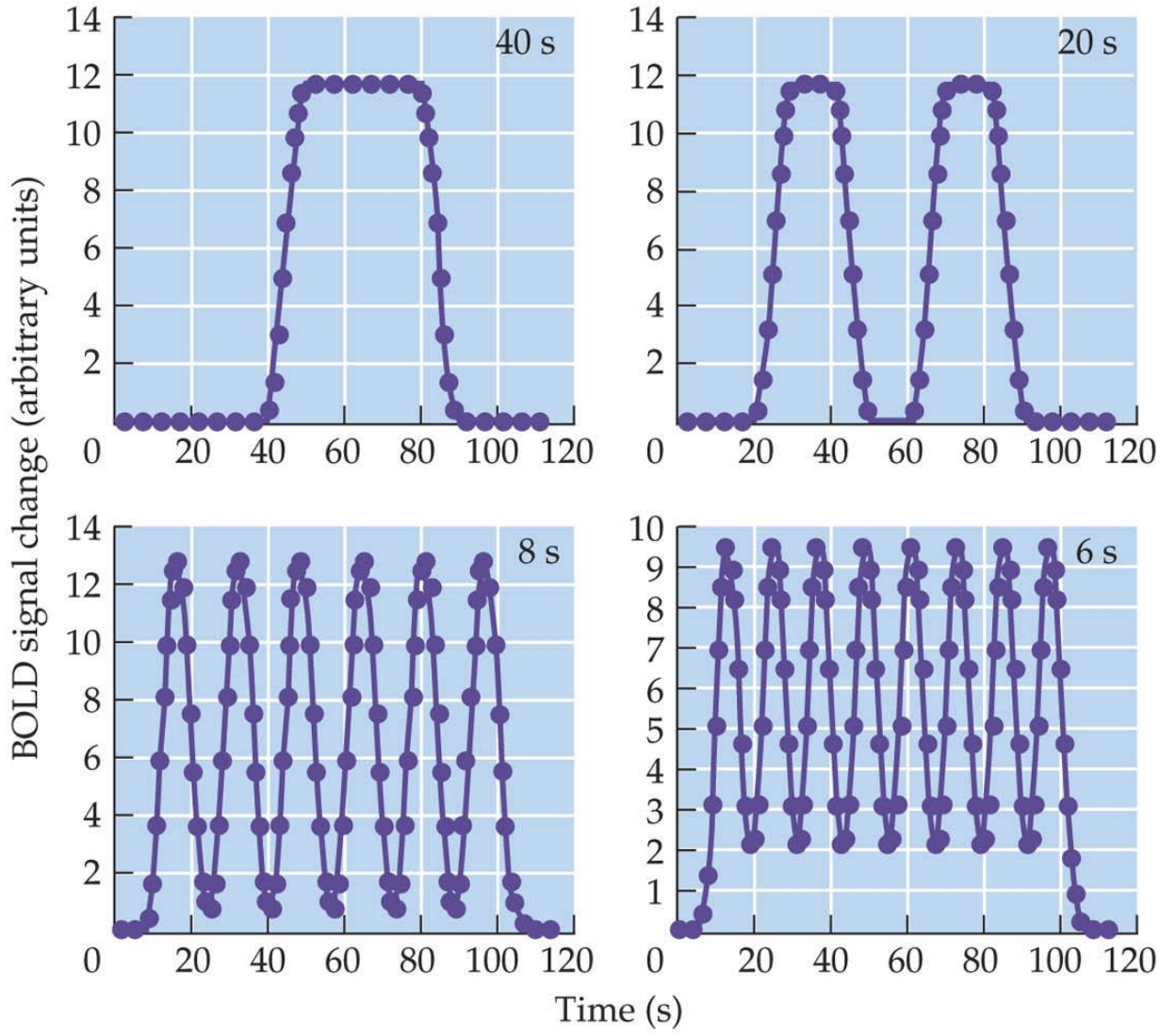
- Comparisons between groups
  - Clinical populations
    - Schizophrenia
    - Alzheimers Disease
  - Other group comparisons
    - Older vs. younger adults
    - Resting, Comatose, Brain-dead
    - Monolinguals vs. Bilinguals?

Other Approaches

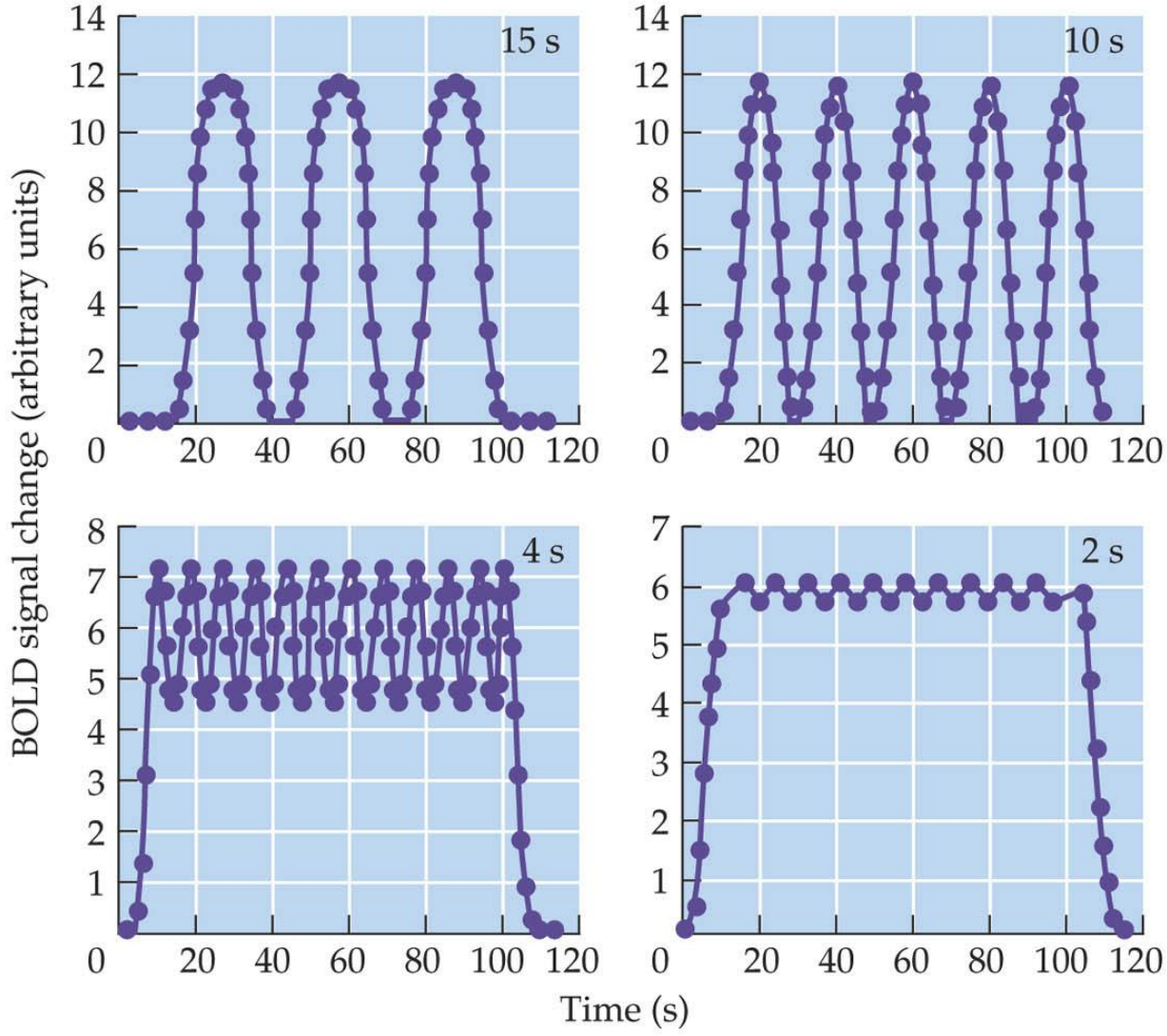
- Anatomical analyses
  - Voxel Based Morphometry
  - Anatomical Region of Interest

4. Your Questions:

Blocked vs. Event-Related Design, Refractory Effects

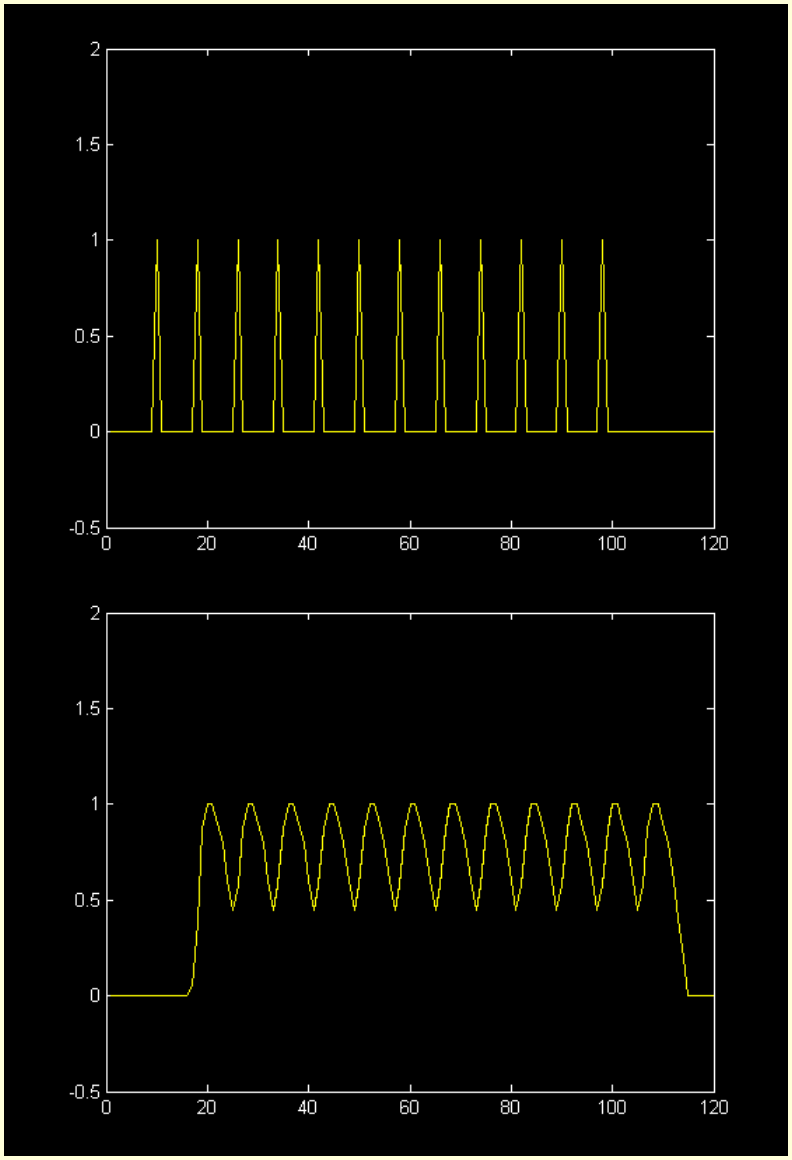


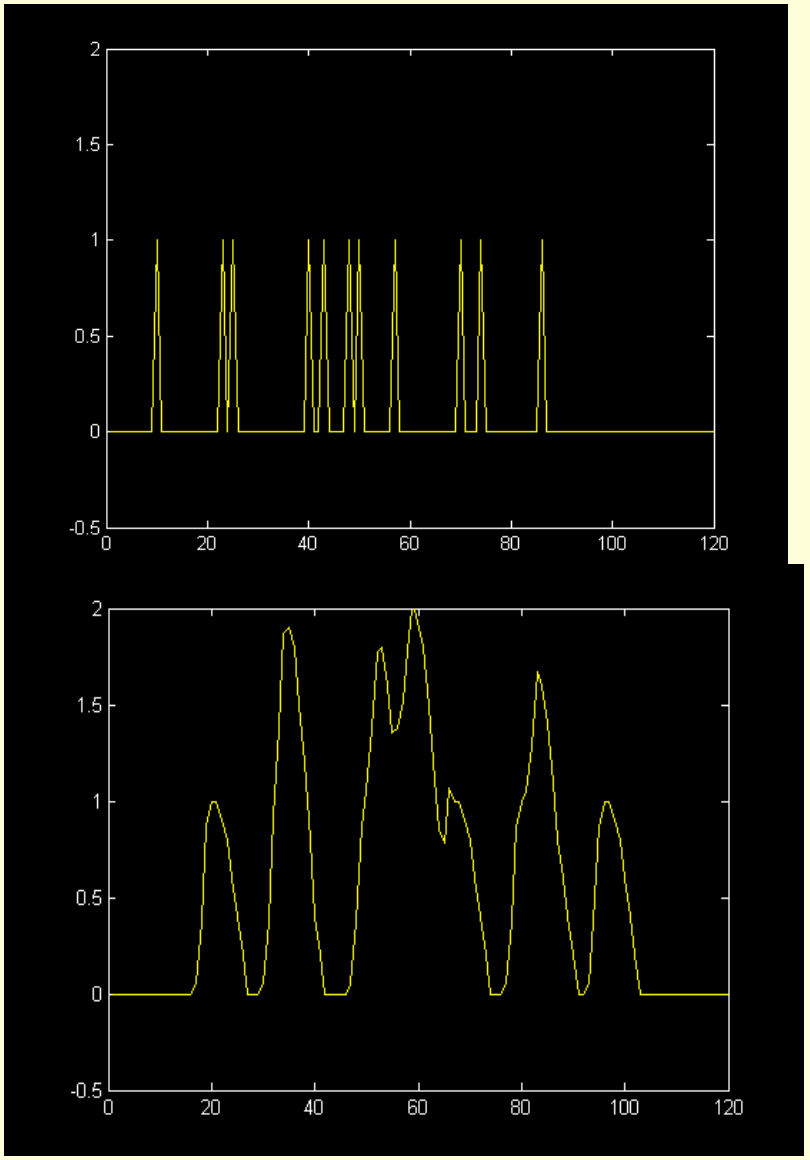
FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 11.10 (Part 1)



FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 11.10 (Part 2)

Effects of Jittering on Stimulus Variance





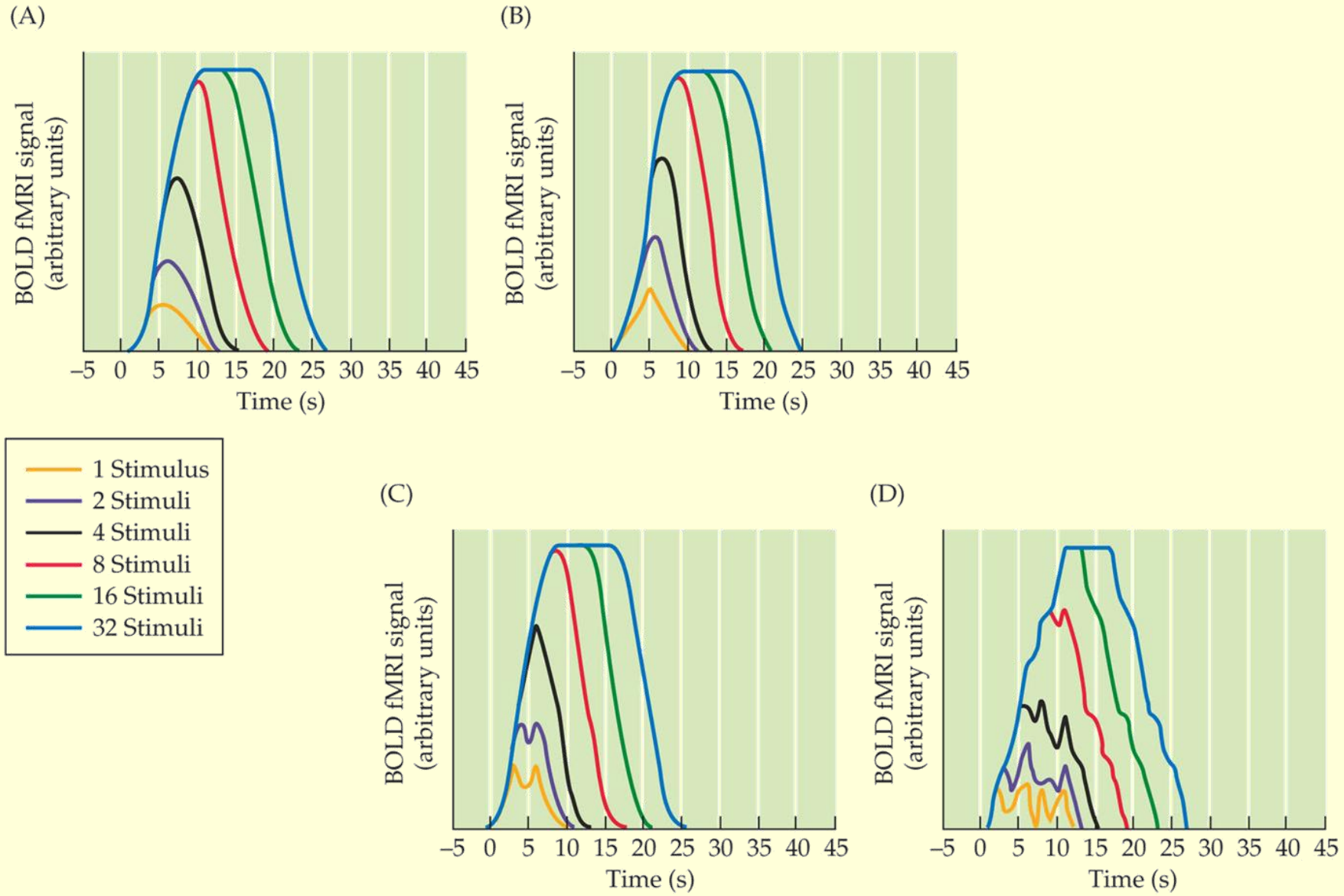
Choosing Length of Blocks

- Longer block lengths allow for stability of extended responses
  - Hemodynamic response saturates following extended stimulation
    - After about 10s, activation reaches max
  - Many tasks require extended intervals
    - Processing may differ throughout the task period

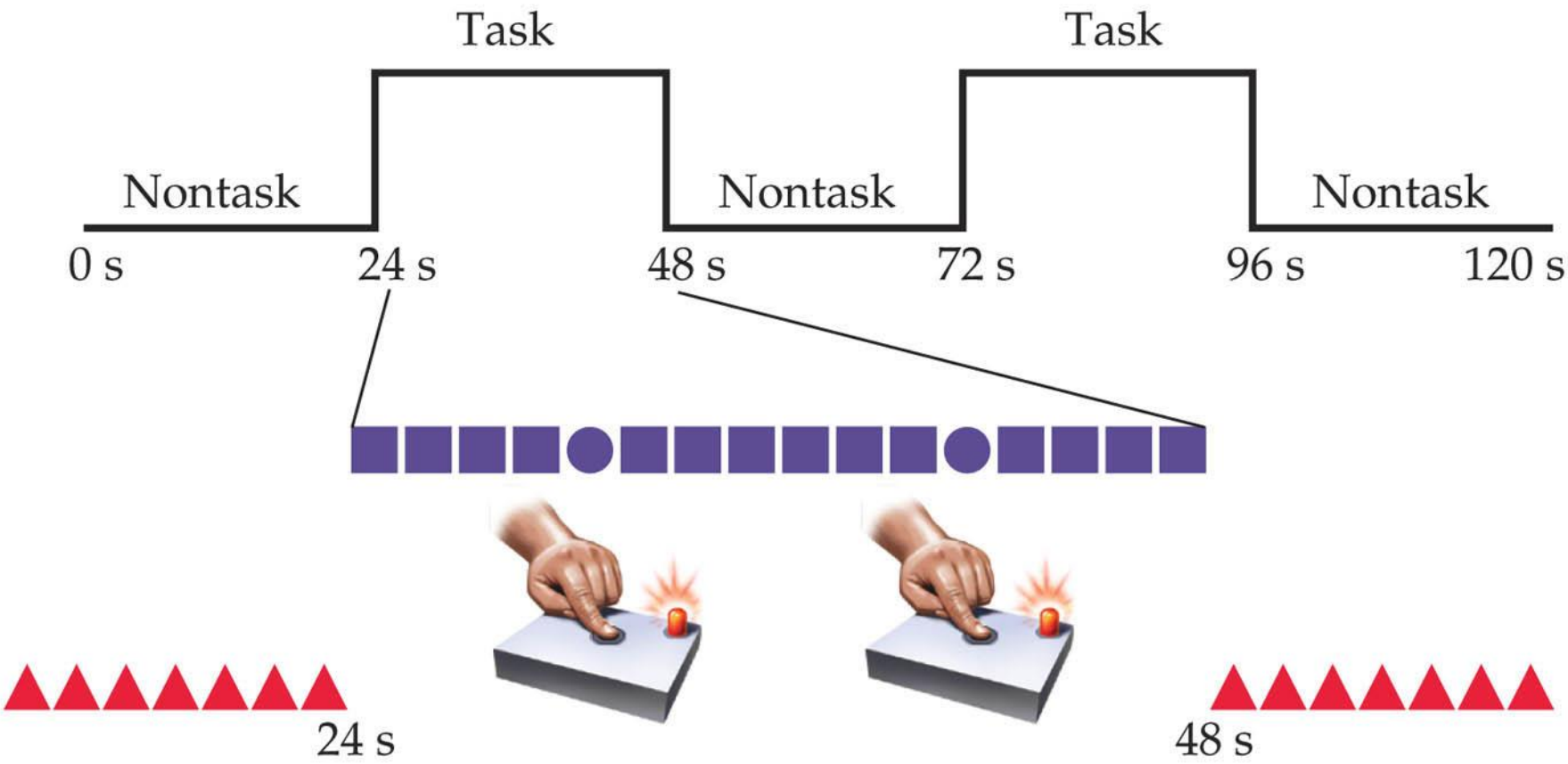
- Shorter block lengths move your signal to higher frequencies
  - Away from low-frequency noise: scanner drift, etc.

- Periodic blocks may result in aliasing of other variance in the data
  - Example: if the person breathes at a regular rate of 1 breath/5sec, and the blocks occur every 10s

HDR Estimation: Blocked Designs

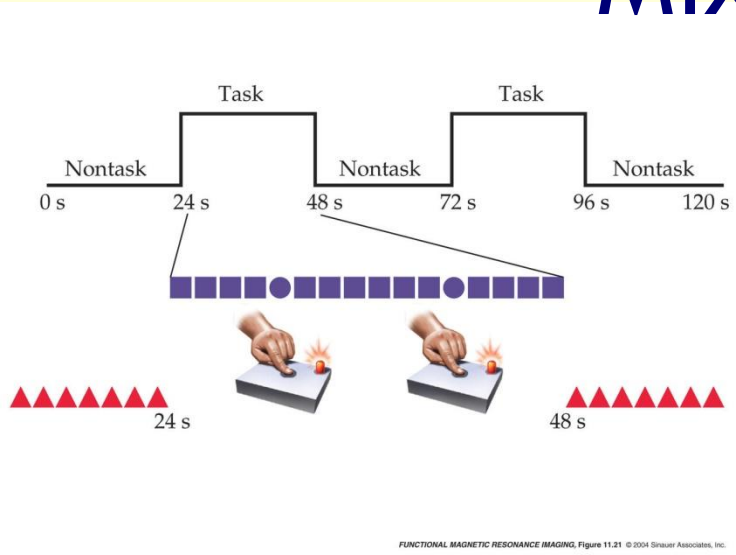


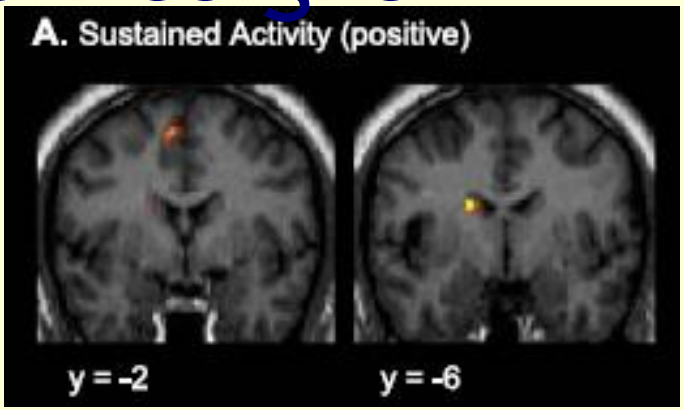
Mixed Designs

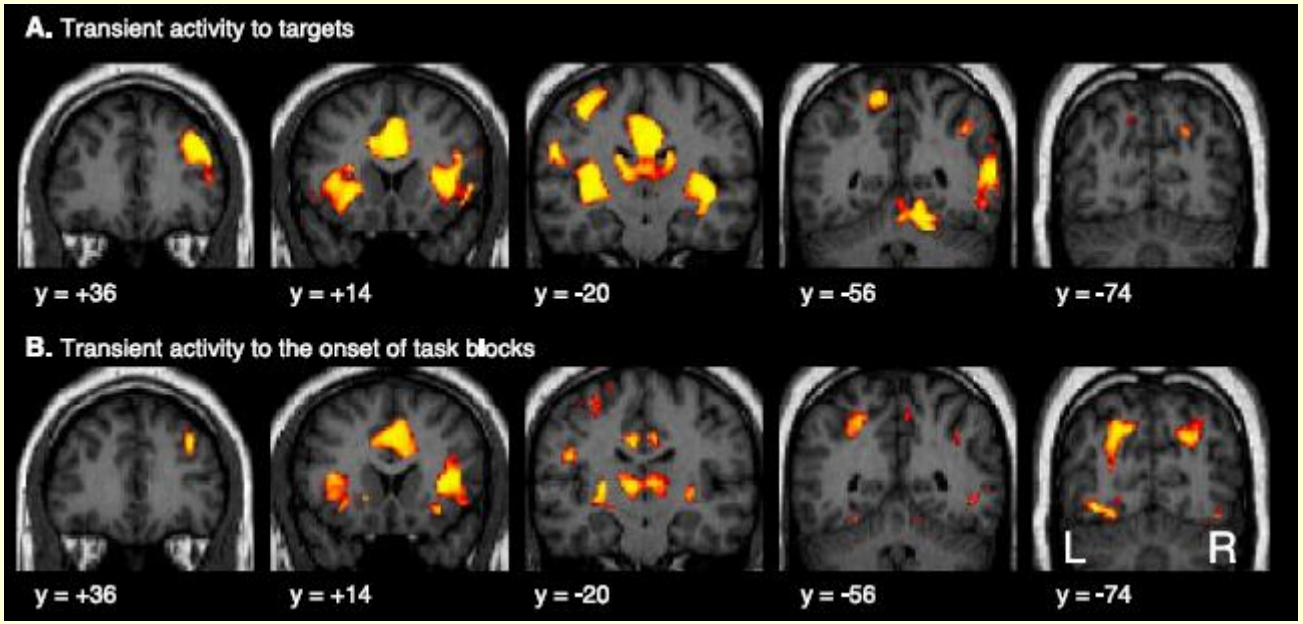


FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 11.21** © 2004 Sinauer Associates, Inc.

Mixed Designs







Questions?