Neuroeconomics:

Background and Methods II

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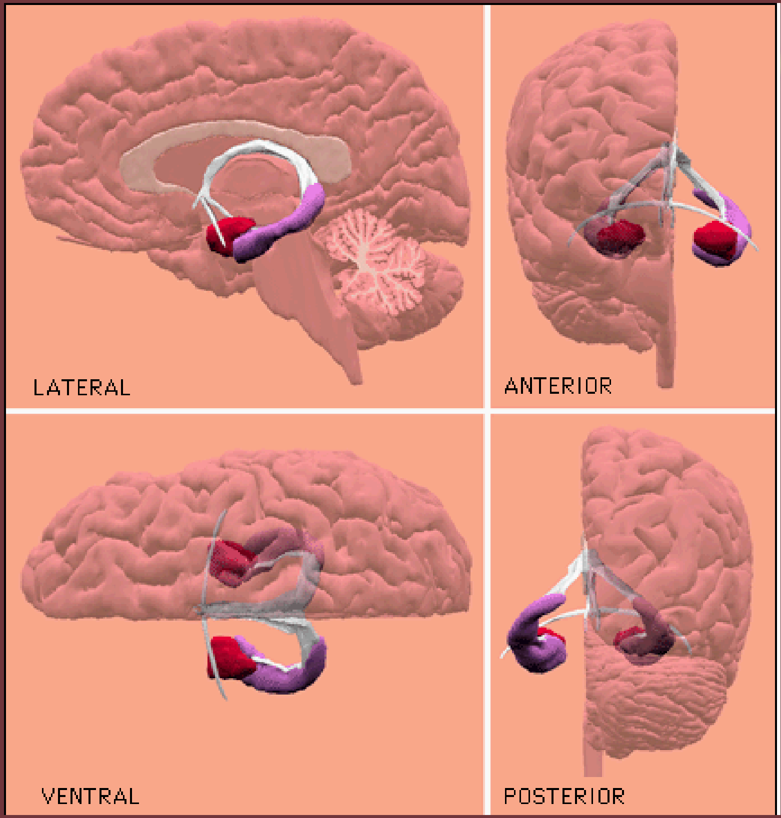
Plan

- Neuroanatomy
  - Terminology
  - Functional neuroanatomy
- Statistical analysis of fMRI data
  - Preprocessing
  - Statistical modeling

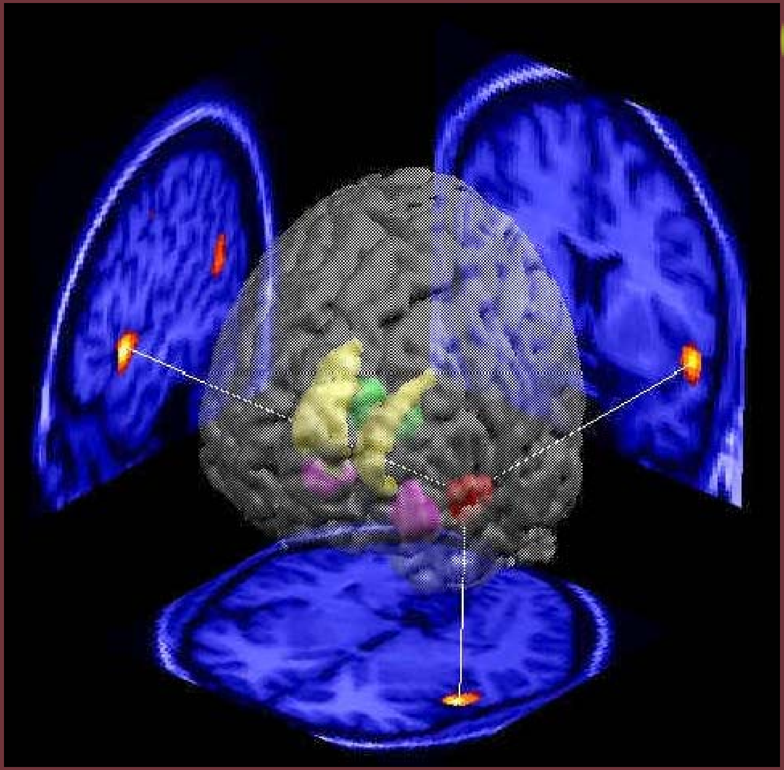
Terminology

- Directions
  - Anterior/Posterior
  - Superior/inferior (dorsal/ventral)
  - Lateral/Medial (also mesial, middle)



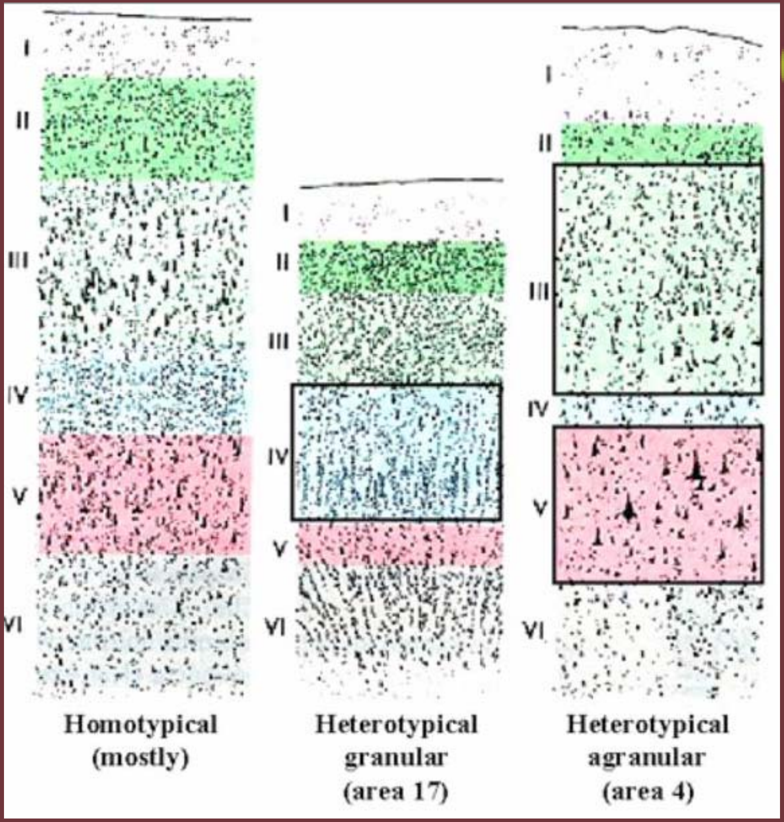
fMRI

- Types of scans
  - Axial: superior - inferior
  - Coronal: anterior - posterior
  - Saggital: left - right



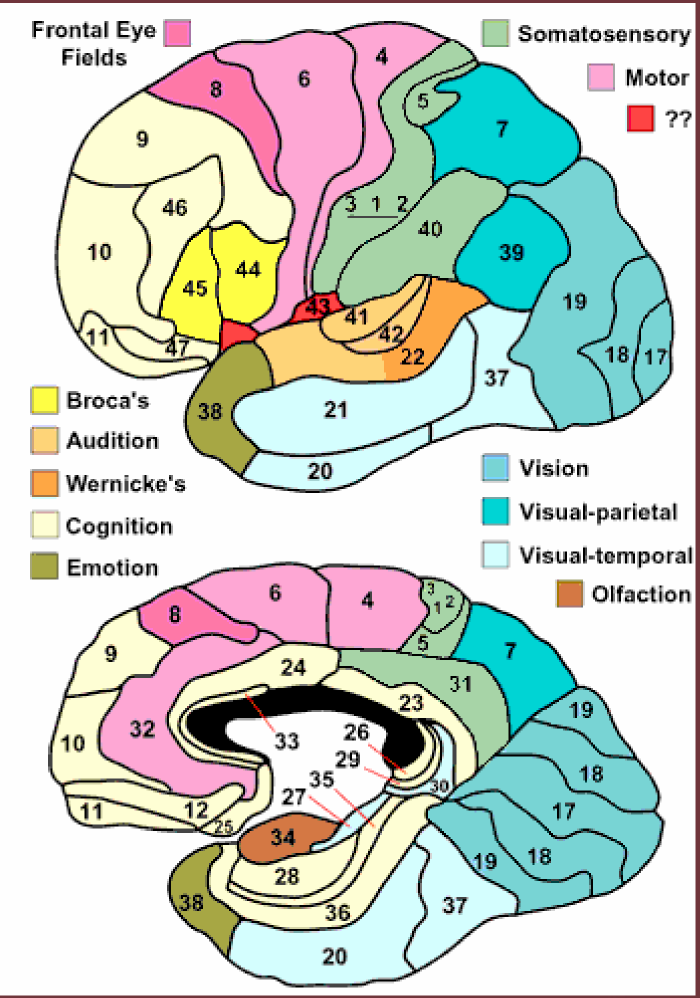
Brodmann Regions

- Cytoarchitecture
  - Cellular composition of a bodily structure
- Cortical columns
  - Group of neurons organized perpendicular to cortical surface
  - Humans 6 layers (~2mm thick), dolphins 5, reptiles 3
- Right: cortical columns of various types

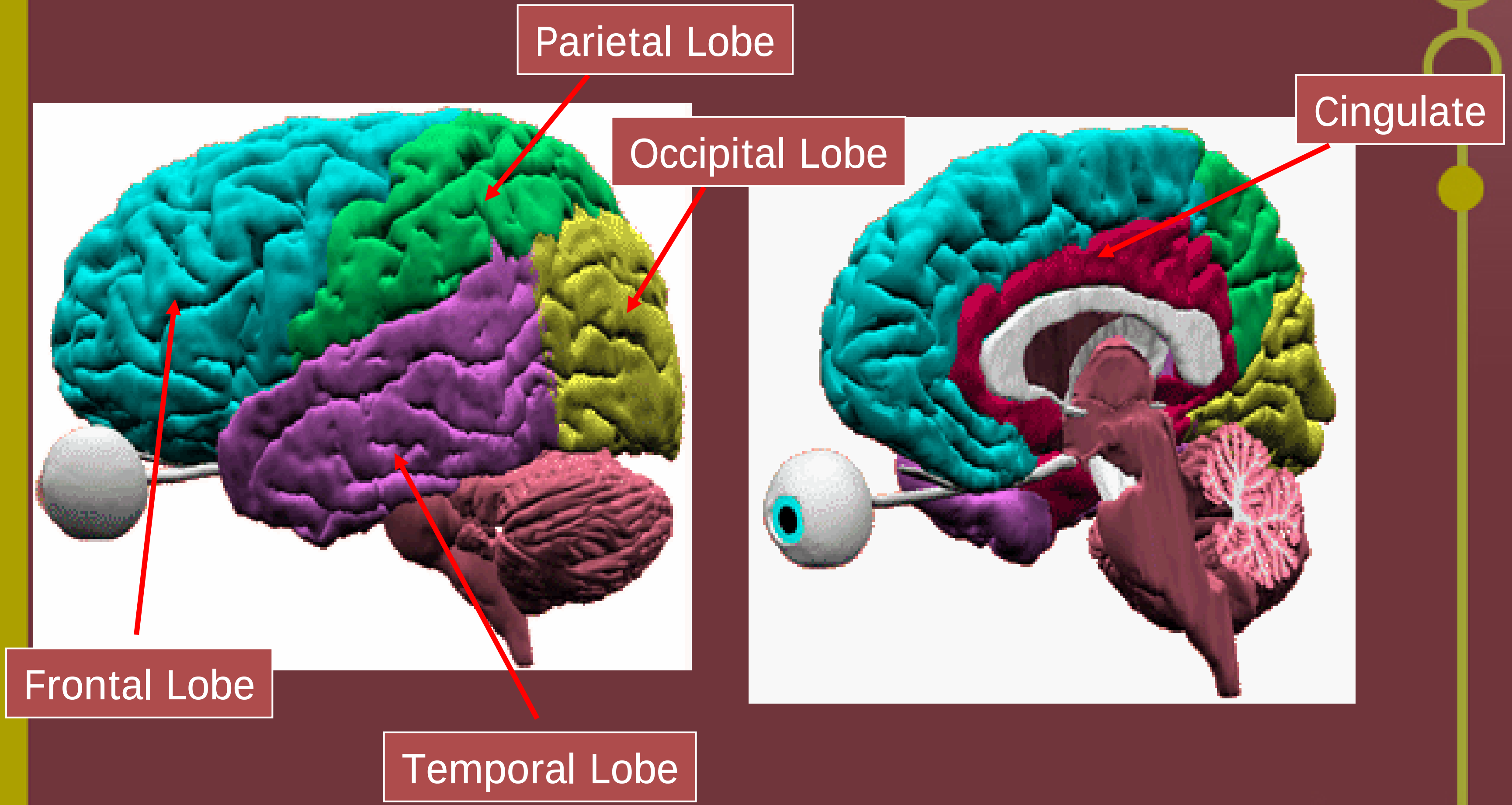


Brodmann Regions

- Korbinian Brodmann
  - Classified cortex according to cytoarchitectural patterns
  - 47 distinct areas
- Model free
  - Assumed nothing about brain functions (perhaps why labeled by numbers)
  - Maps to specific functions surprisingly well (motor cortex)
- Shortcomings

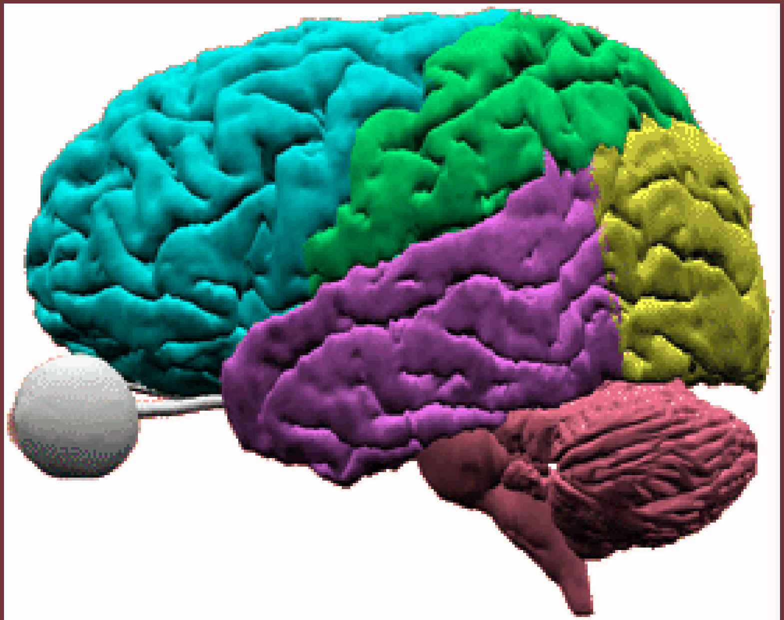


Cerebral Cortex



Frontal Lobe

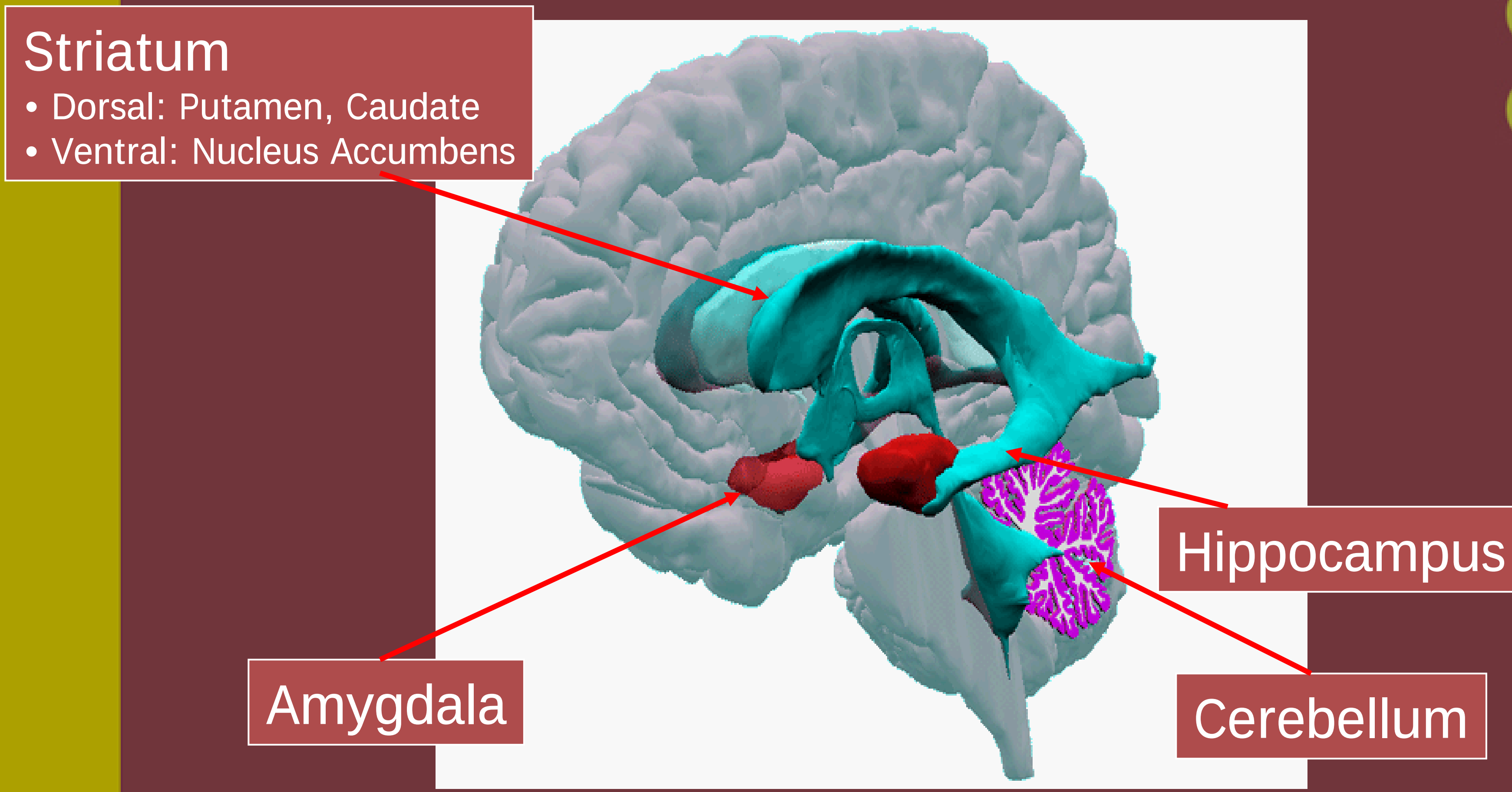
- Orbitofrontal (includes ventromedial and ventrolateral)
  - Reward processing
  - Decision-making
- Dorsolateral
  - Working memory
  - Executive function
- Brodman 8/9
  - Theory of mind
- Lots of other regions, many of them motor/language related



Insula

- Interoception
  - Sense of the physiological condition of the body (Craig)
  - Monitoring of bodily sensations
- Flurry of findings on involvement in decision-making
  - Ultimatum game rejection (Sanfey)
  - Relapsing in smoking (Naqvi)
  - Coding of variance (Preuschoff)
- Caveat

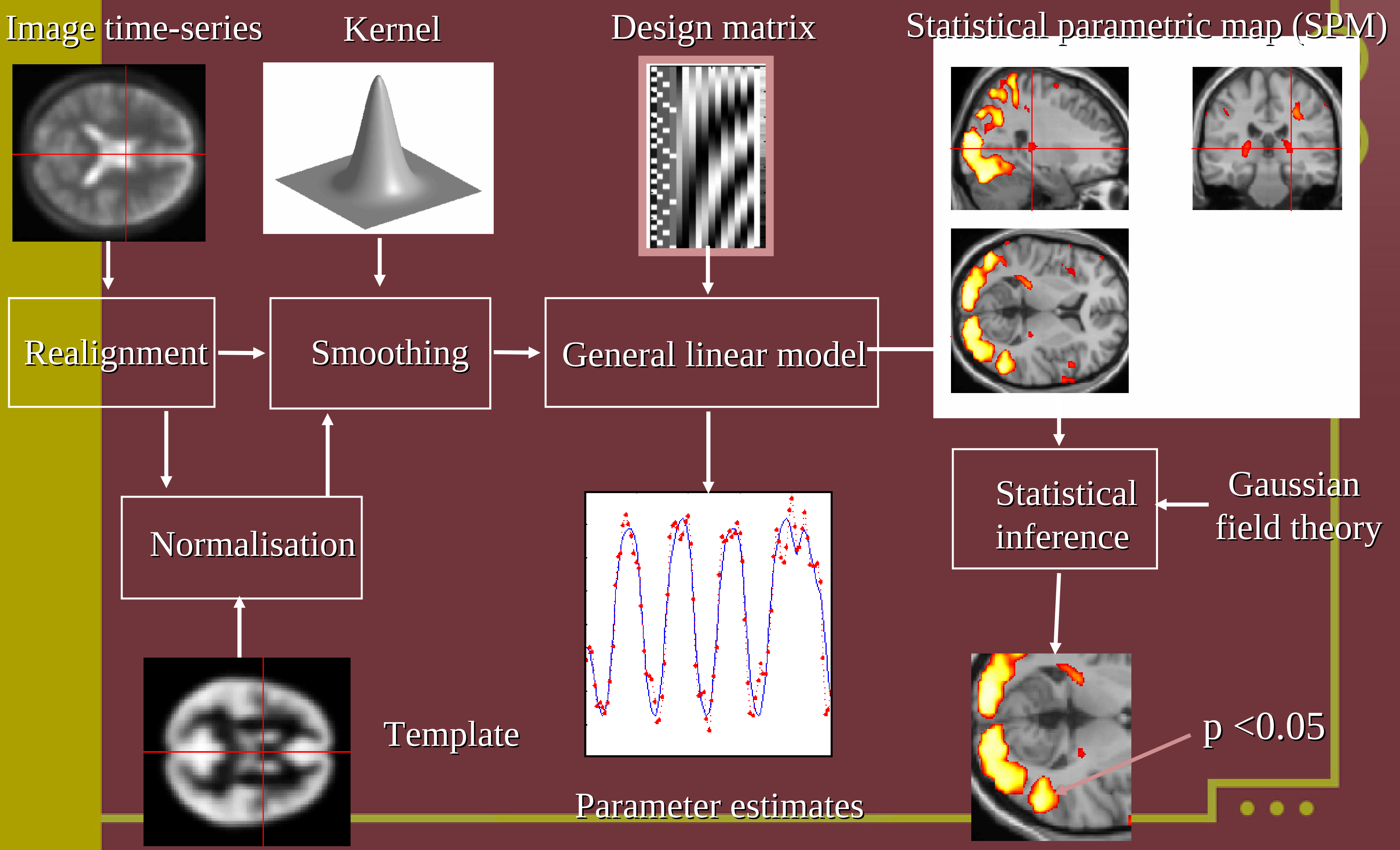
Subcortical Regions



Subcortical Areas

- Striatum: Reward anticipation, reward computation
  - One of the best implicated regions in neuroeconomics
- Amgydala: Fear, vigilance, learning

fMRI Data Analysis

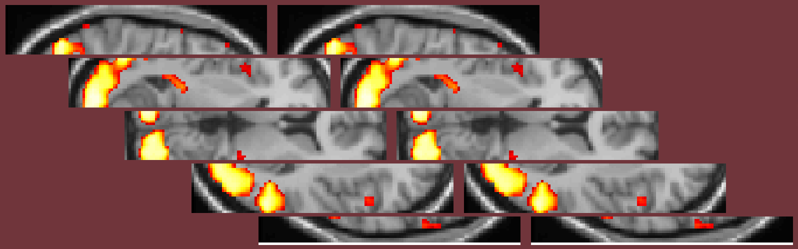


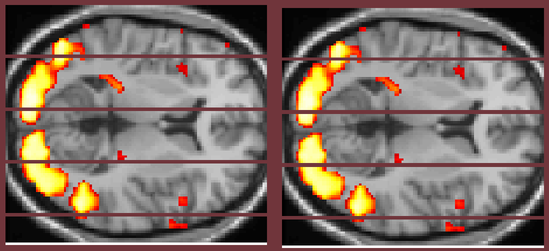
Sources of Noise

- Poor signal to noise ratio in fMRI
  - ~ 0.25 - 0.5% (Huettel et al.)
- Sources of noise
  - Thermal noise (from electrical circuits): biggest contributor, but fortunately white noise.
  - Scanner Drift (small instability in the scanner gradients): Typically introduces linear trend or low frequency noise
  - Subject Motion: Perhaps the most serious source of noise
    - Partial voluming
    - Region misalignment
  - Physiological artifacts: cardiac/respiratory cycles

Slice timing correction

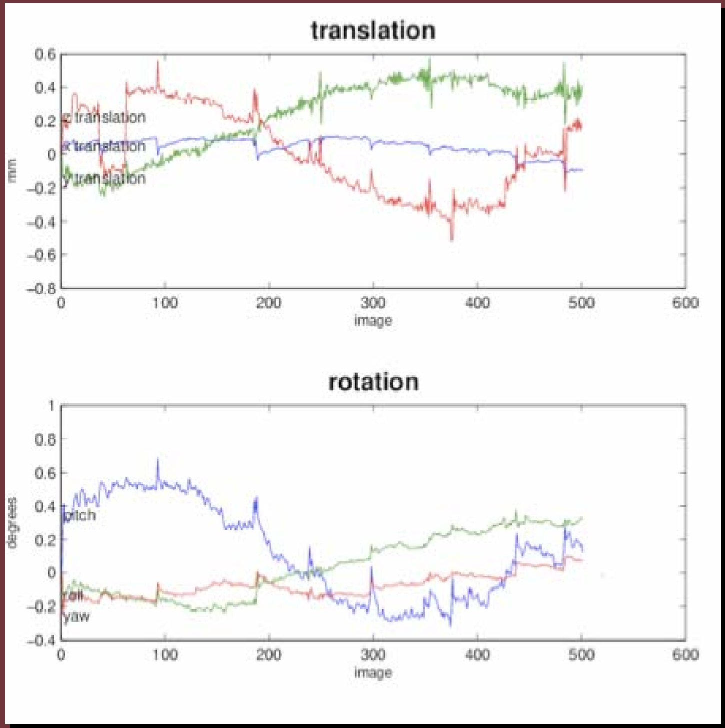
- Different slices acquired at different times
  - ‘Time warp’, as if slices were acquired simultaneously
- Two approaches
  - Shift signal (temporal interpolation)
  - Shift regressor
- Former done for computational constraints





Realignment (Motion Correction)

- Head movements
  - Some degree inevitable
- Assumes head movements do not affect head shape
- Six parameters:
  - 3x translations & 3x rotations
    [x1 y1 z1] = M x [xo yo zo]



Slice timing correction: issues

- Shortcomings of separating slice timing and motion correction
  - Before realignment
    - Assume head is still: one slice of brain per slice of time.
    - Head movements can cause slice-overlap or separation -> interpolation over wrong brain areas
    - Realignment may propagate error to other volumes.
  - After realignment
    - Realignment after head movement may shift voxels onto successive slices -> incorrect temporal ordering

Coregistration

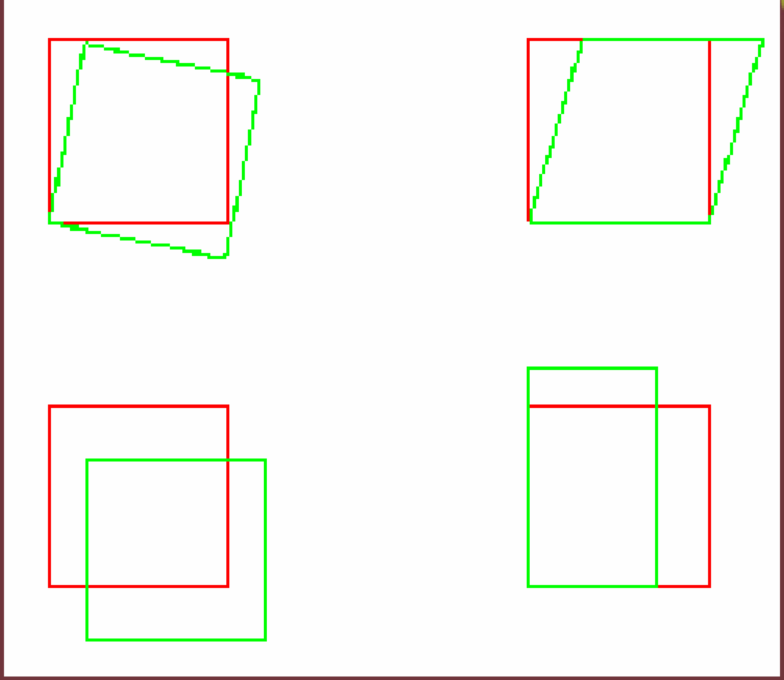
- Align brains between different modalities
  - Within subjects
  - E.g., T1 MRI and functional MRI
  - Not that interesting

Normalization

- Standardize brains across subjects
  - Between subjects
  - Derive group statistics
  - Critical for studying cognitive functions

Normalization

- Two approaches
  - “Standard” brain (exogenous): MNI, Talairach
  - “Group” brain (endogenous): BrainVoyager (less common)
- Affine transform
  - rigid-body + shears and zooms = 12 params
  - zoom fails with insufficient slices (e.g. non-isotropic voxels)
  - prior data helps predict z-zoom from x&y-zoom

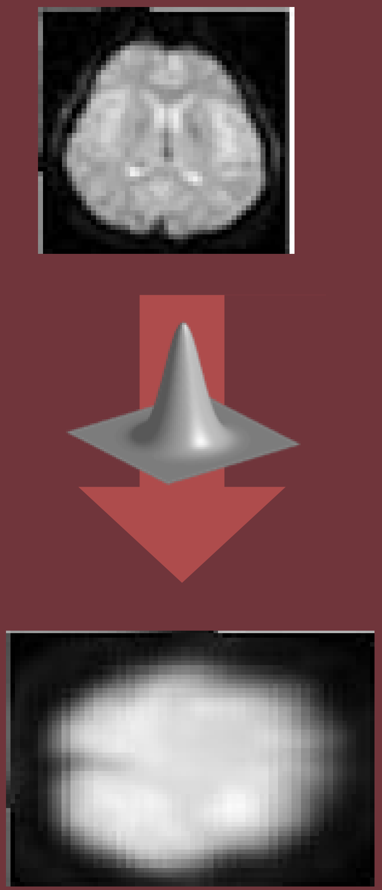


Normalization

- Problems
  - Perfection is not enough
  - Structural alignment doesn't guarantee functional alignment.
  - Fit is limited by differences in gyral anatomy and physiology between subjects.

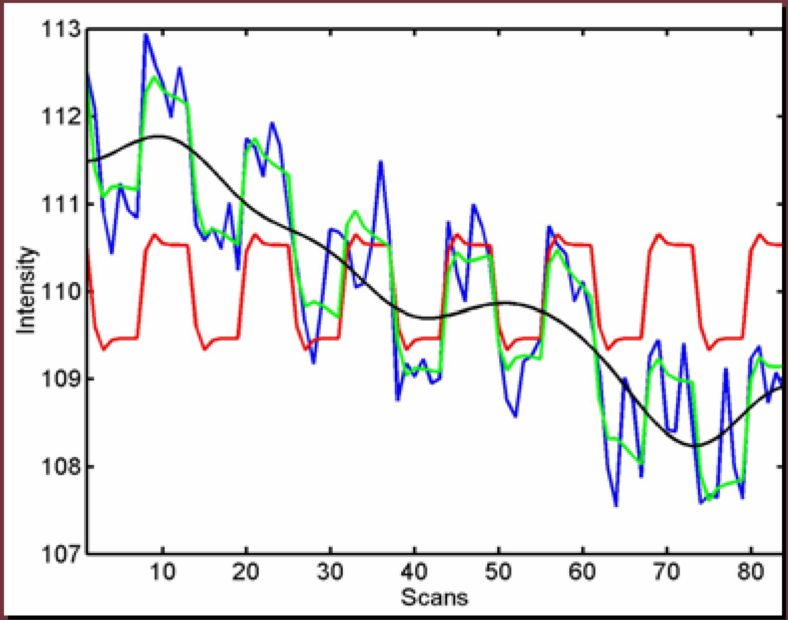
Spatial Smoothing

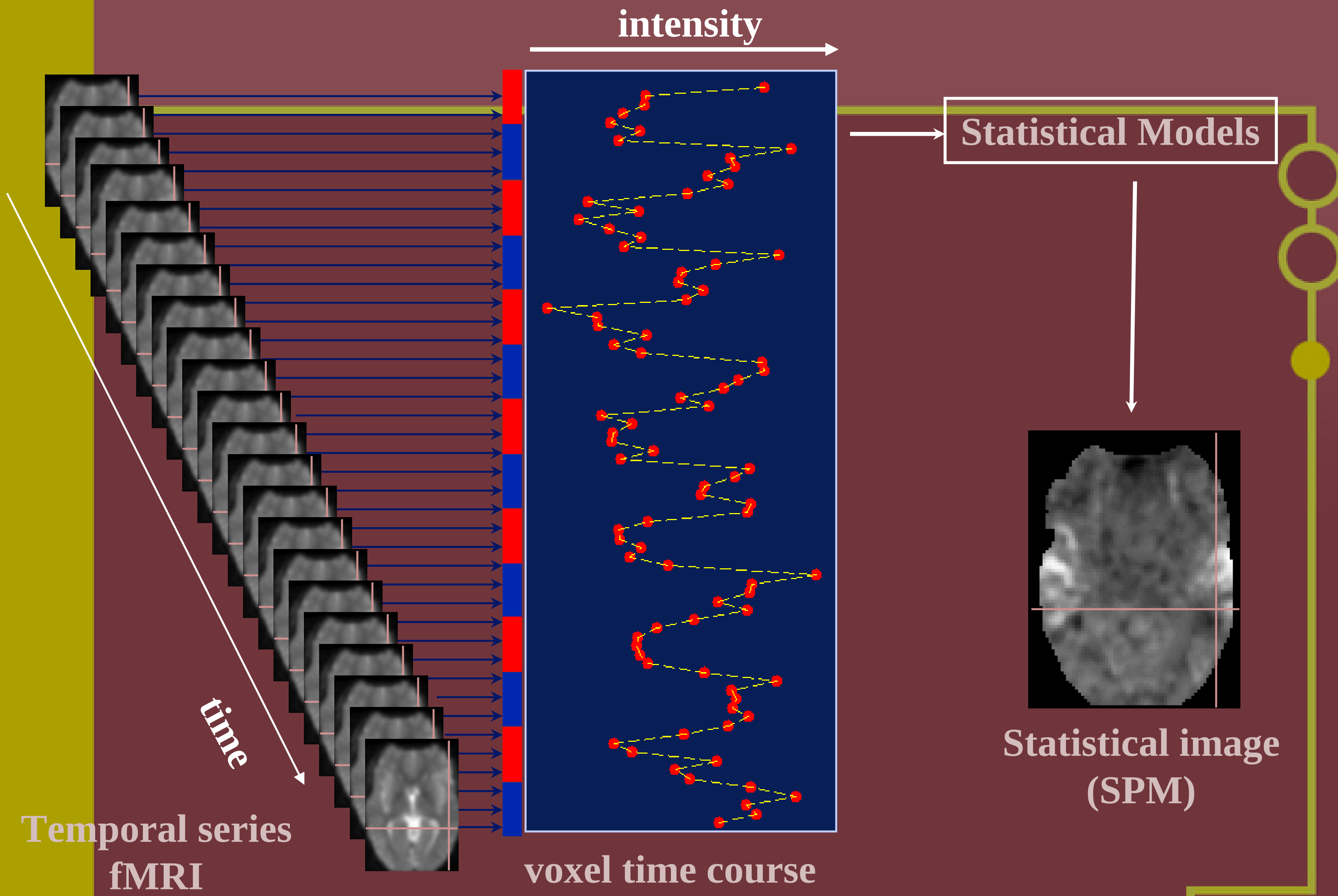
- Increase signal to noise ratio
  - Matched filter theorem
- Challenges
  - FWHM unknown
  - Potentially vary across region/people
  - Current: impose exogenously



Low Frequency Noise

- Sources of noise
  - Cardiac/respiratory
  - Scanner drift
  - Other physiological
- Solutions
  - High-pass filter (most common)
  - Pre-whiten
  - Include in regression



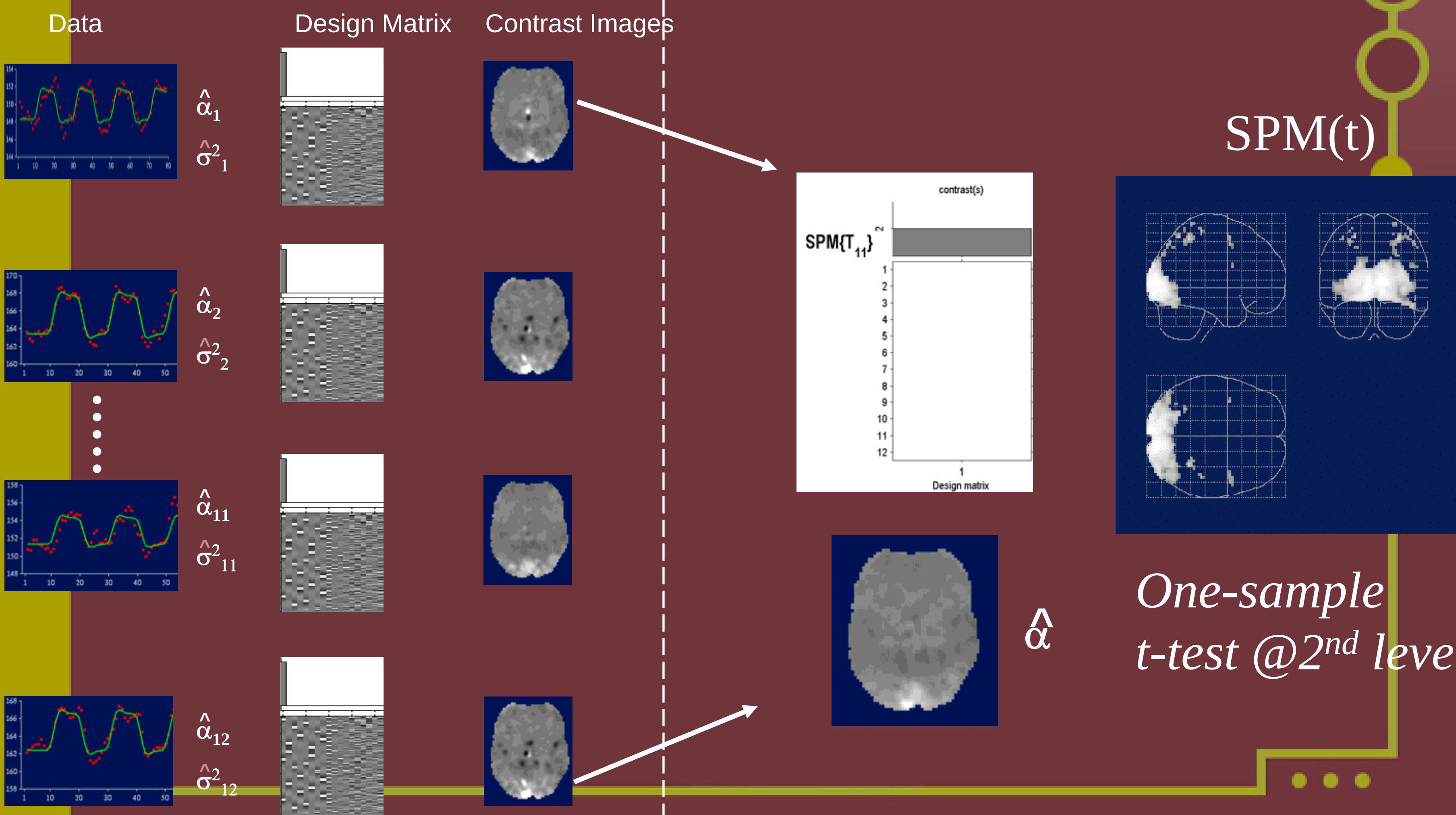

intensity
Statistical Models
time
Temporal series
fMRI
voxel time course
Statistical image
(SPM)

Choice of Techniques

- Model free
  - PCA/ICA
  - Can be difficult to interpret
- Model based
  - Need good prior model
  - Ease of interpretation
  - Most commonly use GLM

Random Effects: “Summary Statistic”

1st Level | 2nd Level



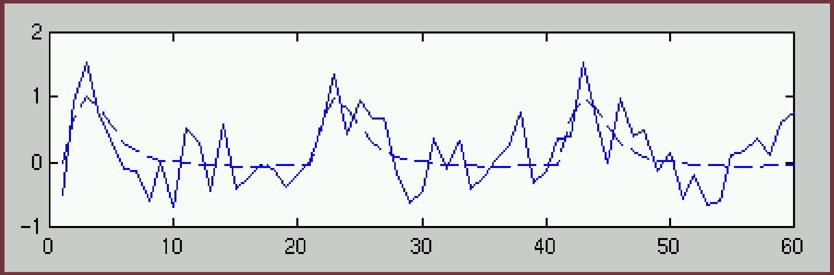
Panel Data

- Classical approach: random effects
  - “Summary statistics” approach (assumes subjects iid)
  - Computationally cheap
  - Require balanced design
- Bayesian (uncommon)
  - Computationally expensive
  - Choice of priors (empirical Bayes)

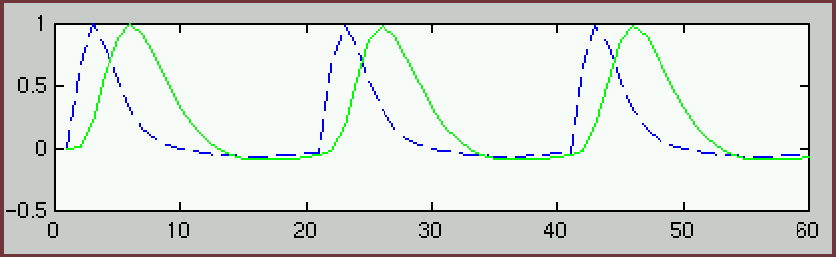
Computational Issues

- 3-Dimensional panel
  - Cross section: ~ 64x64x30 voxels
  - Temporal dimension in the 100s.
  - Group sizes in the 10s.
- Voxel-wise regression
  - Massive computational demand
  - Shortcuts…

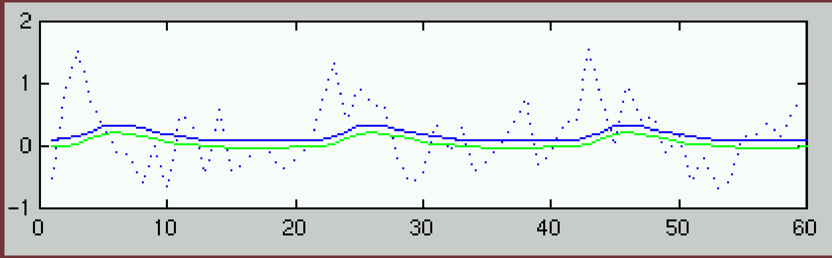
Timing Issues



True signal (-)
observed signal (--)



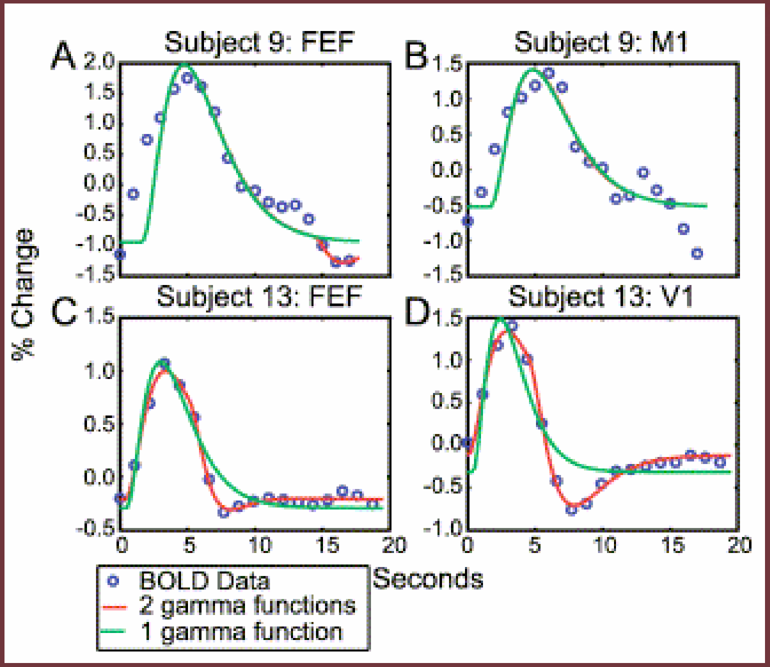
Model (green)
TRUE signal (blue)



Biased estimate

Hemodynamic Response

- Regional Variation (within brain)
  - Derived from visual cortex
  - Some evidence of regional variation
- Individual Differences (between brain)
  - Most clearly violated in elderly and those with pathologies

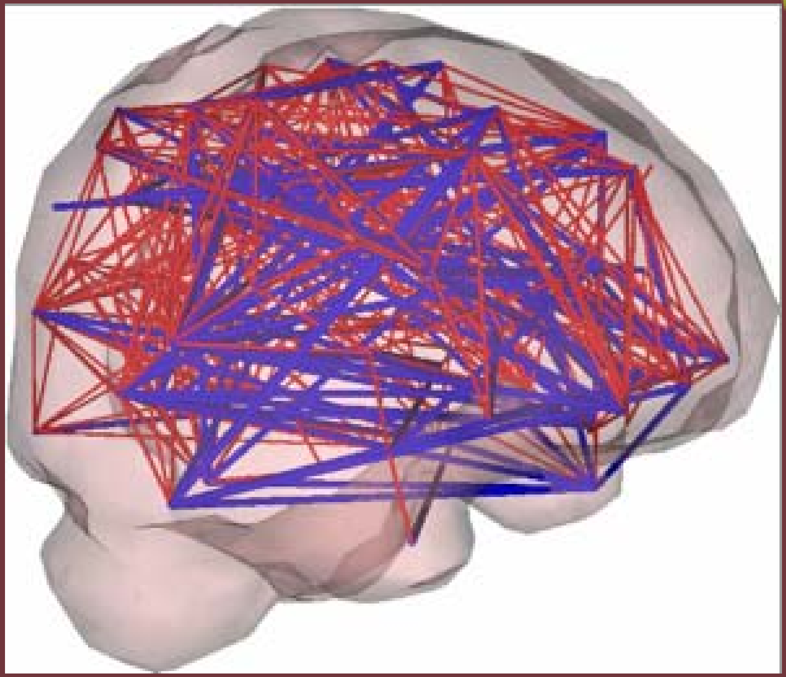


Correlational Structure

- Panel data with both
  - Serial correlation
  - Spatial correlation
- Serial correlation
  - AR(1) appears to be adequate
- Spatial correlation
  - Much more difficult

Spatial Correlation

- Current technique:
  - Average out noise
  - Apply spatial smoothing
  - Ignore neural circuitry



Spatial Correlation: Problems

- Physical distance not representative of synaptic distance
  - E.g., visual cortex in *back* of head, but just a few synapses from retinal neurons
- Incomplete (also asymmetric) knowledge of neural connectivity
  - ~10^{10} neurons in the brain, and up to 15,000 connections between neurons
  - Some regions more explored than others
  - E.g., hippocampus vs. precuneus

Statistical Inference

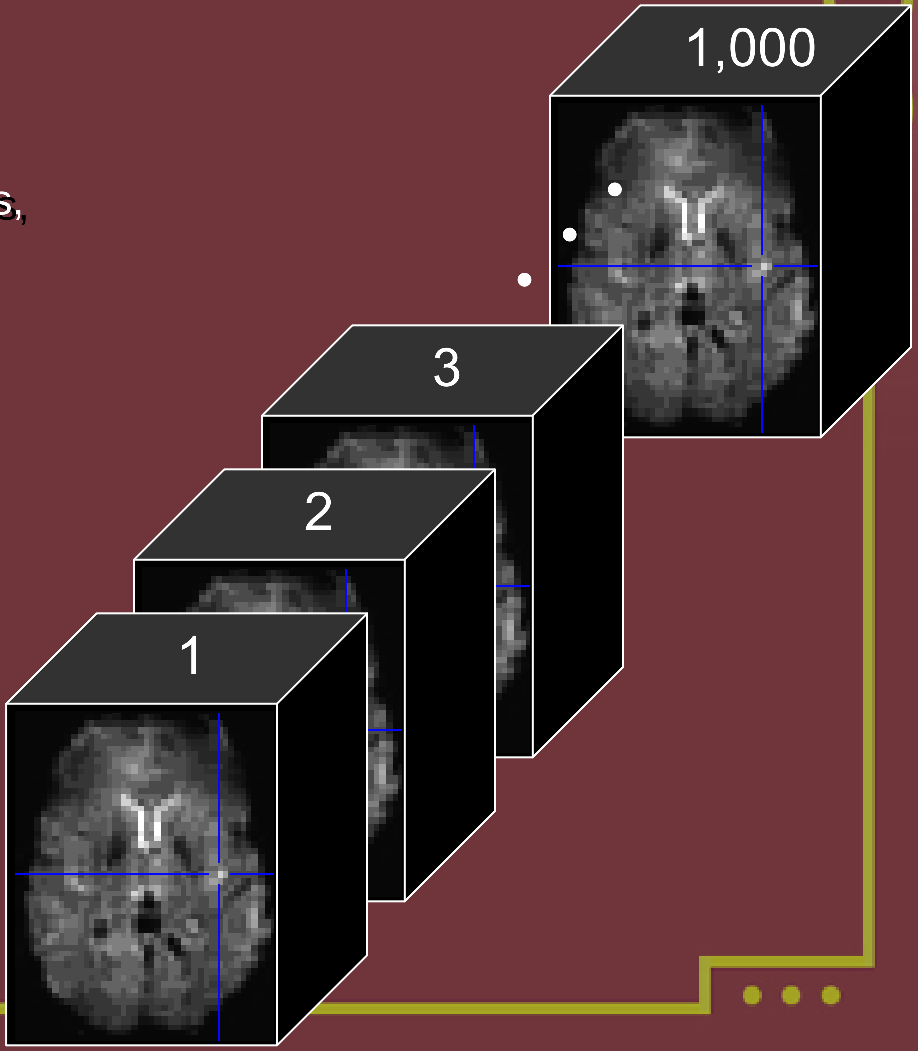
- How do we assess significance?
  - Multiple comparison problem
- Approach
  - Many issues/tradeoffs
  - Many choices
  - Sadly current practice is all over the place

Statistical Inference

- Issues
  - Computational (as always)
  - Cluster-level/voxel level?
  - Incorporate prior information (How?)
- Choices
  - Bonferroni
  - False Discovery Rate

fMRI Multiple Comparisons Problem

- 4-Dimensional Data
  - 1,000 multivariate observations, each with 100,000 elements
  - 100,000 time series, each with 1,000 observations
- Massively Univariate Approach
  - 100,000 hypothesis tests
- Massive MCP!

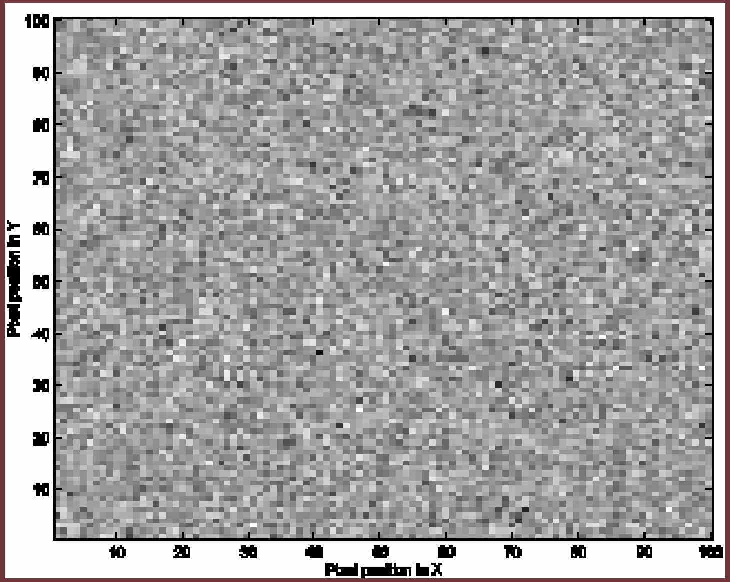


Multiple Comparison Problem

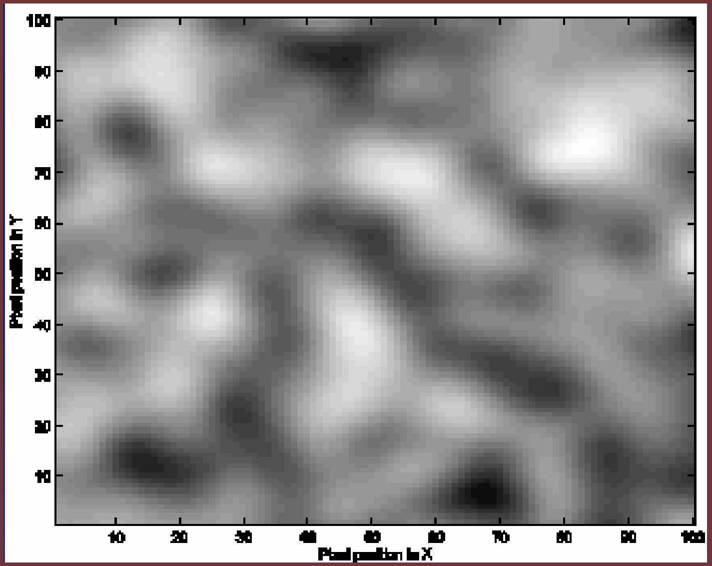
- A MCP Solution Must Control False Positives
  - How to measure multiple false positives?
- Familywise Error Rate (FWER)
  - Chance of any false positives
  - Controlled by Bonferroni & Random Field Methods
- False Discovery Rate (FDR)
  - Proportion of false positives among rejected tests

Bonferroni

Independent Voxels

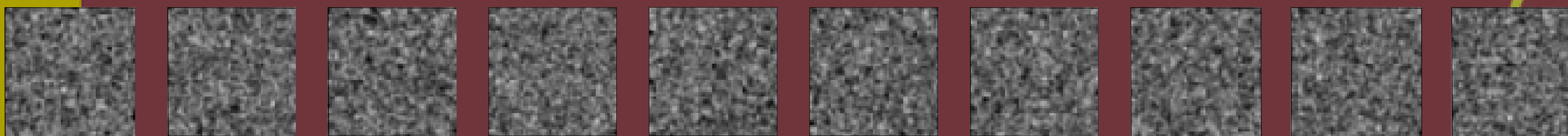


Spatially Correlated

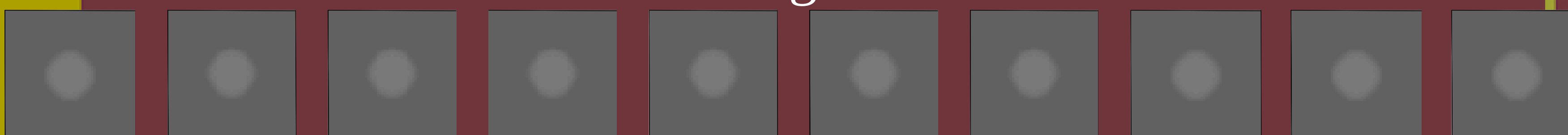


Multiple Comparison Ilustration

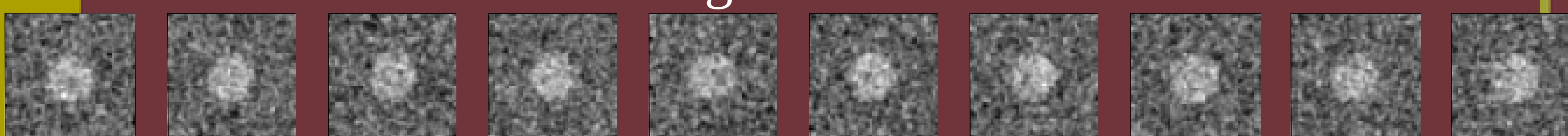
Noise



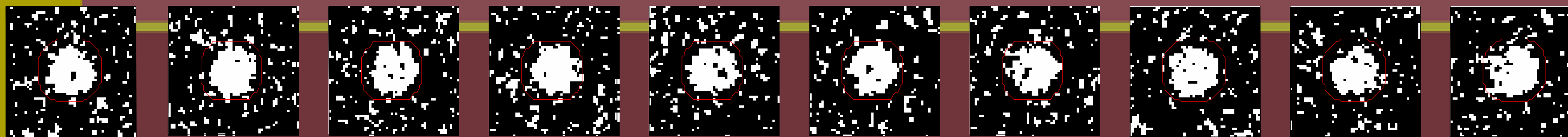
Signal



Signal+Noise



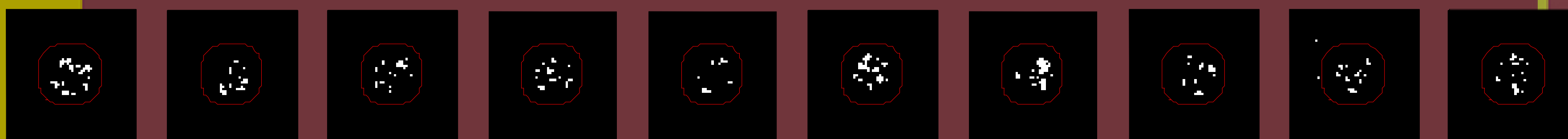
Control of Per Comparison Rate at 10%



11.3% 11.3% 12.5% 10.8% 11.5% 10.0% 10.7% 11.2% 10.2% 9.5%

Percentage of Null Pixels that are False Positives

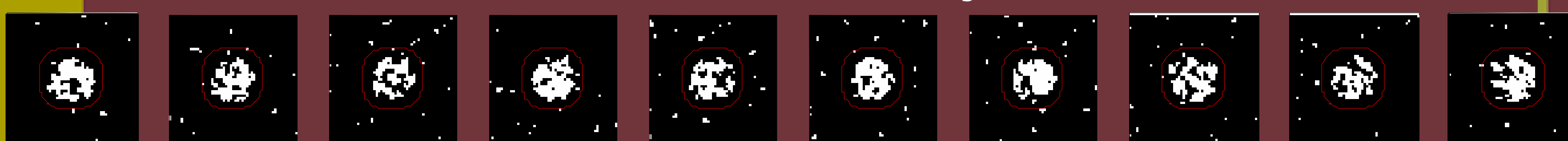
Control of Familywise Error Rate at 10%



FWE

Occurrence of Familywise Error

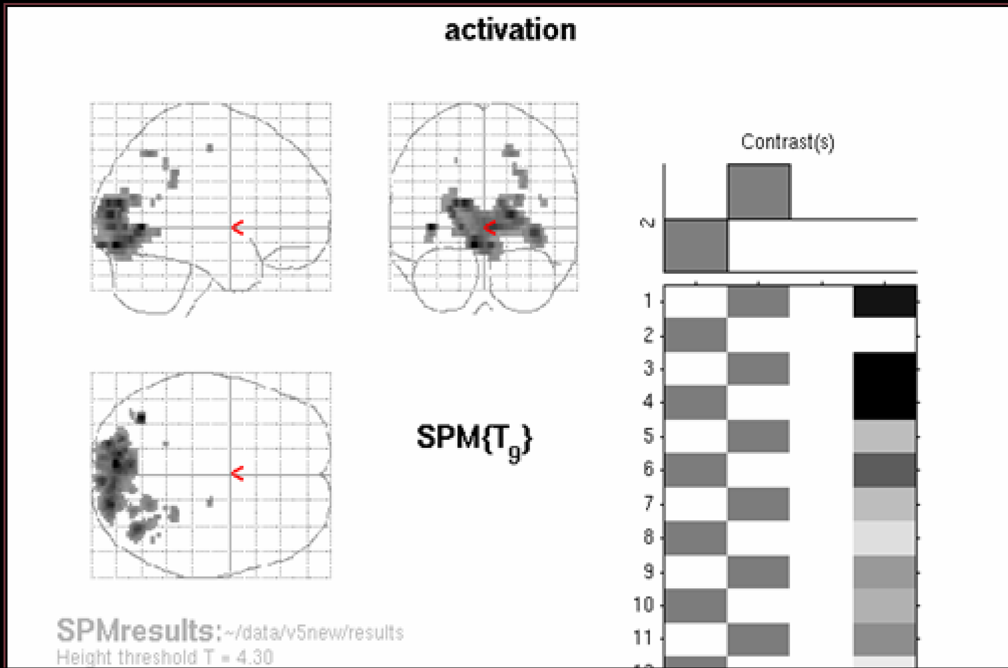
Control of False Discovery Rate at 10%



6.7% 10.4% 14.9% 9.3% 16.2% 13.8% 14.0% 10.5% 12.2% 8.7%

Percentage of Activated Pixels that are False Positives

Cluster vs. Voxel Level



Activations Significant at Cluster level But not at Voxel Level

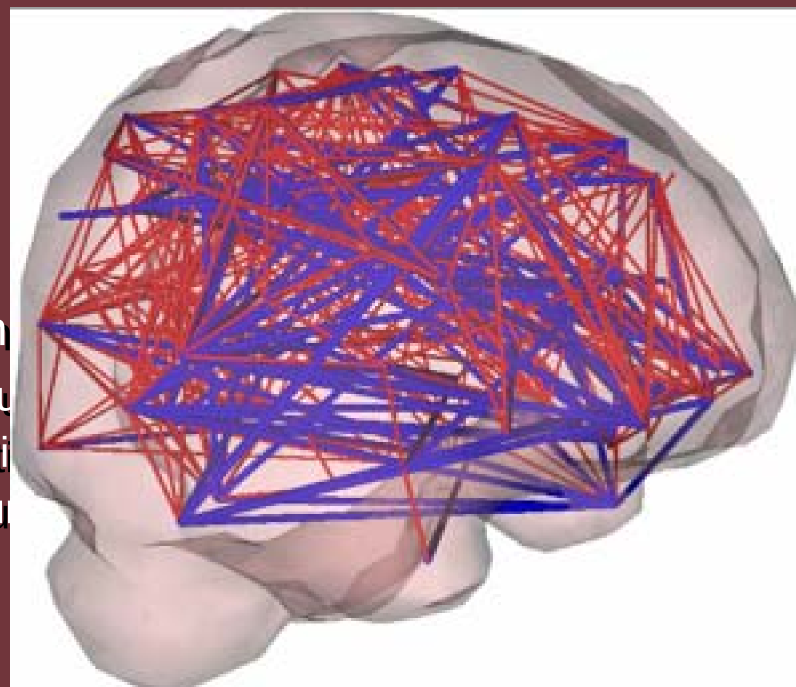
Statistics: *volume summary (p-values corrected for entire volume)*

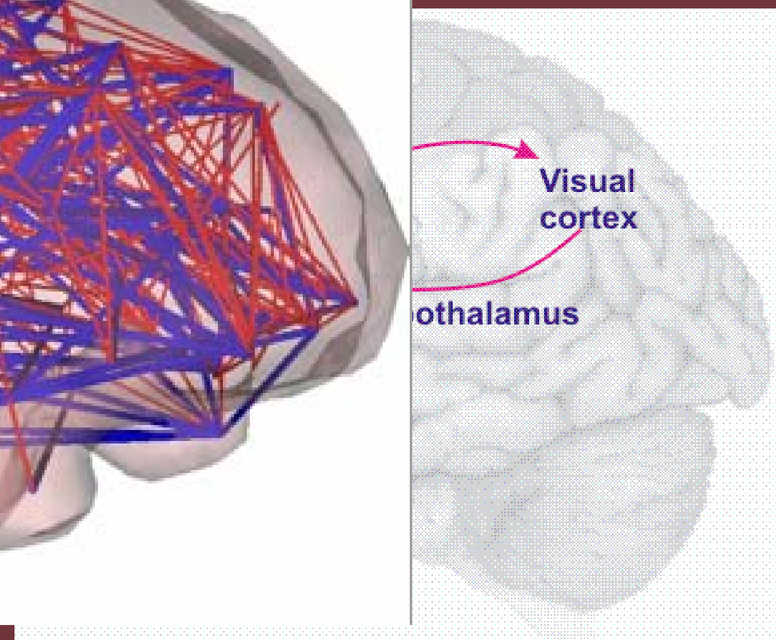
set-level		cluster-level			voxel-level				x,y,z {mm}
p	c	p corrected	k	p uncorrected	p corrected	T	($Z_{\equiv}$)	p uncorrected	
0.964	**11**	**0.000**	**1285**	**0.000**	**0.109**	**12.51**	**(5.01)**	**0.000**	**-8 -82 -12**
					0.269	10.43	(4.71)	0.000	20 -86 8
					0.272	10.40	(4.70)	0.000	-14 -80 16
		0.411	**17**	**0.030**	**0.168**	**11.51**	**(4.87)**	**0.000**	**-38 -64 0**
		0.000	**125**	**0.000**	**0.465**	**9.16**	**(4.48)**	**0.000**	**36 -66 -4**
					0.997	5.74	(3.63)	0.000	28 -52 -4

END

Spatial Correlation

- Current techn
  - Average ou
  - Apply spati
  - Ignore neu



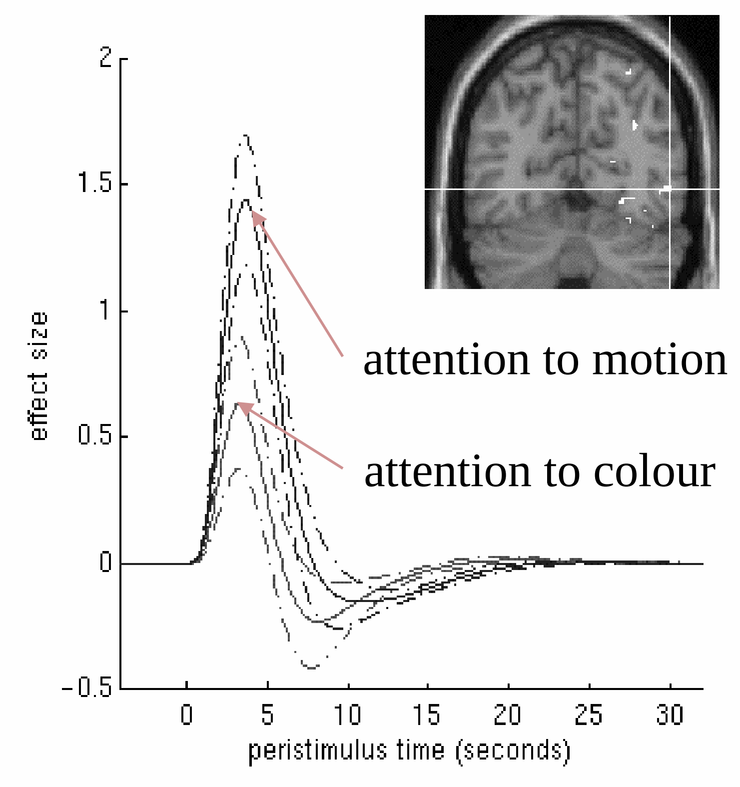


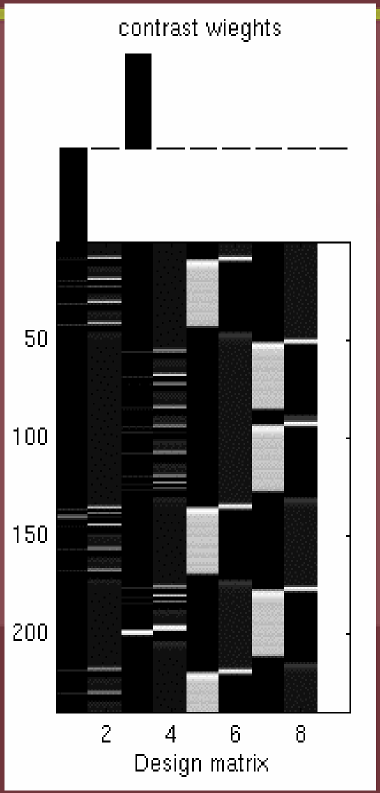
Choices …

- Time domain / frequency domain?
- AR / ARMA / state space models?
- Linear / non-linear time series model?
- Fixed HRF / estimated HRF?
- Voxel / local / global parameters?
- Fixed effects / random effects?
- Frequentist / Bayesian?

Interactions between set and event-related responses:

Attentional modulation of V5 responses





Benjamini & Hochberg Procedure

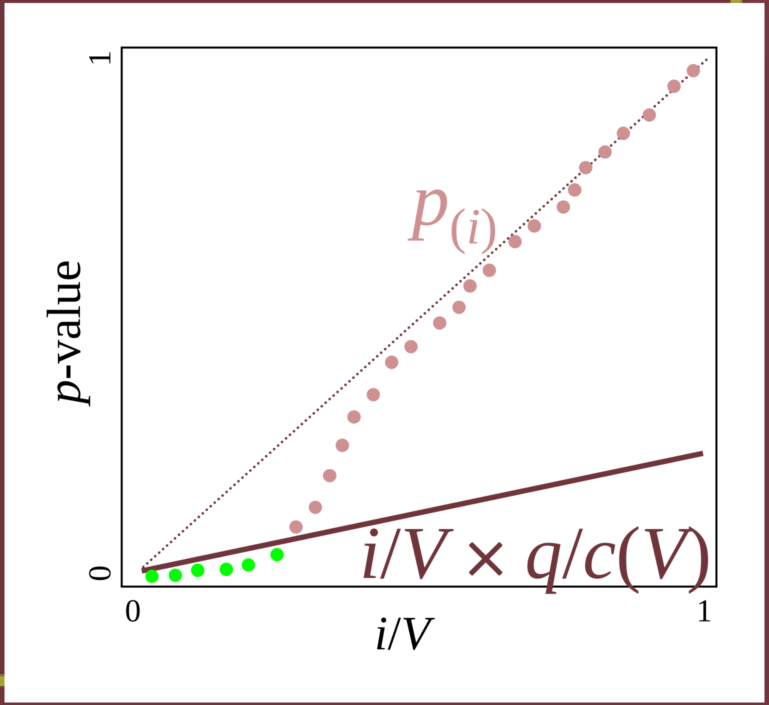
- $c(V) = 1$
  - Positive Regression Dependency on Subsets
    - Technical condition, special cases include
      - Independent data
      - Multivariate Normal with all positive correlations
    - Result by Benjamini & Yekutieli
- $c(V) = \Sigma_{i=1,\ldots,V}\ 1/i \approx \log(V)+0.5772$
  - Arbitrary covariance structure

Benjamini & Hochberg Procedure

- Select desired limit q on E(FDR)
- Order p-values, $p_{(1)} \leq p_{(2)} \leq \ \dots \leq p_{(V)}$
- Let r be largest i such that

$$p_{(i)} \leq \ i/V \times q/c(V)$$

- Re corresponding to $p_{(1)}, \dots , p_{(r)}$.



JRSS-B (1995) 57:289-300

False Discovery Rate

Consider testing $H_1, H_2, \ldots, H_m$ based on the corresponding p-values $P_1, P_2, \ldots, P_m$. Let $P_{(1)} \leqslant P_{(2)} \leqslant \ldots \leqslant P_{(m)}$ be the ordered p-values, and denote by $H_{(i)}$ the null hypothesis corresponding to $P_{(i)}$. Define the following Bonferroni-type multiple-testing procedure:

$$\text{let } k \text{ be the largest } i \text{ for which } P_{(i)} \leqslant \frac{i}{m} q^*;$$

$$\text{then reject all } H_{(i)} \; i = 1, 2, \ldots, k. \tag{1}$$

Theorem 1. For independent test statistics and for any configuration of false null hypotheses, the above procedure controls the FDR at q^*.

Theorem 2. The FDR controlling procedure given by expression (1) is the solution of the following constrained maximization problem:

$$\text{choose } \alpha \text{ that maximizes the number of rejections at this level, } r(\alpha),$$

$$\text{subject to the constraint } \alpha m / r(\alpha) \leqslant q^*. \tag{3}$$