

# Functional Brain MRI

Part IV: fMRI Paradigm Design & Analysis

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## Lecture Handouts

[http://www.meduniwien.ac.at/hochfeld-mr/de/page/page\\_77.html](http://www.meduniwien.ac.at/hochfeld-mr/de/page/page_77.html)

## Outline

- fMRI design
  - blocked design
  - event-related design
- BOLD imaging sequences
- Stimuli

## fMRI Experiment

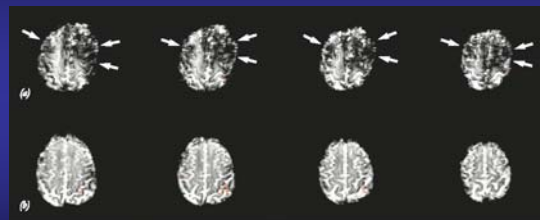
- Brain images are repeatedly acquired during an fMRI measurement, up to several thousand times
- Matrix sizes: from 64x64 to 128x128
- Repetition times: from a few hundred milliseconds to several seconds
- Stimulation types
  - visual (projected on a screen or via goggles)
  - acoustic

## BOLD-fMRI Acquisition Problems

- Shimming quality
- Susceptibility artifacts
- Physiological noise

## EPI-Acquisition

- Shimming quality

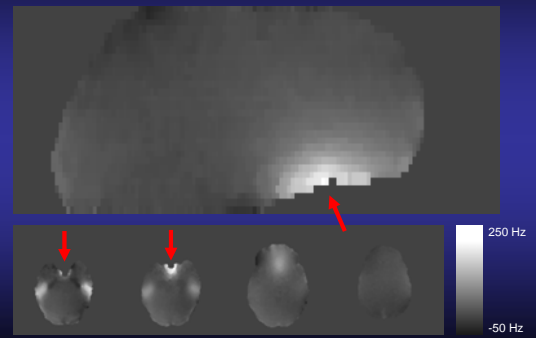


MA=128x128, TE/TR=80/4000  
Motor task, block-design

## Susceptibility Artifacts

- Local magnetic field is distorted around areas of changing susceptibility
  - bone/tissue boundaries
  - air cavities
- Field inhomogeneities cause
  - signal loss via intra-voxel dephasing
  - geometrical distortions
    - pixel shifts in EPI sequences
    - blurring in spiral sequences

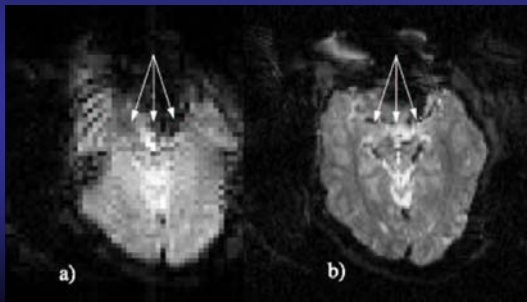
## Field Distribution in the Brain



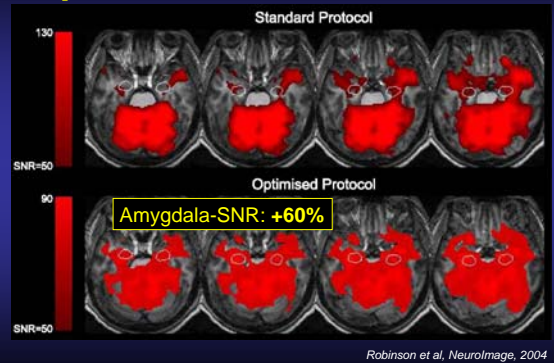
## Signal Loss

Low-resolution EPI  
Voxel size 47  $\mu$ l

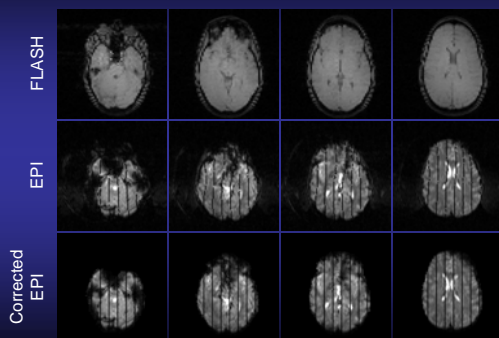
High-resolution EPI  
Voxel size 6  $\mu$ l



## Spatial Resolution and SNR



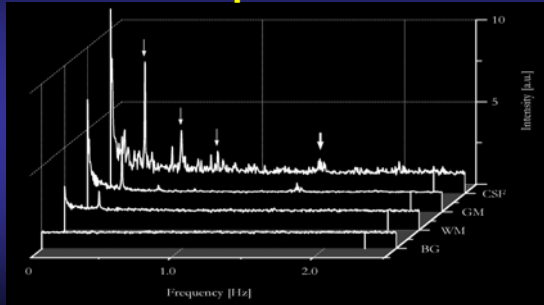
## Geometrical Distortions



## Physiological Artifacts

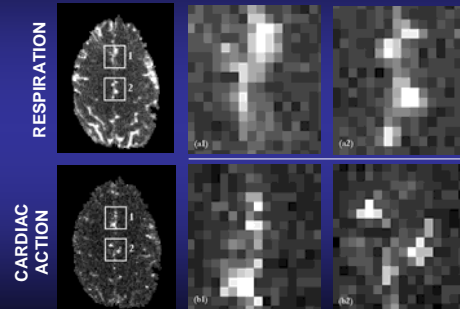
- Cardiac action  $\rightarrow$  Blood flow pulsation
- Respiration  $\rightarrow$  B<sub>0</sub>-fluctuation, Hb-changes
- Significant source of temporal instabilities
- Increase with higher fields
- Main concern for fMRI in deep brain regions

## Physiological Artifacts: Spectra



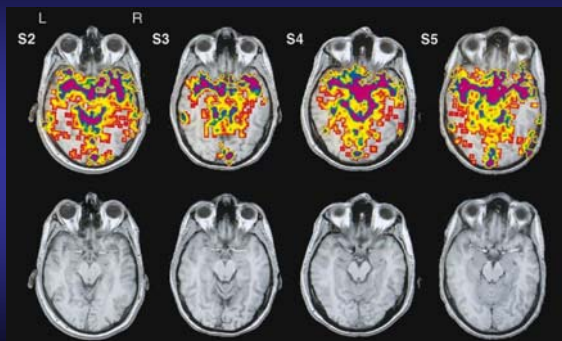
Windischberger et al, MRI, 2002

## Physiological Artifacts: Arteries vs. Veins



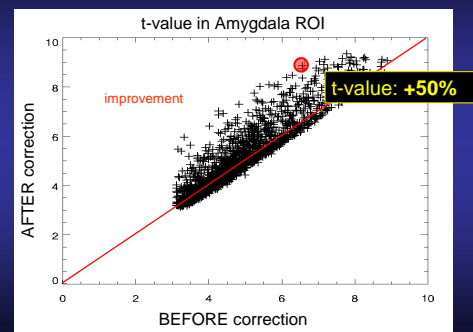
Windischberger et al, MRI, 2002

## Cardiac artifacts



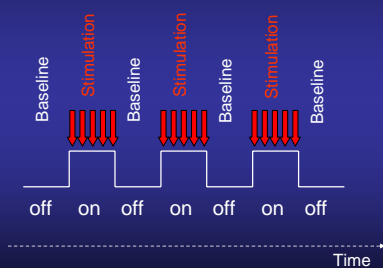
Dagli et al, NeuroImage, 1999

## Physiological artifacts in the Amygdala



Windischberger et al, HBM, 2004

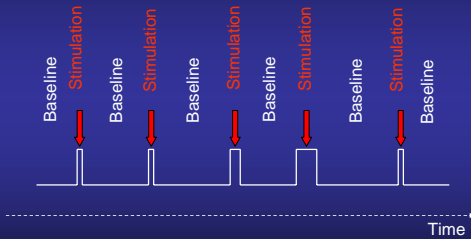
## Blocked fMRI Experiment



## Block design

- compare long periods (e.g., 16 sec) of one condition with long periods of another
- traditional approach
- most statistically powerful approach
- less dependent on how well you model the haemodynamic response

## Event-Related fMRI Experiment



## Event-related design

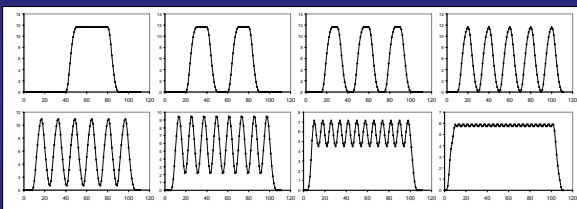
- compare brief trials (e.g., 1 sec) of one condition with brief of another
- quite new (since ~1997) approach
- less statistically powerful but has many advantages
- trials can either be well-spaced to allow the MR signal to return to baseline between trials (e.g., 12+ seconds between trials) or closely spaced (e.g., every 2 sec)

## Block Designs

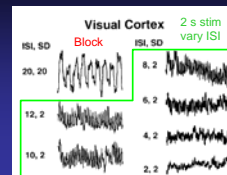
## Choosing Length of Blocks

- **Longer block lengths allow for stability of extended responses**
  - Haemodynamic 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 allow for more transitions**
  - Task-related variability increases (relative to non-task) with increasing numbers of transitions
- **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

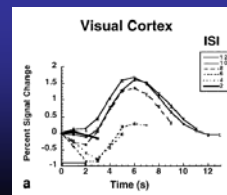
## Effects of Block Interval upon HDR



## Spaced Mixed Trial: Constant ITI



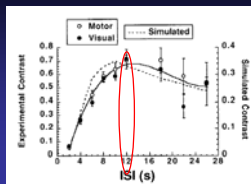
Bandettini et al. (2000)  
What is the optimal trial spacing (duration + intertrial interval, ITI) for a Spaced Mixed Trial design with constant stimulus duration?



Sync with trial onset and average

Source: Bandettini et al., 2000

## Optimal Constant ITI



Source: Bandettini et al., 2000

Brief (< 2 sec) stimuli:  
optimal trial spacing = 12 sec

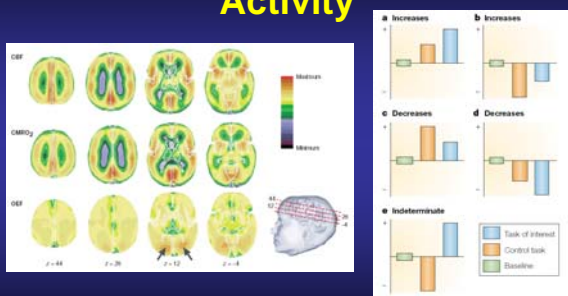
For longer stimuli:  
optimal trial spacing =  $8 + 2 \times \text{stimulus duration}$

Effective loss in power of event related design:  
= -35%  
i.e., for 6 minutes of block design, run ~9 min ER design

## What baseline should you choose?

- **Task A vs. Task B**
  - Example: Squeezing Right Hand vs. Left Hand
  - Allows you to distinguish differential activation between conditions
  - Does not allow identification of activity common to both tasks
    - Can control for uninteresting activity
- **Task A vs. No-task**
  - Example: Squeezing Right Hand vs. Rest
  - Shows you activity associated with task
  - Problem: Rest is not a very well defined state

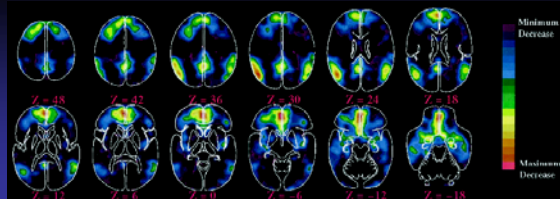
## Interpreting Baseline Activity



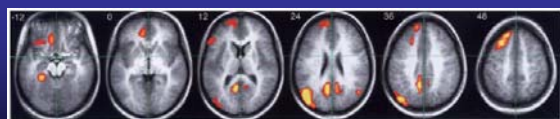
From Gusnard & Raichle, 2001

## Non-Task Processing

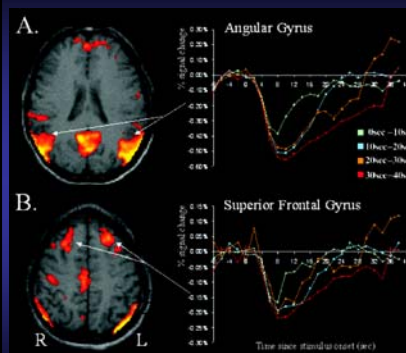
- Sometimes activation is greater in baseline conditions than in task conditions
- Suggests the idea of baseline/resting mental processes
  - Emotional processes
  - Gathering/evaluation about the world around you
  - Awareness (of self)
  - Online monitoring of sensory information
  - Daydreaming



From Shulman et al., 1997 (PET data)



From Binder et al., 1999



From Huettel et al., 2002

From Huettel et al., 2001 (Change Detection)

## Limitations of Blocked Designs

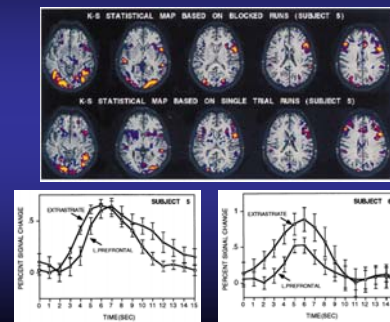
- Very sensitive to signal drift
  - Sensitive to head motion, especially when only a few blocks are used.
- Poor choice of baseline may preclude meaningful conclusions
- Many tasks cannot be conducted repeatedly
- Difficult to estimate the HDR

## Event-Related Designs

## Why use event-related designs?

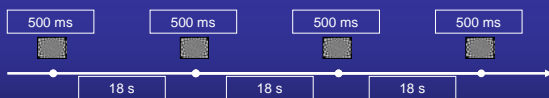
- Some experimental tasks are naturally event-related
- Allows studying of trial effects
- Simple analyses
  - Selective averaging
  - No assumptions of linearity required

## Event-Related and Blocked Designs give Similar Results

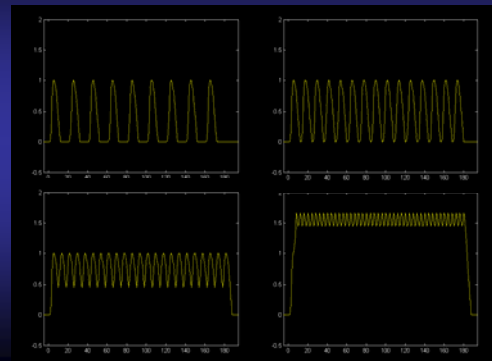


## Periodic Single Trial Designs

- Stimulus events presented infrequently with long interstimulus intervals

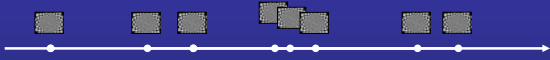


## Trial Spacing Effects: Periodic Designs



## Jittered Single Trial Designs

- Varying the timing of trials within a run



## Effects of Jittering on Stimulus Variance

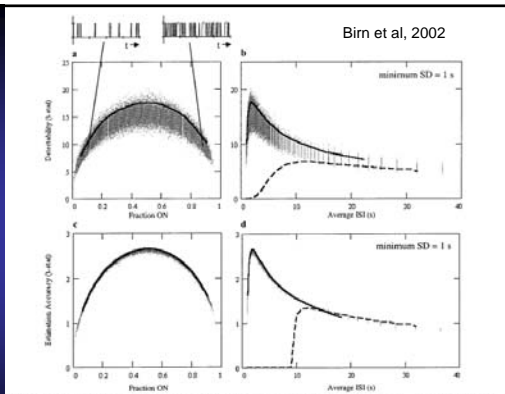
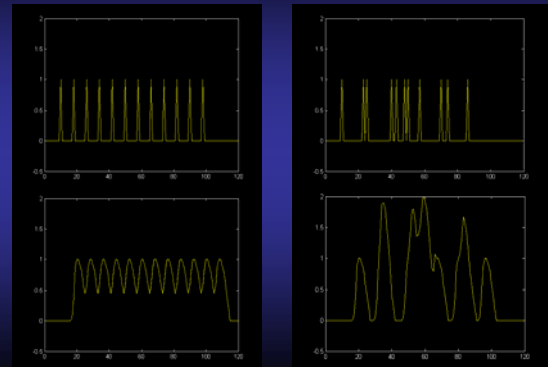
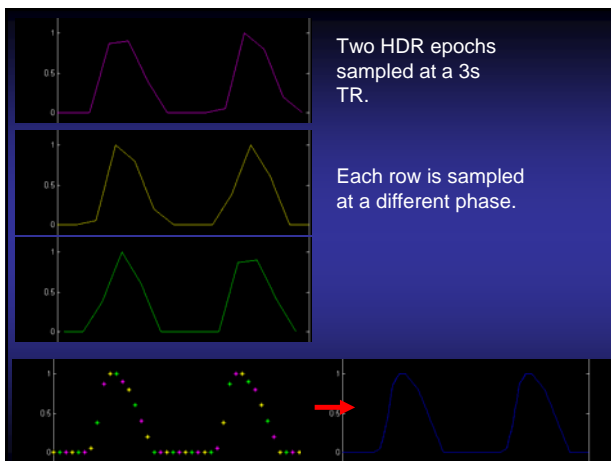


FIG. 2. (a) Detectability of simulated BOLD signal vs fraction of stimulus in the task state for stimulus time series with a varying ISI. (b) Detectability vs average ISI. (c) Accuracy of estimating the impulse response function vs fraction of signal in the task state for stimuli with varying ISI. (d) Estimation accuracy vs average ISI. Each point represents the detectability or estimation accuracy for one time series. Thick line represents the top 5% of stimulus patterns. The dashed line is the detectability for stimuli with a constant ISI. Maximum detectability and IEF estimation accuracy occurs when exactly half the stimuli are in the task state, and half are in the control state, which occurs at an ISI of 2 s for a minimum stimulus duration of 1 s.

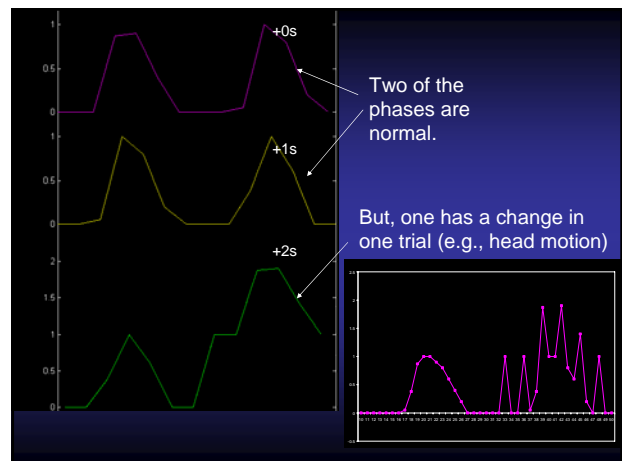
## Staggered Single Trial

- By presenting stimuli at different timings, relative to a TR, you can achieve sub-TR resolution
- Significant cost in number of trials presented
  - Resulting loss in experimental power
- Very sensitive to scanner drift and other sources of variability



Two HDR epochs sampled at a 3s TR.

Each row is sampled at a different phase.



Two of the phases are normal.

But, one has a change in one trial (e.g., head motion)

## Limitations of Event-Related Designs

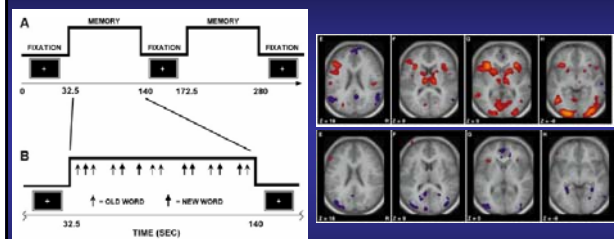
- **Differential effects of interstimulus interval**
  - Long intervals do not optimally increase stimulus variance
  - Short intervals may result in refractory effects
- **Detection ability dependent on form of HDR**
- **Length of “event” may not be known**

## Mixed Designs

## Combination Blocked/Event

- **Both blocked and event-related design aspects are used (for different purposes)**
  - Blocked design is used to evaluate *state-dependent* effects
  - Event-related design is used to evaluate *item-related* effects
- **Analyses are conducted largely independently between the two measures**
  - Cognitive processes are assumed to be independent

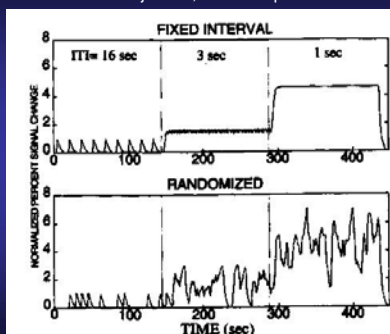
## Mixed designs



Donaldson et al., 2001

## Fixed vs. Random Intervals

If trials are jittered,  $\downarrow$  ITI  $\rightarrow$   $\uparrow$  power



Source: Burock et al., 1998

## Blocked vs. Event-related

BLOCKED:



SPACED MIXED TRIAL:



RAPID MIXED TRIAL:



## Advantages of Event-Related

- 1) **Flexibility and randomization**
  - eliminate predictability of block designs
  - avoid practice effects
- 2) **Post hoc sorting**
  - (e.g., correct vs. incorrect, aware vs. unaware, remembered vs. forgotten items, fast vs. slow RTs)
- 3) **Can look at novelty and priming**
- 4) **Rare or unpredictable events can be measured**
- 5) **Can look at temporal dynamics of response**
  - Dissociation of motion artifacts from activation
  - Dissociate components of delay tasks
  - Mental chronometry

## Summary of Experiment Design

- **Main Issues to Consider**
  - What design constraints are induced by my task?
  - What am I trying to measure?
  - What sorts of non-task-related variability do I want to avoid?
- **Rules of thumb**
  - Blocked Designs:
    - Powerful for detecting activation
    - Useful for examining state changes
  - Event-Related Designs:
    - Powerful for estimating time course of activity
    - Allows determination of baseline activity
    - Best for post hoc trial sorting
  - Mixed Designs
    - Best combination of detection and estimation
    - Much more complicated analyses

## Preprocessing

## 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**

## fMRI Preprocessing

- **Slice timing correction**
  - Temporally shift slices according to their acquisition sequence
- **Realignment**
  - Correction for motion during the experiment
- **Normalization**
  - Registration to a standard brain
- **Spatial Smoothing**
  - Enhance SNR
  - Necessary for group analyses

## Data Preprocessing Options

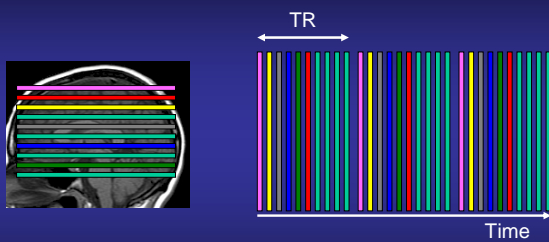
- reconstruction from raw k-space data
  - frequency space → real space
- artifact screening
  - not standard, but one should screen data after acquisition to get information about scanner artifacts, spikes, and head motion
  - if detected, session can be repeated
  - online screening would be ideal
- vessel suppression
  - reduce the effects of large vessels (which are further away from activation than capillaries)
- spatial interpolation (zero-padding)
  - 64x64 → 128x128
- temporal interpolation (with multiple shots)
  - compute intermediate time points
- mean intensity adjustment
  - adjust for average value of MR signal
- slice time correction
  - correct for sampling of different slices at different times
  - not available for multishot images in BV
- motion correction
- spatial filtering
  - smooth the spatial data
- temporal filtering
  - remove low frequency drifts (e.g., linear trends)
  - smooth time courses
- normalisation
- Coregistration
- Segmentation

## Tools for Preprocessing

- SPM
- FSL
- Brain Voyager
- AFNI
- Custom scripts
- .... And many more

## Slice Timing Correction

## Slice timing correction

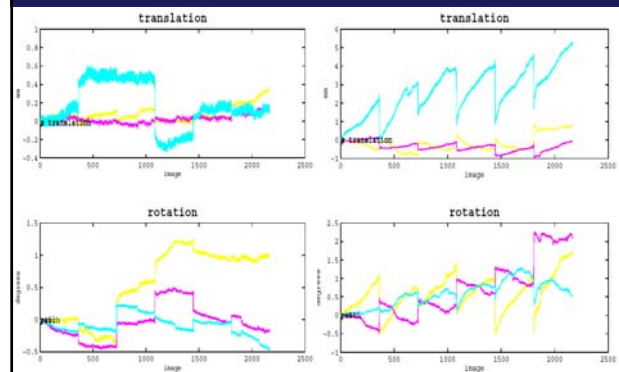


## Why do we correct for slice timing?

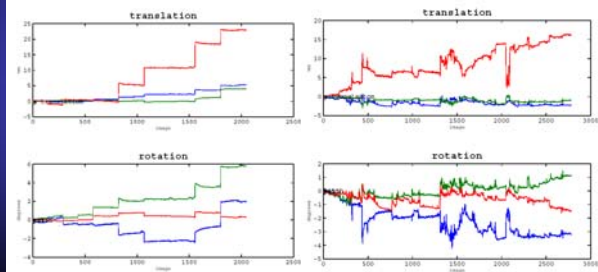
- **Corrects for differences in acquisition time within a TR**
  - Especially important for long TRs (where expected HDR amplitude may vary significantly)
  - Accuracy of interpolation also decreases with increasing TR
- **Might interfere with motion correction**
  - Before motion correction: interpolates data from (potentially) different voxels
  - After motion correction: if voxel position is changing to a different slice this also changes the point of time within TR of that specific voxel

## Motion Correction

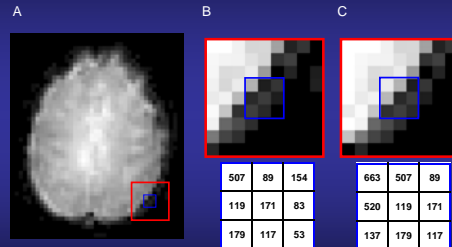
## Head Motion: Good, Bad,...



## ... and catastrophically bad

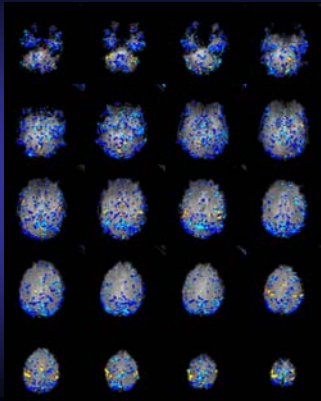


## Why does head motion introduce problems?



## Severe Head Motion

Two 4s movements of 8mm in -Y direction (during task epochs)

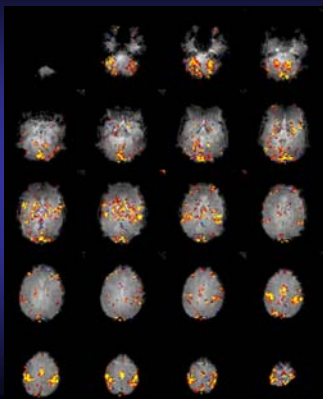


Motion ↑

## Correcting Head Motion

- **Rigid body transformation**
  - 6 parameters: 3 translation, 3 rotation
- **Minimization of some cost function**
  - E.g., sum of squared differences

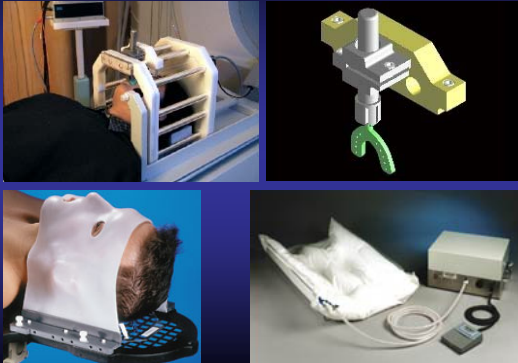
## Effects of Head Motion Correction



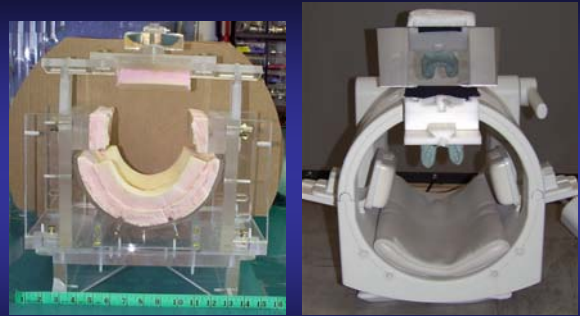
## Limitations of Motion Correction

- **Artifact-related limitations**
  - Loss of data at edges of imaging volume
  - Ghosts in image do not change in same manner as real data
- **Distortions in fMRI images**
  - Distortions may be dependent on position in field, not position in head
- **Intrinsic problems with correction of both slice timing and head motion**

## Prevention is the best medicine



## Head Restraint



Head Vice

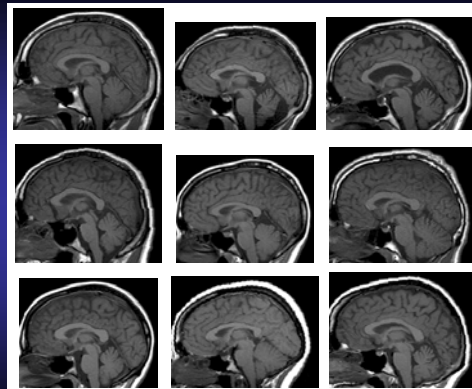
Bite Bar

## Coregistration

## Should you Coregister?

- **Advantages**
  - Aids in normalization
  - Allows display of activation on anatomical images
  - Allows comparison across modalities
  - Necessary if no coplanar anatomical images
- **Disadvantages**
  - May severely distort functional data
  - May reduce correspondence between functional and anatomical images

## Normalization



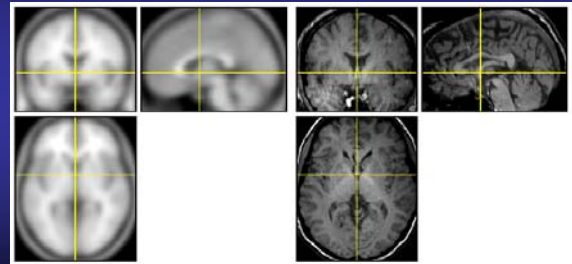
## Standardized Spaces

- **Talairach space (proportional grid system)**
  - From atlas of Talairach and Tournoux (1988)
  - Based on single subject (60y, Female, Cadaver)
  - Single hemisphere
  - Related to Brodmann coordinates
- **Montreal Neurological Institute (MNI) space**
  - Combination of many MRI scans on normal controls
    - All right-handed subjects
  - Approximated to Talairach space
    - Slightly larger
    - Taller from AC to top by 5mm; deeper from AC to bottom by 10mm
  - Used by SPM, National fMRI Database, International Consortium for Brain Mapping

## Normalization to Template

Normalization Template

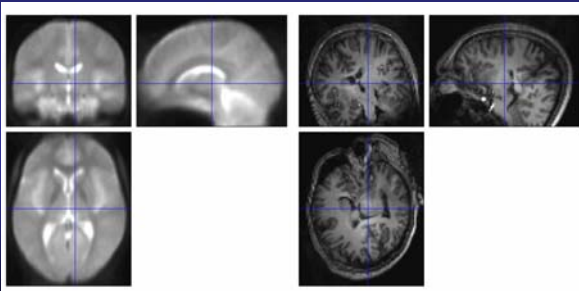
Normalized Data



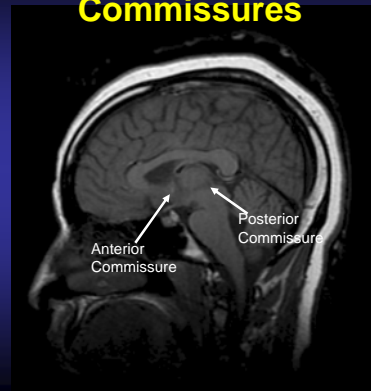
## Normalization to the wrong template

Normalization Template

Normalized Data



## Anterior and Posterior Commissures



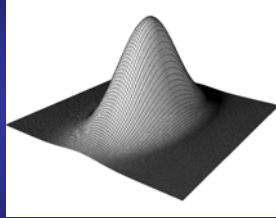
## Should you normalize?

- **Advantages**
  - Allows generalization of results to larger population
  - Improves comparison with other studies
  - Provides coordinate space for reporting results
  - Enables averaging across subjects
- **Disadvantages**
  - Reduces spatial resolution
  - May reduce activation strength by subject averaging
  - Time consuming, potentially problematic
    - Doing bad normalization is much worse than not normalizing

## Spatial Smoothing

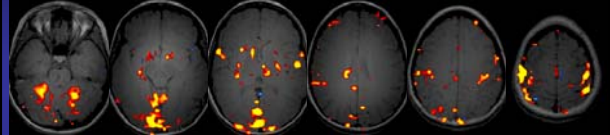
## Techniques for Smoothing

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

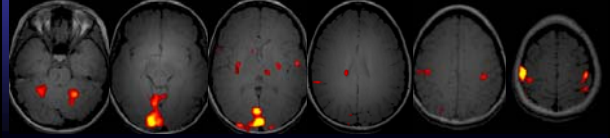


## Effects of Smoothing on Activity

Unsmoothed Data



Smoothed Data (kernel width 5 voxels)

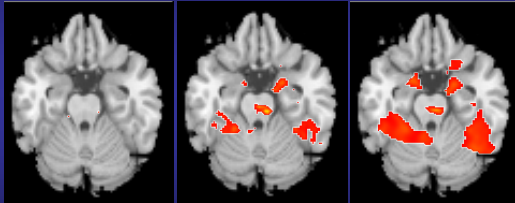


## Smoothing and Activation

No smoothing

6mm FWHM

9mm FWHM



## Should you spatially smooth?

- **Advantages**
  - Increases Signal to Noise Ratio (SNR)
    - Matched Filter Theorem: Maximum increase in SNR by filter with same shape/size as signal
  - Reduces number of comparisons
    - Allows application of Gaussian Field Theory
  - May improve comparisons across subjects
    - Signal may be spread widely across cortex, due to intersubject variability
- **Disadvantages**
  - Reduces spatial resolution
  - Challenging to smooth accurately if size/shape of signal is not known

## Segmentation

- **Classifies voxels within an image into different anatomical divisions**
  - Gray Matter
  - White Matter
  - Cerebro-spinal Fluid (CSF)

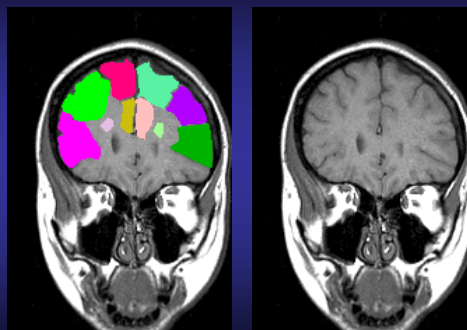


## Region of Interest Drawing

## Why use an ROI-based approach?

- **Allows direct, unbiased measurement of activity in an anatomical region**
  - Assumes functional divisions tend to follow anatomical divisions
- **Improves ability to identify topographic changes**
  - Motor mapping (central sulcus)
  - Social perception mapping (superior temporal sulcus)
- **Complements voxel-based analyses**

## ROI Examples



## fMRI Analysis

## fMRI Analysis

- **Model-based analysis approaches**
  - Time courses of individual pixels are compared to some reference function
- **Exploratory analysis approaches**
  - Time courses of individual pixels are grouped together without using a reference function ("clustering")
  - Some time course feature is assessed and assumed to be different in "activated" voxels (auto-correlation, Hurst-coefficient)

## Model-based fMRI Analysis

- **Cross-correlation**
  - Only a single reference function possible
- **Multidimensional regression, General linear model (GLM, SPM)**
  - Multiple reference functions (regressors) possible
  - Voxel time courses are modeled as a linear combination of weighted regressors

## Types of Errors

		Hypothesis	
		$H_1$ (Active)	$H_2$ (Inactive)
Output of Statistical Test	Accept $H_1$ (Active)	HIT TP	Type I Error FP
	Reject $H_1$ (Active)	Type II Error FN	Correct Rejection TN

## Statistical Corrections

- If more than one test is made, then the collective alpha value is greater than the single-test alpha and the overall Type I error increases
- One option is to adjust the alpha value of the individual tests to maintain an overall alpha value at an acceptable level
  - This procedure controls for overall Type I error
  - Known as Bonferroni Correction

## Correction for Multiple Comparisons

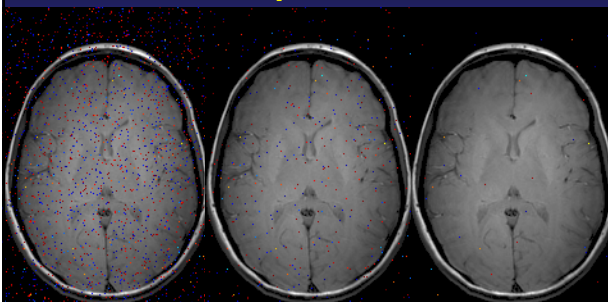
With conventional probability levels (e.g.,  $p < .05$ ) and a huge number of comparisons (e.g.,  $64 \times 64 \times 12 = 49,152$ ), a lot of voxels will be significant purely by chance  
 e.g.,  $.05 * 49,152 = 2458$  voxels significant due to chance

How can we avoid this?

### 1) Bonferroni correction

- divide desired p value by number of comparisons  
 Example:  
 desired p value:  $p < .05$   
 number of voxels: 50,000  
 required p value:  $p < .05 / 50,000 \rightarrow p < .00001$
- quite conservative
- can use less stringent values
  - e.g., use the number of voxels in the cortical surface

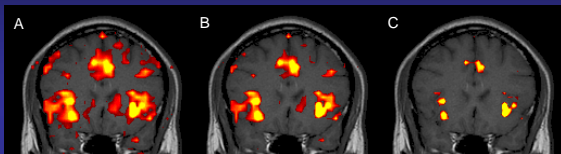
## The Problem of Multiple Comparisons



$P < 0.05$  (1682 voxels)       $P < 0.01$  (364 voxels)       $P < 0.001$  (32 voxels)

## Bonferroni Correction

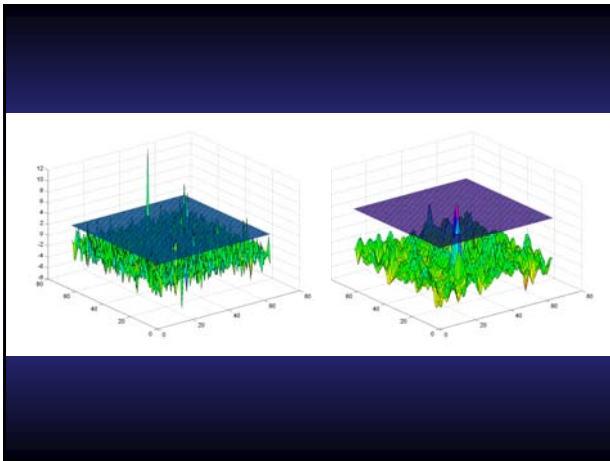
- **Very severe correction**
  - Results in very strict significance values for even medium data sets
  - Typical brain may have about 15,000-20,000 functional voxels
    - Corrected alpha ~ 0.000003
- **Increases Type II error rate**
- **Is not appropriate for correlated data**
  - If data contain correlated data points, then the effective number of statistical tests may be greatly reduced
  - Most fMRI data has significant correlation



A:  $t = 2.10, p < 0.05$  (uncorrected)  
 B:  $t = 3.60, p < 0.001$  (uncorrected)  
 C:  $t = 7.15, p < 0.05$ , Bonferroni Corrected

## Gaussian Field Theory

- Used in SPM
- Provides false positive rate for fMRI data based upon the smoothness of the data
- If data are very smooth, then the chance of noise points passing threshold is reduced



## Neighborhood criteria

- Assumption: Areas of true fMRI activity will typically extend over multiple voxels (clusters)
  - falsely activated voxels should be randomly dispersed
  - Only activated pixels which have pixels in the neighborhood which are also activated are considered activated
- => Cluster size thresholds can be used to reject false positive activity
- Efficacy of cluster analysis depends upon shape and size of fMRI activity
    - Not as effective for non-convex regions
    - Power drops off rapidly if cluster size > activation size

## ROI Comparisons

- Changes basis of statistical tests
  - Voxels: ~16,000
  - ROIs: ~1 – 100
- Each ROI can be thought of as a very large volume element (e.g., voxel)
  - Anatomically-based ROIs do not introduce bias
- Potential problems with using functional ROIs
  - Functional ROIs result from statistical tests
  - Therefore, they cannot be used (in themselves) to reduce the number of comparisons

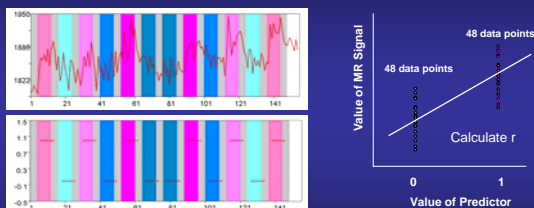
## Correlation

- Special case of General Linear Model
  - Blocked t-test is equivalent to correlation with square wave function
  - Allows use of any reference waveform
- Correlation coefficient describes match between observation and expectation
  - Ranges from -1 to 1
  - Amplitude of response does not affect correlation directly

## Statistical Analyses: Correlation

### Correlation analysis

- voxels with time course correlated with reference function
- can incorporate hemodynamic response function (HRF) to predict time course more accurately

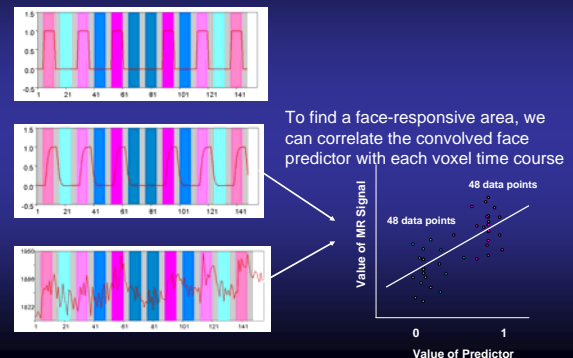


For each voxel:

- Find the correlation between the predictor and the MR signal
- Extract the correlation (r value) and find the corresponding p value.
- Determine whether it is statistically significant
- In this example, similar in spirit to a t-test.

## Correlation: Using the HRF

We can model the expected curve of the data by convolving our predictor with the hemodynamic response function.



## Problems with t-tests and correlations

- 1) How do we evaluate runs with different orders?
- 2) If we test more subjects, how can we evaluate the subjects together?
- 2) We can get nice haemodynamic predictors for different conditions, but how can we compare them accurately?

**Solution: General Linear Model**

## Basic Concepts of the GLM

- **GLM treats the data as a linear combination of model functions plus noise**
  - Model functions have known shapes
  - Amplitude of functions are unknown
  - Assumes linearity of HDR; nonlinearities can be modeled explicitly
- **GLM analysis determines set of amplitude values that best account for data**
  - Usual cost function: least-squares deviance of residual after modeling (noise)

## General Linear Model (GLM)

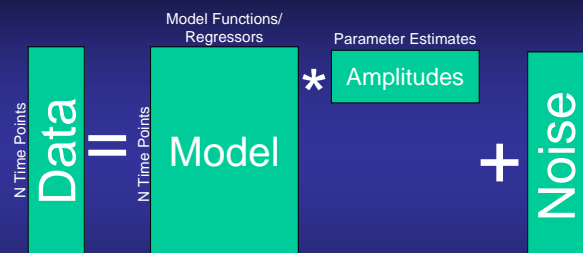
$$y(t) = \sum_n x_n(t) \cdot \beta_n + \epsilon$$

weight:  $\beta_n$   
 error term:  $\epsilon$   
 time course of a single voxel:  $y(t)$   
 reference function, regressor:  $x_n(t)$

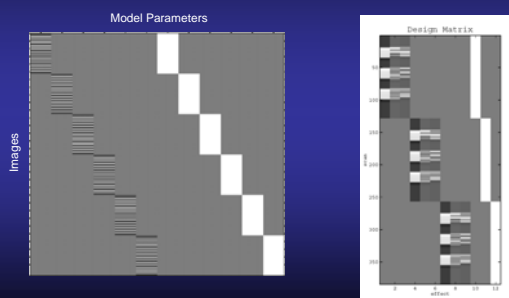
Matrix formulation  
(for all voxels in the data set)

$$Y = XB + E$$

## Form of the GLM



## Implementation of GLM in SPM

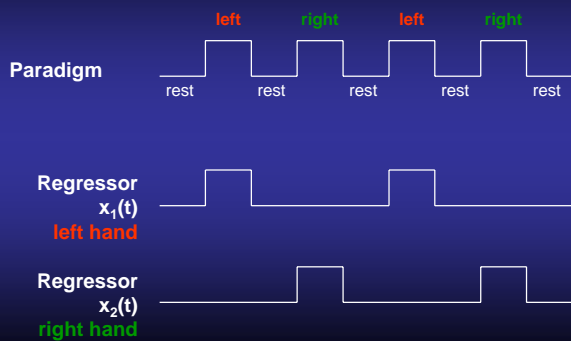


## GLM Example

- **Simple blocked-design experiment**
- **2 conditions**
  - Finger movement left hand
  - Finger movement right hand
- **2 blocks for each condition**



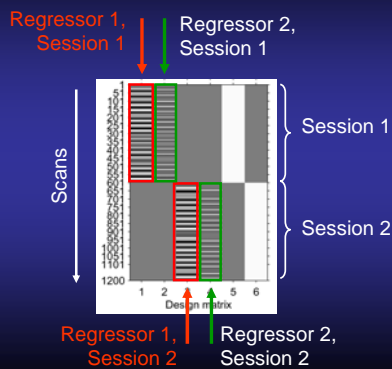
## GLM Example



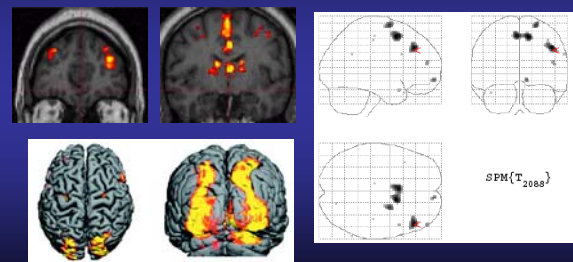
## GLM Example

- During analysis the individual weights  $\beta_1$  and  $\beta_2$  are calculated and statistically tested against the error term  $\epsilon$
- Linear combinations of  $\beta_1$  and  $\beta_2$  (“contrasts”) yield different activation:
  - $\beta_1$ : Activation during left tapping
  - $\beta_2$ : Activation during right tapping
  - $\beta_1 + \beta_2$ : Activation during left and right tapping
  - $\beta_1 - \beta_2$ : More activation during left than during right tapping

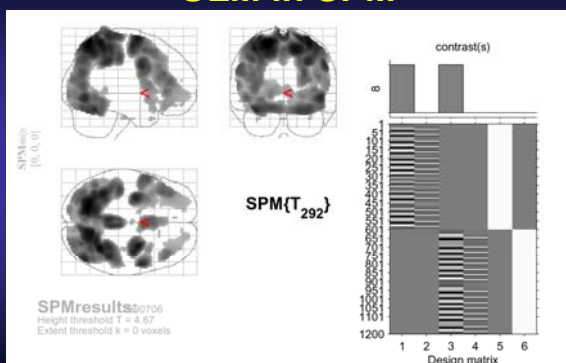
## GLM in SPM



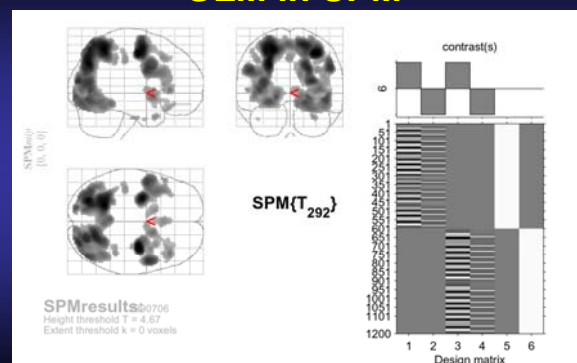
## Representing fMRI Analyses



## GLM in SPM



## GLM in SPM

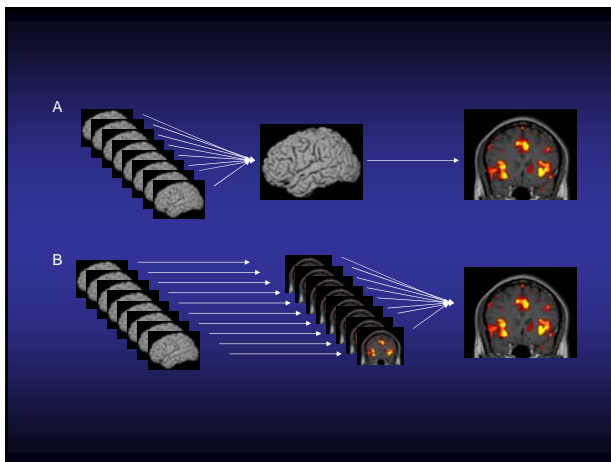


## Fixed and Random Effects Comparisons

## Fixed and Random Effects Comparisons

How do we compare across subjects?

- **Fixed-effects Model**
  - 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 Model**
  - Accounts for inter-subject variance in analyses
  - Allows inferences to population from which subjects are drawn
  - Especially important for group comparisons



## How are random-effects models run?

- **Assumes that activation parameters may vary across subjects**
  - Since subjects are randomly chosen, activation parameters may vary within group
  - Fixed-effects models assume that parameters are constant across individuals
- **Calculates statistic for each subject**
  - i.e., *t*-test for each subject based on correlation
- **Uses all subjects' statistics in a one-sample *t*-test**
  - i.e., another *t*-test based only on significance maps

## RFX Analysis

- Single subject parameter estimates are entered into one sample *t*-tests
- RFX assesses the variance in parameter estimates (“activation amplitudes”) across subjects
- RFX (in the SPM implementation) ignores activation significances of single subject analyses

## Summary of Hypothesis Tests

- **Simple experimental designs**
  - Blocked: *t*-test, Fourier analysis
  - Event-related: correlation, *t*-test at time points
- **Complex experimental designs**
  - Regression approaches (GLM)
- **Critical problem: Minimization of Type I Error**
  - Strict Bonferroni correction is too severe
  - Cluster analyses improve
  - Accounting for smoothness of data also helps
- **Use random-effects analyses to allow generalization to the population**

## Why conduct exploratory analyses?

- **Powerful tools for exploring data**
  - PCA, ICA: Intrinsic, spatially stationary patterns of activity in dataset
  - Clustering: Collections of voxels with similar time courses of activity
  - PLS: How those patterns of activity maximally differentiate experimental conditions
- **Allows segmentation of nuisance factors**
- **Provides check on hypothesis-driven analyses**

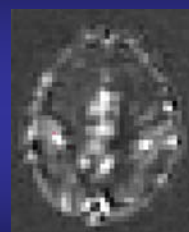
## Exploratory fMRI Analysis

- **Fourier Analysis**
- **Clustering algorithms**
  - Fuzzy Cluster Analysis (FCA)
- **Principal component analysis (PCA)**
- **Independent component analysis (ICA)**
- **Neural network algorithms (NN)**
- **Fractal algorithms**

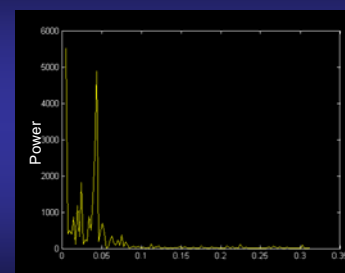
## Fourier Analysis

- **Fourier transform: converts information in time domain to frequency domain**
  - Used to change a raw time course to a power spectrum
  - Hypothesis: any repetitive/blocked task should have power at the task frequency
- **Equivalent to correlation in frequency domain**
  - At short durations, like a sine wave (single frequency)
  - At long durations, like a trapezoid (multiple frequencies)
- **Subset of multiple regression**
  - Same as if sine and cosine used as regressors

## Fourier Analysis



12s on, 12s off



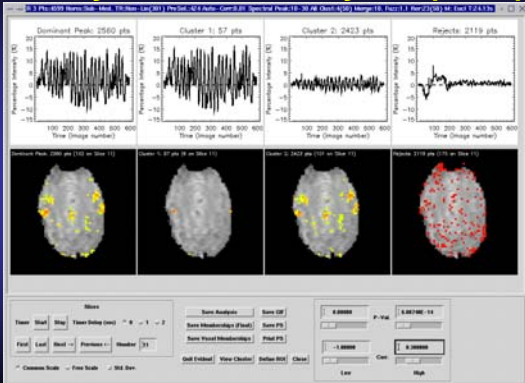
Frequency (Hz)

## Clustering Methods

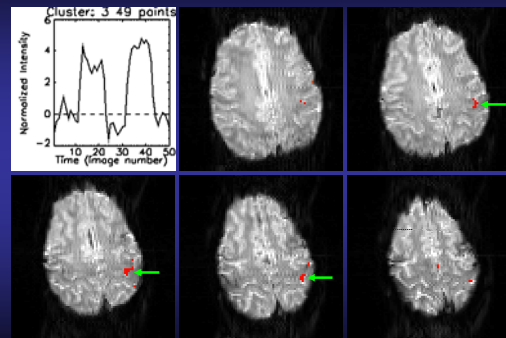
- Algorithm looks for similar time courses (pixel-by-pixel)
- Pixels with similar timecourses are put in one cluster
- Algorithm minimizes differences within cluster and maximizes differences between clusters iteratively
- Fuzzy clustering: "Fuzzyness" enables that one pixels does not belong exclusively to one cluster (membership ranges between 0 and 1)
- Result depicts the average time course of a cluster and the membership value of a pixels

## Fuzzy Cluster Analysis (FCA)

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## FCA Result



Finger tapping paradigm; block design; off-on-off-on-off

