FMRI Pre-Processing and Model-Based Statistics

• Brief intro to FMRI experiments and analysis
• FMRI pre-stats image processing
• Simple Single-Subject Statistics
• Multi-Level FMRI Analysis
• Advanced FMRI Analysis
FMRI Pre-Statistics

- Brief intro to FMRI analysis

FMRI pre-statistical image processing:

- Reconstruction from k-space data
- Motion correction
- Slice timing correction
- Spatial filtering
- Temporal filtering
- Global intensity normalisation
**FMRI Experiments**

- Simple paradigm design:
  - stimulus vs baseline
  - constant stimulus “intensity”
  - constant block lengths
  - many repetitions: ABABABA

- Need baseline (rest) condition to measure *change*
The Haemodynamic Response

- Field changes (perturbations) --> dephasing --> $T_2^*$ effect
- BOLD-tuned MRI ($T_2^*$-weighted) is sensitive to this effect
Predicted Response

• The process can be modelled by convolving the activity curve with a "haemodynamic response function" or HRF
FMRI Experiments: Analysis

- Each voxel contains a time-varying signal (BOLD signal)
FMRI Experiments: Analysis

- Each voxel contains a time-varying signal (BOLD signal)

- Model the stimulus-induced change in BOLD signal (predicted response)

- Find which voxels have signals that match the model

- Good match implies activation related to stimulus
Standard GLM Analysis

• Correlate model at each voxel separately
• Measure residual noise variance
• $t$-statistic = model fit / noise amplitude
• Threshold $t$-stats and display map
Predicted Response (model)

Fitted Amplitude
Residual Noise
Standard GLM Analysis

- Correlate model at each voxel separately
- Measure residual noise variance
- $t$-statistic = model fit / noise amplitude
- Threshold $t$-stats and display map

Signals of no interest (e.g. artifacts) can affect both activation strength and residual noise variance

Use pre-processing to reduce/eliminate some of these effects
FMRI Pre-Statistics

FMRI pre-statistical image processing:

- Reconstruction from k-space data
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Image Reconstruction

• Convert k-space data to images:
  • reconstruction algorithms
• Occasionally get problematic data
  • e.g. slice timing errors, RF spikes, RF interference

• Correct using custom-built initial analysis stages
• Scanner artefacts can be found by:
FMRI Pre-Statistics

FMRI pre-statistical image processing:

- Reconstruction from k-space data
- **Motion correction**
- Slice timing correction
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Motion Correction: Why?

• People always move in the scanner

• Even with padding around the head there is still some motion

• Need each voxel to correspond to a consistent anatomical point for each point in time

• Motion correction realigns to a common reference

• Very important correction as small motions (e.g. 1% of voxel size) near strong intensity boundaries may induce a 1% signal change > BOLD
Motion Correction

= multiple registration

Select a MC target (reference) for all FMRI volumes.

Can use either one original volume, mean of several, standard space image etc.

Register each FMRI volume to target separately

Use rigid body (6 DOF)
Effect of Motion Correction

Uncorrelated Motion

Stimulus Correlated Motion

Without MC

With MC
Motion Parameter Output

Summary of total motion (relative and absolute)

Relative = time point to next time point - shows jumps
Absolute = time point to reference - shows jumps & drifts

Note that large jumps are more serious than slower drifts, especially in the relative motion plot.
FMRI Pre-Statistics

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Slice Timing Correction

Almost all FMRI scanning takes each slice separately.

Each slice is scanned at a slightly different time.

Slice order can be interleaved (as shown) or sequential (up or down).
Slice Timing

Without any adjustment, the model timing is always the same

Slice 9 acquired 1.5 secs after slice 10

acquisition timing (TRs)
Slice Timing

... but the timing of each slice’s data is different

Slice 9 acquired 1.5 secs after slice 10
Slice Timing

Can get consistency by shifting the data

Slice 9 acquired 1.5 secs after slice 10

acquisition timing (TRs)
Slice Timing

... and then interpolating the data
= slice timing correction

Slice 9 acquired 1.5 secs after slice 10
Slice Timing

... and then interpolating the data = slice timing correction

Slice 9 acquired 1.5 secs after slice 10
Slice Timing

The result of slice timing correction is that the data is changed (degraded) by interpolation.

Slice 9 acquired 1.5 secs after slice 10.
Slice Timing

Alternatively, can get consistency by shifting the model

Slice 9 acquired 1.5 secs after slice 10
One way to shift the model is to use the *temporal derivative in the GLM*.

Based on Taylor approx:

\[ m(t+a) = m(t) + a.m'(t) \]
Slice Timing

Shifting the model also accounts for variations in the HRF delay
• as the HRF is known to vary between subjects, sessions, etc.

This is the recommended solution for slice timing
Motion Problems

Motion correction eliminates gross motion changes but assumes \textit{rigid-body motion} - not true if slices acquired at different times.

Other motion artefacts persist including:
- Spin-history changes,
- \( B_0 \) (susceptibility) interactions &
- Interpolation effects

Such artefacts can severely degrade functional results.
Severity usually worse for \textit{stimulus-correlated} motion.
Motion Problems

Motion correction eliminates gross motion changes but assumes *rigid-body motion* - not true if slices acquired at different times

Other motion artefacts persist including:
  Spin-history changes, $B_0$ (susceptibility) interactions & Interpolation effects

Such artefacts can severely degrade functional results
Severity usually worse for *stimulus-correlated* motion

Some *potential* analysis remedies for motion artefacts include:
- including *motion parameter regressors* in GLM
- removing artefacts with ICA denoising
- *outlier* timepoint detection and exclusion (via GLM)
- rejection of subjects displaying “excessive” motion

No simple rule of thumb defining "too much" motion
FMRI Pre-Statistics

FMRI pre-statistical image processing:

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• Temporal filtering
• Global intensity normalisation
Spatial Filtering

Why do it?

1. Increases signal to noise ratio if size of the blurring is less than size of activation

2. Need minimum "smoothness" to use *Gaussian random field theory* for thresholding

However:

- Reduces small activation areas
- Safest option is to do a small amount of smoothing
- Alternative thresholding/stats eliminates the need for smoothing (e.g. randomise, TFCE)
Spatial Filtering: How?

Spatial filtering done by a 3D convolution with a Gaussian (cf. 1D convolution with HRF for model)

Each voxel intensity is replaced by a **weighted** average of neighbouring intensities

A Gaussian function in 3D specifies weightings and neighbourhood size

<table>
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<tr>
<th>Weights</th>
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Spatial Filtering: How?

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Each voxel intensity is replaced by a weighted average of neighbouring intensities

Specify amount by Full Width Half Maximum (FWHM) = distance between 0.5 values

Weights

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Spatial Filtering: Results at Different FWHM
FMRI Pre-Statistics

FMRI pre-statistical image processing:

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- Slice timing correction
- Spatial filtering
- **Temporal filtering**
- Global intensity normalisation
Temporal Filtering: Why?

• Time series from each voxel contain scanner-related and physiological signals + high frequency noise
• Scanner-related and physiological signals (cardiac cycle, breathing etc) can have both high and low frequency components
• These signals + noise hide activation

What is temporal filtering?

• Removal of high frequencies, low frequencies or both, *without removing signals of interest*
Temporal Filtering: Highpass

- Removes low frequency signals, including linear trend
- Must choose cutoff frequency carefully (lower than frequencies of interest = longer period)
Temporal Filtering: Lowpass

Removes high frequency noise

Only useful if the predicted model does not also contain high frequencies...
Filtering & Temporal Autocorrelation

Some designs also contain high frequency content in the model, e.g. Dense Single-Event Model:

- In these cases, lowpass filtering removes too much signal
- Also, need noise data to correctly estimate autocorrelation (to make statistics valid - see later) ➔ avoid lowpass filtering

Recommendations:
- Use Highpass only
- Ensure cutoff frequency higher than model frequencies (can use the Estimate button in the GUI - see practical)
- Lower limit on cutoff frequency for good autocorrelation estimation (e.g. for TR=3s, cutoff period > 90s )
Effect of Temporal Filtering

No Temporal Filtering

Highpass Temporal Filtering
FMRI Pre-Statistics

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Global Intensity Normalisation

- Mean intensity of the whole dataset changes between subjects and sessions
  - due to various uninteresting factors (e.g. caffeine levels)
- Want the same mean signal level for each subject (taken over all voxels and all timepoints: i.e. 4D)
- Scale each 4D dataset by a single value to get the overall 4D mean (dotted line) to be the same
- Automatically done within FEAT
## Summary

<table>
<thead>
<tr>
<th>Process</th>
<th>Description</th>
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<tbody>
<tr>
<td>Reconstruction</td>
<td>Create image and remove gross artefacts</td>
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<tr>
<td>Motion Correction</td>
<td>Get consistent anatomical coordinates (always do this)</td>
</tr>
<tr>
<td>Slice Timing</td>
<td>Get consistent acquisition timing (use temporal derivative instead)</td>
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<tr>
<td>Spatial Smoothing</td>
<td>Improve SNR &amp; validate GRF</td>
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<td>Temporal Filtering</td>
<td>Highpass: Remove slow drifts Lowpass: Avoid for autocorr est.</td>
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<tr>
<td>Intensity Normalisation</td>
<td>4D: Keeps overall signal mean constant across sessions</td>
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