Functional MRI data preprocessing

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Data have been acquired, what’s next?

No matter the design, multiple volumes (made from multiple slices) have been acquired in time. Before getting data out, we need to make sure the signal from each voxel contains the right temporal and spatial information.

Picture credit: http://home.kpn.nl/raema005/functional_magnetic_resonance_imaging_fmri.html
Slice timing and Realignment

normalisation

Anatomical reference

fMRI time-series

kernel

smoothing

Statistics
Slice Timing Correction

R. Henson, C. Buechel, O. Josephs, K. Friston
The slice-timing problem in event-related fMRI
Slice Timing Correction

- Most of the time, fMRI data are acquired using sequential 2D imaging like single shot EPI. Since fMRI statistics are about analyzing the time course of the BOLD signal, exact timing with regard to the stimulus presentation is crucial.

- For instance, if you set a TR of 2 sec and acquire 30 slices, the acquisition time of 1 slice is \(~66.66\) ms (2000/30) and STC compensates for these sampling differences.

STC consists in shifting the signal phase by a given amount to temporally align data. It is therefore mandatory to select a reference slice. The reference slice is usually the slice acquired in the middle of the sequence (maximum interpolation of TR/2) but any slice can be used.

Data are acquired either in sequential or interleaved mode and the middle of the sequence is not the middle of the brain!
Slice Timing Correction

- TR of e.g. 2 sec with the middle temporal slice as reference is comparable to a dataset with a TR of 1 sec when the first (or last) slice acquired are used as a reference slice. This can be a reasonable practice, if the region of interest and putative activations are located near the first (or last) slice because it suppresses temporal interpolation effects in these areas.

Note that all regressors in the GLM also need to be adjusted for this shift in time according to the reference slice (e.g. TR / 2).
Slice Timing Correction

- Possible introduction of aliasing effects for signals at frequencies above the Nyquist sampling limit. Given a typical TR of 2 s ($f = 0.25 \ Hz$) a minimal inter-stimulus interval (ISI) of more than 4 s is recommended. When using the slice acquired in the middle of the acquisition period (TR) as a reference slice, the signal needs to be shifted by TR / 2, therefore reducing the suggested minimal ISI to 2 s.

- It is sometimes advocated to not do the STC especially for TR<2 sec. However, Sladky et al. showed that is always beneficial. When not performed, the reduction of parameter estimates (effects) were more pronounced for long TRs, event-related designs and designs with shorter SOA (up to 63% !).
motion correction
(realignment)

JV. Hajnal, R. Myers, A. Oatridge, JE. Schwieso, IR. Young, GM. Bydder
Artifacts due to stimulus-correlated motion in functional imaging of the brain.
Motion artefacts

- Subjects will always move in the scanner: swallowing for instance lead to motion along the x axis or some movements may be related to the tasks performed.

- Motion will result in a mismatch of the location of subsequent images in the time-series. Since the sensitivity of the statistical analysis is determined by the amount of residual noise in the image series, mismatch of the location will add to this noise and reduce the sensitivity.

- This type of motion problem corresponds to wholesale movements (*bulk-motion*) and is well corrected by realignment algorithms.
Motion correction: How?

- Determine the rigid body transformation that minimises some cost function (a way to define the difference between 2 images as e.g. least square (SPM) or normalized correlation ratio (FSL)).

- Rigid body transformation is defined by: 3 translations in X, Y & Z directions and 3 rotations around the X, Y & Z axes.

Illustration taken from Jesper Andersson
Motion correction: Quality check

- Plots the estimates from the head motion algorithm
  (might be useful to change angles into degrees and also plot the 1\textsuperscript{st} derivative – outlier detection can then be run to identify ‘bad’ scans)
- Compute whole head distance between volumes and to the mean (mean square difference)
- Inspect the realigned data as a movie

Lots of tools available on websites
For SPM users, I wrote a script to do this automatically
see https://sourceforge.net/projects/spm-ga-tools
Motion correction: Quality check

Plots of head motion

Translation

Rotation

Mean square displacement

Scan to scan translation

Scan to scan rotation
Motion correction: Quality check

Whole head distances

![Graph showing mean squared distance to the average and volume to volume mean squared distance](image)

- Mean squared distance to the average
- Volume to volume mean squared distance
Motion correction: Quality check

Movies
Even more motion artefacts

Motion can also alter the MR signal because protons that moves into a voxel from a neighbouring slice have an excitation different from that expected by the scanner and the signal will not reflect well the tissue in that voxel. This *spin history effect* is not corrected using motion correction algorithms and Independent Component Analysis (ICA) or dedicated methods must be used.

The *spin history effect* is seen as alternating bright and dark stripes with interleaved acquisitions. One can mitigate this by modelling bad images as dummy regressors and include movement parameter estimates into the analysis.

Picture credit: http://wagerlab.colorado.edu/wiki/doku.php/help/fmri_quality_control_overview
Even more motion artefacts

- Physiological artefacts

respiratory-induced noise is dominant near the edges of the brain as well as near in the larger veins and in the ventricles.

cardiac-induced noise is dominant near larger vessels (e.g. medial cerebral artery and Circle of Willis)

→ Physio monitoring
→ Don’t trust those regions

Spatial Normalization

M, Holden
A review of geometric transformations for nonrigid body registration.
Normalization: Why?

- Inter-subject averaging
  - extrapolate findings to the population as a whole
  - increase activation signal above that obtained from single subject
  - increase number of possible degrees of freedom allowed in statistical model

- Enable reporting of activations as co-ordinates within a known standard space
  - e.g. the space described by Talairach & Tournoux, or the MNI space (SPM, FSL)
Current methods work mainly on T1 weighted images (i.e. anatomical), so in practice one uses a 3 steps approach in which one i) coregister T1 and T2* (fMRI) data so that they are aligned and in the same space and ii) normalize the anatomical image (i.e. transform it to match the template) and iii) apply the parameters obtained to the fMRI images.
The anatomical image is 1\textsuperscript{st} preprocessed, depending on the method this includes: i) **Noise reduction**: improves local features using local smoothing (SUSAN algorithm in FSL), ii) **Bias correction**: from 3 Teslas, there is often broad intensity variations in space that need to be corrected, iii) **Brain extraction**: remove non brain tissue, iv) **Segmentation**: separate grey matter, white matter and CSF.

In SPM, the unified segmentation approach (Ashburner and Friston (2005) NeuroImage, 26, 839-851) combines/optimizes bias correction, segmentation, and normalization all in one, such as the prior probability of a voxel to belong to a tissue class is determined using a probabilistic atlas. In this framework 2 voxels with the same values can be classified differently using anatomical knowledge.
T1 image preprocessing

Original T1-weighted → Noise reduction → Brain extraction

Bias correction → Segmentation
Volume-based normalization

- The first part of spatial normalisation is a 12 parameter affine transformation:
  - 3 translations
  - 3 rotations
  - 3 scaling
  - 3 shears

Rigid body transformation (realignment) → does not change the size or shape of images

Allow change in overall size and shape

Affine transformation: any set of points that fell on a line prior transformation will continue to fall on a line after the transformation
Volume-based normalization

- The second part of the normalization uses non-linear deformations.
- DARTEL toolbox in SPM or FNIRT in FSL rely on diffeomorphism, that is the transformation from one image to the other can be represented as a vector field, describing the movements to apply at each voxel.
Surface-based Normalization

- Often more accurate to register cortical features than ‘old’ volume based methods. Often limited to cortical surface.
- A combined method (surface based for cortical and volume based for deep brain structures) is available in Freesurfer.

Image credit: Sarah Whittle & Dominic Dwyer free-surfer talk
Normalization: quality check

- Visual inspection using e.g. CheckReg in SPM
- Mean T2*, T1, Template

Allows checking the coregistration and normalization worked
Normalization: quality check

- Segmented (normalized) gray matter and white matter vs. priors (i.e. the gray and white matter images used with the template)

Sometimes the overall shape looks ok but the segmentation was not too good – best to check this as well
Normalization: quality check

- Outlines of template vs. normalized T1
- Average normalized images
- Distance of normalized data to the template
- Movie

Lots of tools available on websites
For SPM users, I wrote a script to do this automatically
see [https://sourceforge.net/projects/spm-qa-tools](https://sourceforge.net/projects/spm-qa-tools)
Normalization: quality check

Average of Normalized T2* Image

Outlines Average/T1
Interpolation methods

P. Thevenaz, T. Blu & M Unser
Interpolation revised
Write down the new images

- Each transformation (realignment, segment, normalize) comes with different methods of interpolation.
- Each time an image is transformed, voxels don’t align with the original ones and new voxels have to be created – their value is inferred from neighbours.

There is no need to apply each transformation. Parameters are stored in the header and for a new transform, previous parameters are applied and the new transform computed. Only when all is computed, one has to write images. At this stage all parameters are applied. This allows to interpolate voxel values only once.
Interpolation methods include i) nearest neighbour ii) linear interpolation iii) higher-order interpolation like sinc interpolation or spline.

http://imp4-2008.blogspot.co.uk/

Loss of resolution tends to blur images.

http://www.hyperzoid.com/csc492/rendering.html
Interpolation methods include i) nearest neighbour ii) linear interpolation iii) higher-order interpolation like sinc interpolation or spline.
Smoothing
Smoothing: Why?

- Increase signal to noise by removing high-frequency information (small-scale changes in the image)

- Inter-subject averaging as spatial normalization cannot perfectly align all structures

- Increase validity of statistics when using random field theory.
Smoothing: How?

Each voxel, after smoothing, effectively becomes the result of applying a weighted region of interest. In SPM, smoothing is a convolution with a 3D Gaussian kernel, and the kernel is defined in terms of FWHM (full width at half maximum).

Before convolution  Convolved with a circle  Convolved with a Gaussian

2D illustration using the conv2 function in Matlab
Smoothing: How much?

- Depends on effects to be detected → Matched filter theorem: smoothing kernel = expected signal.
- Practically FWHM 2 times the voxel size is appropriate for random fields theory, whilst improving SNR.
- May consider varying kernel size if interested in different brain regions (e.g. hippocampus -vs- parietal cortex))

Picture credit: http://fcp-indi.github.com/docs/user/smoothing.html