fMRI Preprocessing

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Image time-series

Realignment → Smoothing → Design matrix → Statistical Inference

Normalisation

Spatial filter

Anatomical reference

Parameter estimates

Statistical Parametric Map

Realignment

Smoothing

Design matrix

General Linear Model

Statistical Inference

Spatial filter

Statistical Parametric Map

p < 0.05

RFT
Realign fMRI time series

Structural MRI

Template

Smoothed fMRI

1. Realign
2. Coregister
3. Normalise/Segment
4. Write Normalised
5. Smooth

\[
\begin{pmatrix}
m_{11} & m_{12} & m_{13} & m_{14} \\
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Contents

- Registration basics
- Motion and realignment
- Inter-modal coregistration
- Spatial normalisation
- Gaussian smoothing
Contents

- **Registration basics**
  - Voxel-to-world mapping
  - Transformation
  - Similarity measure
  - Optimisation
  - Interpolation

- **Motion and realignment**

- **Inter-modal coregistration**

- **Spatial normalisation**

- **Gaussian smoothing**
Representation of imaging data

- Three dimensional images are made up of voxels.

- Voxel intensities are stored on disk as lists of numbers.

- Meta-information about the data:
  - The image dimensions
    - Allowing conversion from list to 3D array
  - The “voxel-to-world mapping”
    - Spatial transformation that maps from data coordinates (voxel column $i$, row $j$, slice $k$) into a real-world position ($x, y, z$ mm) in a coordinate system e.g.:
      - Scanner coordinates
      - T&T/MNI coordinates
Image registration

- Process of transforming different set of images into one coordinate system.

- Two key ingredients:
  
  - **Transformation type:**
    - Rigid
    - Affine
    - Non-linear

  - **Similarity measure:**
    - Mean-squared difference
    - Correlation coefficient
    - Mutual information
Optimisation

- Automatic image registration is done by using an optimisation algorithm.

- Optimisation involves finding some “best” parameters according to an “objective function”, which is either minimised or maximised.

![Graph showing objective function with local optima and most probable solution.](image-url)
Applying the transformation parameters, and re-sampling the data onto the same grid of voxels as the target image
- reslicing, interpolation, regridding, transformation, and writing
Simple Interpolation

- Nearest neighbour
  - Take the value of the closest voxel

- Tri-linear
  - Just a weighted average of the neighbouring voxels
    - $f_5 = f_1 x_2 + f_2 x_1$
    - $f_6 = f_3 x_2 + f_4 x_1$
    - $f_7 = f_5 y_2 + f_6 y_1$
B-spline Interpolation

A continuous function is represented by a linear combination of basis functions.

B-splines are piecewise polynomials.

2D B-spline basis functions of degrees 0, 1, 2 and 3.

Nearest neighbour and trilinear interpolation are the same as B-spline interpolation with degrees 0 and 1.
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Motion correction

- Head movement is a very large source of variance in fMRI data.

- Motion correction: realign a time-series of images acquired from the same subject.
  - Within-subject transformation: rigid-body (6 parameters)
  - Within-modality: least squares objective function
Residual Errors from aligned fMRI

- Slices are not acquired simultaneously
  - rapid movements not accounted for by rigid body model

- Resampling can introduce interpolation errors
  - especially tri-linear interpolation

- Image artefacts may not move according to a rigid body model
  - image distortion
  - image dropout

- Functions of the estimated motion parameters can be modelled as confounds in subsequent analyses
Movement by Distortion Interaction of fMRI

- Subject disrupts $B_0$ field, rendering it inhomogeneous
  - Distortions in phase-encode direction

- Subject moves during EPI time series
  - Distortions vary with subject orientation
  - Shape varies (non-rigidly)

- “Realign & Unwarp”: generative model that combines a model of geometric distortions and a model of subject motion to correct images.
Movement correction strategies

- No correction
- Correction by covariation
- Correction by Unwarp
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Coregistration (intra-subject, inter-modal)

- Inter-modal registration.

- Match images from same subject but different modalities:
  - anatomical localisation of single subject activations
  - achieve more precise spatial normalisation of functional image using anatomical image.
Coregistration maximises Mutual Information

Between-modality registration:
Seek to measure shared information in some sense.

Joint histogram sharpness correlates with image alignment.
Mutual information and related measures attempt to quantify how well one image predicts the other.
Coregistration

L/R translation (mm)
-50 -40 -30 -20 -10 0 10 20 30 40 50

Normalised mutual information
1 1.02 1.04 1.06 1.08 1.1 1.12

Final Joint Histogram

/coreg_demo/T2w.nii
/coreg_demo/T1w.nii

Normalized mutual information

L/R translation (mm)
-50 -40 -30 -20 -10 0 10 20 30 40 50
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  - Unified segmentation
- Gaussian smoothing
Spatial Normalisation
Spatial Normalisation - Reasons

- Inter-subject averaging
  - Increase sensitivity with more subjects
    - Fixed-effects analysis
  - Extrapolate findings to the population as a whole
    - Random-effects analysis

- Make results from different studies comparable by aligning them to standard space.
The MNI template follows the *convention* of T&T, but doesn’t match the *particular brain* (http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach)
Unified Segmentation

- Normalising segmented tissue maps should be more robust and precise than using the original images.

- Tissue segmentation benefits from spatially-aligned prior tissue probability maps.

- Combining normalisation and segmentation in a unified model:
  - Gaussian mixture model segmentation
  - Intensity inhomogeneity (bias field) correction
  - Warping (non-linear registration)
Tissue intensity distributions (T1-weighted MRI)
Mixture of Gaussians

Classification is based on a Mixture of Gaussians model, which represents the intensity probability density by a number of Gaussian distributions.
Non-Gaussian Intensity Distributions

- Multiple Gaussians per tissue class allow non-Gaussian intensity distributions to be modelled.
  - E.g. accounting for partial volume effects
Modelling inhomogeneity

- A multiplicative bias field is modelled as a spatially smooth image (a linear combination of basis functions).
Tissue Probability Maps

- Each TPM indicates the prior probability for a particular tissue at each point in MNI space.

- SPM12’s TPMs are derived from the IXI dataset initialised with the ICBM 452 atlas and other data.
Deforming the Tissue Probability Maps

- Tissue probability images are warped to match the subject.
- The inverse transform warps to the TPMs.
- Warps are constrained to be reasonable by penalising various distortions (regularisation).
Without regularisation, the non-linear normalisation can introduce unnecessary deformation.

Non-linear registration using regularisation. (SSE = 302.7)

Non-linear registration without regularisation. (SSE = 287.3)

Affine registration. (SSE = 472.1)
Spatial Normalisation – Results

Affine registration

Non-linear registration
Spatial Normalisation – Limitations

- Seek to match **functionally** homologous regions, but...
  - No exact match between structure and function
  - Different cortices can have different folding patterns
  - Challenging high-dimensional optimisation, many local optima

- Compromise
  - Correct relatively large-scale variability (sizes of structures)
  - Smooth over finer-scale residual differences
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Smoothing

- Why would we deliberately blur the data?
  - Improves spatial overlap by blurring over minor anatomical differences and registration errors
  - Averaging neighbouring voxels suppresses noise
  - Increases sensitivity to effects of similar scale to kernel (matched filter theorem)
  - Makes data more normally distributed (central limit theorem)
  - Reduces the effective number of multiple comparisons

- How is it implemented?
  - Convolution with a 3D Gaussian kernel, of specified full-width at half-maximum (FWHM) in mm
Effect of smoothing

3D Gaussian smoothing with FWHM: 0, 2, 4, 6, 8, 10, 12, 14, 16 mm isotropic
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