METHODS FOR DUMMIES 2020

Pre-processing: Co-registration, spatial normalisation and smoothing

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With thanks to our expert John Ashburner



Typical SPM analysis sequence









Typical pre-processing steps

- 1. Remove dummy scans.
- 2. **Realign**: correct images for movement over time.
- 3. Slice timing: correct for different slice acquisition times.
- 4. **Co-register**: match image modalities in individual subjects (e.g. structural and functional).
- 5. **Normalise**: match images to a template across subjects (sometimes preceded by segmentation of tissue types).
- 6. **Smooth**: apply spatial filter to adjust for residual differences and alignment errors

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Coregistration



Anatomical MRI



Coregister

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 m_{23}

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1

Template



Estimate Spatial Norm

Deformation

Normalisation







Why Coregister?

- Intermodal
- Intrasubject
- Aim match images of same subject but different modalities
 - Link functional images (T2* weighted) with a structural image (T1)
 - Superior anatomical localisation
 - More precise spatial normalisation



FUNCTIONAL – T2*

Note the poor structural definition



STRUCTURAL – T1

CO-REGISTRATION

How Coregister? – Procedure

- It's not simple...
 - Cannot rely on simply using intensity difference
 - o Identifying individual landmarks too labour intensive
- Need a measure of similarity...
 - Seek to measure shared information
 - Registration intuitively relies on the concept of aligning images to increase their similarity
- Two-step process
 - i. Registration
 - ii. Reslicing (optional)



How Coregister? – i. Registration

- Similar to realignment
- Affine transformation
 - Estimate parameters
 - Apply these transformation
- Fit source image to reference image (static)
 - $_{\circ}$ \rightarrow Intensity nonuniformity (INU) in T1



How Coregister? - ii. Reslicing (optional)



- Resliced to the same dimensions, voxel sizes, orientation etc.
 - E.g., Match 3mm fMRI with 1mm T1 → produce 1mm fMRI that fill up the disk

Coregistration – advise ESTIMATE only

- [Coregister (Estimate)]
- The algorithm only changes the headers of the images in order to reflect their new orientation/position
 - The changed headers are accounted for by the spatial normalisation routines



Measure of similarity

- SPM mathematically measures the similarity of the two images
 - Images are too different to use mean squared difference
 - \circ \rightarrow Mutual Information (Information Theory)
 - More flexible measures of image similarity





 $\begin{aligned} \mathsf{MI} &= \int_{ab} \mathsf{P}(a,b) \log_2 \left[\mathsf{P}(a,b) / (\mathsf{P}(a) \mathsf{P}(b)) \right] \\ & * \text{ Related to entropy: } \mathsf{MI} = -\mathsf{H}(a,b) + \mathsf{H}(a) + \mathsf{H}(b) \\ & * \text{ Where } \mathsf{H}(a) = -\int_a \mathsf{P}(a) \log_2 \mathsf{P}(a) \text{ and } \mathsf{H}(a,b) = -\int_a \mathsf{P}(a,b) \log_2 \mathsf{P}(a,b) \end{aligned}$

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Statistics or

Spatial Normalisation





Spatial Normalisation

- Inter-subject
- Aim voxel to voxel correspondence between the subjects
 - Motivation a shared space to compare subjects



Different individuals' structural scans



Why Normalise?

- Increases statistical power
- Generalise to population level
- Allows group-level analysis
- Allows cross-study comparisons



How Normalise? – Templates

- Native Space → Standard Space
- Montreal Neurological Institute (MNI)
 - Different templates (e.g., Colin27, MNI305)
- Talairach and Tournoux (1988) atlas
 - Based on left hemisphere of 60-year-old woman
 - Smaller than MNI templates (→ mni2tal.m can convert)
- Individual/ averaged structural scans from own study
- SPM uses MNI ICBM152!



MNI Space



Normalise outcome – Localisation

23

37 19

- Standard coordinates [x y z] in mm
 - [0 0 0] = middle of brain
- Brodmann's area
 - Cytoarchitectonic map: areas with the same physiology



Original Brodmann's





Roll

How Normalise? – Procedure 1

i. Affine Linear transformation

- optimum 12-parameter
- Translations across axes (3 dof)
- Rotations around axes (3 dof)
- **Scaling** or Zooming (3 dof)
- **Shearing** or Skewing (3 dof)



Major differences in size, shape and position





How Normalise? – Procedure 2

- ii. Non-linear transformation Warping
 - Constructs non-linear deformations to move voxels from original location to template location
- Small-scale differences
 - Very flexible (1000s dof's)





Affine Registration

Non-linear Registration



2. Warping: how does it work?

Warping in SPM12: segment the source image into tissue types, using a Gaussian Mixture Model of signal intensities.





2. Warping: how does it work?

Alignment with the standard Tissue Probability Maps





2. Warping in more detail

Deformations: modelled with a linear combination of basis functions

 \rightarrow Using another updated algorithm



Bad Normalise? – problems of overfitting

- · Flexibility of warping can lead to unrealistic results
- \rightarrow Regularisation constraints to protect against overfitting

Non-linear registration using regularisation.



Non-linear registration without regularisation.

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Statistics or

Smoothing





Smoothing

- Blurs over residual anatomical differences and registration errors
- Evens out signal across space.
- Removes high spatial frequencies (signal that changes rapidly across voxels).







Why do Smoothing?

- Suppresses noise
 - signal reinforced and noise averaged out
- Superior special overlap
- Data becomes more normally distributed
- Increases sensitivity to effects of similar scale to kernel



No smoothing Smoothing in X direction X&Y direction

How to Smooth? - applying a kernel / filter

- A square section of the image is multiplied in an element wise fashion by the filter and summed
- The central voxel is reassigned to this new value
- A square filter is run across the whole image







Here is an example of an average filter being applied to an image Outlier pixels with lower values than the rest of the image are smoothed out



How to Smooth? - The Gaussian filter

- Rather than an average Kernel the central information can be more heavily weighted
- A gaussian does this and can be turned into a discreate kernel with varying widths
- This can then be applied to an image as in the previous slide





Smoothing: FWHM

- Defined by full-width at half maximum (FWHM)
- Width of smoothing kernel at half its maximum amplitude





Smoothing: FWHM value

- Ideally, size of smoothing kernel should match the expected signal ("matched filter" theorem)
- However, signal rarely known and varies across regions
- Typically, 5-8 mm FWHM
- The larger the FWHM, the more sensitive the statistical analyses, but less spatial resolution





Smoothing: disadvantages?

- Reduction of spatial resolution of the data
- Edge Artifacts
- Merging
- Extinction
- Misslocalisation of activation peaks



Summary

- Coregistration links functional data with a structural image →Intrasubject
- Normalisation links images from one subject to standardised space

→Intersubject

 Smoothing blurs over any residual errors and anatomical differences



Keep in mind

 Multiple data adjustments are made during fMRI analysis, and these alter the raw data considerably



References

- John's Lecture
- Ged Ridgway's preprocessing lecture
- SPM Homepage
- Mfd Resources 2018



Tutorial – Pre-processing #2

- We will use the Unwarped auditory data from last week
- Find the data @

https://www.fil.ion.ucl.ac.uk/spm/data/auditory/

& Select 'Auditory - single subject'

- Steps:
 - 1) Co-register fMRI data to structural image
 - 2) Spatially normalise structural images and apply to fMRI data
 - 3) Smooth the fMRI data
- Additional info on using 'segment' tool

Step 1) Co-register to Structural image

- Open SPM by typing:
 'spm fmri' into Matlab
- Select Coregister (Estimate)
- Coregister (Est & Res) will reslice the fMRI data to the same resolution as the structural data





Step 1) Select Reference image

- Click new subject
- Then click 'Reference image'
- · Go to structural image folder and select it
- Then press 'Done' button





Step 1) Select image to Co-register

- Select the first
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 Select all fMRIs already matched to the 016 image to also co-register

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Step 1) Objective function

- As the images are different sequences ensure one of the 'Mutual information' options is selected
- Then press 'Run' to process



Registration involves finding parameters that either maximise or minimise some objective function. For inter-modal registration, use Mutual Information, Normalised Mutual Information, or Entropy Correlation Coefficient.

For within modality, you could also use Normalised Cross Correlation.

Step 1) SPM- Coregistration Output

Very important to check your images- it automatically loads these up for you!

Normalised Mutual Information Coregistration X1 = 3.000'X +0.024'Y +0.019'Z +28.444

Y1 = -0.024*X +3.000*Y +0.045*Z +33.018

Z1 = -0.006*X -0.015*Y +1.000*Z -8.394



.\sM00223_002.img



.\sM00223_002.img





Step 1) Check Co-registration with 'Check Reg'

- Use can also use the 'Check Reg' function to ensure alignment worked
- Select structural image, original fMRI image and Co-registered fMRI image (still has a u prefix as doesn't make new images)

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Step 1) Check Reg

 You Can see good alignment with the T1 structural image of the same subject!



Original

fMRI

image



Structural image

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Step 1) Check Reg – contour option

 Right click the structural image and go to the contour option









Co-registered fMRI image



Structural image



Step 2) Spatial normalisation

- Use the Normalise (Est & Wri) tool which normalises to 'MNI space'
- Select the structural image to align



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Step 2) Select images to write

- Select all the coregistered fMRI images to spatially normalised
- Also select the structural images to check the normalisation if you want
- Press run and have a cup of tea!

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Step 2) Check against MNI space

 Go to the 'canonical' folder in the spm12 directory to find the MNI MRI images

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Step 2) Results

 You can use the 'Check Reg' function to check the results



Step 3) Smoothing

- Select 'Smooth' function
- You can alter the width of the smooth by changing on the FWHM section
- 8mm is selected here
- The images will be prefixed with an s







Step 3) Smoothing

- Select all images which were spatially normalised
- Prefixed here with w for warped

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Step 3) Check results

- Use 'Check Reg' to compare smoothed and unsmoothed images
- The smoothed images are prefixed with s
- And you're done!

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Unsmoothed







Smoothed



Alternate Step 2) Segment tool

- The segment tool can be used instead of the normalisation tool
- This is just here for extra info
- We include the following as an alternative to Step 2)

Spatial normalisation using 'Segment'

- Use the Segment tool
 which normalises to MNI
- It also produces a tissue segmentation and extracts the brain
- Select the structural image





Segment tool: 'Deformation Fields'

- Ensure the 'Forward' option is selected for the Deformation Fields
- Then press run

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Deformation Fields

Deformation fields can be saved to disk, and used by the Deformations Utility. For spatially normalising images to MNI space, you will need the forward deformation, whereas for spatially normalising (eg) GIFTI surface files, you'll need the inverse. It is also possible to transform data in MNI space on to the individual subject, which also requires the inverse transform. Deformations

Structural image Results

 You can use the 'Check Reg' function to check the results



UCL

Segmentation Results

 A set of tissue segments are also produced



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Skull stripping using segment output

- ImCalc can be used to extract the brain see expression
- the 'm' prefixed image is intensity nonuniformity corrected
- Tissue segmentations will be prefixed by 'c'
- Load 'm' image first then then c1 ,(grey matter) c2 (white matter) and c3 (CSF)

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lator



Skull stripping result

- See final INU and brain extracted result
- This new image can produce better co-registration results in step 1
- This help especially with severly effected INU images e.g. 7T MRI



Now Apply spatial normalisation to fMRI data

- Now you can use the 'Deformation / vector field' to warp the fMRI images
- Select the 'Normalise (Write)' tool

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- Go to the structural image folder
- The deformation field will have a y prefix

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Select fMRI data

- Press 'Images to Write'
- Select all fMRI images
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- Press run
- You can now proceed with step 3 / smoothing

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Q & A