SPM'99 Usage

Preface

This document provides step-by-step guidelines for those who are not yet familiar with the use of SPM'99.

SPM has an extensive web site at:

http://www.fil.ion.ucl.ac.uk/spm.

Practical information regarding the downloading and installation of SPM can be found at: http://www.fil.ion.ucl.ac.uk/spm/distrib.html.

Academic peer-reviewed papers providing a theoretical reference for SPM are available at: http://www.fil.ion.ucl.ac.uk/spm/dox.html.

Information about SPM courses and course notes can be accessed from:

http://www.fil.ion.ucl.ac.uk/spm/course.

Example data sets (which are also used in this manual) are available for downloading from: http://www.fil.ion.ucl.ac.uk/spm/data.

Help is available via the **Help** option of the SPM interface, and more detailed help in using SPM is available through the SPM *e*mail list:

http://www.fil.ion.ucl.ac.uk/spm/help.

Third party documentation is also available.

An extensive site describing many aspects of neuroimaging, including the use of SPM and links to image display software [Matthew Brett – matthew.brett@mrc-cbu.cam.ac.uk] can be found at:

http://www.mrc-cbu.cam.ac.uk/Imaging.

Protocols and tools for use with SPM99 [Kalina Christoff – kalina@psych.stanford.edu] can be found at:

http://www-psych.stanford.edu/~kalina/SPM99//.

Some useful snippets of code from the SPM *e*mail list for manipulation of images and results display [Tom Nichols - nichols@sph.umich.edu] can be found at:

http://www.sph.umich.edu/~nichols/JohnsGems.html

MRIcro - SPM compatible, Windows based software package for viewing medical images, converting image formats and identifying regions of interest [Chris Rorden chris.rorden@nottingham.ac.uk] can be freely downloaded from:

http://www.psychology.nottingham.ac.uk/staff/cr1/mricro.html.

Apologies if there are other useful sites that are not included here. Please remind us about them via the SPM email list.

Requirements

The present version of SPM requires core MATLAB (version 5.2 or higher; Maths Works, Inc., Natick, MA, USA) to run. The image format used is the simple header and image file format of ANALYZE (Biomedical Imaging Resource, Mayo Foundation). In SPM, image headers can be edited (and created) using the **HDR edit** option (described in section 5 below). Several researchers have developed routines for conversion of other image formats to ANALYZE format, (e.g. MRIcro). Other information about image converters is also available via the *e*mail list.

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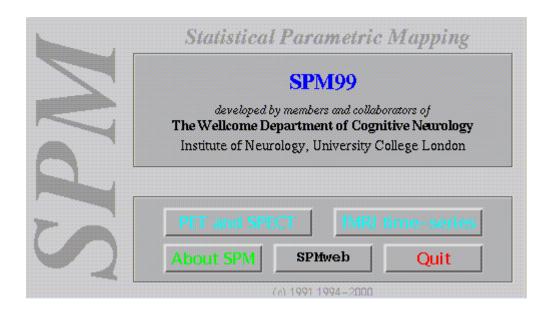
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1. Getting started



For start-up from Matlab, type **spm**.

Select from:

PET and SPECT (or enter **spm pet**)

Studies are considered as a series of independent scans

fMRI (or enter **spm fmri**)

Studies are considered as a temporally correlated time-series

N.B. The interface and usage for the above models of operation are similar. Differences between these components are indicated in this appendix.

About SPM

SPM'99 information

SPMweb

Link to the SPM-pages of the Wellcome Dept of Cognitive Neurology website (http://www.fil.ion.ucl.ac.uk/spm)

Quit

Exits SPM, closes windows and clears workspace variables

N.B. The directory from which SPM is started becomes the SPM working directory, to which a graphical output file **spm99.ps** (postscript file containing displays) and the results of statistical analyses are written. The **spm99.ps** file is appended when written to, SPM signals the risk of overwriting previous statistical results.

The SPM graphical user interface

	spatial pre	–processing		
Realign	Slice	timing	Smooth	
Coregiste	r Norn	nalize	Segment	
model	specification &	: parameter es	timation	
fMRI models Basic models				
Explore design		Esti	mate	
statistical inference				
	Res	sults		
	SPM for fur	ictional MRI		
Display	Check Reg	Render =	FMRI	
oolboxes 🚄	Means 🚚	ImCalc	HDR edi	
	***************************************	Defaults	Quit	

The SPM graphical user interface (shown above) is divided into three panels: the upper for spatial pre-processing of data, the middle for model specification/estimation and statistical inference, and the lower for general utilities (shown above for fMRI).

Spatial pre-processing functions are:

Realign: realignment of functional time-series

Coregister: Coregistration of same modality and multi-modality image volumes

Slice timing: Adjustment for timing differences in multi-slice image acquisition (fMRI)

Normalize: Spatial normalisation of image volumes to a template **Smooth**: Convolution of image volume with a Gaussian kernel

Segment: Segmentation of MRI volume(s) into CSF, grey and white matter

Model specification & parameter estimation:

fMRI and **PET/SPECT models**: set-up of modality-specific models

Basic models: basic statistical models for independent data

Explore design: review a previously specified model

Estimate: estimation of a previously specified model and configuration

Statistical inference:

Results: analysis and display of regional effects

The lower panel includes miscellaneous and general utility functions.

2. Spatial pre-processing

2.1 Realignment (spm_realign_ui.m)

Realignment of an image time-series of the same modality.

Realign	Slice timing	Smooth
Coregister	Normalize	Segment

Speci	fy:	_
	number of subjects 1	
Speci	fy (for fMRI only):	
	num sessions for subject 1	

Select scans:

Previous	Directories				=	pwd
/home/dv	/eltman/men	_fMRI2/C	PRICE/s	cans/scans	s/asc/asc1	
SubDirec	tories				=	home
Filter	*.img	All	Edit	Keybd	Reset	Done

Clicking the *.img will select those images, clicking the preceding number (in white) will show individual scans. SPM displays the total number of selected scans (lower part of window).

Other options:

- **Filter** disables filter
- **All** selects all images shown
- **Edit** allows editing of image file names
- Keybd allows command line input of image file names
- Reset will undo selection
- **Done** completes selection.

Specify:



Coregister only: determines parameters used to realign to the first image in the selected series. For multiple sessions, the first scan of each session is realigned to the first scan of the first session; then the images within each session are realigned to the first scan of the session.

Saves the transform parameters for each *filename*.img in *filename*.mat. Realignment parameters are saved for each session as **realignment_params_*.txt**, which can be used as a set of 6 covariates to regress out movement-related activations.

N.B.

- The first image = the first selected image. This need not be the first acquired in time.
- For each realignment, the current *.mat files are used and updated.
- All output images are written to the same directory as the input images. The mean*.img is written to the directory containing the images for the first session.
- In PET, realignment is in two steps: all images are realigned to the first and a mean image is computed to which all images are realigned in a second pass.

Reslice only: reslices and saves images using the transforms specified by *.mat files. Transforms *filename*.img using *filename*.mat and saves as *rfilename*.img.

Coregister & Reslice (=default): above steps combined. Saves transform parameters for *filename*.img in *filename*.mat. Reslices and saves images as *rfilename*.img.

Specify:



Trilinear interpolation: uses trilinear interpolation to resample images.

Sinc interpolation (default): uses a truncated (kernel is 9x9x9 voxels) sinc interpolation. Slower than trilinear but more accurate; recommended for fMRI time-series.

Fourier space interpolation: added option also found in other packages (AIR). Performs rigid body rotations as shears in Fourier space (Eddy et al. 1996, MRM 36, 923-931). For isotropic voxels only.

Specify:



All images (1-n): reslices all images including the first which is untransformed (i.e., SPM duplicates the first and saves it as *rfirstimage*).

Images 2-n: reslices all images except the first (useful when the first image has a different modality).

All images + **Mean Image** (default): reslices all images and creates a mean of all resliced images, which is saved as **mean** filename.img.

Mean Image only: creates mean image only.

N.B.

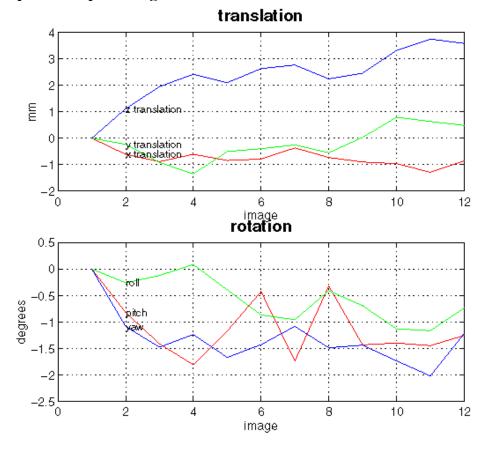
- Because each reslicing slightly degrades the images, this may be postponed until the normalisation step. It is useful, however, to create a mean image to determine parameters from at the normalisation stage (2.4) or to coregister to a structural MR (2.3). Select Coregister & Reslice, Trilinear or Sinc interpolation (trilinear is probably sufficient and much faster) and Mean Image Only. The other images will have only their *.mat files updated.
- If the ORIGIN coordinates in the image headers need adjustment, this should be done prior to realignment (because SPM will ignore the ORIGIN coordinates in the header once a *.mat file is created). Select the Display option (lower panel), select an image, and place the crosshair at the anterior commissure. Select HDRedit, select 'set Origin', and copy & paste the coordinates (in voxels) from the Graphics window. Apply to all time-series images (see 5 for discussion of utilities).

Specify (for fMRI only):

Adjust sampling errors? yes no

This removes interpolation errors arising from reslicing of the data by doing a regularised fit for motion-related variance and removes estimated variance from resliced images. However, if there is any motion-related variance that is correlated with the task, this option may remove variance of interest (i.e. true positives).

Output from spm_realign:



Display (shown here for a 12-scan PET study): **spm_realign** displays realignment parameters in graphic form. This display is written to the **spm99.ps** file in the working directory. This file can be viewed using a postscript reader package such as ghostview or pageview.

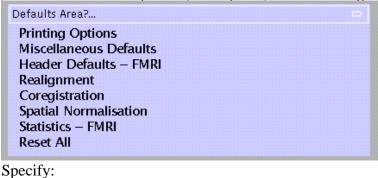
Files: the realigned images \mathbf{r}^* .img, \mathbf{r}^* .hdr, and the updated .mat files are written to the input file directory. The mean*.img and mean*.hdr are written to the input file directory for the first session. Realignment parameters are saved as realignment_params_*.txt to the input file directory for each session.

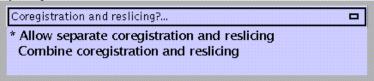
Customisations for realignment (optional):

N.B.

Changes in default settings are valid only during one session. After quitting and restarting SPM, these adjustments need to be renewed.

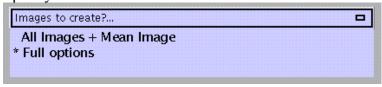
From the 'Defaults' options (lower panel), select 'Realignment':





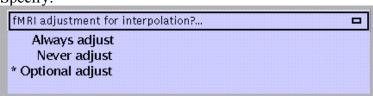
- allow separate coregistration and reslicing (default)
- always combine coregistration and reslicing

Specify:



- always create all images & mean image
- full options (default, see above)

Specify:



- always adjust for interpolation errors
- never adjust for interpolation errors (e.g., when realignment parameters are used as covariates)
- optional adjust (default)

Specify:



- always mask images (=default): to avoid movement-related artefactual variance at the edge of the FOV
- optional mask

Specify:



which refers to the density of voxel sampling for computation of realignment parameters. The quality improves with higher density, which is also more time-consuming.

2.2 Coregistration (spm_coreg_ui.m)

Between and within modality image coregistration.

S	spatial pre-processin	S		
Realign	Slice timing	Smooth		
Coregister	Normalize	Segment		
Specify:				
Specify:				
Which option? Coregister only Reslice Only * Coregister & Resli	ice	0		

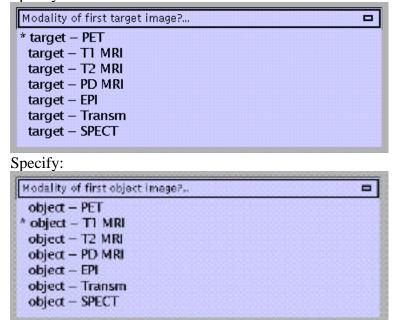
Coregister only: determines parameters used to coregister to one image to another. This option saves the transform parameters *filename*.img in *filename*.mat.

Reslice only: reslices and saves images using the transforms specified by the *.mat files. Transforms *filename*.img using *filename*.mat and saves as *rfilename*.img.

Coregister & Reslice (=default): above steps combined. Saves transform parameters for *filename*.img in *filename*.mat. Reslices and saves images as *rfilename*.img.

FOR 'Coregister only' AND 'Coregister & Reslice':

Specify:



Select:

select target image for subject 1

Select:

select object image for subject 1

Select (or press 'Done'):

select other images for subject 1

The TARGET image is the image to which the OBJECT image is realigned. OTHER images (if any) are transformed in the same way as the OBJECT image.

For example, to realign a structural T1-MRI to a fMRI time-series:

- TARGET: mean EPI

- OBJECT : T1 - OTHER : -

To realign a sequence of PET-images to a structural T1-MRI:

- TARGET: T1

- OBJECT: mean PET

- OTHER: PET1.img, PET2.img,....

N.B.

• If the target and object images have different modalities, an image segmentation (see **2.6**) is performed to partition target and object into CSF, white and grey matter. These partitions are then used in the coregistration.

FOR 'Reslice Only':

Select:

select image defining space for subject 1

The space of this image (i.e. the space defined by the .mat file associated with this image) will be used to reslice the object image.

Select:

select images to reslice 1

This image is the object image that will be resliced in the space of the previously selected image. The image will be resliced at the voxel size and origin of the previously selected image and will have the same space defined by the corresponding .mat file.

Output from spm_coregister:

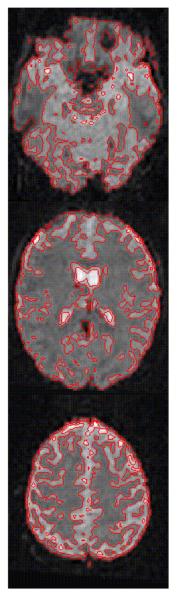
Coregistration

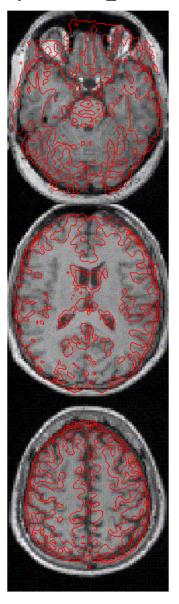
X1 = 0.028*X -1.938*Y +0.492*Z +212.782

Y1 = 0.038*X +0.493*Y +1.938*Z +68.358

Z1 = -1.333*X -0.012*Y +0.029*Z +107.141

..c1/nrfM01800_0016.img..rals/sM01742_0002.img





3M99 (dveltman): **22**:00:11 = 07/11/2000

Display: spm_coregister displays the coregistered images with the contours of the OBJECT image overlaid on both sets of images. This display is written to the **spm99.ps** file in the working directory. If OBJECT and TARGET image have different modalities, a segmentation is also carried out for both images. This is displayed as in **spm_segment** (see **2.6**) and written to the **spm99.ps** file.

Files: the coregistered images **r***filename*.**img** and **r***filename*.**hdr** are written to the same directory as the input images if 'reslice' is specified. The current **r***filename*.**mat** files are updated.

Customisations for coregistration (optional):

N.B. Changes in default settings are valid only during one session. After quitting and restarting SPM, these adjustments need to be renewed.

From the 'Defaults' options (lower panel), select 'coregistration':



- use default registration
- use mutual information registration (advisable when default between-modality coregistration doesn't work due to e.g. poor grey/white contrast, so that the segmentation step fails)

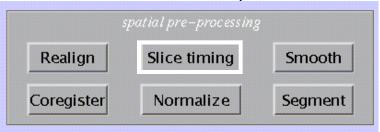
Specify (for default between-modality coregistration only):



- do all three coregistration steps (i.e., (1) 6-parameter (rigid body) normalisation of object and target image to a template of its own modality, (2) segmentation of object and target image, (3) coregistering the segmented images using the results of (1) as a starting point; =default)
- do first coreg step only (6-parameter normalisation of object and target image, each to a template of its own modality), e.g. when coregistering two images with poor grey/white contrast such as a PET transmission scan and a CT-scan, or as a first step prior to mutual information registration

2.3 Slice timing (spm_slice_timing.m)

Correction for differences in slice acquisition time.



This is only for fMRI. Corrects for differences in acquisition time between slices during sequential imaging (as in echo-planar imaging). Especially relevant for *event-related* designs. This routine performs a phase shift, resulting in each time series having the values that would have been obtained had the slice been acquired at (for example) the beginning of each TR.

N.B.

Specify:

Reference Slice (1=bottom)

- This step can be performed either before or after realignment (but before normalisation). Both procedures have potential disadvantages:
 - slice time correction before realignment may interpolate signals from different brain regions if there is significant head movement (which may be particularly problematic near the edge of the brain, where large signal differences occur across nearby voxels);
 - slice time correction after realignment however may shift voxels to adjacent slices (and hence different time points).
- The latter problem is especially relevant for *interleaved acquisitions*, where the time difference between adjacent slices may be _ TR. It is therefore recommended to perform *slice time correction first* for *interleaved* sequences.
- The latter problem is less relevant to *sequential* (*ascending*/*descending*) *acquisitions*, where the time difference between adjacent slices is small, and so *realignment* may be better first for *ascending*/*descending* sequences, to allow for movement effects.

Specify:
number of subjects/sessions 1
Select:
Select images to acquisition correct for
Specify:
Select sequence type
ascending (first slice=bottom) descending (first slice=top) interleaved (first slice=top) user specified
ascending (first slice = bottom; e.g. 1 2 368) descending (first slice = top; e.g. 68 67 661) interleaved (first slice = top; e.g. 68 66 642 67 65 631) user specified (e.g., other interleaved sequences; SPM will prompt for a vector specifying slice acquisition order, where the slices are numbered in Analyze format)

SPM will suggest the middle slice (in space) as the default (in the example above: slice 34). This is particularly useful for ascending/descending sequences because the phase shift interpolation tends to become less accurate with increasing shifts, and slices further away from the middle slice tend to be of less interest. When the regions of interest do lie in extreme (top or bottom) slices however, the reference slice may be chosen to correspond to these regions, so that interpolation artefacts are minimised (the signal in the reference slice itself is unchanged by the interpolation).

N.B.

- For fMRI analyses, SPM divides each TR into a number of time bins (by default this number=16). SPM by default then uses the first time bin as the reference or sampled bin. This bin provides the values from which the covariates are constructed.
- When the first slice in time is **NOT** used as the reference slice during slice-timing correction, the default sampled bin (=1) must be adjusted prior to statistical analysis.
- For example, if the middle slice was chosen as the reference slice for slice timing correction, the middle time bin must be set to the sampled time bin. If the number of time bins =16 for example, the sampled time bin should =8.
- To change these settings, select Defaults, select 'Statistics fMRI', set 'Sampled bin' to 8. This change must be made before creating the design matrix.

Specify:		
Interscan interval (TR) {secs}	4.162	
Specify:		
Acquisition Time (TA) {secs}	4.1008	

TR is defined as the time between the first slice of one scan and the first slice of the next scan; TA is the time between the first and the last slice within one scan. Without an interscan time delay, TA=TR-(TR/N), where N= number of slices (= default). When there is an interscan delay, TA must be adjusted.

N.B.

• In this example, TR>4sec. Although slice timing correction is potentially more important for long TRs, interpolation also becomes less accurate. It is therefore advised to omit slice time correction for TR>3sec and model timing differences by including temporal derivatives as an additional regressor, or using a phase-invariant Fourier set (see 3.1).

Output from spm_slice_timing:

Files: afilename.hdr, afilename.img and afilename.mat files are written to the input file directory.

2.4. Normalisation (spm_sn3d.m)

Three-dimensional spatial normalisation of PET, SPECT and (f)MRI images to a standard space.



Normalisation consists of two steps: first the determination of an optimum 12-parameter (translations, rotations, zooms & shears) affine transformation (from an image to a template), followed by a nonlinear estimation of deformations. These parameters can be used to reslice other images coregistered to the image from which the parameters were determined.

Select:



Determine parameters only: determines parameters (linear and nonlinear) used to normalise image to a template. Saves normalisation parameters in *filename_sn3d.mat*.

Write normalised only: reslices and saves images using normalisation parameters specified by the selected **sn3d.mat** file. Applies parameters to *filename.*img (*.hdr, *.mat) and saves as *nfilename.*img (n*.hdr, n*.mat).

Determine parameters and write normalised (=default): the above steps combined. Saves normalisation parameters for *filename*.img in *filename*_sn3d.mat. Saves normalised images as nfilename.img (n*.hdr, n*.mat).

N.B.

- All output images, headers and *.mat files as well as the *_sn3d.mat file are written to the input directory.
- To assure optimal normalisation, image and template should be in a similar starting position. This can be tested with the Check Reg option in the lower panel. Use the Display option to reposition the image (see section 5).

Specify:		
	н эпресс	
Select:		
subi 1 - Ima	ge to determine no	arameters

for example, a coregistered T1 structural image or a mean functional (PET or EPI) image.

Select:

subj 1 – Images to write normalised Select: Template image(s)

The selected template image which should be the same modality (and have very similar contrast) as the image from which the parameters are to be determined.

N.B.

- The space of the template images in SPM is based upon the Talairach system, but does not make assumptions about brain symmetry, and includes the cerebellum.
- The stereotactic space is based on 152 brains from the Montréal Neurological Institute, and will eventually be replaced in due course by a 450-brain version for the entire ICBM consortium ().
- The 152 subject average brain was chosen rather than the MNI305 official standard brain because from the 152 subjects T2- and PD-weighted images were also available, allowing much more flexibility in the range of different MR contrasts that can be spatially normalized to the same stereotaxic space. See **spm_templates.man** for details.
- A combination of templates may be used when the image to determine parameters from is different (e.g., intensity with a new MRI sequence) from the templates provided by SPM.
 For other purposes, e.g. normalising PET-ligand scans, creating a user-specified template should be considered.

Specify:



Nearest neighbour: fast but not very accurate and therefore not usually recommended.

Bilinear (=default): recommended for fMRI images which have been resliced at the realignment stage, and PET.

Sinc interpolation: uses a modified sinc interpolation (9x9x9 voxels kernel); slowest, recommended for fMRI data which have not been resliced at the realignment stage.

Output from spm_sn3d:

Spatial Normalisation

Image : /home/dveltman/men_fMRI2/temp/sM01742_0002.imgParameters : /home/dveltman/men_fMRI2/temp/sM01742_0002_sn3d

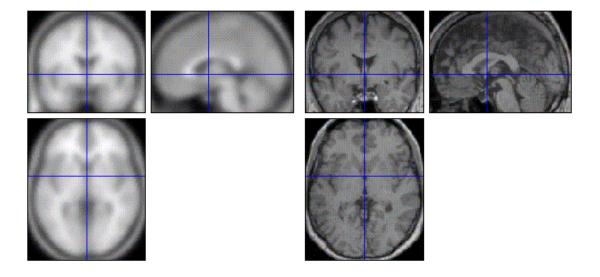
Linear {affine} component - image flipped

X1 = -1.014*X +0.031*Y -0.027*Z -2.990

Y1 = 0.011*X +1.013*Y +0.301*Z -18.126

Z1 = -0.018*X -0.336*Y +1.162*Z -22.571

12 nonlinear iterations 7 x 8 x 7 basis functions



SPM 99 (dveltman): 19:39:48 - 08/11/2000

Display: **spm_sn3d** displays the normalised image and the template. The display is written to the **spm99.ps** file in the working directory.

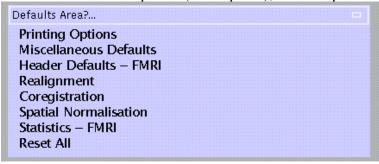
Files: the normalisation parameters *filename_sn3d.mat* are written to the same directory as the input image(s). The normalised images *nfilename.img* (*n*.hdr*, *n*.mat*) are written to the input directory if 'write normalised' is specified.

Customisations for normalisation (optional):

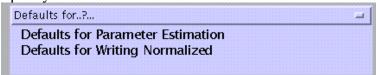
N.B.

Changes in default settings are valid only during one session. After quitting and restarting SPM, these adjustments need to be renewed.

From the 'Defaults' options (lower panel), select 'Spatial Normalisation':

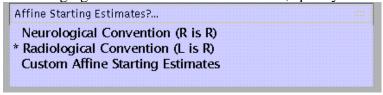


Specify:



- Defaults for Parameter Estimation (first step)
- Defaults for Writing Normalised (second step)

For changing Parameter Estimation defaults, specify:



- Neurological Convention (R=R): SPM assumes that the images are in neurological convention (as used by SPM) so the starting estimates won't include a L-R flip (0 0 0 0 0 0111000
- Radiological Convention (L=R; default): SPM assumes that the images are in radiological convention so the starting estimates will include a L-R flip (0 0 0 0 0 -1 1 1 0 0 0)
- **Custom Starting Estimates:**

[12] Enter Affine Starting 00000-111000 enter these in the following order: x translation (mm) y translation (mm) z translation (mm)

x rotation 'pitch' (radians)

y rotation 'roll' (radians)

z rotation 'yaw' (radians)

x scaling

y scaling

z scaling

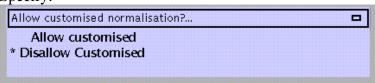
x shear y shear

z shear

N.B.

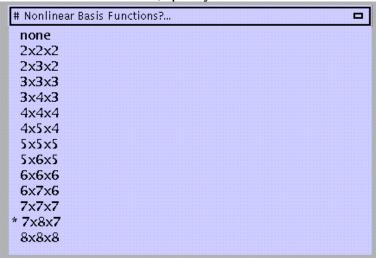
• As an alternative to customising starting estimates, prior to normalisation the images may be repositioned using the Display option (see above).

Specify:



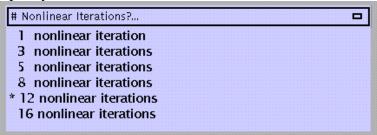
- Allow customised (options for # nonlinear basis functions and iterations, type of regularisation, and masking)
- Disallow customised normalisation (=default; standard options for # nonlinear basis functions and iterations, type of regularisation, and masking)

If customised is selected, specify:



The default is 7x8x7 functions. A large number of functions will improve the quality of the normalisation provided the images do not contain gross lesions and/or have different contrasts compared to the template. More functions will be computationally slower, however.

Specify:



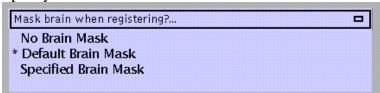
The default is 12 iterations. Again, the more iterations the better the result, but memory demands will similarly increase.

Specify:



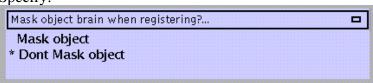
Regularisation involves stabilising the estimation of the deformations by penalising large deformations. Heavy regularisation basically means that more weight is applied to the penalty term. Therefore, if the spatial normalisation introduces excessive warping that is clearly wrong, more regularisation is needed. Conversely, if the images do not get warped enough to match the template, the amount of regularisation needs to be decreased. The default is medium regularisation.

Specify:



Masks template brain (1 1 1 1 .. for voxels within the brain, 0 0 0 0 .. for voxels outside the brain) in order to perform normalisation based on the shape of the brain instead of the skull. Not necessary when normalising a mean EPI image to the EPI template, in which case unmasked normalisation may give better results.

Specify:



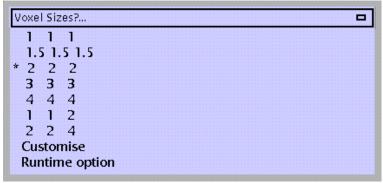
Similarly using $1\ 1\ 1\ 1$.. for voxels within the brain, $0\ 0\ 0$.. for voxels outside the brain. An object brain mask might be used e.g. to prevent an abnormal region (lesion) influencing the normalisation.

For changing Writing Normalised defaults, specify:

```
* -78:78 -112:76 -50:85 (Default)
-64:64 -104:68 -28:72 (SPM95)
-90:91 -126:91 -72:109 (Template)
-95:95 -112:76 -50:95
Customise
Runtime option
```

In mm distances (x y z) from the anterior commissure. When choosing 'Runtime option', SPM will prompt for bounding box dimensions during specification of the normalisation.

Specify:

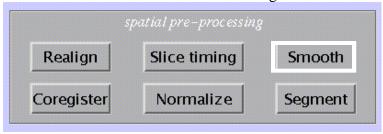


In mm (x y z):

- 111
- 1.5 1.5 1.5
- 2 2 2 (=default; may lead to oversampling of the data; the advantage is that the data will require less smoothing to meet the assumptions of Gaussian field theory, disadvantage is that resulting *.img files will use more disk space)
- 333
- 444
- 1 1 2 (e.g., for structural MRI's with 1mm interslice gap)
- 2 2 4 (e.g., for EPI images with 2mm in-plane resolution and 2mm interslice gap)
- Customise
- Runtime option (i.e., SPM will prompt for voxel sizes during specification of the normalisation)

2.5. Smooth (spm_smooth.m)

Three-dimensional convolution of an image with a Gaussian kernel.



Specify:	
smoothing {FWHM in mm}	

Gaussian filter width. This can be a scalar (for isotropic voxels) or a vector of length 3 (sx sy sz) for anisotropic voxels. Suggested is 2-3 times the voxel size.

Select:

select scans

N.B.

Spatial smoothing has three important objectives:

- it increases signal to noise ratio
- it conditions the data so that they conform more closely to a Gaussian field model. This is important if Gaussian field theory is used to make statistical inferences about regionally specific effects (i.e., assign *p*-values)
- it ensures that effects between different subjects are assessed on a reasonable spatial scale with respect to functional anatomy.

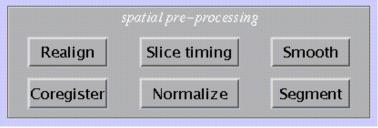
See also Matthew Brett's basic tutorial on smoothing at: http://www.mrc-cbu.cam.ac.uk/Imaging/smoothing.html

Output from spm_smooth:

Images are saved as sfilename.img (s*.hdr, s*.mat) in the same directory as the input files.

2.6. Segmentation (spm_segment.m)

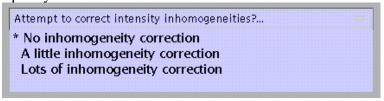
Segments MRI-image(s) into grey and white matter, CSF, and other.



Specify:		
number of subjects	1	
Select:		
Select MRI(s) f	or subject .	1
if more than one, they should be	e coregistered	l .
Specify:		
Are they spatially normalised?	yes	no
Are they spatially normalised?	yes	no
Are they spatially normalised? If not, specify:	yes	no
	yes	no

to match with a template which will be used for affine normalisation of the image(s). This is required for probabilistic segmentation.

Specify:



this option attempts to model intensity inhomogeneities using smooth basis functions.

If inhomogeneity correction is to be applied, specify:



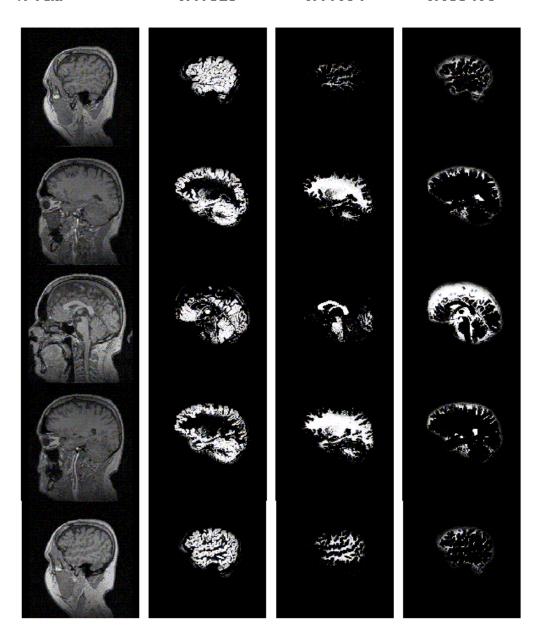
Inhomogeneity-corrected images may be saved as **corr**_filename.**img** for inspection.

Output from spm_segment.m:

Segmentation

Image: /home/dveltman/men_fMRI2/temp/sM01742_0002.ir

Means:90.4381110.320457.1711Std devs:8.78876.305515.9038N vox:0.179250.110840.059406

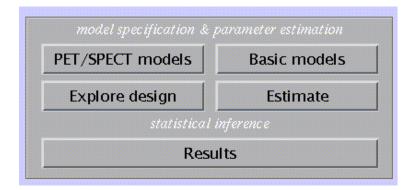


\$RM99 (dweltman): 20:51:18 - 08/11/2000

Display: spm_segment displays the segmentation results. This display is written to the spm.ps file in the working directory. N vox is the proportion of voxels belonging to each class, worked out from a subregion of the volume that encloses the brain.

Files: the segmented images are written as *filename_seg1.img*, *filename_seg2.img*, and *filename_seg3.img* for grey and white matter, and CSF. These images are saved to the input directory.

3. Model specification & parameter estimation



This section deals with the specification of a model to analyse imaging data, and subsequent parameter estimation. Statistical inference is performed using the Results option (see 4). SPM distinguishes three classes of models:

- for modality-specific, independent data (PET/SPECT models; 3.1)
- for modality-specific, serially correlated data (fMRI models, 3.2)
- basic models for independent data, which include random effects (RFX) analyses (3.3).

3.1 PET/SPECT models (spm_spm_ui.m)

SPM offers a number of PET/SPECT prototype models, which limits the number of necessary specifications for easy use.

N.B. All data entered in the model need to be in the same position (i.e., coregistered), and have identical dimensions and voxel sizes.

```
Select design type.....

Single—subject: conditions & covariates
Single—subject: covariates only
Multi—subj: conditions & covariates
Multi—subj: cond x subj interaction & covariates
Multi—subj: covariates only
Multi—group: conditions & covariates
Multi—group: conditions & covariates
Multi—group: covariates only
Population main effect: 2 cond's, 1 scan/cond (paired t—test)
Dodgy population main effect: >2 cond's, 1 scan/cond
Compare—populations: 1 scan/subject (two sample t—test)
```

- **Single-subject, conditions & covariates**: e.g. analysis of an individual subject, 12 scans (ARARARARAR), with habituation (time) as a covariate. See example 1 below
- **Single-subject, covariates only**: e.g., analysis of an individual subject, 12 scans during which a task is performed, with covariate = task score (this example is discussed in Matthew Brett's tutorial on SPM statistics; see http://www.mrc-cbu.cam.ac.uk/Imaging/spmstats.html)
- **Multi-subject, conditions & covariates**: e.g., a study with 10 subjects, each performing a task with three levels of difficulty, with reaction time as a covariate (i.e, a condition x covariate interaction)

- **Multi-subject, cond x subj interaction & covariates**: conditions are modelled separately for each subject, which allows assessment of condition x subject interactions. See example 2 below
- **Multi-subject, covariates only**: e.g., a study with 6 spider phobic patients shown slides of spiders during each of 12 scans, with anxiety ratings as a covariate
- **Multi-group: conditions & covariates**: e.g., a factorial design with two groups of subjects both performing an ARARARARAR experiment. This design allows assessment of main effects (task vs. rest) for each group separately and both groups combined, as well as task x group interaction effects
- **Multi-group, covariates only**: e.g., the 'Multi-subject, covariates only' spider study with a group of non-phobic controls added
- **Population main effect**: 2 conditions, 1 scan/condition (= modality-adjusted paired t-test), e.g., a PET or SPECT study using a dopaminergic ligand in subjects with Parkinson's disease scanned both pre- and post-therapy
- **Dodgy population main effect**: > 2 conditions, 1 scan/condition; 'dodgy' because sphericity assumptions are likely to be violated (see example 1 below)
- **Compare-populations**: 1 condition, 1 scan/condition (=modality-adjusted two-sample t-test), e.g., a PET or SPECT ligand study comparing patients to normal controls
- **Compare-populations (AnCova)**: 1 condition, 1 scan/condition, with nuisance variable(s) added, e.g. the preceding study with age entered as a possible confound
- **The Full Monty**: 'asks you everything'; an amalgam of 'Multi-subject, cond x subjinteraction & covariates' and 'Multi-group' options

Example 1: single-subject: conditions & covariates

Select:	
select image	<i>?s</i>
Specify a vector whose length equal	s the number of scans, e.g. 1 2 1 2 1 2 1 2 1 2 1 2:
[12] condition?	
Specify:	
# covariates 0	1 2 3 4
If a covariate is modelled, specify a	vector whose length also equals the number of scans:
[12] covariate	
Specify (e.g., time):	
covariate name?	
Specify:	
covariate: interaction?	to I
* <none> with condition</none>	

'none' will model the covariate (=time) as one parameter (time x session) or column in the design matrix (see below); 'with condition' as two (time x cond1 and time x cond2).

Specify:



centring of a covariate ensures that main effects of the interacting factor are not affected by the covariate, therefore SPM suggests centring around the overall mean. If 'interaction by condition' had been specified, the default becomes 'centring around condition means'.

Specify:

nuisance variables 0 1 2 3 4

(=0 in this example; otherwise, specification of nuisance variables is similar to covariates)

Specify:



Scan to scan differences in global flow can be

- modelled as a nuisance variable (AnCova),
- adjusted for by scaling the voxel values for each scan to the mean (**proportional scaling**)
- ignored.

AnCova is advised for multi-subject studies unless differences in global flow are large (e.g., due to variability in injected tracer dose). Because **AnCova** also uses one degree of freedom for each subject/group, **proportional scaling** may be preferable for single-subject studies.

If **proportional scaling** is selected, specify:

PropSca global mean to 50

the default of which scales the global flow to a physiologically realistic value of 50 ml/dl/min.

Specify:

Threshold masking absolute prop'nal

to ensure that only grey-matter voxels are included in the analysis, by masking out from all scans voxels which fail to reach the specified threshold.

If 'proportional' is selected, specify:

analysis thresh (prop'n of global) 0,8

the default being 80% of the mean global value. If thresholding is to be omitted, specify '-Inf'.

Specify:



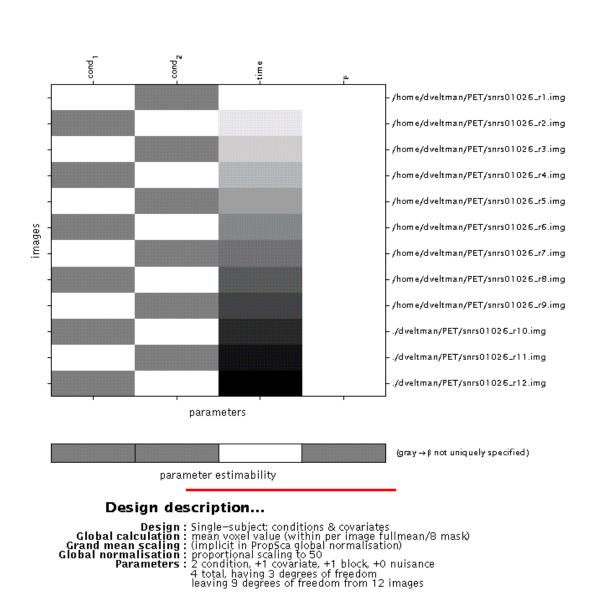
the default is a two-step process in which first the overall mean is computed, after which voxels which do not reach a threshold of overall mean/8 (i.e., those which are extra-cranial) get masked out, followed by a second computation of the mean of the remaining voxels.

yes	no
	yes

sphericity assumes equal variance and independency of measures across replications, condition types, and/or subjects. If this assumption is not met, without a correction statistical inference might produce biased (i.e., inflated) results. If a correction is to be applied, SPM will prompt to specify violations.

Output from PET/SPECT models (spm_spm_ui) for example 1:

Statistical analysis: Design



Display: SPM displays a design matrix having columns for each parameter (in this example, two conditions, one covariate, and one constant (block)) and a row for each scan. The greyand-white bar below the design matrix signals that the matrix is rank deficient (columns 1,2 and 4 are linearly dependent) which limits selection of meaningful contrasts (parameter weights) for condition effects to those which sum up to zero (see 4).

File: the design matrix will be saved as **SPMcfg.mat** in the working directory.

Specify:		
estimate?	now	later

to begin parameter estimation now or at a later stage. If 'later', select 'Estimate' (middle panel) and select the appropriate **SPMcfg.mat** file.

Example 2: Multi-subject, cond x subj interaction & covariates.

Consider a study in which five subjects perform an attention task with two stimulus types alternated with rest (ABRABRABRABR, suitably randomised across subjects) where individual differences in arousal (measured as skin conductance (GSR)) may interact with performance.

Specify (5):							
	#subject's	1	2	3	4	5	
Select:							
s	ubject 1: selec	t ii	ma	iges	Ţ		

Specify (for each subject) a vector whose length equals the number of scans, e.g. A B R R A B B R A A R B:

BBKAAKB:				
	[12] condition?			
Specify (1):				
	# covariates	0 1 2 3	4	
Specify a vector	whose length ed	quals the total r	number of scans:	
	[60] covariate			
Specify (GSR):				
	covariate name?			

Specify (with subject):



'none' will model the covariate (=GSR) as one parameter (GSR x session) or column in the design matrix (see below); 'with condition' as three (GSR x cond1-3) and 'with subject' as five (GSR x subj1-5).

Specify:



centering of a covariate ensures that main effects of the interacting factor are not affected by the covariate, therefore SPM here suggests centering around subject means.

Specify (0):



Select:

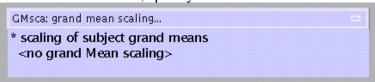


Scan to scan differences in global flow can be

- modelled as a nuisance variable (AnCova),
- adjusted for by scaling the voxel values for each scan to the mean (**proportional scaling**)
- ignored.

AnCova is advised for multi-subject studies unless differences in global flow are large (e.g., due to variability in injected tracer dose). Because AnCova also uses one degree of freedom for each subject/group, **proportional scaling** may be preferable for single-subject studies.

If **AnCova** is selected, specify:



the default corrects for subject to subject differences in mean global flow (within-subject differences were modelled during the previous step).

Specify (50):



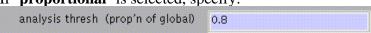
the default of which scales the global flow to a physiologically realistic value of 50 ml/dl/min.

As in example 1, specify:

 	-	,			
		Threshold masking	absolute	prop'nal	

to ensure that only grey-matter voxels are included in the analysis, by masking out voxels which fail to reach the specified threshold.

If 'proportional' is selected, specify:



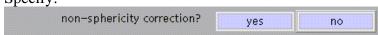
the default being 80% of the mean global value. If thresholding is to be omitted, specify '-Inf'.

Specify:



the default is a two-step process in which first the overall mean is computed, after which voxels which do not reach a threshold of overall mean/8 (i.e., extracranial) get masked out, followed by a second computation of the mean of the remaining voxels.

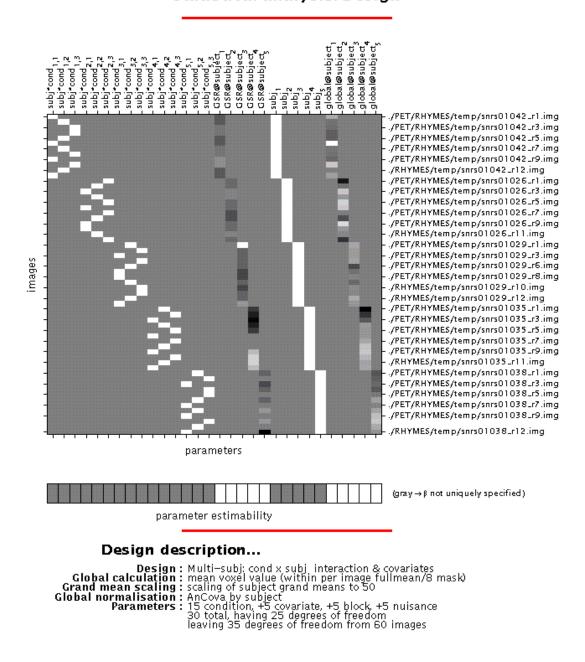
Specify:



Sphericity assumes equal variance and independency of measures across replications, condition types, and/or subjects. If this assumption is not met, without a correction statistical inference might produce unrealistic (i.e., inflated) results. If a correction is to be applied, SPM will prompt to specify violations.

Output from PET/SPECT models (spm_spm_ui) for example 2:

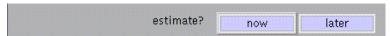
Statistical analysis: Design



Display: SPM displays a design matrix having columns for each parameter (in this example, fifteen conditions (three conditions, modelled separately for each subject), one covariate (GSR for each subject), five constants (block) and five nuisance variables (GBF)), and a row for each scan. The grey-and-white bar below the design matrix signals that the matrix is rank deficient (columns 1-15 and 21-25 are linearly dependent) which limits selection of meaningful contrasts (parameter weights) for condition effects to those which sum up to zero (see 4).

File: the design matrix will be saved as **SPMcfg.mat** in the working directory.

As in example 1, specify:



to begin parameter estimation now or at a later stage. If 'later', select 'Estimate' (middle panel) and select the appropriate SPMcfg.mat file.

N.B. Model estimation may also be launched via the 'Explore design' option. SPM will prompt you to select a SPMcfg.mat file for inspection. Clicking 'Design' (lower left window) will activate a pull-down menu which allows selection of displays for the design matrix, details of design orthogonality (surfable), selected scans and specified conditions, and covariates. It does *not* provide options to edit the model.

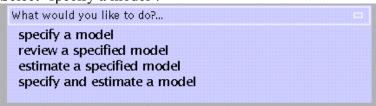
Output from PET/SPECT parameter estimation (spm_spm.m):

- **beta_0001.img/hdr, beta_0002.img/hdr, beta_0003.img/hdr,**: images containing parameter estimates for each column in the design matrix
- **mask.hdr/img**: mask image consisting of 0's and 1's indicating which voxels within the image volume are to be assessed
- **ResMS.hdr/img**: image of estimated residual variance
- **RPV.hdr/img**: image of estimated resels per voxel
- **SPM.mat file**: contains details of design matrix, analysed images, search volume, smoothness estimates and results files. See Appendix for more details.
- **xCon.mat file**: contains default F-contrast (so-called 'effects of interest') which are used for selecting 'interesting' voxels at which to save raw data for future plotting
- **Y.mad file**: contains (in compressed form) the raw (unsmoothed) data at voxels with an F-statistic higher than the default. Each column corresponds to one voxel, each row to an input image
- **Yidx.mat file**: contains a 1 x N vector of column indices used in the **Y.mad file** (where N = number of available voxels)

Other equipment such as the key response pad will send bytes other than zero to Cogent. Therefore when logging serial bytes it is easy to distinguish between pulses from the scanner and pulses from other apparatus. fMRI models (spm_fmri_spm_ui.m)

3.2.1 Specification of a model – first step:

Select 'specify a model':



As with PET/SPECT, SPM'99 allows separate model specification & inspection, and parameter estimation, for fMRI designs. However, fMRI model building is more flexible, the main distinction being between epoch- and event-related designs.

N.B. Whereas model specification & parameter estimation occurs in two stages for PET/SPECT studies, for fMRI there are three: (i) specification of conditions, timings, user-specified covariates, and regressor types (e.g. boxcar), (ii) selecting scans, modelling nuisance variables and other confounds, i.e. low-frequency drifts and temporal autocorrelation, (iii) parameter estimation. This permits the use of a single design matrix (i.e., the first step) for different data sets (sessions/subjects) acquired with the same paradigm, and also for designing an experiment (stochastic designs, see below). In SPM, the first step is termed 'specify a model', the second and third 'estimate a specified model'.

N.B. In the 'specify and estimate a model' option, the order of the prompts is slightly different; moreover, SPM does not display graphs of the specified regressor(s) and design orthogonality (these can be displayed using the 'review a specified model' option and selecting the appropriate **SPM_fMRIDesMtx.mat** file).

Specify:

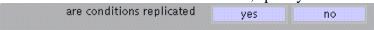
specify.		
spm_fMRI_d	esign: Basic parameters	
Int	erscan interval {secs}	

N.B. As with PET/SPECT, all data entered in the model need to be in the same position (i.e., coregistered), and have identical dimensions and voxel sizes. In addition, the TR needs to be identical.

Specify:
scans per session e.g. 64 64 64

Here SPM does not distinguish between sessions and subjects: e.g., for a design with 4 subjects each having two sessions of 96 scans, enter 96 96 96 96 96 96 96.

When more than one session is entered, specify:



If 'no', SPM will prompt for the number (and names) of conditions / trials for each session. If 'yes', specify:

			988
are timing/parameters the same	yes	no	

If 'no' (as will be usually the case, i.e. when replications are randomised across sessions), SPM will prompt for onset times/trial lengths for each session.

Specify:

number of co	anditions or	teleda			81727187		
number of co	oriuluons or	triais	0 1	7	2	4	
			V	-	201 - 100	-	

for all sessions combined when conditions are replicated, or otherwise for each session separately.

Specify:

name	for condition/trial 1 ? trial 1	1
	<u> </u>	

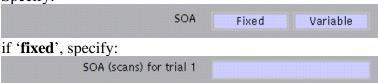
for each condition.

Specify:

stochastic design	yes	no

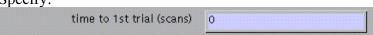
This option allows building an (event-related) experiment rather than analysing one. If 'yes', SPM will prompt to specify (i) whether to include a null event, (ii) a fixed time delay between consecutive events of the same type (SOA, see below), (iii) the relative frequency of event types (e.g., 1/1), and (iv) whether this frequency should be stationary or modulated across the experiment. The resulting design matrix can be used for both conducting and analysing an experiment. Otherwise, select 'no'.

Specify:



SOA = stimulus onset asynchrony = time (in scans) between the onset of two consecutive appearances of the same condition/trial type. This must be entered for each trial/condition.

Specify:



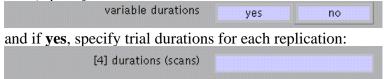
for each trial/condition. For example, if the 1st trial occurs at the beginning of the first scan, enter 0, if it occurs halfway through the 3rd scan, enter 2.5.

If SOA = 'variable', specify:

```
vector of onsets (scans) – trial 1
```

again for each trial/condition. Enter the onset in scans for each occurrence of the trial. The length of this vector should equal the number of times the trial occurs (replications).

Next, specify:



N.B. SOA = stimulus onset asynchrony = time (in scans) between the onset of two consecutive appearances of the same condition/trial type. As an example, consider a time series of 96 scans with conditions A, B, and R, each block lasting 8 scans; if the scanning order is ABRABRABR, SOA = fixed (24 scans), onset time = 0/8/16 for A/B/R. If the scanning order is randomised to ABRRBABARRAB, SOA = variable, vector of onsets = 0 40 56 80/8 32 48 88/16 24 64 72 for A/B/R.

N.B. If block lengths *within a condition* are different, it should be analysed as an event-related design (see below). Alternatively, it can be specified as an epoch design with separate conditions for each block length. For example, consider a simple ARAR... study in which condition A alternately lasts 7 or 8 scans; this can be modelled as A1RA2R... where A1 = 7-scan activation blocks, and A2 = 8-scan activation blocks.

N.B. In these examples, a resting condition is included for clarity. A resting condition (baseline) need not be explicitly modelled in SPM, however.

Specify:			
parametric modulation	none	time	other

This option allows modelling changes over replications of conditions/trials across session. If 'time' or 'other', select:

expansion	linear	exponen	polynom

to model linear, exponential, or polynomial changes. (When choosing 'polynomial', SPM will prompt for the order of the polynomial, the default being 2 generating a polynomial with linear + squared components).

Next, specify condition or trial numbers in which a parametric term should be included (e.g. for 2 trials, select 1, 2 or both):

which trial[s] 1 to 2 1	

If 'other', SPM will also prompt for a vector whose length is equal to the number of replications (e.g., 10):

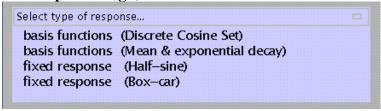
[10] parameters for trial 1	

For two or more condition/trial types, specify:

are these trials	events	epochs	mixed

For each condition, trials should be either events or epochs. If **mixed**, SPM prompts to specify '**events**' or '**epochs**' for each condition separately. If there is only one condition, SPM will also prompt to specify '**events**' or '**epochs**'.

For an **epoch design**, select:



i.e., a function or set of functions which, convolved with the timings specified earlier, provides the most adequate modelling of the data. Basis functions are more flexible than fixed response models but their components usually cannot be interpreted in a physiologically meaningful way; therefore multivariate or *F*-contrasts are required for statistical inference (see 4). A **discrete cosine set** may be useful when a steady-state response does not occur; SPM will prompt for the number of functions (default = 2). Similarly, **mean & exponential decay** may be chosen when the response decreases over time within an epoch (as opposed to across replications, see above).

Next, select:

1 (0/11, 501001.		
convolve with hrf	yes	no

Convolving with the canonical hemodynamic response function (**hrf**) will add a delayed onset, early peak, and late undershoot to the model.

Select:

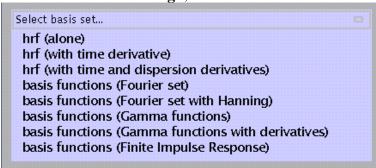
Beleet.		
add temporal derivatives	yes	no

if **yes**, the partial derivative of e.g. the box-car function with respect to time is added as an additional regressor, which will enable modelling of slight onset differences.

Finally, specify for each condition modelled as epochs:

epoch length {scans} for trial 1

For an event-related design, select:

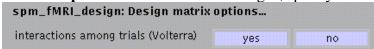


- **hrf (alone)**: canonical hemodynamic response function; based on empirical (visual stimulation) data; consists of two gamma functions (one positive, one negative) shifted 2s apart.
- **hrf (with time derivative)**: hrf with partial derivative for time added; allows modelling of slight (ca. 1s) onset differences.
- **hrf (with time and dispersion derivatives)**: hrf with partial derivatives for time *and* dispersion added; allows modelling of slight onset differences in onset time *and* response width.
- **basis functions (Fourier set)**: uses a set of sines/cosines to model responses. The default window length is 32s (at which time the canonical hrf has returned to baseline), the default number of functions is 4, resulting in 9 basis functions: sines/cosines with frequency 1/32, 2/32, 3/32 and 4/32 Hz, and a constant. The number of functions should be chosen with regard to the TR, as it is doubtful whether one should include components higher than the Nyquist frequency (i.e., 1/(2TR) Hz).
- basis functions (Fourier set with Hanning): similar to the previous option but with an amplitude modulation (Hanning filter) added so that all functions start and end at zero

- **basis functions** (**Gamma functions**): uses three gamma functions (which are asymmetrical) with different onset-to-peak times and orthogonalised with respect to each other.
- **basis functions (Gamma functions with derivatives)**: similar to the previous option but with temporal derivatives for each function added.
- **basis functions** (**Finite Impulse Response**): uses a set of 'mini-boxcars' to model peristimulus time. The default bin size (= 'boxcar length') is 2s, the default number of bins is 8, giving 9 functions (1 constant).

N.B. As with epoch designs, basis functions are more flexible (no prior assumptions regarding the shape of the response, especially the Fourier and FIR sets) but their components cannot be interpreted in a physiologically meaningful way and therefore usually need F-contrasts for inference. When T-contrasts are required (e.g., for a second-level analysis, see **3.3** and **4**), hrf with or without time and dispersion derivatives should be chosen.

For **both epoch and event-related** designs, specify:

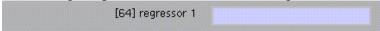


This option allows modelling (regressing out) of non-linearities due to the interaction of successive trials of the same type (for example, repetition suppression (priming)). Use also when the time between successive events is 2s or less.

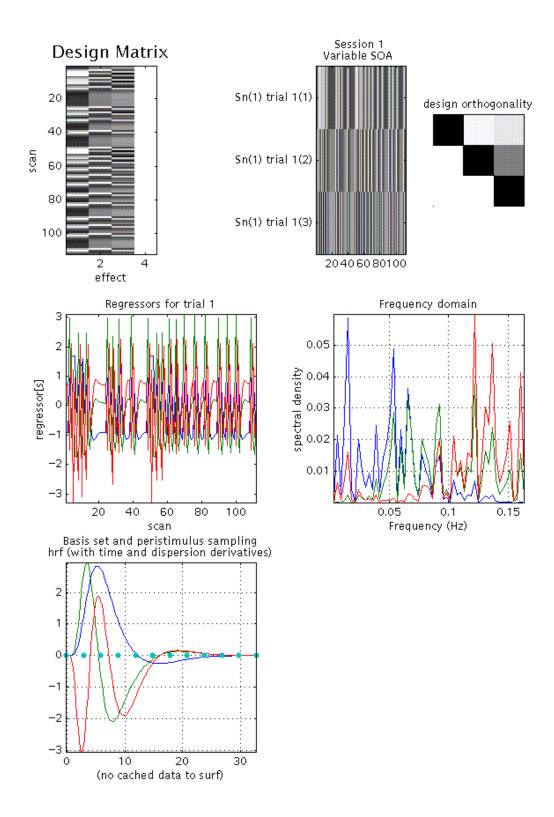
Specify:

Session 1/1: Other regressors							
user specified regressors	0	1	2	3	4	0	

to model any other covariates (i.e., other than modulation across replications (e.g., time) or within a block (=mean and exponential decay, see above)). SPM will prompt for a vector whose length equals the number of scans (e.g., 64):



Output from fMRI model specification (spm_fmri_spm_ui.m) - first step:



Display: shown for an event-related design, 112 scans, one event type, modelled using a canonical hrf with time and dispersion derivatives. There are six panels:

- **upper left**: shows the columns in the design matrix, one for each regressor, one constant (block). This matrix is surfable: R-clicking will show parameter names, L-clicking will show design matrix values for each scan
- **upper middle**: shows the 'columns' of the previous graph (except for the constant) after a 90° rotation, giving a 'bar graph' showing positive (light grey –white) and negative (dark grey black) values across session for regressor(s) used
- **upper right**: graph of design orthogonality: white = orthogonal, black = collinear, grey = between orthogonal and collinear. This matrix is also surfable: L-clicking will give the value of the cosine of the angle between two parameters (0 = orthogonal, 1 = collinear)
- **middle left**: shows a more detailed graph of each regressor across session (cf. upper middle panel)
- **middle right**: shows a Fourier (frequency domain) transform of each regressor
- **lower**: shows a graph of each regressor relative to peristimulus sampling (time bins)

N.B. As shown in this example, the regressors are not completely orthogonal due to the limited number of sampling points (orthogonality therefore varies with TR length).

File: the output of fMRI model specification at this point is saved as **SPM_fMRIDesMtx.mat** in the working directory.

N.B. SPM displays only the first trial/session. To review the model for subsequent trials/sessions, select 'review a model' from 'fMRI models', select the SPM_fMRIDesMtx.mat file, and click 'Explore fMRI design' (lower left window), which will activate a pull-down menu.

3.2.2 Specification of a model – second step:

To complete specification and proceed to estimating your model, select **estimate a specified model** from 'fMRI models':



which provides the option of scaling global activity *within a session* (scaling across sessions/subjects occurs implicitly). This may remove e.g. scanner drifts within a session; on the other hand, large activations may be scaled down as well.

Specify:

spm_fmri_spm_ui: Temporal auto	correlation	options
High—pass filter?	none	specify

Select **specify** if low-frequency confounds are to be removed.

		!	
ses	ssion cutoff p	ierioa (secs)	

The default suggested by SPM for epoch designs is *two times the experimental cycle*, e.g., for an ARAR.... design with A=8 scans and R=6, the default cutoff is 2(8+6)*TR. For event-related designs, the default is *two times the longest interval between two appearances of the most frequently occurring event*. For both epoch- and event-related designs the lower threshold is 32sec, the upper threshold is 512sec.

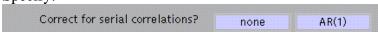
Specify:				
	Low-nass filter?	none	Gaussian	hrf

Because of the temporal autocorrelation in fMRI data, without a correction statistical inference would produce inflated results (the actual number of degrees of freedom is lower than the number of observations (scans)). SPM99 gives two options to deal with this problem: (i) replacing the unknown autocorrelations by an imposed autocorrelation structure, by smoothing the data with a temporal filter which will attenuate high frequency components, hence a 'low-pass filter'. The shape of this filter can be either **Gaussian** or **hrf**. Differences between these two are slight but **hrf** may provide a better sensitivity for event-related data modelled using a hrf-basis function; (ii) by attempting to regress out the unknown autocorrelations (AR(1)-model, see below).

if Gaussian, specify filter width	(default = 4sec):
Gaussian FWHM (secs)	4
dadstall (in the coes)	T .

A large (wide) filter implies that attenuation will occur at lower frequencies (or, put differently, that high frequencies will be suppressed more) than with a small filter. The trade-off is that a large filter may remove interesting data while a small filter will not be adequate to impose a new (known) autocorrelation structure on the data.

Specify:

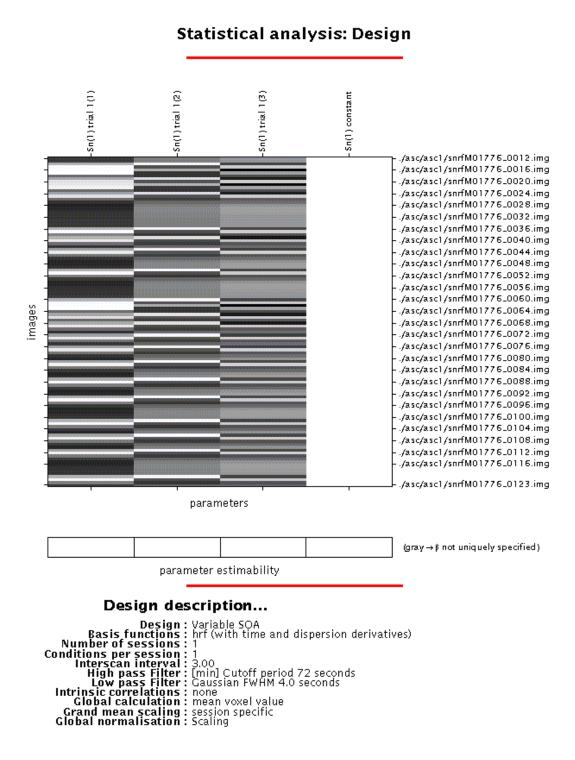


- AR(1) = auto-regression (1) = modelling serial correlations by regressing out the variance explained by the previous observation (scan).
- *N.B.* Either temporal smoothing or AR(1) should be chosen, not both.
- N.B. It is unclear whether the AR(1) option provides adequate correction for serial correlations and hence biased statistics. More extensive autoregression models (AR(n)) are more flexible than low-pass filtering but are computationally demanding.
- *N.B.* Serial correlations affect only statistical inference at the first level. Correction may therefore be omitted when one is only interested in a second-level (random effects) analysis.

spm_fmri_spm_ui: Estimation opt	ions	
Setup trial-specific F-contrasts?	yes	no

i.e., default *F*-contrasts for each trial type will be computed.

Output from fMRI model specification (spm_fmri_spm_ui.m) – 2nd step:

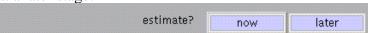


Display: the design matrix shown at this point is simply the left upper panel of the previous graph, with the file names of the scans added, and with other details of the configuration listed underneath.

Output: the configuration for the design matrix is saved as **SPMcgf.mat** in the working directory.

N.B. The design matrix is also shown when the 'specify and estimate a model' option has been chosen.

As with PET/SPECT models, SPM provides the option to begin parameter estimation now or at a later stage:



If 'later', select 'Estimate' (middle panel) and select the appropriate SPMcfg.mat file.

N.B. Model estimation may also be launched via the 'Explore design' option. SPM will prompt you to select a SPMDesMtx.mat or a SPMcfg.mat file for inspection. Clicking 'Design' (lower left window) will activate a pull-down menu which allows selection of displays for the design matrix for each session, details of design orthogonality (surfable), and model estimation (when the SPMcfg.mat file was selected).

Output from fMRI parameter estimation (spm_spm.m):

- **beta_0001.img/hdr, beta_0002.img/hdr, beta_0003.img/hdr,**: images containing parameter estimates for each column in the design matrix
- **mask.hdr/img**: mask image consisting of 0's and 1's indicating which voxels within the image volume are to be assessed
- **ResMS.hdr/img**: image of estimated residual variance
- **RPV.hdr/img**: image of estimated resels per voxel
- **SPM.mat**: contains details of design matrix, analysed images, search volume, smoothness estimates and results files. See Appendix for more details.
- **xCon.mat**: contains default F-contrast (so-called 'effects of interest') which are used for selecting 'interesting' voxels at which to save raw data for future plotting
- Y.mad: contains (in compressed form) the raw (unsmoothed) data at voxels with an F-statistic higher than the default. Each column corresponds to one voxel, each row to an input image
- **Yidx.mat**: contains a 1 x N vector of column indices used in the **Y.mad file** (where N = number of available voxels)

3.3 Customisations for PET/SPECT and fMRI statistics:

Select PET or fMRI statistics from the lower panel:



Defaults for model specification and parameter estimation are few to allow maximal flexibility.

For both PET and fMRI, specify:

Upper tail F prob. threshold	

for the default 'effects of interest'-F-test. The default value for PET is p<0.05 uncorrected (for multiple comparisons), for fMRI p<0.001 uncorrected.

For fMRI only, specify:

		800
Number of Bins/TR	16	

SPM interpolates each TR over this number of time bins to increase temporal resolution. 16 is chosen as default because it provides a reasonable degree of temporal resolution for typical TRs of 3-4s. The number of time bins could be equal to the number of slices, but increasing this number will not gain any real sensitivity (with typical TRs, given the time constants of the HRF and temporal smoothing), and may slow down computation.

Specify:

p v v i j v	
Sampled bin (in [1,16])	1

SPM uses the sampled bin to determine the value of a covariate at each scan. This should be adjusted if slice time correction is selected (e.g. for event-related fMRI) and the middle slice in time has been chosen as a reference slice (see **2.4**). In this case, if the number of bins is 16, the sampled bin should =8 (i.e. the corresponding middle time bin).

3.4 Basic models (spm.spm_ui.m)

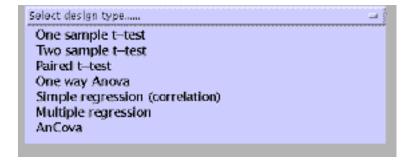
These are basic models for simple statistics, usually at a second level to extend the sphere of inference (random effects (RFX) analysis). Because SPM considers only a single component of variance (the residual error of variance), all analyses involving repeated measures within subjects are to be considered fixed-effects analyses, so that inferences are only valid for the sample under study. To allow inferences valid for the population from which the sample was drawn, a two-stage analysis is required, to account for first or intrasubject and second or between-subject levels of variance. During the first step, scan to scan variance (intrasubject) is modelled for each subject separately, resulting in a summary measure or 'scan'. These summary scans (usually *t*-contrast images (**con*.img**), containing weighted parameter estimates; see **4**) are then fed into a second, between-subjects level analysis, using the 'Basic models' option.

N.B. For second-level analyses, first-level individual subject models should be the same, in other words, it should be a balanced design.

N.B. To compute contrast images for a second-level analysis, either a single-subject OR a subject-separable multi-subject model should be chosen for the first level analysis, i.e. for PET 'Multi-subject, cond x subj interaction & covariates' (single-group design) or 'Full Monty' (multi-group design). For fMRI, each subject should be specified as one session, or contrasts should be specified over sessions. For example, if 10 subjects did two sessions each, this can be analysed as a 20-session experiment, with individual contrast images specified by 1 1 0 0 0 , 0 0 1 1 0 , and so forth.

N.B. The 'Basic models' option may also be used to analyse 'raw' (first-level) data. For this purpose SPM provides options for global normalisation, grand mean scaling and thresholding / implicit masking similar to those discussed for PET/SPECT models. For second-level analyses, however, it is **not** necessary to use these options at this stage because global normalisation etc. has been specified as part of the first level analysis.

Select:



- **One sample t-test**: tests the null hypothesis that the mean of one group of observations is identical to zero. For example, a second level analysis of activation-rest contrast images from a multi-subject experiment.
- Two sample t-test: tests the null hypothesis that the mean of one group of observations is identical to the mean of a second group of observations. For example, a second level

- analysis of activation-rest contrast images from a two-group (e.g., patients and controls) experiment.
- **Paired t-test**: tests the null hypothesis that the mean difference between a group of paired observations is zero. For example, a second level analysis of activation-rest contrast images from a multi-subject experiment with two separate sessions (e.g., pre- and post-therapy).
- **One way Anova**: tests the null hypothesis that the means of two or more groups of observations are identical. For example, a second level analysis of activation-rest contrast images from a three-group (e.g., patients A, patients B, and controls) experiment.
- **Simple regression (correlation)**: tests the null hypothesis that the slope of a fitted (using a least squares solution) regression line describing the relation between a predictor and an outcome variable is zero. For example, a multi-subject PET-ligand study with age as a potential confound.
- **Multiple regression**: regression with two or more predictors and one outcome variable. Tests the null hypothesis that the slope of the regression line for each predictor variable is zero. For example, a multi-subject PET-ligand study with age AND weight as potential confounds.

N.B. Designs in which one or more factors represent repeated measures (eg from the same subject) with more than two levels (eg a one-way Anova on three observations from the same group) are not strictly valid. This is because SPM (currently) assumes that the data are "spherical", which is rarely true in such models. This is why RFX analyses are normally restricted to one- or two-sample t-tests.

N.B. Designs with one measurement of a potential confound per subject (age, weight, education level, etc.) may also be analysed using the PET/SPECT models: 'single subject, covariates only' option, treating each subject as a scan.

- **AnCova**: analysis of covariance: regression with two or more groups of observations and one predictor. Tests the null hypothesis that the distance between parallel regression lines is zero AND the null hypothesis that the means of two or more groups of observations are identical, with the effects of the predictor (confound) removed. For example, a second level analysis of activation-rest contrast images from a two-group (e.g., patients and controls) experiment, with IQ as a potential confound. See example below

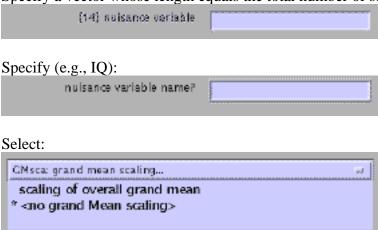
Example: AnCova (two groups, one covariate)

Specify (e.g. 2):



Select (for both groups):

Specify a vector whose length equals the total number of scans:



- scaling of all images to overall grand mean: use only for first-level analyses.
- no grand mean scaling (= default): for second-level analyses (as in this example).

Select (none):

beleet (none).	
Threshold masking	none absolute prop'nal
Select (no):	
Implicit mask lignora zaro's)?	yes no

Thresholding and implicit masking (i.e., ignoring zeros; SPM will automatically disregard zero values indicated by NaN (Not a Number)) should only be performed at the first level.

Select (no):



This option is primarily for analysing raw data; usually, images will be masked at the normalisation stage (2.4).

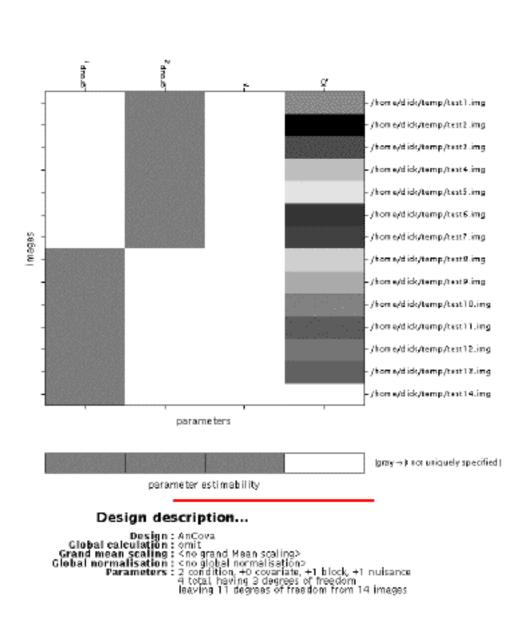
Select (omit):



Again, this option is for first-level analyses only.

Output from Basic models (spm_spm_ui):





Display: SPM displays a design matrix having columns for each parameter (in this example, two groups, one constant (block), and one covariate (IQ in this example), and a row for each scan (subject). Again, the grey-and-white bar below the design matrix signals that the matrix is rank deficient (columns 1-3 are linearly dependent) which limits selection of meaningful contrasts (parameter weights) for group effects to those which sum up to zero (see 4).

File: the configuration for the design matrix will be saved as **SPMcfg.mat** in the working directory.

Finally, specify:

estimate?	now	later
<u>L</u>		10.101

to begin parameter estimation now or at a later stage. If 'later', select 'Estimate' (middle panel) and select the appropriate **SPMcfg.mat** file.

N.B. Model estimation may also be launched via the **'Explore design'** option. SPM will prompt you to select a **SPMcfg.mat** file for inspection. Clicking **'Design'** (lower left window) will activate a pull-down menu which allows selection of displays for the design matrix, details of design orthogonality (surfable), selected scans and specified conditions, and covariates. It does *not* provide options to edit the model.

Output from Basic models parameter estimation (spm_spm.m):

- **beta_0001.img/hdr, ...**: images containing parameter estimates for each column in the design matrix.
- **mask.hdr/img**: mask image consisting of 0's and 1's indicating which voxels within the image volume are to be assessed.
- **ResMS.hdr/img**: image of estimated residual variance.
- **RPV.hdr/img**: image of estimated resels per voxel.
- **SPM.mat**: contains details of design matrix, analysed images, search volume, smoothness estimates and results files. See Appendix for more details.
- **xCon.mat**: contains default F-contrast ('all effects' or 'effects of interest') which is used for selecting voxels at which to save raw data for future plotting.
- Y.mad: contains (in compressed form) the raw (unsmoothed) data at voxels with an F-statistic higher than the default. Each column corresponds to one voxel, each row to an input image.
- **Yidx.mat**: contains a 1 x N vector of column indices used in the **Y.mad** file (where N = number of available voxels).

4. Results assessment (spm_results_ui.m)

This section deals with the interactive exploration and characterisation of the results of a statistical analysis. For this purpose, three data sets will be discussed, which can be found at http://www.fil.ion.ucl.ac.uk/spm/data. These examples are (i) a single-subject epoch (block) fMRI study, (ii) a multi-subject PET study, (iii) a single-subject event-related fMRI study.

4. 1. Example 1: single-subject fMRI block design

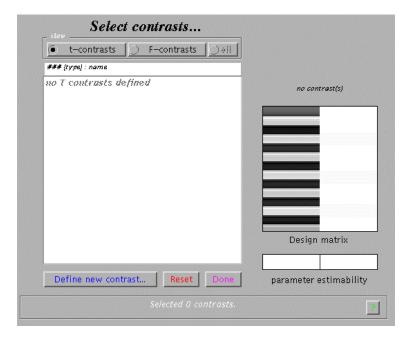
This is a single-subject auditory activation study, with alternating 6-scan blocks of rest and binaural stimulation (speech). Details of model specification and parameter estimation can be found in the README_analysis.txt.

After completing model estimation (this is shown in the lower left SPM and Matlab windows), press 'Results'.

Select:

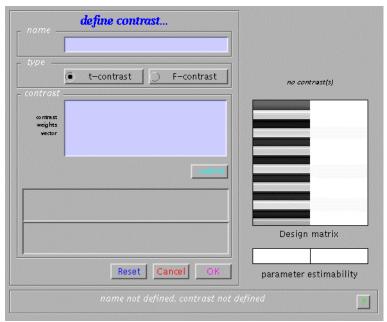
Select SPM.mat

This will invoke the Contrast Manager:

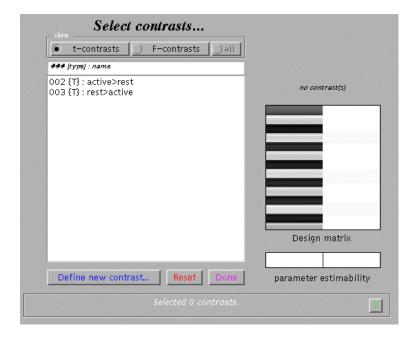


The contrast manager displays the design matrix (surfable) in the right panel and lists specified contrasts in the left panel. Either 't-contrast' or 'F-contrast' can be selected. One F-contrast is predefined ('effects of interest').

To examine statistical results for condition effects, select 'Define new contrast':



Main effects for the active condition (i.e., a one-sided *t*-test) can be specified (in this example) as '1' (active > rest) and '-1' (rest > active). SPM will accept correct contrasts only. Accepted contrasts are displayed at the bottom of the contrast manager window in green, incorrect ones are displayed in red. To view a contrast, select the contrast name (e.g., active>rest) and press 'Done':



Specify (no):



Masking implies selecting of voxels specified by other contrasts. If 'yes', SPM will prompt for (one or more) masking contrasts, the significance level of the mask (default p=0.05 uncorrected), and will ask whether an inclusive or exclusive mask should be used. *Exclusive* will remove all voxels which reach the default level of significance in the masking contrast, *inclusive* will remove all voxels which do not reach the default level of significance in the masking contrast. Masking does **not** affect p-values of the 'target' contrast, it only includes or excludes voxels.

Select (enter a title title fo): or comparison	active>rest	
Specify (yes):			
	ight threshold	yes	no

Select a height/amplitude threshold to examine results that are either corrected for multiple comparisons ('yes'), or uncorrected ('no') at a voxel-level.

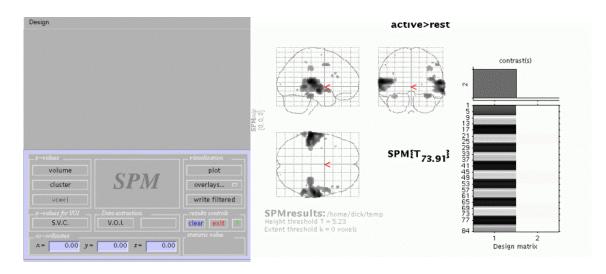


For corrected comparisons, the SPM default is p=0.05, for uncorrected comparisons, p=0.001.



Select the number of voxels to restrict the minimum cluster size. 0 will include single voxel clusters ('spike' activations).

Output from Contrast Manager:



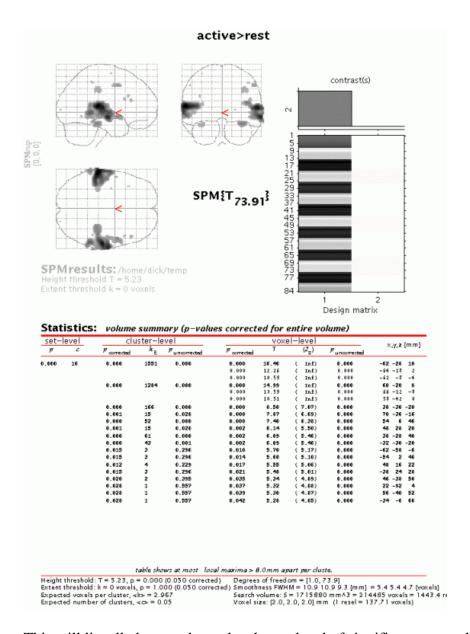
Files: images containing weighted parameter estimates are saved as **con_0002.hdr/img**, **con_0003.hdr/img**, ...etc. in the working directory. Images of *T*-statistics are saved as **spmT_0002.hdr/img**, **spmT_0003.hdr/img**.. etc, also in the working directory.

Display: in the Graphics window, SPM displays

- (i) a **maximum intensity projection** (MIP) on a glass brain in three orthogonal planes. The MIP is surfable: R-clicking in the MIP will activate a pulldown menu, L-clicking on the red cursor will allow it to be dragged to a new position.
- (ii) the design matrix (showing the selected contrast). The design matrix is also surfable: R-clicking will show parameter names, L-clicking will show design matrix values for each scan.

In the SPM Interactive window (lower left panel) a button box appears with various options for displaying statistical results (*p*-values panel) and creating plots/overlays (visualisation panel). Clicking 'Design' (upper left) will activate a pulldown menu as in the 'Explore design' option.

To get a summary of local maxima, press 'volume':



This will list all clusters above the chosen level of significance as well as separate (>8mm apart) maxima within a cluster, with details of significance thresholds and search volume underneath. The columns show, from right to left:

- x, y, z (mm): coordinates in Talairach space for each maximum
- **voxel-level**: the chance (*p*) of finding (under the null hypothesis) a voxel with this or a greater height (*T* or *Z*-statistic), corrected / uncorrected for search volume
- **cluster-level**: the chance (p) of finding a cluster with this or a greater size (k_e), corrected / uncorrected for search volume
- **set-level**: the chance (*p*) of finding this or a greater number of clusters (c) in the search volume

N.B. The table is surfable: clicking a row of cluster coordinates will move the pointer in the MIP to that cluster, clicking other numbers will display the exact value in the Matlab window (e.g. 0.000 = 6.1971e-07).

To inspect a specific cluster (e.g., in this example data set, the R auditory cortex), either move the cursor in the MIP (by L-clicking & dragging the cursor, or R-clicking the MIP

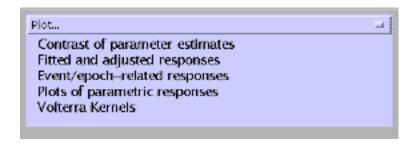
volume table, or type the coordinates in the lower left windows of the SPM Interactive window.

Select 'cluster':

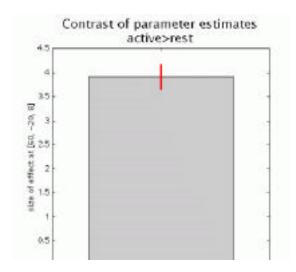
clu	ster-le	vel		VOX	el-level		x,y,z {m m
p corrected	k _E	P _{uncorrected}	p corrected	Ţ	(Z ₌)	^{jp} uncorrected	x,y,z (m m
0.000	1284	0.000	0.000	14.99	(Inf)	0.000	60 -20 8
			0.000	19.59	(Inf)	0.000	66 -12 -8
			0.000	10.51	(Inf)	0.000	58 -42 0
			4.000	8.78	(7.24)	0.000	42 -28 16
			0.000	8.96	(6.99)	0.000	70 -18 -2
			1.111	8.21	(6.90)	0.000	52 4 -8
			1.111	7.97	(6.75)	0.000	86 -88 -6
			0.000	6.75	(5.94)	0.000	50 -12 -8
			0.005	5.97	(5.98)	0.000	58 -24 -8

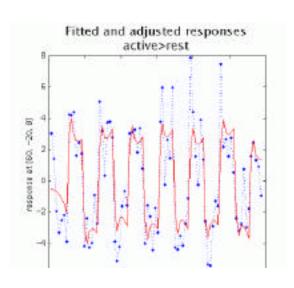
This will show coordinates and voxel-level statistics for local maxima (>4mm apart) in the selected cluster. This table is also surfable.

To plot effect size and/or signal time course from a voxel, e.g. for the cluster maximum, move the cursor to $(60-20\ 8)$. Next, press 'plot':

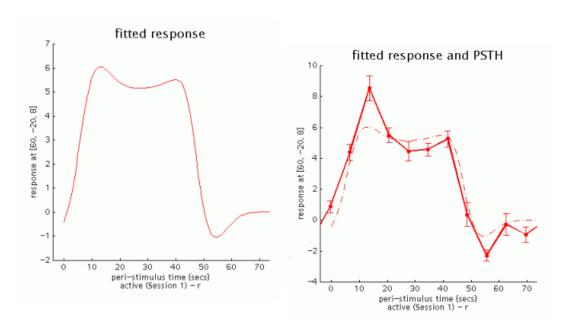


- **Contrast of parameter estimates**: SPM will prompt for a specific contrast (e.g., active>rest). The plot will show effect size and error bars (in %).
- **Fitted and adjusted response**: Plots adjusted data and fitted response across session/subject. SPM will prompt for a specific contrast and provides the option to choose different ordinates ('an explanatory variable', 'scan or time', or 'user specified'). If 'scan or time', the plot will show adjusted BOLD data (in %, blue dashed line) and the regressor(s) used (red solid line):

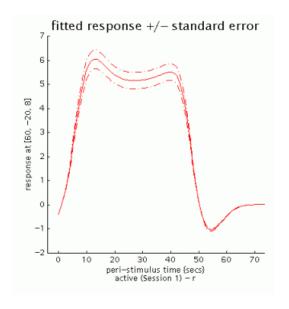


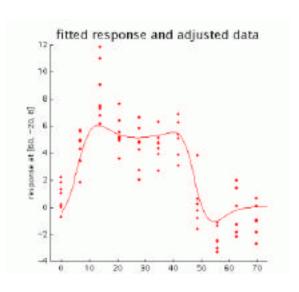


- **Event/epoch-related responses**: Plots adjusted data and fitted response across peristimulus time. SPM provides four options:
- **fitted response:** simple plot of mean (i.e., averaged over session) regressor(s) across PST
- **fitted response and PSTH** (*peri-stimulus time histogram*): plots mean regressor(s) and mean signal +/- SE for each time bin



- **fitted response** +/- **standard error:** plots mean regressor(s) +/- SE
- **fitted response and adjusted data:** plots regressor(s) and individual data (note that in this example the data are shown in columns due to the fixed TR/ISI relationship)



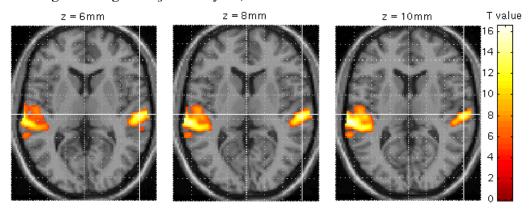


N.B. The values for the fitted response across session/subject for the selected plot can be displayed and accessed in the Matlab window by typing 'Y'. Typing 'y' will display the adjusted data.

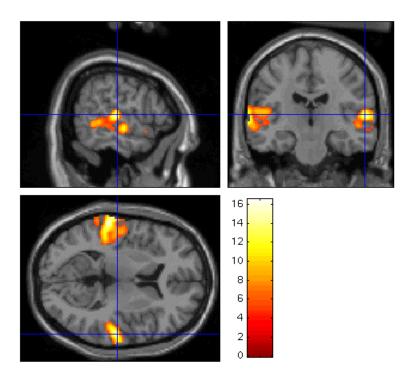
N.B. 'Adjusted' data = adjusted for confounds (e.g., global flow) and high- and low pass filtering.

For anatomical visualisation of a cluster (in this example, R auditory cortex), press 'overlays' which will activate a pulldown menu. There are three options:

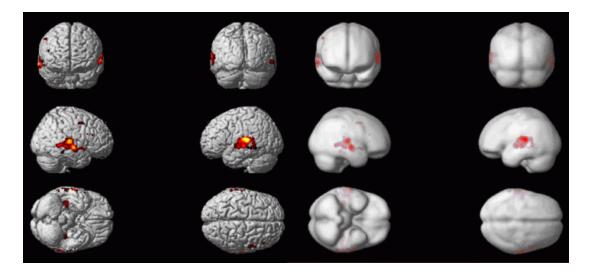
- **slices**: overlay on three adjacent (2mm) transaxial slices. SPM will prompt for an image for rendering (a canonical image (see **spm_template.man**) or an individual T1/mean EPI image for single-subject analyses)



- **sections**: overlay on three intersecting (sagittal, coronal, transaxial) slices. These renderings are surfable: clicking the images will move the crosshair



- **render**: overlay on a volume rendered brain, with options for using a smoothed brain, and old (left) and new (right) style rendering



Renderings can be saved as *filename*.img and *filename*.hdr in the working directory by using the **write filtered** option.

Other options (in the **results controls** panel):

- **clear**: clears lower subpanel of Graphics window
- **exit**: exits the results section
- ?: launches spm_results_ui help

4.2 Example 2: Multi-subject PET study

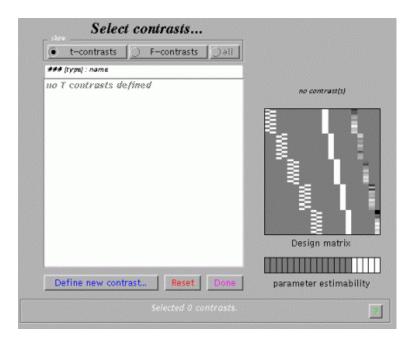
This is a PET word generation study with five subjects, each having 12 scans, with alternating conditions of word shadowing (baseline) and word generation (active), randomised across subjects (see the README.txt). Although this data set can be analysed in several ways, it is suggested to select a subject-separable model (Multi-subj: cond x subj interaction & covariates, see 3.1). Specify: # covariates = 0, # nuisance variables = 0, GloNorm: AnCova by subject.

After completing model estimation (this is shown in the lower left SPM and Matlab windows), press 'Results'.

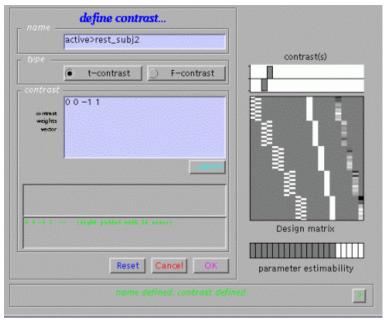
Select:

Select SPM.mat

This will invoke the Contrast Manager:

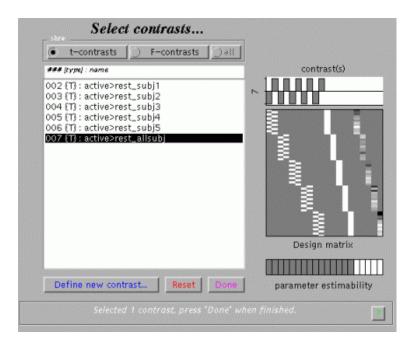


To examine condition effects e.g. for subject 2, select 'Define new contrast'. Specify e.g. 'active>rest_subj2' (name) and '0 0 -1 1' (contrast), and press 'submit':



As shown, SPM will interpret '0 0-1 1' as '0 0-1 1 0 0 0 0 0'. Condition effects for each subject may be assessed as in the previous fMRI example.

To examine group effects, define e.g. 'active>rest_allsubj' as '-1 1 -1 1 -1 1 -1 1 -1 1' and select it (press 'Done'):





Masking implies selecting of voxels specified by other contrasts. If 'yes', SPM will prompt for (one or more) masking contrasts, the significance level of the mask (default p = 0.05 uncorrected), and will ask whether an inclusive or exclusive mask should be used. *Exclusive* will remove all voxels which reach the default level of significance in the masking contrast,

inclusive will remove all voxels which do not reach the default level of significance in the masking contrast. Masking does **not** affect *p*-values of the 'target' contrast.

Specify (yes):

corrected height threshold yes	f ○

Select a height/amplitude threshold to examine results that are either corrected for multiple comparisons ('yes'), or uncorrected ('no') at a voxel-level.

Specify:

specify.		
	corrected a value	0.05

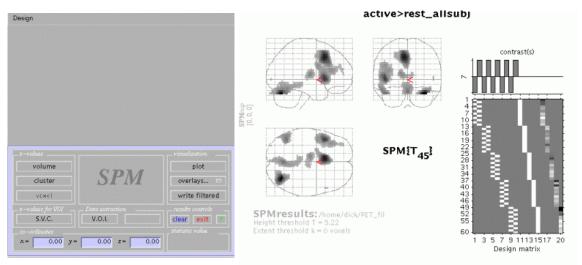
For corrected comparisons, the SPM default is p=0.05, for uncorrected comparisons, p=0.001.

Specify:



Select the number of voxels to restrict the minimum cluster size. 0 will include single voxel clusters ('spike' activations).

Output from Contrast Manager:



Files: images containing weighted parameter estimates are saved as **con_0002.hdr/img**, **con_0003.hdr/img**, ...etc. in the working directory. Images of T-statistics are saved as **spmT_0002.hdr/img**, **spmT_0003.hdr/img**.. etc., also in the working directory.

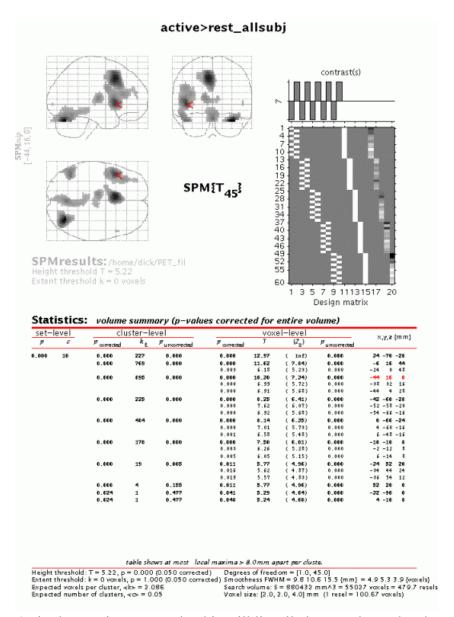
Display: in the Graphics window, SPM displays

(i) a **maximum intensity projection** (MIP) on a glass brain in three orthogonal planes. The MIP is surfable: R-clicking in the MIP will activate a pulldown menu, L-clicking on the red cursor will allow it to be dragged to a new position.

(ii) the design matrix (showing the selected contrast). The design matrix is also surfable: R-clicking will show parameter names, L-clicking will show design matrix values for each scan.

In the SPM Interactive window (lower left panel) a button box appears with various options for displaying statistical results (*p*-values panel) and creating plots/overlays (visualisation panel). Clicking 'Design' (upper left) will activate a pulldown menu as in the 'Explore design' option.

To get a summary of local maxima, press 'volume':



As in the previous example, this will list all clusters above the chosen level of significance as well as separate (>8mm apart) maxima within a cluster, with details of significance thresholds and search volume underneath. The columns show, from right to left:

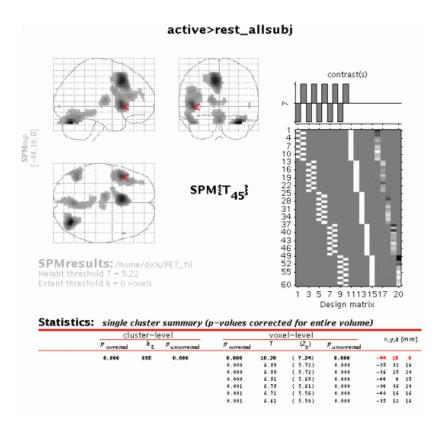
- x, y, z (mm): coordinates in Talairach space for each maximum

- **voxel-level**: the chance (*p*) of finding (under the null hypothesis) a voxel with this or a greater height (*T* or *Z*-statistic), corrected / uncorrected for search volume
- **cluster-level**: the chance (p) of finding a cluster with this or a greater size (k_e), corrected / uncorrected for search volume
- **set-level**: the chance (*p*) of finding this or a greater number of clusters (c) in the search volume

N.B. The table is surfable: clicking a row of cluster coordinates will move the pointer in the MIP to that cluster, clicking other numbers will display the exact value in the Matlab window (e.g. 0.000 = 6.1971e-07).

To inspect a specific cluster (e.g., in this example data set, the L prefrontal cortex), either move the cursor in the MIP (by L-clicking & dragging the cursor, or R-clicking the MIP background which will activate a pulldown menu), or click the cluster coordinates in the volume table, or type the coordinates in the lower left windows of the SPM Interactive window.

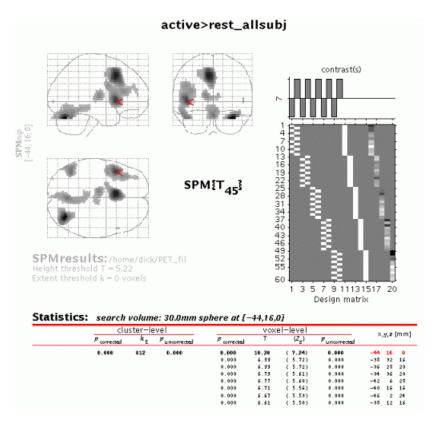
Select 'cluster':



This will show coordinates and voxel-level statistics for local maxima (>4mm apart) in the selected cluster. The table is also surfable.

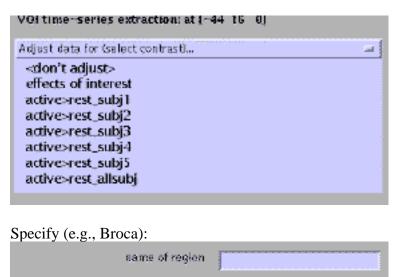
Both in the 'volume' and 'cluster' options, *p*-values are corrected for the entire search volume. If one has an *a priori* anatomical hypothesis (obviously, in the present example, that Broca's area will be activated during this word generation task) one may use the **small volume correction** option (see also Matthew Brett's tutorial at http://www.mrc-cbu.cam.ac.uk/Imaging/vol corr.html). Select 'S.V.C.' (left lower panel), and select a suitable

region, e.g., a 30mm sphere with its center at –44 16 0. Note that the region should be defined using prior knowledge (e.g., a mask image derived from previous imaging data).



N.B. As is shown, only corrected *p*-values change (become smaller) when SVC is used.

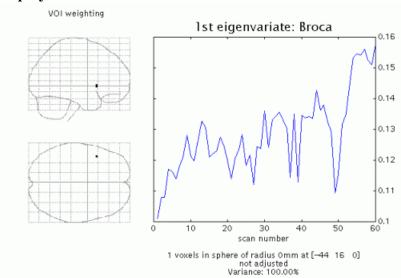
To extract a time course for data in this region of interest (**spm.regions.m**), select V.O.I. (Volume Of Interest) and select ('don't adjust'):



Specify (accept default):

VOI radius (mm)

Display:



SPM displays a graph of the first eigenvariate of the data in or centered around the chosen voxel (or the nearest suprathreshold voxel saved in the Y.mad file), and lists the eigenvariate values (Y) in the Matlab window. If temporal filtering has been specified (fMRI), then the data is temporally filtered. Adjustment is with respect to the null space of a selected contrast, or can be omitted.

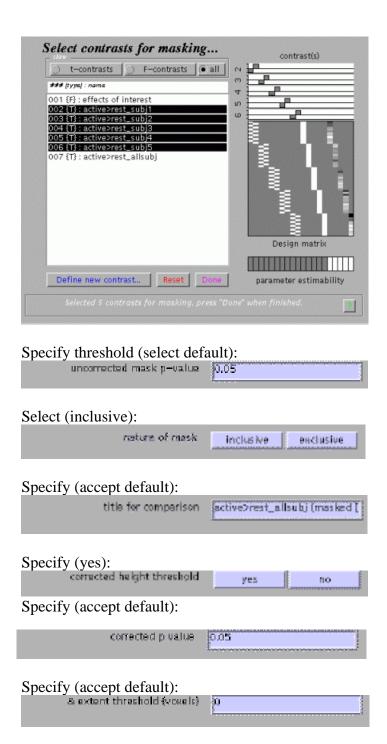
File: Y and VOI details (xY) are saved as VOI_*regionname*.mat in the working directory.

In this example, group effects are calculated averaged across subjects, therefore individual data may bias group results. To assess condition effects common to all subjects, one should either **mask** (inclusively) the 'all_subj' contrast with the individual contrasts, or perform a **conjunction** analysis.

To assess the masked contrast, press 'Results', select the appropriate 'SPM.mat' file, and select the 'all_subj' contrast.



Select all individual contrasts (by pressing [control] while selecting):

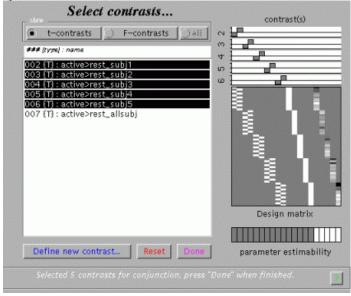


When the MIP appears, press 'volume':

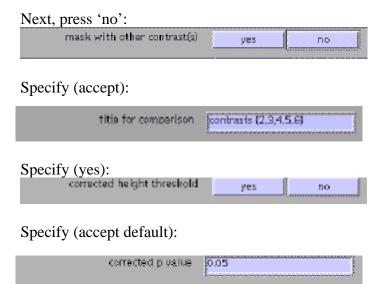
active>rest_allsubj (masked [inclusive] by {2,3,4,5,6} at p=0.05) contrast(s) 19 225 23 34 34 43 44 45 55 SPM{T45} SPMresults:/home/dick/PET_fil Extent threshold k = 0 voxels 60 3 5 7 9 11131517 20 Design matrix Statistics: volume summary (p-values corrected for entire volume) cluster-level $x,y,z \{mm\}$ 34 -76 -28 -6 16 44 -44 16 0 -40 16 16 -35 24 16 -42 -58 -28 -46 -58 -24 6 -50 -16 0.000 0.000 0.000 0.001 0.000 0.000 0.000 0.000 0.000 6.13 5.77 5.56 5.24

The output shows all voxels which are (a) significant at p < 0.05 corrected across all subjects and (b) significant at p < 0.05 uncorrected for each subject individually.

To perform a **conjunction** across subjects, press 'Results', and select all individual contrasts (press 'Control'):



N.B. Sometimes (e.g., if global confounds are used) the contrasts of parameter estimates are not exactly orthogonal (even if the contrast weight vectors are). SPM checks whether the contrasts are orthogonal and if not makes them so (relative to the first contrast specified).

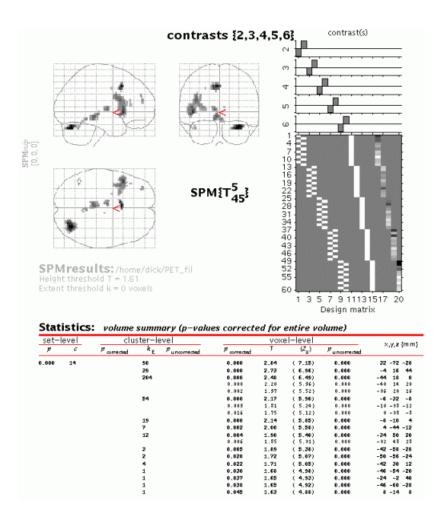


The *p*-value (corrected or uncorrected) refers to the threshold of the conjunction; SPM will compute corresponding thresholds for individual contrasts (for uncorrected thresholds, the individual threshold will be $p^{1/n}$, where p = individual threshold and n = number of contrasts in the conjunction).

N.B. In SPM99b, *uncorrected* p-values were applied by SPM to individual contrasts, so that the threshold of the conjunction was p^n .

N.B. Height, and not extent, is used to specify thresholding because the distributional approximations for the spatial extent of a conjunction SPM are not known (at present), so that inference based on spatial extent is precluded.

When the MIP appears, press 'volume':



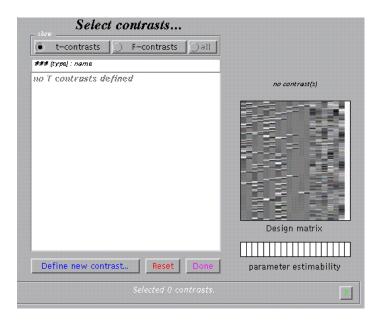
Although the MIP's of the masked group contrast and the conjunction are similar, for the conjunction an intersection SPM or 'minimum T-field' is computed. Conjunctions in SPM99 represent the intersection of several SPMs. This intersection is the same as thresholding a map of the minimum T-values (if the smallest T-value is above the specified threshold then all the T-values associated with the component SPMs are above threshold). These conjunction SPMs are very useful for testing multiple hypotheses (each component hypothesis being specified by a contrast). In this example, the set of hypotheses tested jointly are that the first subject did not activate, the second subject did not activate and so on. In regions that survive a conjunction analysis the null hypothesis is rejected jointly for all subjects. This can be thought of as enabling an inference that subject 1 activated AND subject 2 activated AND subject... etc. Gaussian field theory results are available for SPMs of minimum T- (or F-)statistics and therefore corrected *p*-values can be computed. Note that the minimum T-values do not have the usual Student's T-distribution and small minimum T-values can be very significant.

4. 3. Example 3: single-subject fMRI event-related design

As a third and more sophisticated example, consider the data from a repetition priming experiment performed using event-related fMRI. Again, details regarding the data set can be found in the README.txt. Briefly, this is a 2x2 factorial study where famous and nonfamous faces were presented twice (while the subject was asked to make fame judgements) against a checkerboard baseline. There are thus four event-types of interest (first and second presentations of famous and non-famous faces, ordered in the design matrix N1-N2-F1-F2), each modelled with a canonical HRF and its temporal derivative. Also included are two eventtypes of no interest - the (rare) errors made by this subject on the fame-judgment task - and the subject's realignment parameters, to regress out residual movement-related variance. The latter can be achieved by loading the realignment_*.txt file (output from the realignment stage) as a matrix into the Matlab workspace and entering the matrix name in the SPM input box (rather than specifying 6 vectors of length 351 in this example). Preprocessing of the data includes slice timing correction having the middle slice (12) as the reference slice. Therefore, prior to specifying the model, in the fMRI statistics defaults, the sampled bin should be equal to half the number of bins. For example, enter number of bins = 24 (the number of slices) and the sampled bin=12, using the Defaults button. In addition, stimulus onset times have been specified as a cell array variable, allowing different vector (row) lengths for separate trials.

In addition to analysing the data in the above "categorical" design, an alternative "parametric" design is illustrated in which repetition is viewed as a continuum. In this case, the response to each presentation of famous and non-famous faces is modulated by the time interval (lag) since the previous presentation of that face (for first presentations, this lag is infinite).

To assess the results for the categorical (factorial) analysis, specify and estimate the model (alternatively download the **CatStats** files). Next, press 'Results' and select the appropriate **SPM.mat** file. This will again invoke the contrast manager:

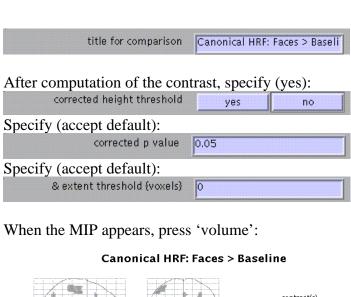


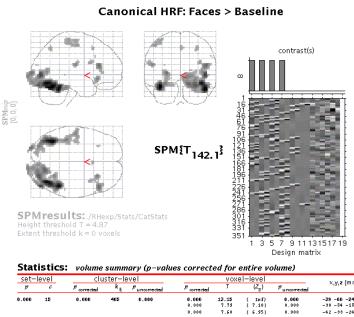
To assess the main effects of viewing faces vs. baseline, select 'Define new contrast' and type 'Canonical HRF: Faces > Baseline' (name) and '1 0 1 0 1 0 1 0' (contrast), and press 'Done'.

Specify (no):

mask with other contrast(s)

Specify (accept default):





set-level		cluster-level		voxel-level				v u a lm m		
р	c	p corrected	k _E	p uncorrected	^p corrected	Ţ	(2 _≡)	p uncorrected	x,y,z {mm}	
0.000	15	0.000	405	0.000	0.000	13.15	(Inf)	0.000	-39 -60	
					0.000	7.79	(7.10)	0.000	-30 -84 -42 -33	
					0.000	7.60	(6.95)	0.000		
		0.000	1045	0.000	0.000	12.85	(Inf)	0.000	45 -48	
					0.000	12.66	(Inf)	0.000	39 -72	
					0.000	11.74	(Inf)	0.000	42 -63	
		0.000	90	0.000	0.000	8.53	(7.65)	0.000		18
					0.001	5.77	(5.46)	0.000	42 36	3
		0.000	57	0.000	0.000	8.12	(7.35)	0.000	-27 -99	3
		0.000	43	0.000	0.000	7.34	(6.75)	0.000	-54 -15	18
		0.000	56	0.000	0.000	7.29	(6.71)	0.000	27 24	-9
					0.007	5.39	(5.13)	0.000	39 27	-6
		0.000	108	0.000	0.000	6.59	(6.15)	0.000	-48 -12	54
					0.000	6.42	(6.01)	0.000	-51 -21	57
					0.000	6.18	(5.81)	0.000	-45 -27	63
		0.000	21	0.001	0.000	6.39	(5.98)	0.000	36 12	24
		0.000	15	0.004	0.000	6.00	(5.66)	0.000	30 -63	51
		0.001	11	0.012	0.001	5.94	(5.60)	0.000	3 15	51
		0.004	5	0.074	0.006	5.41	(5.15)	0.000	-30 27	-9
		0.012	2	0.243	0.016	5.17	(4.94)	0.000	21 -96	9
		0.012	2	0.243	0.025	5.05	(4.84)	0.000	54 -36	
		0.012	2	0.243	0.033	4.98	(4.77)	0.000	-30 -87	18
		0.012	2	0.243	0.046	4.89	(4.70)	0.000	57 21	36

table shows at most | local maxima > 8.0mm apart per cluste

Height threshold: T = 4.87, p = 0.000 (0.050 corrected)

Extent threshold: k = 0 wxcels, p = 1.000 (0.050 corrected)

Expected vxcels per cluster, <x> = 1.580

Expected vxcels per cluster, <x> = 0.005

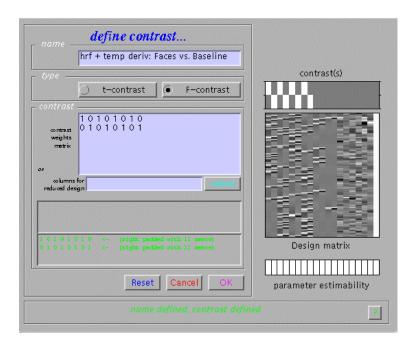
Expected number of clusters, <x> = 0.005

Expected number of clusters, <x> = 0.005

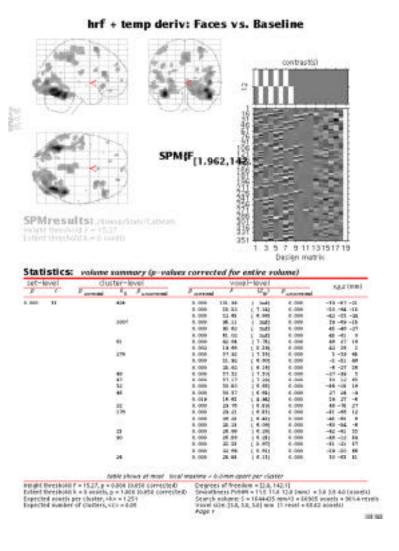
The table lists all areas where the mean of the parameter estimates for the canonical hrf of the four conditions is significantly greater than baseline (zero). To assess both the hrf and its temporal derivative, an F-contrast is required. Press 'Results', select the SPM.mat file, and press 'F-contrast' (radio button). Next, select 'Define new contrast', specify 'hrf + temp deriv: Faces vs. Baseline' (name) and enter

10101010

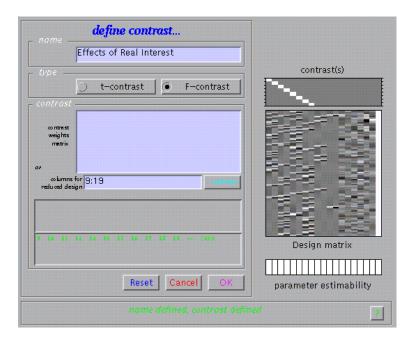
0 1 0 1 0 1 0 1 ' (contrast) and press 'Done':



Select the new contrast, specify 'mask with other images?' (no), specify 'name of comparison' (accept default), specify 'corrected height threshold' (yes), specify 'corrected p value' (accept default). Again, when the MIP appears, press 'volume':

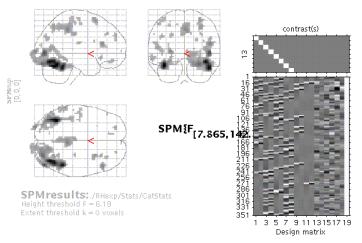


The relative contributions of the canonical hrf and its temporal derivative at a given voxel may also be assessed using F-contrasts to estimate a reduced model, removing all confounds. Press 'Results', select the SPM.mat file, press 'F-contrast' in the contrast manager, and select 'Define new contrast'. Specify 'Effects of Real Interest' (name) and type '9:19' in the small window labeled 'columns for reduced design'. This will remove columns 9 to 19 (i.e., hrf and temporal derivative for events representing error judgements, and nuisance covariates) from the design .



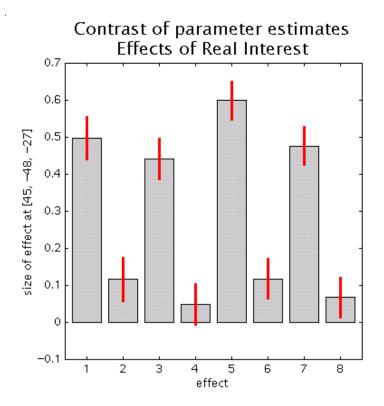
Submit and select the new contrast, specify 'mask with other images?' (no), specify 'name of comparison' (accept default), specify 'corrected height threshold' (yes), specify 'corrected p value' (accept default). Again, when the MIP appears, press 'volume':





set-level		cluster-level			voxel-level				1			
р	с	p corrected	k _E	p uncorrected	p corrected	F		(Z ₌)	p uncorrected	^	×,у, г {m п	
.000	30		294		0.000	26.35	Ç	Inf)	0.000		-57	
					0.000	9.39	- (6.19)	0.000	-42	-33	-24
					0.000	8.81	- (5.97)	0.000	-39	-42	-27
			827		0.000	25.33	- (Inf)	0.000		-69	
					0.000	24.95	- (Inf)	0.000		-48	-27
					0.000	17.37	- (Inf)	0.000	45	-81	0
			47		0.000	12.57	- (7.25)	0.000	48	27	18
			230		0.000	11.93		7.06)	0.000		-39	45
					0.000	9.24		6.14)	0.000		-51	48
					0.000	9.08		6.07)	0.000		-24	36
			37		0.000	11.84		7.03)	0.000		-99	3
			31		0.000	10.01	- (6.42)	0.000	27	15	60
			31		0.000	9.69	- (6.30)	0.000	30	-63	51
			44		0.000	9.38		6.19)	0.000		-42	-12
					0.001	7.82		5.55)	0.000		-51	-6
			47		0.000	9.15		6.10)	0.000		-66	12
			12		0.000	8.99	- (6.04)	0.000	48	-75	27
			16		0.000	8.63	(5.89)	0.000	-24	54	33
			14		0.000	8.35		5.78)	0.000	27	24	-9
			11		0.001	8.14		5.69)	0.000		-81	33
			18		0.001	7.98		5.63)	0.000		-12	54
					0.006	7.14	- (5.25)	0.000	-39	-18	66
			13		0.001	7.96		5.62)	0.000		-15	18
			10		0.002	7.74		5.52)	0.000	-12		-15
			6		0.002	7.52		5.42)	0.000	21	54	24
			8		0.003	7.43	- (5.38)	0.000	27	-24	57

Move the cursor to e.g. the anterior right fusiform blob (the R fusiform face area) by clicking the second set of coordinates in the cluster (45 –48 –27) and press 'plot'. Select 'Contrast of parameter estimates' and select 'Effects of real interest':



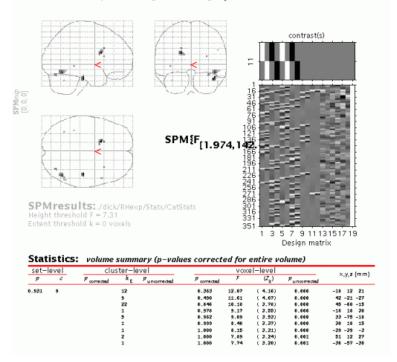
Columns 1,3,5,7 are the canonical hrfs for N1 (non-famous faces, first presentation), N2 (non-famous faces, second presentation), F1 (famous faces, 1st presentation) and F2 (famous faces, 2nd presentation), whereas columns 2,4,6,8 are the temporal derivatives. Note that the amplitude of the canonical hrfs is large compared to the temporal derivatives, suggesting that, for this region at least, the timing of the model is adequate. Also note the repetition x stimulus type interaction (the decrease from N1 to N2 is smaller than for F1 to F2).

To assess further the effects of stimulus repetition, press 'Results', select the SPM.mat file, and press 'F-contrast'. Specify e.g. 'hrf + temp deriv: 1 vs. 2' (name) and '1 0-1 0 1 0 -1 0

 $0\ 1\ 0\ -1\ 0\ 1\ 0\ -1$ ' (contrast). Submit and select the contrast. Specify 'mask with another contrast' (yes), select the 'Canonical HRF: Faces > Baseline' t-contrast, specify 'threshold for mask' (accept default of p=0.05 uncorrected), specify 'nature of mask' (inclusive), specify 'title for comparison' (accept default), specify 'corrected height threshold' (no), specify threshold (0.001).

Again, when the MIP appears, press 'volume':

rivative: 1 vs 2 (masked [inclusive] by Canonical HRF: Faces > Basic



The MIP shows all clusters where the difference between the parameter estimates for first and second presentations for the canonical hrf OR its temporal derivative is significantly different from zero AND the canonical hrf for all four conditions is significantly larger than zero. Note that although the mask does not alter the threshold for the target contrast, the combined probability for a voxel to appear in the masked contrast is in the order of 0.05×0.001 uncorrected due to the orthogonality of the contrasts.

To plot repetition suppression effects for the R fusiform region, select the third cluster from the top (by clicking $48\ 60\ -15$; slightly more posterior to that identified above) and press 'plot'.

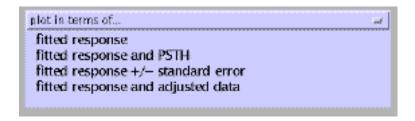
Select 'event/epoch-related responses':

Plot	_
Contrast of parameter estimates	
Fitted and adjusted responses	
Event/epoch-related responses	
Plots of parametric responses	
Volterra Kernels	

α		4 1		•	
· ·	nacity	7	• /	-	٠
٠,	pecify	/ 1	l:4	-	

specify 1.1.	
which trials or conditions (1 to 6)	

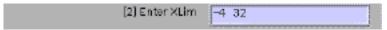
Select 'fitted response':



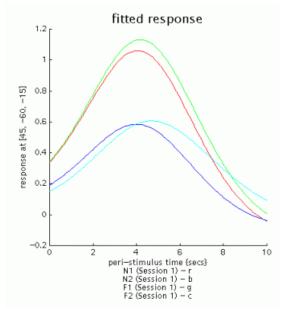
To adjust the scale of the X-axis (time), press 'attrib' from the plot controls panel:



Select Xlim, and change the default (-4 32) to '0 10':



Note the signal decrease between first and second presentations of both famous and non-famous faces:

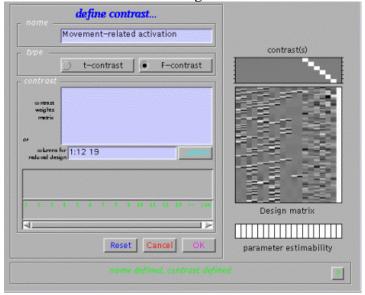


Other options from the plot controls panel:

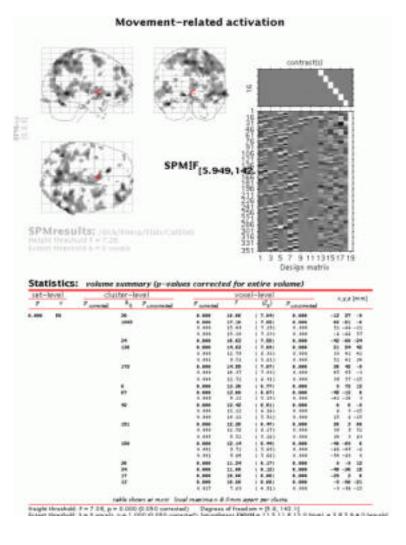
- **hold**: allows overlaying of plots
- **grid**: toggles between grid on/off
- **Box**: toggles between axes/box
- **text**: allows editing of title and/or axis labels.

To assess movement-related activation, press 'Results', select the SPM.mat file, and select 'F-contrast' in the Contrast Manager. Specify e.g. 'Movement-related activation' (name) and either

 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1' in the 'contrasts weights matrix' window, or '1:12 19' in the 'columns for reduced design' window.



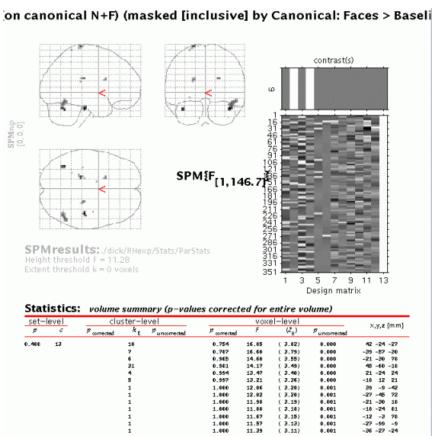
Submit and select the contrast, specify 'mask with other contrasts?' (no), 'title for comparison' (accept default), 'corrected height threshold' (yes), and 'corrected p-value' (accept default). When the MIP appears, press 'volume':



The table displays all clusters where signal changes correlated with any of the six movement parameters are significantly different from zero. Note the large edge effects, which, however, are not apparent in the fusiform regions.

Finally, consider the effects of the interval between first and second presentations of famous and non-famous faces. For this purpose, an alternative statistical model needs to be estimated, with four trial types: (1) first and second presentation of a non-famous face (N1 and N2 collapsed), (2) first and second presentation of a famous face (F1 and F2 collapsed), (3) errors in judging non-famous faces, (4) errors in judging famous faces. These are modelled with the canonical hrf alone, with two parametric (exponential) modulations added for second presentations of non-famous and famous faces. See the README.txt for details of design specification.

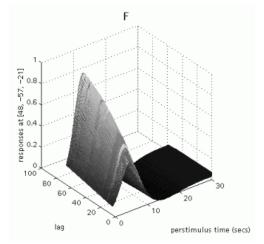
After completion of model estimation, press 'Results' and select the SPM.mat file. When the Contrast Manager appears, define an F-contrast 'Effect of Lag (on canonical N+F)' (name) and '0 1 0 1', and a t-contrast 'Canonical: Faces>Baseline' (name) and '1 0 1 0'. Select the F-contrast, specify 'mask with other contrasts' (yes), select 'Canonical: Faces>Baseline', specify 'uncorrected mask p-value' (accept default), 'nature of mask (inclusive), 'title for comparison' (accept default), 'corrected height threshold' (no), and 'corrected p-value'

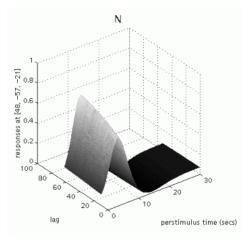


(accept default). When the MIP appears, press 'volume':

The table displays all clusters where the exponential change in activation between first and second presentations for famous OR non-famous faces for the canonical hrf is significantly different from zero AND the canonical hrf for the first two conditions is significantly larger than zero (baseline). To plot these parametric effects, select the R fusiform region (45 –60 –18, similar to the region identified in the previous categorical analysis for repetition effects),

and press 'plot'. Select 'Plots of parametric responses' and select 'F' (or 'N'). Note that the 'attrib' option does not allow adjusting the scale of the Z-axis; therefore, to change the scale for all axes, type e.g. 'figure (1), axis ([0 30 0 100 0 1])' in the Matlab window.

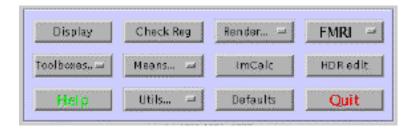




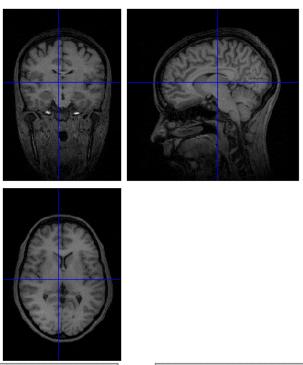
Note that these repetition effects are transient (decrease with increasing intervals between first and second presentations), especially for famous faces.

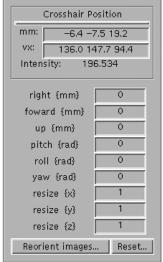
5. Miscellaneous functions and utilities

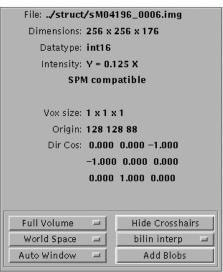
This section describes miscellaneous functions and utilities that are included with SPM.



5.1 Display: Interactive orthogonal display of selected image.







Display utilities:

Bottom left panel:

- Image intensity at crosshair position. Translation, rotation and scaling parameters can be entered to reorient images. Image is displayed with new orientation values.
- **Reorient images...** overwrites the image .mat file with the new transformation as specified by the orientation values entered above.
- **Reset** overwrites the .mat file to contain an estimate of the space of the image.

Bottom right panel: contains information about image, its size and space.

- **Full volume/160x160x160mm/...etc**: displays full image volume or a selected subvolume.
- World Space / Voxel Space: World space displays image in the space of its .mat file. Voxel space displays image in voxel space, i.e. without using .mat file.
- AutoWindow / Manual Window: Auto Window scales image between minimum and maximum values. Manual Window – manually select values to scale image intensity values.
- **Hide Crosshairs** toggles crosshair display on and off.
- NN interp / bilinear interp / sinc interp interpolation used for displayed image.
- **Add/Remove blobs** can add up to 6 sets of blobs from previously executed statistics on displayed image.

5.2 Check Reg(istration)

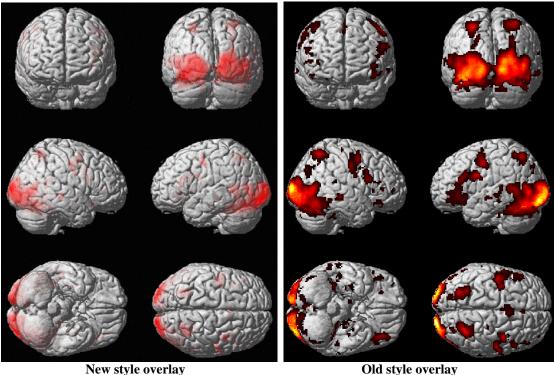


This allows >1 and <15 images to be displayed at the same time, in the space of the .mat file of the first image selected. This utility is VERY useful for checking coregistration results.

5.3 Render...

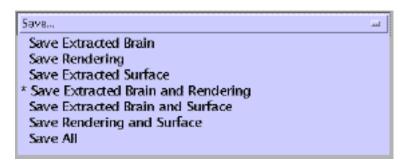


Display – this displays up to 3 sets of activations on a volume rendered brain. There is an option between new style and old style renderings. Examples of these are shown in the figure below (left =new, right=old). For normalised activations it is possible to select one of the canonical rendered brains. Alternatively using the **Xtract Brain** option (below) it is possible to create ones own rendered brain for subject specific renderings.

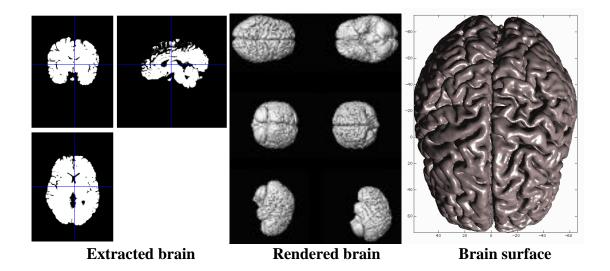


New style overlay

Xtract Brain – this requires that a segmentation has been performed and that grey and white matter segmented images are available (see segmentation, 2.6). Options are:



- Save Extracted Brain extracted brain is saved as a binary mask image (i.e. 1s identifying the brain and 0s elsewhere) with the name brain_filename.img, hdr, .mat. Use display to visualise results (as in figure below).
- Save Rendering rendered brain is displayed (as in figure below) and results are saved as render_filename.mat. This file can be selected to display blobs on a rendered surface (e.g. see x).
- Save Extracted Surface brain surface is saved as surf_filename.mat. The resulting brain surface can be displayed (as in figure below) and rotated. Type help spm_xbrain at the matlab prompt for code to manipulate the surface.



5.4 fMRI/PET



Option to toggle between the PET and the fMRI mode.

5.5. Toolboxes



This option provides access to SPM toolboxes installed in the toolbox subdirectory of the SPM installation directory. A sub-directory must exist under the SPM toolbox directory named after the toolbox. There must be an M-file in this sub-directory whose name ends with the toolbox directory name. E.g. a toolbox for Deformations would contain an M-file called 'spm_Deformations.m' in a subdirectory called Deformations under the SPM toolbox directory.

5.6 Means...



Options:

- **Mean**: creates a mean image from selected images and writes result to **mean.img** in current working directory. Selected images must have same dimensions, voxel sizes and orientations.
- **AdjMean**: creates a mean image from selected images after adjusting for conditions and confounds using the general linear model. The user selects a design, scaling/normalisation and adjustment options in a similar way to doing **SPM-PET** (section 3.1). The adjusted

- means created with this step were previously used for **PET RFX** analyses. See section x for updated RFX analysis.
- adjMean/fMRI creates a mean image from selected images after adjusting for conditions and confounds using the general linear model. The user specifies the design, the required global normalisation and high-pass filtering. An adjusted mean is created for each condition specified in a single session fMRI epoch-related study. The adjusted means created with this step were previously used for fMRI RFX analyses. See section x for updated RFX analysis.

5.7 ImCalc



This option allows basic algebraic calculations to be performed on selected images and the result written as an image. The user must specify the expression to be evaluated in standard matlab form with the selected images referred to in order as i1, i2, i3 ...etc. Logical, relational and trigonometric operators can be used as well as basic arithmetic operators. For information on using these operators in matlab, type 'help arith', 'help relop', 'help slash' and 'help elfun' at the matlab prompt. The user must enter a name for the resulting output image. This will be written to the current working directory.

5.8 HDR edit



This option allows an image header to be edited and applied to selected images. It also allows the creation of image headers. Editing options are:

```
set Image Dimensions – pixels in x, y & z
set Voxel Dimensions – mm in x, y & z
set Scalefactor
set Data Type
set Offset into file – bytes
set Origin – x, y & z coordinate of voxel
set Image description
APPLY to images
QUIT
```

Set options for editing, then select APPLY to images. A new header file will be written for selected images. This utility is especially useful for adjusting the origin of one or more images to provide a better starting point for coregistration with an image where the origin is very different.



This provides a graphical user interface for the help files associated with all buttons in the SPM menu window.

5.10 Utils...



Options:

- **CD** change present working directory
- **PWD** report present working directory
- **delete** file deletion utility
- **Show SPM** pops up figures associated with this SPM session. This is very useful when running >1 SPM at a time
- **Run mFile** run selected Matlab M-file in workspace
- **SPMweb** opens http://www.fil.ion.ucl.ac.uk/spm in web browser

5.11 Defaults



This option allows current defaults to be edited. New default settings are reset to SPM defaults when a new SPM session is started.



Printing Options – allows a variety of different printing options to be selected.

Miscellaneous Defaults:

- Log to file allows user to specify a file in which to log all SPM-user dialogue.
- **Command Line Input** allows user to select GUI or command line input mode.
- **Grid Value** allows user to select intensity for any overlaid grids (e.g. on the MIPS display, slices overlay). The grid is brightest for a value of 1 and disappears for a value of 0.

Header Defaults –PET/FMRI – these values are used as the defaults for the **HDR edit** utility.

The defaults for **Realignment**, **Coregistration**, **Spatial Normalisation**, **Statistics** –**PET**/ **FMRI** are discussed in each of the relevant sections.

Reset All – this reloads the SPM startup defaults from **spm_defaults.m**.

5.12 Quit



This exits SPM and clears the workspace.