# Chapter 1

# Face fMRI data

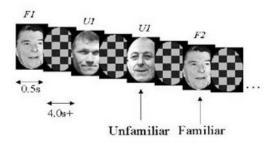
As a third and more sophisticated example, consider the data from a repetition priming experiment performed using event-related fMRI. Briefly, this is a 2x2 factorial study with factors 'fame' and 'repetition' where famous and non-famous faces were presented twice against a checkerboard baseline. The subject was asked to make fame judgements by making key presses. There are thus four event-types of interest; first and second presentations of famous and non-famous faces, which we denote N1, N2, F1 and F2. The experimental design is shown shematically in Figure 1.1.

Images were acquired using continuous Echo-Planar Imaging (EPI) with TE=40ms, TR=2s and 24 descending slices ( $64x64~3x3mm^2$ ), 3mm thick with a 1.5mm gap. The data archive is available from This contains 351 Analyse format functional images  $sM03953\_0005\_*.img$  of dimension 64x64x24 with 3mmx3mmx4.5mm voxels. A strucural image is also provided  $sM03953\_0007.img$  also in Analyse format.

To analyse the data, first create a new directory DIR

eg. c:\home\wpenny\fmri\_analysis\face-rep\all, in which to place the results of your analysis. Then create 3 subdirectories (i) jobs, (ii) designs, (iii) classical and (iv) bayesian. As the analysis proceeds these directories will be filled with job-specification files, design matrices and models estimated using classical or Bayesian methods. Additionally, in each of the designs, classical and bayesian directories create two subdirectories called categorical and parametric as we will show how this data can be analysed in two different ways. In the categoral analysis we will look at the main effects of fame and repetition and in the parameteric analysis we will look at responses as a function of 'lag', that is, the number of faces intervening between repetition of a specific face.

Start up matlab, enter your jobs directory and type  $spm\ fmri$  at the matlab prompt. SPM will then open in fMRI mode with three windows (1) the top-left or 'command' window, (2) the bottom-left or 'interactive' window and (3) the right-hand or 'graphics' window. Analysis then takes place in three major stages (i) spatial pre-processing, (ii) model specification, review and estimation and (iii) inference. These stages organise the buttons in SPM's base window.



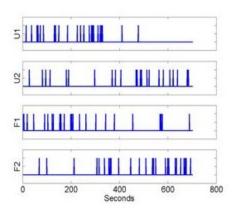


Figure 1.1: Face repetition paradigm. **Left** There were 2 presentations of 26 Famous and 26 Nonfamous Greyscale photographs, for 0.5s each, randomly intermixed. The minimal Stimulus Onset Asynchrony (SOA)=4.5s, with probability 2/3 (ie 1/3 null events). The subject made one of two right finger key presses denoting whether or not the subject thought the face was famous. **Right** The time series of events.

# 1.1 Spatial pre-processing

### 1.1.1 Display

Display eg. the first functional image using the 'Display' button. Note orbitofrontal and inferior temporal drop-out and ghosting. This can be seen more clearly by selecting 'brighten if necessary' from the 'Effects' tab at the top of the graphics window.

### 1.1.2 Realignment

Under the spatial pre-processing section of the SPM base window select 'Realign' from the 'Realign' pulldown menu. This will call up a realignment job specification in the graphics window. Then

- Select 'New Realign:Estimate and Reslice'
- Open the newly created 'Realign:Estimate and Reslice' option.
- Highlight data, select 'New Session', then highlight the newly created 'Session' option.
- Select 'Specify Files' and use the SPM file selector to choose all of your functional images eg. sM03953\_0005\_\*.img.
- Save the job file as eg. DIR/jobs/realign.mat.
- Press the RUN button in the graphics window.

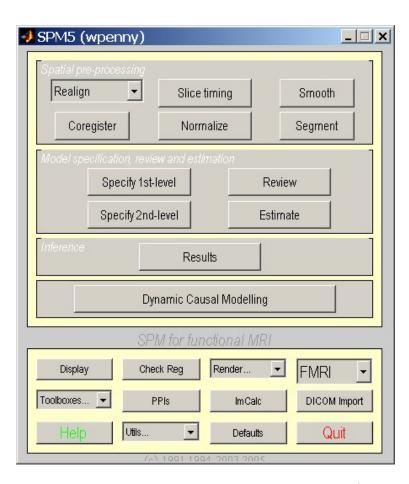
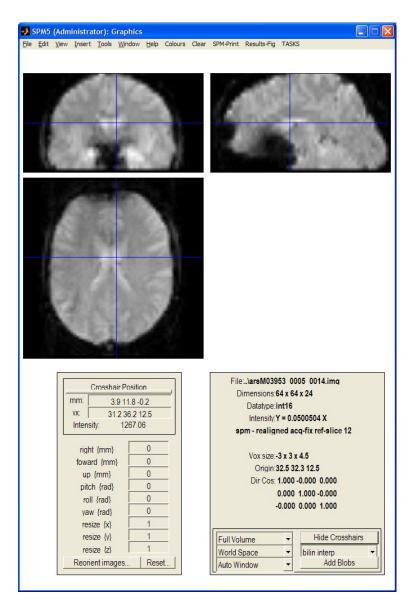


Figure 1.2: The SPM base window comprises three sections i) spatial preprocessing, (ii) model specification, review and estimation and (iii) inference.



 ${\bf Figure~1.3:~Signal~dropout~in~EPI~images.}$ 

This will run the realign job which will write realigned images into the directory where the functional images are. These new images will be prefixed with the letter 'r'. SPM will then plot the estimated time series of translations and rotations shown in Figure 1.4. These data, the realignment parameters, are also saved to a file eg. rp\_sM03953\_0005\_0006.txt, so that these variables can be used as regressors when fitting GLMs. To prepare for this copy the file into the DIR\jobs\ directory and rename it movepars.txt. This allows movements effects to be discounted when looking for brain activations.

SPM will also create a mean image eg. meansM03953\_0005\_0006.img which will be used in the next step of spatial processing - coregistration.

### 1.1.3 Slice timing correction

Press the 'Slice timing' button. This will call up the specification of a slice timing job in the graphics window.

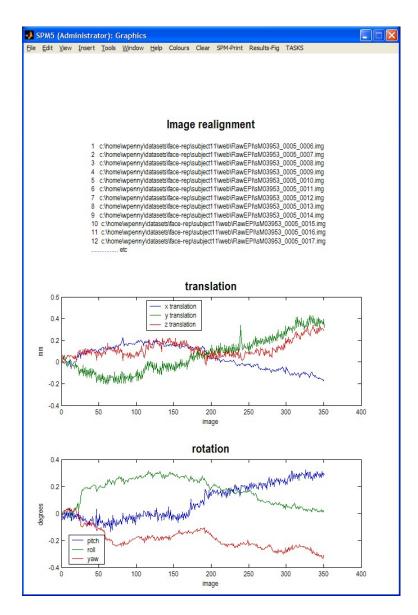
- Open the 'Slice Timing' option
- Highlight 'Data' and select 'New Sessions'
- Highlight the newly create 'Sessions' option, 'Specify Files' and select the 351 realigned functional images using the filter `r.\*.
- Select 'Number of Slices' and enter 24
- Select TR and enter 2
- Select TA and enter 2
- Select 'Slice order' and enter 24:-1:1
- Select 'Reference Slice', and enter 12
- Save the job as slice\_timing.mat and press 'Run'

SPM will write slice-time corrected files with the prefix 'a' in the functional data directory.

### 1.1.4 Coregistration

Press the 'Coreg' button. This will call up the specification of a coregistration job in the graphics window.

- Select New "Coreg:Estimate"
- Double-click on the newly created Coreg:Estimate
- Highlight 'Reference Image' and then select the mean functional image meansM03953\_0005\_0006.img
- Highlight 'Source Image' and then select the structural image eg. sM03953\_0007.img.
- Press the Save button and save the job as coreg.job
- Then press RUN



 ${\bf Figure~1.4:~} Realignment~of~face~data.$ 

SPM will then implement a coregistration between the structural and functional data that maximises the mutual information. The image in figure 1.5 should then appear in the graphics window. SPM will have changed the header of the source file which in this case is the structural image sM03953\_0007.img.

### 1.1.5 Segmentation

Press the 'Segment' button. This will call up the specification of a segmentation job in the graphics window. Highlight the Data field and then select the subjects coregistered anatomical image eg. sM03953\_0007.img. Save the job file as segment.mat and then press RUN. SPM will segment the structural image using the default tissue probability maps as priors. SPM will create, by default, gray and white matter images and bias-field corrected structral image. These can be viewed using the CheckReg facility as described in the previous section (press segement and select. Figure ?? shows the gray matter image, c1sM03953\_0007.img along with the original structural.

SPM will also write a spatial normalisation eg. sM03952\_0007\_seg\_sn.mat file in the original structural directory. This will be used in the next section to normalise the functional data.

#### 1.1.6 Normalize

Press the 'Normalize' button. This will call up the specification of a normalise job in the graphics window.

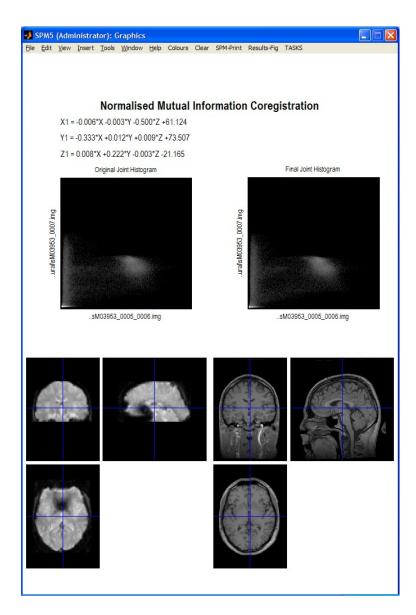
- Select a New "Normalise:Write" field. This allows previously estimated warps to be applied to a series of images.
- Highlight 'Data', select New "Subject"
- Open 'Subject', highlight 'Parameter File' and select the sM03952\_0007\_seg\_sn.mat file that you created in the previous section
- Highlight images to write and select all of the slice-time corrected, realigned functional images 'arsM\*.img'. Note: This can be done efficiently by changing the filter in the SPM file selector to 'ar.\*. SPM will then only list those files beginning with the letter r ie. those that have been realigned. You can then right click over the listed files, choose 'Select all' and press 'Done'.
- Open 'Writing Options', and change 'Voxel sizes' from [2,2,2] to [3,3,3].
- Press 'Save', save the job as normalise.mat and then press 'Run'.

SPM will then write spatially normalised files to the functional data directory. These files have the prefix 'w'.

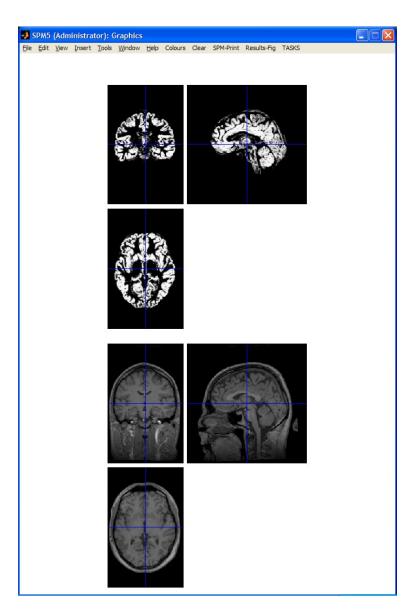
If you wish to superimpose a subject's functional activations on their own anatomy<sup>2</sup> you will also need to apply the spatial normalisation parameters to their (bias-corrected) anatomical image. To do this

<sup>&</sup>lt;sup>1</sup>This step is not strictly necessary. It will write images out at a resolution closer to that at which they were acquired. This will speed up subsequent analysis and is necessary, for example, to make Bayesian fMRI analysis computationally efficient.

<sup>&</sup>lt;sup>2</sup>Beginners may wish to skip this step, and instead just superimpose functional activations on an 'average structural image'.



 $\label{eq:correction} \mbox{Figure 1.5: } \mbox{\it Mutual Information Coeregistration of Auditory data}.$ 



 $\label{eq:Figure 1.6:} \textit{Gray matter image and `registered' structural image}.$ 

- Press 'Normalise', select New "Normalise:Write"
- Open 'Normalise: Write', highlight 'Data', select New "Subject"
- Open 'Subject'
- Highlight 'Parameter File', select the sM03952\_0007\_seg\_sn.mat file that you created in the previous section, press 'Done'.
- Highlight 'Images to Write', select the bias-corrected structural eg. msM03952\_0007.img, press 'Done'.
- Open 'Writing Options', select voxel sizes and change the default [2 2 2] to [1 1 1] which better matches the original resolution of the images [1 1 1.5].
- Save the job as norm\_struct.mat and press 'Run'.

### 1.1.7 Smoothing

Press the 'Smooth' button<sup>3</sup>. This will call up the specification of a smooth job in the graphics window.

- Open 'Smooth', select 'Images to Smooth' and then select the spatially normalised files created in the last section eg. war\*.img.
- Save the job as smooth.mat and press 'Run'.

This will smooth the data by 8mm in each direction, the default smoothing kernel width.

# 1.2 Modelling categorical responses

Before setting up the design matrix we must first load the Stimulus Onsets Times (SOTs) and movement parameters into matlab. SOTs are stored in the sots.mat file in a cell array such that eg. sot{1} contains stimulus onset times in TRs for event type 1, which is N1. Event-types 2,3 and 4 are N2, F1 and F2<sup>4</sup>.

- At the matlab command prompt type 'load sots'
- Then type 'load movepars.txt'

Now press the 'Specify 1st-level' button. This will call up the specification of a fMRI specification job in the graphics window. Then

- Open the fMRI model specification option
- Open the 'Timing paramaters' option

<sup>&</sup>lt;sup>3</sup>The smoothing step is unnecessary if you are only interested in Bayesian analysis of your functional data.

<sup>&</sup>lt;sup>4</sup>Also included included with this data set are variables describing two event-types of no interest - the (rare) errors made by this subject on the fame-judgement task. We will not, however, be using these in our analyses.

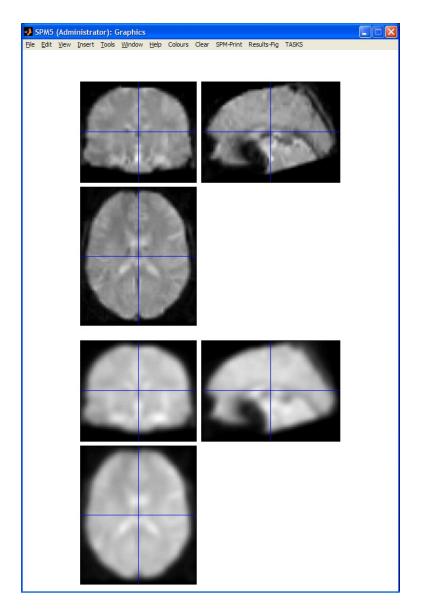


Figure 1.7: Functional image (top) and 8mm-smoothed functional image (bottom). These images were obtained using SPM's 'CheckReg' facility.

- Highlight 'Units for design' and select 'Scans'
- Highlight 'Interscan interval' and enter 2
- Highlight 'Microtime resolution' and enter 24
- Highlight 'Microtime onset' and enter 12. These last two options make the creating of regressors commensurate with the slice-time correction we have applied to the data.
- Highlight 'Data and Design' and select 'New Subject/Session'. Then open the newly created 'Subject/Session' option.
- Highlight 'Scans' and use SPM's file selector to choose the 351 smoothed, normalised, slice-time corrected, realigned functional images ie swarsM.img.
   These can be selected easily using the `swar.\*' filter, and select all. Then press 'Done'.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'N1'. Highlight 'Onsets' and enter 'sot{1}'. Highlight 'Durations' and enter 0.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'N2'. Highlight 'Onsets' and enter 'sot{2}'. Highlight 'Durations' and enter 0.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'F1'. Highlight 'Onsets' and enter 'sot{3}'. Highlight 'Durations' and enter 0.
- Highlight 'Conditions' and select 'New condition'
- Open the newly created 'Condition' option. Highlight 'Name' and enter 'F2'. Highlight 'Onsets' and enter 'sot{4}'. Highlight 'Durations' and enter 0.
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'tx', highlight 'Value', enter movepars(:,1)
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'ty', highlight 'Value', enter movepars(:,2)
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'tz', highlight 'Value', enter movepars(:,3)

- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'pitch', highlight 'Value', enter movepars(:,4)
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'roll', highlight 'Value', enter movepars(:,5)
- Highlight 'Regressors', select 'New Regressor', open the newly created 'Regressor' option, highlight 'Name' enter 'yaw', highlight 'Value', enter movepars(:,6)
- Highlight 'Factorial Design', select 'New Factor', open the newly created 'Factor' option, highlight 'Name' and enter 'Fam', highlight 'Levels' and enter 2.
- Highlight 'Factorial Design', select 'New Factor', open the newly created 'Factor' option, highlight 'Name' and enter 'Rep', highlight 'Levels' and enter 2<sup>5</sup>.
- Open 'Canonical HRF' under 'Basis Functions'. Select 'Model derivatives' and select 'Time derivatives'.
- Highlight 'Directory' and select the DIR/designs/categorical directory you created earlier.
- Save the job as categorical\_spec.mat and press 'RUN'

SPM will then write an SPM.mat file to the DIR/designs/categorical directory. It will also plot the design matrix, as shown in Figure 1.8.

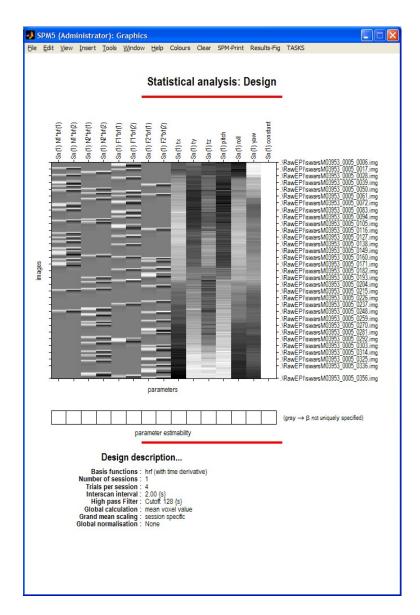
At this stage it is advisable to check your model specification using SPM's review facility which is accessed via the 'Review' button. This brings up a 'design' tab on the interactive window clicking on which produces a pulldown menu. If you select the first item 'Design Matrix' SPM will produce the image shown in Figure 1.8. If you select 'Explore' then 'Session 1' then 'N1', SPM will produce the plots shown in Figure 1.9.

#### 1.2.1 Estimate

Press the 'Estimate' button. This will call up the specification of an fMRI estimation job in the graphics window. Then

- Open the 'fMRI model estimation' option
- Highlight the 'Select SPM.mat' option and then choose the SPM.mat file saved in the DIR/designs/categorical directory
- Highlight the 'Directory' option and then choose the DIR/classical/categorical directory

 $<sup>^5</sup>$ The order of naming these factors is important - the factor to be specified first is the one that 'changes slowest' ie. as we go through the list of conditions N1,N2,F1,F2 the factor 'repetition' changes every condition and the factor 'fame' changes every other condition. So 'Fam' changes slowest and is entered first.



 $\label{eq:prop:prop:sign} \mbox{Figure 1.8: } Design \ matrix.$ 

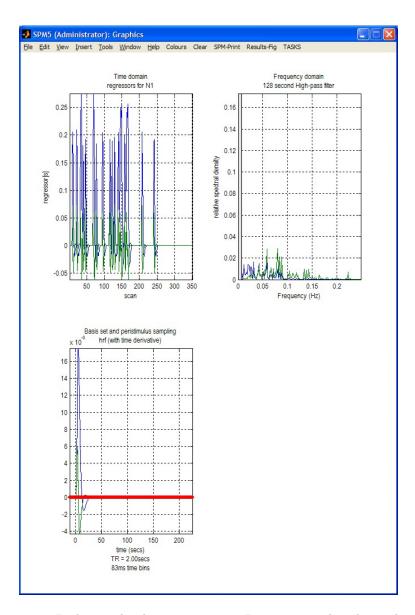


Figure 1.9: Exploring the design matrix in Figure 1.8. This shows the time series of the 'active' regressor (top left), a frequency domain plot of the active regressor (top right) and the basis function used to convert assumed neuronal activity into hemodynamic activity. In this model we used the default option—the canonical basis function. The frequency domain plot shows that the frequency content of the 'N1' regressor is above the set frequencies that are removed by the High Pass Filter (HPF) (these are shown in gray—in this model we accepted the default HPF cut-off of 128s or 0.008Hz).

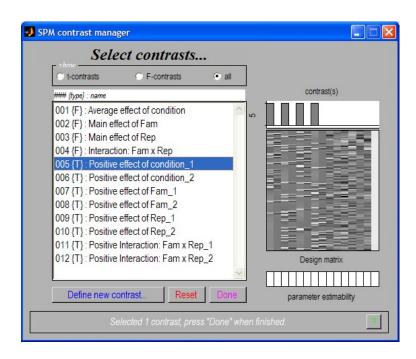


Figure 1.10: Contrast Manager containing default contrasts for categorical design.

• Save the job as categorical\_est.job and press Run

SPM will write a number of files into the selected directory including an SPM.mat file.

# 1.3 Modelling parametric responses

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).

# 1.4 Inference for categorical design

Press 'Results' and select the SPM.mat file from DIR\classical\categorical. This will again invoke the contrast manager. Because we specified that our model was using a 'Factorial design' a number of contrasts have been specified automatically, as shown in Figure ??. 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'.

• Select contrast number 5. This is a t-contrast Positive effect of condition\_1 This will show regions where the average effect of presenting faces (condi-

tion) is significantly positive, as modelled by the first regressor (hence the \_1), the canonical HRF. Press 'Done'.

- Mask with other contrast ? [Yes/No]
- Specify No.
- Title for comparison ?
- Enter 'Canonical HRF: Faces ; Baseline'
- p value adjustment to control: [FWE/FDR/none]
- Select FWE
- Corrected p value(family-wise error)
- Accept the default value, 0.05
- Extent threshold {voxels} [0]
- Accept the default value, 0

SPM will produce a MIP.

#### 1.4.1 Statistical tables

To get a summary of local maxima, press the 'volume' button in the p-values section of the interactive window. 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, as shown in Figure ?? The columns in volume table 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 (FWE or FDR)/uncorrected for search volume.
- cluster-level: the chance (p) of finding a cluster with this many(ke) or a greater number of voxels, corrected / uncorrected for search volume
- set-level: the chance (p) of finding this (c) or a greater number of clusters in the search volume

To assess both the hrf and its temporal derivative, an F-contrast is required.

### 1.4.2 F-contrasts

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'.

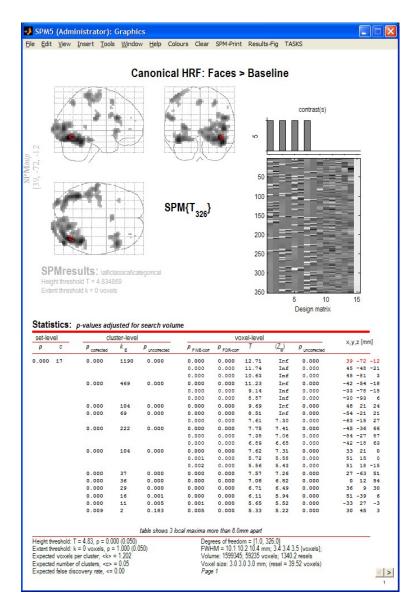


Figure 1.11: MIP and Volume table for Canonical HRF: Faces > Baseline.

Although the MIP of this F-contrast looks similar to the previous t-contrast, note that the present contrast shows the areas for which the mean of the parameter estimates for the canonical hrf OR its temporal derivative for the four conditions are different from zero (baseline). In other words, the F-contrast is two-sided, and tests two t-contrasts simultaneously. Also note that an F- (or t-) contrast such as 1 1 1 1 1 1 1 1, which tests whether the mean of the canonical hrf AND its temporal derivative for all conditions are different from (larger than) zero is not sensible. This is because the canonical hrf and its temporal derivative may cancel each other out while being significant in their own right. Finally, note that single F-contrasts can be regarded as  $t^2$ -contrasts, so that the F-contrasts 1 0 -1 0 1 0 -1 0 and -1 0 1 0 -1 0 are equivalent.

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 labelled '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'.

## 1.4.3 Plotting parameter estimates at a voxel

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).

## 1.4.4 Masking F-contrasts

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'.

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  $0.05 \times 0.001$  uncorrected due to the orthogonality of the contrasts.

### 1.4.5 Plotting event-related responses

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-related responses'.

- Which trials or conditions (1 to 6)
- Specify '1:4'
- Plot in terms of ...
- Select fitted response and PSTH

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.

# 1.4.6 F-contrasts for testing effects of movement

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 [zeros(6,12),eye(6)] 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.

### 1.4.7 Parametric modulation

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). We can now plot these parametric effects at particular voxels.

### 1.4.8 Plotting parametric responses

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 adjustment of 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.