

## **SPM\_SS**

### **Subject-specific analysis toolbox**

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This SPM-compatible toolbox<sup>1</sup> performs **ROI-based** and **voxel-based** multi-subject analyses that use functional localizers to account for inter-subject variability in the loci of activation. This is accomplished by restricting the units of analysis, within each subject, to supra-threshold voxels for a selected *localizer* contrast, while performing inferences about a (possibly different) *effect-of-interest* contrast.

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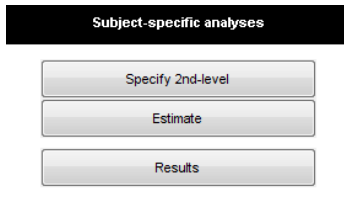
<sup>1</sup> This toolbox is compatible with SPM5 and SPM8. Some or all of its functionality might be compatible with SPM2 (but this has not been extensively tested). The toolbox was developed in Matlab 7.7, but Matlab 6.5 or above should be sufficient for this toolbox to function properly.

## Installation of the toolbox

Add the *spm\_ss* folder to the Matlab path

## Operation of the toolbox

Type *spm\_ss* to start



There are three steps to performing subject-specific analyses:

- 1) (*Specify 2nd-level*) Specify your analyses
- 2) (*Estimate*) Estimate the 2nd-level model
- 3) (*Results*) Explore the results

The following sections describe these steps in detail.

## Step (1): SPECIFY 2ND-LEVEL (*spm\_ss\_design*)

- a) Select the type of analyses: voxel-based or ROI-based (select GcSS for automatically defined fROIs<sup>2</sup>, or manual ROIs for using externally defined ROIs)
- b) Select the output folder (where the analysis files will be written)
- c) Select the first-level contrasts. This can be done in two ways:
  - a. Selecting the first-level SPM.mat files (one SPM.mat file per subject), and then selecting, among the existing first-level contrasts: 1) the contrasts of interest (one or multiple contrasts typically specifying each of the conditions of interest<sup>3</sup>); and 2) the localizer contrast (a single contrast), and its threshold type and value (see also Additional Information below for information on how to do this with a batch script)
  - b. Selecting directly the `con_*.img` files to be used as contrast of interest for each subject, and selecting the `locT*.img` files (or any mask images) to be used as localizers (the option to select these files will appear in the gui when clicking cancel on the selection of SPM.mat files)

note: Contrasts of interest and localizer contrasts must be orthogonal (to ensure that independent subsets of data are used for defining the ROIs vs. for estimating the response in the ROIs (e.g., Kriegeskorte et al., 2009)). If using option (a), the toolbox will automatically check the orthogonality of these contrasts. If they are not orthogonal<sup>4</sup>, the toolbox will implement cross-validation across sessions<sup>5</sup> (it will create additional first-level contrasts by partitioning the selected contrasts across sessions and it will use these new orthogonal contrasts for analyses). This means that the data must contain more than a single session. You can implement other forms of cross-validation manually simply by selecting several contrasts (or files) per subject instead of a single one. These contrasts should represent a partitioning of a single contrast of interest (e.g., across different blocks instead of sessions). In particular, if entering multiple contrasts, all of the effect-of-interest contrasts should be mutually orthogonal, and pairwise orthogonal to the corresponding localizer contrasts (e.g., `A_block1`, `A_block2`, `A_block3` as effect-of-interest contrasts; and `B_block2&3`, `B_block1&3`, and `B_block1&2` as localizer contrasts; this will satisfy the required

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<sup>2</sup> In this analysis, fROIs are automatically defined using some portion of the data under investigation. The term *GcSS (Group-constrained Subject-Specific) fROIs* was introduced in Fedorenko, Hsieh, Nieto-Castañón, Whitfield-Gabrieli & Kanwisher (submitted). This method involves (a) overlaying some number of thresholded individual activation maps on top of one another, (b) parcellating the resulting overlap map using a watershed algorithm, and (c) using the resulting group-level functional partitions to constrain the selection of subject-specific voxels.

<sup>3</sup> Note that you will later (at Step (3) below) be able to specify additional first-level (within-subject) contrasts to explore results that encompass several of the individual effect-of-interest contrasts entered here. For example, in a study with three conditions (A,B,C) you will typically enter three effect-of-interest contrasts (one per condition) at this step. Later when exploring the results you can specify arbitrary within-subject contrasts. For example you can use a within-subjects T-contrast of the form `[1,-1,0]` to explore the “A-B” effect, or a within-subjects F-contrast of the form `[1,-1,0;0,1,-1]` to explore any between-condition differences.

<sup>4</sup> This, for example, may happen if you want to estimate the effect size for the localizer contrast. In this case, you would want to use a subset of the sessions to define the ROIs and the remaining session(s) to extract the response from the ROIs. The toolbox can perform this division of data into subsets automatically under a general cross-validation framework.

<sup>5</sup> “Session” is used throughout to refer to runs.

orthogonality conditions irrespective of whether the original contrasts A and B are orthogonal or not).

- d) [*For manual ROI analyses only*] Select the ROI(s)-defining volume (this should be an analyze or nifti image containing natural numbers, each number referring to a single ROI; e.g. a volume containing 1's for voxels within ROI#1, 2's for voxels within ROI#2, and 0's otherwise)
- e) [*For voxel-based or GcSS fROI analyses only*] Select the level of smoothing (for voxel-based analyses (see Nieto-Castañon, Fedorenko & Kanwisher, submitted, for a detailed discussion of this method) this is used to define the extent of a soft region of interest around each voxel; for GcSS fROI analyses (see Fedorenko et al., submitted, for a detailed discussion of this method) this is used to smooth the estimated inter-subject overlap map to improve the parcellation into functional ROIs). In addition, *for GcSS fROI analyses only* select the percentage overlap threshold (minimal percentage of subjects) used to constrain the extent of the automatically-defined ROIs (for example, you can eliminate from the overlap map voxels where fewer than .10 of subjects show activation, by setting the threshold to .10).
- f) Select and define the 2nd-level analysis model and between-subjects contrast. Currently implemented models include: one-sample t-test (e.g. for single-group analyses), two-sample t-test (e.g. for analyses comparing two subject groups), or multiple regression (e.g. for anova or correlation analyses; Henson & Penny, 2005)

This step will create a SPM\_ss\*.mat file in the target directory (specified in (b) above) containing the specified design. In addition and if the selected contrasts are not orthogonal, this step will create and estimate a series of first-level contrasts for each subject (the new contrasts will be named SESSION####\_\* and ORTH\_TO\_SESSION####\_\*, each of them representing a given contrast estimated from data from a single session, or from all but one of the sessions, respectively)

## **Step (2): ESTIMATE (*spm\_ss\_estimate*)**

- a) Select the *SPM\_ss\*.mat* file containing the design

This step will estimate a 2nd-level model.

It will create the following files in the target directory:

*spm\_ss\_\*beta.img* : 4d-volume with estimated regressor coefficients (one volume per effect of interest contrast and per column of the second-level model<sup>6</sup>)

*spm\_ss\_\*rss.img* : 4d-volume with residual sum squares matrix (as many volumes as the square of the number of effect of interest contrasts)

*spm\_ss\_\*overlap.img* : inter-subjects overlap

In addition, for ROI-based analyses the toolbox will also create the following file:

*spm\_ss\_\*data.csv* : estimated effect sizes and maximum-likelihood weighting per subject & ROI

note: For ROI-based analyses all of the above volumes will contain the ROI-based estimates back-projected to the brain volumes; i.e. all voxels within a given ROI will contain the same values.

In addition, for voxel-based analyses the toolbox will also create the following files:

*spm\_ss\_\*whitening.img* : 4d-volume with estimated ML weights (squared root of inverse covariance)

*spm\_ss\_\*bw.img* : estimated between-/within- subjects variance ratio

This step will modify the *SPM\_ss\*.mat* file adding the estimation step results.

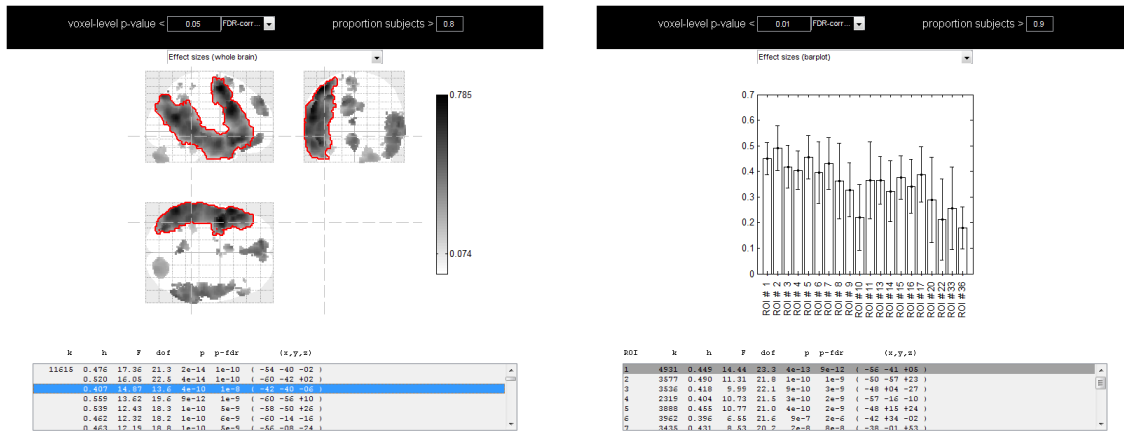
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<sup>6</sup> For example, if you have selected three effect-of-interest contrasts, and you are using a two-sample t-test (looking at two groups of subjects), each *\*beta.nii* file will contain a total of six volumes: the first three containing the estimated effects, for each effect-of-interest contrast, for the first group of subjects, and the next three containing the estimated effects for the second group of subjects.

### Step (3): RESULTS (*spm\_ss\_results*)

- Select the SPM\_ss\*.mat file containing the design
- [if more than one between-subjects regressor<sup>7</sup>] Select the *between-subjects* contrast (or create a new T- or F- contrast)
- [if more than one effect-of-interest] Select the *within-subjects* contrast (or create a new T- or F- contrast)

This step will display the results for the selected contrast:



Depending on the analyses (voxel- or ROI- based) the display options will differ. The resulting statistics can be thresholded by a combination of:

- 1) a false positive control threshold (maximum uncorrected p- values or FDR- corrected q-values)
- 2) a proportion of subjects overlap threshold (minimum proportion of subjects with supra-threshold effects on the localizer contrast)

If the user defines a new contrast (or selects one that has not yet been evaluated) the toolbox will evaluate this contrast, and it will output the following files:

*spm\_ss\_\*con#####.img* : 4-d volume of contrast effect size estimates (one per combined contrast<sup>8</sup>)

<sup>7</sup> For example, for two-sample t-tests or for multiple regression.

<sup>8</sup> The toolbox implements a GLM multivariate analysis of the form  $Y=X*B+E$ , The dependent data Y (for each voxel, or for each ROI) consists of a matrix with as many rows as the number of subjects, and as many columns as the number of effects-of-interest. The matrix of estimated regressors B (for each voxel, or for each ROI) consists of a matrix with as many rows as the number of second-level regressors (one for one-sample t-test, two for two-sample t-test, or arbitrary for multiple regression) and as many columns as the number of effect-of-interest. Hypothesis testing is permitted for any hypothesis of the form:  $C*B*M' = 0$ , where C is the between-subjects contrast (vector or matrix), and M is the within-subjects contrast (vector or matrix). The volume *spm\_ss\_\*con#####.img* will contain (for each voxel) the results of  $h=C*B*M'$  (the individual contrast values that are used to compute the associated statistics). When h is a scalar, the associated p-values are obtained based on a one-sided T- statistic; when h is a vector (row or column vector) the associated p-values are obtained based on a F- statistic; and when h is a matrix the associated p-values are obtained based on a Wilk's lambda statistic (Bartlett's  $\chi^2$  approximation).

*spm\_ss\_\*T#####.img* : T- or F- statistics  
*spm\_ss\_\*dof#####.img* : degrees of freedom  
*spm\_ss\_\*P#####.img* : uncorrected p-values  
*spm\_ss\_\*Pfd#####.img* : whole-brain FDR-corrected p-values

In addition, for ROI-based analyses the toolbox will also create the following file:

*spm\_ss\_\*results#####.csv*: estimated contrast effect sizes, inter-subject overlap, T/F statistics, dof, uncorrected p-values and FDR-corrected p-values, for each ROI.

note: For ROI-based analyses the above volumes will contain the ROI-based estimates back-projected to the brain volumes; i.e. all voxels within a given ROI will contain the same values.

This step will modify the *SPM\_ss\*.mat* file adding the evaluated contrast if new.

## **Additional information:**

### A) batch processing

All of the operations of the toolbox can be performed without user interaction. See *test01.m* for an example and *help spm\_ss\_design* for further information.

### B) *spm\_ss\_crossvalidate\_sessions.m*

This script can be used independently for partitioning a given first-level contrast into multiple contrasts. For each selected first-level contrast this script will create and estimate the following new contrasts:

The `SESSIONn_contrastname` corresponds to the `contrastname` evaluated only on the `n`'th session data.

The `ORTH_TO_SESSIONn_contrastname` corresponds to the `contrastname` evaluated on all except the `n`'th session data.

### C) *spm\_ss\_createlocalizermask.m*

This script can be used independently for thresholding a given first-level contrast (uncorrected p-value or FDR-corrected p-value thresholds are implemented).

For each selected first-level contrast this script will create a new volume named `locT_####.img` containing a binary map resulting from thresholding the selected contrast (`spmT_####.img` file) at the chosen level.