BSMac: Bayesian Spatial Model for Brain Activation and Connectivity

User's Guide

version 2.0

CBIS
Emory University

November 13, 2010

Contents

Chapter 1

Introduction

BSMac is a statistical and graphical visualization MATLAB toolbox for the analysis of fMRI data. It simultaneously performs whole-brain activation analyses at the voxel and region of interest (ROI) levels as well as functional connectivity (FC) analyses using a flexible Bayesian modeling framework [1]. Details of the underlying statistical model, estimation, and interpretations of parameters are provided by Bowman et al. [1]. In the BSMac toolbox, most of the operations can be performed easily within a graphical user interface (GUI).

BSMac runs under both Windows and linux/unix platforms. BSMac implements the following procedures:

✓Load data (Image)
✓Design matrix setup
✓Parameter setup
✓Region selection
✓Model estimation
✓Plot basic summaries of results
✓Plot brain activation maps
✓Plot functional brain connectivity

1.1 System requirements

The BSMac Software is a collection of the MATLAB functions than can be run in a GUI. Users can run (and edit) BSMac functions from any computer with MATLAB, and a non-modifiable executable version of the software can be run from machines without MATLAB. To run without MATLAB, one needs to install the MATLAB Compiler RunTime (MCR) package before launching BAMac. To install the MCR, users must run the MCR installer appropriate for their platform: MCRInstaller.exe for Windows systems or MCRInstaller.bin for UNIX and Linux systems. We provide a link on our web page for installing MCR (*http://www.sph.emory.edu/bios/CBIS/links.html*).

BSMac is a small self-extraction program, around 2MB in size including image templates, such as: AAL [2], Brodmann [3], and MNI152 templates (all are in standard MNI (Montreal Neurological Institute) space). After downloading the software, simply extract it to your computer. BSMac will automatically create four folders to save the necessary files for running BSMac:

✓**anatomical folder**: includes the AAL template image and associated region labels, the Brodmann template image and associated region labels, and the MNI template;

✓**data folder**: for saving extracted image data files, such as .mat files;

✓**results folder**: for saving MCMC results files;

✓**CBIS folder**: includes help files.

BSMac performs parameter estimation based on Markov chain Monte Carlo (MCMC) methods. For some analyses, the toolbox may consume a lot of RAM for storing estimation results, some of which are temporary. More than 1GB RAM is recommended for running BSMac. To reduce the required RAM, you may change the "Thin Factor" to a larger number. You may also decrease the number of iterations or "burn in" runs, although this should be done with caution as it may affect the performance of the MCMC estimation.

1.2 Preprocessing

We assume that the user has already performed some initial preprocessing prior to using our software and that the data are registered to MNI space ($91 \times 109 \times 91$), for example using FSL (http://www.fmrib.ox.ac.uk/fsl/), SPM (http://www.fil.ion.ucl.ac.uk), or other software packages.

Chapter 2

Software structure

BSMac provides an easy to navigate GUI environment based on MATLAB. Figure 2.1 shows a screen capture of the BSMac GUI interface running under Windows. There are five basic steps to implementing the spatio-temporal model in BSMac, namely “Analysis Data File(s)”, which allows the user to read in the image data or saved data/results from previous runs; “Region Selection”, which enables the user to select particular brain regions for inclusion in the analysis; “Parameters”, giving the user to specify hyper-prior parameters in the Bayesian model, select starting values, and MCMC information such as the number of iterations; “Estimate”, which performs estimation; and “Plot”, which provides various options for visualizing the results.

2.1 Analysis Data File

There are three choices to import the data:

- “Import Data” loads image format files, e.g. Analyze or Nifty images from the (raw) preprocessed data.
- “Load Saved Data” loads data from a saved .mat file. This option requires the user has previously loaded the raw image data using ”Import Data” and saved this input in a .mat file.
- “Load Estimation Results” loads results from MCMC, discussed later.

2.1.1 Importing data

“Import data” will allow the user to select the image format and the regional parcellation type (either AAL [2] or Brodmann [3]). When the user clicks the button , it will launch the dialog box in Figure 2.2.

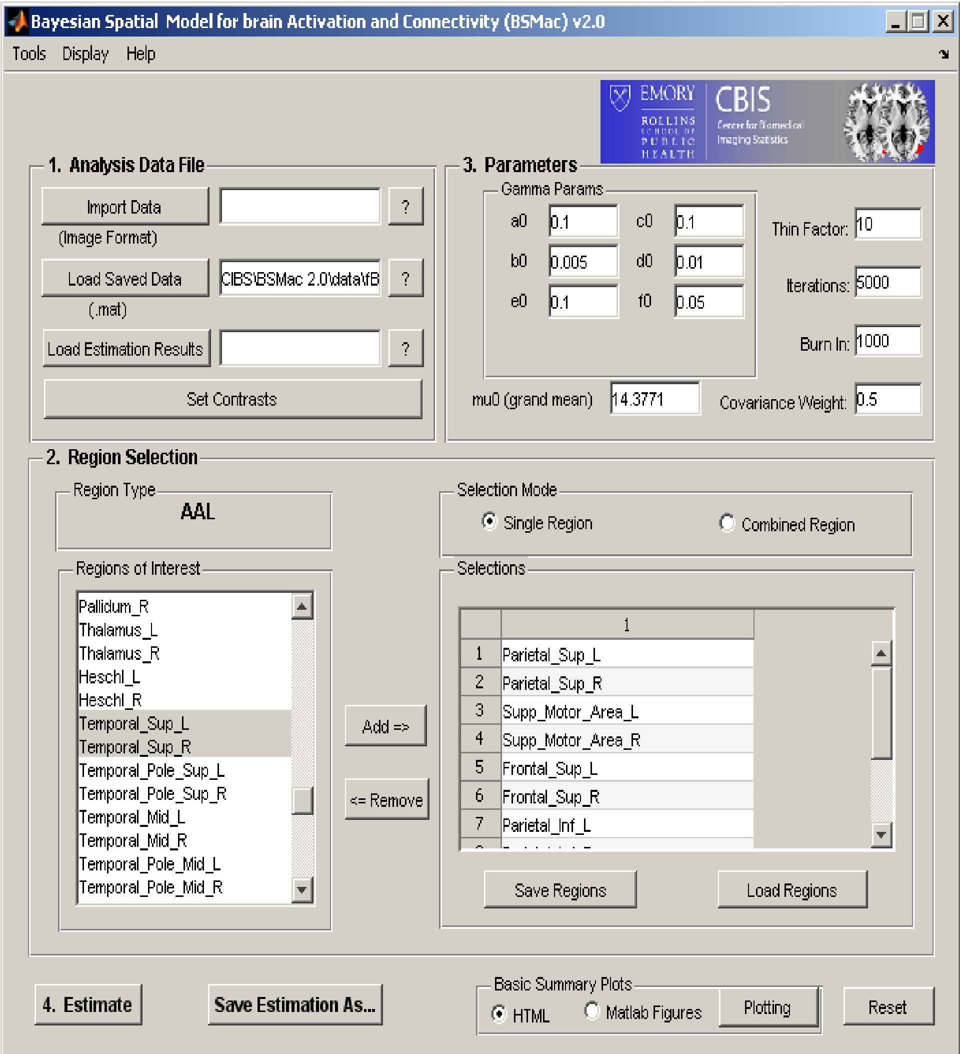

Figure 2.1: BSMac GUI interface

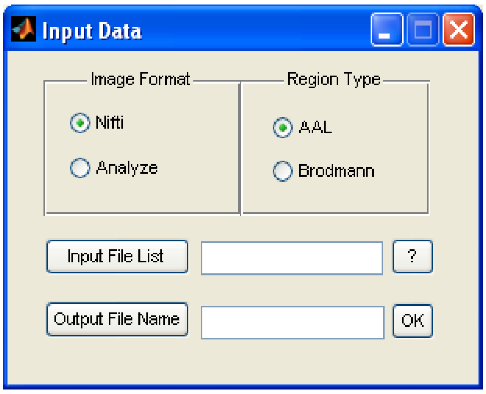

Figure 2.2: Load image data interface

Table 2.1: Input File Format

Path	File-Name	Group(Subject)	Session	Stimulus	Others ...
data1	data2	data3	data4	data5	data...
...	...	...	...	...	...

Besides choosing the data format and the region map (AAL or Brodmann), the user needs to provide a text file which includes additional information about the data. In the text file, the first line (row) contains information on the variable names (no space allowed in the variable name); the following lines contain the data corresponding to the variables. The text file should include at least 5 columns separated by spaces, as shown in Table 2.1 (the first five columns). The total number of columns (exceeding 5) depends on the number of Groups/Sessions/Stimuli and other covariates. The information in the text file will be used to construct the design matrix for modeling.

After completing the information in the dialog box, click the button “Ok”, the BSMac will begin to import the raw image data. When BSMac finishes reading the image data, the toolbox saves the information as a .MAT data file under the folder named *data*, which can be loaded later for future analyses.

After importing the raw data or loading the saved .mat data, the “Set Contrasts” button will become available (the Parameter section of the GUI will also become available) and will guide the user to the next step of setting design matrix.

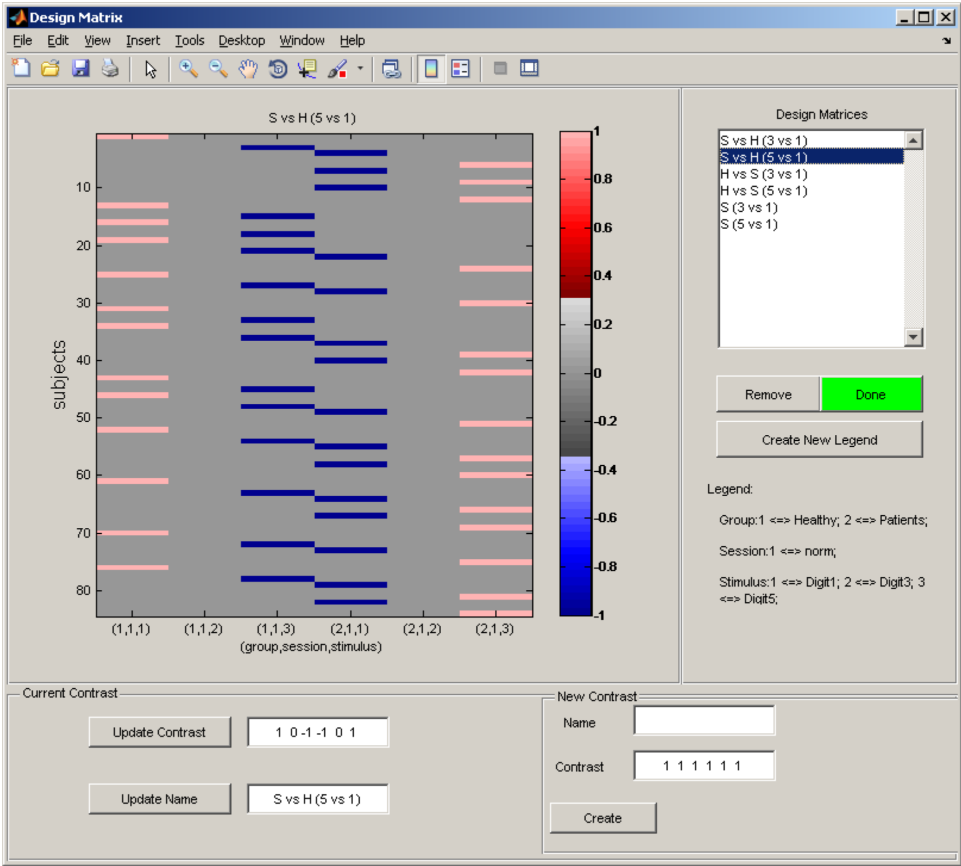

Figure 2.3: Design Matrix for the second level analysis based on the fBIRN data

2.1.2 Design Matrix

The design matrix figure gives an illustration of the design matrix constructed by BSMac from the user-specified text file discussed in section 2.1.1. This dialog box also allows the user to define contrasts between groups, sessions, and tasks. Under "Current Contrast", enter the desired contrast and user-specified label (name), then click "update". The user can define multiple contrasts. Click "Done" when finished. The contrasts will be saved into the default folder *results*.

2.2 Region Selection

Based on the regional parcellation selected in step1 (either AAL or Brodmann), a list will appear with all of the region names. The user can choose regions to be included in the analysis. Regions can be defined as either single regions or as combined regions by clicking "Add" button. The combined regions can include up to 4 individual subregions. Each row in the combined region table constitutes a single defined region for the spatio-temporal model. The selected regions can be saved for reloading later.

IMPORTANT NOTE: We impose a sample size-dependent restriction on the number of regions included in the analysis. Specifically, the number of regions cannot exceed one less than the smallest subgroup size in the data. For example, in a study with 21 healthy controls and 25 patients, we would limit the number of regions to 20. If there are no subgroups present in the data, then the number of regions cannot exceed one less than the total sample size [1]. This restriction is to ensure stability of the estimation procedures, but all regions can be included with a sufficiently large sample size.

2.3 Prior parameters

The toolbox is based on a Bayesian hierarchical parametric model. Thus, the user must specify values of the hyper-prior parameter values at the terminating level of the model. BSMac includes the following default parameter values: $a_0 = 0.1$, $b_0 = 0.005$, $c_0 = 0.1$, $d_0 = 0.01$, $e_0 = 0.1$ and $f_0 = 0.01$, resulting in vague or weakly informative priors. The parameter μ_0 is obtained empirically as the mean across all subjects. The values for a_0, b_0, c_0, d_0, e_0 and f_0 generate densities that place large probability masses on large variances. The rationale for using these vague priors is to ensure that the information in the data primarily governs the results. The user may keep the default values, if there is not specific information available *a priori* to guide particular selections for these values. However, the user may set different values if some additional information about the data is available.

The number of Markov Chain Monte Carlo (MCMC) iterations may vary from one analysis to the next. We suggest running at least a few thousand iterations and discarding the first one thousand. When running a large number of iterations, the "Thin Factor" can be used to reduce the amount of information retained by keeping draws from, say every 5th iteration. Thinning may also help to ensure that draws from subsequent iterations are not highly correlated. **Caution:** If you encounter an "Out of memory" problem, consider thinning or reducing the number of iterations. Reducing the number of covariates included in the model may also help.

2.4 Estimation

Once steps 1-3 have been completed, the model is now set up and ready for Bayesian estimation. The user can execute the estimation step by clicking the "Estimate" button. The MCMC method used here implements Gibbs sampler. Applying MCMC methods in our context is complicated by the massive amount of data, the vast number of spatial locations, and the large number of parameters. However, the Gibbs-friendly model specification facilitates estimation by providing substantial reductions in computing time and memory [1].

Performing estimation is the most time-consuming step in the analysis. The estimation time depends on several factors such as the number of covariates, the number of regions, and the sample size, and the speed of the user's computer. Our experiences have ranged from around 15 minutes to greater than 3 hours.

2.5 Visualization

The last step for this toolbox is devoted to visualization. This includes generating basic summary plots, activity maps, and 3D functional connectivity maps.

2.5.1 Basic Summary Plots

The basic summary plots generate several results. First, a legend of selected regions (Figure 2.4) is shown. A plot of the posterior mean contrast for each region is also generated (see Figure 2.5). The plot gives the contrast estimate for each selected region. BSMac also provides regional posterior probabilities of *activation*, specifically estimating the probability that the contrast is greater than zero. Figure 2.6 shows the posterior probabilities for each region. We also generate a histogram of the voxel-level posterior probabilities of *activation* (Figure 2.7), e.g. giving an indication of the number of highly probable alterations in neural activity across the entire brain (or in the included regions). Figure 2.8 shows intra-regional correlations, separately for each subgroup, say controls and at-risk subjects, and Figure 2.12 shows the group-specific inter-regional correlation matrices, thresholded at 0.1 for ease of visualization.

2.5.2 Activation Maps

After generating the basic summary plots in the above step, the user can plot more detailed maps of distributed patterns of (changes in) neural activity, or what we simply call activation maps from the menu **Display** → **Activation Map**. We provide both region-level and voxel-level activation maps, which are technically posterior probability maps for our analysis.

Figure 2.10 shows a snapshot with the region-level activation map corresponding to a selected contrast. The activation map displays the posterior probabilities associated with the selected contrast in axial, sagittal, and

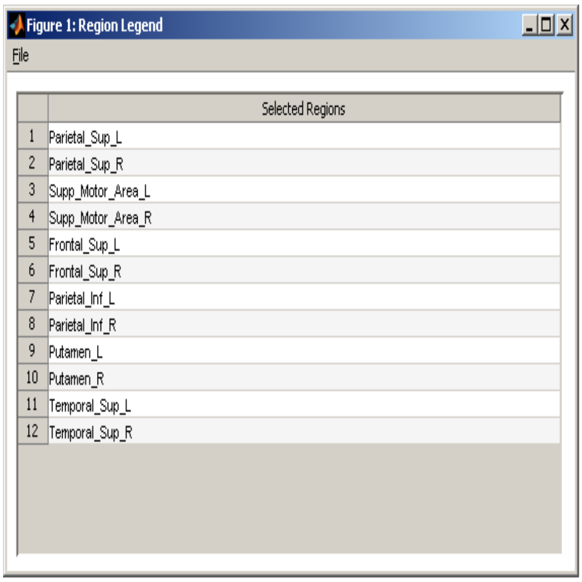

Figure 2.4: Selected regions' labels

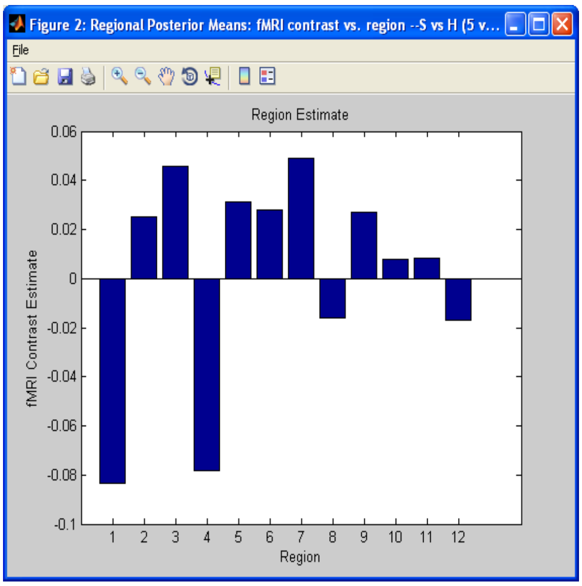

Figure 2.5: Plot of the regional contrast estimates, showing the posterior mean for each region.

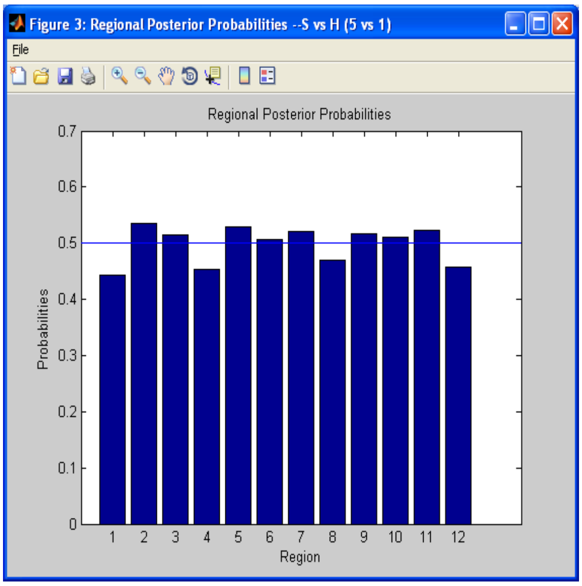

Figure 2.6: Regional posterior probabilities for selected contrast.

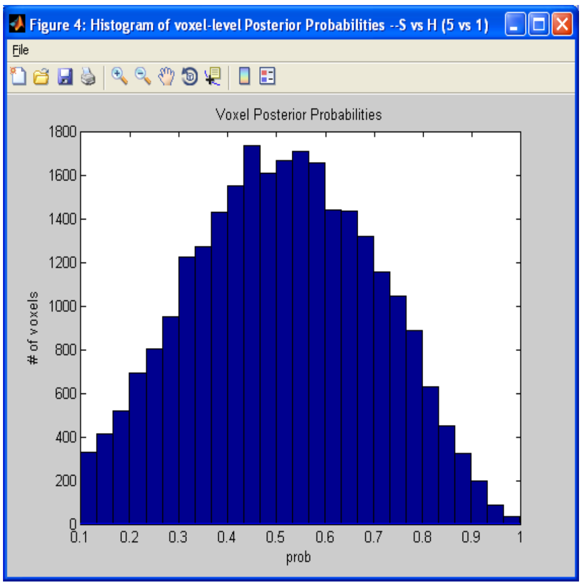

Figure 2.7: Voxel-level posterior probabilities for selected contrast.

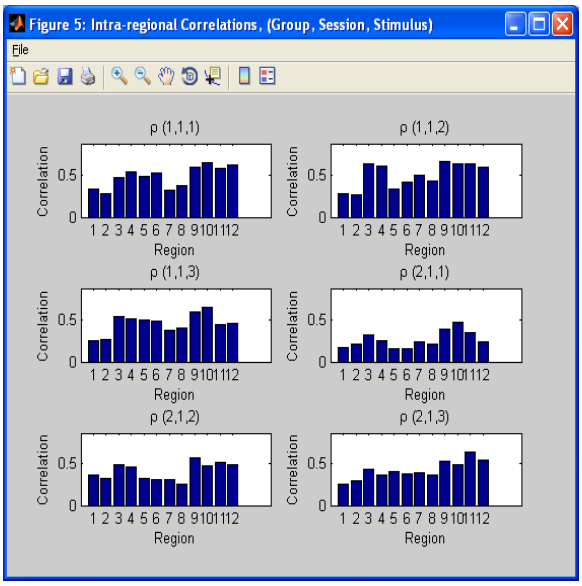

Figure 2.8: Intra-regional correlation estimates.

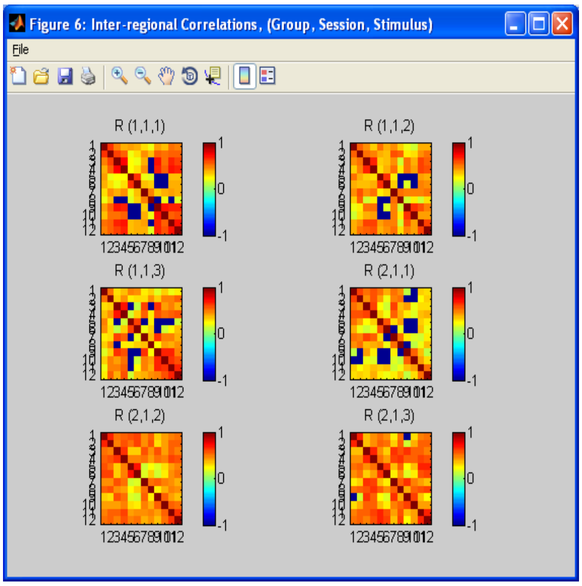

Figure 2.9: Inter-regional correlation estimates.

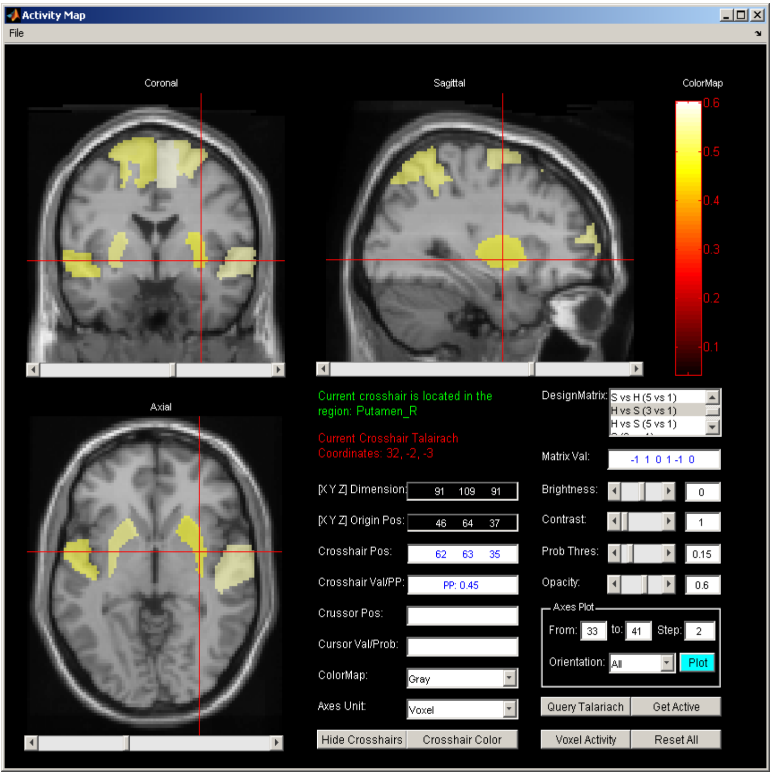

Figure 2.10: Region-level brain activation map.

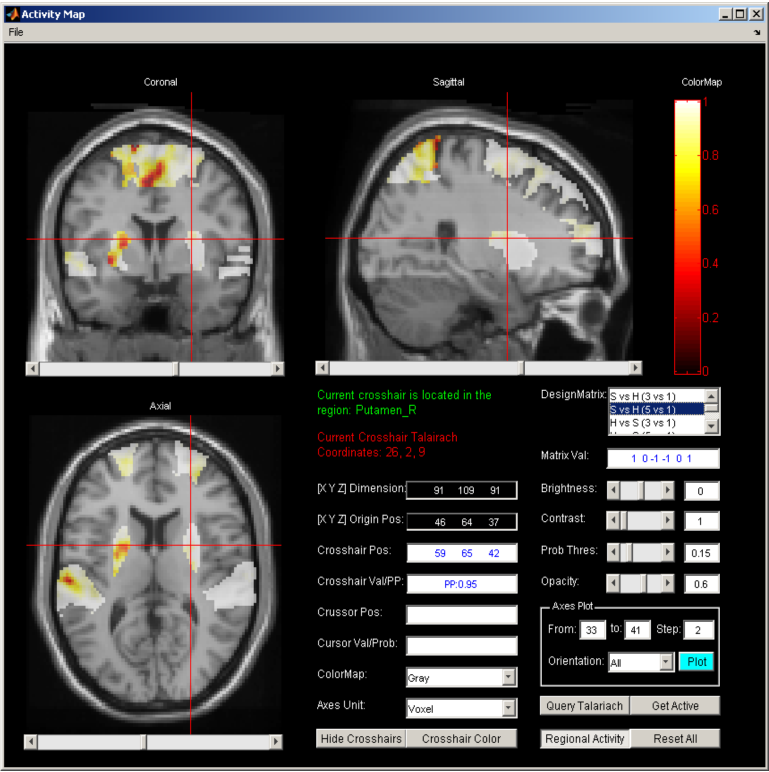

Figure 2.11: Voxel-level brain activation map.

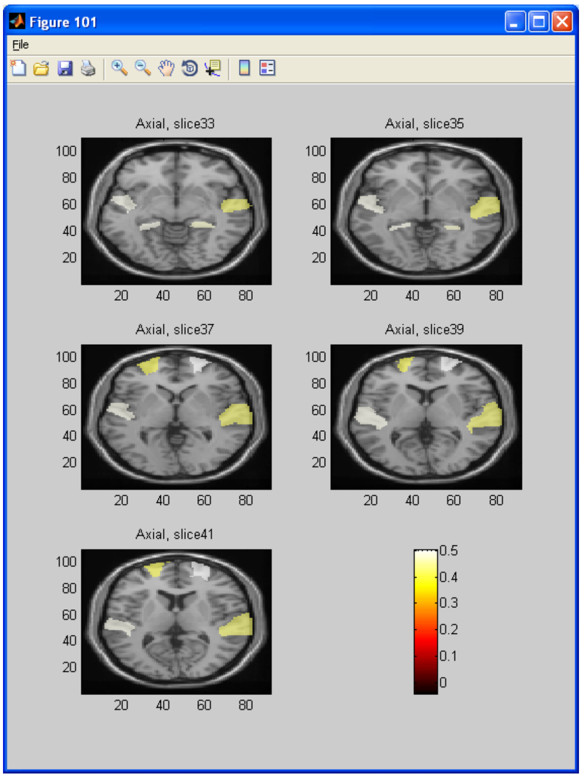

Figure 2.12: Regional activity plot in axial views for every other slice ranging from 33 to 41. The probability threshold is set to 0.2.

coronal views. The lower right part of the figure provides some basic information, such as crosshair/cursor position and the posterior probability value, background brightness and contrast. The user can set the posterior probability threshold and opacity for visualization. By clicking the "Regional Activity" button, the user can switch the activity map between the regional and the voxel view (see Figure 2.11). There are also options that allow the user to plot particular slices, in selected orientations. For example, the user may generate plots in an axial view, slices between 33 to 41, and with the threshold 0.2 (see Figure 2.12).

2.5.3 Functional Connectivity

This toolbox also allows the user to plot inter-regional functional connectivity. To display functional connectivity results, the user can click the "Display" menu at the top, and then click "Functional Connectivity". The user can then select a subset (or all) of the regions included in the analysis and specify the desired connectivity map for display (e.g. corresponding to

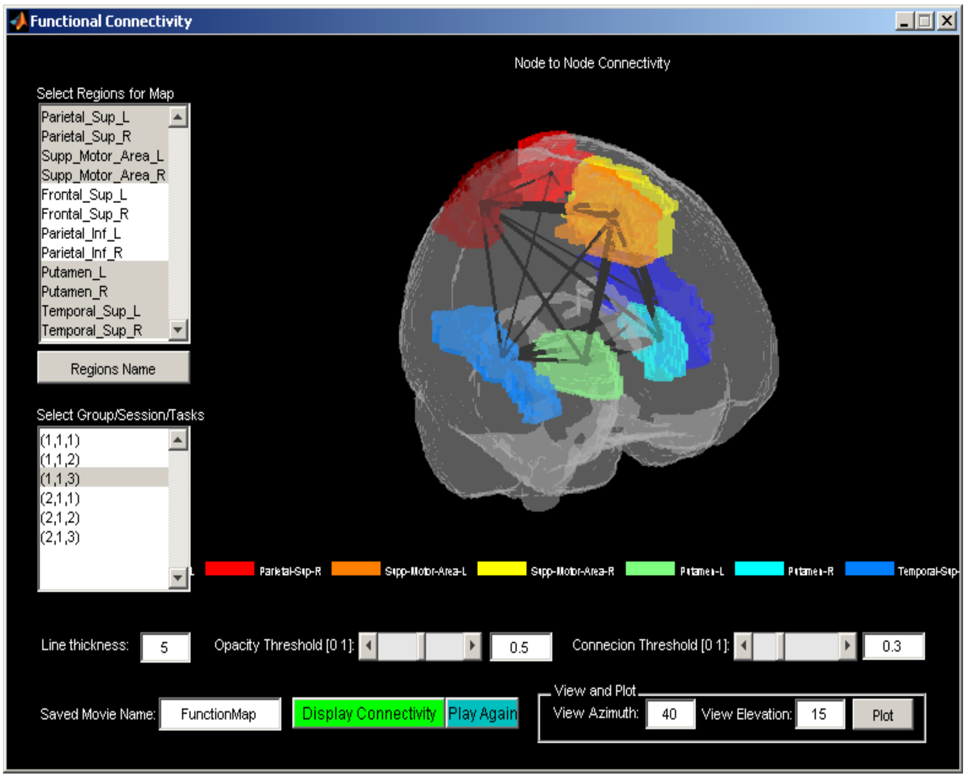

Figure 2.13: Display of functional connectivity results.

a subgroup, session, and task). The functional connectivity map displays all of the selected regions in a dynamically rotating brain, with bars connecting regions that have (posterior median) correlations exceeding a user-specified threshold. The connected regions have different line thicknesses, depending on the strengths of the functional connections between regions.

Figure 2.13 shows the result of the functional connectivity with selected regions. User can also plot the connectivity with special angle view. For example, Figure 2.13 illustrates the connectivity with all selected regions for group/session/stimulus = (2, 1, 1) (corresponding to healthy control subjects during session 1) with the specified threshold of 0.1.

Bibliography

[1] F. D. Bowman, B. Caffo, S. S. Bassett, C. Kilts, A bayesian hierarchical framework for spatial modeling of fmri data, NeuroImage 39 (2008) 146–156.

[2] N. Tzourio-Mazoyer, B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer, M. Joliot, Automated anatomical labelling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single subject brain., NeuroImage 15 (2002) 273–289.

[3] L. Garey, Brodmans localisation in the cerebral cortex: the principles of comparative localisation based on cytoarchitectonics, Springer, London, 1994, english translation of Vergleichende Lokalisationslehre der Grosshirnrinde by Korbinian Brodman.