## SPM Course USA - New Haven, CT
**Wed April 6 through Fri April 8, 2005**

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<thead>
<tr>
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<th>Duration</th>
<th>Event</th>
</tr>
</thead>
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<td><strong>Day 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8:30 AM</td>
<td>0:30</td>
<td>Continental Breakfast</td>
</tr>
<tr>
<td>9:00 AM</td>
<td>0:30</td>
<td>Course Intro</td>
</tr>
<tr>
<td>9:30 AM</td>
<td>1:00</td>
<td>Lect: Spatial Preprocessing</td>
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<tr>
<td></td>
<td></td>
<td>John Ashburner</td>
</tr>
<tr>
<td>10:30 AM</td>
<td>0:30</td>
<td>Coffee</td>
</tr>
<tr>
<td>11:00 AM</td>
<td>1:00</td>
<td>Lect: Computational Neuroanatomy</td>
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<td></td>
<td></td>
<td>John Ashburner</td>
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<tr>
<td>12:00 PM</td>
<td>1:00</td>
<td>Lect: GLM I - Principles</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alexa Morcom</td>
</tr>
<tr>
<td>1:00 PM</td>
<td>1:30</td>
<td>Lunch</td>
</tr>
<tr>
<td>2:30 PM</td>
<td>0:30</td>
<td>Lab 1: SPM Intro &amp; Data checking</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>1:00</td>
<td>Lab 2: Spatial preprocessing</td>
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<tr>
<td>4:00 PM</td>
<td>1:00</td>
<td>Lab 3: VBM preprocessing &amp; (initial) modeling</td>
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<td>5:00 PM</td>
<td></td>
<td>Ajourn</td>
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<tr>
<td>7:00 PM</td>
<td></td>
<td>Welcome Reception</td>
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<tr>
<td><strong>Day 2</strong></td>
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<tr>
<td>8:00 AM</td>
<td>0:30</td>
<td>Continental Breakfast</td>
</tr>
<tr>
<td>8:30 AM</td>
<td>0:30</td>
<td>Review of Day 1 &amp; Questions</td>
</tr>
<tr>
<td>9:00 AM</td>
<td>1:00</td>
<td>Lect: GLM II - fMRI</td>
</tr>
<tr>
<td>10:00 AM</td>
<td>0:45</td>
<td>Lect: GLM III - Variance Components</td>
</tr>
<tr>
<td>10:45 AM</td>
<td>0:30</td>
<td>Coffee</td>
</tr>
<tr>
<td>11:15 AM</td>
<td>0:45</td>
<td>Lect: GLM IV - Contrasts</td>
</tr>
<tr>
<td>12:00 PM</td>
<td>1:30</td>
<td>Lunch</td>
</tr>
<tr>
<td>1:30 PM</td>
<td>1:00</td>
<td>Lect: Classical Inference (thresholding)</td>
</tr>
<tr>
<td>2:30 PM</td>
<td>0:30</td>
<td>Coffee (move to lab)</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>1:00</td>
<td>Lab 4: Single Subject fMRI</td>
</tr>
<tr>
<td>4:00 PM</td>
<td>1:00</td>
<td>Lab 5: Multi-Subject fMRI</td>
</tr>
<tr>
<td>5:00 PM</td>
<td></td>
<td>Ajourn</td>
</tr>
<tr>
<td>5:30 PM</td>
<td>1:00</td>
<td>Football Match</td>
</tr>
<tr>
<td><strong>Day 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8:00 AM</td>
<td>0:30</td>
<td>Continental Breakfast</td>
</tr>
<tr>
<td>8:30 AM</td>
<td>0:30</td>
<td>Review of Day 2 &amp; Questions</td>
</tr>
<tr>
<td>9:00 AM</td>
<td>0:45</td>
<td>Lect: Experimental Design</td>
</tr>
<tr>
<td>9:45 AM</td>
<td>0:45</td>
<td>Lect: fMRI - Epoch &amp; ER</td>
</tr>
<tr>
<td>10:30 AM</td>
<td>0:30</td>
<td>Coffee</td>
</tr>
<tr>
<td>11:00 AM</td>
<td>1:00</td>
<td>Lect: Effective Connectivity &amp; DCM</td>
</tr>
<tr>
<td>12:00 PM</td>
<td>1:30</td>
<td>Lunch</td>
</tr>
<tr>
<td>1:30 PM</td>
<td>1:30</td>
<td>Lab A: Dynamic Causal Modeling</td>
</tr>
<tr>
<td>1:30 PM</td>
<td>1:30</td>
<td>Lab B: Nonparametric Group Modeling w/ SnPM</td>
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<td>1:30 PM</td>
<td>1:30</td>
<td>Lab C: Multivariate Modeling</td>
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<tr>
<td>1:30 PM</td>
<td>1:30</td>
<td>Lab D: Registration alternatives</td>
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<td>1:30 PM</td>
<td>1:30</td>
<td>Lab E: ROI analyses with Marsbar</td>
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<tr>
<td>3:00 PM</td>
<td>0:30</td>
<td>Coffee</td>
</tr>
<tr>
<td>3:30 PM</td>
<td>1:00</td>
<td>Results presentations &amp; conclusion</td>
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<tr>
<td>4:30 PM</td>
<td></td>
<td>Ajourn</td>
</tr>
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## Organizational Notes

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<tr>
<th>Transportation</th>
<th>All lectures are held in the Divinity School, 409 Prospect St., about 1.5 miles from the Omni Hotel (155 Temple St). At <strong>8AM</strong> each morning a shuttle bus will pick up attendees at the Omni and take them to the Divinity School.</th>
</tr>
</thead>
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<td>Lectures</td>
<td>All lectures will be held in the RSV Room in the Divinity School</td>
</tr>
<tr>
<td>Labs</td>
<td>Participants will be split into two groups for labs. Half will use the Social Sciences Stat Lab (140 Prospect St) and half will use the Dunham Lab (10 Hillhouse Ave).</td>
</tr>
<tr>
<td>Breakfast</td>
<td>Continental breakfast will be served at the Divinity School each morning before the lectures.</td>
</tr>
<tr>
<td>Lunch</td>
<td>Lunches are included. On Wednesday, lunch will be served in the Kline Biology Tower (transportation from the Divinity school will be provided). On Thursday and Friday lunch will be served at the Divinity school.</td>
</tr>
<tr>
<td>Dinner</td>
<td>Dinner is not included in the program.</td>
</tr>
<tr>
<td>Welcome Reception</td>
<td>On Wednesday at 7:00pm there will be Welcome Reception in the President’s Room, Woolsey Hall, at the corner of College &amp; Grove Streets. Beer, wine, soft drinks and light refreshments will be served.</td>
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</tbody>
</table>
Yale University

1) Dunham Lab - 10 Hillhouse Ave.
2) Divinity School - 409 Prospect St.
3) Kline Biology Tower - 219 Prospect St.
4) President's Room - College & Grove
5) Social Sciences Stat Lab - 140 Prospect St.
6) Omni Hotel - 155 Temple St.
Lab 1
Introduction to SPM & Data Checking
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Lab 1: Introduction to SPM and data checking

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Lab 1: Introduction to SPM and data checking

Goals of this Lab

After this lab you will...

1. Understand the structure of the SPM package and how to best install and maintain it.
2. Be able to examine data using SPM's single- and multi-volume display facilities.
3. Be able to characterize the susceptibility artifacts and signal voids in functional data, as compared to similar structural data.

Prerequisites

- A standard SPM installation
- The SPM single subject epoch (block) auditory fMRI activation data (see below)

An SPM Installation

Before starting SPM, use the Windows Explorer go to the SPM directory (listed on the board). Note that SPM consists mostly of matlab .m files. There are also .c, .h C source code files, and compiled 'mex' or 'dll' files. The compiled files are custom C language extensions which can be called as if they are matlab .m files, and are used to speed up processing that would be very slow in matlab.

If you install SPM yourself, you can obtain it from

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

but be sure to obtain the latest updates (check regularly!). For SPM2, the updates are here

ftp://ftp.fil.ion.ucl.ac.uk/spm/spm2_updates

When you install SPM yourself, it is a good idea to create a "root" spm directory. In this root SPM directory you can put the released versions of SPM, and in a separate local folder, any local modifications.

For example, our local spm directories look like

/usr/local/spm
/usr/local/spm/spm99
/usr/local/spm/spm99_local
/usr/local/spm/spm2
/usr/local/spm/spm2_local

or for Windows

C:\MatlabToolboxes\spm2
C:\MatlabToolboxes\spm2_local

Never change any files in a SPM release directory (e.g. spm/spm99 or spm/spm2 above), except to incorporate updates from SPM central, even then it is a good idea to backup the old copy of the file being replaced until you are sure the new file has been installed correctly and is working.
If you want to change some SPM code, make a copy of the .m file you want to change and put it in the local directory (e.g. "cp spm2/spm_defaults.m spm2_local/spm_defaults.m" on Unix), and then make changes to that local copy. If you don't do this, your local changes may be overwritten when you download new updates.

**SPM Defaults**

When setting up SPM for the first time it is a good idea to make sure the settings for various default variables are correct for your installation. Default settings are specified in the file spm_defaults.m. This file can be changed in the main spm2 directory where it will affect all users, or individual users can have their own copy with user−specific settings. If you keep your own copy make sure the Matlab path to the copy comes BEFORE the path to the spm2 directory.

**L/R Brain Orientation**

Open the spm_defaults file by typing `edit spm_defaults` at the Matlab prompt.

Look at the entry for defaults.analyze.flip.

Does this installation of SPM expect the images to be in Neurologic (L = L) or Radiologic (L = R) convention? How can you tell?

Display image sM00223_002.img. Assuming this image was made in SPM2 is there any way to tell its orientation?

Now look at image sM00223_002−1.img? Is this in the same or different orientation? How would we want defaults.analyze.flip set for each of these images?

**Memory Use for Data Processing**

How can we tell spm to process the data in bigger or smaller chunks?

**fMRI and PET Analysis Threshold**

Do the defaults tell spm to apply any type of threshold to the data?

If so what is the threshold for fMRI data? _____ for PET data? _____

**Temporal Intervals for fMRI Data**

When setting up designs for fMRI, SPM divides the interscan interval into multiple intervals for finer modeling of the impulse response.

How many intervals is the current interscan interval divided into? _______ (hint: look at defaults.stats.fmri.t)

What interval does SPM use as the starting time point for an event or epoch? _______ (hint: look at defaults.stats.fmri.t0)

How would the starting interval be changed to midway in the TR? _______

Would it matter if the TR was 2 seconds or 4 seconds? _______
Start SPM

Open Matlab. Check that spm is on the Matlab Path by typing

    spm

If an error occurs then you must add the spm path to the Matlab. There are two ways to set the path. You can go under the file menu and use the 'Set path...' command. Click the 'Add Folder...' button to select the spm2 folder. Click 'Close'. (Click save if you want to add the spm2 folder permanently to the Matlab path).

Or you can use the command "addpath" with the path given on the board to add the SPM path to the Matlab path.

    addpath c:\course\spm\spm2

Here is an example of a simple m–file that does this for you. You could save the following 2 lines in a file called spm2.m, and put the file in Matlab's local folder. Typing spm2 would start the fMRI section of spm.

    % Save and name spm2.m
    addpath('C:\path_to_my_spm2_folder\spm2')
    spm('fmri')

The SPM interface

Now that you have run the 'spm' command, you should get a window like this:

Click on the FMRI button. You now get the standard SPM interface. In the top left of the screen you have the SPM buttons window:
Below that you have the SPM input (or Interactive) window:
The large window on the right of the screen is the SPM graphics window. In the example below we are displaying some results:
effects of interest

SPM\{F_{6.345}\}

SPMresults: /mars_eg/SPM2_ana
Height threshold F = 6.35
Extent threshold k = 0 voxels
When SPM requires that you select some files, you will get the SPM file get window:

![Select SPM.mat](image)

**Background on the data**

In this lab you will look at single subject fMRI data from a block auditory activation experiment.

96 acquisitions were made (RT=7s), in blocks of 6, giving 16 42s blocks. The condition for successive blocks alternated between rest and auditory stimulation, starting with rest. Auditory stimulation was with bi–syllabic words presented binaurally at a rate of 60 per minute. The functional data starts at acquisition 4, image fM00223_004. Due to T1 effects it is advisable to discard the first few scans (there were no "dummy" lead–in scans).

These whole brain BOLD/EPI images were acquired on a modified 2T Siemens MAGNETOM Vision system. Each acquisition consisted of 64 contiguous slices (64x64x64 3mm x 3mm x 3mm voxels). Acquisition took 6.05s, with the scan to scan repeat time (RT) set arbitrarily to 7s.

**Download the data:**

The data may already on your PC. If not, copy the MoEApilot data to your hard drive. Look for instructions on the board for where to put the data.
Look at the data!

Start Matlab & SPM

The first thing you should after starting Matlab is to change the working directory to a reasonable place. In the compute lab, the working directory may default to a directory where you do not have write permissions. Use the '...' button at the top of the Matlab window, or use the 'cd' command to change to the 'c:\temp\SPMcourse' directory.

Look at some functional data

Using the 'Display' button view a randomly selected image from among the functional data, in the fM00223 directory. You should always do this to check orientation (and any possible catastrophic problems.)

1. What is the voxel size? _____ _____ _____
2. What are the image dimension? ________ ________
3. What are typical gray matter values? From ____ to ____
4. Bilinear interpolation is default. Select Nearest Neighbor interpolation. Explore the image
5. Select Sinc interpolation. Explore the image.
6. Which one do you prefer? __________ Why?

Find the Susceptibility Voids

Due to the differences in magnetic susceptibility of air and tissue, there are often distortions and signal voices near air–tissue interfaces. Find some of these signal voids in the function data.

1. Use 'Display' to view a single functional image.
2. Position the cursor middle of the brain superior–inferior, so that the axial image shows a full oval brain slice. Now slowly move down (inferiorly) while watching the axial slice. Watch the for a darkening of the medial orbital–frontal region. Clicking further down, find the signal voids above the ear canals in the temporal lobes.

Look for time series artefacts

Almost all FMRI time series have significant artefacts due to the scanner or subject movement. It is important to check for these before we run the analysis. To do this we will use the tsdiffana utility from the CBU SPM tools:

http://www.mrc-cbu.cam.ac.uk/Imaging/Common/downloads/SPMUtils/tsdiffana.tar.gz

Download this archive to a temporary directory – say c:\Temp. Double click to open the archive, and extract into the temporary directory. You should now have some new .m files in this directory including a file tsdiffana.m. Add this directory to your path, for example with:

addpath c:\Temp -end

The "−end" flag just makes sure that c:\Temp goes at the end of the matlab path, so any files in the c:\Temp directory can't interfere with SPM files.
To run the utility, go to the matlab (>>) prompt, and enter

`tsdiffana`

Then select all the raw functional images from the dataset (`FM00223_*_.img`).

You will see the time series diagnostics in the SPM graphics window.

In the top panel you will see the scan-to-scan variance. For the first point, this the mean squared difference (MSD) in signal intensity between the first and second scan; for the second point it is the MSD for scans 2 and 3, and so on. This tells you where there has been global shift in signal between scans.

What do you notice about the scan-to-scan variance time course?

There are more details on the `tsdiffana` utility on the CBU web site:

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

**Review the standard deviation image**

The `tsdiffana` utility also writes out some standard deviation images for the whole time series. These images allow you to see where there may have been artefacts that are larger in particular parts of the image.

1. Click on 'Display'
2. Select the 'std_*.img' in the FMRI data directory

Click around the image. What artefacts do you see? What should we do about these artefacts?

**Compare the functional data to the anatomical data**

In the sM00223 directory you'll find the structural MRI data.

1. Use ‘Check Reg' to "check" the "registration" between the sM00223_002 image and one of the fM00223 functionals.

1. Unlike 'Display', 'Check Reg' lets you view upto 12 volumes. Select the anatomical and then the functional.

1. We haven't registered these two images yet; is this clear from CheckReg?

**ImCalc**

The ImCalc function of spm can be used to manipulate images in a variety of ways. In this section you will learn to make a binary image mask and to average images.

**Make a Binary Mask**

1. Use the spm cd menu to move to a directory you can write to.
2. Click the imcalc button and choose the sM00223_002.img.
3. Enter a filename for the output image. You do not need to include the .img extension.
4. Enter i1 > 0 as the expression to evaluate.
5. Look at the image output using Display. What went wrong? Make a new binary image that fixes this problem.
6. Advanced users: How would you apply the mask to the original image in a single step?

**Make a Mean Image**

1. Click the imcalc button and select the first three EPI images (fM00223_004.img through fM00223_006.img)
2. Given the mean output image a filename – say mean_4_epi (note you do not need the .img extension).
3. Enter the expression (i1+i2+i2)/3.
4. Check this worked by clicking Display, and selecting the output image (mean_4_epi.img in your current working directory). If you can't remember where your current directory is, type pwd in the matlab command window.

**.mat files**

.mat files encode orientation information for images in SPM, and are a major source of confusion.

1. Go to the matlab console window, and type ls mean_4_epi*
2. You should see that there are two files, mean_4_epi.img, and mean_4_epi.hdr. The img file contains the actual image data, and the hdr file contains various bits of information about the image including dimensions etc.
3. If you haven't already done this for the previous exercise, click Display, and select the mean_4_epi.img file.
4. Note the Dir Cos matrix at the bottom right of the graphics window; it should be a 3x3 identity matrix (just zeros with ones on the diagonal).
5. Go to the transformation parameters box at the bottom left of the graphics window (see below for image)
6. Click in the Pitch box, and set the pitch to 0.6, and press return. Notice that the image pitches forward (in fact by 0.6 radians).
7. Click on the Reorient images... button in the bottom left hand corner. Select mean_4_epi.img (the image you are currently working with). The 0.6 pitch value has now been cleared, and you will see the Dir Cos matrix has changed – reflecting the pitch transformation applied to the image
8. Click on the World space drop-down menu box near the bottom mid–right of the graphics window (see below for image).
9. Try toggling between World space and Voxel space. Note that the transformation is not applied in voxel space, but it is in world space.
10. Click on Display and select mean_4_epi.img again. The transformation you saved is still being applied.
11. At the matlab console, type ls mean_4_epi* again. You will see there is a new file mean_4_epi.mat. This file contains the reorientation that you applied to the image.
12. At the matlab console type delete mean_4_epi.mat.
13. Click on Display and select mean_4_epi.img again. The transformation has been lost.
Make a Mean Image
<table>
<thead>
<tr>
<th>File Name</th>
<th>Type</th>
<th>Size</th>
<th>Date/Time</th>
<th>Author</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>spm_get.png</td>
<td>manage</td>
<td>16.2 K</td>
<td>22 Mar 2005 − 23:41</td>
<td>Matthew Brett</td>
<td>SPM get window</td>
</tr>
<tr>
<td>spm_welcome.png</td>
<td>manage</td>
<td>17.2 K</td>
<td>22 Mar 2005 − 23:46</td>
<td>Matthew Brett</td>
<td>SPM welcome window</td>
</tr>
<tr>
<td>orth_trans_params.png</td>
<td>manage</td>
<td>4.0 K</td>
<td>29 Mar 2005 − 19:14</td>
<td>Matthew Brett</td>
<td>Transformation parameters input box</td>
</tr>
<tr>
<td>orth_info_box.png</td>
<td>manage</td>
<td>5.3 K</td>
<td>29 Mar 2005 − 19:22</td>
<td>Matthew Brett</td>
<td>Information box for SPM image display</td>
</tr>
</tbody>
</table>
Lab 2

Spatial
Preprocessing
Lab 2: Spatial Preprocessing

Goals of this Lab

After this lab you will be able to...

1. Perform realignment of image data, correcting for head motion
2. Coregister functional and structural data
3. Spatially Normalize data, accounting for intersubject differences in brain shape

Data needed for this Lab: MoAEpilot, single subject fMRI data.

Ensuring the data are oriented properly

If the images were very out of register we could try to get the images closer by manually setting the origin to the Anterior Commissure (AC).

Q. On the board will be a diagram of how to find the AC on the midsagittal plane. Sketch it here

Now use the Display button view the sM00223 image and locate the AC as best possible. You should be able to see it on the axial slice.

Hint: Once you are close, it helps to "zoom in". In the display facility, click on the "Full Volume" pop-up menu; select "80x80x80 mm"

Q. What is the location of sM00223 AC in voxels?

________    ________    ________   Voxels

Use the Display button view one of the functional fM00223 images and locate the AC as best possible.
Q. What is the location of the functional’s AC in voxels?

_________   __________  ___________   Voxels

_________   __________  ___________   mm ?

At this point we *could* set each image’s origin using "Reorient images..." button in display but we won’t.
But just for reference...

How to change the origin

To change the origin, take the AC location in mm and *multiply* by -1. Enter these three values in the first three boxes on the left ("right {mm}", "forward {mm}", "up {mm}").

Click the bar below the title "Crosshair Position". This brings you to the origin, 0,0,0 mm’s. Check that this origin is correct. If it isn’t, change the shift values and move the cursor to the origin. Repeat as needed.

When the origin is placed appropriately (i.e. when the crosshair position reads 0,0,0 voxels, and the crosshair lies over the AC), click "Reorient images...". Select the set of images (any number!) in the same space whose origin you want to change.

We’re not changing the origin for two reasons. First, the images *should* already be quite close, but there’s a more important reason.

By setting the origin on the Target image (fM00223), we change its "world space"; specifically, the origin of its world space moves from the center of the volume to the AC. Hence it will no longer have the same world space as the functional data *unless* we identically change the origin on all the functional data and any results (beta*, con*, spm_T* etc) we already created.

To summarize, if the images are way off, we can set the origin manually to help the Coregistration. But if we change the origin of the image representing the functional space, we have to similarly change the origin on all functional images.

The images we have for the demo are stored axially. If we had images acquired coronally or sagitally, then they would need to be reoriented to be approximately axial.

Q. How do you tell if a sagittal image in Neurological or Radiological convention?
Realignment
============================================================================

Despite various head restraint methods, subject motion is almost always present. To correct for head motion, we use 'Realign'ment.

1. Click 'Realign'

2. Find the fM00223 directory and select all of the functional data.

X. Note that the image data isn’t actually resampled; only the .mat files have been changed.

Q. Check the plots of motion parameters in the SPM Graphics window. Has any image moved more than 1 pixel (3mm) from the reference image?

Coregistration
============================================================================

SPM’s "Coregister" facility is used for registering different types of images from the same subject (it is a "intermodality, intrasubject" registration). To use it you must specify a "Target" or reference image, which does not move, and a "Source" image, which is moved to match the target.

Recall that the rigid body transformation is recorded in the .mat file of the source image. Hence, it is not necessary to write out the transformed image (the Source transformed into the space of the Target), though it is sometimes convenient to do so.

Before coregistering the low- and high- resolution structural images you should make sure the two images are in the same orientation and not too far from one another (you did this in the previous lab).

You will now "Coregister" the anatomical sM00223 image to the functional image.

Q. What is your "Target" image?

Q. What is your "Source" image?
Click on the Coregister button. You only have one subject and you want to "Coregister & Reslice".

Select the Target and Source images you identified above.

It asks for "Other images". This would be useful if we had other images that were acquired in the same space as the anatomical. We don’t, so just click 'Done’.

Now it will perform the coregistration.

The transformation parameters are written in the .mat file of the source image sM00223.img; this sets the world space of sM00223 to match that of the functionals. Since we asked it to "Reslice", it will also create a rsM00223.img, an image with the same dimensions and world space as the functionals

"Display" the reference functional image and use the "World Space"/"Voxel Space" pop-up button to change between the two spaces.

Q. Does the image move as you flip between the two spaces?

"Display" sM00223.img and do the same again.

Q. Does the image move as you flip between the two spaces?

Q. Why does one move and the other doesn’t?

Check the success of the Coregistration.

Use check reg to check the registration. Make sure to check making sure to compare the following anatomical regions:

i. Frontal pole
ii. Occipital (posterior) pole
iii. Left & Right sides (e.g. superior temporal gyrus)
iv. Corpus collosum: (1) Most anterior, (2) most superior and (3) most posterior extent.

Q. Has the coregistration succeeded?
Spatial Normalization
============================================================================

Spatial Normalization means intersubject registration. It is essential for performing intersubject analyses or, for intrasubject analyses, determining Talairach/MNI coordinates of activation foci.

The "Normalize" button can accept various kinds of image (T1, T2, etc), to register your subject into the standard atlas space. Note that it works by minimising the mean squared difference between the source image and the template(s). This means that the template you use should have a similar visual appearance to the image that is matched to it.

Q. Which of the SPM template images best matches sM00223?

(Check your answer before continuing on!)

Spatial normalisation (or, with an American accent, normalization) takes three types of images

i. "Source images"

These are the high resolution anatomical images from which the spatial transformation is determined. Typically you only specify *one* such image per subject.

ii. "Images to write normalised"

These are other images *with* the *same* world* space* as image (i) above. Typical examples would be statistic or contrast images, or whole set of raw functional images.

iii. "Template image(s)"

Images that define the standard atlas space. You get to choose from images that match the type (or "modality") of the image in (i).

It produces a "*_sn.mat" file, which records the nonlinear transformation from* the atlas space to* the world* space* of image (i).

Q. Now that we have coregistered, what does the world space of sM00223 correspond to?
Q. Thus if we spatially normalize sM00223 the resulting _sn.mat file will not just be good for sM00223, but for...

Click 'Normalize' to start the spatial normalization process.

Select 'Determine Parameters and Write Normalised'.

For "Template images", select T1.mnc. This image is an average of 152 subject’s T1 images, from the MNI/ICBM, smoothed with an 8mm filter. (ICBM=International Consortium for Brain Mapping).

For "Source image, subj 1", select sM00223.img

For "Images to write, subj 1", select sM00223.img and all the functional images.

For now, we are only doing 1 subject; so when it asks for "Source image, subj 2", just click 'done'.

After a short while it will finish. This will create a _sn.mat and reslice the "source", creating a wsM00223.img.

Check the success of the registration, comparing the normalized image (wsM00223.img) to the unsmoothed version of the template image, that is avg152T1.mnc in the spm2/canonical directory.

Q. Has the spatial normalization succeeded?

Smoothing
============================================================================

The only preprocessing step left to do (for an intrasubject analysis) is spatial smoothing.

Click the 'Smooth' button and select all of your r* images.

Apply a 8mm FWHM isotropic smoothing to the data. (Isotropic means "the same in all directions").

Extra for experts Specifying a filter size consisting of a single value implies a isotropic smoothing.
Lab 3

VBM Preprocessing and (initial) Modeling
Lab 3: Voxel Based Morphometry

Goals of this Lab

After this lab you will be able to...

1. Segment an image
2. Use an alternative spatial normalisation strategy
3. Perform necessary spatial pre-processing steps for VBM
4. Evaluate the success of VBM preprocessing and explore the segmentations.
5. Explore the deformations with the deformations toolbox

Data needed for this Lab: MoAEpilot, single subject fMRI data.

Segmentation

Segmentation in SPM involves partitioning an image into different tissue types. Grey matter is stored in a *_seg1.img. White matter in a *_seg2.img, and CSF in a *_seg3.img. A possible by-product of the SPM segmentation is a bias (intensity non-uniformity) corrected image. (m*.img).

Tissue probability maps (TPM) are overlayed on to the image to segment. If the image is already spatially normalised, then this is easy. If the image is not spatially normalised, then TPMs are overlayed by affine registering a template image to the image. The affine transform that overlays the template should also work to overlay the TPMs.

The plan is to segment sM00223. Click ‘Segment’ to start the segmentation process.

You will be prompted to select ‘Image(s), subj 1’. Select sM00223. When it asks for the images of subj 2, select nothing. This will tell SPM that there are no more subjects.

The sM00223 is not a spatially normalised image, so answer "no" to the next question.

The image is a T1 weighted MRI, so specify that this is the modality. At this point, you just need to wait for the segmentation to finish.

Q. What do you think would happen if more than one image was chosen for each subject?
Use the 'Check Reg' button to display sM00223 and msM00223. Change the "window" to manual, choosing a range of [80 120].

Q. Which image has more uniform white matter intensity?

Compare sM00223.img and sM00223_seg1.img using Check Reg.

Q. What happens to grey matter in the thalamus?

Spatial Normalization (again)

One use for the _seg1.img is that it can be used to improve the inter-subject registration. In fMRI, we expect most of the activation to be in the gray matter. If we focus on registering grey matter correctly, then we may get better results.

Q. What image should be used as a template?

Click 'Normalize' to start the spatial normalization process.

Select 'Determine Parameters only'.

For "Template images", select gray.mnc in the apriori directory of spm.

For "Source image, subj 1", select sM00223_seg1.img.

For "Source image, subj 2", select nothing to say that there are no more subjects.
Wait a while.

We now want to apply the deformations that we have just estimated to some images. Usually, spatially normalised images are written at 2mm resolution, often chopping off the base of the cerebellum. We can change this via the Defaults button.

Click 'Defaults'

Choose 'Spatial Normalisation'

Choose 'Defaults for...' 'Writing Normalised'.

Leave this as it is:

Preserve what?...   Preserve Concentrations

To avoid chopping off the bottom of the cerebellum, we can use a larger bounding box. The "Template" bounding box should have the same field of view as the images supplied with SPM, so we can use that.

Choose voxel sizes of [1 1 1], which gives us 1mm isotropic voxels in the spatially normalised images.

Various interpolation methods are available. For speed, we will just use 'Trilinear interpolation'.

Unless you really understand what you are doing, then leave 'Way to wrap images?...' at 'No wrap'.

Now we are ready to write our high resolution spatially normalised images.

Click ‘Normalize’ to start the spatial normalization process.

Select 'Write Normalised Only'.

The deformations are parameterised and stored in a _sn.mat file. Select the one that has just been created (sM00223_seg1_sn.mat).

Choose sM00223.img for 'Images to write'.

You will then be asked for parameters for the second subject. There is no second subject, so select nothing.

This will write out a high resolution spatially normalised image. Use the Check Reg button to compare it with an image in the canonical directory.

The same warps could also be applied to your functional data, although (to save time and disk space) you would probably write these out with 2mm resolution.

Q. If a spatially normalised fMRI dataset at 2mm resolution takes up about 100Mbytes, how much disk space would the same data written at 1mm resolution take up?
Segmentation (again)
============================================================================

The plan is to segment the spatially normalised sM00223. The resulting spatially normalised segmented images can then be used for voxel-based morphometry (VBM).

Q. Should the tissue probability maps be better aligned with wsM00223 than they were during the previous segmentation?

Click 'Segment' to start the segmentation process.

You will be prompted to select ‘Image(s), subj 1’. Select wsM00223. When it asks for the images of subj 2, select nothing. This will tell SPM that there are no more subjects.

wsM00223 is a spatially normalised (warped) image, so answer "yes" to the next question.

Now just wait...

Q. The template images are slightly bigger than most human brains. If the volume of grey matter was computed from wsM00223_seg1.img, (by counting the grey matter voxels and multiplying by the volume of each voxel), then would our estimate be about right, too low, or too high?
Modulation
============================================================================

During spatial normalisation, some regions shrink, whereas others are expanded. If we want to preserve the amount of grey matter from the original data, then this needs to be taken into account. This is what "modulation" does.

Unfortunately, there is no button on the SPM user interface to do this, so you will need to do a bit of typing.

```
P = spm_get(Inf,'*_seg*.img','Select images to "modulate"');
Q = spm_get(size(P,1),'_sn.mat','Select corresponding parameters');
for i=1:size(P,1),
    pi = deblank(P(i,:));
    qi = deblank(Q(i,:));
    spm_write_sn(pi,qi,'modulate');
end;
```

In English, this is how the code translates.

```
Select some files called *_seg*.img
Select the same number of files called *_sn.mat
The selected filenames are stored in a matrix (two dimensional array, where each row is a filename. Loop over each row, where ‘i’ is the row number.

    Select the current row of each matrix of filenames and remove any trailing blanks (’ ’).

    Modulate the current image according to the warps stored in the current parameter file.

If we haven’t finished, then move on to the next row.
```

Use the Check Reg button to see the results.

Q. What would happen if wsM00223.img was modulated before segmenting, rather than the segmented images being modulated?

Smoothing
============================================================================
Finally smooth the modulated, segmented, spatially normalised data by 12mm.

Q. A tricky one. What are the units of the resulting data?

This image is now ready to enter into a VBM statistical analysis, the principles of which are similar to those of analysing PET data.

Deformations Toolbox
============================================================================
The Deformations toolbox contains some utilities for manipulating deformation fields. We will explore some of those options here.

We’ll begin by writing out the sM00223_seg1_sn.mat as a deformation field. Select "Deformations" from the toolbox pulldown. This will produce a little menu in the lower-left window.

Select "Deformations from sn.mat"
Select sM00223_seg1_sn.mat

This will write out a deformation field using the current settings for the voxel sizes and bounding box. This is a y_*\text{.img} file.

We then invert this deformation field:
Select "Deformations" from the toolbox pulldown.
Select "Invert Deformations"
Select the y_*\text{.img} file that has just been created.

When an inverse is created, a range needs to be specified over which the inverse will cover. Select the sM00223.img, and the inverse will have the same dimensions, have the same voxel size, etc.

Suppose we have ROIs in MNI space, which we want to project on to the original data. This can be done by warping an labelled image using the inverse deformation field.

We will use one of the images released with SPM, and warp it so that it overlays our image. Note that the warped image is written in the same directory as the original, so copy one of these images to the current directory.

Select "Deformations" from the toolbox pulldown.
Select "Apply Deformations".

Number of subjects is 1.
Select the iy_*.img (inverse deformation field) that has just been created.

Select the image (that has just been copied) for warping.

Compare the newly created w*.img with sM00223 using Check Reg.
Lab 4

Single Subject fMRI
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Advanced multi-condition event-related design

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Lab 4: Single Subject fMRI

Goals of this Lab

After this lab you will be able to...

1. Specify a single subject categorical fMRI analysis using single condition block (basic analysis) or event-related (advanced analysis) data.
2. Review and explore a single subject categorical design
3. Fit the model and examine the results.
4. Specify and review event-related and parametric designs (Advanced Users)

Choose an Analysis

*Select either the single condition categorical block design or the advanced event-related design depending on your familiarity with SPM. There won't be time to do both analyses in this session.*

Basic single condition categorical block design

Prerequisites (block)

1. Standard SPM installation
2. The SPM single subject epoch (block) auditory fMRI activation data, with all spatial preprocessing applied.

The Experiment (block)

- Conditions for successive blocks alternated between rest and auditory stimulation (starting with rest).
- Auditory stimulation was bi-syllabic words presented binaurally at a rate of 60 per minute.
- These data were acquired on a modified 2T Siemens MAGNETOM Vision system.
- Each acquisition consisted of 64 contiguous slices (64x64x64 3mm x 3mm x 3mm voxels).
- Each acquisition took 6.05s, with the scan to scan repeat time (RT) set arbitrarily to 7s.
- A total of 96 images were acquired in blocks of 6, giving 16–42 second blocks.
- This experiment was conducted by Geraint Rees under the direction of Karl Friston and the FIL methods group. The data have never been written up. Please contact Geraint Rees (Geraint Rees) or the Wellcome Department of Imaging Neuroscience (send an email to the SPM list http://www.jiscmail.ac.uk/lists/spm.html) for permission to use the data.

The Data (block)

The data have been pre-processed as follows:

- Realignment
- Coregistration of the T1 volume to the mean EPI image.
- Normalized to the EPI template.
- Smoothed with a 6 mm Gaussian kernel.
Start in a new directory (block)

Before starting any analysis in SPM, make sure you are in an empty directory. SPM will write many, many files to the current Matlab directory, and no two analyses can share a directory, so always be careful about where you preprocess data or perform an analysis.

Make a new directory:

```markdown
mkdir c:\temp\Auditory
```

for the results of this.

Change into this directory, using either the cd command in the command window, the 'Current directory...' button in the command window bar, or the SPM CD utility.

Specify the model (block)

SPM questions are followed by responses in brackets.

1. Press FMRI
2. Specify design or data [design]
3. Interscan Interval{secs} [7] (This is the TR)
4. Scans per session [84] (Use a vector if there are multiple sessions [84 84 etc.].)
5. Specify design in [Scans]
6. Select basis set... [hrf] (This is the simplest, least flexible option. Adding temporal derivative may often be helpful).
7. Model interactions (Volterra) [no] (You'll always say 'no' here)
8. Number of conditions [1]
9. Name for condition/trial 1 [Words]
10. Vector of onsets – Words [6:12:84] (or, 6, 18, 30, 42, 54, 66, 78)
11. Duration(s)(events = 0) [6] (A block of words was 42 seconds, 6 scans long)
12. Parametric modulation [none]
13. Other regressors (user specified) [0]

SPM has just saved a SPM.mat file with all of the specifications you just gave it.

Review Design (block)

After specifying a model, SPM presents various time and frequency domain graphs of the specified conditions. Graphs for the first condition are displayed after a model is specified, but you can also go to the SPM interactive window (lower−left window) and click on the menu in the upper−left of that window:

'Explore fMRI design' --> 'Session 1' --> 'Words'

The SPM Graphics window shows following plots:

- Upper left: Predictor for this event
- Upper right: Power spectrum of this event
- Lower left: Basis set used (boring, if just 'hrf' was used)
This and other information can be reviewed at any time with the 'Review Design' button. Note that the actual design matrix will not be shown until data are assigned to the model.

**Assign data (block)**

1. Click 'fMRI and select the 'data' option.
2. A file selection dialog will appear: 'Select SPM.mat'
3. Select the scans in your study
4. Remove Global effects [Scale]
   ♦ In this experiment with older data, global scaling will be used. However, the use of global scaling for fMRI data obtained using current equipment, with better stability is a highly debated topic. Current suggestions are that global scaling may not be necessary in this instance.
5. High Pass filter [Specify]
6. Cutoff period(sec) [168] *(All drifts with sinusoidal periodicity of 168 seconds or greater will be modeled.)*
7. Correct for serial correlations? [AR(1)]

After a pause, SPM has will update the SPM.mat file with the information just supplied. The delay is because SPM must compute the global estimates for each image.

**Estimate! (block)**

Start the analysis pressing the 'Estimate' button & selecting the 'SPM.mat' file.

**SPM output files (block)**

Before probing the results with SPM, let's look at the different files SPM has created.

- **SPM.mat**: This file contains information about the entire setup of the design including the conditions, basis set, actual design matrix, non-sphericity corrections, links to data, and links to various estimation images discussed below.
- **beta*.img**: GLM parameter estimates. Beta images are created for each condition in the design.
- **ResMS.img**: Residual Mean Square image; a.k.a. sigma-squared-hat.
- **mask.img**: A binary image indicating what voxels were analyzed.
- **RPV.img**: Resels–Per–Voxel image; image of roughness

Before looking at any results it's useful to look at the mean and standard deviation of the images. Although SPM doesn't write out a standard deviation image, we can make one using ImCalc.

1. Press ImCalc
2. Output filename: [ResStd]
3. Select images to work on: [Select ResMS.img]
4. Evaluated function [$\sqrt{\text{i1}}$]

We can also create an image to look at the local smoothness of the data. SPM's computes an image of local smoothness, or Resels per Voxel (RPV.img). Unfortunately, RPV values aren't very interpretable. However, it's easy to transform RPV into FWHM smoothness using this relationship:

$$\text{FWHM} = \text{RPV}^{-\frac{1}{3}}$$

Using ImCalc, create a 'FWHM.img' image, using RPV.img and the equation [i1.^(-1/3)]. (Steps below, but don't peek until you've tried this on your own).

1. Press ImCalc
2. Output filename: [FWHM]
3. Select RPV image
4. Evaluated function [i1.^(-1/3)] (*Don't forget the "." before "^".*

We don't have to create a mean image because it is one of the parameters in the GLM and was written out as a beta image.

Which beta image (1,2,....) represents the (grand) mean? ______
Now, view both the mean and standard deviation images by clicking 'Check Reg' and selecting the appropriate beta image and the ResStd image you created.

What regions have the largest standard deviation?

________________________________________________

Do regions with signal voids (e.g. in the inferior frontal cortex) have large or small variability (relatively)?

________________________________________________

If the images are too dark or bright, you can use the ‘Effects’ menu in the graphics window to brighten or darken the whole window. Or...

Extra for experts! The colormap of the SPM Graphics figure can be adjusted using facilities within Matlab. Either click on the Edit menu and choose Colormap at the bottom, or right-click at the top of the figure, and in the context menu choose Edit -> Colormap. Matlab will show a colormap editor allowing the user to change various limits.

**Define contrasts (block)**

OK. Now that we have a explored the data, and have a sense where the most variable regions are located. (If there were any horrific spatial artifacts they should have been detected in the ResStd image.)

To make inferences click 'Results' and select the 'SPM.mat' file. The contrast manager will appear. The contrast manager allows you to specify contrasts of the linear model:

- \( t \)-contrasts (consisting of a single contrast vector)
- \( F \)-contrasts (consisting of one or more contrast vectors)

Even though you can only view a single contrast at a time, it is often convenient to create all of your contrasts at once, which we will do now.

1. In the contrast manager, click on 'Define new contrast...'
2. In the 'name' box enter the name 'Words (actives)'
3. In the 'contrast' box enter 1
4. Click OK.

You will notice that after you define each element of the contrast (name and vector), SPM updates information at the bottom of the dialog. Once the contrast has been fully defined the information text turns green, which means the contrast has been defined properly.

Repeat for the other contrast

1. Click 'Define new contrast...'
2. Name = 'Words (passive)'
3. Contrast = −1
4. Click OK.
Now select the 'Words (active)' contrast and click 'Done'. SPM will ask some additional questions.

1. Mask with other contrasts: [No] *(Masking can be useful with complicated experiments with many different conditions, wherein you want to ensure that the results reflect increases rather than decreases in activity. For example, in a [1 −1] contrast, significant voxels may be seen because of increased activity for condition 1 or decreased activity for condition 2.)*
2. Title for comparison: [Press [ENTER] to accept the default text]
3. p-value adjustment to control [FDR] *(Later, you can repeat this with 'none' and 'FWE' and compare. 'FDR' is usually a good starting place.)*
4. p-value' or 'threshold' [0.05]
5. Extent threshold (voxels) [0] *(Using a number greater than zero eliminates blobs smaller than that size.)*

After you see the glass brain view, click on the 'volume' button in the "p-value" section of the interactive window.

Now try the following:

- Drag the cursor around the glass brain view.
- Try to guess where the brightest voxel is in the brain. where is (roughly) in the brain: (Circle one on each line)

Superior | Inferior | Left | Medial | Right | Anterior | Posterior

Right click; use the 'goto global maximum' option. Did you guess correctly? __________

In the tabular output, click on one of the x,y,z locations. What happens to its color? To the cursor?

____________________________________________________________________________

**Additional Results Options (for either experiment)**

Results display in SPM has a number of additional features that enhance the viewing of results. The features are listed below and users are encouraged to search for them to get experience using the interface.

- SPM shows 3 maxima for each cluster of activation. Click on the first activation xyz value in the Results table.
  - Are there additional peaks for this cluster that are not shown, and if there are how can you tell?

____________________________________________________________________________

- Are there any activations that do not have additional peaks? Write down the xyz values for 1 or 2.

____________________________________________________________________________

- How are additional activations displayed? __________
  - How can the results table be printed out as text suitable for copying?

____________________________________________________________________________

- Is there a way to save the results table in a variable?
• Display the results on a normalized brain as follows.
  ♦ Click on the Overlays pop-up menu to the right of the interactive window.
  ♦ Select a normalized brain volume on which to display the activations.
  ♦ Click on one of the activations, then right-click in the upper half of the Graphics window and choose 'goto nearest local maxima'.
  ♦ How would you get the t or F score, p-values, and cluster size of this cluster?
  ♦ If you clicked on the cluster button you got the answer but your orthogonal sections inconveniently disappeared.
  ♦ How can you simultaneously show the brain sections and the results table?

• Display the activations on a rendering of a brain.

The next experiment uses event–related data

Advanced multi–condition event–related design

One subject's data from Henson et al. (2002) Cerebral Cortex – FOR TEACHING PURPOSES ONLY (to illustrate facilities of SPM) – PLEASE DO NOT CITE WITHOUT PERMISSION

This lab assumes some familiarity with basic SPM2 operation.

Prerequisites (event–related)

1. Standard SPM installation
2. The SPM single subject event–related face repetition fMRI activation data, with all spatial preprocessing applied.

The Experiment (event–related)

• 2x2 factorial event–related fMRI.
• One session (one subject)
• (Famous vs. Nonfamous) x (1st vs 2nd presentation) of faces against baseline of chequerboard
• 2 presentations of 26 Famous and 26 Nonfamous Greyscale photographs, for 0.5s, randomly intermixed, for fame judgment task (one of two right finger key presses).
• Parameteric factor "lag" = number of faces intervening between repetition of a specific face + 1
• Minimal SOA=4.5s, with probability 2/3 (ie 1/3 null events)
• Continuous EPI (TE=40ms,TR=2s) 24 descending slices (64x64 3x3mm2), 3mm thick, 1.5mm gap

The Data (event–related)

The data have been pre–processed as follows:

• Realignment and Unwarping
• Slice–timing adjusted with reference to the slice obtained at 1/2 the TR.
• Normalized to the EPI template.
• Smoothed with an 8 mm Gaussian kernel.

Start in a new directory (event–related)

Before starting any analysis in SPM, make sure you are in an empty directory. SPM will write many, many files to the current Matlab directory, and no two analyses can share a directory, so always be careful about where you pre-process data or perform an analysis.

Make a new directory:

```bash
mkdir c:\temp\FacePriming
```

but replace '?' with number of the dataset you're using.

Change into this directory, using either the cd command in the command window, the 'Current directory...' button in the command window bar, or the SPM CD utility.

Modify Defaults (event–related)

Because the data were slice–time corrected to the middle slice, the model should also be synchronised with the middle slice (rather than the default top slice).

1. Press [DEFAULTS] in SPM main window
2. Choose 'Statistics – FMRI'
3. Upper tail F prob. threshold – Hit return to use current value.
4. Number of Bins/TR: [ 24 ]
5. Sampled bin: [ 12 ]

Specify the Model (event–related)

The model include 4 trial types

• N1 – First presentation of Nonfamous face
• N2 – Second presentation of Nonfamous face
• F1 – First presentation of Famous face
• F2 – Second presentation of Famous face

In the top directory for this analysis is the sots.mat file which contains the onset times, stored as cell arrays, for each condition.

1. Type load sots at the Matlab prompt. The onsets are stored in a cell array. If you're not sure where the file is type spm_load . This will bring up a file browser to search for the file.
2. Press fMRI
3. Specify design or data – [ design ]
5. Scans per session: [ 351 ]
6. Specify design in scans or secs: [ scans ]
7. Select basis set: [ hrf with (with time and dispersion derivatives) ]
8. Interactions among trials (Volterra) [ no ]
9. Number of conditions or trials [ 4 ]
10. Condition or trial name 1 [ N1 ]
11. Vector of onsets (N1) [ sots{1} ] (Note the curly braces)
12. Duration[s] (events=0) [ 0 ]
13. Parametric modulation [ none ]
14. Condition or trial name 1 [ N2 ]
15. Vector of onsets (N2) [ sots{2} ]
16. Duration[s] (events=0) [ 0 ]
17. Parametric modulation [ none ]
18. Condition or trial name 1 [ F1 ]
19. Vector of onsets (F1) [ sots{3} ]
20. Duration[s] (events=0) [ 0 ]
21. Parametric modulation [ none ]
22. Condition or trial name 1 [ F2 ]
23. Vector of onsets (F2) [ sots{4} ]
24. Duration[s] (events=0) [ 0 ]
25. Parametric modulation [ none ]
27. [351] regressor1 − [ spm_load ]
28. [select the movement parameters from the realignment, which are in the RealignUnwarp directory as:
    rp_SM03953_0005_0006.txt. This is a text file with 351 rows and 6 columns for the 6 affine params]
29. Name of regressor 1 − [ press 'return' ] (for default as the name doesn't matter. Also press return for the
    next 5 regressor names.)

NOTE: Adding the movement parameters to the design matrix makes the unwarping step of preprocessing
somewhat redundant, but they are added here for teaching purposes.

Review Design (event–related)

1. Press Review Design and select 'SPM.mat'. Click Done.
2. In the upper left of the SPM Interactive window is the Design Menu.
3. Click Design −&gt; Explore −&gt; Session 1 −&gt; and then click the trial–type you wish to view.

The Design has 351 rows (scans) and (4 x 3) + 6 + 1 columns (covariates). Each of the event types has 3 columns
corresponding to the hrf, the temporal derivative of the hrf, and the dispersion derivative of the hrf. Columns 13 −
18 of the design matrix correspond to the movement parameters and the last column represents the intercept or the
mean session effect.

Note: 2nd presentations necessarily later in time on average than 1st, thus the repetition effect below is
confounded with time. This was not true of the analyses reported in Henson et al (2002).

Assign Data (event–related)

1. Press fMRI
2. Specify design or data: [ data ]
3. Select 'SPM.mat' and press Done.
4. Select all 351 'swausM03952_0005_*.img' files and press Done.
5. Remove Global effects: [ none ]
6. High–Pass filter: [ specify ]
7. session cutoff period(secs): [ 128 ]
8. Model intrinsic correlations: [ AR(1) ]

After several seconds while SPM calculates the global values for each volume the Design matrix and analysis choices appear in the graphics window.

**Estimate! (event–related)**

1. Press Estimate
2. In the selection window click pwd in the upper right to return to the analysis directory.
3. Select 'SPM.mat' and press Done.

Pause while parameters estimated, watch progress in Matlab window, watch grass grow outside, go have a cup of coffee, wait for world peace, ... estimation should be done right... about... now.

**Define contrasts (event–related)**

**Main Effect of Faces minus Baseline**

- (t–contrast on canonical activations)

1. Press Results and select the SPM.mat file
2. Press 'Define new contrast'
3. Name: [ Canonical HRF: Faces > Baseline ]
4. Contrast: [ 1 0 0 1 0 0 1 0 0 1 ] (SPM automatically enters trailing zeros)
5. Click OK
6. Select the contrast you just created: 'Canonical HRF: Faces > Baseline'
7. Click Done.
8. mask with other contrast(s): [ no ]
10. p–value adjustment to control: [ FWE ] (Note that this level of control is quite stringent for initial display)
11. threshold{p value}: [ 0.05 ]
12. & extent threshold{voxels}: [ 0 ]

In Graphics window, notice bilateral temporoccipital, left motor and right frontal activations.

**Explore activations – Main effect (event–related)**

**Tables (Main effect)**

1. List all activations by clicking 'volume' button
2. Click on xyz coordinate at top of table
   1. Where does the MIP cursor move?
3. Click cluster (coordinates should be approximately [39 –72 –18] 1. How does this display differ from what is shown under volume?

**Overlays (Main effect)**

1. Click overlays and choose sections
2. Select 'wsM03953_0007.img' in Structural directory
3. Click Results–Fig at the top of the Graphics window
4. Click cluster. How the cluster data displays in the Results−Fig window. Note: Clicking the xyz coordinates is still linked to the MIP cursor and the cross−hairs on the sections.

5. Click overlays and choose render

6. Choose 'render_no_cereb.mat' in Structural directory

7. Style: [ old ]

Plots (Main effect)

1. Click 'plot'
2. Choose 'Event−related responses'
3. which trials [ N1 ]
4. Choose 'fitted response and adjusted data'
5. After looking at this graph click 'plot'
6. Choose 'Event−related responses'
7. which trials [ N1 ]
8. Choose 'fitted response and PSTH'

How do these two graphs differ? ____________________________

Is a different model being used to plot the graphs? _______

Effects of Interest (reduced model removing all confounds)

1. Click Results
2. Select 'SPM.mat' file
3. Click F−contrasts radio−button
4. Click 'Define new contrast'
5. Name: [ Effects of Real Interest ]

F−contrasts can be specified in two ways, we can specify the columns to be included in the contrast, or the columns to be removed. In this case specifying the columns to be included would be quite laborious. We would have to type:

\[
\begin{bmatrix}
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
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0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\
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0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix}
\]

Instead we can specify the columns to be removed.

1. In the small box below the main contrasts box enter [ 13:19 ]. SPM will then treat columns 13–19 as confounds, leaving 1–12.
2. Click Done.
3. mask with other contras(s): [ no ]
4. title for contrast: press return to accept the default
5. p-value adjustment to control: [ FWE ]
6. threshold{p value}: [ 0.05 ]
7. & extent threshold{voxels}: [ 0 ]
8. Click on red MIP cursor and drag near to anterior right fusiform blob. Will be approximately at [ 45 −48 −27 ]
9. Right click and select 'goto nearest local maxima'

Plots – real effects of interest

Parameter estimates (real effects of interest)

1. Click 'plot'
2. Choose 'Contrast of parameter estimates'
3. which contrast: Choose [ Effects of real interest ]
   1. columns 1,4,7,10 are canonical HRF for N1,N2,F1,F2 – note suppression effect from F1 to F2 greater than from N1 to N2
   2. columns 2,5,8,11 are temporal derivative – note fact that derivatives close to zero suggests model timing is okay
   3. columns 3,6,7,12 are dispersion derivatives

Fitted responses (real effects of interests)

1. Click 'plot'
2. Choose 'Fitted responses'
3. which contrast: Choose [ Effects of Real Interest ]
4. fitted or adjusted: [ adjusted ]
5. plot against: [ Scan or time ]

Model is plotted in red and data in blue across whole timeseries. Click on attrib -> XLim and change to [0 100] to see more clearly.

Effects of Fame (F-contrast for one-tailed test on canonical)

1. Click Results
2. Select 'SPM.mat' file
3. Click on F-contrasts
4. Press 'Define new contrast'
5. Name: [ Canonical HRF: F N ]
6. Contrast: [ −1 0 0 −1 0 0 1 0 0 1 ]
7. Click OK.
8. Select from list of contrasts: [ Canonical HRF: F vs N ]
9. Click Done.
10. mask with other contras(s): [ no ]
11. title for comparison: press return to accept default
12. p-value adjustment: [ none ]
13. threshold {F or p value}: [ 0.001 ]
14. & extent threshold{voxels}: [ 10 ]

Note left mid-temporal, temporal pole and inferior frontal regions showing activation.
Plots – Effects of Fame

Parameter estimates (Effects of Fame)

1. Click volume
2. Click on xyz coordinates at the top of the table or right-click on the Graphics window and choose 'Go to global maxima'. The red cursor on MIP should move to approximately [-63 -21 18] in the left temporal region.
3. Click 'plot'
4. Select from menu: [ Contrast of parameter estimates ]
5. which contrast: [ Effects of real interest ]

Note columns 7 and 10 (canonical HRF for F1 and F2) are positive possibly representing face naming? However, columns 1 and 4 (canonical HRF for N1 and N2) are close to zero.

Effects of Repetition (F–contrast on canonical and derivative)

1. Click Results.
2. Select 'SPM.mat' file
3. Click on F–contrasts
4. Click 'Define new contrast'
5. Name: [ Canonical + Derivatives: 1 vs 2 ]
6. Contrast:

\[
\begin{bmatrix}
1 & 0 & 0 & -1 & 0 & 0 & 1 & 0 & 0 & -1 & 0 & 0 \\
0 & 1 & 0 & 0 & -1 & 0 & 1 & 0 & 0 & -1 & 0 \\
0 & 0 & 1 & 0 & 0 & -1 & 0 & 0 & 1 & 0 & 0 & -1
\end{bmatrix}
\]

1. Click OK.
2. Select contrast: [ Canonical + Derivative: 1 vs 2 ]
3. Click Done.
4. mask with other contrast(s): [ yes ]
5. Select contrast: [ Canonical HRF: Faces > Baseline ]
6. uncorrected mask p−value: [ 0.05 ]
7. nature of mask: [ inclusive ]
8. title for comparison: press return to accept default
9. p−value adjustment: [ none ]
10. threshold \{T or p value\}: [ 0.001 ]
11. & extent threshold\{voxels\}: [ 10 ]

Note combined probability of −.0005 for the activations given orthogonal contrasts.

Plots – Effects of Repetition

Parameter estimates (Effects of Repetition)

1. Click 'Results−fig' at top of Graphics window
2. Click volume
3. Click on xyz coordinates third from top of table, which should be approximately [45 -60 -15] in the right occipitotemporal region.
4. Click plot
5. Select from menu: [ Contrast of parameter estimates ]
6. which contrast: [Canonical + Derivatives: 1 vs 2]

Note positive canonical (and temporal derivative). Given direction of contrast this indicates that 1st presentations are greater than 2nd presentations (see Henson et al (2002) for further details).

**Event−related responses (Effects of Repetition)**

1. Click plot
2. Select from menu: [Event−related responses]
3. which effect?: [F1]
4. plot in terms of...: [fitted response and PSTH]
5. Click on hold to allow plotting more than one curve on the same graph.
6. Click plot
7. Select from menu: [Event−related responses]
8. which effect?: [F2]
9. plot in terms of...: [fitted response and PSTH]

Note that the event−related responses are smaller for F2 than for F1.

Other interesting contrasts, which are left for the interested reader to attempt.

1. F−contrast on movement parameters
2. Trial−specific F−contrasts for N1 and for F1
3. Derivatives only


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<thead>
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<th>Attachment</th>
<th>Action</th>
<th>Size</th>
<th>Date</th>
<th>Who</th>
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Lab 5

Multi-Subject fMRI
Lab 5: Multi Subject fMRI

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Further Reading

Goals

After this lab you will be able to...

1. Run group analyses (or “random effects” analyses, where subjects are treated as a random variable), based on a two-stage approximation to a Mixed Effects model, both with SPM and SnPM.

2. Perform t-tests and repeated-measures Analysis of Variances (ANOVA)

3. Understand the basic problem of nonsphericity and how it is tackled in SPM2

Introduction

We start with an SPM2 group analysis of a single condition per subject (a "one-sample t-test"), where the data represent the contrast of faces versus baseline using SPM’s canonical haemodynamic response function (HRF). We then compare the results with a nonparametric equivalent in SnPM. Finally, we describe an SPM2 group analysis using
multiple conditions per subject (a "one-way ANOVA"), where each condition reflects the contrast of faces versus baseline for one of twelve peri-stimulus timebins of a Finite Impulse Response (FIR) basis set.

Data

The data come from the `implicit' condition (although the design matrices used here do not correspond exactly) of the study:

Henson, R.N.A, Shallice, T., Gorno-Tempini, M.-L. & Dolan, R.J (2002). Face repetition effects in implicit and explicit memory tests as measured by fMRI. *Cerebral Cortex*, 12, 178-186

Briefly, 104 greyscale photographs of faces were presented for 0.5s for a fame judgment (one of two right finger key presses). The minimal SOA (SOAmin) was 4.5s, with faces randomly intermixed with a further 52 null events (i.e, a 2/3 probability of a face every SOAmin). The interstimulus baseline was a stationary chequerboard.

Original images were EPI (TE=40ms, TR=2s) consisting of 24 descending slices (64x64 3x3mm2), 3mm thick, 1.5mm gap. These were spatially realigned, slice-time corrected, normalised to an EPI template and smoothed by 8mm. For further information about the pre-processing, see the single-subject example dataset: [http://www.fil.ion.ucl.ac.uk/~wpenny/datasets/face-rep/SPM2.html](http://www.fil.ion.ucl.ac.uk/~wpenny/datasets/face-rep/SPM2.html).

1. Single condition in SPM2 (one-sample t-test)

The example is also on the web: [http://www.fil.ion.ucl.ac.uk/spm/data/multi_sub.html](http://www.fil.ion.ucl.ac.uk/spm/data/multi_sub.html)

The data come from 12 subjects. They were analysed in a single, large “fixed effects” model (so-called because subjects are treated as a fixed variable in this model). There was only one session per subject, so in fact the 12 subjects were treated as 12 fMRI sessions. For a picture of the design matrix, see Figure 1. Six event-types per session were modelled using only a canonical HRF, though the responses to the different event-types, versus baseline, were averaged by a T-contrast (also shown, for the first subject, in Figure 1).

This model is also called the “first-level” model, as distinct from the “second-level”, or “random effects” model that we will be creating below (which treats subjects as a random variable). Together, these two levels implement a “mixed effects” model, that properly accommodates within- and between-subject variability (provided certain assumptions are met; see Further Reading for more details). The first-level model can be viewed as “summarising” the data for each subject, and it is these summaries that are tested across
subjects (in order to extrapolate from the sample to the population of subjects). This is why this approach is also called a “summary statistic” approach.

Within the first-level model, one T-contrast was evaluated per subject, producing 12 “contrast images” or “con*.img” (con_0006.img to con_0017.img, where the number simply refers to the order of the contrasts in the Contrast Manager). These images are stored in the “CanHRF” sub-directory. (Note that, for the purposes of this analysis, these contrast images could equally well have been produced from 12 separate models for each subject).

Thus the value of each voxel in one of the contrast image reflects the parameter estimate for the canonical HRF, averaged across different face-types, versus interstimulus baseline (a chequerboard).

Press “Check Reg” and select all 12 con*.imgs.

Notice the different intensities reflecting between-subject variability.

**Creation of Design Matrix (and assignment of data)**

Type SPM at the matlab prompt

Now change to a new directory, eg “SPM_Ttest” (this is easy to forget !)

Select either 'PET and SPECT' or 'fMRI time-series'

Press the 'Basic models' button

Select design type ..... [One sample t-test]

Then select the 12 images in the CanHRF directory (con_0006.img to con_0017.img)

GMsca: grand mean scaling [None]

Explicitly mask images [No]

Global calculation [omit]

SPM will then show you the design matrix (simply a single column of 1's which will appear as a white box on a white background).

This is a “second-level” model, since the data are no longer fMRI data (EPI volumes), but some “summary measure” of those data (e.g, the mean response per condition), with the “summarising” done by the first-level model.
**Estimation of the (single) Parameter**

Now press the Estimate button, and select the new “SPM.mat” file that has been created in the current directory (press “pwd” to move the input window to the current directory).

SPM will now estimate the (single) parameter

1. What is this parameter?

The parameter reflects the size of the population effect at each voxel - simply the average of the con*.img's.

**Viewing Results**

Now press the 'Results' button.

Select the SPM.mat file.

In the contrast manager press 'Define new contrast'.

Enter a [1] contrast weight, and name it 'activation'.

2. How would one test for deactivations?

Deactivations can be tested with a [-1] contrast (OR equivalently by a [1] contrast, if the original first-level contrast images were [-1 -1 -1 -1] rather than [1 1 1 1]).

Press the '..submit' button

Press OK

Now press the 'Done' button

Mask with other contrast(s) [No]

Title for comparison [activation]

P-value to control? [FWE]

This stands for “Family-wise error” and uses Random Field Theory (RFT) to correct for multiple comparisons (though see below). The other options are “FDR”, which stands for False Discovery Rate, and “none”, which corresponds to an uncorrected threshold.
Corrected p value [0.05]

& Extent threshold {voxels} [0]

SPM will now display the thresholded t-statistic image. These show the voxels that are significantly active in the population from which the subjects were drawn, correcting for multiple comparisons.

Note that the corrected height threshold used by SPM is $T=9.07$.

(Actually, this SPM threshold is from a Bonferroni correction, rather than from RFT, which is 10.43, since RFT can be too conservative for low df's, so SPM2 takes the minimum of Bonferroni and RFT corrections.)

Press volume

Move the cursor to the global maximum (42 -48 -30)

Press plot

Select [Fitted Responses]

Which contrast [activation]

Predicted or adjusted [adjusted]
(though both give the same answer here)

Plot against? [scan or time]

---

3. What do the twelve points and line represent?

The points are the 12 scans, which here represent 12 subjects; the line indicates the mean effect (at this voxel). All subjects show a positive effect. The units of the y-axis are arbitrary (since it is a function of the contrast weights and the scaling of the regressors for the canonical HRF in the first-level model).

**Going Further**

The "glass brain" MIP viewer is a somewhat crude way to visualize your results. While conveniently summarizing your 3D results in a fixed 2D picture, there is much more to your data.
As in Lab 1, use ImCalc to create a ResStd image (i.e, select the ResMS.img, and enter the output image name ResStd, and the equation sqrt(i1) ).

Use Check Reg to view four images simultaneously

1. OneSubT1 ... For anatomical reference
2. spmT_0002 ... The statistic image of your [1] contrast above
3. con_0002 ... The contrast image for your [1] contrast above (population mean at each voxel)
4. ResStd ... The standard deviation image (as above)

Now explore the statistic image with the cursor

4. Is there a lot of structure in the standard deviation image? Can you see anatomical features?

5. Can you see any correspondences between regions of significance in the t image and structure in the standard deviation image?

6. Go to a region of large positive change (eg a mid-fusiform white blob). Is this due to a large effect size (in the contrast) or a relative dip in the standard deviation ?

Top of the Document

2. Group analysis of a single condition in SnPM

Now we perform a non-parametric version of the same basic group analysis.

In matlab type 'snpm'

Now change to a new directory, e.g, “SNPM_Ttest” (easy to forget !)

SnPM is split up into three components (1) Setup, (2) Compute and (3) Results.
Setup

First press the 'Setup' button. Then type in the following options:

[Multisub: 1 condition, 1 scan per subject]
Select all scans [con_0006.img -> con_0017.img]
Number of confounding covariates [0]
4096 Perms. Use approx test? [No]
(typically, with fewer than 5000 Perms your computer should be quick enough to use an exact test - ie. to go through all permutations)
FWHM(mm) for Variance smooth [0]
See below (and [http://www.fil.ion.ucl.ac.uk/spm/snpm/](http://www.fil.ion.ucl.ac.uk/spm/snpm/)) for more info on the above option.
Collect Supra-Threshold stats [Yes]
Collecting suprathreshold statistics is optional because the file created is huge; it is essentially the "mountain tops" of the statistic image of every permutation. Say "No" if you want to save disk space and time.
Select Global Normalisation [No Global Normalization]
Select global calculation [Mean]
The above option doesn't matter because no normalisation will be done (this is specified in the next step)
Threshold masking [None]
Note, there's no need to use threshold masking since the data are already implicitly masked with NaN's.
Grand Mean Scaling [No Grand Mean Scaling]
SnPM will now create the file SnPMcfg.mat.

Compute

Now press the 'Compute' button and select the above file (SnPMcfg.mat)
The above computation should take between 5 and 10 minutes depending on your computer.

**Results**

Finally press the 'Results' button and select the SnPM.mat file

- Positive or negative effects [+ve]
- Write out statistic img? [yes]
- Write filtered statistic img ? [yes]
- Filename ? [SnPMt_filtered]
- Write full SS adj p-value img ? [yes]
- Corrected p-value for filtering [0.05]
- Assess spatial extent [no]

SnPM will then show the distribution of the maximum t-statistic. If you then press RETURN in the matlab command window, SnPM will then plot a MIP of those voxels surviving the SnPM critical threshold (this value is displayed at the bottom of the image and for this data set should be 7.92).

Note that the SnPM threshold is lower than the SPM threshold (9.07). Consequently, SnPM shows more active voxels.

Note also that you could use this value as the threshold in the previous SPM analysis (pressing Results, saying 'No' to corrected height threshold, and typing in 7.92) and hence take advantage of SPM’s rendering routines (not available in SnPM).

---

**3 Multiple conditions in SPM2 (ANOVA)**

For this example, 12 contrast images per subject are used (i.e, 144 images in total). Each contrast image reflects one timebin of a Finite Impulse Response (FIR) basis set (for further information, see [http://www.fil.ion.ucl.ac.uk/spm/doc/papers/rnah_choice.pdf](http://www.fil.ion.ucl.ac.uk/spm/doc/papers/rnah_choice.pdf)). In other words, the 12 images capture the average signal every 2s from 0-24s poststimulus for faces versus baseline. These contrasts derived from a separate design matrix for each subject. For a picture of one subject’s design matrix, see [Figure 2](#). (Note that only two-event-types were defined in these first-level re-analyses, which are again collapsed here via a contrast for each timebin).
The contrast images are in the “FIR” sub-directory and have been renamed (for ease of selection):

- con_fir_bin01_sub01.img  (FIR bin 1, subject 1)
- con_fir_bin01_sub02.img  (FIR bin 1, subject 2)
  ...
- con_fir_bin02_sub01.img  (FIR bin 2, subject 1)
  ...

These images comprise the data for a "one-way ANOVA" in SPM2.

These data are also available and further discussed at ftp://ftp.fil.ion.ucl.ac.uk/spm/data/rfx-multiple/rfx-multiple.htm

**Creation of Design Matrix (and assignment of data)**

Type SPM at the matlab prompt

Now change to a new directory, e.g, “SPM_ANOVA” (easy to forget !)

Press the 'Basic models' button

Select design type ..... [One way ANOVA]

#group's ... enter [12]

  group 1: filter to "*bin01*.img" and select "all"
  group 2: filter to "*bin02*.img" and select "all"
  etc

GMsca: grand mean scaling [No]

Threshold masking [none]

explicitly mask images [No]

Global calculation [omit]

non-sphericity correction [yes]

replications are over?... [repl(12)]

correlated repeated measures [yes]

(We will explain the last three questions about nonsphericity in more detail below).

SPM will show you the design matrix, which

Now press the Estimate button, and select the new “SPM.mat” file that has been created in the current directory.
**F-contrast and Results**

After estimation, test the "effects of interest" F-contrast:

In the contrast manager press 'Define new contrast'
(select F)

Enter ["eye(12)"] as the contrast weights...
(which in matlab evaluates to a 12x12 identity matrix)
...and "FIR" as the name

7. What is this contrast testing ?

In general terms, this contrast will reveal voxels that show ANY form (shape) of event-related response (within the range 0-24s poststimulus, and with 2s "resolution"). More precisely, it is testing whether the 12 means (i.e, parameter estimates, one per timebin) explain an appreciable amount of the total variance in the data.

Press the '...submit' button

Press OK

Now press the 'Done' button

Mask with other contrast(s) [No]

Title for comparison [FIR]

Corrected height threshold [Yes]

Corrected p value [0.05]

& Extent threshold {voxels} [0]

This will produce a MIP, as usual, showing bilateral ventral temporal and left motor cortex (given the right hand responses).

Press "Volume" to get a table of statistics

The maximum in the resulting SPM{F}is:

42 -57 -24F = 25.3, Z = Inf (beyond SPM's range)

Select this, or any of most of the other voxels, and

Press plot
Select [Contrast of Parameter Estimates]

Which contrast [FIR]

This should reveal a fairly typical BOLD impulse response shape over the 12 timebins (e.g, peaking at FIR timebin 3, ie 4-6 seconds).

**Nonsphericity - theory**

Classical parametric statistics assume that the errors are “i.i.d”, that is "independent and identically distributed" (and furthermore, that the identical distributions are Gaussian). Errors that were i.i.d. would be "spherical". In SPM, "nonsphericity" thus refers to situations where the error is non-identically distributed and/or non-independent (for precise definition, see [http://www.fil.ion.ucl.ac.uk/spm/doc/books/hbf2/pdfs/Ch9.pdf](http://www.fil.ion.ucl.ac.uk/spm/doc/books/hbf2/pdfs/Ch9.pdf) and [http://www.fil.ion.ucl.ac.uk/~wpenny/publications/rik_anova.pdf](http://www.fil.ion.ucl.ac.uk/~wpenny/publications/rik_anova.pdf)). Let's consider non-identical distribution first.

The parameter estimates for the FIR timebins are likely to differ in their variability over subjects. The first timebin (0-2s), for example, is likely to be close to zero for all subjects (since the BOLD response to event onset has not had time to develop), whereas the third timebin (4-6s) is likely to include the peak of the haemodynamic response, which may vary considerably over subjects. This is called "inhomogeniety of variance”.

The parameter estimates for the timebins are also likely to be correlated across subjects (since they are "repeated measures"). The fact that the functions themselves are orthogonal is irrelevant here: the correlation in the parameter estimates is simply because, if the parameter estimate for one timebin is large in one subject, the parameter estimates for other timebins are also likely to be large (i.e, that subject has a large event-related response). These correlations induce nonzero covariances in the error. Classical corrections to this problem include variants of the Satherthwaite approximation, such as Greenhouse-Geisser and Huyn-Feldt corrections for the df's in repeated-measures ANOVAs.

**Nonsphericity - mechanics**

Imagine a 12x12 matrix in which each cell reflects the (co)variance, across subjects, between one timebin and another. This is called a covariance matrix, in which the leading diagonal reflects the variance of each timebin. Inhomogeneity of variance thus reflects unequal values along the leading diagonal. Repeated measures induce non-zero values in off-diagonal cells (note that covariance matrices are symmetrical about the leading diagonal).

8. Why was there no nonsphericity issue for the one-sample t-test above?
Note that for one-sample t-test above, the "covariance matrix" only consists of one cell, so there can be no nonsphericity.

More precisely, what is important is the covariance of the true underlying errors (rather than the data themselves). But we cannot estimate the error covariance independently of estimating the parameters of the model. We need to estimate both simultaneously, and this is where an iterative scheme like Restricted Maximum Likelihood (ReML) is needed (for more information on this algorithm, see http://www.fil.ion.ucl.ac.uk/spm/doc/books/hbf2/pdfs/Ch9.pdf and references therein).

The user needs to specify the type of nonsphericity they want to estimate. This is done in the form of a set of matrices, or “variance components”. These matrices actually have as many rows and columns as there are data points (144x144 in this case).

So, when the user answers “yes” to the question “nonsphericity correction?” above, 12 basis matrices (one per timebin) are generated to model inhomogeniety of variance. To see what one of these looks like, type in matlab:

```matlab
figure,imagesc(SPM.xVi.Vi{2}),colormap('gray'),colorbar
```

This is the one that will be used to estimate the error variance of the second timebin.

Note that the "repl(12)" answer to the "replications are over?" question tells SPM2 that the replications come from the (implicit) factor of "replications", which in this case we know corresponds to subjects, with the other factor "group" corresponding to the repeated measure, namely the FIR timebins. (SPM does not know which factor "rotates fastest" with respect to the order of the data: in our case, subjects rotate fastest in the sense that we first entered all 12 subjects for FIR bin number 1, then all 12 subjects for FIR bin number 2, etc; as above).

When the user answers “yes” to the question “are these correlated measures?” , a further 12*11/2 = 66 matrices are added to model the covariance terms (off-diagonal elements). To see what one of these looks like, type in matlab:

```matlab
figure,imagesc(SPM.xVi.Vi{13}),colormap('gray'),colorbar
```

This is the one that will be used to estimate the covariance of errors between the first and second timebins.

It is the relative weighting, or "hyper-parameters", for each of these 78 variance components that are estimated by ReML. Note that these are, in fact, “global” values that are estimated by "pooling" over all "active" voxels (those that survive an implicit “effects of interest” F-test estimated during an initial pass through the data assuming sphericity). This pooling assumes that the correlation structure of the nonsphericity is invariant across those "active" voxels. If this assumption is true, such pooling allows a much more precise estimation of nonsphericity than would be possible if we only had one voxel. Moreover,
it means that ReML only needs to iterate once, rather than iterating for each voxel separately, which would be computationally demanding. For further information, see http://www.fil.ion.ucl.ac.uk/spm/doc/books/hbf2/pdfs/Ch9.pdf.

Having estimated these "global" hyper-parameters via pooling, the final estimated error covariance derives from scaling the nonsphericity by a voxel-specific value to allow for some differences across voxels in the amount of error.

**Nonsphericity - viewing**

To see the covariance matrix of the data from the subset of voxels that are pooled, type:

```
figure,imagesc(SPM.xVi.Cy),colormap('gray'),colorbar
```

9. Why are there large positive values around the third timebin? Why are there negative values between the third timebin and fifth/sixth timebins?

You can notice: 1) the high variance around timebin 3 (rows 25-36), which corresponds to the peak of the BOLD impulse response, and so is where one would also expect the greatest variability across subjects, 2) the negative co-variances between timebins 3 and 5-7, which reflects the fact that, if the peak response (at timebin 3) is large and positive, then the subsequent BOLD undershoot is likely to be large and negative.

The estimates of the hyper-parameters are stored in SPM.xVi.h. To see the estimated nonsphericity, type

```
figure,imagesc(SPM.xVi.V),colormap('gray'),colorbar
```

You can see that this has captured the qualitative pattern of the error covariance that one would expect given the data covariance above (the error covariance is not the same as the data covariance, but here the simple ANOVA model just removes the mean for each timebin, so the data and error covariances look similar).

**Pre-Whitening**

Note how the design matrix changes after estimation. This is because it has been "pre-whitened" by the inverse of the estimated nonsphericity. Note also that because both the data and design matrix have been pre-whitened our interpretation of the parameter estimates (the 'betas') is unchanged. In other terminology, the parameters have been estimated using 'Weighted Least Squares (WLS)', where the weights relate to the estimated error covariance structure. SPM2 implements WLS by pre-whitening the data and the design matrix and then using 'Ordinary Least Squares' (OLS).
**T-contrast: assuming a response shape**

Returning to the results, one can also test for more constrained shapes of event-related responses within this ANOVA/FIR model. For example, one can test for "typical-shaped" responses by evaluating a contrast whose weights trace out SPM's "canonical HRF" (when binned every 2s).

To do this, switch to the Matlab window for a moment and type:

```matlab
xBF.dt = 1;
xBF.name = 'hrf (with time and dispersion derivative)';
xBF.length = 32;
xBF.order = 1;
xBF = spm_get_bf(xBF);
```

This returns the canonical and two partial derivatives in the matrix "xBF.bf" (type "help spm_get_bf" for more info). For convenience, then define:

```matlab
can = xBF.bf(2:2:24,1)';
```

This variable represents SPM's canonical HRF, downsampled every 2 seconds at 1, 3, 5 ... 23 seconds poststimulus (i.e, the mid-point of each FIR timebin).

In the contrast manager press 'Define new contrast' (select T)

Enter ["can"] as the contrast weights... ...and "Canonical-weighted FIR" as the name.

Press the '..submit' button

Press OK

Now press the 'Done' button

Mask with other contrast(s) [No]

Title for comparison [Canonical-weighted FIR]

Corrected height threshold [Yes]

Corrected p value [0.05]

& Extent threshold {voxels} [0]

Note how there are now more suprathreshold voxels and higher Z-values than in the above F-contrast: this is because most impulse responses in these data match SPM's canonical HRF, and so the more constrained T-test is more sensitive.
Note also that there are more suprathreshold voxels and higher Z-values for this canonical-weighted FIR model than in the earlier one-sample t-test on contrast images, even though those images reflected the fits of the same canonical HRF in the first-level model (above).

9. Why are the statistics “better” for the “canonical HRF” in this ANOVA model than in the previous one-sample t-test?

The main reason for the “better” statistics is the increased statistical power afforded by the extra degrees of freedom (df’s) in the ANOVA model, which allows better estimation of the underlying error (co)variance (though it is possible that, if the FIR parameters were estimated very inefficiently, the extra data might add more noise, outweighing any advantage of higher degrees of freedom). Another reason is that the higher df’s mean that RFT correction for multiple comparison is less conservative (see earlier). But remember that this increased power comes with a strong assumption about the nonsphericity, namely that it has the same structure across (activated) voxels; the "pooling assumption" (see nonsphericity section above).

**F-contrast: testing SPM's canonical HRF derivatives**

In the Matlab window, you can also define:

```matlab
tem = xBF.bf(2:2:24,2)';
dis = xBF.bf(2:2:24,3)';
all = [can; tem; dis];
```

The second variable ("tem") is SPM's "temporal derivative" (first-order partial derivative of the canonical HRF with respect to onset latency); the third variable ("dis") is SPM's "dispersion derivative" (first-order partial derivative of the canonical HRF with respect to dispersion of the gamma function representing the peak). The fourth variable is just a matrix with the above three functions combined (which could be used as an F-contrast).

You can create new F-contrasts for any of these three variables ("tem", "dis" or "all") to see how much variability is captured by the derivatives of SPM's canonical HRF. For example, you will see that some fusiform regions (e.g., 27 -69 -15) show reliable effects of the temporal derivative, and if you plot the "effects of interest" contrast, you will see that this is because the true BOLD impulse response peaks slightly earlier than the canonical HRF.

**F-contrast: testing sufficiency of SPM's canonical HRF**

One can also ask how much event-related variance is NOT captured by SPM's canonical HRF. To do this, first create the variable in Matlab:
nullcan = eye(12) - pinv(can)*can;

This creates a matrix for an F-contrast that spans the "null space" of the canonical HRF.

In the contrast manager press 'Define new contrast'
(select F)

Enter ["nullcan"] as the contrast weights ...
... and "Null space of canonical HRF" as the name

(and then complete the remaining questions about contrast estimation as before).

When looking at a corrected threshold, you will see that several regions express variability not captured by the canonical HRF. This is not surprising, since you will notice that most of these regions appeared above in the individual F-tests on the temporal and dispersion derivatives (e.g., 28 -78 -9, which shows an earlier peak than the canonical HRF). Other regions (e.g., 36 -78 18) appear to show a larger undershoot than the canonical HRF.

So even more interesting is the ability to ask how much event-related variance is NOT captured by the canonical HRF or its two derivatives. To do this, first create the variable in Matlab:

nullall = eye(12) - pinv(all)*all;

This creates a matrix for an F-contrast that spans the "null space" of all three basis functions.

In the contrast manager press 'Define new contrast'
(select F)

Enter ["nullall"] as the contrast weights ...
... and "Null space of canonical and derivatives" as the name

You will see that only 2 voxels (in one cluster with maximum -21 -18 27) express variability not captured by the informed basis set. This reinforces the point that, while there is certainly variability in the HRF across different brain regions, the canonical HRF and its two derivatives are probably sufficient to capture the majority of this regional variability (at least on average across the 12 subjects in this dataset). See http://www.fil.ion.ucl.ac.uk/spm/doc/papers/rnah_choice.pdf for further details.

**Further Reading**

For theoretical background see eg.
http://www.fil.ion.ucl.ac.uk/spm/doc/papers/aph_rfx.pdf (original HBM abstract on the
summary statistic approach),
http://www.fil.ion.ucl.ac.uk/spm/doc/books/hbf2/pdfs/Ch12.pdf (a book chapter on Random Effects Analysis)
http://www.fil.ion.ucl.ac.uk/~wpenny/publications/rik_anova.pdf (notes on ANOVAs and SPM).

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Figure 2

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Lab A

Dynamic Causal Modeling
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Dynamic Causal Modeling

Goals of this Lab

After this lab you will...

1. Understand the types of questions that can be answered using DCM.
2. Be able to extract time series data for use in DCMs.
3. Understand how to specify and estimate the parameters of a DCM
4. Be able to perform statistical tests on DCM parameters.
5. Be able to use Bayesian Model Comparisons to select the optimal model

Prerequisites

- A standard SPM installation
- The attention to motion fMRI dataset (see below)

Background on the data (Attention to Visual Motion)

This dataset was collected by Christian Buchel and is described in the paper. Buchel, C and K. Friston (1997). Modulation of Connectivity in Visual Pathways by Attention: Cortical Interactions Evaluated with Structural Equation Modelling and fMRI, Cerebral Cortex, December, 7, pp 768–778.

This data has been pre−processed using SPM99. This analysis is in SPM2. Therefore ensure ‘defaults.analyze.flip’ is set to 1 in the spm_defaults.m file, before proceeding further. See http://www.fil.ion.ucl.ac.uk/spm/spm2.html#Compat for more details.

The experiment was performed on a 2 Tesla Siemens VISION scanner. Contiguous multislice T2*−weighted fMRI images were obtained with a TR of 3.22 s. The original data had 32− 3 mm slices covering 9.6 cm of the cortex and extending to the upper cerebellum. Subjects were scanned during four runs, each lasting 5 min 22 s. One hundred image volumes were acquired in each run. The first 10 volumes of each run were discarded to allow stabilization of the BOLD signal. Each condition lasted 10 scans or 32.2 seconds. For more on the dataset, see http://www.fil.ion.ucl.ac.uk/spm/data/#epoch.

Experimental paradigm

There were four condition. The onsets are defined in a file called conditions.mat

- F (Fixation): Corresponds to a low level baseline where subjects viewed a fixation point at the centre of a screen
- A (Attention): Subjects viewed 250 dots moving radially and were asked to detect changes in radial velocity
- N (No attention): Subjects were asked simply to view the moving dots
- S (Stationary): Subjects viewed stationary dots

In the current analysis these have been grouped into 3 conditions called

- att(ention) Same as above
mot(in) Motion with or without attention
pho(tic) Any visual stimulation

We will use these 3 factors for this lab.

**GLM–DCM Analysis**

**Specify Design**

In the steps below, responses to questions are in brackets.

1. Start SPM *(spm fmri)*
2. At the Matlab prompt type `load factors`. This file contains the onsets of each epoch.
3. At the Matlab prompt type `who` to look at the variables just loaded. You should see variables called 'att', 'mot', and 'phot'.
4. Click the fMRI button.
5. Specify [design]
6. TR(secs) [3.22]
7. Scans per session [360]
8. Specify design in [scans]
9. Select basis set [hrf]
10. Model interactions (Volterra) [No]
11. Number of conditions [3]
12. Name for condition 1 [Photic]
13. Vector of onsets – Photic [phot]
14. Duration(s) (events=0) [10]
15. Parametric modulation [None]
16. Name for condition 2 [Motion]
17. Vector of onsets – Motion [mot]
18. Duration(s) (events=0) [10]
19. Parametric modulation [None]
20. Name for condition 3 [Attention]
21. Vector of onsets – Attention [att]
22. Duration(s) (events=0) [10]
23. Parametric modulation [None]
24. User specified [0]

SPM now creates an SPM.mat file in your working directory

**Assign Data to Design**

1. Click fMRI
2. Specify design or data [data]
3. Select the SPM.mat file you've just created
4. Select 'All' the scans from the 'functional' directory
5. Remove global effects [none]
6. High–pass filter [specify]
7. Cut–off period(secs) [128]
8. Correct for serial correlations [AR(1)]
SPM will now update your SPM.mat file.

Estimate the model by pressing the 'ESTIMATE' button. Then select the SPM.mat file that's just been updated.

SPM will now compute the hyperparameters and parameters and update the SPM.mat file once again.

View Results

*NOTE*− In the SPMs 'LEFT−IS−RIGHT' (see earlier comment on spm_defaults.m)

Press 'RESULTS'

1. Select the SPM.mat file
2. Choose one of the F−contrasts, e.g., the Motion condition
3. Mask with other contrasts [No]
4. Title for comparison []
5. p value adjustment to control [FWE]
6. p value [0.05]

You should see multiple activations in visual cortex.

By selecting overlays→sections, and selecting the normalised structural image you should be able to identify the anatomy more accurately.

Selecting VOIs

V1 VOI

1. Go to voxel 0,−93,−3. This can be entered in the edit boxes at the bottom of the SPM interactive window.
2. Press VOI
3. Name of region [V1]
4. Adjust data for [effects of interest]
5. VOI definition [sphere]
6. VOI radius(mm) [6]

This saves the data info in VOI_V1_1.mat in the working directory

V5 VOI

1. Go to −39,−81,3
2. Press VOI
3. Name of region [V5]
4. Adjust data for [effects of interest]
5. VOI definition [sphere]
6. VOI radius(mm) [6]

This saves the data in VOI_V5_1.mat in the working directory

At this point you can use corr_look.m to plot the V1 and V5 time series and see how their correlation changes during attention vs. non−attention blocks. Type `corr_look` at the Matlab prompt.
PPC VOI

1. Press Results and this time select the Attention F−contrast
2. Go to −24,−72,54
3. Press VOI
4. Name of region [PPC]
5. Adjust data for [effects of interest]
6. VOI definition [sphere]
7. VOI radius(mm) [6]

This saves the data in VOI_PPC_1.mat in the working directory

PFC VOI

1. Go to −51,33,24
2. Press VOI
3. Name of region [PFC]
4. Adjust data for [effects of interest]
5. VOI definition [sphere]
6. VOI radius(mm) [6]

This saves the data in VOI_PFC_1.mat in the working directory

How would you adjust if you had entered the realignment parameters as user defined regressors?

At this point you can proceed with the DCM analysis.

**DCM Analysis I**

**Specify DCM I**

These steps will set up the DCM analysis described in Friston et al. (2003) Dynamic Causal Modelling, Neuroimage, 19(4), pages 1273–1302.

1. Press DCM
2. Specify or review [specify]
3. Select the SPM.mat file you created above
4. Name for DCM_???.mat [VisFroPar1]
5. Select all VOIs in order VOI_V1_1, VOI_V5_1, VOI_PPC_1, VOI_PFC_1.
6. Include Photic [Yes]
7. Include Motion [Yes]
8. Include Attention [Yes]
9. Make the following intrinsic connections. Connections go from the columns to the rows.
   A. V1 to V5 (first column to second row)
   B. V5 to V1 (second column to first row)
   C. V5 to PPC (second column to third row)
   D. PPC to V5 (third column to second row)
   E. PPC to PFC (third column to fourth row)
   F. PFC to PPC (fourth column to third row)
10. Make the following Driving and Modulatory connections
A. Connect Photic only to V2  
B. Connect Motion to modulate the bottom-up connection from V1 to V5  
C. Connect Attention to modulate the top-down connections from PPC to V5  
D. Connect Attention to modulate the connection PFC to PPC.

11. Estimate the model by pressing DCM 
12. Select estimate 
13. Choose the DCM_VisFroPar1.mat file

SPM will now estimate the model. Go have a cup of coffee.

Review DCM I

1. Press DCM  
2. Specify or review [review]  
3. Select DCM_VisFroPar.mat  
4. Threshold [0]  
5. You can then eg. display -> Effects of [Photic],[Motion],[Attention] etc.

The numerical results will be slightly different from those in the paper (as this is a different subject) but you should still see that motion modulates the bottom-up connection between V1 and V5, and attention modulates the top-down connections between PPC and V5, and PFC and PPC.

To further explore the model, you can also display Intrinsic connections, contrast of connections, locations, inputs, outputs, neuronal and hemodynamic kernels

DCM Analysis II

Specify DCM II

Set up alternative model, where attention modulates the bottom-up and top-down connections

1. Press DCM  
2. Specify or review [specify]  
3. Select the SPM.mat file you created in README_GLM  
4. Name for DCM_???.mat [VisFroPar2]  
5. Select all VOIs in order VOI_V1_1, VOI_V5_1, VOI_PPC_1, VOI_PFC_1  
6. Include Photic [Yes]  
7. Include Motion [Yes]  
8. Include Attention [Yes]  
9. Make the following intrinsic connections  
   A. V1 to V5  
   B. V5 to V1  
   C. V5 to PPC  
   D. PPC to V5  
   E. PPC to PFC  
   F. PFC to PPC  
10. Make the following Driving and Modulatory connections  
   A. Connect Photic only to V2  
   B. Connect Motion to modulate the bottom-up connection from V1 to V5  
   C. Connect Attention to modulate the bottom-up connection from V5 to PPC
D. Connect Attention to modulate the top-down connection from PPC to V5

11. Estimate DCM II
12. Review DCM II

**DCM Model Comparison**

1. Press DCM
2. Specify, review, compare etc. [compare]
3. Number of DCM models to compare [2]
4. Select DCM_VisFroPar1.mat and DCM_VisFroPar2.mat
5. You can see posterior probabilities of models from AIC or BIC

Which model provides a better fit to the data?

What if you had several models with different data instead of different connections? Could these models be compared using DCM Model Comparison?


This Lab based on the DCM dataset put together by: Will Penny, Lee Harrison and Klaas Stephan, September 2003

--- DarrenGitelman – 22 Mar 2005
Lab B

Nonparamametric Group Modeling with SnPM
In this section, we analyze a multi-subject event-related fMRI data with the SnPM software. The aim of this example is:

i. Give another example to demonstrate the steps of an SnPM analysis by analyzing the fMRI data.

The same set of data have also been analyzed by SPM. The details can be found at SPM website ("Multi-subject event-related fMRI – Repetition priming" data set).


We will give two standard methods to analyze the data by using nonparametric methods:

i. **Without smoothed variance t**

ii. **With Smoothed variance t**

### The Example Data

This data is from a study on face repetition effects in implicit and explicit memory tests (Henson et al. 2002; see above).

In this study, twelve volunteers (six male; aged 22–42 years, median 29 years) participated in the experiment. Faces of famous and nonfamous people were presented to the subjects for 500 ms, and replaced by a baseline of an oval chequerboard throughout the interstimulus interval. Each subject was scanned during the experiment and his or her fMRI images were obtained.

Each subject's data was analyzed, creating a difference image between faces and chequerboard (baseline) watchings. So each image here is the contrast image for each subject.

Under the null hypothesis we can permute the labels of the effects of interest. One way of implementing this with contrast images is to randomly change the sign of each subject's contrast. This
sign-flipping approach can be justified by a symmetric distribution for each voxel's data under the null hypothesis. While symmetry may sound like a strong assumption, it is weaker than Normality, and can be justified by a subtraction of two sample means with the same (arbitrary) distribution.

Hence the null hypothesis here is:

H₀: The symmetric distribution of (the voxel values of the) subjects' contrast images have zero mean.

---

**Exchangeability of Second Level fMRI Data**

fMRI data presents a special challenge for nonparametric methods. Because fMRI data exhibits temporal autocorrelation, an assumption of exchangeability of scans within subject is not tenable. However, to analyze a group of subjects for population inference, we need to only assume exchangeability of subjects. The conventional assumption of independent subjects implies exchangeability, and hence a single exchangeability block (EB) consisting of all subjects.

(On a technical note, the assumption of exchangeability can actually be relaxed for the one-sample case considered here. A sufficient assumption for the contrast data to have a symmetric distribution, is for each subject's contrast data to have a symmetric but possibly different distribution. Such differences between subjects violates exchangeability of all the data; however, since the null distribution of the statistic of interest is invariant with respect to sign-flipping, the test is valid.)

---

**Nonparametric Analysis**

**(Without smoothed variance t)**

You can implement a nonparametric random effects analysis using the SnPM software which you can download from [http://www.fil.ion.ucl.ac.uk/spm/snpm/](http://www.fil.ion.ucl.ac.uk/spm/snpm/).

First follow the instructions on the above web page to download and install SnPM (don't forget the patches!).

Then, in matlab (in a new directory!) type

```
  snpm
```

SnPM is split up into three components (1) Setup, (2) Compute and (3) Results.
First click on 

Setup

Then type in the following options (your responses are in square brackets).

Select design type [Multisub: 1 condition, 1 scan per subject]

Select all scan files from the corresponding directory in a window as below [con_0006.img -> con_0017.img]

Number of confounding covariates [0]

4096 Perms. Use approx test? [No]

(typically, with fewer than 5000 Perms your computer should be quick enough to use an exact test – ie. to go through all permutations)

FWHM(mm) for Variance smooth [0]

See below (and http://www.fil.ion.ucl.ac.uk/spm/snpm/) for more info on the above option.

Collect Supra-Threshold stats [Yes]

Collecting suprathreshold statistics is optional because the file created is huge; it is essentially the "mountain tops" of the statistic image of every permutation is saved. Say "No" if you want to save disk space and time.

Select Global Normalisation [No Global Normalization]
Select global calculation [Mean]

The above option doesn't matter because no normalisation will be done (this is specified in the next step)

Threshold masking [None]

Note, there's no need to use threshold masking since the data are already implicitly masked with NaN's.

Grand Mean Scaling [No Grand Mean Scaling]

Finally, the Setup Menu is as below:

```
MultiSub: 1 conditions, 1 scan per subject
# of confounding covariates        0
4096 Perms. Use approx. test?      no
FWHM(mm) for Variance              0
Collect Supra-Threshold stats?     yes
<no global normalisation>
mean voxel value (within per image full mean/8 mask)
Threshold masking                  none
<no grand Mean scaling>
```

SnPM will now create the file SnPMcfg.mat. and show the Design Matrix in the Graphics window.

Now click on

Compute

Select the file (SnPMcfg.mat) as below

```
Select SnPMcfg.mat CfgFile...
```

```
... 1:SnPMcfg.mat
```
The computation should take between 5 and 10 minutes depending on your computer. In one of the SnPM window, it will show the percentage of the completeness, and in the matlab window, the permutation step that is being performed will be listed.

![Permutation Results](image)

Note that it shows how many minutes and seconds spent on each permutation. The number in parentheses is the percentage of time spent on variance smoothing. Since we choose no variance smoothing, this is 0%.

Finally click on **Results**

Select the SnPM.mat file in the corresponding directory as below,

![Select SnPM.mat](image)

In the menu, choose the following options:

- **Positive or negative effects?:** (+ve)
- **Write filtered statistic img?:** (yes)
- **Filename?:** SnPMt_filtered
Finally, the SnPM PostProcess menu will be as below,

```
| Positive or negative effects? | +ve |
| Write filtered statistic img? | yes |
| Filename?                     | SnPM1_filtered |
| Write FWE-corrected p-value img? | yes |
| FWE-Corrected p value threshold | 0.05 |
| Assess spatial extent?        | no  |
```

SnPM will then show the distribution of the maximum t-statistic.

A small dialog box will come out and ask you to review the permutation distributions and to choose either 'Print & Continue' (to print the histogram to spm2.ps file and then to continue) or just 'Continue' only. Click on one of the two buttons.

On next page, SnPM will then show the permutation distributions of the uncorrected P values,
SnPM example

Uncorrected P Permutation Distributions

Choose to print the page to spm2.ps file and then continue or to continue directly by using the prompted small dialog box.

On next page, SnPM will then plot a MIP of those voxels surviving the SnPM critical threshold (this value is displayed at the bottom of the image and for this data set should be 7.92).

SnPM
You can then use this value in SPM (in the RESULTS section, say 'No' to corrected height threshold, and then type in 7.9248 for the threshold) and take advantage of SPMs rendering routines (not available in SnPM).

Note that the SnPM threshold is lower than the SPM threshold (9.07). Consequently, SnPM shows more active voxels.
(With smoothed variance t, Pseudo-t)

Note that the result just obtained looks "jaggedy". That is, while the image data is smooth (check the con* images), the t statistic image is rough. A t statistic is an estimate divided by a square root of the variance of the estimate, and this roughness is due to uncertainty of the variance estimate; this uncertainty is especially bad when the degrees of freedom are low (here, 11). By smoothing the variance before creating a t ratio we can eliminate this roughness and effectively increase our degrees of freedom, increasing our power.

Create a new directory for the smoothed variance results.

First click on

Setup

Then type in the following options (your responses are in square brackets).

[Multisub: 1 condition, 1 scan per subject]
Select all scans [con_0006.img -> con_0017.img]
Number of confounding covariates [0]
4096 Perms. Use approx test? [No]
FWHM(mm) for Variance smooth [8]

A rule of thumb for the variance smoothing is to use the same FWHM that was applied to the data (which is what we've used here), though a little as 2 x VoxelSize may be sufficient.

Collect Supra-Threshold stats [Yes]
Select Global Normalisation [No Global Normalization]
Select global calculation [Mean]

Again, this doesn't matter because no normalisation will be done.

Threshold masking [None]
Grand Mean Scaling [No Grand Mean Scaling]

The final Setup Menu will be as below,
SnPM will now create the file SnPMcfg.mat. In the Graphics window, the design matrix will be shown.

Now click on

Compute

Select the file (SnPMcfg.mat)

In the matlab window, the permutation step that is being performed will be listed.

<table>
<thead>
<tr>
<th>Perm</th>
<th>Time</th>
<th>% Variance Smoothing</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>67</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>68</td>
<td>0' 1&quot;</td>
<td>(39% Sm)</td>
</tr>
<tr>
<td>69</td>
<td>0' 1&quot;</td>
<td>(38% Sm)</td>
</tr>
<tr>
<td>70</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>71</td>
<td>0' 1&quot;</td>
<td>(38% Sm)</td>
</tr>
<tr>
<td>72</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>73</td>
<td>0' 4&quot;</td>
<td>(53% Sm)</td>
</tr>
<tr>
<td>74</td>
<td>0' 1&quot;</td>
<td>(39% Sm)</td>
</tr>
<tr>
<td>75</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>76</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>77</td>
<td>0' 1&quot;</td>
<td>(38% Sm)</td>
</tr>
<tr>
<td>78</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>79</td>
<td>0' 1&quot;</td>
<td>(37% Sm)</td>
</tr>
<tr>
<td>80</td>
<td>0' 1&quot;</td>
<td>(38% Sm)</td>
</tr>
</tbody>
</table>

Note that it shows how many minutes and seconds spent on each permutation. The number in parentheses is the percentage of time spent on variance smoothing. Compare this result with what we get from "Without smoothed variance t" method (0% in that case).

The above computation should take between 10 and 25 minutes depending on your computer.

Finally click on

Results

Select the SnPM.mat file

Make the following choices:

Positive or negative effects?: (+ve)
Write filtered statistic img?: (yes)
Filename?: SnPMt_filtered
Write FWE-corrected p-value img?: (yes)
Use corrected threshold?: (FWE)
FWE-Corrected p value threshold: (0.05)
Assess spatial extent?: (no)

The final Results Setup Menu will be as below,

- Positive or negative effects?: +ve
- Write filtered statistic img?: yes
SnPM will then show the distribution of the maximum *pseudo* t-statistic, or smoothed variance t statistic as below.

A small dialog box will come out and ask you to review the permutation distributions and to choose either 'Print & Continue' (to print the histogram to spm2.ps file and then to continue) or just 'Continue' only. Click on one of the two buttons.

On next page, SnPM will then show the permutation distributions of the uncorrected P values, together with a FDR plot.
Choose to print the page to spm2.ps file and then continue or to continue directly by using the prompted small dialog box.

On next page, SnPM will then plot a MIP of those voxels surviving the SnPM critical threshold (this value is displayed at the bottom of the image and for this data set should be 5.33).

SnPM example

http://www.sph.umich.edu/ni-stat/SnPM/exnew.html
Observe how there are both more suprathreshold voxels, and that the image is smoother. For example, note that the anterior cingulate activation (3,15,45) is now 356 voxels, as compared with 75 with SnPM{t} or 28 with SPM{t}.

**Very important!!!** This is *not* a t image. So you *cannot* apply this threshold to a t image in SPM. You can, however, create overlay images with the following:

1. Use 'Display' to select the image you would like for a background. Via the keyboard only you could do...

   ```
   Img = spm_get(1,'.img','select background reference');
   spm_image('init',Img)
   ```

2. Create filtered image with NaN's instead of zero's.

   ```
   In     = 'SnPMt_filtered';
   Out    = 'SnPMt_filteredNaN';
   f      = 'i1.*(i1./i1)';
   flags  = {0,0,spm_type('float')};
   spm_imcalc_ui(In,Out,f,flags);
   ```

   Ignore the division by zero errors.

3. Overlay the filtered image

   ```
   spm_orthviews('addimage',1,'SnPMt_filteredNaN')
   ```
SnPM example http://www.sph.umich.edu/ni-stat/SnPM/exnew.html

Back to main SnPM page

SnPM by Andrew Holmes of the Astra Zeneca
& Tom Nichols of University of Michigan Biostatistics department

SnPM authors at <snpm-authors at umich.edu> Last modified: Tue Feb 1 08:06:01 EST 2005
Lab C
Multivariate Modeling
Lab C: Multivariate Modeling

Goals of this Lab

After this lab you will...

1. Be able to fit multivariate models to neuroimaging data.
2. Be able to compute PCA, (Principal component analysis), and variation of.
3. Multivariate Linear Models
4. Be able to explore your "noise" and see if something is going on that you didn’t expect in a multivariate way.

The lab will use the standard dataset provided by Rik Henson, and possibly other datasets for specific purposes.

An overview of the documentation of the toolbox can be found at http://www.madic.org/download/MMTBx.

Multivariate methods: a short descriptions

The Multivariate Methods toolbox (MM toolbox for SPM) is a package that implements several multivariate methods for fMRI data analysis. These methods (outlined in red on the figure) are based on Singular Value Decomposition (SVD). They provide the user with an interactive environment to:

* Explore the data without any prior model (Principal Component Analysis : PCA).
* Explore fitted effects and to check the model fit (Projected PCA).
* Explore relations between data and model and help to specify new models (Multivariate Linear Models : MLM - Partial Least Square : PLS ).

The figure in www.madic.org/download/MMTBx summarises briefly various multivariate methods and the ones that are implemented in the MM toolbox are inside the red contour. Note that Canonical Variate Analysis (CVA), although based on SVD, is not implemented since it requires a data reduction step that is problematic with fMRI data. The most relevant references are found in the following. Our work is an extension of Worsley et al., 97 and Friston et al., 96. This toolbox was used in "Multivariate Model Specification for fMRI Data", in Neuroimage 2002 by Kherif et al.
Lab D
Registration Alternatives
USA SPM Short Course April 6-8, 2005 Yale University
Lab D: Registration Alternatives

== Goals of this Lab ==

After this lab you will be able to...
1. Use an alternative realignment protocol (INRIAlign)
2. Understand potential limitations of realignment protocols that employ techniques that minimize the sum of the squares of the differences (i.e., SPM, AIR, AFNI).
3. Understand EPI warping issues.
4. Perform optimized spatial normalization processing for fMRI studies.

---

INRIAlign toolbox for fMRI realignment in SPM99/2

The INRIAlign toolbox enhances the standard SPM realignment routine (see topic: spm_realign_ui in SPM99 documentation). In the latter, rigid registration is achieved by minimization of the sum of squared intensity differences (SSD) between two images. As noted by several SPM users, SSD based registration may be biased by a variety of image artifacts and also by activated areas. To get around this problem, INRIAlign reduces the influence of large intensity differences by weighting errors using a non-quadratic, slowly-increasing function (rho function). This is basically the principle of an M-estimator.

When launching INRIAlign, the user may select a specific rho function as well as an associated relative cut-off distance (which is needed by most of the rho functions). By default, the rho function is that of Geman-McClure while the relative cut-off distance is set to 2.5.

Apart from this distinction, the method is very similar to spm_realign and uses the same editable default parameters. Most of the implementation has been directly adapted from the code written by J. Ashburner.

Author: Alexis Roche, INRIA Sophia Antipolis, EPIDAURE Group, Now working at the CEA anatomo-fonctional neuro-imaging unit, Frederic Joliot Hospital, Orsay, France

References


Matlab routines

- README.txt
- INRIAlign_1.01.zip
- INRIAlign_1.0.zip

Spatial Normalization

1) We will discuss issues associated with differences in the acquisition of EPI data versus T1 MRI data. We will review two options for spatially normalizing fMRI data. One option will be to coregister the EPI mean image to the individual subjects T1 MRI data. Then spatially normalize the subject’s T1 data to the T1 template provided in SPM, dragging the coregistered EPI data along. A second procedure discussed will be to tailor the SPM spatial normalization routines to directly normalize the EPI mean image to the EPI template provided in SPM. Results will be discussed as they pertain to these two options on different scanners (i.e., 1.5T, 3T).
Lab E

ROI Analyses
with
Marsbar
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Region of interest analysis with MarsBaR

Goals

1. Install MarsBaR
2. Learn to work the with the online help
3. Define and combine ROIs
4. Run statistical analyses on ROIs
5. Run MarsBaR batch scripts
6. Extract and plot event–related time courses

Prerequisites

1. Standard installation of SPM
2. MarsBaR example dataset, with preprocessing already run.
3. An estimated three session model for the MarsBaR example dataset (see the run_s3_model batch
   script in the batch subdirectory).
4. A utility to unzip compressed archives (Windows Explorer in XP, WinZip, etc).

Installing MarsBaR

First download MarsBaR 0.37 from The Marsbar Sourceforge Page

Save it into a temporary folder.

Unpack it into this folder. You now have a new subdirectory called marsbar-devel-0.37.

Start matlab. Add the marsbar-devel-0.37 directory to your matlab path:

addpath c:\Temporary_folder\marsbar-devel-0.37

Start SPM, and start MarsBaR

>> spm fmri
>> marsbar

Installing the AAL ROIs

Download the AAL ROI archive into your temporary directory. Unpack the AAL library in the same directory; it
will create a new directory, called something like marsbar-aal-0.2.

The library contains ROIs in MarsBaR format that were anatomically defined by hand on a single brain matched
to the MNI / ICBM templates. The ROI definitions are described in:

anatomical labelling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single
Working your way round the help system

Open a web browser (please don't let that be Internet Explorer. I bet it is).

Chose File -> Open (or whatever)

Navigate to c:\Temporary_folder\marsbar-devel-0.37\doc, and select index.html.

From that page, select the marsbar link, and from that page select marsbar again. This gives you the help documentation from the main MarsBaR program file. Note that you can click on links to find the help for all the MarsBaR functions. The same help is also available online for the latest version at:

http://marsbar.sourceforge.net/doc-devel/latest/

As always with matlab, for help with the marsbar.m function, you can also type

>> help marsbar

at the matlab prompt.

There is also a MarsBaR FAQ

The example dataset


The data consist of three EPI runs, all from one subject. In each run the subject watched a computer screen, and pressed a button when they saw a flashing checker board. An “event” in this design is one presentation of the flashing checker board.

We did this experiment because we were interested to see if events at fast presentation rates give different activation levels from events that are more widely spaced. Each run has a different presentation rate. We randomized the times between events in each run to give an average rate of 1 event every second in run 1, 1 event every 3 seconds for run 2, and 1 event every 10 seconds for run 3.

The first step: defining the ROI

We (your kind organizers) have already run an SPM model for run 2 (and run 1 and run 3). Now we need to find an activation cluster in the visual cortex.

Go to the MarsBaR window, and click on ROI definition.

Defining a functional ROI

We are going to define the functional ROI using the SPM analysis for run 2. Select “Get SPM cluster(s)...”: from the menu. This runs the standard SPM results interface. Use the file selection window that SPM offers to navigate to the sess2/SPM2_ana directory. Select the SPM.mat file and click Done. Choose the stim_hrf t contrast
from the SPM contrast manager, click Done. Then accept all the default answers from the interface, like this:

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>mask with other contrasts:</td>
<td>no</td>
</tr>
<tr>
<td>title for comparison</td>
<td>stim_hrf</td>
</tr>
<tr>
<td>p value adjustment to control</td>
<td>none</td>
</tr>
<tr>
<td>threshold ({T\ or \ p\ value})</td>
<td>0.05</td>
</tr>
<tr>
<td>&amp; extent threshold {voxels}</td>
<td>0</td>
</tr>
</tbody>
</table>

Now you have run the Get SPM cluster(s) interface, you should have an SPM activation map in the graphics window:

Meanwhile, you may have noticed there is a new menu in the SPM input window for saving ROIs.

Another thing you may not have noticed is that the matlab working directory has now changed to the `sess2/SPM2_ana`. SPM2 does this to be able to keep track of where its results files are.

Move the red arrow in the SPM graphics window to the activation cluster in the visual cortex. You can do this by dragging the arrow, or right-clicking to the right of the axial view and choosing goto global maxima.

When the red arrow is in the main cluster, click on the Write ROI(s) menu in the SPM input window and select Write one cluster.

After you have selected Write one cluster, MarsBaR asks for details to save with the ROI, which are a description, and a label. Both provide information about the ROI for statistical output and display. The label should be 20 characters or so, the description can be longer. For the moment, accept the defaults, which derive from the coordinates of the voxel under the red arrow and the title of the contrast:

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description of ROI</td>
<td>stim_hrf cluster at ([-9.0, -93.0, -15.0])</td>
</tr>
<tr>
<td>Label for ROI</td>
<td>stim_hrf (-9,-93,-15)</td>
</tr>
</tbody>
</table>

After this, MarsBaR offers a dialog box to give a filename for the ROI. By default the offered filename will be `stim_hrf\(-9\,-93\,-15\)_roi.mat` in the `sess2/SPM2_ana` directory. For simplicity, why not accept the default name and click Save to save the ROI.

### Review the ROI

We can now review this ROI to check if it is a good definition of the visual cortex. Click on the ROI definition menu in the MarsBaR window, and select View…. Choose the ROI and click Done. Your ROI should be displayed in blue on an average structural image:

### Refining the ROI

Now we have reviewed the ROI, we see that the cluster does include visual cortex, but there also seems to be some connected activation lateral and inferior to the primary visual cortex. Ideally we would like to restrict the ROI to voxels in the primary visual cortex.
We can do this by defining a box ROI that covers the area we are interested in, and combining this with the activation cluster.

### Defining a box ROI

To decide on the box dimensions, click around the ROI in the view interface and note the coordinates of the crosshairs that are shown at the top of the bottom left panel. This may suggest to you, as it did to us, that it would be good to restrict the ROI to between −20 and +20mm in X, −66 to −106mm in Y, and −20 to +7mm in Z.

To define this box ROI, click on ROI definition, and choose Build... . You will see a new menu in the SPM input window:

From the menu, select Box (ranges XYZ). Answer the prompts like this:

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>[2] Range in X (mm)</td>
<td>−20 20</td>
</tr>
<tr>
<td>[2] Range in Y (mm)</td>
<td>−66 −106</td>
</tr>
<tr>
<td>[2] Range in Z (mm)</td>
<td>−20 7</td>
</tr>
<tr>
<td>Description of ROI</td>
<td>box at −20.0&gt;XYZ</td>
</tr>
<tr>
<td>Label for ROI</td>
<td>box_x−20:20_y−106:−66_z−20:7</td>
</tr>
<tr>
<td>Filename</td>
<td>box_x−20_20_y−106_−66_z−20_7_roi.mat</td>
</tr>
</tbody>
</table>

The last three values here are the defaults. To check this is as you want it, choose ROI Definition, View, select both of box_x−20_20_y−106_−66_z−20_7_roi.mat and stim_hrf−9_−93_−12_roi.mat, in that order, and click Done.

You should see the box in blue, with the activation cluster overlaid in red.

We now need to combine the two ROIs, to select only those voxels that are shared by the box and the activation cluster.

### Combining ROIs

Choose ROI Definition, Transform... A new menu comes up in the SPM input window. Choose Combine ROIs; select both the box and the cluster ROIs, click on Done. The prompt now asks for a function with which to combine the ROIs. In this function, the first ROI you selected is \( r_1 \), and the second ROI is \( r_2 \). Here we want to get the overlap, and this is represented by the logical AND operator, which is \( \& \) in Matlab. Enter the function \( r_1 \& r_2 \)

After this, accept the default description, set the label to something like “Trimmed stim run 2”, and save the ROI as trim_stim_roi.mat.

### Writing the ROI as an image

Just for practice, let us write our new ROI as a binary image. You might want to do this so you can review the ROI using another program, such as the excellent MRicro (www.mricro.com). Click on ROI definition, then Export... Select image from the new menu in the SPM input window, and choose the new trim_stim_roi.mat as the ROI to export. Another menu appears, asking for a Space for ROI image. The three options are Base space for ROIs, From image, or ROI native space.
In our case, the data are spatially normalized, and so are in the space of the MNI template. The MNI template space is the default base space for ROIs, so select Base space for ROIs, choose a directory to save the image, and accept the default filename for the image, which should be trim_stim. You can check this has worked, by finding the SPM buttons window, selecting Display, and choosing the new trim_stim.img.

**Running the ROI analysis**

First, let us estimate the activation within the ROI for the first run. There are three stages to the analysis.

1. Choosing the design
2. Extracting the data
3. Estimating the design model with the data

To this basic list I will also add:

- Setting the autocorrelation options

We have already processed the example data to create an SPM model for all three EPI runs, so we already have a design made for the first run. We are going to use this design and the trim_stim ROI to extract ROI data from the functional scans. Then we will use the design and the extracted data to estimate the model.

**Stage 1: choosing the design**

Click on the Design button in the MarsBaR window. Select the Set design from file option in the design menu and choose the SPM.mat file in the sess1/SPM2_ana directory. MarsBaR loads the design into memory and displays the design matrix in the SPM graphics window.

**Stage 2: extracting the data**

Before we can run the model, we need to extract the ROI data from the functional scans. This brings us to the data menu.

Choose Data – Extract ROI data (default); the GUI will ask you to select one or more ROIs files; select the trim_stim_roi.mat file. MarsBaR starts to whirr. As it whirrs, it will:

1. Take each image in the design (you had already set the default design from the design menu);
2. Extract all the data within the ROI for each image, to give voxel time courses for each voxel in the ROI.

When it has finished, MarsBaR will calculate a new summary time course for each ROI. The summary time course has one value per scan, per ROI; by default, this new time course is made up of the means of all the voxel values in the ROI. For example, if there are only 5 voxels in the ROI, the first value in the summary time series will be the mean of the 5 voxel values for scan 1, the second value will be the mean of the 5 voxel values for scan 2, and so on. You can change the method of summarizing voxel data using the Statistics, Data summary function item in the MarsBaR options interface.

As MarsBaR extracts the data you will see its progress printed to the matlab console. When the extraction is done, the data is kept in memory. You can save the data to disk if you want using the Save data to file option on the data menu. Now we have the design and the data we can estimate the model.
The optional stage: setting the autocorrelation

There are a few problems with the autocorrelation estimation in SPM2. For this reason MarsBaR includes the option of using the autocorrelation algorithm from Keith Worsley's fmristat program. This option is faster and more robust than the default in SPM2. To use the fmristat algorithm, choose add/edit filter from the Design menu:

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>High pass filter?</td>
<td>specify</td>
</tr>
<tr>
<td>cutoff period (secs)</td>
<td>60</td>
</tr>
<tr>
<td>Correct for serial autocorrelations?</td>
<td>fmristat AR(n)</td>
</tr>
<tr>
<td>fmristat AR model order</td>
<td>2</td>
</tr>
</tbody>
</table>

This sets an AR(2) model for the data.

Stage 3: estimating the model

Click on the Results menu in the MarsBaR window. Choose the first item on the menu, Estimate results. MarsBaR takes the default design and the extracted data, and runs the model. There are more progress reports to the matlab console; finally you see the suggestion that you use the results section for assessment.

Assessing results in MarsBaR

Basic results: the statistic table

Let us start the assessment by getting some t and F values for the effects in the design. Click on the Results button in the MarsBaR window:

We next need to specify a contrast. In our case the contrast is very simple: just a 1 in the column for the HRF regressor used to model the visual event. Usually the contrast will be more complicated, and you may have already entered it for a previous SPM or MarsBaR analysis. The Import contrasts option allows you to get contrasts from a previous analysis. To show how it works, click on this option. The SPM file selection window should appear. Navigate to the sess1/SPM2_ana directory, and select the SPM.mat file there. The SPM contrast manager comes up, showing all the F and t contrasts in the SPM.mat file. Select the stim_hrf t contrast, and click Done. MarsBaR will put this contrast into the current estimated design. Here we only selected one contrast, but you can select many contrasts by dragging the mouse, shift clicking etc. (depending on your system).

Now click on the Statistic table option in the MarsBaR results menu. Select the stim_hrf contrast and click Done. The results will print out in a rather ugly fashion in the Matlab window. You might want to enlarge your Matlab window to stop the text wrapping in an annoying way.

At the left you see the contrast name. Under this, and to the right, MarsBaR has printed the ROI label that you entered a while ago. The t statistic is self explanatory, and the uncorrected p value is just the one−tailed p value for this t statistic given the degrees of freedom for the analysis. The corrected p is the uncorrected p value, with a Bonferroni correction for the number of regions in the analysis. In this case, we only analyzed one region, so the corrected p value is the same as the uncorrected p value. MarsBaR (like SPM), will not attempt to correct the p value for the number of contrasts, because the contrasts may not be orthogonal, and this will make a Bonferroni correction too conservative.
There is also a column called Contrast value. For a t statistic, as here, this value is an effect size. Remember that a t statistic consists of an effect size, divided by the standard deviation of this effect. Here our contrast is very simple, containing only a single 1, so the contrast value is the same as the value of the first parameter in the model. The value of this parameter will be the best-fitting slope of the line relating the height of the HRF regressor to the FMRI signal. This effect size measure is the number that SPM stores for each voxel in the con_0001.img, con_0002.img ... series, and these are the values that are used for standard second level / random effect analyses. Just for practice, let us also run an F contrast. Click Statistic table again, choose the effects of interest contrast, click Done:

Now the Contrast value has become the Extra SS. This is a measure of the variance that would be added to a model that does not contain the effects in the contrast. The F statistic is this measure, adjusted for the number of effects, and divided by the residual variance for the whole model. There is no simple way of using this Extra SS value in second level analyses.

**Comparing fast and slow events – the difference between run 1 and run 3**

Our results so far show that there is indeed a highly significant effect of visual stimulation on the visual cortex, even for very frequent events. This is not a Nature paper so far. To make things a bit more interesting, we can compare this effect, from run 1, with the effect in run 3, for which the events were much less frequent.

Click on Design in the MarsBaR window, then Set design from file. Choose SPM.mat from sess3/SPM2_ana. Now we need to extract the data; select Extract ROI data (default) from the data menu. MarsBaR will ask you if you want to save the previous data. Why not say 'no' for the moment. Next choose trim_stim_roi.mat again. When that is done, run Estimate results from the Results menu. Again choose 'no' when asked if you want to save the previous estimated design. In the end, you get a new statistic table.

You can see that the contrast value – which is proportional to the change in signal for a single event – is greater for run 3 than for run 1. Despite this, the t statistic for run 3 is lower than for run 1. One explanation for this is that there are many more events in run 1, so the estimate of signal change per event is more reliable (has less variance).

**Using a structural ROI**

So far we have used a functional ROI. This has the advantage that it is usually well tuned to the subject we are analysing. The disadvantages are that we have had to use a whole run of data to define the ROI, which we would have preferred to be able to analyze, and that functional ROIs can be noisy, when the activation signal is not strong. An alternative is to use the anatomy of the brain to estimate the location of functional areas.

Using anatomical ROIs can work well for areas that are naturally defined by brain structure, such as the subcortical nuclei, or the primary sensory and motor cortices, where the functional areas are closely linked to the position of large and relatively invariant sulci. Outside these areas, it can be difficult to define functional areas using anatomy alone. The problems are compounded when anatomical ROIs are defined on one subject, and applied to another, because there is great variability between subject in sulcal anatomy.

In the example experiment, subjects responded with a key-press each time they saw the flashing checker board. We might therefore be interested to know the level of activation in the putamen. This would be a good candidate for an anatomical ROI, because the putamen can be accurately defined on a structural scan, and does not vary much between subjects after spatial normalization. The AAL ROI library contains a definition of the left and right putamen for a single subject after spatial normalization. The images from our subject have been spatially normalized, so the AAL definition of the putamen will probably give a reasonable approximation to the putamen...
in our data.

**Running an analysis using structural ROIs**

is exactly the same as running the analysis with the functional ROI. Select Design from the MarsBaR menu, and
Set design from file. Choose sess1/SPM2_ana/SPM.mat. Click on Data, Extract ROI data (default). When you are
asked for ROI file, navigate to the AAL directory, select MNI_Putamen_L_roi.mat and click Done. When the
data extraction is done, choose Results, Estimate results and wait till MarsBaR has done its thing. Select Results,
Statistic table, enter the stim_hrf contrast, as shown in Figure 17, above. Repeat the same procedure, using the
AAL MNI_Putamen_R_roi.mat ROI.

The subject responded with their right hand, so we expected that the right putamen would have less signal than
the left.

**Batch mode**

MarsBaR has a powerful batch mode. It is also relatively simple. Here we will just rerun our first ROI analysis
above using batch mode.

Go to the matlab (>>) prompt. Type or paste:

```matlab
spm_mat = spm_get(1, 'SPM.mat', 'Select SPM.mat for run 2');
roi_mat = spm_get(1, '*roi.mat', 'Select trimmed ROI for run 2');
```

The SPM file window comes up twice, asking you for the SPM.mat and ROI files. The code above just gets the
file names for the SPM.mat analysis file for run 2, and the ROI file. Type:

```
spm_mat
roi_mat
```

and you will see the paths for the two files.

Now we can batch. Type or paste the following into the matlab window:

```matlab
D = mardo(spm_mat);
R = maroi(roi_mat);
Y = get_marsy(R, D, 'mean');
D = autocorr(D, 'fmristat', 2);
E = estimate(D, Y);
```

What do these lines do? Do you recognize this from the beginning of the tutorial?

Next we set the simple HRF contrast:

```matlab
[E contrast_no] = add_contrasts(E, 'stim_hrf', 'T', [1 0 0]);
```

and finally we evaluate the contrast:

```matlab
stat_struct = compute_contrasts(E, contrast_no);
```

Type `stat_struct` in the matlab window. All the information from the contrast is available in this structure.
Can you identify the contrast P value? Check the help for the compute_contrast function using the online help to
see what the stat_struct structure includes.

For more batch examples, see the MarsBaR FAQ.

There is also an example batch script in the example data set batch directory, called run_tutorial.m. You won't be surprised to hear that this is a batch script that runs most of the steps in this tutorial, as well as extracting and plotting reconstructed event time courses.

**Working with event time courses**

We will often want to estimate the shape of the event time courses within an ROI. For this we will use the three-session model provided by running the `run_s3_model` batch file from the MarsBaR example dataset. This is just a single model including all three of the experimental sessions.

**Set and review the model**

Choose:

1. Design – Set design from file.
2. Design – Add/edit filter for FMRI design

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>High pass filter?</td>
<td>specify</td>
</tr>
<tr>
<td>cutoff period (secs)</td>
<td>60</td>
</tr>
<tr>
<td>Correct for serial correlations?...</td>
<td>fmristat AR(n)</td>
</tr>
<tr>
<td>fmristat AR model order</td>
<td>2</td>
</tr>
</tbody>
</table>

Then choose Design – Explore.

You should see the design in the SPM graphics window. Note that there is text at the bottom of the window reminding you of the filter you've chosen.

**Extract data and estimate the model**

1. Data – extract ROI data (default). Select the trim_stim roi.
2. Results – Estimate results

**Plot a fitted event time course for events in each session**

1. Results – Fitted event time course

Now you get the event type management window:
For now we have no event types. An event type is an event or combination of events in your model. To start, let us add an event type for each session, for the visual stimulation event. Click on the New button. You should see the *event type editing window*:

1. Click on the vis_stim: session 1 event in the bottom list box, and click Add.
2. Change the event type name to *vis_stim_1*
3. Click OK

Repeat these steps for session 2 and 3 (giving *vis_stim_2* and *vis_stim_3*).
You now have 3 event types in the event type management window. Drag the mouse to select all 3 and click OK. Enter 0 for Event duration

You now have 3 event plots, one for each session. Note that the event shape varies a little from session to session. This is so because we have used the HRF and temporal derivative as our model of the event – and this allows some very constrained variation of the event shape, with different values of the temporal derivative parameter.

**Plot mean fitted event time course**

We may want to average across events in different sessions, or even across events in the same session. The event type interface allows us to do this.

1. Click Results − Fitted event time course
2. Click New in the event type manager
3. Drag select all 3 events (sessions 1 to 3) and click Add
4. Enter the name as vis_stim_average
5. Click OK
6. Click OK (the vis_stim_average event type is already selected)
7. Enter event duration of 0

You will see the average time course in the graphics window.

We could have achieved the same effect by using Results − Add event types by name. This finds all the events with the same names in the design, and makes event types which are the average of those events. Try it now:

1. Results − Add event types by name
2. Results − Fitted event time course

You will see a new event type called vis_stim in the event types management window. Click the edit button to see the events that have been included.

**Plot FIR estimate of the event time course.**

We have seen the fitted event time course, but we had a very constrained of the shape of the hemodynamic response for each event (the canonical hemodynamic response function and its temporal derivative). Now we would like to see a less constrained best estimate of the shape of the response following a single event. For this we use the FIR model. For more information on the FIR model, see the relevant section in the MarsBaR FAQ. In brief, the FIR is a way of doing event−related averaging that allows for overlap between events. In fact, if there is no overlap between events, the results of the FIR model are identical to event−related averaging.

1. Results − FIR event time course
2. Select vis_stim_1 through vis_stim_average and click OK

<table>
<thead>
<tr>
<th>Prompt</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal units...</td>
<td>Percent</td>
</tr>
<tr>
<td>Bin length (secs)</td>
<td>2.0273</td>
</tr>
<tr>
<td>No of bins</td>
<td>12</td>
</tr>
</tbody>
</table>

You will then get FIR plots for all three sessions, and the average, in the graphics window, in units of percent signal change.

Plot mean fitted event time course
Question: why don't the FIR plots begin at zero?

Again, see the MarsBaR FAQ for examples of how to batch the extraction of time courses.

**The end**

If you have time, you might want to have a look at the plot functions in the data menu. You might also want to look at the Frequencies – (event+data) option in the Design menu. This can be useful in deciding on the correct high-pass filter.

If not, then – all done.

— MatthewBrett – 23 Mar 2005