CCA-fMRI Toolbox - SPM 5

User's Manual

Version 2.0

Linköping University

Content

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Credits

Author

The toolbox and its documentation were developed by Ph.D. Nils Paulsson, Center for Medical Image Science and Visualization (CMIV), Linköping University, with much appreciated input from Professor Magnus Borga and Ph.Lic. Joakim Rydell, Department of Biomedical Engineering, Linköping University, Sweden.

Scientific work

This toolbox is based on the work in, among others, the following references:

1. Borga M., Learning Multidimensional Signal Processing., Ph.D. thesis, Linköping University, SE-581 83 Linköping, Sweden, 1998. Dissertation No 531, ISBN 91-7219-202-X, http://www.imt.liu.se/mi/Publications/Papers/M_Borga_thesis.pdf

2. Buxton R., Wong E. and Frank L., Dynamics of Blood Flow and Oxygenation Changes During Brain Activation: the Balloon Model.,Magnetic Resonance in Medicine, 39(6):855-864, 1998.

3. Das S. and Sen P., Asymptotic distribution of restricted canonical correlations and relevant resampling methods., Journal of Multivariate Analysis, 56(1):1-19, 1996.

4. Friman O., Borga M., Lundberg P. and Knutsson H., Adaptive Analysis of fMRI Data, NeuroImage 19(3):837-845, July 2003.

5. Friman O., Borga M., Lundberg P. and Knutsson H, Detecting Neural Activity in fMRI Using Maximum Correlation Modeling, NeuroImage, 15(2):386-395, February 2002.

6. Friston K. J., Mechelli A., Turner R. and Price C. J., Nonlinear responses in fMRI: the balloon model, Volterra kernels,and other hemodynamics. NeuroImage, 12:466-477, 2000.

7. Hotelling H., Relations between two sets of variates., Biometrika, 28:321-377, 1936.

8. Rydell J., Adaptive Spatial Filtering of fMRI Data, Linköping Studies in Science and Technology, Thesis No. 1200, Linköping University, SE-581 83 Linköping, Sweden, LiU-TEK-LIC-2005:55, ISBN 91-85457-43-4.

9. Zheng Y., Martindale J., Johnston D., Jones M., Berwick J. and Mayhew J., A model of the hemodynamic response and oxygen delivery to brain., Neuroimage 16: 617-37, 2002.

1. Background

The *CCA-fMRI Toolbox* implements the use of canonical correlation analysis (CCA) for detecting brain activity patterns recorded by functional magnetic resonance imaging (fMRI). CCA was developed by Hotelling [7] and is a method for finding the maximum correlation between linear combinations of two sets of variables. In the *CCA-fMRI Toolbox* CCA is used in a two step process. In the first step, CCA is used to construct a low pass filter that adapts to the environment of each voxel in the brain volume analyzed. In the second step, CCA compare the temporal intensity change of the filtered voxels with an expected activation pattern to determine the level of correlation and, hence, the level of activation. The method is thoroughly described in reference [4].

SPM is a well known and free (GNU General Public License) software package for analysis of brain imaging data sequences. It has a long history and has continuously been released in new versions since at least 1994.

2. Requirements

Hardware requirements

- Any hardware platform that is supported by both Matlab® version 7.4 and SPM 5.
- Minimum 1 GB RAM. For 3-dimensional analysis a minimum of 1.5 GB RAM is recommended.
- CPU running at 2 GHz or above.
- Minimum 1.5 GB available temporary disk storage.

Software requirements

- Matlab® 7.4 or later.
- SPM software package version 5 (http://www.fil.ion.ucl.ac.uk/spm/).
- Linux®, Windows® XP or any other operating system that is supported by both SPM 5 and Matlab® 7.4.

Restrictions

- The *CCA-fMRI Toolbox* version 2.xx was written for SPM 5 and does not support SPM 2. For SPM 2 support, please use version 1.xx of the toolbox.
- The *CCA-fMRI Toolbox* was developed and tested using 32-bit Matlab®, version 7.4. Correct operation under 64-bit Matlab® has neither been tested nor verified.
- SPM 5 is officially only supported on Matlab® versions 6.5 - 7.3. However, besides having successfully developed the *CCA-fMRI Toolbox* using Matlab® 7.4 and SPM 5, there are several external sources reporting that this is indeed a working combination.

Installation

1. Install Matlab® and SPM 5 according to their respective installation instructions.

2. Unzip the *CCA-fMRI Toolbox* zip-file in a temporary directory.

3. Move the extracted folder, named `CCA_fMRI`, to the toolbox folder in the installed SPM 5 directory tree, e.g. `<MatlabPath>\toolbox\spm5\toolbox`. Be sure to have write access to the toolbox folder.

4. Start Matlab® and add the path of the *CCA-fMRI Toolbox*-folder, e.g. `<MatlabPath>\toolbox\spm5\toolbox\CCA_fMRI`, to the Matlab® path by selecting `Set Path...` from the `File`-menu in Matlab's® console window.

5. Install the *CCA-fMRI Toolbox* by entering:

   ```
   >> CCA_fMRI('install');
   ```

   at the Matlab® prompt. When the installation is done the following text will be displayed:

   ```
   CCA-fMRI for SPM has now been installed and the
   toolbox can be reached from within SPM.
   ```

The *CCA-fMRI Toolbox* is now installed and ready to be used. In case SPM 5 is used on a computer where each user has a profile of their own, step 5 above has to be repeated for all users that want to use the *CCA-fMRI Toolbox*. In other words, repeat the following steps for each user:

1. Log on the user
2. Start Matlab®
3. Run `CCA_fMRI('install');`

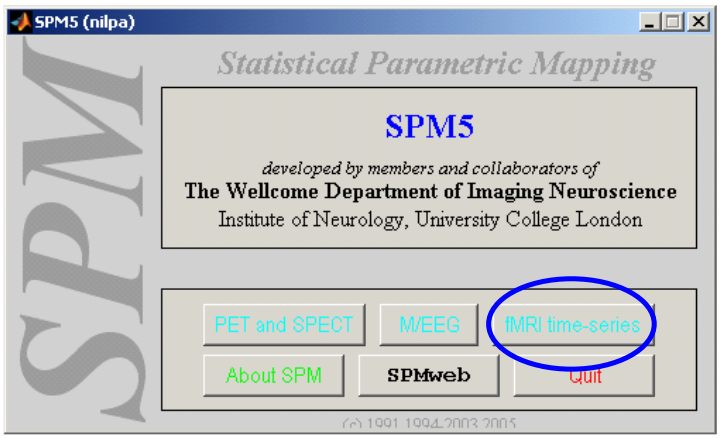
For more information regarding usage of the *CCA-fMRI Toolbox* please see the following chapters in this User's Manual.

3. Start up

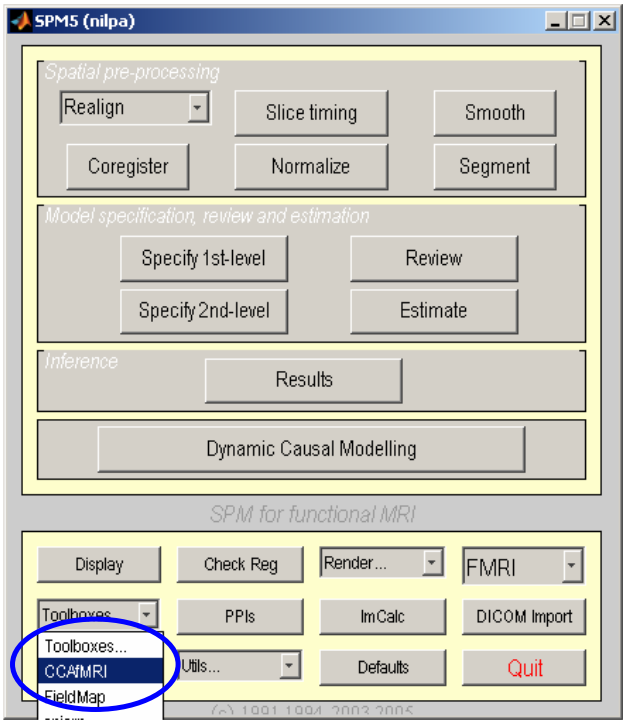
The *CCA-fMRI Toolbox* can be reached from the SPM GUI in the same way as any other SPM toolbox. First, start SPM from the Matlab® prompt:

```
>> spm
```

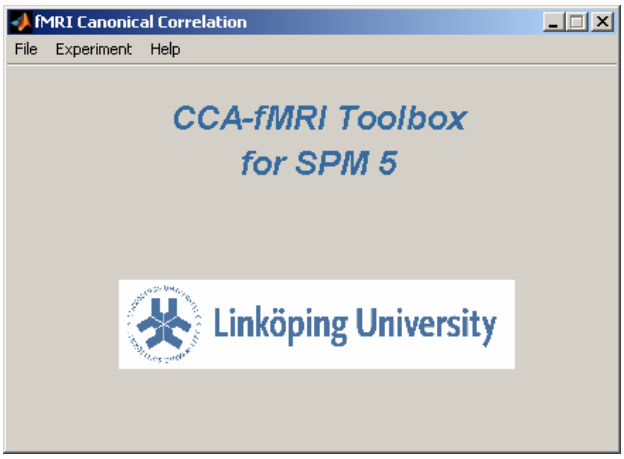
Click the `fMRI time-series` button in the main window:



Three new windows are opened. Open the drop down list named `Toolboxes...` in the lower left corner of the fMRI main window and select `CCAfMRI`.

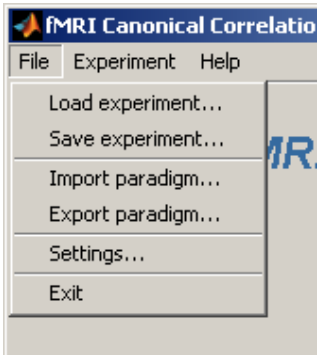


The *CCA-fMRI Toolbox* starts up and opens the main window. The toolbox is now ready to be used.



4. The File Menu

The `File` menu's main purpose is to provide the abilities to save and load experiment settings (see *Setting up an experiment*), import/export paradigms and optimize memory usage.



The `Load Experiment...` loads a previously saved experiment and makes it the currently defined experiment.

The `Save Experiment...` menu stores the current experiment setup to an external Matlab® file (MAT-format) using a user provided file name. The file holds a Matlab® structure named `Experiment` having the following fields:

```
Experiment

    ParadigmDesign: [1x1 struct]
    BalloonLimits: [1x1 struct]
    GammaDiffLimits: [1x1 struct]
    FilterSettings: [1x1 struct]
    ImageFiles: [1x1 struct]
```

`ParadigmDesign` - holds the parameters defining the paradigm of the experiment. For more informaton see `ValidateDesign.m` and the paradigm design dialog box.

`BalloonLimits` - specifies the base and threshold values of the hemodynamic response model used in the experiment for cases when being based on the balloon model. For more information see `ValidateBalloonLimits.m` and the balloon settings dialog box.

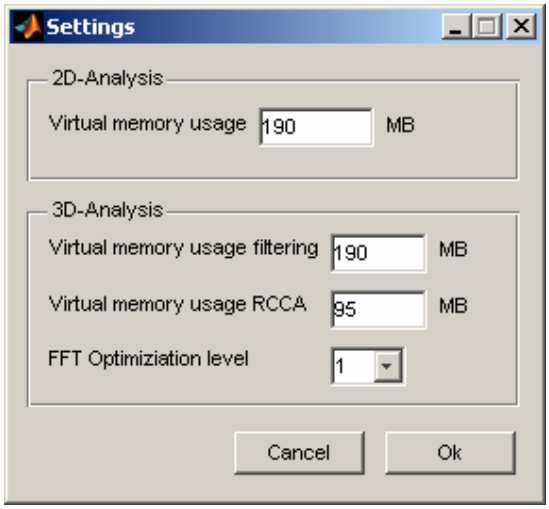
`GammDiffLimmits` - specifies the base and threshold values of the hemodynamic response model used in the experiment for cases when being based on the differential gamma function. For more information see `ValidateGammaDiffLimits.m` and the GammaDiff settings dialog box.

`FilterSettings` - specifies the filter settings of the experiment. For more information see `SteerableBasisFilter3D.m` and the steerable filter settings dialog box.

`ImageFiles` - specifies the set of image files that are analyzed in the experiment. For more information see `frm_ImageFiles.m`.

At times the same paradigm is used in several experiments. To facilitate the experiment setup the two menu items `Import paradigm...` and `Export paradigm...` allows the user to exclusively save and load the paradigm part of an experiment.

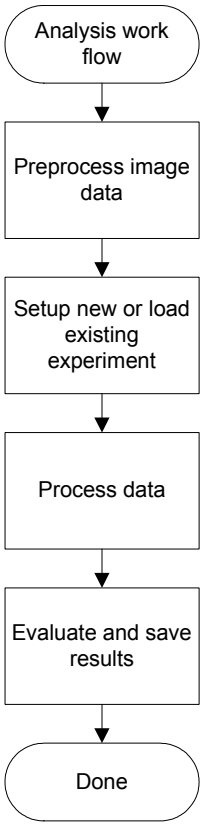
The `Settings` menu opens up the dialog box for managing memory usage and FFT optimization levels. There are different settings depending on if 2-dimensional or 3-dimensional analysis is performed (see *Setting up an experiment*). For 2-dimensional analysis `Virtual memory usage` has to be set to be large enough to hold the entire image set of an experiment.



For 3-dimensional analysis the `Virtual memory usage filtering` parameter has to be set to be large enough to hold the entire image set of an experiment. The `Virtual memory usage RCCA` setting has to be large enough to hold at least one image file. Finally, the `FFT Optimization level` sets the level of optimization performed during filtering with steerable filters. The lowest level is 1 and the highest level is 4. The higher levels may produce lower initial performance than the lower levels but over time Matlab®'s FFT module will learn how to perform an optimal Fourier transform. To determine the size of an image in bytes use the following formula *ImageSizeX* * *ImageSizeY* * *ImageSizeZ* * 4. The image size is expressed as number of pixels. To get the size of an image set just multiply the image size with the number of images.

5. Analysis workflow

The workflow of the CCA-fMRI analysis is straight forward and consists of preprocessing, experiment setup, data processing and finally evaluation of the result.



In the preprocessing step the raw image data is realigned, normalized, etc. to facilitate the subsequent data processing. However, **lowpass filtering must not be performed**. That would significantly degrade the quality of the results. The *CCA-fMRI Toolbox* performs its own lowpass filtering using adaptive filters. In the second step, experiment setup, parameters such as paradigm, BOLD model settings, filter properties and image data set are specified. Experiments can also be stored/loaded from secondary storage (hard drive, CD-ROM, etc). The step of processing data consists of several phases but the process is entirely automatic. Once started there is no need for user interaction until the processing has finished. This is usually the most time consuming step. A 2D-analysis usually takes less than 10 minutes and a 3D-analysis less than an hour, depending on size of data set, amount of available RAM, etc. In the last step the result can be visualized as well as exported to secondary storage. With the exception of preprocessing, all steps are performed within the *CCA-fMRI Toolbox* user interface.

6. Preprocessing

The *CCA-fMRI Toolbox* will usually produce better results when analyzing preprocessed data. Commonly applied preprocessing procedures in SPM are:

- Setting origin
- Realignment
- Reorientation

The only prerequisite of using preprocessed images in the toolbox is that the data is available as standard SPM 5 image files. This is seldom a problem since SPM usually applies preprocessing to the image data files directly or by creating new preprocessed versions of existing image files.

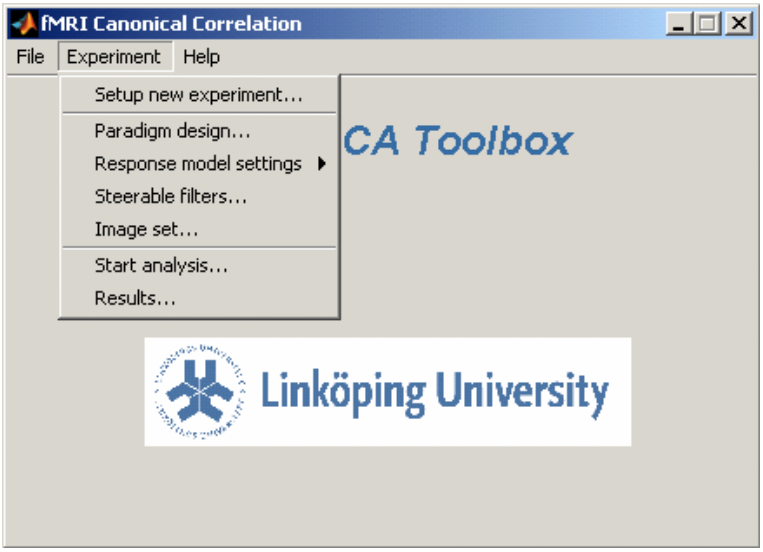
NOTE
Smoothing, or low pass filtering, must not be applied to the data set during preprocessing. Doing so would interfere with the adaptive filtering applied later on by the *CCA-fMRI Toolbox* and significantly degrade the quality of the final analysis results.

7. Setting up an experiment

An analysis setup is defined in terms of an experiment, which defines the parameters necessary for the analysis of a certain fMRI data set. An experiment is defined by the four main property groups:

- Paradigm design
- Response model (BOLD) settings
- Settings of the steerable filters
- Name and location of the image data set to be analyzed

All properties are accessible from the `Experiment` menu in the *CCA-fMRI Toolbox* main window.

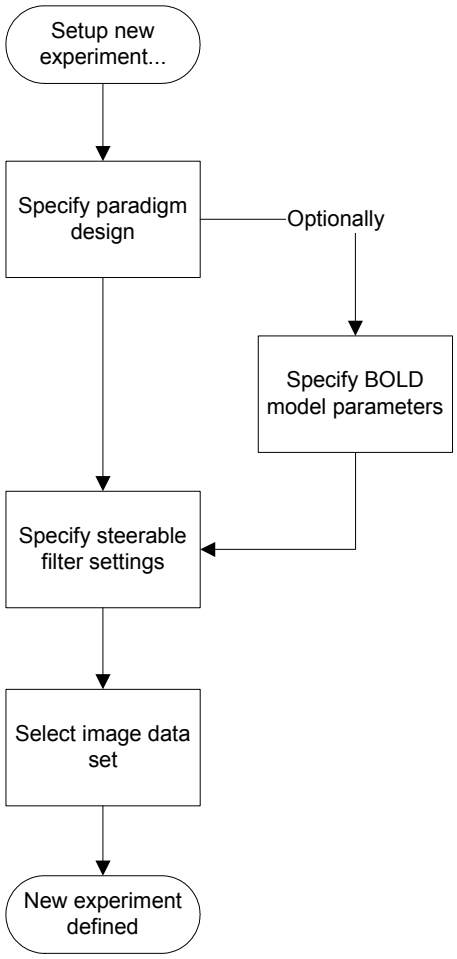


The paradigm design specifies at what time points and for how long the subject is exposed to stimuli. The response model describes how the expected BOLD response, resulting from the stimuli, should look like. The steerable filter settings give the shape and size of the adaptive low pass filters used during the data analysis and the data set points out which image files to analyze.

The Experiment menu

Setup new experiment…

This menu item takes you through all the steps necessary to setup a new experiment, i.e. the paradigm design, the response model (BOLD) settings, the filter settings and the image data file selection. The setup workflow is as follows:

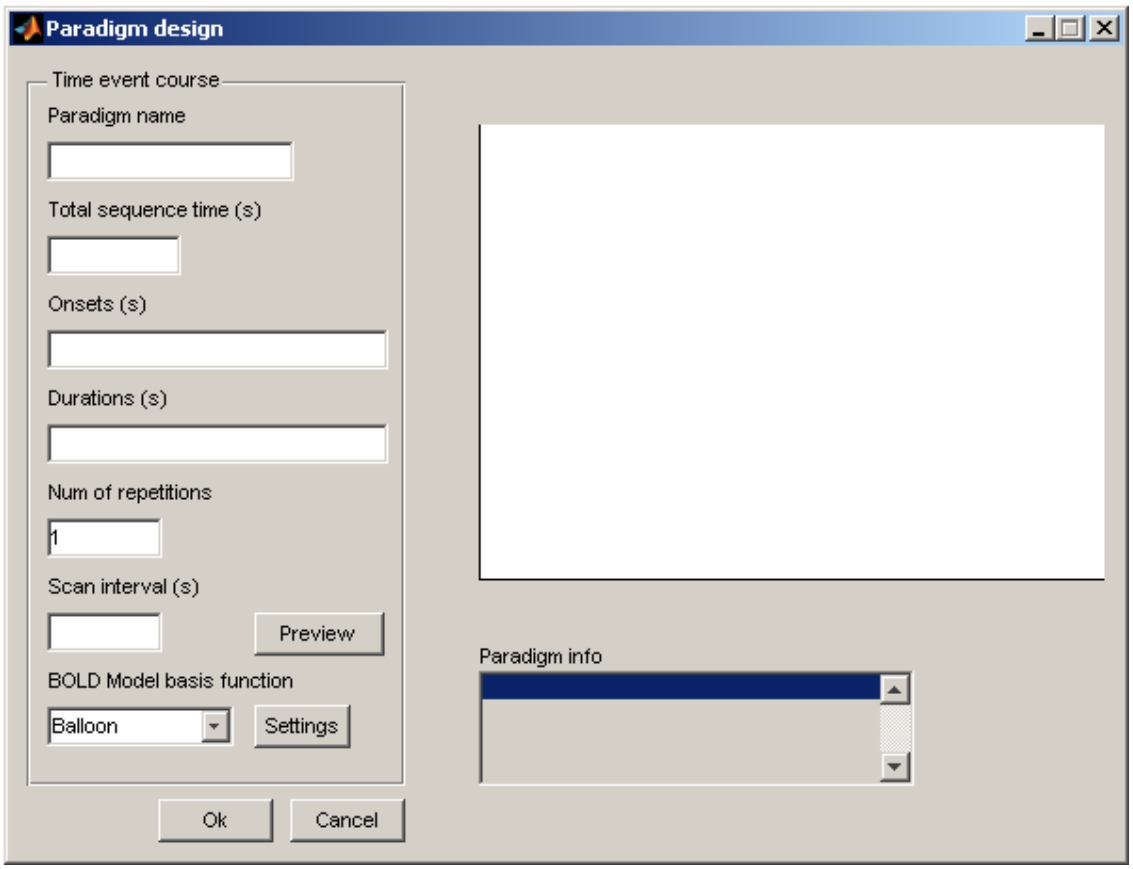


Setting up a new experiment this way is entirely transactional, meaning that the user has to respond `Ok` to all the dialog boxes that appear during the setup procedure. If the user selects `Cancel`, i.e. click the `Cancel`-button, in any of the steps above, none of the settings are saved and any previously specified experiment and results are still intact.

The separate settings are also available under their corresponding menu headline in the `Experiment` menu. Consequently, an experiment can also be setup in a more manual fashion by accessing the menu items `Paradigm design...`, `Response model settings`, `Steerable filters` and `Image set...`. Please see below for more information about how to use the separate settings dialog boxes.

Paradigm design…

The paradigm design outlines at what times and for how long the CCA-fMRI data analysis should look for activity, i.e. BOLD responses, in the fMRI data.



On the left side of the dialog box the paradigm properties are entered and the right side shows how the paradigm looks as well as some basic information about it. The paradigm parameters are:

`Paradigm name` – Any name you want to give the paradigm.

`Total sequence time` – The total time of the paradigm in integer seconds.

`Onsets` – The time points at which stimuli are presented to the subject investigated. `Onsets` are specified in integer seconds and the different time points are separated by space when entered in the field.

`Durations` – The length of the stimulation period beginning at the corresponding `Onset` time points. `Durations` are specified in integer seconds and the different time periods are separated by space when entered in the field.

`Num of repetitions` – Specifies the number of times the `Onset/Duration` settings should be repeated **within** the total sequence time. As such, the `Onset/Duration` settings may not be repeated beyond the total sequence time.

`Scan interval` – The sampling interval at which fMRI image volumes are recorded by the MR scanner. `Scan interval` is given in decimal seconds.

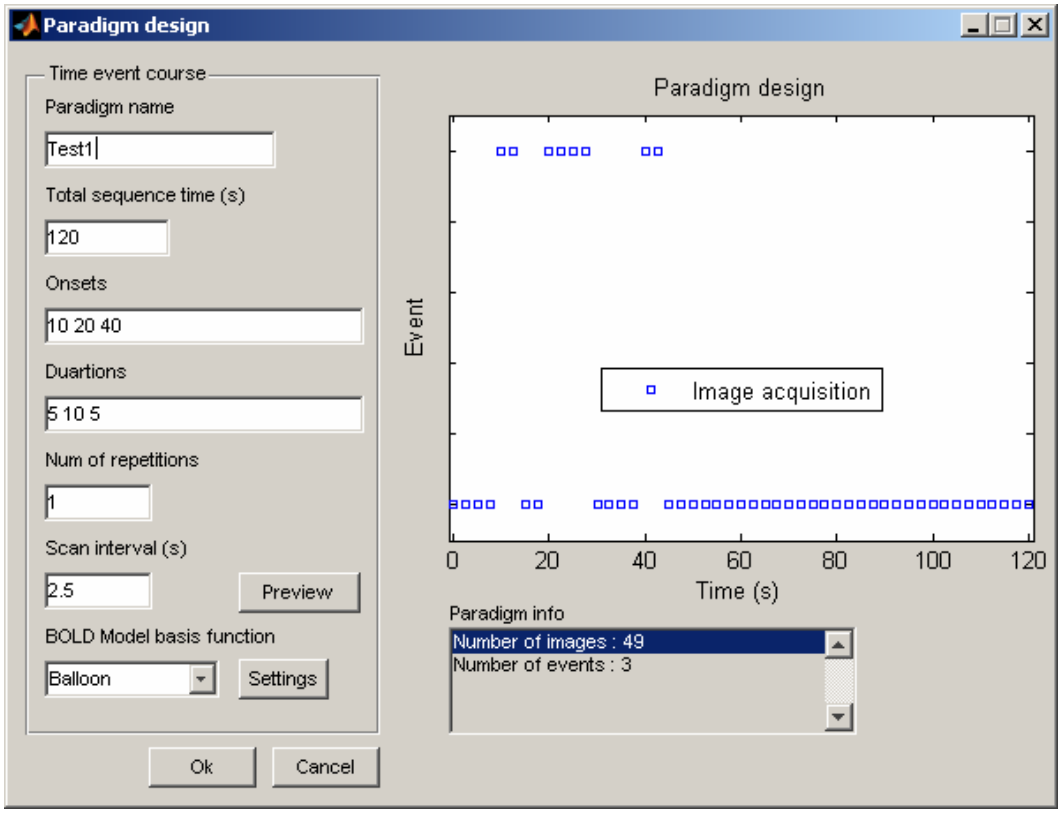
`BOLD Model basis function` – Specifies what mathematical model should be used to approximate the BOLD response. The two options are the *Balloon model* and the *Differential gamma model*. Default model selection is the *Balloon model*.

The dialog box also has four buttons. Besides the standard `Ok/Cancel`-buttons, there is also a `Preview`-button for plotting the resulting paradigm design and a `Setting`-button that allows direct access to the dialog boxes for adjusting the parameters of the selected BOLD model basis function. Please see menu item `Response model settings` for more information.

Examples

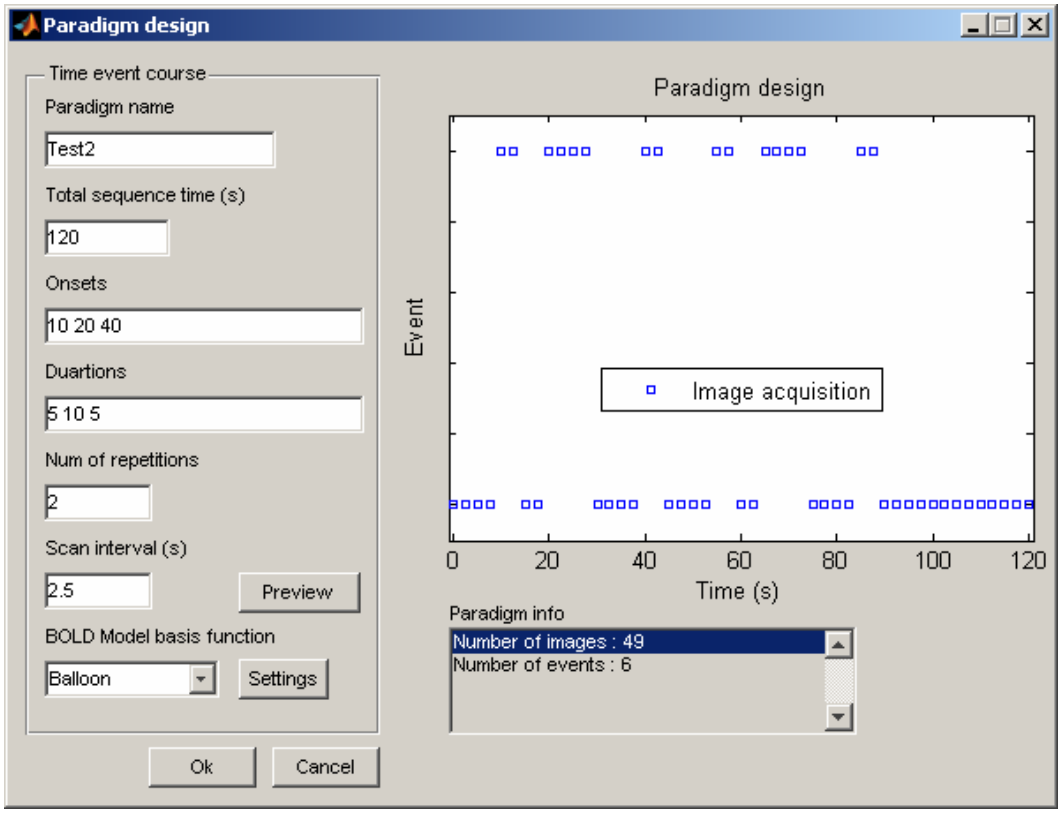
Example 1.

The total sequence time is 120 seconds. Three events occur at 10 s, 20 s and 40 seconds respectively (onsets). The duration of the first event is 5 seconds, the duration of the second event is 10 seconds and the duration of the final event is 5 seconds. The MR-scanner samples a new image volume every 2.5th second. The paradigm is entered in the dialog box the following way:



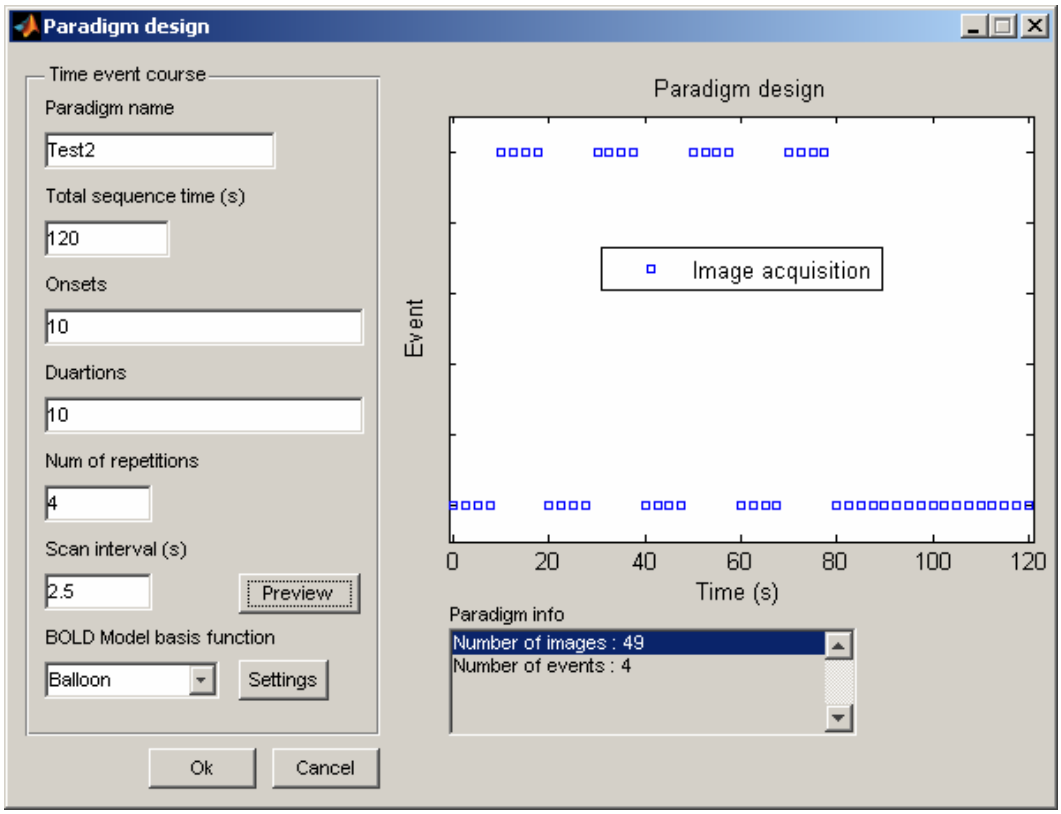
Onsets are entered after each other separated by a space character, as are the corresponding durations. Click the `Preview`-button to plot the sampling points.

Example 2.
In this example almost all parameters are the same as in Example 1 with the notable exception of the `Num of repetitions`. This time we would like to repeat the `Onset/Duration` sequence owing to repetitive patterns of stimuli presentations. By setting `Num of repetitions` to 2 the Onset/Duration sequence will be repeated one time directly after the last data point of the last stimuli event, ending at 45 seconds (Onset 40 s + Duration 5 s = 45 seconds).



Again, click the `Preview`-button to plot the new paradigm. The limitation of the `Num of repetitions`-parameter is that the `Onset/Duration` sequence can't be repeated beyond the `Total sequence time`-setting.

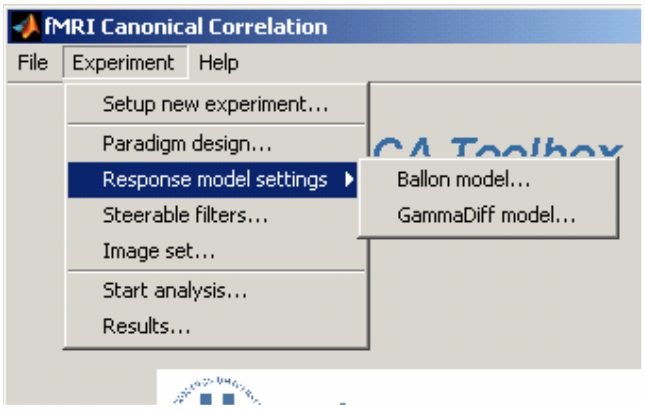
Example 3
A consequence of having the possibility to repeat the sequence of events, the setting `Onset` = [10 30 50 70] and `Duration` = [10 10 10 10] can also be defined as `Onset`=10 s, `Duration`=10 s and `Num of repetitions`=4 :



Response model settings

The response model describes the expected BOLD response for a given paradigm. In other words, the model is considered to be the approximate true activation pattern for any subject exposed to the stimuli paradigm used in the experiment. The level of activation in a brain voxel is, simplified, determined by comparing the temporal intensity change of the voxel with the intensity change of the response model. High correlation means high level of activation and vice versa. This comparison is performed for each voxel in the sample data.

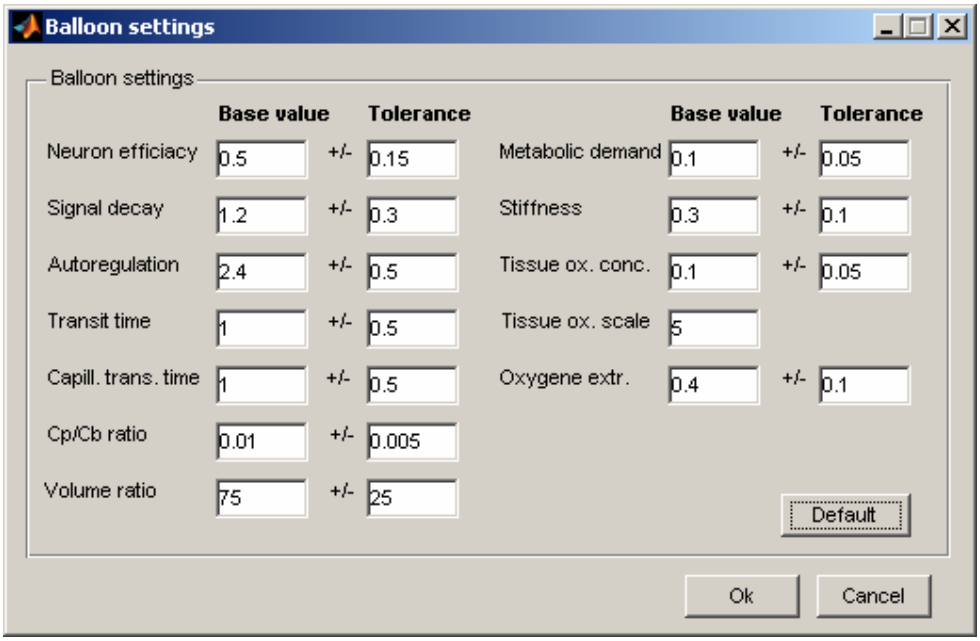
There are two different BOLD basis functions available in the toolbox; the *Balloon* model and the Differential Gamma model, also called *GammaDiff* in the toolbox. Of the two, the *Balloon* model is considered more accurate but also somewhat more demanding for the computer to generate. For a fairly up to date computer there is little incentive not to use the *Balloon* model.



The two models have their own sets of adjustable parameters, accessible from the `Response model settings` menu. Disregarding what basis function is used, the BOLD model is generated in the same way. First, 500 plausible response curves are generated by randomizing the values of corresponding parameters. To assure plausible curves the parameters are only allowed random variations within a specific tolerance interval. The 500 plausible responses are then reduced, by principal component analysis, to a compressed format, which is also the expected BOLD response used in the subsequent data analysis.

Balloon model settings

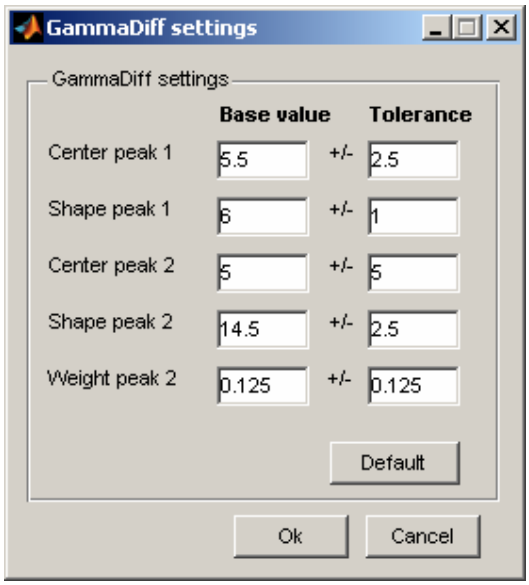
The *Balloon* model is a fairly complicated model having a number of adjustable parameters corresponding to, among other things, properties of an expanding blood vessel forming a local balloon of oxygenated blood. The model, and its parameters, is explained in references [2] and [6].



The default parameter settings are adequate in most cases and have been compiled from data in references [2], [6] and [9].

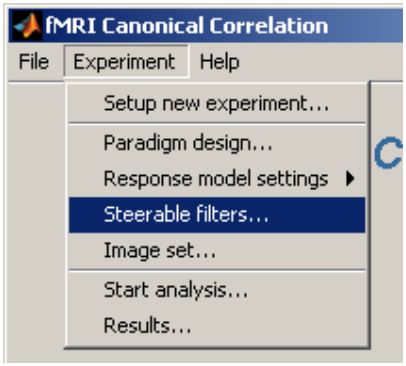
GammaDiff model settings

The *GammaDiff* model is a simpler model and uses the difference of two Gamma functions to model the BOLD response. The default settings are adequate for most cases and have been compiled from data in reference [5].

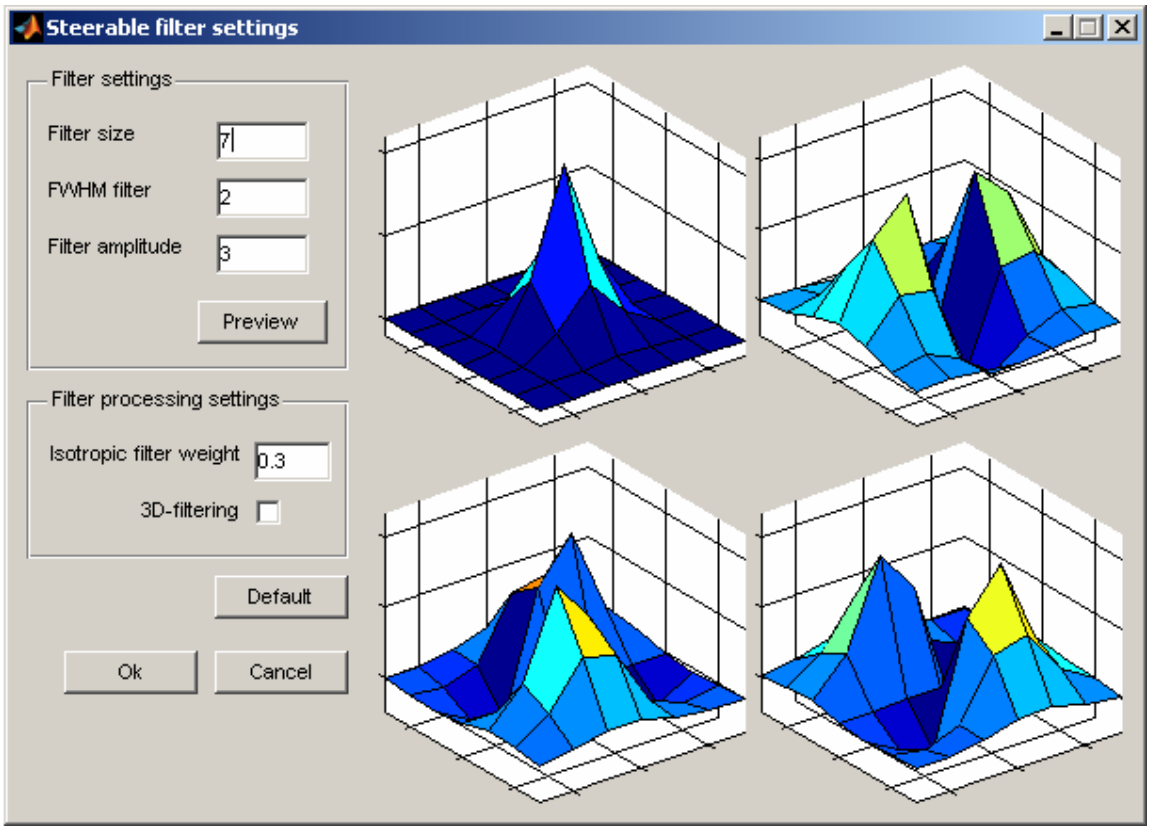


Steerable filters…

A steerable filter, or adaptive filter, is a special set of spatial low pass filter kernels that can be combined and optimized in accordance with the nature of the data on which they are applied. The *CCA-fMRI Toolbox* utilizes these properties by only applying filter configurations that are favorable to the CCA-fMRI analysis.



From the perspective of the *CCA-fMRI Toolbox* user they have similar set of parameters as ordinary low pass filters, e.g. filter matrix size and FWHM (Full Width Half Maximum).



In the left side of the dialog box the filter and processing parameters are set and the right side shows previews of the filter kernel shapes. The filter kernel views are updated by clicking on the `Preview`-button using the currently entered values.

NOTE
Even when selecting 3-dimensional analysis the filter kernels will still be drawn as 2-dimensional kernels in the previews.

Filter settings

The filter parameters are:

> `Filter size` – The size of the adaptive filter given as the number of pixels (or voxels) of one side if the filter kernel. The filter size is symmetric in all directions forming a squared matrix or cube depending on whether 2-dimensional or 3-dimensional analysis should be performed. Only odd sizes are allowed.
>
> `FWHM filter` – The full width half maximum of the filter kernels expressed as number of pixels. This is the same as the effective width of the filter.
>
> `Filter amplitude` – The amplitude of the final filter.

Large settings for `FilterSize` and `FWHM filter` tend to favor large regions of activation and suppress small. Small settings allow small regions of activation to remain but also increase the spatial noise level.

Filter processing settings

The filter processing parameters defines how the adaptive filter is applied during the data analysis phase. The parameters are:

> `Isotropic filter weight` – Defines the importance of the center voxel during filtering. Weight 0.0 means that the center voxel is given no special importance, i.e. only anisotropic filtering, and weight 1.0 gives the center voxel the same importance as the anisotropic filter.
>
> `3D-filtering` – Enables 3-dimensional filtering. When unchecked, 2-dimensional filtering is used.

Using 3-dimensional filtering is the preferred setting since that would take into account the entire 3-dimensional neighborhood. 2-dimensional only takes into account the neighborhood in the X/Y-plane, which typically is the horizontal plane through the brain.

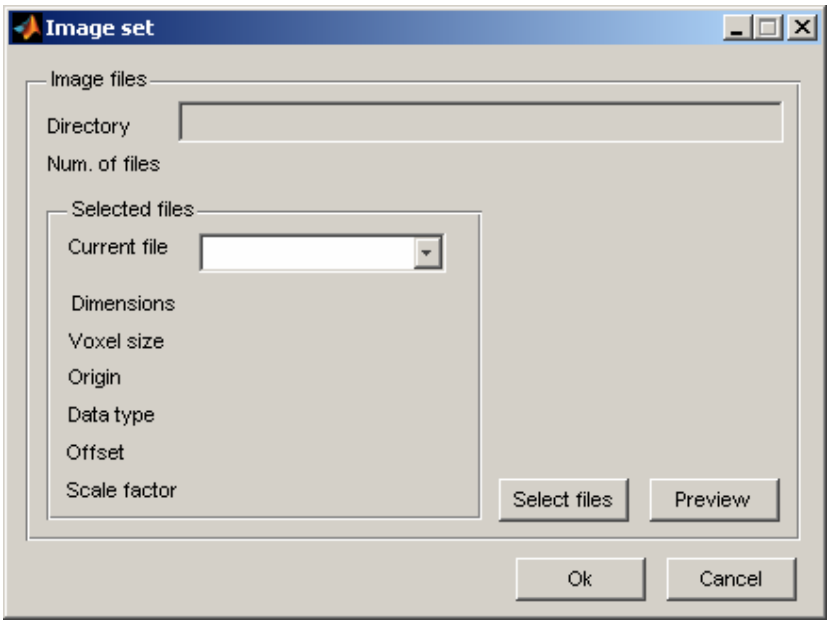
The drawback of using 3-dimensional filtering is that the complexity of the fMRI analysis grows exponentially meaning significantly longer processing time, compared to 2-D filtering. On a fairly modern computer a 2-dimensional analysis would take 5-

10 minutes. The same analysis performed in 3 dimensions would take from 40 minutes up to an hour.

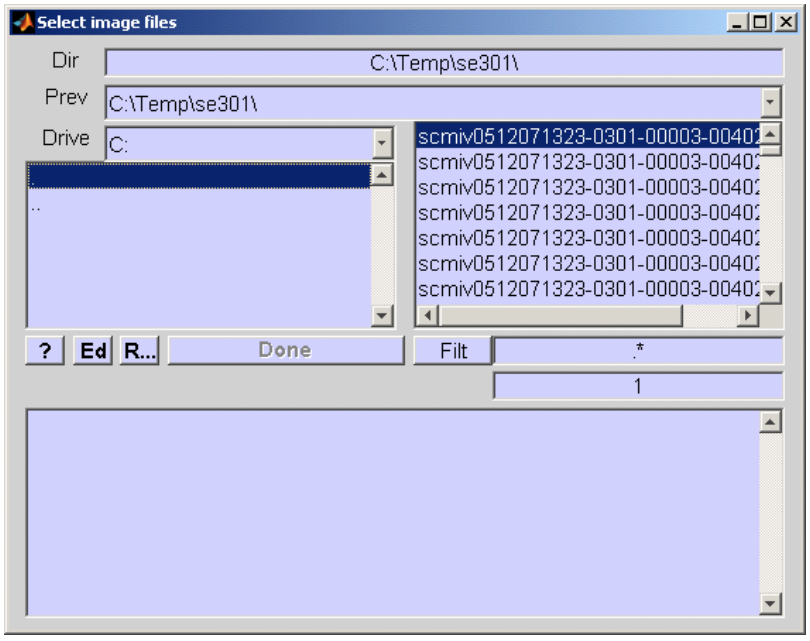
NOTE
The most important factor for maximizing the 3-D performance is to have a lot of random access memory (RAM). The analysis generates between 1 and 2 GB of temporary data. Large amount of RAM prevents data from being written to disk during the analysis, hence increasing performance. See *Requirements* for more information regarding the recommended hardware platform.

Image set …

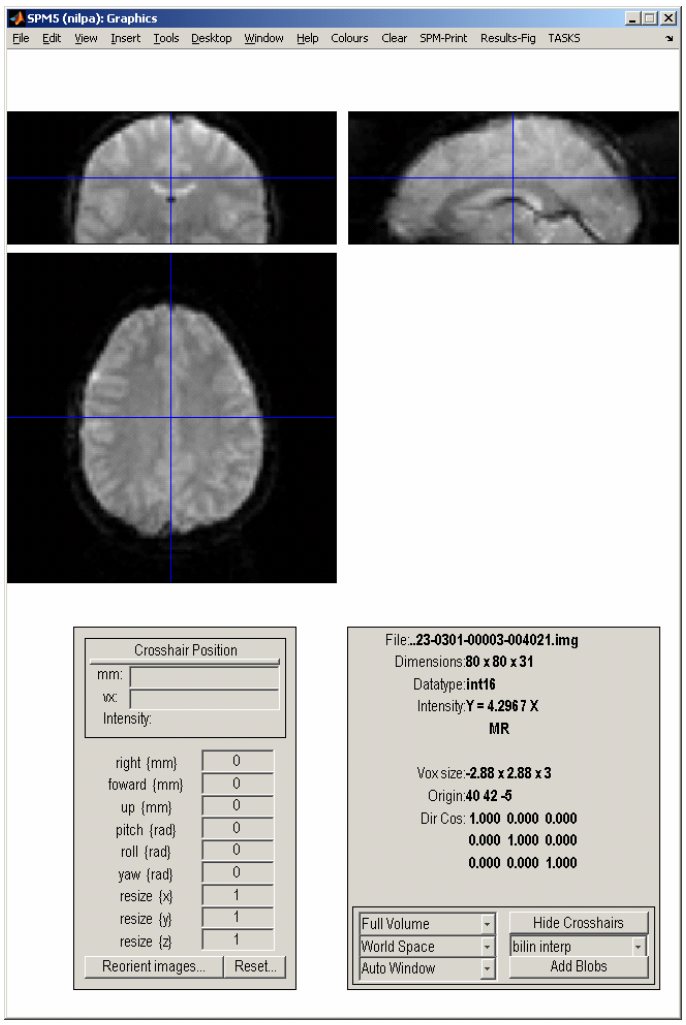
The `Image set` window is used for selecting the image set to be analyzed by the *CCA-fMRI Toolbox*. The data set is defined by clicking on the `Select files` button.



The CCA-fMRI Toolbox uses the standard SPM file dialog box to select the image set. In case the images have been preprocessed be sure to select the image files having the correct name prefix.

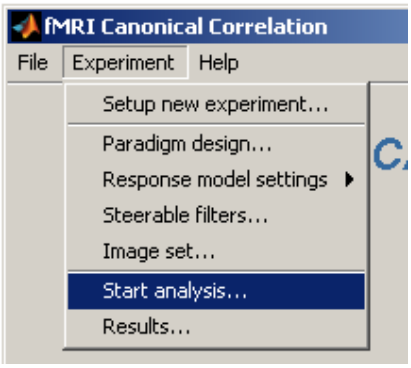


Information about separate image files in the set, selectable from the drop down list `Current file`, is displayed in the panel. The currently selected image can also be viewed using the `Preview`-button.

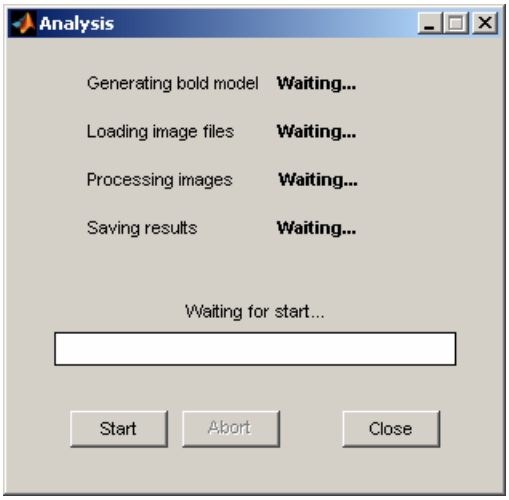


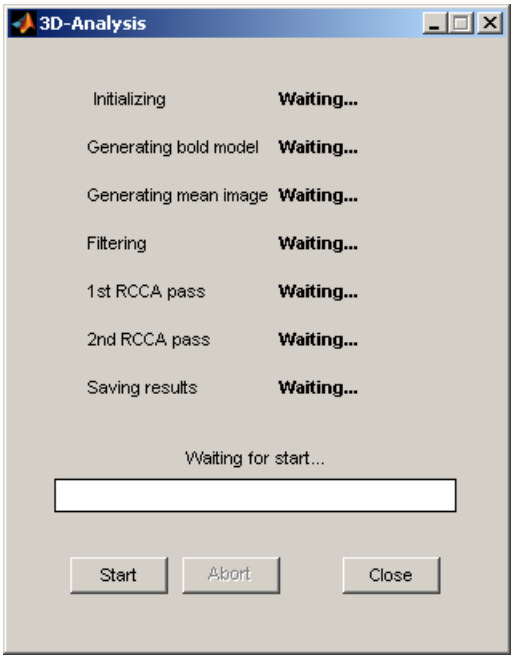
8. Data analysis

The data analysis is an automated process with little need for manual intervention. Depending on whether 2-dimensional or 3-dimensional analysis has been chosen one of the dialog boxes below will be opened.



Besides the `Start`-button, which commences the analysis process, there is also an `Abort`-button for interrupting an analysis in progress and a progress bar showing the progress of each separate phase.





2-Dimensional analysis ***3-Dimensional analysis***

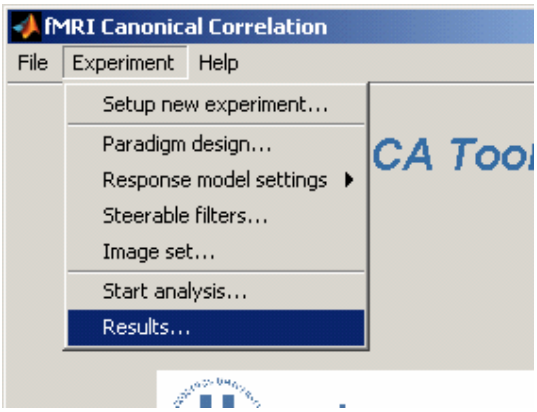
The analysis is divided into separate phases, shown in the dialog boxes above. The phases are listed in the order of execution and each phase has a status displayed to the right. The valid statuses are `Waiting...`, `Working...`, `Done` and `Aborted`. The toolbox keeps track of these statuses meaning that when a previously aborted analysis

is restarted only the phases not yet finished, i.e. not having the `Done`-status, will be reprocessed. Some parts of the analysis process may be reprocessed in cases when experiment settings influencing the phase have been changed. Which phases to reprocess is entirely handled by the *CCA-fMRI Toolbox*. Once the analysis has finished the result is reachable from the `Results…` dialog box. The results are also stored in two standard SPM image files in the same directory as the original image file sets analyzed. The two images are named `CorrelationMap_#TIMESTAMP#` and `MeanVolume_#TIMESTAMP#`, where `#TIMESTAMP#` is on the format MMM-DD-HH-MM-SS, e.g. `CorrelationMap_Jan-15_14-27-23.img` (or `.hdr`).

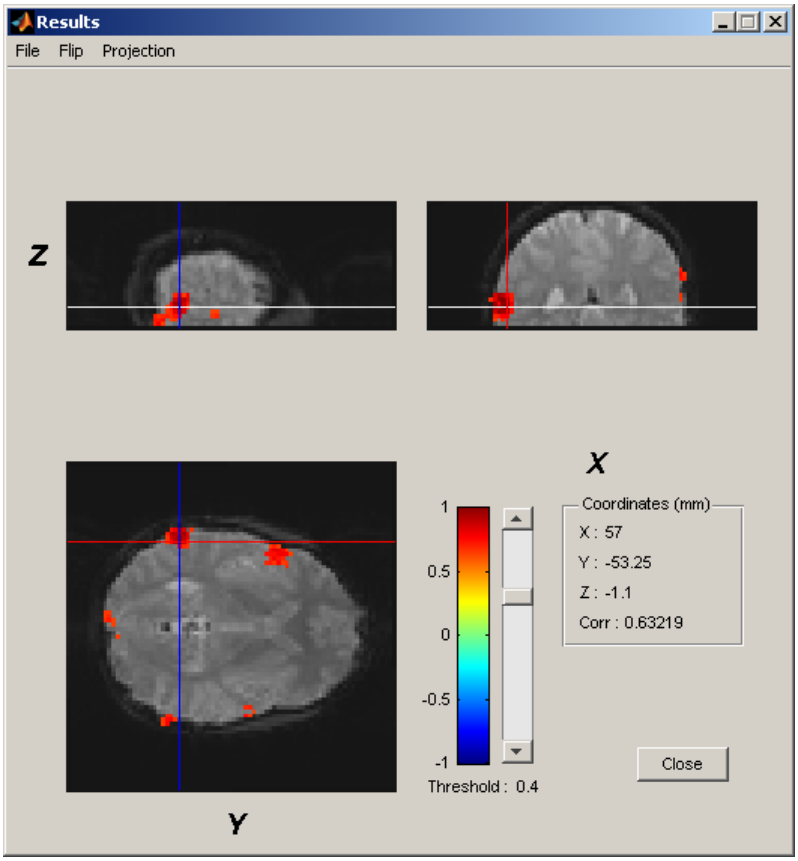
NOTE
When aborting an analysis the toolbox usually takes a while before actually aborting. The reason is that owing to limitations in Matlab® the abort of the analysis has to be synchronized with an update of the horizontal progress bar which only happen a limited number of times during each phase. The toolbox will, however, in time abort the analysis process.

9. Results

The `Results...` menu provide basic functionality for displaying, printing and saving the analysis results from the current experiment.



The `Results` dialog box displays the correlation as color coded levels superimposed on a background image of the brain analyzed. The brain is segmented along the X-, Y- and Z- dimensions forming 3 image segments. The lower left image is the Y/X-segment, the upper left is the Y/Z-segment and the right is the X/Z-segment.

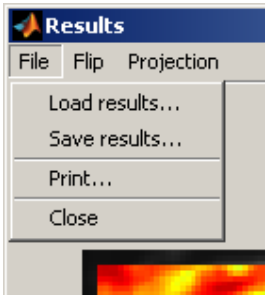


The background image is the mean image of the entire image set. The projection honors reorientation and other preprocessing procedures applied in advance of the canonical correlation analysis.

In the lower right corner information about the current voxel is displayed, i.e. voxel coordinate in millimeters as well as its corresponding correlation coefficient. The current voxel is selected using the mouse to select and clicking in one of the three projections. The voxel information and hair cross are updated accordingly. The vertical slider is used to manually determines the smallest correlation threshold value for which correlation should be superimposed on the background image.

The File Menu

In the `File` menu current results can be saved to disk and already saved results can be loaded and displayed.



Load results…

Loads and displays the results from a Matlab® data file previously saved using `Save results...` Results from a current experiment setup is **not** erased by this. The next time the `Results` window is opened existing results from an ongoing experiment is re-displayed.

Save results…

Saves the currently displayed results in a Matlab® data file. The format of the data saved is a Matlab® structure (`Results`) having the following structure and fields:

```
Results
        SPM: [1x1 struct]
        xSPM: [1x1 struct]
        CorrelationMapFile: [1x1 struct]
        CorrelationMap: [COLxROWxDEPTH single]
        MeanImageFile: [1x1 struct]
        MeanImageVolume: [COLxROWxDEPTH single]
```

`Results.SPM` is the `SPM` structure associated with the correlation map. Please see the SPM documentation for more information.

`Results.xSPM` is the `xSPM` structure associated with the correlation map. Please see the SPM documentation for more information.

`Results.CorrelationMapFile` is the `SPM` file header structure pointing to the file where the correlation map is stored externally. The file is a standard SPM image file.

`Results.CorrelationMap` is the resulting 3-dimensional correlation map calculated during the analysis step organized as a 3-dimensional Matlab® matrix.

`Results.MeanImageFile` is the SPM file header structure pointing to the file where the mean image of all the image volumes in the set is stored externally. The file is a standard SPM image file.

`Results.MeanImage` is the resulting 3-dimensional mean image calculated during the analysis step organized as a 3-dimensional Matlab® matrix.

Print…

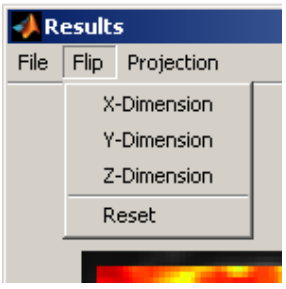
Prints a copy of the currently displayed results.

Close

Closes the results dialog box and returns to the main window.

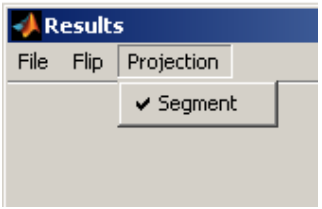
The Flip Menu

The `Flip` menu provides the ability to flip the dimensions of the displayed projections 180 degrees. The `Reset` menu item resets the dimensions to default orientation.



The Projection Menu

The `Projection` menu allows to change between various ways of displaying the results. Currently only segmented projection is supported.



10. Scripting

Great efforts have been made to keep the graphical user interface separated from the actual image processing modules. As a consequence it is straight forward to use the *CCA-fMRI Toolbox*, and its modules, in Matlab®. An advantage of running the toolbox in script mode is that repetitive tasks for large analysis series can be automated. Script mode also reduce the memory footprint significantly, thereby allowing larger datasets to be analyzed than is the case when using the graphical user interface.

Below are two examples of how to use the toolbox in scripts. The first example is a 2-dimensional analysis and the second example is a 3-dimensional analysis. The two sample scripts are located in the `SampleScripts` folder located within the *CCA-fMRI Toolbox* directory. The wrapper functions are located in the main toolbox directory and have names prefixed by `scr`.

NOTE
Make sure that the path to the sample directory has been added to the Matlab® path before trying to use the samples.

Script for 2-dimensional analysis

The script `Sample2DAnalysis.m` uses analysis wrappers functions, also provided in the toolbox, for the actual processing. Their usage and calling parameters and are described in *Appendix A – Scripting wrapper functions*. The wrapper functions used for 2-dimensional analysis are:

1. `scrCreateHemodynModel()`
2. `scrRCCA()`

```
function [CorrelationMap MeanImageVolume] = Sample2DAnalysis()


   % GET IMAGE VOLUME FILES TO PROCESS
   disp('Getting image files...');

   % Query the user for the files in the data set. The is not the usual way
   % of specifying what files to analyze in a script...
   warning off;
   % ImageFiles = spm_get([],'.img','Select image files',pwd);
   [ImageFiles Cancel] = spm_select([1 Inf], 'image','Select image files', '',pwd);
   spm_Headers = spm_vol(ImageFiles);
   warning on;


   % CREATE HEMODYNAMIC RESPONSE MODEL
   disp('Creating hemodyn model...');

   % Setup parameters for balloon model
   BalloonLimits.NeuronEffBase = 0.5;
   BalloonLimits.NeuronEffMinMax = 0.15;
   BalloonLimits.SigDecayBase = 1.2;
   BalloonLimits.SigDecayMinMax = 0.3;
   BalloonLimits.AutoRegBase = 2.4;
   BalloonLimits.AutoRegMinMax = 0.5;
   BalloonLimits.TransTimeBase = 1;
   BalloonLimits.TransTimeMinMax = 0.5;
   BalloonLimits.CapTransTimeBase = 1.0;
   BalloonLimits.CapTransTimeMinMax = 0.5;
   BalloonLimits.CpbRatioBase = 0.01;
   BalloonLimits.CpbRatioMinMax = 0.005;
   BalloonLimits.VolRatioBase = 75;
```

```
BalloonLimits.VolRatioMinMax = 25;
BalloonLimits.MetabolicBase = 0.1;
BalloonLimits.MetabolicMinMax = 0.05;
BalloonLimits.StiffnessBase = 0.3;
BalloonLimits.StiffnessMinMax = 0.1;
BalloonLimits.TissueOxConcBase = 0.1;
BalloonLimits.TissueOxConcMinMax = 0.05;
BalloonLimits.TOScale = 5;
BalloonLimits.RestExtractBase = 0.4;
BalloonLimits.RestExtractMinMax = 0.1;

% In case default values are appropriate use the following instead
% BalloonLimits = GetDefBalloon();

% Setup the paradigm. The model basis function can also be set to 'Gamma
% diff' in which case the structure GammaDiffLimits should replace
% BalloonLimits below.
ParadigmDesign.ModelBasisFunction = 'Balloon';
ParadigmDesign.Name = 'Test paradigm';
ParadigmDesign.TotalSequenceTime = 360;
ParadigmDesign.NumberOfRepetitions = 1;
ParadigmDesign.SamplingInterval = 2.7;
Onsets = [40 120 200 280];
Durations = [40 40 40 40];
ParadigmDesign.RelaxStimEvents = Compatibility('OnsetDuration2EventTime', Onsets, Durations);
HemoDynRespModel = scrCreateHemodynModel(ParadigmDesign, BalloonLimits);


% LOAD IMAGE DATA SET

% Check that the number of files is equal to the number of expected data
% points in the paradigm
NumberOfFiles = size(spm_Headers,1);
SampleCount = size(HemoDynRespModel,1);
if (NumberOfFiles > SampleCount)

   % Adjust the number of images
   disp ('Clipping trailing image files');
   spm_Headers = spm_Headers(1:SampleCount);
elseif (NumberOfFiles < SampleCount);

   % Not enough image files
   disp ('Not enough image files');
```

```
   return;
end;

% Init image storage
disp ('Initiating image storage...');
MemFileName = 'c:\temp\memfile.dat';
ImageStorage = InitImageFileStorage(MemFileName, spm_Headers);

% Load images into memory mapped file
disp ('Loading images...');
LoadImageFiles(spm_Headers, ImageStorage, 0);


% GET MEAN IMAGE AND BRAIN SEGMENTATION MASK OF ORIGINAL IMAGE VOLUMES
disp('Calculating mean image...');

% Calculate the mean image volume
[MeanImageVolume SegMask] = scrCalcMeanImage(spm_Headers);


% SETUP FILTERS
disp('Setting up filters...');
FilterSettings.FilterSize = 7;
FilterSettings.FWHMLowPass = 5;
FilterSettings.FWHMFilter = 2;
FilterSettings.IsoFilterWeight = 0.3;
FilterSettings.Filter3D = false;


% PROCESS THE IMAGE DATA
disp('Processing images...');
CorrelationMap = scrRCCA(HemoDynRespModel, FilterSettings, ImageStorage, SegMask);


% FINISH UP
disp ('Saving results...');

% Put together the results. Warning is disabled to prevent numerous
% "Warning: Cant get default Analyze orientation - assuming
% flipped" -messages in case SPM isn't currently running.
warning off;
Results = GenerateResults(ParadigmDesign, spm_Headers, CorrelationMap, MeanImageVolume, SegMask);
warning on;
```

```
% Save the results to a file that is readable by the CCA-fMRI toolbox's
% Results window.
ResultsFileName = 'c:\temp\Results2D.mat';
save (ResultsFileName, 'Results');

% Done
disp('Done!!!');
```

Script for 3-dimensional analysis

The script `Sample3DAnalysis.m` uses analysis wrapper functions, also provided in the toolbox, for the actual processing. Their usage and calling parameters are described in *Appendix A – Scripting wrapper functions*. The wrapper functions 3-dimensionala analysis are:

3. `scrCreateHemodynModel()`
4. `scrFilterVolumes()`
5. `scrCalcMeanImage()`
6. `scrRCCAPass1()`
7. `scrRCCAPass2()`

```
function [CorrelationMap MeanImageVolume] = Sample3DAnalysis()

   % GET IMAGE VOLUME FILES TO PROCESS
   disp('Get image files...');

   % Query the user for the files in the data set. The is not the usual way
   % of specifying what files to analyze in a script.
   warning off;
   ImageFiles = spm_get([],'.img','Select image files',pwd);
   spm_Headers = spm_vol(ImageFiles);
   warning on;


   % CREATE HEMODYNAMIC RESPONSE MODEL
   disp('Create hemodyn model...');

   % Setup parameters for balloon model
   BalloonLimits.NeuronEffBase = 0.5;
   BalloonLimits.NeuronEffMinMax = 0.15;
   BalloonLimits.SigDecayBase = 1.2;
   BalloonLimits.SigDecayMinMax = 0.3;
   BalloonLimits.AutoRegBase = 2.4;
   BalloonLimits.AutoRegMinMax = 0.5;
   BalloonLimits.TransTimeBase = 1;
   BalloonLimits.TransTimeMinMax = 0.5;
   BalloonLimits.CapTransTimeBase = 1.0;
   BalloonLimits.CapTransTimeMinMax = 0.5;
```

```
BalloonLimits.CpbRatioBase = 0.01;
BalloonLimits.CpbRatioMinMax = 0.005;
BalloonLimits.VolRatioBase = 75;
BalloonLimits.VolRatioMinMax = 25;
BalloonLimits.MetabolicBase = 0.1;
BalloonLimits.MetabolicMinMax = 0.05;
BalloonLimits.StiffnessBase = 0.3;
BalloonLimits.StiffnessMinMax = 0.1;
BalloonLimits.TissueOxConcBase = 0.1;
BalloonLimits.TissueOxConcMinMax = 0.05;
BalloonLimits.TOScale = 5;
BalloonLimits.RestExtractBase = 0.4;
BalloonLimits.RestExtractMinMax = 0.1;

% In case default values are appropriate use the following instead
% BalloonLimits = GetDefBalloon();

% Setup the paradigm
ParadigmDesign.TotalSequenceTime = 360;
Onsets = [40 120 200 280];
Durations = [40 40 40 40];
ParadigmDesign.RelaxStimEvents = Compatibility('OnsetDuration2EventTime', Onsets, Durations);
ParadigmDesign.NumberOfRepetitions = 1;
ParadigmDesign.SamplingInterval = 2.7;
HemoDynRespModel = scrCreateHemodynModel(ParadigmDesign, BalloonLimits);


% SETUP FILTERS
disp('Setup filters...');
FilterSettings.FilterSize = 7;
FilterSettings.FWHMLowPass = 5;
FilterSettings.FWHMFilter = 2;
FilterSettings.IsoFilterWeight = 0.3;
FilterSettings.Filter3D = true;

% Create the 3D-filters
[IsoFilt AnisoFilt_1 AnisoFilt_2 AnisoFilt_3 AnisoFilt_4 AnisoFilt_5 AnisoFilt_6] = GetFilters3D(FilterSettings);
Filters3D = {IsoFilt AnisoFilt_1 AnisoFilt_2 AnisoFilt_3 AnisoFilt_4 AnisoFilt_5 AnisoFilt_6};


% SETUP TEMPORARY STORAGE
disp('Setup temporary storage...');
```

```
% Specify names of temporary storage used during the processing
FilteredFileName = 'C:\temp\memmapfile1.dat';
RCCAFileName = 'C:\temp\memmapfile2.dat';

% Setup the temporary files (memory mapped files)
VolumeSize = spm_Headers(1).dim(1:3);
VolumeCount = size(spm_Headers,1);
[FilteredStorage RCCAStorage] = InitImageFileStorage3D(VolumeSize, VolumeCount, FilteredFileName, RCCAFileName);


% GET MEAN IMAGE AND BRAIN SEGMENTATION MASK OF ORIGINAL IMAGE VOLUMES
disp('Calculate mean image...');

% Calculate the mean image volume
[MeanImageVolume SegMask] = scrCalcMeanImage(spm_Headers);


% FILTER VOLUMES
disp('Filter image volumes...');

% Filter all volumes with all filters
scrFilterVolumes(spm_Headers, Filters3D, FilteredStorage, RCCAStorage);

% Clean up
clear Filters3D;
clear FilteredStorage;


% RUN 1ST RCCA PASS
disp('1st RCCA pass...');

% Perform 1st RCCA pass reusing the temporary file used during the
% filtering step as output file
SizeRCCAArray = scrRCCAPass1(HemoDynRespModel, FilterSettings.IsoFilterWeight, ...
   RCCAStorage, FilteredFileName, VolumeCount, VolumeSize, SegMask);
clear RCCAStorage;


% RUN 2ND RCCA PASS
disp('2nd RCCA pass...');

% Perform 2nd RCCA pass using the input file from the 1st pass
CorrelationMap = scrRCCAPass2(HemoDynRespModel, FilteredFileName, SizeRCCAArray, VolumeSize, SegMask);
```

```
% FINISH UP
disp ('Saving results...');

% Put together the results. Warning is disabled to prevent numerous
% "Warning: Cant get default Analyze orientation - assuming
% flipped"-messages in case SPM isn't currently running
warning off;
Results = GenerateResults(ParadigmDesign, spm_Headers, CorrelationMap, MeanImageVolume, SegMask);
warning on;

% Save the results to a file that is readable by the CCA-fMRI toolbox's
% Results window.
ResultsFileName = 'c:\temp\scrResults3D.mat';
save (ResultsFileName, 'Results');

% Done
disp('Done!!!');
```

11. Appendix A – Scripting wrapper functions

scrCreateHemodynModel()

Definition

```
[HemoDynRespModel] = scrCreateHemodynModel(ParadigmDesign,
BalloonLimits)
```

Description

Creates a hemodynamic response model based on the settings of `ParadigmDesign`. The model is returned in `HemoDynRespModel`. The `ParadigmDesign` parameter has the following fields:

```
ParadigmDesign.TotalSequenceTime;
ParadigmDesign.RelaxStimEvents;
ParadigmDesign.NumberOfRepetitions;
ParadigmDesign.SamplingInterval;
```

The hemodynamic model created is based on the balloon model using the parameters specified in the `BalloonLimits` structure having the following fields:

```
BalloonLimits.NeuronEffBase;
BalloonLimits.NeuronEffMinMax;
BalloonLimits.SigDecayBase;
BalloonLimits.SigDecayMinMax;
BalloonLimits.AutoRegBase;
BalloonLimits.AutoRegMinMax;
BalloonLimits.TransTimeBase;
BalloonLimits.TransTimeMinMax;
BalloonLimits.CapTransTimeBase;
BalloonLimits.CapTransTimeMinMax;
BalloonLimits.CpbRatioBase;
BalloonLimits.CpbRatioMinMax;
BalloonLimits.VolRatioBase;
BalloonLimits.VolRatioMinMax;
BalloonLimits.MetabolicBase;
BalloonLimits.MetabolicMinMax;
BalloonLimits.StiffnessBase;
BalloonLimits.StiffnessMinMax;
BalloonLimits.TissueOxConcBase;
BalloonLimits.TissueOxConcMinMax;
BalloonLimits.TOScale;
BalloonLimits.RestExtractBase;
BalloonLimits.RestExtractMinMax
```

See Also

```
ValidateDesign.m
ValidateBalloonLimits.m
```

scrFilterVolumes()

Definition

```
scrFilterVolumes(spm_Headers, Filters3D, FilteredStorage,
RCCAStorage)
```

Description

Applies the 3-dimensional filter kernels `Filters3D` to the image volumes defined by `spm_Headers`. `scrFilterVolumes`() uses the memory mapped file `FilteredStorage` for intermediate storage. After the filtering has been performed the final results are rearranged and copied to the memory mapped file `RCCAStorage`, which is used by the subsequent canonical correlation analysis.

`spm_Headers` is a standard SPM image file header vector. `Filters3D` is a cell array holding the different filter kernels that should be applied to the image volumes. `FilteredStorage` and `RCCAStorage` are structures of the type `ImageStorage` having the following fields:

```
ImageStorage.TotalSize
ImageStorage.TotNumOfObjects
ImageStorage.ObjectSize
ImageStorage.CurrentObjectIndex
ImageStorage.RepeatValue
ImageStorage.MemFileHandle
ImageStorage.MemFileHandle.data[].Object
ImageStorage.MemFileHandle.format
ImageStorage.MemFileHandle.offset
ImageStorage.MemFileHandle.repeat
ImageStorage.MemFileHandle.writable
```

See Also

```
InitImageFileStorage3D.m
GetFilters3D.m
Filter3D.m
spm_get()
spm_vol()
```

scrCalcMeanImage()

Definition

```
[MeanImageVol SegMask] = scrCalcMeanImage(spm_Headers)
```

Description

Calculates the mean image volume and the brain segmentation mask for the image files specified by `spm_Headers`. The resulting mean image is returned as a standard Matlab® matrix in `MeanImageVol` and the segmentation mask is returned as a logical matrix in `SegMask`. The `spm_Headers` is the same headers as returned by e.g. `spm_vol()`.

See Also

scrRCCA()

Definition

```
[CorrelationMap MeanImageVolume] = scrRCCA(HemoDynRespModel,
FilterSettings, ImageStorage, Segmask)
```

Description

Performs a 2-dimensional correlation analysis and returns the correlation map in `CorrelationMap` and the mean image in `MeanImageVolume`.

`HemoDynRespModel` is the hemodynamic response model to which the MRI-data should be compared. `FilterSettings` specifies the size and shape of the steerable filters and have the following fields:

```
FilterSettings.FilterSize;
FilterSettings.FWHMLowPass;
FilterSettings.FWHMFilter;
FilterSettings.IsoFilterWeight;
FilterSettings.Filter3D;
```

`ImageStorage` specifies the memory mapped file into which the images to analyzed have been loaded and `SegMask` is the brain segmentation mask as returned by `scrCalcMeanImage()`.

See Also

`ValidateSteerableFilter.m`
`InitImageFileStorage.m`
`LoadImageFiles.m`

scrRCCAPass1()

Definition

```
[SizeRCCAArray] = scrRCCAPass1(HemoDynRespModel,
IsoFilterWeight, RCCAStorage, OutputFileName, VolumeCount,
ValidVolumeSize, SegMask)
```

Description

Performs the first phase of the 3-dimensional canonical correlation analysis and returns the size of the output data from phase 1 in `SizeRCCAArray`.

`HemoDynRespModel` is the hemodynamic response model to which the MRI-data should be compared. `IsoFilterWeight` specifies the amount of isotropic filtering to add to the anisotropic filtered images (see headline *Steerable Filters…* for more information about this parameters). `RCCAStorage` is the very same memory mapped file storage used by `scrFilterVolumes`() to store filtered image volumes. `OutputFileName` is the name of a temporary file in which `scrRCCAPass1()` can store intermediate results that subsequently will be processed by the second phase of the canonical correlation analysis. If the file doesn't exists it will be created during the first phase. `VolumeCount` specifies the number of image volumes/files in the original SPM data file set, i.e. `size(spm_Headers,1)`. `ValidVolumeSize` specifies the size of the volumes that are valid after filtering. The valid volume size can be calculated the following way using the first image data file in the set to get the original image size:

```
SkipVoxels = fix(FilterSettings.FilterSize/2);
ValidVolumeSize = spm_Headers(1).dim(1:3) - SkipVoxels * 2;
```

`SegMask` is the brain segmentation mask as returned by `scrCalcMeanImage()`.

See Also

`spm_get()`
`spm_vol()`
`Filter3D.m`
`RestrictedCCA.m`

scrRCCAPass2()

Definition

```
[CorrelationMap] = scrRCCAPass2(HemoDynRespModel,
InputFileName, SizeRCCAArray, ValidVolumeSize, SegMask)
```

Description

Performs the second and final step of the 3-dimensional canonical correlation analysis and returns the correlation map in `CorrelationMap`. The correlation map has the same size as an image volume in the original SPM data set analyzed. `HemoDynRespModel` is the hemodynamic response model earlier created by `scrCreateHemodynModel`(). `InputFileName` is the name of the temporary file used in phase 1 as output file (`OutputFileName`). `SizeRCCAArray` is the size of the input data object as returned by `scrRCCAPass1`(). `ValidVolumeSize` is the same valid volume size used by `scrRCCAPass1`(). `SegMask` is the brain segmentation mask as returned by `scrCalcMeanImage()`.

See Also

`RestrictedCCA.m`

12. Appendix B - Software License

The GNU General Public License (GPL)

Version 2, June 1991

Preamble

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