REX: Response Exploration for Neuroimaging Datasets

Guide and Tutorial

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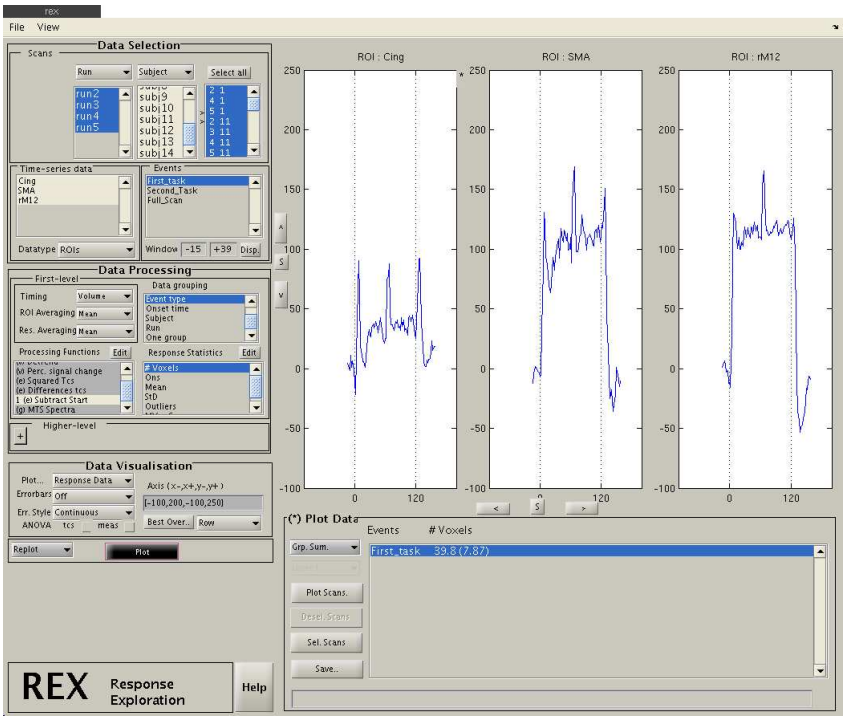
1 Introduction

1.1 Overview

The REX (Response Exploration) software is a prototype fMRI dataset exploration tool designed to enable the real-time processing and visualisation of response data from across large experimental datasets. REX can complement the spatial characterisation of experimental effects provided by General Linear Modelling approaches. REX makes fast navigation of datasets possible by integrating the specific organisation of an experiment's scans and events for data selection. The experimental organisation can be automatically identified from FSL or SPM GLM analysis design files or defined manually. The series of data processing steps applied to the data before plotting can also be rapidly specified and adjusted. New processing modules can defined using simple MATLAB scripts. REX's interface enables either simultaneous side-by-side plotting of selected ROI responses, or they can be overlaid. A set of user-defined response statistics can be calculated and tabulated below the plots.

This document details the basic organisation of REX, and provides a tutorial that illustrates its core functions. Users interested in quickly gaining an understanding of the tool could jump directly to the tutorial after reading this introduction.



1.2 System Requirements and data formats

REX has been designed to run in MATLAB 7 on all major operating systems. It has been tested in the Linux and Mac OS X environments, but has not yet been fully tested in the Windows environment.

Some processing modules require MATLAB's Statistics or Signal Processing toolboxes.

REX can read Analyze and NIFTI image formats, including compressed NIFTI files.

1.3 Installation

Email eduff@pcomm.hfi.unimelb.edu.au or check www.neuroimaging.org.au/nig/REX/ to obtain the latest version of REX. Please join the email list for updates.

REX needs to be extracted from the zip file using an unzipping programme. REX consists of a set of MATLAB functions that are stored in a series of subdirectories.

The fastest way to set up an analysis is by providing REX with a SPM or FSL FEAT design file, from which it can identify image file locations, scan organisation, and the timing and type of task periods. To take advantage of the import facility, the initial REX session must be run on a machine that has access to the unaltered FSL or SPM analysis directories.

1.4 Trouble shooting

REX is currently in development and has not yet been fully tested. We offer no guarantee for the accuracy or reliability of the software. Please email problems, comments and suggestions to REX@pcomm.hfi.unimelb.edu.a A message board and help ticketing service are planned on the Neuroimaging Informatics Tools and Resources Clearinghouse website (www.neuroimaging.org.au/n

The current implementation of REX should be effective in importing and exploring relatively simple experiments that have been analysed in a straightforward manner using FSL FEAT or SPM 2. Datasets with complex designs or that have been moved may cause problems, and need to be set up manually. Importation of data in Windows has not yet been tested.

1.5 Reference

A paper has recently been published that describes the approach and design of REX:

REX: response exploration for neuroimaging datasets. Neuroinformatics. 2007 Winter; 5(4):223-34.

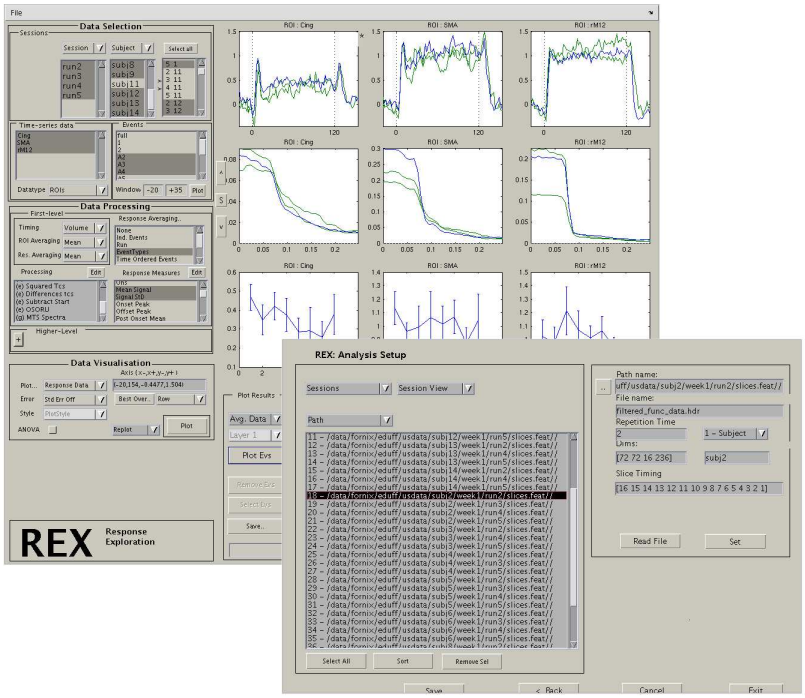
2 User Guide

2.1 Overview

Basic organisation of REX

REX utilises two main graphical interfaces. The setup interface allows users to import or manually define the organisation of an experimental dataset, and extract ROI time courses from the raw data. ROIs must defined as binary masks, or SPM VOI files, outside of REX. The setup procedure produces a data structure that stores all the data required for exploration with REX. This data structure can be saved to disk and used and copied independently of the original data. New ROIs and aspects of experimental structure can be added on an ongoing basis.

The exploration interface consists of a control panel, a data visualisation window, and a data table. In the control panel, users can select the subset of the dataset for visualisation, the sequence of data processing steps, and visualisation settings. A 'Plot' button initiates data processing and displays the output in a selected row of axes within the plot window. User defined response statistics are tabulated in the data panel below. This output can saved for further analysis in MATLAB or text format.



2.1.1 Applications

REX can be used for an initial exploration of a dataset, helping in the identification of artefacts and unexpected features of responses, or following a GLM analysis, to explore the results. REX enables the assessment of regional responses associated with activated clusters, or ROIs that were expected to activate. A set of averaged subject responses can be rapidly generated to identify subjects with unusual responses or artefacts that may have affected modelling. Grouping and averaging repsonses according to factors such as task-type can provide show the effects that they have on responses, informing modelling and experimental design. Factors central to a prior experimental hypothesis should not be explored before the formal statistical analysis. REX also enables the comparison of the effects of different processing strategies on the BOLD signal and ROI responses, and visual assessment of the quality of different models. REX can generate time-plots showing changes in average signal or other signal statistics, and it can be used to extract and process data for use in connectivity analyses.

2.1.2 Data organisation

REX's data structure, RX, has three core data-elements - **scans**, **scan events** , and **time-series data**, that are defined and classified to specify the experimental organisation and store its data. **Scans** refer to the separate scanning periods during which experimental data was continuously recorded. **Scan events** refer to specific segments of these periods, and are defined by an onset and duration. They could refer to periods of task performance, certain behavioural or physiological states, or artefacts identified in the BOLD signal. **Time-series data** refers to specific measurements recorded during a given **scan**, such as BOLD signal time-course data, stored as regions-of-interest (ROIs), as well as additional "covariates" such as recorded measures of physiological variables, head-motion estimates, or reaction-time measures.

The organisation of the experiment is defined by classifying these data elements (Figure 2.3). For example, subjects can be identified by associating a subject ID with each scanning run. Scan sessions and subject groups can be defined similarly. Event classification will indicate the types task being performed, artefact contaminated scans, and can specify reaction times and other data. Voxel-data time-series classifications identify spatial areas of the images, such as ROIs, image slices, or functional networks. In the current implementation of REX, the sets of voxel time-series corresponding to ROIs are preloaded into memory as single time-course data elements.

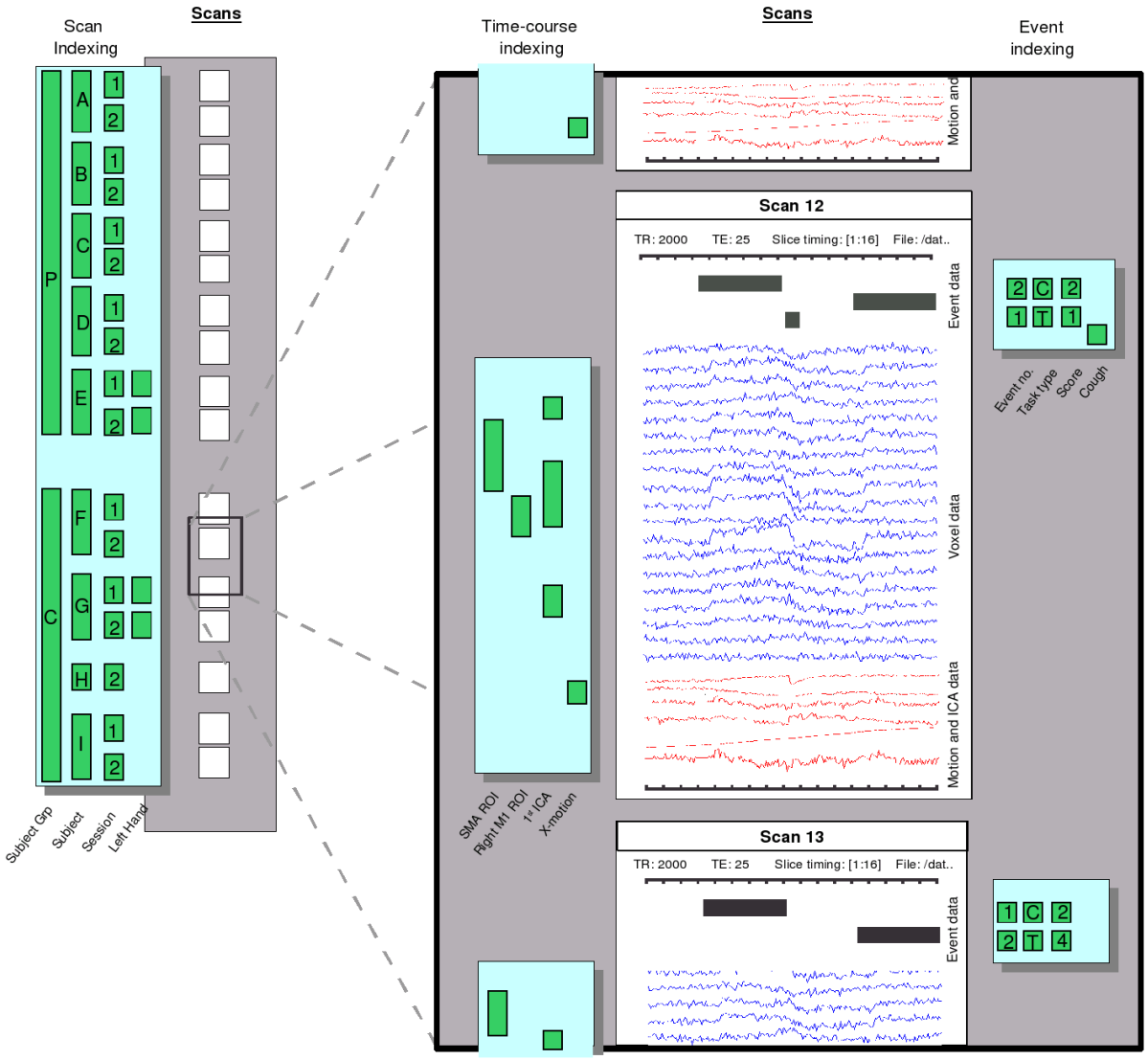


Figure 2.1: *Schematic of REX data structure. The three core data dimensions - scans, events, and voxels - may indexed in a flexible manner, which permits the rapid navigation of the dataset. Behavioural, motion estimates, and other auxiliary data can also be included in the schema.*

2.1.3 Processing

Processing of the selected data is organised around hard-coded event extraction and response averaging processing stages, around which a range of inbuilt or user-defined processing modules can be set to be applied to the data. Signal statistics can also be calculated from the data at any stage of processing, to be are tabulated alongside the resulting data plots, or plot themselves.

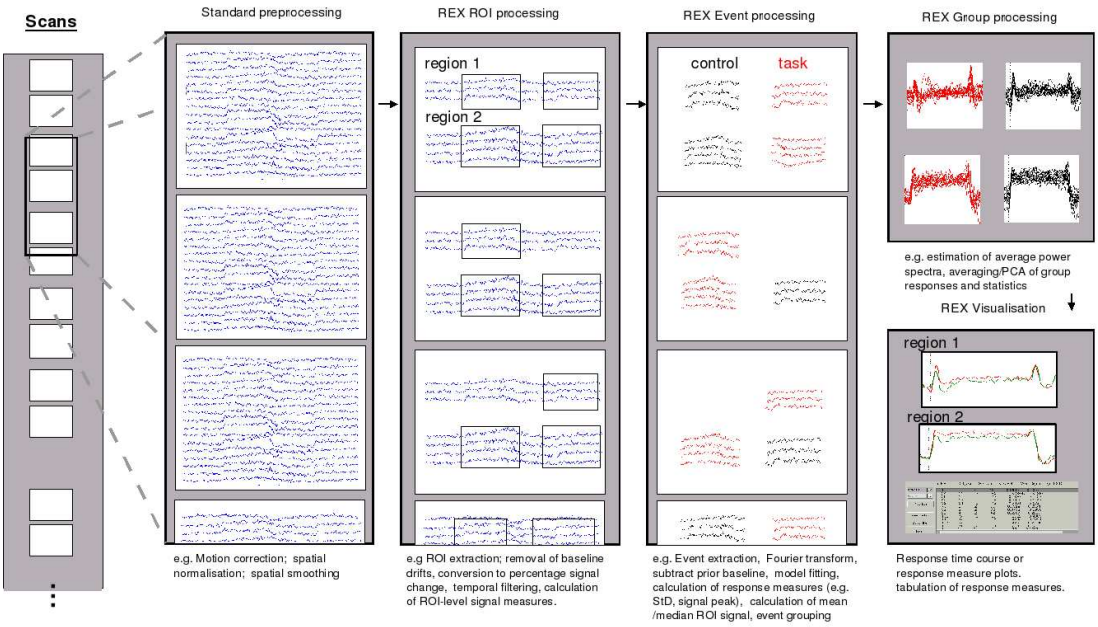


Figure 2.2: *The REX processing stream. A series of user defined data processing steps can be defined prior to and following ROI averaging and event extraction, and following event grouping. Multiple signal statistics can be defined, that are calculated and averaged in parallel to the main processing stream. Both time-course data and statistics can be visualised.*

2.1.4 Starting REX

Start MATLAB.

```
eduff@soma:~$ cd /data/contr/sbj1/r1/run.feat eduff@soma:/data/cntrl/
matlab
```

```
< MATLAB >
Copyright 1984-2006 The MathWorks, Inc.
Versions 7.2 (R2006a)

>>
```

The directory where REX was installed needs to be in the MATLAB path. To add the path from the command line:

```
>> addpath /usr/local/REX/
```

REX can be added permanently to the path the “Set Path” option in the “File” drop down menu.

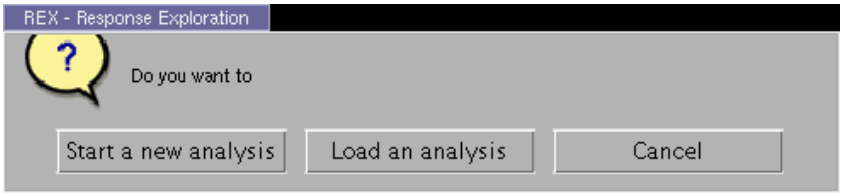
REX is run with the lowercase command `rex`. If a REX data structure exists in the workspace it can be provided as an argument to load the analysis, i.e.:

```
>> rex(Rx);
```

The name of a MATLAB file containing a `Rx` structure can also be provided as an argument to load in a previously generated analysis file.

```
>> rex('/data/RxMotor.mat');
```

Otherwise, REX will provide the following options:



2.2 Data Setup

The Setup interface opens if 'Start a new analysis' is selected. It can also be accessed from the File menu in the main exploration window.

The REX data setup interface reflects the underlying Rx data structure, with separate areas for defining each of the core elements of the dataset. Timecourse data is separated in to "ROIs" for data extracted from the fMRI image series, and "covariates", for other data.

2.2.1 Overview

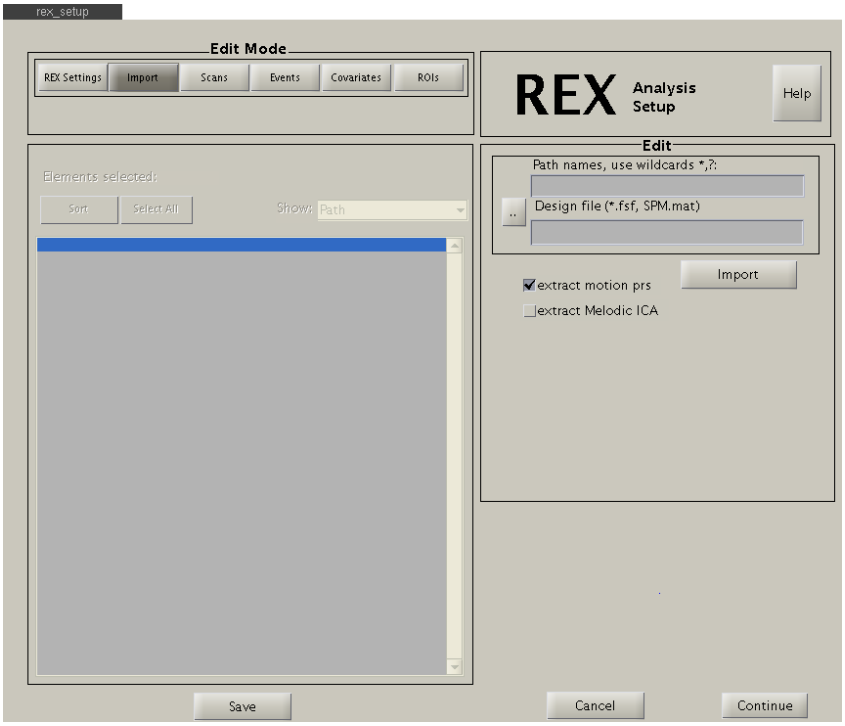
Scans, events, covariates, and ROIs are defined in separate sections of the setup interface, which can be navigated by the buttons in the top section of the interface. In each section, all the data elements for the entire experiment can be scrolled through and edited en-masse. New elements can be created, as can new classification schemes for the elements.

2.2.2 Importing settings

REX can determine a wide range of experimental settings from the GLM design files produced by FSL FEAT and SPM. FEAT saves a text file `design.fsf` into its output directory. This file specifies file locations and analysis settings. In an hierarchical analyses a design file is saved for each lower-level analysis, and for higher level analyses. A design file can be saved from the FEAT setup GUI without performing the analysis. SPM 2 produces a MATLAB format file `SPM.mat` in its working directory that stores the analysis settings and results.

To import data from the FEAT design file, REX may use FSL functions. The FSL can be identified automatically, but can be set in the General Settings menu. This can be set prior to running REX, or can be added in the General Settings area of of REX. To import data from a SPM analysis, REX uses SPM commands, which also need to be accessable by MATLAB.

Data from FEAT and SPM files can be imported in the Import section of the setup window:



Low-level design files will most reliably import data. REX attempts to access file locations defined in the original analysis. If data has been moved, it will be necessary to edit the links to the scan images and other files.

To quickly import data from multiple design files, the "*" wild card can be used to stand for any series of characters, and the "?" wild card to stand for any individual character. For example, `/data/subj*/run?/run.feat/` will select design files from all runs of all subjects. In Linux and Mac, square brackets can also be used to identify a set of acceptable characters. "run[125]" would accept run1, run2, or run5).

REX creates new scan and event data elements based on the design files, and creates classifications for different scan and event types. Continuous regressors, which may refer to ongoing in-scan measurements, are automatically stored as covariate time-series, so that they can be processed and visualised in the same way as the ROI data. REX can also automatically load motion parameters and FSL Melodic ICA time-courses as covariates. For FEAT, the spatial normalisation settings are identified, to be later used to enable extract data associated with ROIs defined in standard space. REX can work with the 3-D file series sometimes used in SPM 2.

2.2.3 Scans

Scans should be the first elements of the experiment to be specified, as events and time-series elements are always linked to a specific scan. If scans have not been defined using the import function, they can be added manually. REX can read Analyze, NIFTI, and g-zipped NIFTI formats. As for the design files, multiple scans can be added at once using wild cards. It is best to define all scans of an experiment at the same time, which enables all the experimental information to be adjusted en-masse. Note that specifying scans does not load their

Data element	Determined from..	Indexed by..
Scans	Image files SPM .mat files FSL .fsl files	Directory hierarchy Group-level designs
Events	Discrete GLM regressors	Regressor name Event number Onset time Event duration
Covariates	Motion parameters Continuous GLM regressors	Motion param Regressor name
ROIs	MNI or native space mask SPM VOI file	File name

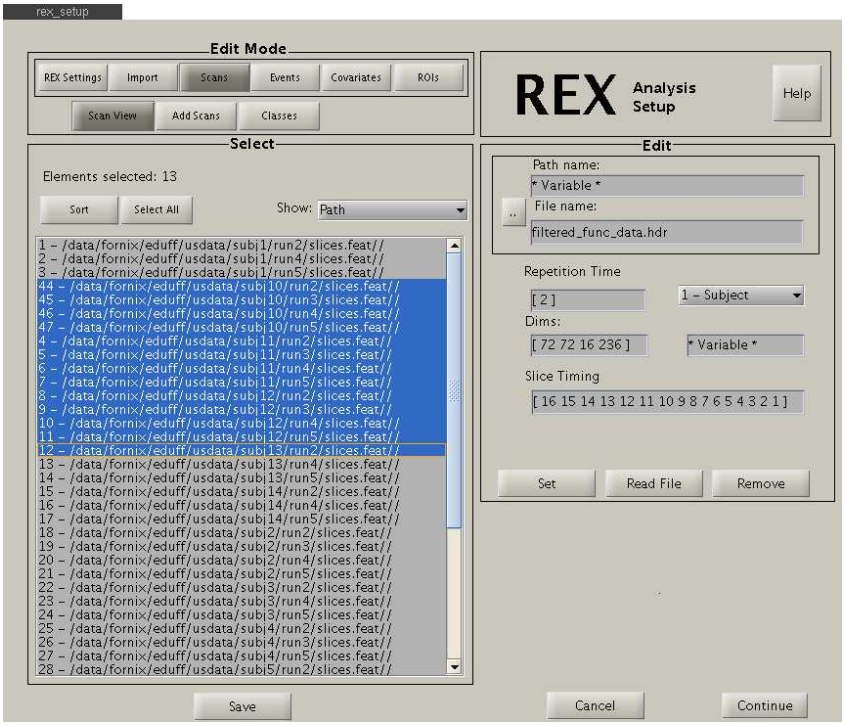
Table 2.1: Data extraction and indexing

time-course data. At present, timecourse data can be extracted from scans when ROIs are defined.

Once scans are specified, they can be edited in the Scans section of the interface. As for all data elements, sets of scans can be selected in the left Select window, and their settings adjusted in the Edit window. The menu above the scan list in the Select window enables a range of scan properties to be displayed in the list. The Sort button will sort the list alpha-numerically according to the displayed property. Sorting the display list is useful to quickly select specific groups of data elements for editing.

Remember to press 'Set' after changing settings

When multiple scans are selected, settings that have a common value for all selected scans will be displayed, otherwise settings will be indicated as `' ** Variable **'`. Changing scan data settings will alter the settings of all the selected scans. Changes made to scan settings must be confirmed with the Set button.



Scan classification

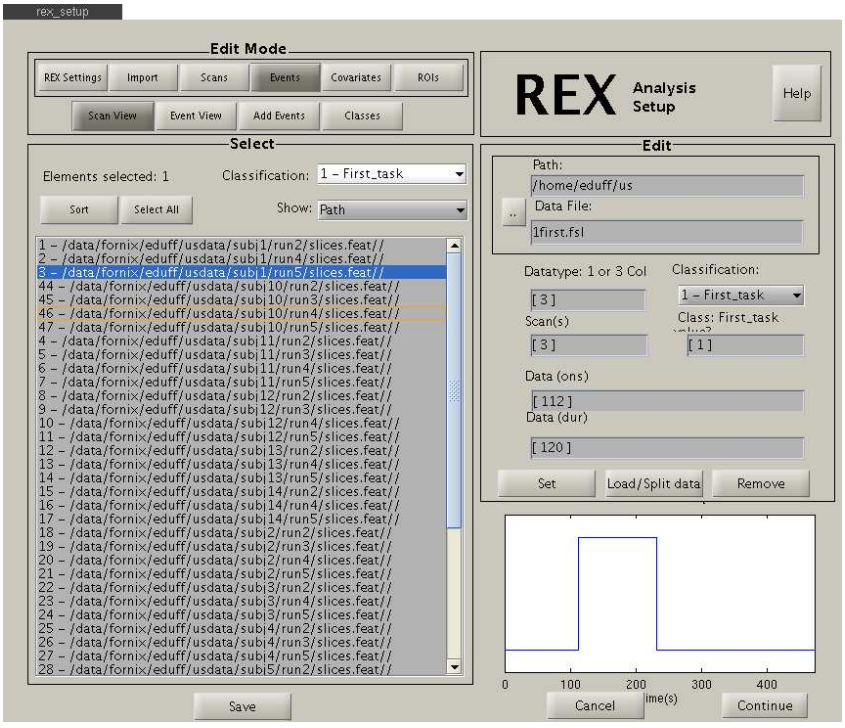
Any number of scan classifications can be created in the Classes section of the scan setup area. Classifications may specify subject IDs or session numbers, and can be numeric or strings. With the Generate button, in the Add classification menu, REX attempts to automatically generate scan classifications based on the directory structure. REX is able to detect the three-level-hierarchy of an experiment with a directories, '/data/patients/subject10/run3' etc.. REX will not successfully interpret experiments with redundant directory naming conventions, such as '/data/pat/patsubj10/patsubj10srun3/'. By selecting existing classification types in the Select area, Classifications be edited or removed.

The class membership of individual scans can be set en-masse in the scan view area, where the classification to be set is selected in the drop-down menu.

2.2.4 Editing non-scan data elements

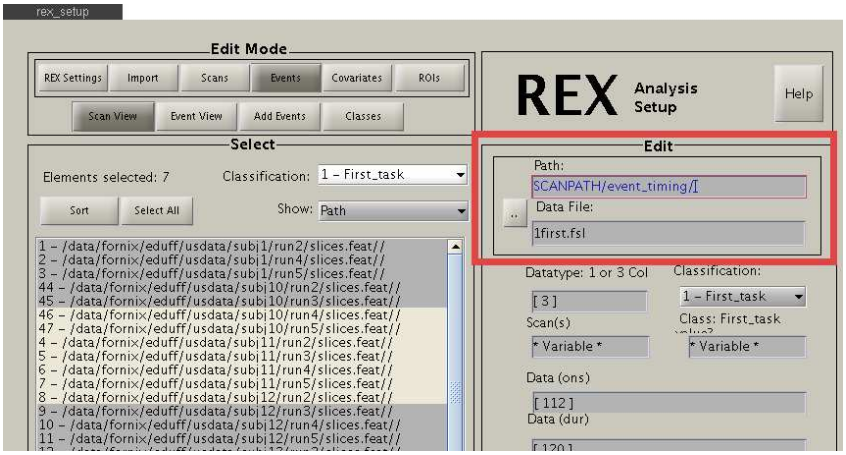
Scan view

Event, ROI and covariate setup areas have the same organisation as the scan setup area, with sub-areas for the generation of new data elements and indexing. As these elements are tied to a specific scan, two edit views are provided. Data elements can be viewed either as a list of all elements for the entire experiment, like the view available for scans e.g. Event view or in a Scan view. The Scan view shows specified data elements for a given scan. Different classes of the data elements (e.g. Control Task) can be chosen in the third drop-down menu. A given scan may have zero, one, or more events of a given type, i.e. there may be three Control events in a given scan.



REX has an autofill feature to enable the rapid specification of file locations for event, covariate, and ROI, data. The text, SCANPATH, is contained in a file path section , it will be automatically expanded to

the path of the associated scan image file. This enables file locations that can be defined relative to the scan directory to be quickly specified. For example, the following specifies the normalisation file to found in the `./reg/` subdirectory of the Scan directory for all selected scans:



2.2.5 Events

To create new events, move to Add Event. Often, one will want to define a new event that occurs in all or many scans of the experiment. For this reason, this sub-area uses the Scan view. A new, empty, event will be created for all selected scans. A new Classification for the scan can also be specified (i.e. 'Control'). The event details can now be edited together in the Scan or Event view subareas.

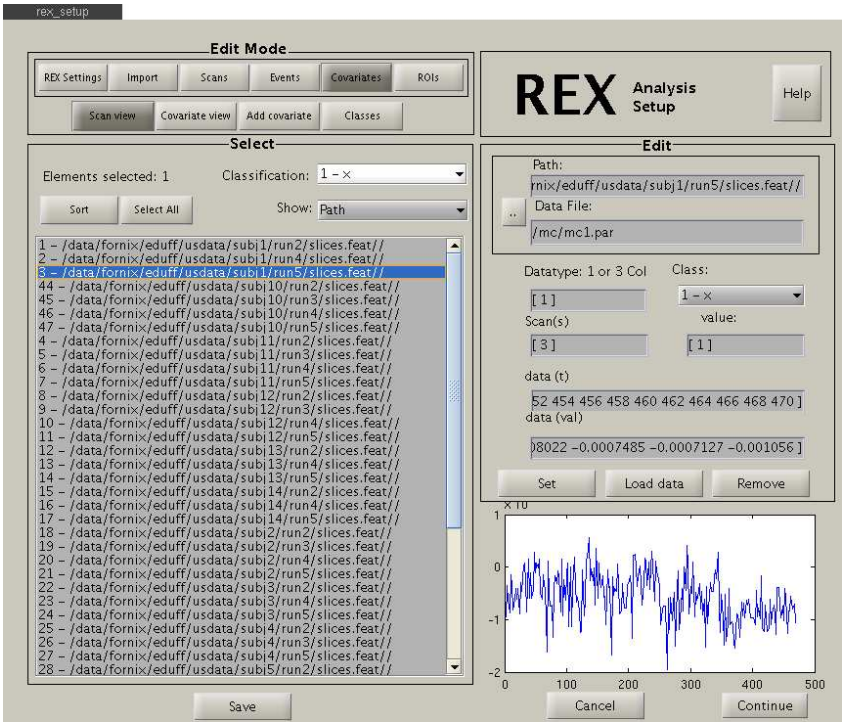
REX can read standard text files containing event timings, either in a 1-column format, with a zero or a one for each time-point, or a three-column format, listing `<onset> <duration> <value>`. `SCANPATH` can be used to specify the location files relative to the individual scan locations. The Read file button enables the event files to be re-read if they have been changed. Event data files that specify multiple events of the same type are automatically split and stored as separate event elements, to enable the events to be assessed and classified individually. Event timings can also be specified manually. Series of multiple events can be input, e.g. `[ 20 50 80 ]`, and are automatically split up by REX.

! → The classification of the non-scan data elements is at present slightly different from that of scan elements. REX only recognises binary classifications of these elements, meaning, for example, Trained and Control events must be defined by two classifications, one indicating whether an event is a Task event, the other whether it is a Control event. This arrangement does not reduce the flexibility of the indexing schemes.

! → Some care is required in classifying events. For event-related averaging, the condition immediately prior to the onset of a selected event-type may not always be the same. An analysis of different transitions might reveal interesting differences in transient signal responses reflecting the cognitive demands of specific task-switches. These different transitions can be defined in an event classification, and investigated with REX.

2.2.6 Covariates

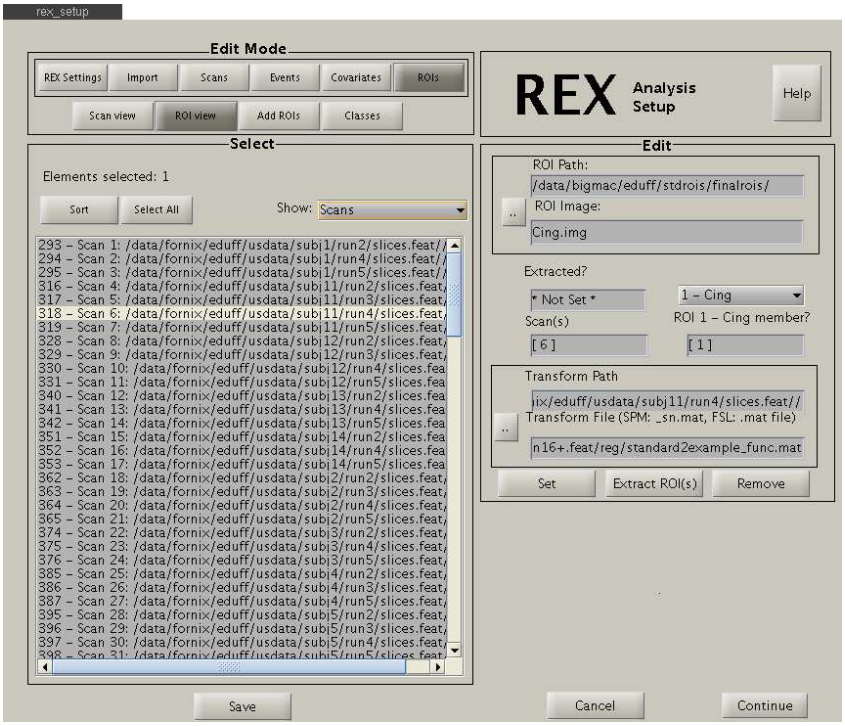
Covariates are set up in an identical manner to Events, with the only difference being that covariate data must be time series data in one-column format. The sampling rate of the covariate time series does not have to match scan acquisitions, allowing data such as high-rate physiological measurements or irregularly obtained subjective ratings of factors such as comfort.



2.2.7 ROIs

ROIs are defined by specifying 3D mask images or SPM volume-of-interest files. The Add ROIs area is used to specify new ROIs. Separate ROI files can be provided for each scan or subject, or a single ROI file in standard space can be used for all subjects. SCANPATH can be used to load scan-specific ROIs that stored in the scan directories. If the ROI is in a different space to the scan data, REX can use SPM or FSL tools to invert a provided spatial normalisation file. When experimental data is imported from SPM or FSL design files, the spatial normalisation settings are automatically identified. This functionality enables data to be rapidly extracted from native space. Extracting ROI timecourses from native space allows slice timing information to be used in the processing of signals, and enables accurate assessment of ROI homogeneity.

When new ROIs are defined, an ROI classification is automatically created, based on the file name of the ROIs. Multiple classifications of ROIs are not at present accomodated for.



ROI extraction

After ROIs are defined, time course data can be extracted into the RX structure using the Extract data button. Extraction can take some time for large datasets. Extraction is fastest if performed for all ROIs at once, as REX orders the extraction process such that each scan image is opened only one. However, a test extraction of one or two ROIs should be performed first to ensure that the time-courses are loading successfully.

2.2.8 REX settings

An additional area of the RX structure stores general analysis settings. The experiment's name, the default save path, and the locations of FSL and SPM can be specified here.

2.3 Exploration tool

→ see section 3.2

The tutorial provides a walk-through of the exploration interface. This section describes its features in detail.

The exploration interface consists of a control panel, a data visualisation window, and a data table. The control panel is split into data selection, processing and visualisation sections that fully define the processing sequence.

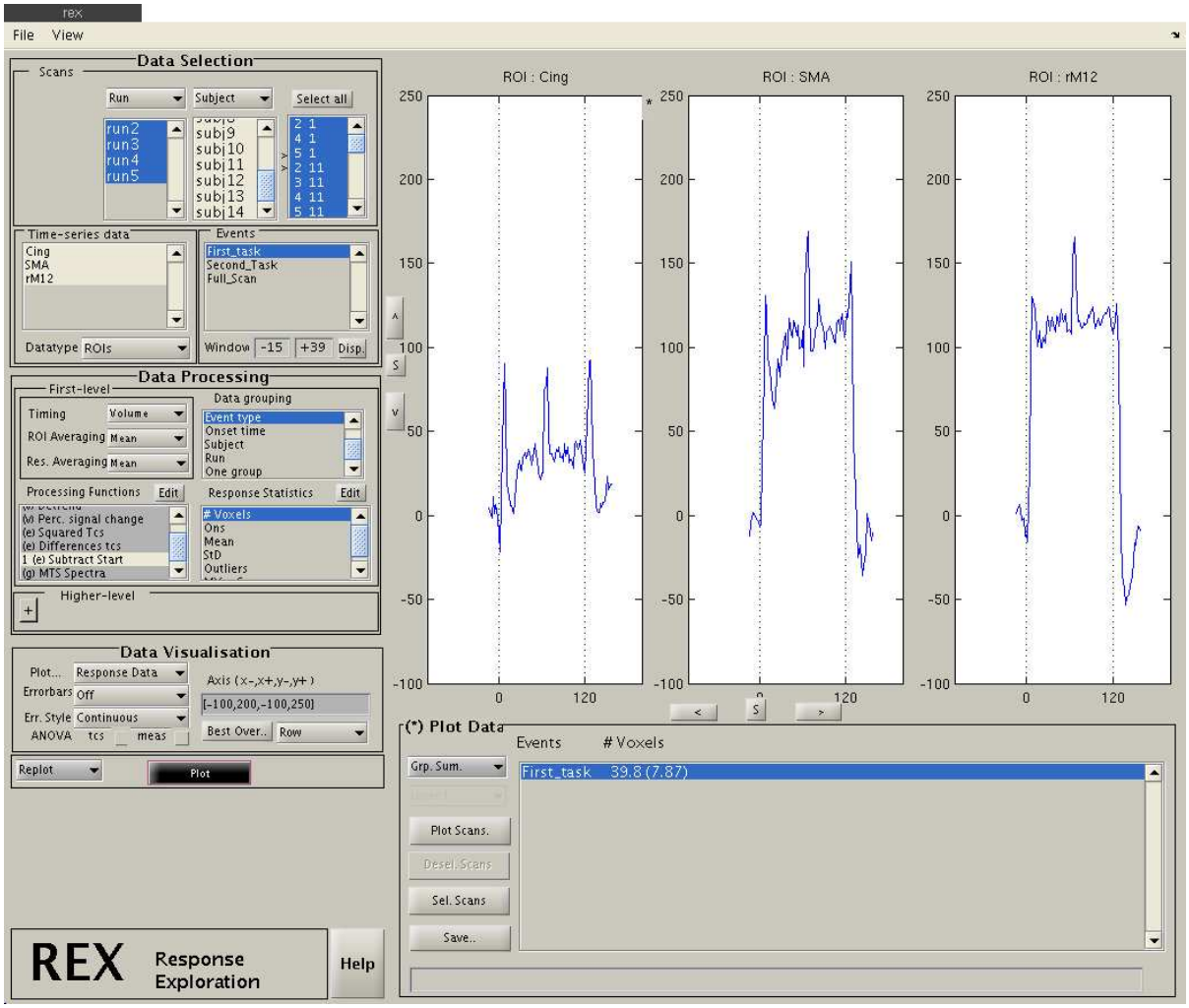


Figure 2.3: The REX exploration interface.

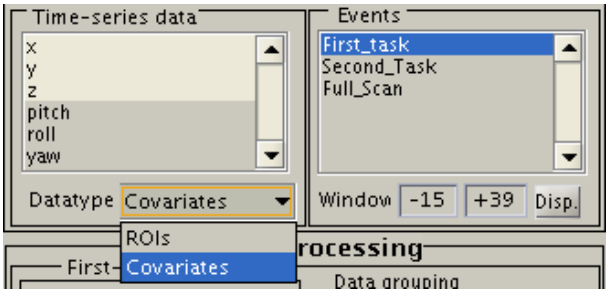
2.3.1 Data selection

Scans The top row of list-boxes enables selection of the scans that will be included in the processing. The rightmost list-box provides a list of all scans, identified by abbreviated names that indicate the various classes each scan belongs to. The listboxes to the left list all the classes of the different scan classifications. The drop-down menus above each allow selection of any additional scan classifications. The

selection or de-selection of different scan classes alters the overall selected pool of scans in the rightmost list-box.

Time-courses

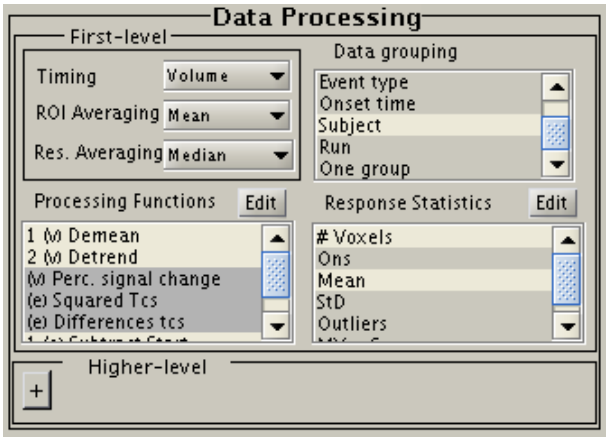
The rightmost list-box below the scan selection area enables the selection of the time-course data to be selected. Either ROI or the Covariate data can be selected from the drop down menu. Any number of ROIs or Covariates can be selected for simultaneous processing, with the resulting data plotted horizontally across the plot axes.



Events

Events are selected from a single menu that lists all the defined event classes. Choosing two event classes extracts all events that are members of at least one of these classes. The “Window” settings specify the amount of time around each event that will be retained when the events are extracted. The first box sets the time point of the start of the data extraction. A negative value specifies the number of seconds prior to the onset of the task period that is retained in the extraction. The second box specifies the number of seconds after the completion of the event that will be retained. Care needs to be taken that data exists in the extraction window for all events in the exeriment. Otherwise, different timepoints of the final data will reflect differing numbers of subjects.

2.3.2 Data processing



Slice timing

REX can utilise slice timing information to achieve sub-TR resolution of averaged BOLD signal responses. When slice timing is selected, REX calculates the acquisition times for each slice of the input data, based on the slice timing information provided in the setup procedure. To enable successful averaging of this data, an appropriate interpolation processing step must be used. Slice timing will be useful primarily

for experiments where the task onset times were specifically jittered for sub-TR resolution.

ROI and response grouping and averaging

The averaging menus enable specification of how the ROI data and grouped responses are averaged. The options are mean, median, and a first eigenvariate of a SVD. A final option is not to apply any of these methods and instead use a processing module that calculates a different summary of the set of responses. The ROI data averaging occurs immediately after event extraction.

Data grouping

The top right menu lists a range of data classifications that can be used to group the data for averaging or further processing. These include Run, Individual Events and All, as well as event classes determined from the data file. If multiple classifications are selection, subgroups are formed through the intersection of the groups defined by each of the classifications. The order that these classifications are selected (shown by a numbering of items), affects the the order in which factors are described in the summary tables, and how the data is displayed in some plots (section 2.3.2).

Processing pipeline

The entire processing workflow is defined within a single list-box. Each processesing module is defined to be applied within one of three sections of the overall workflow - prior to event extraction, following event extraction, and following data grouping. The first stage involves processing of voxel or covariate time-courses prior to the extraction of events, and might include detrending of the data, or conversion to percentage signal change. Event-level processing is applied after event extraction and averaging. At this stage the response data might be normalised with respect to the signal prior to the response, or the transformed. Following data grouping, the processing is again performed on a set of time-courses. A PCA decomposition of the group of time-courses, or the fitting of a model across all responses. Note that group level processing currently only functions when all events have the same timing of sample points.

Processing modules are defined for a specific processing stage. They are all listed in a single processing menu, and chosen simply by the order of their selection.

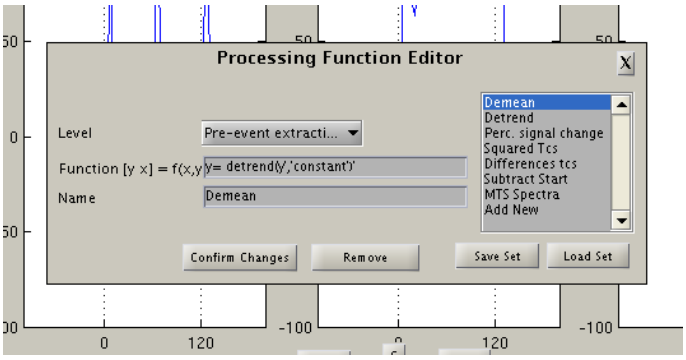
Creating and editing processing modules

The Edit button above the Processing list-boxes opens a window that enables the editing of modules. Processesing functions must be defined to either be applied prior to event extraction, following event extraction, or following event grouping. Any accessible MATLAB function can be called to act on the signal (**y**) and the sampling points (**x**). For example, `y = y * 10;` or `[x y] = interp(y,x);`. Functions can utilise and alter both the signal variable, **y**, and the time variable, **x**. Prior to ROI averaging **y** and **x** will be $\mathbf{v} \times \mathbf{t}$ matrices, where **v** is the number of voxels and **t** is the number of time points, unless prior processing has altered their dimensions. Post-event extraction, **y** and **x** will be an $\mathbf{1} \times \mathbf{t}$ matrices, unless no ROI averaging is selected. Following grouping, **y** will be an $\mathbf{e} \times \mathbf{m}$ matrix, with **e** being number of data elements in the specific group. During processing, **y** and **x** must remain 2-D matrices. Sets of processing functions can be saved, and loaded for use with different datasets.

The MATLAB programming language is intuitive, and has has an extensive Help section. Note that certain functions, such as `mean`, will have altered behaviour acting on $(n \times m)$ matrices when $n = 1$. In this case, `mean` usually averages rows, producing a $(1 \times m)$ matrix,

however when $n = 1$, `mean` takes the mean of the entire column's data, producing a single value.

The set of processing modules can be saved for use in other analyses. They are stored in the `Rx` structure, so are retained when data is reopen for analysis.

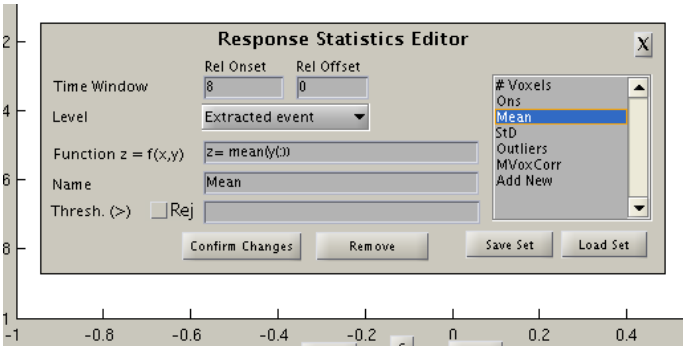


Response statistics

In addition to the primary processing stream, Response statistics can be calculated to provide useful single-value summaries of different aspects of the response data, such as mean signal or power in a certain spectral band. A response statistic can set to be calculated immediately prior to ROI averaging, or following event processing, and are grouped and averaged in the same manner as the main processing stream. See section 2.3.3 and 2.3.2 for the visualisation of response statistics.

Creating and editing response statistics

Response statistics are be created and edited in the same manner as processing modules. They must be defined either for application prior to event extraction, or following event extraction. Response statistics are defined as MATLAB functions of **y** and **x** producing a new variable, **z**. For example, `z = mean(y(:))`. The functions must output a single numerical value. A time window for the calculation allows the calculation to be constrained to a more limited section of data than is being displayed. This is helpful, for example, to calculate the mean of the signal during only the task period. Finally, a threshold can be specified. Responses with statistics exceeding this value are rejected from the processing and not displayed.



ANOVA

A two-way ANOVA can be applied to the response data, with factors of time and the chosen response groupings. A plot is flagged if there are any significant effects. There may be an effect of time (e.g. any

	Function	Acting on..	Notes
Processing Module	Remove mean	scans	
	Detrend	scans	does not remove mean
	High pass filter	scans	Butterworth > 0.005 Hz
	Percentage signal change	scans	Based on mean scan signal
	Low pass filter	scans	Butterworth < 0.1 Hz
	Difference time-series	scans	for assessment of avg. motion
	Subtract prior baseline	events	Ten seconds prior to onset
***	Multitaper Spectrum	group	assesses change in signal fluctuations
Response statistics	Number of voxels	scans	
	Signal mean	events	period 8 seconds post-onset to offset
	Signal standard deviation	events	period 8 seconds post-onset to offset
	Onset	events	indicates onset time
	Outlier count	events	signal $>$ time points > 3 from mean
	Onset/offset signal	events	

Table 2.2: Default processing and response-statistic modules

consistent response time course over all groups), group (e.g. different average levels of signal across the response periods across groups), or a significant interaction effect (e.g. a significant difference in response shape between groups). In addition, ANOVAs will be calculated for all response statistics, testing for between-group differences. The results of these statistical tests are intended to be used as pointers to interesting effects, useful for directing the exploration and identification of potential confounds. For example, this can indicate when a statistic indicating the amount of motion is significantly different across subject groups.

Higher-level analysis

The higher-level functionality is currently in development. This enables calculation of functions across the output of multiple first-level processes. Two (or more) separate first-level plots, with the same data grouping scheme (e.g. individual responses, or subject-level grouping), can be selected, and functions selected to process the paired time series. As well as inter-regional correlation and connectivity analyses, this feature can enable multi-level averaging, the regression of motion or other experimental time series from the voxel data, and the generation of difference-plots across task-types.

2.3.3 Visualisation

REX can visualise both the data output produced by the main processing stream, and any of the defined response statistics. The output can be selected in the Plot.. menu. Error bar settings can be selected in the menu underneath. When the `Plot` button is pressed the processing stream is executed, and the chosen output displayed in the visualisation window. Response statistics are plot as connected plots of the average response statistics for the different classes of the data. If two classifications have been used to group the data, with n and m classes each, the data is grouped as n connected plots of m points, with the order of the classifications determined by the order they were selected.

Plot window

The plot window can be split twice both horizontally and vertically, using the S buttons, so can display between one and nine axes. The

arrow buttons move focus to a specific set of axes. When data is plot the data of the selected ROIs are displayed across the row of the highlighted axis. This row of plots can extend off the right of the screen. Axes can also extended downwards, enabling any number of data plots to be maintained in memory.

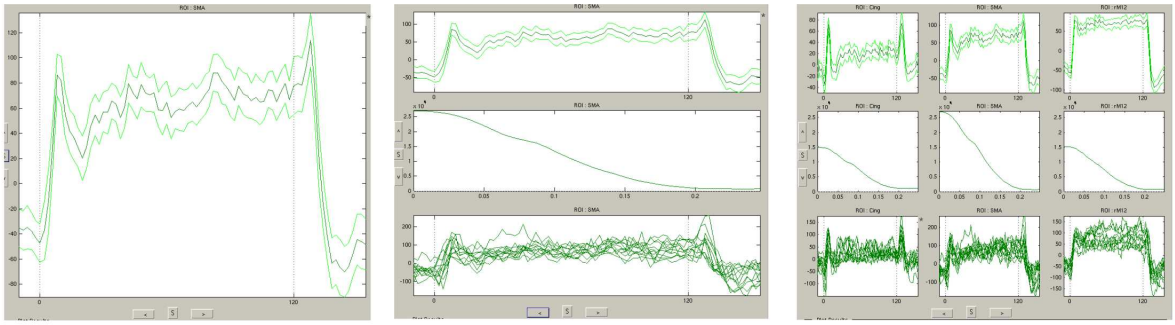
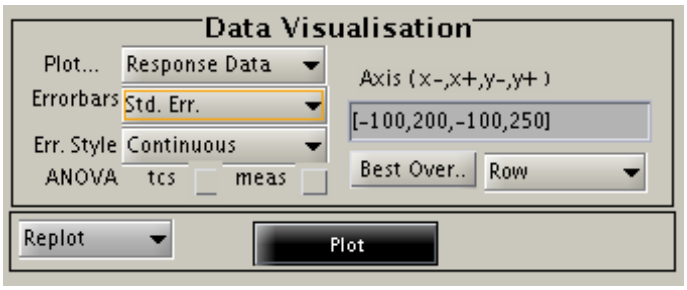


Figure 2.4: Three possible organisations of the plot window

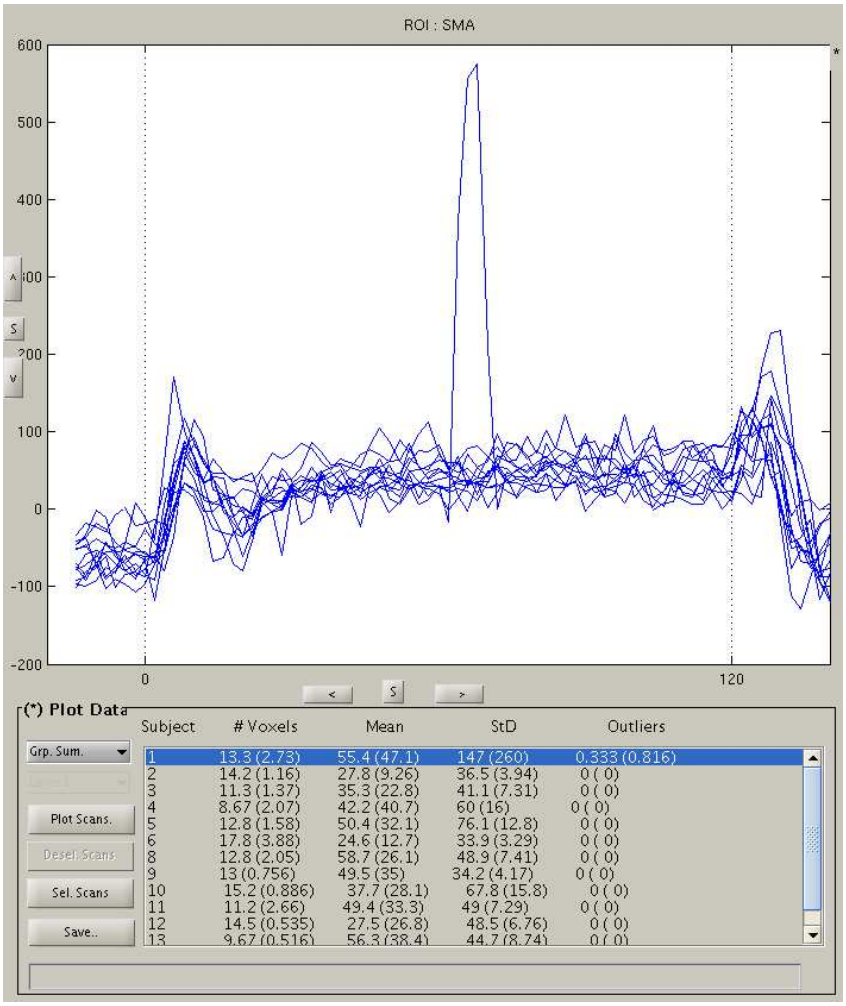
The menu immediately adjacent to the Plot button has the options Overwrite, Overlay, and Replot. Overwrite means that the new data will overwrite the data in the currently selected row. When plots are Overlaid, the old plot remains, and the axes are adjusted to fit all data. When the Replot option is selected, the current data in the selected axis is replot with the current visualisation options. With this option, the axis-set box becomes active, enabling the adjustment of the x and y axes scales The Best over.. menu calculates optimal axes for the plots in the current Row, Column, or across all plots.



Plot data-structure Processing produces a data-structure that contains the processed data and information regarding the applied processing and visualisation options. This structure is used when the data is replot. It can also be saved for further analysis.

Data table Below the plot window is the data table which lists the response statistic data associated with the highlighted axis. Two views are available, via the top menu, a group summary view, showing the mean and standard deviation of response statistics for each data group, and an individual response view, which lists response statistics for all responses. If multiple plots have been overlayed in this axis, the different plots can be selected in the Layer menu below this. In

the summary view, the Plot Scans button adjacent to the table will highlight the specified response in the display. In the individual response view, selected individual responses can be overlaid upon the average data. The individual list will include responses whose statistics exceeded specified rejection thresholds; these are designated with a *. If an ANOVA has been applied to the data, responses with significant effects are indicated by a * next to their summary row in the group list. A * alongside a statistic column indicates that it displays significant differences across groups. Desel. Scans removes the selected scans from the main data selection list, while Sel. Scans keeps only those scans on the list. Data can be saved in text or MATLAB format'



In Event Data display mode, the Deselect button deselects runs associated with the chosen responses from the main processing-menu scan-selection box, enabling the analysis to be re-run on a refined dataset. The Select button alters the main scan-selection box to select only runs associated with highlighted events.

The Save button enables the data associated with the selected plot to be saved, either the original MATLAB structure or in a simple text format.

3 Tutorial

This tutorial describes the exploration of a simple example dataset using REX. The tutorial can be used prior to reading the remainder of the documentation. The tutorial dataset involves scans consisting of two-minute periods of continuous motor-tasks interspersed with rest. The data can be found on the download page (www.neuroimaging.org.au/REX). This data file was generated using REX's Setup procedure, which shall be briefly demonstrated towards the end of the tutorial. The exploration process outlined here investigates the dataset for time effects, and is intended to show the basic functionality of REX, and indicate some of the signal dynamics and experimental factors that can be detected with the tool.

3.1 Starting REX

REX installation instructions can be found in Section 1.2.

Start MATLAB:

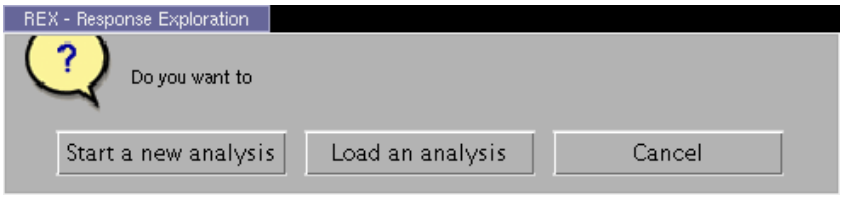
eduff@cingulate:/data/$ `matlab`

Add the REX directory to the matlab path if required e.g.

```
>> addpath('/usr/local/REX/');
```

Start REX.

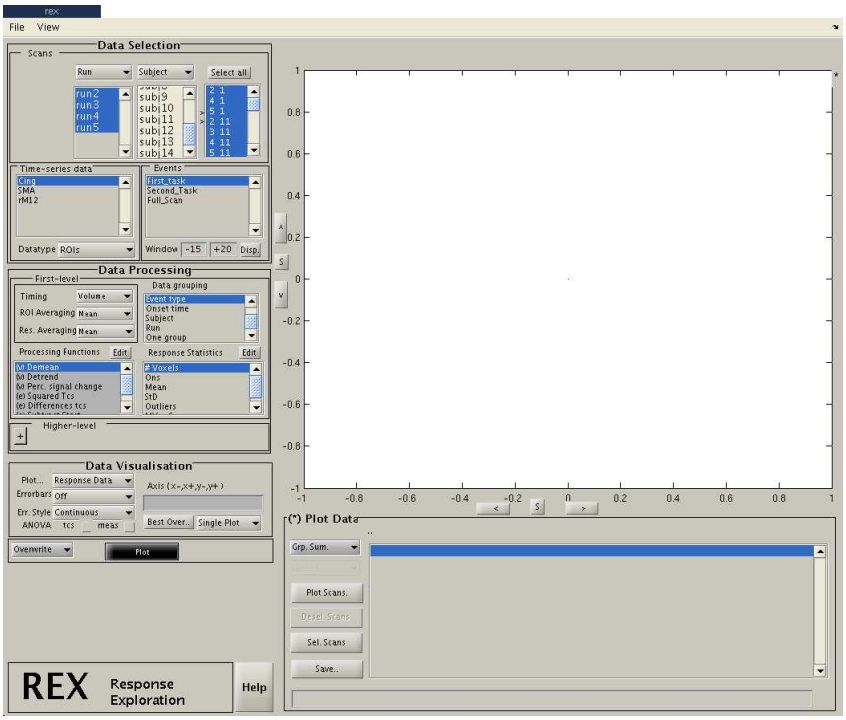
```
>> rex;
```



REX stores information regarding experimental organisation and ROI time-courses in a MATLAB structure that can be saved to disc and updated in an ongoing manner (see 2.1.1).

Select the 'Load an Analysis' button, and select the example dataset, RxExample.mat.

This brings up the main processing and visualisation window. The exploration interface consists of a control panel, a data visualisation window, and a data table. An online help system can be initiated by pressing the Help button (note: this may not work correctly on Windows).

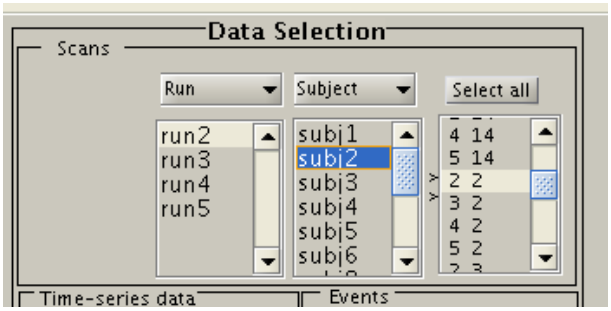


3.2 Exploration

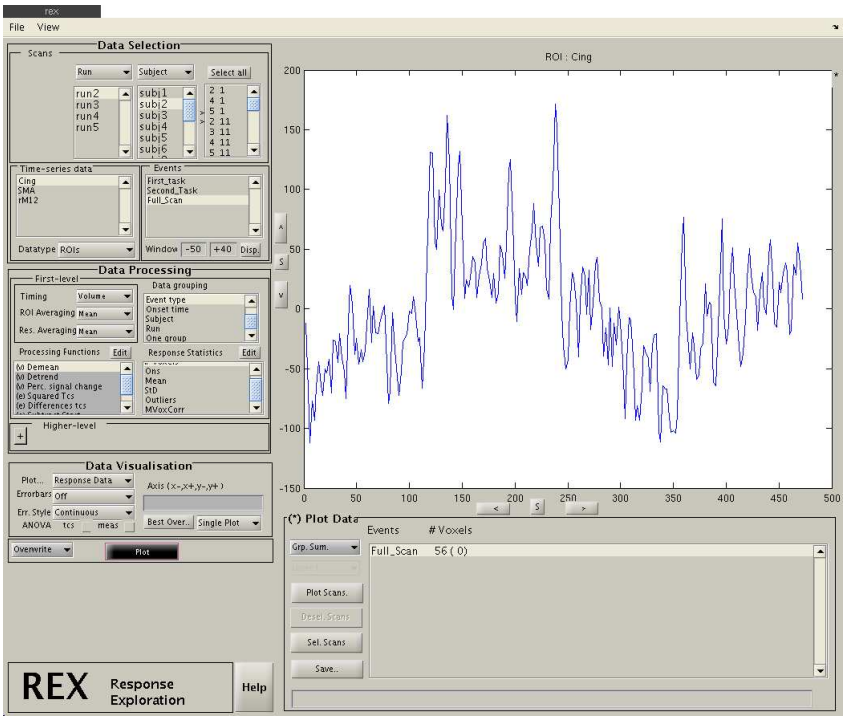
Data selection

The main control panel on the left is split into data selection, processing and visualisation sections. The top row of menus enables the selection of the scanning runs to be included in the data processing. Selection or deselection of different scan classes alters the overall pool of scans, which is shown in the rightmost listbox.

Select Run 2 and Subject 2



Press the Plot button at the bottom of the control panel



The main screen shows the average signal for the selected scans for the first selected ROI, the Cingulate.

Below the scan selection area, the ROIs that will be processed can be chosen, along with one or more event classes. The default event class for any is “Full_Scan” which specifies the period consisting of the entire scan duration. All the scans in this dataset consist of two motor-task periods, the first from t = 120s to t = 180s, and the second from t = 360 until the end of the scan. The event elements corresponding to these periods have been tagged as either “First_Task” or “Second_Task” to enable these elements to be selected separately.

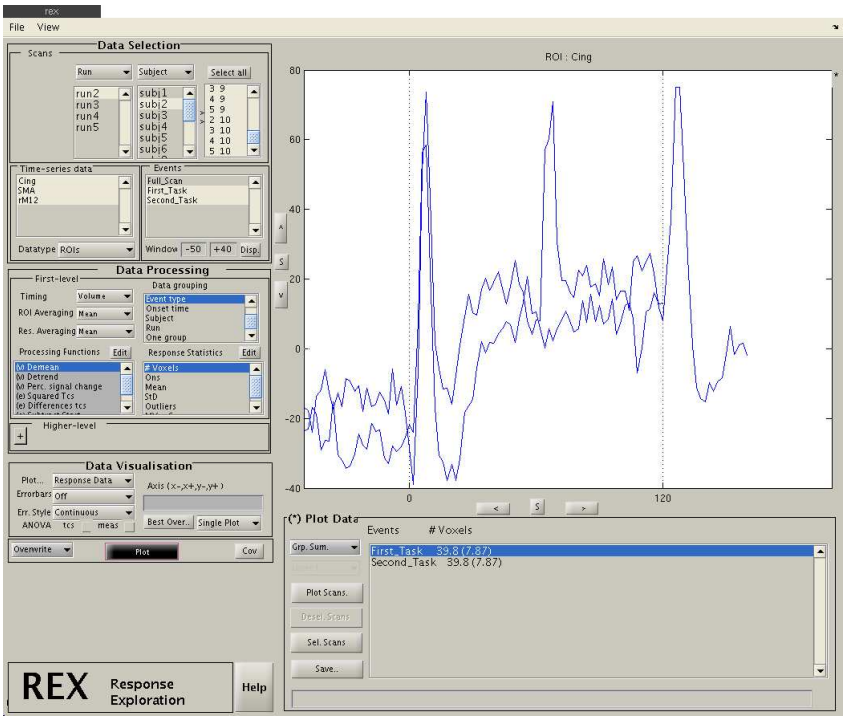
Press Select all in the Scans section of the Data Selection panel

Select all ROIs and events “First_Task” and “Second_Task”

Change the Events extraction window to: (-50, +40)

Press Plot

Events that match any selected event class are extracted for processing. The extaction window specifies the size in seconds of the data window that is retained around the events for processing. The current data has long task blocks, and benefits from an increased window size. The temporal indexing of the plotted data is relative to the time of onset of the events.



Processing

2.3.1 ←

Processing is organised as a configurable, semi-structured workflow, with two hard-coded processing steps - the event-related response extraction and the grouping of responses. The first option of the processing panel enables the specification of the mode of voxel timing utilised in processing. Options are volume, ROI, or slice timing. Unless an experiment has been specifically designed for sub-TR resolution, volume timing should be used. Below, the methods used to generate a representative signal from the ROI voxel data, and from the sets of grouped responses, are selected.

> *Experiment with the effects of the different Averaging options Mean, Median, and SVD, pressing* Plot *after each adjustment. Return both options to Mean afterwards.*

The option to select none enables you to define your own data-averaging method as a processing module.

The Data grouping menu lists a range of data classifications that can be used to group the data for averaging. For example, the selection of 'Subject' will result in the data being averaged in subject groups. Multiple classifications can be used to group the data. Selection of 'Subject' and 'Event Type' will generate an average response for each event type, for each subject.

> *Experiment with the different grouping settings. Finish with the "Event type" setting.*

2.3.2 ←

Processing streams can be defined at three stages of the processing - prior to event extraction, following event extraction, and following data grouping. The first stage of processing involves processing of the full scan voxel time-series. Appropriate processing steps could involve detrending of the data, or conversion to percentage signal.

After this processing, the event data is extracted, and the averaging of the voxel data occurs. This is followed by further user-defined processing. Here, processing may include the subtraction of average pre-onset signal levels or a Fourier tranform of the selected data. After this stage of processing, the data is grouped according to the specified classifications. Before the final built-in averaging of the data, further processing can be applied to the sets of averaged responses produced by the grouping. Alternate averaging approaches could be used, such as an estimation the average power spectra, or ICA.

Processing modules must be defined for a specific stages of analysis. They are listed in a single processing menu. Their order of application is specified by the order of their selection.

> *Select, in order (by holding down the control button during selection), the ROI-level processing modules: Percentage Signal Change, Detrend, Subtract Start.*

Note that Subtract start is numbered as (1), as it is the first selected event-level processing model.

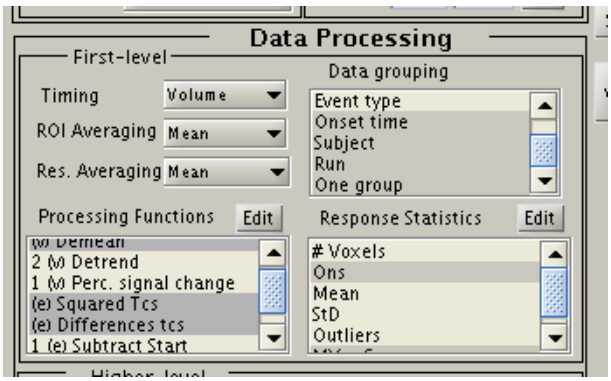
> *Press Plot*

Response statistics

2.3.2 ←

In addition to the primary processing stream, additional "response statistics" can be employed to provide single-value summaries of the response data. Response statistics are calculated immediately prior to the averaging response groups. They are averaged in the same manner as the main processing stream, and the results tabulated below the visualisation screen. These statistics enable the rapid assessment of the sensitivity of basic aspects of responses to experimental factors. Predefined response statistics include mean signal, signal standard deviation, a voxel count, and diagnostic statistics.

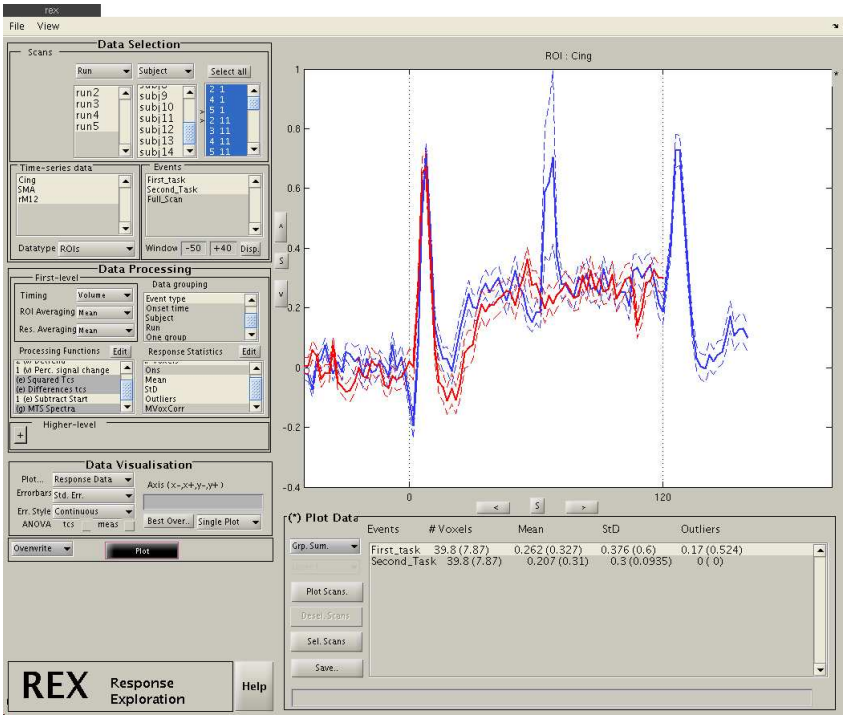
> *Select response statistics "# Voxels", "Mean", "StD", and "Outliers".*



Visualisation settings can be specified and adjusted in the Data Visualisation panel.

> *Select Std Err on from the Data Visualisation panel*
>
> *Press Plot*

The plot display will have the title 'ROI:Cing' and show the data averaged into First_Task and Second_Task responses:



Window navigation

The average cingulate response shows signal spikes at onset and offset. Note also the strange effect approximately half way through the averaged response.

Click on the right arrow (>) below the plot window

This moves to the second ROI, SMA. All ROIs are tiled horizontally and can be scrolled through. We recommend a large number of ROIs be used in exploration (> 10), to enable assessment of a wide range of responses.

Click on the 'S' button

This splits the screen vertically. Clicking again splits the screen into three, revealing the motor cortex ROI. Clicking a further time returns the display to one plot. The 'S' button to the left of the plot window splits the screen vertically in an identical manner, enabling a maximum of nine axes on the screen at once. A "*" identifies the currently selected set of axes. Data is alway plot in the row that contains this axes.

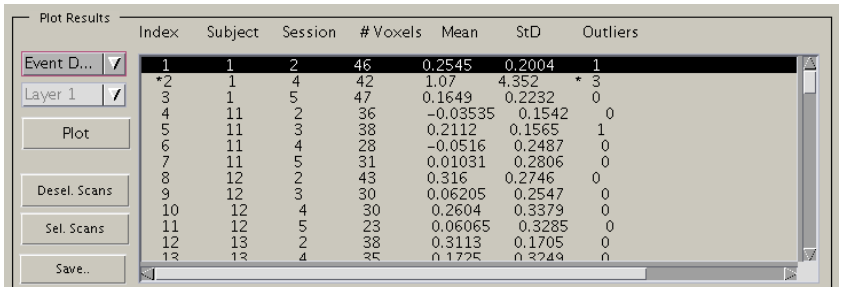
Return to the full screen view of the cingulate ROI.

Data window

Below the plot window are tabulated the selected Response statistics for the selected plot.

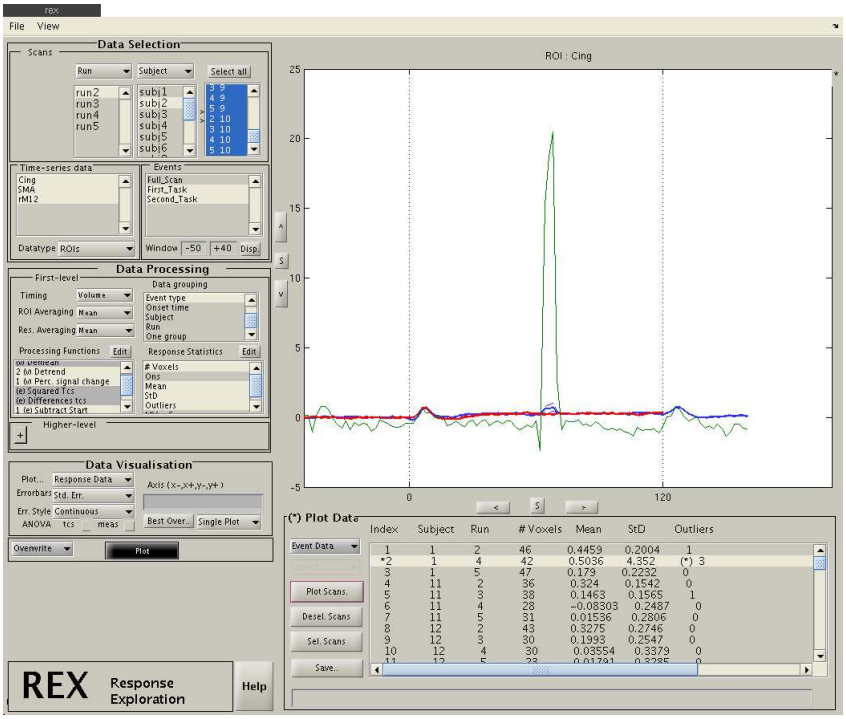
Click on the Grp. Sum. menu in the data table, and select Event data.

Now response statistics for individual event-related responses are displayed.



Note the second event is highlighted with a '*'. This indicates that the outlier count response statistic has exceeded the threshold defined for this module. The module counts the number of points > 4 Std Dev from the response mean, and the thresshold is set to one. This suggests that the scan could be affected by an artefact, such as a slice dropout.

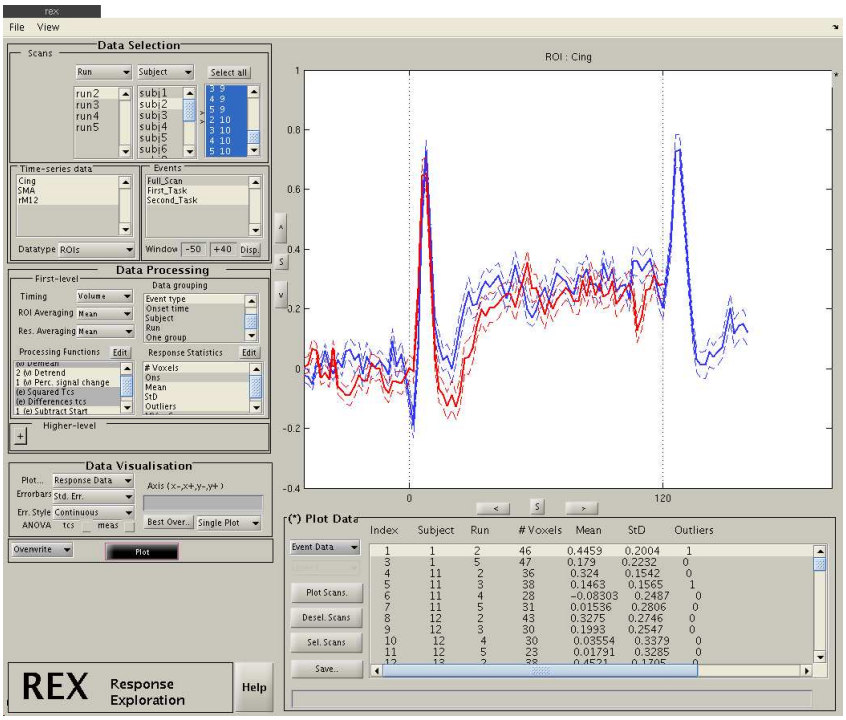
Select the highlighted (second) response and click on the Plot Scans *button to the left of the data table.*



This plots the specified response. Clearly, this response contains an artefact that causes the spike in the middle of the task period.

Click the Desel. Scans *button. Now click on the main* Plot *button.*

Deselect removes the scan associated with the selected response from the data selection menu. At present it is not possible to remove only the selected response period is not automated.



Responses with statistics that exceed a threshhold can also be set to be automatically excluded from the processing. Here, the Outlier module could be edited to include this automatic rejection:

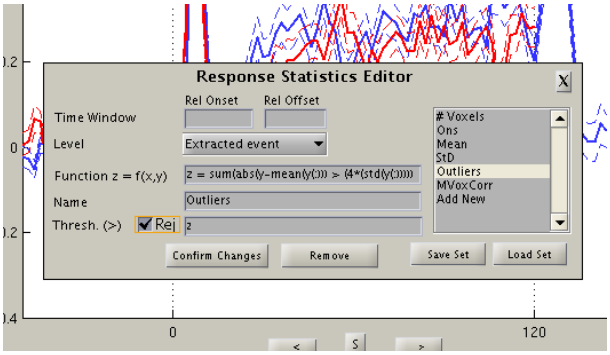
Click Select all in the Scan Selection panel

Click the Edit button above the Response statistics menu

This brings up the module editor for response statistics. The core component of a response statistic module is a single line of MATLAB code that produces that variable z, the response statistic, from x and y, and time-course data. A time window can be specified to restrict that section of the extracted response that is included in the calculation. New modules can be created by moving to the bottom of the list.

Move to the Outlier module and click on the check-box Rej.

Press Confirm changes



This specifies that any responses exceeding the Outlier threshhold of 2 should be rejected from processing. The set of processing and response statistic modules can be saved for use with other datasets using the Save Set button.

Close the editing menu with the (X) button.

Data grouping

Change data grouping to Subject

Set Errorbars to Off

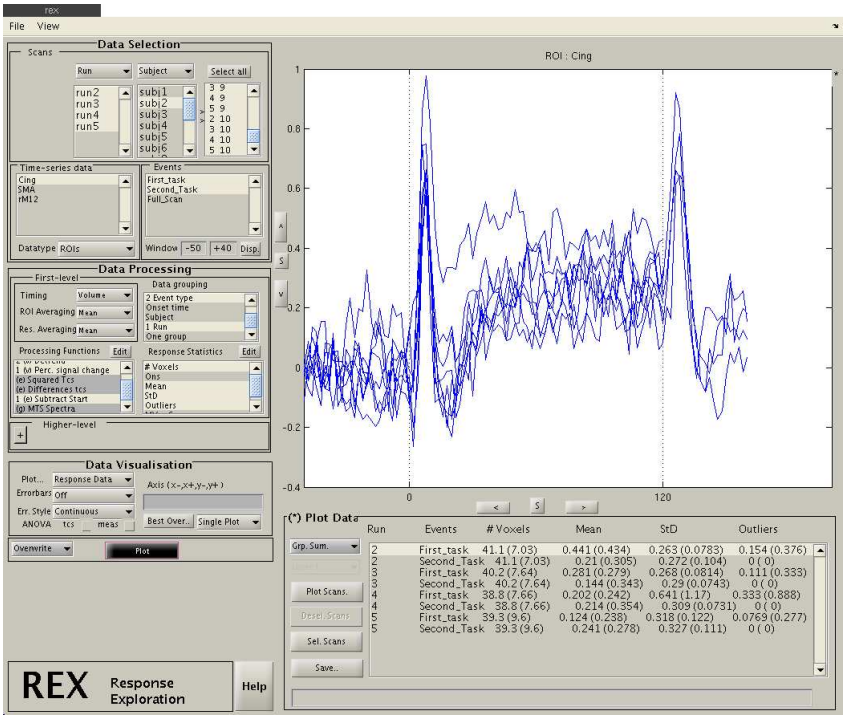
Change data table from Event data to Grp. Sum

Press Plot

The data is now split into subject-averaged responses. By clicking Plot Scans in the group summary table, the responses of individual subjects are highlighted.

Select both Run and Event Type (in that order) in the data grouping menu.

Press Plot

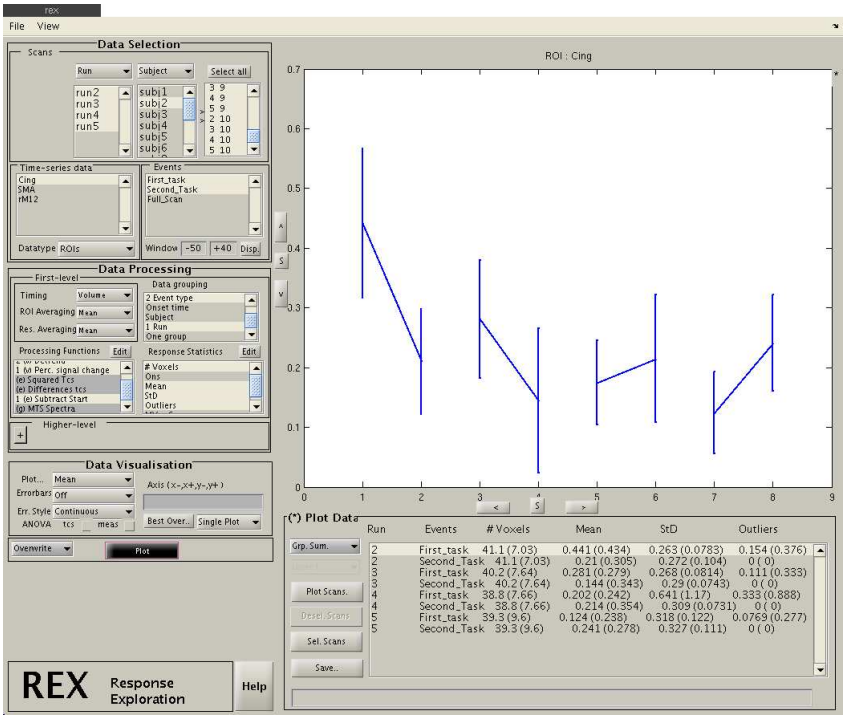


Now the data is grouped according to both event number and scan number, producing eight averaged plots. A tendency for a greater signal reduction following the initial spike, over the scanning scan, is apparent for the Cingulate. A similar effect can be seen in the SMA.

Response statistics can also be displayed graphically:

In the visualisation panel, change the Plot.. menu to Mean

Press Plot



This plots an ordered series of the Mean response statistic across the scan, revealing a reduction in the mean over time for the Cingulate. The SMA shows a similar effect. The Mean statistic has been defined to calculate the mean of the signal only during the task period. However, given the observed shape of the responses, particularly the cingulate, the mean signal is probably not an optimal statistic for assessing response patterns.

Change the Plot.. menu to StD

Press Plot

Note the very consistent changes in this parameter.

Motion parameters

REX can additionally assess motion parameters, which are automatically loaded when settings are imported from FSL analyses.

Select subject 4

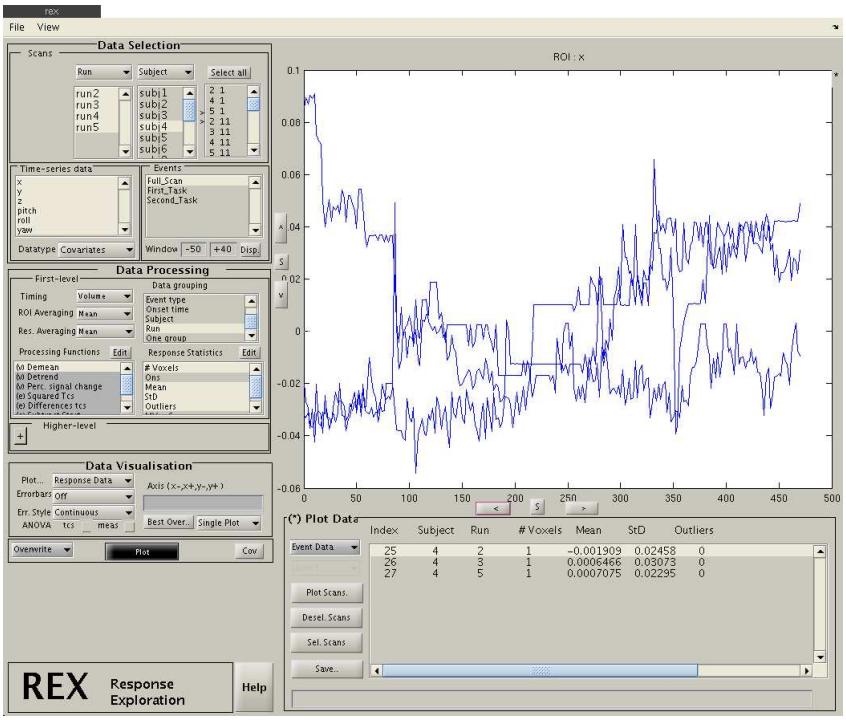
In the Data Selection window change the Data-type menu to Covariates

Select all motion parameters (x, y, z, pitch, roll, yaw).

Change the Event to helv Full_Scan

Set the processing workflow to Demean, and Data grouping to Run

Set Plot.. to Response Data, and press Plot



The motor parameters can be scrolled through across the row. A steady scanner-induced drift can be seen in the y-direction.

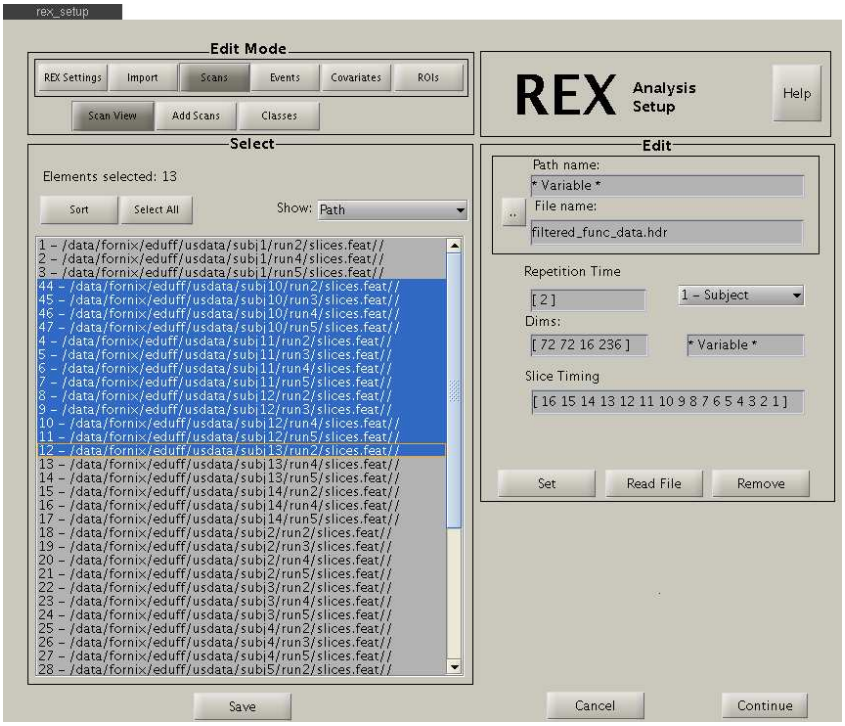
3.3 Data Setup

Change the Datatype *back to ROIs*

Go to the File *menu at the top left of the window, and select* Edit..

This brings up the REX setup window, where new experimental datasets are loaded and their organization defined. REX can read FSL FEAT and SPM experimental design files to rapidly set up an exploration. Data and data classifications can be added, altered, or removed at any stage.

The setup interface involves a number of Edit Modes for specifying and adjusting the Scan, Event, Covariate, and ROI data elements. It opens in the Scan area.



The Select window enables the selection of components for editing. The right Edit window allows the editing of these components. When multiple scans are selected, settings that are not consistent across the selected scans display ** Variable **.

Press the Classes button in the second row of buttons in the Edit Mode frame.

This area allows scan classifications for scans to be created, edited, or removed.

In the classification menu, select Add Classification.

As the Classification name, add "Group" and press Add.

This has created a new scan classification. The values of this classification can now be set in the Scan View area.

Move to the Scan View area

In the Show menu, select Subject

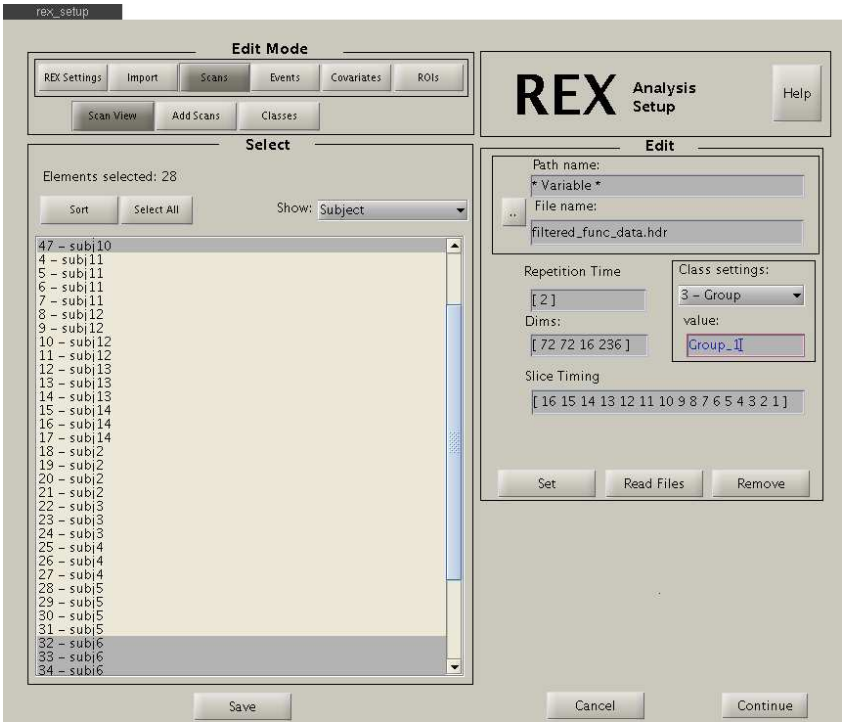
The Sort button above the window will sort the scan entries according to the displayed scan setting. This can be useful for the mass selection of elements during editing.

Select a random set of subjects.

In the Class settings subpanel, select the "Group" class and set its value to "Group_1".

Press Set.

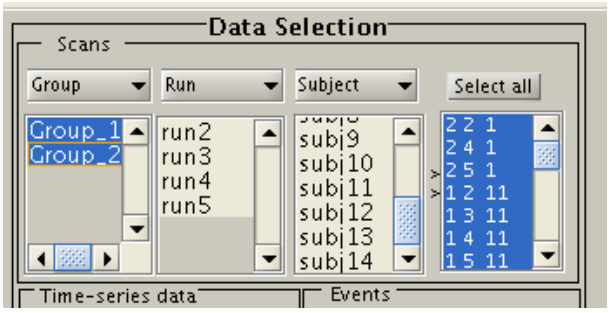
Set another group of subjects to "Group_2".



The Save button saves the updated REX file.

Click on the Continue at the bottom right of the screen

The adjusted data is now loaded into the exploration window, enabling the newly defined scan groups to be quickly selected and displayed.



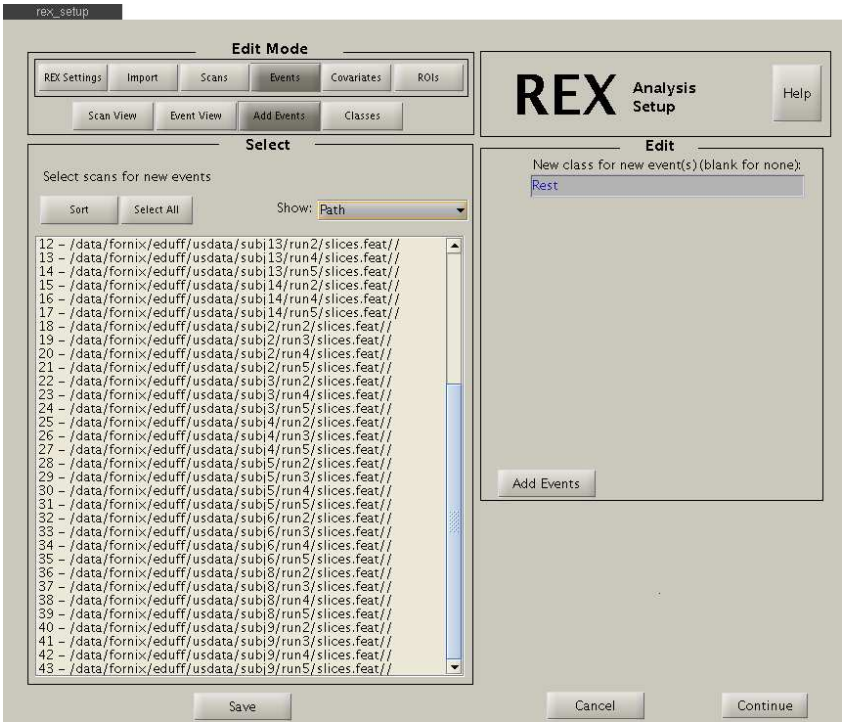
New events can be defined in a similar manner. In the final component of the tutorial, a new event will be defined for all subjects.

Go back to the data setup interface using File.. Edit, and move to the Event section

Go to the Add event section using the button in the second row.

Select all of the subjects in the select panel.

Call the new class to be associated with the events "Rest".



Press Set

This has created one new event elements associated with each scan, of class “Rest”.

Back in the Event view section, change the Show: menu setting to New_Event.

Select all the New_events, and in the Edit menu set data(ons) to be 232 and data(duration) to be 120

Press Set

Events of the same class may have different times of onset during their scans. Usually the duration of all events in a class will be the same, however REX is able to process events with differing durations.

Press Continue.

Now the second rest period of the scans can be rapidly accessed in the exploration window. Further details describing the setup procedures can be found in section 2.2.

3.4 Overview

This tutorial has demonstrated how REX can be used to explore experimental datasets. The range of signal features and effects identified in this dataset are common, and can motivate alterations to preprocessing and modelling, and provide further insight into the dynamics elicited in the experiment.