

SAfE: Straightforward Analysis of fMRI and EEG-fMRI

Manual

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July 10, 2014

Introduction

If you use S_AfE in a publication, please cite:

Beltramini GC, Covolan RJM (2013) Straightforward Analysis of fMRI and EEG-fMRI (S_AfE): A toolbox for SPM8. Proceedings of the 19th Annual Meeting of the Organization for Human Brain Mapping, Seattle, WA, USA, June 16-20 2013

S_AfE is a toolbox for SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/>). It allows one to perform straightforward analyses of almost any fMRI experiment, from the preprocessing until the statistical maps. The user must only complete a spreadsheet with the experimental paradigm and file names. Even a person with little training in fMRI analysis can use this interface very easily.

S_AfE is especially suited for situations when the number of conditions and timing of the events vary among subjects. This is one of the reasons why a spreadsheet is used to organize the paradigm.

This is particularly the case of one type of EEG-fMRI analysis. When the onset and duration of the events are obtained from the EEG, a VBA macro in Microsoft Excel reads the EEG markers file and creates the spreadsheet that will be used by S_AfE.

By requiring little user input, fMRI (or EEG-fMRI) analyses become less prone to human error and can be performed in a fast way. S_AfE uses SPM's default options for all the parameters that are not accessible through the GUI except when stated otherwise in this manual. The scripts must be manually edited to customize these parameters.

S_AfE has been tested with MATLAB R2010, using Windows and Linux operational systems. It may not work as predicted when MS Excel is not installed.

If you have any suggestion, contribution or bug report about S_AfE or this manual, do not hesitate to contact the author. Feedback from the users is very important.

Installation

To install S_AfE, unzip the contents of *safe.zip* and save them in any folder of your computer. Then add this directory to the MATLAB search path:

a) MATLAB, File, Set Path..., Add with Subfolders..., select the S_AfE directory, Save, Close

or

b) `>> addpath(genpath('full_path_to_SAfE_directory')); savepath;`

Spreadsheets

There are two different types of spreadsheet used by S_AfE:

- a) To create a spreadsheet for fMRI analysis, follow the instructions in the worksheet "Readme" of file *fMRI-events.xls*. When MS Excel is not installed, it is suggested to test first MATLAB's function "xlsread", because sometimes part of or even the full worksheet is not read¹.

Worksheet "Readme":

	A	B	C	D	E	F	G	H	I	J	K	L	M
1													
2													
3													
4													
5													
6													
7													
8													
9													

Worksheet manually created:

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1														
2														
3														
4														
5														
6														
7														
8														
9														
10														
11														
12														
13														
14														
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29														
30														
31														
32														
33														
34														
35														

- b) To create a spreadsheet for EEG-fMRI analysis, follow the instructions in the worksheet "INPUT" of file *EEG_fMRI-events.xls*. The macro works only with the markers files that were exported from Brain Vision Analyzer (Brain Products, Munich, Germany), but it could be customized to read different types of files. The expected format is an ASCII file with the sampling rate, and onset and duration of the MRI scanner triggers and marked events. For example, for an EPI acquisition with TR=2 s:

Sampling rate: 250Hz, SamplingInterval: 4.00ms
 Type, Description, Position, Length, Channel
 Response, R128, 9465, 1, All
 Response, R128, 9965, 1, All
 Response, R128, 10465, 1, All

¹ It may help to save the spreadsheet in MS Excel 5.0/95 format, or to remove all formatting from the worksheet or to remove the protected worksheets.

...
(only the first scanner trigger “R128” is used)

Stimulus, Spike, 18110, 168, Fp1
Response, R128, 18465, 1, All

...
Response, R128, 98966, 1, All

The worksheets are shown below:

Worksheet “INPUT”:

	A	B	C	D	E	F
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
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23						
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25						
26						
27						
28						
29						

Subject ID: XYP
Name: Patient Name
Struct. scan: PATIENT_NAME_T1W3D_03.nii
TR (s): 2.00
Markers folder: D:\EEG-fMRI\Epilepsy\XYP\EEG\Export

	fMRI	EEG	EEG marker
1	PATIENT_NAME_EPI_04.nii	XYP-epi01_04.eeg	XYP-epi01_04-markers
2	PATIENT_NAME_EPI_05.nii	XYP-epi02_05.eeg	XYP-epi02_05-markers
3	PATIENT_NAME_EPI_06.nii	XYP-epi03_06.eeg	XYP-epi03_06-markers
4			
5			
6			
7			
8			
9			
10			

INSTRUCTIONS:

- The fields "fMRI" and "EEG" must be filled. If there is no marker, "EEG marker" can be empty.
- Use Ctrl+Shift+S to run the macro (the spreadsheets "INPUT" and "Aux-Import" are necessary).
- NEVER modify the spreadsheet created by the macro, because it is a complete record of the experiment (all files and markers done).
- If you wish to edit the markers (e.g., rename, delete, etc.), copy the spreadsheet created by the macro, rename it to a different name (e.g., XXy, where XX is the subject ID and y = a, b, ...), edit it and write in the "OBSERVATION:" field what was done.

Automatically created worksheet:

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1																
2																
3																
4																
5																
6																
7																
8																
9																
10																
11																
12																
13																
14																
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29																
30																
31																
32																
33																
34																
35																
36																
37																
38																
39																
40																
41																

Subject: Subject Name
Struct. scan: PATIENT_NAME_T1W3D_03.nii
TR (s): 2.00

fMRI: PATIENT_NAME_EPI_04.nii
EEG: XYP-epi01_04.eeg
EEG-marker: XYP-epi01_04-markers

Type	Description	Position	Length	Channel	Description	Onset (s)	Duration (s)	Channel
Response	R128	6520	1	All				
Stimulus	Seizure	9242	70	F8	Seizure	2.9	0.3	F8
Stimulus	GSW	33569	194	F6	GSW	100.2	0.8	F6

fMRI: PATIENT_NAME_EPI_05.nii
EEG: XYP-epi02_05.eeg
EEG-marker: XYP-epi02_05-markers

Type	Description	Position	Length	Channel	Description	Onset (s)	Duration (s)	Channel
Response	R128	7789	1	All				
Stimulus	LTL_Spike	43841	62	T7	LTL_Spike	144.2	0.2	T7
Stimulus	LTL_Spike	49965	125	T5	LTL_Spike	168.7	0.5	T5

fMRI: PATIENT_NAME_EPI_06.nii
EEG: XYP-epi03_06.eeg
EEG-marker: XYP-epi03_06-markers

Type	Description	Position	Length	Channel	Description	Onset (s)	Duration (s)	Channel
Response	R128	7183	1	All				
Stimulus	GSW	87431	156	F8	GSW	321.0	0.6	F8
Stimulus	LTL_Spike	84967	75	T7	LTL_Spike	311.1	0.3	T7
Stimulus	LTL_Spike	95488	95	T7	LTL_Spike	353.2	0.4	T7

Description	Count
GSW	2
LTL_Spike	4
Seizure	1
TOTAL	7
Check	7

OBSERVATION:
- Any relevant information

Using SArE via a graphical user interface

SArE can be used through a GUI to perform fMRI analyses using SPM.

1. Open MATLAB.
2. Type “safe” in the Command Window. The following window will appear (the colors may differ depending on your operating system):

Basic input

Select the spreadsheet, the worksheet names and the corresponding data directories. The spreadsheet contains the fMRI paradigm and must follow the correct template.

3. Select at least one XLS file.
4. Select at least one worksheet for each of the selected XLS files (the worksheets will be asked sequentially for each XLS file).
5. Select the directories for each worksheet (the directories will be asked sequentially for each XLS file). The order is important. These directories must contain the files listed in the corresponding worksheet.
6. Check the box if it is an EEG-fMRI experiment. Otherwise, it is an fMRI experiment. The only difference in the analysis is that S_AfE expects a different spreadsheet organization.

Preprocessing

S_AfE will read the spreadsheets to get the file names and will preprocess the fMRI files. The preprocessing can be done outside S_AfE using SPM directly (or other toolbox) for more customized options.

7. To perform the preprocessing, check the corresponding box. The options will be enabled.
8. To perform slice timing correction, check the corresponding box.
9. To perform spatial normalization, check the corresponding box. Choose the normalization factor for the structural and functional scans.

The normalization factor is a 1×3 vector with the voxel size of the normalized image. For negative numbers, the absolute value is taken, and the result represents a multiplicative factor of the original voxel size. For example: if the normalization factor is [-2 2 4] and the original voxel size is 1.5×1.5×1.5 mm³, the resolution of the normalized image will be 3×2×4 mm³.

10. To perform spatial smoothing, check the corresponding box. Choose the FWHM for the Gaussian kernel. Negative values have the same meaning as above.

SAfE will perform the preprocessing in this order: realignment, slice timing correction (optional), co-registration, normalization (optional), smoothing (optional). The following options are different from the SPM defaults and can only be changed inside the scripts:

- Realignment: wrap in Y (both estimation and reslice options); “mean image only” as resliced image if the normalization is done.
- Slice timing: ascending slice order; middle slice as the reference slice.
- Co-registration: co-register the mean functional image and the structural image.
- Normalization using the unified segmentation approach (Ashburner J, Friston KJ. NeuroImage 26:839-851, 2005)
 - Segmentation: the output files are grey matter, white matter and CSF images in native space and their normalized versions with and without modulation
 - Normalization: wrap in Y

Design & Estimate

SAfE will read the spreadsheet to get the information of all conditions (names, onsets and durations), create the design matrix and estimate the parameters.

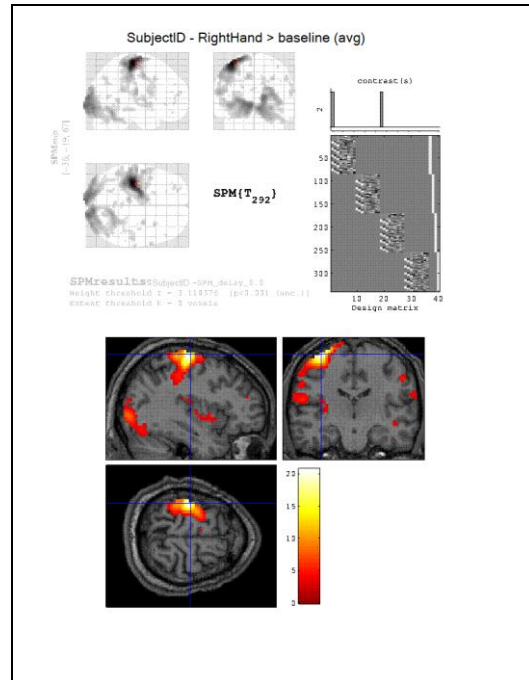
11. To create the model and estimate the parameters, check the corresponding box. The options will be enabled.
12. Choose the functional file prefix that was prepended to the fMRI file names after the preprocessing.
13. Choose the high-pass filter period (in seconds). The cutoff frequency in Hz is the reciprocal.
14. To use the 6 realignment parameters as confounders, check the corresponding box.
15. Choose the HRF, the number of basis functions (maximum 3 for the canonical HRF), the length and the delay(s). “Delay” is the size of the shift applied to the HRF (inspired by Bagshaw AP, et al. Human Brain Mapping 22:179-192, 2004)

Results

SAfE will read the SPM.mat file to create the thresholded images.

16. To generate the results, check the corresponding box. The options will be enabled.
17. To create the contrasts, check the corresponding box. T-tests are performed to test if the beta values of the conditions are greater or smaller than zero (positive

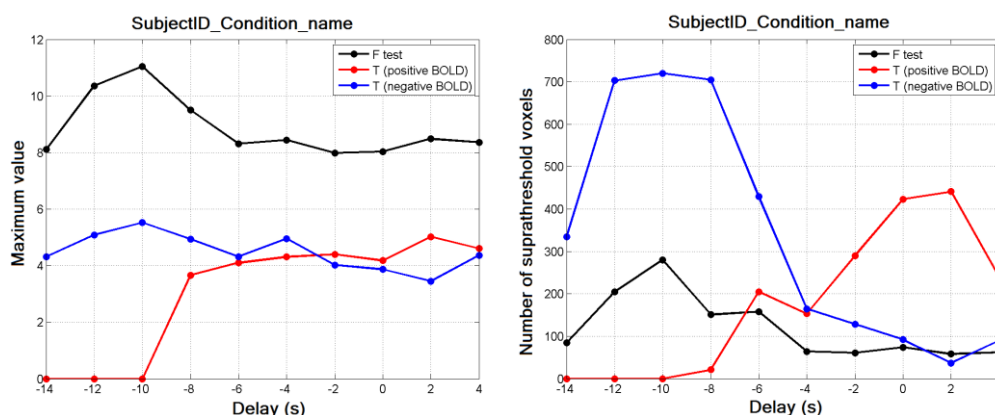
a. PS file: glass brain view, whole brain p-values and brain sections with the crosshair indicating the most significant voxel (for each contrast). For example:



20. Check the appropriate box the save a slice view image for each condition (the options will be chosen in a different window). One possible output is:



21. Check the appropriate box to make a union of the delays of the HRF (the options will be chosen in a different window). The options chosen for the slice view apply here as well. The output images are the same as above but for each group of delays. The maximum T-value and the number of suprathreshold voxels are also recorded for each group (in an ASCII file and in plots in PNG and FIG formats).
22. Check the appropriate box to save the delay images in a sequence of slice views with the statistical scale adjusted (the options will be chosen in a different window). The options chosen for the slice view apply here as well. The output is analogous to the union of delays. Two of the possible output plots are shown below:



23. Choose the file prefix of the underlay image that was prepended to the file name after the preprocessing. If the model design is also performed, SAfE will use the structural image as the underlay image; otherwise, it will look for the file in the subject folder.
24. When the file prefix is empty or ambiguous, it may be necessary to specify an additional text to uniquely identify the underlay image (part of its file name).
25. To remove the temporary files (mostly thresholded images), check the Clean up box.

Options

The screenshot shows the 'SAfE: Options for the results' dialog box. It has three main sections:

- Slice view:** Includes a 'Number of slices' dropdown set to 36, and 'Slice orientation' checkboxes for Axial (checked), Coronal, and Sagittal.
- Union of delays:** Includes 'No. of delays per group' set to 3, an 'Adjust scale' checkbox (checked), and radio buttons for 'Maximum value of all delays' (selected) and 'Specify maximum values'. Below are input fields for 'F-test', 'T (positive BOLD)', and 'T (negative BOLD)'.
- Sequence of delays:** Includes an 'Adjust scale' section with radio buttons for 'Maximum value of all delays' (selected) and 'Specify maximum values'. Below are input fields for 'F-test', 'T (positive BOLD)', and 'T (negative BOLD)'.

At the bottom are 'OK' and 'Cancel' buttons.

26. Slice view: choose the number of slices, the step size (in mm) or the coordinates of the slices, and the slice orientation(s).
27. Union of delays: choose the number of delays that will be put together in each group; choose also if the statistical scale will be adjusted for all groups and, if

so, if it will be done using the maximum value among all delays or with custom maximum values.

28. Sequence of delays: adjust the statistical scale using the maximum value among all delays or with custom maximum values.

Load, save, run

All the chosen parameters can be saved and loaded afterwards. They can be then edited in the GUI or through the command line. To run the analysis, click on the Run button.

Using SAE via command line

In addition to the GUI, complete analyses with SAE can be done using the command line. There are two easy ways:

- a) Edit and run the file `safe_INPUT.m`, based on `safe_INPUT_template.m` (with the default options) or `safe_INPUT_example.m` (with some dummy values). The available options in the scripts and in the GUI are practically the same.
- b) Choose some or all parameters in the GUI, save them, load the created file, edit the variable and run the analysis with the script `safe_preproc_stat.m`.

The script `safe_preproc_stat.m` (the GUI also calls this function) basically calls all the functions in an organized way to perform the complete analysis. Alternatively, all the functions can be called independently. The file names of the scripts that are directly called by SAE start with “safe_”. For example, the preprocessing is performed by `safe_preproc.m`. To learn more about what each script does, check the corresponding help text.

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