

This toolbox was developed as part of a project funded by the European Union under the MUR PNRR grant for young researchers (Project No. SOE_0000127; CUP H97G2200032006), titled "PRISM: Profiling the risk for schizophrenia with machine learning." It was first utilized in the following paper: Valt, C., López-Caballero, F., Tavella, A., Altamura, M., Bellomo, A., Barrasso, G., ... & Salisbury, D. F. (2024). "Abnormal inter-hemispheric effective connectivity from left to right auditory regions during Mismatch Negativity (MMN) tasks in psychosis. *Psychiatry Research*, 342, 116189. Doi: 10.1016/j.psychres.2024.116189.

Please cite the Valt et al., (2024). *Psychiatry Research* paper, along with Brainstorm (Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM (2011) Brainstorm: A User-Friendly Application for MEG/EEG Analysis Computational Intelligence and Neuroscience, vol. 2011, ID 879716), and the toolbox as: Valt (2024) Toolbox for Computing Source-based Spectral Granger Causality in Sliding Time Windows retrieved from github ...

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Disclaimer:

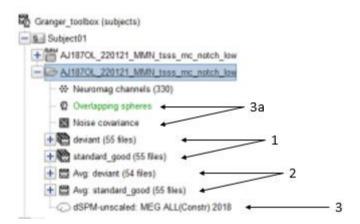
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This toolbox utilizes the spectral Granger Causality function of Brainstorm to analyze concatenated segments of source-reconstructed signals within sliding time-windows. First, the program concatenates all artifact-free trials. It then selects and combines moving data windows from each segment. Granger causality analysis is subsequently applied to the concatenated file of these data windows.

PREPARATION OF DATA WITH BRAINSTORM

Imported data organized as follow:

- 1) Imported segments of interests.
- 2) Average
- 3) **The kernel of a source model** (for sLORETA or other see specification below). To process it you need the Noise Coviariance (computed from an empty room recording or all data) and the head model (here, computed as Overlapping spheres) [these two files are not necessary in the three for the Granger analysis]. IMPORTANT, the kernel should be on constrained vertices.

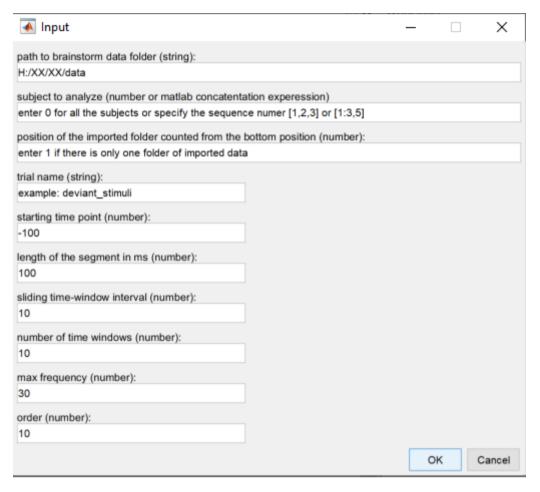


RUNNING THE TOOLBOX

Run the script directly from the Matlab editor window or by calling it by name in the Matlab command window when it is current folder or the folder is saved in the Matlab path.

IMPORTANT: Brainstorm must be running

INPUT WINDOW 1



1) path to brainstorm data folder

Enter the path to the folder containing your data. To find this path, right-click the data folder, select 'Properties,' and copy the path. Then, paste it into the input window and append '\data' to the end. You can use either forward slashes (/) or backslashes (\), but be consistent throughout.

Example:

H:\Granger toolbox\data or H:/Granger toolbox/data

This part is used by the script to identify the folder that holds all the data required for Granger Causality analysis.

2) Subjects to analyze

Specify the ordinal positions of the subjects you wish to analyze as they appear in the Brainstorm tree. To include all subjects in the protocol, enter [0]. Alternatively, you can enter a concatenated sequence (using [...]) of the ordinal positions for specific subjects.

Example_2:

[1:3,5] or [1] or [0]

With the settings of Example_2, the analysis will consider 1) the first three subjects and the fifth subject in the brainstorm tree, or 2) only the first subject, or 3) all the subjects.

3) Position of the imported folder counted from the bottom position

Imported folders might be more than one with different names, for example when there is more than one experimental run. In the brainstorm tree, these folders are saved after pre-processed entries. The toolbox will select the position of the imported folder of interest looking from the last position in the brainstorm tree. Hence, if there is only one imported folder, finding it is easy (enter 1 if there is only one file). However, if there are more than one imported folders, finding the correct one might be more complicated. In this case, you should enter the position of the imported file in the brainstorm tree counting from the last.

Example_3:

3 or 1

Consider a scenario with three experimental runs, where the imported folders in the Brainstorm tree are labeled as run1, run2, and run3. By entering '3,' the Granger Analysis will process the first branch, which is run1. Conversely, if you input '1,' the analysis will target the last branch, run3.

4) Trial name

The name of the trials you want to analyze.

Examples_4:

deviant or standard_good

The toolbox can process only one trial type a time. This entry is key-sensitive.

5) Starting time

Specify the starting time for the Granger Causality time windows. This can be the beginning of the segment or another specific time point within it, such as the moment of marker onset, which is typically represented as the 0 point.

Example_5:

-100

With the setting in Example_5, the first time-window will be created from -100 ms before the stimulus of interest

6) Length of the time-window

Specify the length of the time-window for the Granger Causality analysis. A suggested length is 100 ms. Longer time-windows may diminish the Granger Causality effect, as it represents an average over time, while shorter time-windows might reduce the analysis's sensitivity to low frequencies.

Example:

100

Here, the Granger Causality analysis will consider a 100-ms-long time window for each trial. With the input in Example_5, this setting determines a time-window that goes from -100 to 0.

7) Number of time windows

The movement interval from one time-window to the next.

Example_7:

10

With this setting, the time-windows will have 10 ms gaps between them. Adjusting this number higher or lower will decrease or increase the temporal resolution of the analysis, respectively. Taking into account the settings in Examples_5:6, the first time window spans from -100 ms to 0 ms, the second from -90 ms to 10 ms, and this pattern continues accordingly."

8) Sliding time-window interval

The number of time windows to be considered.

Example_8:

10

Here, the Granger Causality analysis will be performed on ten different time-windows. With the inputs in Examples_5:7, the analysis will start with the time-window -100:0, move in steps of 10ms to -90:10, -80:20... until -10:90.

9) Max frequency

The highest frequency you want to consider. This frequency must not be higher than the low-pass filter, if used in the pre-processing. Frequencies are than calculated in steps of 2Hz.

Example 9:

30

With the setting in Example 9, the program will consider 15 frequencies (2Hz, 4Hz, 6Hz,, 30Hz)

10) Order

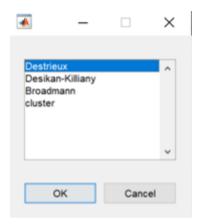
The number of previous time points considered when estimating the causal relationships between time series. A higher order allows the analysis to incorporate more historical data, potentially capturing more complex dynamics. However, setting the order too high can lead to overfitting, while a low order might miss important causal influences. Typically, it's important to find a balance based on the characteristics of your data and the specific analysis goals.

Example 10:

10

The Brainstorm tutorial suggests an order or 10, estimating the Granger causality based on 10-ms data before the time of interest in a 1000Hz recording, but 40ms in a 250Hz recording. Select this number wisely depending on the SAMPLE RATE of your data.

INPUT WINDOW 2

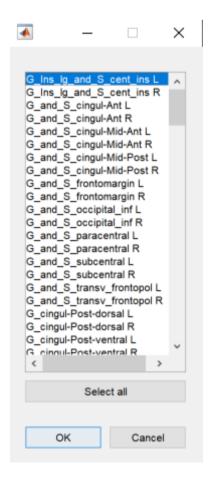


Select the atlas of interest.

Atlas files are stored in the toolbox folder. To add a new atlas, simply save it in the toolbox folder and replace the word 'cluster' with the name of the new atlas in lines 49 and 60, or add a new entry.

You also have the option to create personal scouts by merging different parcellations. However, this approach is not recommended, as it may cause issues when working with individual anatomical data.

INPUT WINDOW 3



Select the parcellations of interest.

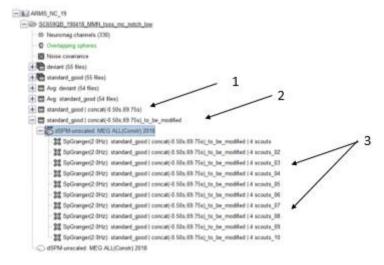
WARNING: the computational time increases exponentially with the number of vertices. In case of many parcellation (for a total number of vertices larger than 200), use mean before instead of mean after (see below changes within the script)

SUMMARY WINDOW

```
SETTINGS:
data folder: H:/toolbox_test/data
number of subjects: 1
data folder: standard_good
starting time: -100
window length: 100
sliding interval: 10
number of time-windows: 10
number of frequencies: 30
order: 10
ATLAS: Destrieux
Number of parcellations: 2
Parcellations: G_Ins_Ig_and_S_cent_ins L; G_Ins_Ig_and_S_cent_in...
   OK
              Restart
                           Cancel
```

Summary of the inputs. Press OK to run the script if the entered settings are correct. Press Restart to modify the setting. Press Cancel to exit the toolbox.

OUTPUT IN BRAINSTORM



- 1) Concatenated segments of all artifact-free trials.
- 2) Concatenated segments of in the last window.
- 3) Spectral Granger causality in the different time-windows

SUMMARY OUTPUT FILE

A Matlab structure with a summary of the toolbox setting and output. This .mat file is saved in the same folder of the Toolbox folder, with a name Granger_Causality_*subject name*_*date_time*.

File (cell array):

a table with the output files created in the brainstorm space.

Column1 = number of created files;

Column2 = name of the Granger causality file in Brainstorm

Column3 = the starting data point in the segment

Column4 = the ending data point in the segment

Column5 = the correspondent starting time point in the segment

Column6 = the correspondent ending time point in the segment

Column7 = the link file used by Brainstorm to run the Granger causality Brainsotrm function

Column8 = the name of the .mat file in the Brainstorm data folder

Saving data (cell)

The date and time of the saved file

Input_setting (string array)

The input settings entered in the toolbox by the user

current (string array)

The folders and files used for by the toolbox

Design_description (string array)

A summary of experimental parameters extracted from the Brainstorm structure

Frequencies

The frequencies considered in the Granger causality analysis

Regions (cell array)

The brain regions considered in the Granger causality analysis

Column1: atlas

Column2: parcellation

Column3: number of vertices

Changes within the script.

Different source-reconstruction model

If your source-reconstruction model is sLORETA change "filesStartingWith4Kernel" (line 135)

Example

filesStartingWith4Kernel = dir(fullfile('results_dLORETA*.*'));%%%

Average data before Granger Causality

This procedure speeds-up the analysis but might decrease the sensitivity of the effective connectivity estimation. Change 'scouttime', 'after', ...

Example

'scouttime', 'before' ...

Use PCA before Granger Causality

This procedure speeds-up the analysis but might substantially decrease the sensitivity of the effective connectivity estimation. Change 'scouttime', 'after', ... and 'scoutfunc', 'mean', ... % PCA. Afterwards, the PCA settings should be checked.

.Example

'scouttime', 'before' ...

'scoutfunc', 'PCA', ... % PCA