

Graph Theoretical Analysis of Task-related Functional Dynamics (GAT-FD) Toolbox Manual

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1. Introduction

1.1. What is GAT-FD?

Graph Theoretical Analysis of Task-related Functional Dynamics (GAT-FD) integrates the complete pipelines for estimating the task-related dynamic brain functional connectivity (FC) metrics and quantifying the topological dynamics and its statistical property of the functional brain network. The GAT-FD toolbox is developed using MATLAB version 2019b (The MathWorks Inc., Natick, MA, US), under a 64-bit Windows (Microsoft Corp., Redmond, WA, US) environment.

1.2. What can GAT-FD do?

The GAT-FD toolbox includes the following modules:

- Sliding-window analysis: generation of the FC matrices using time points within defined sliding-window.
- Task design: generation of temporal mask based on the task design.
- Network analysis: calculation of the functional network property dynamics.
- Result display: visualization of the intermediate processes and results of the functional dynamics.

This toolbox has been successfully tested in MATLAB under a variety of operating systems with SPM12 and brain connectivity toolbox, including Windows 10 and Mac OS 10.14 in 64-bit versions.

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2. Installation

2.1. Before using GAT-FD

- The GAT-FD toolbox package can be downloaded from https://www.nitrc.org/projects/gat_fd and https://centers.njit.edu/cnnl/gat_fd/
- Required MATLAB Toolboxes:
 - Imaging Processing Toolbox
 - Signal Processing Toolbox
 - (Optional) Parallel Computing Toolbox
- Two prerequisite toolboxes need to be installed:
 - The brain connectivity toolbox (BCT) (download from <https://sites.google.com/site/bctnet/>)
 - Statistical Parametric Mapping (SPM) (download from <https://www.fil.ion.ucl.ac.uk/spm/software/download/>).
- The format of the initial imported image files must be preprocessed functional MRI data using SPM (.nii) or FMRIB Software Library (FSL) (.nii.gz).
- Before you start, always make sure that the preprocessed functional MRI data are in the standard space (usually in the MNI space). If you use customized masks (details are discussed in Chapter 3.1.6), make sure your preprocessed functional MRI data are in the same space with your regions of interest (ROI) masks.

2.2. Run GAT-FD on a PC with MATLAB

- Run MATLAB. (A version of R2018a or above is recommended)
- Add GAT-FD toolbox package to MATLAB search path:

Click 'File' in MATLAB menu -> Click 'Set Path' -> Click 'Add with Subfolders...' button in the popup dialog-> Select the 'GAT_FD' folder on the machine -> Click 'OK' button -> Click 'Save' Button.
- Add prerequisite BCT and SPM toolbox packages to MATLAB search path using the same way.
- Run GAT-FD:

Type 'GAT_FD' in the command window of MATLAB.

The main user interface below (**Fig. 2.1**) will be shown after successfully running the GAT_FD. Details of the 4 modules will be explained in Chapter 3.

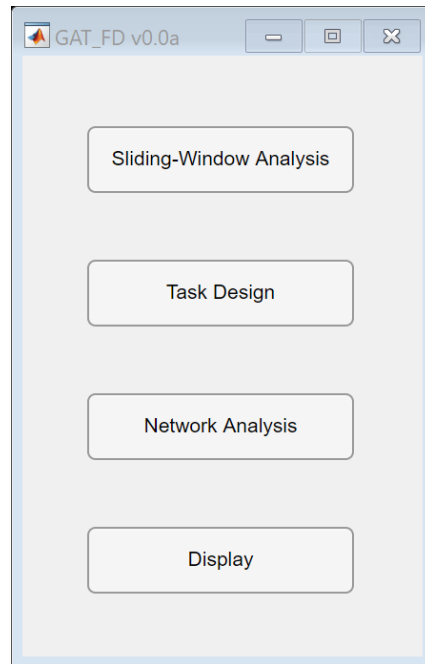


Fig. 2.1 The main user interface of the GAT-FD

3. GAT-FD Graphical User Interface (GUI) Basics

3.1. Sliding-Window Analysis

The sliding-window approach is the most common analytical method to explore the network dynamics in fMRI studies [1]. In this approach, a window with the current time points and a fixed number of previous time points is first selected, to construct the FC matrix of the current time point. Then the sliding-window moves to next time point and the process repeats till the end of the task period to generate a series of FC metrics. [2-10].

Press the **Sliding Window Analysis** button in the main use interface.

You can find the interface below (**Fig. 3.1.1**) after successfully running the **Sliding-Window Analysis**.

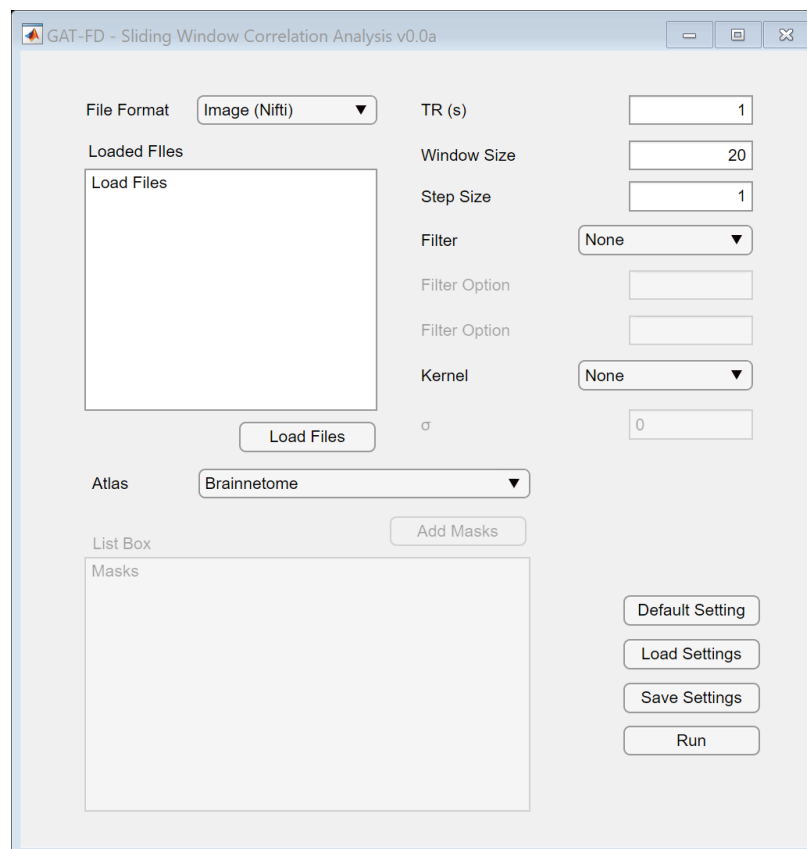


Fig. 3.1.1 The interface of sliding-window analysis

3.1.1. Load Files

Two types of imaging files can be imported for the slide-window analysis, including the raw fMRI data (Nifti format images) and time series data (.mat format, time x ROIs)

Raw Image File:

Click **Load Files** button, select files to import (**Fig. 3.1.2**). In the current version, the GAT-FD only support “*.nii” or “*.nii.gz” format data as input.

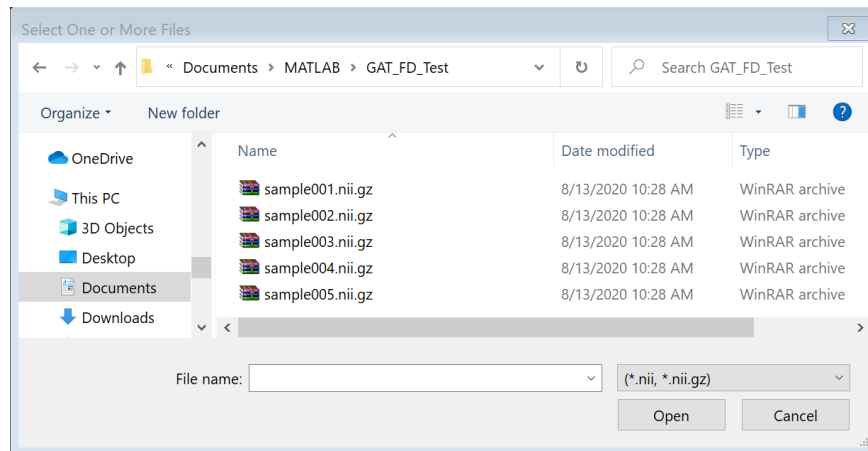


Fig. 3.1.2 Import files for sliding window analysis

Click Open, then you can find your imported image files in the **Loaded Files** window (**Fig. 3.1.3**).

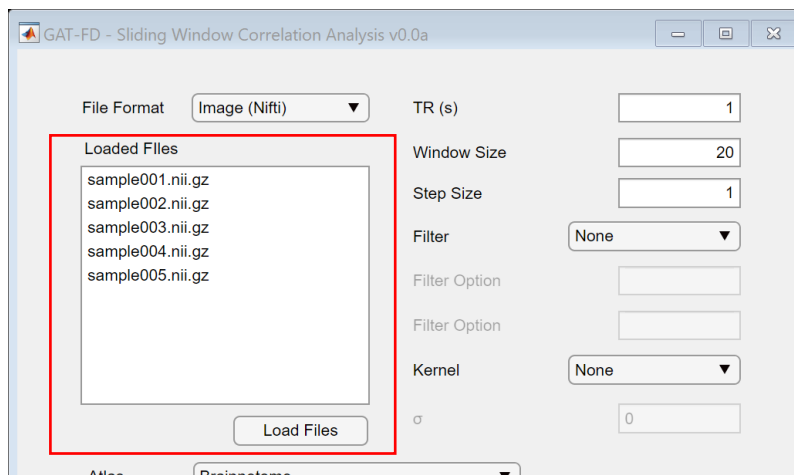


Fig. 3.1.3 Imported files for sliding window analysis

Time series data:

You can also import MAT-format matrix which contains the time series of the brain regions based on your own research interest. This allows users to apply customized temporal processes to the data before analysis.

3.1.2. Window Size

Window size is the size of the window, which is the length of the sequence you're looking at each time in the analysis. For block-designed tasks, the window size is usually smaller than the

block duration. For the illustration data, the repetition time (TR) is 1s, duration of each block is 30s, we set the window size as 20 TRs (20s).

Type your window size value in number of TRs.

3.1.3. Step Size

Step size is the moving length of the "sliding" action. For the illustration data, we set the step size as 1TR=1s.

Type your step size value in number of TRs.

3.1.4. Temporal Filter

Four options including high-, low-, band-pass filtering, and wavelet filtering are offered to help minimize the undesired noises of the imaging data (**Fig. 3.1.4**).

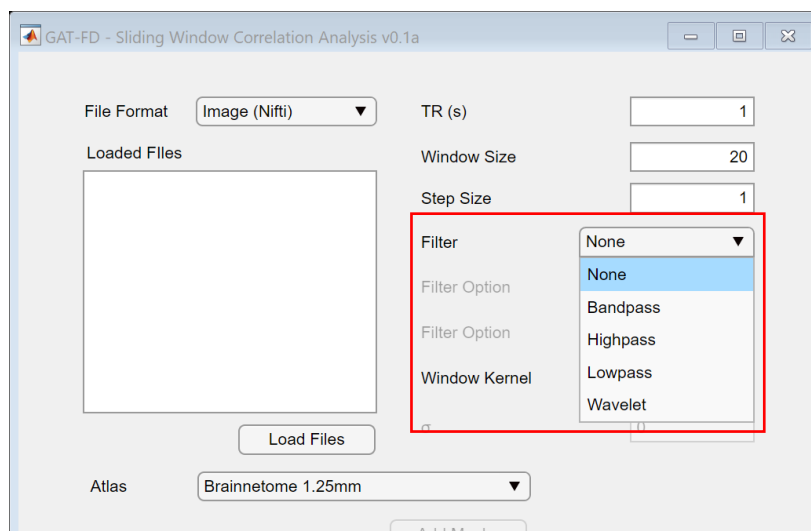


Fig. 3.1.4 Filter selection

Wavelet decomposition is a frequently used tool in task-based fMRI data analysis. It increases sensitivity in detecting signal correlation against a noisy background, especially when motion artifacts related spikes occur. If the wavelet filtering function is selected (**Fig. 3.1.5**), the sliding-window module will first decompose each activation time series with specified number of levels, and then transfer back with selected levels of coefficients.

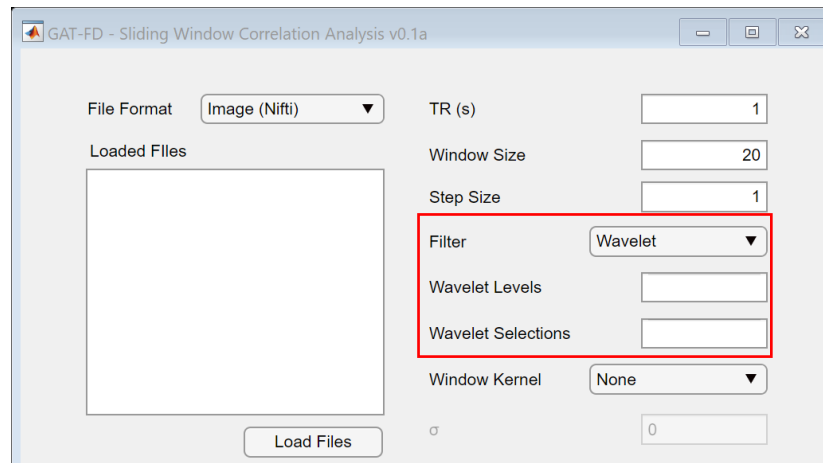


Fig. 3.1.5 Wavelet Options

3.1.5. Window Kernel

You can also apply kernel when calculating the correlation of the network within a sliding window, which increase the weight of the center points for correlation calculation. Current version only supports Gaussian kernel.

You can select Gaussian kernel from the Kernel drop-down list (**Fig. 3.1.6**). Then you can type your sigma (σ) value (standard deviation) for the Gaussian kernel.

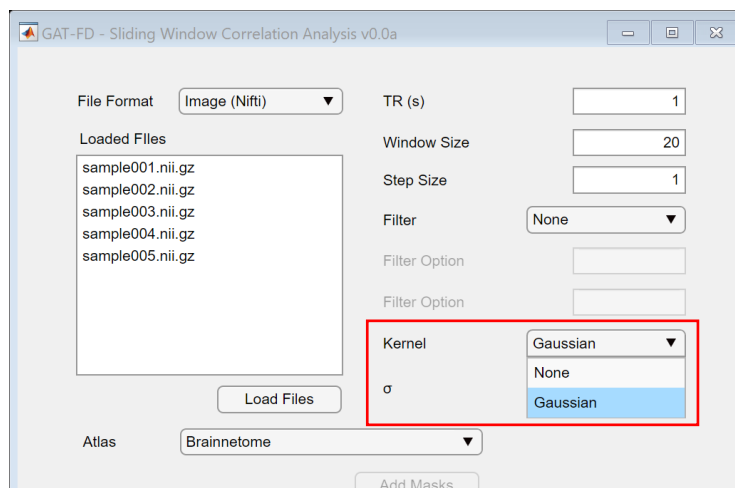


Fig. 3.1.6 Kernel selection

3.1.6. Atlas

The GAT-FD toolbox provides two options for region-of-interest (ROI) determination, including the build-in atlas and customized brain masks (**Fig. 3.1.7**). For the build-in atlas, the current version of GAT-FD offers two options, the Brainnetome atlas and Automated Anatomical Labeling (AAL) atlas, which are most used in neuroimaging studies [11, 12].

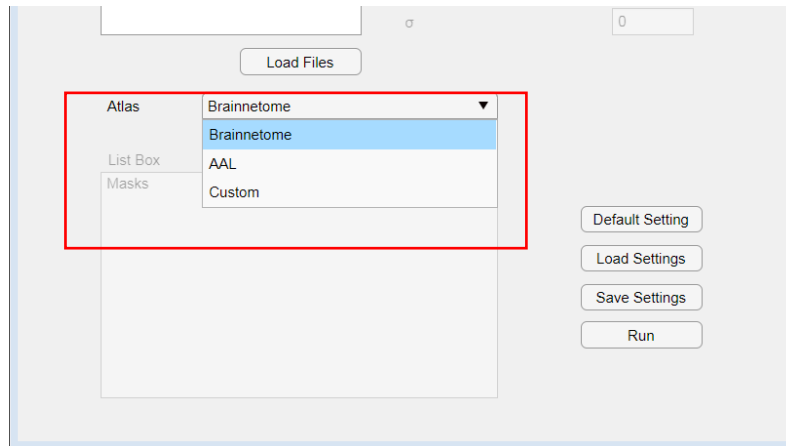


Fig. 3.1.7 Atlas selection

The GAT-FD also provides selections of customized brain masks. The customized brain masks need to be prepared in the Montreal Neurological Institute (MNI) space to avoid miscalculations during extraction of blood-oxygen-level-dependent (BOLD) responses. When select your customized brain masks, click on “Atlas” and choose “custom” from the drop-down list. Then click on “Add masks”, and select your customized brain masks (**Fig. 3.1.8**).

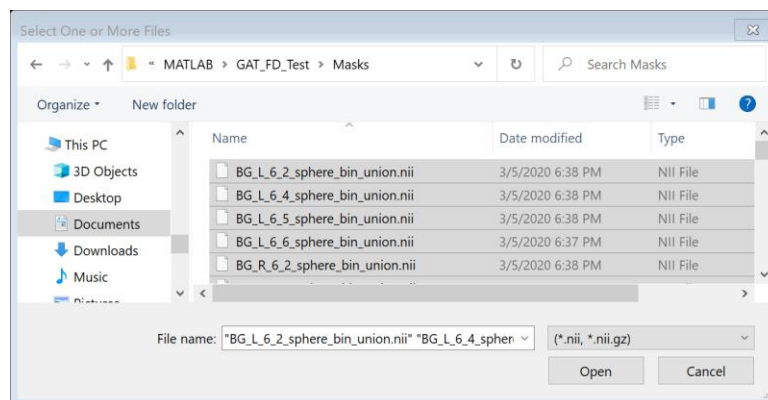


Fig. 3.1.8 Customized brain masks selection

Click “open”, then you will find the selected brain masks in the “List Box” window (**Fig. 3.1.9**). You can either select one file that contains all masks or multiple individual masks in this step.

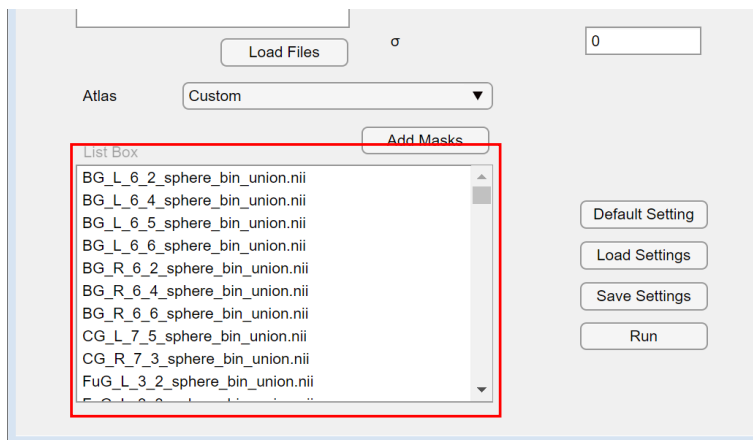


Fig. 3.1.9 Selected customized brain masks

3.1.7. Default Setting

The GAT-FD provides a default setting which included parameters utilized for the illustration data analysis. To process the data using default setting parameters, click on the “default setting” button. Then click “Run”.

3.1.8. Load Settings / Save Settings

The “load settings” allows you to select your pre-saved setting for your customized sliding-window analysis. Click on the “Load Settings” button, select your pre-saved setting, click “open”, and then click “Run”.

Click ‘Save Settings’ button to save your current setting for future use.

3.1.9. Run

After clicking the ‘Run’ button, a destination directory selection dialog will be shown. Select your output directory and click ‘OK’ (**Fig. 3.1.10**).

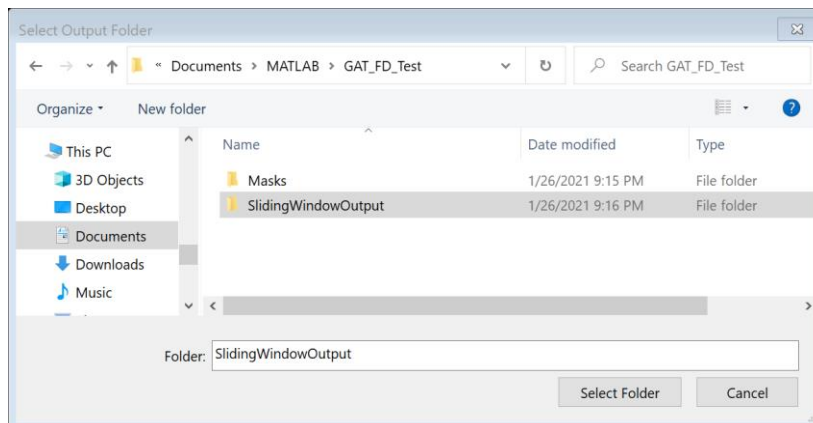


Fig. 3.1.10 Output folder selection

When successfully running sliding-window analysis, you will find a window (**Fig. 3.1.11**) showing you the current processing status.

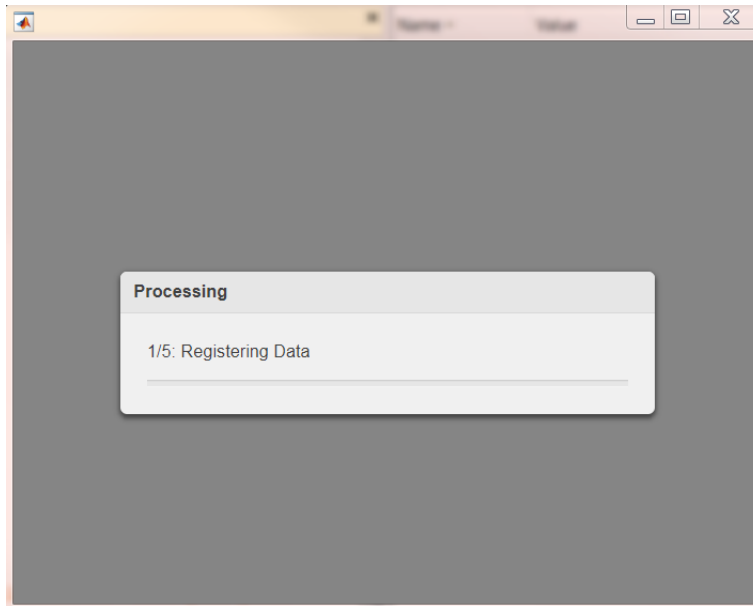


Fig. 3.1.11 Processing status window of sliding-window analysis

3.1.10. Output Data

After successfully running the sliding-window analysis, a “Finished” window will be shown (**Fig. 3.1.12**), and a *.mat file will be generated in your output folder for each subject (**Fig. 3.1.13**). These files will be used in the following network analysis (details are explained in Chapter 3.3.1).

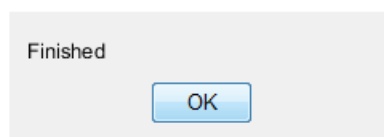


Fig. 3.1.12 Finished window after successfully running sliding-window analysis

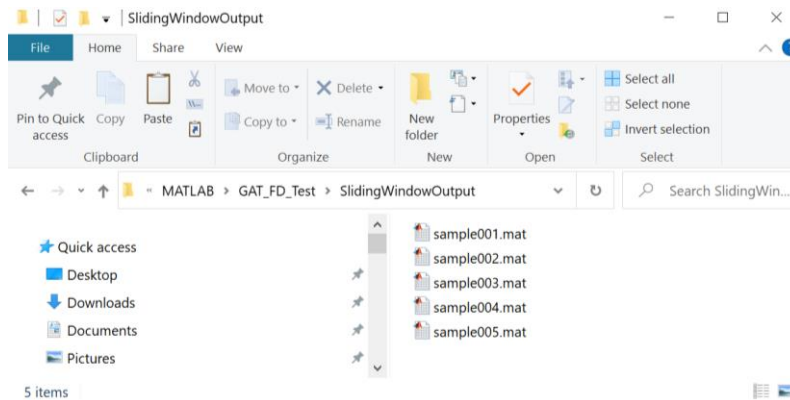


Fig. 3.1.13 Output data of sliding-window analysis

3.2. Task Design

The GAT-FD provides dynamic functional connectivity analysis for functional MRI data collected during block-designed tasks. The task design function is designed for generating task condition files based on the task design information. Generated task condition will be used for the future dynamic functional network connectivity analysis.

When creating task condition files, click the **'Task Design'** button from the toolbox main menu.

You can find the interface below (**Fig. 3.2.1**) after successfully running the **Task Design**.

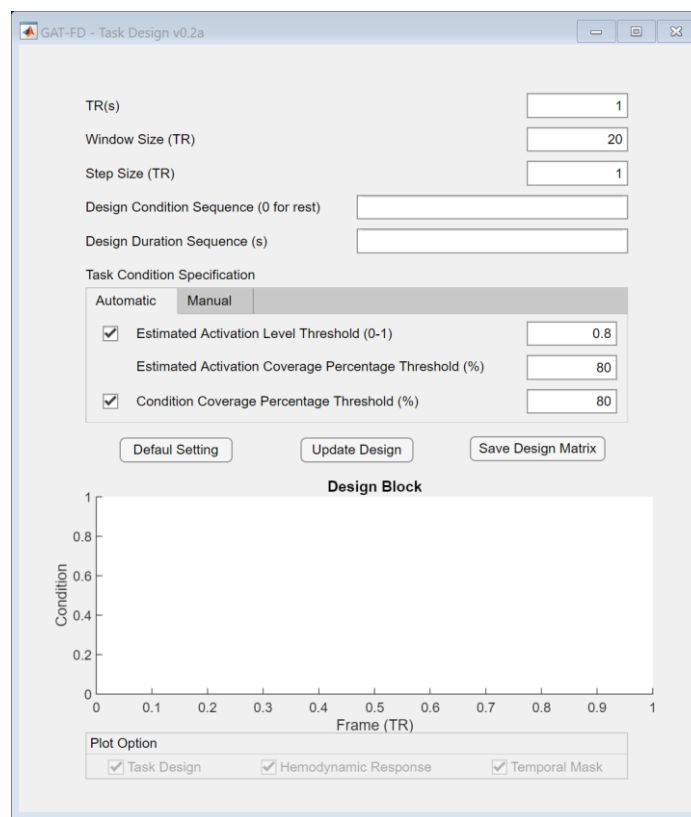


Fig. 3.2.1 The interface of task design

3.2.1. TR / Window Size (TR) / Step Size (TR)

Type the **TR** value of your functional MRI data. For the sample data, the TR is 1s.

Type the same **window size** (in TRs) that you used when calculating the sliding windows.

Type the same **step size** (in TRs) that you used when calculating the sliding windows.

3.2.2. Design Vector (0 for rest)

The condition list for the design. For example, "0 1 0 1 0 1 0 1 0 1". Use 0 for rest, and 1 for task.

3.2.3. Duration Vector (second)

The duration list for each condition. For example, "30 30 30 30 30 30 30 30 30 30". In number of TRs.

3.2.4. Estimated Activation Level Threshold (0-1)

The level of activation of a time point that will be considered as task condition. (default is 0.8, full activation is 1)

3.2.5. Estimated Activation Coverage Threshold (%)

The percentage of task time points (higher activation response than the threshold set in chapter 3.2.2) in a window for that window to be included in the variance and mean calculation. (Default is 80%)

3.2.6. Condition Coverage Percentage Threshold (%)

The percentage of time points within task block in a window for that window to be included in the variance and mean calculation. (Default is 80%)

3.2.7. Manual Condition Input

The toolbox also supports manually defined conditions (one task condition and one rest condition in the current version). As shown in **Fig. 3.2.2**.

After defining the sliding window options, design condition, and design duration, the total number of frames can be calculated by clicking on "calculate".

Then the stage condition and duration can be manually set. 0 for rest and 1 for desired condition.

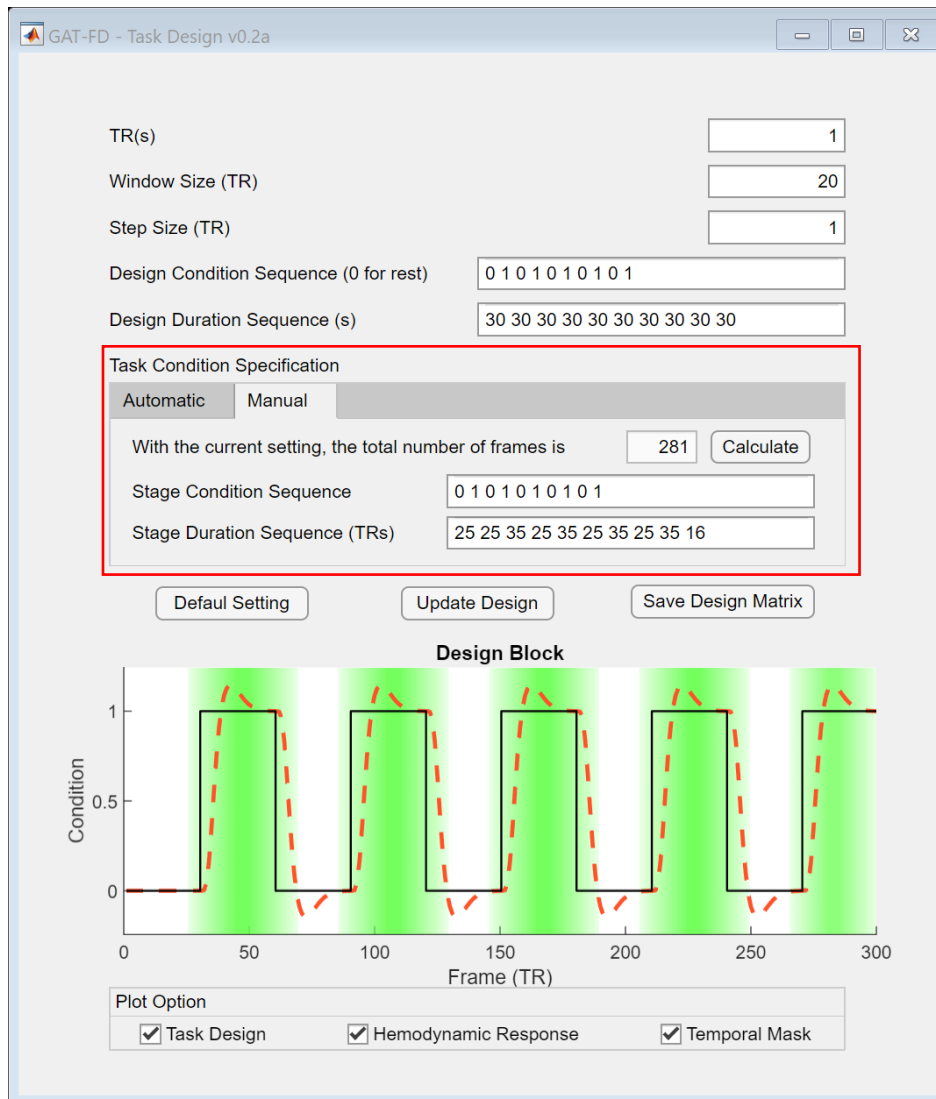


Fig. 3.2.2 Define condition using manual option

3.2.8. Default setting

Restore default settings.

3.2.9. Update Design

After clicking the 'Update Design' button, you will find a plot showing the task design for the current settings (**Fig. 3.2.3**). The green areas represent frames that covered by task windows. Yellow areas represent the frames that are in task condition. The black solid line is the task design while the red dash line is the calculated hemodynamic response.

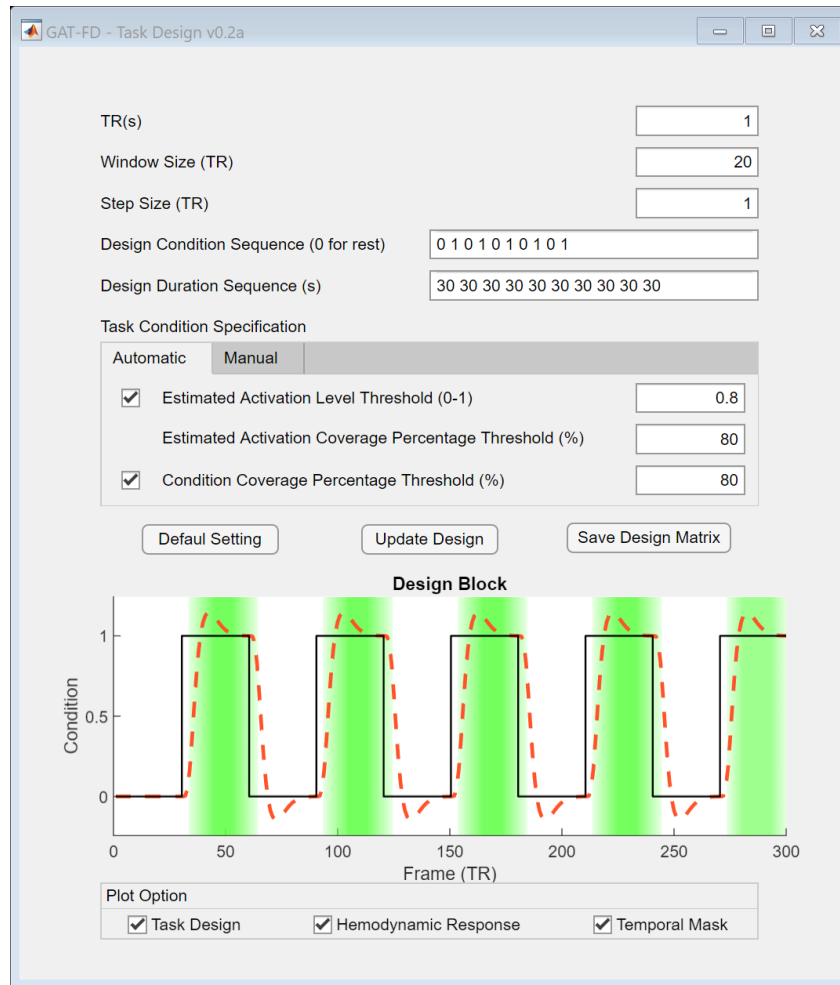


Fig. 3.2.3 Plot of the task design

The GAT-FD provides options for plotting the task design. Uncheck the option you do not need, the updated plot will be shown in the 'Design Block' window immediately (**Fig. 3.2.4 a-c**).

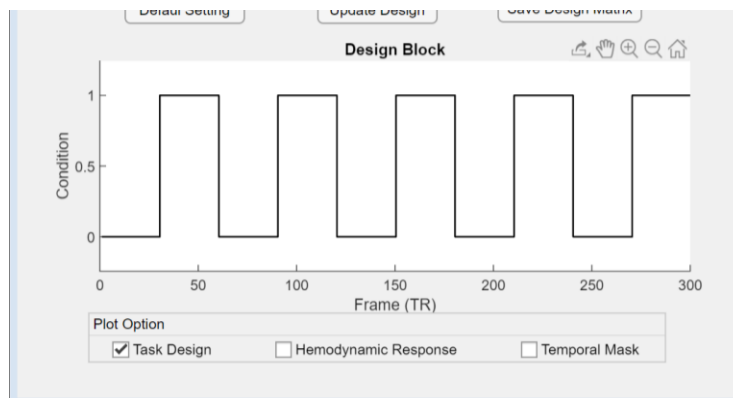


Fig. 3.2.3a Plot showing task design only

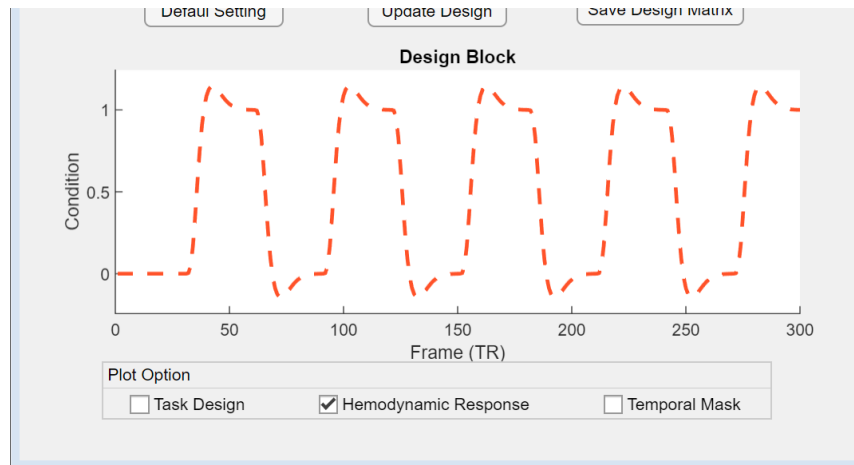


Fig. 3.2.3b Plot showing hemodynamic response only

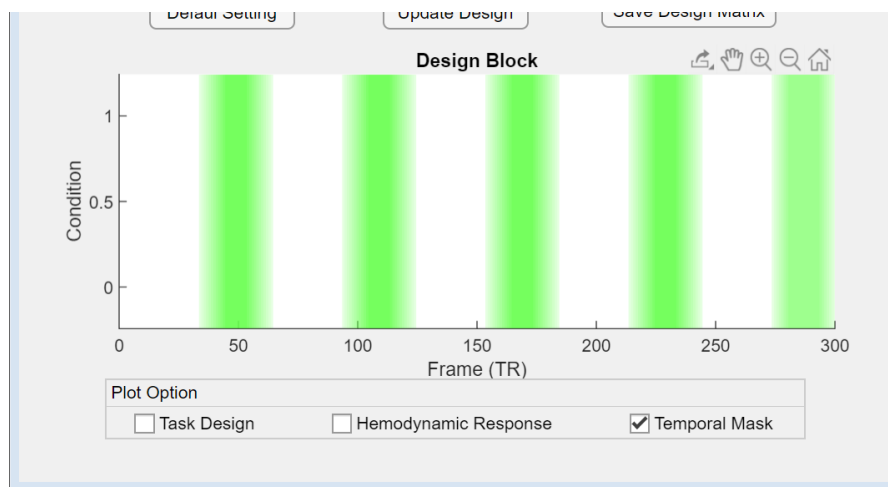


Fig. 3.2.3c Plot showing selected window

3.2.10. Save Design Matrix

Click on 'Save Design Matrix' to save the task condition file (default name is `dynamic_condition.mat`) (**Fig. 3.2.4**). After successfully saving the task condition file, you will find the `dynamic_condition.mat` file in your selected output folder (**Fig. 3.2.5**).

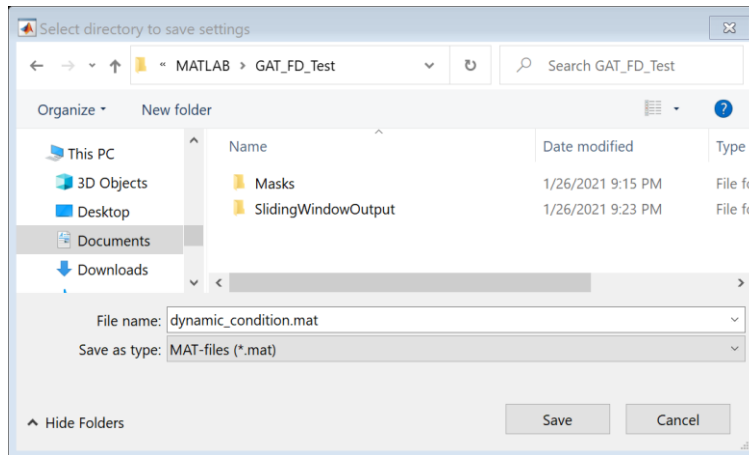


Fig. 3.2.5 Select output folder for saving task condition file

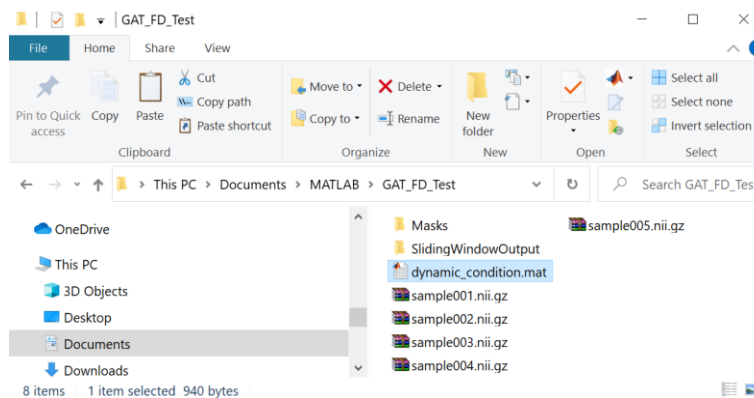


Fig. 3.2.6 Successfully generated task condition file

3.3. Network Analysis

Network analysis is a popular method in characterizing the dynamics of functional topological properties. GAT-FD provide tools to evaluate the variability of functional network properties using the well-developed graph theoretical techniques [13].

Click **'Network Analysis'** button from the toolbox main menu.

A warning window will be shown if the BCT has not been correctly installed (**Fig. 3.3.1**). Click **'OK'**, check the BCT installation and re-run this step.

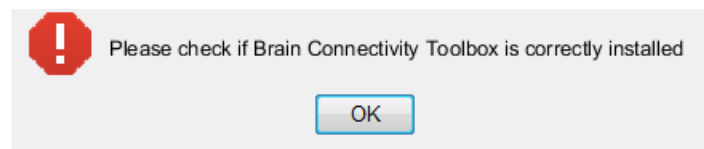


Fig. 3.3.1 BCT installation warning window

Then you can find the interface below (**Fig. 3.3.2**) after successfully running the **Network Analysis**.

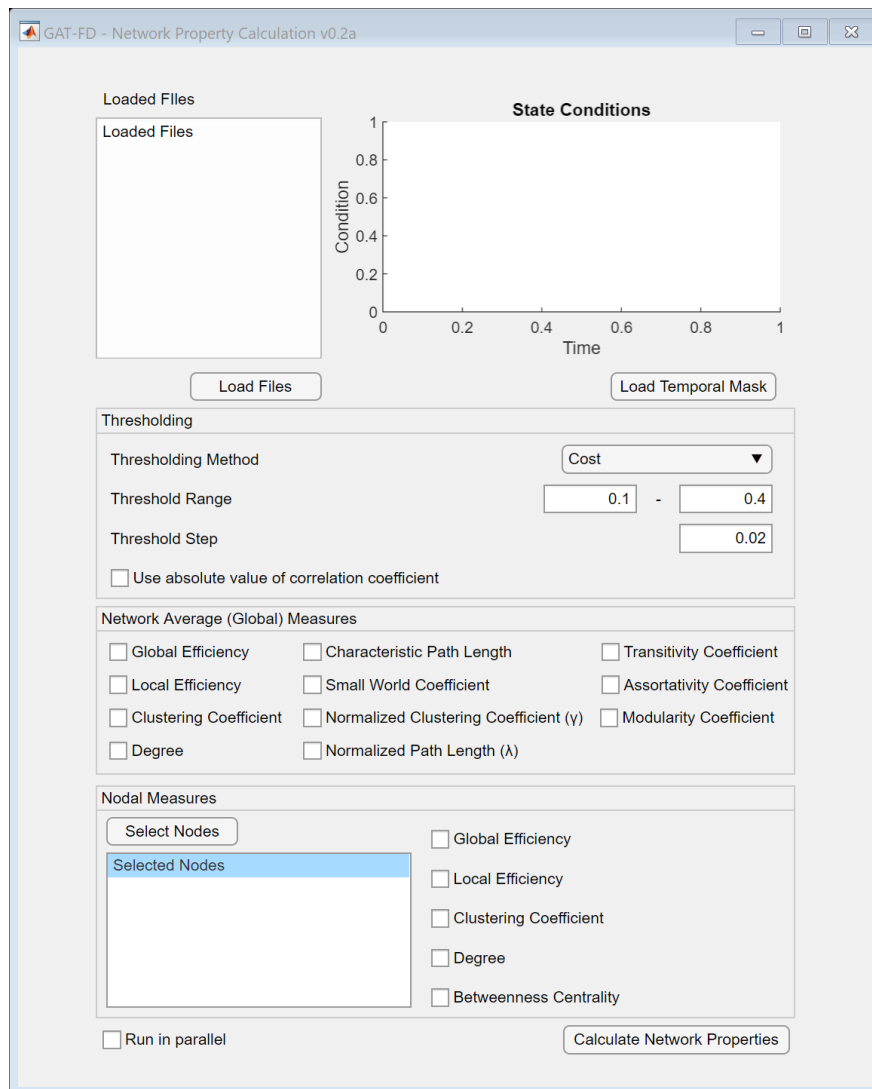


Fig. 3.3.2 The interface of dynamic functional network connectivity analysis

3.3.1. Load Files

Click 'Load File' button, select *.mat files for individual which generated from the Sliding Window Calculation step (**Fig. 3.3.3**).

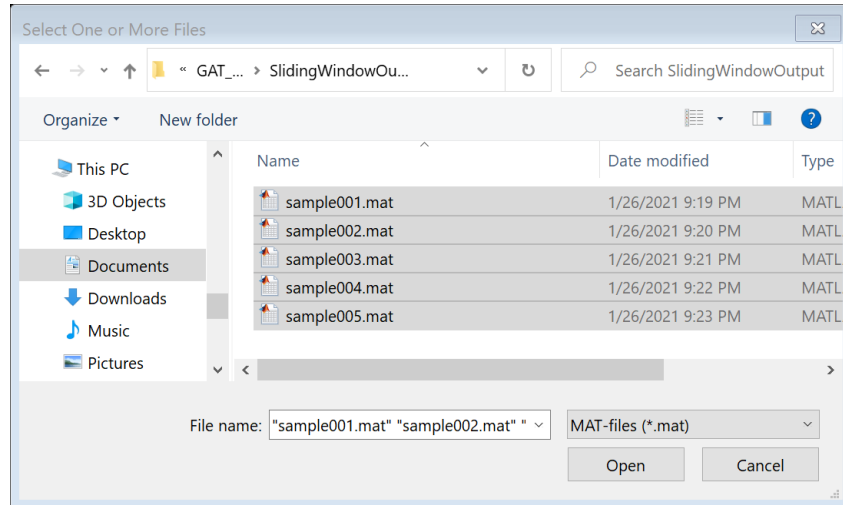


Fig. 3.3.3 Input data selection for network analysis

Click 'Open', then you will find your selected files in the 'loaded files' window (Fig. 3.3.4).

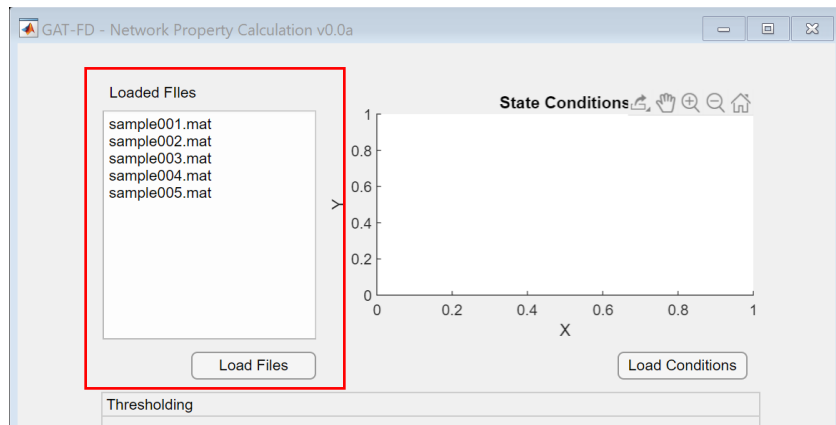


Fig. 3.3.4 Selected input files for network analysis

3.3.2. Load Conditions

Click 'Load Condition' button, select *.mat file which generated from the Task Design step (Fig. 3.3.5). (Note: Current version only support condition matrix generated in Task Design step)

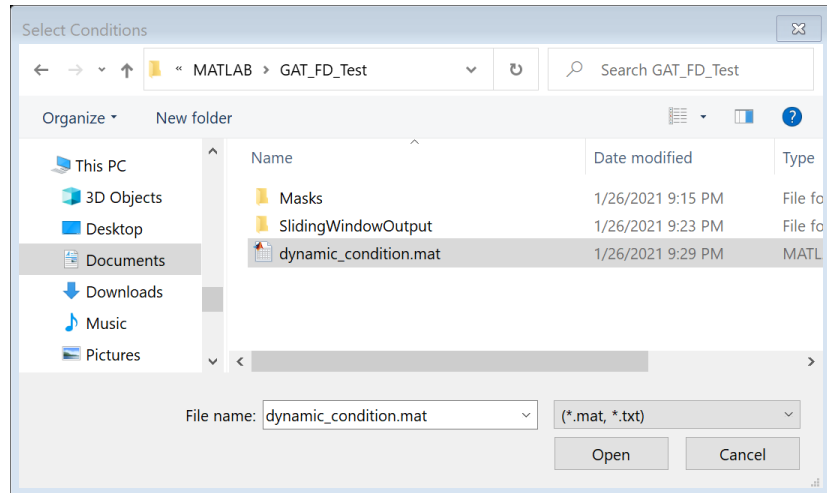


Fig. 3.3.5 Select task condition file for network analysis

Click 'Open', then you will find a plot showing your imported task design in the 'State Condition' window (**Fig. 3.3.6**).

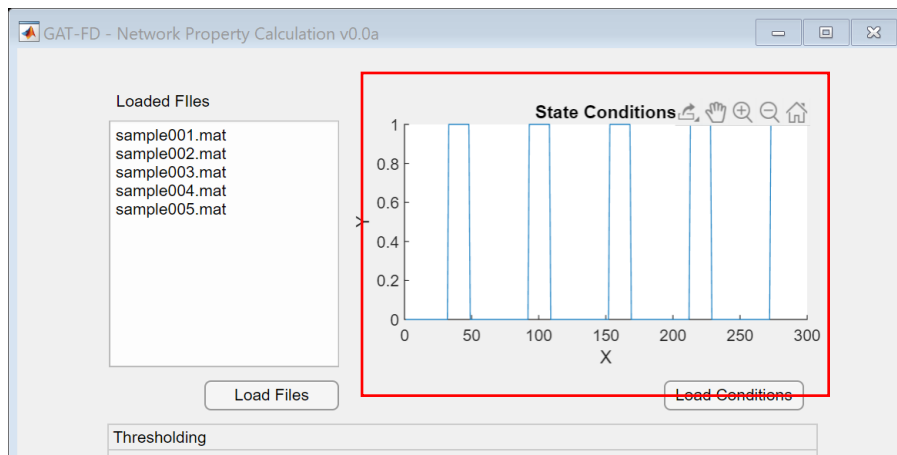


Fig. 3.3.6 Plot showing successfully loaded task condition file

3.3.3. Thresholding Method

The GAT-FD provides three thresholding methods including “Cost”, “Proportional”, and “Absolute”, which allows you to use the network cost, a proportional value or an absolute value to threshold your functional network (**Fig. 3.3.7**).

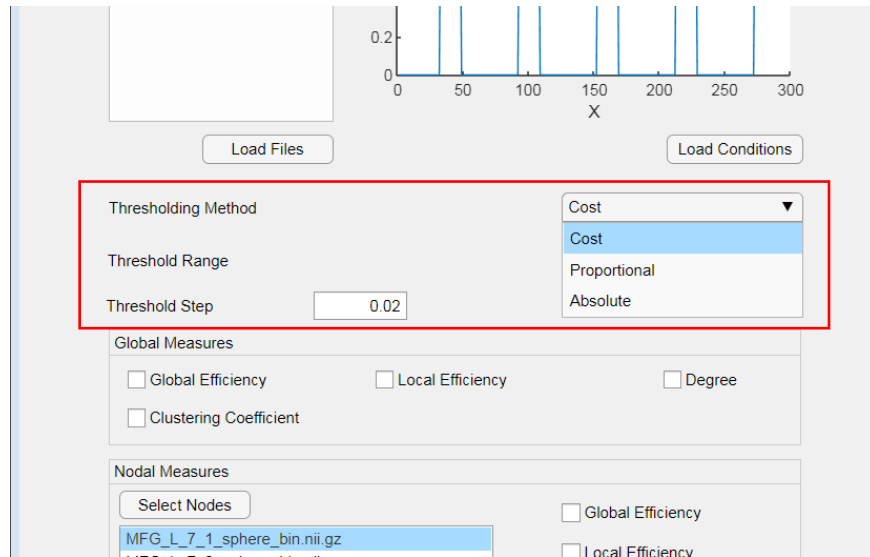


Fig. 3.3.7 Thresholding methods provided by the GAT-FD

3.3.4. Threshold Range

Type your threshold range here. Because functional network exhibit small-world properties with a high level of local clustering. The selection of threshold is usually based on the wiring efficiency and wiring cost. In order to increase the reliability of calculated network properties, calculations will be performed in a range of thresholds that satisfy the small-world properties. For our sample data, we use 0.1-0.4 (**Fig. 3.3.8**). If you don't check "Output data for each step", the result matrix will only include mean values over the specified threshold range.

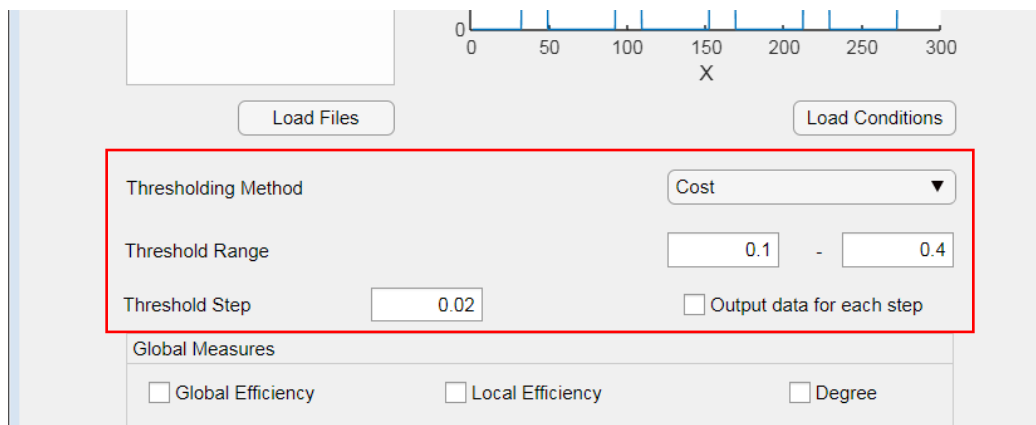


Fig. 3.3.8 Selection of threshold range

3.3.5. Threshold Step

Type the step size for thresholding range. For sample data, we use 0.02.

3.3.6. Global and Nodal Measures

The GAT-FD toolbox provides calculation of global-level and nodal-level measurements including global efficiency, local efficiency, degree, clustering coefficient, and betweenness

centrality. Select the measures you need for network analysis (Here we select global efficiency and local efficiency as examples). Please check Brain Connectivity Toolbox for detailed calculation.

For network properties calculation, your pre-selected Nodes will be loaded in the ‘Select Node’ window. You can also manually select desired node for network properties calculation by clicking ‘Select Node’.

3.3.7. Calculate Network Properties

When calculating network properties, click ‘Calculate Network Properties’ button, select a folder for saving your output file (a network_properties.csv file), and click ‘save’ button (**Fig. 3.3.9**).

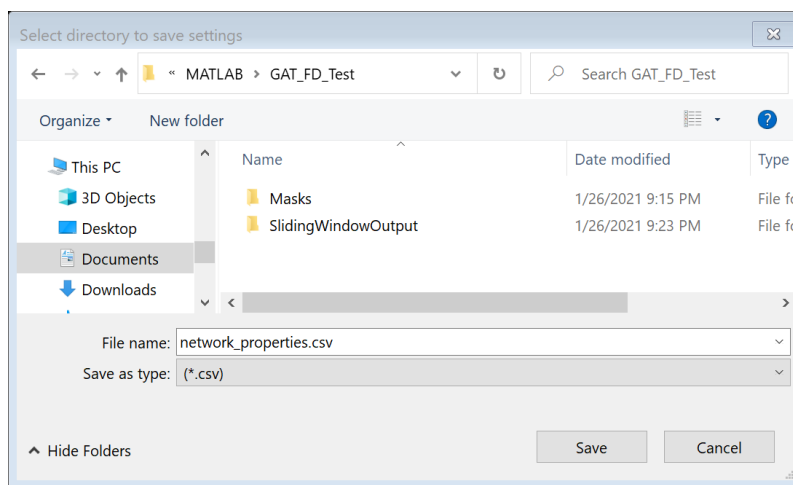


Fig. 3.3.9 Output folder selection for network analysis

When successfully running network properties calculation, you will find a window (**Fig. 3.3.10**) showing you the current processing status.

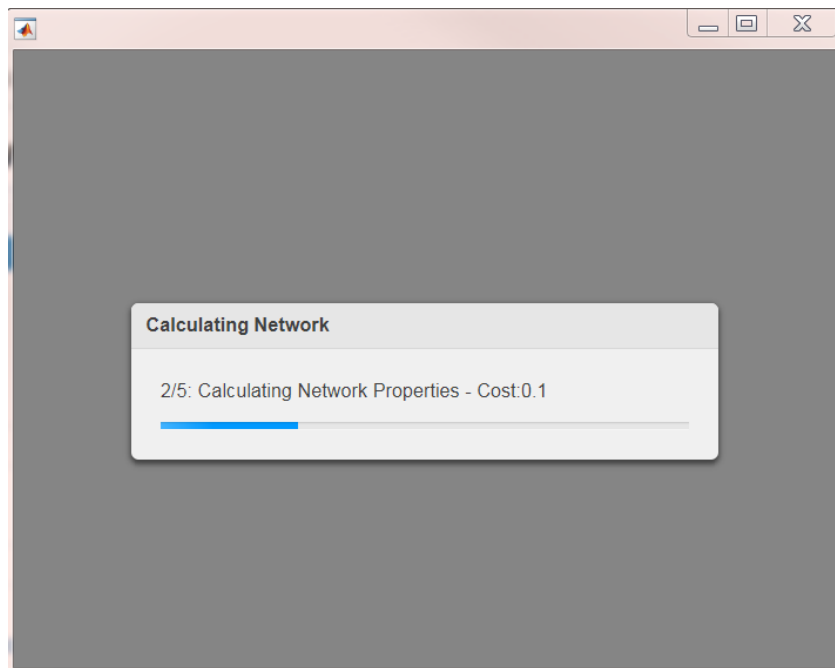


Fig. 3.3.10 Processing status window of network properties calculation

3.3.8. Output Data

After successfully running the network properties calculation, a “Finished” window will be shown (Fig. 3.3.11).

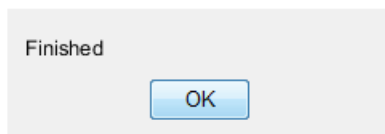


Fig. 3.3.11 Finished window showing successfully running network properties calculation

The output data will be a *.csv file and a *.csv.mat file (Fig. 3.3.12).

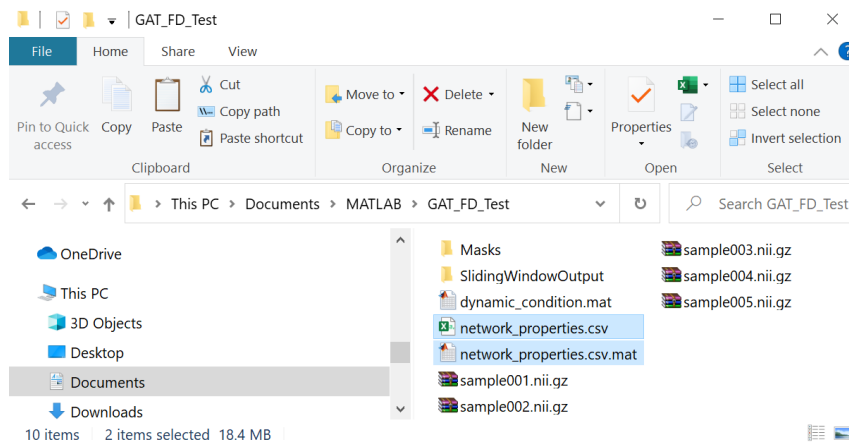


Fig. 3.3.12 Output data of network properties calculation

The *.csv file contains the mean and variance values of the network properties across the sliding windows (**Fig. 3.3.13**). Each row represents information of one subject.

	A	B	C	D	E	F	G	H	I	J	K
1	filename	glo_eff_va	glo_eff_m	glo_lef_va	glo_lef_m	nod_eff_N	nod_eff_M	nod_lef_N	nod_lef_M	nod_eff_N	nod_eff_M
2	sample001	0.000525	0.129937	0.010274	0.049315	0.0083	0.032877	0.01855	0.02226	0.004485	0.016895
3	sample002	0.000622	0.128425	0.009349	0.021575	0.007925	0.057135	0.003377	0.003425	0.009408	0.048231
4	sample003	0.00064	0.131678	0.011233	0.032877	0.010654	0.051541	0.006564	0.006849	0.009016	0.094349
5	sample004	0.000533	0.134047	0.006678	0.013356	0.010018	0.059817	0.010987	0.011986	0.009497	0.059189
6	sample005	0.000707	0.130023	0.011353	0.034932	0.009156	0.069578	0.020691	0.025685	0.006233	0.022774
7											
8											
9											
10											
11											
12											

Fig. 3.3.13 Example of *.csv file

The *.csv.mat file is used for the validation of the time series (details are explained in Chapter 3.4.4). You can also access the calculated network properties for each step, node, and subject when load the csv.mat file into matlab.

dnet_data_data_mat_global: Global network properties, window (frames) × measures count × threshold steps × subjects.

dnet_data_data_mat_nodal: Nodal network properties, window (frames) × measures count × threshold steps × nodes × subjects.

dnet_data_files: Subject file names.

dnet_data_measures_global: Global network properties' names.

dnet_data_measures_nod: Nodal network properties' names.

dnet_data_nodes_list: Selected nodes for calculation.

dnet_data_threshold_list: All threshold steps.

3.4. Result Display

The GAT-FD toolbox also provides a tool to visually check the connectivity matrix for each sliding window and network properties over time series.

Click '**Display**' button from the main menu.

You can find the interface below (**Fig. 3.4.1**) after successfully running the **Display**.

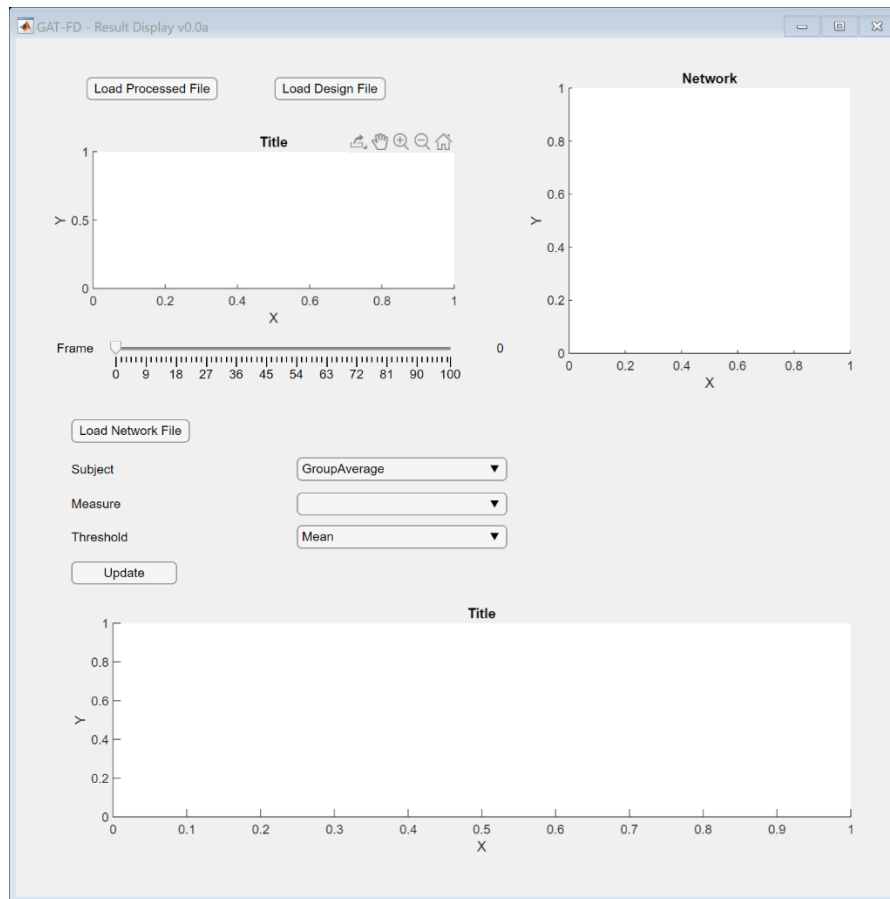


Fig. 3.4.1 The interface of Display

3.4.1. Load Files

Click 'Load Processed File' button, select *.mat file of one subject (generated from the sliding window analysis step) (**Fig. 3.4.2**), and click 'Open'.

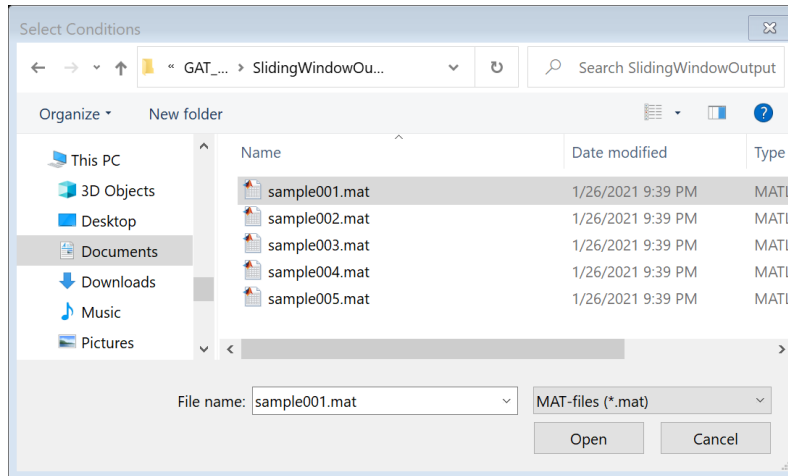


Fig. 3.4.2 Load processed file

3.4.2. Load Design File

Click 'Load Design File' button, select *.mat file generated from the task design step (**Fig. 3.4.3**), and click 'Open'.

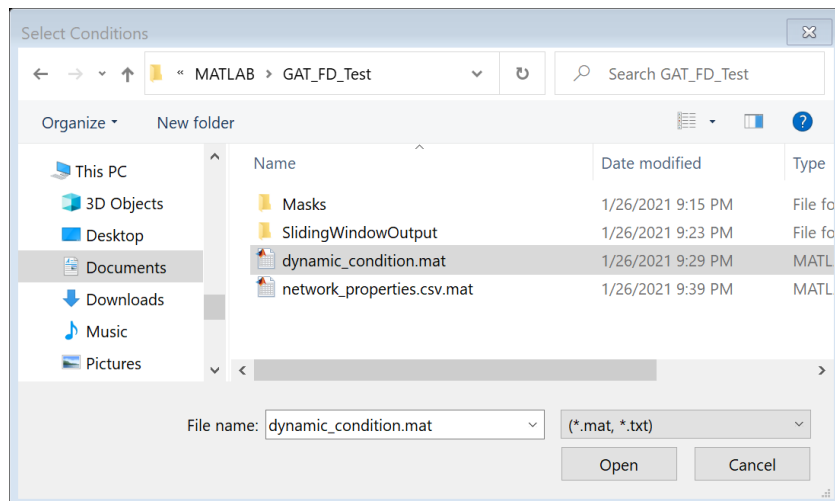


Fig. 3.4.3 Load design file

3.4.3. Navigate Through Sliding Windows

You can click on the slider to find desired frame or you can use left and right arrow to navigate the frame (**Fig. 3.4.4**).

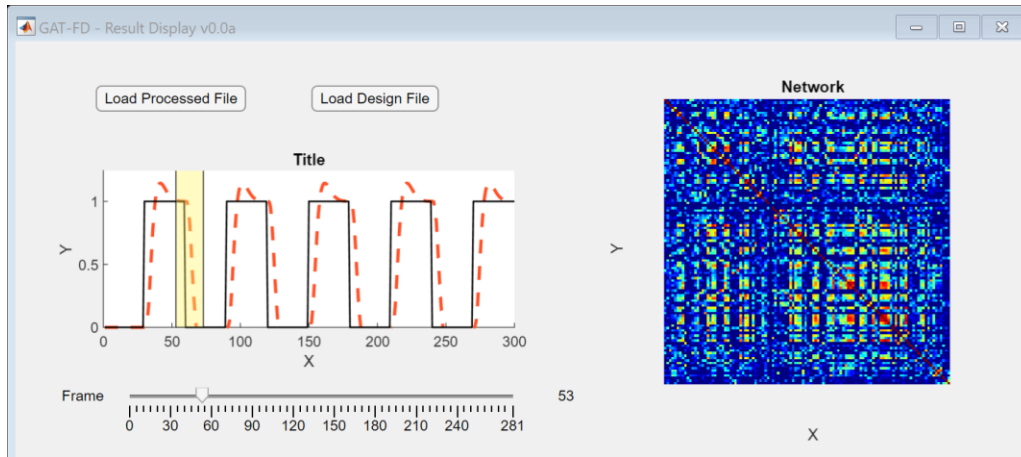


Fig. 3.4.4 Check functional connectivity matrix for each subject

3.4.4. Check Network Properties Across Sliding Windows

Click 'Load Network File' button, select *.csv.mat file generated after network analysis step (**Fig. 3.4.5**).

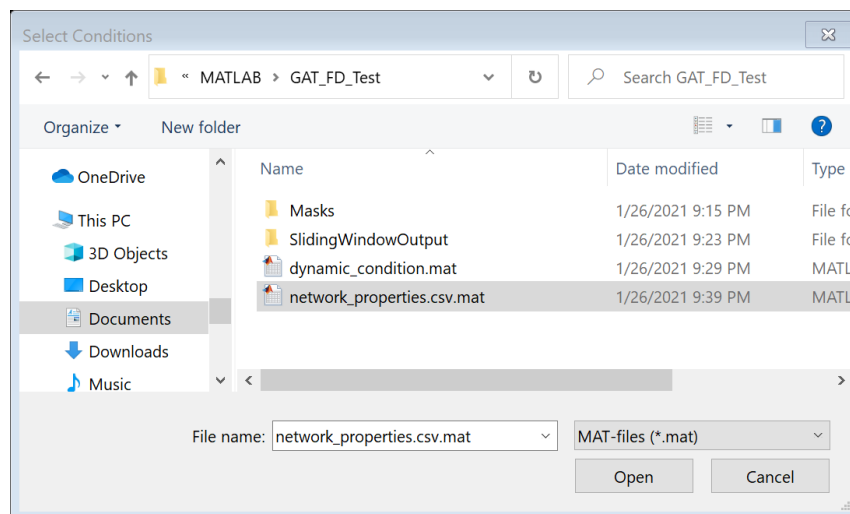


Fig. 3.4.5 Load network properties file

You can select desired subject, measures, and threshold in the drop-down menus (**Fig. 3.4.6**).

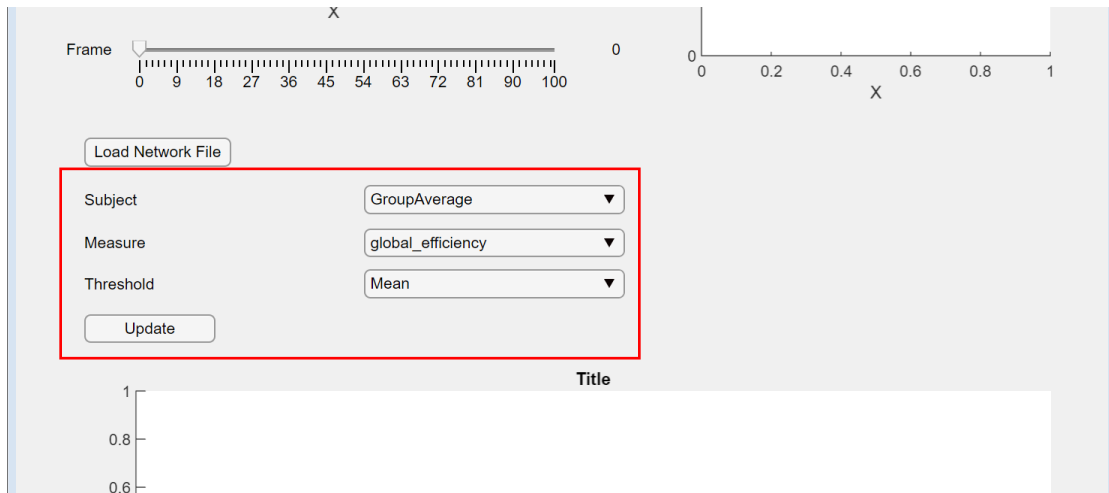


Fig. 3.4.6 Drop-down menus for network properties display

Then you can click update to display the selected network property over frames (**Fig. 3.4.7**).

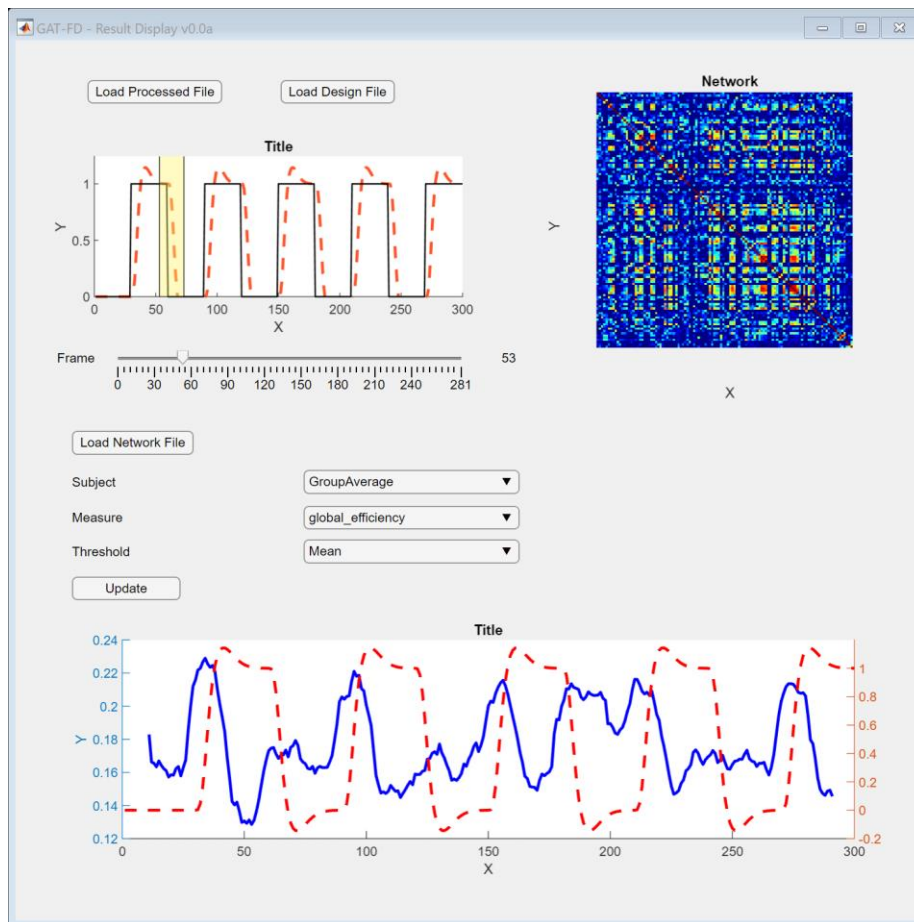


Fig. 3.4.7. Network property vs. hemodynamic response

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MATLAB: www.mathworks.com/products/matlab/

SPM: www.fil.ion.ucl.ac.uk/spm/

Brain Connectivity Toolbox: <https://sites.google.com/site/bctnet/>

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