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 **A**nalysis of **T**ask-related **F**unctional **D**ynamics (GAT-FD) is an integrated toolbox for analyzing dynamic functional connectivity and time-varying network topological properties in task-based functional MRI. 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 GAT-FD do?

The GAT-FD toolbox includes the following modules:

- Sliding window analysis: extraction of the functional connectivity matrix for sliding windows with predefined or customized atlas.
- Task design configuration: categorization of sliding windows into different conditions based on the task design.
- Functional network connectivity dynamics analysis: quantification of the variability of the functional connectivity dynamics using variance of the topological properties across sliding windows.
- Result visualization: validation 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.

This manual will explain the parameters in detail for each step. Sample data will be provided and will be used to demonstrate each step accordingly.

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GAT-FD User Manual 0.1, January 2021

2. Installation

2.1.Before using GAT-FD

- The GAT-FD toolbox package can be downloaded from https://centers.njit.edu/cnnl
- 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).
- We offered 5 sample data preprocessed by FSL. The sample data can be downloaded from: https://centers.njit.edu/cnnl.
- 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.

You can find the interface below (**Fig. 2.1**) after successfully running the GAT_FD. The main program provides 4 different tools, which will be explained in Chapter 3.

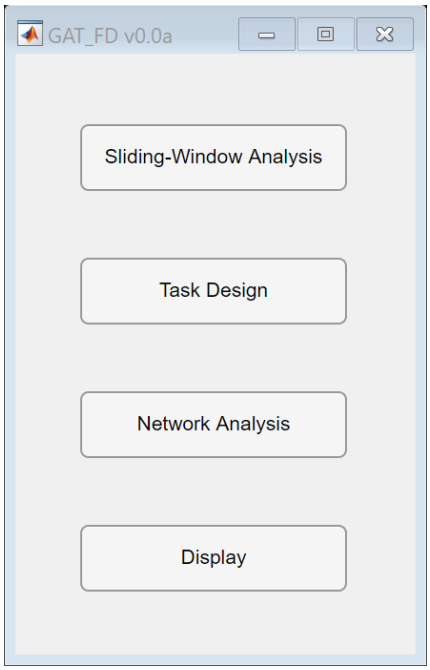


Fig. 2.1 The interface of GAT-FD

3. GAT-FD GUI Basics

3.1 Sliding Window Analysis

The sliding window analysis is a straightforward and common approach for evaluating functional connectivity dynamics [1]. It calculates connectivity matrix over consecutive windowed segments of the data, with a fixed window length and fixed time shift, which can be used to evaluate the fluctuations in functional topological properties [2-10].

Press the **Sliding Window Analysis** button.

You can find the interface below (**Fig. 3.1**) after successfully running the **Sliding Window Analysis**.

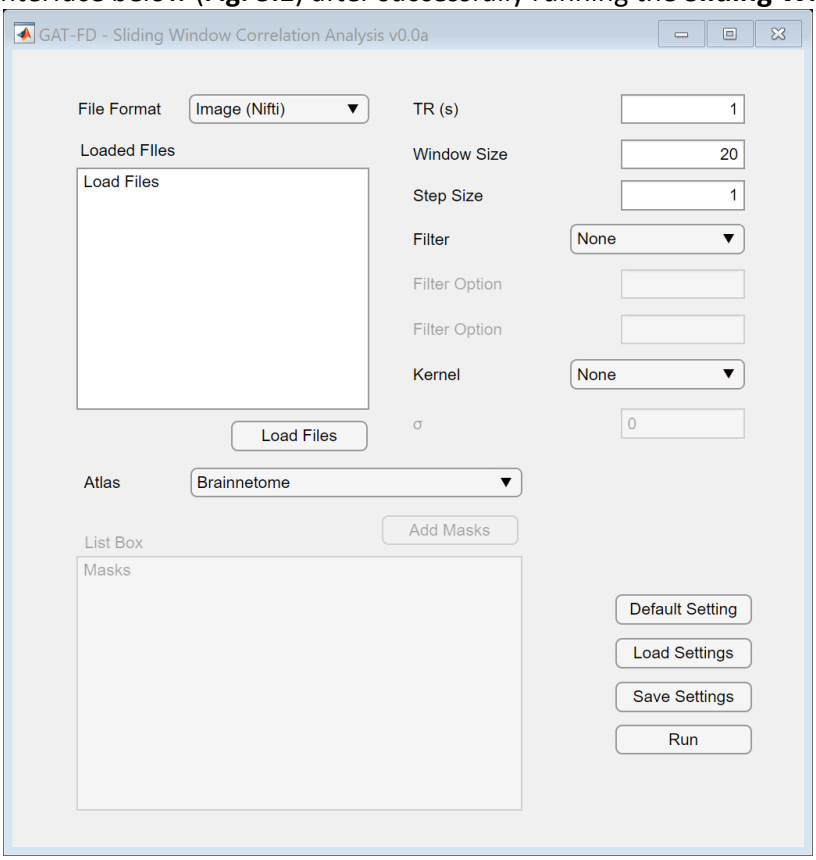


Fig. 3.1 The interface of sliding window analysis

3.1.1 Load Files

Two types of files can be imported to extract sliding windows, raw fMRI data (Nifti format images) or time-series data (.mat format, time x ROIs)

Raw Image File:
Click **Load Files** button, select files to import (**Fig. 3.2**). In the current version, the GAT-FD only support *.nii or *.nii.gz format data as input.

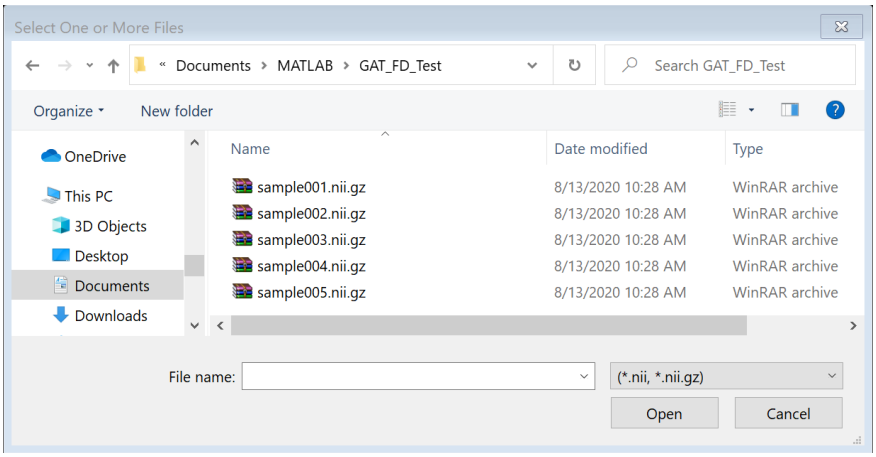


Fig. 3.2 Import files for sliding window analysis

Click Open, then you can find your imported image files in the **Loaded Files** window (**Fig. 3.3**).

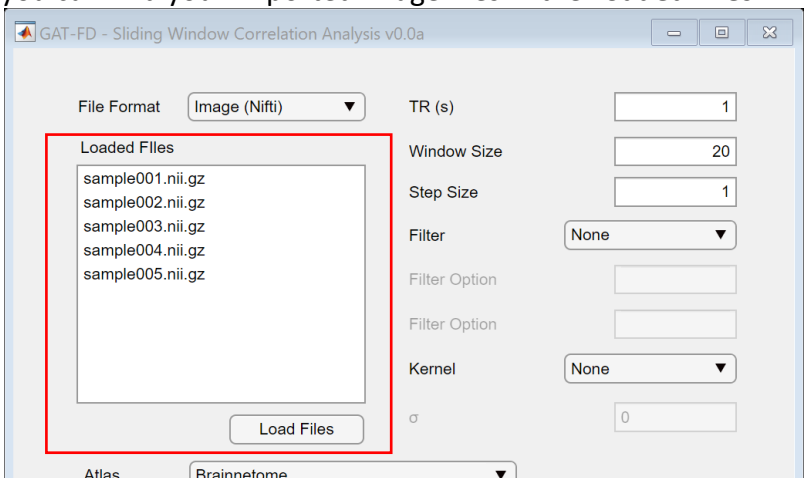


Fig. 3.3 Imported files for sliding window analysis

Time series data:
MAT-format matrix contains the time series of each region-of-interest can also be imported. 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 sample data, the repetition time (TR) is 1s, duration of each block is 30s, we use a window size of 20 TRs (20s).

Type your window size value in number of TRs.

3.1.3 Step Size

Step size is the size of the "sliding" action, which is the length of sequence you move between each window. For the sample data, we set the step size as 1TR=1s.

Type your step size value in number of TRs.

3.1.4 Cut-off Frequency

The GAT-FD provides a “Cur-off Frequency” option for sliding window analysis. This is a high-pass filter which allows you to minimize the effects of the oscillation between rest and task blocks when calculating correlations within sliding windows.

Type your cut-off frequency value if needed. The cut-off frequency will be the inverse of the input value. For example, input 55 if you want the cut-off frequency to be 1/55 Hz.

3.1.5 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. 3.4**). Then you can type your sigma value for the Gaussian kernel.

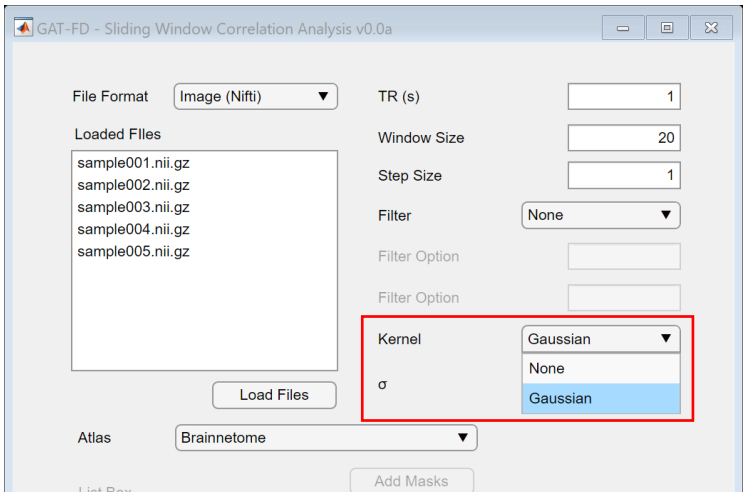


Fig. 3.4 Kernel selection

3.1.6 Atlas

The GAT-FD toolbox provides two types of atlas, including the standard atlas and customized ROI masks (**Fig. 3.5**). For the standard atlas, the current version of GAT-FD offers two options, the Brainnetome and Automated Anatomical Labeling (AAL), which are the two most commonly applied atlases in neuroimaging studies [11, 12].

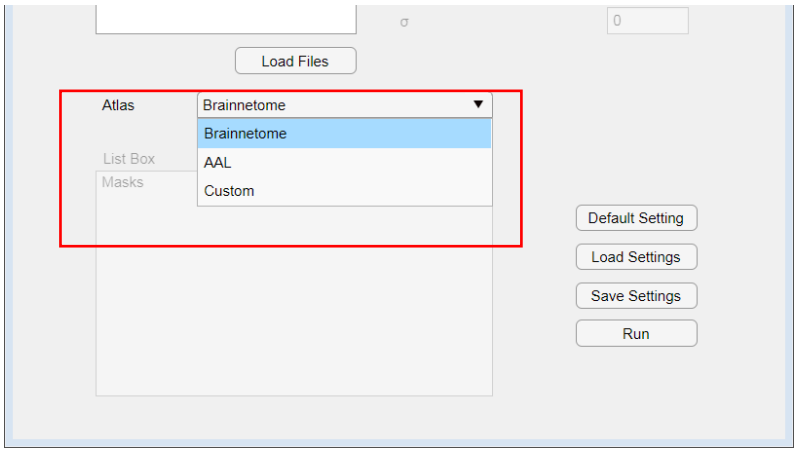


Fig. 3.5 Atlas selection

GAT-FD also provides selections of customized ROI masks. The customized ROI masks need to be prepared and in the same space with the functional MRI data. When select your customized ROI masks, click on “Atlas” and choose “custom” from the drop-down list. Then click on “**Add masks**”, select your customized ROI masks (**Fig. 3.6**).

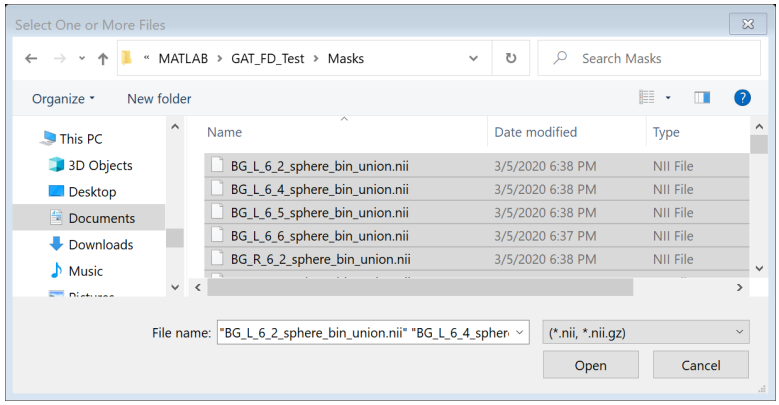


Fig. 3.6 Customized ROI masks selection

Click “open”, then you will find the selected ROI masks in the “List Box” window (**Fig. 3.7**). You can either select one file that contains all masks or multiple individual masks in this step.

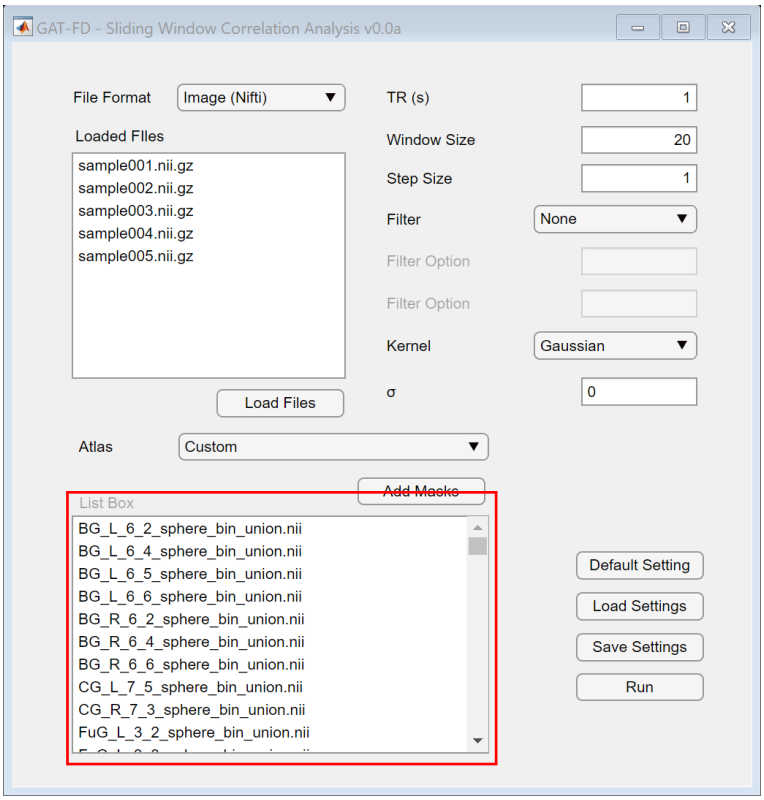


Fig. 3.7 Selected customized ROI masks

3.1.7 Default Setting

The GAT-FD provides a default setting which included parameters utilized for sample data analysis. To practice on the sample data, 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 usage.

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. 3.8**).

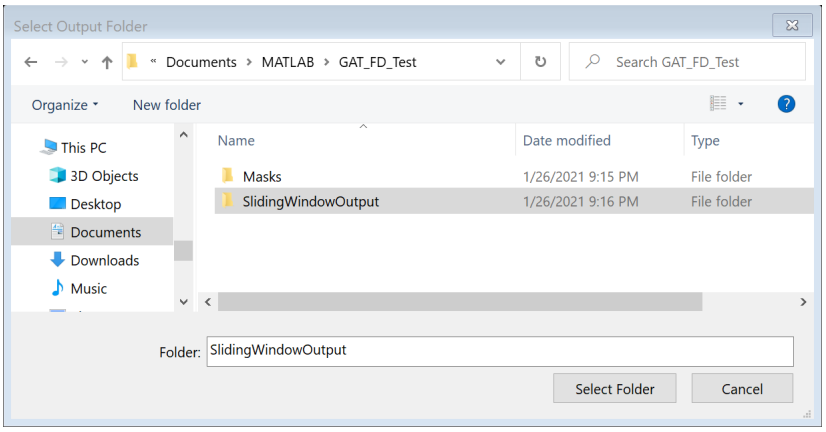


Fig. 3.8 Output folder selection

When successfully running sliding window analysis, you will find a window (**Fig. 3.9**) showing you the current processing status.

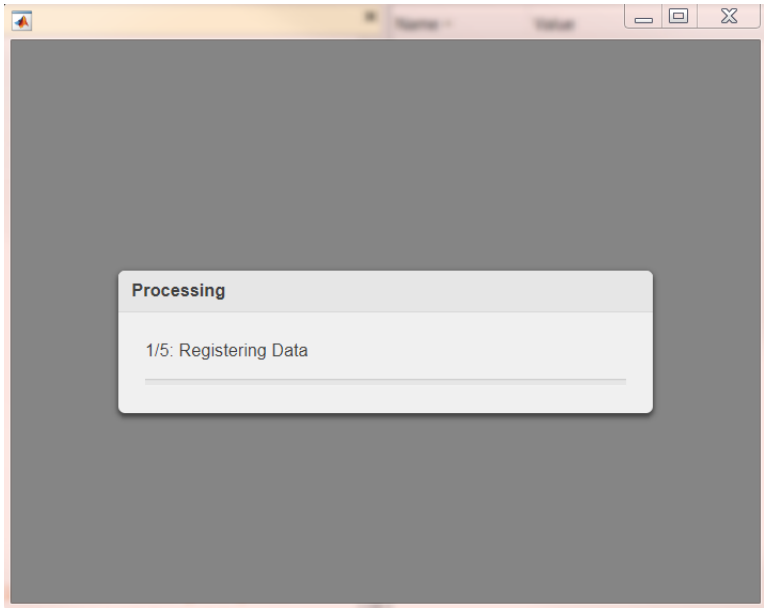


Fig. 3.9 Processing status window of sliding window analysis

3.1.10 Output Data

After successfully running the sliding window analysis, a “Finished” window will be shown (**Fig. 3.10**), and a *.mat file will be generated in your output folder for each subject (**Fig. 3.11**). These files will be used in the following network analysis (detailed are explained in Chapter 3.3.1).

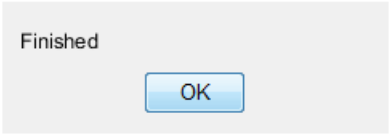


Fig. 3.10 Finished window after successfully running sliding window analysis

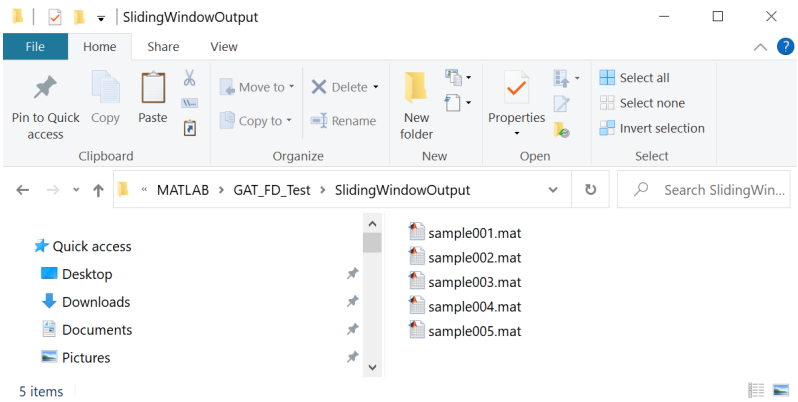


Fig. 3.11 Output data of sliding window analysis

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. 3.12**) after successfully running the **Task Design**.

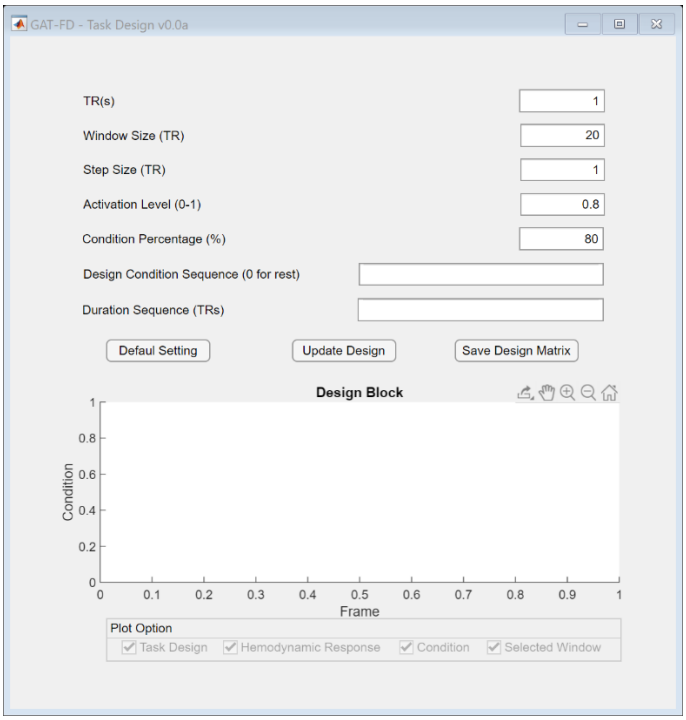


Fig. 3.12 The interface of task design

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 Activation Level

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

3.2.3 Condition Percentage (%)

Percentage of frames that in a window to that for a window to be considered as task condition. (Default is 80%)

3.2.4 Design Condition Sequence (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.

3.2.5 Duration Sequence (TRs)

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

3.2.6 Default setting

Restore default settings.

3.2.7 Update Design

After clicking the ‘Update Design’ button, you will find a plot showing the task design for the current settings (**Fig. 3.13**). 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.

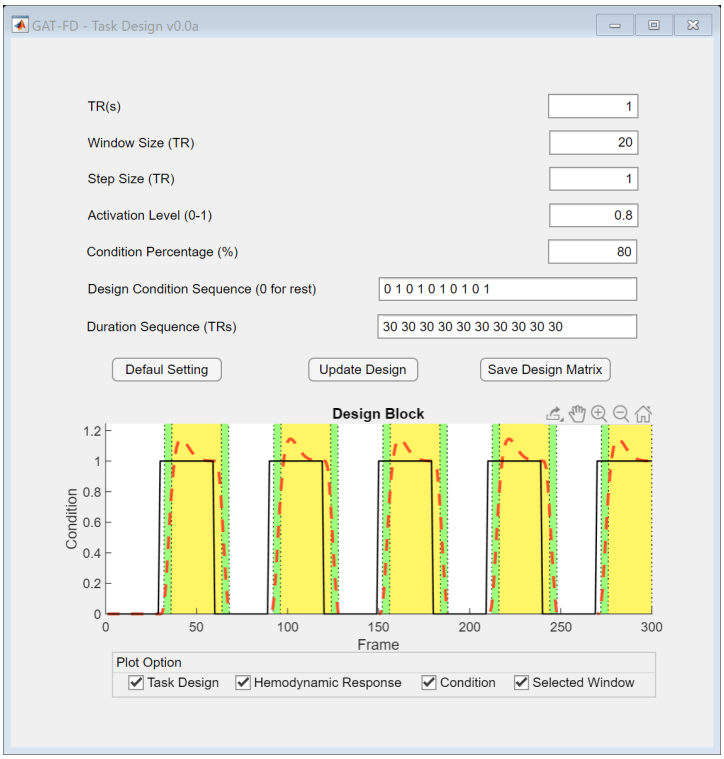


Fig. 3.13 Plot of the task design

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. 3.14 a-d**).

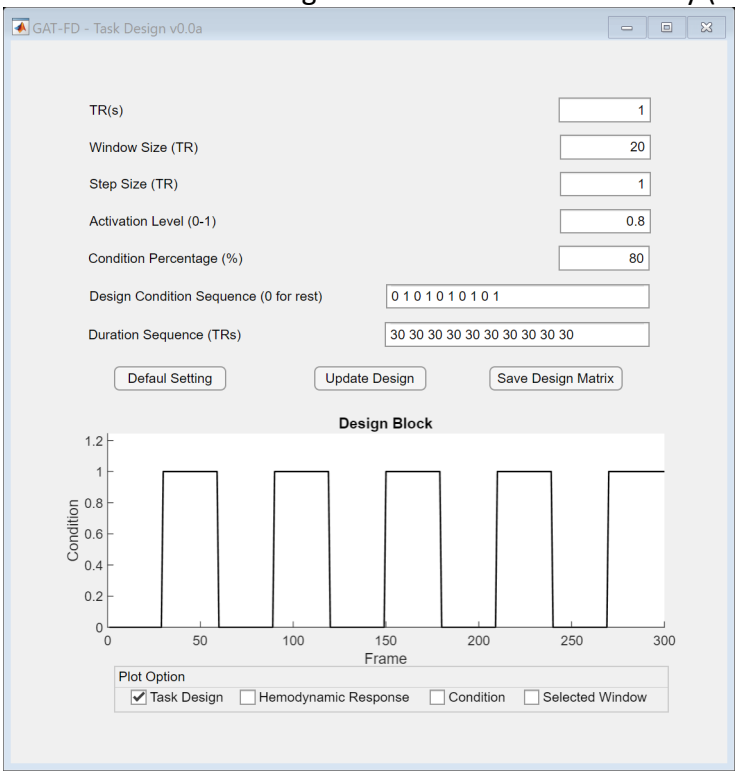


Fig. 3.14a Plot showing task design only

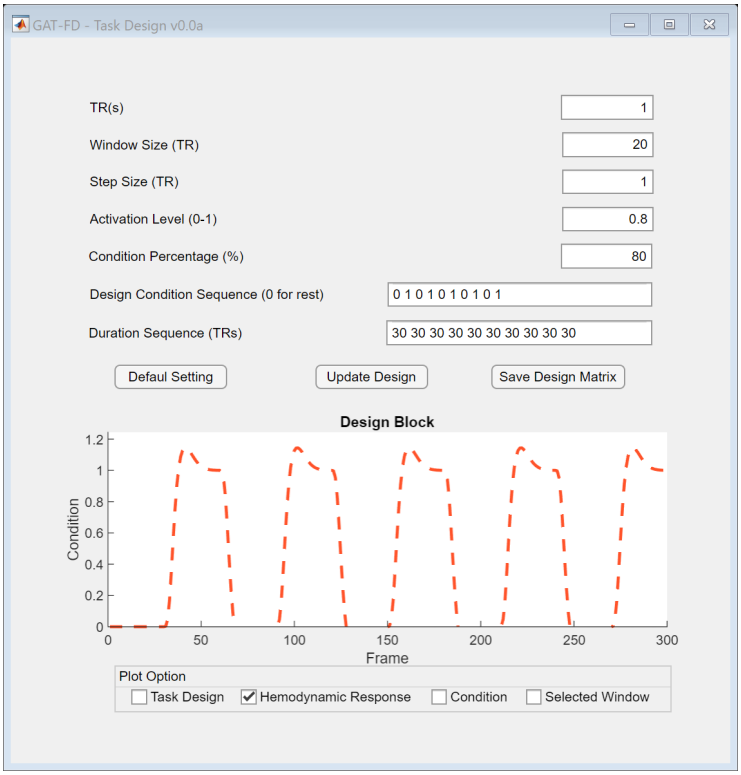


Fig. 3.14b Plot showing hemodynamic response only

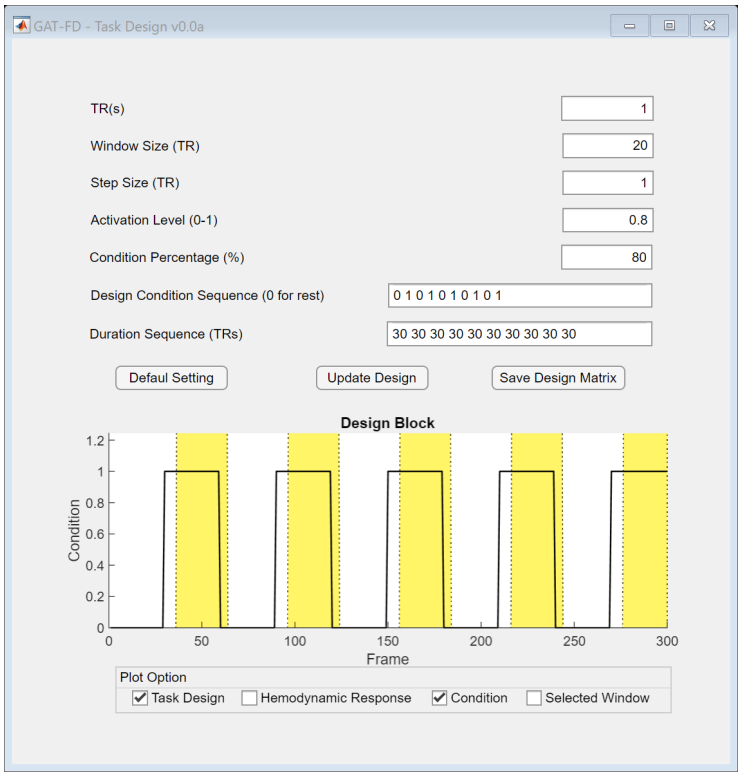


Fig. 3.14c Plot showing task design and condition percentage

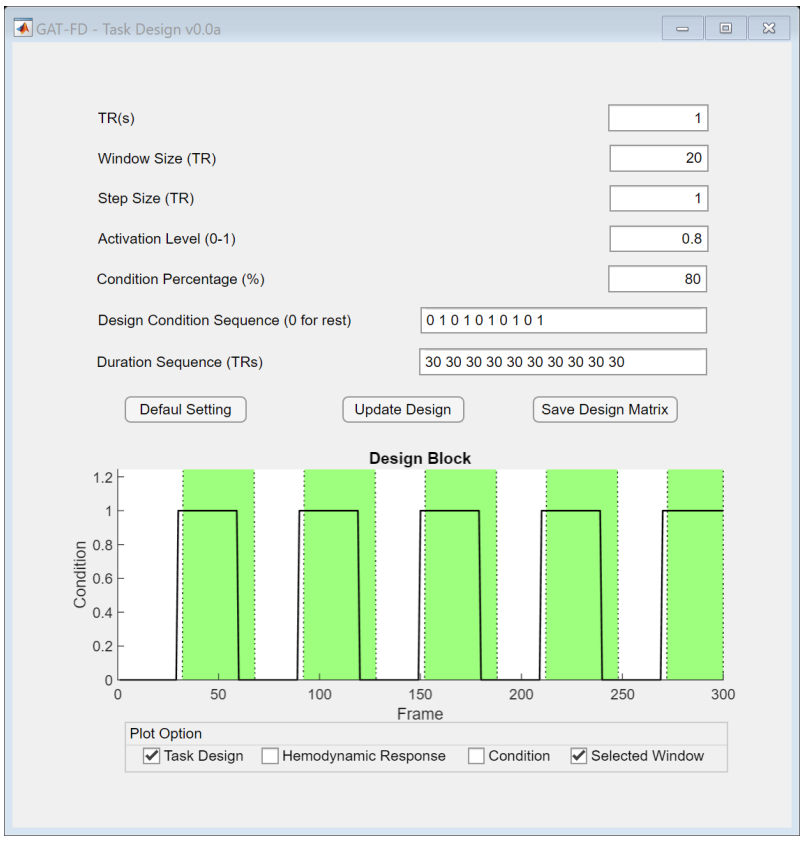


Fig. 3.14d Plot showing task design and selected window

3.2.8 Save Design Matrix

Click on 'Save Design Matrix', select an output folder to save the task condition file (called dynamic_condition.mat) (**Fig. 3.15**). Click 'open', then click 'save'. After successfully saving the task condition file, you will find the dynamic_condition.mat file in your selected output folder (**Fig. 3.16**).

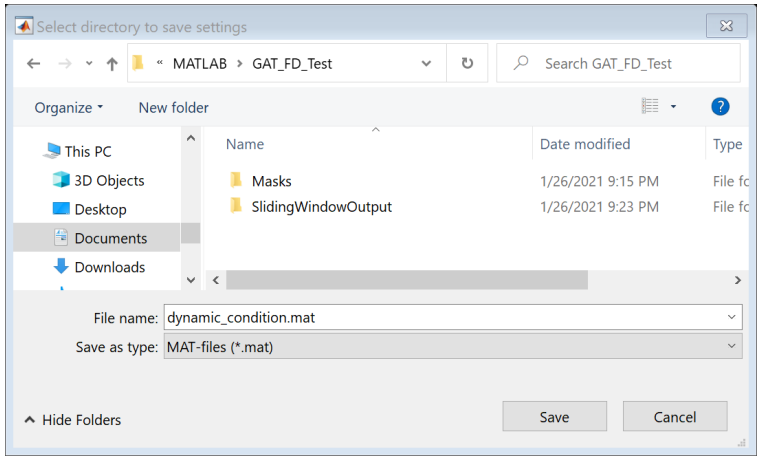


Fig. 3.15 Select output folder for saving task condition file

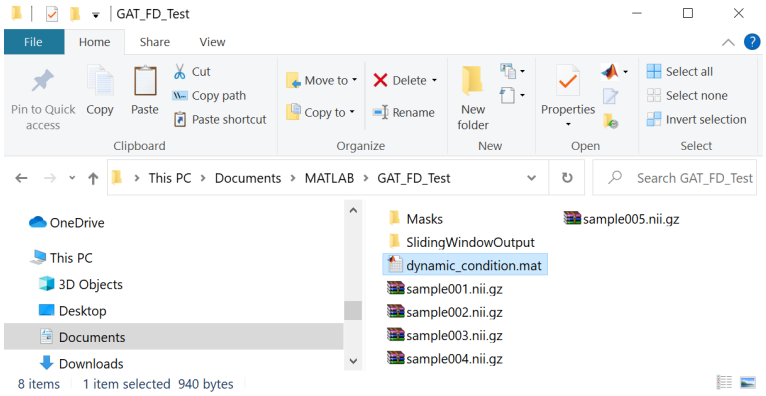


Fig. 3.16 Successfully generated task condition file

3.3 Analysis of Functional Network Connectivity Dynamics

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. 3.17**). Click 'OK', check the BCT installation and re-run this step.

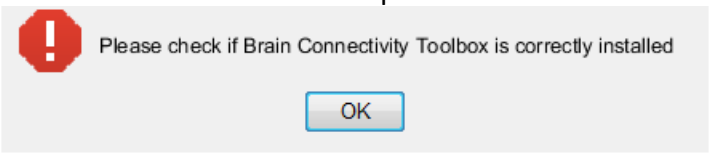


Fig. 3.17 BCT installation warning window

Then you can find the interface below (**Fig. 3.18**) after successfully running the **Network Analysis**.

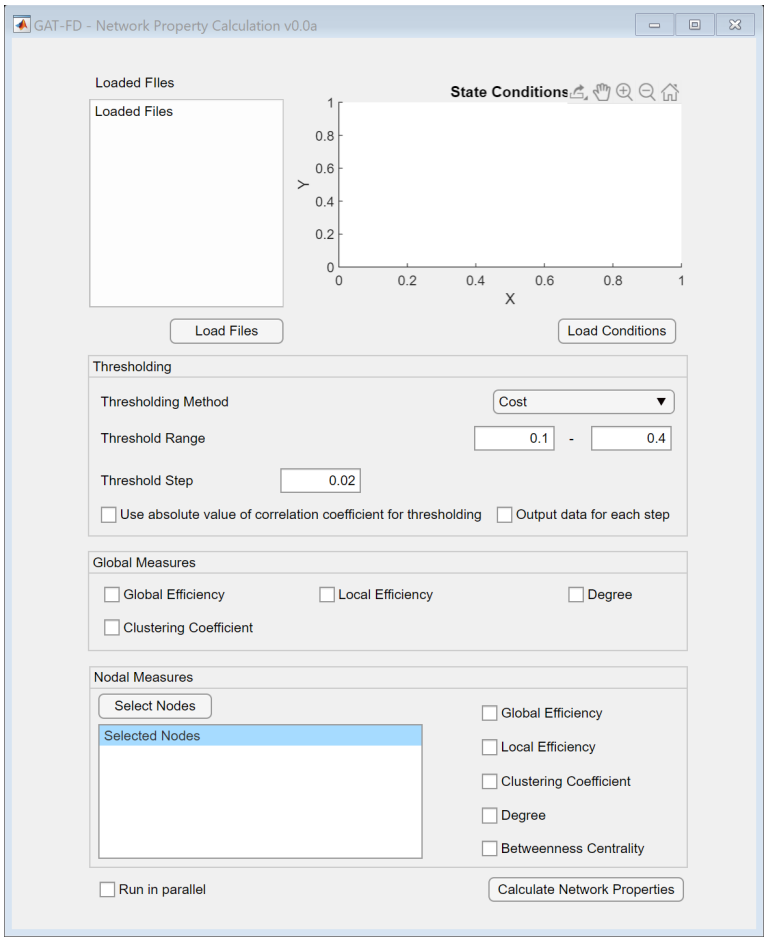


Fig. 3.18 The interface of dynamic functional network connectivity analysis

3.3.1 Load Files

Click 'Load File' button, select *.mat files for individual which generated from the Sliding Window Calculation step (**Fig. 3.19**).

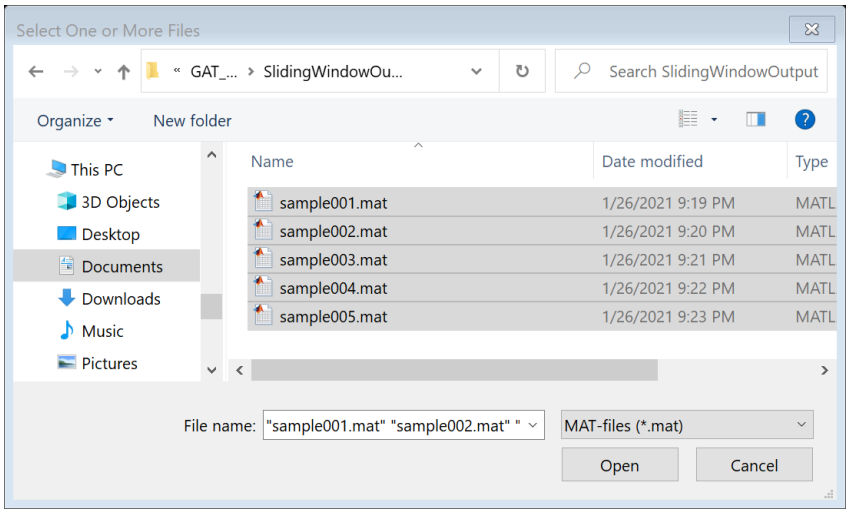


Fig. 3.19 Input data selection for network analysis

Click ‘Open’, then you will find your selected files in the ‘loaded files’ window (**Fig. 3.20**).

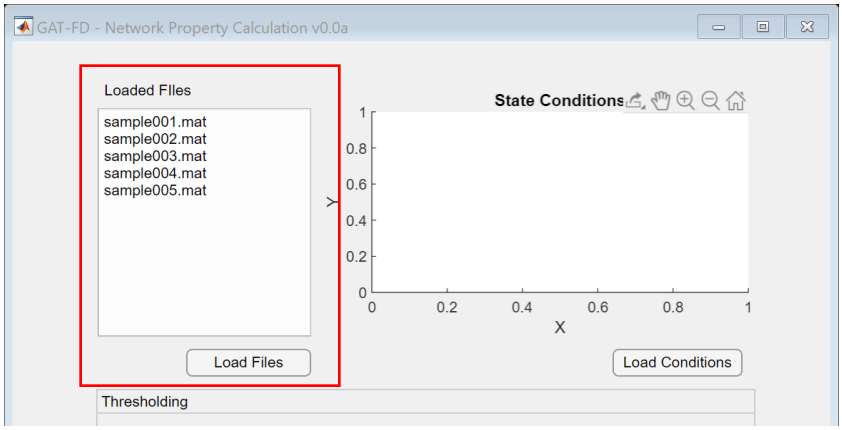


Fig. 3.20 Selected input files for network analysis

3.3.2 Load Conditions

Click ‘Load Condition’ button, select *.mat file which generated from the Task Design step (**Fig. 3.21**). (Note: Current version only support condition matrix generated in Task Design step)

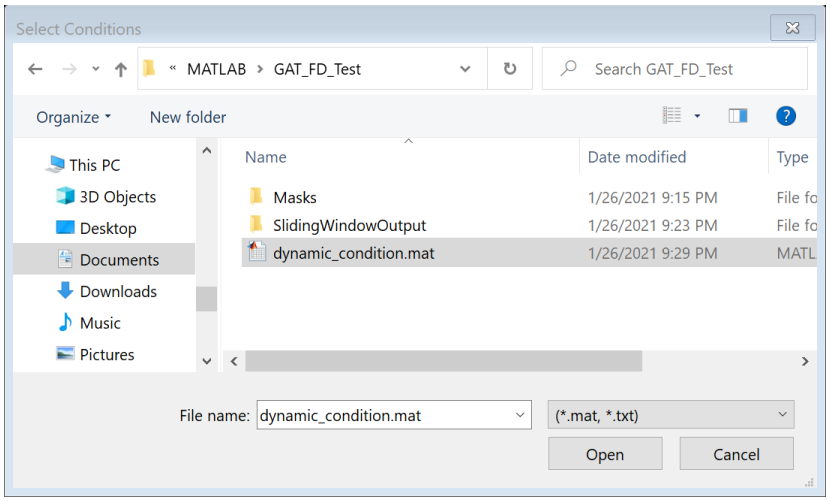


Fig. 3.21 Select task condition file for network analysis

Click ‘Open’, then you will find a plot showing your imported task design in the ‘State Condition’ window (**Fig. 3.22**).

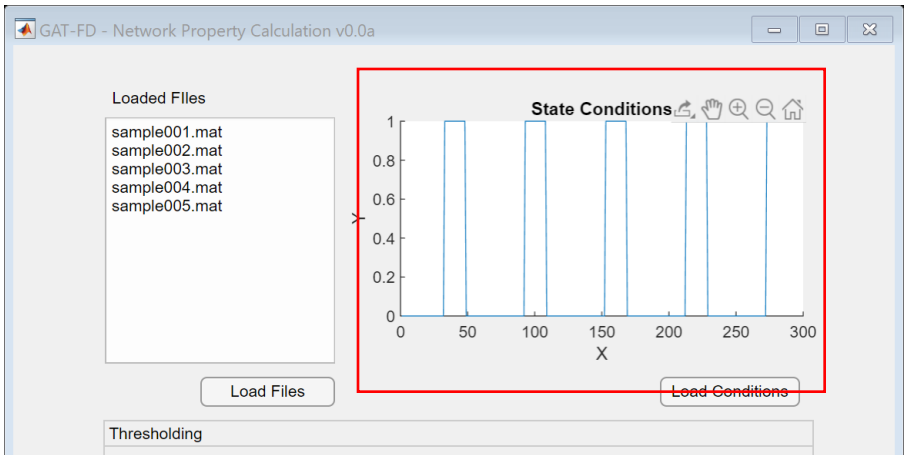


Fig. 3.22 Plot showing successfully loaded task condition file

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. 3.23**).

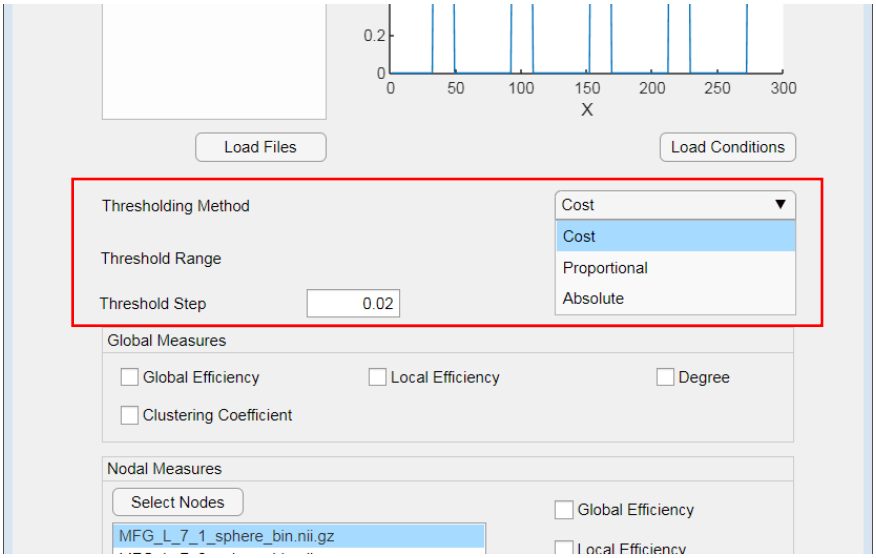


Fig. 3.23 Thresholding methods provided by the GAT-FD

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. 3.24**). If you don't check "Output data for each step", the result matrix will only include mean values over the specified threshold range.

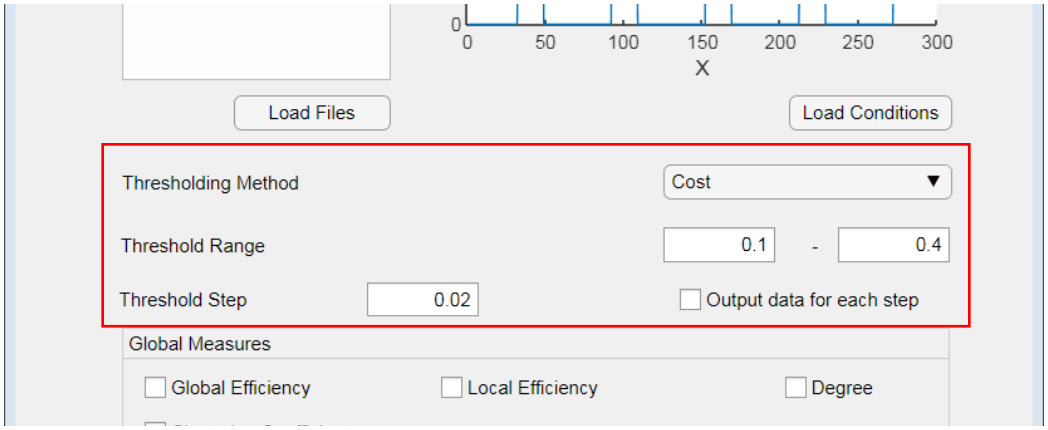


Fig. 3.24 Selection of threshold range

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. 3.25**).

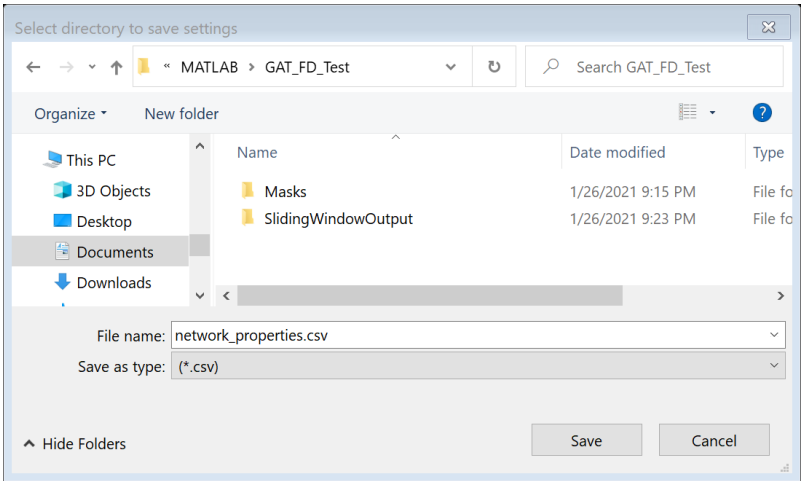


Fig. 3.25 Output folder selection for network analysis

When successfully running network properties calculation, you will find a window (**Fig. 3.26**) showing you the current processing status.

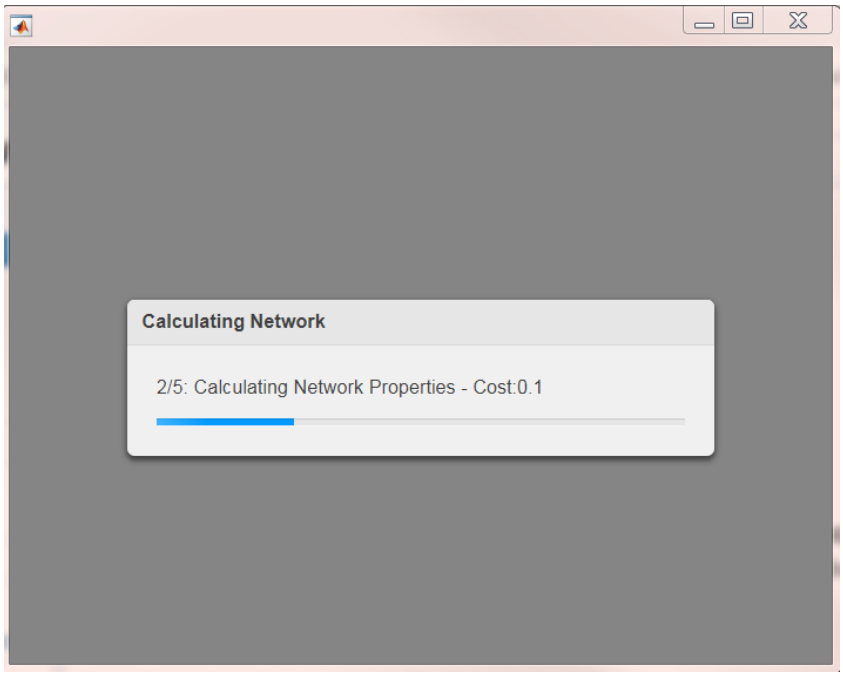


Fig. 3.26 Processing status window of network properties calculation

3.3.8 Output Data

After successfully running the network properties calculation, a "Finished" window will be shown (**Fig. 3.27**).

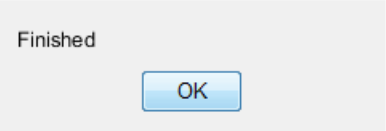


Fig. 3.27 Finished window showing successfully running network properties calculation

The output data will be a *.csv file and a *.csv.mat file (**Fig. 3.28**).

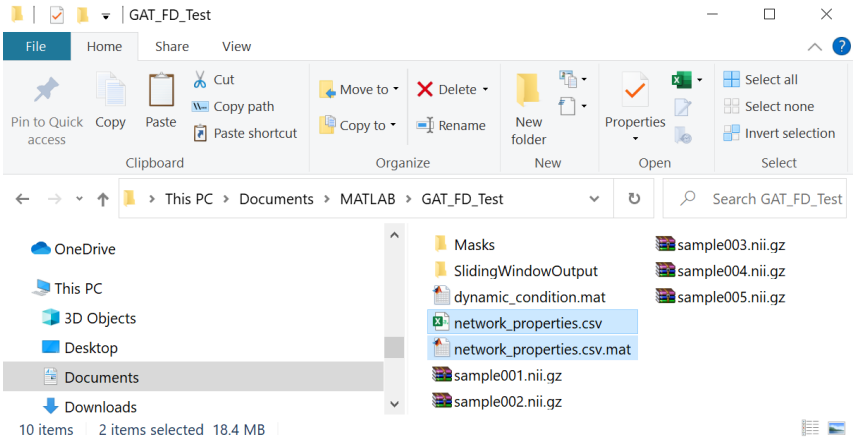
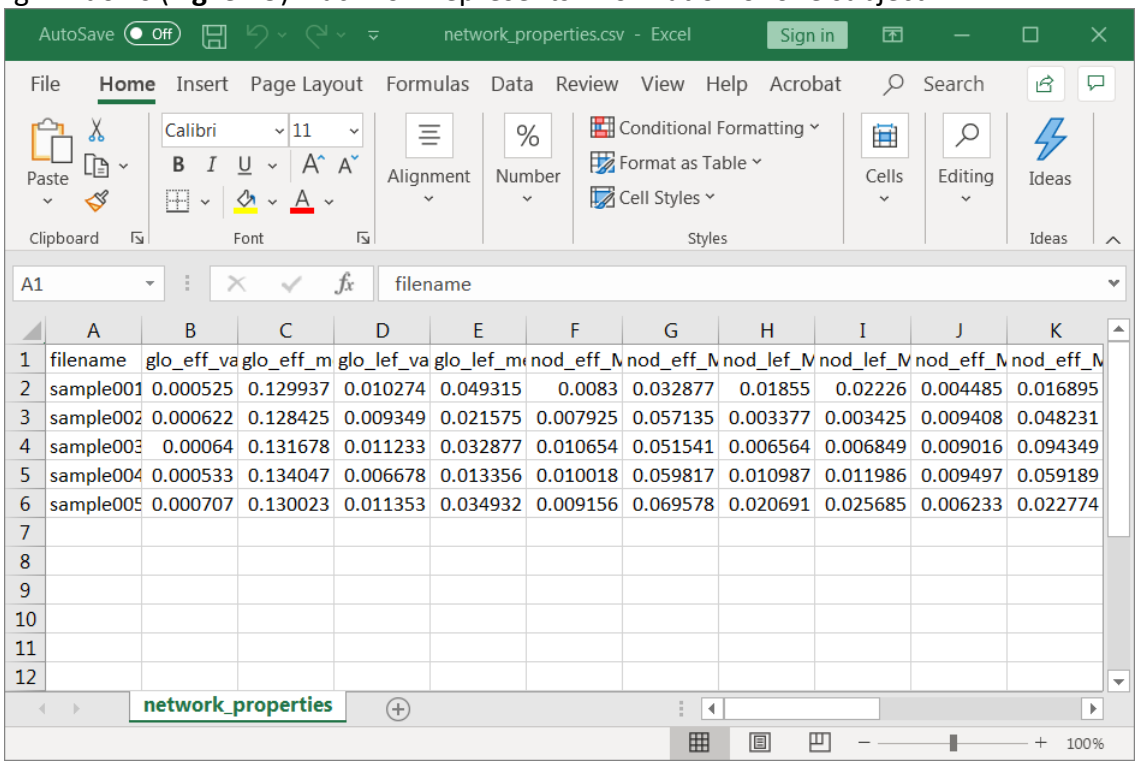


Fig. 3.28 Output data of network properties calculation

The *.csv file contains the mean and variance values of the network properties across the sliding windows (**Fig. 3.29**). 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_M	nod_eff_M	nod_lef_M	nod_lef_M	nod_eff_M	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. 3.29 Example of *.csv file

The *.csv.mat file is used for the validation of the time series (details are explained in Chapter 3.4.3).

3.4 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. 3.30**) after successfully running the **Display**.

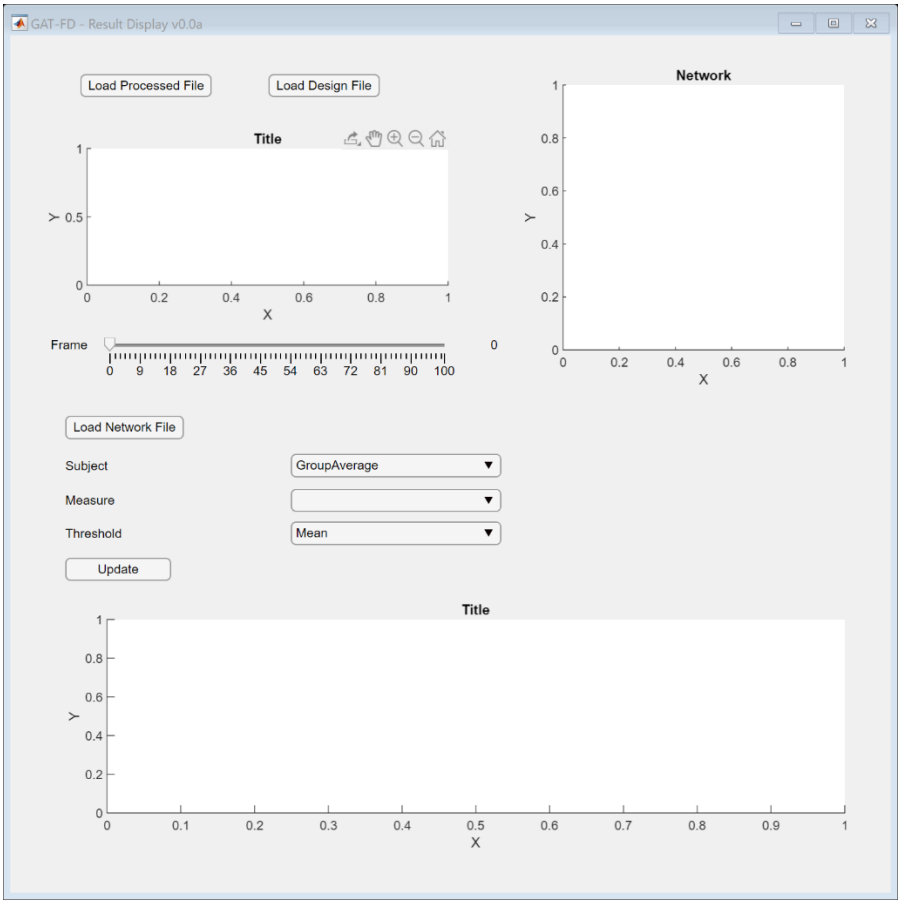


Fig. 3.30 The interface of Display

3.4.1 Load Files

Click 'Load Processed File' button, select *.mat file of one subject (generated from the sliding window analysis step) (**Fig. 3.31**), and click 'Open'.

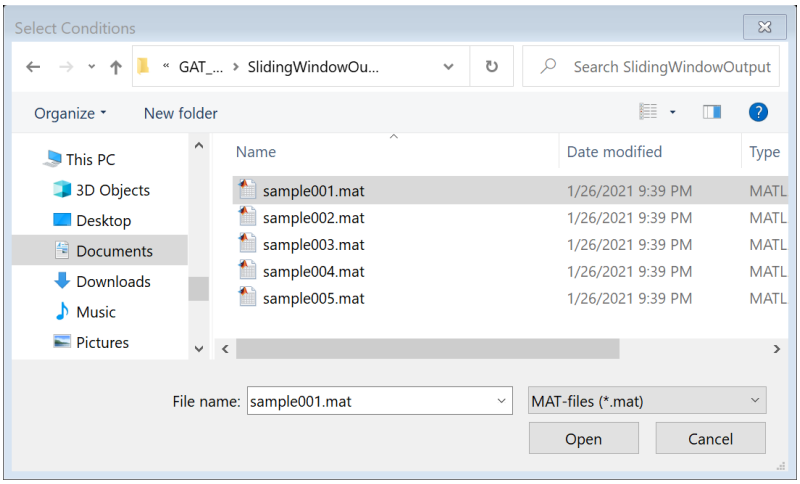


Fig. 3.31 Load processed file

3.4.2 Load Design File

Click 'Load Design File' button, select *.mat file generated from the task design step (**Fig. 3.32**), and click 'Open'.

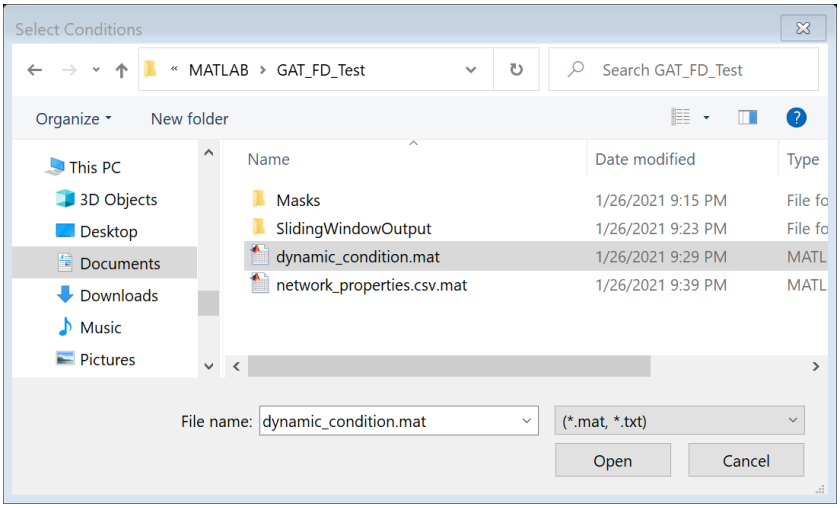


Fig. 3.32 Load design file

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. 3.33**).

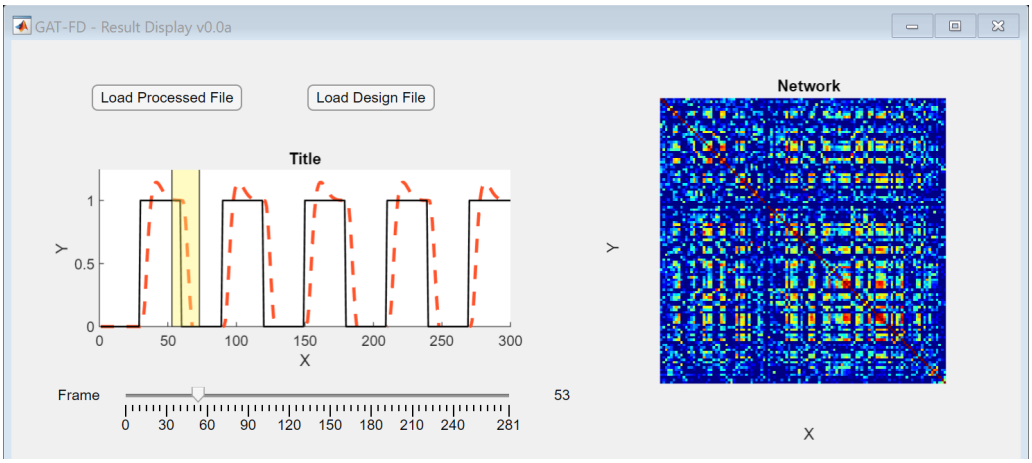


Fig. 3.33 Check functional connectivity matrix for each subject

3.4.4 Check Network Properties Across Sliding Windows

Click 'Load Network File' button, select *.csv.mat file generated after network analysis step (**Fig. 3.34**).

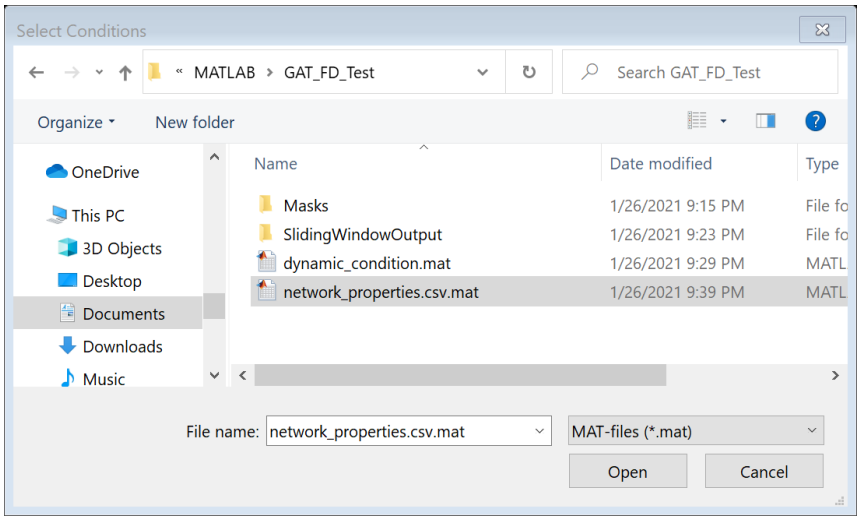


Fig. 3.34 Load network properties file

You can select desired subject, measures, and threshold in the drop-down menus (**Fig. 3.35**).

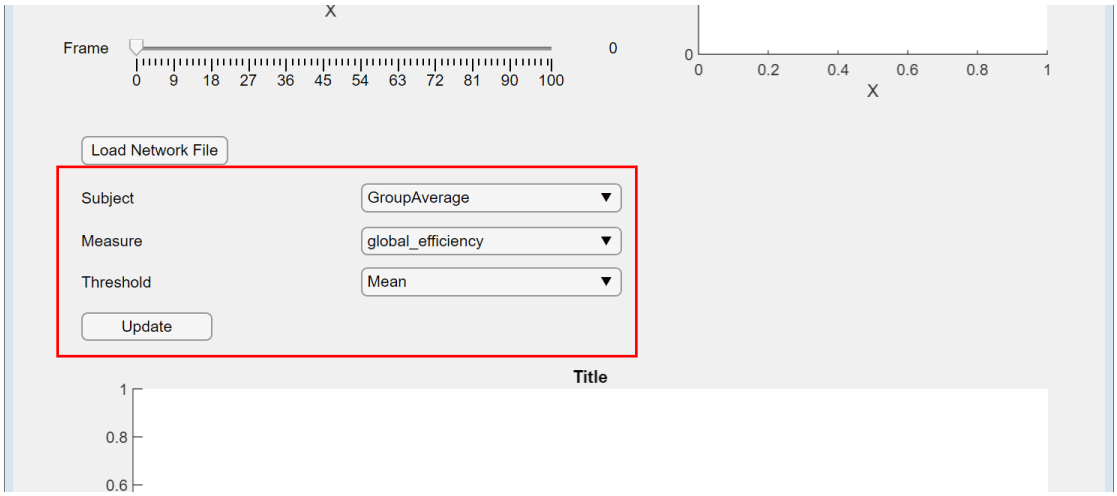


Fig. 3.35 Drop-down menus for network properties display

Then you can click update to display the selected network property over frames (**Fig. 3.36**).

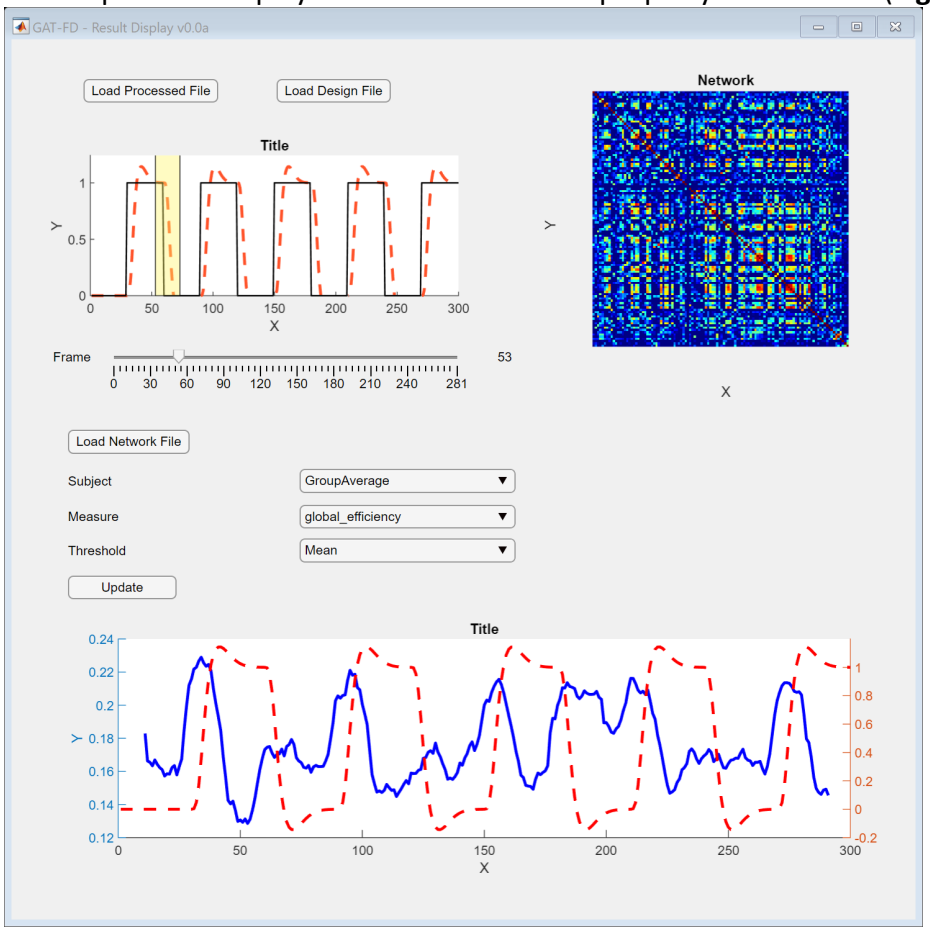


Fig. 3.36. Network property vs. hemodynamic response

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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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