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Introduction

BRAPH is an object-oriented toolbox written in MatLab that uses graph theory to characterize brain connectivity. BRAPH permits one to calculate brain connectivity matrices from various kinds of neuroimaging techniques, including structural magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and positron emission tomography (PET). Once these networks have been built, BRAPH can calculate several graph theory measures.

BRAPH provides a graphical user interface (GUI) that guides the user through all the steps of an analysis of brain connectivity using graph theory: definition of a brain atlas; construction of the connectivity matrices; calculation of global and local measures; comparison between groups and with random graphs using permutation tests; and, finally, visualization of the results. The initial GUI is presented in figure 1.

In this chapter, we briefly introduce the overall architecture of BRAPH.

While the current version of BRAPH does not allow analyzing data from diffusion tensor imaging (DTI), this will be available in future releases.

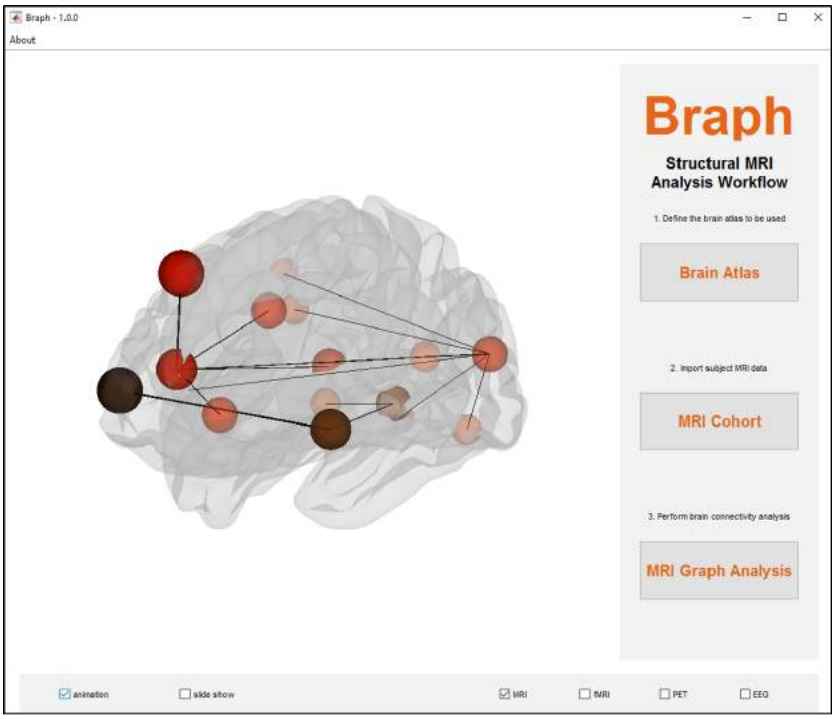


Figure 1: Initial GUI that appears when BRAPH is launched. From this GUI, it is possible to select the neuroimaging modality (checkboxes on the bottom right) and to launch the software from different stages of the workflow: brain atlas, cohort or graph analysis (buttons on the right).

Getting started

1. Download BRAPH from `http://braph.org/software/`.
2. Unzip the downloaded file into the desired directory.
3. Launch MatLab and change the current folder to the directory chosen in step 2.
4. Execute *braph.m* by typing `braph` in the command line panel of MatLab. This loads all the files necessary to use BRAPH and opens the initial GUI shown in figure 1.

Initial GUI

The initial GUI Braph is shown in figure 1 and consists of three main work areas:

1. **Animation panel** (on the left). By default, it shows an animation of a sample graph on a brain surface. Alternatively, by checking the corresponding checkbox in the bottom left, it can also feature a slide show of some select graph measures.
2. **Imaging modality selection** (at the bottom). A set of four checkboxes permits the user to choose the imaging modality corresponding to the data to be analyzed. Currently, BRAPH can analyze:
   - structural magnetic resonance imaging (**MRI**) data;
   - functional magnetic resonance imaging (**fMRI**) data;
   - positron emission tomography (**PET**) data;
   - electroencephalography (**EEG**) data.
3. **Workflow panel** (on the right). Series of push buttons that permit to launch various stages of the graph analysis for the selected imaging modality. For example, for MRI:
   - `Brain Atlas` defines the atlas used in the analysis;
   - `MRI Cohort` imports the MRI data of the subjects;[1]
   - `MRI Graph Analysis` performs the brain connectivity analysis.[2]

[1] Depending on the selected imaging modality, this can also be `fMRI Cohort`, `PET Cohort`, or `EEG Cohort`.

[2] Depending on the selected imaging modality, this can also be `fMRI Graph Analysis`, `PET Graph Analysis`, or `EEG Graph Analysis`.

General workflow

The workflow of BRAPH is organized along a series of GUIs that guide the user into the analysis of brain connectivity. This is illustrated in figure 2.

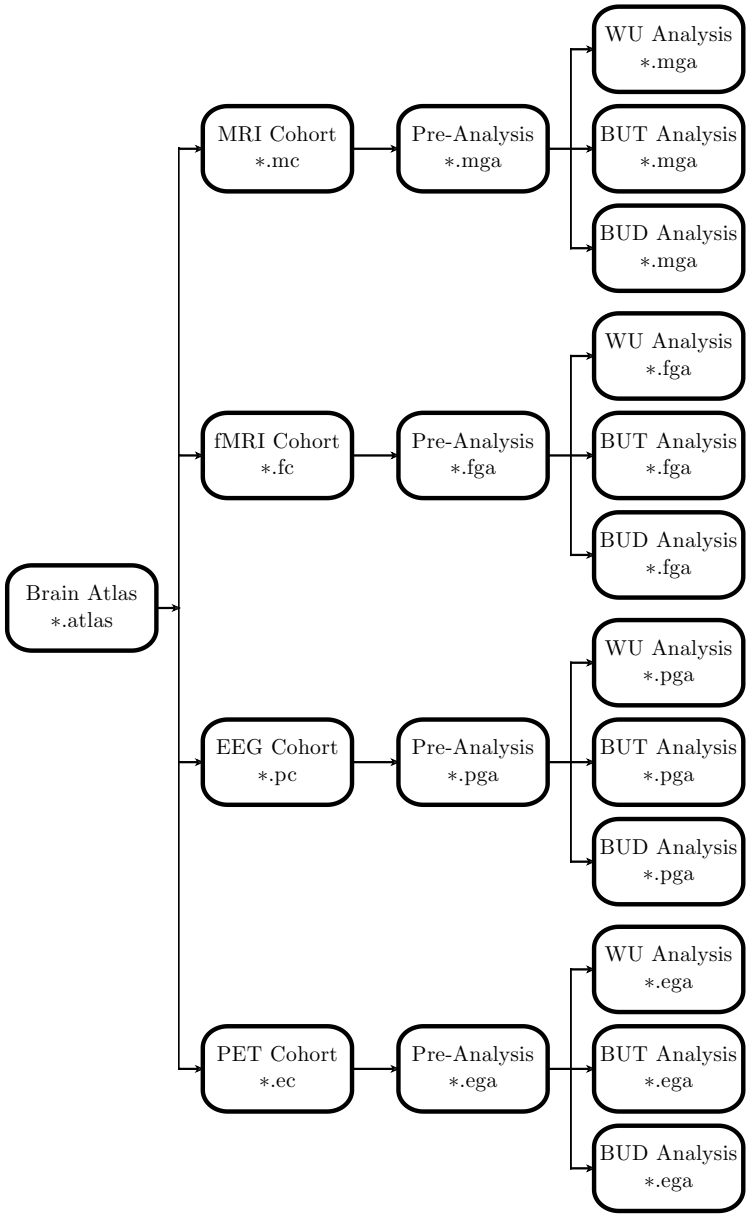


Figure 2: General workflow of BRAPH for MRI, fMRI, EEG, and PET data analysis. Each box represents a GUI available in BRAPH, while the arrows indicate the typical workflow. The formats of the BRAPH files are indicated within each box. The abbreviation WU refers to weighted undirected graphs, BUD to binary undirected graphs at a fixed density of connections, and BUT to binary undirected graphs at a fixed threshold.

1. **Brain Atlas** permits the user to create and manage a brain atlas.
2. **MRI/fMRI/PET/EEG Cohort** permits the user to create a cohort of subjects and upload their data.
3. **MRI/fMRI/PET/EEG Graph Analysis** permits the user to define the parameters for the graph analysis. After deciding the type of analysis, the user is redirected to a specialized GUI:
   - **MRI/fMRI/PET/EEG Graph Analysis WU** to perform a graph analysis using weighted undirected graphs.
   - **MRI/fMRI/PET/EEG Graph Analysis BUD** to perform a graph analysis using binary undirected graphs at a fixed density of connections.
   - **MRI/fMRI/PET/EEG Graph Analysis BUT** to perform a graph analysis using binary undirected graphs at a fixed threshold.

Example data

MRI and fMRI data sets are provided on the website `http://braph.org`. They are provided only for trainign purposes. They have been randomly generated and do not correspond to real clinical data.

Brain Graphs

In order to perform brain connectivity analysis, the first essential step is to obtain information about the *brain connectivity matrix*. To this end, the brain is divided into several (typically between 50 and 1000) regions, and the connection strength between each pair of regions is measured. The definition and measurement of this strength depends on the neuroimaging modality used to acquire the data. Currently, BRAPH deals with two categories of data:

1. **Structural data** acquired with magnetic resonance imaging (MRI) or **glucose metabolism data** acquired with static positron emission tomography (PET). These neuroimaging techniques provide a brain image for each subject of a group, i.e. a value (e.g. cortical thickness, gray matter volume, glucose metabolism) for each brain region of each subject. The connectivity strength between two regions can be measured as the correlation between the values corresponding to these two regions *across the group*. A possible underlying assumption is that connected regions will grow or shrink together or show similar levels of glucose metabolism. Therefore, these techniques provide a *single* brain connectivity matrix for each group.

2. **Functional data** acquired with functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). Functional neuroimaging techniques provide a sequence of images that show the activation of various brain regions as a function of time for each subject. The connectivity strength between brain regions can be measured as the correlation between their activation levels as a function of time. The underlying assumption is that functionally connected regions get activated together. Therefore, this technique provides an *individual* brain connectivity matrix for each subject.

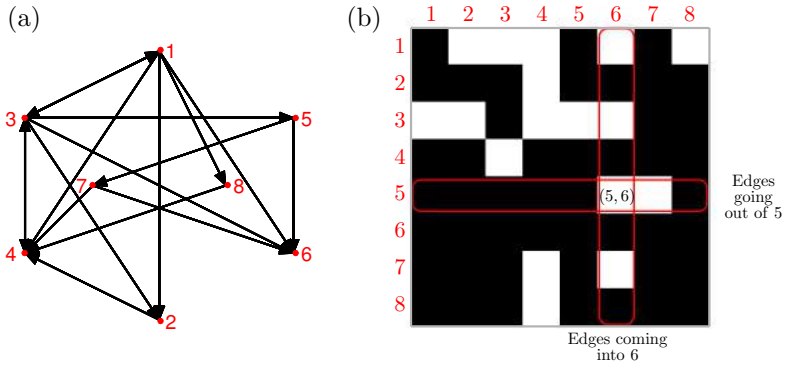


Figure 3: (a) A binary graph and (b) the corresponding connectivity matrix.

Graphs

A graph consists of a set of *nodes* that are connected by *edges*. Figure 3(a) shows an example of a simple graph, where the nodes are represented by circles and the edges by lines. This representation of a graph is very intuitive, but can become very complex and cluttered as soon as the numbers of nodes and edges start to grow.

Figure 3(b) shows that an alternative way to represent a graph is using a *connectivity matrix*.[3] The use of connectivity matrices permits one to employ highly-optimized algorithms based on linear algebra.[4] The *elements* of the matrix represent the edges between nodes; for example, the element (j, k) represents the edge that goes from node j to node k. Each *row* of the connectivity matrix represents the edges that are going out from a node; for example, row j represents the edges that are going out from node j. And each *column* of the matrix represents the nodes that arrive to a node; for example, column k represents the edges that are arriving to node k.

[3] The specific order of the nodes in the matrix does not affect the calculation of the graph measures, but only the graphical representation of the connectivity matrix.

[4] J. Kepner and J. Gilbert. *Graph algorithms in the language of linear algebra*. SIAM, 2011

Based on the nature of the edges' weight and directionality, four types of graphs can be identified (figure 4):

- **Weighted directed (WD) graphs.** The edges are associated with a real number indicating the *strength* of the connection and are *directed* (therefore, node j can be connected to node k without node k needing to be connected to node j).
- **Weighted undirected (WU) graphs.** The edges are associated with a real number indicating the *strength* of the connection and are *undirected* (therefore, if node j is connected to node k, then node k is also connected to node j). The connectivity matrix is symmetric.
- **Binary directed (BD) graphs.** The edges can be either 0 (absence of connection) or 1 (existence of connection) and are *directed*.
- **Binary undirected (BU) graphs.** The edges can be either 0 (absence of connection) or 1 (existence of connection) and are *undirected*. The connectivity matrix is symmetric.

As shown in figure 4, it is possible to transform these graphs in the following ways:

1. **Weighted to binary.** It is possible to transform a weighted graph into a binary one by *thresholding*, i.e. by assigning a value of 1 to the edges above a given threshold and 0 to those below the threshold. The value of the threshold can be either assigned a priori or determined so that the graph has a given density (fraction of edges that are connected); this choice becomes relevant when different binarized graphs need to be compared either at fixed threshold or at fixed density.

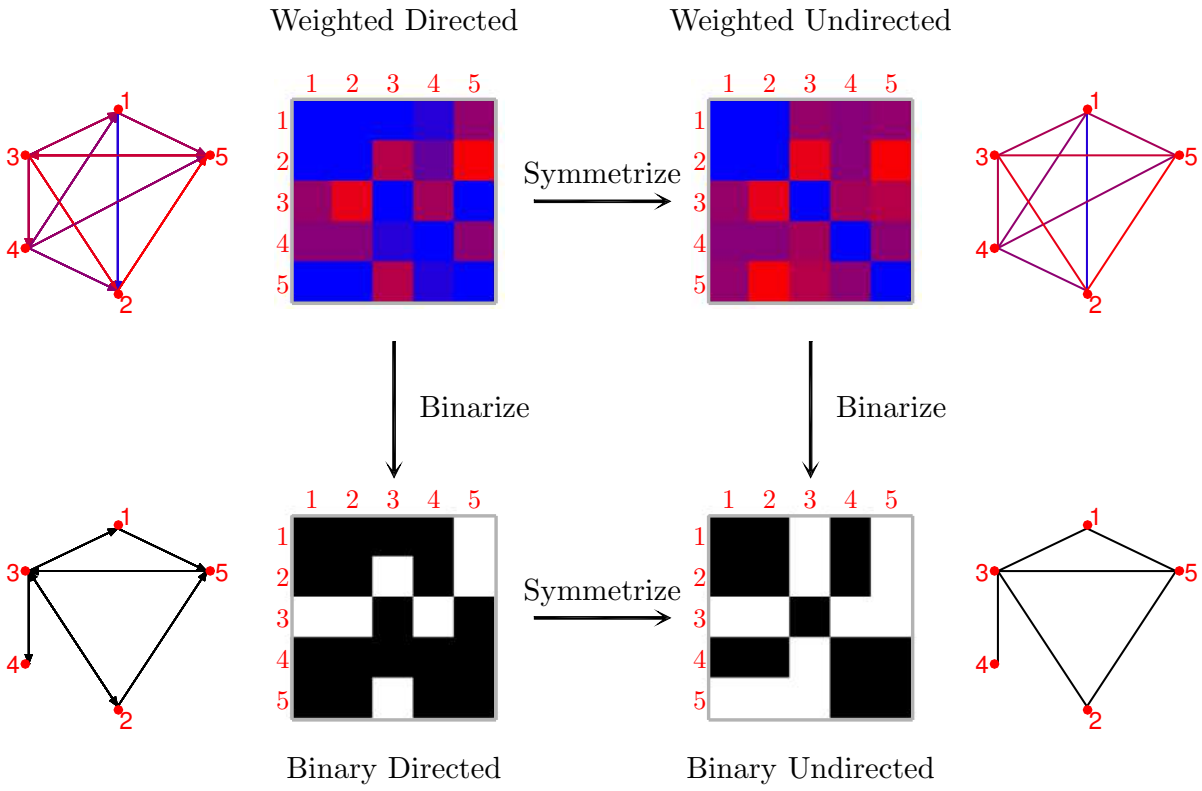


Figure 4: Graphs can be classified based on their edge weights (weighted/binary) and directionality (directed/undirected). It is possible to transform a directed graph into an undirected one by symmetrization (i.e. by removing the information about the edge directions), and a weighted graph into a binary one by thresholding (i.e. by assigning a value of 1 to the edges above a given threshold and 0 to those below the threshold).

2. **Directed to undirected.** It is possible to transform a directed graph into an undirected one by *symmetrization*, i.e. by removing the information about the edge directions. This is done by binarizing the connectivity matrix representing the directed graph. There are several possible rules for the symmetrization, e.g.:

   - **Sum.** Addition of the connectivity matrix and its transpose.
   - **Average.** Average of the connectivity matrix and its transpose.
   - **Minimum.** Connectivity matrix and its transpose are compared and the smallest value for each entry is used.
   - **Maximum.** Connectivity matrix and its transpose are compared and the largest value for each entry is used.

Nodes: Brain regions

The nodes are brain regions. The nodes should be chosen so that they do not overlap with each other and cover the whole brain.[5] The

[5] M. Rubinov and O. Sporns. Complex network measures of brain connectivity: Uses and interpretations. *Neuroimage*, 52: 1059–1069, 2010

choice of nodes is not unique and can be derived from many anatomical atlases used in MRI, fMRI and PET, or from the locations of the electrodes in EEG. The choice of the nodes is very important because it influences the topology of the brain graphs, the strength of the connections, and also the values of the calculated graph measures[6]. Therefore, two brain graphs can only be quantitatively compared if they are built using the same brain atlas.

In BRAPH the choice of the parcellation scheme is inputted in the GUI Brain Atlas interface. In this manual, we use the AAL90 (Automated Anatomical Labeling - 90 regions) atlas[7] and the Desikan atlas[8].

[6] J. Wang, L. Wang, Y. Zang, H. Yang, H. Tang, Q. Gong, Z. Chen, C. Zhu, and Y. He. Parcellation-dependent small-world brain functional networks: A resting-state fMRI study. *Hum. Brain Mapp.*, 30:1511–1523, 2009

[7] N. Tzourio-Mazoyer, B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer, and M. Joliot. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage*, 15: 273–289, 2002

[8] R. S. Desikan, F. Ségonne, B. Fischl, B. T. Quinn, B. C. Dickerson, D. Blacker, R. L. Buckner, A. M. Dale, R. P. Maguire, B T Hyman, M. S. Albert, and R. J. Killianya. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*, 31:968–980, 2006

Edges: Brain connections

The edges represent the connections between brain regions. As we have seen in the previous section, the edges can indicate absence/presence of connections (binary graphs) or the strength of the connections (weighted graphs). Depending on the nature of the neuroimaging data, the edges can be interpreted in different ways. For example, in the case of structural MRI (T1-weighted) or static PET the edges represent the correlation coefficients between couples of brain regions. In the case of *functional* connectivity data, the edges may represent the time correlations between the activation of pairs of brain regions. In the following sections, we will explain how to build the connectivity matrices for some of the most common brain imaging techniques.

Building the connectivity matrix

MRI

Magnetic resonance imaging (MRI)[9] is a non-invasive and non-ionizing imaging technique that gives quickly-obtainable and easy-to-interpret images acquired as 3D data sets. MRI uses relatively low magnetic fields and is able to distinguish between different tissues by sending radio-frequency (RF) pulses with various frequencies and strengths thanks to the fact that different tissues have different proton density, and proton density determines the strength of the interaction with the external magnetic field.

In neuroimaging, MRI can be used to show the shape and structure of the grey and white matter in the brain. Since more cell bodies are present in the gray matter (where neurons and glial cells are present) compared to the white matter (in which mostly long nerve fibers are present), their MRI signals are different. The contrast in the image is obtained by observing the different relaxation times of the

[9] R. W. Brown, Y.-C. N. Cheng, E. M. Haacke, M. R. Thompson, and R. Venkatesan. *Magnetic resonance imaging: Physical principles and sequence design*. John Wiley & Sons, 2014

protons present in different tissues. One of the most common images obtained with MRI are *T1-weighted images*.

Before the connectivity matrix can be built, all T1-weighted images obtained with MRI need to be preprocessed using an external software (e.g. FreeSurfer[10]). The preprocessing may include several steps, e.g. correction for spatial distortions due to field inhomogeneity, tissue segmentation and normalization to a template. After preprocessing the images, the gray matter volume or cortical thickness should be extracted for each region of the brain atlas. Finally, a linear regression can be applied to the regions in order to exclude the effects due to variables such as age, gender, education.[11]

[10] B. Fischl. Freesurfer. *Neuroimage*, 62: 774–781, 2012

[11] Y. He, Z. J. Chen, and A. C. Evans. Small-world anatomical networks in the human brain revealed by cortical thickness from mri. *Cereb. Cortex*, 17: 2407–2419, 2007

In order to be uploaded into BRAPH, the data need to have a single value (e.g. cortical thickness, subcortical volume) per brain region per subject. Therefore, the nodes in the connectivity matrix need to correspond to the brain regions of the brain atlas employed in the analysis. The edges are calculated as the statistical correlations of the values between pairs of brain regions across a group of subjects. A group typically includes the subjects sharing a common property (e.g. the same clinical diagnosis). Therefore, a single connectivity matrix is obtained for each group of subjects and consequently all the measures calculated for the connectivity matrix reflect the group's properties. The workflow for the calculation of the connectivity matrix is shown in figure 5. Note that:

- all self-connections are eliminated (i.e. the diagonal entries of the connectivity matrix, which correspond to the autocorrelations, are set to zero);
- the negative correlations can be (1) excluded from the analysis by setting them to zero, (2) substituted by their absolute values, or (3) left unchanged (however, in this latter case, some graph measures are not defined for negative correlations).

In BRAPH, a connectivity matrix can be built using any of the following correlation functions:

- The **Pearson correlation coefficient** is calculated as

$$\rho_{jk} = \frac{\text{cov}\left(x_j, x_k\right)}{\sigma_j \sigma_j} , \tag{1}$$

  where x_j and x_k are the values corresponding to regions j and k, $\text{cov}\left(x_j, x_k\right)$ is their covariance, and σ_j and σ_j are their standard deviations. This coefficient measures the linear relation between the two sets of data x_j and x_k: when the data are plotted in a scatter plot, the coefficient measures how far the data points are from the line of best fit drawn through the data. The value of the

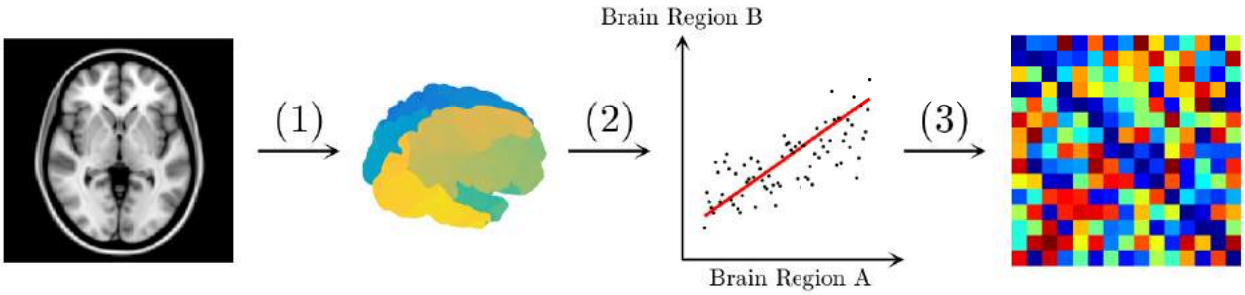


Figure 5: Flowchart exemplifying the building of the connectivity matrices in the brain for MRI structural data. (1) A T1-weighted MRI image is preprocessed to account for some artifacts and a meaningful variable is extracted for each brain region defined by the chosen parcellation scheme (e.g. cortical thickness, subcortical volume). (2) Correlation coefficients are calculated for each pair of brain regions in the brain across the subjects of a group. (3) The connectivity matrix is built such that the rows and the columns represent the brain regions and the entries are the correlation coefficients between each pair of brain regions.

coefficient can range between -1 and 1: a value of 1 denotes a perfect positive linear relation (as one variable increases, the other increases linearly); a value of -1 signifies a perfect negative linear relation (as one variable increases, the other decreases linearly); and a value of 0 denotes no linear correlation between the two variables (importantly, a value of 0 does not state that there is no correlation between the two variables, just that the correlation is not linear). Note that the Pearson coefficient assumes the data to be normally distributed, it can be sensitive to outliers or a skewed distribution, and it does not reveal a difference between dependent and independent variables.

- The **Spearman rank correlation coefficient** is defined as the Pearson correlation coefficient between the ranked variables. This coefficient measures the correlation between two ranked variables with monotonic relation between them. The ranks are assigned to each value in the data such that the highest value is ranked 1 (if there is a "tie", i.e. two values of same rank, their average rank is assigned to both). The coefficient ranges from -1 to 1 with the same interpretations of the positive and negative values as explained in the Pearson correlation coefficient. The Spearman's rank coefficient is a non-parametric version of Pearson coefficient and as such the relation between the ranks of the data it reveals (monotonic) is less restrictive than the one of the Pearson coefficient (linear).

- The **Kendall rank correlation coefficient** is a non-parametric test that measures the correlation between two ranked quantities. It can be calculated by considering all the pairings between the data sets x and y. Consider the pairs (x_i, y_j) and (x_j, y_i), where x_i and x_j are the ranks for i^{th} and j^{th} data value in the x data set. Then, if $x_i < x_j$ and $y_i < y_j$ is valid or equivalently $x_i > x_j$ and $y_i > y_j$ is valid the pair is considered concordant. Otherwise, the pair is discordant. In the case $x_i = x_j$ or $y_i = y_j$ the pair is tied. The range

for the correlation is -1 to 1, where 1 indicates perfect agreement, -1 indicates perfect disagreement, and 0 shows that the ranks are independent.

- **Partial correlation coefficients.** Partial correlation coefficients are the correlation coefficients between two sets of data after removing the influence of one or more variables on the two data sets. Both Pearson and Spearman partial correlation coefficients can be calculated in BRAPH.

fMRI

Functional magnetic resonance imaging (fMRI)[12] is a neuroimaging technique that is used to measure the blood-oxigen-level-dependent (BOLD) activity of the brain, differently from structural MRI which measures the anatomical properties of the brain.

The foundation for fMRI lies on the observation that an increased activity in a part of the brain results in an enhancement of the corresponding magnetic resonance signal. The reason is that neural activity is associated with increases in blood flow and oxygenation. Since oxygen-rich and oxygen-poor blood has different magnetic properties, this results in a contrast in the magnetic resonance signal. This information can be obtained for subjects performing some special tasks (e.g. looking at a picture) or also while no explicit task is performed (*resting state fMRI*). In both cases, multiple images are obtained which show the brain activity as a function of time.

In contrast to MRI, fMRI data provide a time-series of values corresponding to each brain region. Therefore, an *individual* connectivity matrix can be obtained for each subject by calculating the temporal correlations between the activation of couples of brain regions, and the graph measures are calculated for each subject. As in the case of structural MRI, the nodes are the brain regions and the edges are calculated as correlation coefficients. The groups of subjects are built by grouping subjects sharing some common properties (e.g. same clinical diagnosis).

[12] S. A. Huettel, A. W. Song, and G. McCarthy. *Functional magnetic resonance imaging*. Sinauer Associates Sunderland, 2004

EEG and PET

In addition to MRI and fMRI data, BRAPH permits the analysis of the data obtained by static PET[13] and EEG[14]. Since their workflow is similar to the one of MRI and fMRI, respectively, we refer the reader to the respective sections for more details.

[13] R. C. Walker, G. L. Purnell, L. B. Jones-Jackson, K. L. Thomas, J. A. Brito, and E. J. Ferris. Introduction to PET imaging with emphasis on biomedical research. *Neurotoxicology*, 25:533–542, 2004

[14] M. Teplan. Fundamentals of EEG measurement. *Meas. Sci. Rev.*, 2:1–11, 2002

Statistical significance

Permutation test

Statistical significance tests are used to determine whether a measured effect is genuine or is a statistical glitch due to the randomness associated with the selection of the sample. BRAPH employs a non-parametric permutation test to assess the significance of the differences between groups (reported as p-values) and to determine the confidence intervals (typically the 95% confidence intervals).

The *null hypothesis* is the statement that an observed effect is due to randomness. The permutation test evaluates whether the null hypothesis can be rejected by calculating the associated p-value (i.e. the probability to observe a value of the measure that is as extreme or more extreme than the observed value just by chance) and comparing it with a predetermined threshold (typically, $p = 0.05$ or $p = 0.01$). This concept is illustrated in figure 6.

In particular, the permutation test is employed to compare the measures calculated for two groups of subjects. In detail:

1. Determine the difference between the measures calculated for the two groups.

2. Permute the subjects between the two groups; calculate the difference between the measures calculated for the permuted groups. Repeat this step several times (typically 1000 times) and obtain the histogram of the differences.

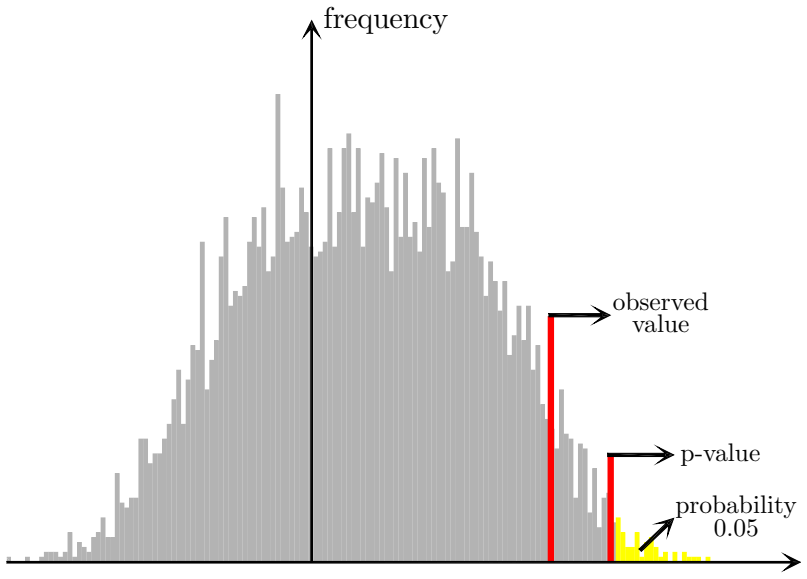


Figure 6: The permutation test evaluates whether the null hypothesis can be rejected by calculating the associated p-value (i.e. the probability to observe a value of the measure that is as extreme or more extreme than the observed value just by chance) and comparing it with a predetermined threshold (typically, $p = 0.05$ or $p = 0.01$).

3. Determine where the difference between the measures calculated in the two groups lies within the histogram and compare this value with the chosen threshold (as shown in figure 6).

Comparison with random graphs

To compare the measures calculated for one group to those of corresponding random graphs, the following procedure is employed:

1. Determine the value of the measure for the group.
2. Calculate the distribution of the measure on a set (typically 1000) of random graphs[15] and obtain the corresponding histogram.
3. Determine where the value of the measure falls within the histogram.

[15] These random graphs typically are chosen to preserve the degree and strength distributions of the original graph.

False discovery rate (FDR)

In the case of nodal measures, the permutation test tests multiple null hypotheses simultaneously (one for each brain region). This means that the likelihood of false significance increases.[16] Therefore, the significance level needs to be adjusted for multiple comparisons and

[16] For example, using a 0.05 threshold for the p-value, one would expect to reject the null hypothesis 5 times in 100 trials just by chance.

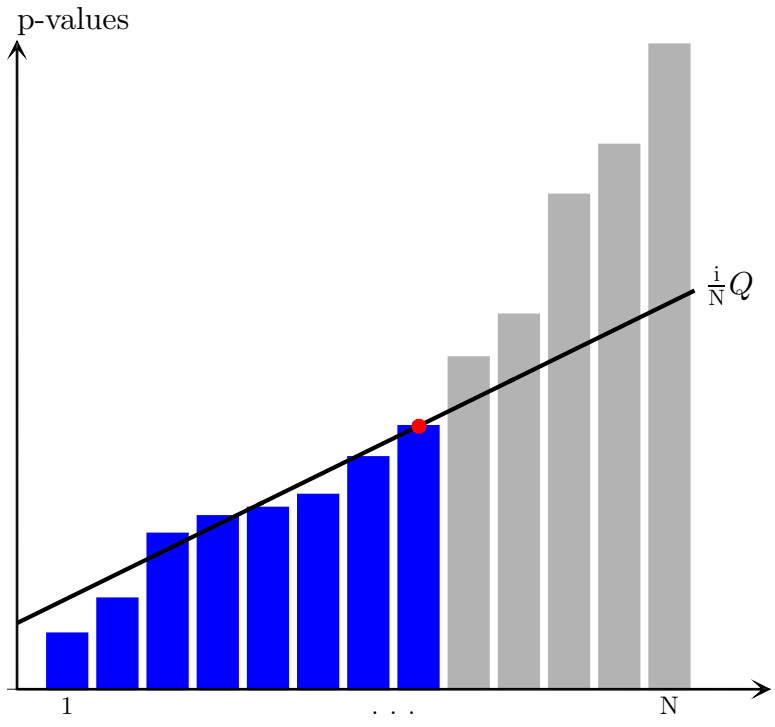


Figure 7: The individual p-values for each hypothesis testing are arranged in order starting from the smallest one and compared to their false-rate-corrected values calculated as $\frac{i}{N}Q$ (here, $Q = 0.10$). The largest p-value that is smaller than the corresponding false-rate-corrected value is significant as well as all hypothesis having smaller p-values (regardless of whether they are larger than the corresponding false rate corrected values).

the p-values need to be corrected accordingly. BRAPH does this by using the *false discovery rate* (FDR) algorithm.

The false discovery rate is corrected by using the Benjamini-Hochberg procedure, which follows the ensuing steps (figure 7):

1. Obtain all the individual p-values for each hypothesis testing and arrange them in order starting from the smallest one (i.e. the smallest one has rank $i = 1$, the largest $i = N$, where N is the number of hypotheses tested).

2. Choose the false discovery rate Q (typically, $Q = 0.05$).

3. Compare each of the individual p-values with their false-rate-corrected values calculated by $\frac{i}{N}Q$.

4. Find the largest p-value that is smaller than the corresponding false-rate-corrected value.

5. The value in the previous point is significant as well as all p-values that are smaller; therefore, all hypothesis having smaller p-values pass the test, regardless of whether they are larger than the corresponding false-rate-corrected values.

Graph Measures

A graph consists of a series of *nodes* connected by *edges*. The edges can be either *weighted* (**W**), in which case they are associated with a real number that indicates the strength of the connection, or *binary* (**B**), in which case they are either 0 (absence of connection) or 1 (existence of connection). Furthermore, the edges can be either *directed* (**D**), if the connections have a directionality (e.g. node j can be connected to node k but not viceversa), or *undirected* (**U**), if the connections do not have a preferential directionality (i.e. if node j is connected to node k, then automatically node k is connected to node j). The connections of a graph can be efficiently represented with a connectivity matrix, where the jth row represents the out-going connections from node j and the kth column represents the in-coming connections to node k. U graphs are symmetric. Typically, the diagonal elements of the connectivity matrix are set to 0, i.e. a node is not connected to itself.

Graph measures can be classified within two broad categories:

1. **global** measures refer to global properties of a graph and, therefore, consist of a single number for each graph;
2. **nodal** measures refer to properties of the nodes of a graph and, therefore, consist of a vector of numbers — one for each node of the graph.

Furthermore, we will indicate to which kind of graph a given measure belongs by using **W** (= weighted graphs) or **B** (= binary graphs), and **D** (= directed graphs) or **U** (= undirected graphs). If no letter is indicated it means that the measure applies to both cases.

Degree

Degree (nodal): Total number of edges connected to a node.
Average degree (global): Average of the degrees of all nodes.
In-degree (nodal, D): Number of inward edges going into a node.
Average in-degree (global, D): Average of the in-degrees of all nodes.
Out-degree (nodal, D): Number of outward edges originating from a node.
Average out-degree (global, D): Average of the out-degrees of all nodes.
Methodological notes: For BU graphs, the degree is calculated as the sum of the number of connections across the rows or columns of the connectivity matrix. For BD graphs, the in-degree is calculated as sum over columns, while the out-degree is calculated as sum over the rows; the degree is the sum of in-degree and out-degree. For W

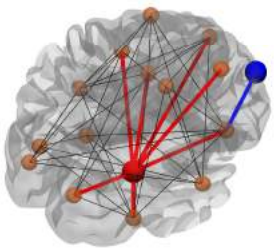


Figure 8: Degree of a node. The red node has a high degree (i.e. a large number of connections), while the blue node has a low degree (i.e. a low number of connections).

graphs, the weights of the connections are ignored in the calculations by binarizing the connectivity matrix so that only edges with nonzero weights are considered connected.

Strength

Strength (nodal, W): Sum of the weights of all edges connected to a node.[17]
Average strength (global, W): Average of the strengths of all nodes.
In-strength (nodal, WD): Sum of the weights of inward edges going into a node.
Average in-strength (global, WD): Average of the in-strengths of all nodes.
Out-strength (nodal, WD): Sum of the weights of outward edges originating from a node.
Average out-strength (global, WD): Average of the out-strengths of all nodes.
Methodological notes: For WU graphs, strengths are calculated as sums over either rows or columns of the weighted connectivity matrix. For WD graphs, in-strengths (out-strengths) are calculated as sums over columns (rows), and strengths are calculated as sums of in-strengths and out-strengths.

[17] A. Barrat, M. Barthelemy, R. Pastor-Satorras, and A. Vespignani. The architecture of complex weighted networks. *Proc. Natl. Acad. Sci. U.S.A.*, 101:3747–3752, 2004

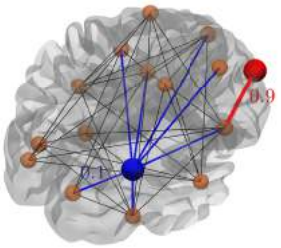


Figure 9: Strength of a node. Despite having less connections, the red node has a higher strength (only one connection with a high strength of 0.9), while the blue node has a lower strength (it has 7 connections, each with strength of only 0.1).

Eccentricity

Eccentricity (nodal): Maximal distance between a certain node and any other node.[18]
Average eccentricity (global): Average of the eccentricities of all nodes.
In-eccentricity (nodal, D): Maximal incoming distance from all other nodes to a node.
Average in-eccentricity (global, D): Average of the in-eccentricities of all nodes.
Out-eccentricity (nodal, D): Maximal outgoing distance from a node to all other nodes.
Average out-eccentricity (global, D): Average of the out-eccentricities of all nodes.
Radius (global): Minimum eccentricity of all nodes.
Diameter (global): Maximum eccentricity of all nodes.
Methodological notes: The distances (the shortest path lengths) between a node and any other node in the graph can be calculated and stored in a distance matrix. The eccentricity of a node is the maximum of all distances calculated for this node. For D graphs, the in-eccentricity (out-eccentricity) is the maximum along columns (rows) of the distance matrix and the eccentricity is the larger value

[18] J. M. Harris, J. L. Hirst, and M. J. Mossinghoff. *Combinatorics and graph theory*. Springer Verlag, 2008

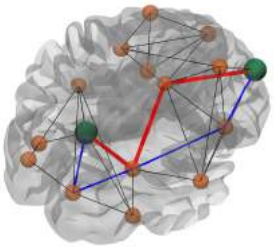


Figure 10: Distance between nodes. The distance between the two green nodes is the shortest possible path between them (e.g. the red path). Other (longer) paths between the two nodes can also exist (e.g. the blue path).

of the the in-eccentricity and out-eccentricity. For disconnected nodes, the eccentricity is set to NaN.

Path length

Path length (nodal): Average distance from a node to all other nodes.
Characteristic path length (global): Average of the path lengths of all nodes.
In-path length (nodal, D): Average distance from all other nodes to a particular node.
Characteristic in-path length (global, D): Average of the in-path lengths of all nodes.
Out-path length (nodal, D): Average distance from a particular node to all other nodes.
Characteristic out-path length (global, D): Average of the out-path lengths of all nodes.
Methodological notes: The distance between two nodes is defined as the length of the shortest path between those nodes (figure 10). For B graphs, the length of a path is the number of edges. For W graphs, the length of an edge is a function of its weight; typically, the edge length is inversely proportional to the edge weight because a high weight implies a shorter connection.[19] For D graphs, the path length of a node is the average of its in- and out-path lengths. The shortest path lengths between all pairs of nodes can be found using *Dijkstra's algorithm* on W graphs and using *breadth-first search* on binary graphs.[20]

[19] M. Rubinov and O. Sporns. Complex network measures of brain connectivity: Uses and interpretations. *Neuroimage*, 52: 1059–1069, 2010

[20] J. Kepner and J. Gilbert. *Graph algorithms in the language of linear algebra*. SIAM, 2011

Triangles

Triangles (nodal): Number of neighbors of a node that are also neighbors of each other.[21]
Methodological notes: For BU graphs, given a connectivity matrix A, the number of triangles is the diagonal of A^3 divided by two. For WU graphs, a contribution of the triangles around the node is defined as the geometric mean of the weights of the edges forming the triangle; it can be calculated by taking each element of the connection matrix to the power of $1/3$ and the diagonal entries of the third power of the resulting matrix divided by two. For D graphs, we will consider that there is a triangle only if the directed edges between the three nodes (vertices of the triangle) are arranged so that they form a closed cycle (but other conventions are also possible).

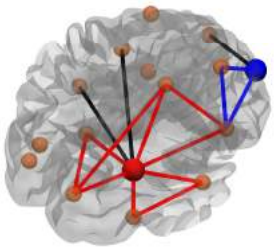


Figure 11: Triangles around a node. The red node has a high number of triangles (only the red edges contribute as the black edges are not connected between themselves), while the blue node has a low number of triangles (only 1 triangle is formed by the blue edges).

[21] J.-P. Onnela, J. Saramäki, J. Kertész, and K. Kaski. Intensity and coherence of motifs in weighted complex networks. *Phys. Rev. E*, 71:065103, 2005; and G. Fagiolo. Clustering in complex directed networks. *Phys. Rev. E*, 76: 026107, 2007

Clustering coefficient

Clustering coefficient (nodal): Fraction of triangles present around a node.[22]

[22] D. J. Watts and S. H. Strogatz. Collective dynamics of 'small-world' networks. *Nature*, 393:440–442, 1998

Clustering coefficient (global): Average of the clustering coefficients of all nodes.
Methodological notes: The clustering coefficient is calculated as the ratio between the number of triangles present around a node and the maximum number of triangles that could possibly be formed around that node. See also **triangles** for how the number of triangles is calculated. For U graphs, the total number of possible triangles is calculated as $\frac{1}{2}d(d-1)$, where d is the degree of a node. For D graphs, we consider a triangle only if the directed edges between any three nodes form a cycle; the total number of possible triangles is calculated as $d_{\text{in}} * d_{\text{out}} - d_{\text{ii}}$, where d_{in} and d_{out} are the in-degree and out-degree of the node, respectively, and d_{ii} is the number of connections that cannot form triangles (i.e. the number of neighboring nodes that are connected with both inward and outward edges).

Transitivity

Transitivity (global): Ratio of total number of triangles to the number of (unordered) triplets in the graph.
Methodological notes: The transitivity is calculated as $3N_{\text{triangles}}/N_{\text{triplets}}$, where $N_{\text{triangles}}$ is the total number of triangles and N_{triplets} is the total number of triplets in the graph. $N_{\text{triplets}} = \sum_i d_i(d_i - 1) - d_{\text{ii}}$, where the sum runs over all nodes in the graph, d_i is the total degree of each node and d_{ii} are the false pairs that do not result in triplets.[23]

[23] M. E. J. Newman. Ego-centered networks and the ripple effect. *Social Networks*, 25:83–95, 2003

Closeness centrality

Closeness centrality (nodal): Inverse of the path length of a node.
In-closeness centrality (nodal, D): Inverse of the in-path length of a node.
Out-closeness centrality (nodal, D): Inverse of the out-path length of a node.
Methodological notes: See **path length** for the calculation of the path length.

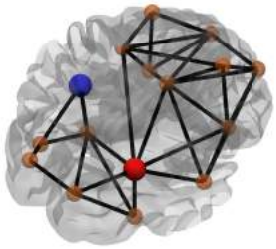


Figure 12: Betweeness centrality of a node. The red node has a high betweeness centrality (many shortest paths that connect the nodes from left to right pass through the red node), while the blue node has a low betweeness centrality (no shortest path passes through the blue node).

Betweenness centrality

Betweenness centrality (nodal): Fraction of all shortest paths in the graph that pass through a node. Nodes with high values of betweenness centrality participate in a large number of shortest paths.
Methodological notes: An algebraic method used to calculate the betweenness centrality is presented by Kintali.[24]

[24] S. Kintali. Betweenness centrality: Algorithms and lower bounds. *arXiv*, 0809.1906, 2008

Global efficiency

Global efficiency (nodal): Average of the inverse shortest path length from a node to all other nodes.[25]

[25] V. Latora and M. Marchiori. Efficient behavior of small-world networks. *Phys. Rev. Lett.*, 87:198701, 2001

Global efficiency (global): Average of the global efficiencies of all nodes.
In-global efficiency (nodal, D): Average of the inverse shortest in-path lengths of a node.
In-global efficiency (global, D): Average of the in-global efficiencies of all nodes.
Out-global efficiency (nodal, D): Average of the inverse shortest out-path lengths of a node.
Out-global efficiency (global, D): Average of the out-global efficiencies of all nodes.
Methodological notes: See **path length** for the calculation of the path length. After the path lengths from a node to all other nodes are calculated, they are inverted and the average gives the global efficiencies of the nodes. For D graphs, the global efficiencies of the nodes are the average of their in- and out-global efficiencies.

Local efficiency

Local efficiency (nodal): Global efficiency of a node calculated on the subgraph created by the node's neighbors.
Local efficiency (global): Average of the local efficiencies of all nodes.
Methodological notes: See **global efficiency** for the calculation of the global efficiency. The local efficiency is calculated by applying the same steps on the subgraph formed by the node's neighbors. In the case of W graph, the weighted connections of the neighbors of node i are calculated as $d_{jk}^{\text{subgraph}} = d_{jk}\sqrt{d_{ij}d_{ik}}$, where the nodes j and k are two neighbors of i, and d_{ij}, d_{ik} and d_{jk} are the weights of the edges.

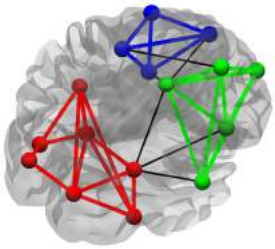


Figure 13: High modularity. This graph is composed by 3 clearly separated communities with a high number of within-module connections and a low number of between-module connections.

Modularity

Modularity (global): Extent to which a graph can be divided into clearly separated communities (i.e. subgraphs or modules). Its calculation requires a previously determined community structure.
Methodological notes: The modularity is calculated as

$$\frac{1}{l}\sum_{ij}\left[A_{ij} - \frac{k_i k_j}{l}\right]\delta_{ij}$$

where l is the number of edges in the graph, A_{ij} represents the connectivity matrix, k_i (k_j) is the degree of the node i (j), and δ_{ij} is 1 if the two nodes belong to the same community and 0 otherwise, while the sum is performed over all pairs of nodes in the graph.

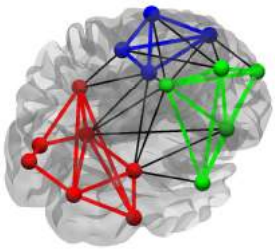


Figure 14: Low modularity. This graphs is the one shown in Figure 13 with some extra between-module connections. The graph can no longer be clearly separated into a collection of communities.

Within-module z-score

Within-module z-score (nodal): Extent to which a node is connected to the other nodes in the same community. It is a within-module version of degree. Its calculation requires a previously determined community structure.
Within-module in-z-score (nodal, D): Z-score calculated only by considering the contribution of in-path lengths.
Within-module out-z-score (nodal, D): Z-score calculated only by considering the contribution of out-path lengths.
Methodological notes: The z-Score is calculated as

$$Z_i = \frac{K_i - K_{S_i}}{\sigma_{S_i}}$$

where K_i is the degree of the node in the community S_i to which the node belongs, K_{S_i} is the average degree of all nodes in the community S_i, and σ_{S_i} is the standard deviation of the degree of the nodes within the community S_i.

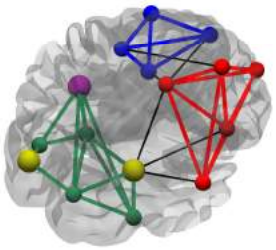


Figure 15: Within-module z-score of a node. A node can have low z-score because it has a low number of connections (leftmost yellow node) or because it has a lot of connections outside of the community to which it belongs (rightmost yellow node). Nodes with lots of connections within their community have high z-score (e.g. violet node).

Participation coefficient

Participation coefficient (nodal): Quantifies the relation between the number of edges connecting a node outside its community and its total number of edges. Its calculation requires a previously determined community structure.
Methodological notes: The participation coefficient can be calculated as

$$P_i = 1 - \sum_s \left(\frac{K_{S_i}}{K_i} \right)^2$$

where the sum runs over all communities, K_{S_i} is the number of edges connecting the node i within its community S_i, and K_i is the total number of edges of node i. Nodes with a high participation coefficient (known as connector hubs) are connected to many communities and are likely to facilitate global intermodular integration.

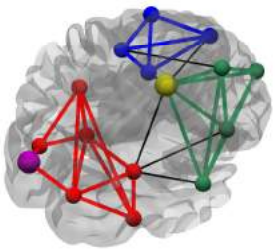


Figure 16: Participation coefficient of a node. A node has low participation coefficient if most of its connections are within its community (violet node). It has high participation coefficient if a lot of its connections are with nodes in different communities (yellow node).

Assortativity coefficient

Assortativity coefficient (global): The assortativity coefficient is a correlation coefficient between the degrees/strengths of all nodes on two opposite ends of an edge.[26]
Methodological notes: The assortativity is calculated as

$$r = \frac{l^{-1} \sum_{i,j \in L} k_i k_j - [l^{-1} \sum_{i,j \in L} \frac{1}{2}(k_i + k_j)]^2}{l^{-1} \sum_{i,j \in L} \frac{1}{2}(k_i^2 + k_j^2) - [l^{-1} \sum_{i,j \in L} \frac{1}{2}(k_i + k_j)]^2}$$

where k_i and k_j are the respective degrees of the nodes i and j, and l is the number of edges in the graph. The corresponding coefficient for directed and weighted networks is calculated by using the

[26] M. E. J. Newman. Assortative mixing in networks. *Phys. Rev. Lett.*, 89:208701, 2002

weighted and directed variants of degree/strength. A positive assortativity coefficient indicates that nodes tend to link to other nodes with similar degree/strength.

Small-worldness

Small-worldness (global): A small-world graph has a similar characteristic path length as a random graph with the same degree distribution but is significantly more clustered.[27]

Methodological notes: The small-worldness coefficient is calculated as

$$C_{\text{sw}} = \frac{C/C_{\text{rnd}}}{L/L_{\text{rnd}}}$$

where C and L are the clustering coefficient and characteristic path length of the graph, and C_{rnd} and L_{rnd} are the corresponding expected measures calculated on random graphs (typically averaging more than 100 random graphs). If $C_{\text{sw}} \gg 1$, then the network has a small-world organization.

[27] D. J. Watts and S. H. Strogatz. Collective dynamics of 'small-world' networks. *Nature*, 393:440–442, 1998; and M. D. Humphries and K. Gurney. Network 'small-world-ness': A quantitative method for determining canonical network equivalence. *PloS One*, 3:e0002051, 2008

Brain Atlas

GUIBrainAtlas is a graphical user interface that allows the user to create a custom brain atlas or import one from data files in xml, txt, or xls format. GUIBrainAtlas provides numerous options to visualize the brain atlas and to manipulate brain regions. The brain atlas can be saved in a file **.atlas* for future use within BRAPH; it can also be exported in txt or xml format for use within other applications.

The layout of GUIBrainAtlas is shown in figure 17. It is composed of four main work areas:

- **Menu** permits one to access the basic functionalities of GUIBrainAtlas, including loading, saving, editing, and visualizing a brain atlas, as well as creating a cohort for further analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading, saving, editing, and visualizing a brain atlas.
- **Table view** shows the brain regions and their properties in a table. Permits one to select, add, remove, move, and edit brain regions and their properties.
- **Brain view** visualizes the brain regions on a brain surface. Permits one to adjust the visualization parameters. The brain image can be exported as a MatLab figure.

Example data and a tutorial video can be found on `http://braph.org/manual/brain-atlas/`

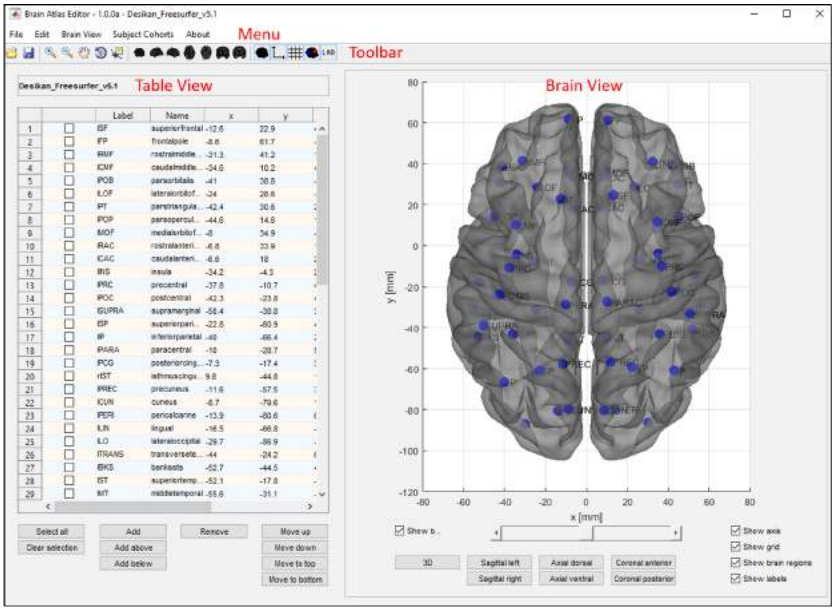


Figure 17: Screenshot of GUIBrainAtlas. On the top there are the menu and the toolbar; below there are a table view (on the left) and a brain view (on the right) of the brain regions.

Getting Started

As a first example of the use of GUIBrainAtlas, we will proceed to import the Desikan brain atlas[28] from the Excel file desikan_atlas.xlsx. We will then proceed to modify the atlas by adding a new brain region. Finally, we will save it as a **.atlas* file.

[28] R. S. Desikan, F. Ségonne, B. Fischl, B. T. Quinn, B. C. Dickerson, D. Blacker, R. L. Buckner, A. M. Dale, R. P. Maguire, B T Hyman, M. S. Albert, and R. J. Killianya. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*, 31:968–980, 2006

1. Select `File` → `Import (xls)` and select your file as shown in figure 18. After you select the file, the table and the brain surface are updated to show the brain atlas.

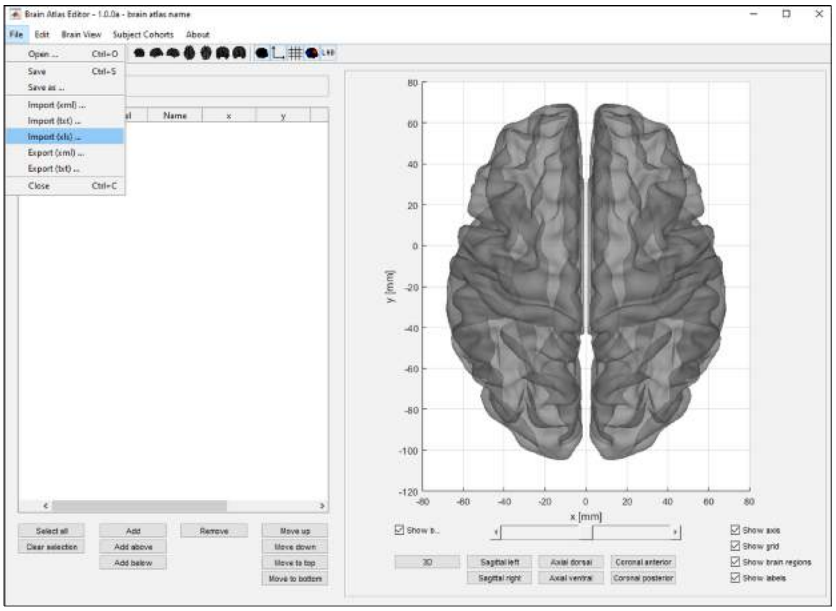


Figure 18: Importing a brain atlas saved as an Excel file into GUIBrainAtlas.

2. As shown in figure 19, a region can be selected by clicking on its checkbox on the left side of the table. A selected region appears red on the brain surface. Alternatively, right-click on the desired region on the brain surface and push `Select` on the popup menu; if a region is already selected, then `Deselect` appears on the popup menu.

3. Push `Add` at the bottom of the table to add a new brain region. A default region is added with label 'BR', name 'br name', and coordinates $(0, 0, 0)$ – see brain region 69 in figure 20. You can now edit these properties by clicking on them in the table. This new brain region has been added at the end of the table; to add it at a different position in the table, select a brain region and push `Add below` or `Add above`.

   A series of options is available to edit and modify the brain atlas.

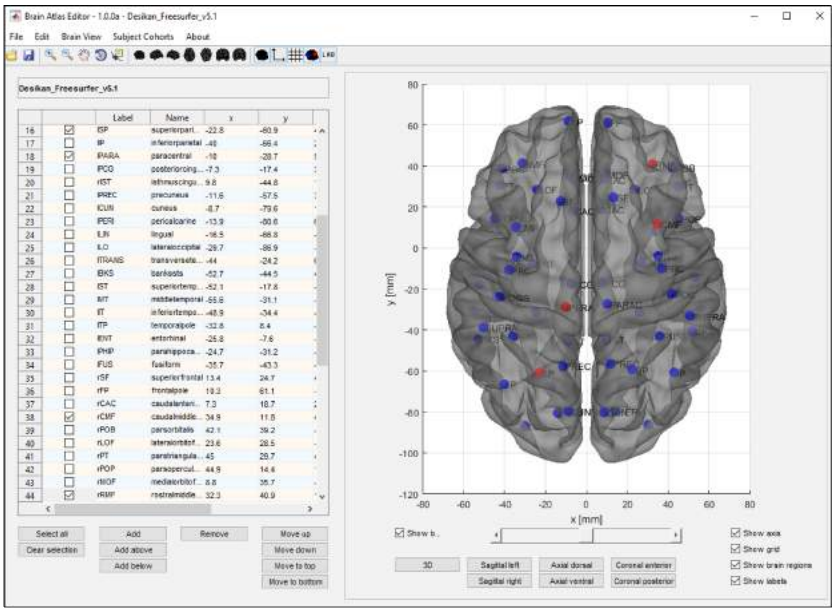


Figure 19: Brain regions can be selected by clicking on the corresponding checkbox or by right-clicking on the desired region on the brain surface. When selected, they appear red on the brain surface.

These are accessible both through the buttons at the bottom of the table and through the menu on the top of the interface. These are:

- `Select all` selects all the brain regions.
- `Clear selection` clears the current selection.
- `Add` adds a brain region at the end of the table.
- `Add above` adds brain regions above the selected ones.
- `Add below` adds brain regions below the selected ones.
- `Remove` removes the selected brain regions.
- `Move up` moves the selected brain regions up by one place.
- `Move down` moves the selected brain regions down by one place.
- `Move to top` moves the selected brain regions to the top of the table.
- `Move to bottom` moves the selected brain regions to the bottom of the table.

4. Push `3D` in the brain view to change the visualization of the brain atlas on the brain surface, as shown in figure 21. By selecting `Brain View` → `Generate figure`, the brain view can be exported as a MatLab figure; the same can be achieved with `Ctrl+F`.

5. Select `File` → `Save` to save the brain atlas as a **.atlas* file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.

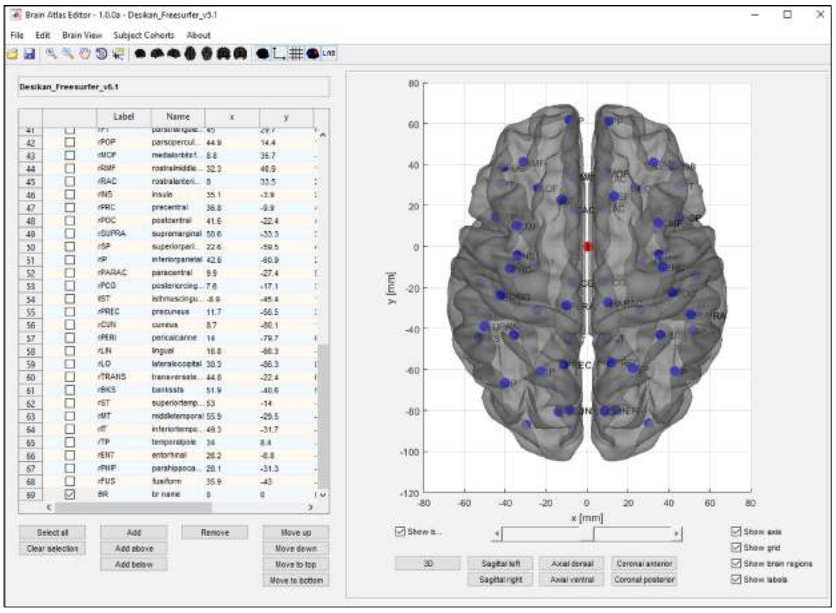


Figure 20: Adding a new brain region to a brain atlas.

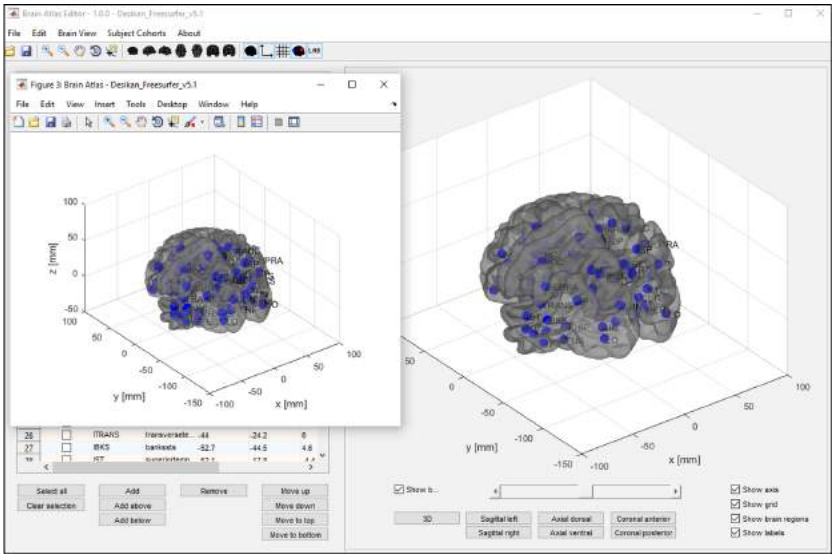


Figure 21: Changing visualization of the brain and exporting a 3D view of the brain to a MatLab figure.

6. Select `File` → `Open` to open a brain atlas previously saved with GUIBrainAtlas; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

File formats that can be imported

A brain atlas can be imported from Excel (**.xls* or **.xlsx*), text (**.txt*), or xml (**.xml*) files only if these files are in the correct format. For examples, see the files desikan_atlas.xlsx, desikan_atlas.txt, and desikan_atlas.xml.

In order to be imported correctly the Excel file should have the format shown in figure 22. It must include only one sheet. The first row must include the metainformation about the brain atlas, i.e. the atlas name (A1) and the atlas surface (B1). Each of the following rows (e.g. row 2) must contain the information relative to a brain region, including code (e.g. A2), name (e.g. B2), x-coordinate (e.g. C2), y-coordinate (e.g. D2), z-coordinate (e.g. E2), hemisphere ('left' or 'right', e.g. F2), and notes (e.g. G2). Importantly, the note column must contain some values (in our sample file we just added '.').

	A	B	C	D	E	F	G
1	Desikan_Freesurfer_v5.1	BrainMesh_ICBM152.nv					
2	ISF	superiorfrontal	-12.6	22.9	42.4	left	.
3	IFP	frontalpole	-8.6	61.7	-8.7	left	.
4	IRMF	rostralmiddlefrontal	-31.3	41.2	16.5	left	.
5	ICMF	caudalmiddlefrontal	-34.6	10.2	42.8	left	.
6	IPOB	parsorbitalis	-41	38.8	-11.1	left	.
7	ILOF	lateralorbitofrontal	-24	28.6	-14.4	left	.
8	IPT	parstriangularis	-42.4	30.6	2.3	left	.
9	IPOP	parsopercularis	-44.6	14.6	13.1	left	.
10	IMOF	medialorbitofrontal	-8	34.9	-14.9	left	.

Figure 22: Format of the Excel file containing a brain atlas required to be imported correctly.

The format for the text file is essentially the same, including a first row with the name and brain surface, and the following rows with the information about the brain regions (see desikan_atlas.txt).

The xml format is slightly more complex, but can be easily inferred from the sample file desikan_atlas.xml.

Brain view

The brain view permits one to visualize the brain regions on top of a brain surface based on the ICBM152 template.[29] The brain surface can be visualized in different ways by using the buttons below the brain view:

- `3D`
- `Sagittal left`
- `Sagittal right`
- `Axial dorsal`

[29] J. Mazziotta, A. W. Toga, A. Evans, P. Fox, and J. Lancaster. A probabilistic atlas of the human brain: theory and rationale for its development the international consortium for brain mapping (ICBM). *Neuroimage*, 2:89–101, 1995; and J. *et al.* Mazziotta. A probabilistic atlas and reference system for the human brain: International consortium for brain mapping (ICBM). *Phil. Trans. Royal Soc. London B: Biol. Sci.*, 356:1293–1322, 2001

- `Axial ventral`
- `Coronal anterior`
- `Coronal posterior`

The slider adjusts the transparency of the brain. The checkboxes are used to turn on and off the brain surface (`Show brain`), the axis (`Show axis`), the grid (`Show grid`), the brain regions (`Show brain regions`), and the labels (`Show labels`). To visualize the information about a brain region (i.e. label, name, position, hemisphere, and notes), right-click on it, and push `Info` on the popup menu.

Menu

`File` provides various options for importing and saving a brain atlas:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an atlas saved in **.atlas* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIBrainAtlas.
- `File` → `Save` (`Ctrl+S`) saves the current atlas in **.atlas* format.
- `File` → `Save as` opens a popup window to save the current atlas in **.atlas* format possibly in a different file.
- `File` → `Import (xml)` imports an atlas from an xml file.
- `File` → `Import (txt)` imports an atlas from a text file.
- `File` → `Import (xls)` imports an atlas from an Excel file.
- `File` → `Export (xml)` exports the current atlas to an xml file.
- `File` → `Export (txt)` exports the current atlas to a text file.

`Edit` provides various options to edit or change brain regions:

- `Edit` → `Select all` selects all the brain regions.
- `Edit` → `Clear selection` clears the current selection.
- `Edit` → `Add` (`Ctrl+A`) adds a brain region at the end of the table.
- `Edit` → `Add above` adds brain regions above the selected ones.
- `Edit` → `Add below` adds brain regions below the selected ones.
- `Edit` → `Remove` (`Ctrl+R`) removes the selected brain regions.

- `Edit` → `Move up` (`Ctrl+U`) moves selected brain regions up by one place.
- `Edit` → `Move down` (`Ctrl+D`) moves selected brain regions down by one place.
- `Edit` → `Move to top` (`Ctrl+T`) moves selected brain regions to the top of the table.
- `Edit` → `Move to bottom` (`Ctrl+B`) moves selected brain regions to the bottom of the table.

`Brain View` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`Subject Cohorts` provides a series of options to launch the cohort manager programs for various imaging modalities using the current brain atlas:

- `Subject Cohorts` → `MRI Cohort` launches GUIMRICohort.
- `Subject Cohorts` → `fMRI Cohort` launches GUIfMRICohort.
- `Subject Cohorts` → `PET Cohort` launches GUIPETCohort.
- `Subject Cohorts` → `EEG Cohort` launches GUIEEGCohort.

`About` → `About` provides information about the current version of GUIBrainAtlas and BRAPH.

Toolbar

The toolbar provides different options to open, save, and visualize the brain surface. It is shown in figure 23.

Figure 23: GUIBrainAtlas toolbar.

Open and save commands

These commands allow the user to open and save a brain atlas in the **.atlas* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an atlas saved in **.atlas* format.

 saves the current atlas in **.atlas* format.

Visualization commands

These commands allow the user to control the visualization of the brain view.

 zooms in brain view.

 zooms out brain view.

 drags brain view.

 rotates brain view

 shows/hides data cursor.

 standard 3D view.

 sagittal left view.

 sagittal right view.

 axial dorsal view.

 axial ventral view.

 coronal anterior view.

 coronal posterior view.

 switches brain surface on/off.

 switches axis on/off.

 switches grid on/off.

 switches brain regions on/off.

switches brain region labels on/off.

MRI Cohort

GUIMRICohort is a graphical user interface that allows the user to create an MRI cohort by adding individual subjects or by importing groups of subjects from data files in xls, txt, or xlm format. The user can also edit the data and anagraphic details of the subjects, as well as create groups of subjects. Furthermore, GUIMRICohort provides numerous options to visualize the data relative to individual subjects, groups, and comparisons between groups. The MRI cohort can be saved in a file **.mc* for future use within BRAPH; it also can be exported in xml format for use within other programs.

The layout of GUIMRICohort is shown in figure 24. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIMRICohort, including loading, saving, editing, and visualizing an MRI cohort, as well as creating a new MRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an MRI cohort, as well as visualizing the data corresponding to individual subjects, to groups, and to comparisons between groups.
- **Brain atlas panel** permits one to select a brain atlas for the MRI cohort or, if a brain atlas has already been selected, to view the brain atlas properties in GUIBrainAtlas.
- **Group panel** shows the subject groups and their properties in a table. Permits one to select, add, re-

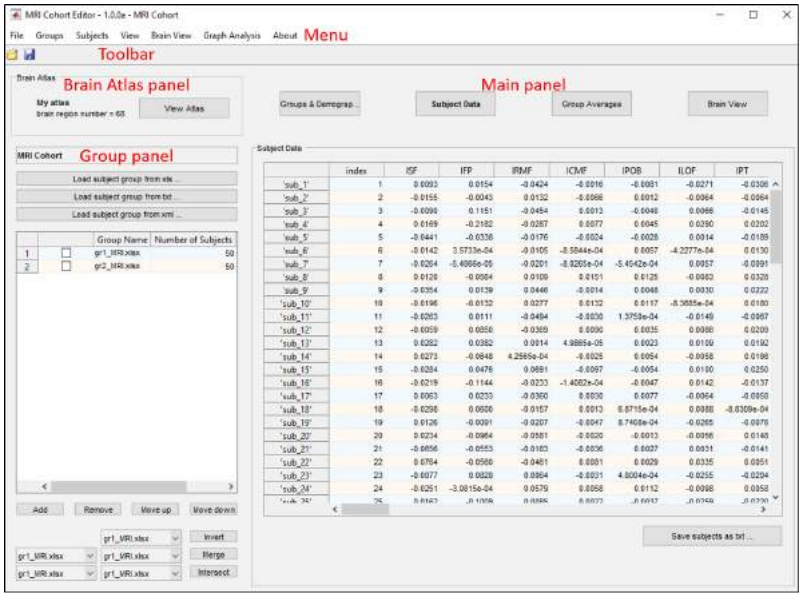


Figure 24: Screenshot of GUIMRICohort. On the top there are the menu and the toolbar; below there are a brain atlas panel (on the top left), a group panel (on the bottom left), and a main panel (right) in which subject data can be visualized.

move, move, and edit the existing groups, and to create new groups from the existing ones.

- **Main panel** consists of four tabs: `Groups & Demographics` to visualize the group data; `Subject Data` to edit the subjects' data; `Group Averages` to calculate the averages and standard deviations of the group data; and `Brain View` to visualize the data on a brain surface (this brain image can be exported as a MatLab figure).

  Example data and a tutorial video can be found on `http://braph.org/manual/mri/mri-cohort/`

Getting Started

As a first example of the use of GUIMRICohort, we will proceed to import the brain atlas my_atlas.atlas. Then, we will proceed to import two groups of subjects from the Excel files gr1_MRI.xlsx and gr2_MRI.xlsx, and to calculate a comparison between the data. Finally, we will save the MRI cohort in a **.mc* file.

1. Push `Select Atlas` to select a brain atlas as shown in figure 25. The atlas must be in **.atlas* format. After you select the file, the brain atlas panel is updated to show the properties of the atlas. The select button is changed to `View Atlas`; pushing this button opens the uploaded atlas in GUIBrainAtlas with restricted access (i.e. no further changes to the atlas are allowed).

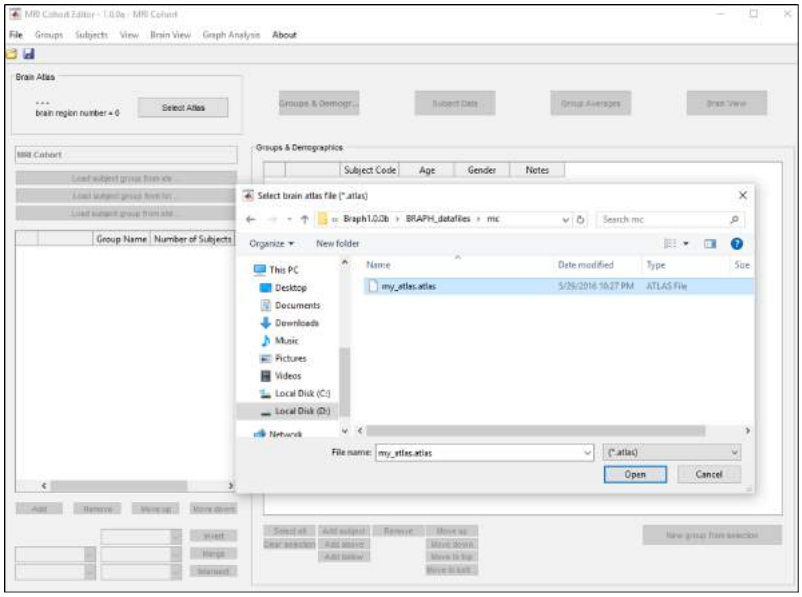


Figure 25: Importing a brain atlas from a **.atlas* file into GUIMRICohort.

2. Push `Load subject group from xls ...` to add a group from an xls file. Locate and choose the file gr1_MRI.xlsx. After the file is selected, the group panel is updated to show to group's properties: the group name (editable), the number of subjects, and the notes

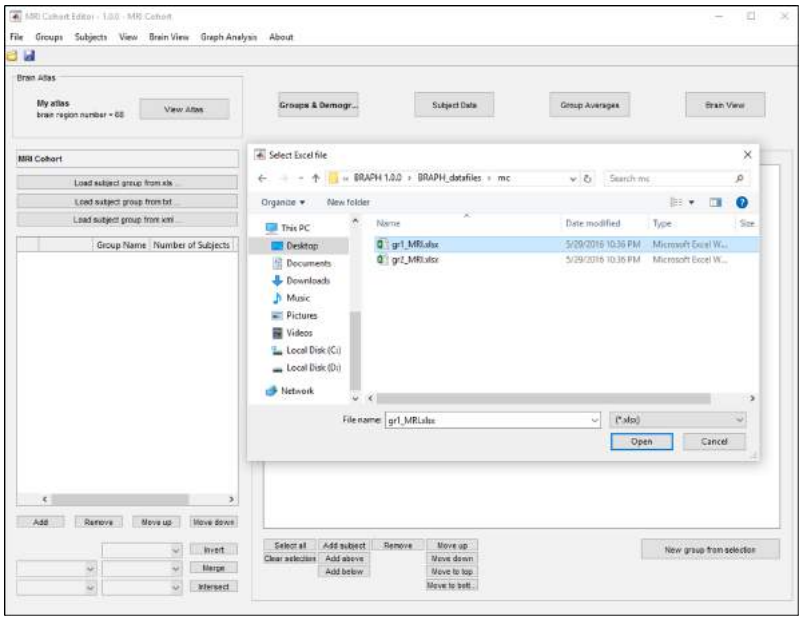


Figure 26: Importing a group of subjects from an xls file into GUIMRICohort.

(editable). The main panel is updated to show the subject data tab, as shown in figure 26.

A series of options are available to create new groups from the existing ones. They are accessible both through the buttons at the bottom of the group panel and through the menu. These are:

- `Add` adds new group at the bottom of the list.
- `Remove` removes the selected group.
- `Move up` moves the selected group up by one place.
- `Move down` moves the selected group down by one place.
- `Invert` creates a new group from the subjects not belonging to the group selected in the neighboring popup menu.
- `Merge` creates a new group by merging the subjects participating to the two groups currently selected in the neighboring popup menus.
- `Intersect` creates a new group by selecting the subjects participating to both groups selected in the neighboring popup menus.

3. Repeat step 2 selecting the file gr2_MRI.xlsx to import also this group of subjects. The main panel shows all subjects in the MRI cohort. If you select a group in the group panel, the main panel will show only the subject data corresponding to that group.

4. Push `Group Averages` in the main panel to visualize the average and standard deviation of the data corresponding to each

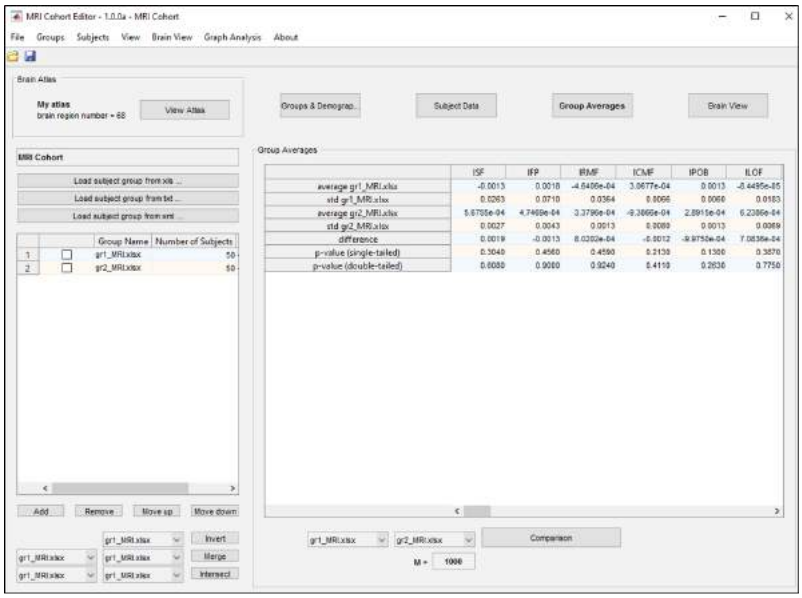


Figure 27: The group averages tab in the main panel shows the average and standard deviation for the data corresponding to each brain region for each group. Pushing `Comparison` also the differences between two groups can be visualized, together with their statistical significance calculated with a permutation test (in the screenshot 1000 permutations are used) in terms of single-tailed and double-tailed p-values.

brain region for each group. Choose two groups from the popup menus at the bottom of the main view and compare their data by pushing `Comparison` next to the popup menus. This performs a permutation test (the number of permutations can be entered in the neighboring edit box; the default number is 1000) that provides the significance of the difference by calculating single-tailed and double-tailed p-values. Figure 27 shows these values for the comparison between the groups gr1_MRI and gr2_MRI.

5. `Select File` → `Save` to save the MRI cohort as a **.mc* file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.

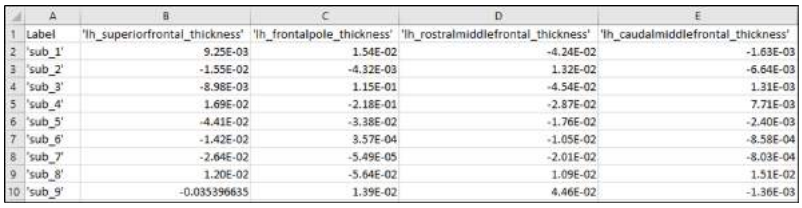
6. `Select File` → `Open` to open an MRI cohort previously saved with GUIMRICohort; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

File formats that can be imported

To create an MRI cohort, you need a brain atlas and the data corresponding to the groups of subjects. A brain atlas can be imported only if previously saved as a **.atlas* file (e.g. by using GUIBrainAtlas). Groups of subjects can be imported from Excel (**.xls* or **.xlsx*), text (**.txt*), or xml (**.xml*) files only if these files are in the correct format. For examples, see the files gr1_MRI.xlsx, gr1_MRI.txt, and gr1_MRI.xml.

In order to be imported correctly the Excel file should have the format shown in figure 28. It must include only one sheet. The first row must include the names of the brain regions consistent with the uploaded brain atlas starting from cell `B1`. Each of the following rows (e.g. row 2) must contain the IDs of a subject in the first cell (e.g. A2) and the numerical information for each brain region in the subsequent cells (e.g. B2, C2, D2, ...).



	A	B	C	D	E
1	Label	'lh_superiorfrontal_thickness'	'lh_frontalpole_thickness'	'lh_rostralmiddlefrontal_thickness'	'lh_caudalmiddlefrontal_thickness'
2	'sub_1'	9.25E-03	1.54E-02	-4.24E-02	-1.63E-03
3	'sub_2'	-1.55E-02	-4.32E-03	1.32E-02	-6.64E-03
4	'sub_3'	-8.98E-03	1.15E-01	-4.54E-02	1.31E-03
5	'sub_4'	1.69E-02	-2.18E-01	-2.87E-02	7.71E-03
6	'sub_5'	-4.41E-02	-3.38E-02	-1.76E-02	-2.40E-03
7	'sub_6'	-1.42E-02	3.57E-04	-1.05E-02	-8.58E-04
8	'sub_7'	-2.64E-02	-5.49E-05	-2.01E-02	-8.03E-04
9	'sub_8'	1.20E-02	-5.64E-02	1.09E-02	1.51E-02
10	'sub_9'	-0.035396635	1.39E-02	4.46E-02	-1.36E-03

Figure 28: Format required for the the Excel file containing the data of a group of subjects to be imported correctly.

The format for the text file is essentially the same, including a first column with the subjects' ID codes, first row with the names of the brain regions, and the following rows with the corresponding data about the brain regions (see gr1_MRI.txt).

The xml format is slightly more complex, but can be easily inferred from the sample file gr1_MRI.xml.

Main panel

The main panel permits one to explore the data of the subjects. There is a series of four console buttons at the top that can be used to switch between various tabs. The following information can be displayed:

- `Groups & Demographics` shows the profiles of the subjects (see figure 29). It is possible to change the age, gender, and notes of the subjects. The composition of the groups can be altered by checking the appropriate checkboxes corresponding to each group. The buttons at the bottom allow various options for the user to manipulate, remove, and add subjects:
  - `Select all` selects all the subjects.
  - `Clear selection` clears the current selection.
  - `Add subject` adds a subject at the end of the table.
  - `Add above` adds subjects above the selected ones.
  - `Add below` adds subjects below the selected ones.
  - `Remove` removes the selected subjects.
  - `Move up` moves the selected subjects up by one place.
  - `Move down` moves the selected subjects down by one place.

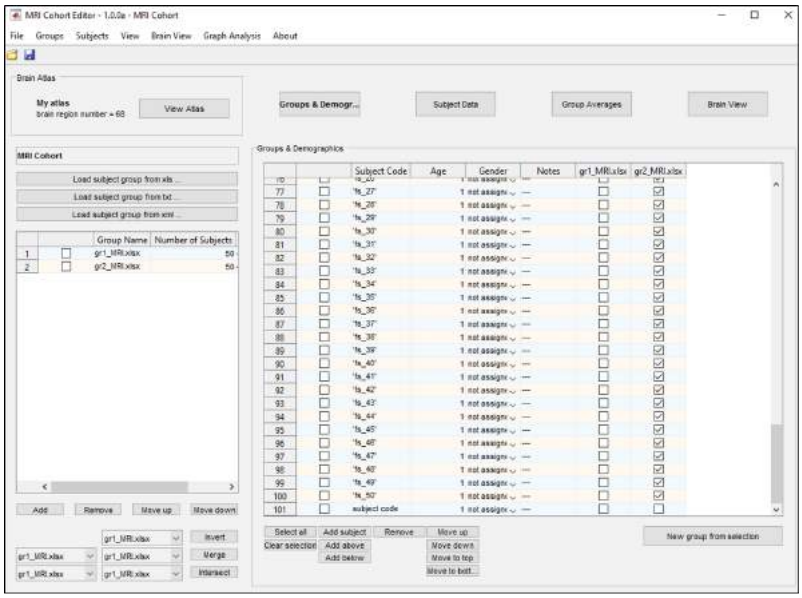


Figure 29: The groups & demographics tab of the main panel shows the profiles of the subjects. It permits one to alter the composition of the groups, to manipulate the demographic information regarding the subjects, to remove subjects, and to add new subjects.

  - `Move to top` moves the selected subjects to the top of the table.
  - `Move to bottom` moves the selected subjects to the bottom of the table.
  - `New group from selection` creates a new group from the selected subjects. Subjects can be selected by clicking the checkboxes next to them on the left side.

  When a new subject is added (see, e.g., subject 101 in figure 29), it is assigned some default code ('subject code'), age ('1'), gender ('not assigned'), and notes ('...'), it is not included in any group, and its data is set to zero for all brain regions. The subject properties can be edited by clicking on them in the table and subjects can be assigned to groups by clicking on the corresponding checkboxes.[30] This new subject has been added at the end of the table; to add it at a different position in the table, select a subject and push `Add below` or `Add above`.

- `Subject Data` shows the data for each subject in the cohort for each brain region in the brain atlas (figure 30). By default, the data are shown for all the subjects in the cohort. If a group is selected in the group panel, the data are shown only for the subjects belonging to the selected group. The header of the table shows the brain region labels, while the first column shows the subject codes. Each of the following rows contains the numerical information for each brain region of the corresponding subject. The numerical data can be edited by clicking on the desired field.

[30] The data corresponding to the brain region can be edited as explained below when discussing the subject data tab.

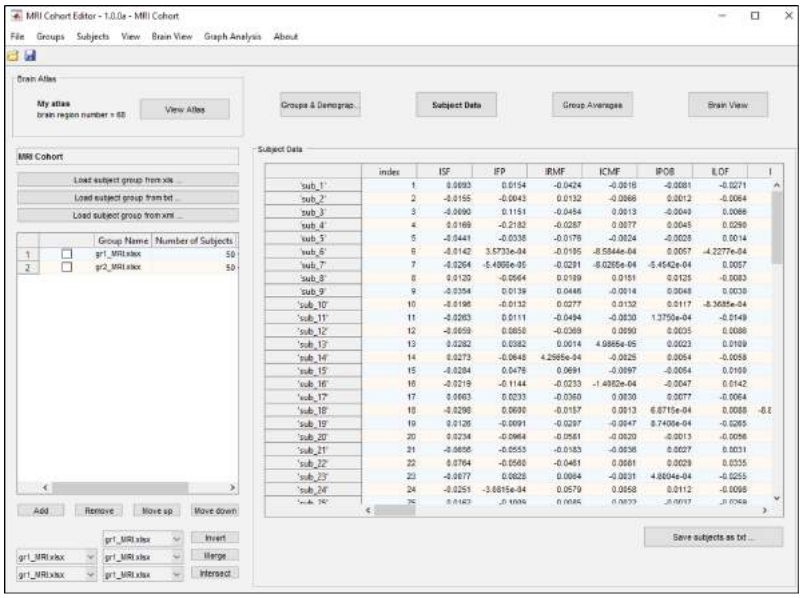


Figure 30: The subject data tab of the main panel shows a table containing the data corresponding to each subject and each brain region.

Subject IDs and brain region names are not editable.[31] The subjects and their data can be exported as a **.txt* file by pushing `Save subjects as txt ...`.

[31] They are editable in the groups & demographics tab.

- `Group Averages` shows the average and the standard deviation of all brain regions' data for each group (figure 31). A comparison can be performed between any two groups specified by the popup menus at the bottom by pushing `Comparison`. The significance of the differences between values are calculated by permutation test;

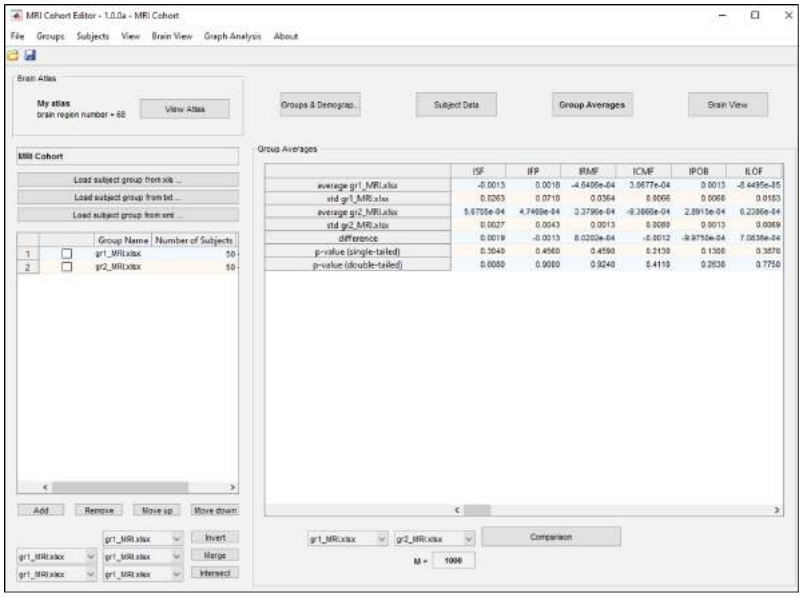


Figure 31: The group averages tab of the main panel shows the average and the standard deviation of the data of each group. It also permits one to compare two groups.

the number of permutations can be entered as the parameter M (by default $M = 1000$). After the calculation, the table is updated to show the differences between the values of the two groups as well as single-tailed and double-tailed p-values.

- `Brain View` visualizes the data on a brain surface (figures 32, 33, and 34). The user can visualize subject data, group data, or group comparisons on a brain surface by pushing one of the three buttons at the bottom. Each opens an interface that allows the user to specify the parameters to plot the data:
  - `View subjects` visualizes the data for each brain region at the level of single subjects. This opens a new interface shown in figure 32. The list on the left shows all the subjects in the cohort. The user can offset and rescale the data by entering the desired values in the corresponding field. Alternatively, the offset and rescale can be computed automatically to scale the data between 0 and 1 pushing `Automatic rescaling`. The negative data are substituted with their absolute values if the absolute value check box is checked, otherwise all negative values are set to zero.

    The value of the data can be plotted with various graphical conventions:

    * **Symbol size.**
    * **Symbol color.**
    * **Sphere radius.**
    * **Sphere color.**
    * **Sphere transparency.**
    * **Label size.**

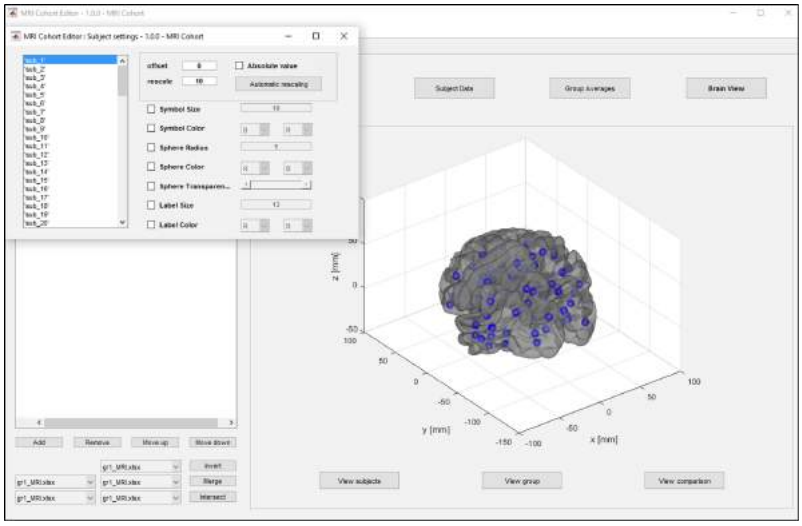


Figure 32: The brain view tab of the main panel shows subject data, group data, or group comparisons on a brain surface by pushing one of the three buttons at the bottom. For each option, an interface is provided allowing the user to specify the parameters for the plot. This snapshot correspond to the subject-level brain view.

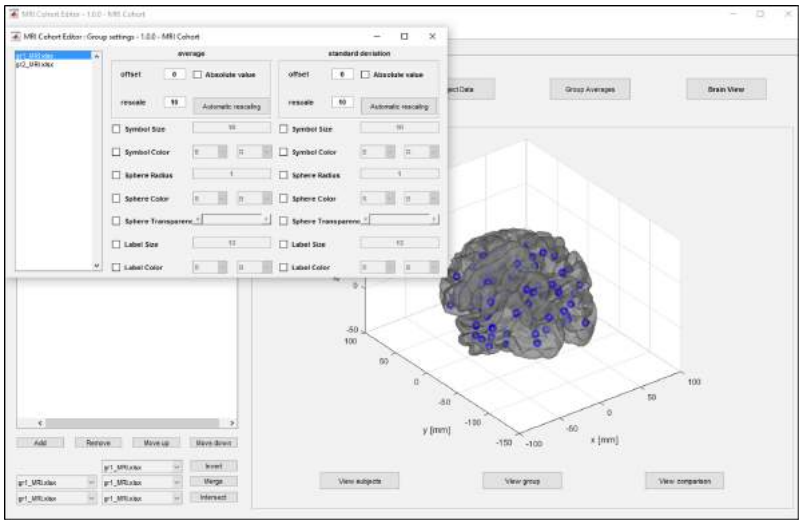


Figure 33: This snapshot correspond to the group-level brain view.

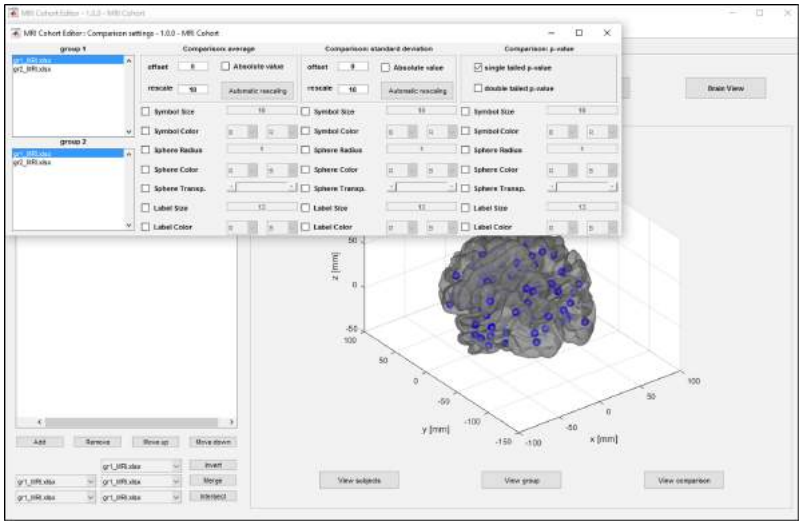


Figure 34: This snapshot correspond to the comparison brain view.

* **Label color.**

– `View group` visualizes the data for each brain region at the group level. This opens the new interface shown in figure 33. The list on the left shows all the groups in the cohort. The average and standard deviation of each group can be visualized according to the graphical conventions selected on the left and right columns, respectively. The graphical conventions and rescaling parameters can be chosen analogously to the ones detailed in the view subjects section.

– `View comparison` visualizes a comparison between two groups. The interface in this case is shown in figure 34. The groups are selected from the lists on the left.[32] The user can choose to view the difference between the average values and standard

[32] The order of the groups is that specified by the popup menus. Thus, the comparison between the groups gr1_MRI and gr2_MRI is not equivalent to comparison between gr2_MRI and gr1_MRI.

deviations of the two groups as well as the single-tailed or double-tailed p-values calculated by the permutation test. The graphical conventions and rescaling parameters can be chosen analogously to the ones detailed in the view subjects section.

By right-clicking on the brain surface, one has access to four popup menus where the parameters for visualization of the brain regions can be set:

- **Brain settings** (figure 35) permits one to set the parameters of the brain surface, including the edge color, face color, and transparency.
- **Brain region symbol settings** (figure 36) allows one to change the type, size, edge, and face color of the symbols representing the brain regions. Furthermore, brain regions can be set visible or hidden. The regions on which to apply the changes can be selected from the list that appears on the left-hand side of the menu.
- **Brain region sphere settings** (figure 37) allows one to change the radius, edge color, face color, and transparency of the spheres representing the brain regions. Also, brain regions can be set visible or hidden. The regions on which to apply the changes can be selected from the table at the left.
- **Brain region label settings** (figure 38) allows one to change the font, color, and interpreter for the labels representing the brain regions. Also, brain regions can be set visible or hidden. The regions on which to apply the changes can be selected from the table at the left.

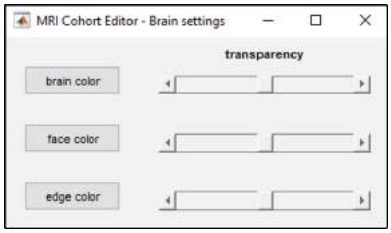


Figure 35: Brain settings.

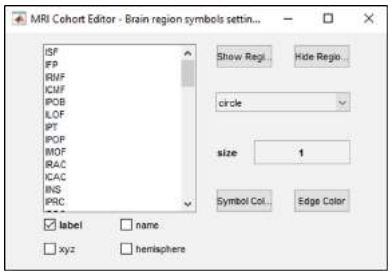


Figure 36: Brain region symbol settings.

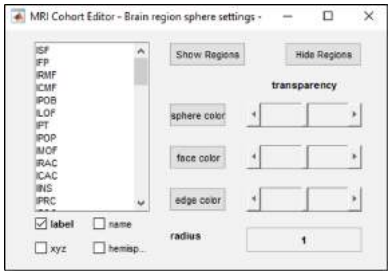


Figure 37: Brain region sphere settings.

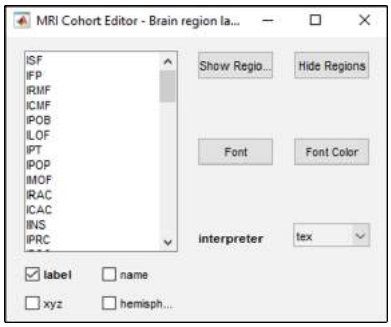


Figure 38: Brain region label settings.

Menu

`File` provides various options for importing and saving an MRI cohort:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an MRI cohort saved in **.mc* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIMRICohort.
- `File` → `Save` (`Ctrl+S`) saves the current MRI cohort in **.mc* format.
- `File` → `Save as` opens a popup window to save the current MRI cohort in **.mc* format possibly in a different file.
- `File` → `Import (xml)` imports an MRI cohort from an xml file.
- `File` → `Export (xml)` exports the current MRI cohort to an xml file.

`Groups` provides various options to edit subject groups:

- `Groups` → `Load subject group from xls ...` loads subject group from xls.
- `Groups` → `Load subject group from txt ...` loads subject group from txt.
- `Groups` → `Load subject group from xlm ...` loads subject group from xlm.
- `Groups` → `Add` adds a group at the end of the table.
- `Groups` → `Remove` removes the selected group.
- `Groups` → `Move up` moves the selected group up by one place.
- `Groups` → `Move down` moves the selected group down by one place.

`Subjects` provides various options to edit subjects:

- `Subjects` → `Select all` selects all the subjects.
- `Subjects` → `Clear selection` clears the current selection.
- `Subjects` → `Add subject` adds a subject at the end of the table.
- `Subjects` → `Add above` adds subjects above the selected ones.
- `Subjects` → `Add below` adds subjects below the selected ones.
- `Subjects` → `Remove` removes the selected subjects.
- `Subjects` → `Move up` moves selected subjects up by one place.
- `Subjects` → `Move down` moves selected subjects down by one place.
- `Subjects` → `Move to top` moves selected subjects to the top of the table.
- `Subjects` → `Move to bottom` moves selected subjects to the bottom of the table.

`View` switches the main view to display various types of information:

- `View` → `Groups & Demographics` shows group data and the profiles of the subjects.
- `View` → `Subject Data` shows the data for each subject in the cohort.
- `View` → `Group Averages` shows the average and the standard deviation for each group.

– `View` → `Brain View` visualizes the data on a brain surface.

`Brain View` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`Graph Analysis` → `New MRI graph analysis` launches GUIMRIGraphAnalysis, a graph analysis manager program, using the current cohort.

`About` → `About` provides information about the current version of GUIMRICohort and BRAPH.

Toolbar

The toolbar provides different options to open and save the MRI cohort and visualize the brain surface. It is shown in figure 39.

Figure 39: GUIMRICohort toolbar.

Open and save commands

These commands allow the user to open and save an MRI cohort in the **.mc* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an MRI cohort in **.mc* format.

 saves the current MRI cohort in **.mc* format.

Visualization commands

These commands allow the user to control the visualization of the brain view.

 zooms in brain view.

 zooms out brain view.

 drags brain view.

 rotates brain view

 shows/hides data cursor.

 standard 3D view.

 sagittal left view.

 sagittal right view.

 axial dorsal view.

 axial ventral view.

 coronal anterior view.

 coronal posterior view.

 switches brain surface on/off.

 switches axis on/off.

 switches grid on/off.

switches brain region symbols on/off.

switches brain region spheres on/off.

switches brain region labels on/off.

MRI Graph Analysis

GUIMRIGraphAnalysis is a graphical user interface that allows the user to define the parameters to create the connectivity matrices to analyze MRI data, while simultaneously visualizing the resulting weighted or binary matrices. Binary connectivity matrices can be visualized as a function of density or threshold. The user can also define a community structure and restrict the analysis to a subset of brain regions. A list of the measures available for calculation is shown at the bottom of the interface. The MRI graph analysis can be saved in a file **.mga* for future use within BRAPH; it also can be exported in xml format for use within other programs.

The layout of GUIMRICohort is shown in figure 40. It is composed of six main work areas:

- **Menu** permits one to access the basic functionalities of GUIMRIGraphAnalysis, including loading and saving an MRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an MRI graph analysis as well as manipulating the graphic representations of the connectivity matrices.
- **Cohort panel** permits one to select an MRI cohort for the graph analysis or, if already selected, to view the cohort properties in GUIMRICohort.
- **Graph analysis panel** permits one to choose the properties of the graph analysis, to set a community structure, and to choose whether to perform the analysis on a subgraph.

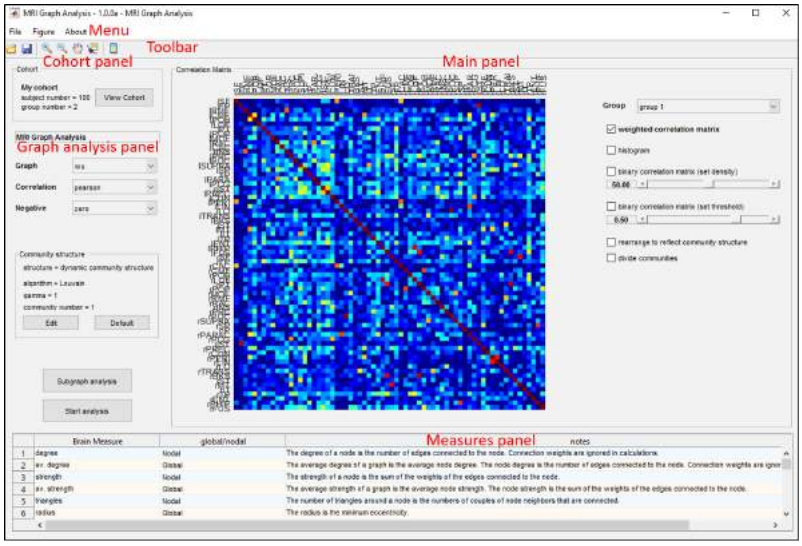


Figure 40: Screenshot of GUIMRIGraph-Analysis. On the top, there are the menu and the toolbar; in the middle there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right); on the bottom, there is the measures panel.

- **Main panel** visualizes the connectivity matrix that will be used for the analysis.
- **Measures panel** shows the available measures for each type of graph (binary or weighted).

Example data and tutorial videos can be found on `http://braph.org/manual/mri/mri-graph-analysis/`

Getting Started

As a first example of the use of GUIMRIGraphAnalysis, we will proceed to import the MRI cohort stored in the my_cohort.mc file. Then, we will define a binary undirected graph analysis with fixed density and positive Pearson correlation coefficients. We will further specify a dynamic community structure calculated with the Louvain algorithm by using the subject group gr1_MRI. Finally, we will choose to perform the analysis on the full connectivity matrix and save it as a **.mga* file.

1. Push `Select Cohort` to select an MRI cohort as shown in figure 41. The cohort must be in **.mc* format. After you select the file, the cohort panel is updated to show the properties of the cohort. The select button state is changed to `View Cohort`; pushing this button opens the uploaded cohort in GUIMRICohort with restricted access (i.e. no further changes to the cohort are allowed).

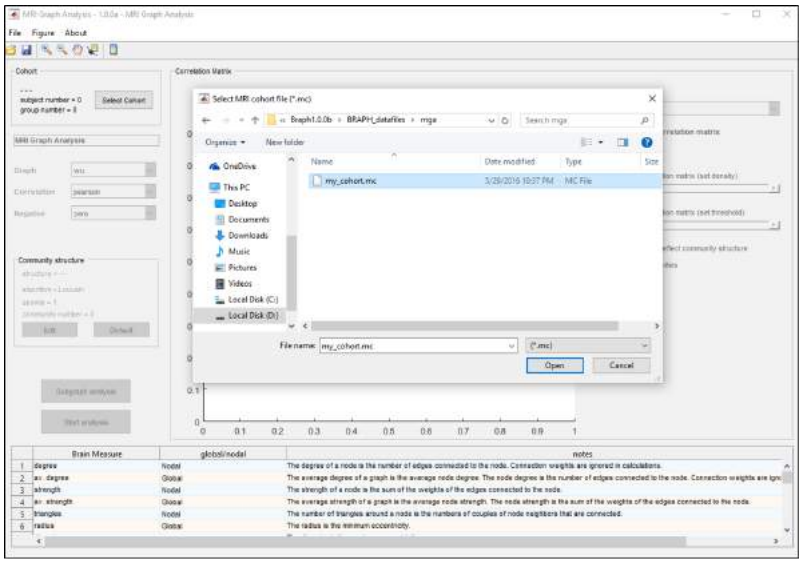


Figure 41: Importing an MRI cohort from a **.mc* file into GUIMRIGraphAnalysis.

2. Select `BUD` from the 'Graph' popup menu in the graph analysis panel, `Pearson` from the 'Correlation' popup menu, and `zero` from the 'Negative corrs.' popup menu. With these settings, the connectivity matrix will be calculated using Pearson correlation coefficients where all negative coefficient are set to zero; this matrix will then be binarized at a fixed density.

A number of settings are available to create different types of graph analyses. More details about how these options affect the graphs can be found in the chapter 'Brain Graphs'. These options are accessible through the popup menus in the graph analysis panel:

- **Graph** sets the type of graph to be analyzed:
  - `WU` analyzes weighted undirected graphs.
  - `BUT` analyzes binary undirected graphs, i.e. graphs whose connectivity matrices are binarized by specifying the threshold.
  - `BUD` analyzes binary undirected graphs, i.e. graphs whose connectivity matrices are binarized by specifying the density.
- **Correlation** sets the correlation used to calculate connectivity matrix coefficients:
  - `Pearson` is the Pearson correlation coefficient.
  - `Spearman` is the Spearman rank correlation coefficient.
  - `Kendall` is the Kendall rank correlation coefficient.
  - `partial Pearson` is the partial Pearson correlation coefficient.
  - `partial Spearman` is the partial Spearman correlation coefficient.
- **Negative corrs.** sets how to deal with the negative correlation coefficients:
  - `zero` sets all negative correlation coefficients to zero.
  - `none` leaves all negative correlation coefficients as as they are.[33]
  - `abs` replaces all negative correlation coefficients with their absolute values.

[33] Not all measures can be calculated in the presence of negative correlation coefficients.

3. Push `Edit` in the panel 'Community structure' to define a community structure. This opens a new interface where the parameters for the calculation of the community structure can be set. Check the `Dynamic structure` checkbox to define a dynamic structure, choose the Louvain algorithm and select the group group1 from the popup menu, as shown in figure 42.

   The community structure interface consists of five main working areas as shown in figure 42:

   - **Menu** permits one to generate the brain view of the community structure. This can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

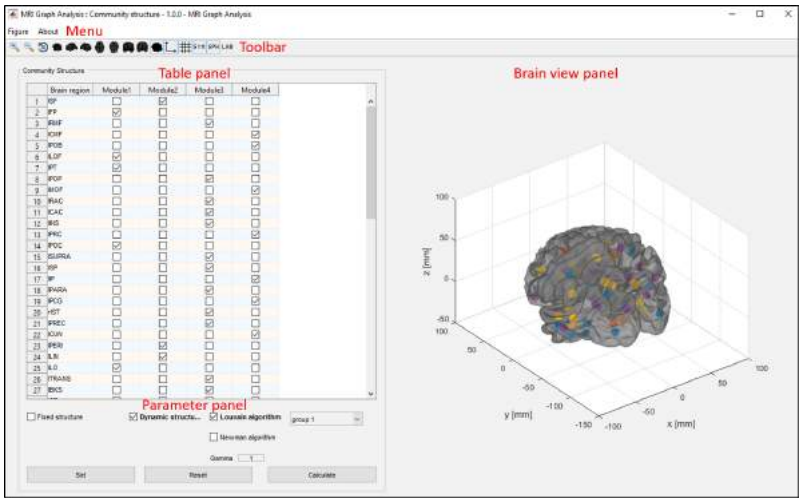


Figure 42: Interface to define a community structure for the graph analysis.

- **Toolbar** gives direct access to various brain views and allows the user to choose how to represent the brain regions (spheres, symbols, or labels).
- **Table panel** lists all brain regions and designates their participation to a particular module. By checking the corresponding checkbox, the brain regions can be assigned to different modules.
- **Brain view panel** visualizes the community structure on a brain surface. Different modules are represented with different colors.
- **Parameter panel** allows one to choose the parameters for the calculation of the community structure. The following parameters can be specified:
  - `Fixed structure` fixes the community structure. The same structure will be used throughout the analysis.
  - `Dynamic structure` creates a dynamic structure with the specified parameters. The structure will be recalculated with the selected parameters whenever needed throughout the analysis.
  - `Louvain algorithm` calculates the structure using the Louvain algorithm.
  - `Newman algorithm` calculates the structure using the Newman algorithm.
  - `Gamma` sets the parameter $\gamma > 0$ determining the resolution of the algorithm. The default setting is $\gamma = 1$. Larger values ($\gamma > 1$) lead to more modules and smaller values ($0 < \gamma < 1$) to less modules.
  - `Group` permits one to choose the group whose data serve as basis for the community structure calculation.

The structure is calculated by pushing `Calculate` and reset by pushing `Reset`. Once all parameters are choosen, the structure can be set by pushing `Set`.

Alternatively, one can choose to perform the graph analysis with the default community structure by pushing `Default`. The default structure is a dynamic structure calculated with the Louvain algorithm with $\gamma = 1$.

4. To start the graph analysis on the full connectivity matrix, push `Start analysis`. This opens a new interface, GUIMRIGraph-AnalysisBUD, which allows one to calculate and visualize the graph measures. The details of this interface are discussed in chapter 'MRI Graph Analysis BUD'. After this, the parameters of the analysis become fixed and, if any change is needed, a new graph analysis with different parameters should be created.

5. The analysis can be performed only on a subset of brain regions. To do this, push `Subgraph analysis`. This opens a new interface, shown in figure 43, with five main working areas:

   - **Menu** permits one to generate the subgraph brain view, which can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.
   - **Toolbar** gives direct access to various brain views and allows the user to choose how to represent the brain regions (spheres, symbols, or labels).
   - **Table panel** shows all brain regions. If the checkbox next to a brain region is checked, the region is included into the subgraph.

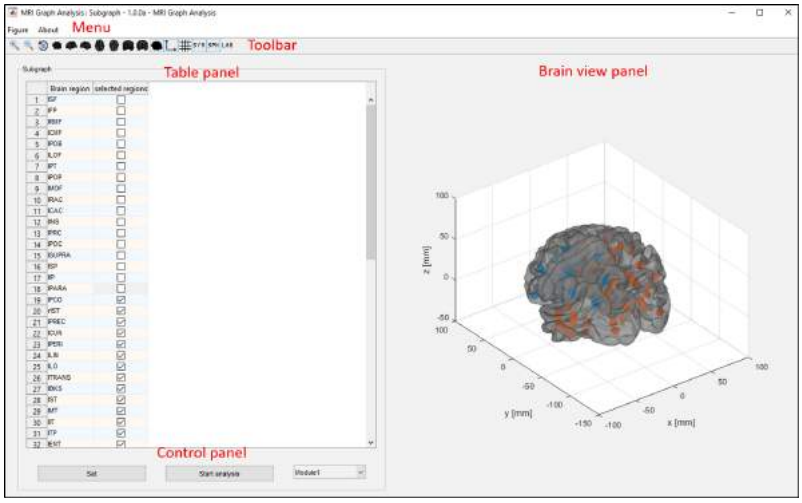


Figure 43: Interface to determine a subgraph on which to perform the graph analysis.

- **Brain view panel** permits one to visualize the subgraph on a brain surface. The included brain regions are highlighted with an orange color.
- **Control panel** allows one to choose the parameters for the calculation of the subgraph analysis as follows: (1) One of the modules from a previously calculated community structure can be selected as subgraph from the popup menu on the right. (2) `Set` sets the subgraph that will be used in the analysis. (3) `Start analysis` starts the analysis by opening a new interface, GUIMRIGraphAnalysisBUD. The analysis can be performed only after the subgraph has been set.

6. `Select File` → `Save` to save the MRI graph analysis as a **.mga* file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.

7. `Select File` → `Open` to open an MRI graph analysis previously saved with GUIMRIGraphAnalysis; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar. Opening a **.mga* file with with GUIMRIGraphAnalysis interface opens a new interface (i.e. GUIMRIGraphAnalysisWU, GUIMRIGraphAnalysisBUT, or GUIMRIGraphAnalysisBUD) depending on the type of analysis specified (weighted undirected, binary undirected fixed threshold, or binary undirected fixed density, respectively).

Additional information

Main panel

The main panel allows one to visualize the connectivity matrix based on the parameters specified by the set of checkboxes on the right (figure 40). The available options are:

- **Group** selects the group whose connectivity matrix to show.
- **Weighted correlation matrix**, if checked, visualizes the correlation coefficients between any two brain regions: warmer colors denote higher coefficients.
- **Histogram** shows the distribution of the correlation coefficients.
- **Binary correlation matrix (set density)** shows the binarized connectivity matrix at the set density (text field and slider below).
- **Binary correlation matrix (set threshold)** shows the binarized connectivity matrix at the set threshold (text field and slider below)

- **Rearrange to reflect community structure** rearranges the rows and columns of the connectivity matrix to reflect the community structures (i.e. keeping together regions belonging to the same module).
- **Divide communities** draws lines (squares around each module) to emphasize the division of the brain into different modules. This option is available only if the matrix has been previously rearranged to reflect the community structure by selecting the option **Rearrange to reflect community structure**.

Measures panel

The measures panel lists the measures (together with a short description) that are available for calculation given the kind of graph that has been selected (WU, BUT, BUD).

Menu

`File` provides various options for importing and saving an MRI graph analysis:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an MRI graph analysis saved in **.mga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIMRIGraphAnalysis.
- `File` → `Save` (`Ctrl+S`) saves the MRI current graph analysis in **.mga* format.
- `File` → `Save as` opens a popup window to save the current MRI graph analysis in **.mga* format possibly in a different file.
- `File` → `Import (xml)` imports an MRI graph analysis from an xml file.
- `File` → `Export (xml)` exports the current MRI graph analysis to an xml file.

`Brain View` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIMRIGraphAnalysis and BRAPH.

Toolbar

The toolbar provides different options to open and save the MRI graph analysis as well as to visualize the connectivity matrix. It is shown in figure 44.

Figure 44: GUIMRIGraphAnalysis toolbar.

Open and save commands

These commands allow the user to open and save an MRI graph analysis in the **.mga* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an MRI graph analysis saved in **.mga* format.

 saves the current MRI graph analysis in **.mga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations of the connectivity matrix.

 zooms in image.

 zooms out image.

 drags image.

 shows/hides data cursor.

 shows the colorbar.

MRI Graph Analysis WU

GUIMRIGraphAnalysisWU is a graphical user interface that allows the user to perform a brain graph analysis of MRI data using weighted undirected graph (WU = Weighted Undirected). The user can calculate group measures, compare them with random graphs, and compare the measures of two groups by permutation test. Significance intervals and single/double-tailed p-values are provided (the p-values can be corrected for false discovery rate (FDR) in the case of nodal measures). Global and nodal measures are displayed separately; for nodal measures the user has the option to visualize the results on a brain surface. The graph analysis can be saved in a file **.mga* for future use within BRAPH; it can also be exported in xml format for use within other programs.

The layout of GUIMRIGraphAnalysisWU is shown in figure 45. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIMRIGraphAnalysisWU, including loading and saving an MRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an MRI graph analysis.
- **Cohort panel** permits one to view the MRI cohort properties.
- **Graph analysis panel** permits one to choose which measures to calculate or compare, view the community structure, and, if needed, start a new graph analysis.

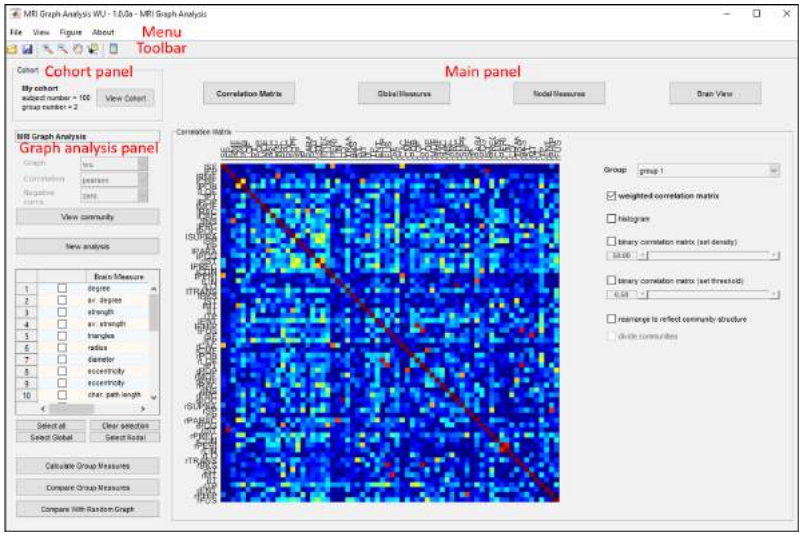


Figure 45: Snapshot of GUIMRIGraphAnalysisWU. On the top, there are the menu and the toolbar; below, there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right).

- **Main panel** allows one to view the connectivity matrix as well as the calculated global and nodal measures and comparisons.

Getting Started

As a first example of the use of GUIMRIGraphAnalysisWU, we will proceed to calculate some global (average strength, diameter) and local (strength, triangles) measures, and to compare the results for two groups. Then, we will visualize these results on the brain surface. Finally, we will save the graph analysis in a **.mga* file.

1. In the graph analysis view, select from the list of measures the average strength, diameter, strength, and triangles measures.

   To quickly select more than one measure, use the buttons below the measure list:

   - `Select all` selects all the measures.
   - `Clear selection` clears the current selection.
   - `Select Global` selects all global measures.
   - `Clear Nodal` selects all nodal measures.

2. Push `Calculate Group Measures` in the graph analysis panel (figure 45) to calculate the selected measures. This opens a new interface, shown in figure 46. On the left of the interface, there is a list with the selected measures to be calculated. On the right,

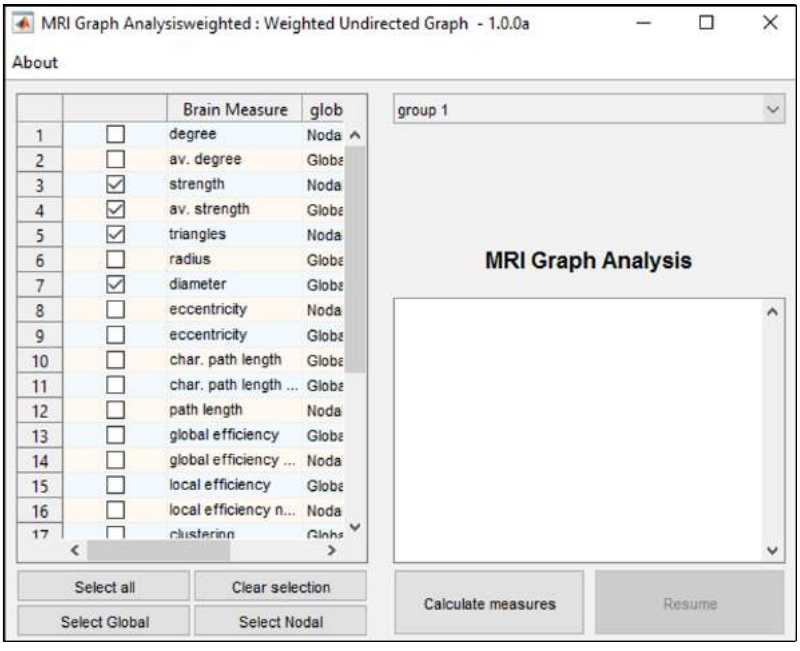


Figure 46: Interface to calculate group measures.

there is a popup menu to select the group for which the measures will be calculated. The calculation is started by pushing `Calculate measures`. When the calculation is in progress, the status of the button changes to `stop` and pushing it stops the calculation; the calculation can then be resumed by pressing `Resume`.

3. Push `Compare with Random Graph` in the graph analysis panel (figure 45) to calculate measures that are normalized by the results obtained from random graphs. This opens the interface shown in figure 47. This interface is analogous to that to calculate group measures, which we have seen in the previous step, but two new parameters can be inputted:

   - **random matrix no.** sets how many random graphs are used in the comparison.
   - **random swaps no.** sets how many times each edge is rewired to randomize the original graph.

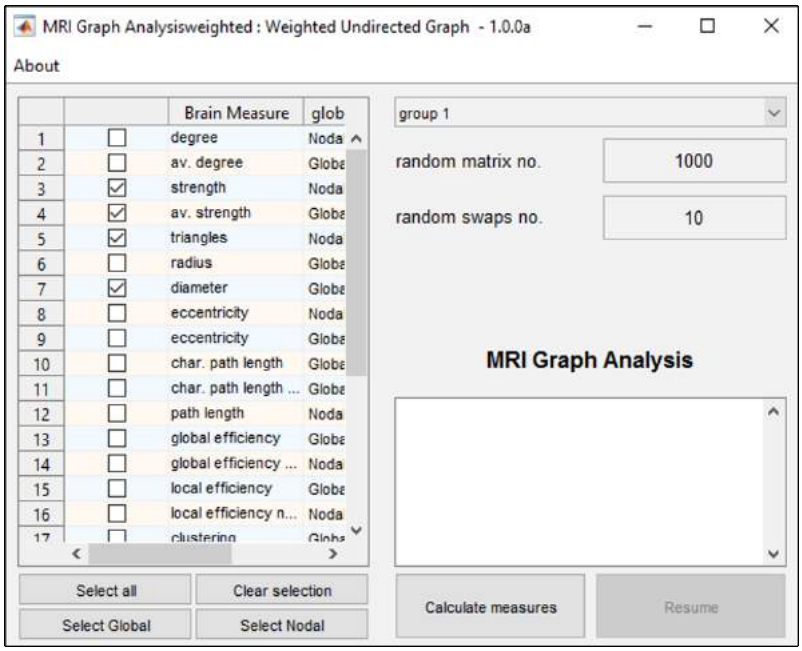


Figure 47: Interface to calculate group measures normalized by comparison with random graphs.

4. Push `Compare Group Measures` in the graph analysis panel (figure 45) to compare the measures between two groups. This opens the interface shown in figure 48. This interface is analogous to that to calculate group measures, but with two new parameters:

   - **permutation number** sets how many permutations are performed in the permutation test.

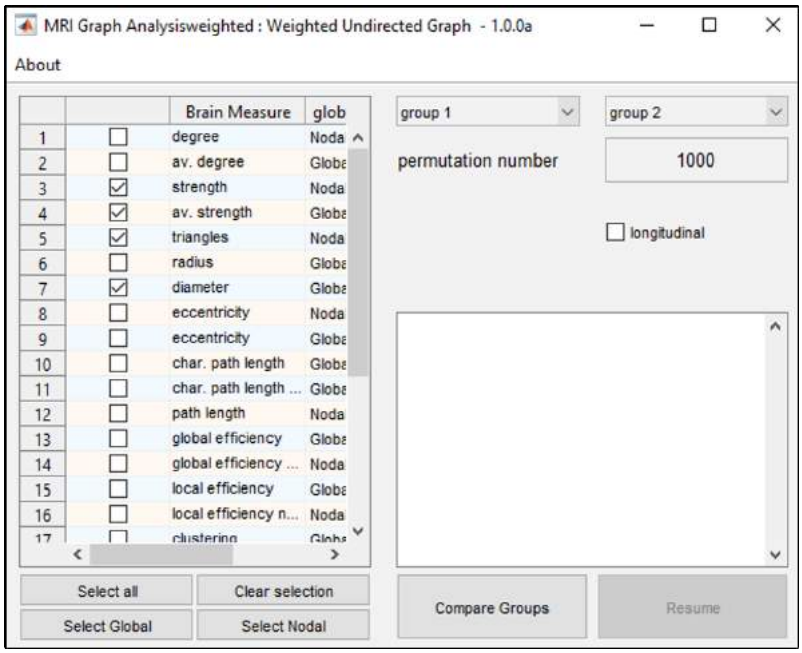


Figure 48: Interface to compare the measures of two groups.

- **longitudinal** sets whether the comparison is done for longitudinal data.

5. Push `Global Measures` in the main panel to visualize the results for the global measures (figure 49).

   If the **measure** checkbox is checked, group measures are displayed (the measure and the group are selected using the popup menus at

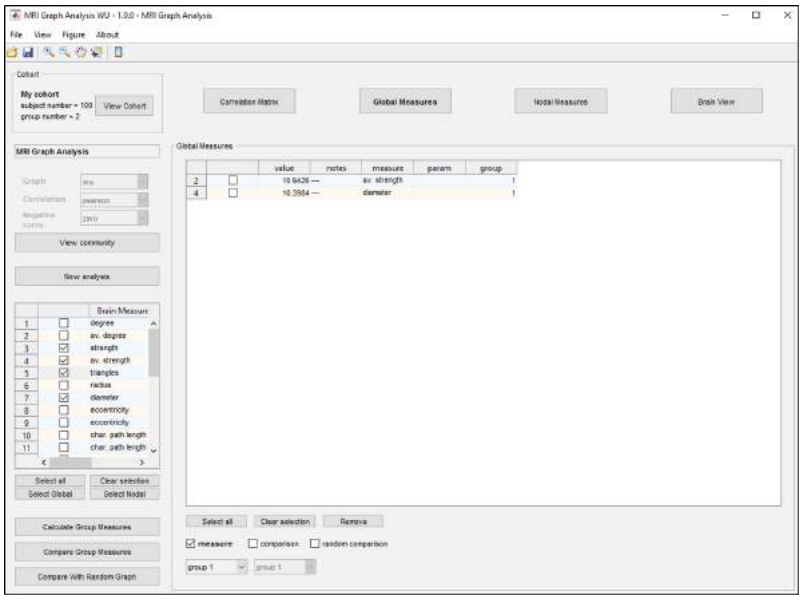


Figure 49: Global measures tab.

the bottom). If the **comparison** checkbox is checked, comparisons between two groups are displayed (the measure and the groups are selected using the popup menus at the bottom). If the **random comparison** checkbox is checked, measures normalized by comparison with random graphs are displayed (the measure and the group are selected using the popup menus at the bottom).

The main panel shows a **table view** that displays the numerical information about the selected measure. Among other data, this includes the value of the measure and the group for which it was calculated. If it is a comparison between groups or with random graphs, the difference between the values and the single/double-tailed p-values are also displayed. A series of options are available below the table view:

- `Select all` selects all the measures.
- `Clear selection` clears the current selection.
- `Remove` removes the selected measure.

6. Push `Nodal Measures` in the main panel to visualize the results for nodal measures (figure 50). This interface is very similar to that explained above for the global measures. The main difference is that now it is possible to select also the brain region.

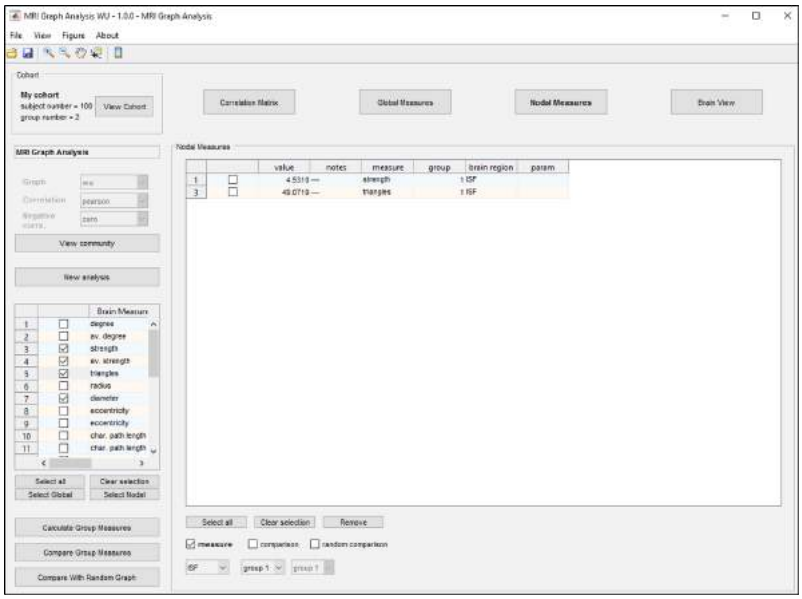


Figure 50: Nodal measures tab.

7. Push `Brain View` in the main panel to visualize the nodal measures on a brain surface. By pushing the buttons at the bottom of this panel, the user can visualize the brain graph, the group measures, the comparisons between two groups, and the comparisons with random graphs.

- `View brain graph` visualizes the brain graph, as shown in figure 51. The graph parameters that can be specified are:
  - **fix density** draws the binary brain graph with the selected density of connections. The density can be specified by entering the value in the corresponding field or by using the slider.
  - **fix threshold** draws the binary brain graph with all connections having larger weight than the given threshold. The threshold can be specified by entering the value in the corresponding field or by using the slider.
  - **weighted** plots all the connection of the weighted brain graph. The weight of the connections can be encoded by color and/or thickness (by checking the corresponding checkboxes).
  - `Show` shows the current graph on the brain surface.
  - `Hide` hides the current graph from the brain surface.
  - `Color` plots the current graph in the specified color.
  - **Set thickness** sets the thickness of the connections.

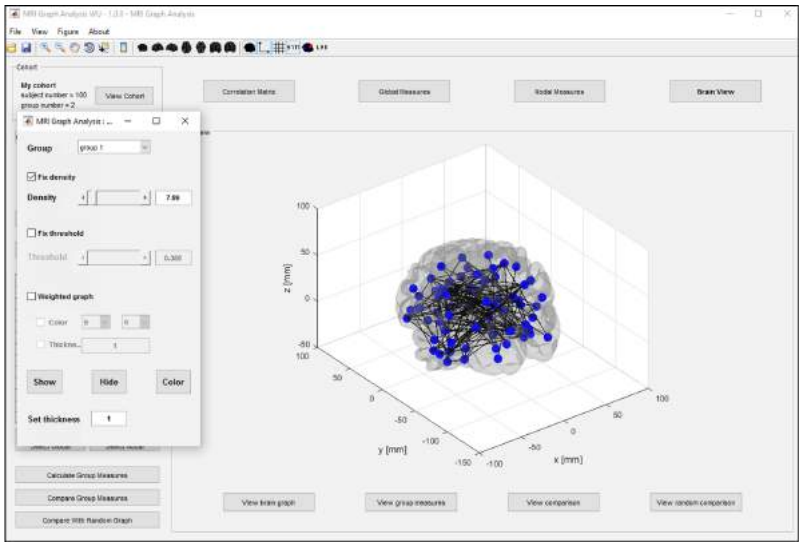


Figure 51: Visualization of the brain graph on the brain surface.

- `View group measures` visualizes the nodal measures calculated for a given group, as shown in figure 52.[34] The group for which the measures are to be shown is selected from the popup menu in the top left. The list on the left shows the measures that have been calculated.
- `View comparison` visualizes the measures comparison between two groups, as shown in figure 53. The two popup menus on the left specify the two groups that are compared and the list

[34] For more information about the rescaling and the filters needed to be applied to visualize the data, refer to the *Main panel* subsection in the chapter MRI Cohort.

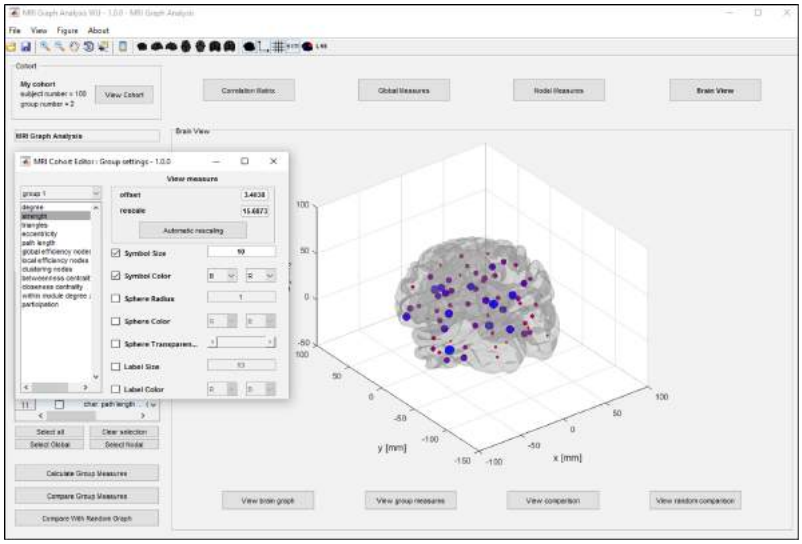


Figure 52: Visualization of the nodal measures on the brain surface.

below them show the measures for which they have been calculated. The other functionalities are analogous to the interface for viewing group measures with two new options:

- **fdr (1-tailed)**, if checked, corrects the p-values for single-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.
- **fdr (2-tailed)**, if checked, corrects the p-values for double-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.

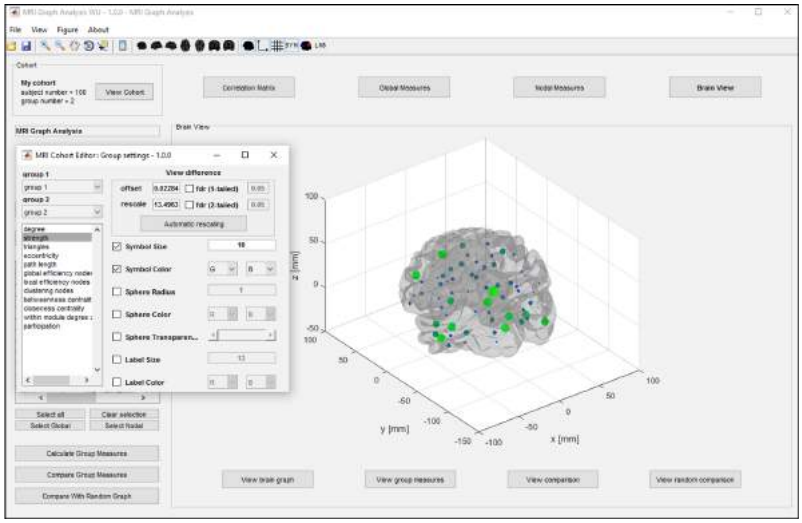


Figure 53: Visualization of the comparison between two groups on the brain surface.

- `View random comparison` visualizes the measures normalized by comparing them with random graphs, as shown in figure 54. All the functionalities of this interface are analogous to those of

the interface to visualize a comparison between groups.

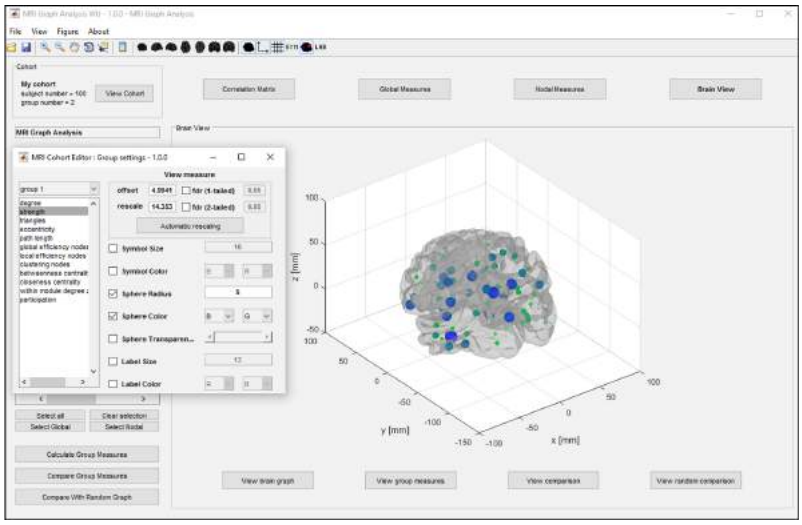


Figure 54: Visualization of the measures normalized by random comparison on the brain surface.

- `Select File` → `Save` to save the MRI graph analysis WU as a *.mga file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.
- `Select File` → `Open` to open an MRI graph analysis WU previously saved with GUIMRIGraphAnalysisWU; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

Cohort panel

The cohort is already uploaded when GUIMRIGraphAnalysisWU is launched. The cohort view shows the cohort's properties including name, number of subjects, and groups. Moreover, all cohort's properties can be viewed in the GUIMRICohort interface with restricted access by pushing `View Cohort`.

Graph analysis panel

The graph analysis panel shows the information relative to the graph analysis and gives the user the ability to calculate measures. The available features are:

- **Graph analysis properties**. These three popup menus show the properties of the graph analysis: graph type, correlation type, and how to deal with negative correlations. As all these properties were set in GUIMRIGraphAnalysis, here all the popup menus are disabled and the properties cannot be changed. If the user wishes

to change any of the properties, a new graph analysis should be started.

- `View community` opens the interface to view the community structure that is set. Also the community structure cannot be changed.

- `New analysis` opens a new GUIMRIGraphAnalysis interface where a new graph analysis with different parameters can be launched.

- **Measure list** lists all measures available for calculation for weighted graphs. The user can choose which measure to calculate by checking the checkboxes next to them.

- `Calculate Group Measures` opens an interface allowing the user to set parameters to calculate the selected measures.

- `Compare Group Measures` opens an interface allowing the user to set parameters to compare the selected measures between two groups.

- `Compare With Random Graphs` opens an interface allowing the user to set parameters to compare the selected measures with random graphs.

Main panel

The main panel consists of a main table that displays different information about the graph analysis and the calculated measures. The console buttons are used to switch between the various types of information shown in the table. The following information can be displayed:

- `Correlation Matrix` visualizes the connectivity matrix based on the parameters set on the right. For more detailed information about how to visualize the connectivity matrix please refer to the section *Main view* of the chapter MRI Graph Analysis.

- `Global Measures` allows the user to visualize global measures.

- `Nodal Measures` allows the user to visualize nodal measures.

- `Brain View` allows the user to visualize the brain graph and the calculated nodal measures on a brain surface.

Menu

`File` provides various options for importing and saving an MRI graph analysis WU:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an MRI graph analysis WU saved in **.mga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIMRIGraphAnalysisWU.
- `File` → `Save` (`Ctrl+S`) saves the current MRI graph analysis WU in **.mga* format.
- `File` → `Save as` opens a popup window to save the current MRI graph analysis WU in **.mga* format possibly in a different file.
- `File` → `Import (xml)` imports an MRI graph analysis WU from an xml file.
- `File` → `Export (xml)` exports the current MRI graph analysis WU to an xml file.

`View` switches the main view to display various types of information:

- `View` → `Correlation Matrix` visualizes the connectivity matrix.
- `View` → `Global Measures` visualizes global measures.
- `View` → `Nodal Measures` visualizes nodal measures.
- `View` → `Brain View` visualizes the data on a brain surface.

`Figure` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIMRIGraphAnalysisWU and BRAPH.

Toolbar

The toolbar provides different options to open and save the MRI graph analysis WU and visualize the figures. It is shown in figure 55.

Figure 55: MRIGraphAnalysisWU toolbar.

Open and save commands

These commands allow the user to open and save an MRI graph analysis WU in the **.mga* format. These are equivalent to the open and save menu options in the `File` menu.

opens a popup window to load an MRI graph analysis WU saved in **.mga* format.

saves the current MRI graph analysis WU in **.mga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations.

zooms in image.

zooms out image.

drags image.

shows/hides data cursor.

shows color scale.

standard 3D view.

sagittal left view.

sagittal right view.

axial dorsal view.

axial ventral view.

coronal anterior view.

coronal posterior view.

switches brain surface on/off.

switches axis on/off.

switches grid on/off.

SYM switches brain region symbols on/off.

`SPH` switches brain region spheres on/off.

`LAB` switches brain region labels on/off.

MRI Graph Analysis BUT

GUIMRIGraphAnalysisBUT is a graphical user interface that allows the user to perform a brain graph analysis of MRI data using binary undirected graphs at a fixed threshold (BUT = Binary Undirected Threshold). The user can calculate group measures, compare them with random graphs, and compare the measures of two groups by permutation test. Significance intervals and single/double-tailed p-values are provided (the p-values can be corrected for false discovery rate (FDR) in the case of nodal measures). Global and nodal measures are displayed separately; for nodal measures the user has the option to visualize the results on a brain surface. The graph analysis can be saved in a file **.mga* for future use within BRAPH; it can also be exported in xml format for use within other programs.

The layout of GUIMRIGraphAnalysisBUT is shown in figure 56. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIMRIGraphAnalysisBUT, including loading and saving an MRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an MRI graph analysis.
- **Cohort panel** permits one to view the MRI cohort properties.
- **Graph analysis panel** permits one to choose which measures to calculate or compare, view the community structure, and, if needed, start a new graph analysis.

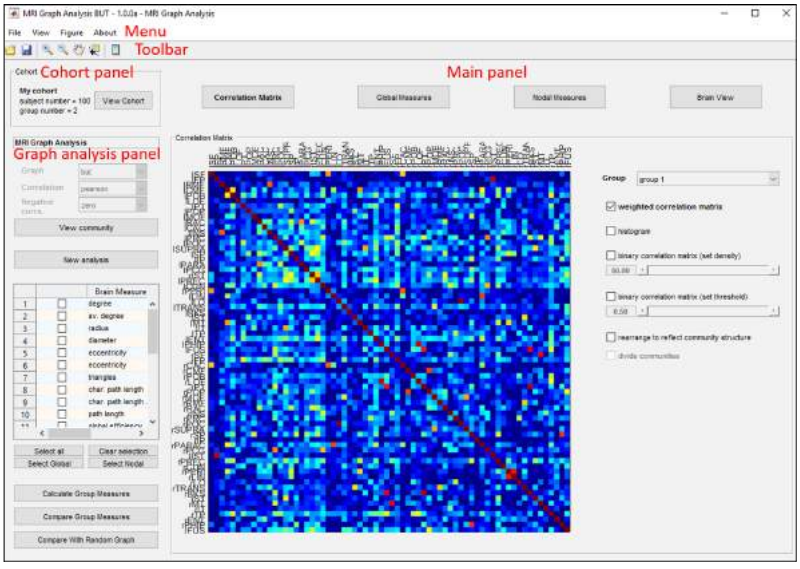


Figure 56: Snapshot of GUIMRIGraphAnalysisBUT. On the top, there are the menu and the toolbar; below, there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right).

- **Main panel** allows one to view the connectivity matrix as well as the calculated global and nodal measures and comparisons.

Getting Started

As a first example of the use of GUIMRIGraphAnalysisBUT, we will proceed to calculate some global (average degree, diameter) and local (degree, triangles) measures, and to compare the results for two groups. Then, we will visualize these results and the graph on the brain surface. Finally, we will save the graph analysis in a **.mga* file.

1. In the graph analysis view, select from the list of measures the average degree, diameter, degree, and triangles measures.

   To quickly select more than one measure, use the buttons below the measure list:

   - `Select all` selects all the measures.
   - `Clear selection` clears the current selection.
   - `Select Global` selects all global measures.
   - `Clear Nodal` selects all nodal measures.

2. Push `Calculate Group Measures` in the graph analysis panel (figure 56) to calculate the selected measures. This opens a new interface, shown in figure 57. On the left of the interface, there is a list with the selected measures to be calculated. On the right, there

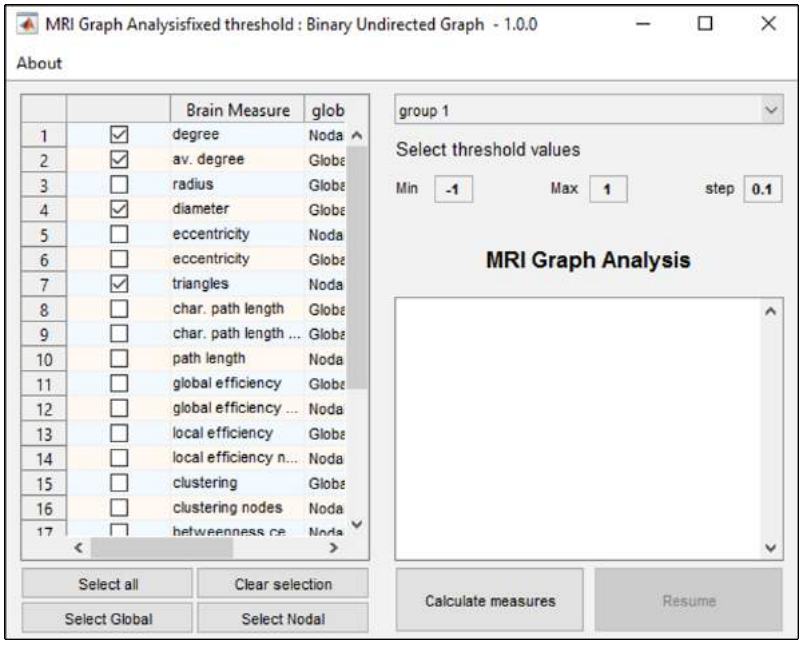


Figure 57: Interface to calculate group measures.

are a popup menu to select the group for which the measures will be calculated and a series of fields to enter the threshold values (including the minimum threshold, the maximum threshold, and the threshold step). The calculation is started by pushing `Calculate measures`. When the calculation is in progress, the status of the button changes to `stop` and pushing it stops the calculation; the calculation can then be resumed by pressing `Resume`.

3. Push `Compare with Random Graph` in the graph analysis panel (figure 56) to calculate measures that are normalized by the results obtained from random graphs. This opens the interface shown in figure 58. This interface is analogous to that to calculate group measures, which we have seen in the previous step, but two new parameters can be inputted:

   - **random matrix no.** sets how many random graphs are used in the comparison.
   - **random swaps no.** sets how many times each edge is rewired to randomize the original graph.

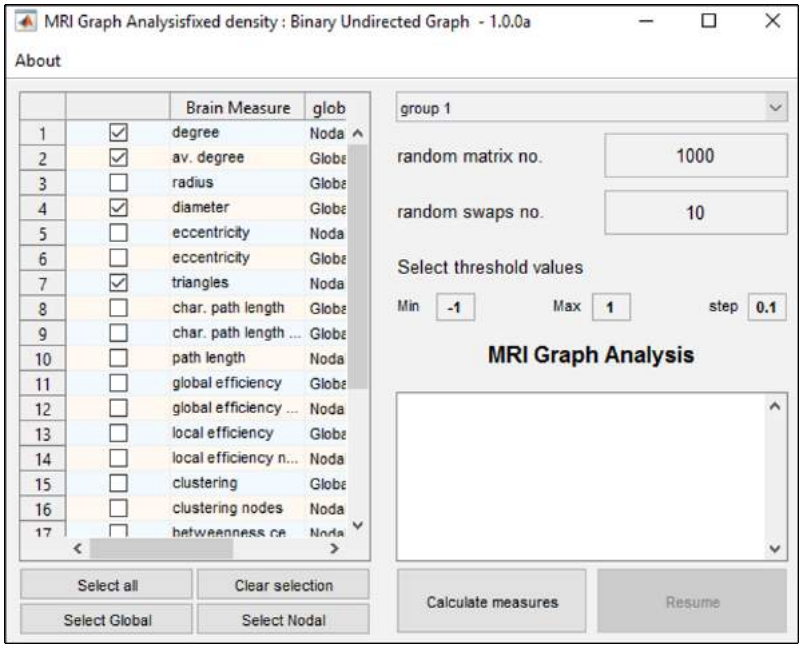


Figure 58: Interface to calculate group measures normalized by comparison with random graphs.

4. Push `Compare Group Measures` in the graph analysis panel (figure 56) to compare the measures between two groups. This opens the interface shown in figure 59. This interface is analogous to that to calculate group measures, but with two new parameters:

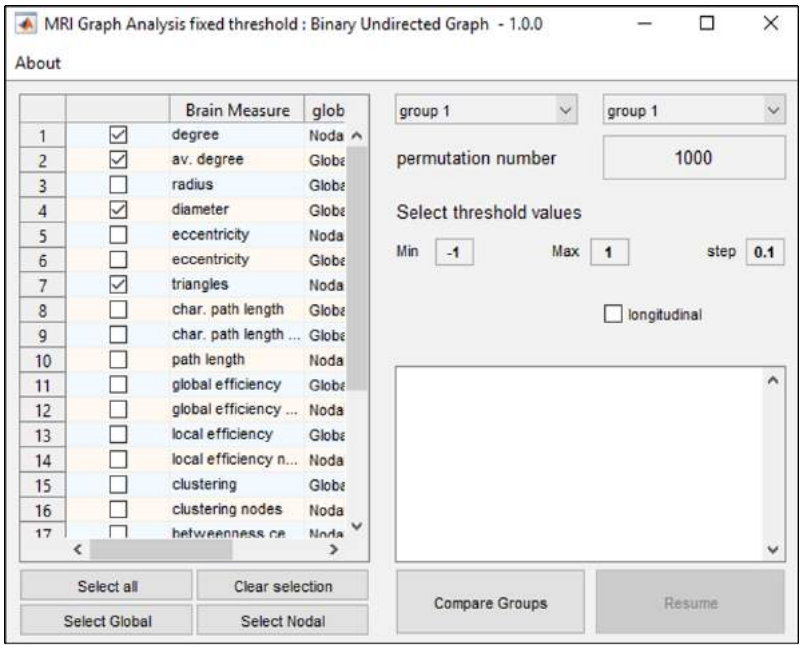


Figure 59: Interface to compare the measures of two groups.

- **permutation number** sets how many permutations are performed in the permutation test.
- **longitudinal** sets whether the comparison is done for longitudinal data.

5. Push `Global Measures` in the main panel to visualize the results for the global measures (figure 60).

   If the **measure** checkbox is checked, group measures are displayed

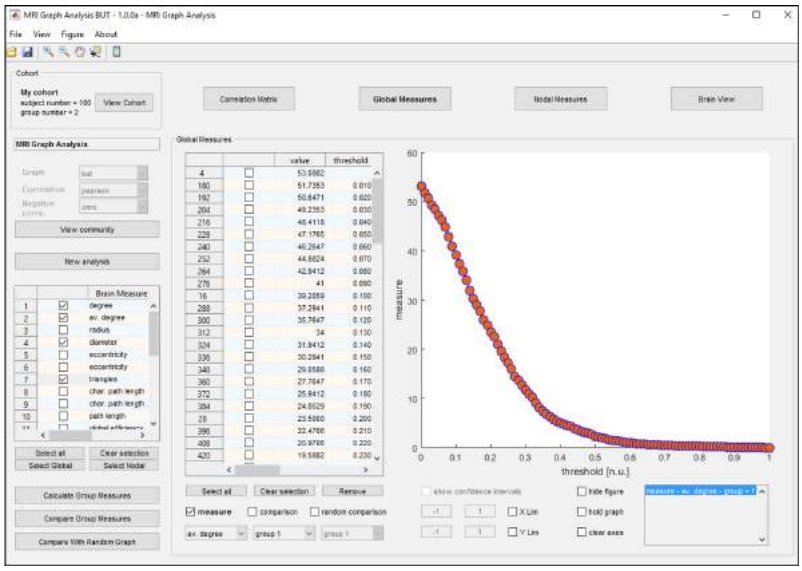


Figure 60: Global measures tab. Here the average degree is shown as a function of the threshold.

(the measure and the group are selected using the popup menus at the bottom). If the **comparison** checkbox is checked, comparisons between two groups are displayed (the measure and the groups are selected using the popup menus at the bottom). If the **random comparison** checkbox is checked, measures normalized by comparison with random graphs are displayed (the measure and the group are selected using the popup menus at the bottom).

The main panel now shows two parts:

(a) A **table view** on the left shows the numerical information about the selected measure. Among other data, this includes the value of the measure, the group for which it was calculated, and the density and threshold of the graph on which it was calculated. If it is a comparison between groups or with random graphs, the difference between the values and the single/double-tailed p-values are also displayed. A series of options are available below the table view:

- `Select all` selects all the measures.
- `Clear selection` clears the current selection.
- `Remove` removes the selected measure.

(b) A **graph view** plots a graph of the selected measure as a function of threshold. By pressing `Ctrl+F` the graph can be exported as a figure that can be customized using the standard MatLab plotting tools; then, the figure can be exported in several standard graphic formats. Below the graph, several options are available to customize the plot:

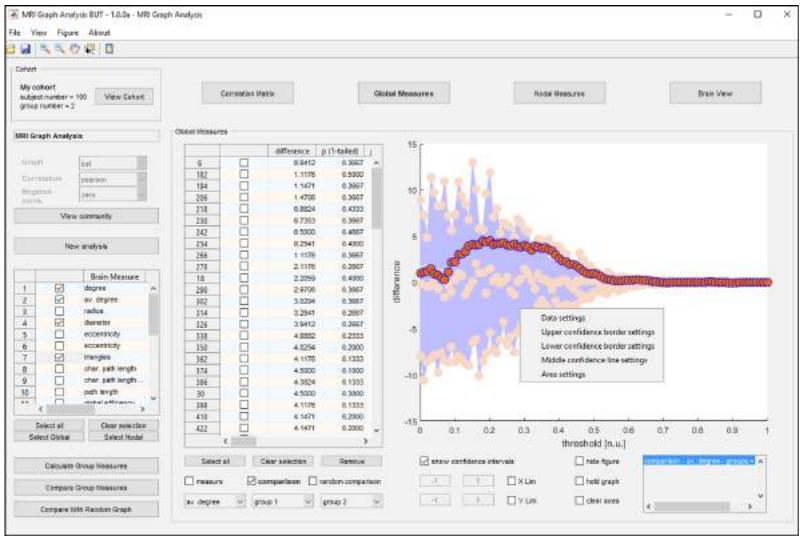


Figure 61: Confidence intervals when comparing two groups.

- **show confidence intervals** shows the 95% confidence intervals as shown in figure 61. This option is only available for comparisons between groups and with random graphs. As can be seen in the figure 61 by right-clicking on the confidence intervals, a popup menu appears which allows the user to change the properties of the data values, lower, middle, and higher borders of the confidence interval as well as of the area plot properties.
- When **X Lim** is checked, the x-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **Y Lim** is checked, the y-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **hide figure** is checked, the graph is hidden and the table is extended.
- When **hold graph** is checked, more than one data set can be plotted on the same graph. The plotted measures are listed below the graph on the right.
- **clear axes** erases all the data plotted on the graph.

6. Push `Nodal Measures` in the main panel to visualize the results for nodal measures (figure 62). This interface is very similar to that explained above for the global measures. The main difference is that now it is possible to select also the brain region.

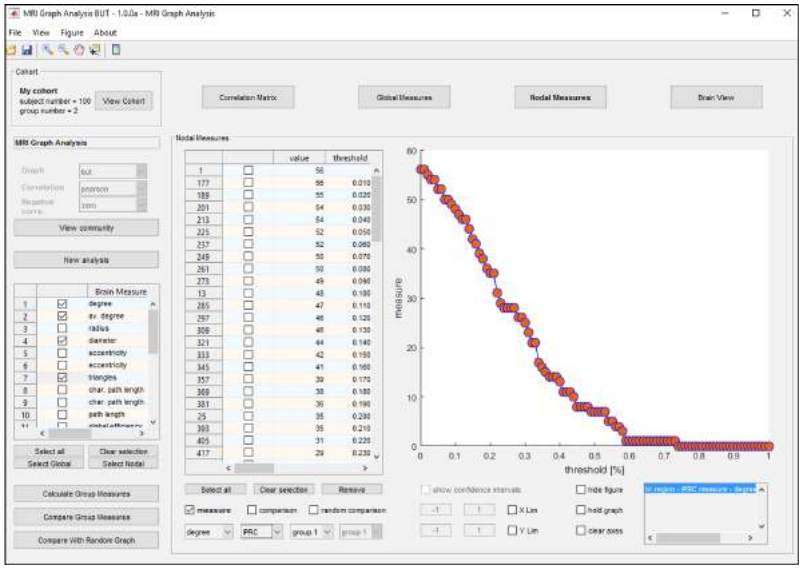


Figure 62: Nodal measures tab.

7. Push `Brain View` in the main panel to visualize the nodal measures on a brain surface. By pushing the buttons at the bottom of

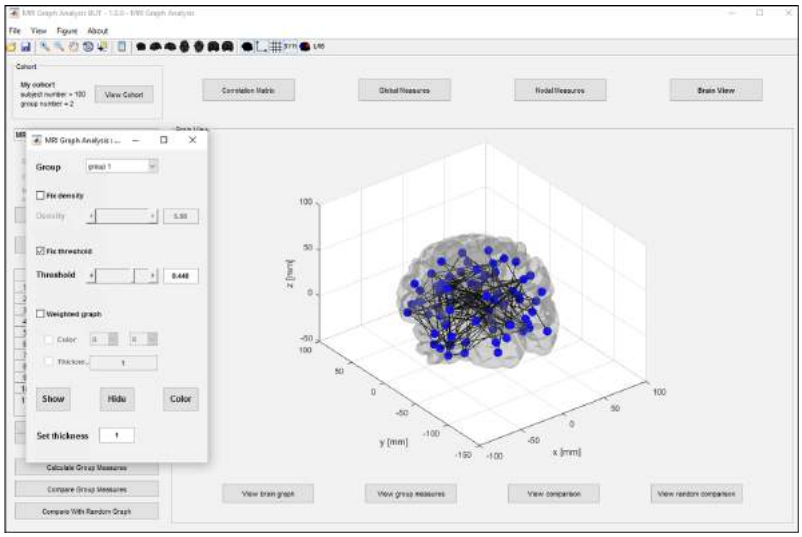


Figure 63: Visualization of the brain graph on the brain surface.

this panel, the user can visualize the brain graph, the group measures, the comparisons between two groups, and the comparisons with random graphs.

- `View brain graph` visualizes the brain graph, as shown in figure 63. The graph parameters that can be specified are:
  - **fix density** draws the binary brain graph with the selected density of connections. The density can be specified by entering the value in the corresponding field or by using the slider.
  - **fix threshold** draws the binary brain graph with all connections having larger weight than the given threshold. The threshold can be specified by entering the value in the corresponding field or by using the slider.
  - **weighted** plots all the connection of the weighted brain graph. The weight of the connections can be encoded by color and/or thickness (by checking the corresponding checkboxes).
  - `Show` shows the current graph on the brain surface.
  - `Hide` hides the current graph from the brain surface.
  - `Color` plots the current graph in the specified color.
  - **Set thickness** sets the thickness of the connections.
- `View group measures` visualizes the nodal measures calculated for a given group, as shown in figure 64.[35] The group for which the measures are to be shown is selected from the popup menu in the top left. In the first list below it, the user can select the measure; the list on the left shows the thresholds for which the measure have been calculated.

[35] For more information about the rescaling and the filters needed to be applied to visualize the data, refer to the *Main panel* subsection in the chapter MRI Cohort.

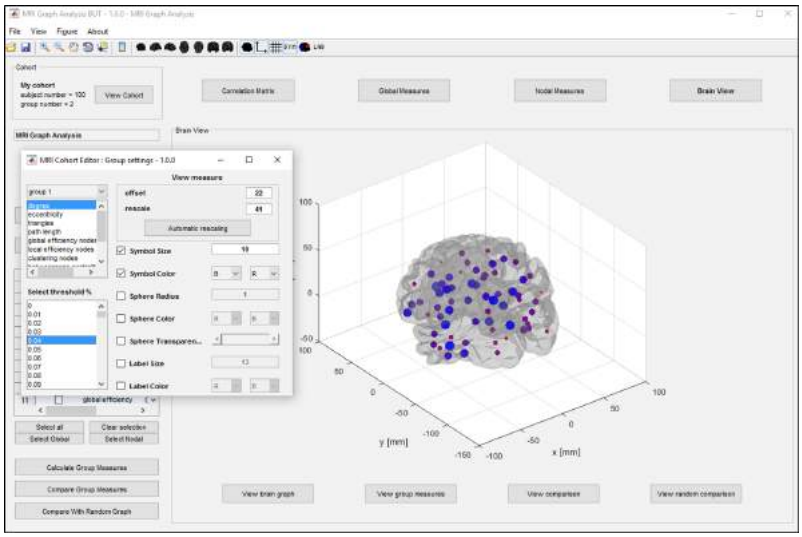


Figure 64: Visualization of the nodal measures on the brain surface.

- `View comparison` visualizes the comparison between two groups, as shown in figure 65. The two popup menus on the left specify the two groups that are compared and the lists below them show the measures and the thresholds for which they have been calculated. The other functionalities are analogous to the interface for viewing group measures with two new options:
  - **fdr (1-tailed)**, if checked, corrects the p-values for single-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.
  - **fdr (2-tailed)**, if checked, corrects the p-values for double-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.

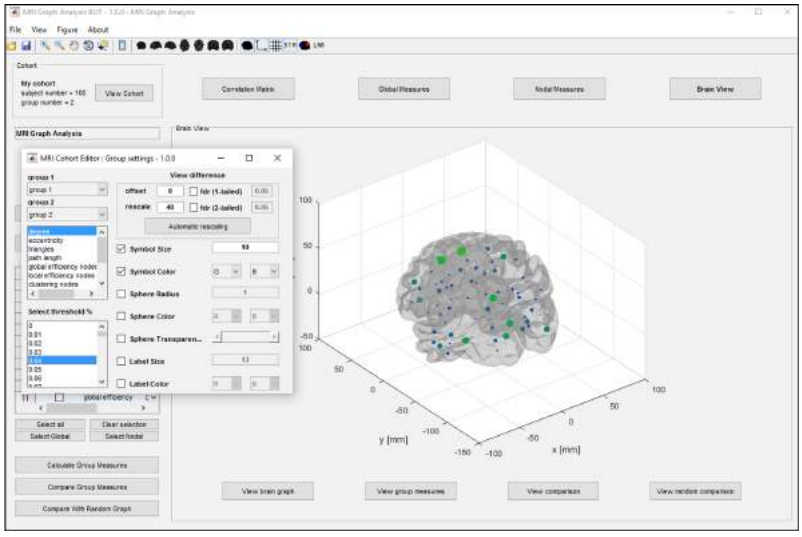


Figure 65: Visualization of the comparison between two groups on the brain surface.

- `View random comparison` visualizes the measures normalized by comparing them with random graphs, as shown in figure 66. All the functionalities of this interface are analogous to those of the interface to visualize a comparison between groups.

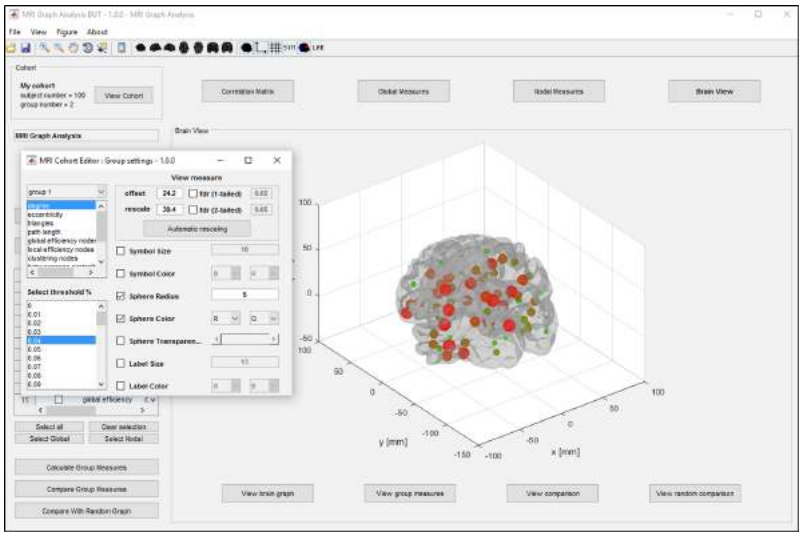


Figure 66: Visualization of the measures normalized by random comparison on the brain surface.

- `Select File` → `Save` to save the MRI graph analysis BUT as a *.mga file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.
- `Select File` → `Open` to open an MRI graph analysis BUT previously saved with GUIMRIGraphAnalysisBUT; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

Cohort panel

The cohort is already uploaded when GUIMRIGraphAnalysisBUT is launched. The cohort view shows the cohort's properties including name, number of subjects, and groups. Moreover, all cohort's properties can be viewed in the GUIMRICohort interface with restricted access by pushing `View Cohort`.

Graph analysis panel

The graph analysis panel shows the information relative to the graph analysis and gives the user the ability to calculate measures. The available features are:

- **Graph analysis properties**. These three popup menus show the properties of the graph analysis: graph type, correlation type, and

how to deal with negative correlations. As all these properties were set in GUIMRIGraphAnalysis, here all the popup menus are disabled and the properties cannot be changed. If the user wishes to change any of the properties, a new graph analysis should be started.

- `View community` opens the interface to view the community structure that is set. Also the community structure cannot be changed.
- `New analysis` opens a new GUIMRIGraphAnalysis interface where a new graph analysis with different parameters can be launched.
- **Measure list** lists all measures available for calculation for binary graphs. The user can choose which measure to calculate by checking the checkboxes next to them.
- `Calculate Group Measures` opens an interface allowing the user to set parameters to calculate the selected measures.
- `Compare Group Measures` opens an interface allowing the user to set parameters to compare the selected measures between two groups.
- `Compare With Random Graphs` opens an interface allowing the user to set parameters to compare the selected measures with random graphs.

Main panel

The main panel consists of a main table that displays different information about the graph analysis and the calculated measures. The console buttons are used to switch between the various types of information shown in the table. The following information can be displayed:

- `Correlation Matrix` visualizes the connectivity matrix based on the parameters set on the right. For more detailed information about how to visualize the connectivity matrix please refer to the section *Main view* in the chapter MRI Graph Analysis.
- `Global Measures` allows the user to visualize global measures.
- `Nodal Measures` allows the user to visualize nodal measures.
- `Brain View` allows the user to visualize the brain graph and the calculated nodal measures on a brain surface.

Menu

`File` provides various options for importing and saving an MRI graph analysis BUT:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an MRI graph analysis BUT saved in **.mga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIMRIGraphAnalysisBUT.
- `File` → `Save` (`Ctrl+S`) saves the current MRI graph analysis BUT in **.mga* format.
- `File` → `Save as` opens a popup window to save the current MRI graph analysis BUT in **.mga* format possibly in a different file.
- `File` → `Import (xml)` imports an MRI graph analysis BUT from an xml file.
- `File` → `Export (xml)` exports the current MRI graph analysis BUT to an xml file.

`View` switches the main view to display various types of information:

- `View` → `Correlation Matrix` visualizes the connectivity matrix.
- `View` → `Global Measures` visualizes global measures.
- `View` → `Nodal Measures` visualizes nodal measures.
- `View` → `Brain View` visualizes the data on a brain surface.

`Figure` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIMRIGraphAnalysisBUT and BRAPH.

Toolbar

The toolbar provides different options to open and save the MRI graph analysis BUT and visualize the figures. It is shown in figure 67.

Figure 67: MRIGraphAnalysisBUT toolbar.

Open and Save commands

These commands allow the user to open and save an MRI graph analysis BUT in the **.mga* format. These are equivalent to the open and save menu options in the `File` menu.

opens a popup window to load an MRI graph analysis BUT saved in **.mga* format.

saves the current MRI graph analysis BUT in **.mga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations.

zooms in image.

zooms out image.

drags image.

shows/hides data cursor.

shows color scale.

standard 3D view.

sagittal left view.

sagittal right view.

axial dorsal view.

axial ventral view.

coronal anterior view.

coronal posterior view.

switches brain surface on/off.

switches axis on/off.

switches grid on/off.

SYM switches brain region symbols on/off.

`SPH` switches brain region spheres on/off.

`LAB` switches brain region labels on/off.

MRI Graph Analysis BUD

GUIMRIGraphAnalysisBUD is a graphical user interface that allows the user to perform a brain graph analysis of MRI data using binary undirected graphs at a fixed density of connections (BUD = Binary Undirected Density). The user can calculate group measures, compare them with random graphs, and compare the measures of two groups by permutation test. Significance intervals and single/double-tailed p-values are provided (the p-values can be corrected for false discovery rate (FDR) in the case of nodal measures). Global and nodal measures are displayed separately; for nodal measures the user has the option to visualize the results on a brain surface. The graph analysis can be saved in a file **.mga* for future use within BRAPH; it can also be exported in xml format for use within other programs.

The layout of GUIMRIGraphAnalysisBUD is shown in figure 68. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIMRIGraphAnalysisBUD, including loading and saving an MRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an MRI graph analysis.
- **Cohort panel** permits one to view the MRI cohort properties.
- **Graph analysis panel** permits one to choose which measures to calculate or compare, view the community structure, and, if needed, start a new graph analysis.
- **Main panel** allows one to view the connectivity matrix as well as the calculated global and nodal

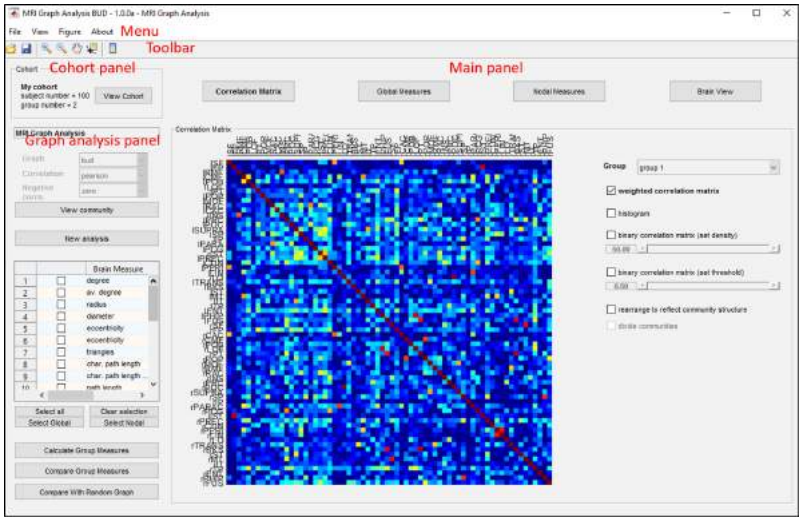


Figure 68: Snapshot of GUIMRIGraphAnalysisBUD. On the top, there are the menu and the toolbar; below, there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right).

measures and comparisons.

Getting Started

As a first example of the use of GUIMRIGraphAnalysisBUD, we will proceed to calculate some global (average degree, clustering coefficient) and local (degree, triangles) measures, and to compare the results for two groups. Then, we will visualize these results and the graph on the brain surface. Finally, we will save the graph analysis in a **.mga* file.

1. In the graph analysis view, select from the list of measures the average degree, diameter, degree, and triangles measures.

   To quickly select more than one measure, use the buttons below the measure list:

   - `Select all` selects all the measures.
   - `Clear selection` clears the current selection.
   - `Select Global` selects all global measures.
   - `Clear Nodal` selects all nodal measures.

2. Push `Calculate Group Measures` in the graph analysis panel (figure 68) to calculate the selected measures. This opens a new interface, shown in figure 69. On the left of the interface, there is a list with the selected measures to be calculated. On the right,

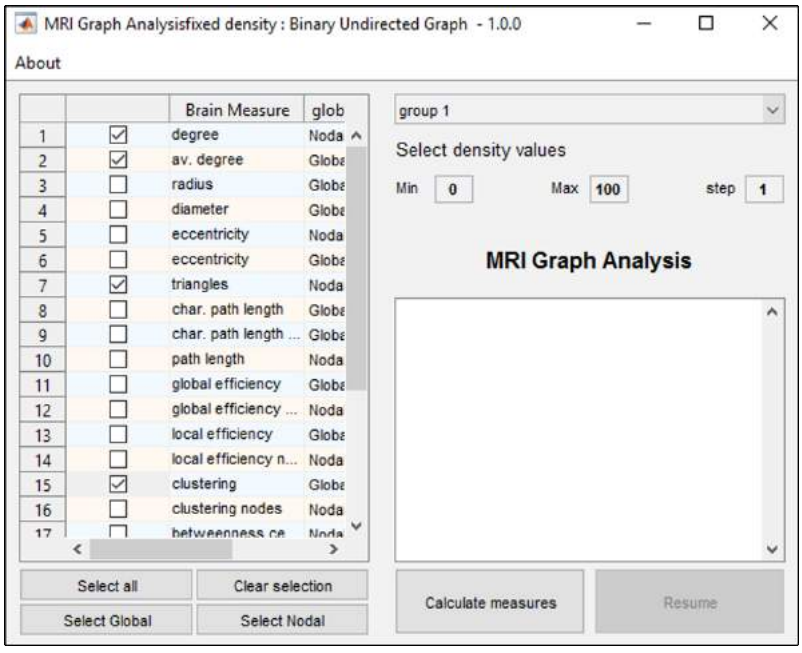


Figure 69: Interface to calculate group measures.

there are a popup menu to select the group for which the measures will be calculated and a series of fields to enter the density values (including the minimum density, the maximum density, and the density step). The calculation is started by pushing `Calculate measures`. When the calculation is in progress, the status of the button changes to `stop` and pushing it stops the calculation; the calculation can then be resumed by pressing `Resume`.

3. Push `Compare with Random Graph` in the graph analysis panel (figure 68) to calculate measures that are normalized by the results obtained from random graphs. This opens the interface shown in figure 70. This interface is analogous to that to calculate group measures, which we have seen in the previous step, but two new parameters can be inputted:

   - **random matrix no.** sets how many random graphs are used in the comparison.
   - **random swaps no.** sets how many times each edge is rewired to randomize the original graph.

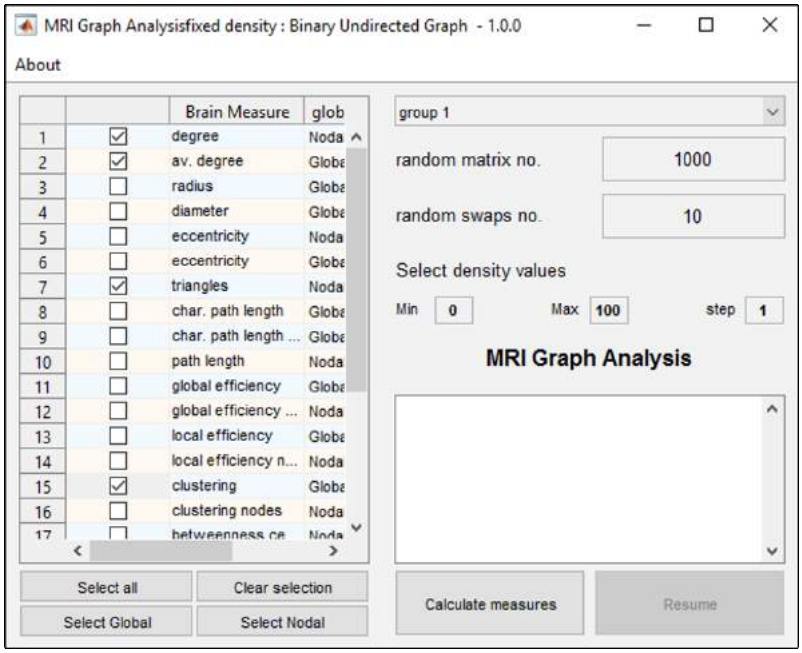


Figure 70: Interface to calculate group measures normalized by comparison with random graphs.

4. Push `Compare Group Measures` in the graph analysis panel (figure 68) to compare the measures between two groups. This opens the interface shown in figure 71. This interface is analogous to that to calculate group measures, but with two new parameters:

   - **permutation number** sets how many permutations are performed in the permutation test.

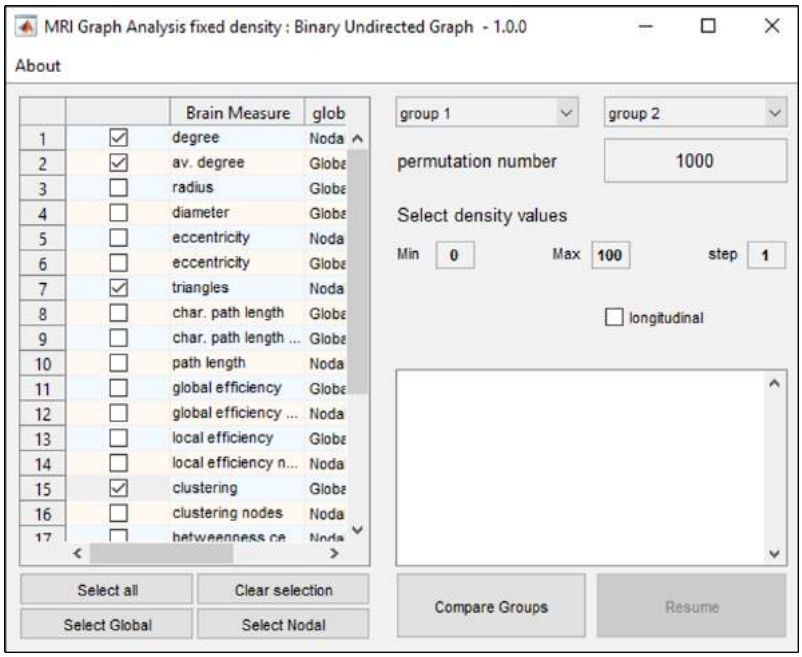


Figure 71: Interface to compare the measures of two groups.

- **longitudinal** sets whether the comparison is done for longitudinal data.

5. Push `Global Measures` in the main panel to visualize the results for the global measures (figure 72).

   If the **measure** checkbox is checked, group measures are displayed (the measure and the group are selected using the popup menus at the bottom). If the **comparison** checkbox is checked, comparisons between two groups are displayed (the measure and the groups

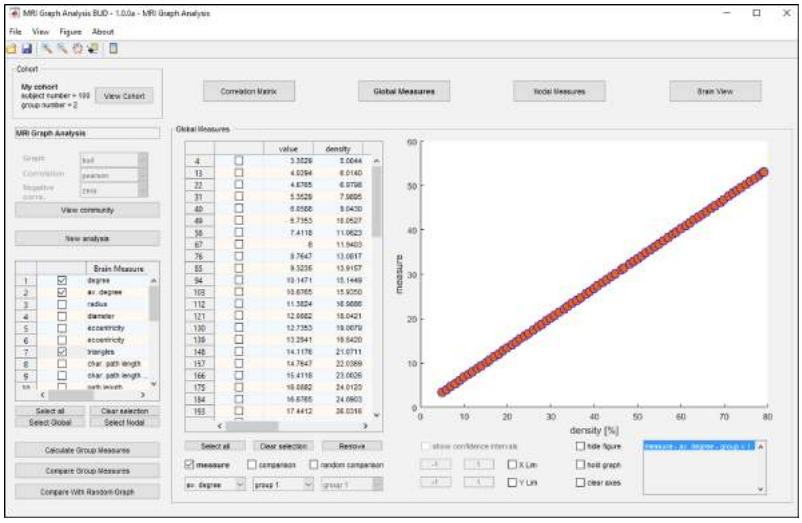


Figure 72: Global measures tab. Here the average degree is shown as a function of the density.

are selected using the popup menus at the bottom). If the **random comparison** checkbox is checked, measures normalized by comparison with random graphs are displayed (the measure and the group are selected using the popup menus at the bottom).

The main panel now shows two parts:

(a) A **table view** on the left shows the numerical information about the selected measure. Among other data, this includes the value of the measure, the group for which it was calculated, and the density and threshold of the graph on which it was calculated. If it is a comparison between groups or with random graphs, the difference between the values and the single/double-tailed p-values are also displayed. A series of options are available below the table view:

- `Select all` selects all the measures.
- `Clear selection` clears the current selection.
- `Remove` removes the selected measure.

(b) A **graph view** plots a graph of the selected measure as a function of density. By pressing `Ctrl+F` the graph can be exported as a figure that can be customized using the standard MatLab plotting tools; then, the figure can be exported in several standard graphic formats. Below the graph, several options are available to customize the plot:

- **show confidence intervals** shows the 95% confidence intervals as shown in figure 73. This option is only available for comparisons between groups and with random graphs. As

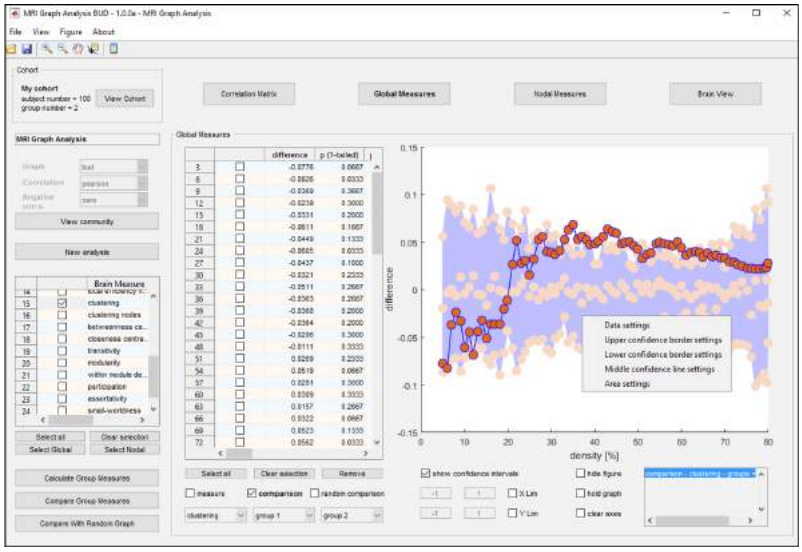


Figure 73: Confidence intervals when comparing two groups.

can be seen in the figure 73 by right-clicking on the confidence intervals, a popup menu appears which allows the user to change the properties of the data values, lower, middle, and higher borders of the confidence interval as well as of the area plot properties.

- When **X Lim** is checked, the x-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **Y Lim** is checked, the y-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **hide figure** is checked, the graph is hidden and the table is extended.
- When **hold graph** is checked, more than one data set can be plotted on the same graph. The plotted measures are listed below the graph on the right.
- **clear axes** erases all the data plotted on the graph.

6. Push `Nodal Measures` in the main panel to visualize the results for nodal measures (figure 74). This interface is very similar to that explained above for the global measures. The main difference is that now it is possible to select also the brain region.

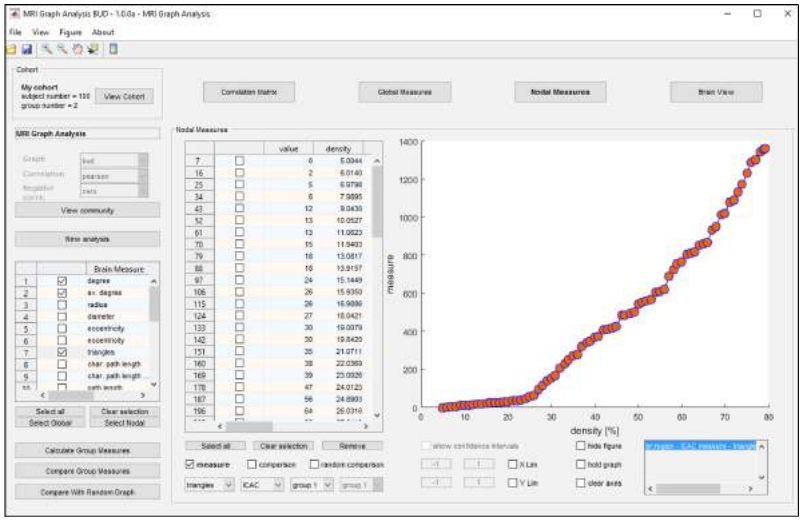


Figure 74: Nodal measures tab.

7. Push `Brain View` in the main panel to visualize the nodal measures on a brain surface. By pushing the buttons at the bottom of this panel, the user can visualize the brain graph, the group measures, the comparisons between two groups, and the comparisons with random graphs.

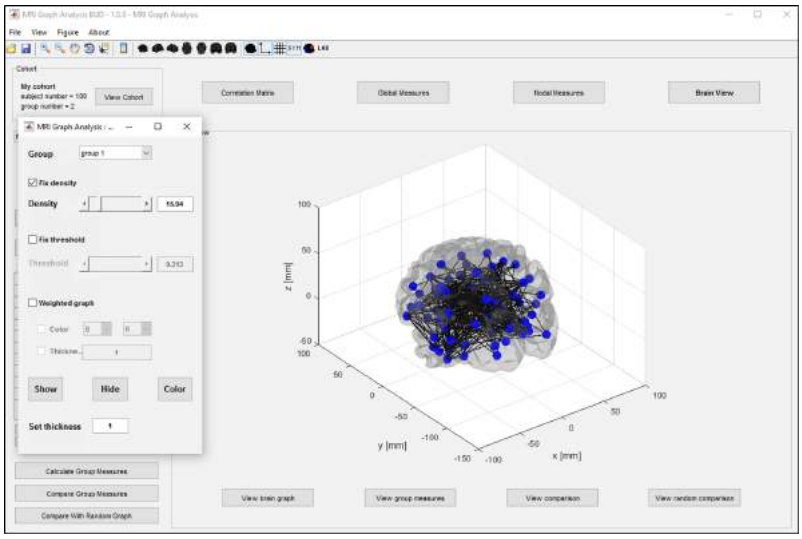


Figure 75: Visualization of the brain graph on the brain surface.

- `View brain graph` visualizes the brain graph, as shown in figure 75. The graph parameters that can be specified are:
  - **fix density** draws the binary brain graph with the selected density of connections. The density can be specified by entering the value in the corresponding field or by using the slider.
  - **fix threshold** draws the binary brain graph with all connections having larger weight than the given threshold. The threshold can be specified by entering the value in the corresponding field or by using the slider.
  - **weighted** plots all the connection of the weighted brain graph. The weight of the connections can be encoded by color and/or thickness (by checking the corresponding checkboxes).
  - `Show` shows the current graph on the brain surface.
  - `Hide` hides the current graph from the brain surface.
  - `Color` plots the current graph in the specified color.
  - **Set thickness** sets the thickness of the connections.
- `View group measures` visualizes the nodal measures calculated for a given group, as shown in figure 76.[36] The group for which the measures are to be shown is selected from the popup menu in the top left. In the first list below it, the user can select the measure; the list on the left shows the densities for which the measure have been calculated.
- `View comparison` visualizes the comparison between two groups, as shown in figure 77. The two popup menus on the left specify the two groups that are compared and the lists below

[36] For more information about the rescaling and the filters needed to be applied to visualize the data, refer to the *Main panel* subsection in the chapter MRI Cohort.

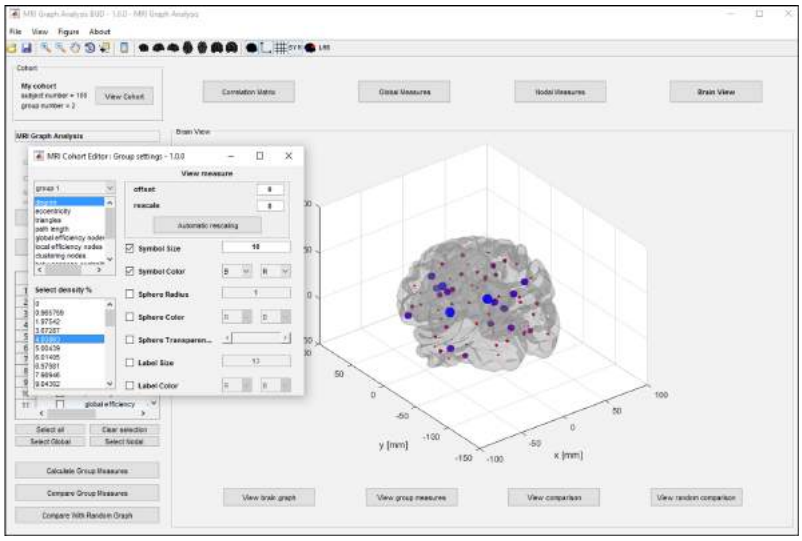


Figure 76: Visualization of the nodal measures on the brain surface.

them show the measures and the densities for which they have been calculated. The other functionalities are analogous to the interface for viewing group measures with two new options:

- **fdr (1-tailed)**, if checked, corrects the p-values for single-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.
- **fdr (2-tailed)**, if checked, corrects the p-values for double-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.

- `View random comparison` visualizes the measures normalized by comparing them with random graphs, as shown in figure 78. All the functionalities of this interface are analogous to those of

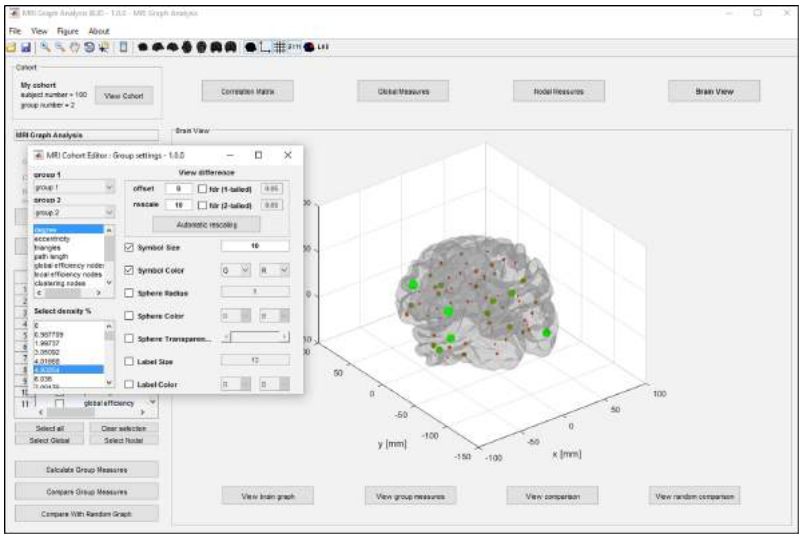


Figure 77: Visualization of the comparison between two groups on the brain surface.

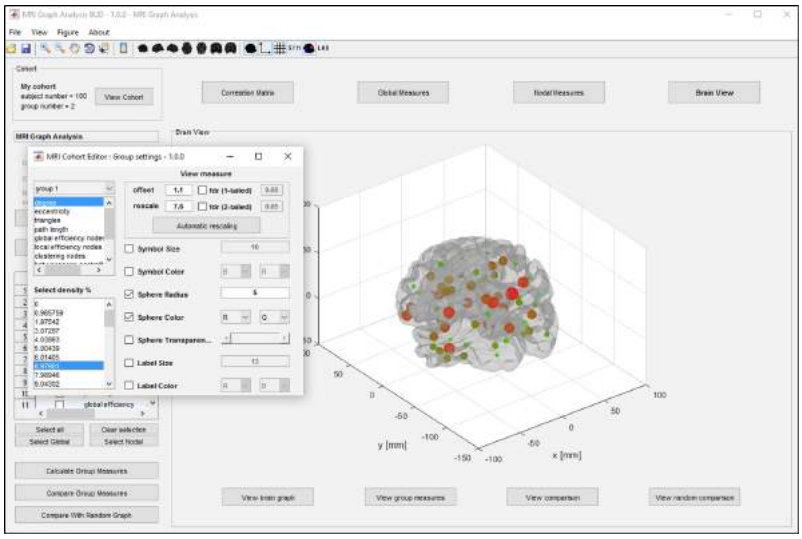


Figure 78: Visualization of the measures normalized by random comparison on the brain surface.

the interface to visualize a comparison between groups.

- `Select File` → `Save` to save the MRI graph analysis BUD as a *.mga file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.
- `Select File` → `Open` to open an MRI graph analysis BUD previously saved with GUIMRIGraphAnalysisBUD; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

Cohort panel

The cohort is already uploaded when GUIMRIGraphAnalysisBUD is launched. The cohort view shows the cohort's properties including name, number of subjects, and groups. Moreover, all cohort's properties can be viewed in the GUIMRICohort interface with restricted access by pushing `View Cohort`.

Graph analysis panel

The graph analysis panel shows the information relative to the graph analysis and gives the user the ability to calculate measures. The available features are:

- **Graph analysis properties**. These three popup menus show the properties of the graph analysis: graph type, correlation type, and how to deal with negative correlations. As all these properties were set in GUIMRIGraphAnalysis, here all the popup menus are disabled and the properties cannot be changed. If the user wishes

to change any of the properties, a new graph analysis should be started.

- `View community` opens the interface to view the community structure that is set. Also the community structure cannot be changed.

- `New analysis` opens a new GUIMRIGraphAnalysis interface where a new graph analysis with different parameters can be launched.

- **Measure list** lists all measures available for calculation for binary graphs. The user can choose which measure to calculate by checking the checkboxes next to them.

- `Calculate Group Measures` opens an interface allowing the user to set parameters to calculate the selected measures.

- `Compare Group Measures` opens an interface allowing the user to set parameters to compare the selected measures between two groups.

- `Compare With Random Graphs` opens an interface allowing the user to set parameters to compare the selected measures with random graphs.

Main panel

The main panel consists of a main table that displays different information about the graph analysis and the calculated measures. The console buttons are used to switch between the various types of information shown in the table. The following information can be displayed:

- `Correlation Matrix` visualizes the connectivity matrix based on the parameters set on the right. For more detailed information about how to visualize the connectivity matrix please refer to the section *Main view* of the chapter MRI Graph Analysis.

- `Global Measures` allows the user to visualize global measures.

- `Nodal Measures` allows the user to visualize nodal measures.

- `Brain View` allows the user to visualize the brain graph and the calculated nodal measures on a brain surface.

Menu

`File` provides various options for importing and saving an MRI graph analysis BUD:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an MRI graph analysis BUD saved in **.mga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIMRIGraphAnalysisBUD.
- `File` → `Save` (`Ctrl+S`) saves the current MRI graph analysis BUD in **.mga* format.
- `File` → `Save as` opens a popup window to save the current MRI graph analysis BUD in **.mga* format possibly in a different file.
- `File` → `Import (xml)` imports an MRI graph analysis BUD from an xml file.
- `File` → `Export (xml)` exports the current MRI graph analysis BUD to an xml file.

`View` switches the main view to display various types of information:

- `View` → `Correlation Matrix` visualizes the connectivity matrix.
- `View` → `Global Measures` visualizes global measures.
- `View` → `Nodal Measures` visualizes nodal measures.
- `View` → `Brain View` visualizes the data on a brain surface.

`Figure` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIMRIGraphAnalysisBUD and BRAPH.

Toolbar

The toolbar provides different options to open and save the MRI graph analysis BUD and visualize the figures. It is shown in figure 79.

Figure 79: MRIGraphAnalysisBUD toolbar.

Open and save commands

These commands allow the user to open and save an MRI graph analysis BUD in the **.mga* format. These are equivalent to the open and save menu options in the `File` menu.

opens a popup window to load an MRI graph analysis BUD saved in **.mga* format.

saves the current MRI graph analysis BUD in **.mga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations.

zooms in image.

zooms out image.

drags image.

shows/hides data cursor.

shows color scale.

standard 3D view.

sagittal left view.

sagittal right view.

axial dorsal view.

axial ventral view.

coronal anterior view.

coronal posterior view.

switches brain surface on/off.

switches axis on/off.

switches grid on/off.

SYM switches brain region symbols on/off.

`SPH` switches brain region spheres on/off.

`LAB` switches brain region labels on/off.

fMRI Cohort

GUIfMRICohort is a graphical user interface that allows the user to create an fMRI cohort by adding individual subjects or by importing groups of subjects from data files in xls, mat, or xlm format. The user can also edit the data and anagraphic details of the subjects, as well as create groups of subjects. Furthermore, GUIfMRICohort provides numerous options to visualize the data relative to individual subjects and groups. The fMRI cohort can be saved in a file **.fc* for future use within BRAPH; it also can be exported in xml format for use within other programs.

The layout of GUIfMRICohort is shown in figure 80. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIfMRICohort, including loading, saving, editing, and visualizing an fMRI cohort, as well as creating a new fMRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an fMRI cohort.
- **Brain atlas panel** permits one to select a brain atlas for the fMRI cohort or, if a brain atlas has already been selected, to view the brain atlas properties in GUIBrainAtlas.
- **Group panel** shows the subject groups and their properties in a table. Permits one to select, add, remove, move, and edit the existing groups, and to create new groups from the existing ones.

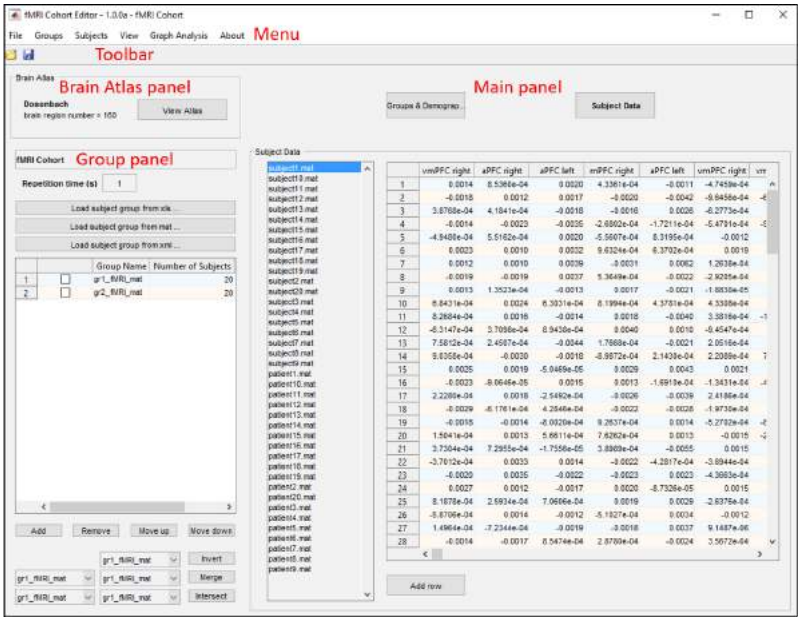


Figure 80: Screenshot of GUIfMRICohort. On the top there are the menu and the toolbar; below there are a brain atlas panel (on the top left), a group panel (on the bottom left), and a main panel (right) in which subject data can be visualized.

- **Main panel** consists of two tabs: `Groups & Demographics` to visualize the group data; and `Subject Data` to edit the subjects' data.

  Example data and a tutorial video can be found on `http://braph.org/manual/fmri/fmri-cohort/`

Getting Started

As a first example of the use of GUIfMRICohort, we will proceed to import the Dosenbach brain atlas from the file dosenbach_atlas.atlas.[37] Then, we will proceed to import two groups of subjects from the folders gr1_fMRI_mat and gr2_fMRI_mat (the subjects' data is imported from a series of MatLab files). Finally, we will save the fMRI cohort in a **.fc* file.

[37] N. U. F. Dosenbach, B. Nardos, A. L. Cohen, D. A. Fair, J. D. Power, J. A. Church, S. M. Nelson, G. S. Wig, A. C. Vogel, C. N. Lessov-Schlaggar, K. A. Barnes, J. W. Dubis, E. Feczko, R. S. Coalson, J. R. Pruett Jr., D. M. Barch, S. E. Petersen, and B. L. Schlaggar. Prediction of individual brain maturity using fMRI. *Science*, 329:1358–1361, 2010

1. Push `Select Atlas` to select a brain atlas as shown in figure 81. The atlas must be in **.atlas* format. After you select the file, the brain atlas panel is updated to show the properties of the atlas. The select button is changed to `View Atlas`; pushing this button opens the uploaded atlas in GUIBrainAtlas with restricted access (i.e. no further changes to the atlas are allowed).

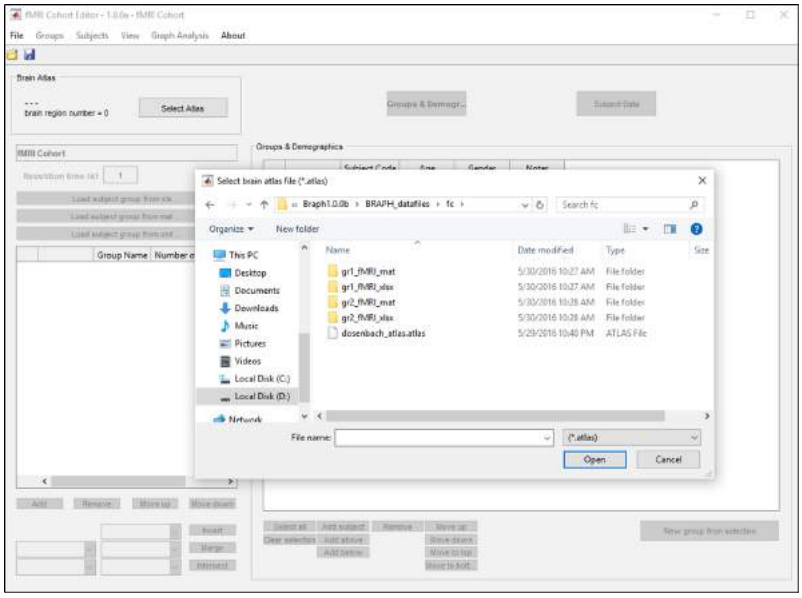


Figure 81: Importing a brain atlas from a **.atlas* file into GUIfMRICohort.

2. Push `Load subject group from mat ...` to add a group of subjects from a series of MatLab files. Locate and choose the folder gr1_fMRI_mat which contains the subjects' files. After the folder is selected, the group panel is updated to show to group's properties: the group name (editable), the number of subjects, and the notes (editable). The main panel is updated to show the subject data tab, as shown in figure 82.

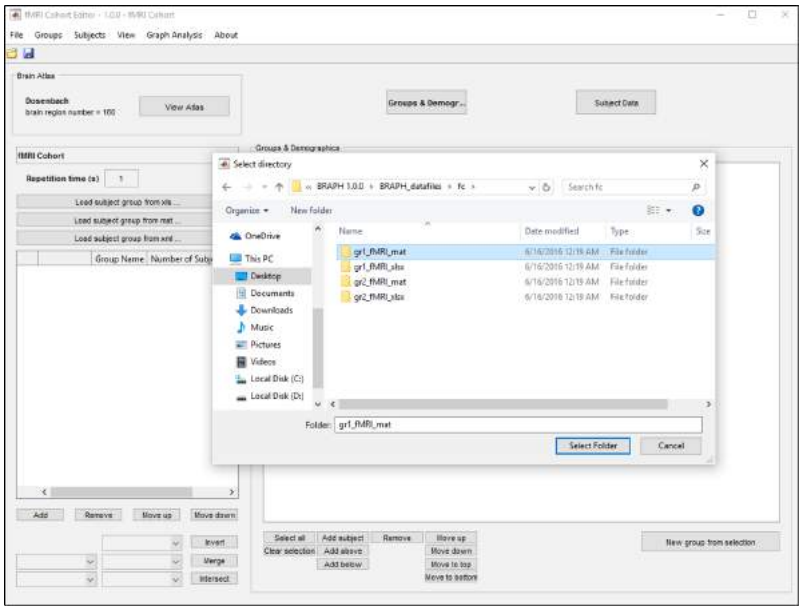


Figure 82: Importing a group of subjects from a folder containing MatLab files file into GUIfMRICohort.

A series of options are available to create new groups from the existing ones. They are accessible both through the buttons at the bottom of the group panel and through the menu. These are:

- `Add` adds new group at the bottom of the list.
- `Remove` removes the selected group.
- `Move up` moves the selected group up by one place.
- `Move down` moves the selected group down by one place.
- `Invert` creates a new group from the subjects not belonging to the group selected in the neighboring popup menu.
- `Merge` creates a new group by merging the subjects participating to the two groups currently selected in the neighboring popup menus.
- `Intersect` creates a new group by selecting the subjects participating to both groups selected in the neighboring popup menus.

3. Repeat step 2 selecting the folder gr2_fMRI_mat to import also this group of subjects. The main panel shows all subjects in the fMRI cohort. If you select a group in the group panel, the main panel will show only the subject data corresponding to that group.

4. `Select File` → `Save` to save the fMRI cohort as a **.fc* file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.

5. `Select File` → `Open` to open an fMRI cohort previously saved with GUIfMRICohort; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

File formats that can be imported

To create an fMRI cohort, you need a brain atlas and the data corresponding to the groups of subjects. A brain atlas can be imported only if previously saved as a **.atlas* file (e.g. by using GUIBrainAtlas). A group of subjects can be imported from a folder containing multiple files with the data of each subject as Excel (**.xls* or **.xlsx*), MatLab (**.mat*), or xml (**.xml*) files, only if these files are in the correct format. For examples, see the files subject1.mat, subject1.xlsx and gr1_fMRI.xml.

In order to be imported correctly a MatLab file must contain a single matrix whose columns represent brain regions; the values in a column are the values measured for a specific brain region as a function of time.

The format for the Excel file is essentially the same (see subject1.xlsx).

The xml format is slightly more complex. It can be easily inferred from the sample file gr1_fMRI.xml.

Repetition time

The user can enter the repetition time for the fMRI measurement in the edit box below the name for the fMRI cohort. The repetition time designates the time that passes between the subsequent excitation pulses (measured in seconds). It is the factor that determines the time at which the fMRI images are obtained.

Main panel

The main panel permits one to explore the data of the subjects. There are two console buttons at the top that can be used to switch between various tabs. The following information can be displayed:

- `Groups & Demographics` shows the profiles of the subjects (see figure 83). It is possible to change the age, gender, and notes of the subjects. The composition of the groups can be altered by checking the appropriate checkboxes corresponding to each group. The buttons at the bottom allow various options for the user to manipulate, remove, and add subjects:

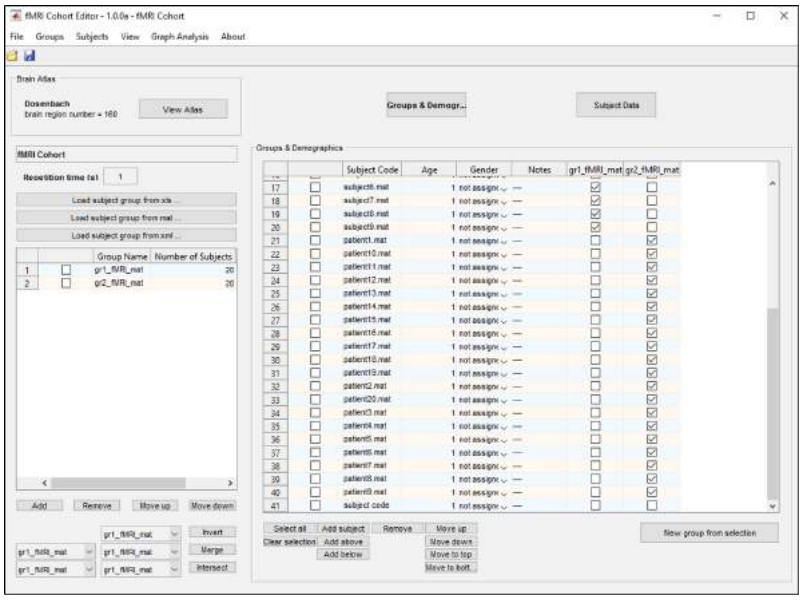


Figure 83: The groups & demographics tab of the main panel shows the profiles of the subjects. It permits one to alter the composition of the groups, to manipulate the demographic information regarding the subjects, to remove subjects, and to add new subjects.

- `Select all` selects all the subjects.
- `Clear selection` clears the current selection.
- `Add subject` adds a subject at the end of the table.
- `Add above` adds subjects above the selected ones.
- `Add below` adds subjects below the selected ones.
- `Remove` removes the selected subjects.
- `Move up` moves the selected subjects up by one place.
- `Move down` moves the selected subjects down by one place.
- `Move to top` moves the selected subjects to the top of the table.
- `Move to bottom` moves the selected subjects to the bottom of the table.
- `New group from selection` creates a new group from the selected subjects. Subjects can be selected by clicking the checkboxes next to them on the left side.

When a new subject is added (see, e.g., subject 41 in figure 83), it is assigned some default code ('subject code'), age ('1'), gender ('not assigned'), and notes ('...'), it is not included in any group, and its data is set to zero for all brain regions. The subject properties can be edited by clicking on them in the table and subjects can be assigned to groups by clicking on the corresponding checkboxes.[38] This new subject has been added at the end of the table; to add it at a different position in the table, select a subject and push `Add below` or `Add above`.

[38] The data corresponding to the brain region can be edited as explained below when discussing the subject data panel.

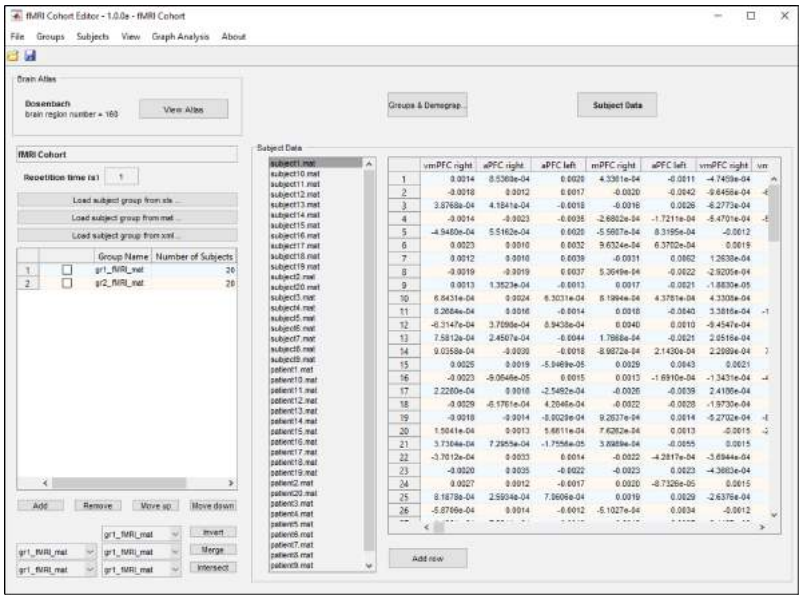


Figure 84: The subject data tab of the main panel shows a list of the subjects and a table containing the data of the subjects corresponding to each brain region as a function of time.

- `Subject Data` (figure 84) features a list on the left showing all the subjects. When a subject is selected, the corresponding data are shown in the table on the right. By default, all the subjects in the cohort are added to the list. If a group is selected in the group panel, only the subjects belonging to the selected group are listed. The header of the table shows the brain region labels. Each of the following rows contains the numerical information for each brain region of the corresponding subject at a given time. The numerical data can be edited by clicking on the desired field. Subject IDs and brain region names are not editable. A new row with all zeros can be added to the data by pushing `Add row`.

Menu

`File` provides various options for importing and saving an fMRI cohort:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load a cohort saved in **.fc* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIfMRICohort.
- `File` → `Save` (`Ctrl+S`) saves the current cohort in **.fc* format.
- `File` → `Save as` opens a popup window to save the current cohort in **.fc* format possibly in a different file.
- `File` → `Import (xml)` imports an fMRI cohort from an xml file.

- `File` → `Export (xml)` exports the current fMRI cohort to an xml file.

`Groups` provides various options to edit subject groups:

- `Groups` → `Load subject group from xls ...` loads subject group from xls.
- `Groups` → `Load subject group from mat ...` loads subject group from mat.
- `Groups` → `Load subject group from xlm ...` loads subject group from xlm.
- `Groups` → `Add` adds a group at the end of the table.
- `Groups` → `Remove` removes the selected group.
- `Groups` → `Move up` moves the selected group up by one place.
- `Groups` → `Move down` moves the selected group down by one place.

`Subjects` provides various options to edit subjects:

- `Subjects` → `Select all` selects all the subjects.
- `Subjects` → `Clear selection` clears the current selection.
- `Subjects` → `Add subject` adds a subject at the end of the table.
- `Subjects` → `Add above` adds subjects above the selected ones.
- `Subjects` → `Add below` adds subjects below the selected ones.
- `Subjects` → `Remove` removes the selected subjects.
- `Subjects` → `Move up` moves selected subjects up by one place.
- `Subjects` → `Move down` moves selected subjects down by one place.
- `Subjects` → `Move to top` moves selected subjects to the top of the table.
- `Subjects` → `Move to bottom` moves selected subjects to the bottom of the table.

`View` switches the main view to display various types of information:

- `View` → `Groups & Demographics` shows the group data and the profiles of the subjects.
- `View` → `Subject Data` shows the data for each subject in the cohort.

`Brain View` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`Graph Analysis` → `New fMRI graph analysis` launches GUIfMRI-GraphAnalysis, a graph analysis manager program using the current cohort.

`About` → `About` provides information about the current version of GUIfMRICohort and BRAPH.

Toolbar

The toolbar provides the options to open and save the fMRI cohort. It is shown in figure 85.

Figure 85: GUIfMRICohort toolbar.

Open and save commands

These commands allow the user to open and save an fMRI cohort in **.fc* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an fMRI cohort in **.fc* format.

 saves the current fMRI cohort in **.fc* format.

fMRI Graph Analysis

GUIfMRIGraphAnalysis is a graphical user interface that allows the user to define the parameters to create the connectivity matrices to analyze fMRI data, while simultaneously visualizing the resulting weighted or binary matrices. Binary connectivity matrices can be visualized as a function of density or threshold. The user can also define a community structure and restrict the analysis to a subset of brain regions. A list of the measures available for calculation is shown at the bottom of the interface. The fMRI graph analysis can be saved in a file **.fga* for future use within BRAPH; it also can be exported in xml format for use within other programs.

The layout of GUIfMRIGraphAnalysis is shown in figure 86. It is composed of six main work areas:

- **Menu** permits one to access the basic functionalities of GUIfMRIGraphAnalysis, including loading and saving an fMRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an fMRI graph analysis as well as manipulating the graphic representations of the connectivity matrices.
- **Cohort panel** permits one to select an fMRI cohort for the graph analysis or, if already selected, to view the cohort properties in GUIfMRICohort.

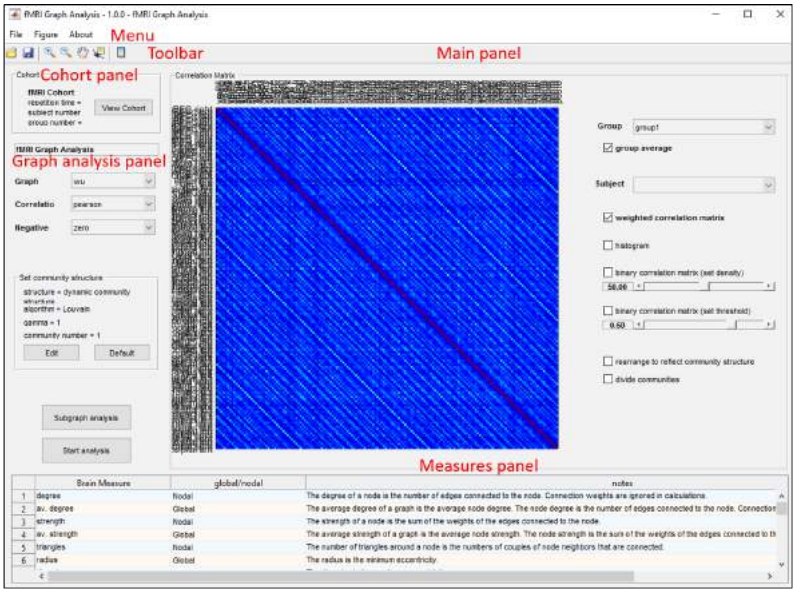


Figure 86: Screenshot of GUIfMRIGraphAnalysis. On the top, there are the menu and the toolbar; in the middle there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right); on the bottom, there is the measures panel.

- **Graph analysis panel** permits one to choose the properties of the graph analysis, to set a community structure, and to choose whether to perform the analysis on a subgraph.
- **Main panel** visualizes the connectivity matrix that will be used for the analysis.
- **Measures panel** shows the available measures for each type of graph (binary or weighted).

Example data and tutorial videos can be found on `http://braph.org/manual/fmri/fmri-graph-analysis/`

Getting Started

As a first example of the use of GUIfMRIGraphAnalysis, we will proceed to import the fMRI cohort stored in the my_cohort.fc file. Then, we will define a binary undirected graph analysis with fixed density and positive Pearson correlation coefficients. We will further specify a dynamic community structure calculated with the Louvain algorithm by using the first subject group. Finally, we will choose to perform the analysis on the full connectivity matrix and save it as a **.fga* file.

1. Push `Select Cohort` to select an fMRI cohort as shown in figure 87. The cohort must be in **.fc* format. After you select the file, the cohort panel is updated to show the properties of the cohort. The select button state is changed to `View Cohort`; pushing this button opens the uploaded cohort in GUIfMRICohort with restricted access (i.e. no further changes to the cohort are allowed).

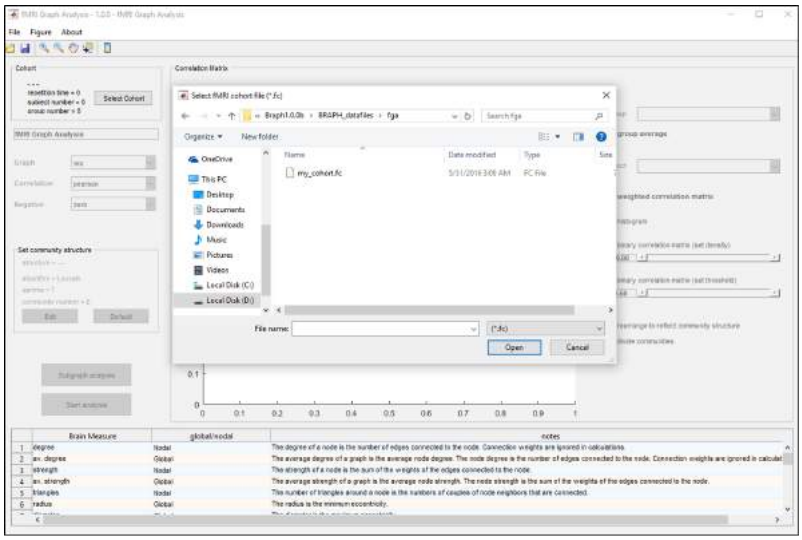


Figure 87: Importing an fMRI cohort from a **.fc* file into GUIfMRIGraphAnalysis.

2. Select `BUD` from the 'Graph' popup menu in the graph analysis panel, `Pearson` from the 'Correlation' popup menu, and `zero` from the 'Negative corrs.' popup menu. With these settings, the connectivity matrix will be calculated using Pearson correlation

coefficients where all negative coefficient are set to zero; this matrix will then be binarized at a fixed density.

A number of settings are available to create different types of graph analysis. More details about how these options affect the graphs can be found in chapter 'Brain Graphs'. These options are accessible through the popup menus in the graph analysis panel:

- **Graph** sets the type of graph to be analyzed:
  - `WU` analyzes weighted undirected graphs.
  - `BUT` analyzes binary undirected graphs, i.e. graphs whose connectivity matrices are binarized by specifying the threshold.
  - `BUD` analyzes binary undirected graphs. i.e. graphs whose connectivity matrices are binarized by specifying the density.
- **Correlation** sets the correlation used to calculate connectivity matrix coefficients:
  - `Pearson` is the Pearson correlation coefficient.
  - `Spearman` is the Spearman rank correlation coefficient.
  - `Kendall` is the Kendall rank correlation coefficient.
  - `partial Pearson` is the partial Pearson correlation coefficient.
  - `partial Spearman` is the partial Spearman correlation coefficient.
- **Negative corrs.** sets how to deal with the negative correlation coefficients:
  - `zero` sets all negative correlation coefficients to zero.
  - `none` leaves all negative correlation coefficients as as they are.[39]
  - `abs` replaces all negative correlation coefficients with their absolute values.

[39] Not all measures can be calculated in the presence of negative correlation coefficients.

3. Push `Edit` in the panel 'Define community structure' to define a community structure. This opens a new interface where the parameters for the calculation of the community structure can be set. Check the `Dynamic structure` checkbox to define a dynamic structure, choose the Louvain algorithm, check the `Group` checkbox, and select the first group from the popup menu, as shown in figure 88.

   The community structure interface consists of five main working areas as shown in figure 88:

   - **Menu** permits one to generate the brain view of the community structure. This can be customized using the standard MatLab

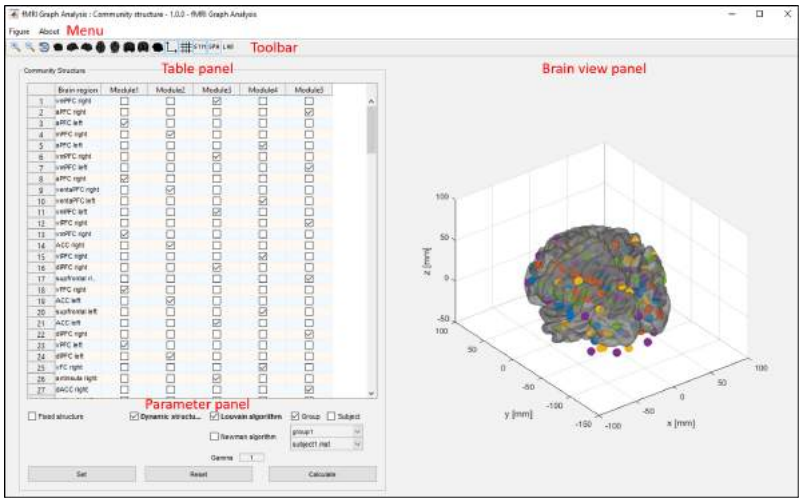


Figure 88: Interface to define a community structure for the graph analysis.

plotting tools. The figure can then be exported in several standard graphic formats.

- **Toolbar** gives direct access to various brain views and allows the user to choose how to represent the brain regions (spheres, symbols, or labels).
- **Table panel** lists all brain regions and designates their participation to a particular module. By checking the corresponding checkbox, the brain regions can be assigned to different modules.
- **Brain view panel** visualizes the community structure on a brain surface. Different modules are represented with different colors.
- **Parameter panel** allows one to choose the parameters for the calculation of the community structure. The following parameters can be specified:
  - `Fixed structure` fixes the community structure. The same structure will be used throughout the analysis.
  - `Dynamic structure` creates a dynamic structure with the specified parameters. The structure will be recalculated with the selected parameters whenever needed throughout the analysis.
  - `Louvain algorithm` calculates structure using the Louvain algorithm.
  - `Newman algorithm` calculates structure using the Newman algorithm.
  - `Gamma`. Sets the parameter $\gamma > 0$ determining the resolution of the algorithm. The default setting is $\gamma = 1$. Larger values ($\gamma > 1$) lead to more modules and smaller values ($0 < \gamma < 1$) to less modules.

- `Group`, if checked, permits one to select the group whose data serve as basis for the community structure calculation.
- `Subject`, if checked, permits one to select the subject whose data serve as basis for the community structure calculation.

The structure is calculated by pushing `Calculate` and reset by pushing `Reset`. Once all parameters are choosen, the structure can be set by pushing `Set`.

Alternatively, one can choose to perform the graph analysis with the default community structure by pushing `Default`. The default structure is a dynamic structure calculated with the Louvain algorithm with $\gamma = 1$.

4. To start the graph analysis on the full connectivity matrix, push `Start analysis`. This opens a new interface, GUIMRIGraphAnalysisBUD, which allows one to calculate and visualize the graph measures. The details of this interface are discussed in chapter 'fMRI Graph Analysis BUD'. After this, the parameters of the analysis become fixed and, if any change is needed, a new graph analysis with different parameters should be created.

5. The analysis can be performed only on a subset of brain regions. To do this, push `Subgraph analysis`. This opens a new interface, shown in figure 89, with five main working areas:

   - **Menu** permits one to generate the subgraph brain view, which can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.
   - **Toolbar** gives direct access to various brain views and allows

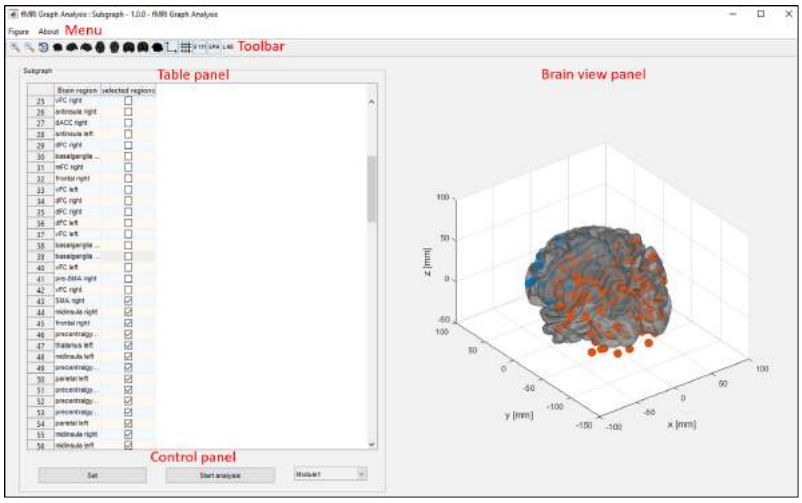


Figure 89: Interface to determine a subgraph on which to perform the graph analysis.

the user to choose how to represent the brain regions (spheres, symbols, or labels).

- **Table panel** shows all brain regions. If the checkbox next to a brain region is checked, the region is included into the subgraph.
- **Brain view panel.** Permits one to visualize the subgraph on a brain surface. The included brain regions are highlighted with an orange color.
- **Control panel** allows one to choose the parameters for the calculation of the community structure as follows: (1) choose a module as subgraph (modules from previously calculated community structure can be selected from the popup menu on the right); (2) `Set` sets the subgraph that will be used in the analysis; and (3) `Start analysis` starts the analysis by opening the corresponding interface (GUIMRIGraphAnalysisBUD, GUIMRIGraphAnalysisBUT and GUIMRIGraphAnalysisWU) depending on the graph type to be analysed. The analysis can performed only after the subgraph has been set.

6. `Select File` → `Save` to save the fMRI graph analysis as a **.fga* file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.

7. `Select File` → `Open` to open an fMRI graph analysis previously saved with GUIfMRIGraphAnalysis; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar. Opening a **.fga* file with with GUIfMRIGraphAnalysis interface opens a new interface (i.e. GUIfMRIGraphAnalysisWU, GUIfMRIGraphAnalysisBUT, or GUIfMRIGraphAnalysisBUD) depending on the type of analysis specified (weighted undirected, binary undirected fixed threshold, or binary undirected fixed density, respectively).

Additional information

Main panel

The main panel allows one to visualize the connectivity matrix based on the parameters specified by the set of checkboxes on the right (figure 86). The available options are:

- **Group** selects the group whose connectivity matrix to show.
- **Weighted correlation matrix**, if checked, visualizes the correlation coefficients between any two brain regions: warmer colors denote higher coefficients.

- **Histogram** shows the distribution of the correlation coefficients.
- **Binary correlation matrix (set density)** shows the binarized connectivity matrix at the set density (text field and slider below).
- **Binary correlation matrix (set threshold)** shows the binarized connectivity matrix at the set threshold (text field and slider below)
- **Rearrange to reflect community structure** rearranges the rows and columns of the connectivity matrix to reflect the community structures (i.e. keeping together regions belonging to the same module).
- **Divide communities** draws lines (squares around each module) to emphasize the division of the brain into different modules. This option is available only if the matrix has been previously rearranged to reflect the community structure by selecting the option **Rearrange to reflect community structure**.

Measures panel

The measures panel lists the measures (together with a short description) that are available for calculation given the kind of graph that has been selected (WU, BUT, BUD).

Menu

`File` provides various options for importing and saving an fMRI graph analysis:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an fMRI graph analysis saved in **.fga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIfMRIGraphAnalysis.
- `File` → `Save` (`Ctrl+S`) saves the current fMRI graph analysis in **.fga* format.
- `File` → `Save as` opens a popup window to save the current fMRI graph analysis in **.fga* format possibly in a different file.
- `File` → `Import (xml)` imports an fMRI graph analysis from an xml file.
- `File` → `Export (xml)` exports the current fMRI graph analysis to an xml file.

`Brain View` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIfMRIGraphAnalysis and BRAPH.

Toolbar

The toolbar provides different options to open and save the fMRI graph analysis as well as to visualize the connectivity matrix. It is shown in figure 90.

Figure 90: GUIfMRIGraphAnalysis toolbar.

Open and Save commands

These commands allow the user to open and save an fMRI graph analysis in the **.fga* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an fMRI graph analysis saved in **.fga* format.

 saves the current graph analysis in **.fga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations of the connectivity matrix.

 zooms in image.

 zooms out image.

 drags image.

 shows/hides data cursor.

 shows the colorbar.

fMRI Graph Analysis WU

GUIfMRIGraphAnalysisWU is a graphical user interface that allows the user to perform a brain graph analysis of fMRI data using weighted undirected graph (WU = Weighted Undirected). The user can calculate group measures, compare them with random graphs, and compare the measures of two groups by permutation test. Significance intervals and single/double-tailed p-values are provided (the p-values can be corrected for false discovery rate (FDR) in the case of nodal measures). Global and nodal measures are displayed separately; for nodal measures the user has the option to visualize the results on a brain surface. The graph analysis can be saved in a file **.fga* for future use within BRAPH; it can also be exported in xml format for use within other programs.

The layout of GUIfMRIGraphAnalysisWU is shown in figure 91. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIfMRIGraphAnalysisWU, including loading and saving an fMRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an fMRI graph analysis.
- **Cohort panel** permits one to view the fMRI cohort properties.
- **Graph analysis panel** permits one to choose which measures to calculate or compare, view the community structure, and, if needed, start a new graph analysis.

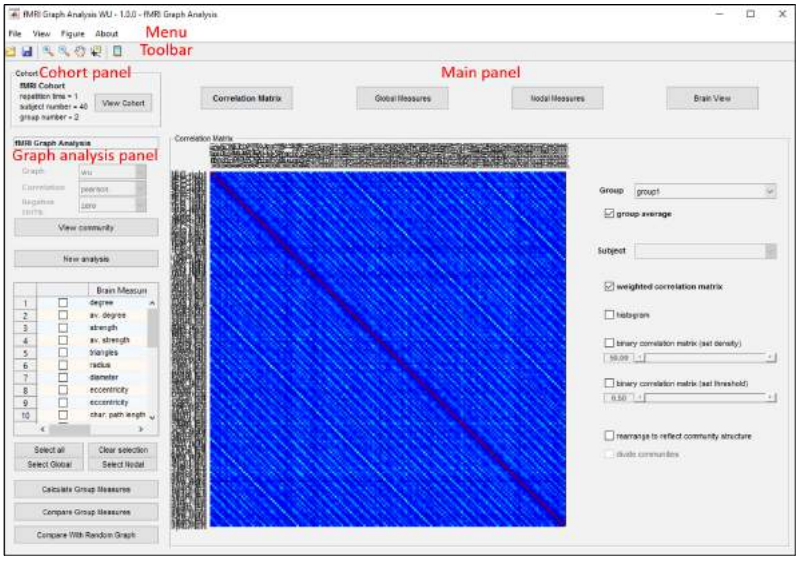


Figure 91: Snapshot of GUIfMRIGraph-AnalysisWU. On the top, there are the menu and the toolbar; below, there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right).

- **Main panel** allows one to view the connectivity matrix as well as the calculated global and nodal measures and comparisons.

Getting Started

As a first example of the use of GUIfMRIGraphAnalysisWU, we will proceed to calculate some global (average strength, diameter) and local (strength, triangles) measures, and to compare the results for two groups. Then, we will visualize these results on the brain surface. Finally, we will save the graph analysis in a **.fga* file.

1. In the graph analysis view, select from the list of measures the average strength, diameter, strength, and triangles measures.

   To quickly select more than one measure, use the buttons below the measure list:

   - `Select all` selects all the measures.
   - `Clear selection` clears the current selection.
   - `Select Global` selects all global measures.
   - `Clear Nodal` selects all nodal measures.

2. Push `Calculate Group Measures` in the graph analysis panel (figure 91) to calculate the selected measures. This opens a new interface, shown in figure 92. On the left of the interface, there is a list with the selected measures to be calculated. On the right,

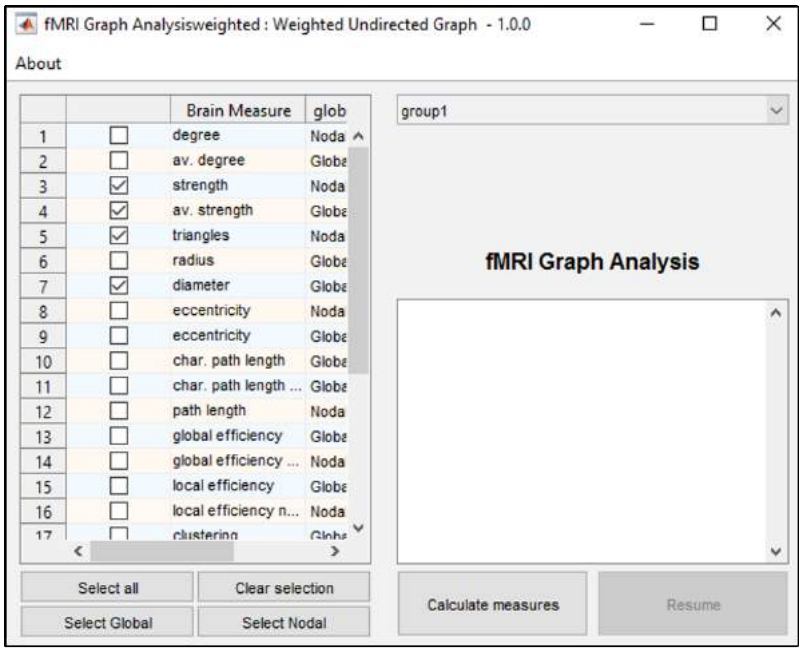


Figure 92: Interface to calculate group measures.

there is a popup menu to select the group for which the measures will be calculated. The calculation is started by pushing `Calculate measures`. When the calculation is in progress, the status of the button changes to `stop` and pushing it stops the calculation; the calculation can then be resumed by pressing `Resume`.

3. Push `Compare with Random Graph` in the graph analysis panel (figure 91) to calculate measures that are normalized by the results obtained from random graphs. This opens the interface shown in figure 93. This interface is analogous to that to calculate group measures, which we have seen in the previous step, but two new parameters can be inputted:

   - **random matrix no.** sets how many random graphs are used in the comparison.
   - **random swaps no.** sets how many times each edge is rewired to randomize the original graph.

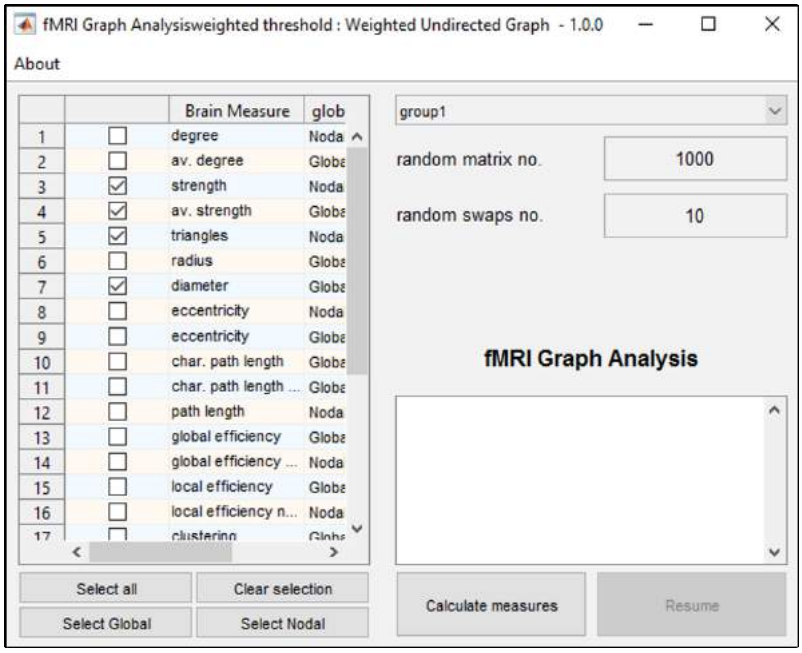


Figure 93: Interface to calculate group measures normalized by comparison with random graphs.

4. Push `Compare Group Measures` in the graph analysis panel (figure 91) to compare the measures between two groups. This opens the interface shown in figure 94. This interface is analogous to that to calculate group measures, but with two new parameters:

   - **permutation number** sets how many permutations are performed in the permutation test.

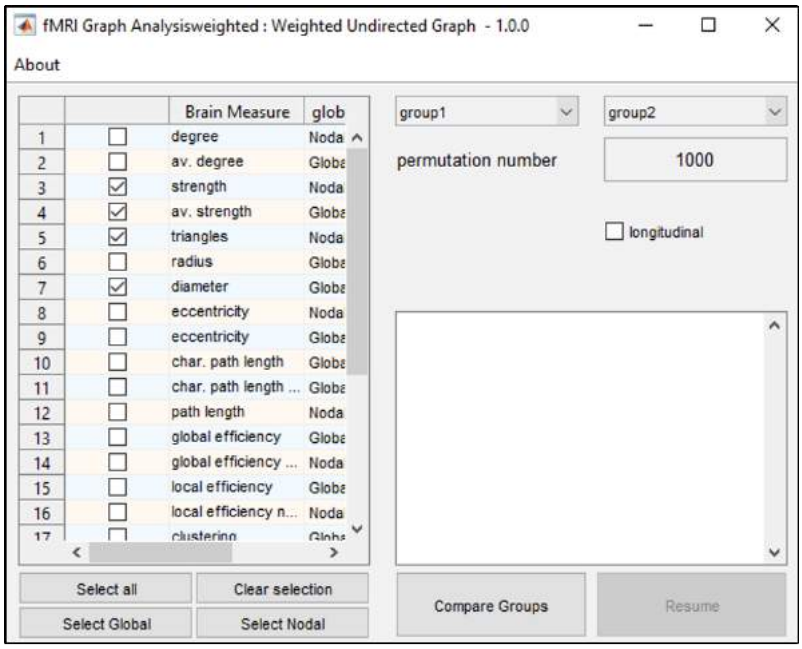


Figure 94: Interface to compare the measures of two groups.

- **longitudinal** sets whether the comparison is done for longitudinal data.

5. Push `Global Measures` in the main panel to visualize the results for the global measures (figure 95).

   If the **measure** checkbox is checked, group measures are displayed (the measure and the group are selected using the popup menus at the bottom). If the **comparison** checkbox is checked, comparisons

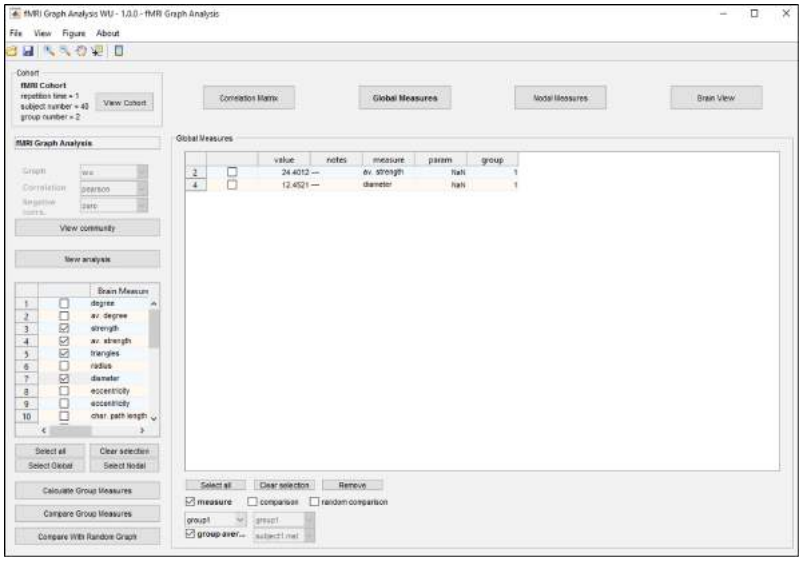


Figure 95: Global measures tab.

between two groups are displayed (the measure and the groups are selected using the popup menus at the bottom). If the **random comparison** checkbox is checked, measures normalized by comparison with random graphs are displayed (the measure and the group are selected using the popup menus at the bottom). By default the **group average** checkbox is checked; the results shown are averaged over all group subjects. To view the measure for each subject separately, uncheck this checkbox and select the subject from the neighboring popup menu.

The main panel shows a **table view** that displays the numerical information about the selected measure. Among other data, this includes the value of the measure and the group for which it was calculated. If it is a comparison between groups or with random graphs, the difference between the values and the single/double-tailed p-values are also displayed. A series of options are available below the table view:

- `Select all` selects all the measures.
- `Clear selection` clears the current selection.
- `Remove` removes the selected measure.

6. Push `Nodal Measures` in the main panel to visualize the results for nodal measures (figure 96). This interface is very similar to that explained above for the global measures. The main difference is that now it is possible to select also the brain region.

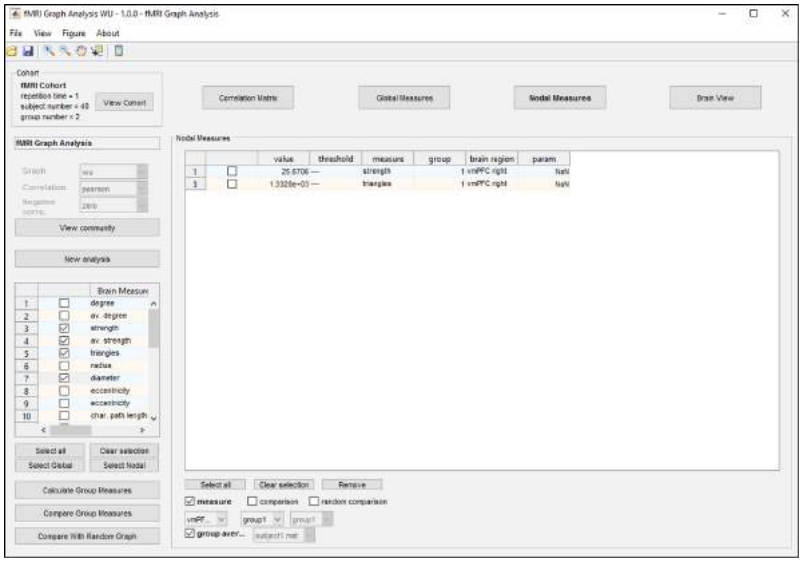


Figure 96: Nodal measures tab.

7. Push `Brain View` in the main panel to visualize the nodal measures on a brain surface. By pushing the buttons at the bottom of

this panel, the user can visualize the brain graph, the group measures, the comparisons between two groups, and the comparisons with random graphs.

- `View brain graph` visualizes the brain graph, as shown in figure 97. The graph parameters that can be specified are:
  - **fix density** draws the binary brain graph with the selected density of connections. The density can be specified by entering the value in the corresponding field or by using the slider.
  - **fix threshold** draws the binary brain graph with all connections having larger weight than the given threshold. The threshold can be specified by entering the value in the corresponding field or by using the slider.
  - **weighted** plots all the connection of the weighted brain graph. The weight of the connections can be encoded by color and/or thickness (by checking the corresponding checkboxes).
  - `Show` shows the current graph on the brain surface.
  - `Hide` hides the current graph from the brain surface.
  - `Color` plots the current graph in the specified color.
  - **Set thickness** sets the thickness of the connections.

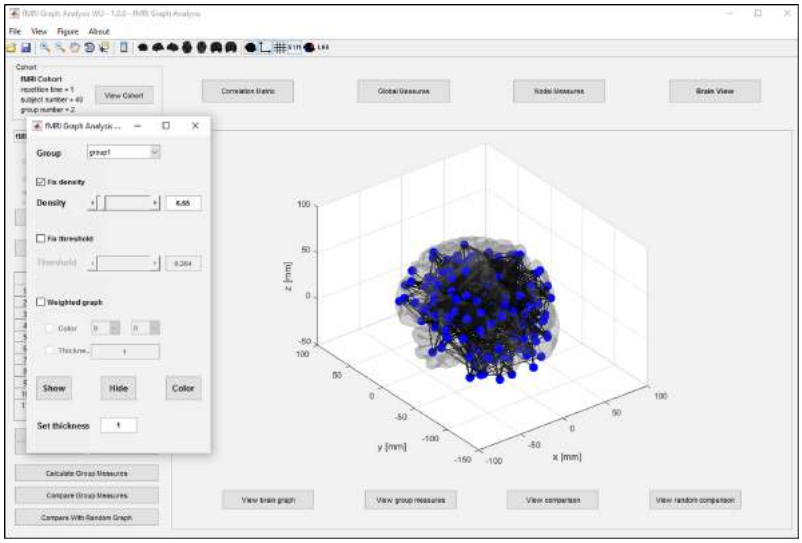


Figure 97: Visualization of the brain graph on the brain surface.

- `View group measures` visualizes the nodal measures calculated for a given group, as shown in figure 98.[40] The group for which the measures are to be shown is selected from the popup menu in the top left. The list on the left shows the measures that have been calculated.

[40] For more information about the rescaling and the filters needed to be applied to visualize the data, refer to the *Main panel* subsection in the chapter MRI Cohort.

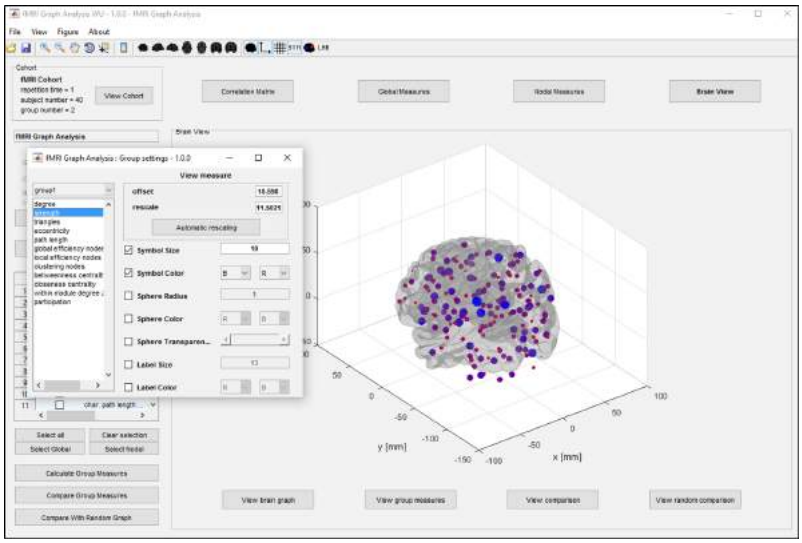


Figure 98: Visualization of the nodal measures on the brain surface.

- `View comparison` visualizes the comparison between two groups, as shown in figure 99. The two popup menus on the left specify the two groups that are compared and the list below them shows the measures for which they have been calculated. The other functionalities are analogous to the interface for viewing group measures with two new options:
  - **fdr (1-tailed)**, if checked, corrects the p-values for single-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.
  - **fdr (2-tailed)**, if checked, corrects the p-values for double-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.

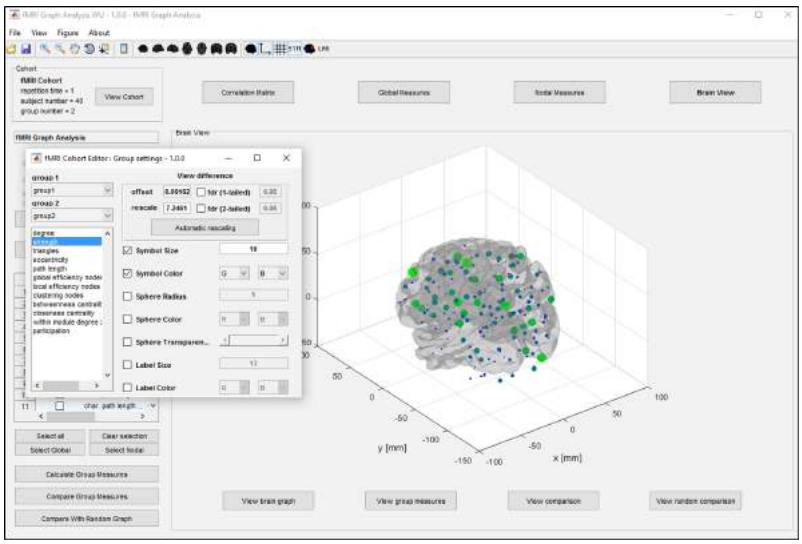


Figure 99: Visualization of the comparison between two groups on the brain surface.

- `View random comparison` visualizes the measures normalized by comparing them with random graphs, as shown in figure 100. All the functionalities of this interface are analogous to those of the interface to visualize a comparison between groups.

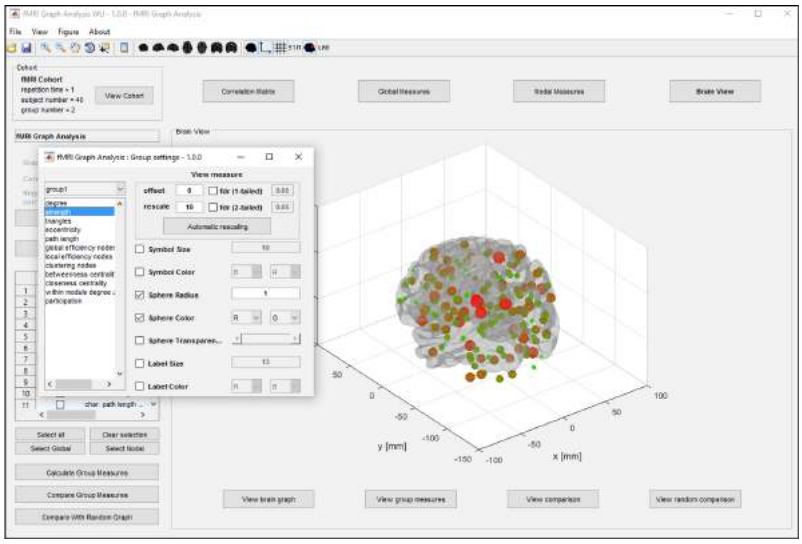


Figure 100: Visualization of the measures normalized by random comparison on the brain surface.

- `Select File` → `Save` to save the fMRI graph analysis WU as a *.fga file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.
- `Select File` → `Open` to open an fMRI graph analysis WU previously saved with GUIfMRIGraphAnalysisWU; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

Cohort panel

The cohort is already uploaded when GUIfMRIGraphAnalysisWU is launched. The cohort view shows the cohort's properties including name, number of subjects, and groups. Moreover, all cohort's properties can be viewed in the GUIfMRICohort interface with restricted access by pushing `View Cohort`.

Graph analysis panel

The graph analysis panel shows the information relative to the graph analysis and gives the user the ability to calculate measures. The available features are:

- **Graph analysis properties**. These three popup menus show the properties of the graph analysis: graph type, correlation type, and how to deal with negative correlations. As all these properties were set in GUIfMRIGraphAnalysis, here all the popup menus are disabled and the properties cannot be changed. If the user wishes to change any of the properties, a new graph analysis should be started.
- `View community` opens the interface to view the community structure that is set. Also the community structure cannot be changed.
- `New analysis` opens a new GUIfMRIGraphAnalysis interface where a new graph analysis with different parameters can be launched.
- **Measure list** lists all measures available for calculation for weighted graphs. The user can choose which measure to calculate by checking the checkboxes next to them.
- `Calculate Group Measures` opens an interface allowing the user to set parameters to calculate the selected measures.
- `Compare Group Measures` opens an interface allowing the user to set parameters to compare the selected measures between two groups.
- `Compare With Random Graphs` opens an interface allowing the user to set parameters to compare the selected measures with random graphs.

Main panel

The main panel consists of a main table that displays different information about the graph analysis and the calculated measures. The console buttons are used to switch between the various types of information shown in the table. The following information can be displayed:

- `Correlation Matrix` visualizes the connectivity matrix based on the parameters set on the right. For more detailed information about how to visualize the connectivity matrix please refer to the section *Main view* in the chapter fMRI Graph Analysis.
- `Global Measures` allows the user to visualize global measures.
- `Nodal Measures` allows the user to visualize nodal measures.
- `Brain View` allows the user to visualize the brain graph and the calculated nodal measures on a brain surface.

Menu

`File` provides various options for importing and saving an fMRI graph analysis WU:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an fMRI graph analysis WU saved in **.fga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIfMRIGraphAnalysisWU.
- `File` → `Save` (`Ctrl+S`) saves the current fMRI graph analysis WU in **.fga* format.
- `File` → `Save as` opens a popup window to save the current fMRI graph analysis WU in **.fga* format possibly in a different file.
- `File` → `Import (xml)` imports an fMRI graph analysis WU from an xml file.
- `File` → `Export (xml)` exports the current fMRI graph analysis WU to an xml file.

`View` switches the main view to display various types of information:

- `View` → `Correlation Matrix` visualizes the connectivity matrix.
- `View` → `Global Measures` visualizes global measures.
- `View` → `Nodal Measures` visualizes nodal measures.
- `View` → `Brain View` visualizes the data on a brain surface.

`Figure` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIfMRIGraphAnalysisWU and BRAPH.

Toolbar

The toolbar provides different options to open and save the fMRI graph analysis WU and visualize the figures. It is shown in figure 101.

Figure 101: fMRIGraphAnalysisWU toolbar.

Open and save commands

These commands allow the user to open and save an fMRI graph analysis WU in the **.fga* format. These are equivalent to the open and save menu options in the `File` menu.

opens a popup window to load an fMRI graph analysis WU saved in **.fga* format.

saves the current fMRI graph analysis WU in **.fga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations.

zooms in image.

zooms out image.

drags image.

shows/hides data cursor.

shows color scale.

standard 3D view.

sagittal left view.

sagittal right view.

axial dorsal view.

axial ventral view.

coronal anterior view.

coronal posterior view.

switches brain surface on/off.

switches axis on/off.

switches grid on/off.

SYM switches brain region symbols on/off.

`SPH` switches brain region spheres on/off.

`LAB` switches brain region labels on/off.

fMRI Graph Analysis BUT

GUIfMRIGraphAnalysisBUT is a graphical user interface that allows the user to perform a brain graph analysis of fMRI data using binary undirected graphs at a fixed threshold (BUT = Binary Undirected Threshold). The user can calculate group measures, compare them with random graphs, and compare the measures of two groups by permutation test. Significance intervals and single/double-tailed p-values are provided (the p-values can be corrected for false discovery rate (FDR) in the case of nodal measures). Global and nodal measures are displayed separately; for nodal measures the user has the option to visualize the results on a brain surface. The graph analysis can be saved in a file **.fga* for future use within BRAPH; it can also be exported in xml format for use within other programs.

The layout of GUIfMRIGraphAnalysisBUT is shown in figure 102. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIfMRIGraphAnalysisBUT, including loading and saving an fMRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an fMRI graph analysis.
- **Cohort panel** permits one to view the fMRI cohort properties.
- **Graph analysis panel** permits one to choose which measures to calculate or compare, view the community structure, and, if needed, start a new graph analysis.

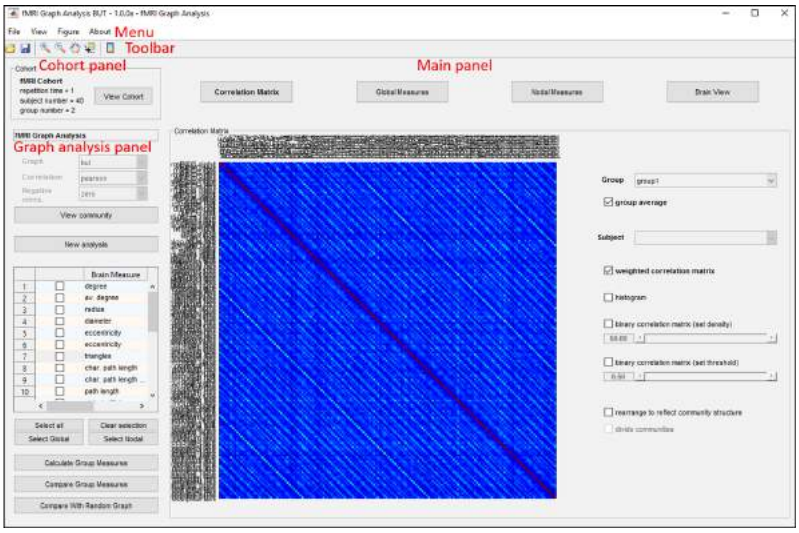


Figure 102: Snapshot of GUIfMRIGraphAnalysisBUT. On the top, there are the menu and the toolbar; below, there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right).

- **Main panel** allows one to view the connectivity matrix as well as the calculated global and nodal measures and comparisons.

Getting Started

As a first example of the use of GUIfMRIGraphAnalysisBUT, we will proceed to calculate some global (average degree, diameter) and local (degree, triangles) measures, and to compare the results for two groups. Then, we will visualize these results and the graph on the brain surface. Finally, we will save the graph analysis in a **.fga* file.

1. In the graph analysis view, select from the list of measures the average degree, diameter, degree, and triangles measures.

   To quickly select more than one measure, use the buttons below the measure list:

   - `Select all` selects all the measures.
   - `Clear selection` clears the current selection.
   - `Select Global` selects all global measures.
   - `Clear Nodal` selects all nodal measures.

2. Push `Calculate Group Measures` in the graph analysis panel (figure 102) to calculate the selected measures. This opens a new interface, shown in figure 103. On the left of the interface, there is a list with the selected measures to be calculated. On the right,

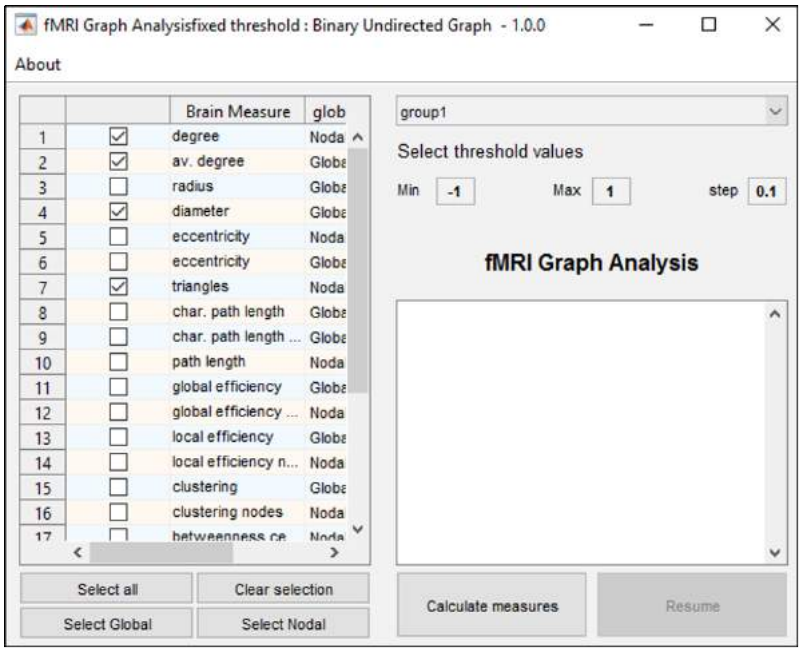


Figure 103: Interface to calculate group measures.

there are a popup menu to select the group for which the measures will be calculated and a series of fields to enter the threshold values (including the minimum threshold, the maximum threshold, and the threshold step). The calculation is started by pushing `Calculate measures`. When the calculation is in progress, the status of the button changes to `stop` and pushing it stops the calculation; the calculation can then be resumed by pressing `Resume`.

3. Push `Compare with Random Graph` in the graph analysis panel (figure 102) to calculate measures that are normalized by the results obtained from random graphs. This opens the interface shown in figure 104. This interface is analogous to that to calculate group measures, which we have seen in the previous step, but two new parameters can be inputted:

   - **random matrix no.** sets how many random graphs are used in the comparison.
   - **random swaps no.** sets how many times each edge is rewired to randomize the original graph.

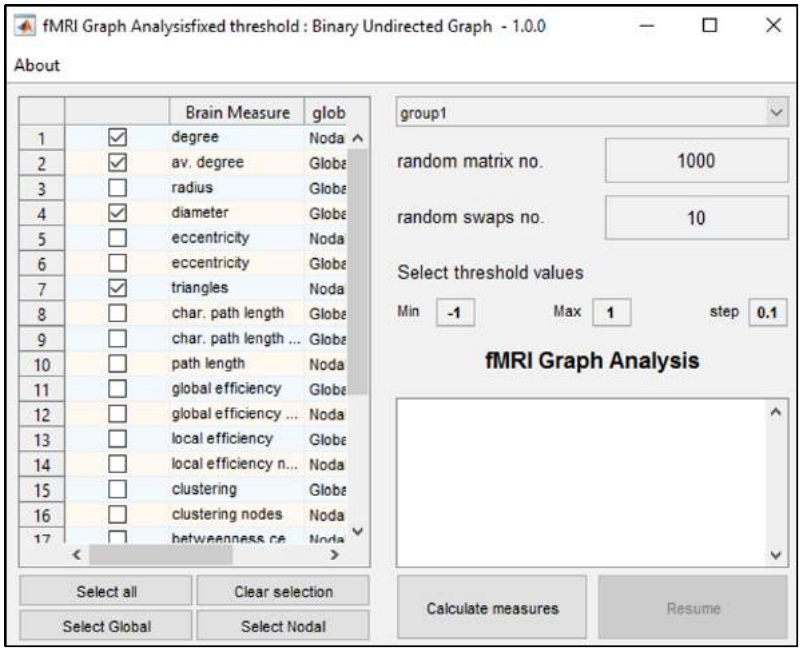


Figure 104: Interface to calculate group measures normalized by comparison with random graphs.

4. Push `Compare Group Measures` in the graph analysis panel (figure 102) to compare the measures between two groups. This opens the interface shown in figure 105. This interface is analogous to that to calculate group measures, but with two new parameters:

   - **permutation number** sets how many permutations are performed in the permutation test.

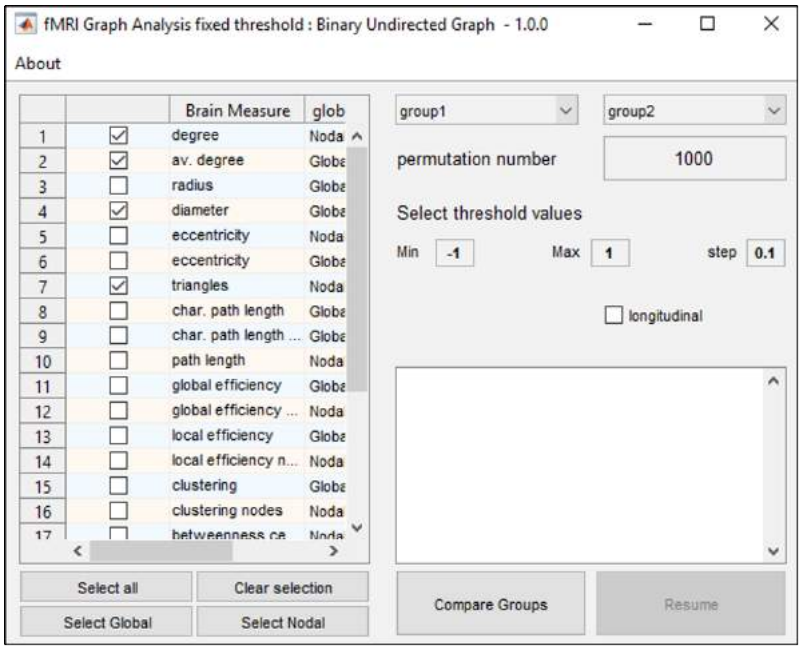


Figure 105: Interface to compare the measures of two groups.

- **longitudinal** sets whether the comparison is done for longitudinal data.

5. Push `Global Measures` in the main panel to visualize the results for the global measures (figure 106).

   If the **measure** checkbox is checked, group measures are displayed (the measure and the group are selected using the popup menus at the bottom). If the **comparison** checkbox is checked, comparisons between two groups are displayed (the measure and the groups

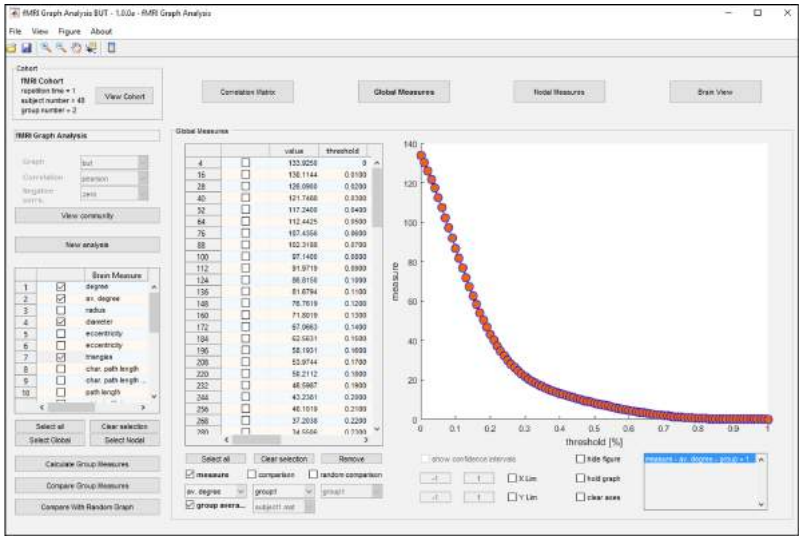


Figure 106: Global measures tab. Here the average degree is shown as a function of the threshold.

are selected using the popup menus at the bottom). If the **random comparison** checkbox is checked, measures normalized by comparison with random graphs are displayed (the measure and the group are selected using the popup menus at the bottom). By default the **group average** checkbox is checked; the results shown are averaged over all group subjects. To view the measure for each subject separately, uncheck this checkbox and select the subject from the neighboring popup menu.

The main panel now shows two parts:

(a) A **table view** on the left shows the numerical information about the selected measure. Among other data, this includes the value of the measure, the group for which it was calculated, and the density and threshold of the graph on which it was calculated. If it is a comparison between groups or with random graphs, the difference between the values and the single/double-tailed p-values are also displayed. A series of options are available below the table view:

- `Select all` selects all the measures.
- `Clear selection` clears the current selection.
- `Remove` removes the selected measure.

(b) A **graph view** plots a graph of the selected measure as a function of threshold. By pressing `Ctrl+F` the graph can be exported as a figure that can be customized using the standard MatLab plotting tools; then, the figure can be exported in several standard graphic formats. Below the graph, several options are available to customize the plot:

- **show confidence intervals** shows the 95% confidence intervals as shown in figure 107. This option is only available for comparisons between groups and with random graphs. As can be seen in the figure 107 by right-clicking on the confidence intervals, a popup menu appears which allows the user to change the properties of the data values, lower, middle, and higher borders of the confidence interval as well as of the area plot properties.
- When **X Lim** is checked, the x-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **Y Lim** is checked, the y-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **hide figure** is checked, the graph is hidden and the table is extended.

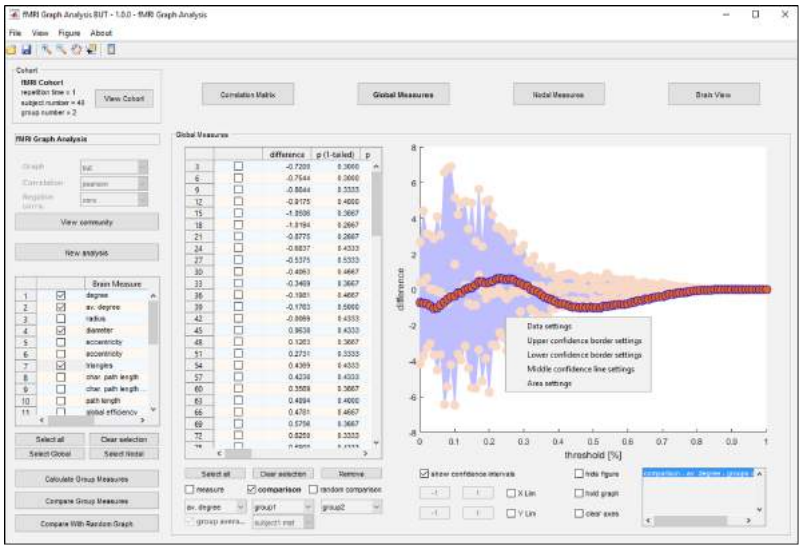


Figure 107: Confidence intervals when comparing two groups.

- When **hold graph** is checked, more than one data set can be plotted on the same graph. The plotted measures are listed below the graph on the right.
- **clear axes** erases all the data plotted on the graph.

6. Push `Nodal Measures` in the main panel to visualize the results for nodal measures (figure 108). This interface is very similar to that explained above for the global measures. The main difference is that now it is possible to select also the brain region.

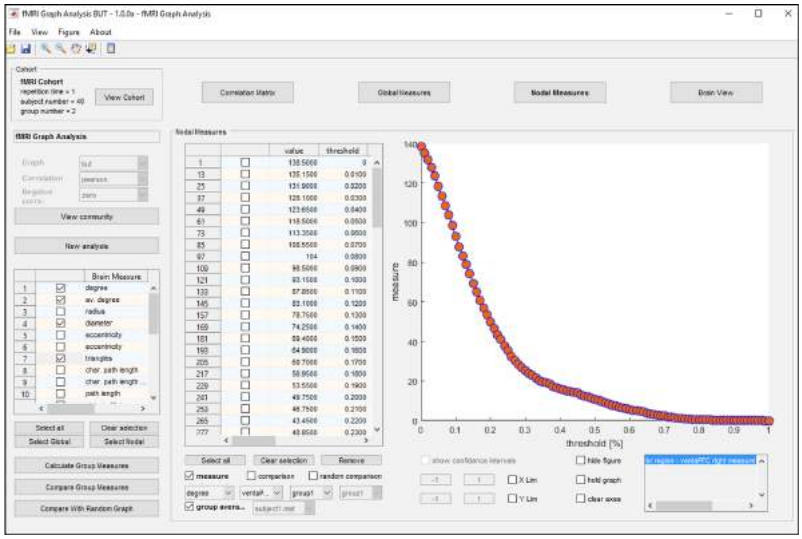


Figure 108: Nodal measures tab.

7. Push `Brain View` in the main panel to visualize the nodal measures on a brain surface. By pushing the buttons at the bottom of

this panel, the user can visualize the brain graph, the group measures, the comparisons between two groups, and the comparisons with random graphs.

- `View brain graph` visualizes the brain graph, as shown in figure 109. The graph parameters that can be specified are:
  - **fix density** draws the binary brain graph with the selected density of connections. The density can be specified by entering the value in the corresponding field or by using the slider.
  - **fix threshold** draws the binary brain graph with all connections having larger weight than the given threshold. The threshold can be specified by entering the value in the corresponding field or by using the slider.
  - **weighted** plots all the connection of the weighted brain graph. The weight of the connections can be encoded by color and/or thickness (by checking the corresponding checkboxes).
  - `Show` shows the current graph on the brain surface.
  - `Hide` hides the current graph from the brain surface.
  - `Color` plots the current graph in the specified color.
  - **Set thickness** sets the thickness of the connections.

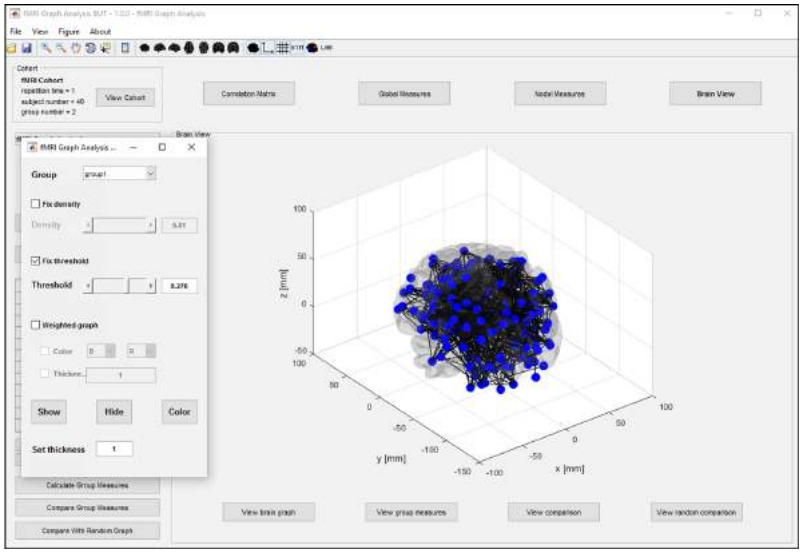


Figure 109: Visualization of the brain graph on the brain surface.

- `View group measures` visualizes the nodal measures calculated for a given group, as shown in figure 110.[41] The group for which the measures are to be shown is selected from the popup menu in the top left. In the first list below it, the user can select

[41] For more information about the rescaling and the filters needed to be applied to visualize the data, refer to the *Main panel* subsection in the chapter MRI Cohort.

the measure; the list on the left shows the thresholds for which the measure have been calculated.

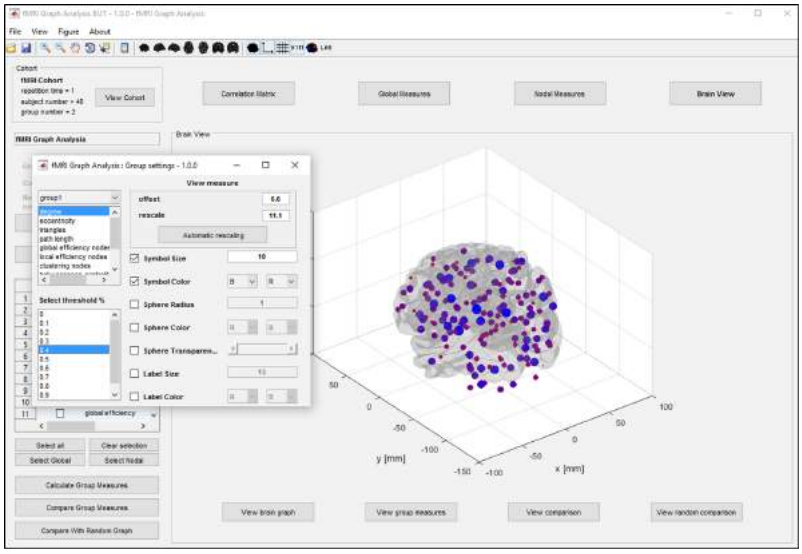


Figure 110: Visualization of the nodal measures on the brain surface.

- `View comparison` visualizes the comparison between two groups, as shown in figure 111. The two popup menus on the left specify the two groups that are compared and the lists below them show the measures and the thresholds for which they have been calculated. The other functionalities are analogous to the interface for viewing group measures with two new options:
  - **fdr (1-tailed)**, if checked, corrects the p-values for single-tailed false discovery rate. Only brain regions with significant

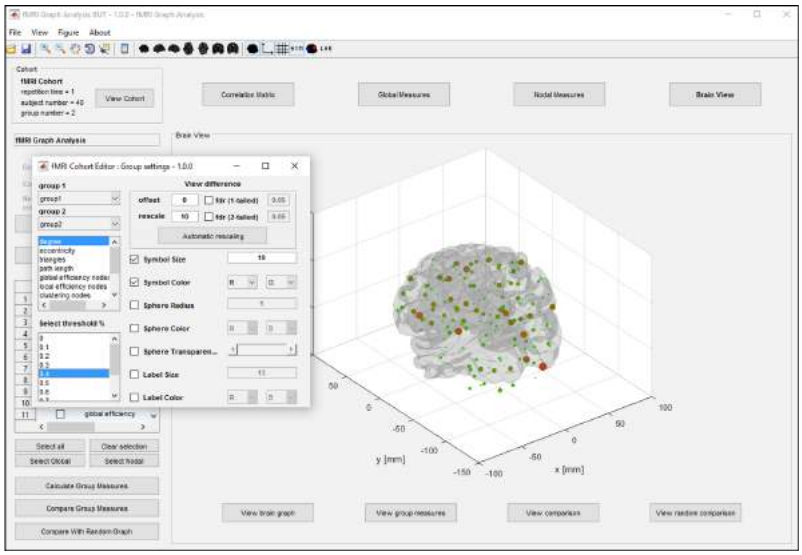


Figure 111: Visualization of the comparison between two groups on the brain surface.

p-values are then shown on the brain surface.

  - **fdr (2-tailed)**, if checked, corrects the p-values for double-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.

- `View random comparison` visualizes the measures normalized by comparing them with random graphs, as shown in figure 112. All the functionalities of this interface are analogous to those of the interface to visualize a comparison between groups.

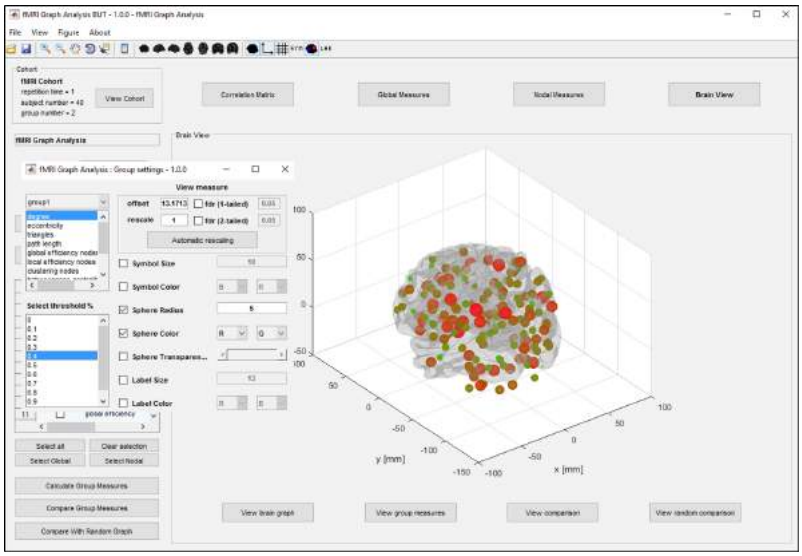


Figure 112: Visualization of the measures normalized by random comparison on the brain surface.

- `Select File` → `Save` to save the fMRI graph analysis BUT as a *.fga file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.
- `Select File` → `Open` to open an fMRI graph analysis BUT previously saved with GUIfMRIGraphAnalysisBUT; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

Cohort panel

The cohort is already uploaded when GUIfMRIGraphAnalysisBUT is launched. The cohort view shows the cohort's properties including name, number of subjects, and groups. Moreover, all cohort's properties can be viewed in the GUIfMRICohort interface with restricted access by pushing `View Cohort`.

Graph analysis panel

The graph analysis panel shows the information relative to the graph analysis and gives the user the ability to calculate measures. The available features are:

- **Graph analysis properties**. These three popup menus show the properties of the graph analysis: graph type, correlation type, and how to deal with negative correlations. As all these properties were set in GUIfMRIGraphAnalysis, here all the popup menus are disabled and the properties cannot be changed. If the user wishes to change any of the properties, a new graph analysis should be started.
- `View community` opens the interface to view the community structure that is set. Also the community structure cannot be changed.
- `New analysis` opens a new GUIfMRIGraphAnalysis interface where a new graph analysis with different parameters can be launched.
- **Measure list** A list of all measures available for calculation for binary graphs. The user can choose which measure to calculate by checking the checkboxes next to them.
- `Calculate Group Measures` opens an interface allowing the user to set parameters to calculate the selected measures.
- `Compare Group Measures` opens an interface allowing the user to set parameters to compare the selected measures between two groups.
- `Compare With Random Graphs` opens an interface allowing the user to set parameters to compare the selected measures with random graphs.

Main panel

The main panel consists of a main table that displays different information about the graph analysis and calculated measures. The console buttons are used to switch between the various types of information shown in the table. The following information can be displayed:

- `Correlation Matrix` visualizes the connectivity matrix based on the parameters set on the right. For more detailed information about how to visualize the connectivity matrix please refer to section *Main view* of the chapter fMRI Graph Analysis.

- `Global Measures` allows the user to visualize global measures.
- `Nodal Measures` allows the user to visualize nodal measures.
- `Brain View` allows the user to visualize the brain graph and the calculated nodal measures on a brain surface.

Menu

`File` provides various options for importing and saving an fMRI graph analysis BUT:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an fMRI graph analysis BUT saved in **.fga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIfMRIGraphAnalysisBUT.
- `File` → `Save` (`Ctrl+S`) saves the current fMRI graph analysis BUT in **.fga* format.
- `File` → `Save as` opens a popup window to save the current fMRI graph analysis BUT in **.fga* format possibly in a different file.
- `File` → `Import (xml)` imports an fMRI graph analysis BUT from an xml file.
- `File` → `Export (xml)` exports the current fMRI graph analysis BUT to an xml file.

`View` switches the main view to display various types of information:

- `View` → `Correlation Matrix` visualizes the connectivity matrix.
- `View` → `Global Measures` visualizes global measures.
- `View` → `Nodal Measures` visualizes nodal measures.
- `View` → `Brain View` visualizes the data on a brain surface.

`Figure` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIfMRIGraphAnalysisBUT and BRAPH.

Toolbar

The toolbar provides different options to open and save the fMRI graph analysis BUT and visualize the figures. It is shown in figure 113.

Figure 113: fMRIGraphAnalysisBUT toolbar.

Open and save commands

These commands allow the user to open and save an fMRI graph analysis BUT in the **.fga* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an fMRI graph analysis BUT saved in **.fga* format.

 saves the current fMRI graph analysis BUT in **.fga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations.

 zooms in image.

 zooms out image.

 drags image.

 shows/hides data cursor.

 shows color scale.

 standard 3D view.

 sagittal left view.

 sagittal right view.

 axial dorsal view.

 axial ventral view.

 coronal anterior view.

 coronal posterior view.

 switches brain surface on/off.

 switches axis on/off.

 switches grid on/off.

 switches brain region symbols on/off.

 switches brain region spheres on/off.

 switches brain region labels on/off.

fMRI Graph Analysis BUD

GUIfMRIGraphAnalysisBUD is a graphical user interface that allows the user to perform a brain graph analysis of fMRI data using binary undirected graphs at a fixed density of connections (BUD = Binary Undirected Density). The user can calculate group measures, compare them with random graphs, and compare the measures of two groups by permutation test. Significance intervals and single/double-tailed p-values are provided (the p-values can be corrected for false discovery rate (FDR) in the case of nodal measures). Global and nodal measures are displayed separately; for nodal measures the user has the option to visualize the results on a brain surface. The graph analysis can be saved in a file **.fga* for future use within BRAPH; it can also be exported in xml format for use within other programs.

The layout of GUIfMRIGraphAnalysisBUD is shown in figure 114. It is composed of five main work areas:

- **Menu** permits one to access the basic functionalities of GUIfMRIGraphAnalysisBUD, including loading and saving an MRI graph analysis.
- **Toolbar** gives direct access to some of the most commonly employed functionalities, in particular loading and saving an fMRI graph analysis.
- **Cohort panel** permits one to view the fMRI cohort properties.
- **Graph analysis panel** permits one to choose which measures to calculate or compare, view the commu-

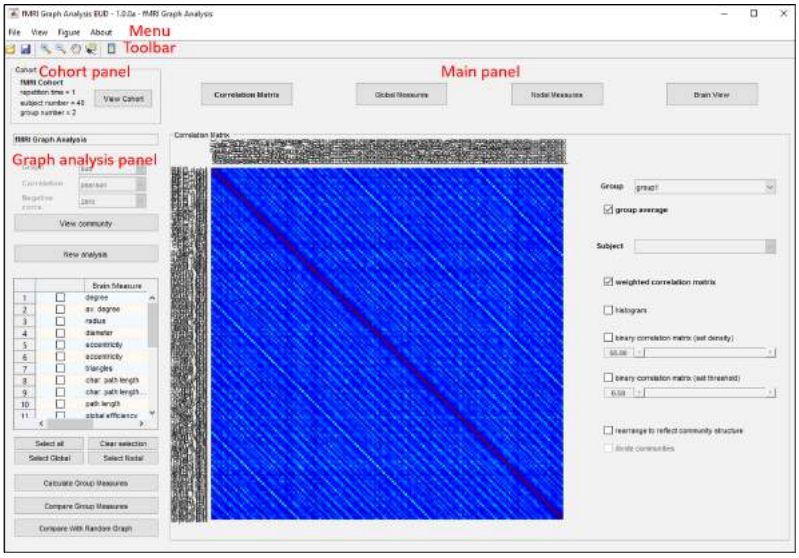


Figure 114: Snapshot of GUIfMRIGraph-AnalysisBUD. On the top, there are the menu and the toolbar; below, there are the cohort panel and the graph analysis panel (on the left), and the main panel (on the right).

nity structure, and, if needed, start a new graph analysis.

- **Main panel** allows one to view the connectivity matrix as well as the calculated global and nodal measures and comparisons.

Getting Started

As a first example of the use of GUIfMRIGraphAnalysisBUD, we will proceed to calculate some global (average degree, diameter) and local (degree, triangles) measures, and to compare the results for two groups. Then, we will visualize these results and the graph on the brain surface. Finally, we will save the graph analysis in a **.fga* file.

1. In the graph analysis view, select from the list of measures the average degree, diameter, degree, and triangles measures.

   To quickly select more than one measure, use the buttons below the measure list:

   - `Select all` selects all the measures.
   - `Clear selection` clears the current selection.
   - `Select Global` selects all global measures.
   - `Clear Nodal` selects all nodal measures.

2. Push `Calculate Group Measures` in the graph analysis panel (figure 114) to calculate the selected measures. This opens a

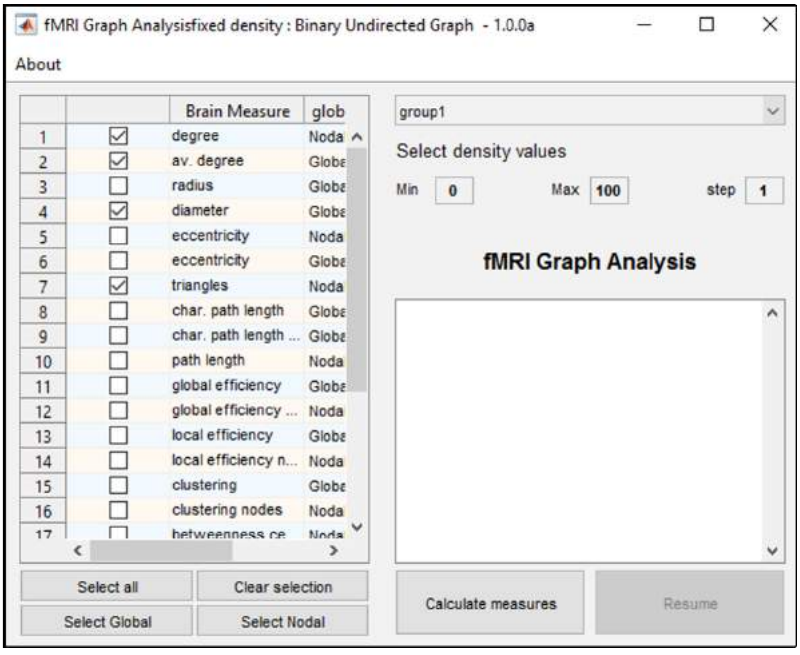


Figure 115: Interface to calculate group measures.

new interface, shown in figure 115. On the left of the interface, there is a list with the selected measures to be calculated. On the right, there are a popup menu to select the group for which the measures will be calculated and a series of fields to enter the density values (including the minimum density, the maximum density, and the density step). The calculation is started by pushing `Calculate measures`. When the calculation is in progress, the status of the button changes to `stop` and pushing it stops the calculation; the calculation can then be resumed by pressing `Resume`.

3. Push `Compare with Random Graph` in the graph analysis panel (figure 114) to calculate measures that are normalized by the results obtained from random graphs. This opens the interface shown in figure 116. This interface is analogous to that to calculate group measures, which we have seen in the previous step, but two new parameters can be inputted:

   - **random matrix no.** sets how many random graphs are used in the comparison.
   - **random swaps no.** sets how many times each edge is rewired to randomize the original graph.

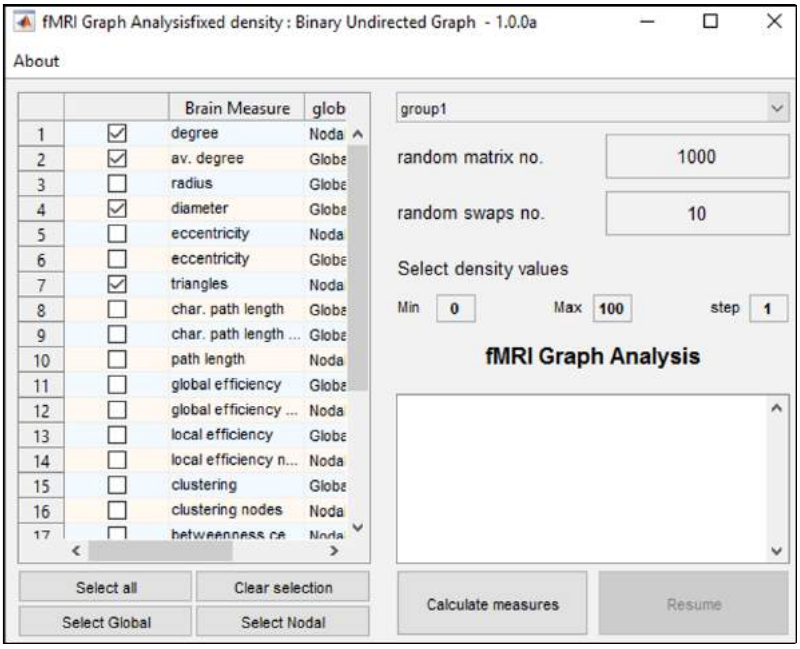


Figure 116: Interface to calculate group measures normalized by comparison with random graphs.

4. Push `Compare Group Measures` in the graph analysis panel (figure 114) to compare the measures between two groups. This opens

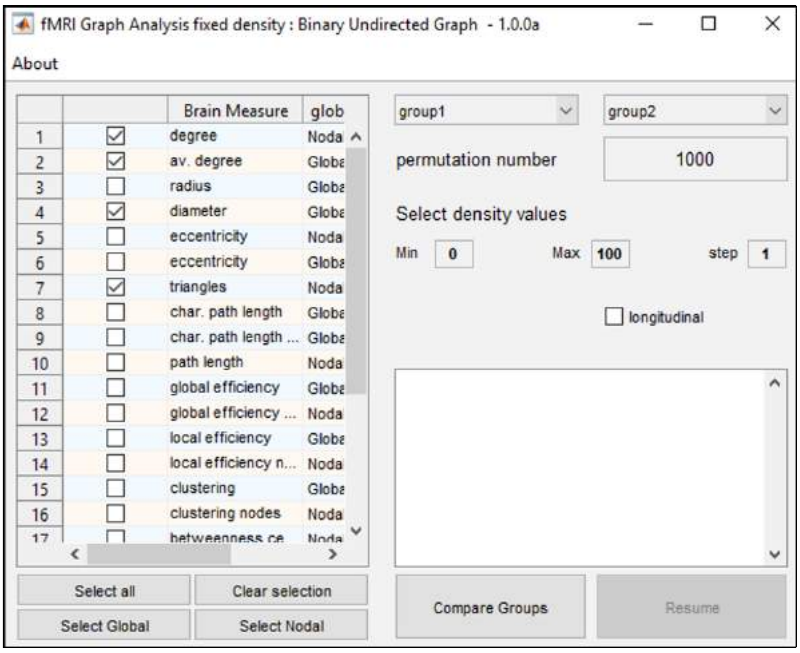


Figure 117: Interface to compare the measures of two groups.

the interface shown in figure 117. This interface is analogous to that to calculate group measures, but with two new parameters:

- **permutation number** sets how many permutations are performed in the permutation test.
- **longitudinal** sets whether the comparison is done for longitudinal data.

5. Push `Global Measures` in the main panel to visualize the results

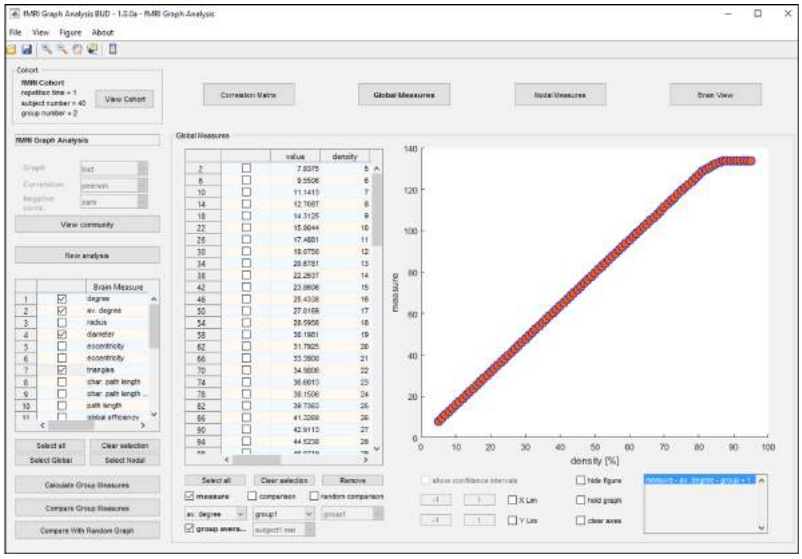


Figure 118: Global measures tab. Here the average degree is shown as a function of the density.

for the global measures (figure 118).

If the **measure** checkbox is checked, group measures are displayed (the measure and the group are selected using the popup menus at the bottom). If the **comparison** checkbox is checked, comparisons between two groups are displayed (the measure and the groups are selected using the popup menus at the bottom). If the **random comparison** checkbox is checked, measures normalized by comparison with random graphs are displayed (the measure and the group are selected using the popup menus at the bottom). By default the **group average** checkbox is checked; the results shown are averaged over all group subjects. To view the measure for each subject separately, uncheck this checkbox and select the subject from the neighboring popup menu.

The main panel now shows two parts:

(a) A **table view** on the left shows the numerical information about the selected measure. Among other data, this includes the value of the measure, the group for which it was calculated, and the density and threshold of the graph on which it was calculated. If it is a comparison between groups or with random graphs, the difference between the values and the single/double-tailed p-values are also displayed. A series of options are available below the table view:

- `Select all` selects all the measures.
- `Clear selection` clears the current selection.
- `Remove` removes the selected measure.

(b) A **graph view** plots a graph of the selected measure as a function of density. By pressing `Ctrl+F` the graph can be exported as a figure that can be customized using the standard MatLab plotting tools; then, the figure can be exported in several standard graphic formats. Below the graph, several options are available to customize the plot:

- **show confidence intervals** shows the 95% confidence intervals as shown in figure 119. This option is only available for comparisons between groups and with random graphs. As can be seen in the figure 119 by right-clicking on the confidence intervals, a popup menu appears which allows the user to change the properties of the data values, lower, middle and higher borders of the confidence interval as well as of the area plot properties.
- When **X Lim** is checked, the x-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.

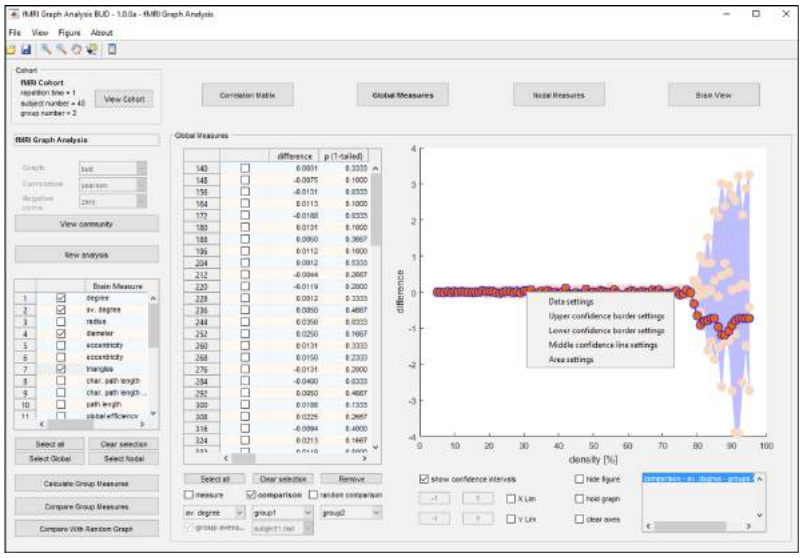


Figure 119: Confidence intervals when comparing two groups.

- When **Y Lim** is checked, the y-limits of the axes can be entered from the two neighboring edit boxes. If not checked, the limits are automatically set.
- When **hide figure** is checked, the graph is hidden and the table is extended.
- When **hold graph** is checked, more than one data set can be plotted on the same graph. The plotted measures are listed below the graph on the right.
- **clear axes** erases all the data plotted on the graph.

6. Push `Nodal Measures` in the main panel to visualize the results

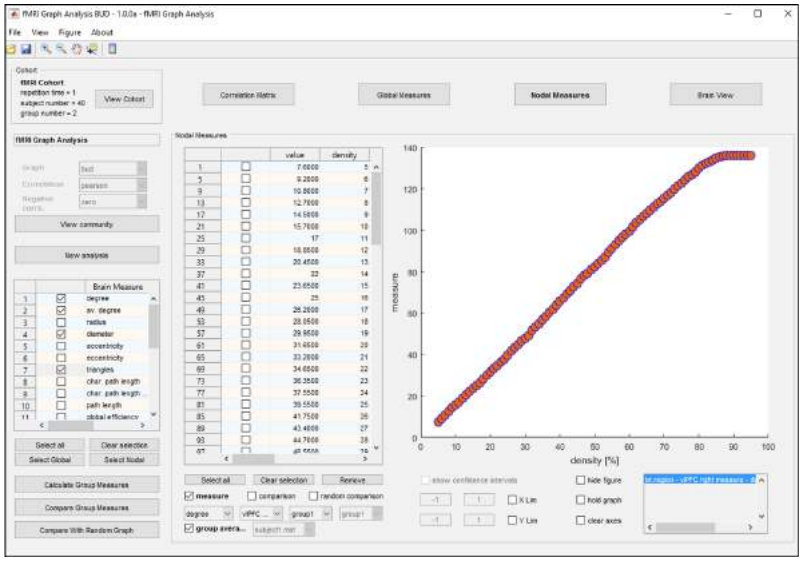


Figure 120: Nodal measures tab.

for nodal measures (figure 120). This interface is very similar to that explained above for the global measures. The main difference is that now it is possible to select also the brain region.

7. Push `Brain View` in the main panel to visualize the nodal measures on a brain surface. By pushing the buttons at the bottom of this panel, the user can visualize the brain graph, the group measures, the comparisons between two groups, and the comparisons with random graphs.

   - `View brain graph` visualizes the brain graph, as shown in figure 121. The graph parameters that can be specified are:
     - **fix density** draws the binary brain graph with the selected density of connections. The density can be specified by entering the value in the corresponding field or by using the slider.
     - **fix threshold** draws the binary brain graph with all connections having larger weight than the given threshold. The threshold can be specified by entering the value in the corresponding field or by using the slider.
     - **weighted** plots all the connection of the weighted brain-graph. The weight of the connections can be encoded by color and/or thickness (by checking the corresponding check-boxes).
     - `Show` shows the current graph on the brain surface.
     - `Hide` hides the current graph from the brain surface.
     - `Color` plots the current graph in the specified color.
     - **Set thickness** sets the thickness of the connections.

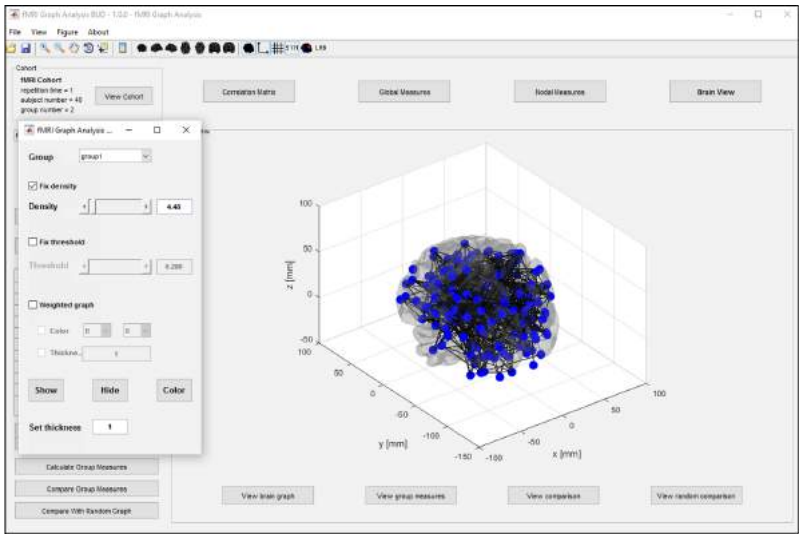


Figure 121: Visualization of the brain graph on the brain surface.

- `View group measures` visualizes the nodal measures calculated for a given group, as shown in figure 122.[42] The group for which the measures are to be shown is selected from the popup menu in the top left. In the first list below it, the user can select the measure; the list on the left shows the densities for which the measure have been calculated.

[42] For more information about the rescaling and the filters needed to be applied to visualize the data, refer to the *Main panel* subsection in the chapter MRI Cohort.

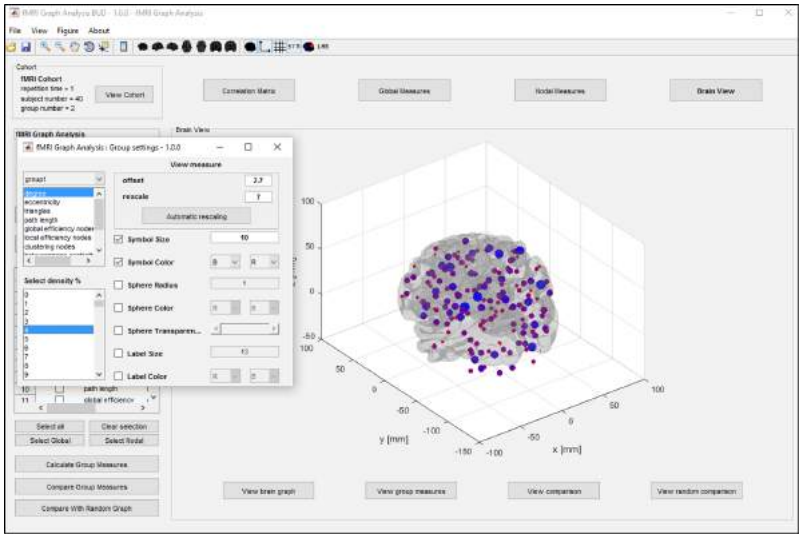


Figure 122: Visualization of the nodal measures on the brain surface.

- `View comparison` visualizes the comparison between two groups, as shown in figure 123. The two popup menus on the left specify the two groups that are compared and the lists below them show the measures and the densities for which they have been calculated. The other functionalities are analogous to the interface for viewing group measures with two new options:

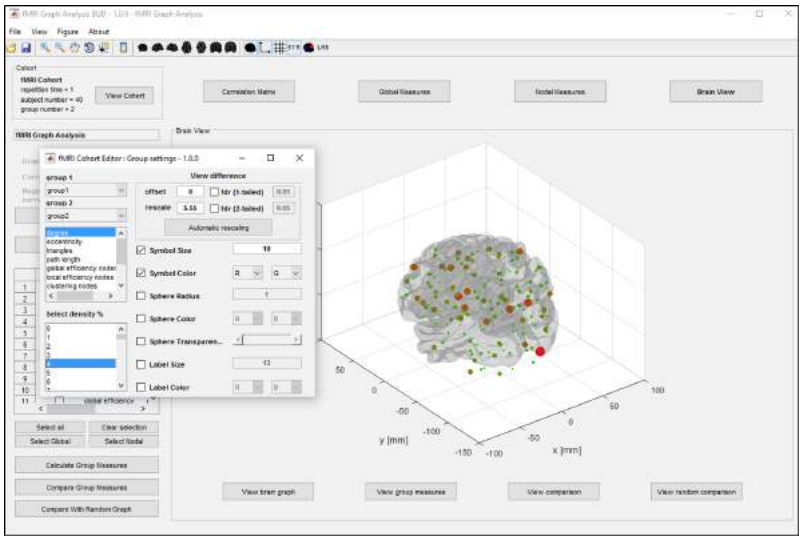


Figure 123: Visualization of the comparison between two groups on the brain surface.

  - **fdr (1-tailed)**, if checked, corrects the p-values for single-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.
  - **fdr (2-tailed)**, if checked, corrects the p-values for double-tailed false discovery rate. Only brain regions with significant p-values are then shown on the brain surface.
- `View random comparison` visualizes the measures normalized by comparing them with random graphs, as shown in figure 124. All the functionalities of this interface are analogous to those of the interface to visualize a comparison between groups.

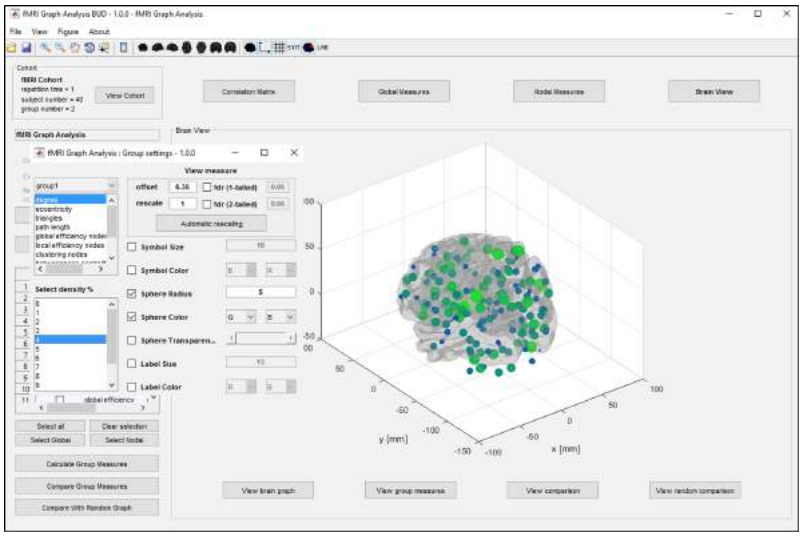


Figure 124: Visualization of the measures normalized by random comparison on the brain surface.

- `Select File` → `Save` to save the fMRI graph analysis BUD as a *.fga file; alternatively you can also use the shortcut `Ctrl+S` or the `Save` icon on the toolbar.
- `Select File` → `Open` to open an fMRI graph analysis BUD previously saved with GUIfMRIGraphAnalysisBUD; alternatively you can also use the shortcut `Ctrl+O` or the `Open` icon on the toolbar.

Additional information

Cohort panel

The cohort is already uploaded when GUIfMRIGraphAnalysisBUD is launched. The cohort view shows the cohort's properties including name, number of subjects, and groups. Moreover, all cohort's properties can be viewed in the GUIfMRICohort interface with restricted access by pushing `View Cohort`.

Graph analysis panel

The graph analysis panel shows the information relative to the graph analysis and gives the user the ability to calculate measures. The available features are:

- **Graph analysis properties**. These three popup menus show the properties of the graph analysis: graph type, correlation type, and how to deal with negative correlations. As all these properties were set in GUIfMRIGraphAnalysis, here all the popup menus are disabled and the properties cannot be changed. If the user wishes to change any of the properties, a new graph analysis should be started.
- `View community` opens the interface to view the community structure that is set. Also the community structure cannot be changed.
- `New analysis` opens a new GUIfMRIGraphAnalysis interface where a new graph analysis with different parameters can be launched.
- **Measure list** lists all measures available for calculation for binary graphs. The user can choose which measure to calculate by checking the checkboxes next to them.
- `Calculate Group Measures` opens an interface allowing the user to set parameters to calculate the selected measures.
- `Compare Group Measures` opens an interface allowing the user to set parameters to compare the selected measures between two groups.
- `Compare With Random Graphs` opens an interface allowing the user to set parameters to compare the selected measures with random graphs.

Main panel

The main panel consists of a main table that displays different information about the graph analysis and calculated measures. The console buttons are used to switch between the various types of information shown in the table. The following information can be displayed:

- `Correlation Matrix` visualizes the connectivity matrix based on the parameters set on the right. For more detailed information about how to visualize the connectivity matrix please refer to section *Main view* of the chapter fMRI Graph Analysis.

- `Global Measures` allows the user to visualize global measures.
- `Nodal Measures` allows the user to visualize nodal measures.
- `Brain View` allows the user to visualize the brain graph and the calculated nodal measures on a brain surface.

Menu

`File` provides various options for importing and saving an fMRI graph analysis BUD:

- `File` → `Open` (`Ctrl+O`) opens a popup window to load an fMRI graph analysis BUD saved in **.fga* format.
- `File` → `Close` (`Ctrl+C`) closes the GUIfMRIGraphAnalysisBUD.
- `File` → `Save` (`Ctrl+S`) saves the current fMRI graph analysis BUD in **.fga* format.
- `File` → `Save as` opens a popup window to save the current fMRI graph analysis BUD in **.fga* format possibly in a different file.
- `File` → `Import (xml)` imports an fMRI graph analysis BUD from an xml file.
- `File` → `Export (xml)` exports the current fMRI graph analysis BUD to an xml file.

`View` switches the main view to display various types of information:

- `View` → `Correlation Matrix` visualizes the connectivity matrix.
- `View` → `Global Measures` visualizes global measures.
- `View` → `Nodal Measures` visualizes nodal measures.
- `View` → `Brain View` visualizes the data on a brain surface.

`Figure` → `Generate figure` (`Ctrl+F`) generates a figure that can be customized using the standard MatLab plotting tools. The figure can then be exported in several standard graphic formats.

`About` → `About` provides information about the current version of GUIfMRIGraphAnalysisBUD and BRAPH.

Toolbar

The toolbar provides different options to open and save the fMRI graph analysis BUD and visualize the figures. It is shown in figure 125.

Figure 125: fMRIGraphAnalysisBUD toolbar.

Open and save commands

These commands allow the user to open and save an fMRI graph analysis BUD in the **.fga* format. These are equivalent to the open and save menu options in the `File` menu.

 opens a popup window to load an fMRI graph analysis BUD saved in **.fga* format.

 saves the current fMRI graph analysis BUD in **.fga* format.

Visualization commands

These commands allow the user to control the visualization of the graphical representations.

 zooms in image.

 zooms out image.

 drags image.

 shows/hides data cursor.

 shows color scale.

 standard 3D view.

 sagittal left view.

 sagittal right view.

 axial dorsal view.

 axial ventral view.

 coronal anterior view.

 coronal posterior view.

 switches brain surface on/off.

 switches axis on/off.

 switches grid on/off.

 switches brain region symbols on/off.

 switches brain region spheres on/off.

 switches brain region labels on/off.