Practice in resting-state fMRI (rs-fMRI) Analysis: PART III

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Course Arrangement

PART I
- REST toolbox http://restfmri.net/forum/index.php?q=rest
- ReHo, ALFF, fALFF, Statistics

PART II
- REST toolbox
- Functional connectivity (seed-based, atlas-based)
- FC strength mapping

Course Arrangement

PART III
- Large-scale network analysis
- Graph theory: topological properties (degree, strength, efficiency, clustering…)

PART IV
- Dynamic functional connectivity

Employed Software/Package

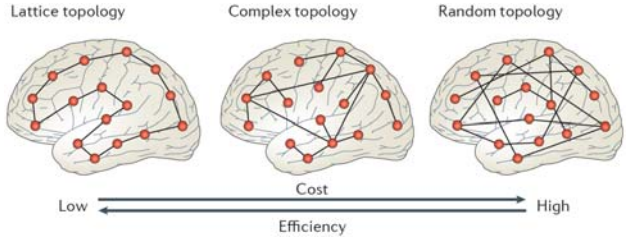
1. **SPM** preprocessing
   - http://www.fil.ion.ucl.ac.uk/spm/
2. **REST** functional connectivity, ReHo, ALFF, fALFF, VMHC
   - http://restfmri.net/forum/index.php?q=rest
3. **IBASPM 64-bit**
   - http://www.ym.edu.tw/~cflu/software/Ibaspm_64.zip
4. **Brain Connectivity Toolbox/Network Based Statistic Toolbox**
   - https://sites.google.com/site/bctnet/
5. **GraphVar**
   - http://www.rfmri.org/graphvar

Complex Network Analysis

Human brain networks

Wiring costs ⇔ efficiency

- Clusters of lattice-like short-distance connections between spatially neighboring nodes
- Topologically direct interconnections between spatially remote brain regions → increase efficiency of information processing
- Nodes aggregated topologically and anatomically as modules → minimize wiring cost



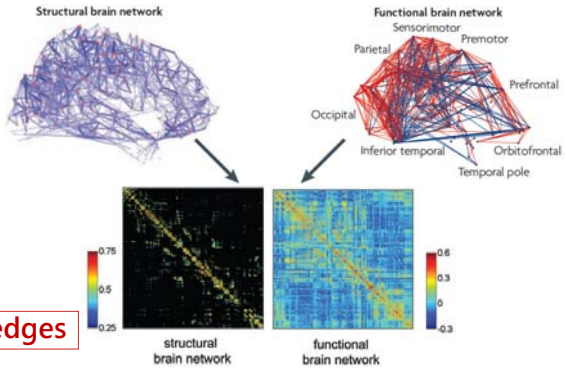
Bullmore et al., Nature Reviews Neuroscience, 13: 336-349, 2012.

Network construction

Nodes
- Cortical regions

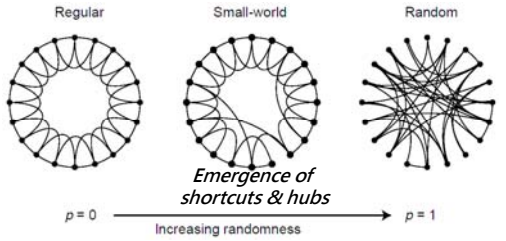
Edges
- Cortical thickness correlations
- Fiber connections
  - DSI, DTI, transneuronal tracers
- Functional connectivity
  - fMRI, EEG, MEG

Network = nodes + edges

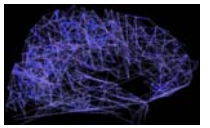


Complex networks

- Brain have a small-world architecture.



Complex networks
- Social network
- WWW internet
- Biological system
- Brain network



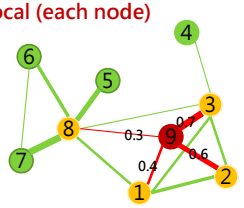
➢ *High local clustering* ➢ *Local segregation*
➢ *Low separation* ➢ *Global integration*

high signal-propagation speed, computational power, and synchronizability

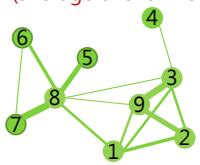
Watts DJ, Strogatz SH, *Nature* 393:440-442, 1998.

Graph theory: topological properties

Local (each node)



Global (average over all nodes)

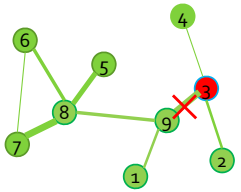


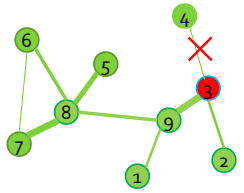
- **degree** (the number of neighbors)
  e.g. degree of node 9 = 4
- **strength** (the connected correlation coefficient)
  e.g. strength of node 9
  = (0.3+0.4+0.6+0.7)/4 = 0.5
- **clustering coefficient** (the connection between neighbors, [0~1])
  e.g. clustering coefficient of node 9
  = 5/6 = 0.83
- **shortest path length (separation)** (the minimal steps for connection)
  e.g. path length from node 9 to node 6
  = 2 steps (9 → 8 → 6)

Salvador et al, *Philos Trans R Soc Lond B Biol Sci*, 360, 937-946, 2005

Network properties

- The topological observations can reveal a "hidden" or "high-level" relations between nodes.





Brain Connectivity Toolbox

NeuroImage 52 (2010) 1059–1069

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Complex network measures of brain connectivity: Uses and interpretations

Mikail Rubinov [a,b,c], Olaf Sporns [d,*]

[a] Black Dog Institute and School of Psychiatry, University of New South Wales, Sydney, Australia
[b] Mental Health Research Division, Queensland Institute of Medical Research, Brisbane, Australia
[c] CSIRO Information and Communication Technologies Centre, Sydney, Australia
[d] Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN 47405, USA

Topological Measurements

Basic Measures
- degree, strength, shortest path length

Measures of integration
- global efficiency

Measures of segregation
- Clustering coefficient, local efficiency, modularity

Measures of centrality
- Betweenness, within-module degree, participation coefficient

Network motifs

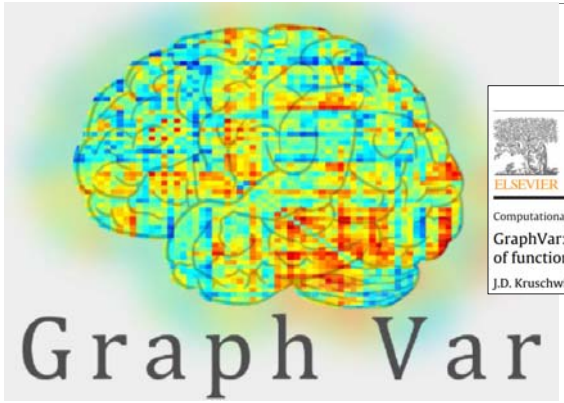
Measures of resilience
- Degree distribution, neighbor degree, assortativity coefficient

Network small-worldness

Network Analysis Using GraphVar

MATLAB R2013b or older version is recommended.

GUI for network analysis




Journal of Neuroscience Methods 245 (2015) 107–115

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

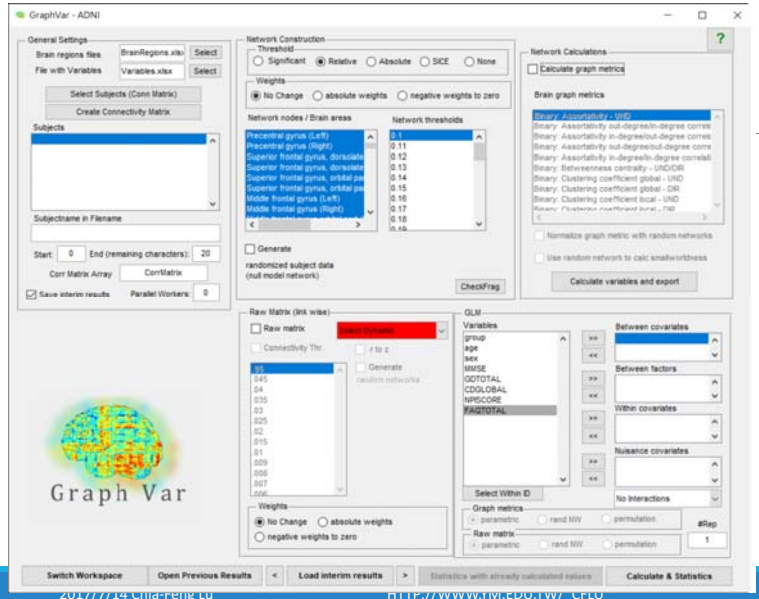
journal homepage: www.elsevier.com/locate/jneumeth

Computational Neuroscience

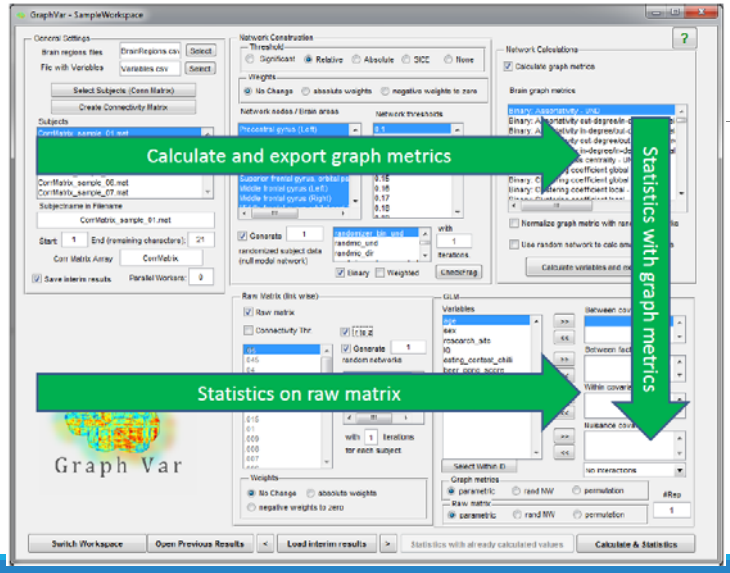
GraphVar: A user-friendly toolbox for comprehensive graph analyses of functional brain connectivity

J.D. Kruschwitz[a,b,*,1], D. List[a,b,*,1], L. Waller[a], M. Rubinov[c], H. Walter[d]

Set Path
>> start_GraphVar



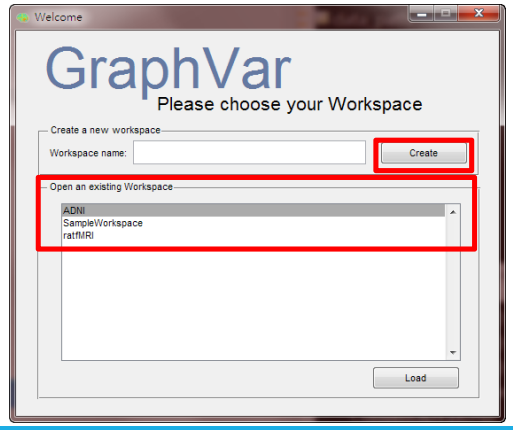
GraphVar
using BCT toolbox



Workflow

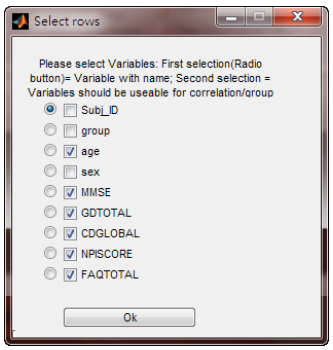
Step 1: Preparation of Workspace

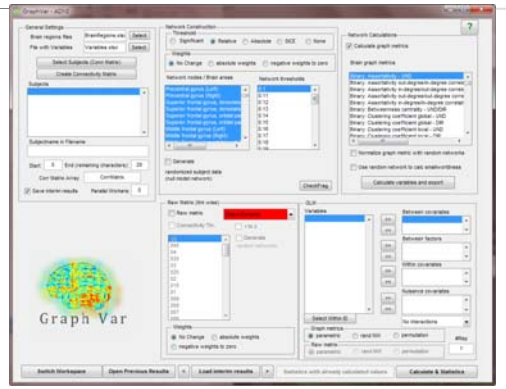
Set Path
>> start_GraphVar



Use pre-prepared workspace folder may be better!

Step 1: Preparation of Workspace



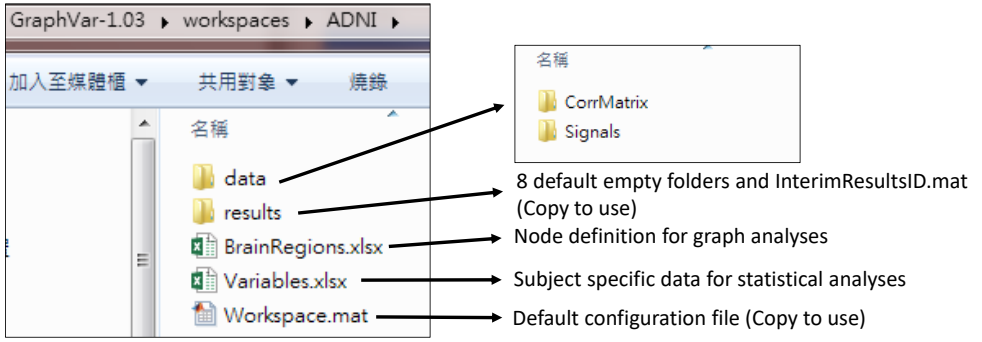


↑ This query window displays only when the "**ImportSettings.mat**" file is absent in the study folder.
(delete ImportSettings.mat file and restart GraphVar to reset configuration)

Step 1: Preparation of Workspace

Under **..\GraphVar-1.03\workspaces**

Create a Folder for your study (ex: ADNI, ratfMRI)



8 default empty folders and InterimResultsID.mat (Copy to use)

Node definition for graph analyses

Subject specific data for statistical analyses

Default configuration file (Copy to use)

Step 1: Preparation of Workspace

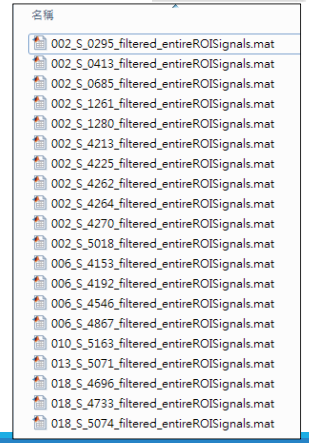
(1) **data** folder

CorrMatrix

- One mat-file of connectivity matrix (Node x Node) for each subject.
- Should have 20 files for 20 subjects.

Signals (recommended for GraphVar)

- One mat-file of preprocessed regional signals (Time frame x Node) for each subject.
- Should have 20 files for 20 subjects.

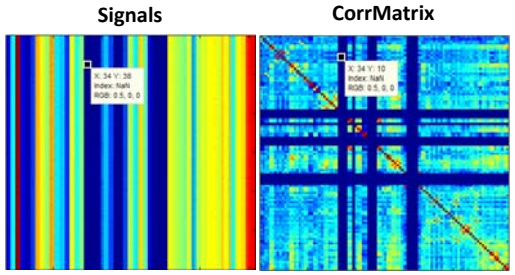


Step 1: Preparation of Workspace

Nan in Signals/CorrMatrix (caused by empty brain regions) will cause calculation error later!

tlstsq dgelsd error !!

(nan when polyfit) during GLM

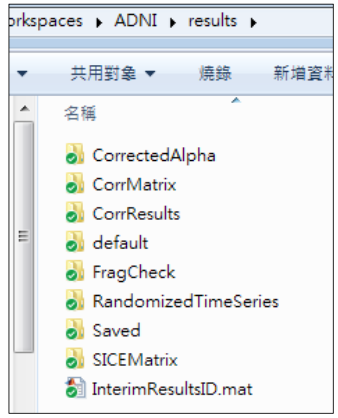


Exclude empty regions for all subjects!!

Step 1: Preparation of Workspace

(2) **result** folder

8 default empty folders and InterimResultsID.mat



Step 1: Preparation of Workspace

(3) **BrainRegions.xlsx** file (default: AAL 116)

Category **Node (abbr.)** **Node (full name)** **Coordinates (X, Y, Z)**

	A	B	C	D	E	F
1	1	Precentral_L	Precentral gyrus (Left)	-40	-6	51
2	1	Precentral_R	Precentral gyrus (Right)	40	-8	52
3	1	Frontal_Sup_L	Superior frontal gyrus, dorsolateral (Left)	-19	35	42
4	1	Frontal_Sup_R	Superior frontal gyrus, dorsolateral (Right	20	31	44
5	1	Frontal_Sup_Orb_L	Superior frontal gyrus, orbital part (Left)	-18	47	-13
6	1	Frontal_Sup_Orb_R	Superior frontal gyrus, orbital part (Right)	17	48	-14
7	1	Frontal_Mid_L	Middle frontal gyrus (Left)	-34	33	35
8	1	Frontal_Mid_R	Middle frontal gyrus (Right)	37	33	34
9	1	Frontal_Mid_Orb_L	Middle frontal gyrus orbital part (Left)	-32	50	-10
10	1	Frontal_Mid_Orb_R	Middle frontal gyrus orbital part (Right)	32	53	-11
11	1	Frontal_Inf_Oper_L	Inferior frontal gyrus, opercular part (Left	-49	13	19
12	1	Frontal_Inf_Oper_R	Inferior frontal gyrus, opercular part (Righ	49	15	21

(1 for default selection)

The order must comply with that listed in data!

Step 1: Preparation of Workspace

(4) **Variables.xlsx** file

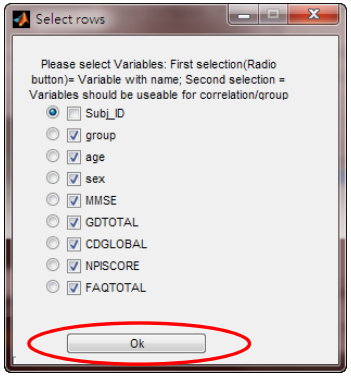
Subject ID **group** **Personal/Clinical Data**

	A	B	C	D	E	F	G	H	I
1	Subj_ID	group	age	sex	MMSE	GDTOTAL	CDGLOBAL	NPISCORE	FAQTOTAL
2	002_S_5018	AD	74.4	M	22	2	1	3	17
3	006_S_4153	AD	81.4583333	M	19	2	0.5	0	8
4	006_S_4192	AD	84.3416667	M	17	1	0.5	3	7
5	006_S_4546	AD	71.5777778	M	24	3	1	2	14
6	006_S_4867	AD	75.6527778	M	24	1	2	12	22
7	010_S_5163	AD	67.4111111	M	23	2	0.5	0	8
8	013_S_5071	AD	76.5777778	M	21	4	1	14	20
9	018_S_4696	AD	73.5333333	F	16	0	1	5	20
10	018_S_4733	AD	75.8472222	M	21	1	1	4	26
11	018_S_5074	AD	74.8166667	F	25	1	1	4	26
12	002_S_0295	NC	90.9083333	M	22	0	0	0	0
13	002_S_0413	NC	83.3611111	F	30	0	0	0	0

Subject ID must be included in the filename.

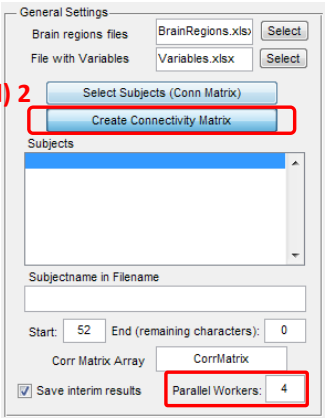
Step 2: General Settings

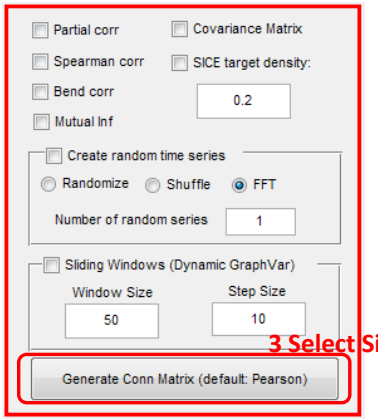
Select Variables (First column: Subject ID; Second column: other variables)



The "**ImportSettings.mat**" file will be generated in the study folder (delete ImportSettings.mat file and restart GraphVar to reset configuration)

Step 2: General Settings





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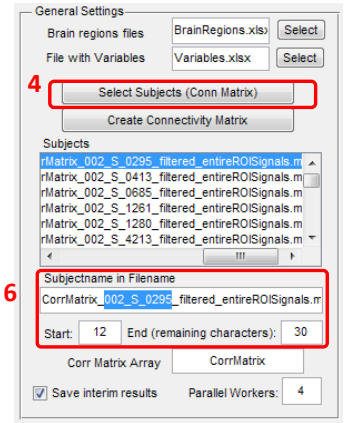
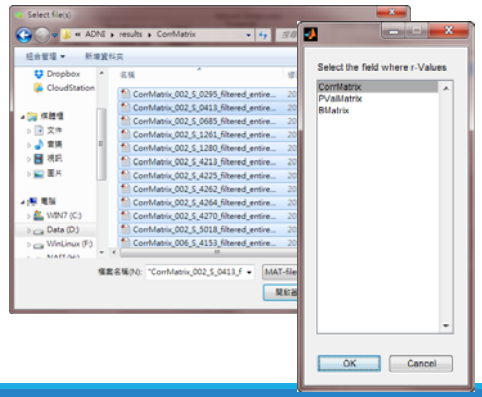
Mouse-over help

Step 2: General Settings

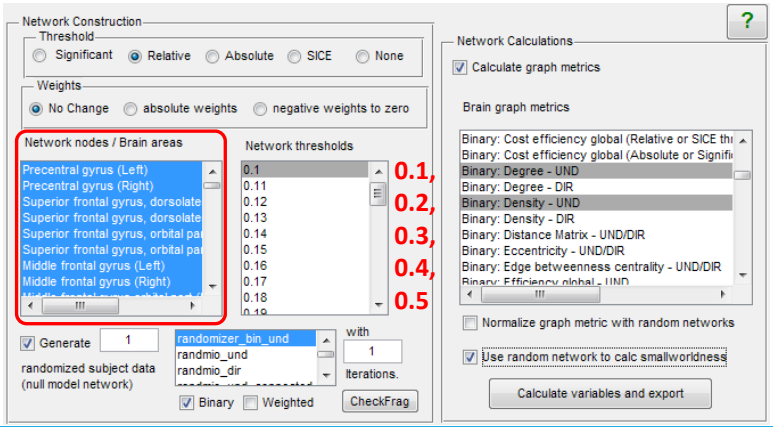


5 Select results/CorrMatrix



Step 3: Network Construction

Can select a subset for the subnetwork analysis



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Step 3: Network Construction

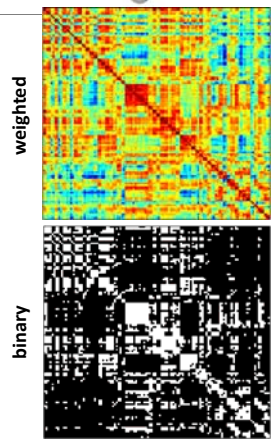
(1) **Threshold** method

Significant
- Thresholded based on the p-values.

Relative
- Thresholded in a proportional way.

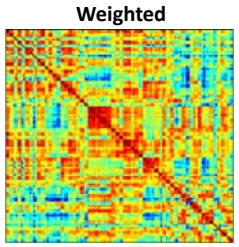
Absolute
- Thresholded based on the correlation coefficients.

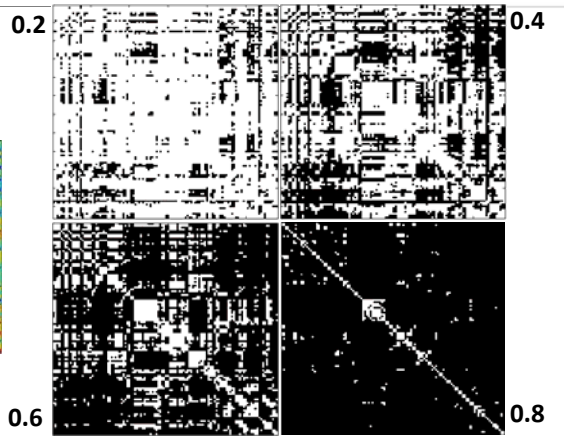
None
- No thresholding. Preserve full graph.



Step 3: Network Construction

(1) **Threshold** effects





Step 3: Network Construction

Common Abbreviations in Network Analysis
- bin/BIN: binary graph
- und/UND: undirected graph
- dir/DIR: directed graph
- w/W: weighted graph
- wu/WU: weighted and undirected graph
- bu/BU: binary and undirected graph

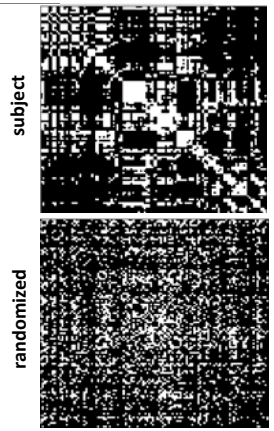
Step 3: Network Construction

(2) Generate **null-model network**

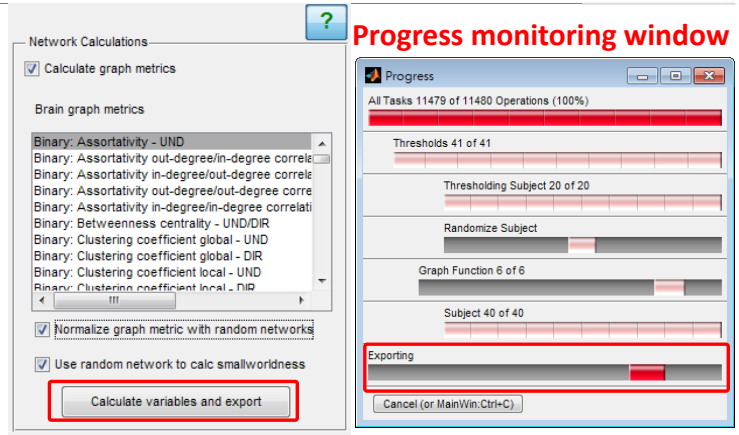
Usage
- Used for normalization of the network topological measures.
- Non-parametric testing of the significance against random networks.

BCT functions
- *randomizer_bin_und, randmio_und, randmio_und_connected, null_model_und_signed*.

https://sites.google.com/site/bctnet/Home/functions



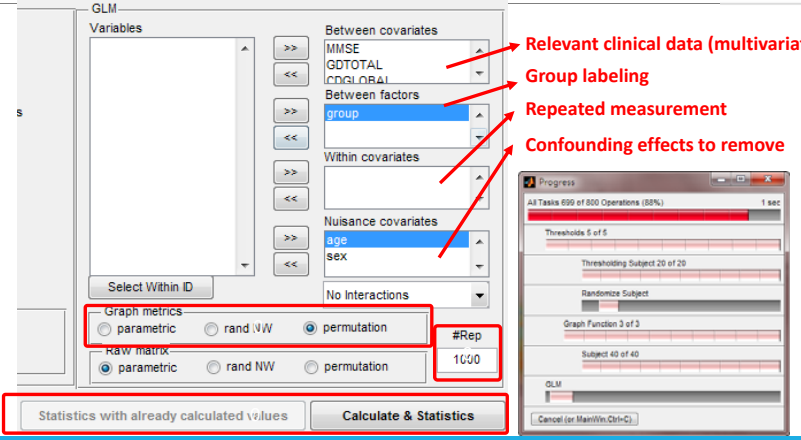
Step 3: Network Construction



Calculate & export to Excel files

Progress monitoring window

Step 4: Statistics (GLM)



Relevant clinical data (multivariate regression)

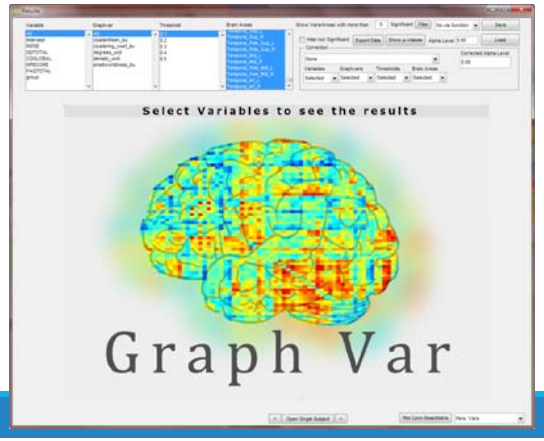
Group labeling

Repeated measurement

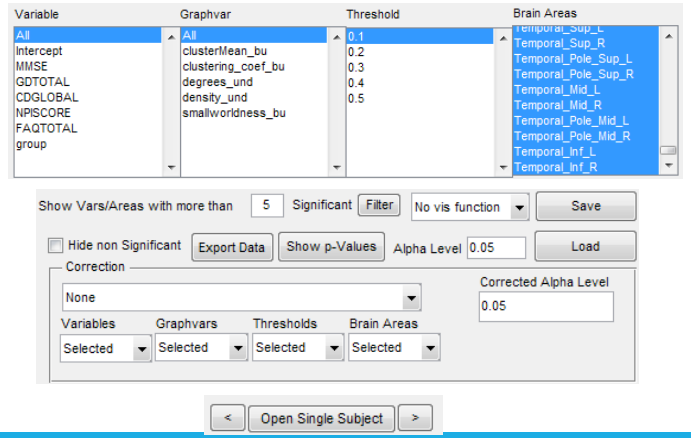
Confounding effects to remove

Step 5: Results viewer

Automatically pop-out once the **[Calculate & Statistics]** is done.



Step 5: Results viewer



Left upper panel

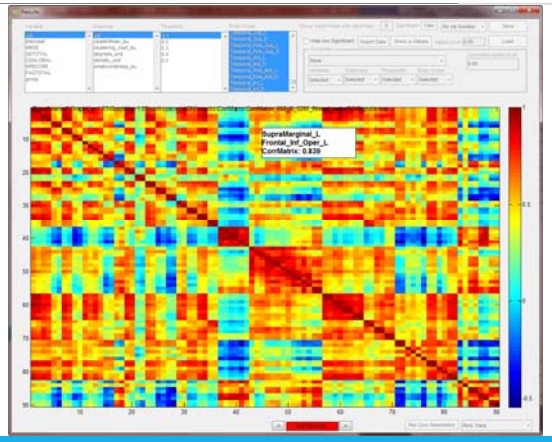
Right upper panel

Bottom

Step 5: Results viewer

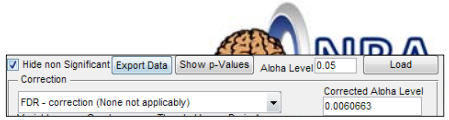
Display of single subject's CorrMatrix

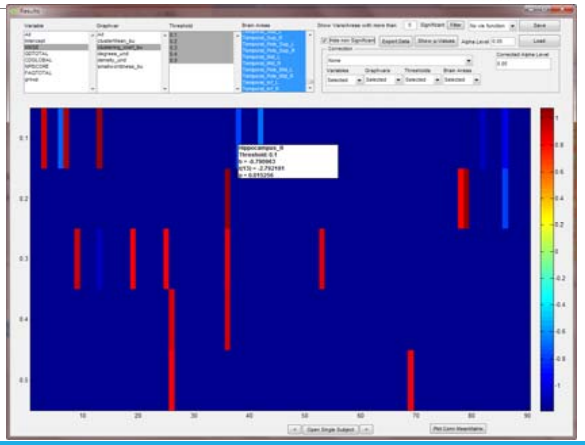
ADNI dataset



Step 5: Results viewer

Display of regression results

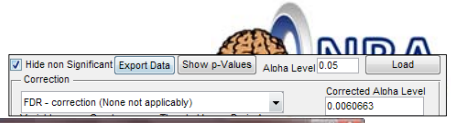


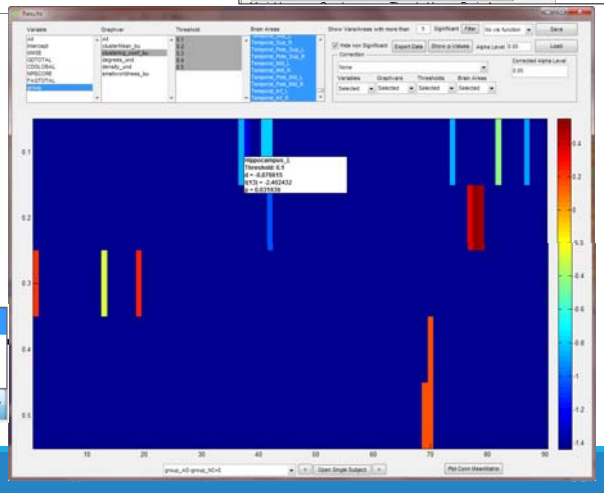


Step 5: Results viewer

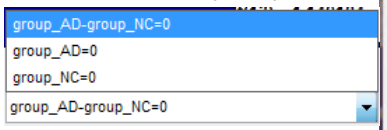
Display mode for local measurements:

Threshold x Brain regions





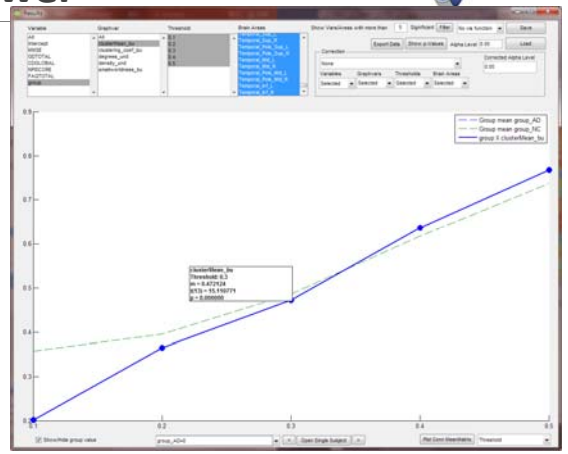
Group Comparisons:

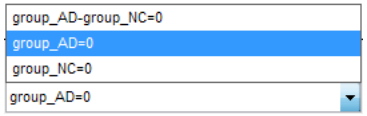


Step 5: Results viewer

Display mode for global measurements:

Measures under different thresholds

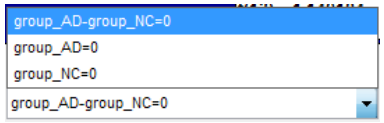


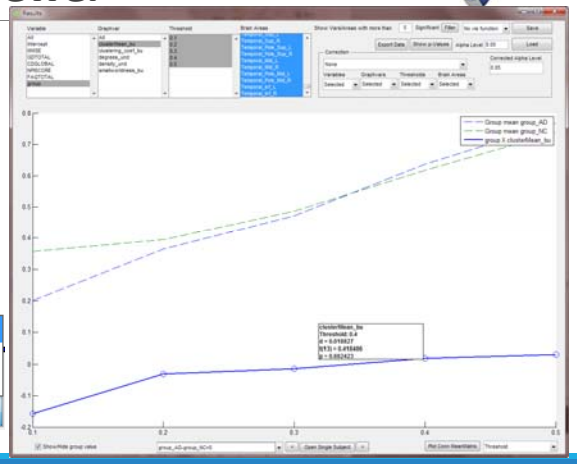


Step 5: Results viewer

Display mode for global measurements:

Measures under different thresholds





Q & A