Graph Analysis of fMRI data

UCLA/Semel Advanced Neuroimaging Summer Program 2015

Sepideh Sadaghiani, PhD

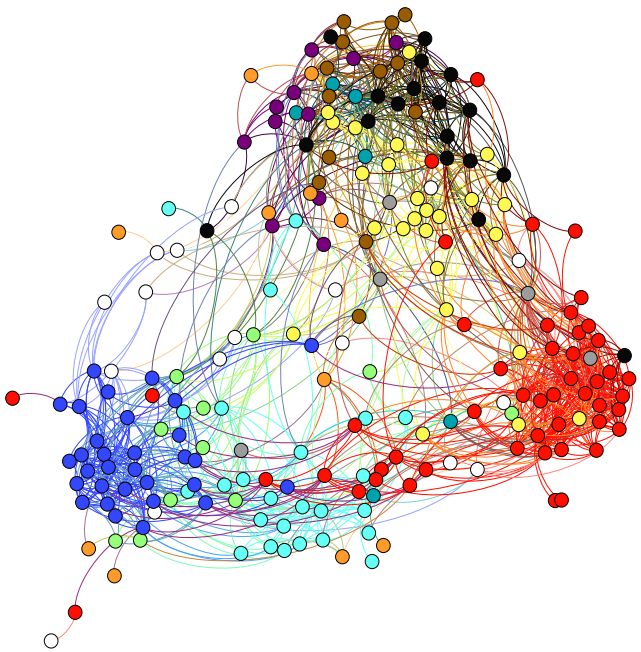
Contents

Introduction

- What is graph analysis?
- Why use graphs in fMRI?

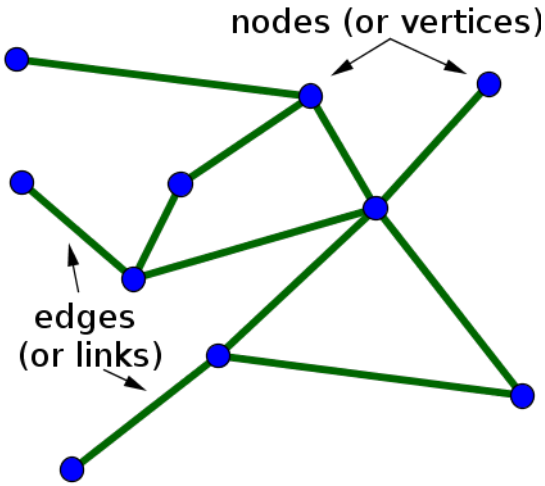
Decisions

- Which fMRI data?
- Which nodes?
- Which edges?
- Which modules?
- Which graph metrics?

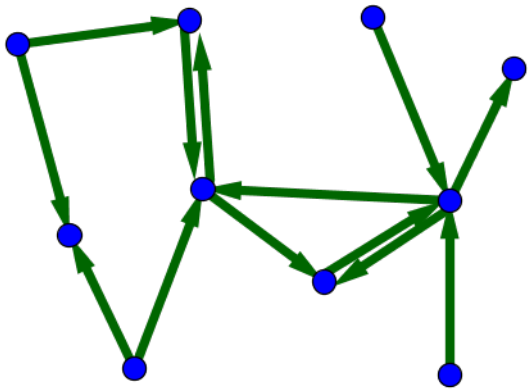


What is a graph?

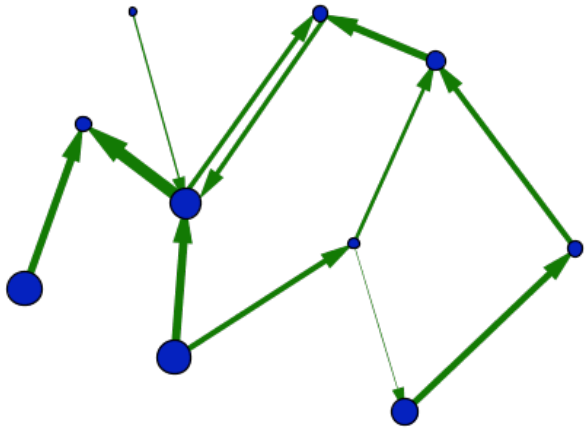
- Mathematical representation of a real-world network with pairwise relations between objects



undirected
unweighted



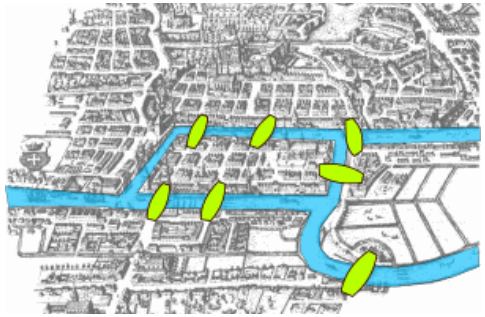
directed



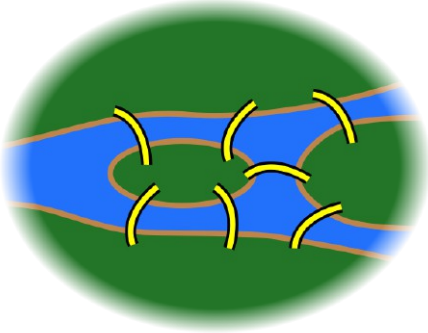
directed
weighted

Why graphs?

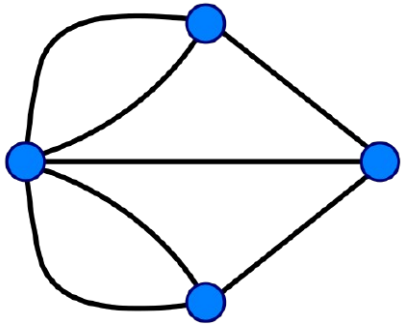
Euler 1736: The bridge puzzle of Königsberg



Physical space



Topological space



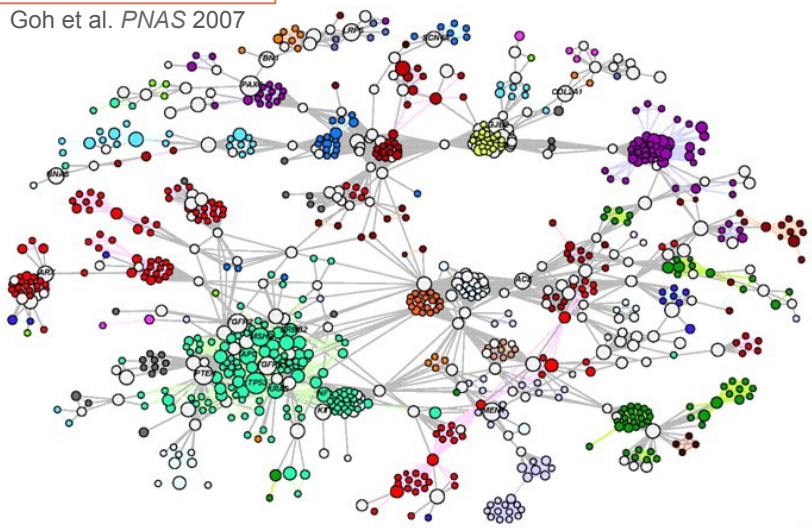
Necessary condition for the walk crossing each bridge exactly once:
Zero or two nodes with odd <u>degree.</u>

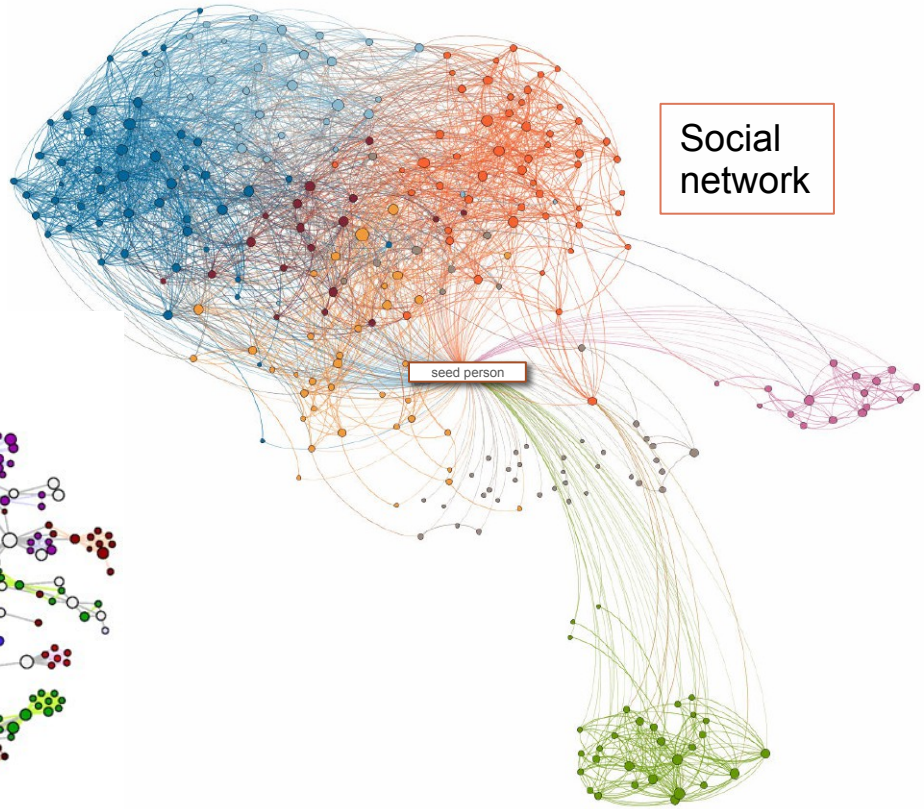
Real-world networks

Protein-protein “interactome”

Disease gene network

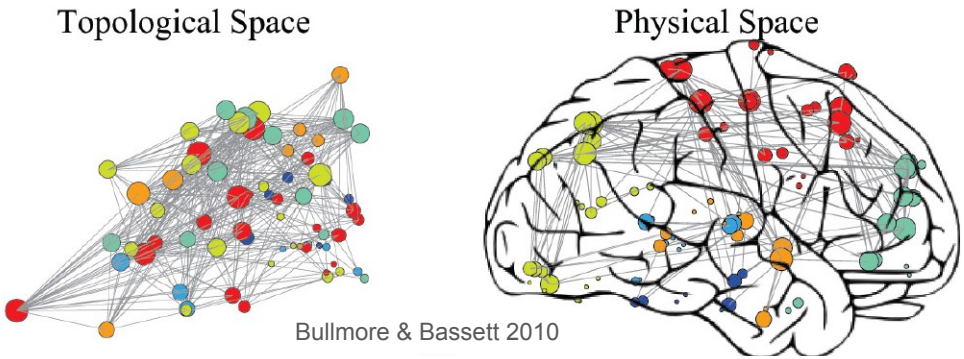
Goh et al. *PNAS* 2007





Social network

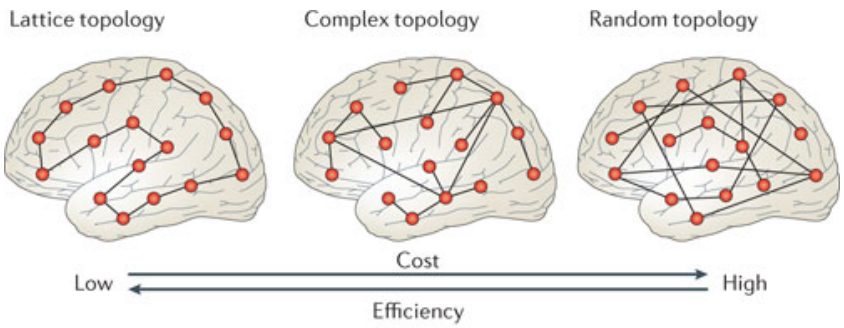
Brain connectome



Bullmore & Bassett 2010

Graph Theory

- Real-life networks are complex



Bullmore & Sporns, 2012

- Graph theory allows mathematical study of complex networks

- Describe properties of a complex system:
  Quantify topological characteristics of its graph representation

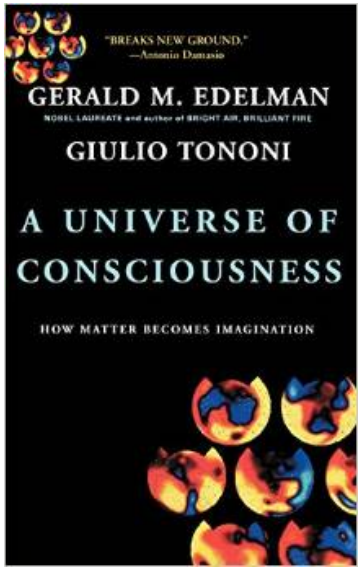
Why use graphs analyses in fMRI?

Quantification of global properties of spatio-temporal network organization

- Early motivation:

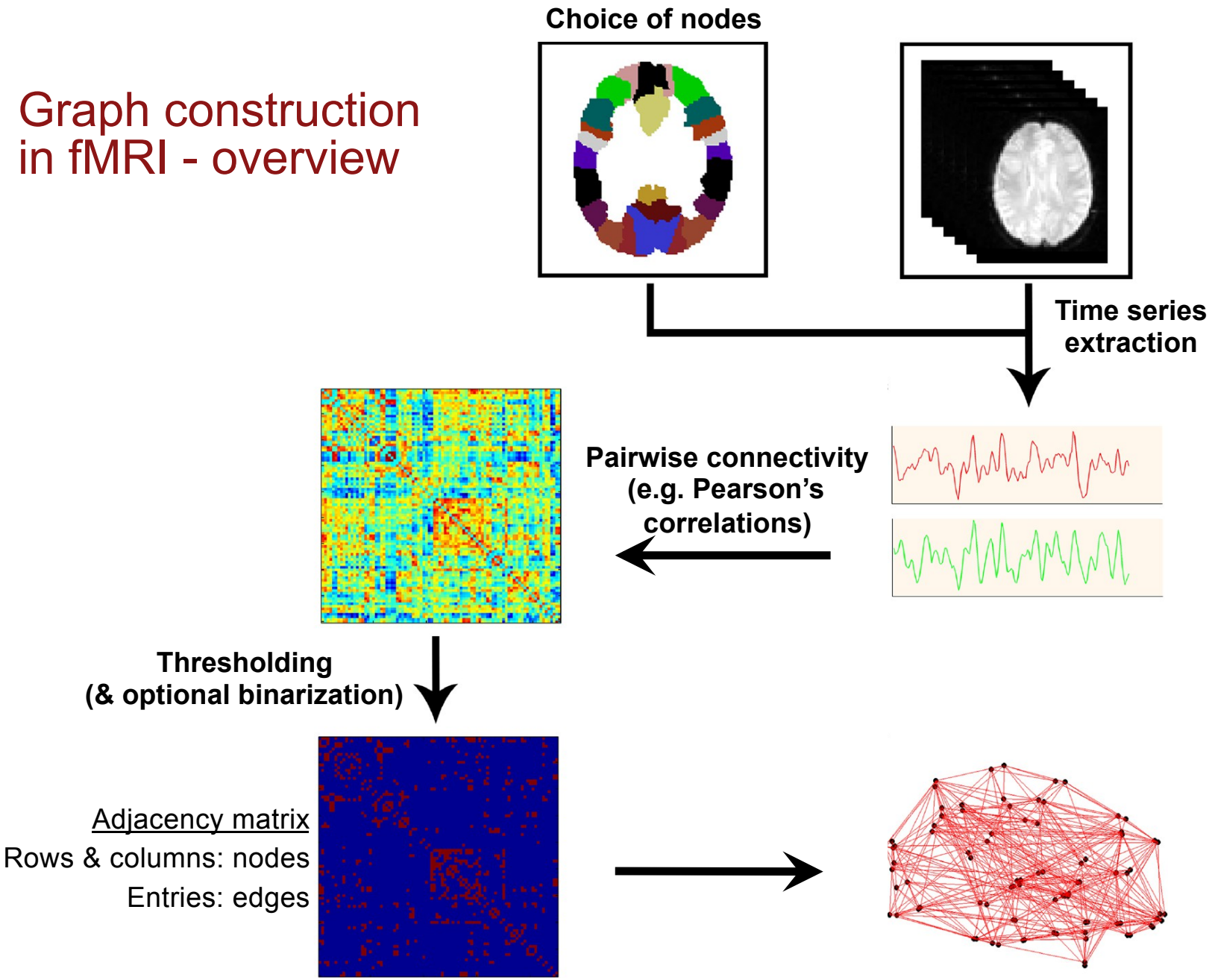
A testable theory of consciousness (Edelman & Tononi 2000)

Based on global network integration (information theory)



- Structural connectivity ↔ functional connectivity
- Comparisons across individuals (e.g. in disorders)
- Comparison across mental and functional states

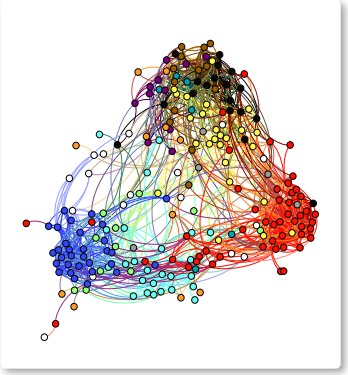
Graph construction in fMRI - overview



Wang et al., 2010

Which datasets?

MENTAL STATE,
PREPROCESSING



fMRI Datasets

Connections most commonly derived from resting state, but task data possible in principle

Session length most commonly 5-10min

- Long enough for multiple cycles of infraslow (<0.1Hz) frequencies
- Short enough to minimize mental state change

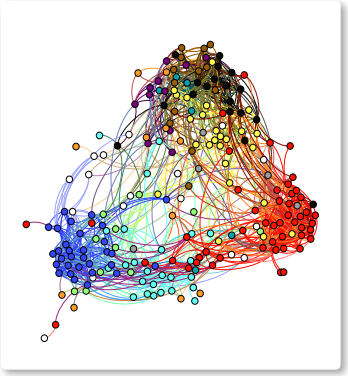
- Shorter term time-varying dynamics (e.g. sliding window)

Preprocessing: same considerations as any fMRI connectivity study:

- What motion correction?
- Slice time correction?
- Physiological nuisance measures?
- Compartment signal regression (GM, WM, CSF)?

Which nodes?

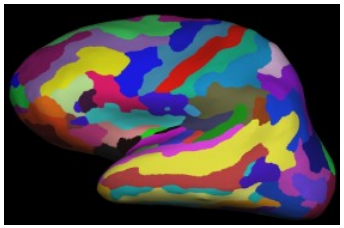
ANATOMICAL VS. FUNCTIONAL
ATLAS VS. DATA-DRIVEN



Anatomical atlases

Nodes:

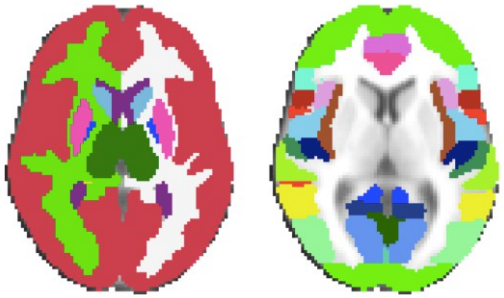
- Internally coherent / homogeneous (connectivity)
- Externally independent



FreeSurfer (Destrieux)

Anatomical atlases

- Automated Anatomical Labeling (AAL) template
- Eickhoff-Zilles (Cytoarchitectonic)
- FreeSurfer (Gyral. Individual surface-based possible)
- Harvard-Oxford
- Talairach & Tournoux



21subcortical 48 cortical
Harvard-Oxford

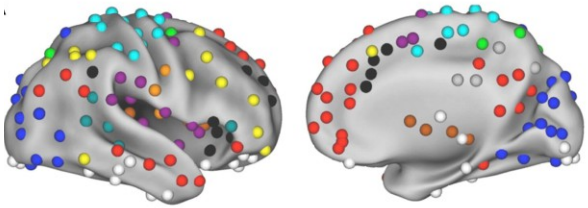
- ☺ Comparability (across subjects and modalities)
- ☹ Highly variable node size. Not functionally coherent.

Functional atlases

Craddock et al. 2012

Functional atlases

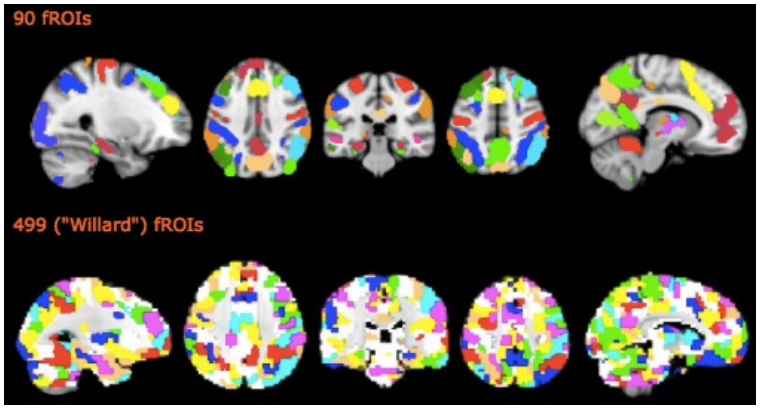
- Craddock (local homogeneity of connectivity)
- Power (resting state seed-based & task)
- Stanford Atlas FIND lab (ICA-based)
- ☺ Comparability across subjects.
- ☺ Functionally coherent (☹ but suboptimal for individuals)



Power et al. 2011: 164 peak locations

Functional subject-specific parcellations

- ICA
- (Seed-based)
- Connectivity homogeneity: Craddock
- ☺ Functionally coherent
- ☹ Time-intensive

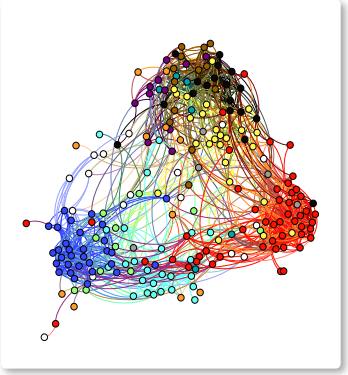


FINDlab, Shirer et al. 2012

List of atlases: https://en.wikibooks.org/wiki/SPM/Atlases

Which edges?

CONNECTIVITY AND THRESHOLDING



Edges in fMRI

Based on magnitude of temporal covariation

- Pearson's cross-correlations (by far most common)
- Partial correlations
- Mutual information

- → symmetric adjacency matrices (undirected graphs)

Directionality problematic in fMRI
(but measures of effective connectivity possible)

Other Data Modalities

Structural (e.g. DTI, histological tracing)

- Nodes: cf. fMRI
- Edges: e.g. number of reconstructed fibers

EEG / MEG

- Nodes: sensors or reconstructed sources
- Edges: Correlation in oscillation amplitudes
  Oscillation phase synchrony (coherence of phase locking)

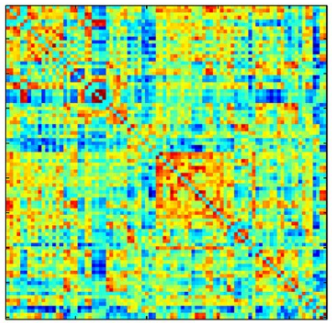
Thresholding

Most metrics require **sparse** graphs

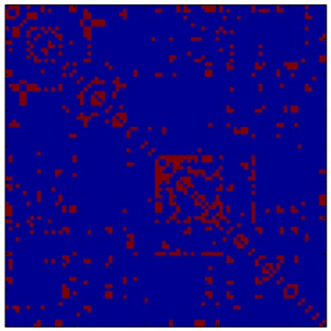
Threshold to remove weak connections

Use proportional thresholds (vs. absolute thresholds)

Use broad range of proportions



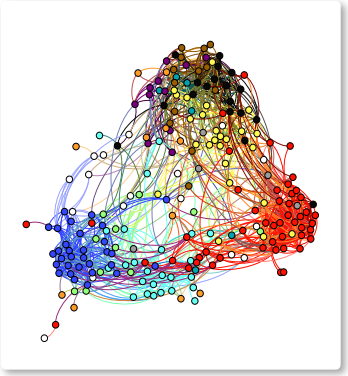
Thresholding (& optional binarization)



Adjacency matrix

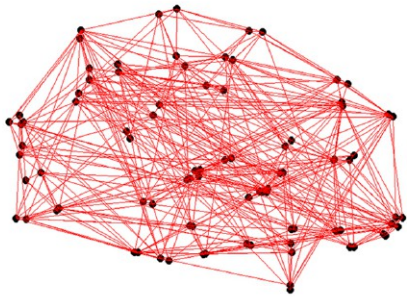
Which Modules?

COMMUNITY DETECTION



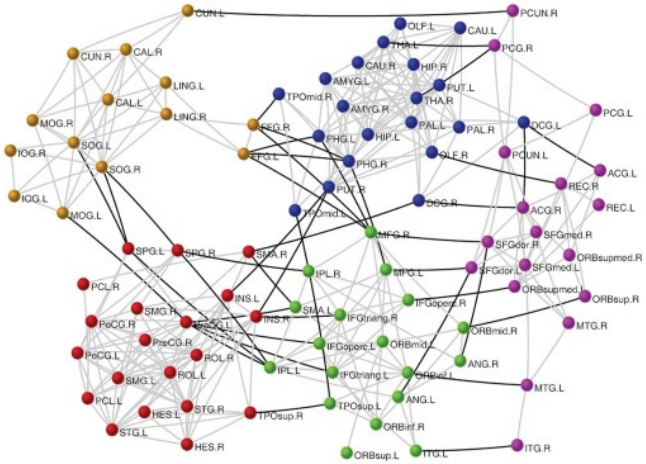
Modules

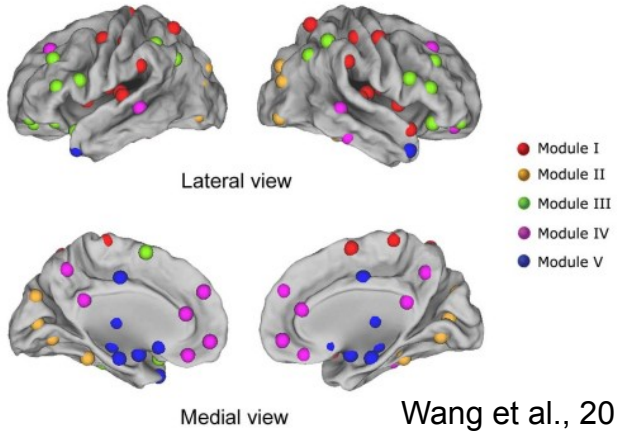
Communities of densely interconnected nodes



Community detection

Optimization algorithms





Wang et al., 2010

Community Detection Algorithms

Modularity-base algorithms

Maximize number of within-community edges (compared to random network)

- Newman's Modularity (Newman, 2006)
- Louvain method (Blondel et al. 2008)

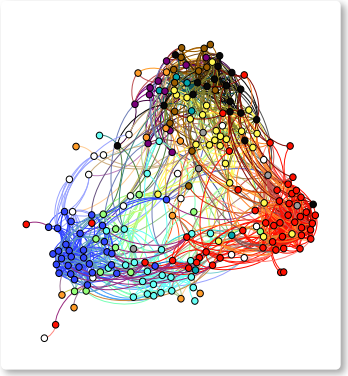
Infomap algorithm (Rosvall and Bergstrom, 2008)

Minimize information theoretic descriptions of random walks on the graph

Review: Fortunato, 2010

Which graph metrics?

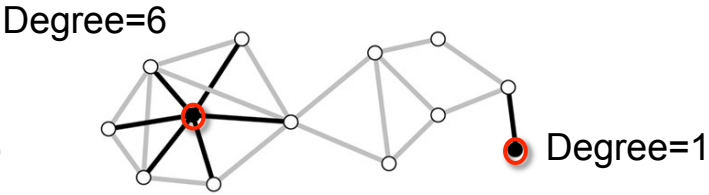
NODAL AND GLOBAL



Nodal Measures

Degree

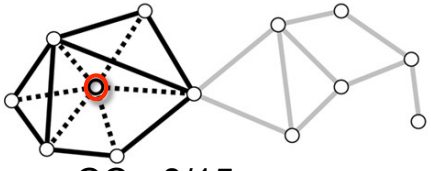
Number of edges connected to a node



Nodal Clustering Coefficient (➔ basis for measure of global segregation)

Fraction of all possible edges realized among a node's neighbors

= Fraction of all possible triangles around a node

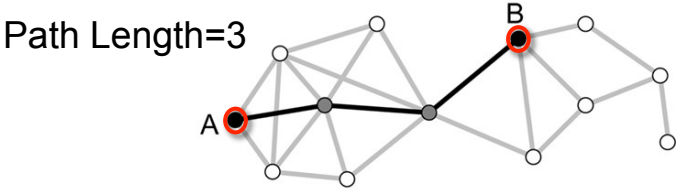


CC =8/15
=0.53

(n(n-1)/2)

Shortest Path Length (➔ basis for measure of global integration)

Number of edges on shortest geodesic path between two nodes



➔ Distance matrix

Sporns, 2011

Nodal Measures

<u>Measures of centrality</u>:

Closeness Centrality

Inverse of the node's average Shortest Path Length

Betweenness Centrality

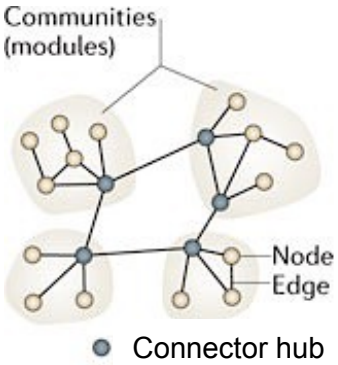
Fraction of all shortest paths passing through the node

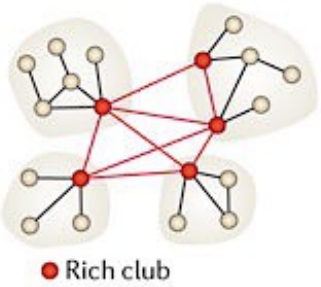
Participation Coefficient

Diversity of intermodular connections

Within-Module Degree (z-score)

Degree$_{intra\text{module}}$ z-scored within the node's module





"Provincial hubs": high within-module degree & low participation coefficient
"Connector hubs": high participation coefficient
"Rich club": densely interconnected connector hubs

Bullmore & Sporns, 2012

Global Measures

Measures of Integration

Characteristic Path Length

$\frac{1}{n}\sum_{nodes}$ average Shortest Path Length to all other nodes

Global Efficiency

$\frac{1}{n}\sum_{nodes}$ average *inverse* Shortest Path Length to all other nodes

Measures of Segregation

Clustering Coefficient

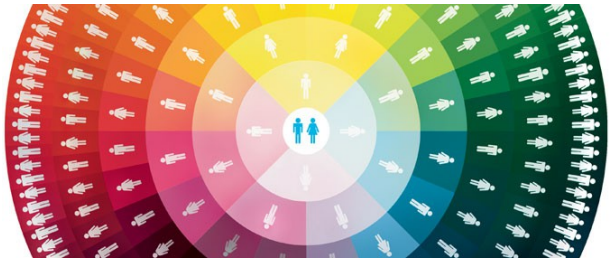
$\frac{1}{n}\sum_{nodes}$ nodal Clustering Coefficient

Modularity (Newman's)

$\sum_{Modules}$ Fraction of edges falling within the module minus expected fraction in a random network

→Often used to detect community structure

Rubinov & Sporns, 2010

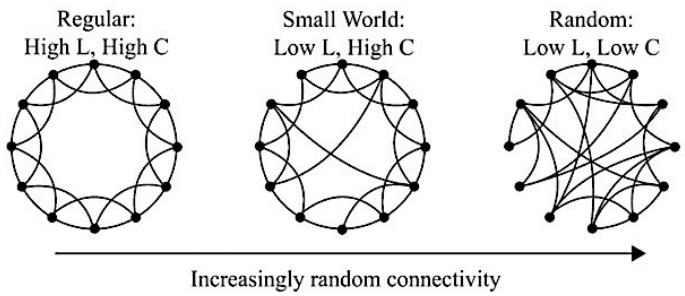


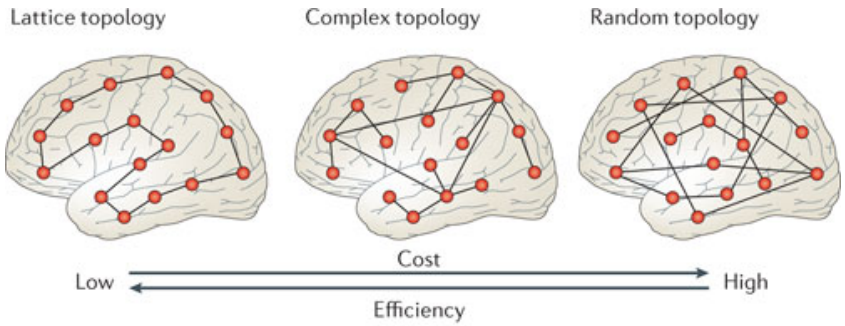
Global Measures

Small-worldness

Optimal balance between functional segregation and integration

$$\frac{\text{Clustering Coefficient}_{real} \,/\, \text{Clustering Coenfficient}_{random}}{\text{Characteristic Path Length}_{real} \,/\, \text{Characteristic Path Length}_{random}}$$





☺ Functionally specialized (segregated) modules *AND* intermodular (integrating) edges

Watts & Strogatz, 1998

Resources

Analysis Software

- MATLAB-based: **Brain Connectivity Toolbox (**Rubinov & Sporns, 2010)
  https://sites.google.com/site/bctnet/

- Python-based: **NetworkX** (Hagberg et al., 2008)
  https://networkx.github.io

Visualization

- General: **Gephi** http://gephi.github.io
- Anatomical space: **Multimodal Connectivity Database**
  http://umcd.humanconnectomeproject.org
- Anatomical space: **Connectome Visualization Utility**
  https://github.com/aestrivex/cvu

Reading

- Rubinov M, Sporns O. Complex network measures of brain connectivity: Uses and interpretations. NeuroImage. 2010 Sep;52(3):1059–69.

- Bullmore ET, Bassett DS. Brain Graphs: Graphical Models of the Human Brain Connectome. Annu Rev Clin Psychol. 2010 Apr;7(1):113–40.

References

- Blondel, V.D., Guillaume, J.-L., Lambiotte, R., Lefebvre, E., 2008. Fast unfolding of communities in large networks. J. Stat. Mech. 2008, P10008
- Bullmore E, Sporns O. The economy of brain network organization. Nat Rev Neurosci. 2012 May;13(5):336–49.
- Craddock RC, James GA, Holtzheimer PE, Hu XP, Mayberg HS. A whole brain fMRI atlas generated via spatially constrained spectral clustering. Hum Brain Mapp. 2012 Aug 1;33(8):1914–28.
- Fortunato, S. (2010). Community detection in graphs. Phys. Rep. *486*, 75–174.
- Newman MEJ. Modularity and community structure in networks. PNAS. 2006 Jun 6;103(23):8577–82.
- Hagberg, A.A., Schult, D.A., Swart, P.J., 2008. Exploring network structure, dynamics, and function using networkx. In: Varoquaux, G., Vaught, T., Millman, J. (Eds.), Proceedings of the 7th Python in Science Conference (SciPy2008). Pasadena, CA USA, pp. 11–15.
- Power JD, Cohen AL, Nelson SM, Wig GS, Barnes KA, Church JA, et al. Functional Network Organization of the Human Brain. Neuron. 2011 Nov 17;72(4):665–78.
- Rosvall, M., and Bergstrom, C.T. (2008). Maps of random walks on complex networks reveal community structure. Proc. Natl. Acad. Sci. USA *105*, 1118– 1123.
- Shirer WR, Ryali S, Rykhlevskaia E, Menon V, Greicius MD. Decoding Subject-Driven Cognitive States with Whole-Brain Connectivity Patterns. Cerebral Cortex. 2012 Jan 1;22(1):158–65.
- Sporns O. The non-random brain: efficiency, economy, and complex dynamics. Front Comput Neurosci. 2011;5:5.
- Wang J, Zuo X, He Y. Graph-based network analysis of resting-state functional MRI. Frontiers in Systems Neuroscience. 2010. doi: 10.3389/fnsys.2010.00016
- Watts DJ, Strogatz SH. Collective dynamics of “small-world” networks. Nature. 1998 Jun 4;393(6684):440–2.