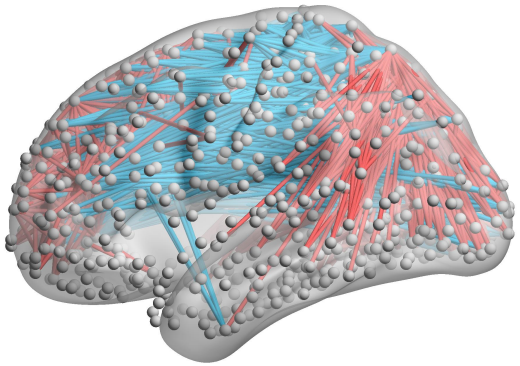
Graph theory and connectomics

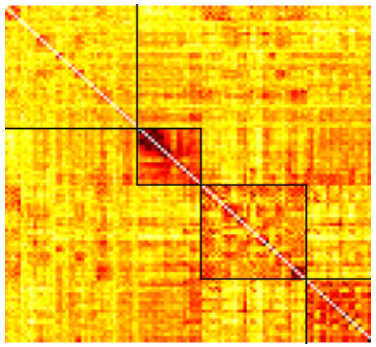
an introduction

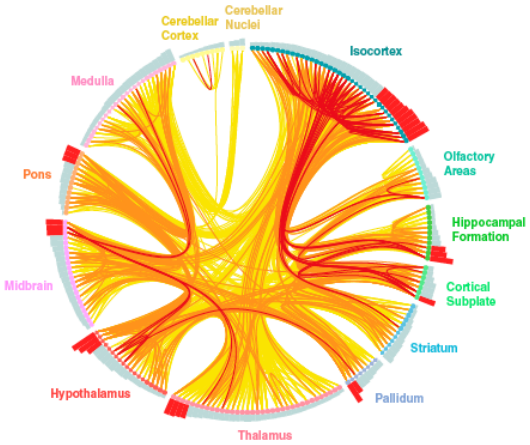
Alex Fornito

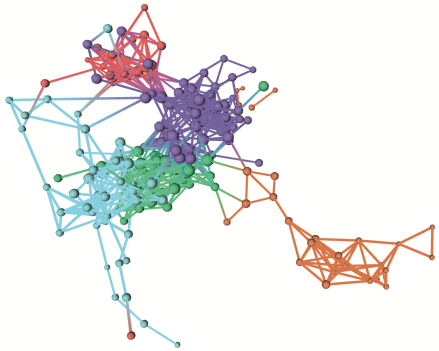
Monash Clinical and Imaging Neuroscience
Monash University

email: alex.fornito@monash.edu
twitter: @AFornito









overview

Why graph theory?

Building a brain graph
Defining nodes
Defining edges
Matrices and graphs

Network analysis
Connectivity
Topology

Null models
Edge rewiring

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PLoS COMPUTATIONAL BIOLOGY

Review

The Human Connectome: A Structural Description of the Human Brain

Olaf Sporns*, Giulio Tononi, Rolf Kötter

connectome:

a comprehensive structural description of the network of elements and connections forming the human brain.

Sporns, Tononi, Kötter, PLoS Comp Biol, 2005

OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Review

The Human Connectome: A Structural Description of the Human Brain

Olaf Sporns*, Giulio Tononi, Rolf Kötter

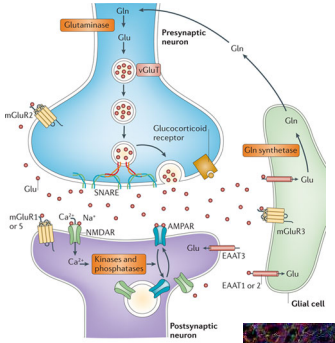
connectome:

a comprehensive map of neural connections in the brain.

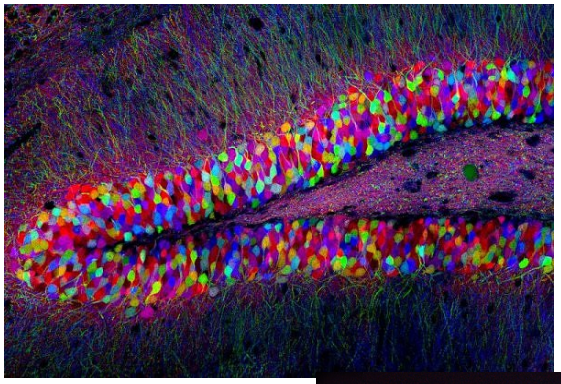
The production and study of connectomes, known as connectomics, may range in scale from a detailed map of the full set of neurons and synapses within part or all of the nervous system of an organism to a macro scale description of the functional and structural connectivity between all cortical areas and subcortical structures.

http://en.wikipedia.org/wiki/Connectome

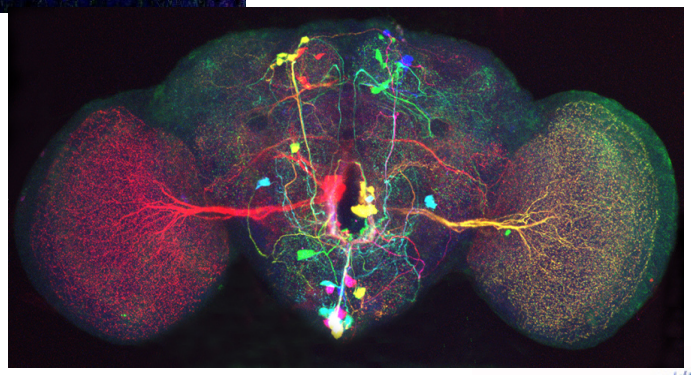
the brain is a multiscale system



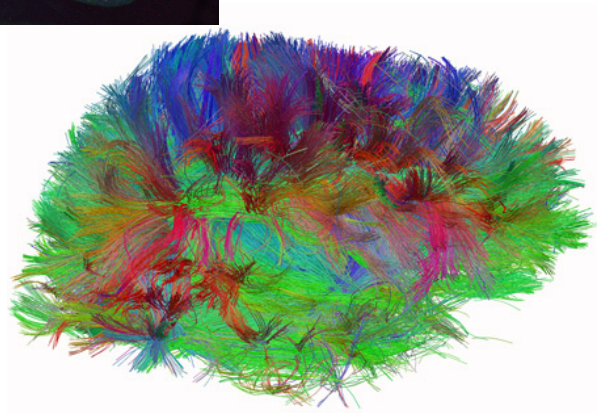
molecular
nm



microscale
nm to μm

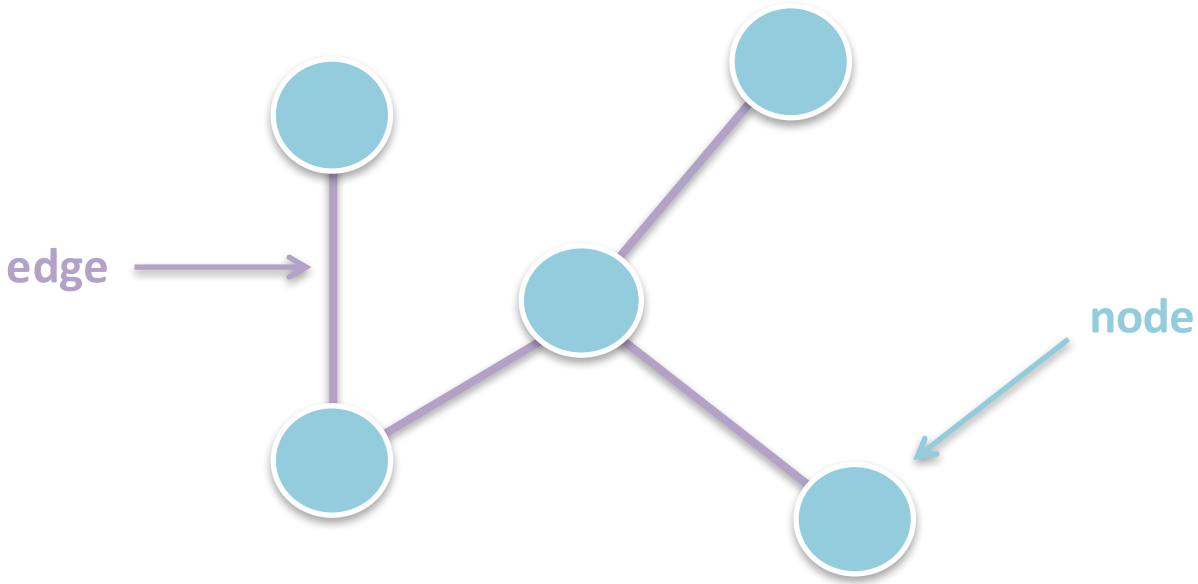


meso
μm to mm



macroscale
mm to cm

fundamental assumptions of network neuroscience



any network can be modelled as a graph of nodes connected by edges

Nodes represent fundamental processing units

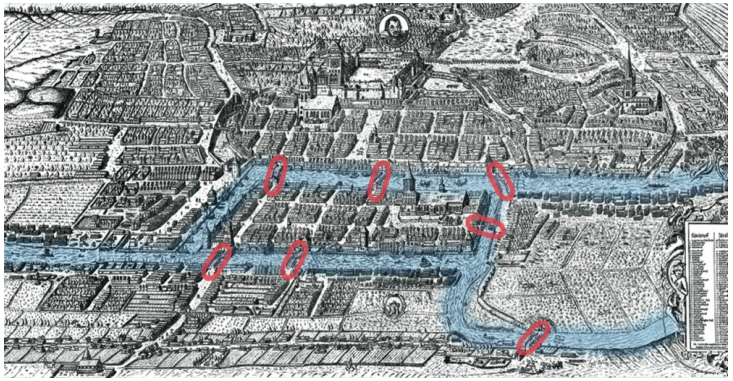
Edges represent the interactions between nodes

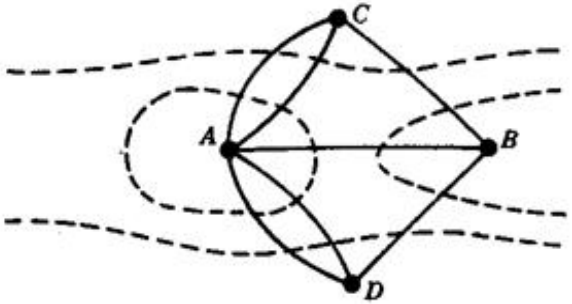
connectomes are networks

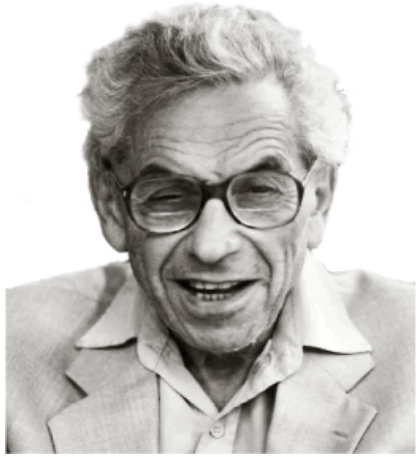
graphs should provide useful models of connectomes

major discoveries in graph theory & network science

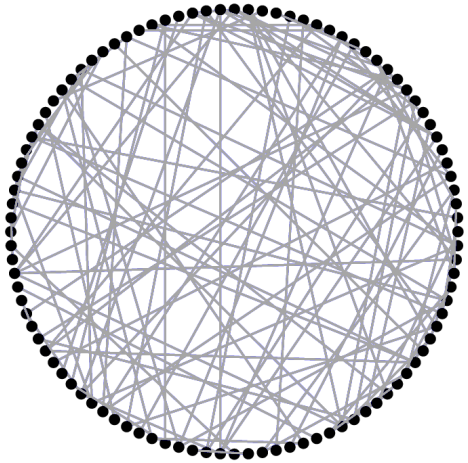
Leonhard Euler
(1707-1783)

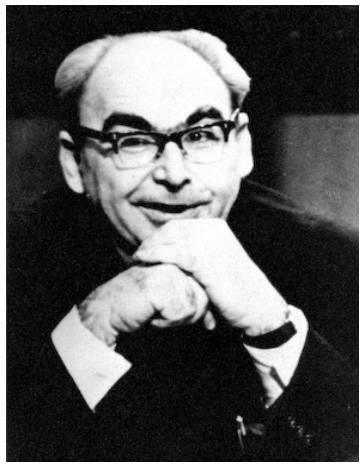






Paul Erdős
(1913-1996)





Alfréd Rényi
(1921-1970)

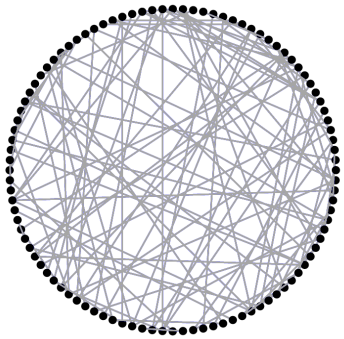
major discoveries in graph theory & network science

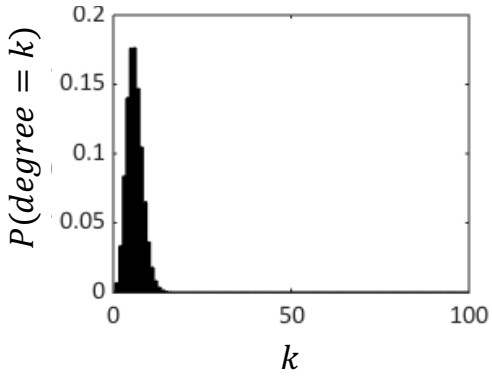
graph

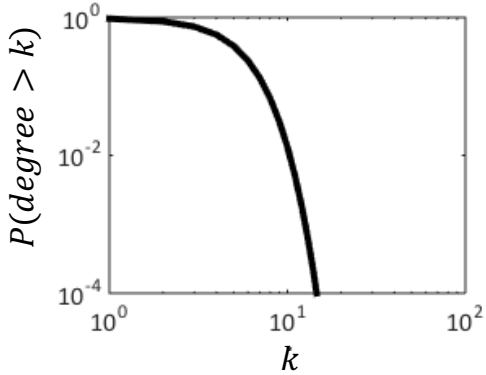
pdf

cdf

random

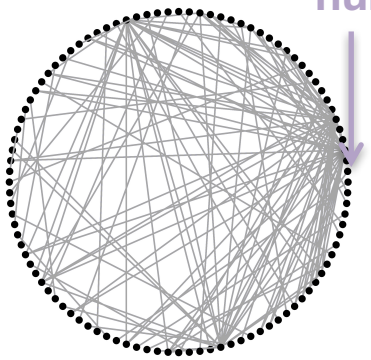


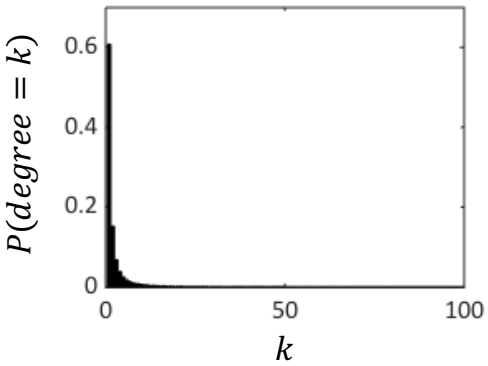


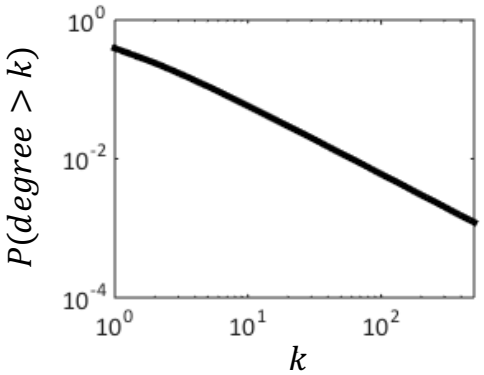


hub

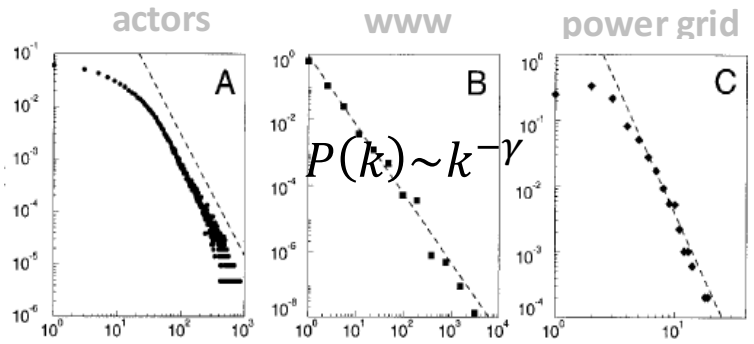
scale-free







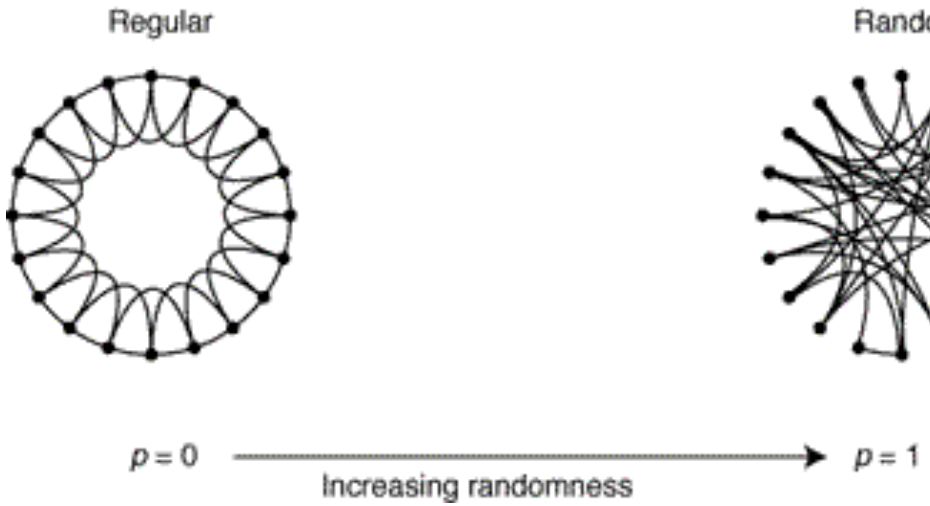
actors www power grid



Barabási & Albert, Science, 1999; see also Clauset, Shalizi, Newman, SIAM Rev, 2009

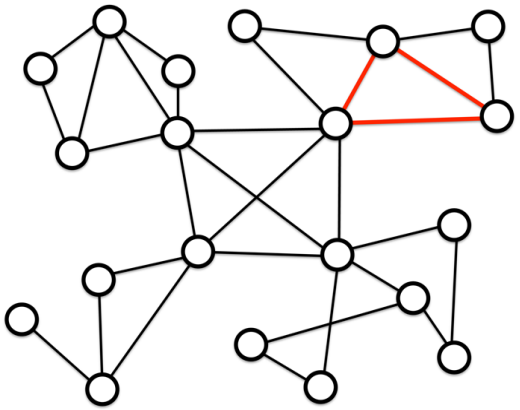
major discoveries in graph theory & network science

↑ clustering
↑ path length

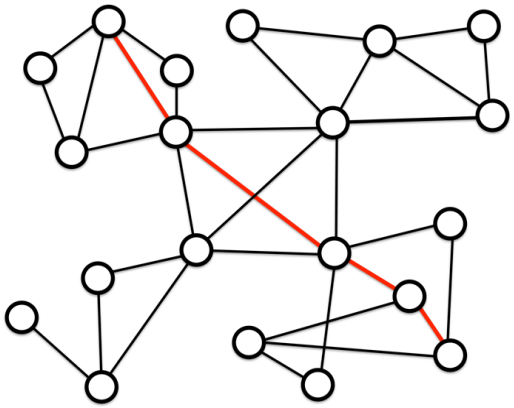


↓ clustering
↓ path length

clustering



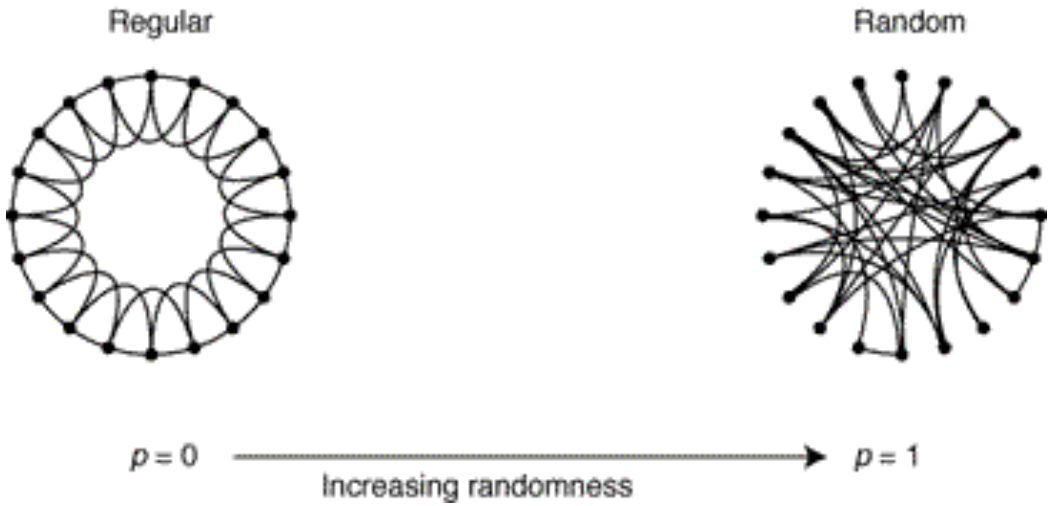
path length



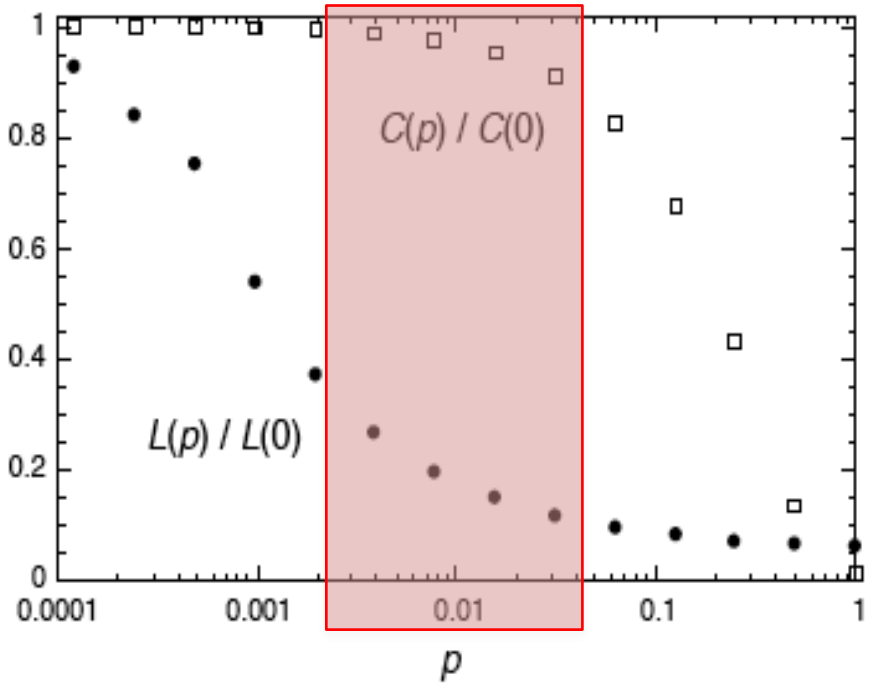
Watts and Strogatz, Nature, 1999

major discoveries in graph theory & network science

↑ clustering
↑ path length

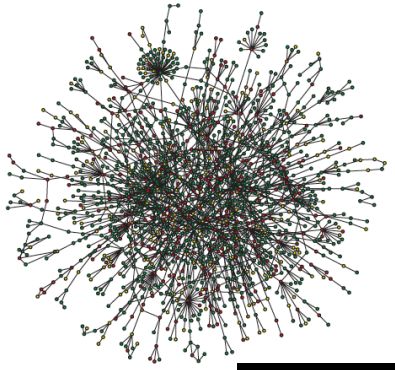


↓ clustering
↓ path length

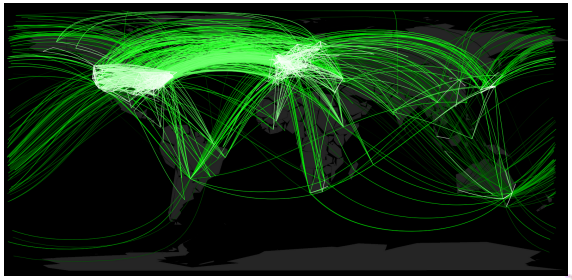


Watts and Strogatz, Nature, 1999

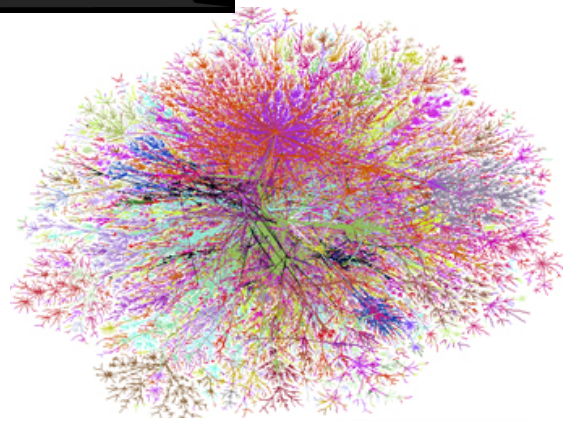
real-world networks



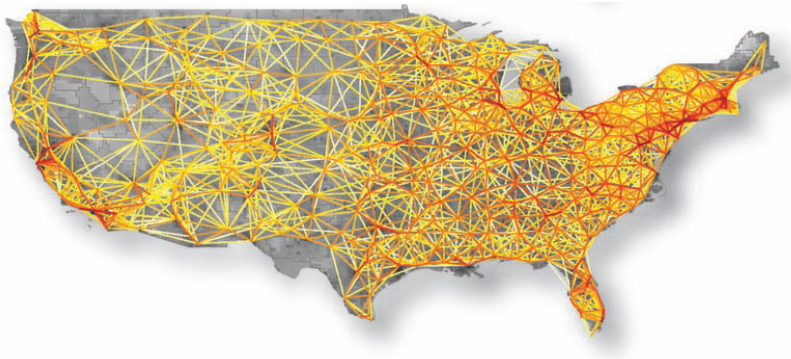
protein interactions



academic collaborations



world wide web



commuters

overview

Why graph theory?

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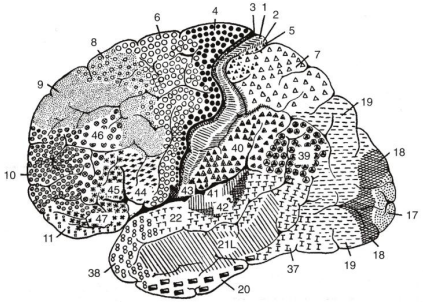
defining nodes

Brain nodes should have:

1. Intrinsic consistency
2. Extrinsic differentiation
3. Spatially constrained

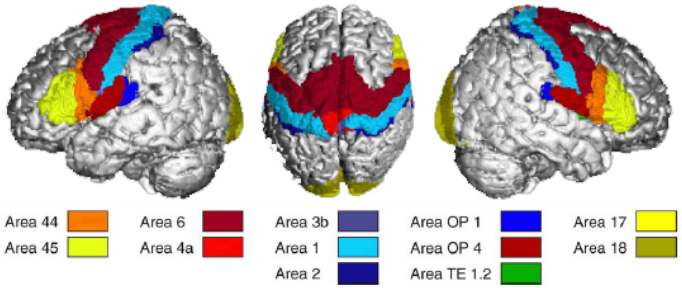
Fornito et al. NeuroImage, 2013

cytoarchitecture



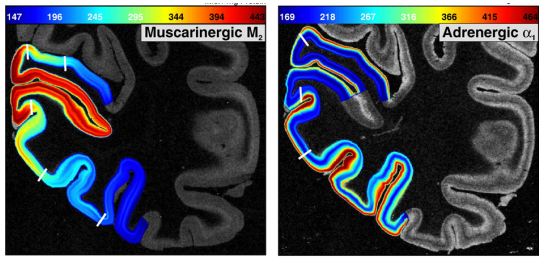
Brodmann, 1909

probabilistic



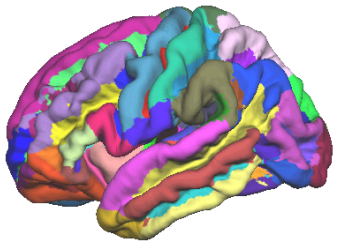
Eickhoff et al. NeuroImage, 2006

chemoarchitecture



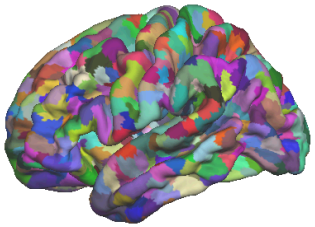
Eickhoff et al. NeuroImage, 2007

anatomical



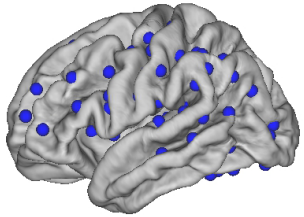
Tzuorio-Mazoyer, et al. NeuroImage, 2002
Desikan, et al. NeuroImage, 2006

random



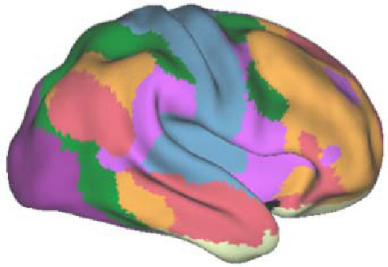
Hagmann, et al. PLoS One, 2007
Zalesky, et al. NeuroImage, 2010
Fornito et al. Font Sys Neurosci, 2010

functional



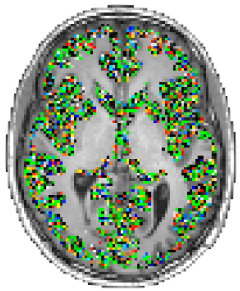
Dosenbach, et al. Science, 2010
Fornito et al. PNAS, 2012

data-driven



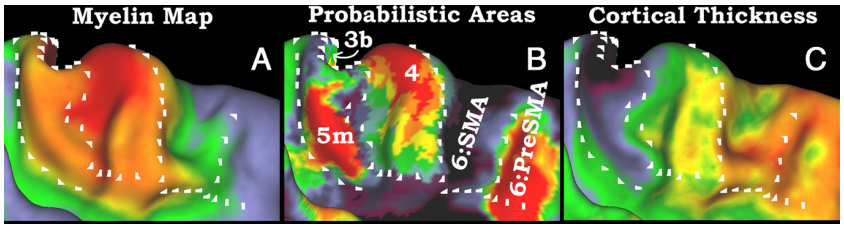
Yeo et al. J Neurophysiol, 2011
Craddock et al. Hum Brain Mapp, 2012
Power et al. Neuron, 2011

voxel-based



van den Heuvel et al. NeuroImage, 2009
Hayasaka & Laurienti, NeuroImage, 2010

myeloarchitecture



Glaser & Van Essen J Neurosci 2011

overview

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Structural connectivity

The physical (anatomical) connections between brain regions

- Invasive methods can resolve directionality
- Non-invasive methods cannot resolve directionality

Functional connectivity

A statistical dependence between spatially distinct neurophysiological signals

- Estimated at level of measured signals
- Can be directed or undirected

Effective connectivity

The influence that one neuronal system exerts over another

- Usually model-based
- Describes causal (directed) interactions at the neuronal level

Friston et al, 1994, Hum Brain Mapping; Fornito et al, 2015, Nat Rev Neurosci

defining edges

structural

electron microscopy

Bock et al. Nature, 2011
White et al. PTRS, 1986

tract-tracing

Oh et al. Nature, 2014
http://connectivity.brain-map.org

genetic labelling

Chiang et al. Curr Biol, 2011
www.flycircuit.tw

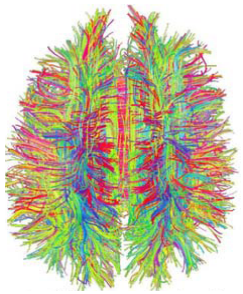
informatics

Modha & Singh PNAS, 2010
Shanahan et al. Fron Comp Neurosci,2013
http://cocomac.org

PLI

Axer, et al. NeuroImage, 2011

DWI



Hagmann et al. PLoS One, 2007

functional

electrophysiology

Yu et al. Cereb Cortex, 2008

ECoG

Bastos et al. Neuron, 2015
Brovelli, et al. PNAS, 2004

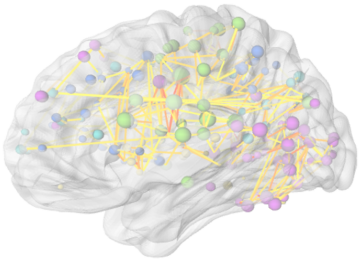
calcium imaging

Ahrens et al. Nat Methods, 2013

M/EEG

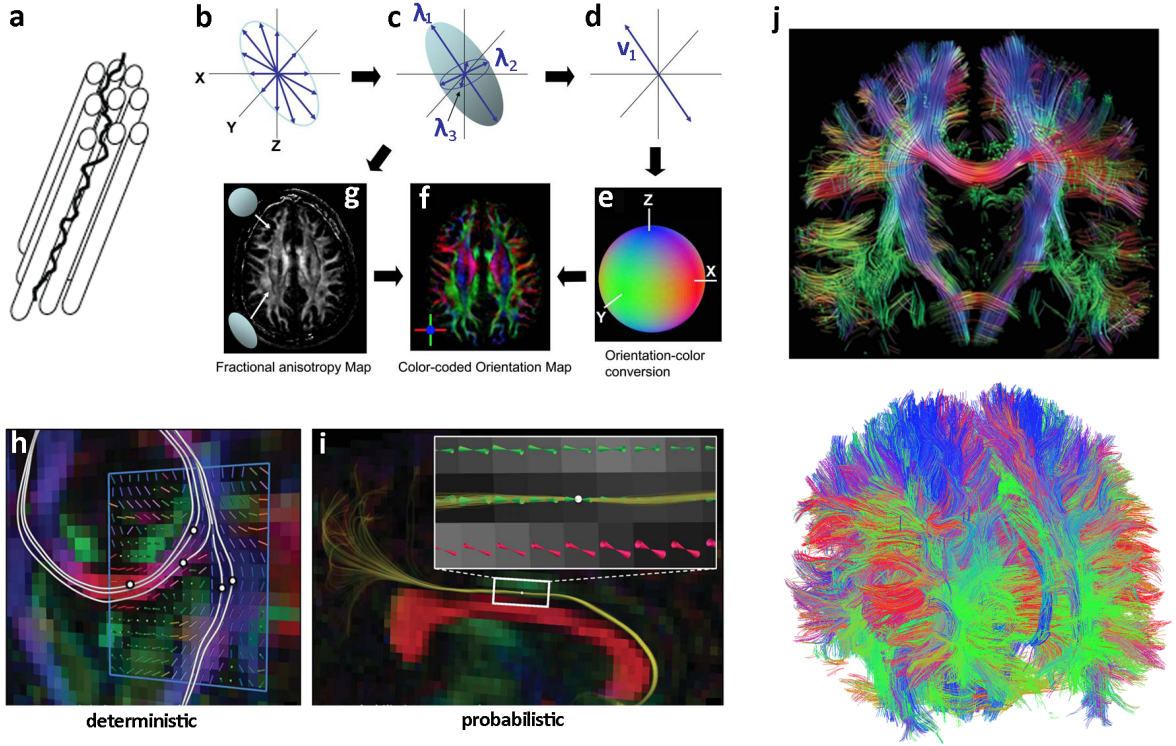
Engel et al. Neuron, 2013

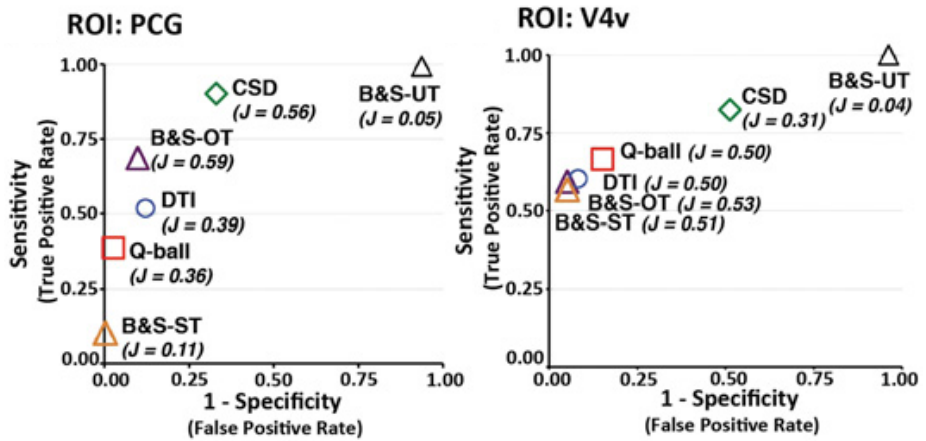
fMRI



Smith et al. NeuroImage, 2011

mapping structural connectivity in humans with DWI





Johansen-Berg & Rushworth, Ann Rev Neurosci, 2014; Mori & Zhang, Neuron, 2008; Tournier et al. Magn Res Med, 2011; Isenberg, 2011; Thomas, et al. PNAS, 2014

measuring connection weights with diffusion MRI

connection weights typically estimated as:

number of connecting streamlines

average tract FA or other diffusivity index

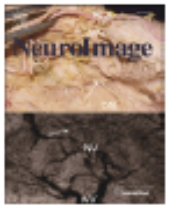
but:

Neuroimage 73 (2013) 239–254

Contents lists available at SciVerse ScienceDirect

NeuroImage

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



Comments and Controversies

White matter integrity, fiber count, and other fallacies: The do's and don'ts of diffusion MRI

Derek K. Jones[a,b,*], Thomas R. Knösche[c], Robert Turner[c]

[a] Cardiff University Brain Research Imaging Centre (CUBRIC), School of Psychology, Cardiff University, Park Place, Cardiff, CF10 3AT, UK
[b] Neuroscience and Mental Health Research Institute, Cardiff University, Cardiff, CF10 3AT, UK
[c] Max Planck Institute for Human Cognitive and Brain Sciences, Stephanstrasse 1A, 04013 Leipzig, Germany

emerging approaches include:

axon morphology (Assaf & Basser, NeuroImage, 2005)

axon diameter & density (Alexander et al. NeuroImage, 2010; Assaf et al. Magn Res Med, 2011)

track density imaging (Calamante, et al. NeuroImage, 2011)

myelin content (Deoni et al. Magn Res Med, 2008)

defining edges

structural

electron microscopy

Bock et al. Nature, 2011
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tract-tracing

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Modha & Singh PNAS, 2010
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http://cocomac.org

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Axer, et al. NeuroImage, 2011

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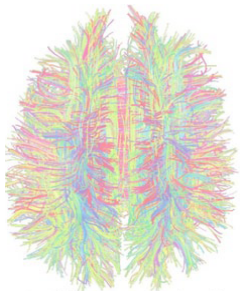

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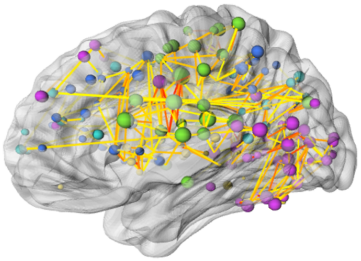
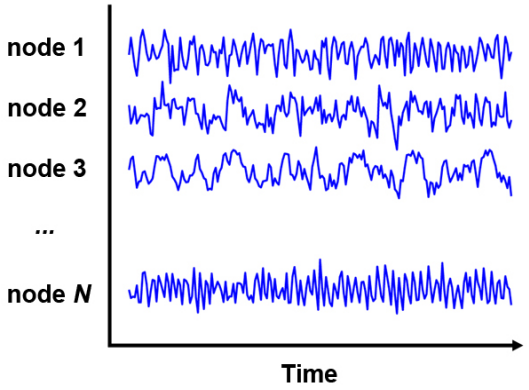


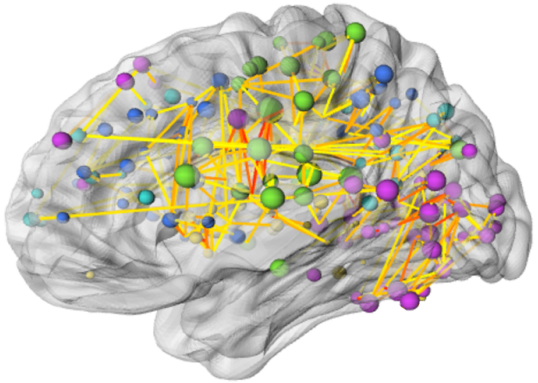
Fornito et al. NeuroImage, 2013
Smith et al. NeuroImage, 2011

mapping functional connectivity with fMRI

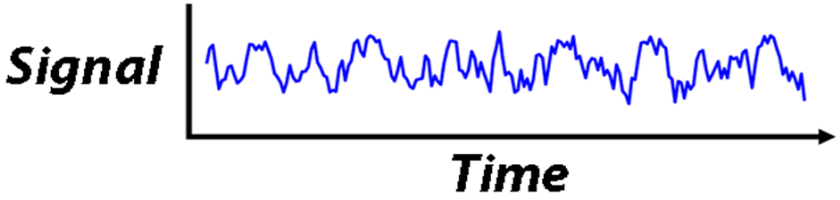


statistical dependence

correlation
partial correlation
mutual information
...
etc

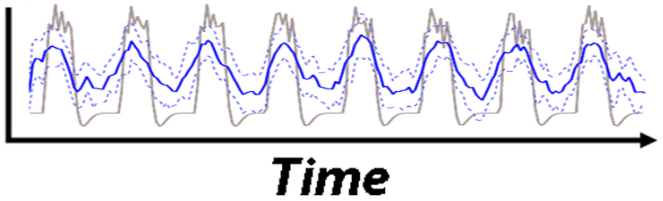


rest



Fox & Raichle, Nat Rev Neurosci, 2002
Achard et al. J Neurosci, 2005
Smith et al. NeuroImage, 2011

task



Fornito et al. PNAS, 2012
Fornito et al. Biol Psychiatry, 2012
Cole et al. Nat Neurosci, 2013

dynamics

Zalesky et al. PNAS, 2014
Hutchison, et al. NeuroImage, 2013

overview

Why graph theory?

Building a brain graph
Defining nodes
Defining edges
Matrices and graphs

Network analysis
Connectivity
Topology

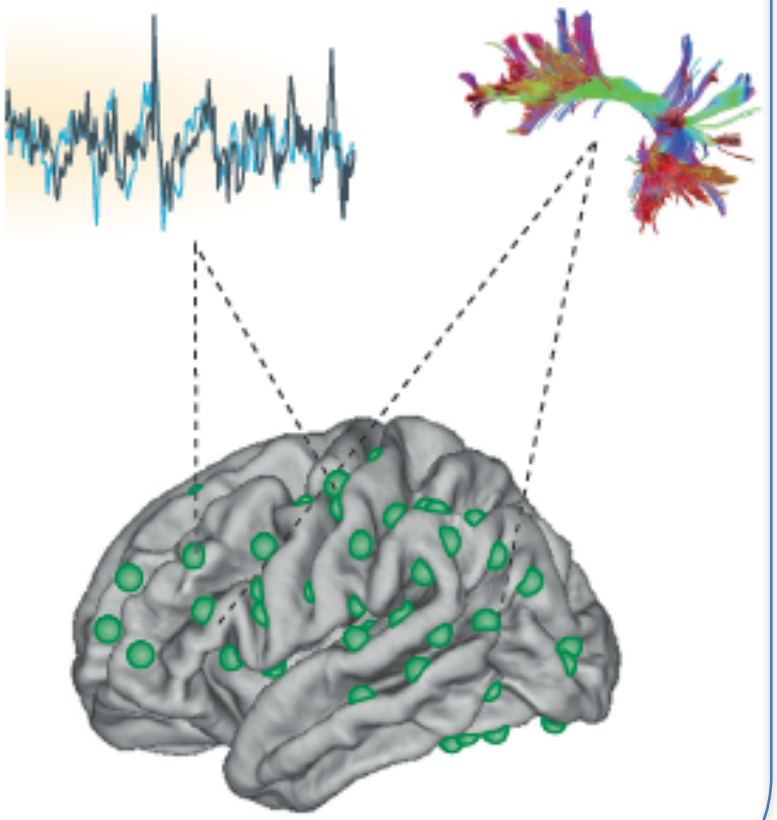
Null models
Edge rewiring

from data to graph

define nodes & edges

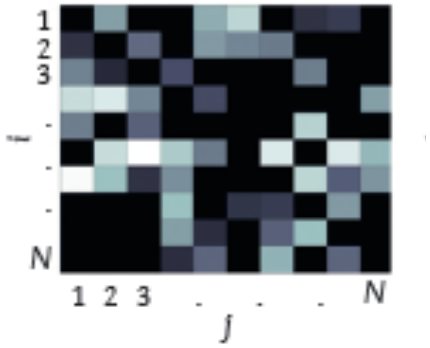
functional connectivity

structural connectivity



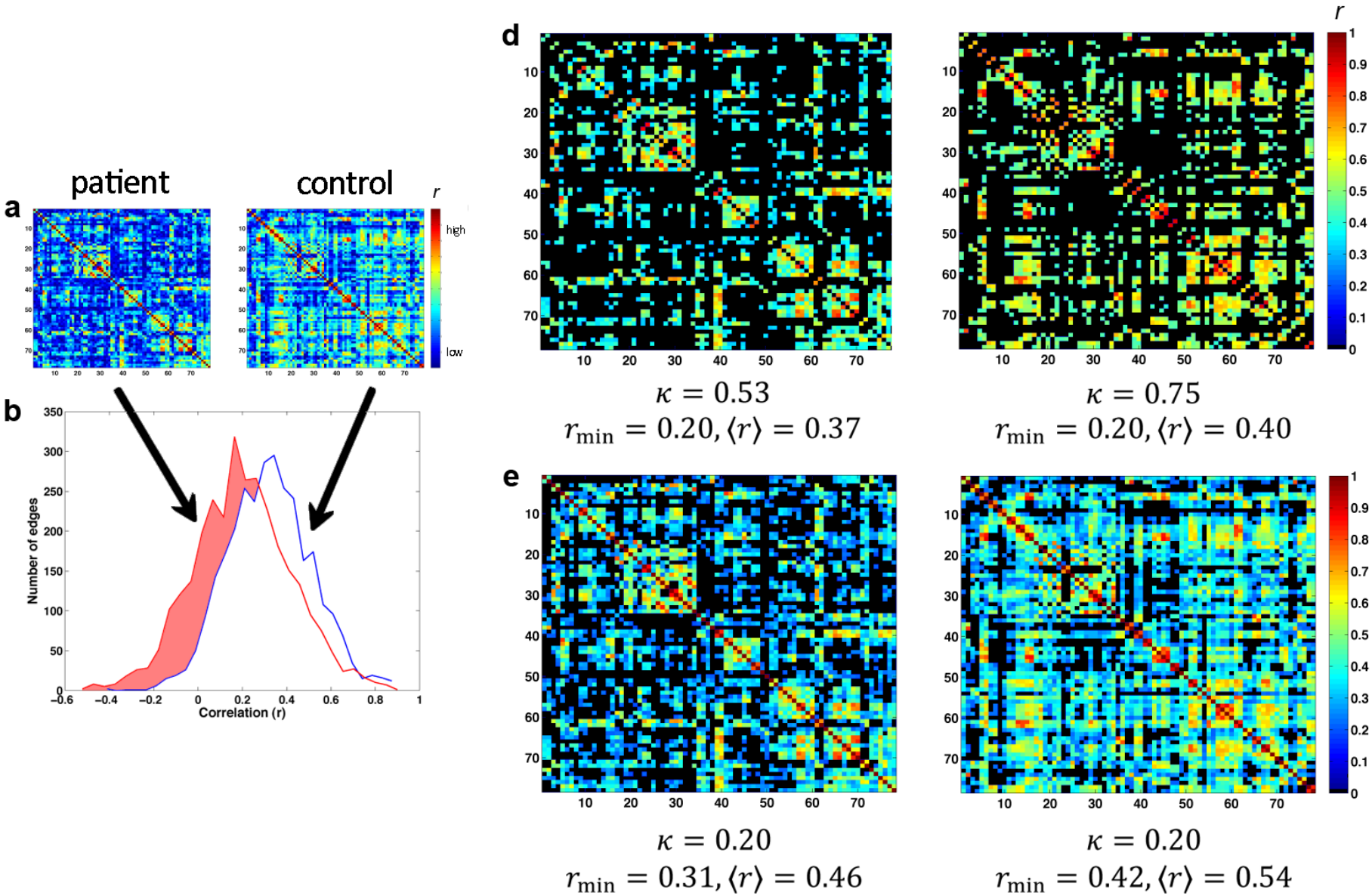
build graph

adjacency matrix



Fornito, Zalesky, & Breakspear. 2015, Nat Rev Neurosci

matrix thresholding



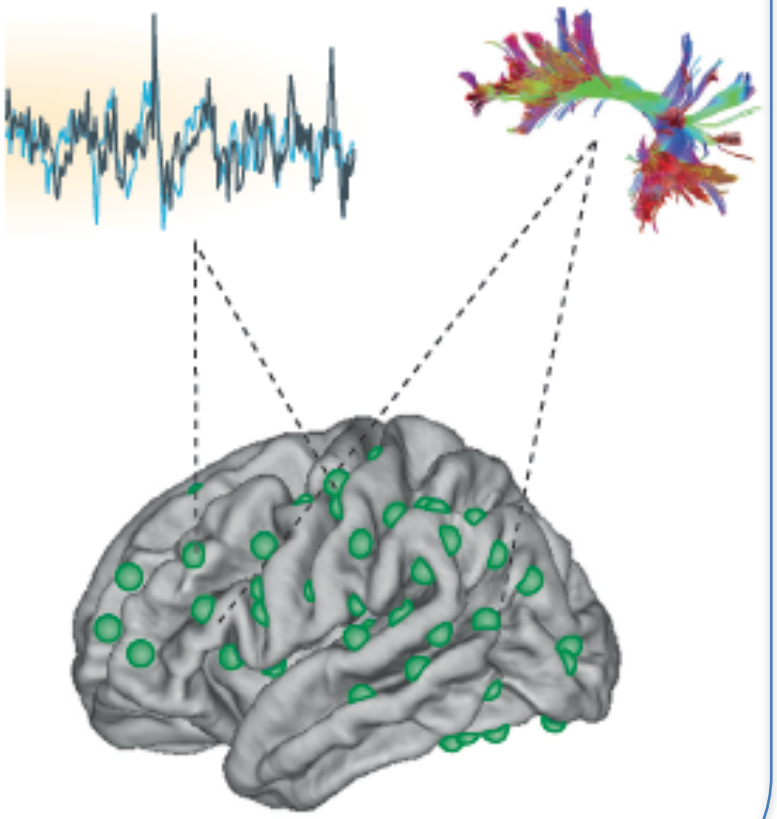
Fornito, Zalesky & Breakspear. 2013, NeuroImage; see also van Wijk et al. PLoS One, 2010

from data to graph

define nodes & edges

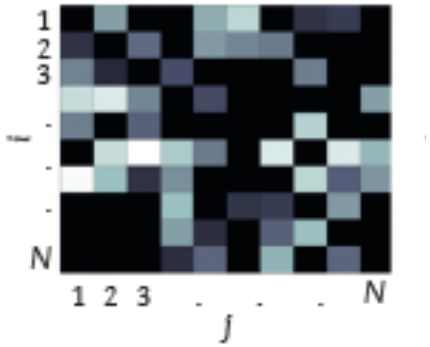
functional connectivity

structural connectivity

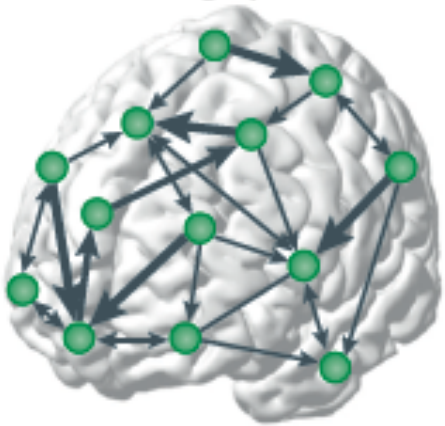


build graph

adjacency matrix



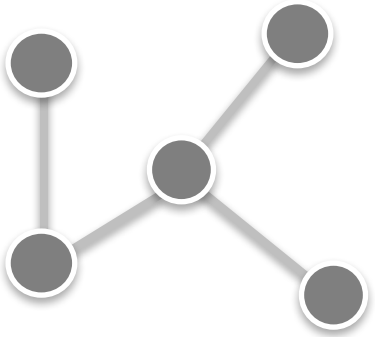
brain graph



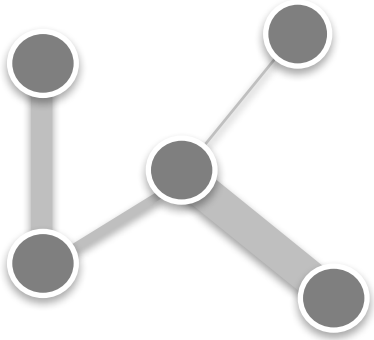
Fornito, Zalesky, & Breakspear. 2015, Nat Rev Neurosci

which graph best represents the brain?

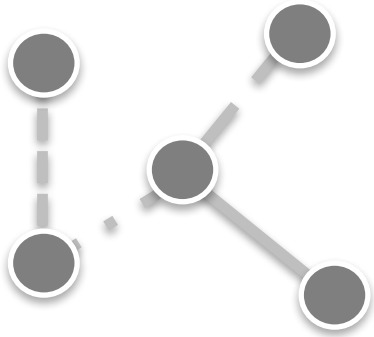
binary



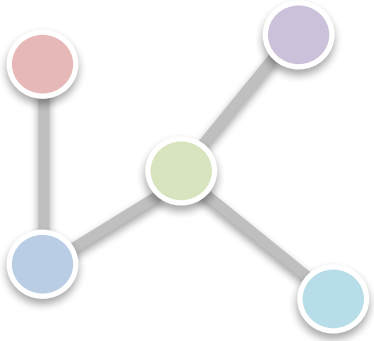
weighted



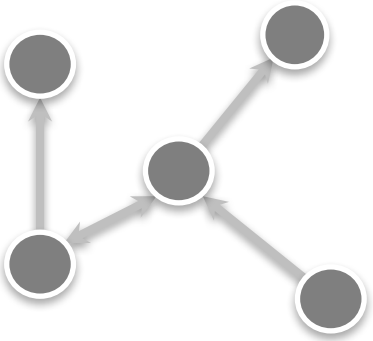
heterogeneous edges



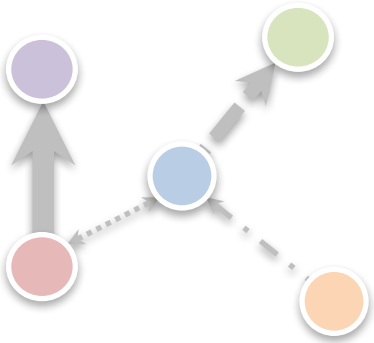
heterogeneous nodes



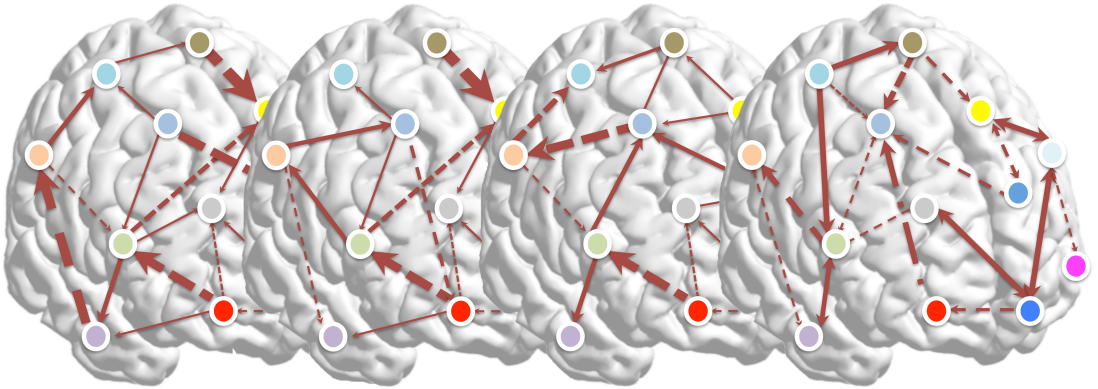
directed



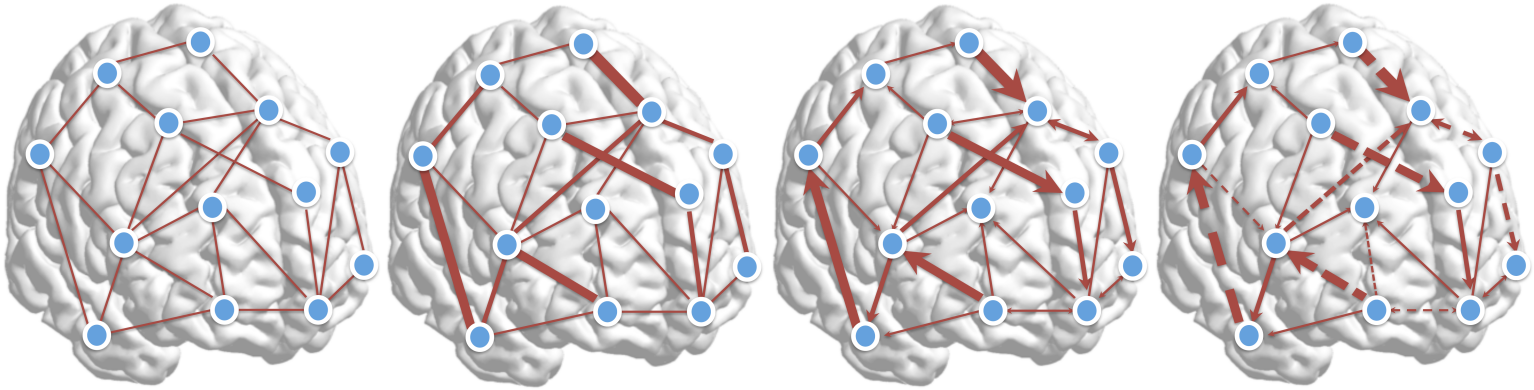
hybrid



which graph best represents the brain?



time (milliseconds to years)



nodes	homogeneous	homogeneous	homogeneous	homogeneous
edges	homogeneous	homogeneous	homogeneous	heterogeneous
weight	binary	weighted	weighted	weighted
directionality	undirected	undirected	directed	directed
method	all	all	electron microscopy tract-tracing most functional imaging	electron microscopy tract-tracing + some functional imaging

Fornito, Zalesky, & Breakspear. 2013, NeuroImage; Fornito, Zalesky, Bullmore, 2016, *Fundamentals of Brain Network Analysis*

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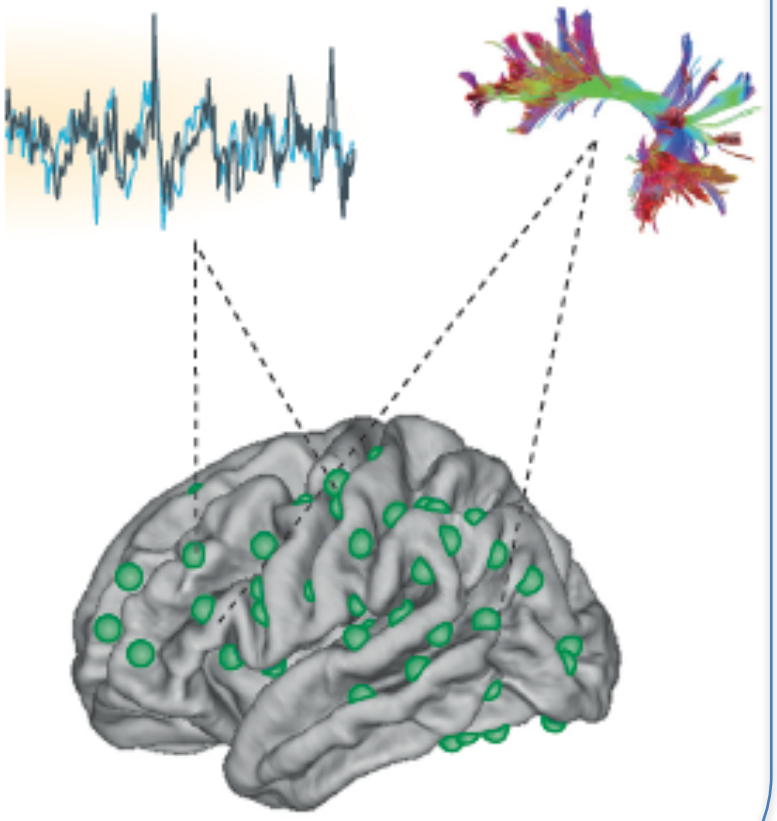
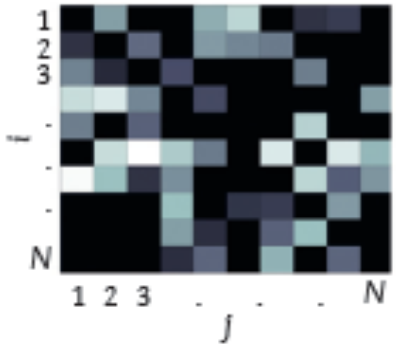
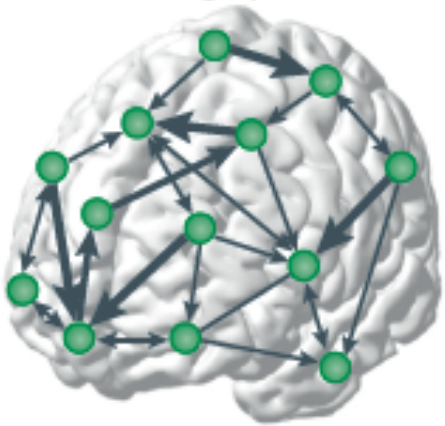


build graph

adjacency matrix

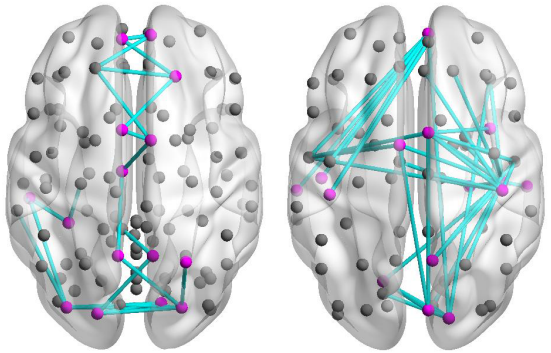


brain graph

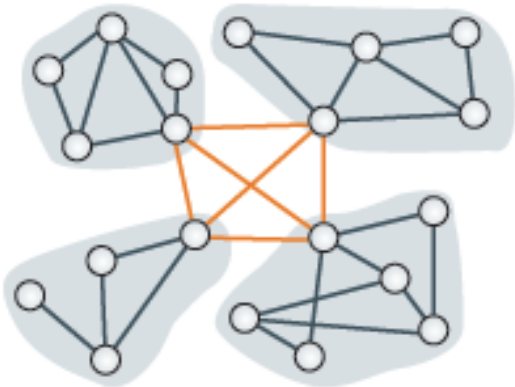


network analysis

connectivity



topology

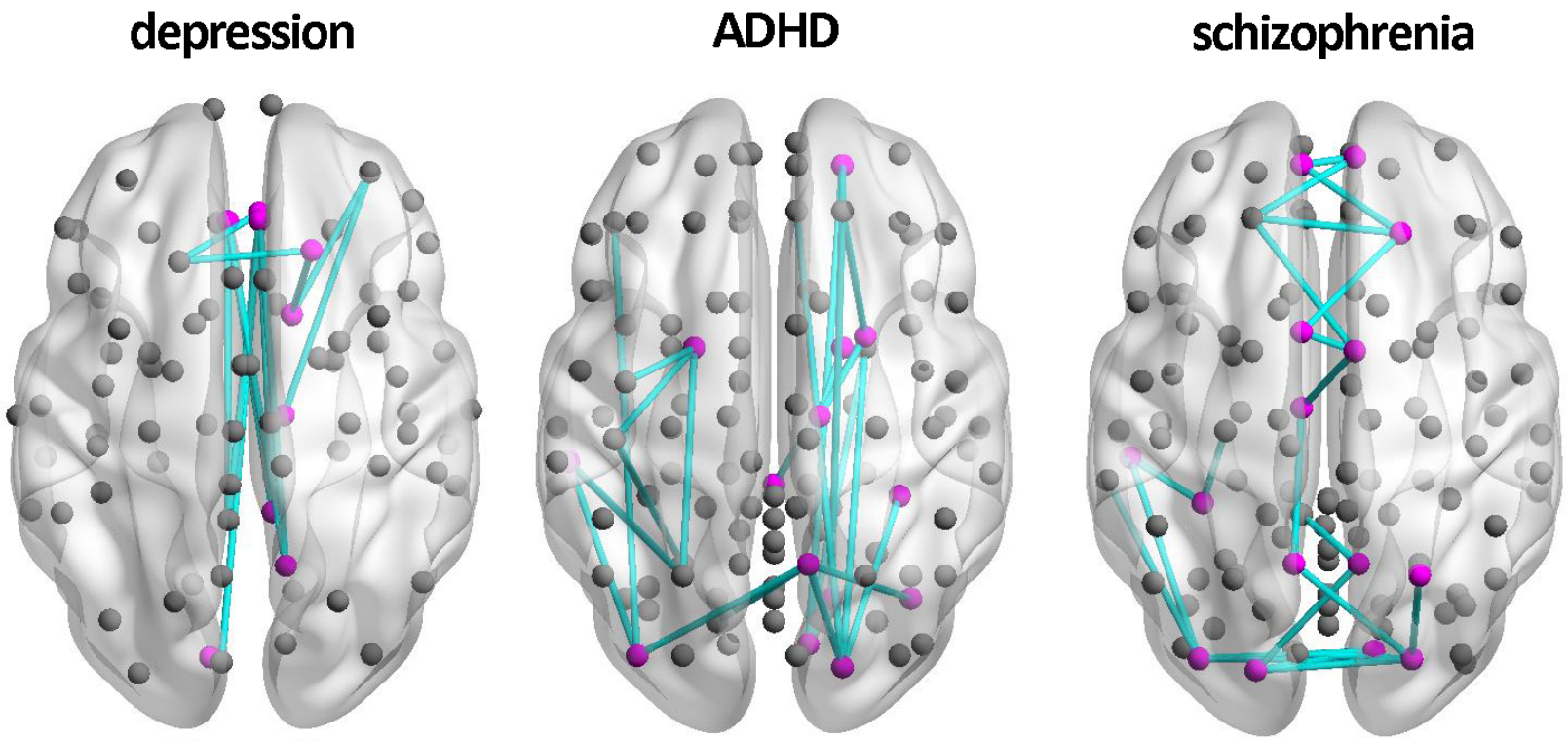


Fornito, Zalesky, & Breakspear. 2015, Nat Rev Neurosci

network analysis: connectivity

connectivity can be studied at level of edges or regions

see talk by Andrew Zalesky

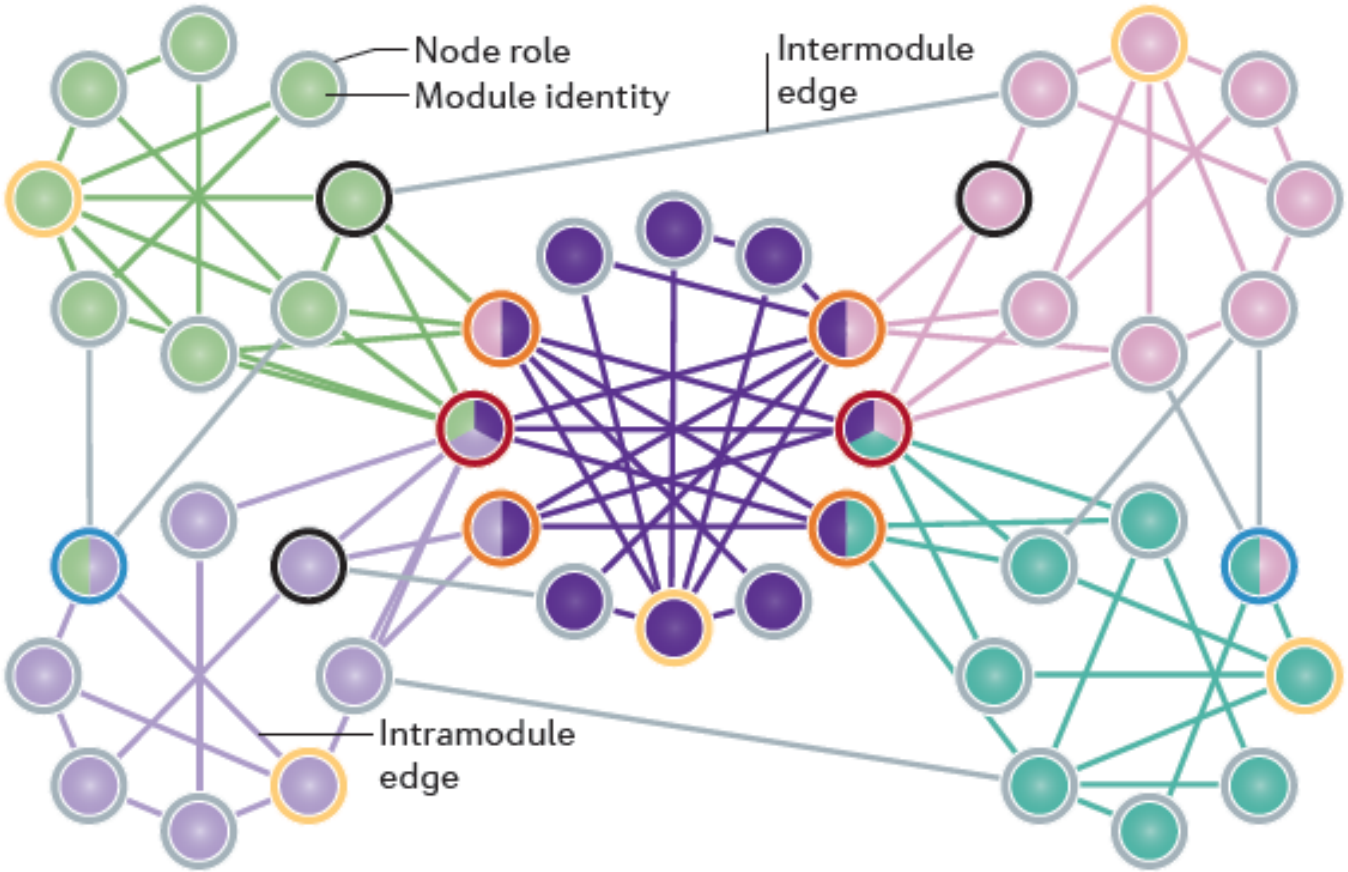


Korgaonkar, et al. 2014, Biol Psychiatry; Hong et al. Biol Psychiatry, 2014, Zalesky et al. Biol Psychiatry, 2011

network analysis: topology

modules facilitate functional specialization and segregation

see talk by Damien Fair

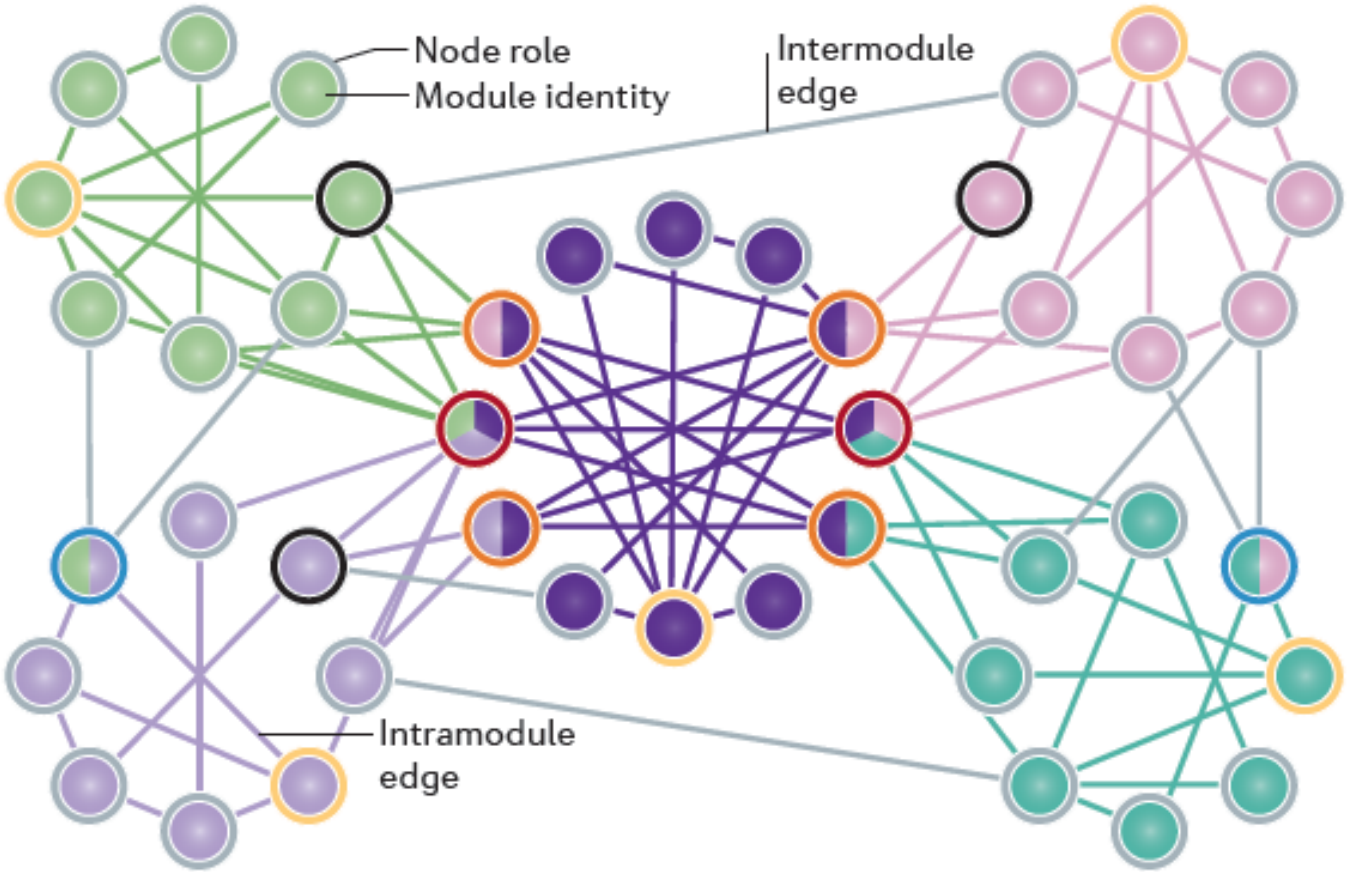


Fornito, Zalesky, & Breakspear. 2015, Nat Rev Neurosci

network analysis: topology

modules facilitate functional specialization and segregation
see talk by Damien Fair

hubs form a topologically central core (rich club) that facilitates integrated communication
see talks by Bratislav Misic & Martijn van den Heuvel



Fornito, Zalesky, & Breakspear. 2015, Nat Rev Neurosci

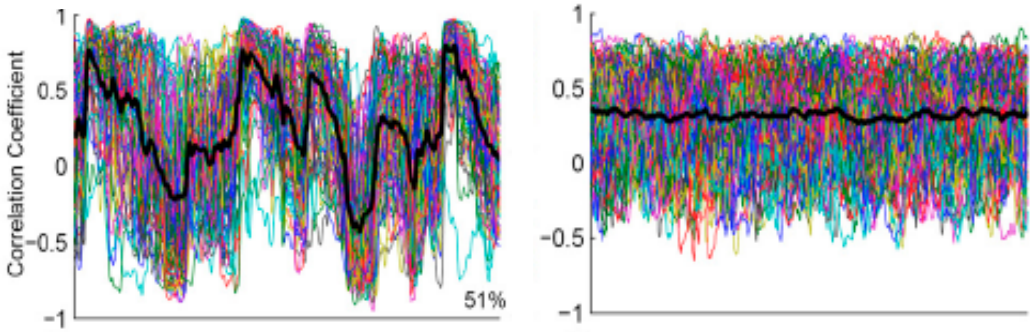
network analysis: topology

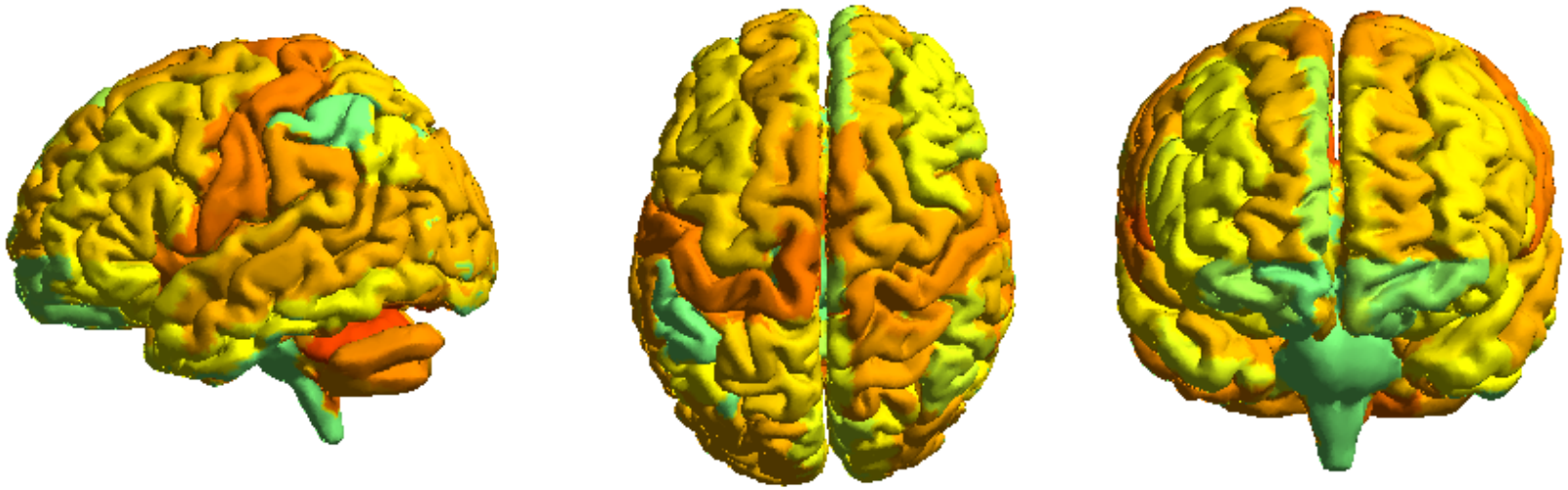
brain networks are dynamic

see talks by Mark Woolrich & Danielle Bassett

observed

null



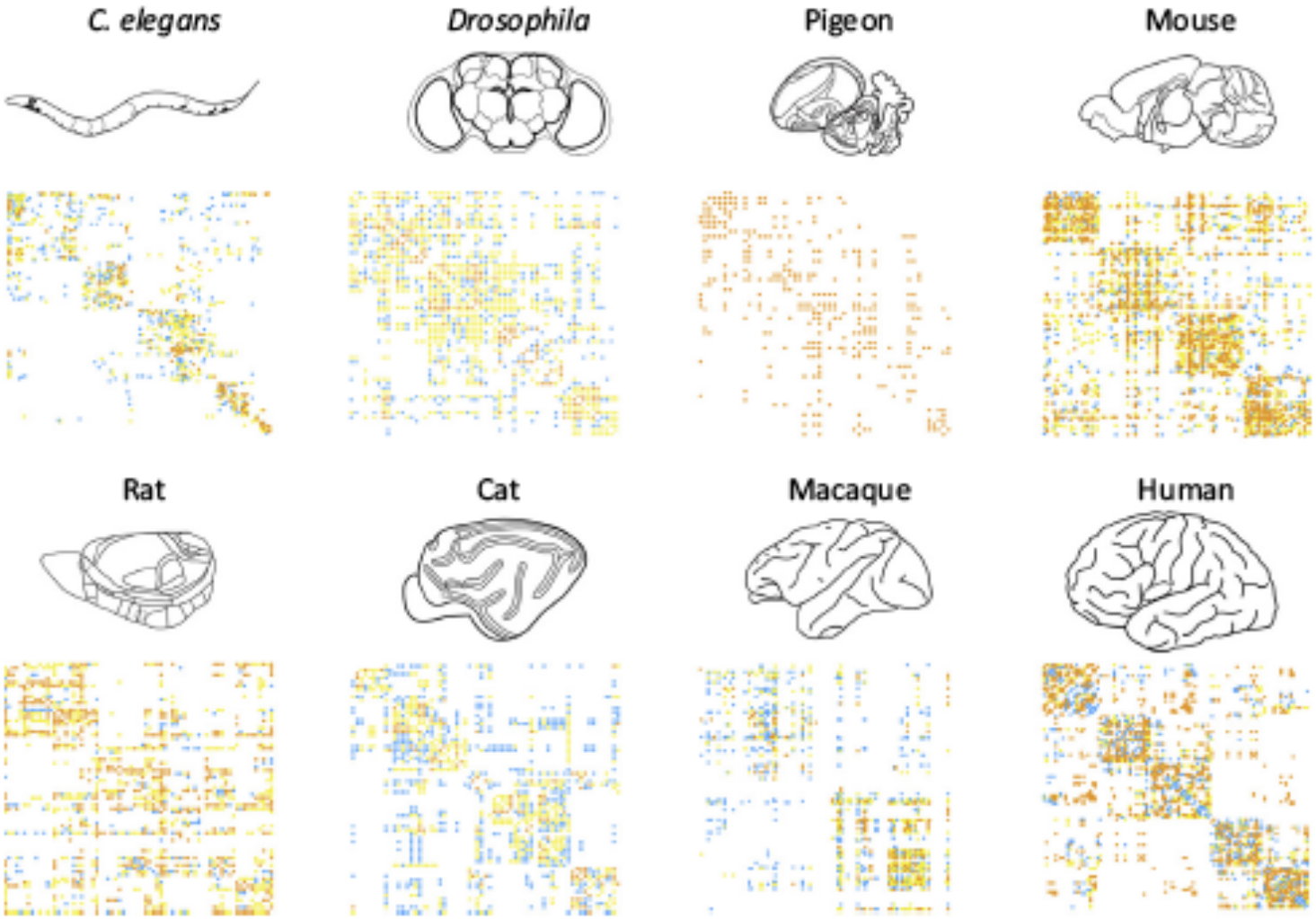


Zalesky, Fornito, Cocchi, Gollo & Breakspear, PNAS, 2014

network analysis: topology

many topological properties are conserved across scales and species

see talk by Ed Bullmore

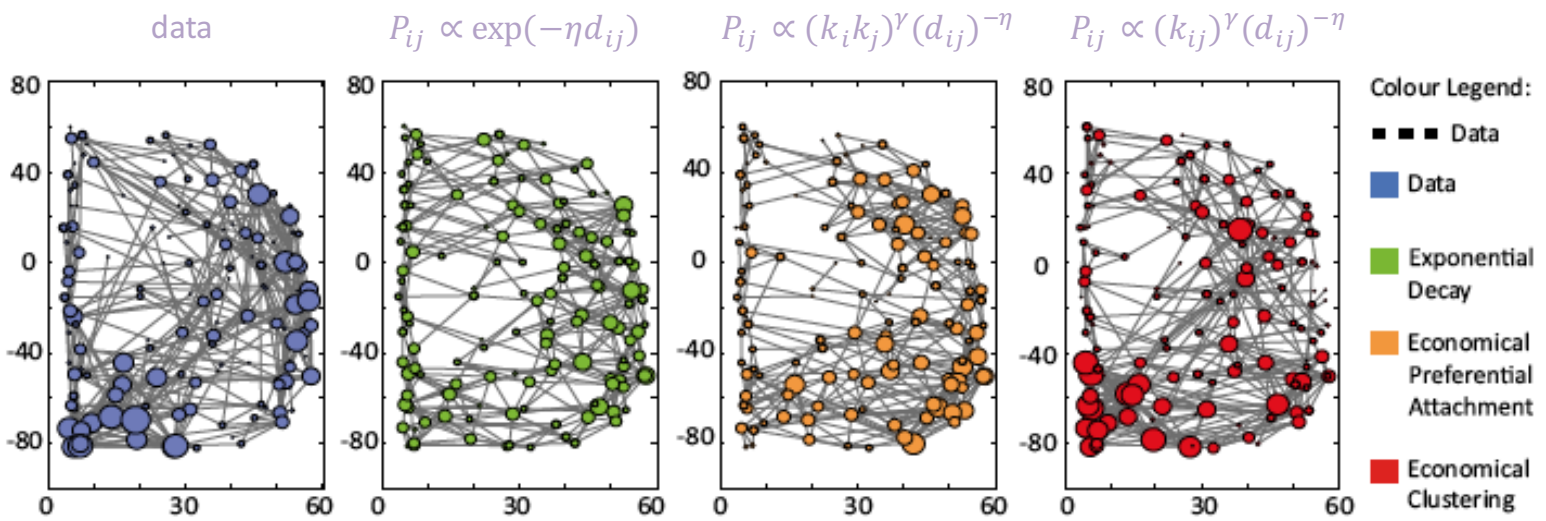


van den Heuvel, Bullmore & Sporns, 2016, TICS

network analysis: topology

many topological properties can be explained by cost-value trade-offs

see talk by Rick Betzel

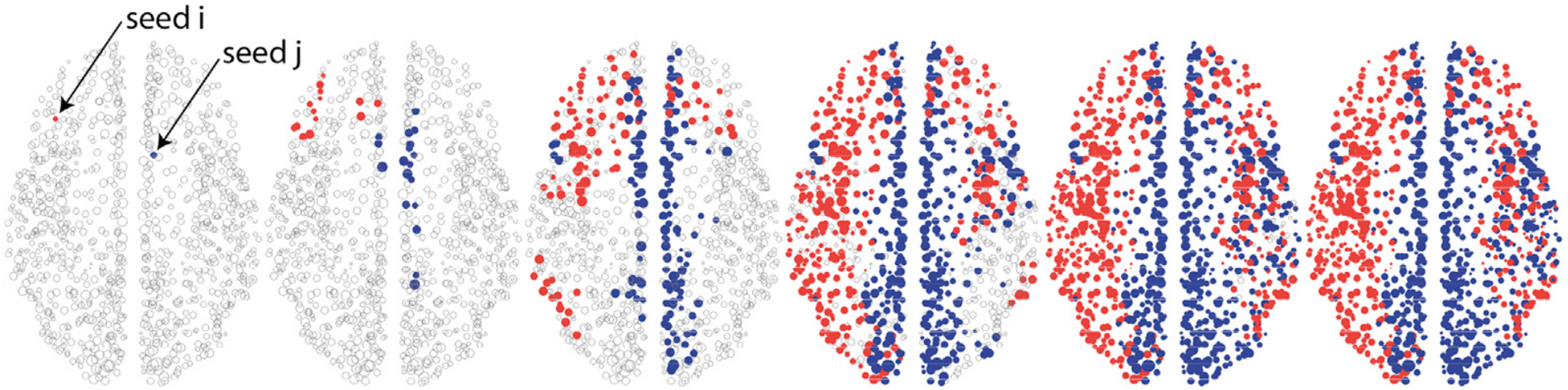


Vertes et al. 2012, PNAS

network analysis: topology

network topology shapes dynamics and disease evolution

see talks by Bratislav Mišić & Ashish Raj



Mišić et al. 2015, Neuron

overview

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Topology

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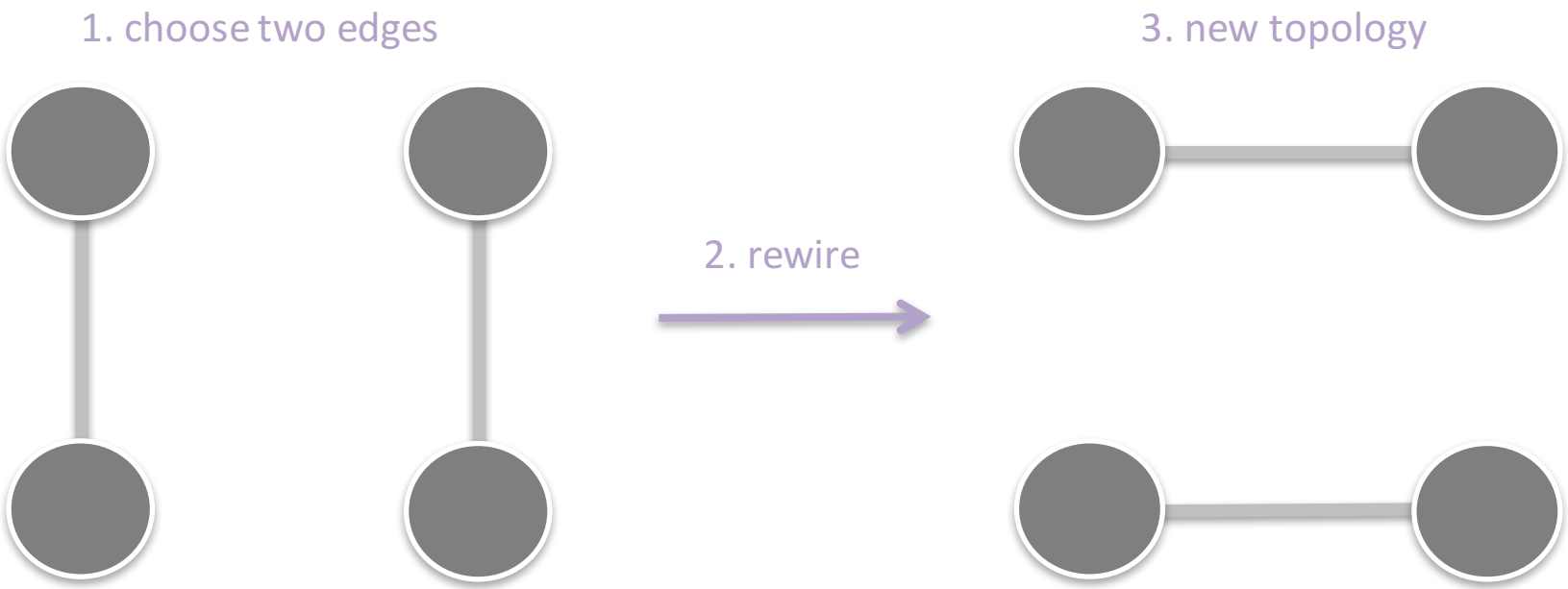
Edge rewiring

null models

Maslov & Sneppen rewiring (Science, 2002)



preserves number of nodes, edges, and degree sequence

other algorithms are also available

preserve strength distributions (Rubinov & Sporns, NeuroImage, 2011)
preserve spatial properties (Samu et al. PLoS Comp Biol, 2014; Roberts et al, NeuroImage, 2016)
preserve correlation structure (Zalesky et al. NeuroImage, 2012)

summary

Graphs provide useful models of brain networks
A unified framework for representing multiscale organization

There are different methods for defining brain nodes and edges
Each has pros and cons, and constrains interpretation of findings

Brain networks can be analysed at the level of connectivity or topology
Effects can be mapped at individual edges, nodes, or globally

Null models should be chosen carefully
Different methods/measures/questions require specific null models

resources (and shameless plugs)

graph theory/network science

Newman (2010) Networks: An introduction.

Newman (2003) SIAM Rev.

Albert & Barabasi (2002) Rev Modern Physics

graph theory and the brain

Sporns (2011) Networks of the brain.

Sporns (2012) Discovering the human connectome.

Bullmore & Sporns (2009) Nat Rev Neurosci.

Bullmore & Bassett (2011) Annu Rev Clin Psychol.

Fornito, Zalesky & Breakspear (2013) NeuroImage.

software

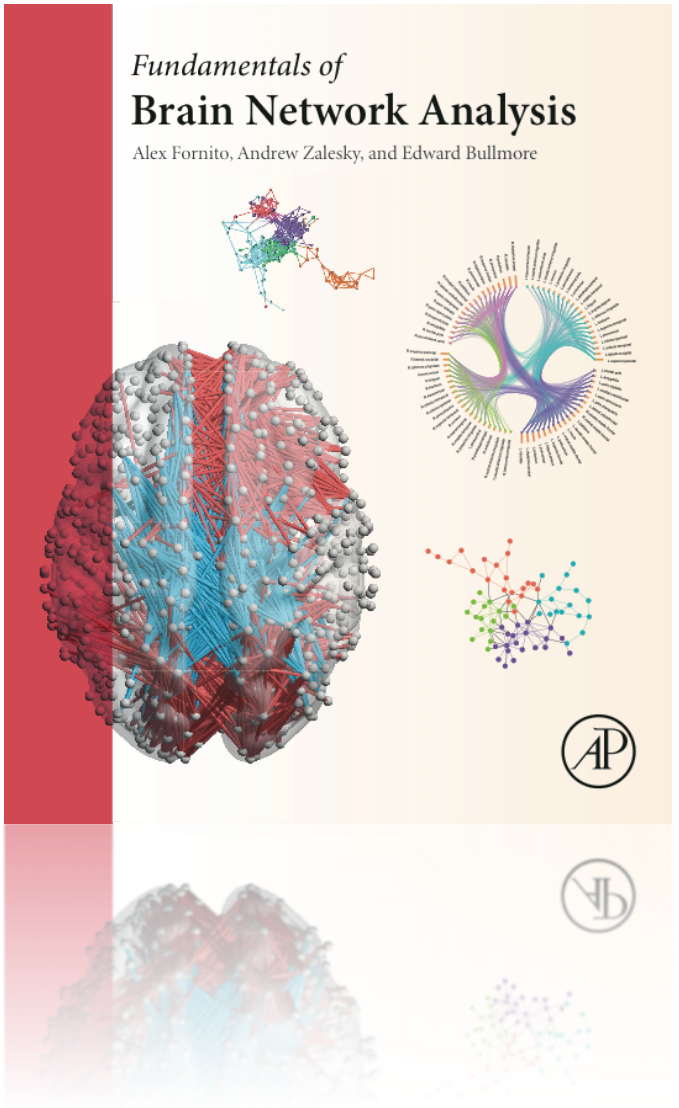
Brain connectivity toolbox:
https://sites.google.com/site/bctnet/

Graph analysis toolbox:
https://www.nitrc.org/projects/gat/

Network-based statistic:
http://www.nitrc.org/projects/nbs/

Task-related functional connectivity (cPPI):
http://www.nitrc.org/projects/cppi_toolbox/

Network visualization (beta)
http://immersive.erc.monash.edu.au/neuromarvl/



Amazon: http://amzn.to/1MLgMhU

Elsevier: http://bit.ly/1Hp29OZ