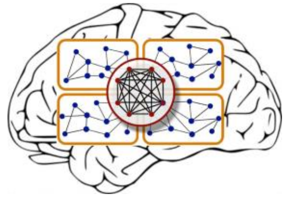
Complex structure and dynamics in neural systems



Rafael Romero-Garcia
Department of Psychiatry
rr480@cam.ac.uk

Cambridge MPhil in Computational Biology
University of Cambridge
February 2017

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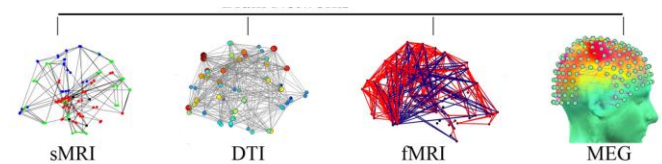
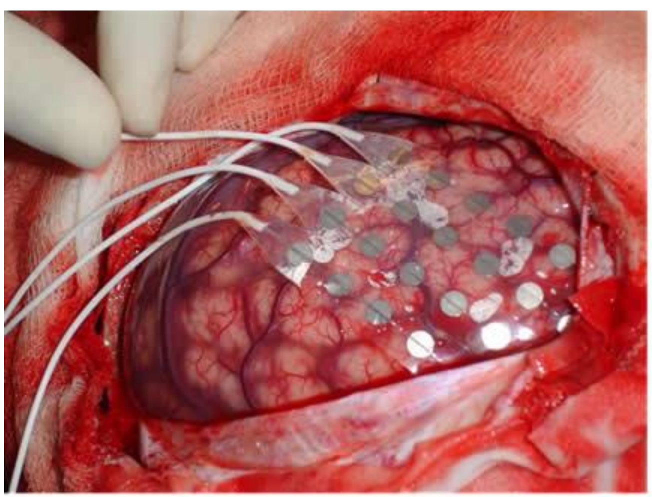
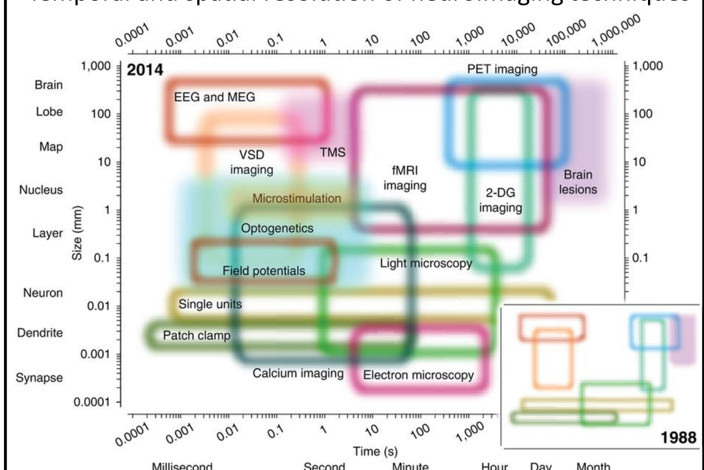
Complex networks are a universal framework for representation of multimodal brain connectivity

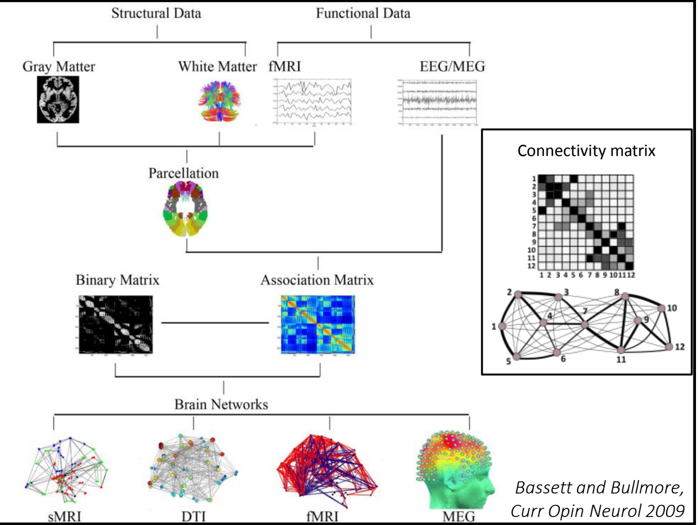


Bassett and Bullmore, Curr Opin Neurol 2009

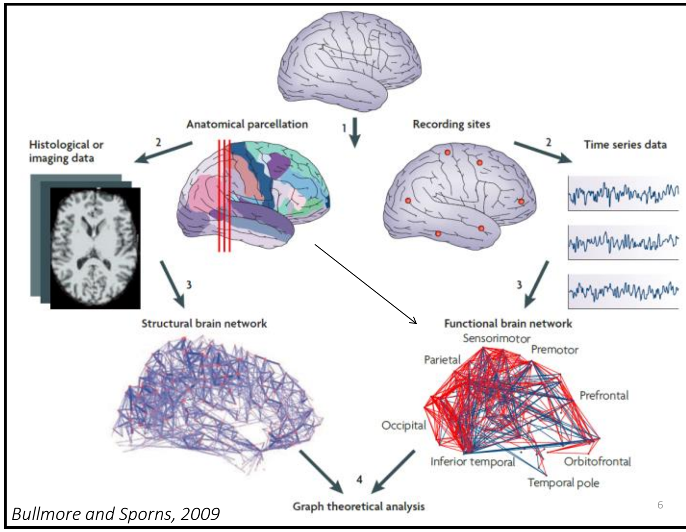


Temporal and spatial resolution of neuroimaging techniques





Bassett and Bullmore, Curr Opin Neurol 2009



Bullmore and Sporns, 2009

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Complexity is not easy to define

- Complexity
  - The quality or state of not being simple: the quality or state of being complex
  - The state or quality of being intricate or complex
  - Something with many parts where those parts interact with each other in multiple ways
- Complex
  - Involving a lot of different but related parts
  - The complexity of a physical system or a dynamical process expresses the degree to which components engage in organized structured interactions

There are three distinct notions of complexity

1st notion: Difficulty of “creation”

- Computational complexity.
- Wiring cost (although it’s not usual to describe wiring cost in these terms).

Thanks to Seth Lloyd, MIT

There are three distinct notions of complexity

2nd notion: Difficulty of "description"

- Kolmogorov complexity, entropy.
  - Lowest for ordered organizations:
    - E.g. abababababababababa
  - Highest for random organizations.
    - E.g 4c1j5b2p0cv4w1x8rx2y

Thanks to Seth Lloyd, MIT

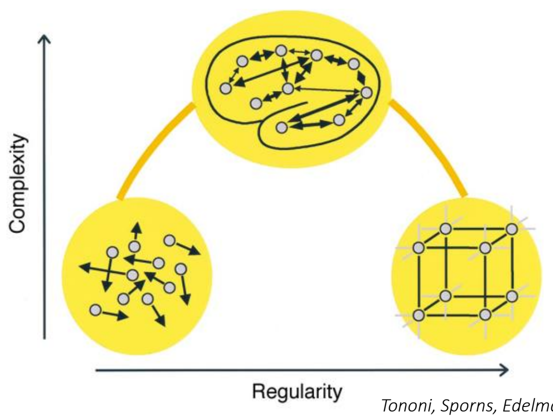
There are three distinct notions of complexity

<u>3rd notion: "Richness" of organization.</u>

- Low for ordered organizations,
  High between order and randomness
  Low for random organizations

Thanks to Seth Lloyd, MIT

"Richness" of organization



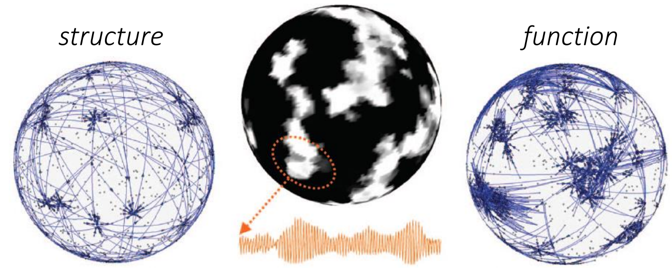
Tononi, Sporns, Edelman, 1998

We are interested in <u>structural</u>, <u>dynamical</u> (and <u>functional</u>) complexity of this third kind.

dynamics

structure

function



Sporns and Honey, 2006

Overview

Structure: Complex topology of brain-wiring diagrams

- small-worldness

Dynamics: Complex brain activity

- multistability
- neuronal avalanches
- neural complexity

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STRUCTURE:
COMPLEX TOPOLOGY OF BRAIN-WIRING DIAGRAMS

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Review

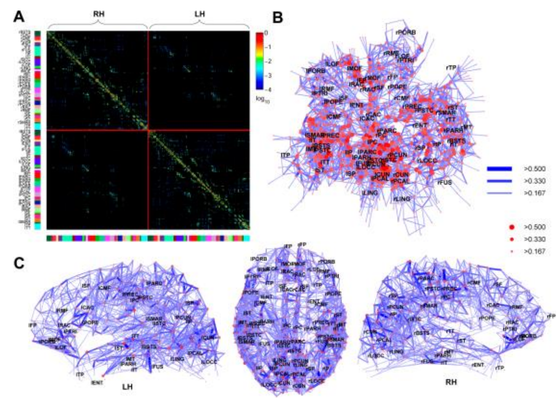
The Human Connectome: A Structural Description of the Human Brain

Olaf Sporns*, Giulio Tononi, Rolf Kötter

To understand the functioning of a network, one must know its elements and their interconnections. The purpose of this article is to discuss research strategies aimed at a comprehensive structural description of the network of elements and connections forming the human brain. We propose to call this dataset the human "connectome," and we argue that it is fundamentally important in cognitive neuroscience and neuropsychology. The connectome will

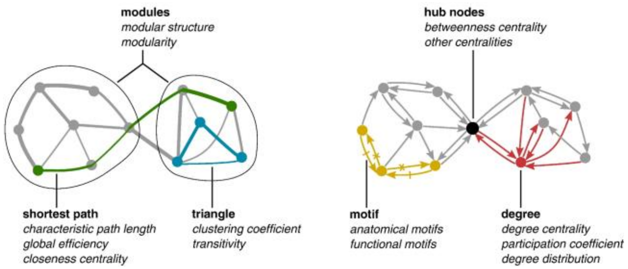
Sporns et al., 2005.

Topological complexity of brain-wiring diagrams



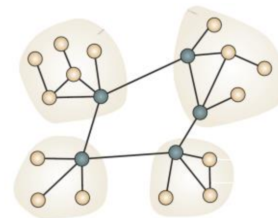
Hagmann et al., 2008

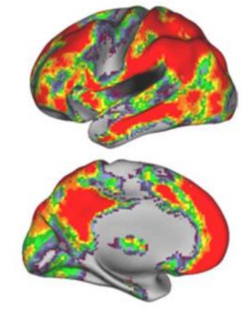
Topological complexity of brain-wiring diagrams



Rubinov and Sporns, 2010

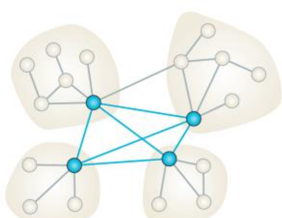
Measures of network microscale describe properties of single nodes

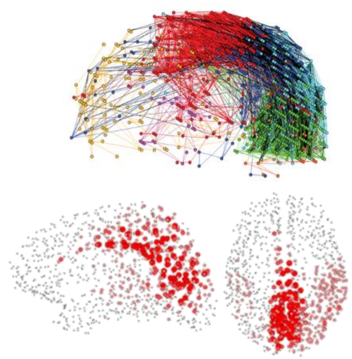




Buckner et al., 2009.

Measures of network mesoscale describe properties of groups of nodes





Hagmann et al., 2008; Meunier et al., 2011.

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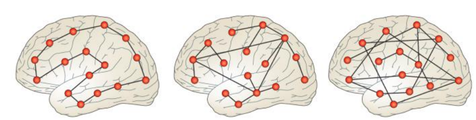
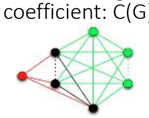
Measures of network macroscale summarize properties of the whole network in a single statistic



Clustering coefficient: C(G)



$C_{red} = \frac{2*2}{3*(3-1)} = 0.66$

Path length: L(G)

Small-world: σ(G)

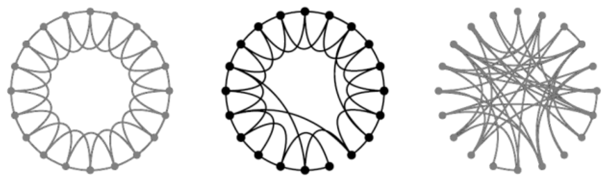
$$\sigma(G) = \frac{C(G)}{L(G)}$$

Bullmore and Sporns, 2012.

Small-worldness is a simple measure of topological complexity: the combination of high clustering and low path length

$$\sigma(G) = \frac{C(G)}{L(G)}$$

Lattice	Small-world	Random
High clustering	High clustering	Low clustering
High path length	Low path length	Low path length



Watts and Strogatz, Nature 1998

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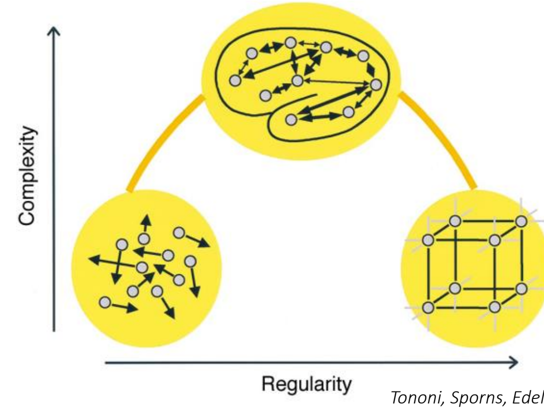
"Richness" of organization



Tononi, Sporns, Edelman, 1998

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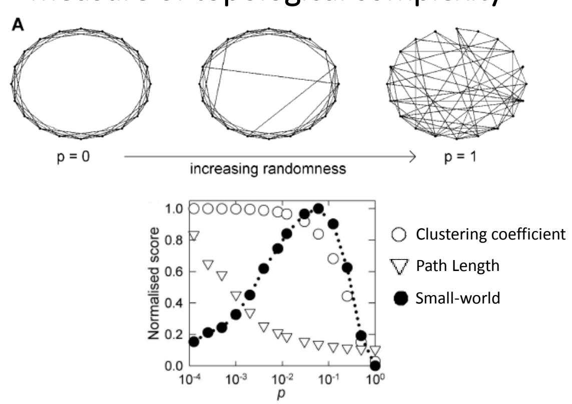
Small-worldness is a simple (simplistic) measure of topological complexity



Humphreys and Gurney, 2008

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DYNAMICS:
COMPLEX BRAIN ACTIVITY

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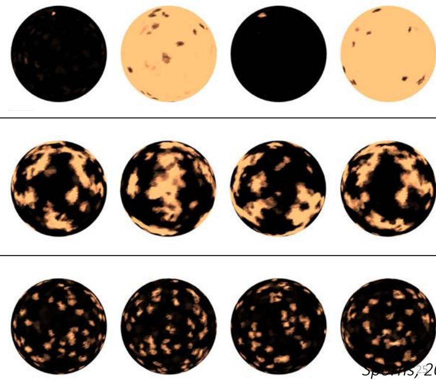
Dynamical complexity lies between order and randomness

Ordered
(low complexity)

Intermediate
(high complexity)

Random
(low complexity)



Sporns, 2007

We consider three popular notions of dynamical complexity

1. MULTISTABILITY
2. AVALANCHE DYNAMICS
3. NEURAL COMPLEXITY

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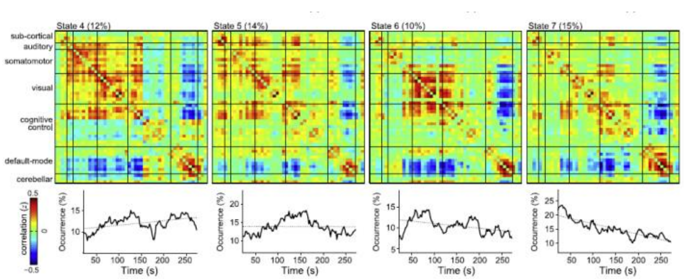
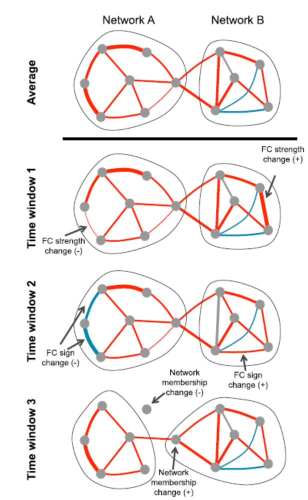
1. Multistability is the repeated exploration of distinct dynamical states



Hutchison et al., 2013



Hutchison et al., 2013

Real-time spontaneous brain activity in the mouse

Voltage sensitive dye imaging of spontaneous activity in isoflurane anesthetized mouse

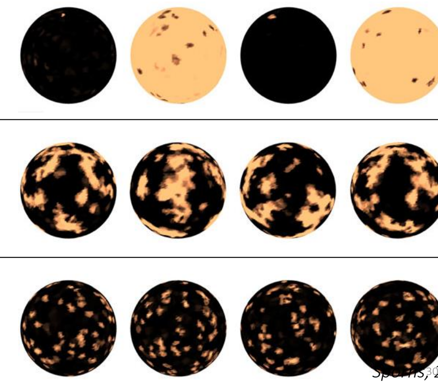
Mohajerani et al., 2013.

Multistability lies between order and randomness

Ordered
Monostable
low complexity

Intermediate
Multistable
high complexity

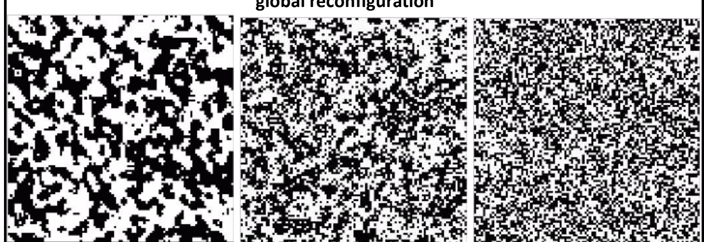
Random
Unstable
low complexity



Sporns, 2007

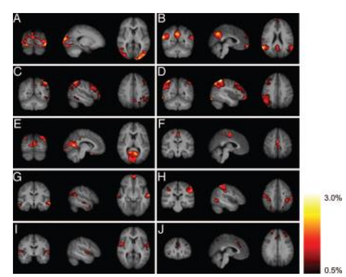
Cortical networks operate near a critical point

Dynamic based on local coupling | **Dynamic based on local coupling and global reconfiguration** | **Dynamic based on global reconfiguration**

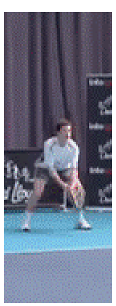


Beggs and Timme , 2012

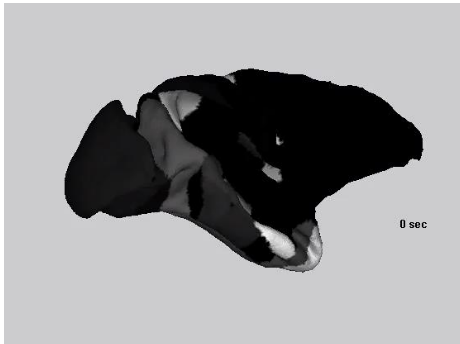
Multistability: alternating between temporality stable states provides a fast response to any stimulus



Damoiseaux et al., PNAS 2006



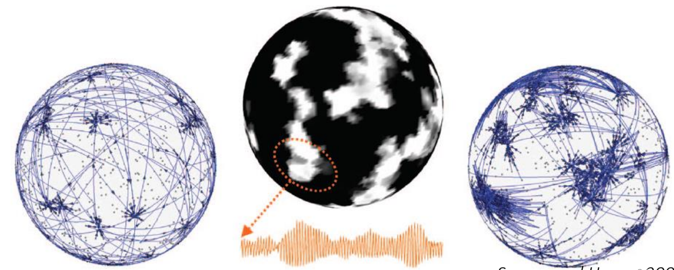
Models of brain dynamics shed light on the origin of multistability



Honey et al., 2007

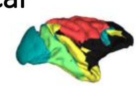
Dynamics are less significantly constrained by anatomical connectivity on short time-scales.

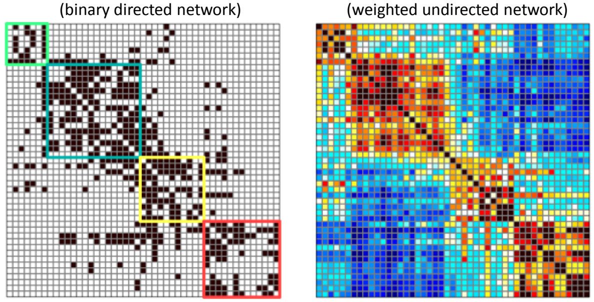
Dynamics are more significantly constrained by anatomical connectivity on long time-scales.



Sporns and Honey, 2006

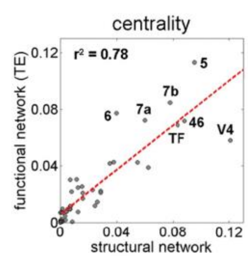
Dynamics/functional connectivity is significantly constrained by anatomical connectivity on long time-scales.

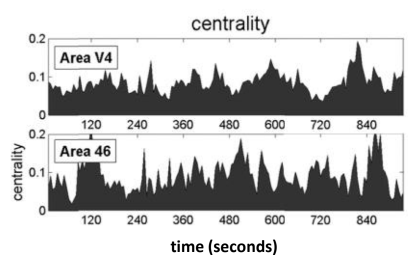




Rubinov and Sporns, 2010

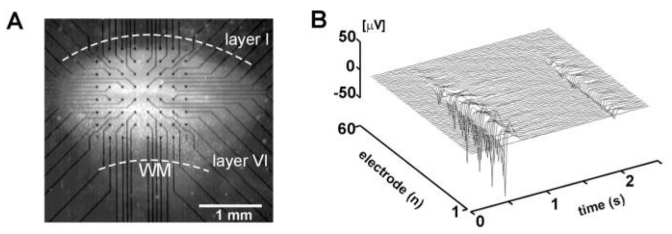
Dynamics/functional connectivity is less constrained by anatomical connectivity and is more variable on short time-scales.





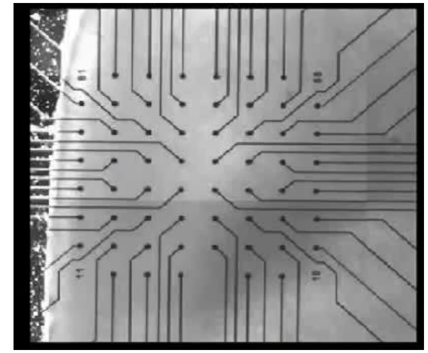
Honey et al., 2007

2. Dynamical complexity of neuronal avalanches



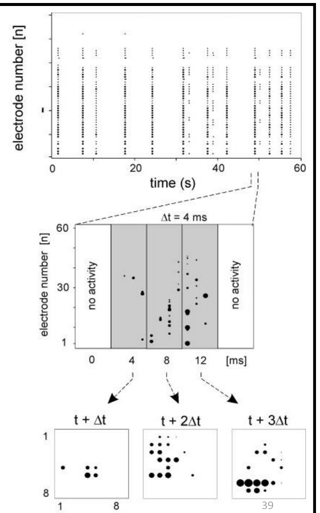
Beggs and Plenz, 2003

Neuronal avalanches are discrete spatio-temporal patterns of spontaneous activity



Dietmar Plenz Lab, NIH

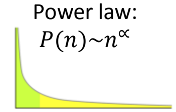
Neuronal avalanches are discrete spatio-temporal patterns of spontaneous activity

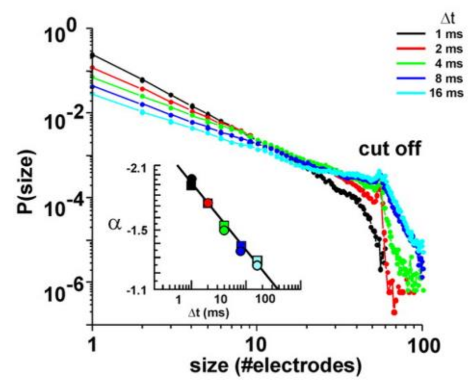


Beggs and Plenz, 2003

Sizes and durations of neuronal avalanches scale as "power laws" *in vitro* and *in vivo*

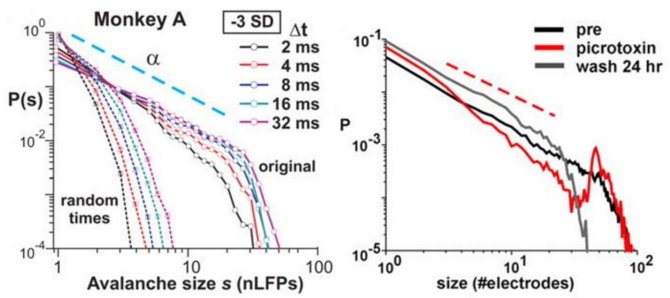
Power law:
$P(n) \sim n^{\propto}$





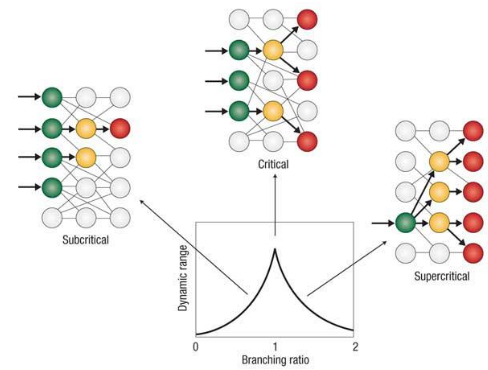
Beggs and Plenz, 2003

Such scaling of neuronal avalanches lies between order and randomness



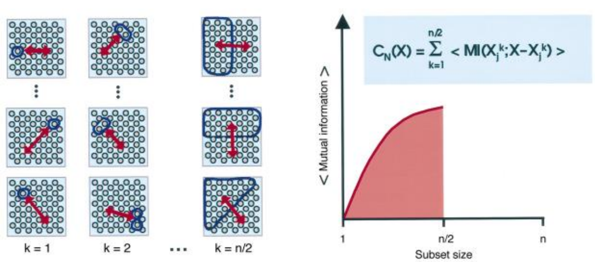
Beggs and Plenz, 2003; Petermann, et al., 2008

Such scaling is associated with functional benefits such as maximized dynamic range



Chialvo et al., 2006

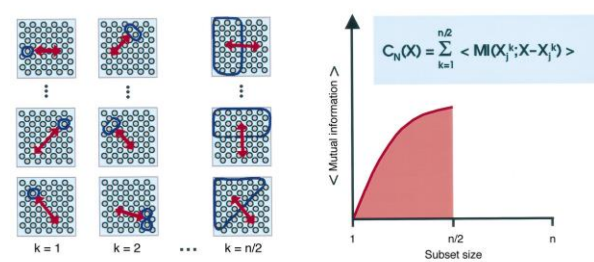
3. Neural complexity is an information theoretic measure of the simultaneous presence of segregation and integration



Tononi, Sporns and Edelman 1994

Segregation: small subsets of the system behave independently

Integration: large subsets of the system behave coherently



Tononi, Sporns and Edelman 1994

Entropy is a measure of uncertainty or variability

$$H(X) = -\sum_{m=1}^{M} p_m \log_2(p_m)$$

X is a system composed of a set of elements $\{x_i\}$, that assumens a number m=1..M of discrete states with a probability p_m

Extreme case:

System with only one possible state ($M=1$, $p_m=1$)

$$H(X) = -1 \cdot \log_2(1) = 0$$

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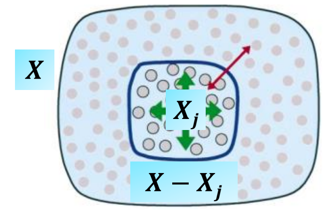
Mutual Information (MI) between X_j and X is the uncertainty in states of X_j which is accounted by states of X



$$MI(X_j; X - X_j) = H(X_j) + H(X - X_j) - H(X)$$

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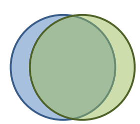
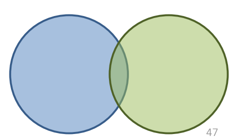
High neural complexity lies between order and randomness

<u>ordered</u>: low initial uncertainty
low remaining uncertainty

<u>complex</u>: high initial uncertainty
low remaining uncertainty



<u>random:</u> high initial uncertainty
high remaining uncertainty



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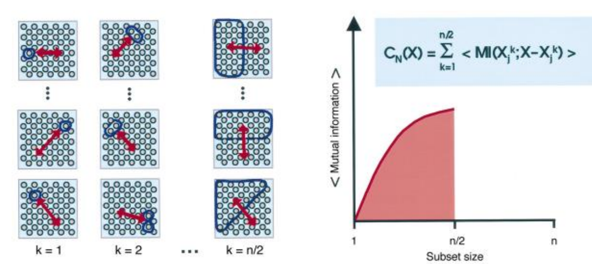
<u>Definition of neural complexity:</u>

Sum of the average mutual information (MI) across all bipartitions of the system.



Tononi, Sporns and Edelman 1994

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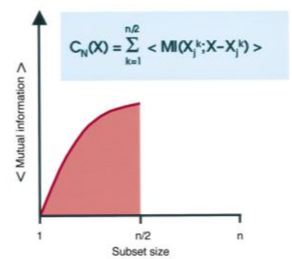
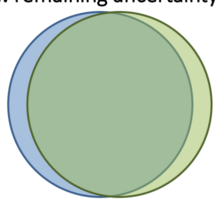
Interpretation: neural complexity is high when subsets exhibit diverse states (segregation), which influence each other (integration).



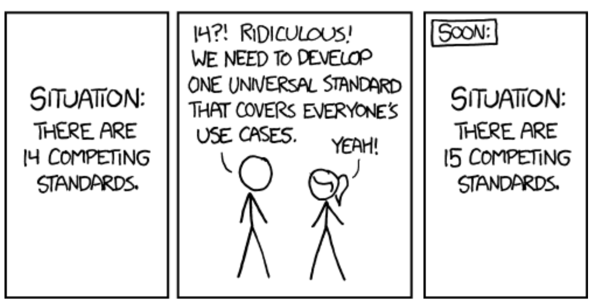
Complex:
high initial uncertainty
low remaining uncertainty



Tononi, Sporns and Edelman 1994

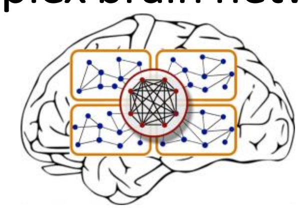
Some take home thoughts

- Relevant complexity of neural systems captures a "rich" organization between order and randomness.
- Many measures which capture distinct patterns of structural, dynamical (functional) brain organization have been independently studied *in silico*, *in vitro* and *in vivo.*
- The present myriad of measures would be clarified with development of a unifying complexity (this is a longstanding question).



XKCD

Generative and null models of complex brain networks



Rafael Romero-Garcia
Department of Psychiatry
rr480@cam.ac.uk

Cambridge MPhil in Computational Biology
University of Cambridge
February 2016

Ramón y Cajal on the need for generative models

"That apparent disorder of the cerebral jungle conceals a profound organization of the utmost subtility which is at present inaccessible"

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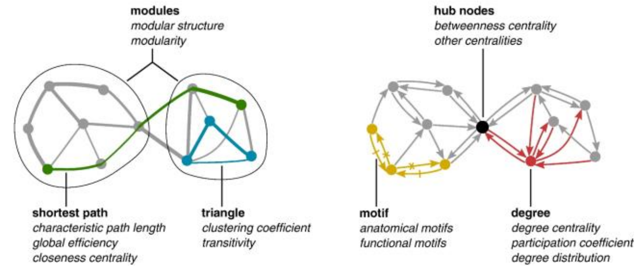
Generative and null models aim to 1) describe and 2) explain topological complexity of brain-wiring diagrams



Rubinov and Sporns, 2010

Overview

Generative models of brain networks

Principle of brain economy

Null models of brain networks

Random networks

More sophisticated networks

Brain networks in schizophrenia

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GENERATIVE MODELS

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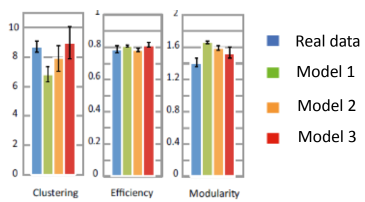
A generative model is a rule, mechanism or equation ('proto-theory') for generating a class of networks

Generative models should preferably:

1. Reproduce a sufficient degree of observed structural complexity

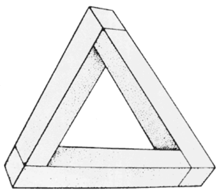


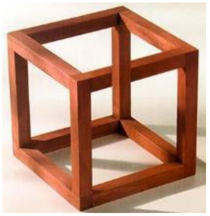
Vertes et al., PNAS 2012

A generative model is a rule, mechanism or equation ('proto-theory') for generating a class of networks

Generative models should preferably:

2. Be biologically meaningful or plausible





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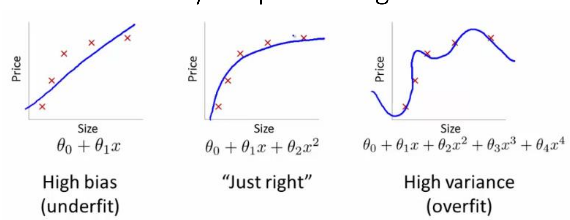
A generative model is a rule, mechanism or equation ('proto-theory') for generating a class of networks

Generative models should preferably:

3. Be relatively simple or elegant



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Preferential attachment rule (Barabási-Albert model) rule generates networks with power-law degree distributions

The probability p_i that the new node is connected to node *i* is :

$$p_i = \frac{k_i}{\sum_j k_j},$$

Where k_i is the degree of node *i* and the sum is made over all pre-existing nodes *j*

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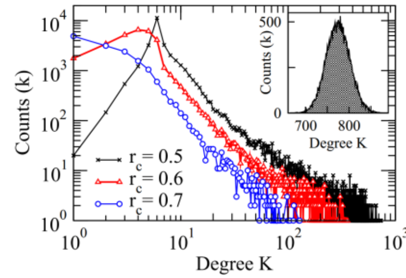
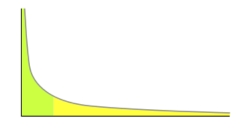
Preferential attachment rule (Barabási-Albert model) rule generates networks with power-law degree distributions

Edwin Grappin, Centre de Recherche en Economie et Statistique

Example 1: Preferential attachment model





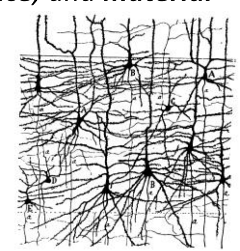
Barabasi and Albert, 1999; Eguiluz et al., 2005

Preferential attachment rule as a generative model of brain networks.

- Reproduces a sufficient degree of observed structural complexity ☹
- Is biologically meaningful or plausible ☹
- Is relatively simple or elegant ☺

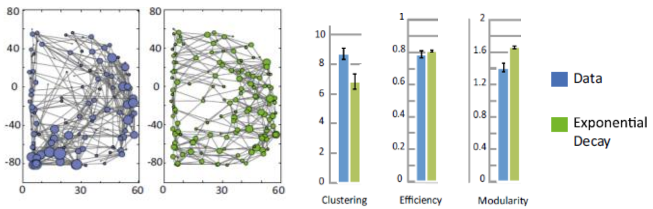
Ramón y Cajal's principle of economy as generative model

"all of the various conformations of the neuron and its various components are simply morphological adaptations governed by laws of conservation for ***time***, ***space***, *and* ***material****"*



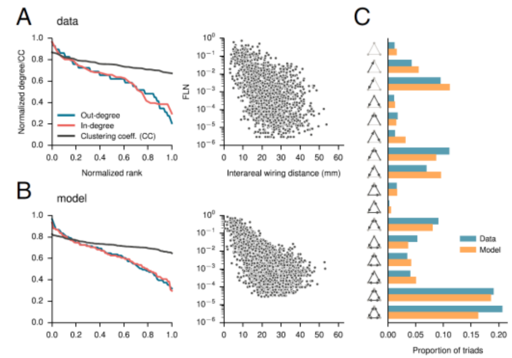
Ramón y Cajal, 1899

Recently, investigators report a exponential decay with distance as a good generative model of the brain



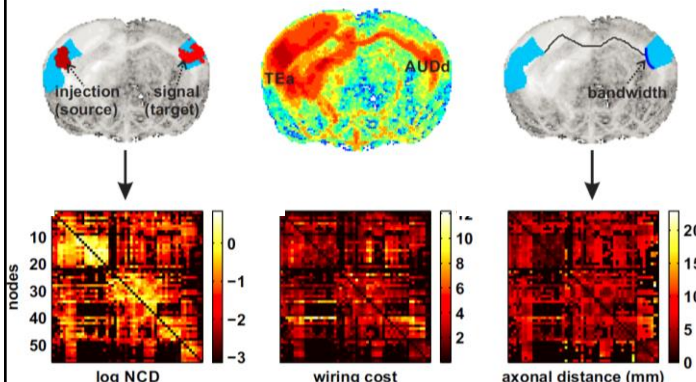
Vertes et al., PNAS 2012

This caused a stir in complex-brain-networks neuroscience circles



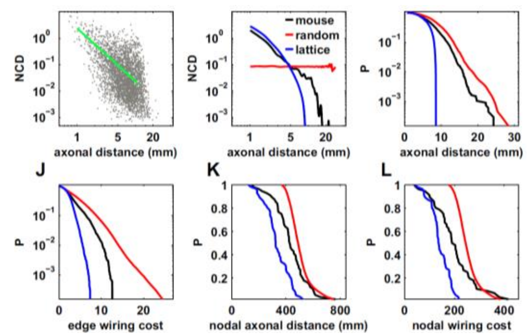
Ercsey-Ravasz, 2013; Song et al., 2014.

We evaluated this model in a new mouse brain dataset



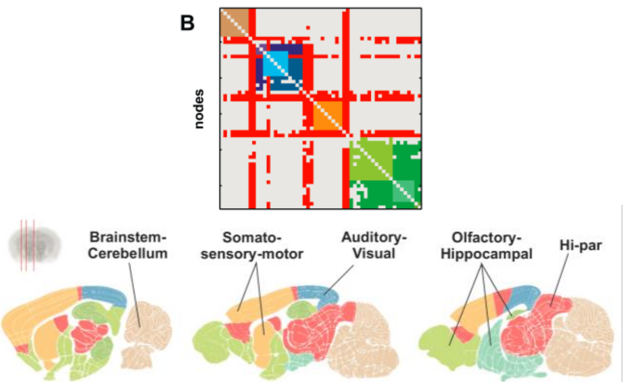
Rubinov, Ypma, Watson, Bullmore, 2015.

Our results argue against distance minimization as an accurate generative model of the mouse brain connectome.



Rubinov, Ypma, Watson, Bullmore, 2015.

We decompose the mouse brain into modules and hubs



Rubinov, Ypma, Watson, Bullmore, 2015.

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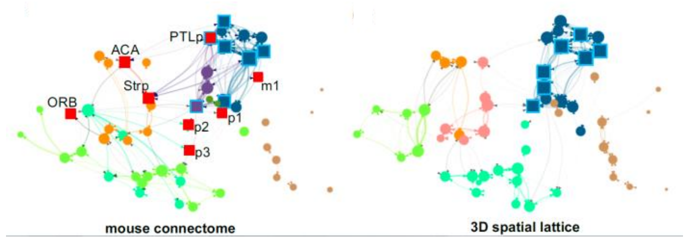
The distance minimization model reproduces the modules but not the hubs



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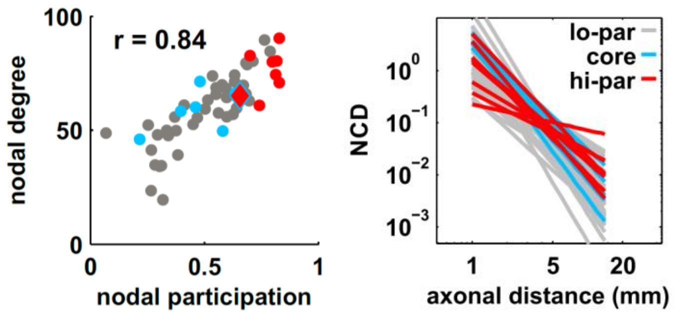
Hi-par nodes a higher distance than would be expected with distance minimization.



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How good is Ramón y Cajal's principle of economy as a generative model?

It depends...

Economy of space and material

- Reproduces a sufficient degree of observed structural complexity ☹
- Is biologically meaningful or plausible ☺
- Is relatively simple or elegant ☺

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How good is Ramón y Cajal's principle of economy as a generative model?

It depends…

Economy of space, **time** and material

- Reproduces a sufficient degree of observed structural complexity ☺
- Is biologically meaningful or plausible ☺
- Is relatively simple or elegant ☹ ? ☺

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NULL MODELS

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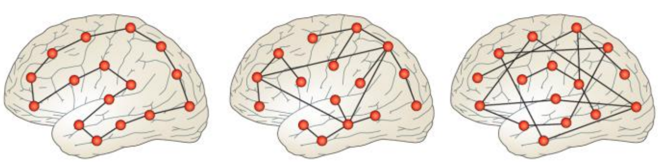
Nontrivial properties of network topology can only be claimed through comparisons with "null model" networks



Watts and Strogatz, Nature 1998

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Null models are networks which preserve "trivial" properties of empirical networks

A good null model should preserve

- all the "trivial" properties and
- none of the "nontrivial" properties

of the original empirical network

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Null models are networks which preserve "trivial" properties of empirical networks

Algorithms to create null models

- should sample the space of all possible null models in an unbiased way
- should run in reasonable time
- do not need to be biological or elegant

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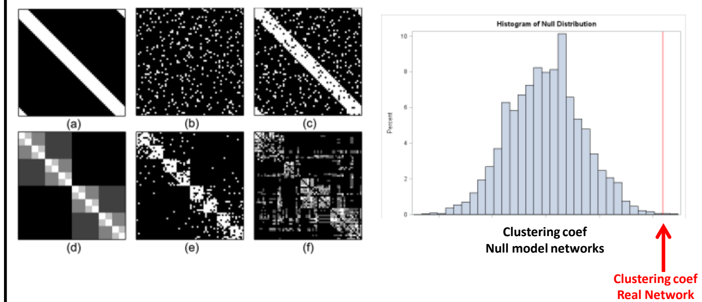
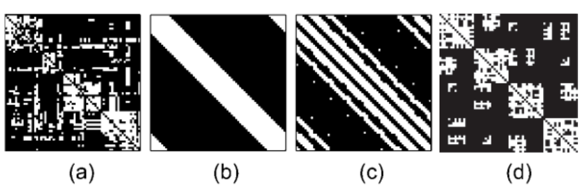
In general these null models are overly simplistic and too easy to "reject"



Robinson et al., 2009 78

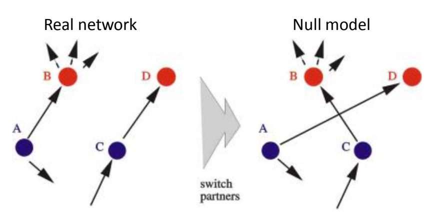
More sophisticated null modes, such as 2D and 3D lattices, are more interesting



Henderson and Robinson., Phys Rev Lett 2011 79

Edge permutation as a null Model

Permuting edges to create null models preserve the number of nodes, edges (and degree distribution)



Maslov, 2002 80

Some take home thoughts

- Generative models are akin to 'proto-theories' of brain-network organization.
- Null models are akin to 'null hypotheses' of brain-network organization.

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BRAIN NETWORKS IN SCHIZOPHRENIA

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Schizophrenia is a disorder characterized by a mixture of heterogeneous symptoms

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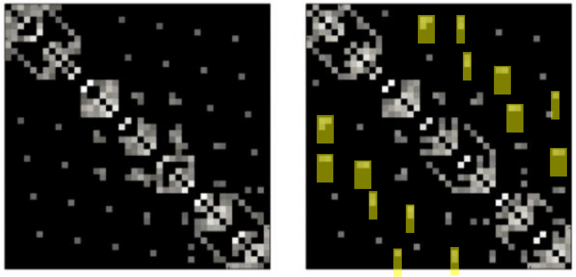
Schizophrenia is associated with a subtle randomization of whole-brain network topology



Rubinov et al., 2009.

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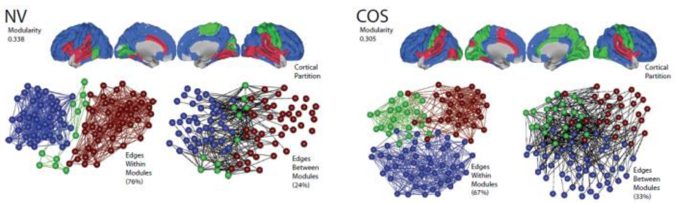
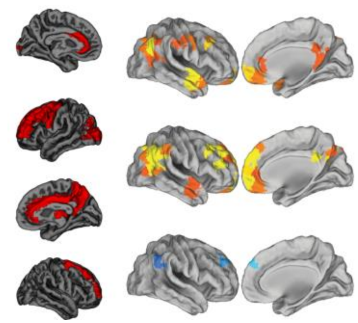
Schizophrenia is associated with a subtle randomization of whole-brain network topology



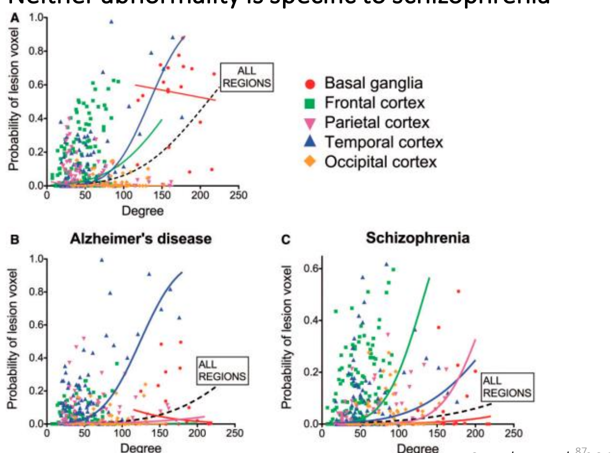
Alexander-Bloch et al., Frontiers Syst Neurosci 2011

Schizophrenia associates with abnormal association and limbic hubs



Rubinov and Bullmore, 2013.

Neither abnormality is specific to schizophrenia



Crossley et al., 2014

Review

The Human Connectome: A Structural Description of the Human Brain

Olaf Sporns*, Giulio Tononi, Rolf Kötter

To understand the functioning of a network, one must know its elements and their interconnections. The purpose of this article is to discuss research strategies aimed at a comprehensive structural description of the network of elements and connections forming the human brain. We propose to call this dataset the human "connectome," and we argue that it is fundamentally important in cognitive neuroscience and neuropsychology. The connectome will

fundamental vs sufficient

Sporns et al., 2005.

Review

Cell PRESS

Special Issue: The Connectome

Fledgling pathoconnectomics of psychiatric disorders

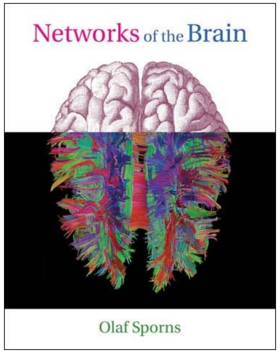
Mikail Rubinov[1,2,3] and Ed Bullmore[1,2,4]

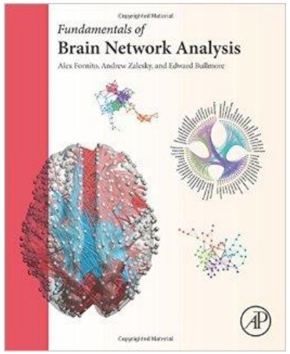
We use the term sufficient phenotype to denote the simplest-known specific biological phenotype of a disorder. We note that the main tenet of pathoconnectomics postulates that abnormal brain-networks are sufficient phenotypes of psychiatric disorders. We consider the available evidence for this tenet below.

Rubinov and Bullmore, 2013.

Any questions: rr480@cam.ac.uk

Further reading





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