Conservation, Constraints, and Comparisons

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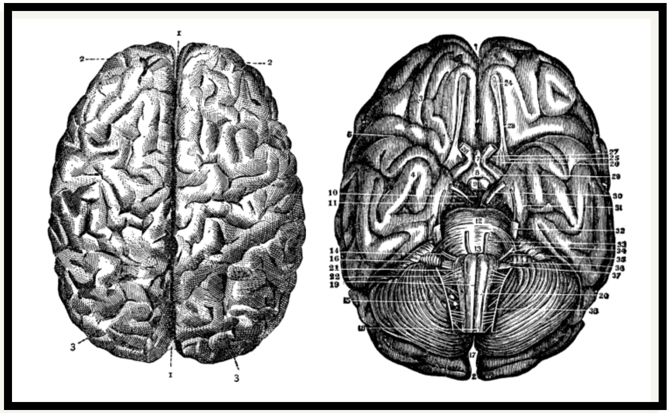
Complexity in the Human Brain

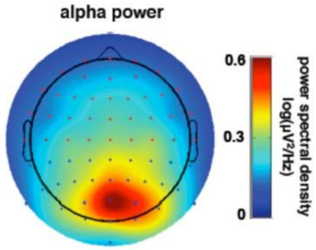
The human brain is complex over multiple scales of space and time …

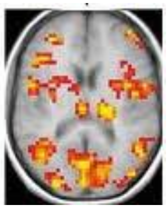


and can be examined using both low and high order statistics.

Univariate Measures – Magnitude, Power, etc.

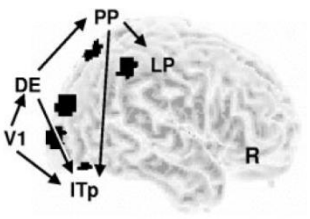
- Single regions





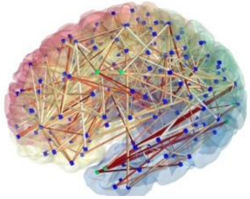
Bivariate Measures – Functional Connectivity

- Two regions



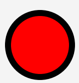
Multivariate Measures – Network Analysis

- Many Regions



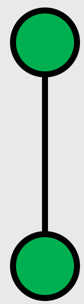
Complexity in the Human Brain

Univariate



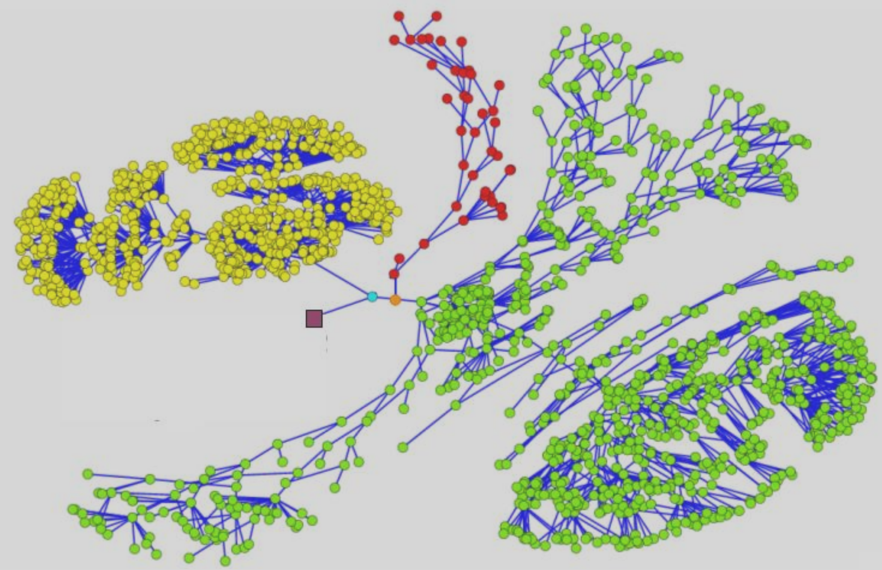
Process

Bivariate



Interaction

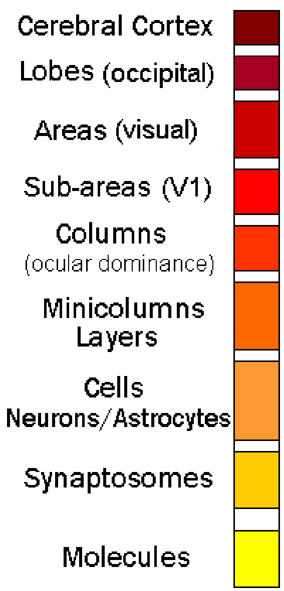
Multivariate

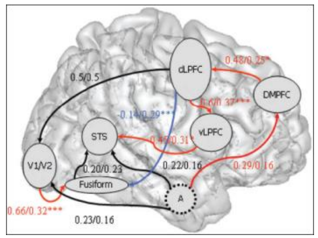


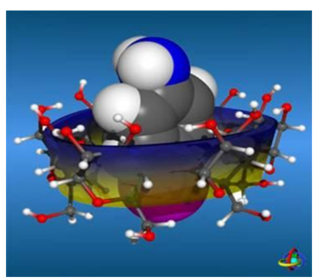
Pattern

Why Higher Order Statistics?

Interactions







The function of the brain is built on multi-scale interactions.

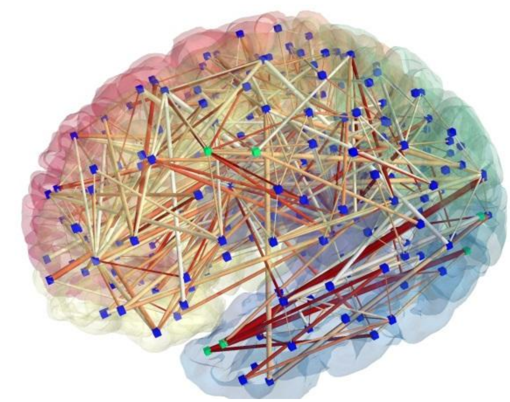
Patterns

While the function of the brain is built on multi-scale interactions, **cognition** is only possible through the combined interactions of neurons, ensembles of neurons, and larger-scale brain regions that make **oscillatory activity** and subsequent information transfer possible.

Necessitates an examination of not just **bivariate** interactions but also **multivariate** interactions over a range of spatial scales.

Complex Network Theory in Neuroimaging

- A modeling endeavor that provides a set of representational rules that can be used to describe the brain in terms of its subcomponents (brain regions / nodes) and their relationships to one another (white matter tracts / edges)



Tools:
Graph Theory and
Statistical Mechanics

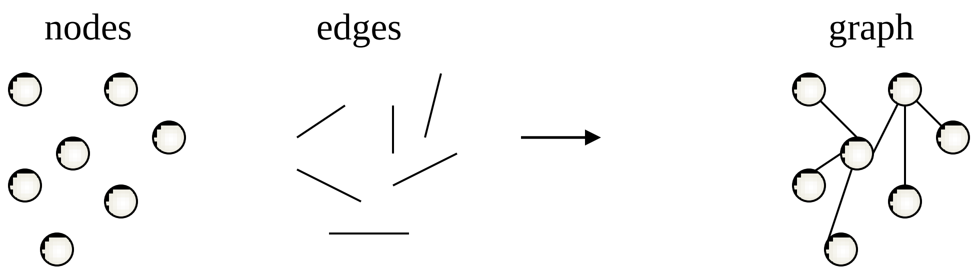


Image Credit: http://web.med.unsw.edu.au/bcw08/, http://public.kitware.com/ImageVote/

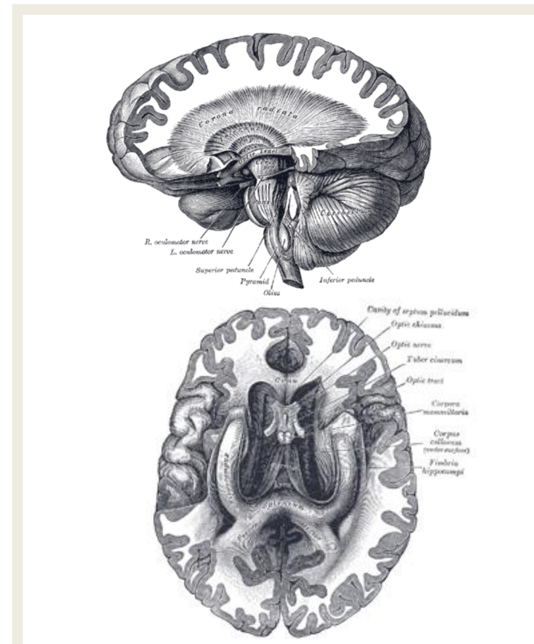
Biological Relevance of Network Architecture

Complex brain networks have been shown to be sensitive to:

- **behavioral variability** (Bassett et al., 2009)
- **cognitive ability** (van den Heuvel et al., 2009; Li et al., 2009)
- **shared genetic factors** (Smit et al., 2008)
- **genetic information** (Schmitt et al., 2008)
- **experimental task** (Bassett et al., 2006; De Vico Fallani et al., 2008b)
- **age** (Meunier et al., 2009; Micheloyannis et al., 2009)
- **gender** (Gong et al., 2009)
- **drug** (Achard et al., 2007)
- disease such as **Alzheimer's** (He et al. 2008, Buckner et al. 2009, Supekar et al. 2008, Stam et al. 2007, Stam et al. 2009) and
  schizophrenia (Bassett et al. 2008, Lynall et al. 2010, Liu et al. 2008, Rubinov et al. 2009, Bassett et al. 2009, Micheloyannis et al., 2006)
  other clinical states such as **epilepsy** (Raj et al., 2010; Horstmann et al., 2010; van Dellen et al., 2009), **multiple sclerosis** (He et al., 2009b), **acute depression** (Leistedt et al., 2009), **seizures** (Ponten et al., 2009, Ponten et al., 2007), **attention deficit hyperactivity disorder** (Wang et al., 2009), **stroke** (De Vico Fallani et al., 2009; Wang et al., 2010), **spinal cord injury** (De Vico Fallani et al., 2008a), **fronto-temporal lobar degeneration** (de Haan et al., 2009), and **early blindness** (Shu et al., 2009).

Brain Networks & Robustness

Construction of brain networks



Multiple Means of Uncertainty:

1. Building a Model Based on Choices:
   - Nodes
   - Edges

2. Experimental variability

3. Individual variability

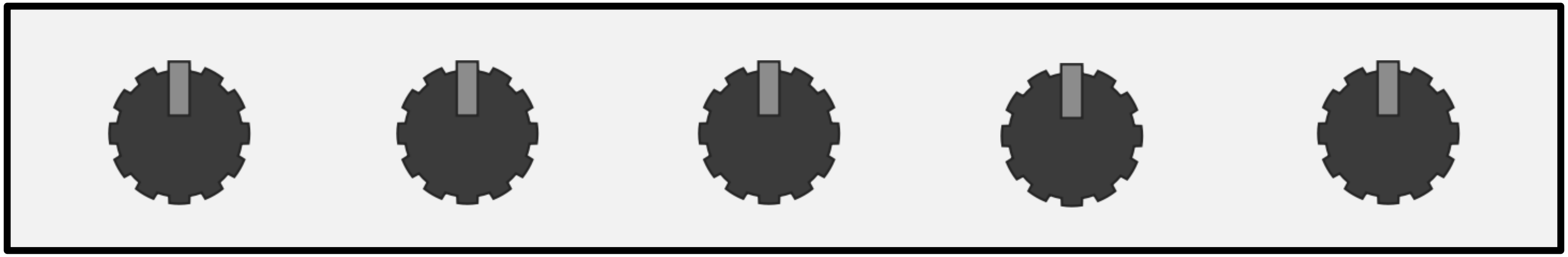
4. Population variability

How can we measure the robustness of our network-based results?

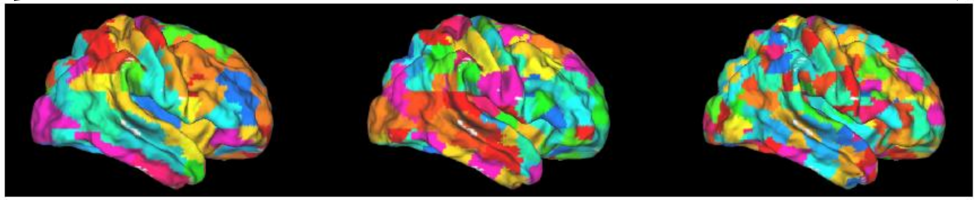
Conserved Architecture

Bassett et al. 2011

Tuning Knobs:



Individual Variability	Temporal Dependence	Imaging Modality	Anatomical Parcellation	Spatial Resolution
7 individuals	3 scanning sessions	DSI/DTI	AAL/HO/LPBA40	4 Granularities



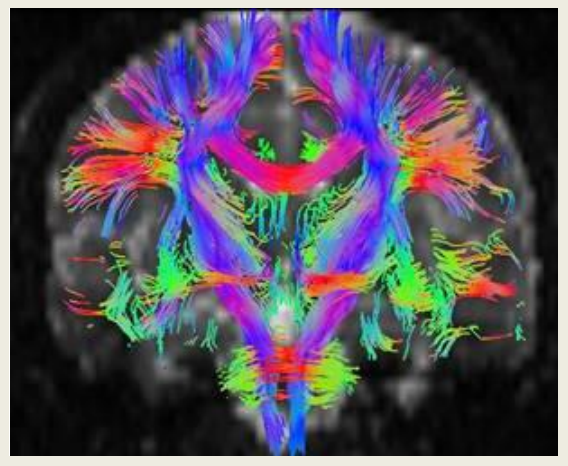
2x 4x 8x

Look for organizational "principles" which are robust to these variations.

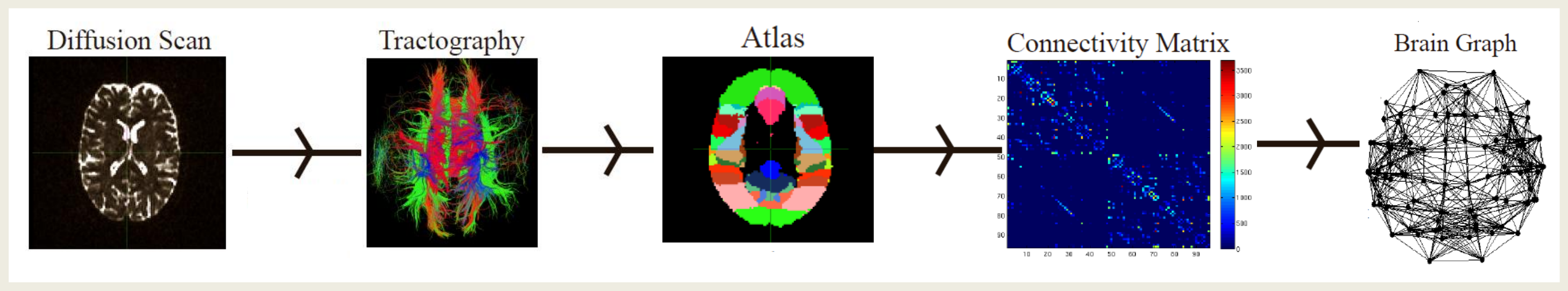
Building Cortical Connectivity Maps

from White Matter Structure

Bassett et al. 2011



How do we build a large-scale anatomical brain network?

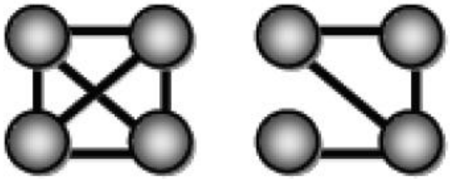


Diffusion imaging allows us to measure the diffusion of water molecules within the cortex, and thus track the paths of white matter fibers, which connect different parts of the brain.

Conserved Architecture - Sparsity

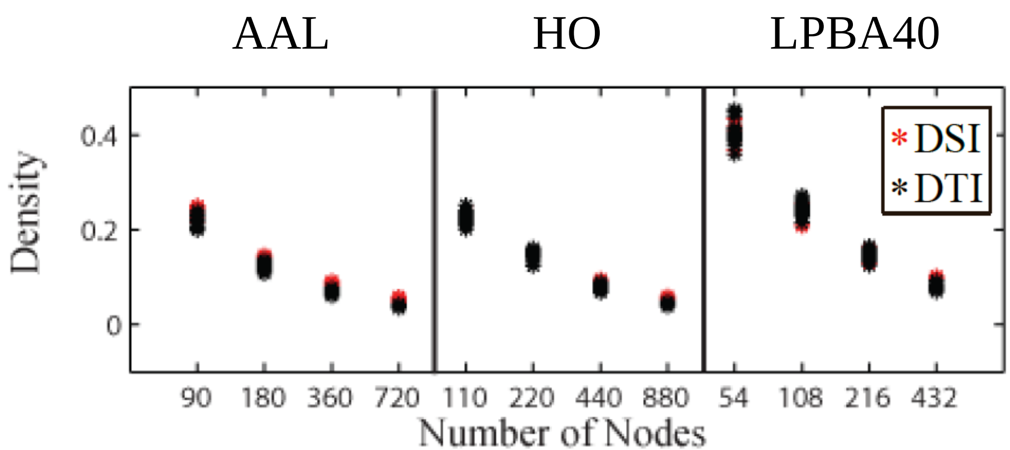
Bassett et al. 2011

Density of edges in the graph is relatively sparse.



Complete Graph

Sparse Graph



Sparsity:

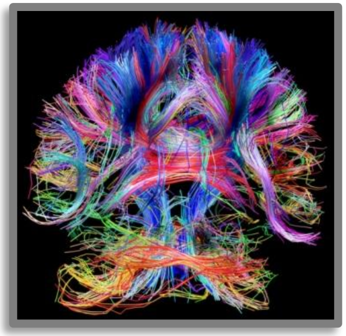
• Sparse networks, unlike fully connected networks, may vary topologically from perfectly random to highly organized

• Sparse connectivity is thought to be caused by an evolutionary pressure for energy efficiency

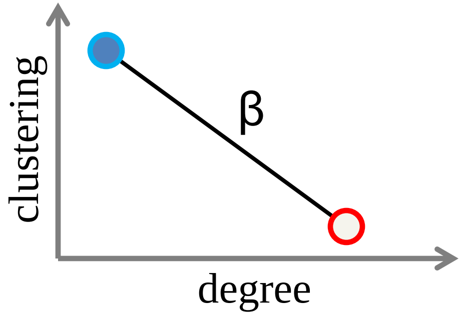
Attwell and Laughlin, 2001;
Niven and Laughlin, 2008

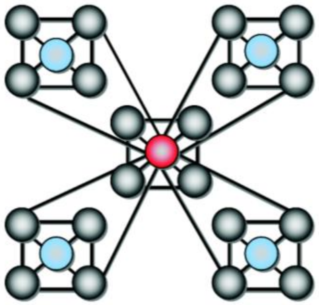
Structural Organization: Hierarchy

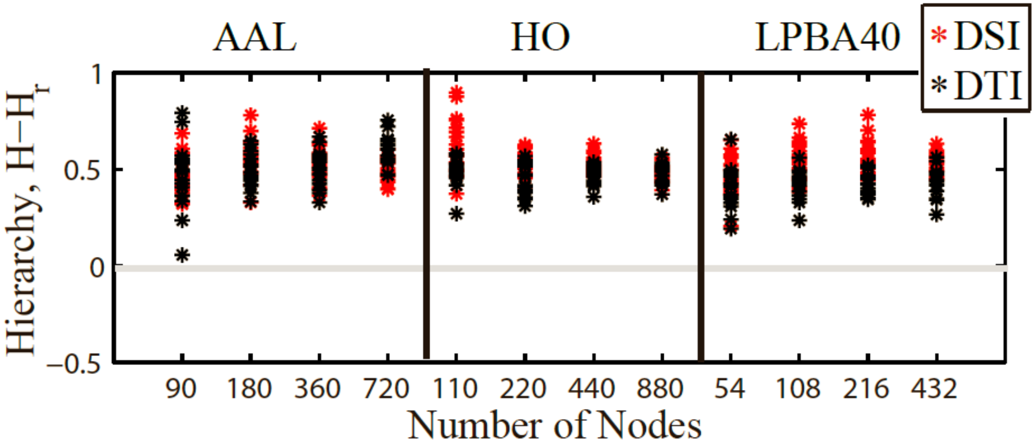
Bassett et al. 2011, Neuroimage



Anatomical connectivity is characterized by network hierarchy.



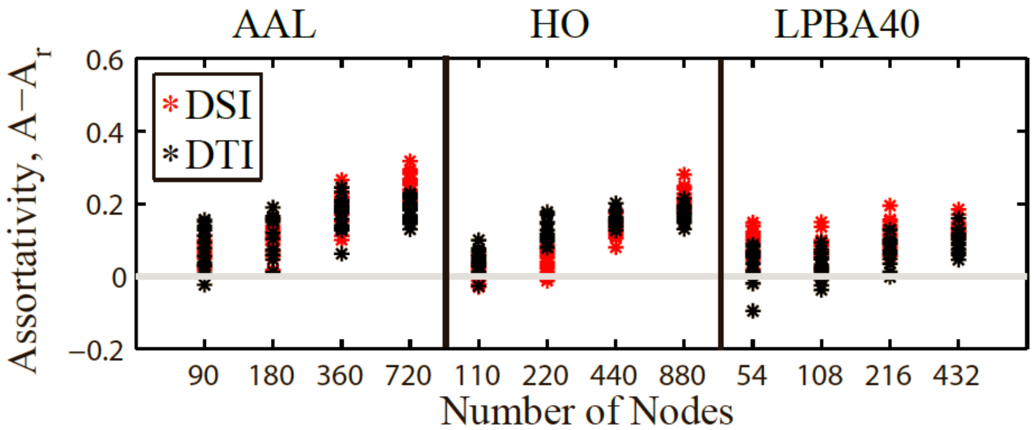


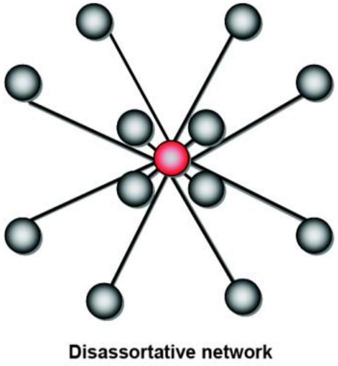


Structural Organization: Assortativity

Bassett et al. 2011, Neuroimage

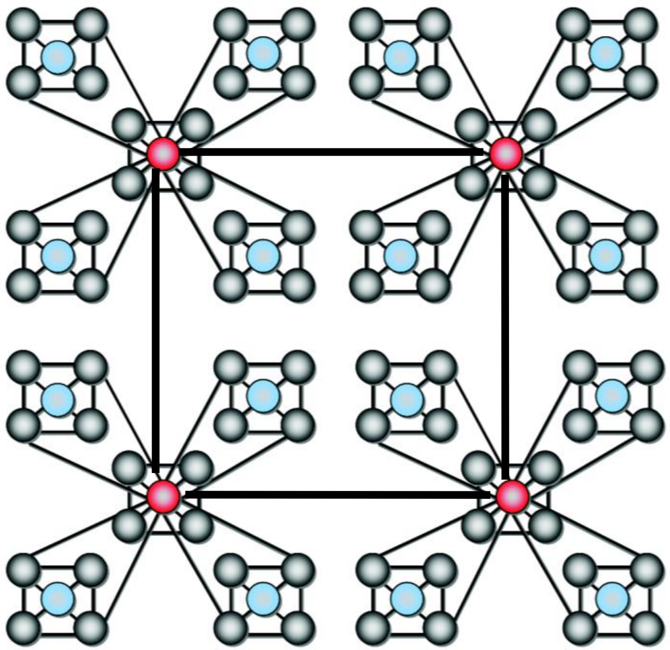
Anatomical connectivity is characterized by degree-degree correlations (or degree *assortativity*).





Hierarchical Modularity

Bassett et al. 2011



Function:
Segregation and Integration (Fodor, 1983, “Modularity of Mind”)

Structure:
Heterogeneous, non-random cortex
Cytoarchitectonic boundaries
Laminar organization
Segregation of white and gray matter
Separation of visual cortical areas
Organization of basal ganglia
Existence of topographic maps
Retinotopic maps
Ocular dominance patterns
Organization of cortical columns
Symmetric modular structure of genetic expression

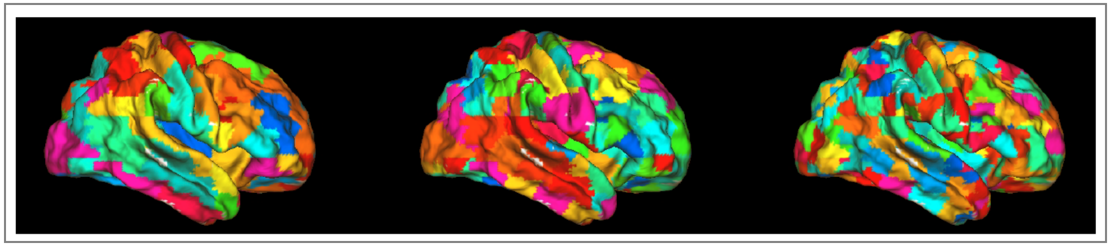
Theoretically, modular structure of such “nearly decomposable systems” (Simon, 1962) maximizes efficiency, evolvability, and adaptability.

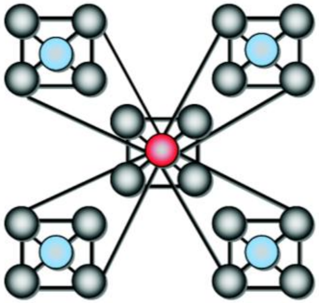
Experimentally, hierarchical modularity in connectivity profiles has also been identified in the C. elegans neuronal network and in very large scale integrated computer circuits.

Structural Organization: Spatial Scaling

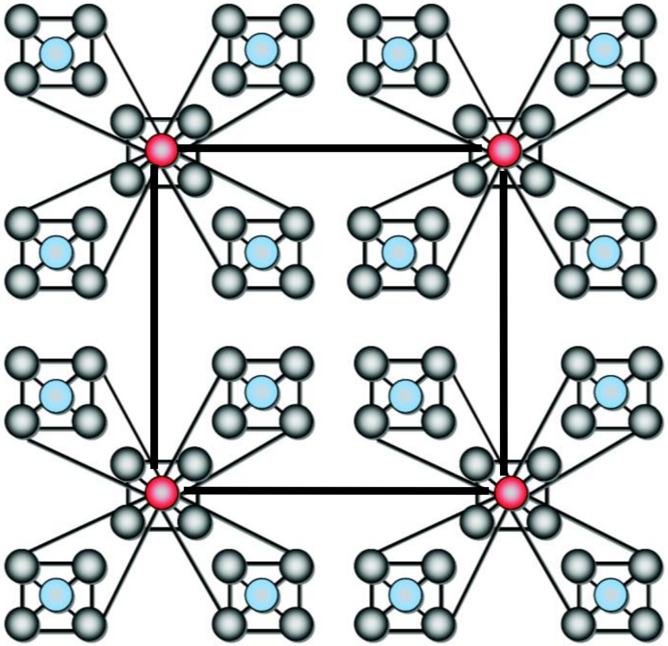
Bassett et al. 2011, Neuroimage

Vertical Spatial Scaling



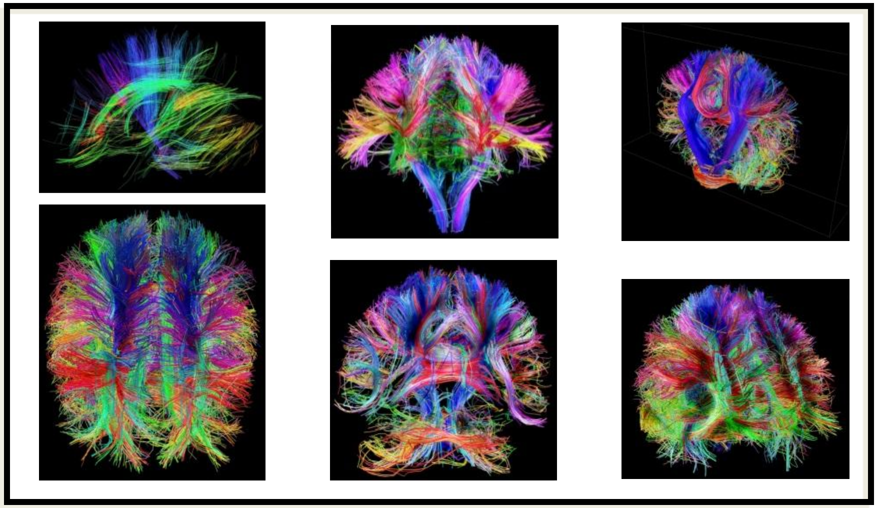


Horizontal Spatial Scaling

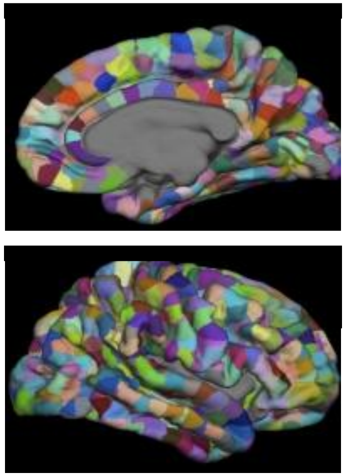


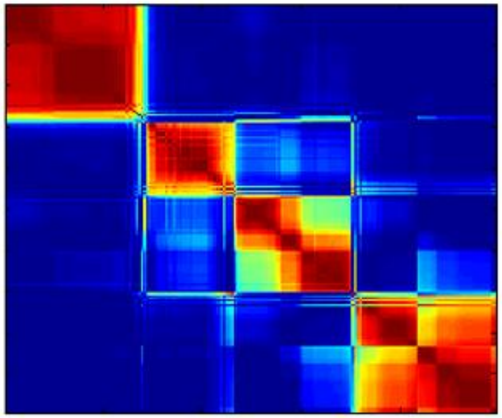
The Structurally Modular Brain

Diffusion Imaging Data



Whole-Brain Parcellation





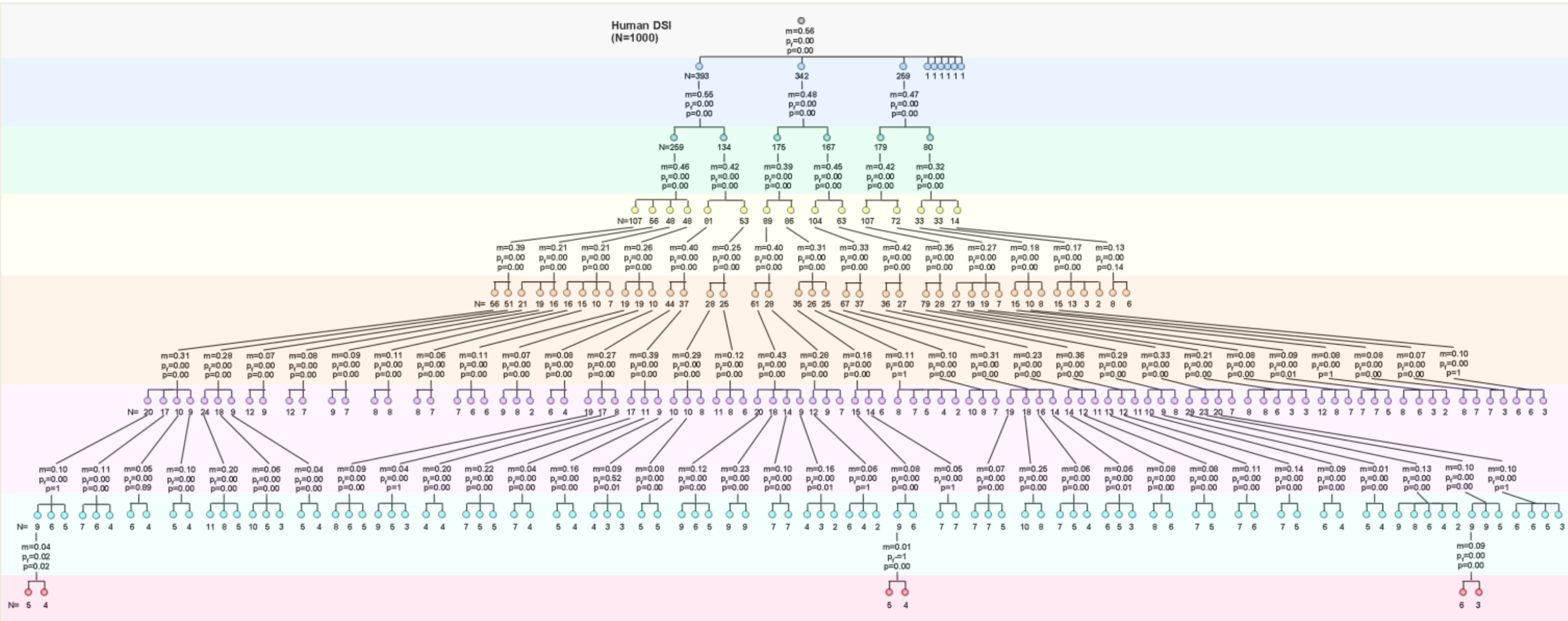
Hagmann et al. 2008 PLoS Biology

Bassett et al. 2010 PLoS Comp Biol

Bassett et al. 2011 NeuroImage

Hierarchical Modularity

Tree-based visualization

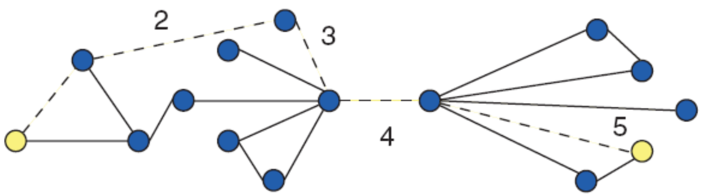


Bassett et al. 2010 PLoS Comp Biol

Topological and Physical Architecture

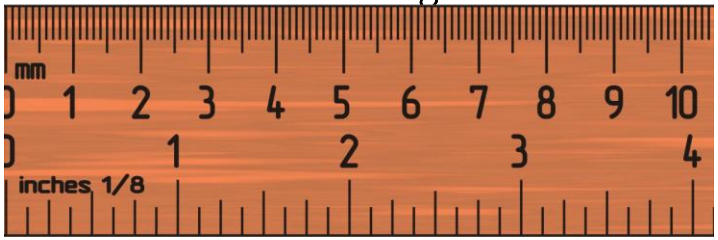
Bassett et al. 2011

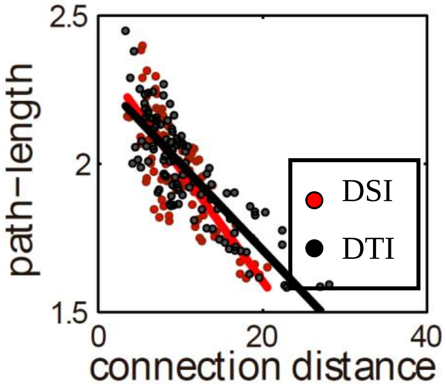
In a network, the distance between two nodes is measured in units of connections:



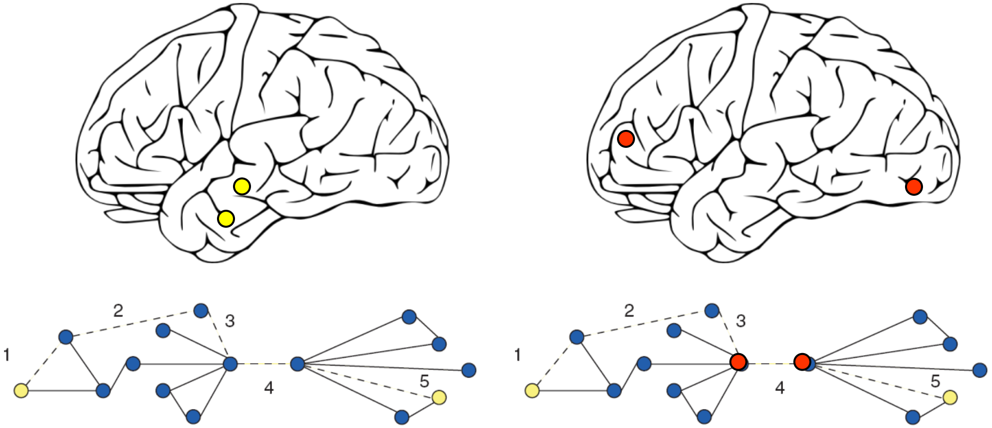
Path-length = 5

In a physical system, the distance between two points is measured in units of length.



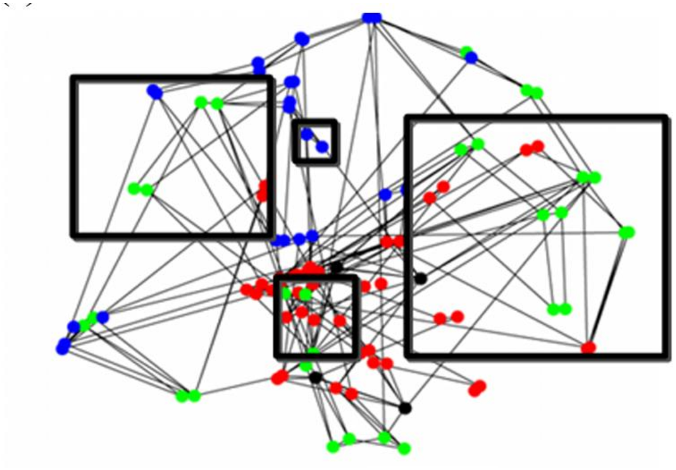


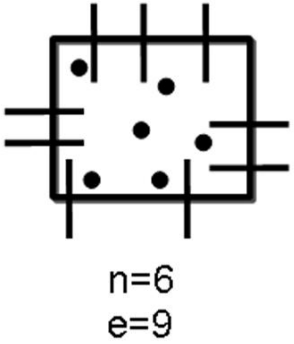
- Strong interdependence between topological distance and physical distance. Suggests there may be physical analogs to our other results. For example, network ‘modules’ may be anatomically localized.

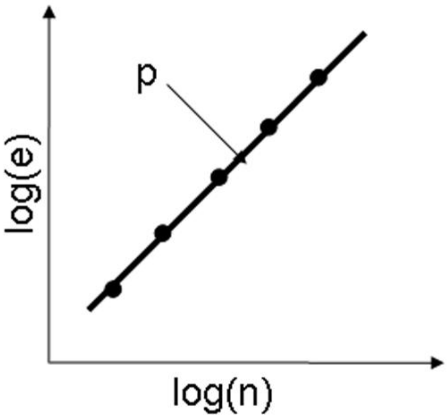


Rentian Scaling

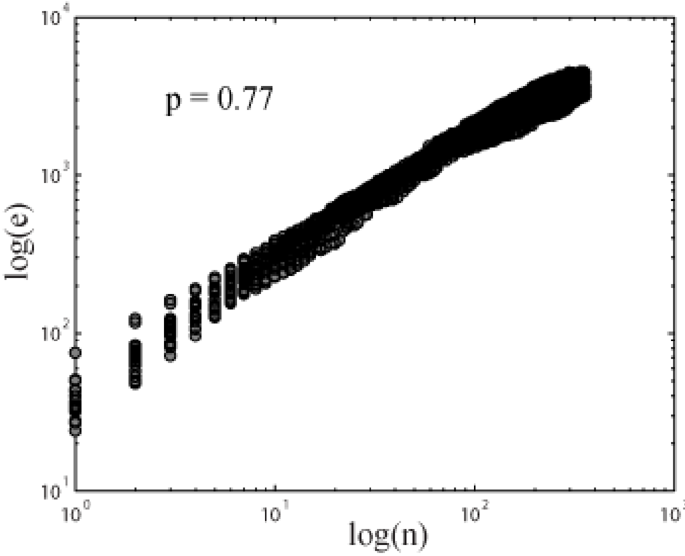
topo-physical property of efficient embedding







Rent's rule indicates a scaling relationship between the number of nodes in a box and the number of connections crossing the boundary of the box.

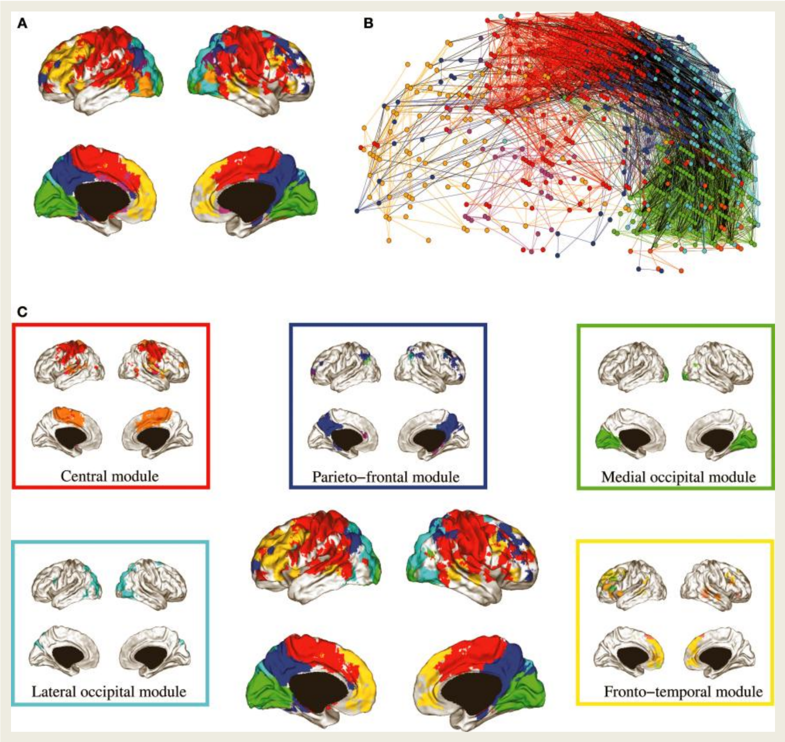


Rentian scaling has been found in systems that have been cost-efficiently embedded into physical space, for example brains, neuronal networks, and computer circuits.

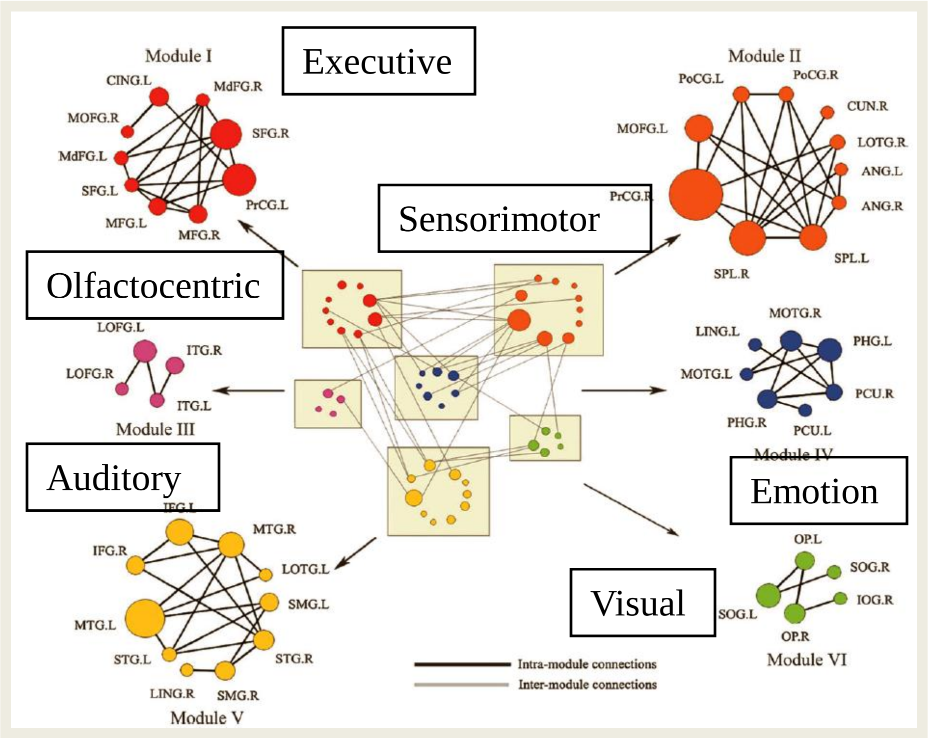
Bassett et al. 2010

Anatomical Localization of Modules

While anatomical localization of modules has not yet been demonstrated in white matter networks, it has been demonstrated in resting state fMRI and morphometric networks.



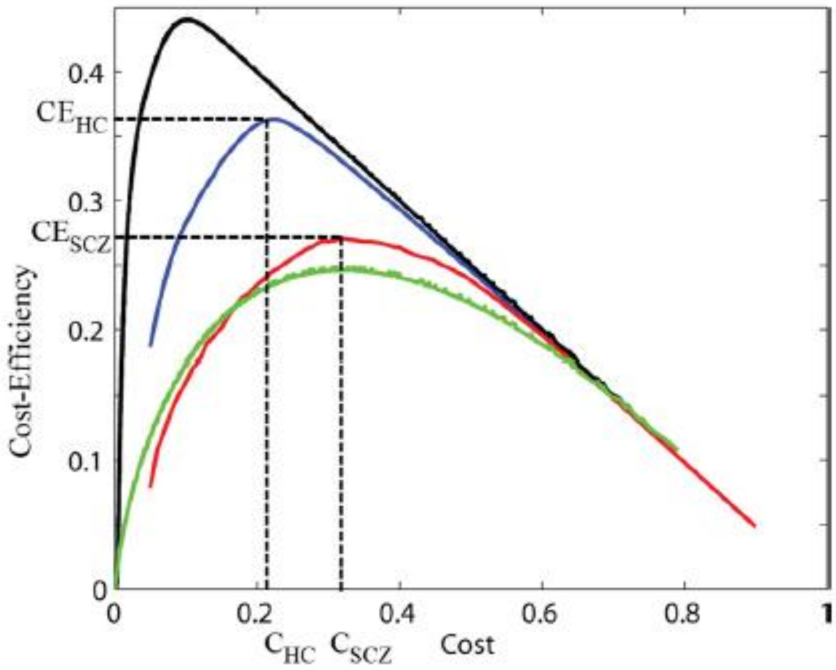
Meunier et al. 2009



Chen et al. 2008

Physical versus Topological Constraints

Topological diagnostic of Cost-Efficiency (does not use ANY physical information)

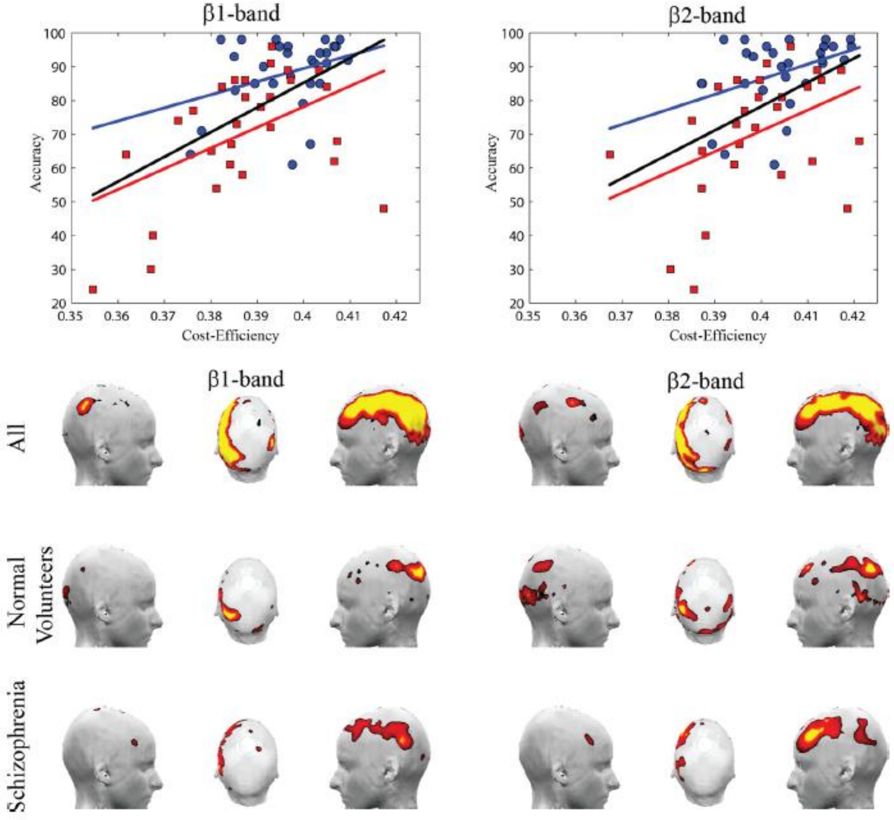


Efficiency is defined by the inverse of the path-length (Latora & Marchiori PRL 2001)
Cost is defined as the number of connections present in the network (density).

Topological Cost-Efficiency and Behavior

Bassett et al. 2009, PNAS

People with Schizophrenia and controls performing an N-back working memory task.

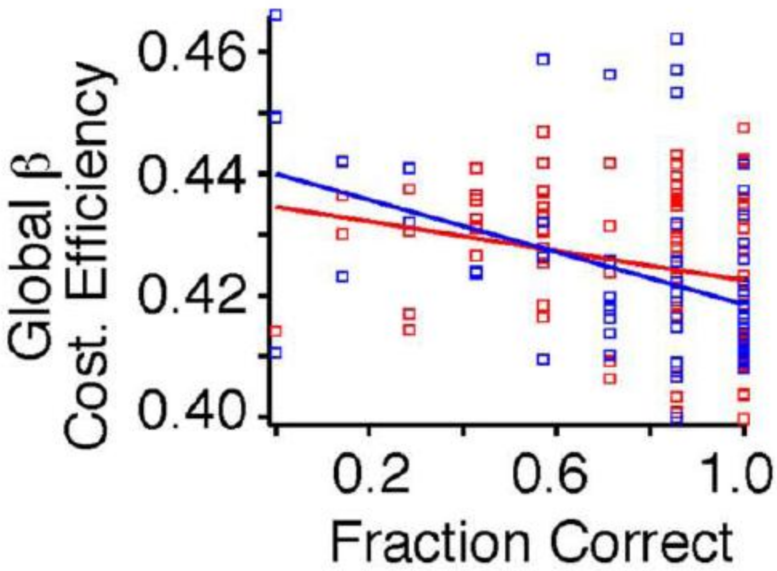


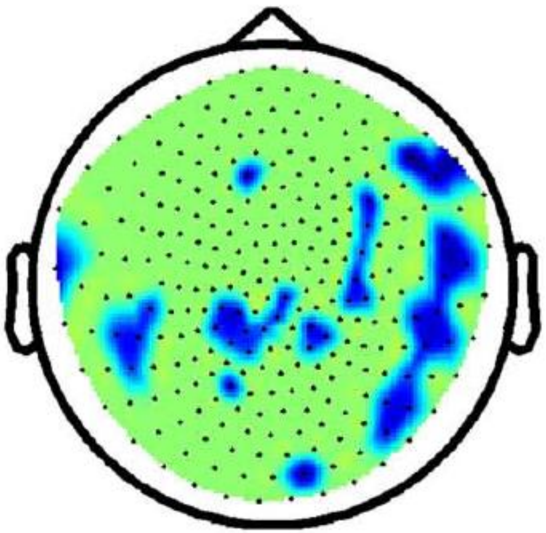
Cost-Efficiency is positively correlated with accuracy.

Topological Cost-Efficiency and Behavior

Weiss et al. 2011, Frontiers in Human Neuroscience

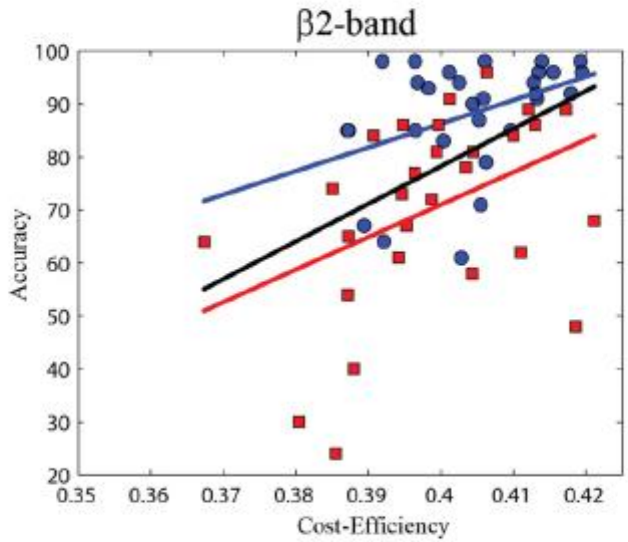
People with Schizophrenia and controls performing an auditory task for the purposes of cognitive remediation.

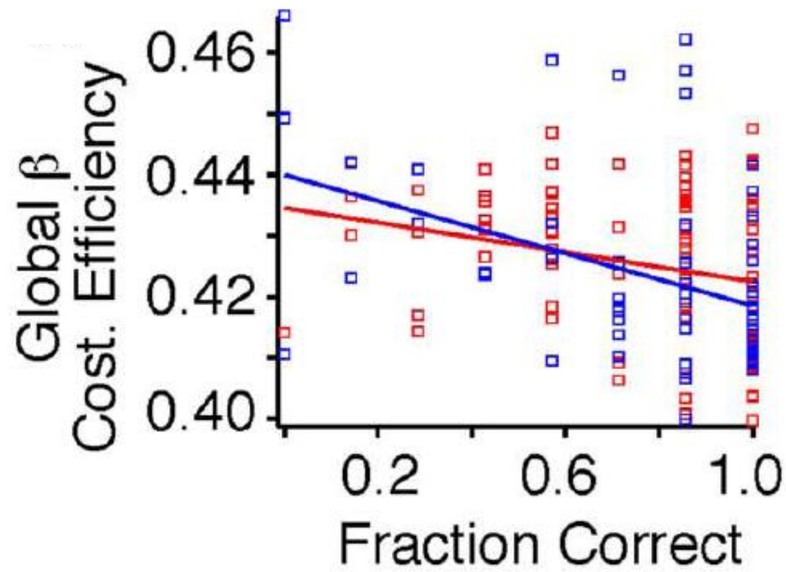




Cost-Efficiency is negatively correlated with accuracy.

Are Cost-Efficient Networks Cost-Efficient?



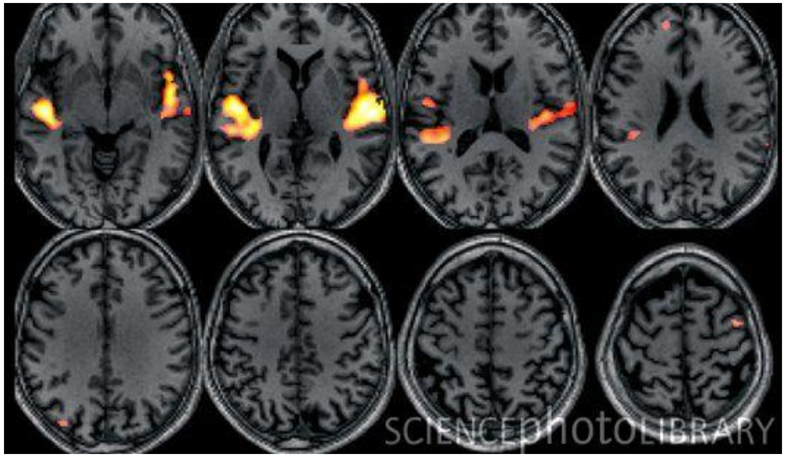


Possible Conclusions: 1) A network with high efficiency is not necessarily efficient. 2) A network with high cost is not necessarily costly. 3) Topological Cost-Efficiency is not a fundamental principle.

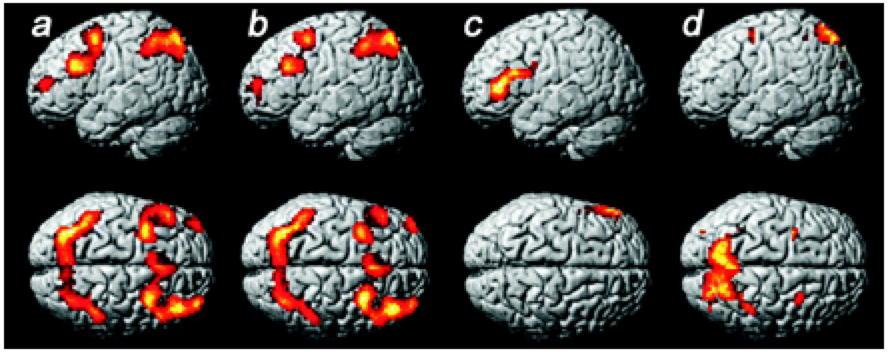
Low and High cost-efficiency can be equally useful to a brain depending on the task at hand.

Task-Dependence of Topology

Single domain task



More complex task



High local clustering
Low Efficiency (Long path-length)

Less local clustering
Higher Efficiency (Shorter path-length)

The Question of Interpretation

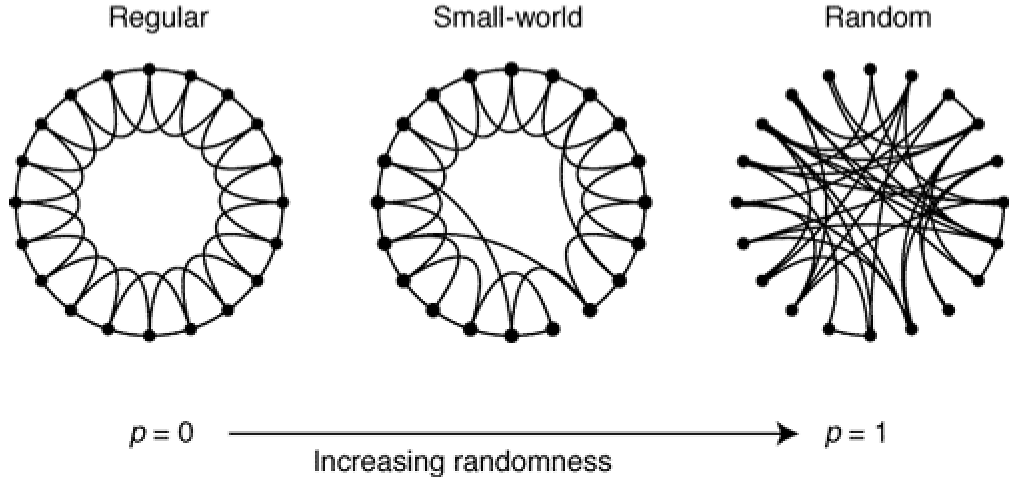
"A brain network with a higher small-world index will have more optimal information transfer."

"A brain network with higher topological efficiency is more efficient at information processing."

"A brain network with a higher clustering coefficient has more/better local information processing."

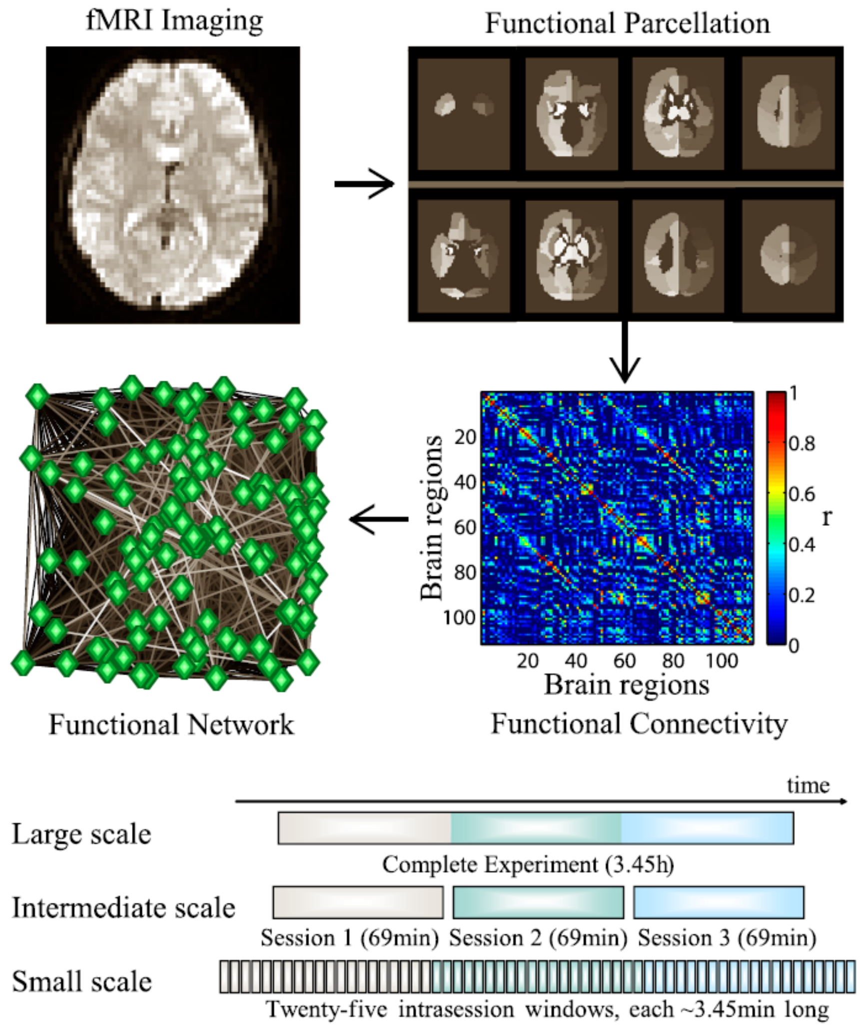
Comparisons

"A brain network with a higher small-world index will have more optimal information transfer." Many of these interpretations are based on simulation results from networks of coupled oscillators. Is this the right comparison?



Benchmark networks of regular and random graphs. In the majority of brain networks studies, we compare graph diagnostic values to their counterparts in regular or random graphs. How insightful are these comparisons? What do we learn from them? How can we use what we are learning about physical constraints to construct other benchmark networks for comparison?

Dynamic Brain Networks & Learning

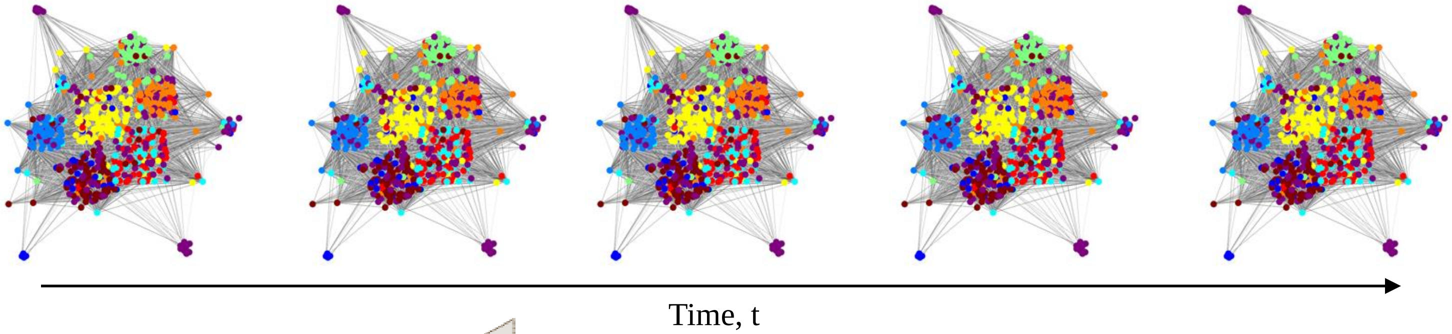


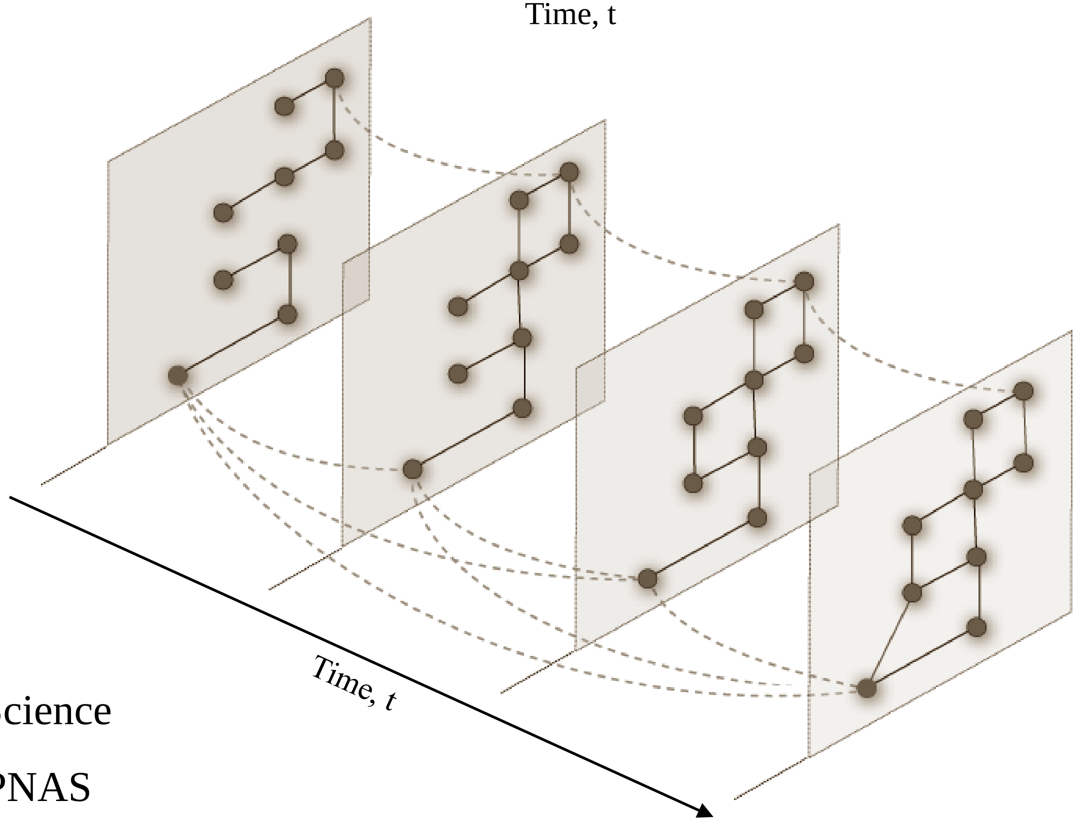
Construction of Functional Brain Network

Dynamic network slices

Bassett et al. 2011 PNAS

Investigating Dynamic Modularity





Dynamic extension of previous static modularity optimization

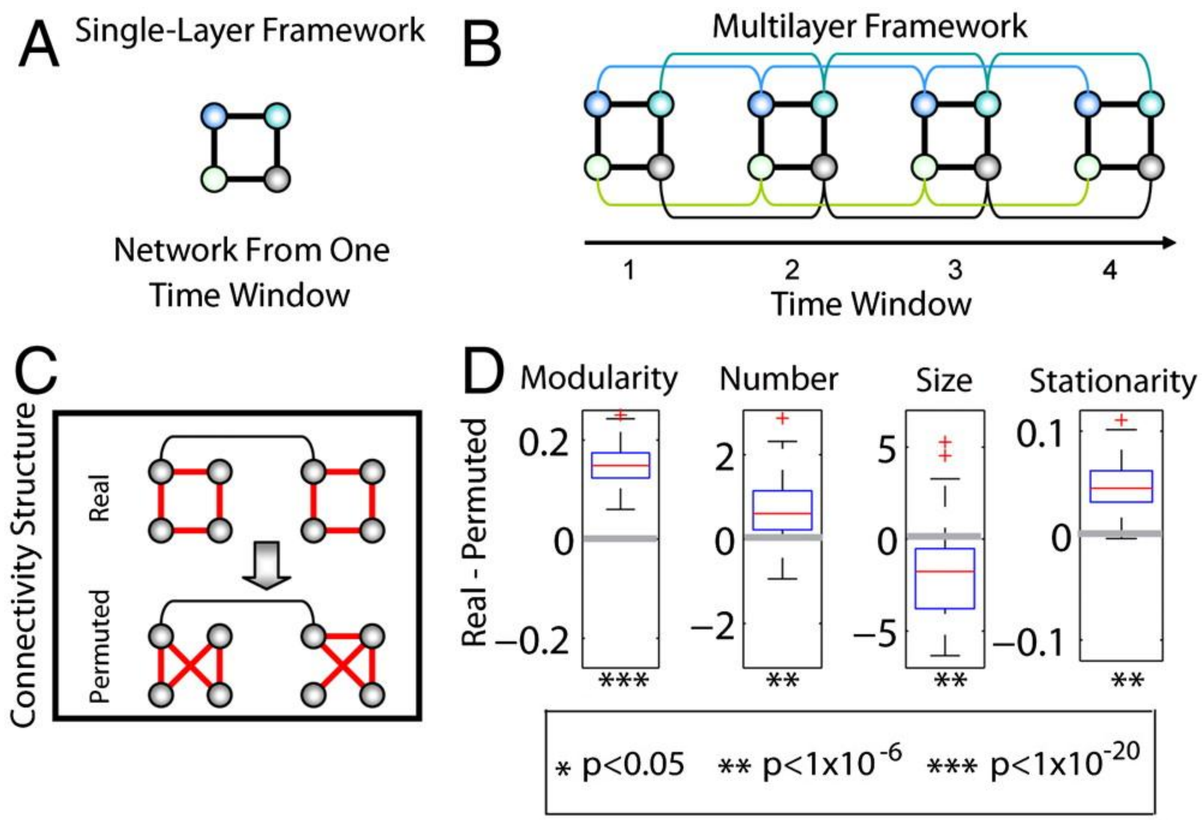
Mucha et al. 2010 Science

Bassett et al. 2011 PNAS

Robust Statistical Testing

Bassett et al. 2011, PNAS

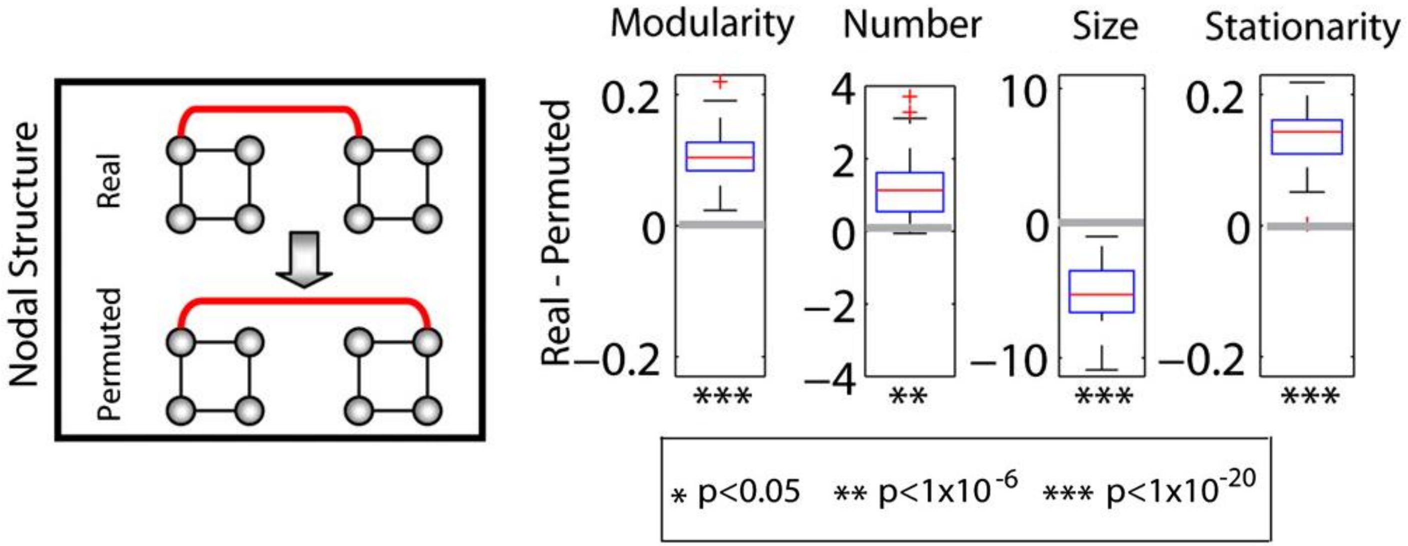
Simplest statistical comparison: compare to random graph connectivity.



Conclusion: The topological organization of cortical connectivity is highly structured.

Robust Statistical Testing II

Second statistical comparison: Scramble Node-Node (Inter-slice) Connectivity.

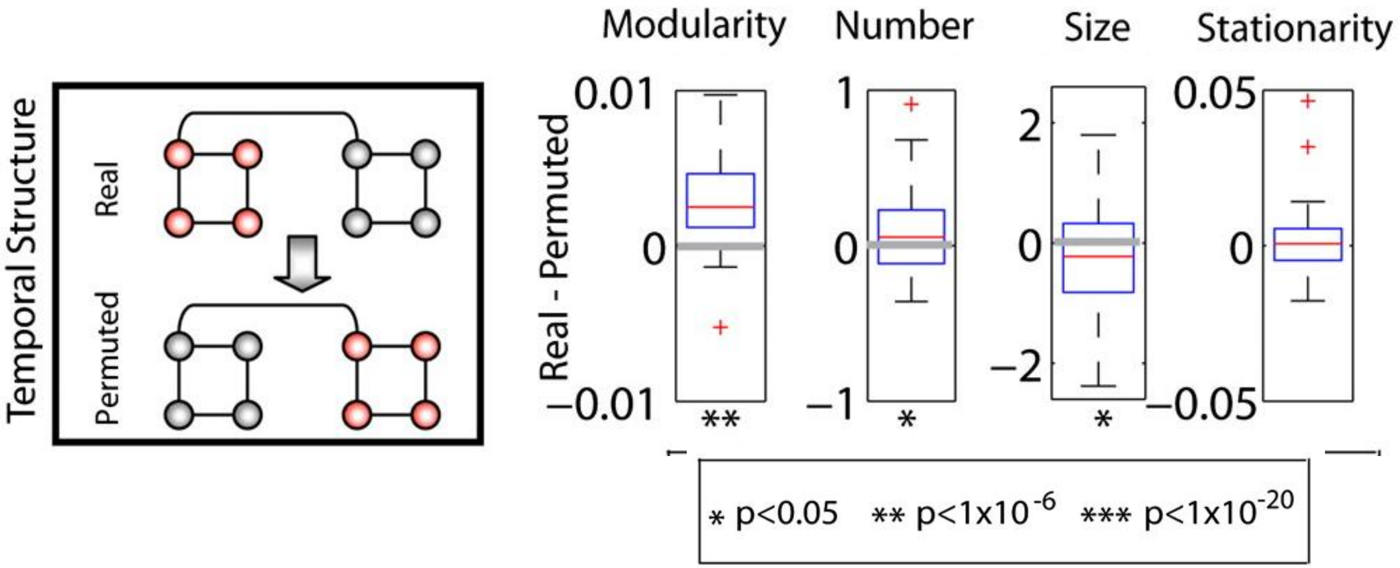


Conclusion: Diverse brain regions perform distinct non-interchangeable tasks throughout the experiment.

Bassett et al. 2011, PNAS

Robust Statistical Testing III

Third statistical comparison: Scramble Time Window Order.



Conclusion: The evolution of modular architecture in human brain function is cohesive in time.

Bassett et al. 2011, PNAS

Summary

Possible path for the meaningful examination of network organization in the brain:

1) Look for conserved properties that are independent of a range of methodological/data variations.

2) Use these properties to gain insight about constraints on brain structure and function.

3) Use what we learn about constraints to help construct meaningful benchmark comparisons.

Bassett et al. 2011, PNAS

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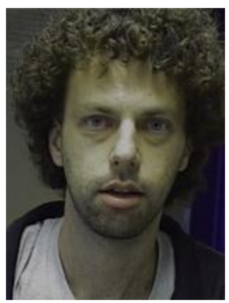

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