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

Bivariate

Multivariate

Process

Interaction

Pattern
Why Higher Order Statistics?

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

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)

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).
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

Tuning Knobs:

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

Look for organizational “principles” which are robust to these variations.
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.
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
Anatomical connectivity is characterized by network hierarchy.

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

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.

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Structural Organization: Spatial Scaling

Bassett et al. 2011, Neuroimage
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
In a network, the distance between two nodes is measured in units of connections:

\[ \text{Path-length} = 5 \]

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.

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Bassett et al. 2011
Rentian Scaling

Rentian Scaling is a topo-physical property of efficient embedding. Rentian scaling has been found in systems that have been cost-efficiently embedded into physical space, for example brains, neuronal networks, and computer circuits. 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.
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.
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

High local clustering
Low Efficiency (Long path-length)

More complex task

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

Functional Parcellation

fMRI Imaging

Functional Network

Construction of Functional Brain Network

Large scale

Intermediate scale

Small scale

Complete Experiment (3.45h)

Session 1 (69min) Session 2 (69min) Session 3 (69min)

Twenty-five intrasession windows, each ~3.45min long

Bassett et al. 2011 PNAS
Investigating Dynamic Modularity

Mucha et al. 2010 Science
Bassett et al. 2011 PNAS

Dynamic extension of previous static modularity optimization
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
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
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
**Structural Networks:**

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Complex Systems  
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**Dynamic Networks:**

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**Network Constraints:**

ONR MURI: Next Generation Network Science