SFI 2009

Complex Brain Networks: Patterns of Functional Connectivity

Olaf Sporns
Department of Psychological and Brain Sciences
Indiana University, Bloomington, IN 47405
http://www.indiana.edu/~cortex , osporns@indiana.edu

Outline

Brain Dynamics
- *Structure, Function, Information, Complexity*

Linking Structure to Function
- *Multiple Time Scales*
- *Comparing Structural and Functional Connectivity*
- *Modeling the Human Brain*

Network Damage and Clinical Applications
- *Modeling Human Brain Lesions*

Neural Information Processing

Two major organizational principles of cortex:

Segregation (anatomical/functional) ← clustering coefficient

Integration (anatomical/functional) ← path length

These principles are complementary and interdependent.

Two major challenges for information processing in the brain:

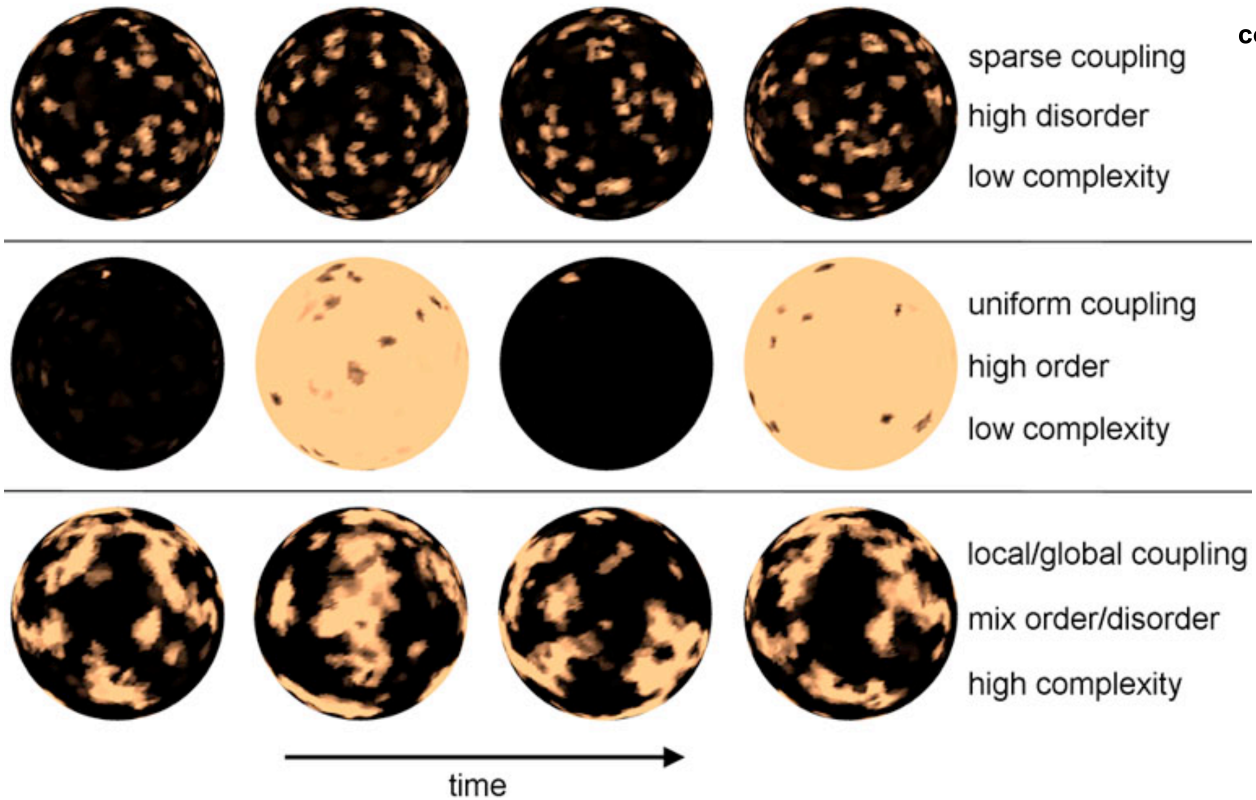
Rapid extraction of information (elimination of redundant dimensions, efficient coding, maximum information transfer)

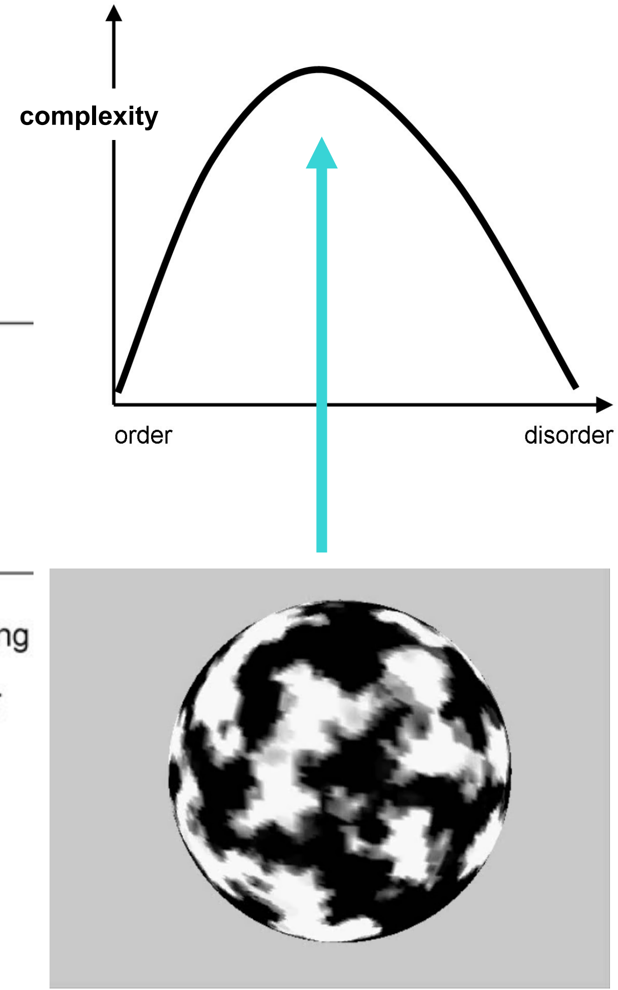
Coordination of distributed resources to create coherent states

Both challenges must be solved simultaneously, within a common neural architecture.

Complex Dynamics and Small-World Connectivity

Small-World Connectivity and Complex Dynamics

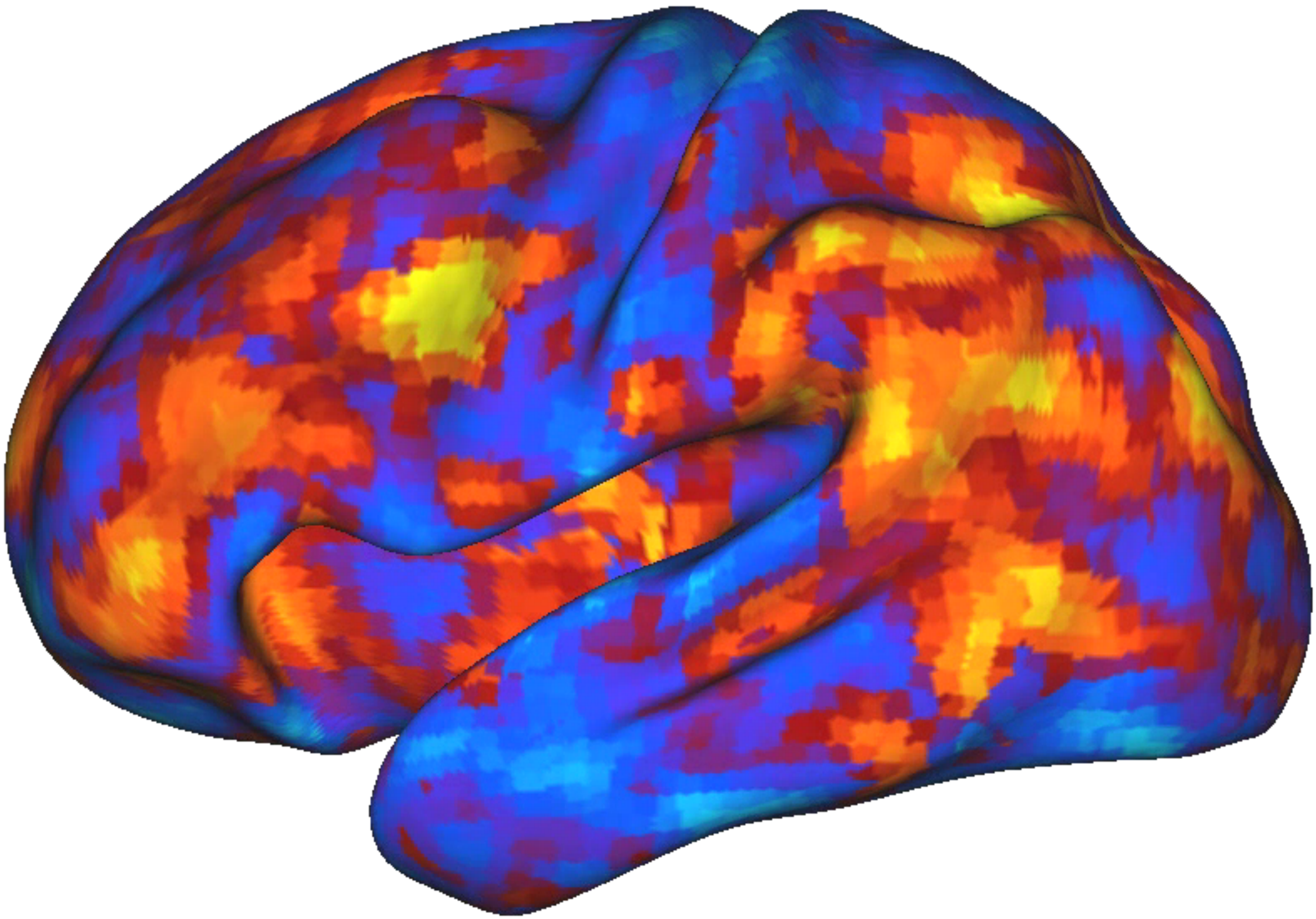




complexity: coexistence of local and global structure

$$C(\boldsymbol{X}) = H(\boldsymbol{X}) - \sum_i H(x_i | \boldsymbol{X} - x_i).$$

Sporns (2007) Complexity. www.scholarpedia.org



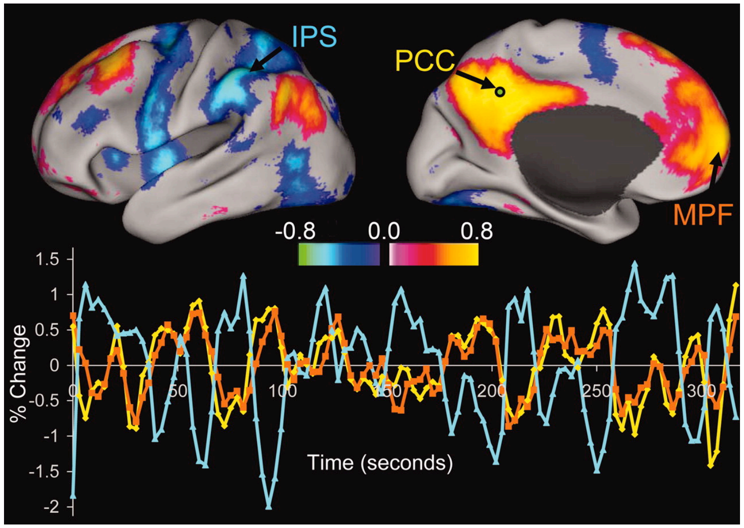
Movie courtesy of Vincent, Raichle, Snyder et al (Washington University)

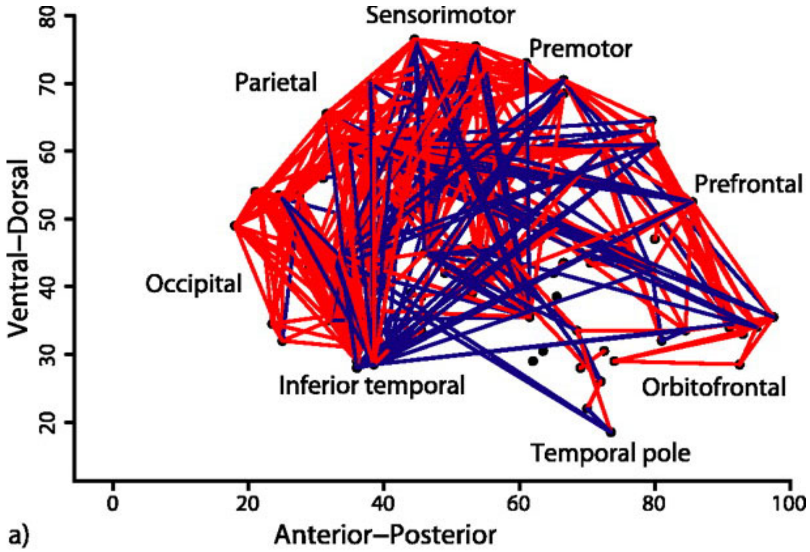
Endogenous Neural Activity in the Human Brain

Slow fluctuations in fMRI signal at rest may reflect neuronal baseline activity.

Patterns of resting state BOLD signal change are consistent across subjects.

Spontaneous fluctuations reveal the existence of two distributed and anti-correlated resting state networks.





fMRI resting state functional networks of wavelet coefficients show small-world attributes. Small-world networks (in wavelet space) may be fractal across multiple frequency ranges.

Fox et al. (2005) *PNAS*
Bassett et al. (2006) *PNAS*
Achard et al. (2006) *J. Neurosci*. 26, 63

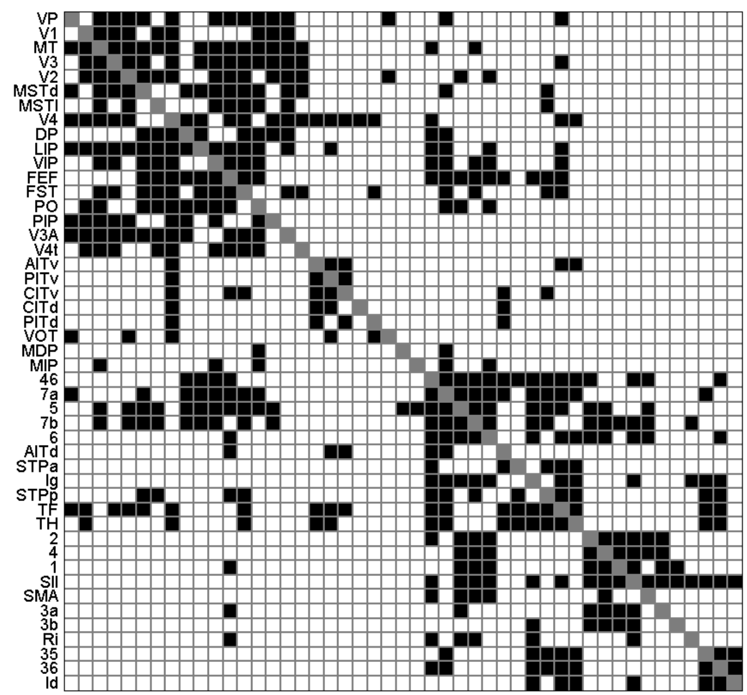
Modeling Endogenous Brain Activity - Connectivity

Structural matrix of regions of macaque neocortex connected by inter-regional pathways.

Connection matrix is generated in CoCoMac following the parcellation scheme of Felleman and Van Essen (1991), including visual, somatosensory and motor cortical regions as well as their interconnections.

Key features of structural connections as used in the model:

- one node = one brain region
- no intra-regional connections
- binary connection weights
- no conduction delays
- no distinction between absent and unknown connections



Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity - Dynamics

Neural mass model, exhibiting spontaneous activity, including intermittency, phase synchrony and marginal stability/chaos.

Neural dynamics are based on voltage- and ligand-gated calcium, potassium and sodium channels. Model parameters are set to previously verified physiologically plausible values.

Morris and Lecar, *Biophys. J.* (1981); Larter et al., *Chaos* (1999); Breakspear et al., *Network* (2003)

$$\frac{dV(\mathbf{x}_i)}{dt} = -\left(g_{Ca} + (1-c)r_{NMDA}a_{ee}Q_V(\mathbf{x}_i) + cr_{NMDA}a_{ee} < Q_V(\mathbf{x}) >\right)m_{Ca}\left(V(\mathbf{x}_i) - V_{Ca}\right) - g_K W\left(V(\mathbf{x}_i) - V_K\right)$$
$$- g_L\left(V(\mathbf{x}_i) - V_L\right) - \left(g_{na}m_{na} + (1-c)a_{ee}Q_V(\mathbf{x}_i) + ca_{ee} < Q_V(\mathbf{x}) >\right)\left(V(\mathbf{x}_i) - V_{na}\right) \quad \text{(A6)}$$
$$+ a_{ie}ZQ_Z(\mathbf{x}_i) + a_{ne}I_\delta,$$

Coupling between *N* nodes is introduced as competitive agonist excitatory action at populations of NMDA and AMPA receptors.

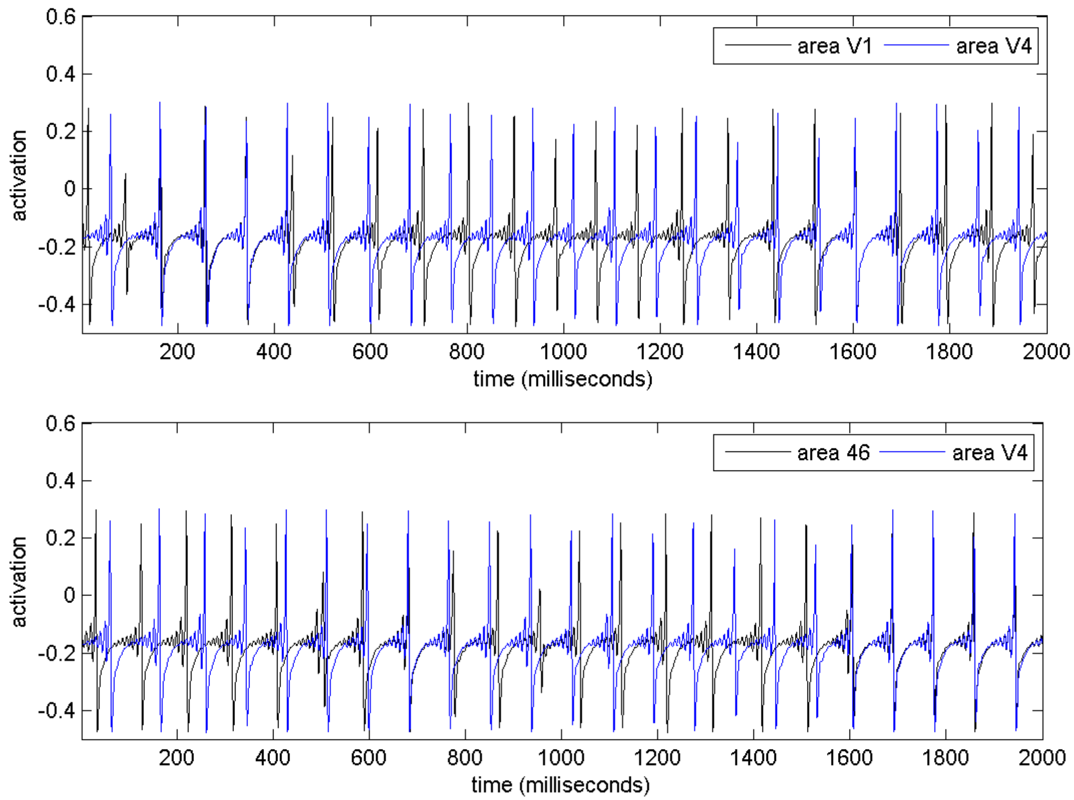
Coupling (*c*) is set such that the model resides in a weak coupling regime.

Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity - Dynamics

Inter-node coupling generates weakly stable synchronous dynamics allowing spontaneous switching between synchronous epochs and desynchronous bursts.

examples of neuronal dynamics



Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity – Analysis Tools

Model Analysis at Different Time Scales

- Long Time Scale: 240 – 960 secs., 0.1-0.01 Hz
- Intermediate Time Scale: 2 - 30 secs., 1-0.1 Hz
- Fast Time Scale: 100 msec. – 1 sec., 10 Hz

Model Analysis with Different Tools and Modalities

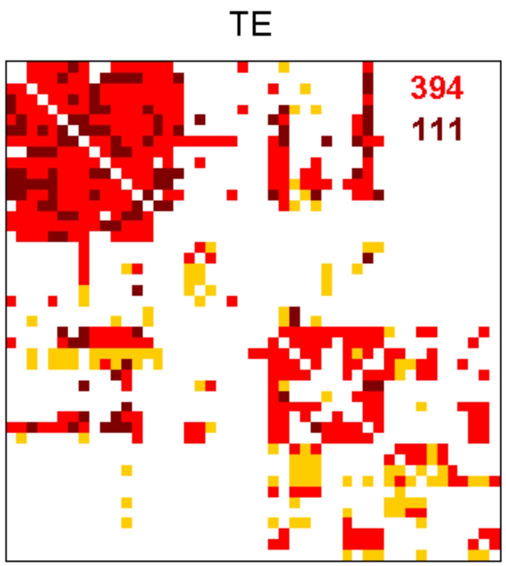
- Methods for extraction of functional connectivity based on information theory and wavelet analysis (data segments of 30-960 secs., 6 second resolution)
- Measures of instantaneous phase synchrony, e.g. phase locking value (data segments of varying length, millisecond resolution)
- Computation of “BOLD” analogue from fast dynamics of glutamatergic neural activity (data segments of 1-30 seconds, 1-6 second resolution)

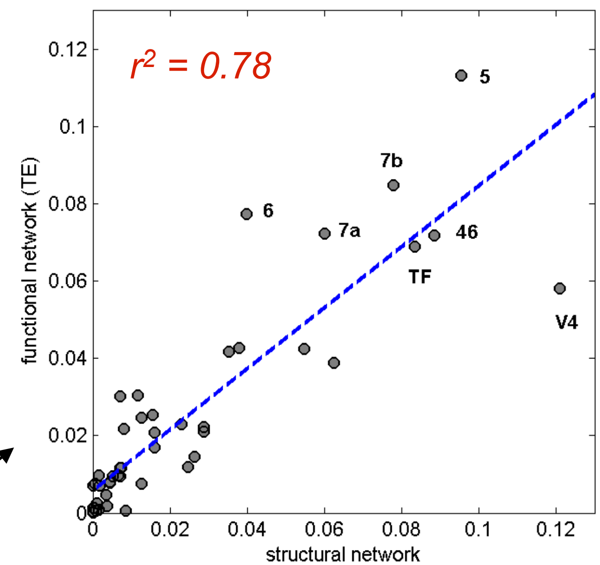
Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity

Extracting Functional Networks

When using long samples (~240 secs.), transfer entropy functional networks show high overlap with the underlying structural network (~80%).



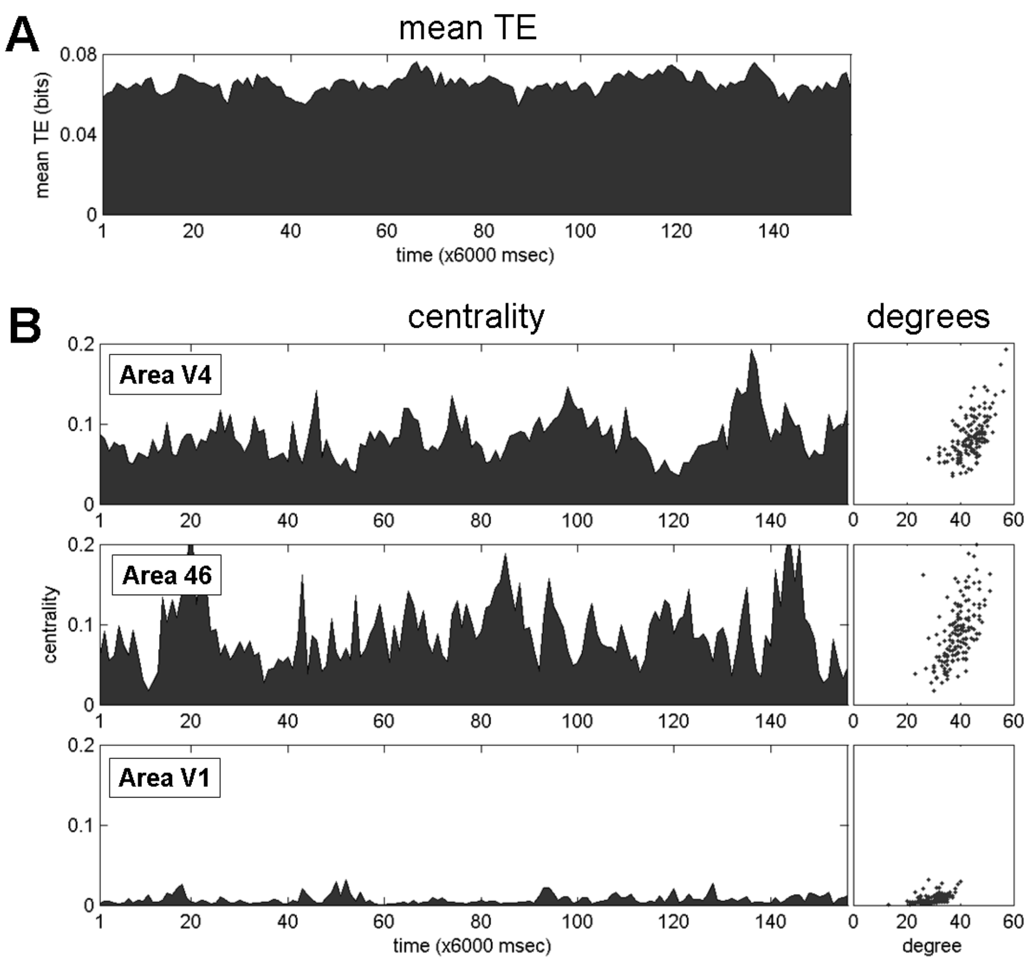


Structural and functional networks show significant correlations in betweenness centrality.

Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity – Hub Dynamics

Functional Networks Change Across Time (Intermediate Time Scale)



Aggregate information flow (transfer entropy) across all regions.

Centrality of nodes in the functional network fluctuates over time.

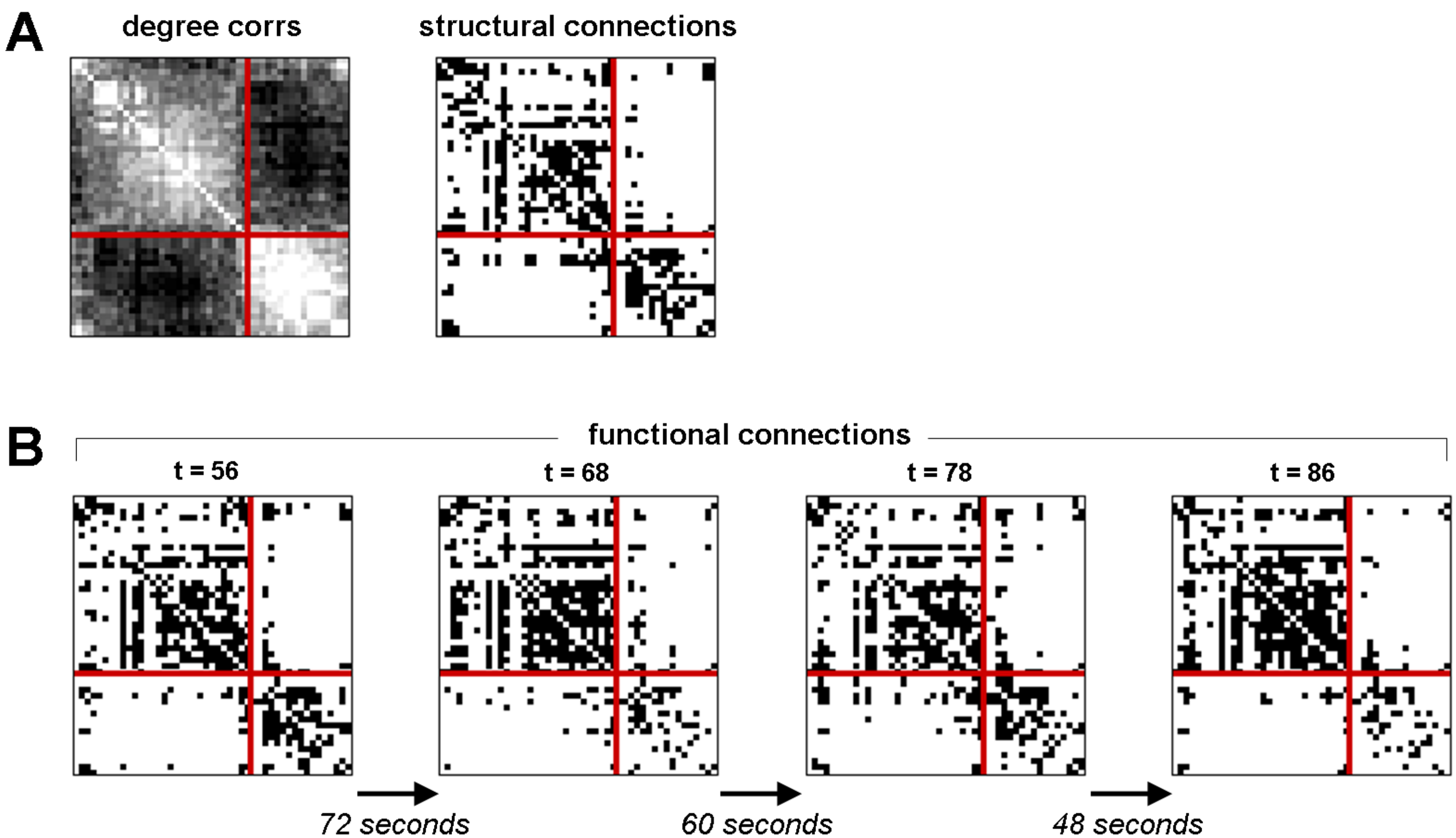
Putative hub regions exhibit significant variations in their "hubness" relative to other nodes.

This is partly due to gain and loss of functional connections (degree).

Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity – A Functional Repertoire?

Functional Networks form a Variable Repertoire

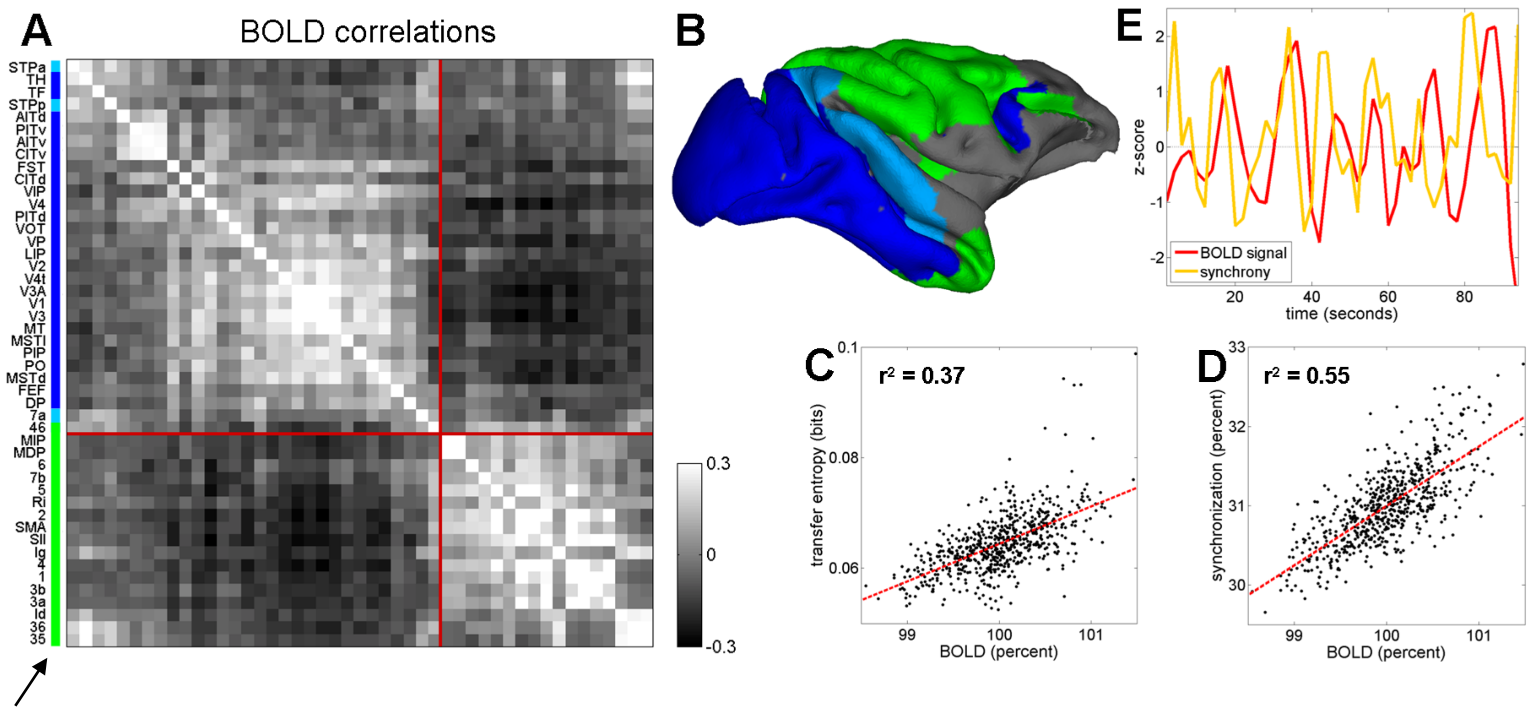


Honey et al. (2007) *PNAS* 104, 10240.

Modeling Endogenous Brain Activity – Multiple Time Scales

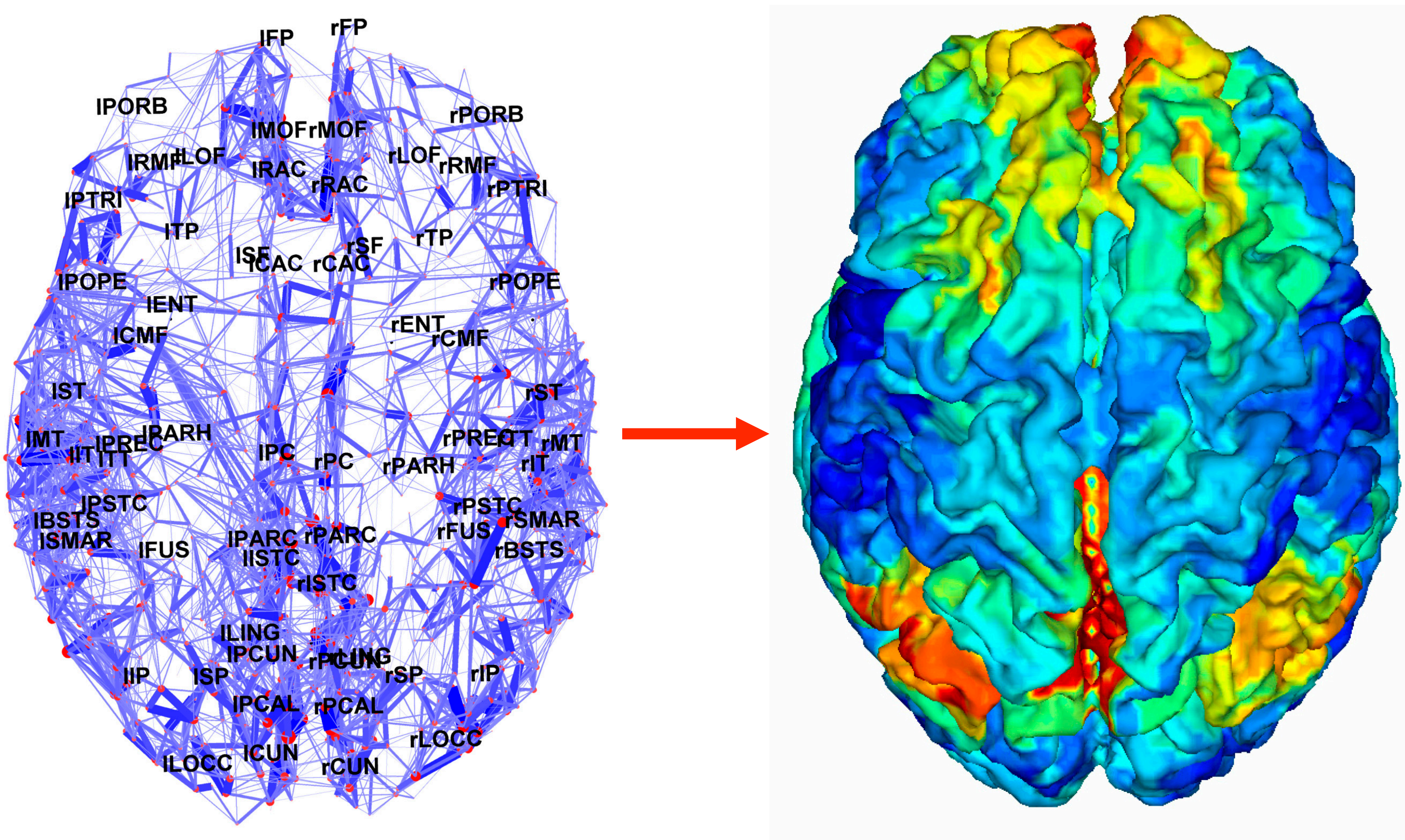
Fast fluctuations in neural synchrony drive slower fluctuations in neural population activity.

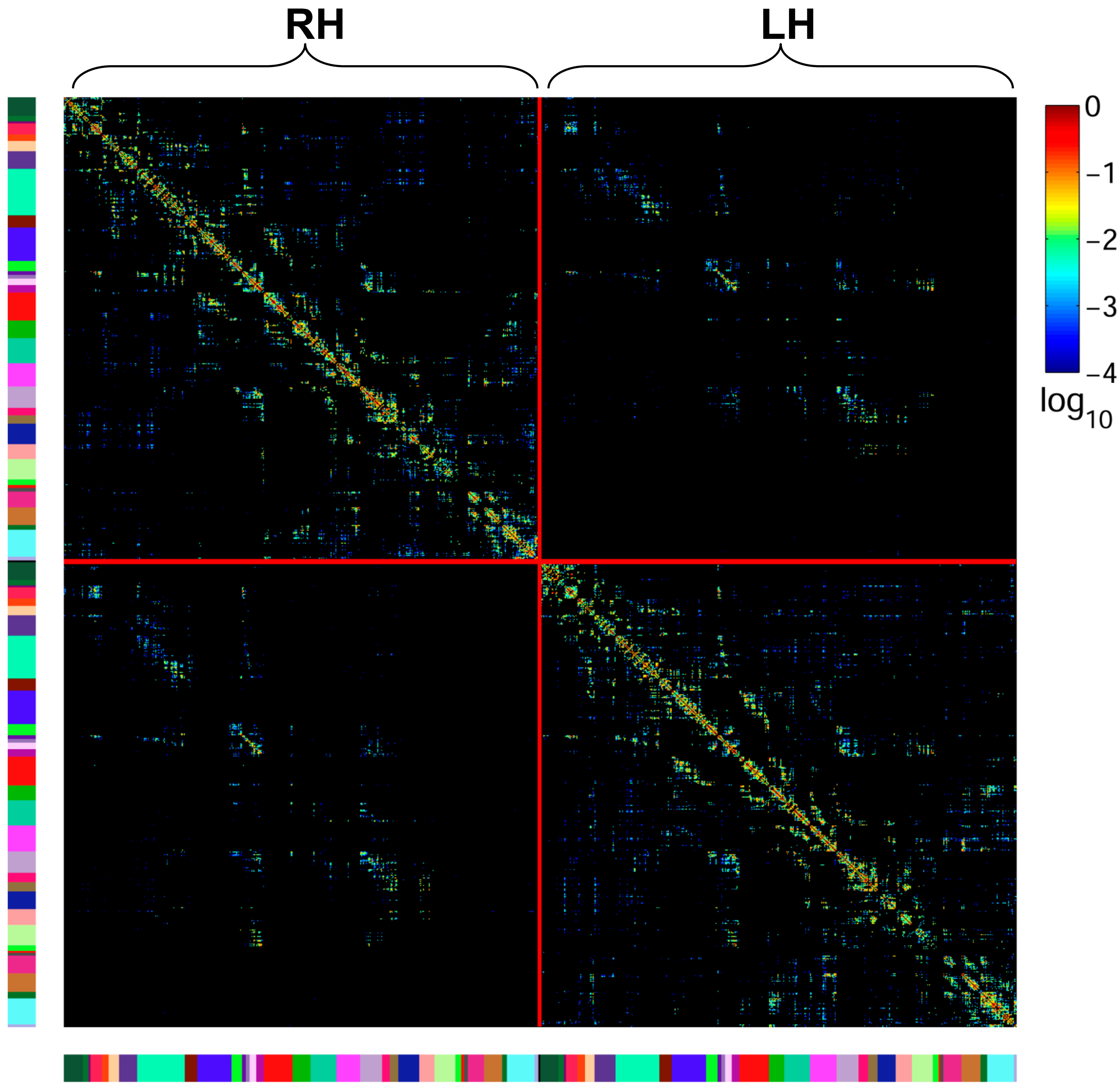
Functional brain networks reflect the small-world architecture of their underlying structural substrate (structural/functional modularity).

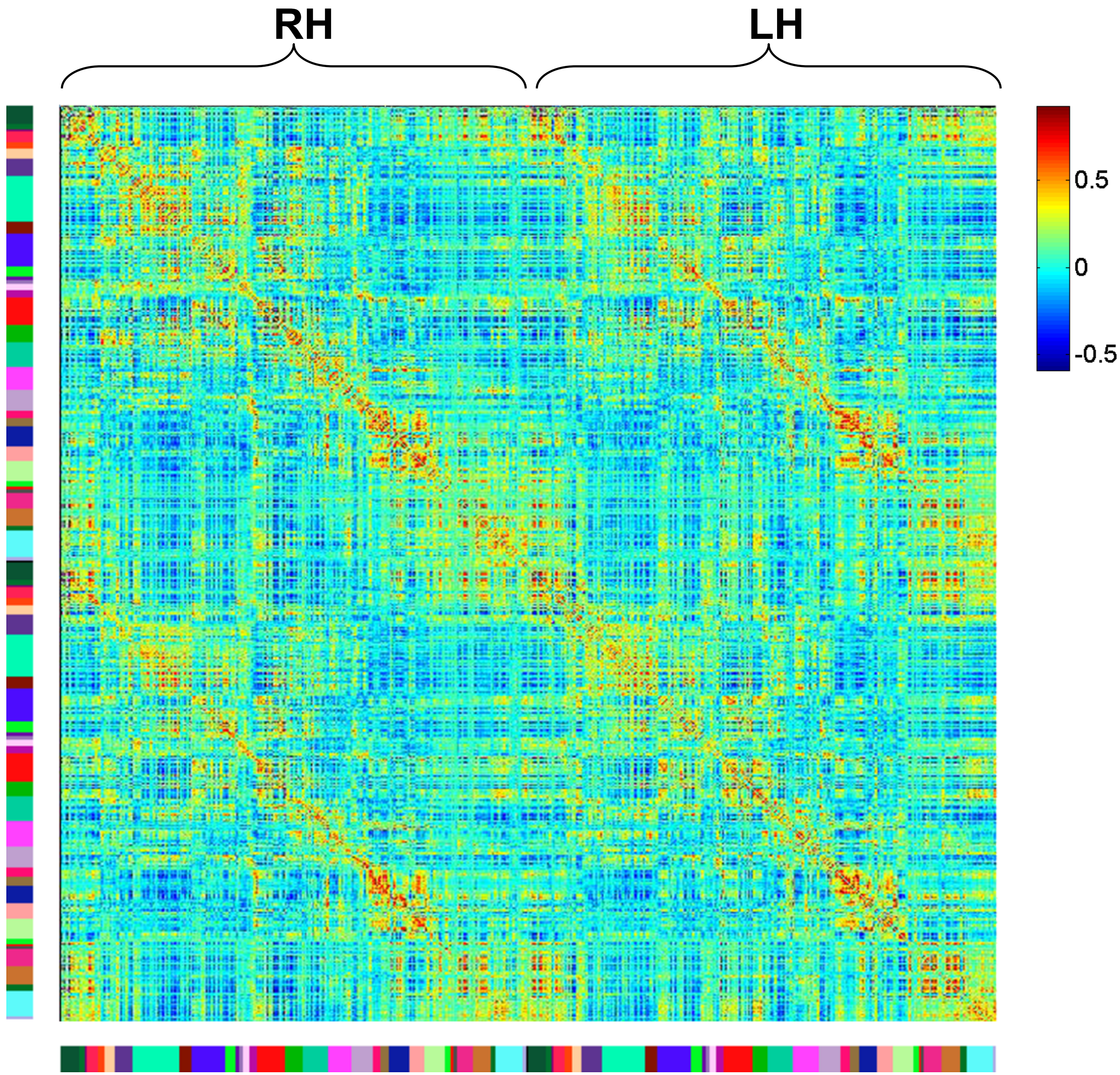


simulated fMRI cross-correlations

Direct Comparison of Structural and Functional Connections



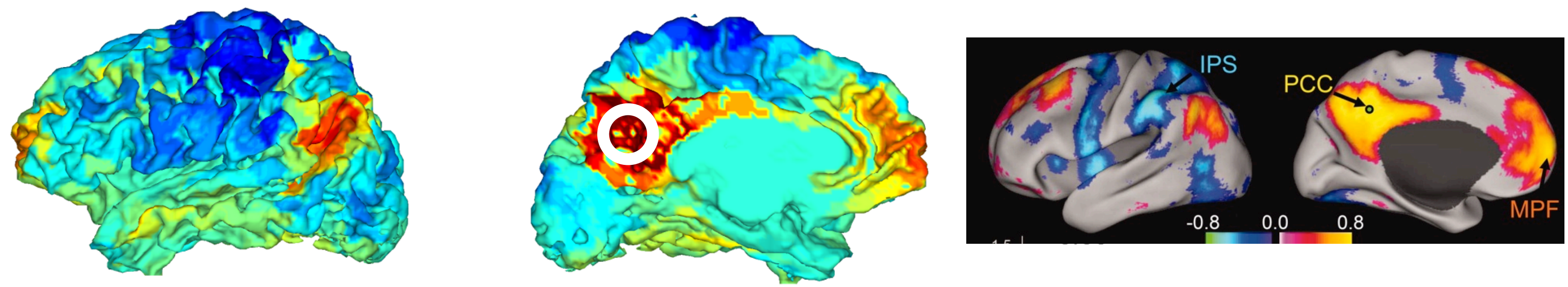

RH
LH
0
−1
−2
−3
−4
log10


RH
LH
0.5
0
-0.5

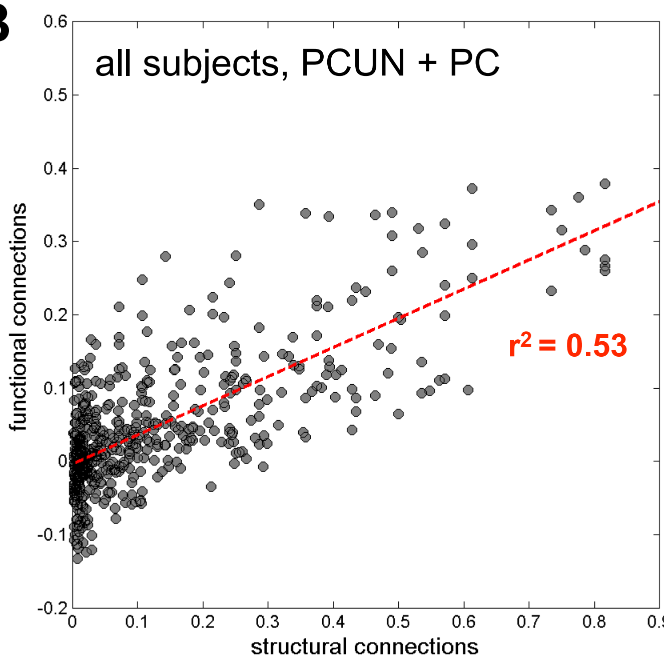
Direct Comparison of Structural and Functional Connections

Structural and Functional Connections are Highly Correlated

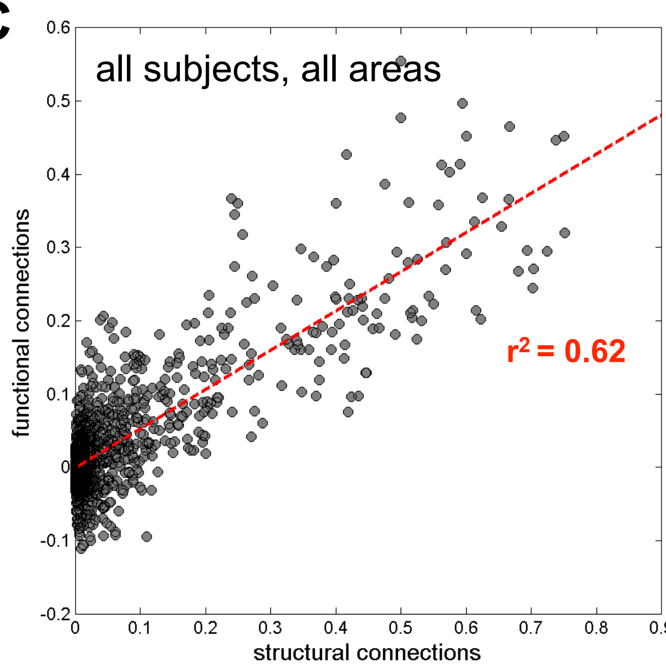
A



B



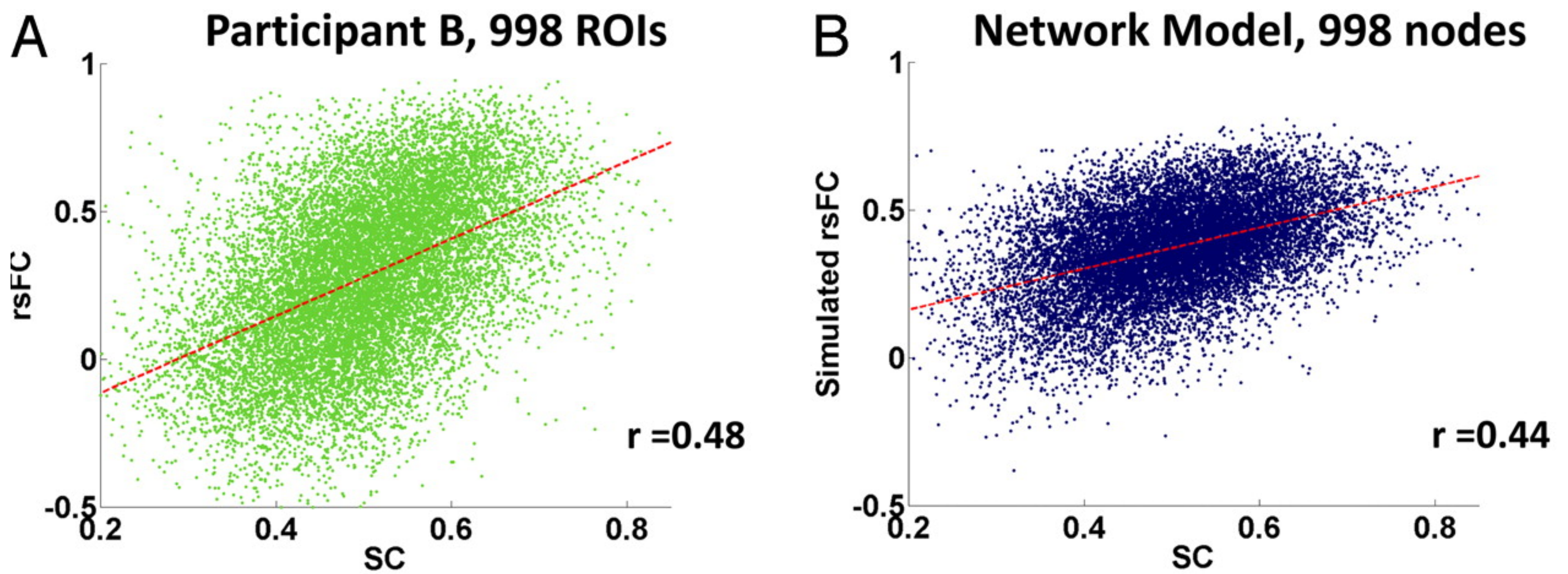
C



Hagmann et al. (2008) *PLoS Biol.* 6, e159

Prediction and Modeling of Functional Connections

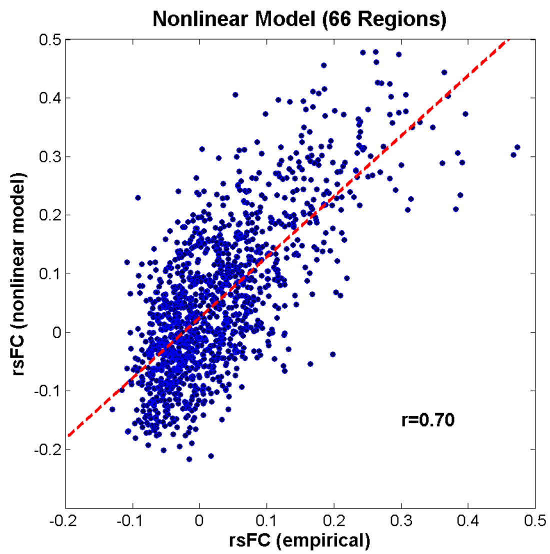
Computational Models Capture Large-Scale Human Brain Activity



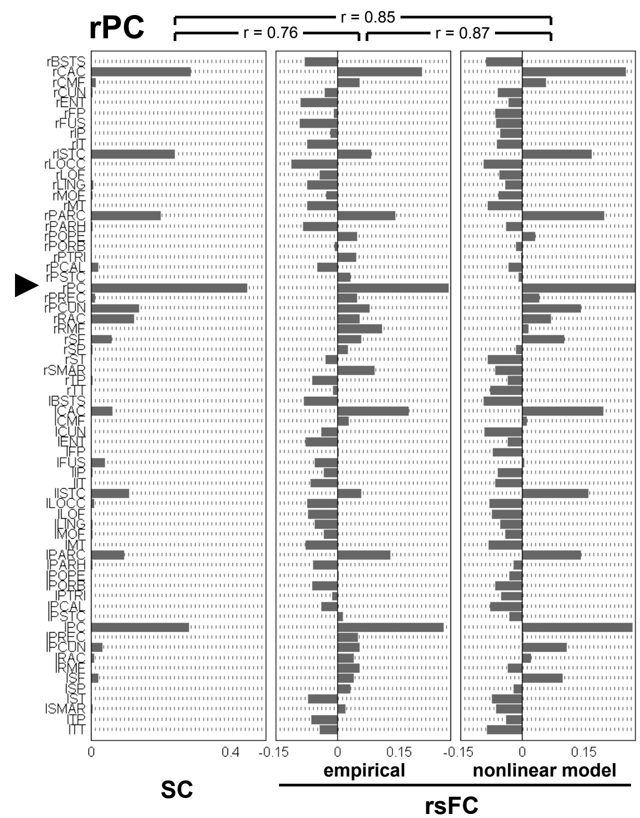
Relation between SC and rsFC for empirical data (left) and computational model (right). Note that the fully deterministic (nonlinear and chaotic) model does not yield a “simple” linear SC-rsFC relationship.

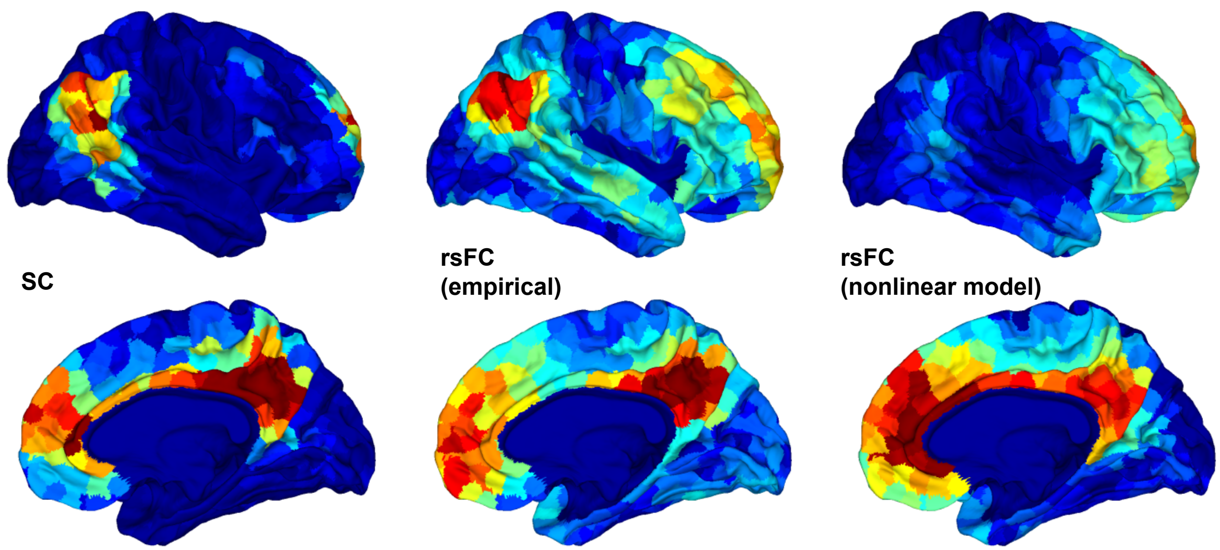
Honey et al. (2009) *PNAS* 106, 2035

Models Capture Human Resting State Functional Connectivity



Structural connections of the human brain can explain much of the patterns seen in resting state functional connectivity.



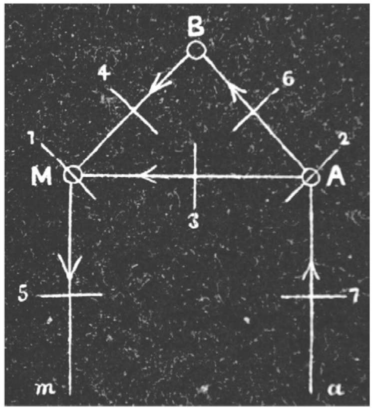


Honey et al. (2009) *PNAS* 106, 2035.

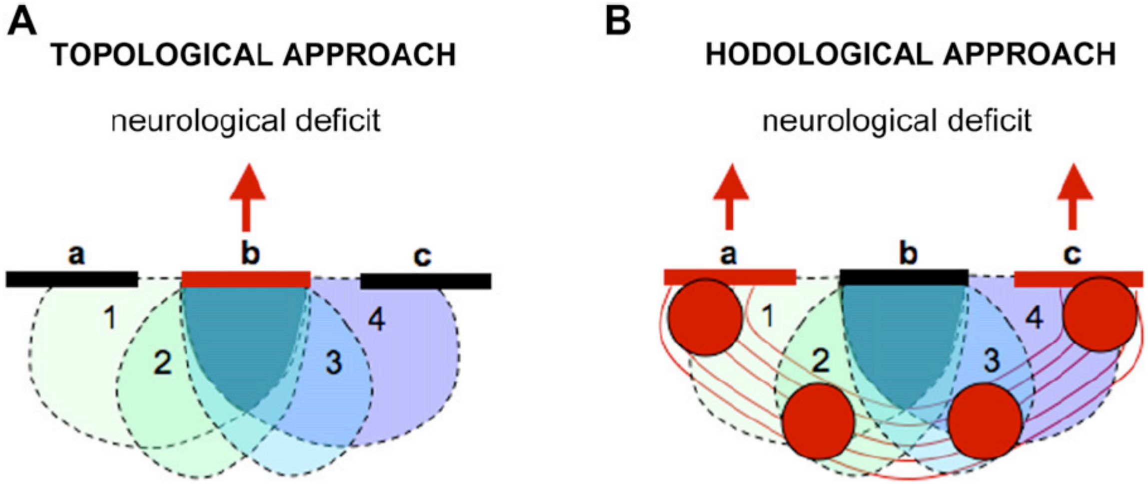
Nonlocal Lesion Effects and Disconnection

The generally accepted theory according to which aphasia, agnosia, apraxia etc. are due to destruction of narrowly circumscribed appropriate praxia, gnosia, and phasia centres, must be finally discarded on the basis of more recent clinical and anatomical studies. It is just in the case of these focal symptoms that the concept of complicated dynamic disorders in the whole cortex becomes indispensable.

Constantin von Monakow (1914)



Lichtheim Aphasia

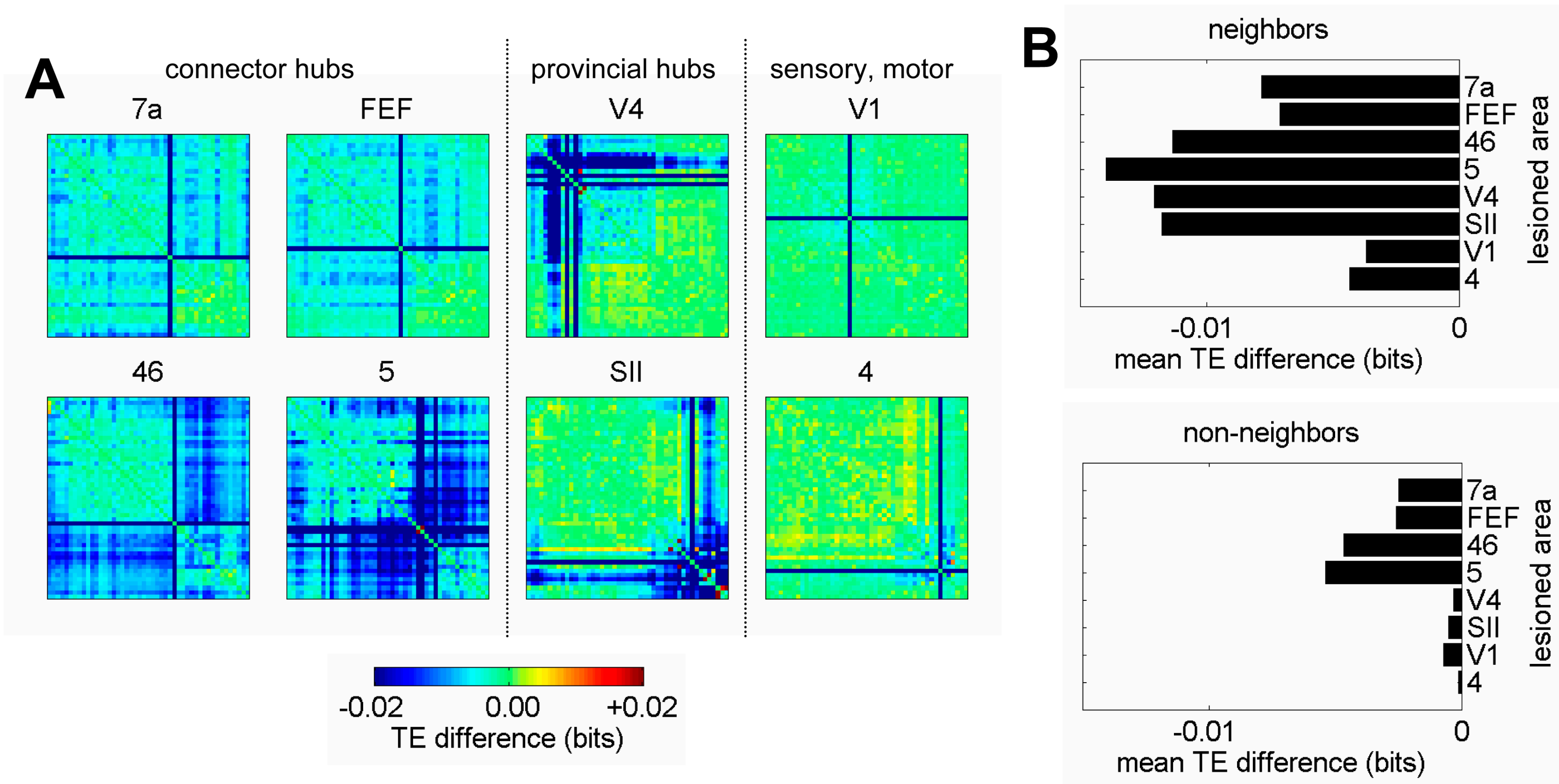


Von Monakow (1914) *Die Lokalisation im Grosshirm und der Abbau der Funktion durch Kortikale Herde*
Catani and Mesulam (2008) *Cortex* 44, 953

Modeling the Impact of Lesions in the Macaque Brain

Lesions may induce global changes in the pattern of spontaneous activity across a large network.

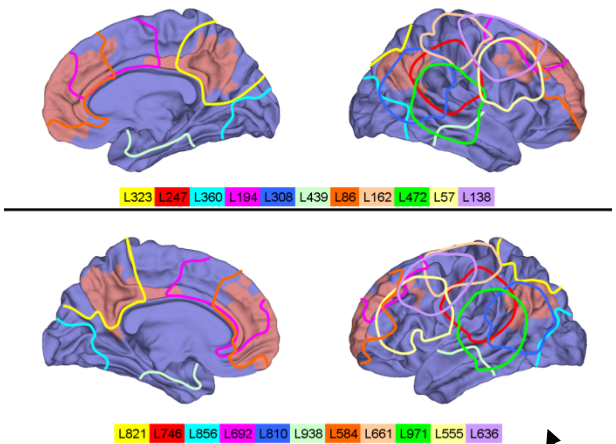
Lesions of hub regions have the greatest potential to disrupt integrative aspects of cortical function.



Honey and Sporns (2008) Human Brain Mapping

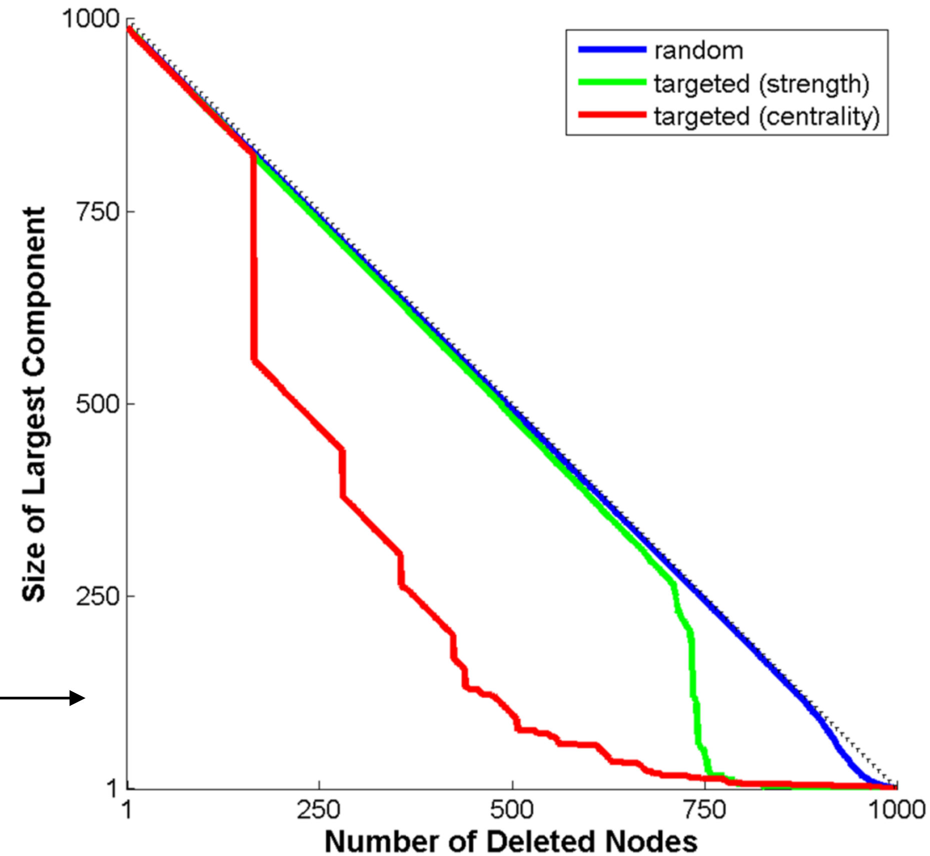
Networks in Brain Injury and Disease

Modeling the Impact of Lesions in the Human Brain



Modeled lesion locations

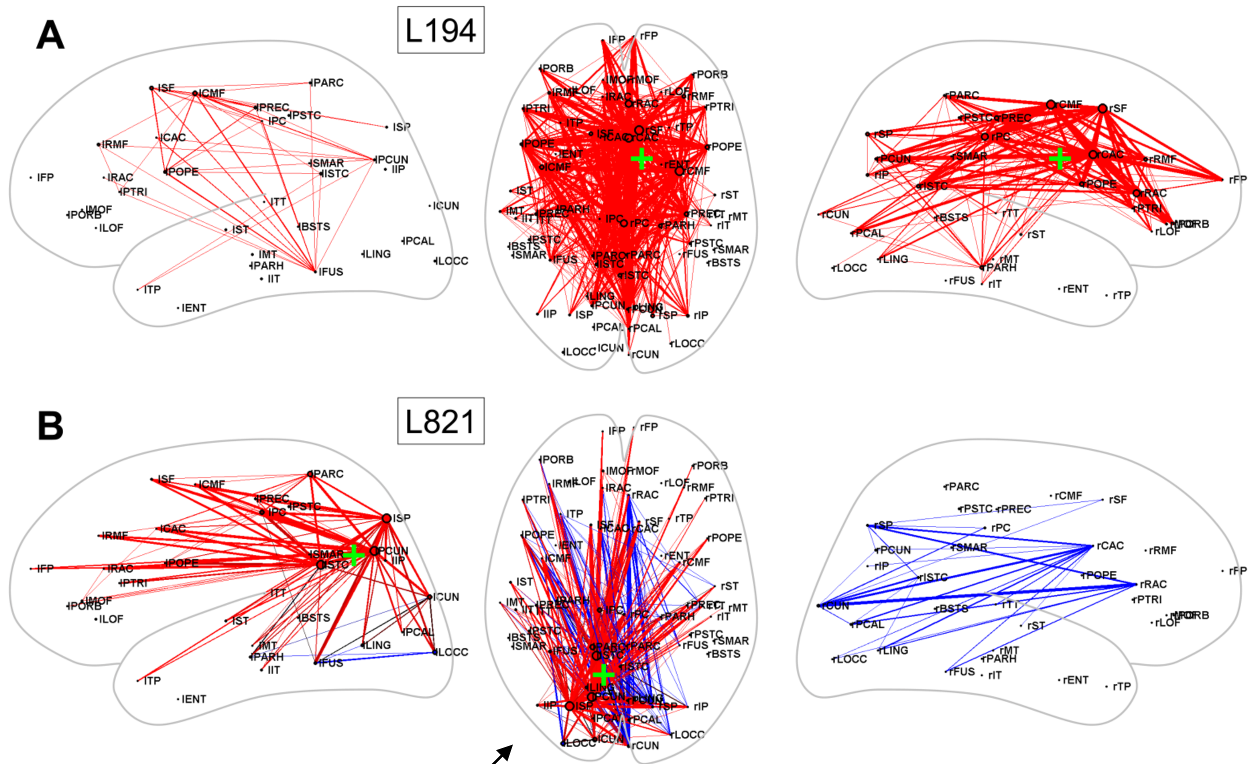
Effect of random or targeted node deletion



The structural network is vulnerable to deletion of highly central nodes, but more resilient to deletion of strong nodes, or randomly selected nodes.

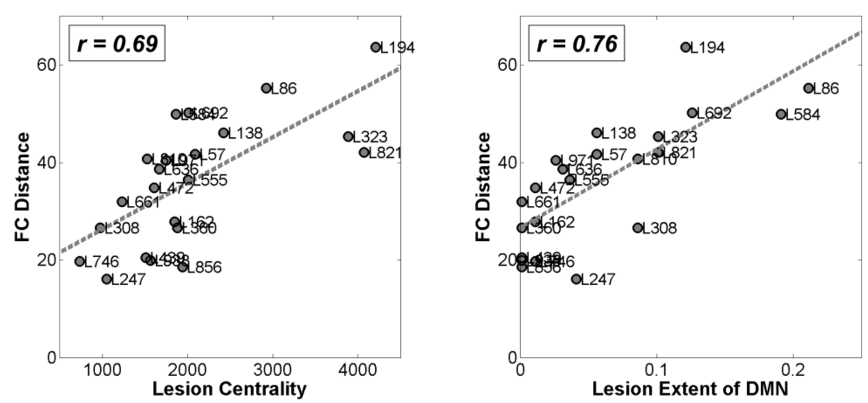
Alstott et al. (2009) *PLoS Comput Biol* (in press)

Modeling the Impact of Lesions in the Human Brain



Effects of lesions in anterior cingulate (L194) or precuneus (L821)

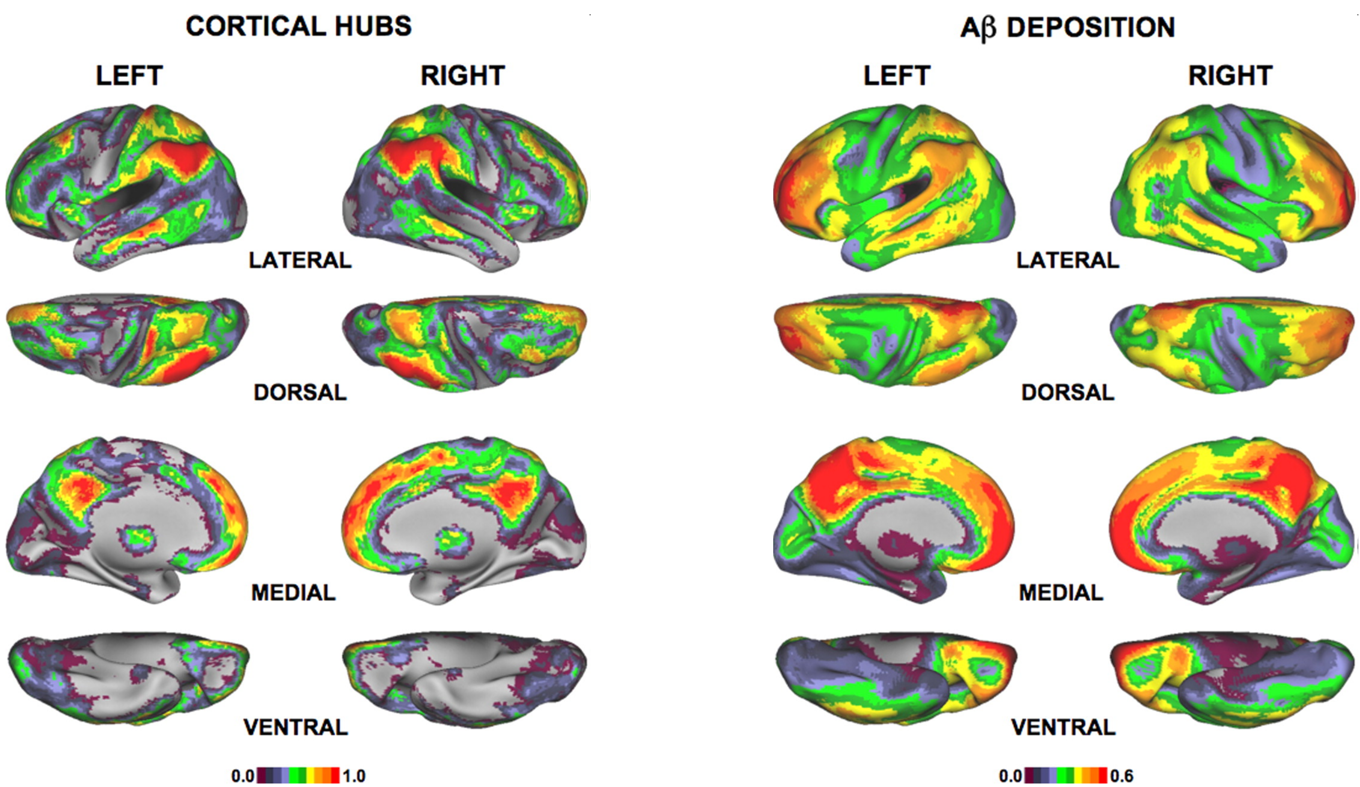
Centrality of lesion site partially predicts lesion effects



Alstott et al. (2009) *PLoS Comput Biol* (in press)

Network Hubs and Alzheimer's Disease

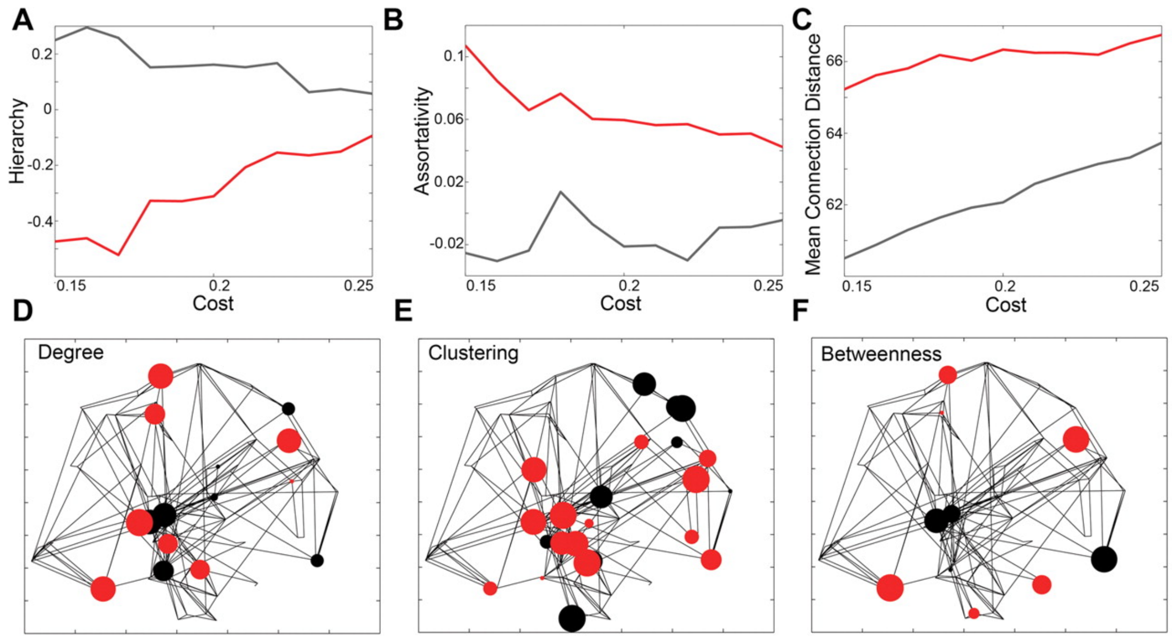
Buckner et al. (2009)
Identification of network hubs in resting state / task-evoked fcMRI
Mapping of Aβ deposition with PET imaging

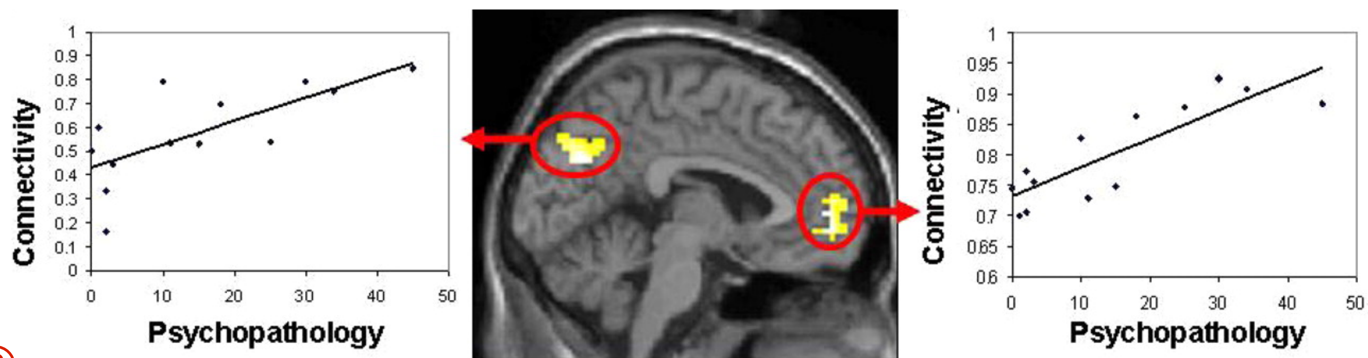


Buckner et al. (2009) *J. Neurosci.* 29, 1860

Disturbed Connectivity in Schizophrenia

① Structural brain networks of people with schizophrenia show reduced hierarchy, longer connection distance, and abnormal hub distribution





②

Functional connectivity at rest correlates with psychopathology

① Bassett et al. (2008) *J. Neurosci.* 28, 9239
② Whitfield-Gabrieli et al. (2009) *PNAS* 106, 1279

Clinical and Translational Aspects

Several neurological and psychiatric disorders can be described as disconnection or dysconnectivity syndromes.

Network approaches may provide new diagnostic criteria – brain connectivity measures may discriminate between patient and control populations.

- Loss of small-world network properties might provide a clinically useful diagnostic marker of AD (EEG: Stam et al., 2007, Cereb Cortex; fMRI: Supekar et al., 2008, PLoS Comp Biol)
- Impaired network properties in patients with schizophrenia (Rubinov et al., 2007, Human Brain Mapping; Bassett et al., 2008, J Neurosci)

Measures of network topology may provide endophenotypes (biological marker) mediating the genetic risk for neuropsychiatric disorder.

Deletion of nodes or of connections between them may allow the exploration of how disease-related damage to specific regional nodes can impact the overall performance of brain networks

Network measures may aid in the understanding of therapeutic effects of pharmacological or psychological therapies

Bullmore and Sporns (2009) *Nature Rev. Neurosci.* 10, 186

Summary

Complexity = Segregation + Integration

Mixture of local specialization and global interaction
Maps onto small-world architecture

The Brain is Always Active – Even "at Rest"

Endogenous processes vs. exogenous perturbations
Multiple time scales – functional repertoire?

Structural and Functional Connectivity are Related…

… up to a point
… and the relationship is reciprocal

Computational Models Capture Large-Scale Human Brain Activity

Possibility of a global brain simulator
Models as tools for exploring mechanistic substrates of human cognition

Clinical Applications of Network Approaches

Modeling of lesion effects reveal non-local mechanisms
Network analysis as a way to diagnose clinical conditions

Funded by the JS McDonnell Foundation