Symposium “Cognition and Connectomics” - ICON 2014

How Brain Structure Constrains Brain Function

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What is the Connectome?

Structural connectivity (anatomical, synaptic):

- Physical/material in nature
- Finite (enumerable) set of elements and connections
- Complex attributes (including density, strength, conduction speed, biophysics)
- Changes across time (development, plasticity)
- Multiscale organization
- Methodological convergence onto a single map is possible

Functional connectivity:

- Statistical/dynamic in nature
- Large and virtually infinite set of network configurations
- Complex attributes (including strength, directionality, temporal persistence)
- Rapid changes across time (moment-to-moment, input- and task-dependent)
- Multiscale organization
- Methodological convergence onto a single “functional connectome” is uncertain

Structural connectivity is the connectome…
Functional connectivity is what the connectome does…

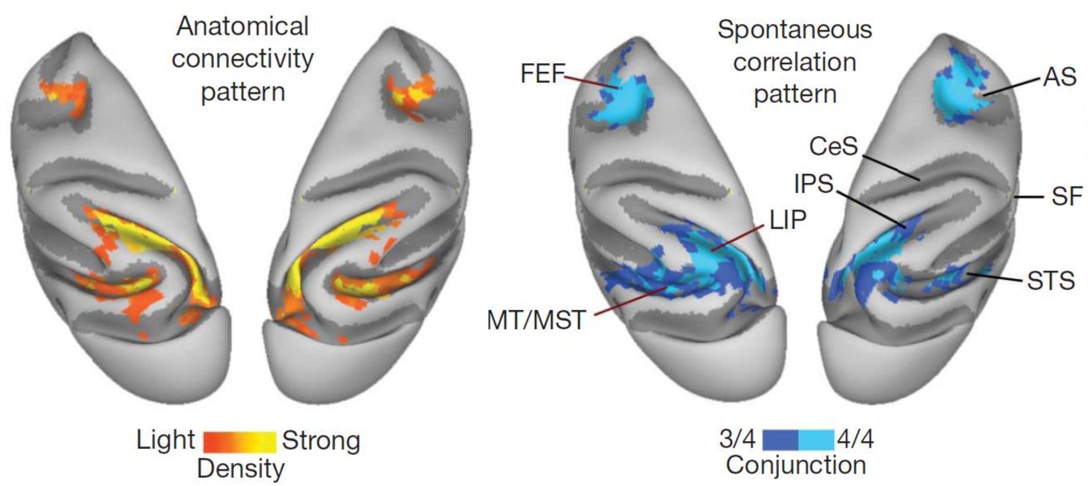
Connectomics

Relating Structural and Functional Connectivity

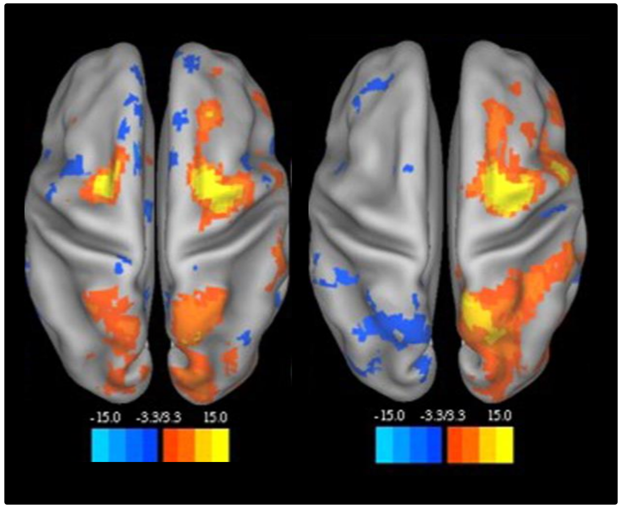
FC has an anatomical/structural basis:

- Robust (but complex) relationship between SC and rs-FC (Vincent et al., 2007; Hagmann et al., 2008; Honey et al., 2009)
- RSNs are internally linked via structural projections (e.g. Greicius et al., 2009; van den Heuvel et al., 2009)
- Cutting SC results in immediate changes in FC (Johnston et al. 2008; O'Reilly et al. 2013)

Vincent et al (2007)

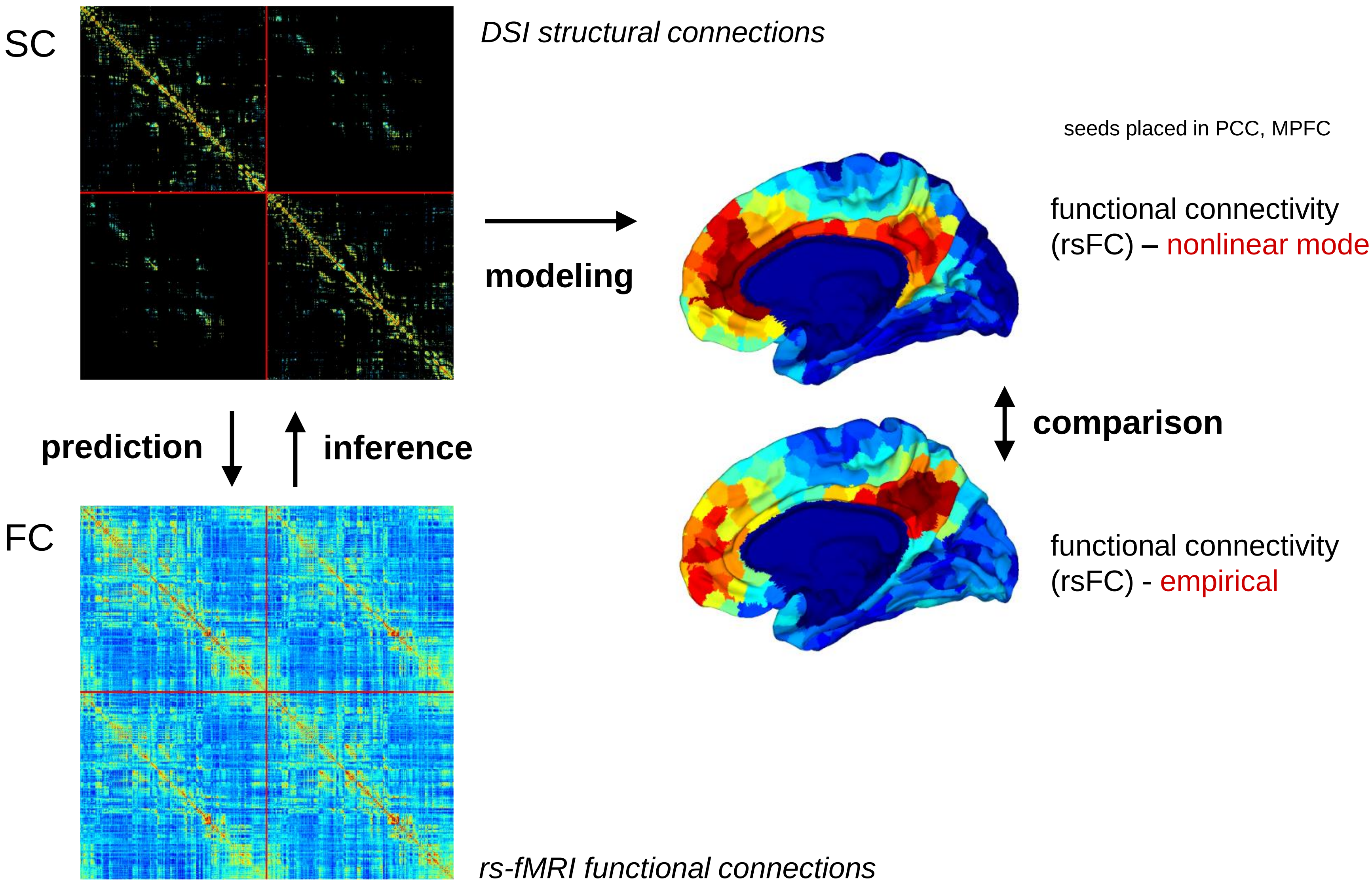


Johnston et al (2008)



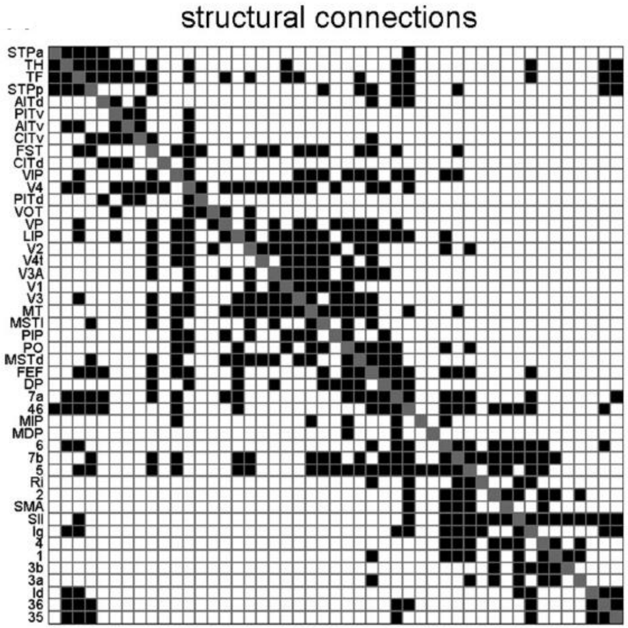
Vincent et al. (2007) Nature 447, 83. -- Hagmann et al. (2008) PLoS Biol. 6, e159. -- Honey et al. (2009) PNAS 106, 2035.
Greicius et al. (2009) *Cerebr Cortex* 19, 72. -- van den Heuvel et al. (2009) *Hum Brain Mapp* 30, 3127.
Johnston et al. (2008) J Neurosci 28, 6453. – O'Reilly et al. (2013) PNAS 110, 13982.

Relating Structural and Functional Connectivity



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

Computational Modeling of FC



perturbations

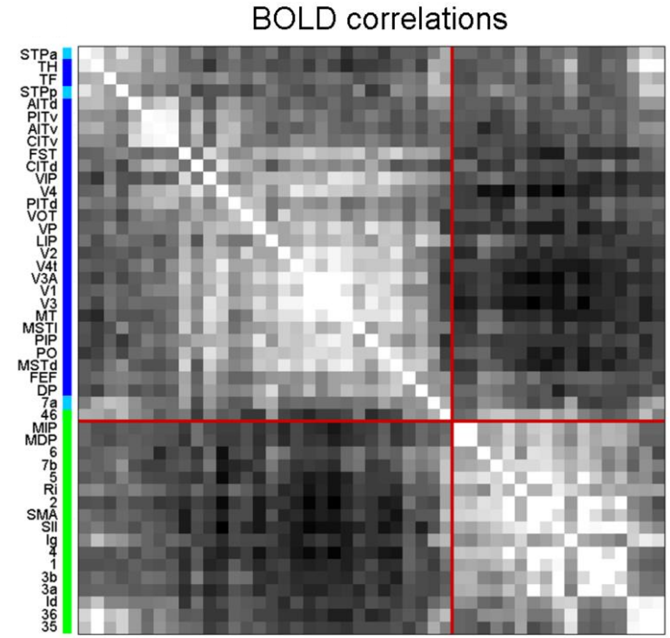
connectome

+

biophysical equations

rest

task



$$\frac{dV}{dt} = -\left(g_{Ca} + r_{NMDA} a_{ee} Q_V\right) m_{Ca}\left(V - V_{Ca}\right) - \left(g_{na} m_{na} + a_{ee} Q_V\right)\left(V - V_{na}\right) - g_K W\left(V - V_K\right)$$
$$- g_L\left(V - V_L\right) + a_{ie} Z Q_Z + a_{ne} I_\delta,$$

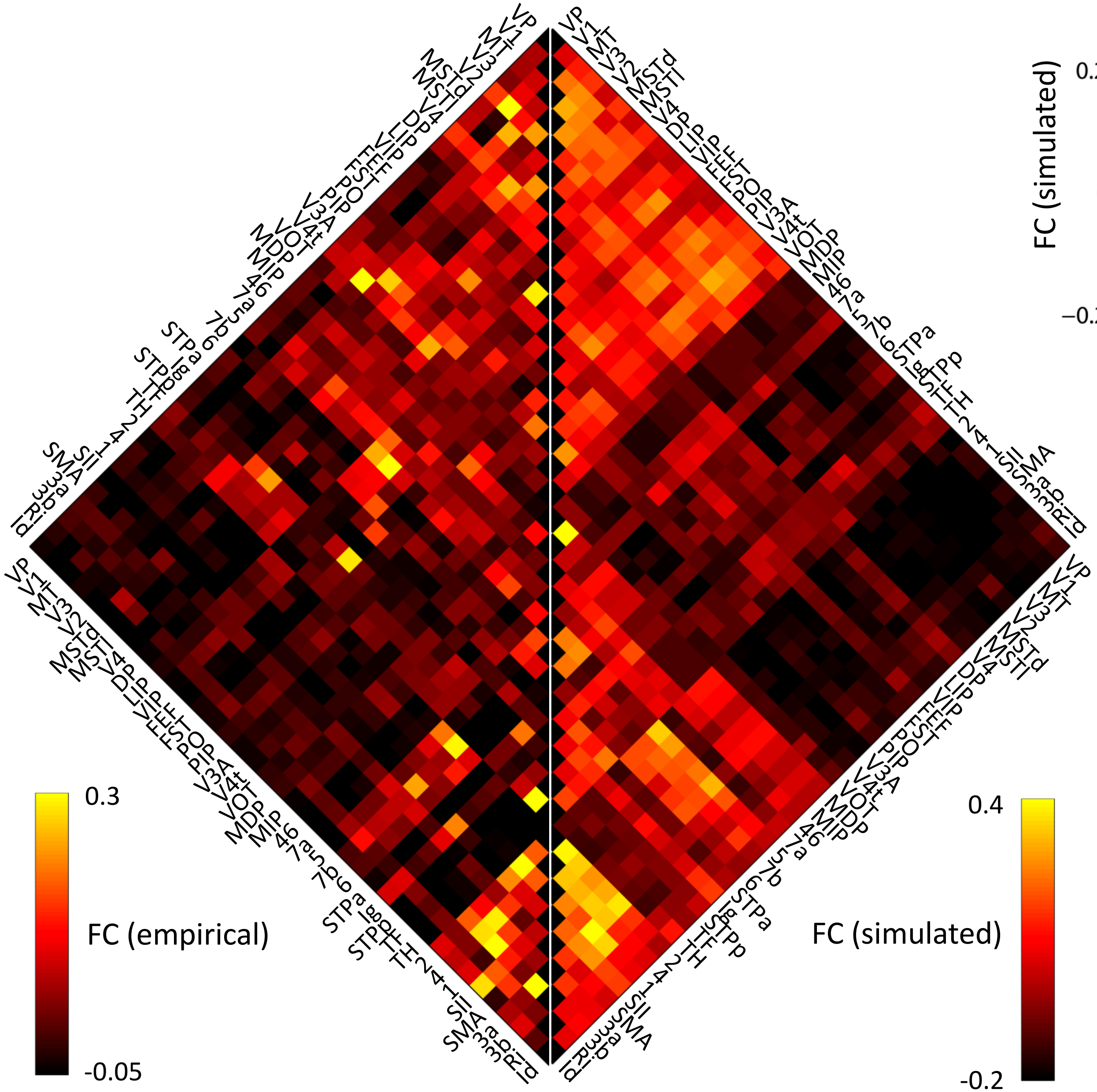
$$\frac{dZ}{dt} = b\left(a_{ni} I_\delta + a_{ei} V Q_V\right),$$

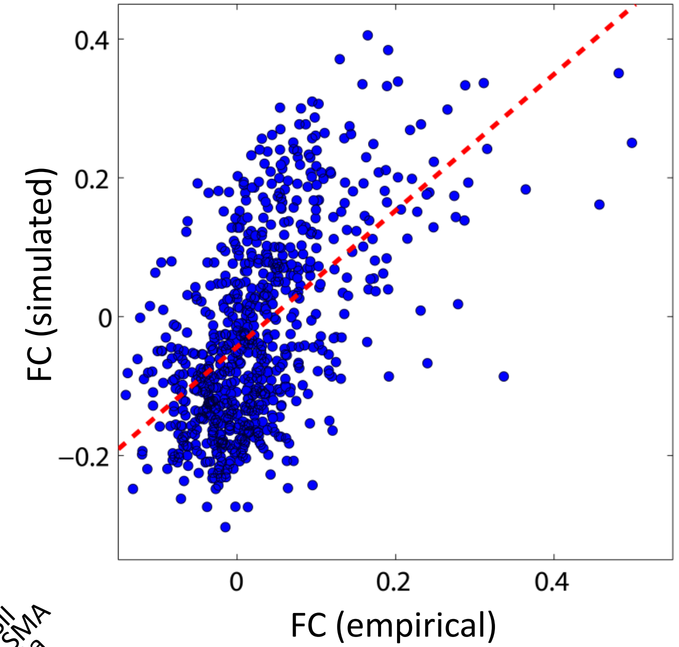
inputs

R = 0.55 correlation with empirical macaque rs-fMRI data
Adachi et al. (2012) *Cereb Cortex*

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

Deco et al. (2011) *Nature Rev Neurosci* 12,

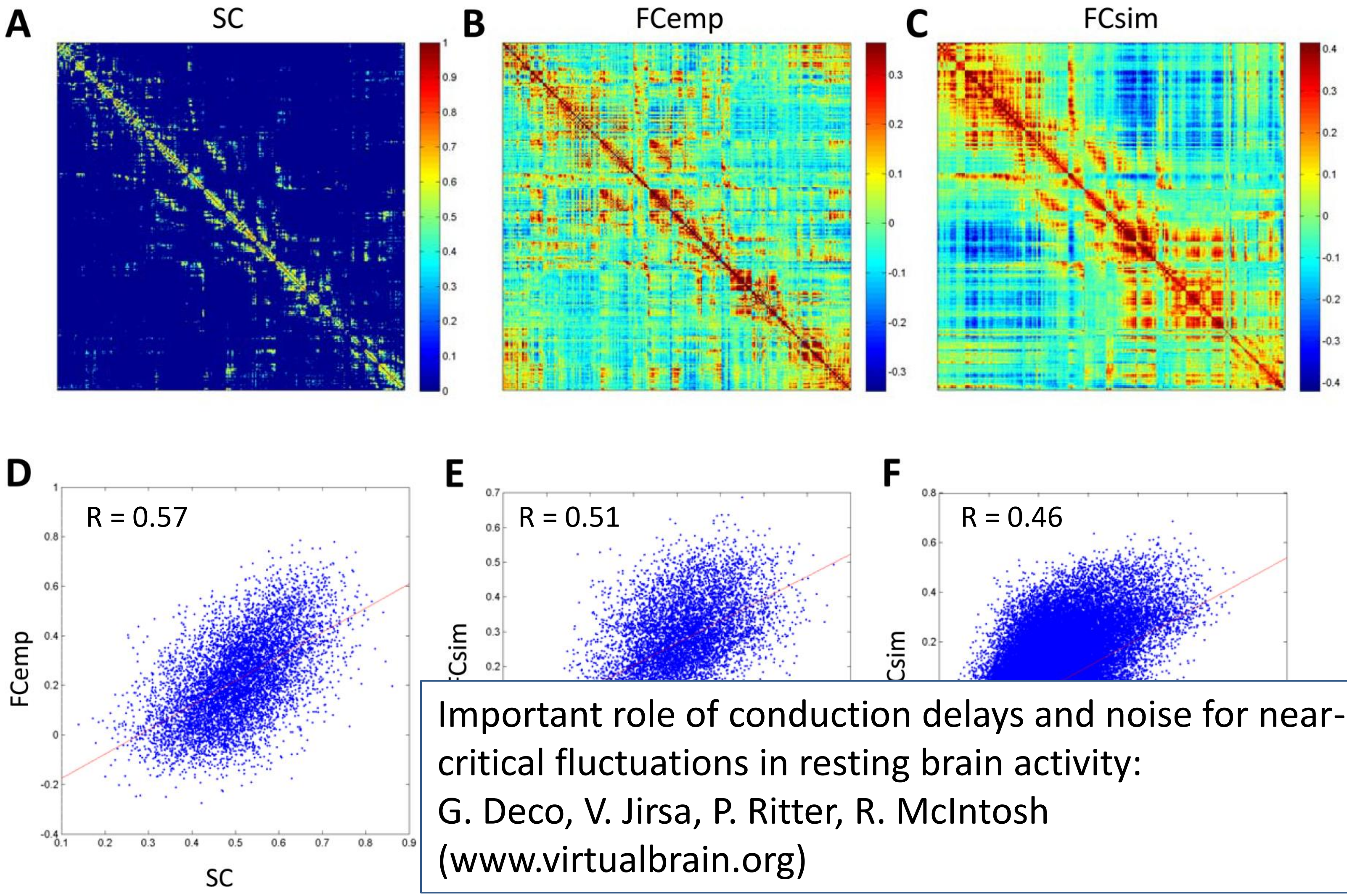




Adachi et al (2012) Cereb Cortex 22, 1586

Computational Modeling of FC

A network model of human resting-state fMRI functional connectivity.



Important role of conduction delays and noise for near-critical fluctuations in resting brain activity:
G. Deco, V. Jirsa, P. Ritter, R. McIntosh
(www.virtualbrain.org)

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

Functional Connectivity and Communication Processes

Many networks (technological, social, biological) involve the transportation of mass/energy/people/molecules or the communication of signals/messages.

Network performance is often efficient, with particles or signals traveling along short routes, maximizing transmission speed and minimizing energy expenditure.

The brain is an example of a communication network:

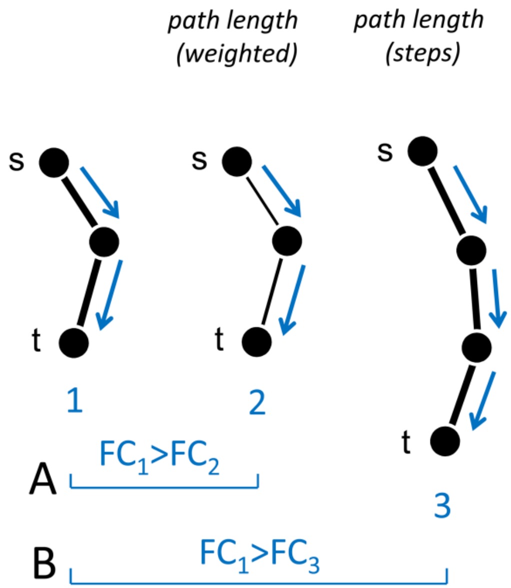
- Efficient signaling related to communication paths
- Selection pressure on connectivity structure to enable efficient signaling
- Trade-off: Conserving network cost while maximizing performance

The strength of functional connectivity may be thought of as reflecting network communication:

- Stronger functional connectivity among node pairs that are more directly linked (i.e. shorter topological distance or path length)
- Other potential predictors: physical distance, community structure

Using SC Graph Metrics to Predict FC

Graph metrics that capture patterns of network communication:



Search information quantifies the “hiddenness” of a path, i.e. the information needed to access it.

Path transitivity quantifies the density of “local detours” surrounding a given path.

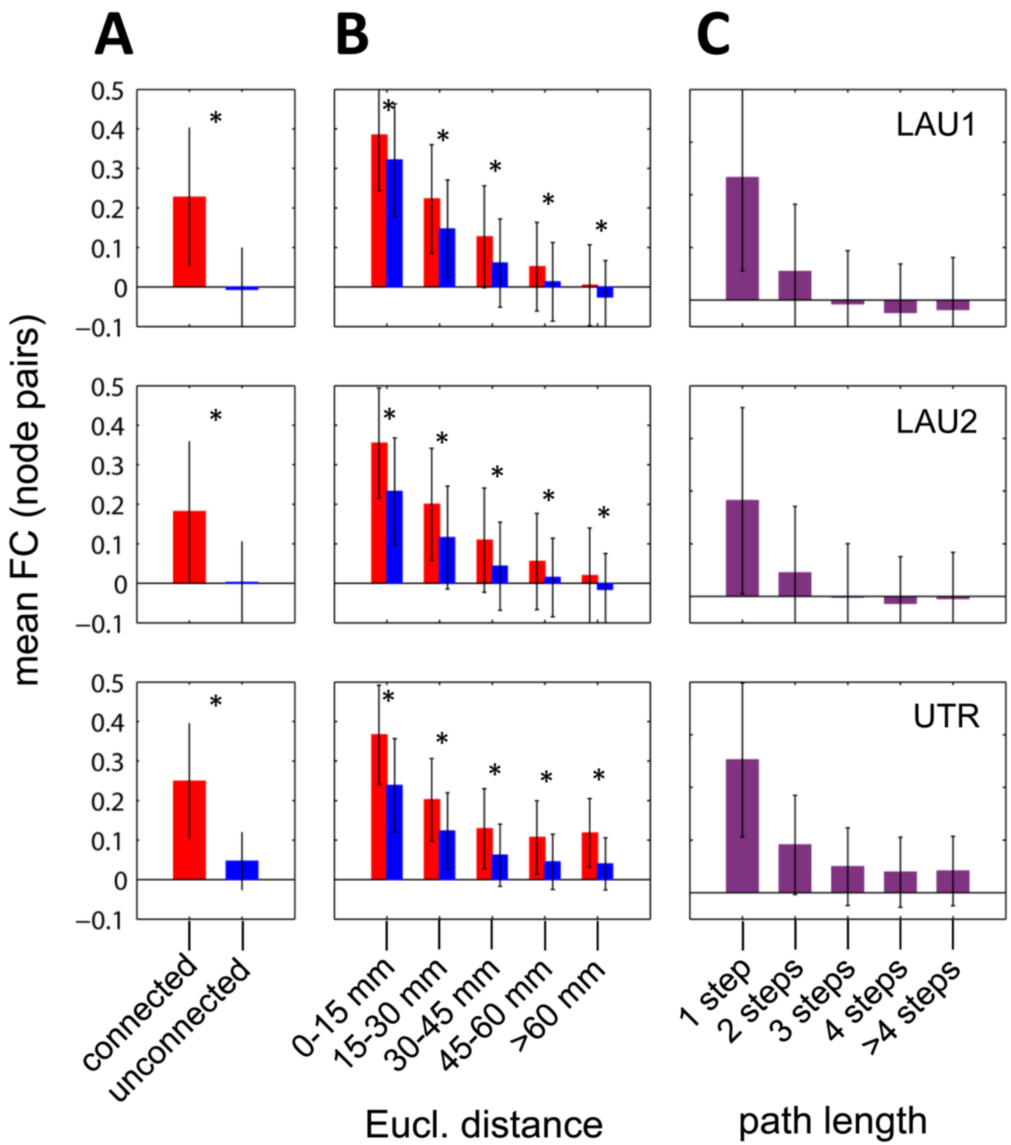
Predictions:

- [s,t] node pairs requiring greater search information exhibit weaker FC*
- [s,t] node pairs with higher path transitivity exhibit stronger FC**

* holding path length constant
** holding path length and search information constant

Goñi et al. (2014) *PNAS* 111, 833.

Connectome-Based Models for Functional Connectivity



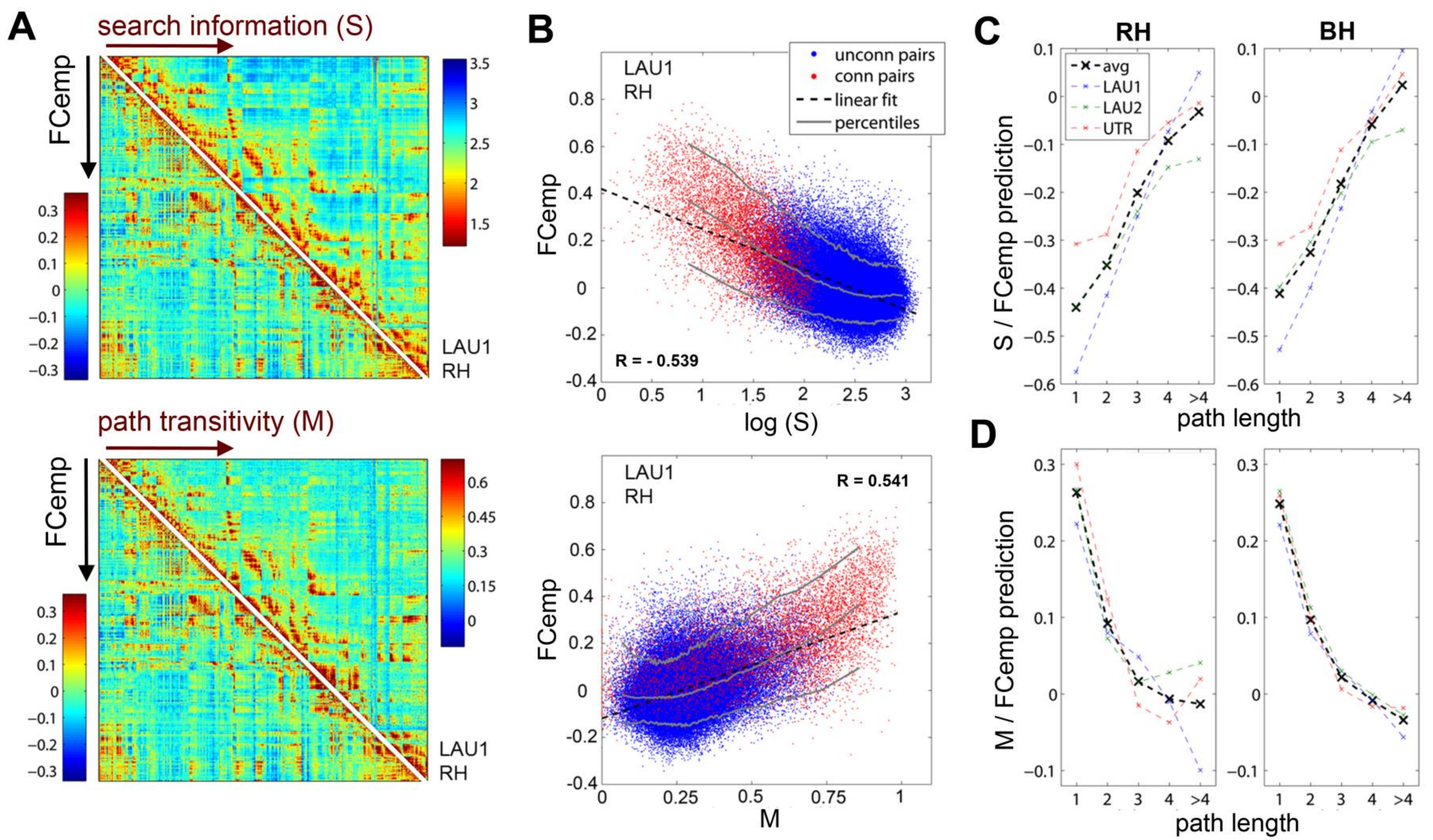
Three independently acquired data sets

Relationship of structural connectivity and functional connectivity:

- Stronger on connected node pairs
- Diminishes with spatial distance
- Diminishes with path length

Goñi et al. (2014) *PNAS* 111, 833.

Connectome-Based Models for Functional Connectivity



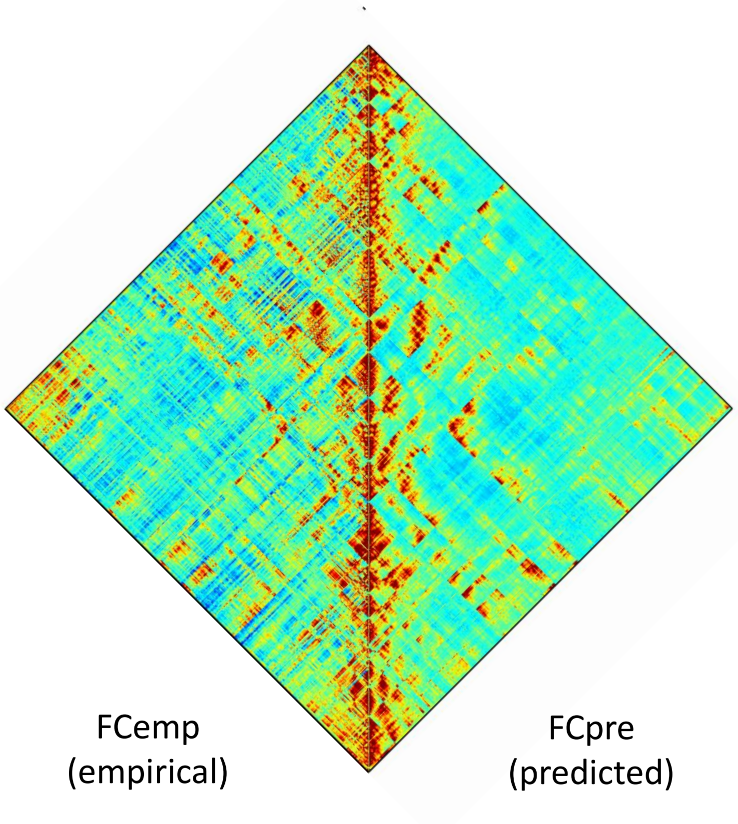
Search information and path transitivity are negatively/positively correlated with FC.

Relationship remains significant when accounting for path length.

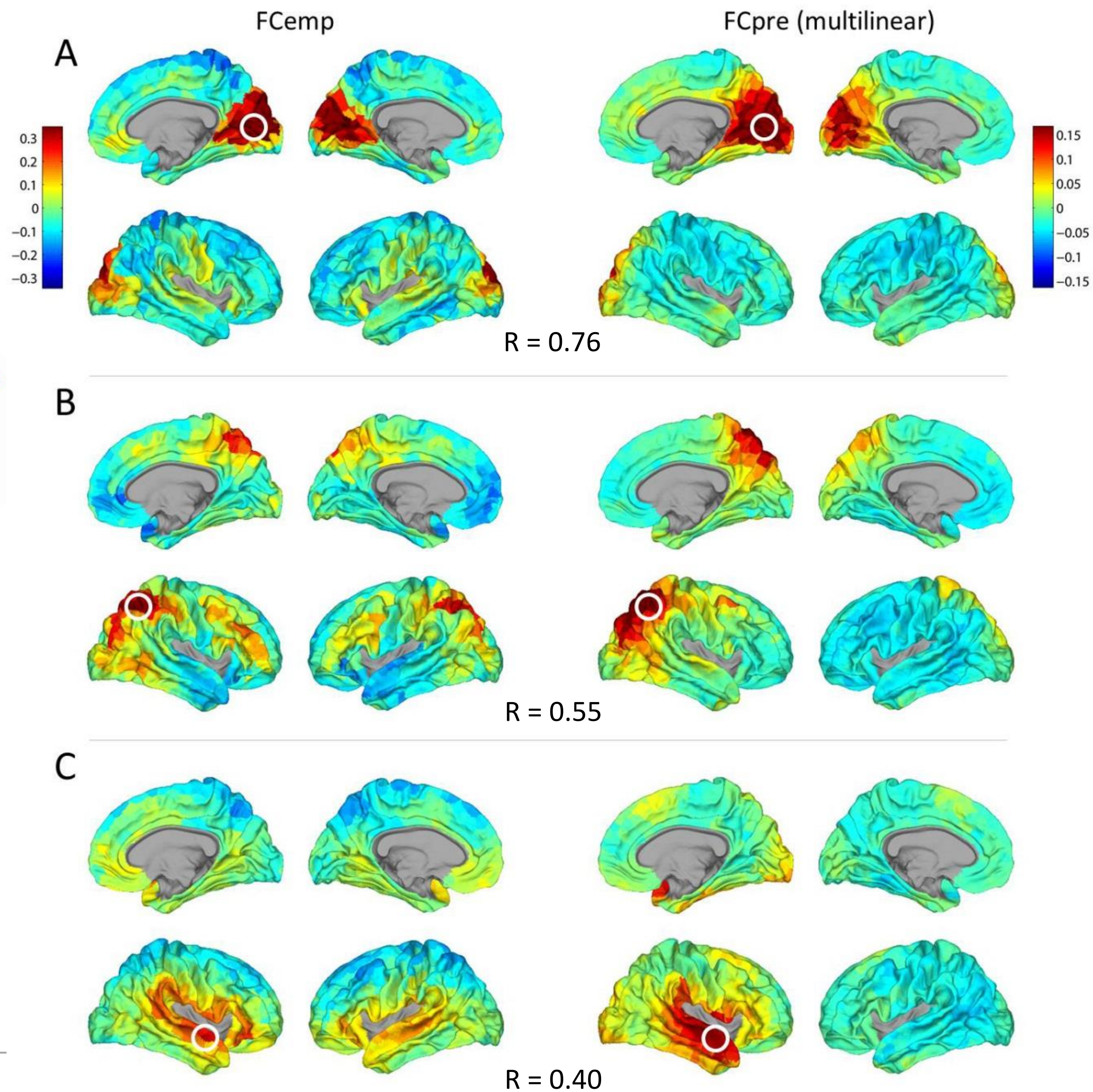
Goñi et al. (2014) *PNAS* 111, 833.

Connectome-Based Models for Functional Connectivity

Analytic measures of network communication can predict functional connectivity.



R = 0.60



Goñi et al. (2014) *PNAS* 111, 833.

Connectome-Based Models for Functional Connectivity

Table S1. FC predictions of neural mass model, linear model, and Euclidean distance, as well as single-predictor and multipredictor models based on shortest paths computed from the SC after applying a log transform to convert edge weights to distances

			Both hemispheres			Right hemisphere		
FC predictors			LAU1	LAU2	UTR	LAU1	LAU2	UTR
Neural mass model		R_{all}	0.359	0.317	0.363	0.464	0.365	0.441
		R_{conn}	0.346	0.340	0.436	0.354	0.317	0.406
		R_{unconn}	0.237	0.202	0.197	0.313	0.223	0.218
Linear model		R_{all}	0.347	0.251	0.332	0.453	0.296	0.423
		R_{conn}	0.474	0.197	0.079	0.517	0.192	0.090
		R_{unconn}	0.217	0.144	0.162	0.279	0.156	0.214
Euclidean distance	ED	R_{all}	−0.421	−0.370	−0.256	−0.489	−0.441	−0.328
		R_{conn}	−0.578	−0.568	−0.547	−0.571	−0.620	−0.562
		R_{unconn}	−0.341	−0.313	−0.171	−0.393	−0.379	−0.219
Path length (weighted)	*D*	R_{all}	−0.310	−0.270	−0.215	−0.473	−0.370	−0.352
		R_{conn}	−0.527	−0.317	−0.174	−0.573	−0.373	−0.202
		R_{unconn}	−0.200	−0.181	−0.110	−0.324	−0.260	−0.206
Path length (steps)	*K*	R_{all}	−0.281	−0.235	−0.220	−0.408	−0.323	−0.343
		R_{conn}	−0.096	−0.026	−0.110	−0.103	0.008	−0.106
		R_{unconn}	−0.169	−0.144	−0.116	−0.256	−0.210	−0.192
Search information	log(*S*)	R_{all}	−0.410	−0.352	−0.325	−0.565	−0.449	−0.451
		R_{conn}	−0.520	−0.400	−0.319	−0.570	−0.438	−0.320
		R_{unconn}	−0.256	−0.238	−0.168	−0.380	−0.319	−0.247
Path transitivity	*M*	R_{all}	0.405	0.366	0.347	0.524	0.439	0.451
		R_{conn}	0.501	0.458	0.374	0.536	0.454	0.397
		R_{unconn}	0.248	0.248	0.177	0.338	0.298	0.238
All predictors		R_{all}	0.478	0.409	0.402	0.598	0.491	0.500
		R_{conn}	0.570	0.491	0.423	0.616	0.519	0.446
		R_{unconn}	0.312	0.292	0.216	0.403	0.357	0.263
All predictors (ED regressed)		R_{all}	0.338	0.280	0.326	0.441	0.352	0.405
		R_{conn}	0.482	0.366	0.353	0.504	0.344	0.344
		R_{unconn}	0.219	0.186	0.175	0.289	0.242	0.219

Correlation values are Pearson correlations computed for all pairs (R_{all}), only structurally connected pairs (R_{conn}), and only structurally unconnected pairs (R_{unconn}). All correlations were significant ($P < 0.001$).

NMM prediction

ED prediction

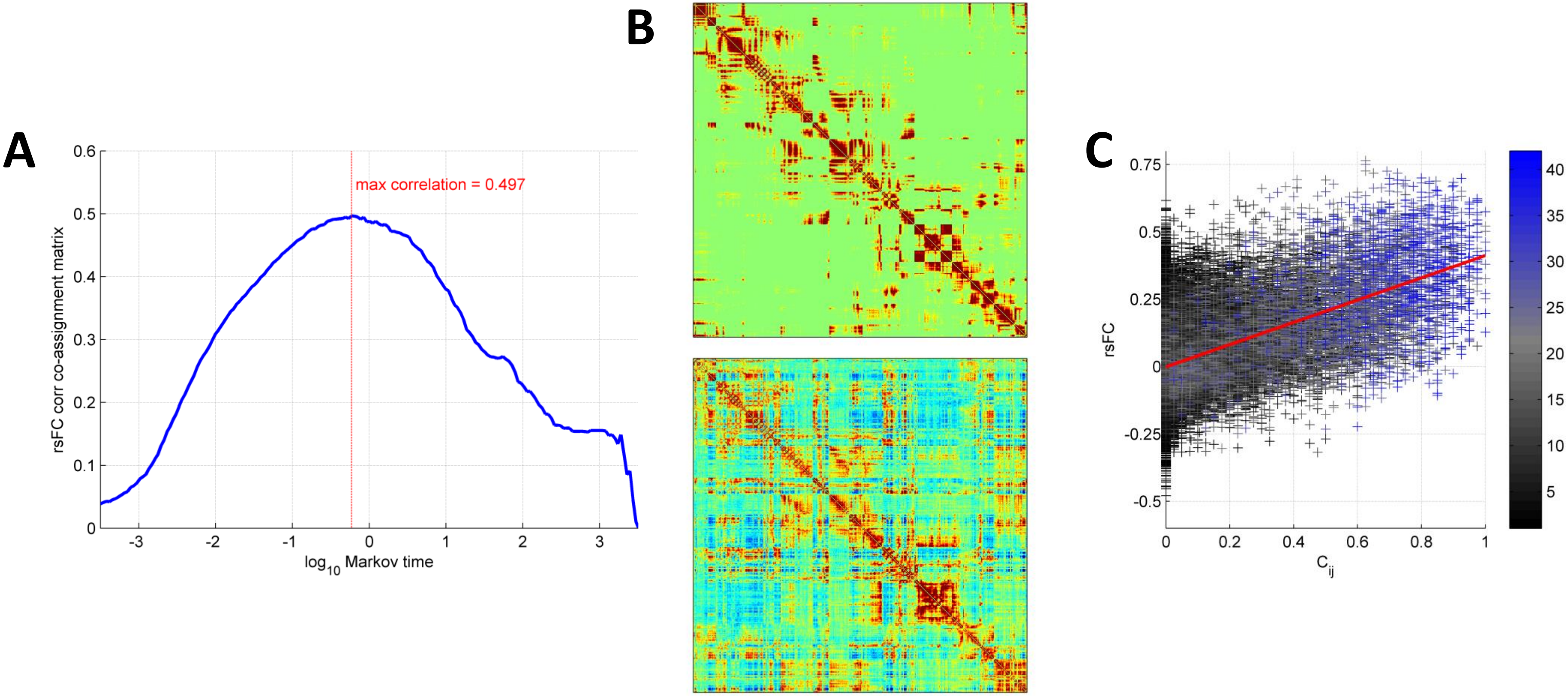
Search information alone

Multilinear model

Goñi et al. (2014) *PNAS* 111, 833.

Other Models: Multiscale Community Structure

Diffusion processes can be utilized to assess network communities (e.g. infomap).
Evidence suggests multiscale organization of network communities in the connectome.



Betzel et al. (2013) *Network Science 1, 353*
See also: Abdelnour et al. (2014) Neuroimage 90, 335
Meunier et al. (2010) *Front. Neurosci*. 4, 200.
Mucha et al. (2010) *Science* 328, 876.
Lewis et al. (2012) *BMC Systems Biol.* 4, 100.

Summary and Conclusion

SC (the connectome) and (resting-state) FC are robustly related.

SC can serve as a coupling matrix for computational neural models of (spontaneous or resting) FC.

Analytic measures (derived from SC) that capture aspects of network communication processes are powerful predictors of the strength and pattern of FC.

Measures and models of network diffusion appear to capture many features of FC topology.

Challenges:

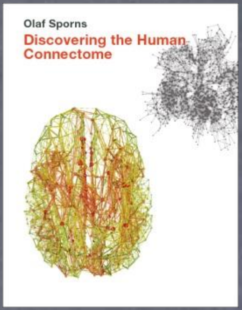
- Modeling temporal fluctuations in FC
- Modeling patterns of task-evoked FC

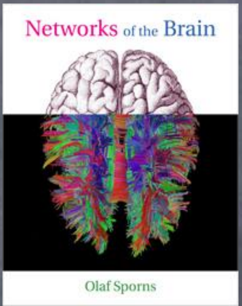
Future work modeling SC/FC relations may provide further insight into the nature of large-scale brain communication.

Further Reading and Acknowledgements

Further Reading:

• van den Heuvel MP, Sporns O (2013) Network hubs in the human brain. *Trends Cogn Sci* 17, 683.
• Bullmore ET, Sporns O (2012) The economy of brain network organization. *Nature Rev Neurosci* 13, 336-349.
• Behrens TEJ, Sporns O (2012) Human connectomics. *Curr Opin Neurobiol* 22, 144-153.
• Rubinov M, Sporns O (2010) Complex network measures of brain connectivity: Uses and interpretations. *Neuroimage* 52, 1059-1069.
• Bullmore, ET, Sporns, O (2009) Complex brain networks: Graph-theoretical analysis of structural and functional systems. *Nature Rev Neurosci* 10, 186-198.





Lab: www.indiana.edu/~cortex

NIH Human Connectome Project:
www.humanconnectome.org

The Virtual Brain Project:
http://thevirtualbrain.org

Network Analysis Toolbox (Matlab):
www.brain-connectivity-toolbox.net

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