NETWORK SCIENCE CHALLENGES IN HUMAN NEUROSCIENCE

SIAM NS15
MAY 16, 2015

Danielle S. Bassett

University of Pennsylvania
Department of Bioengineering

Complex Biological Systems

Utilize networks of mechanical, electrical, or informational signals to perform complex functions

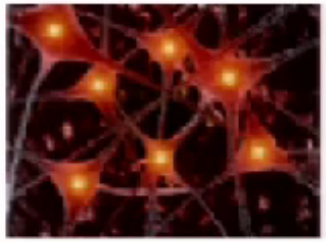
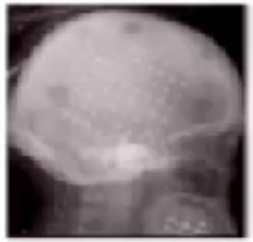
The Human Brain

Utilizes networks of mechanical, electrical, or informational signals to perform complex functions

Networks at Each Scale

Small Scales ⟷ Larger Scales



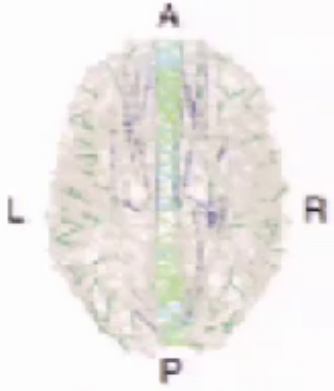




Network neuroscience provides a systems approach to the study of the brain, and enables the examination of interactions between scales.

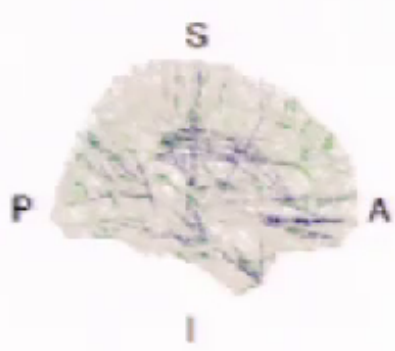
A Network of Anatomy (Type I)

Structural Pathways:
Neuronal Fiber Bundles

Coronal View



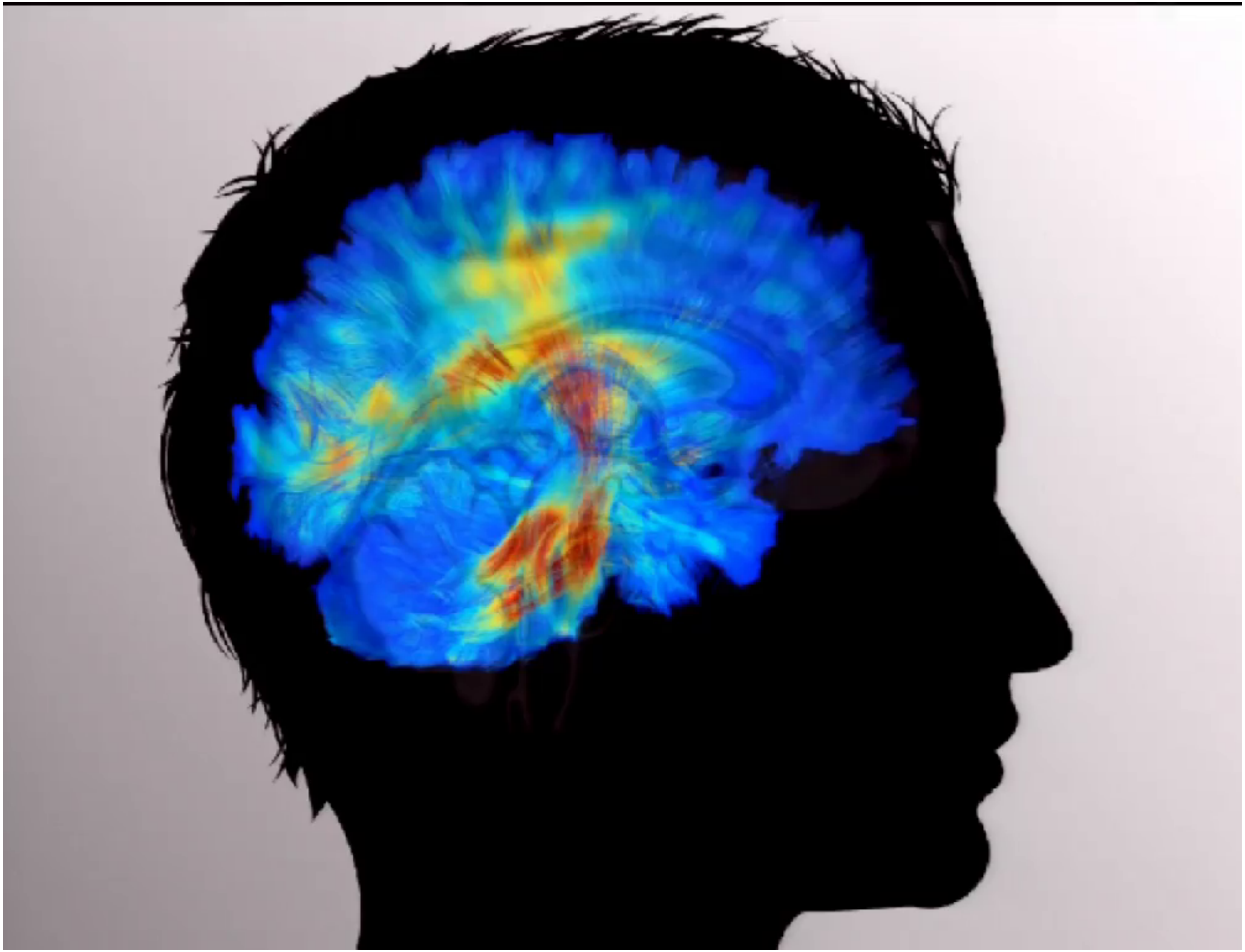
Axial View



Sagittal View

- Anatomically distinct brain areas are represented as **network nodes**
- Fiber bundles that link these areas are represented as **network edges**

Hermundstad et al. 2013 PNAS



Li et al. 2009 PLoS Comp Biol

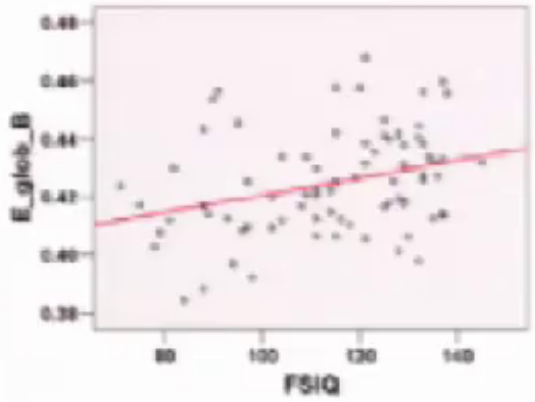
Efficient Brains are Smarter Brains

The global efficiency of a network can be defined as:

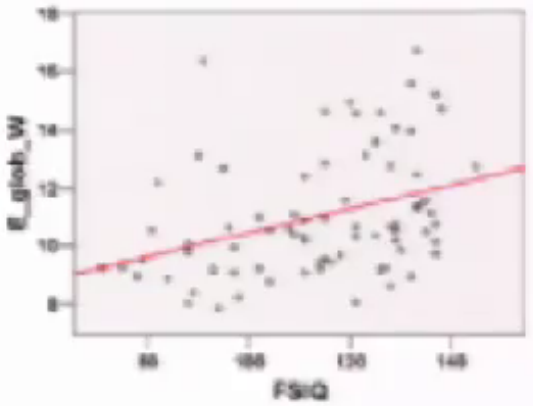
$$E = \frac{1}{n}\sum_{i \in N} E_i = \frac{1}{n}\sum_{i \in N} \frac{\sum_{j \in N, j \neq i} d_{ij}^{-1}}{n-1},$$

where E_i is the efficiency of node i, and d_{ij} is the shortest path between node i and node j.

Binary



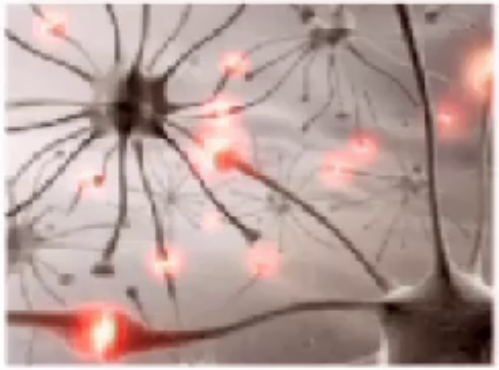
Weighted

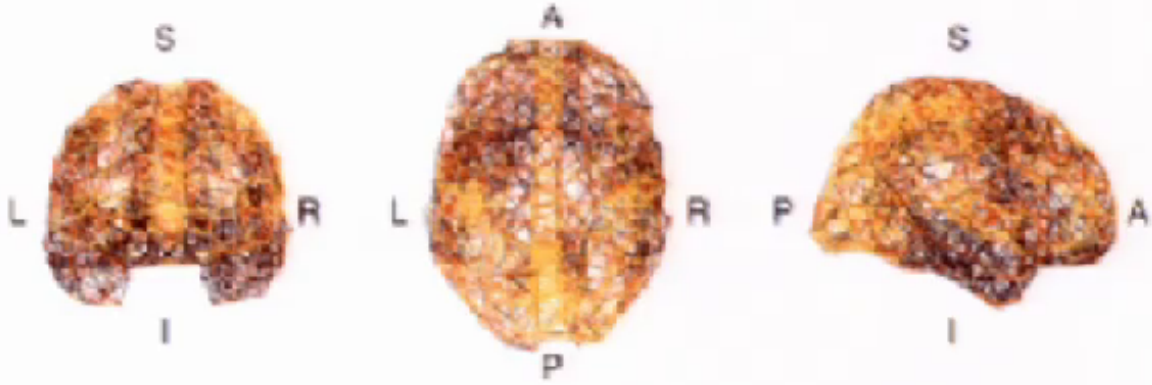


People with higher global efficiency have higher IQs.

A Network of Utilization (Type II)

Functional Pathways:
Coherent Time Series

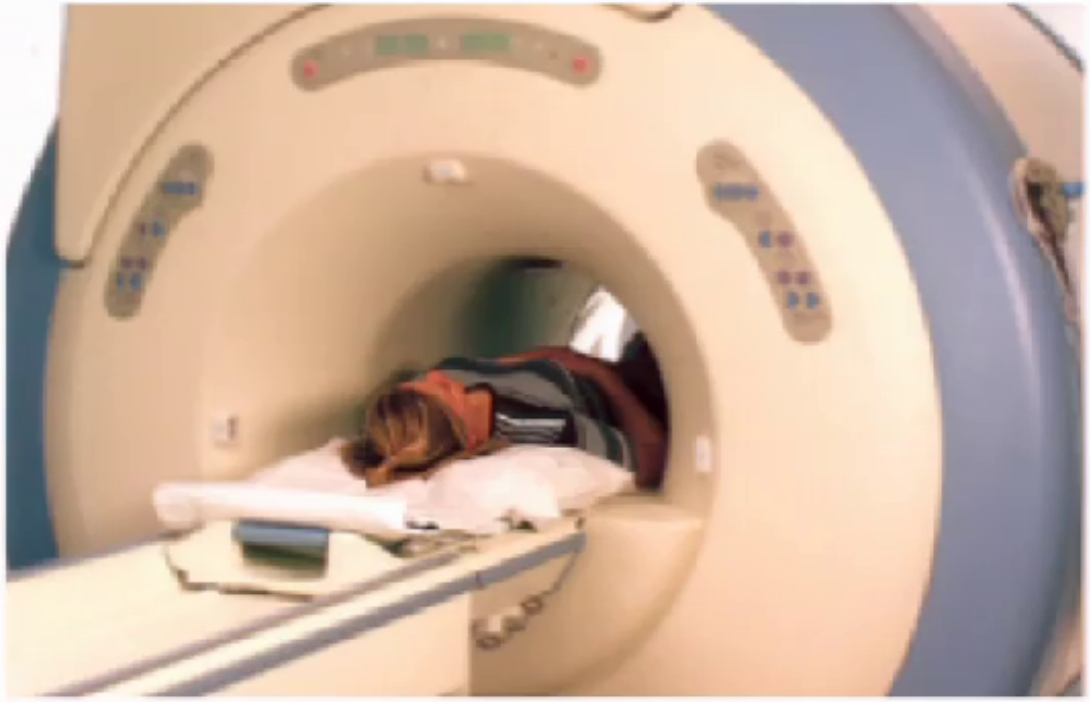




- Anatomically distinct brain areas are represented as **network nodes**
- Coherence between area activity is represented as a **network edge**
- Complements efforts in brain mapping to understand how distributed networks function to enable cognition

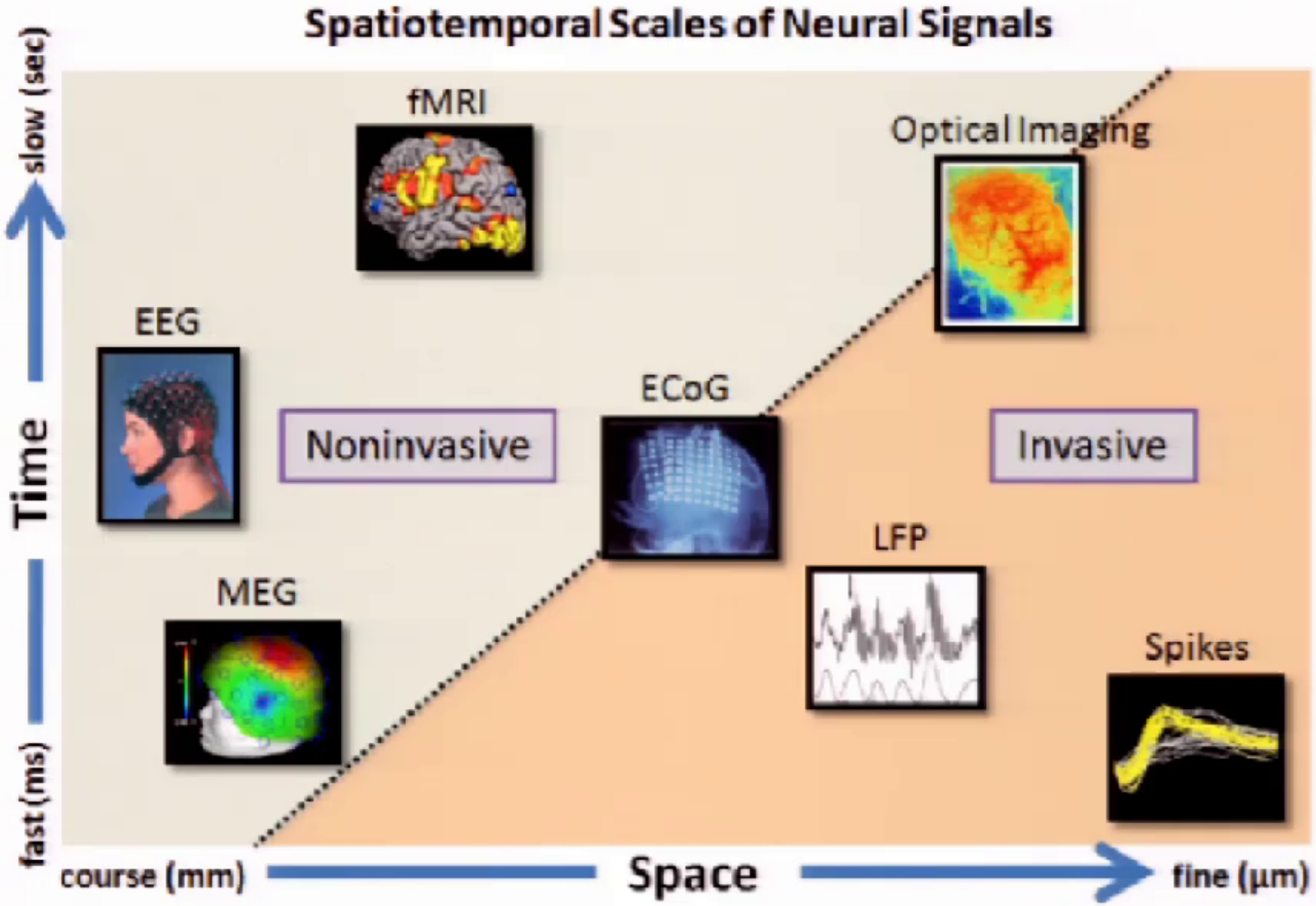
Hermundstad et al. 2013 PNAS

How do we measure brain activity?
What are the time series?



functional magnetic resonance imaging (fMRI)

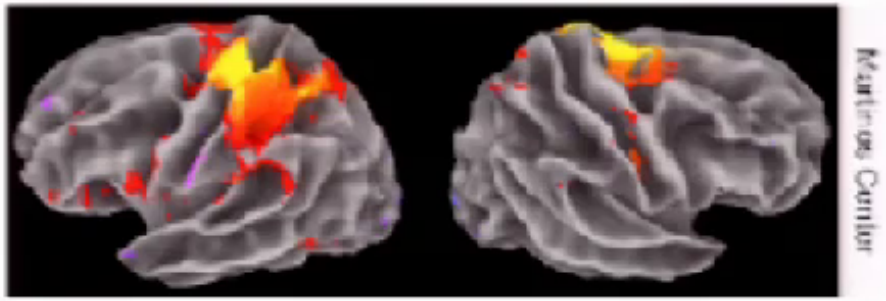
Non-invasive imaging techniques provide a window into brain function in awake, behaving humans.


Spatiotemporal Scales of Neural Signals
slow (sec)
Time
fast (ms)
fMRI
Optical Imaging
EEG
ECoG
Noninvasive
Invasive
LFP
MEG
Spikes
course (mm)
Space
fine (µm)

Traditional View of Brain Function

What "Lights Up" and When?

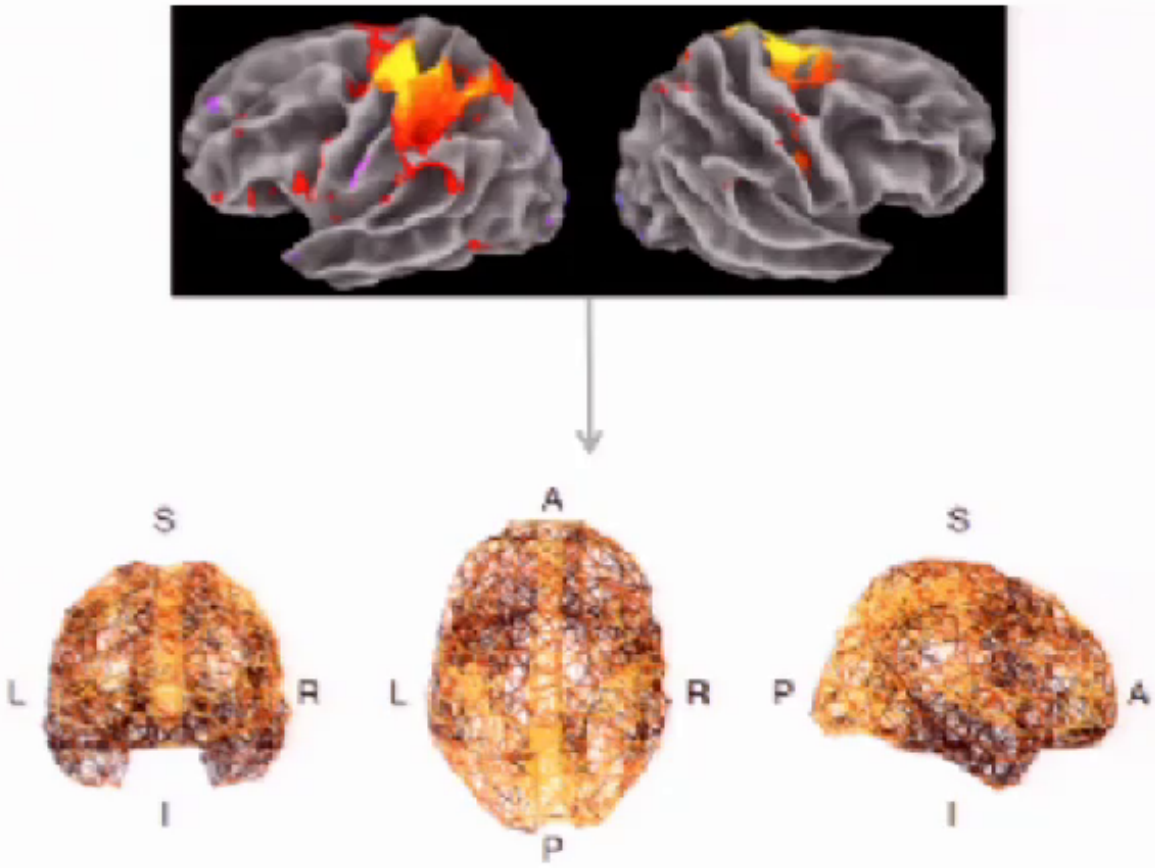
Cortical Activity During Hand Movement



Left Hemisphere Right Hemisphere

Different patters of brain areas show heightened blood-oxygen-level-dependent signals during different tasks.

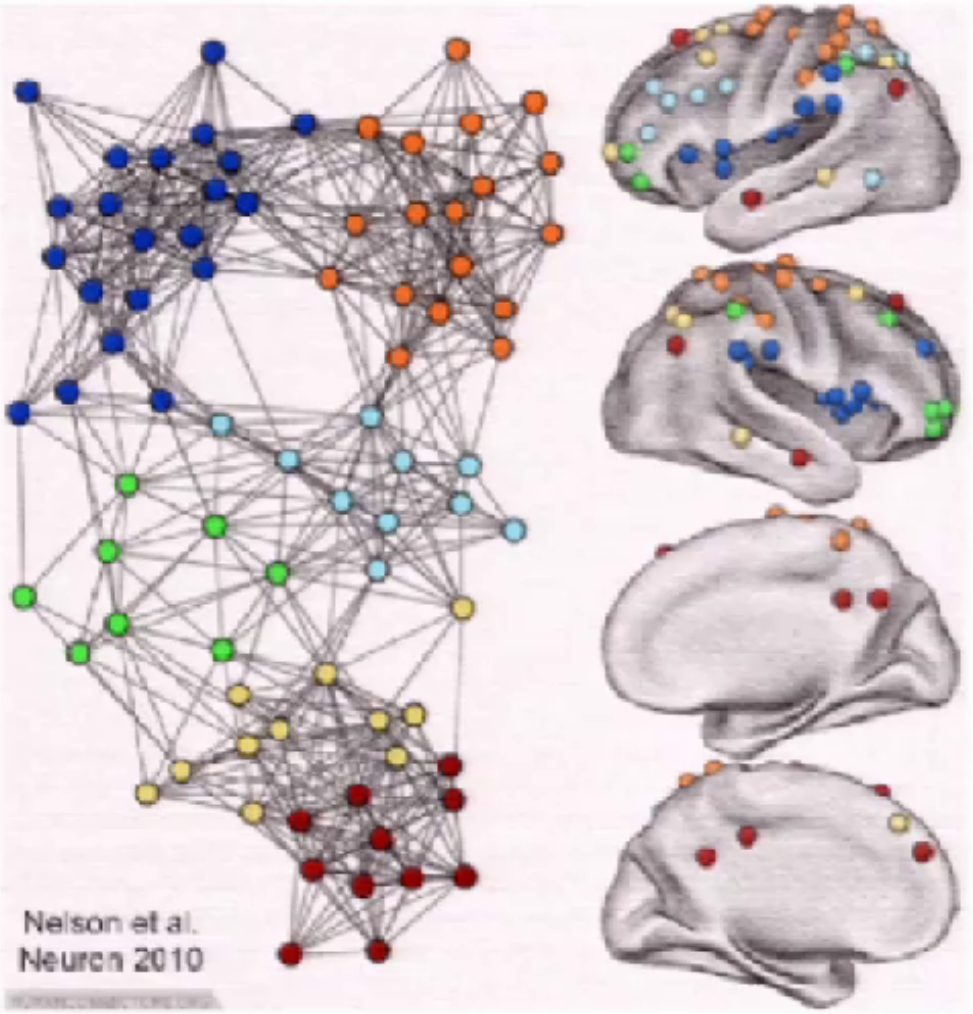
Network Science Provides a Paradigm Shift



Functional network analysis complements efforts in brain mapping to understand how distributed networks function to enable cognition

Hermundstad et al. 2013 PNAS

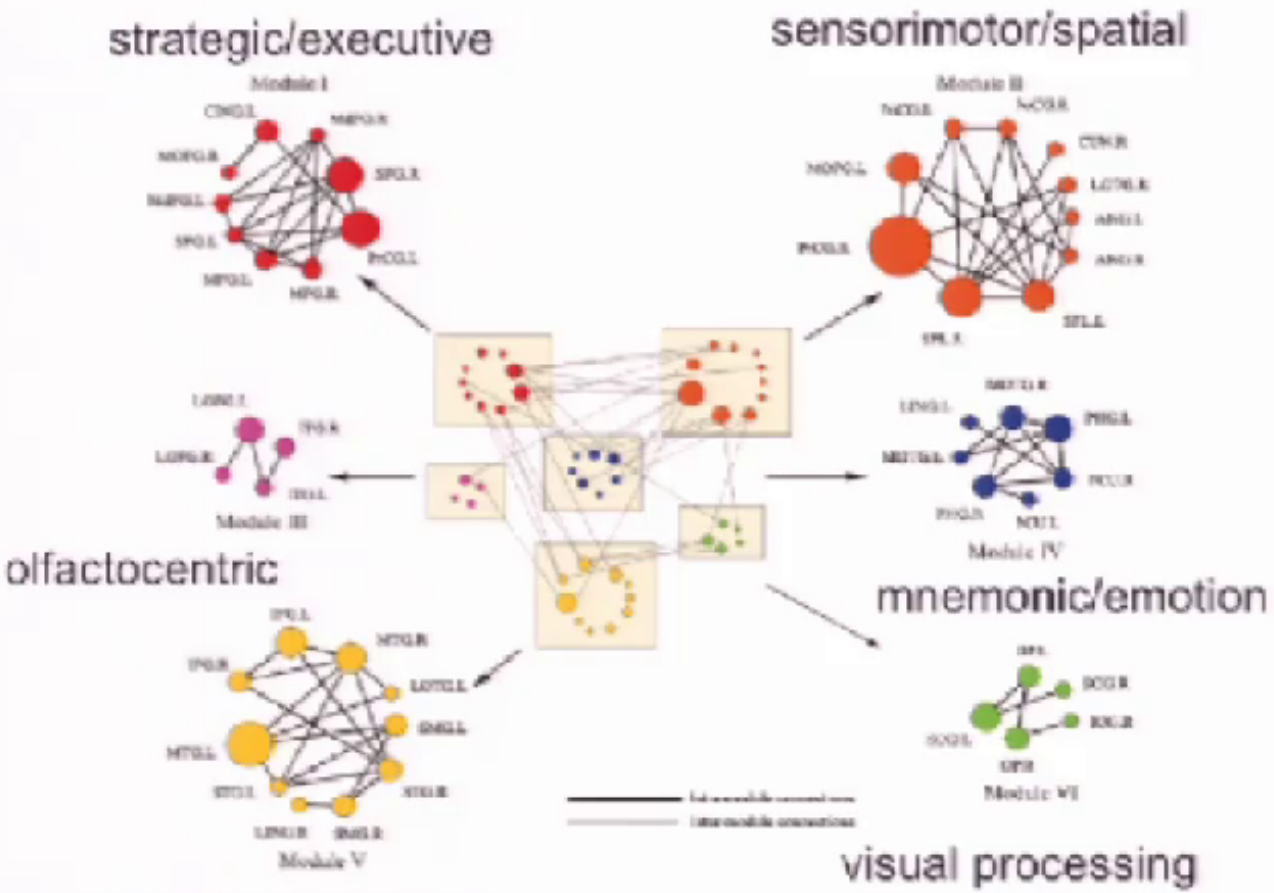
Community Structure



In a single time window, the network of interactions between brain regions displays community structure.

Open Question: How does community structure relate to cognitive function?

Communities Map to Cognitive Functions

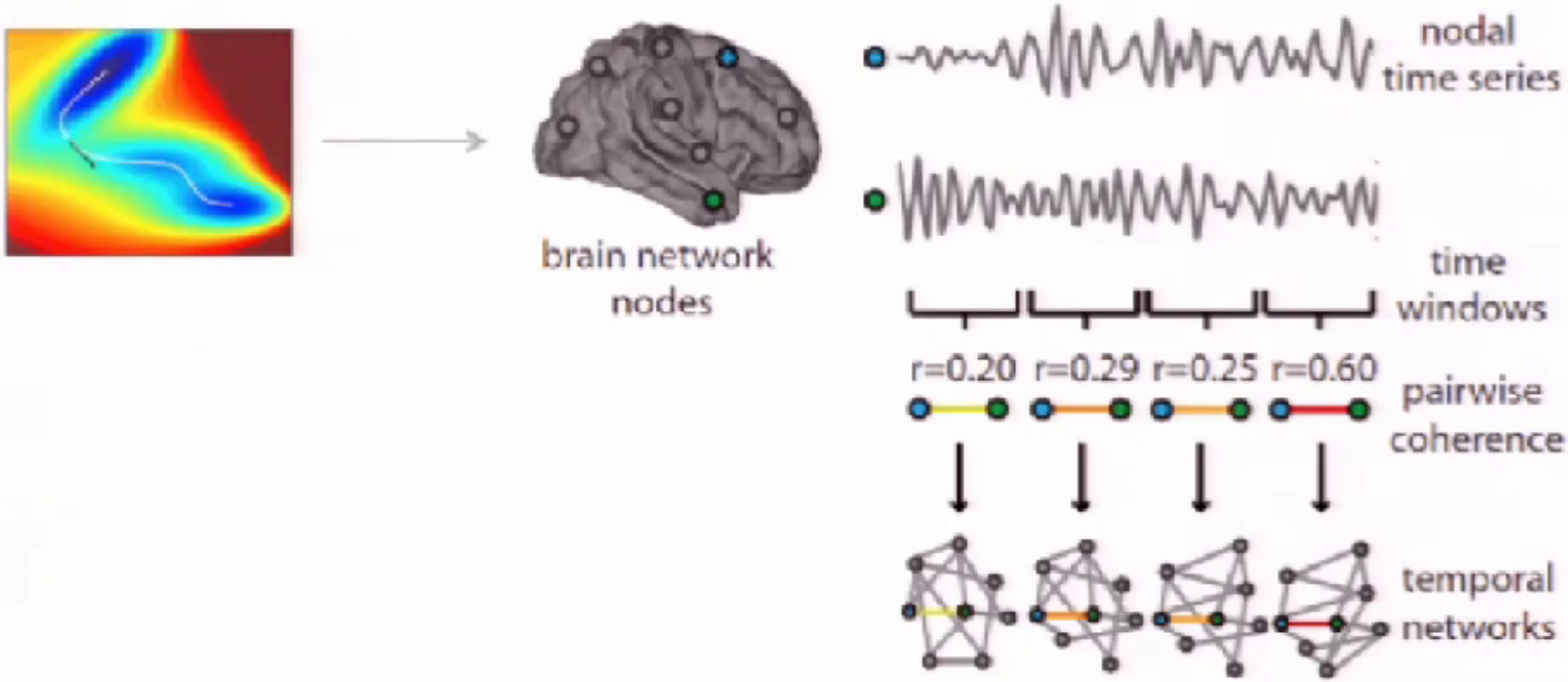


Chen et al. Cereb Cortex 2008

Community structure provides insight on how the brain functions.

But is this the optimal way to be studying cognitive processes?

A Network of Dynamics (Type III)



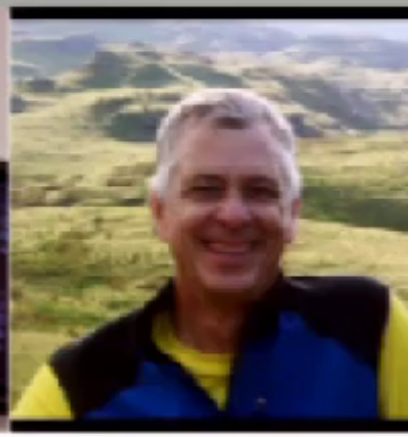
How do brain communication patterns change over time?

Bassett et al. PNAS 2011

Motor Skill Learning (a.k.a. Guitar Hero)

Bassett et al. 2011 PNAS

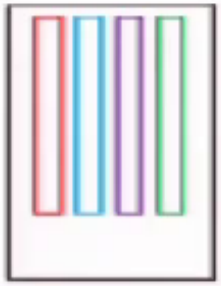
Nicholas Wymbs



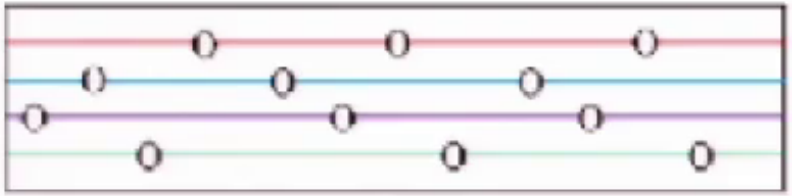
Scott Grafton

Experimental Paradigm:

Sequential Movement Task Over 3 Days



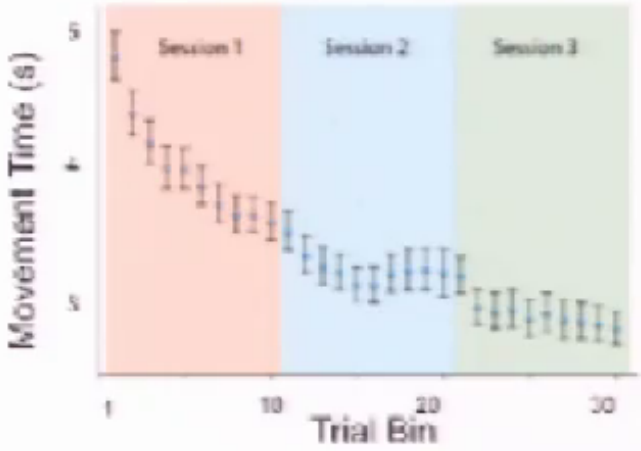
Response Button Box



Pseudo-Musical Staff

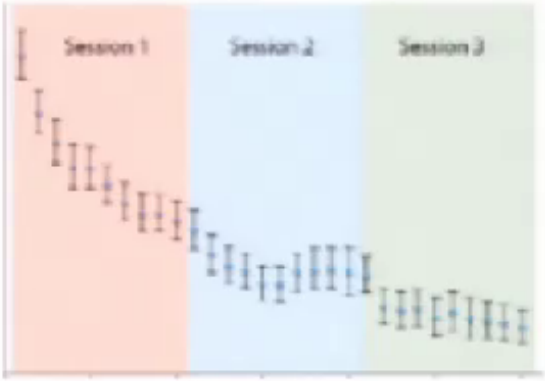
Estimate Learning:

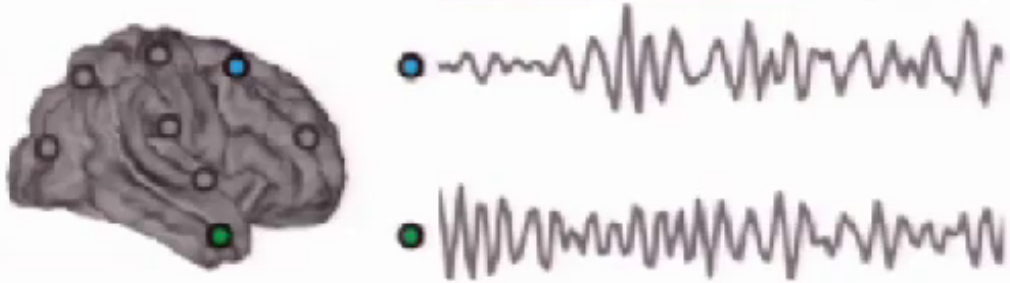
Exponential drop-off parameter of movement time versus trial bin

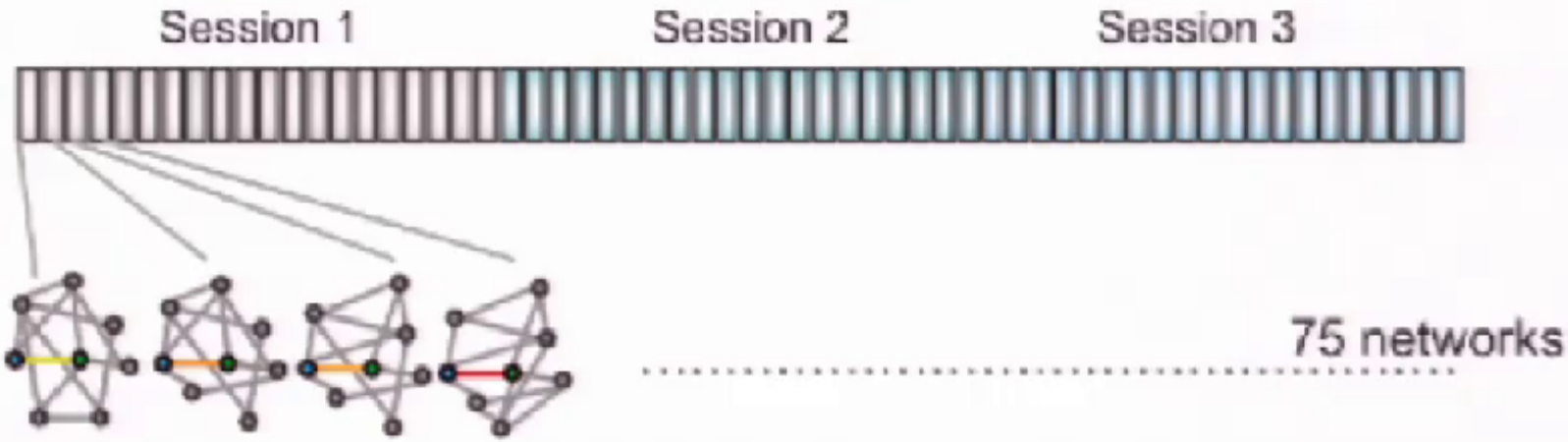


- What is happening in the brain during learning?

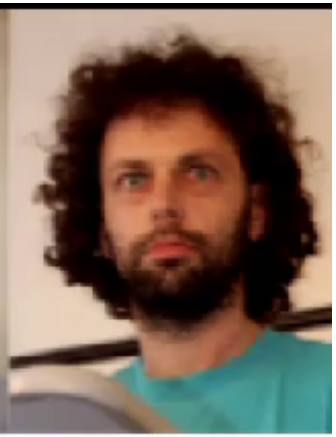
What is happening in the brain during learning?







Dynamic Modules

Peter Mucha Mason A. Porter

We use multilayer modularity to estimate dynamic community structure.

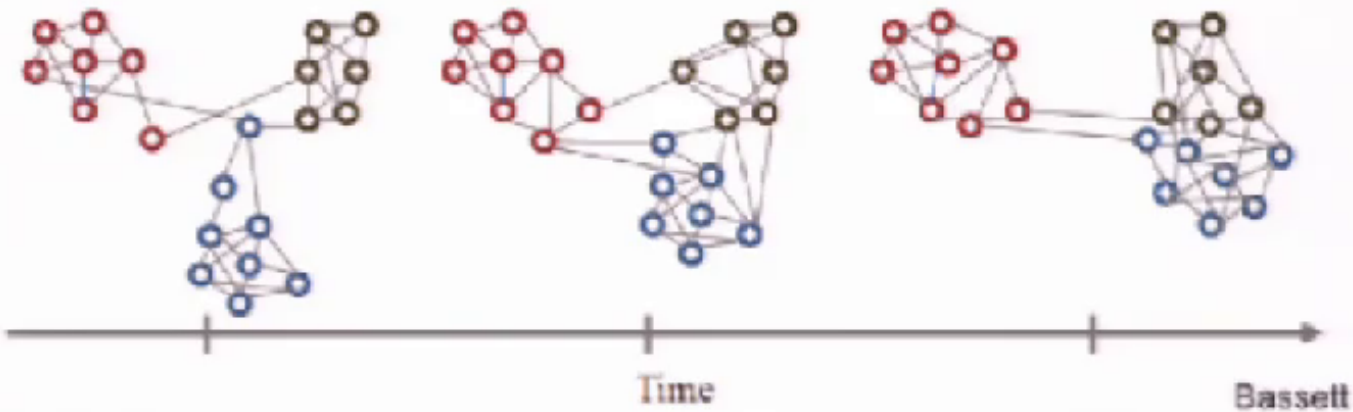
Optimize using a Louvain-like locally greedy algorithm

Blondel et al. 2008

$$Q = \frac{1}{2\mu} \sum_{ijlr} \left\{ \left(A_{ijl} - \gamma_l P_{ijl} \right) \delta_{lr} + \delta_{ij} \omega_{jlr} \right\} \delta(g_{il}, g_{jr}),$$

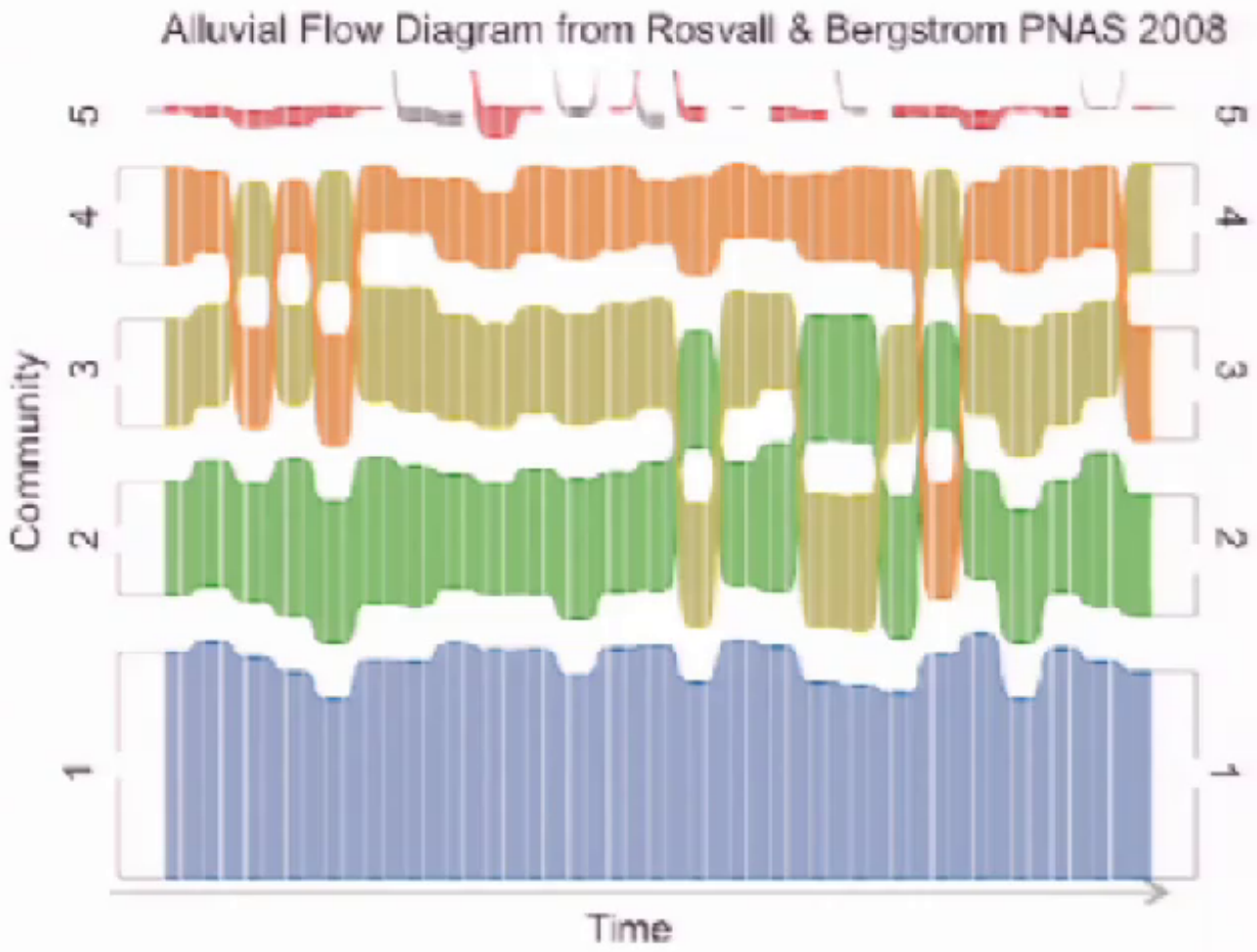
- A_{ijl}: Adjacency Matrix
- γ_l: Resolution Parameter For Module Size
- P_{ijl}: Null Model Adjacency Matrix
- δ_{ij}: For i and j in same community
- ω_{jlr}: Resolution Parameter for Module Dynamics
- $\delta(g_{il}, g_{jr})$: Community i in time slice l; Community j in time slice r

Mucha et al. 2010 Science



Bassett et al. 2013 Chaos

Flexibility of Dynamic Community Structure



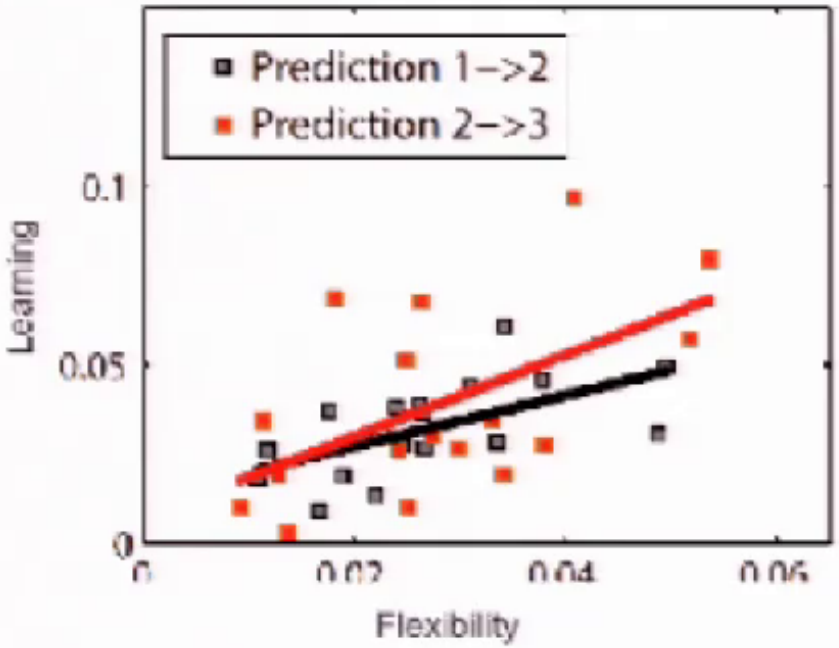
Flexibility of node i is the fraction of times that node i changes community allegiance

Bassett et al. PNAS 2011
Doron et al. PNAS 2012
Bassett et al. Chaos 2013

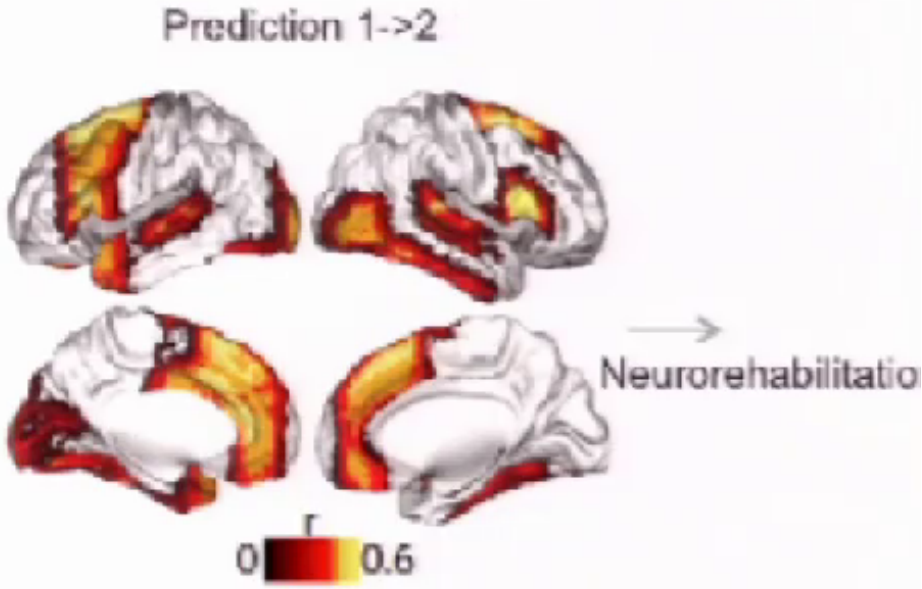
Bassett et al. 2011 PNAS
Bassett et al. 2013 PLoS CB
Bassett et al. 2015 Nature Neuroscience

Flexibility Predicts Learning

Global Results | Regional Results



People with higher flexibility on one day will learn better on the following day than people with lower flexibility.



Regional flexibility is critical in association cortex rather than primary sensorimotor cortex.

Personal, Cultural, & Clinical Implications

NeuroRehabilitation

Who do we train? And when?

Brain State

Can we tune flexibility?

Neuromodulation

Can we optimize flexibility?

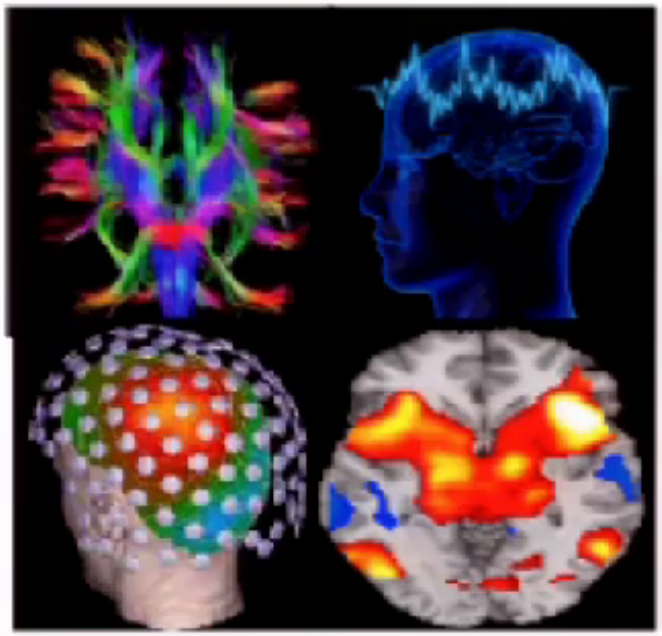
Classroom Environment

What environments engender flexibility?

Open Challenges

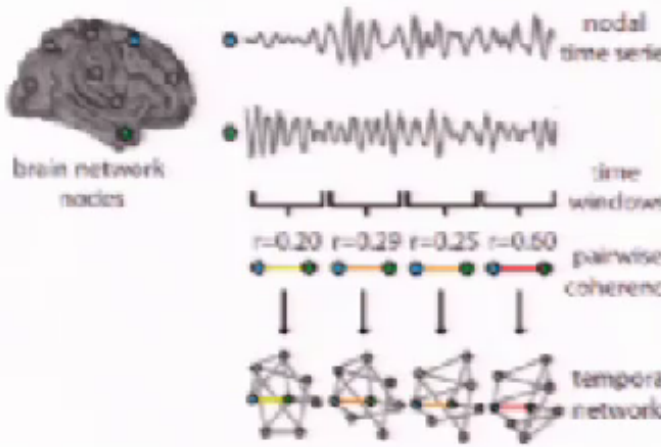
Multilayer Networks

Many Imaging Modalities
(Edge Types)



Many People
(Network Layers)

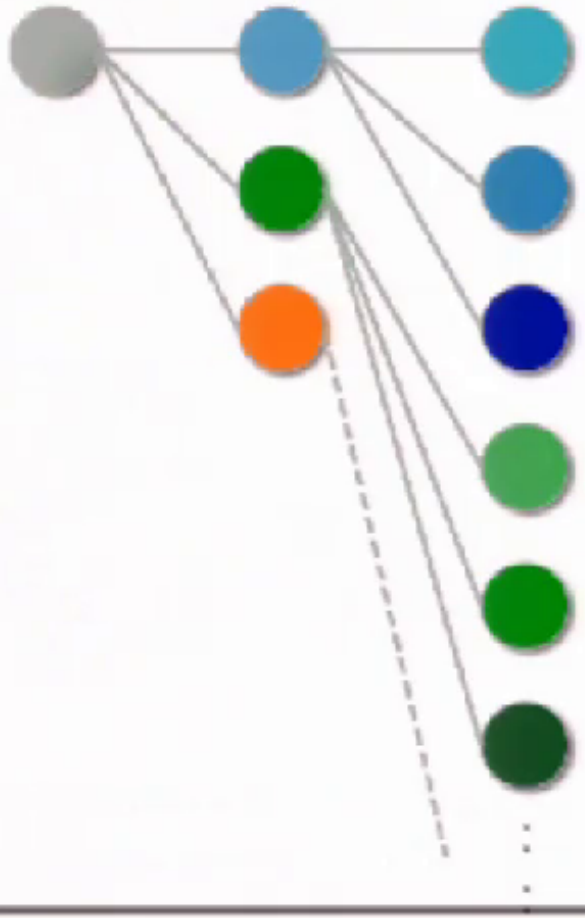
Many Time Windows
(Network Layers)



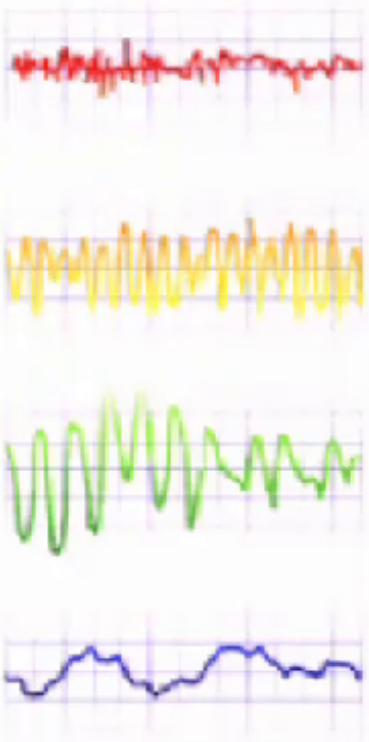
- How does function depend on structure?
- What is conserved or variable across people?
- Cognition and Disease

Node and Edge Hierarchies

Node Hierarchies
(Multi-Resolution Measurements)



Temporal Scales of Dynamics
(Edge Types have Nontrivial Dependencies)



Beta (More than 13 cps)

Alert

Alpha (8 – 13 cps)

Relaxed

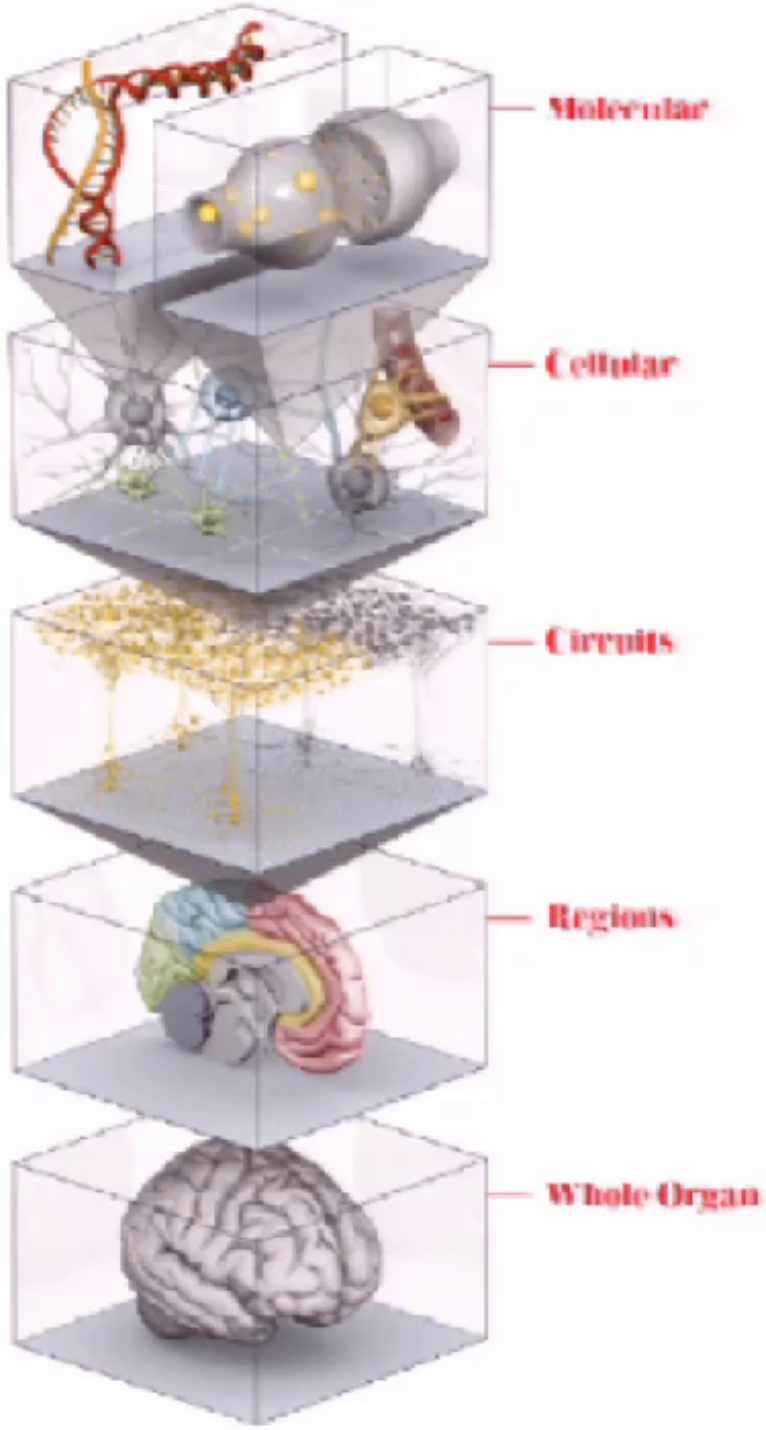
Theta (4 – 8 cps)

Drowsy

Delta (Less than 4 cps)

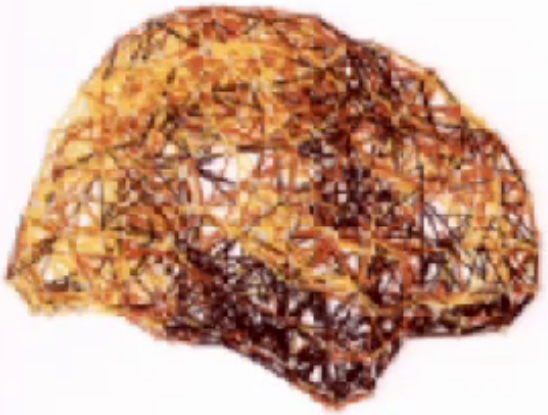
Asleep

Nodes at the top level are composed of nodes at the bottom level.



Edges at the top level are driven by edges at the bottom level.

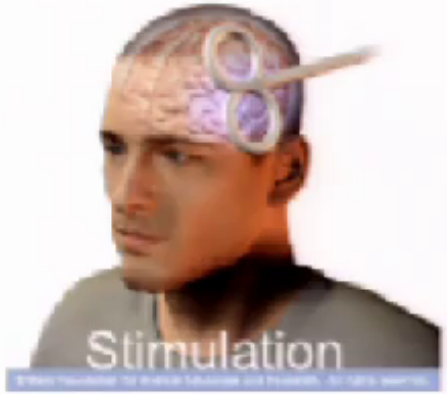
Network Control



Brain Network

Control Point

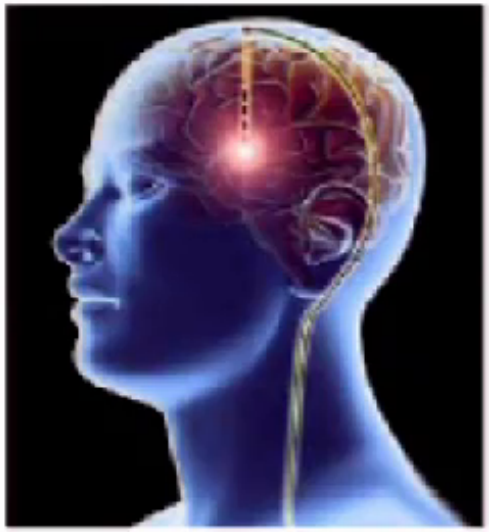
Drugs



Gu et al. arxiv 1406.5197

Clinical Control Applications for Network Control

Deep Brain Stimulation

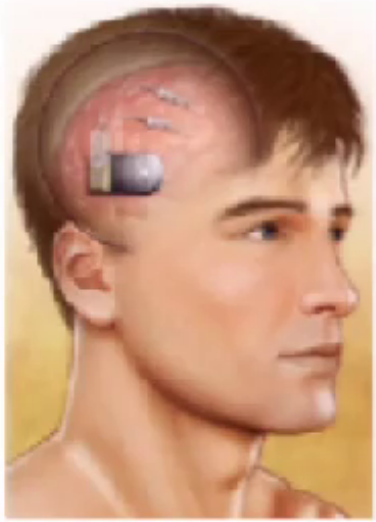


Treatment of Parkinson's

Transcranial Magnetic Stimulation

Treatment of Depression

NeuroPace

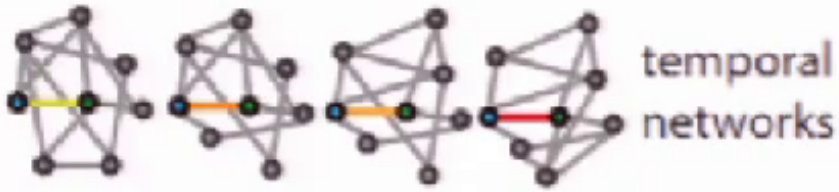


Treatment of Epilepsy

Work from Sri Sarma (John Hopkins), ShiNung Ching (WUSTL), Mark Kramer (Boston University), etc.

Modeling & Statistical Inference

- Distinguishing dynamics from noise



Application: Confidence and uncertainty

- Predicting future dynamics

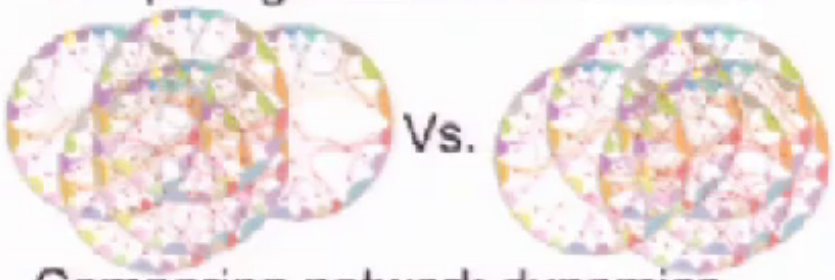
Application: disease progression, degeneration, decision-making

- Building spatially informed null models

Application: Understanding physical constraints on evolution and function

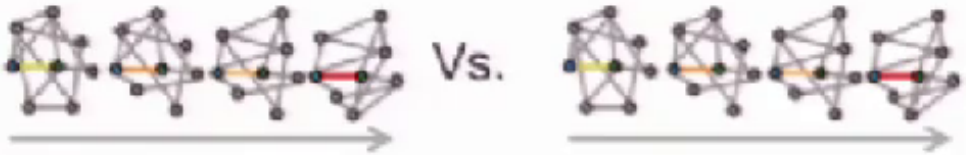
Modeling & Statistical Inference

- Comparing network ensembles



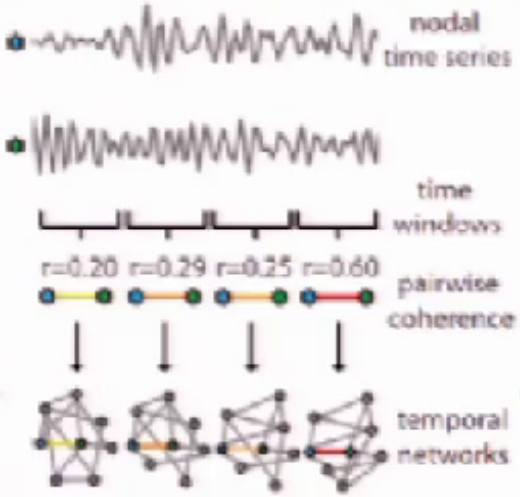
Application: Alterations in psychiatric disease and neurological disorders

- Comparing network dynamics



Application: Different cognitive strategies in autism, ADHD, and other conditions

- Extracting Temporal Networks from Time Series Data



Application: Extracting network states; distinguishing differences in network state dynamics across people

Prediction, Perturbation, Intervention

Personalized Training
Personalized Rehabilitation and Therapies
Brain-machine Interfaces

Acknowledgments

Our group &Affiliated Members:

Sarah Muldoon

Shi Gu

Qawi Telesford

John Medaglia

Chad Giusti

Lucy Chai

Muzhi Yang

David Baker

Marcelo Mattar

Ankit Khambhati

Urs Braun

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Peter Mucha (University North Carolina) & **Mason Porter** (Oxford)

Brian Litt, Sharon Thompson-Schill, Roy Hamilton, Geoff Aguirre (PENN)

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Office of Naval Research

National Science Foundation

National Institutes of Health

Open postdoc position!

(dsb@seas.upenn.edu)

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