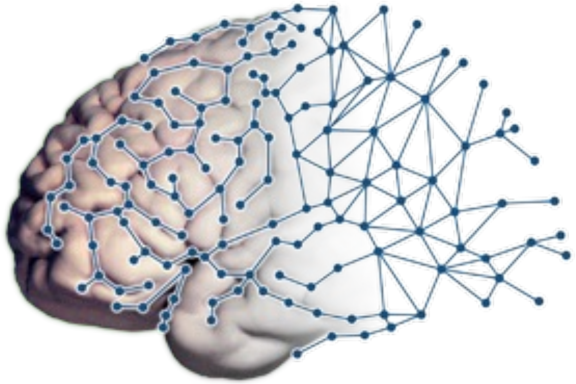
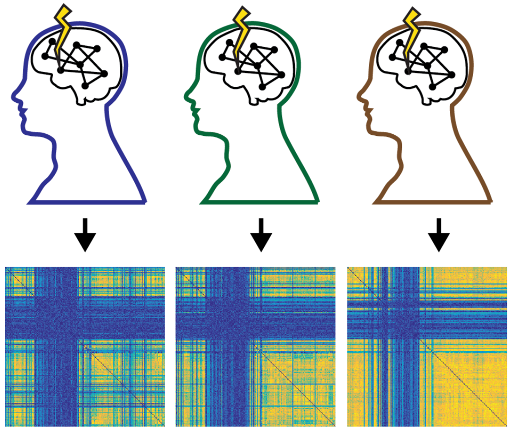
Personalized brain network models augment individual differences





Sarah F. Muldoon

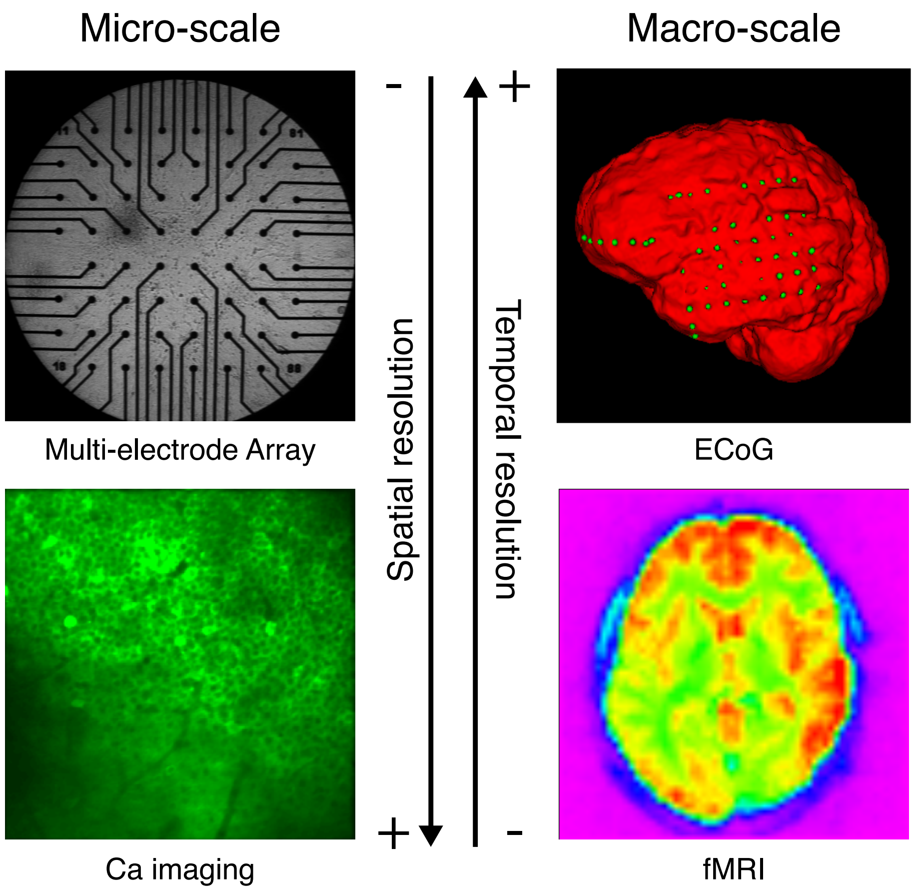
IPAM - Mathematical Approaches for Connectome Analysis

February 14, 2024

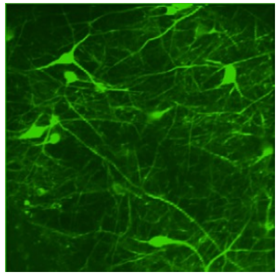
Types of neuroscience data

Lots of different data from which we build networks

- Structural data
- Time series data (functional data)
- Simultaneous recordings across modalities
- Data across multiple scales

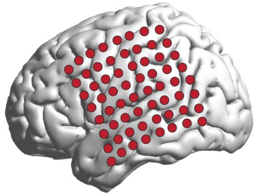


My lab: Multi-scale exploration



Micro-scale: calcium imaging data

- Community structure to find similar groups of neurons
- TDA for performing cell detection/segmentation
- Applications in epilepsy – seizure prediction/control
- Collaborations: Ethan Goldberg (CHOP – NSF Brain Initiative Grant); Caroline Bass (UB); Valerie Crepel (INMED, France)



Meso-scale: sensor data (EEG)

- Individual differences
- Collaborations: Jean Vettel, Javi Garcia (ARL); David Shucard (UB); Tom Covey (UB); Janet Shucard (UB)

Macro-scale: MRI data (structural/functional)

- Personalized Brain Network Models (BNM)
- Individual differences
- Applications in epilepsy - epileptogenesis
- Collaborations: David Shucard (UB); Tom Covey (UB); John Leddy (UB); Barry Willer (UB); Dave Poulsen(UB), Ferdinand Schweser (UB); Anca Radesculu (New Platz); Vijaya Prakash Krishnan Muthaiah (UB); Kostas Slavakis (UB) and John Medaglia (Drexel); David Wack (UB)

Outline

1. Personalized Brain Network Models

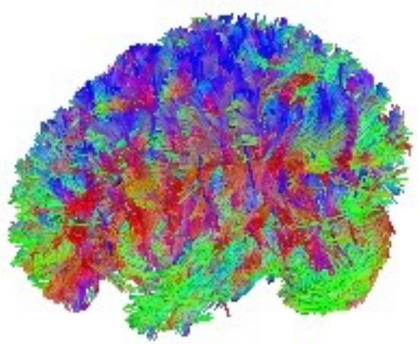
2. Predicting Task Performance with pBNMs

3. Quantifying Variability with pBNMs

Part 1: Personalized Brain Network Models

Building brain networks

Structural networks



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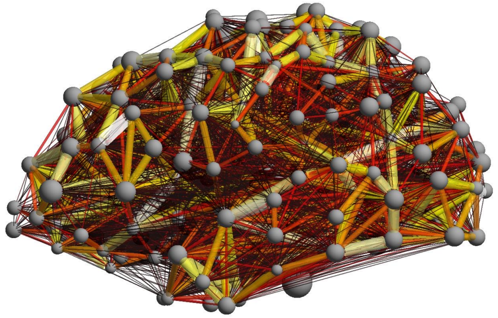
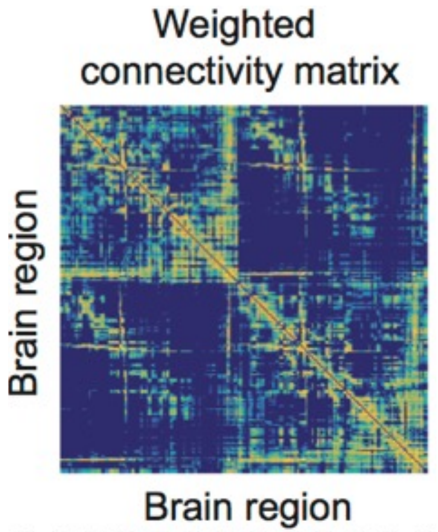




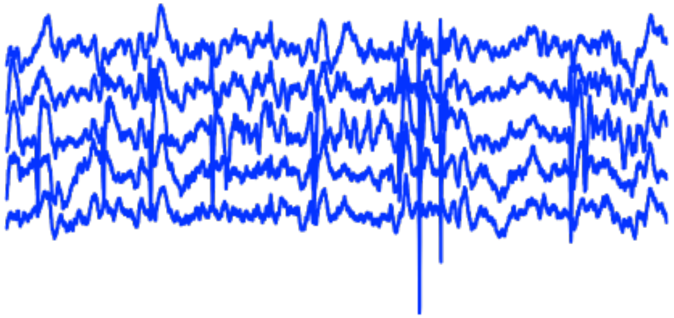
Nodes: brain regions

Edges: white matter tracts

(streamlines – DSI data)

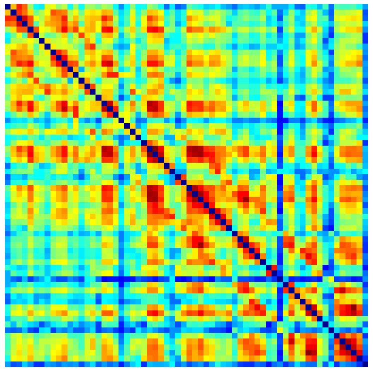
Building brain networks

Functional networks



Statistical
Relationships
(correlations)

Functional
Connectivity

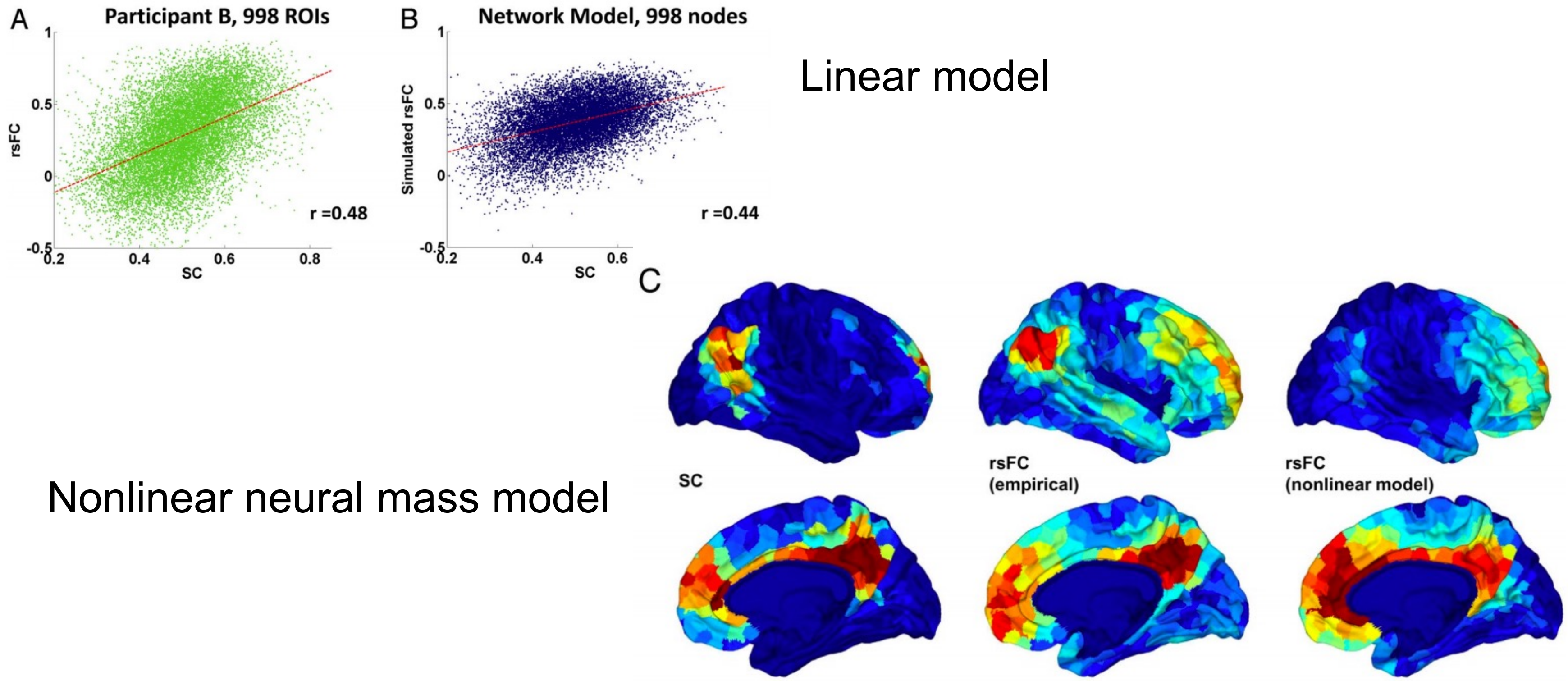


Nodes: brain regions

Edges: statistical relationships
between dynamics of
brain regions

Structure-function relationships

Initial work using computational models to assess the relationship between structure and function – also included empirical data



Linear model

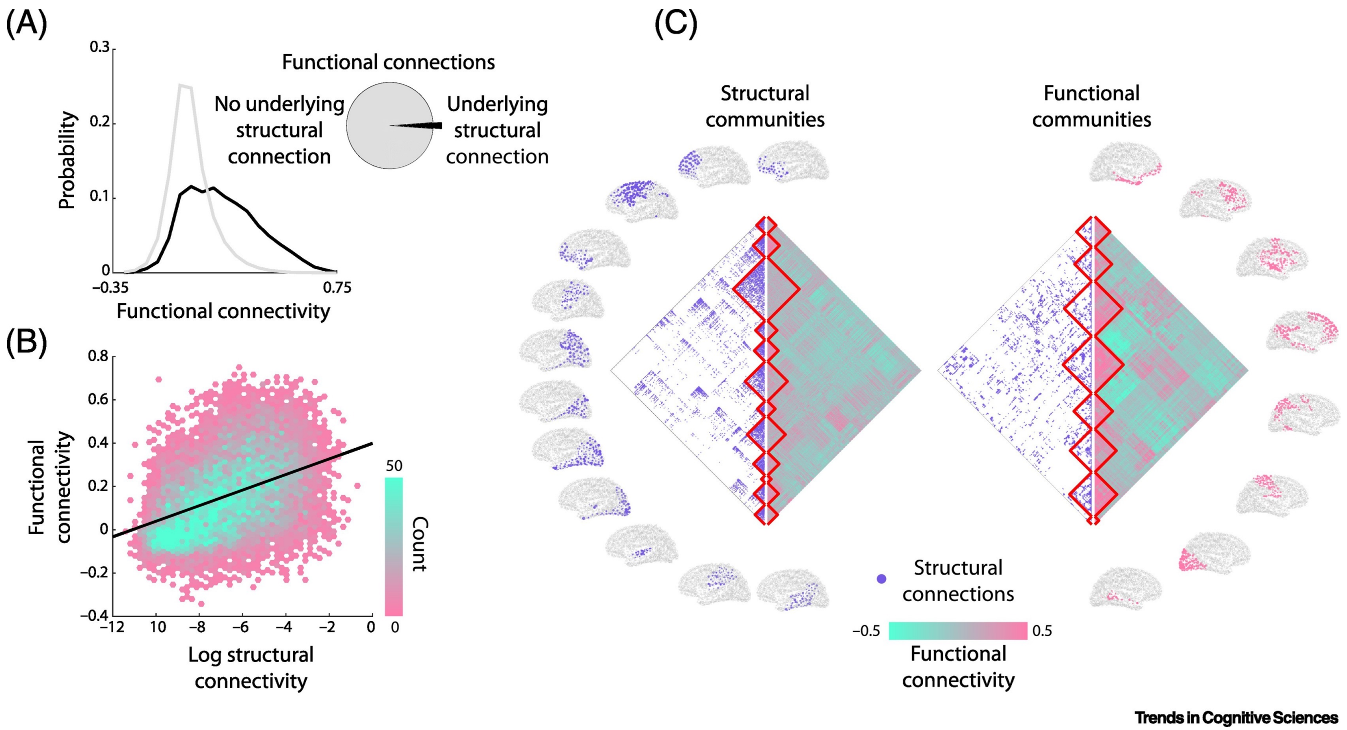
Nonlinear neural mass model

Honey et. al (2009) PNAS

Review Article: Linking Structure and Function in Macroscale Brain Networks

Laura E. Suárez, Ross D. Markello, Richard F. Betzel, Bratislav Misic

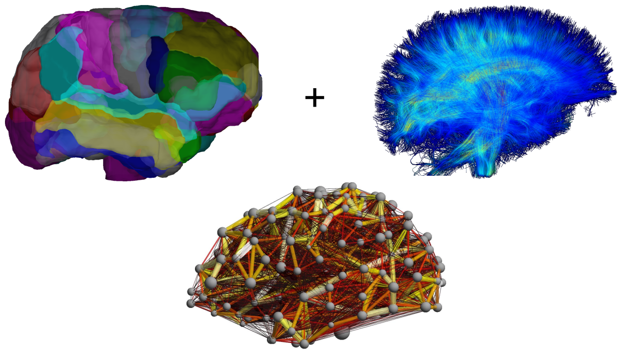
Trends in Cognitive Sciences - April 2020



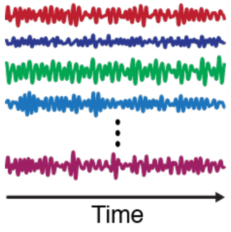
Building a virtual brain

- Use structural matrices derived from human imaging data to model brain network connectivity
- Add simulated brain dynamics to each node (brain region)

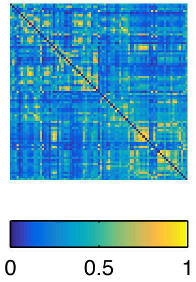
Anatomical Network Structure



Mathematical Model of Dynamics



Functional Connectivity

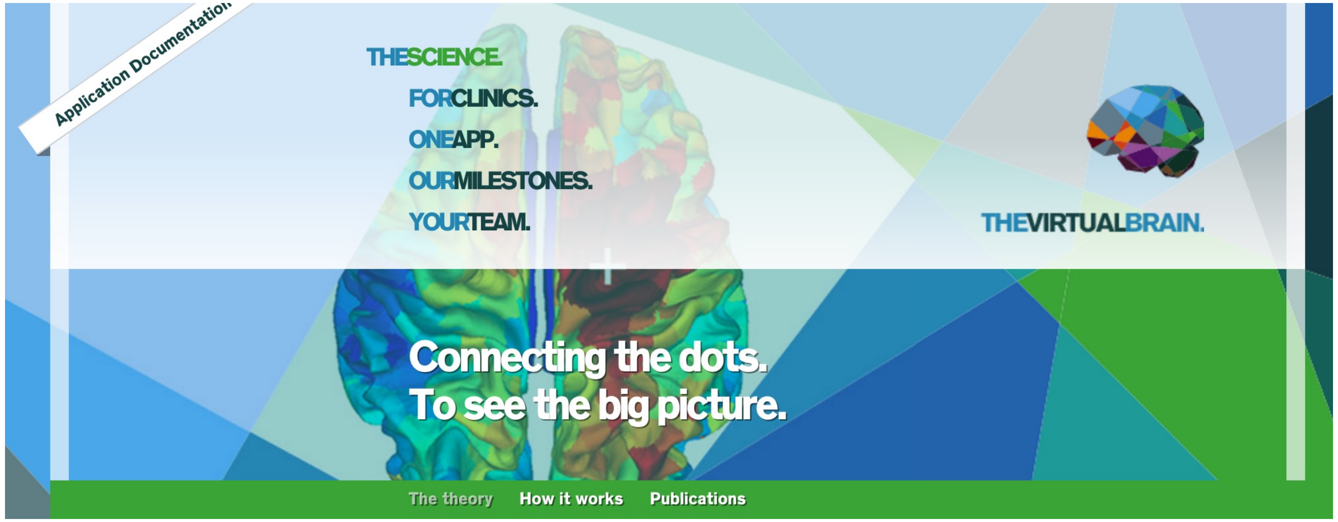


Run virtual experiments in a controlled environment

(Stimulation of brain regions with nonlinear dynamics)

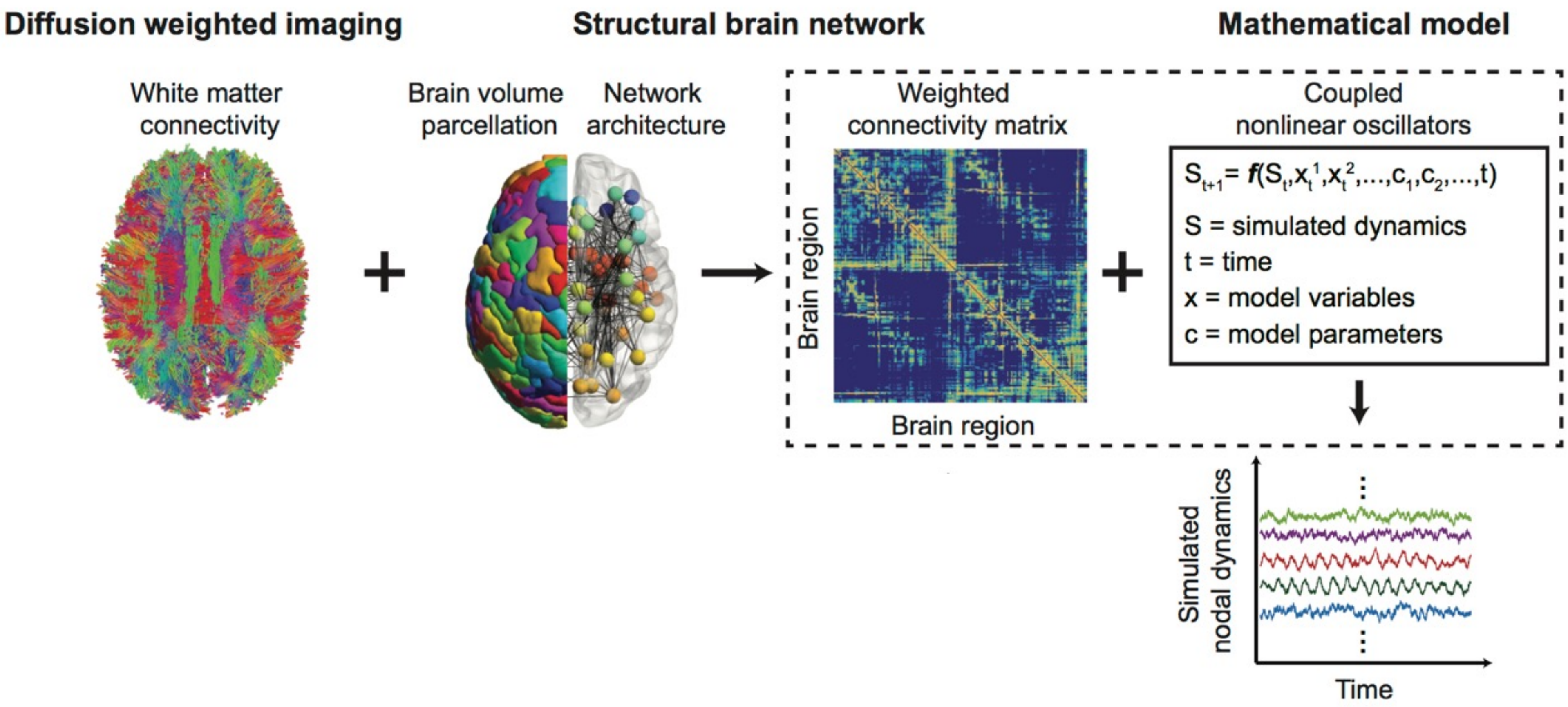
Brain network models

Used to study a wide variety of brain features



Resting state dynamics
tDCS
Stroke
Epilepsy

Computational brain network models



Bansal et al. (2018) Curr Opin Neurobiol

Network dynamics

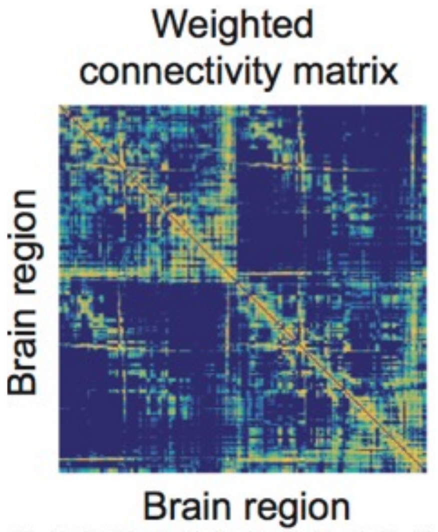
Wilson-Cowan Oscillators

Biologically derived nonlinear oscillator modeling firing rates of regional populations of neurons

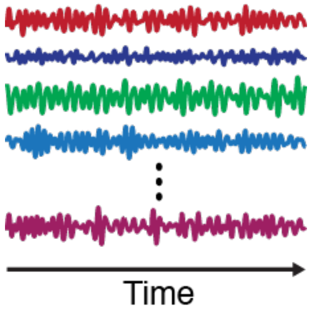
Excitatory population

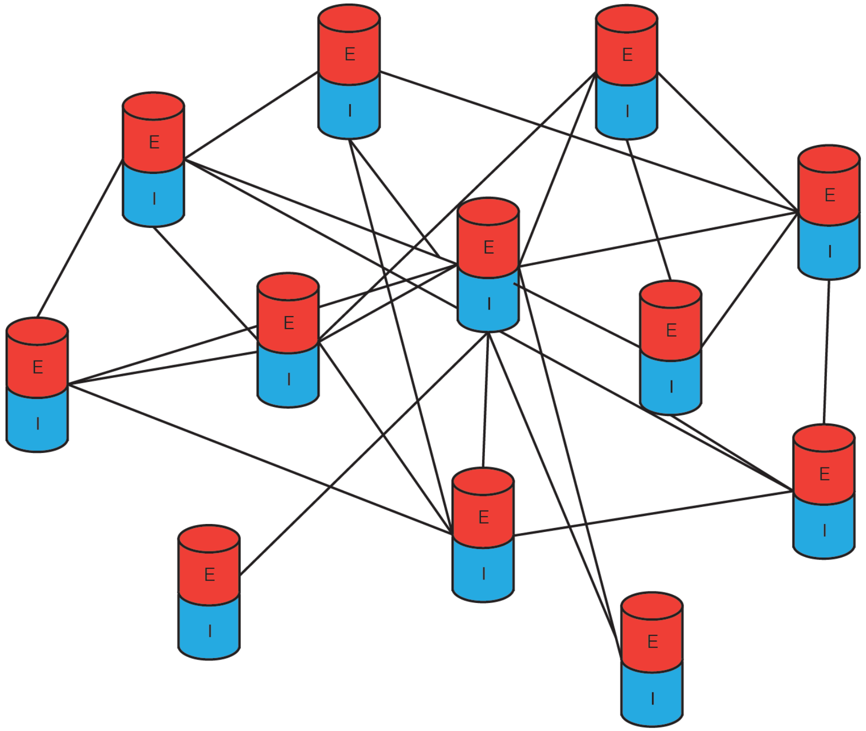
Inhibitory population

Network Structure



Dynamics





Wilson-Cowan dynamics

Excitatory population

$$\tau\frac{dE_i}{dt} = -E_i(t) + \left(S_{E_m} - E_i(t)\right)S_E\left(c_1E_i(t) - c_2I_i(t) + \overbrace{c_5\sum_j A_{ij}E_j(t-\tau_d^j)}^{\text{Excitatory coupling term}} + P_i\right) + \sigma w_i(t)$$

External Stimuli

Noise

Inhibitory population

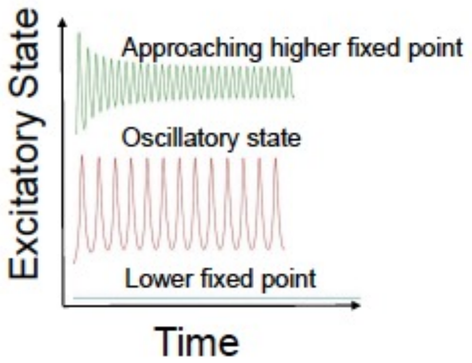
$$\tau\frac{dI_i}{dt} = -I_i(t) + \left(S_{I_m} - I_i(t)\right)S_I\left(c_3E_i(t) - c_4I_i(t) + \underbrace{c_6\sum_j A_{ij}I_j(t-\tau_d^j)}_{\text{Inhibitory coupling term}} + Q_i\right) + \sigma v_i(t)$$

where

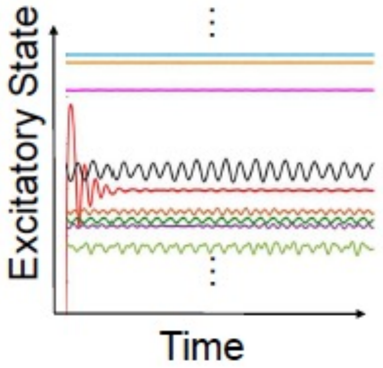
$$S_{E,I}(x) = \frac{1}{1+e^{(-a_{E,I}(x-\theta_{E,I}))}} - \frac{1}{1+e^{a_{E,I}\theta_{E,I}}}$$

$\tau = 8$
$c_1 = 16$
$c_2 = 12$
$c_3 = 15$
$c_4 = 3$
$\sigma = 10^{-5}$
$a_E = 1.3$
$a_I = 2$
$\theta_E = 4$
$\theta_I = 3.7$

Allowed single oscillator states

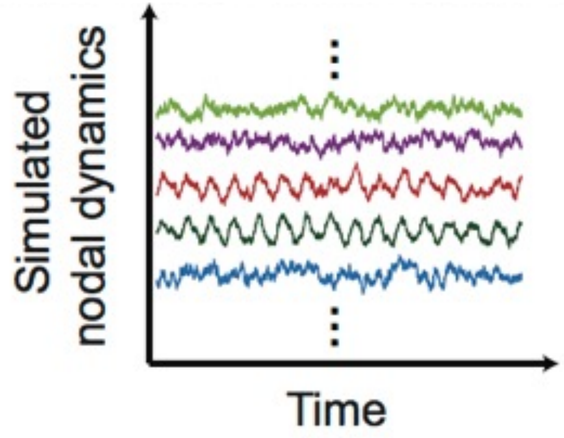


Typical coupled system



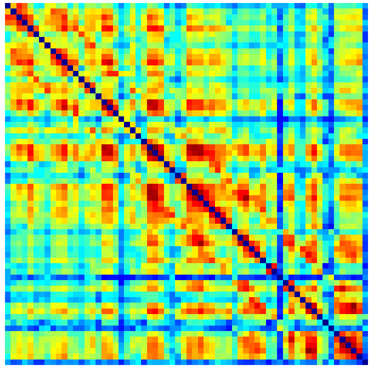
Building brain networks

Functional networks



Statistical Relationships (correlations)

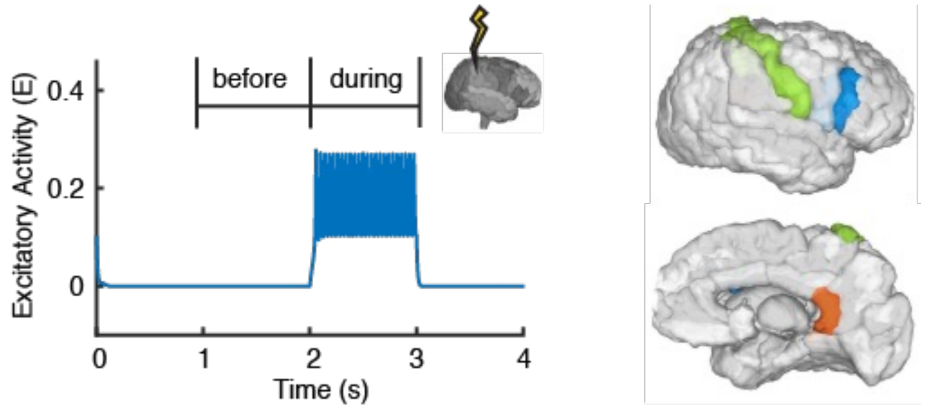
Functional Connectivity

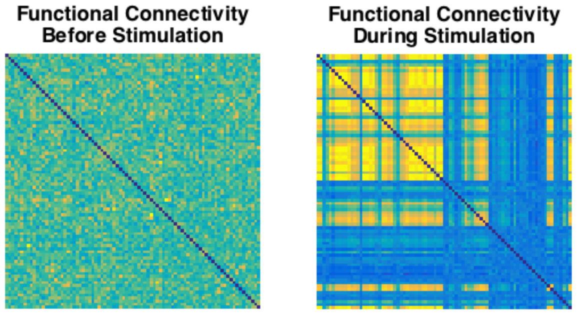


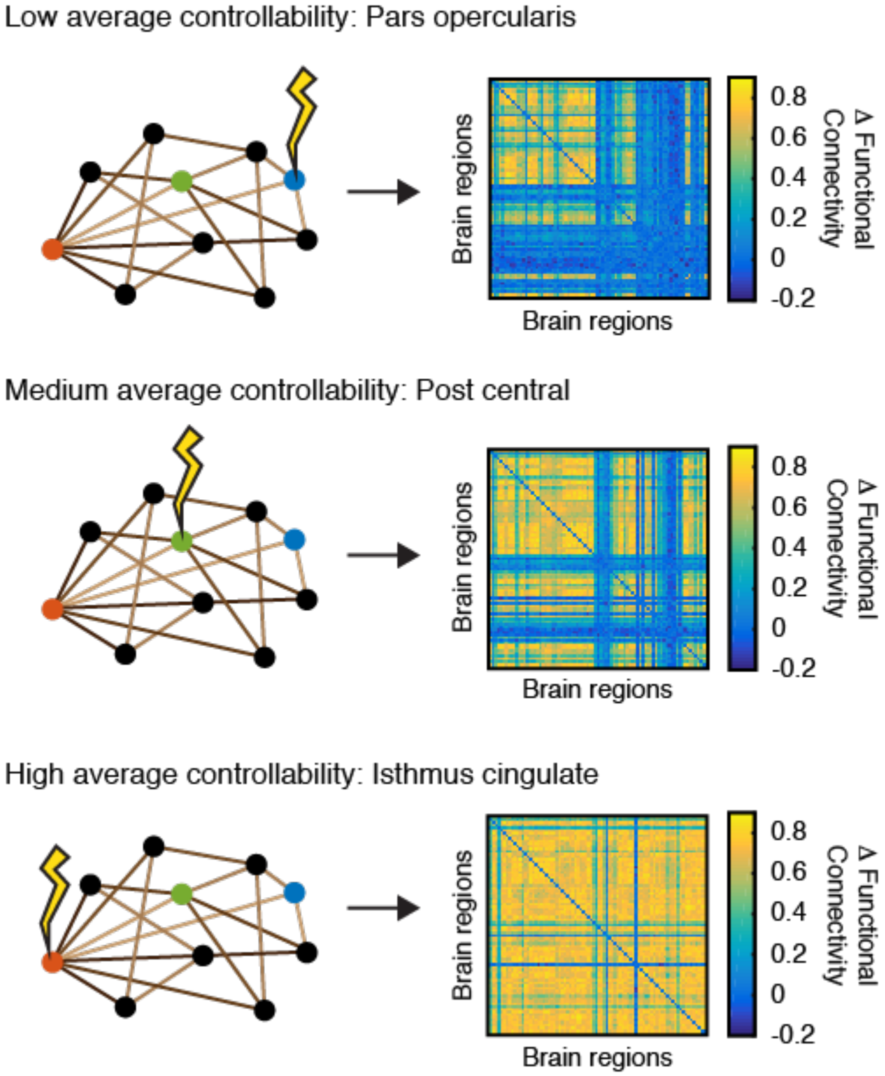
Nodes: brain regions

Edges: statistical relationships between dynamics of brain regions

Virtual experiments: Effects of stimulation





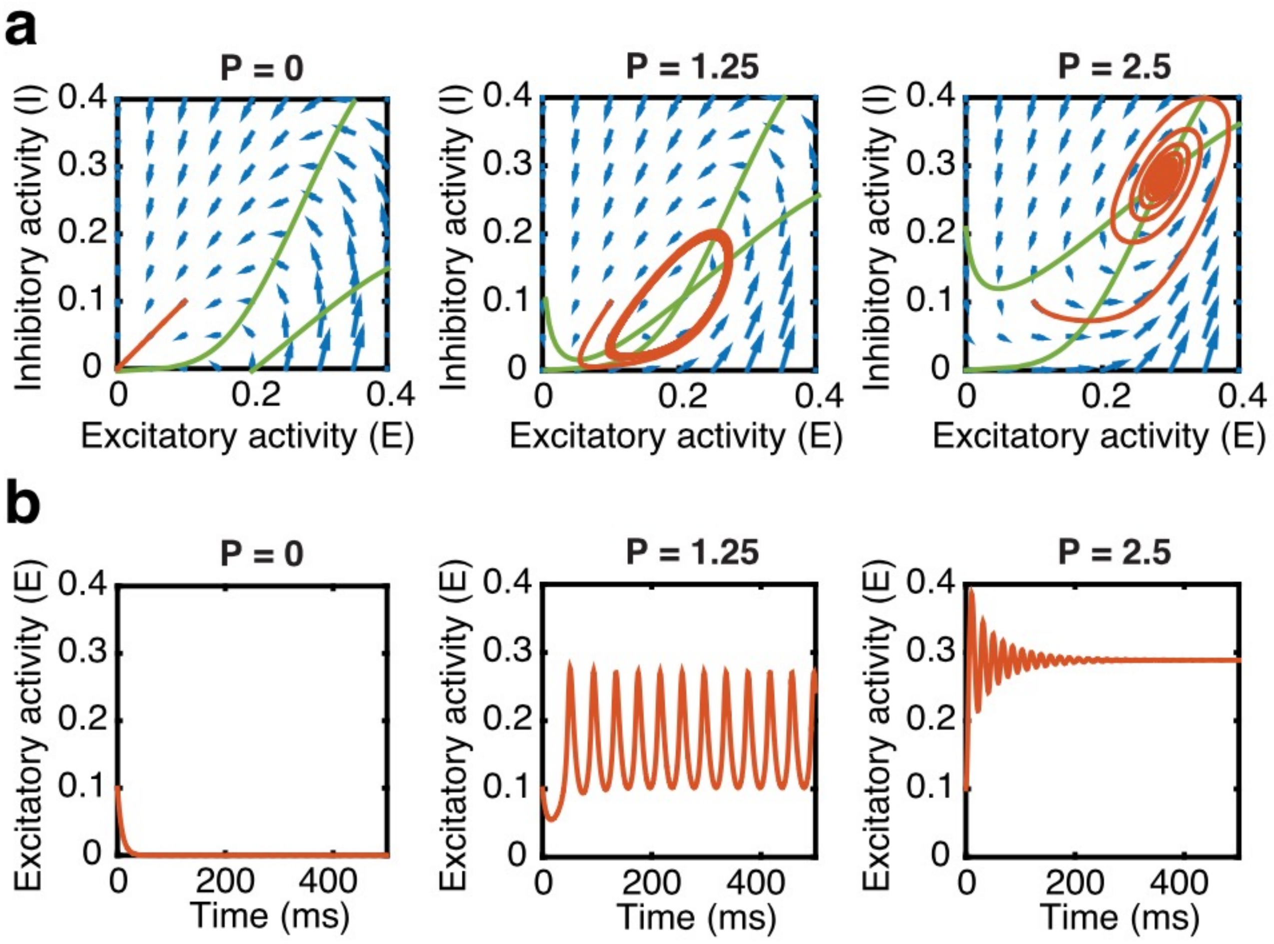


Muldoon et al. (2016) PLOS Comp Bio

Nonlinear Dynamics – Single Oscillator

Three states:

1. Low fixed point
2. Limit cycle
3. High fixed point

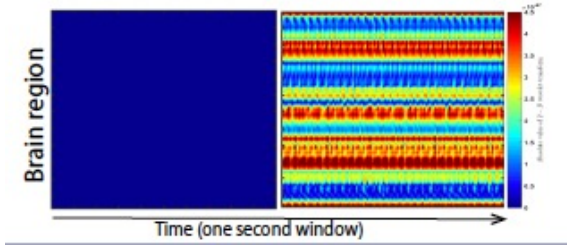


Muldoon et al. (2016) PLOS Comp Bio

Variability in transition point

Triplicate data set

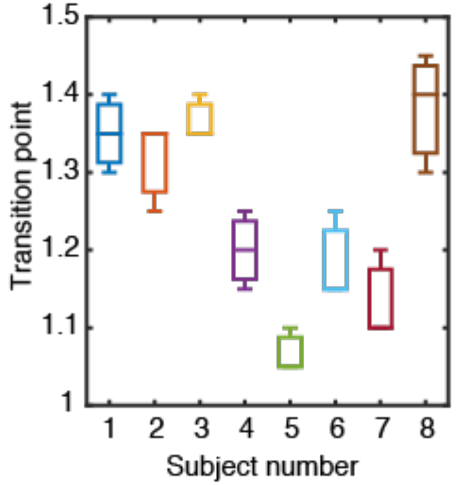
- 8 subjects
- 3 scans per subject

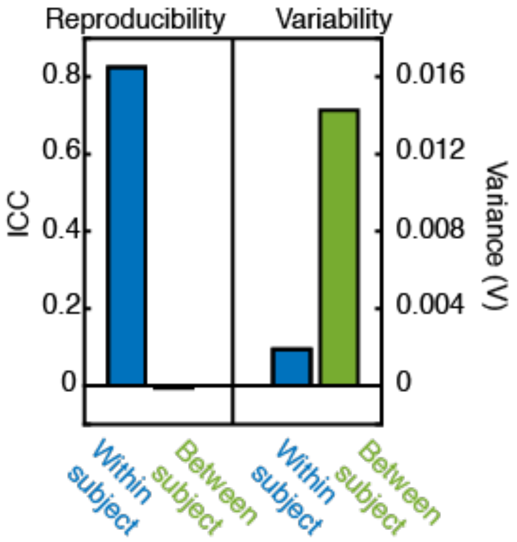


Excitatory population

$$\tau \frac{dE_j}{dt} = -E_j(t) + (S_{e\_max} - E_j(t))\, S_e \left(c_1 E_j(t) - c_2 I_j(t) + c_5 \sum_k A_{jk} E_k(t - \tau_d^k) + P_j(t) \right) + \sigma w_j(t)$$

Global coupling parameter



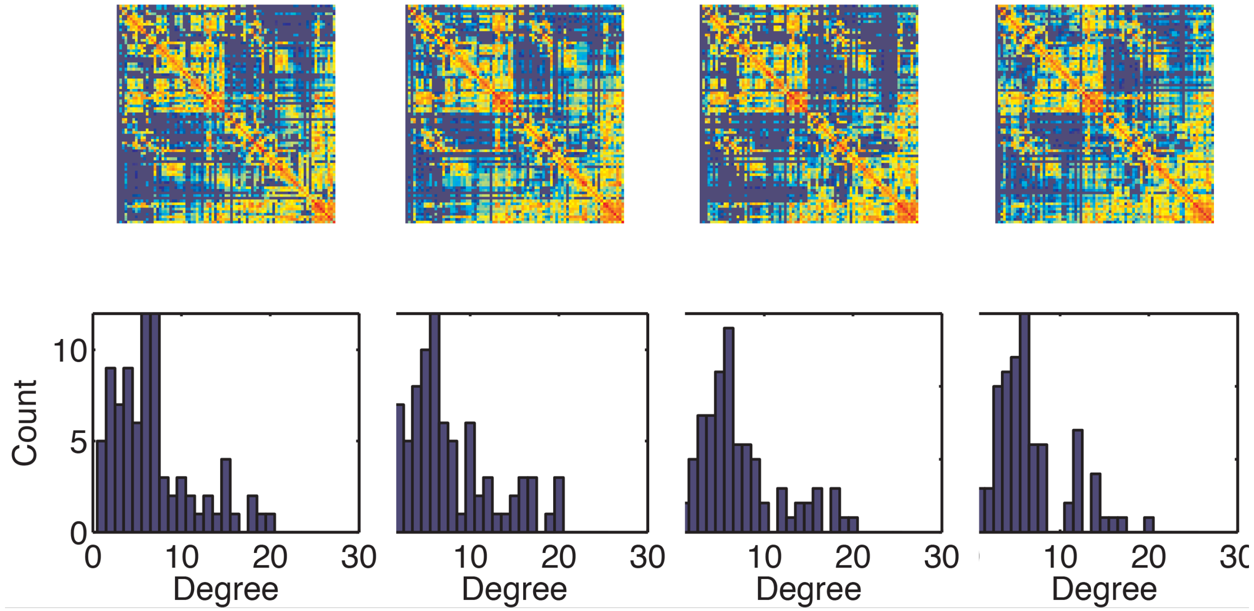


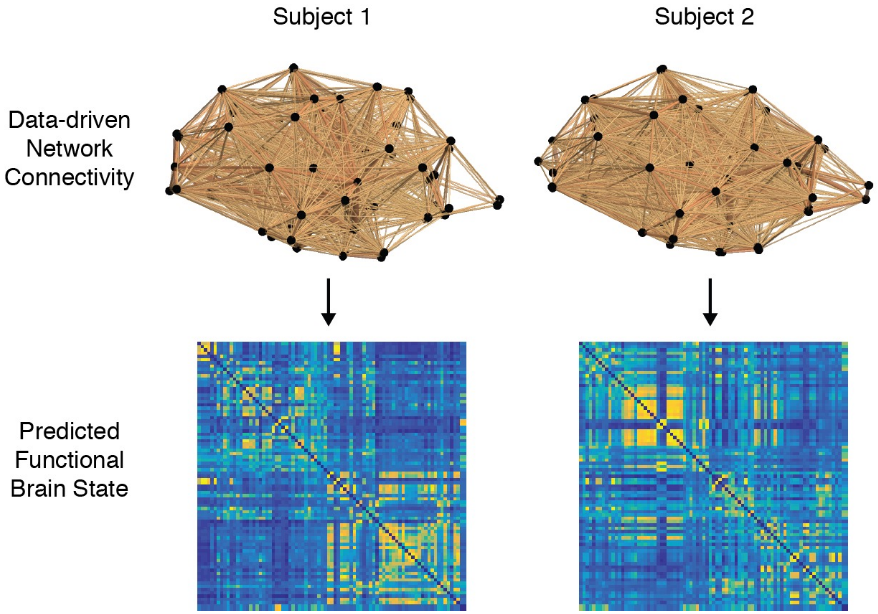
Sensitive to individual differences in brain network structure!

Muldoon et al. (2016) PLOS Comp Bio

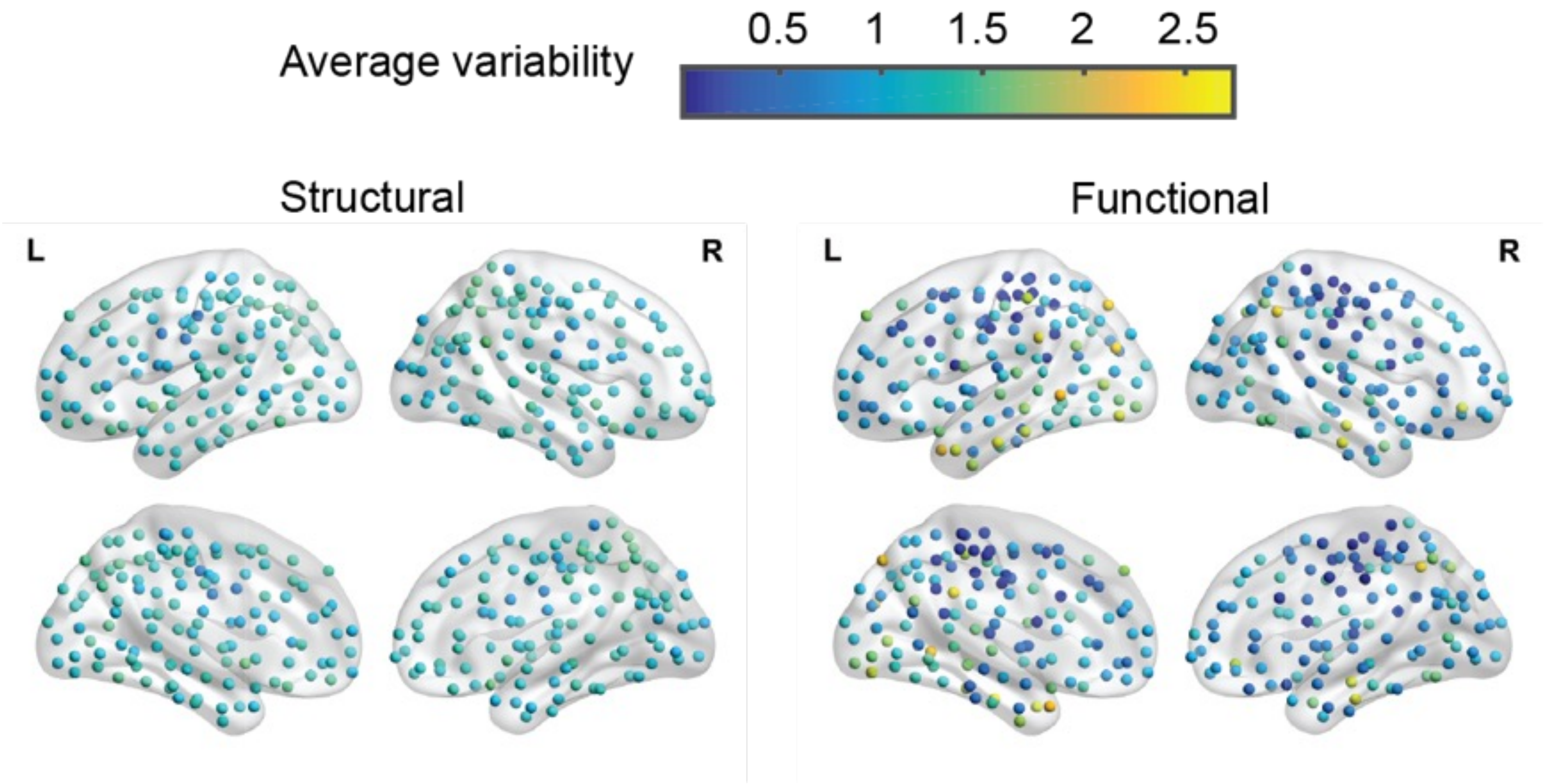
Brains 'appear' structurally similar

Individual differences





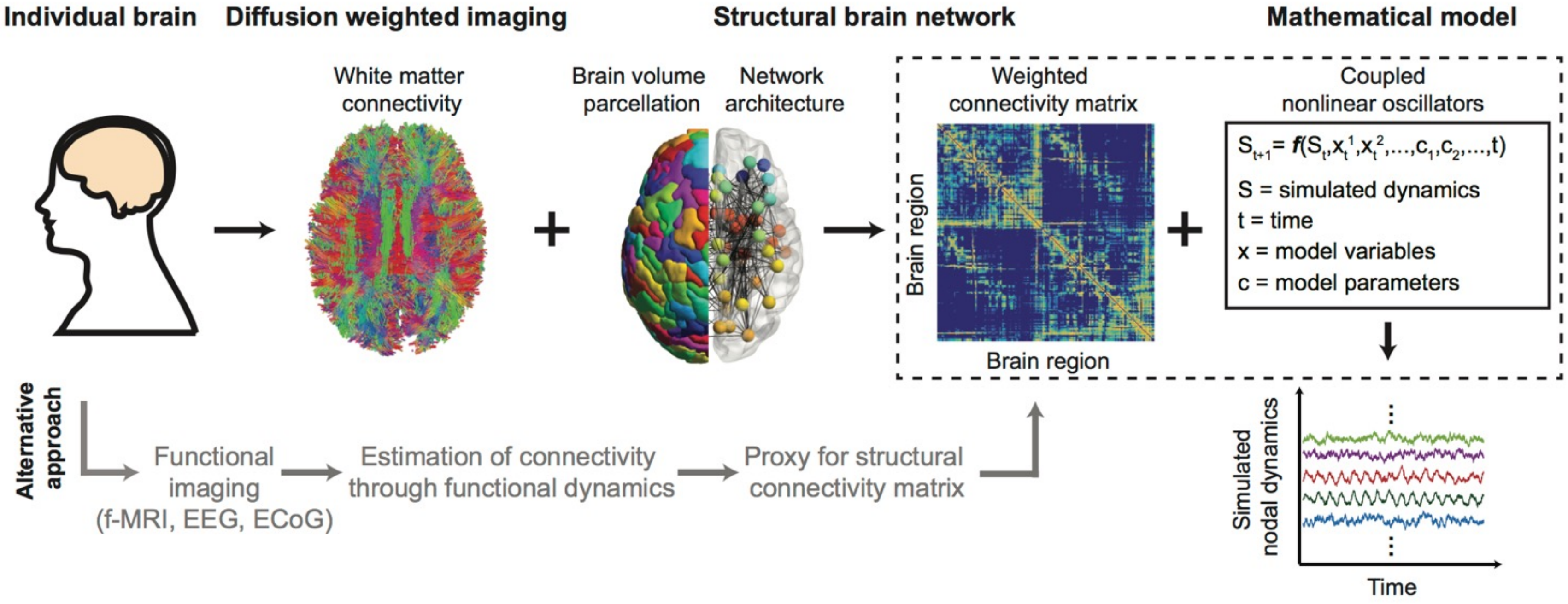
Model accentuates structural differences



Bansal et al. (2018) PLoS Comp Bio

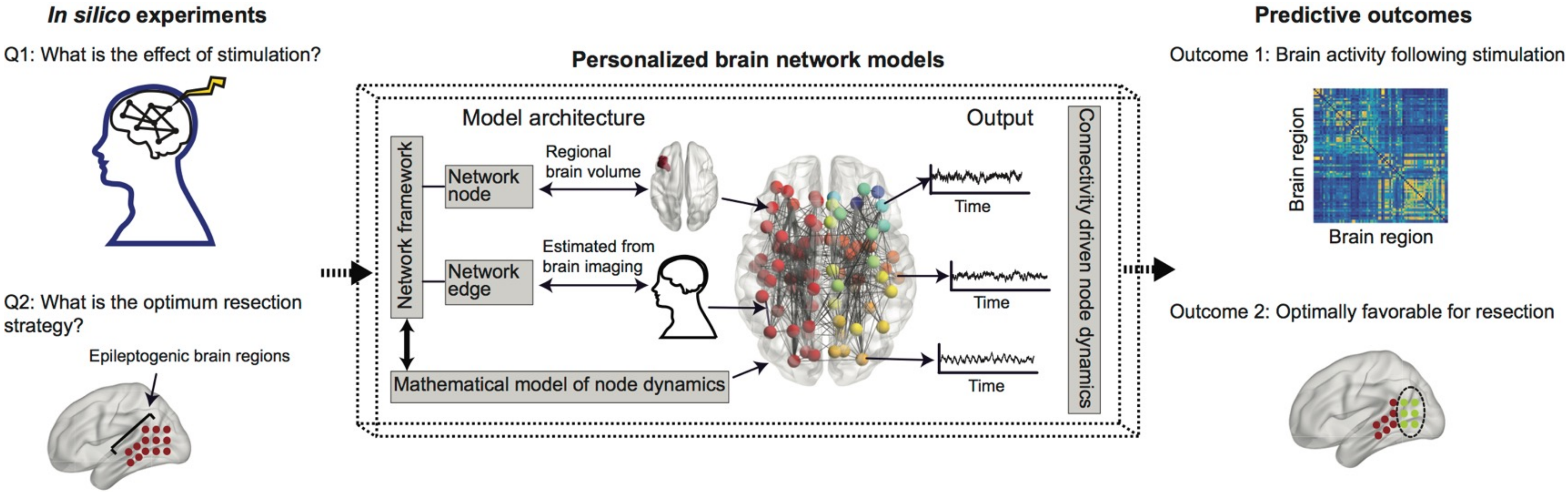
Personalized brain network models

Brain network models are especially sensitive to perturbations in the underlying connectivity



Bansal et al. (2018) Curr Opin Neurobiol

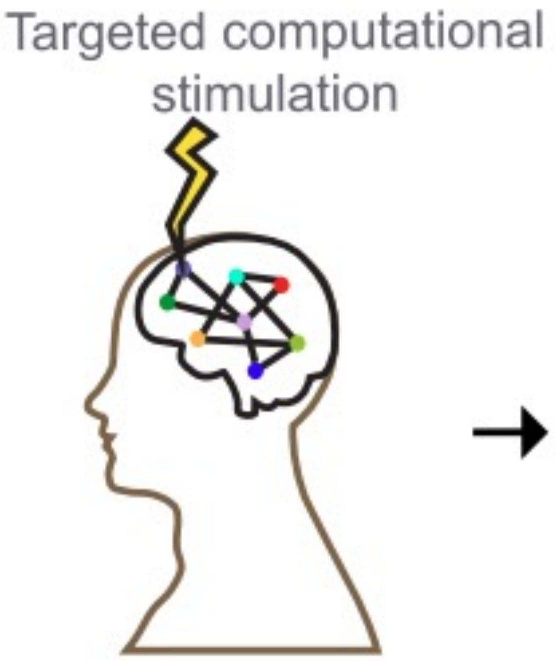
Personalized brain network models



Bansal et al. (2018) Curr Opin Neurobiol

Perform computational experiments

Study differential effects of stimulation across cohort of individuals



Can simulated brain activity be used as a parameter to differentiate individual behavior?

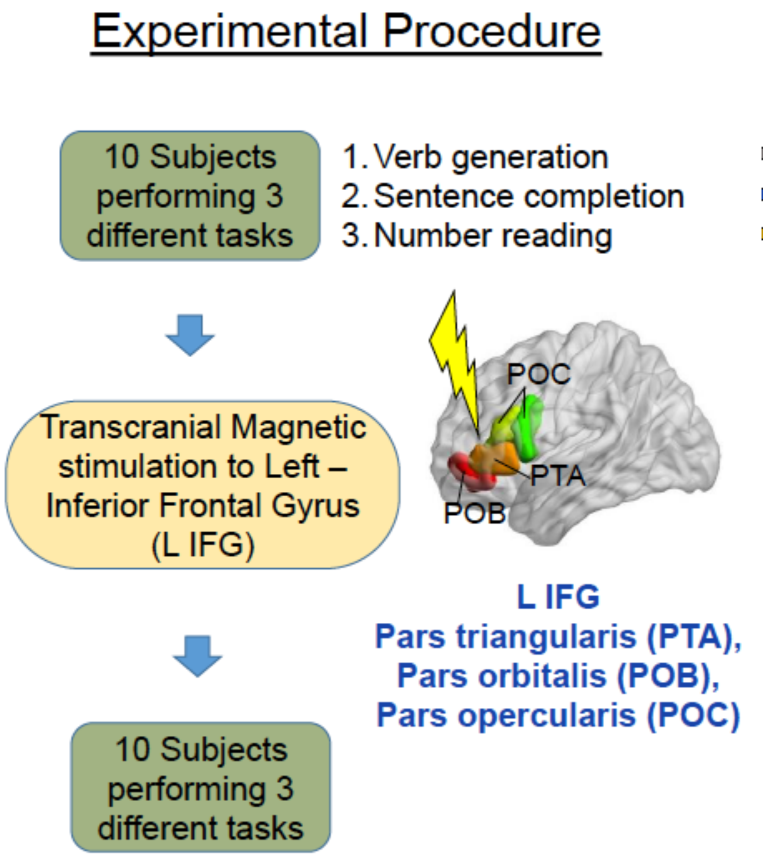
Part 2: Predicting Task Performance

Individual differences: task performance

Can simulated brain activity be used as a parameter to differentiate individual behavior?

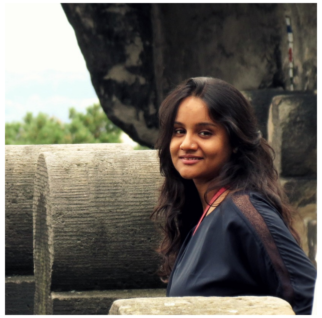
Data from Medaglia and Bassett at Penn

- 10 subjects, 3 cognitive tasks
- TMS stimulation to L-IFG
- task performance before stim
- task performance after stim



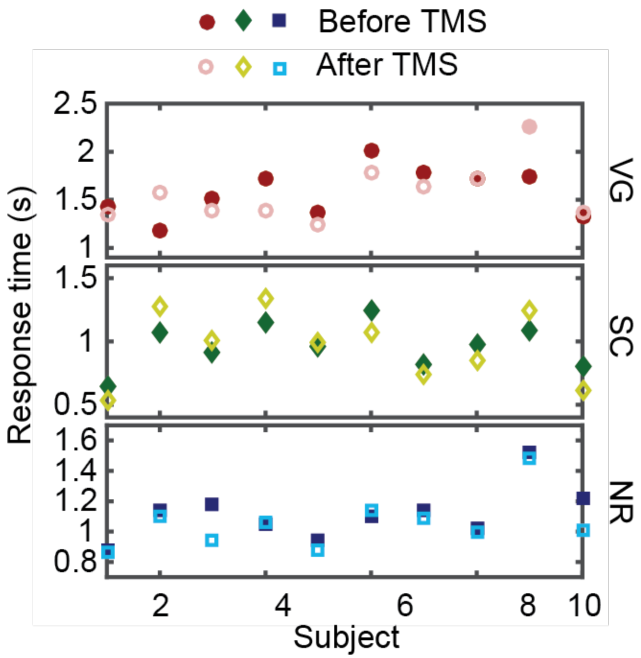
Individual variability

Postdoc Kanika Bansal

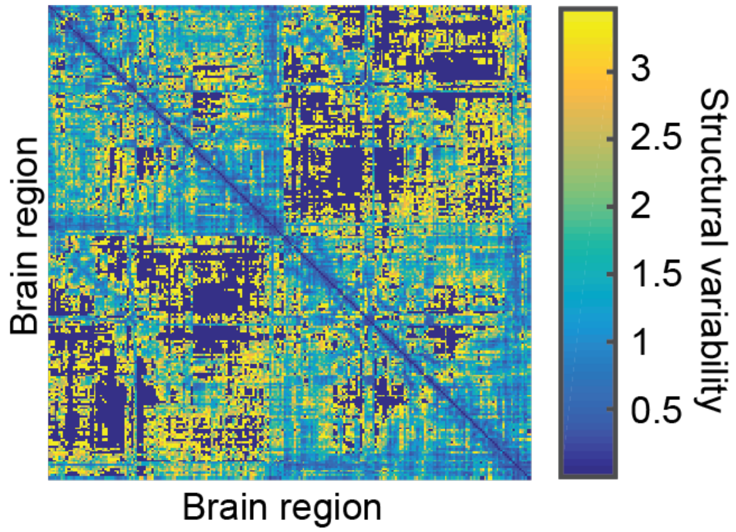


Individual differences in task performance

Performance variability



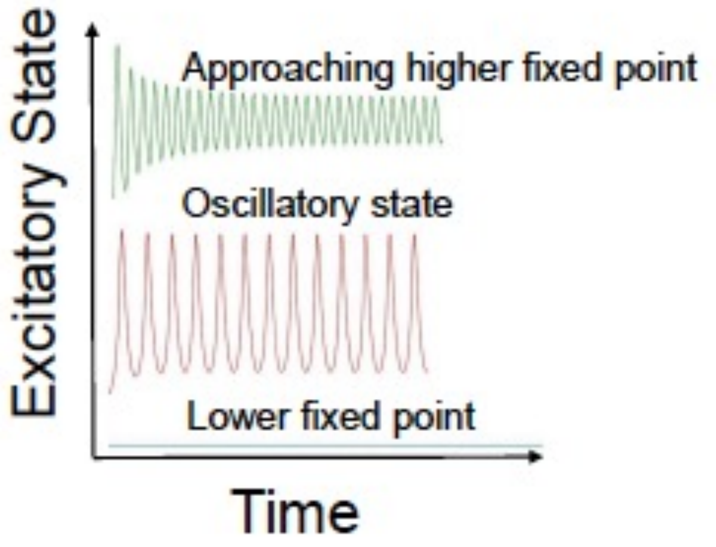
Structural variability



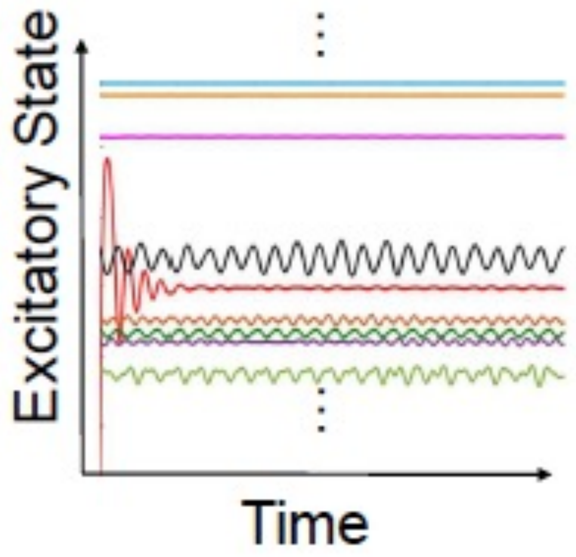
Bansal et al. (2018) PLoS Comp Bio

Variability in the model

Allowed single oscillator states

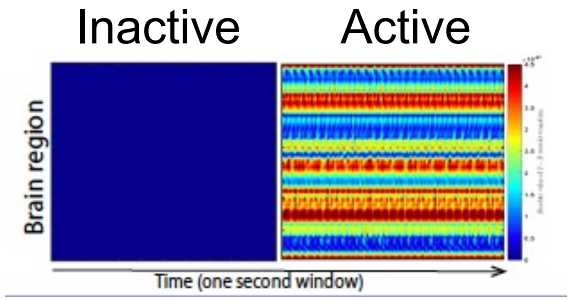


Typical coupled system



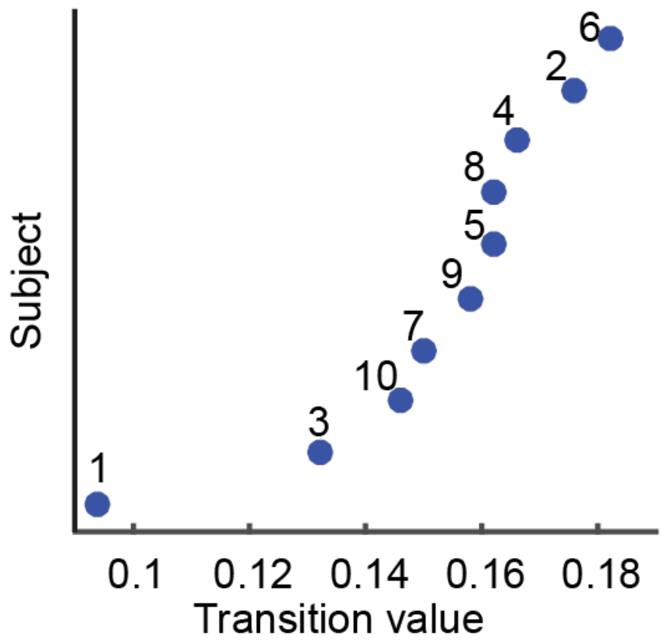
Excitatory population

$$\tau \frac{dE_i}{dt} = -E_i(t) + \left(S_{E_m} - E_i(t)\right)S_E\left(c_1E_i(t) - c_2I_i(t) + \overbrace{c_5\sum_j A_{ij}E_j\left(t-\tau_d^j\right)}^{\text{Excitatory coupling term}} + \underbrace{P_i}_{\text{External Stimuli}}\right) + \underbrace{\sigma w_i(t)}_{\text{Noise}}$$

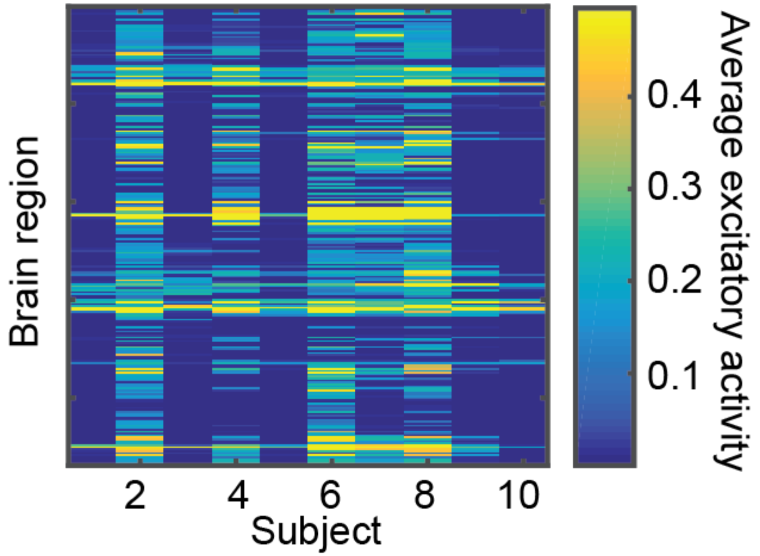


Variability in the model

Model transition value



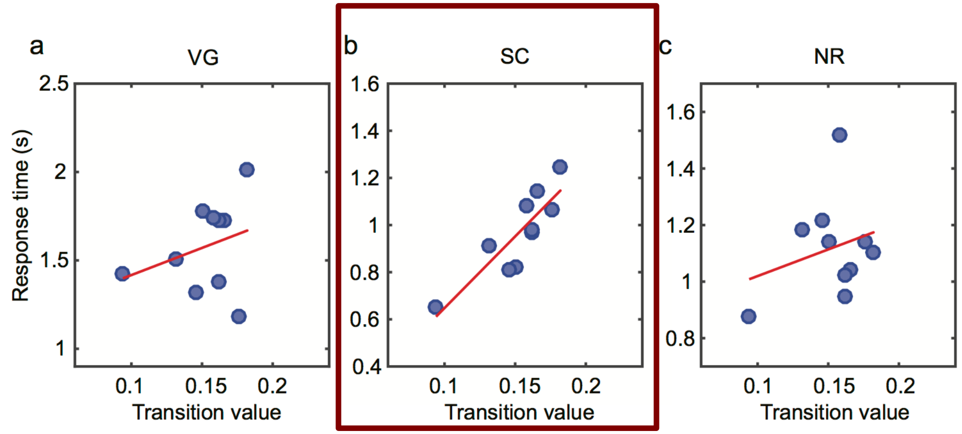
Output model dynamics



Bansal et al. (2018) PLoS Comp Bio

Correlations with transition value

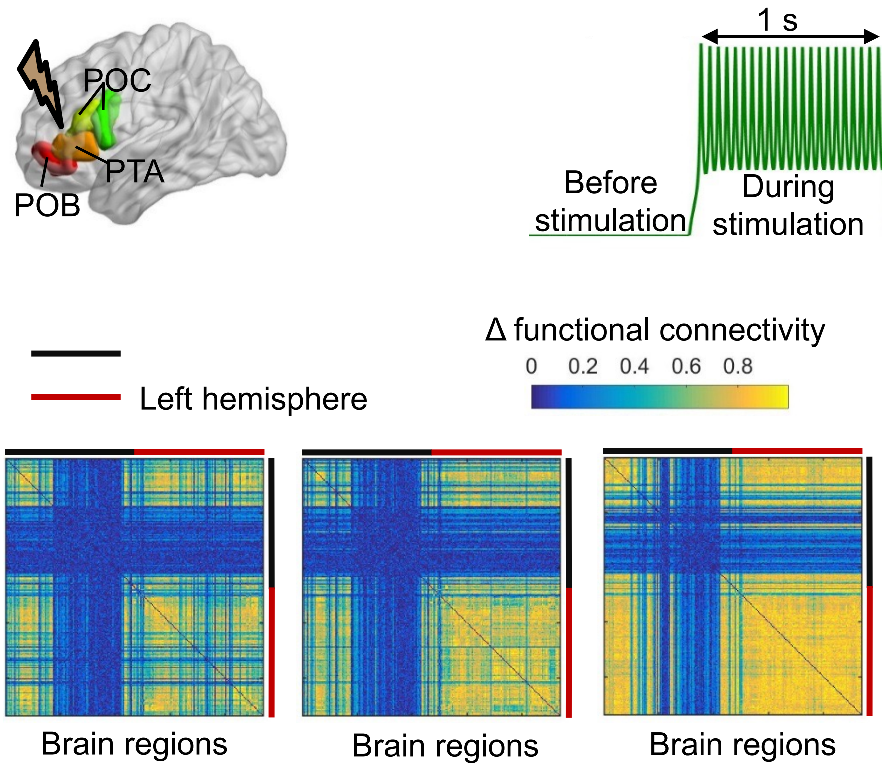
Only see correlation between transition value and task performance for Sentence Completion (SC) task



Model feature	VG		SC		NR	
	r	p	r	p	r	p
Transition value	0.30	0.39	**0.86*•**	**0.001**	0.27	0.45
	[-0.27, 0.80]		[0.68, 0.95]		[-0.52, 0.69]	

Virtual stimulation experiments

To mimic experimental data, apply stimulation to LIFG in computational brain (Lausanne parcellation, 234 regions)



Functional Effect: average change in functional connectivity

Hypothesis: The spread of synchronization through the brain (functional effect), will correlate with the performance

Bansal et al. (2018) PLoS Comp Bio

Correlations with functional effect

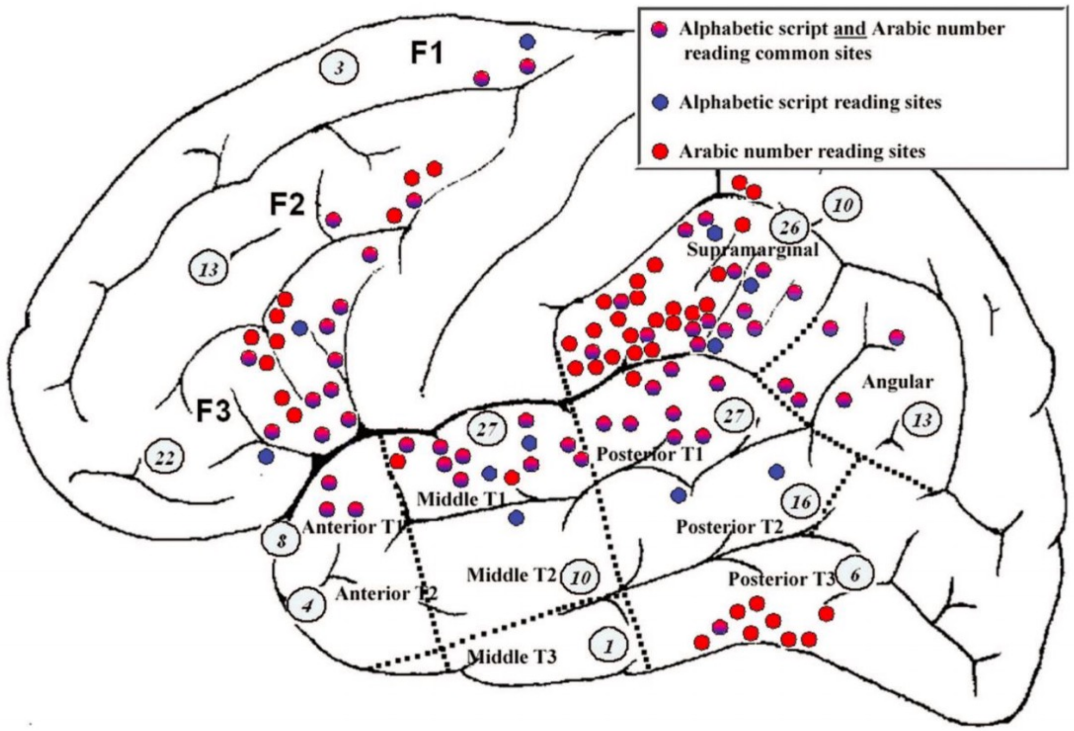
No correlations!

Model feature	VG r	VG p	SC r	SC p	NR r	NR p
Transition value	0.30 [-0.27, 0.80]	0.39	**0.86*•** [0.68, 0.95]	**0.001**	0.27 [-0.52, 0.69]	0.45
Functional effect (global brain)	-0.04 [-0.52, 0.44]	0.91	0.39 [-0.27, 0.80]	0.26	0.23 [-0.31, 0.72]	0.52

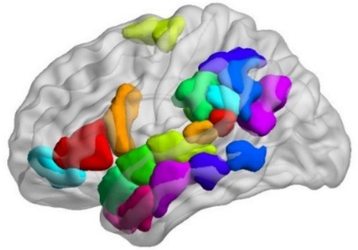
Bansal et al. (2018) PLoS Comp Bio

Task circuits

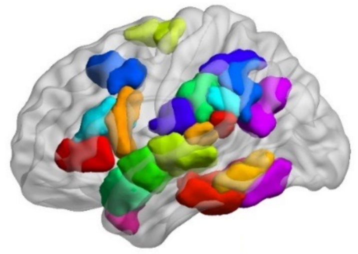
Examine activation of subnetworks associated with language or number reading



Task circuit for processing alphabets



Task circuit for processing numbers

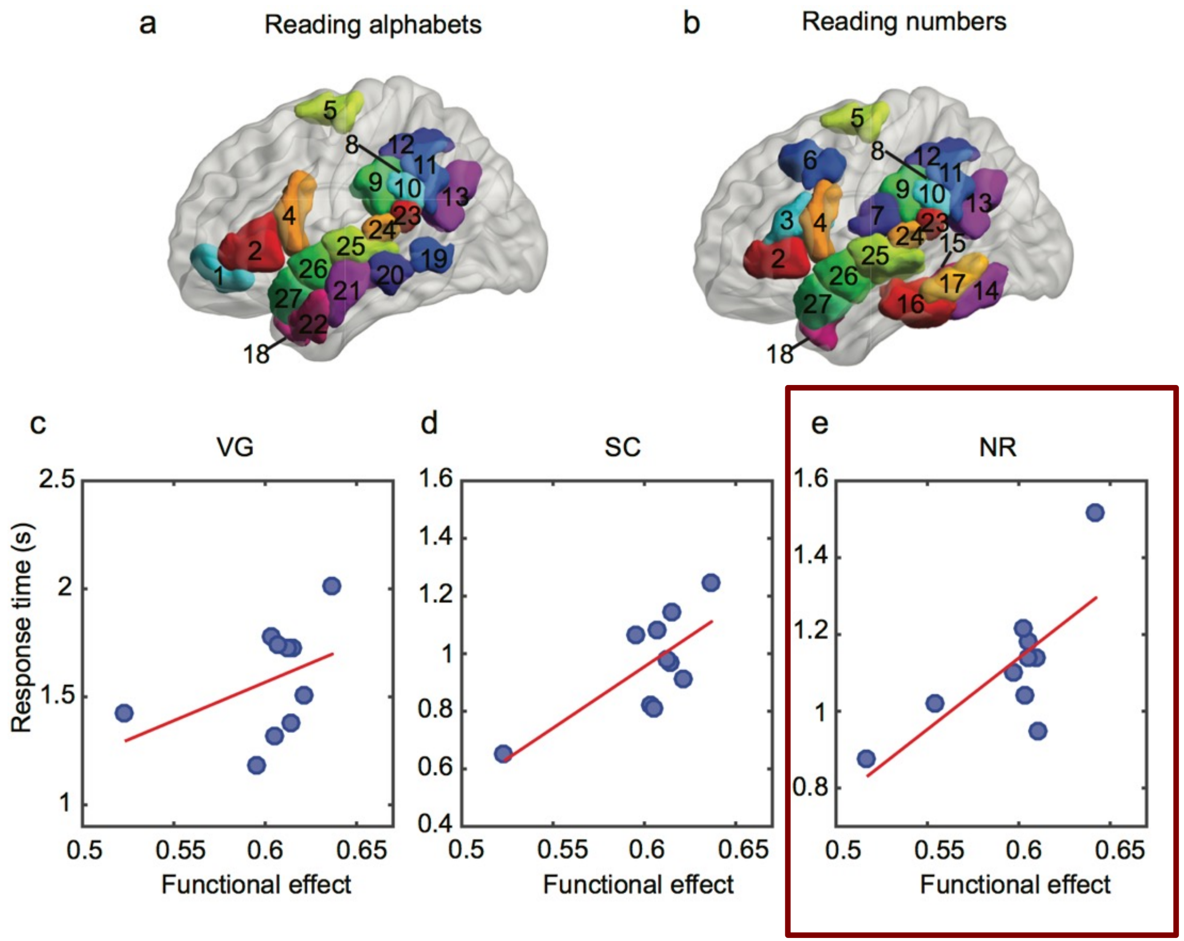


Roux et al. (2008) Neurology

Correlation within task circuits

Only see a correlation between the functional effect within the task circuit and task performance in the Number Reading (NR) task!

Model feature	VG r	VG p	SC r	SC p	NR r	NR p
Transition value	0.30 [-0.27, 0.80]	0.39	**0.86*•** [0.68, 0.95]	**0.001**	0.27 [-0.52, 0.69]	0.45
Functional effect (global brain)	-0.04 [-0.52, 0.44]	0.91	0.39 [-0.27, 0.80]	0.26	0.23 [-0.31, 0.72]	0.52
Functional effect (task circuit)	0.42 [0.12, 0.82]	0.22	**0.73*** [0.01, 0.90]	**0.017**	**0.74*•** [0.20, 0.94]	**0.016**

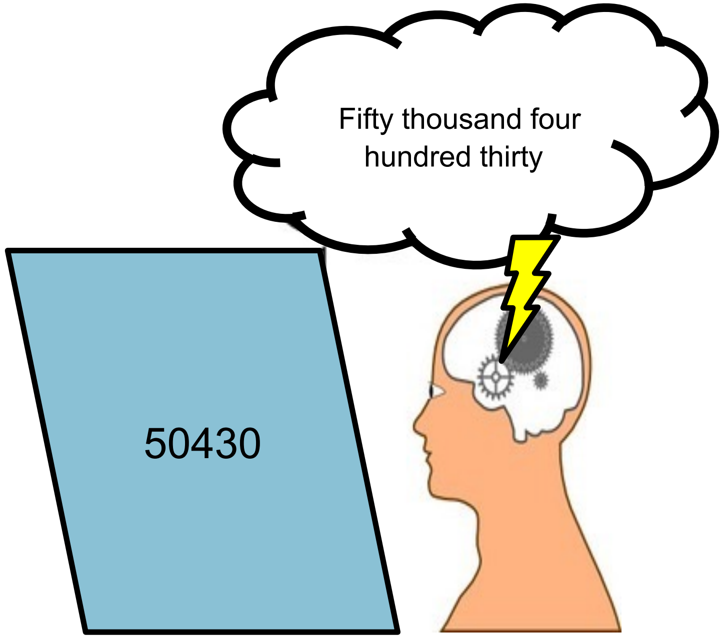


Local vs global computation

Task circuits are for letter and number reading

Does the task require other cognitive effort?

Do other brain regions play a role?



Local vs global complexity

Sentence completion – requires involvement of more cognitive systems

- Global brain task
- Transition value = global brain excitation

Number reading – simpler task involving local sub-circuit

- Localized brain task
- Functional effect within task circuit – localized computation

To summarize

Personalized brain network models accentuate differences in structural variability

Use to perform virtual experiments otherwise not possible to assess how patterns of brain activity differ across individuals or across stimulation sites

Useful for developing personalized medicine treatments

Promising results but need better understanding of task circuitry and larger sample size! Now working with larger data set and auditory/visual cues during task.

Part 3: Quantifying Variability

Quantifying individual differences

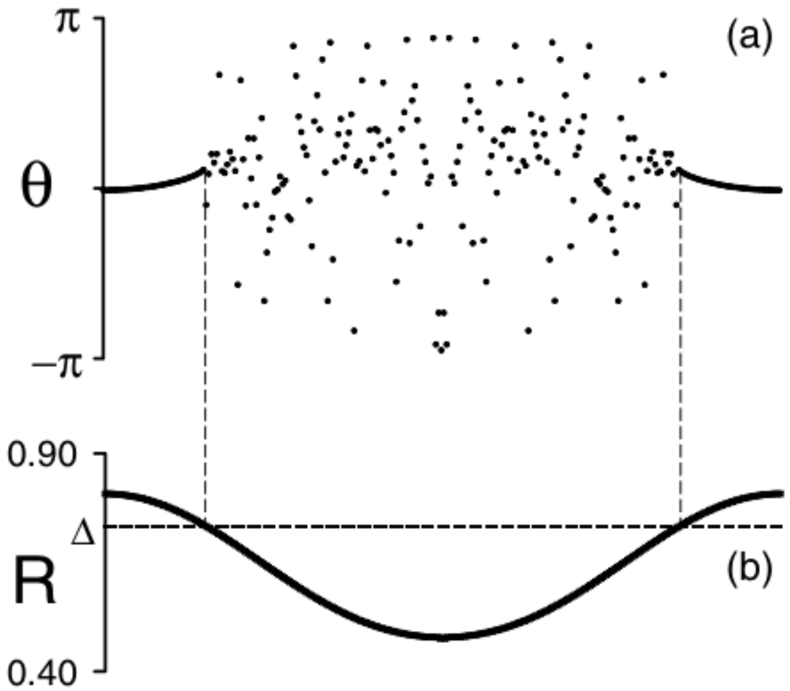
Functional effect (average pairwise synchronization across brain/sub-circuit) is a very unsophisticated measure of synchronized brain activity patterns

Need to develop tools to quantify and understand patterns of brain activity and how the differ across individuals

Cognitive chimera states

What is a chimera state?

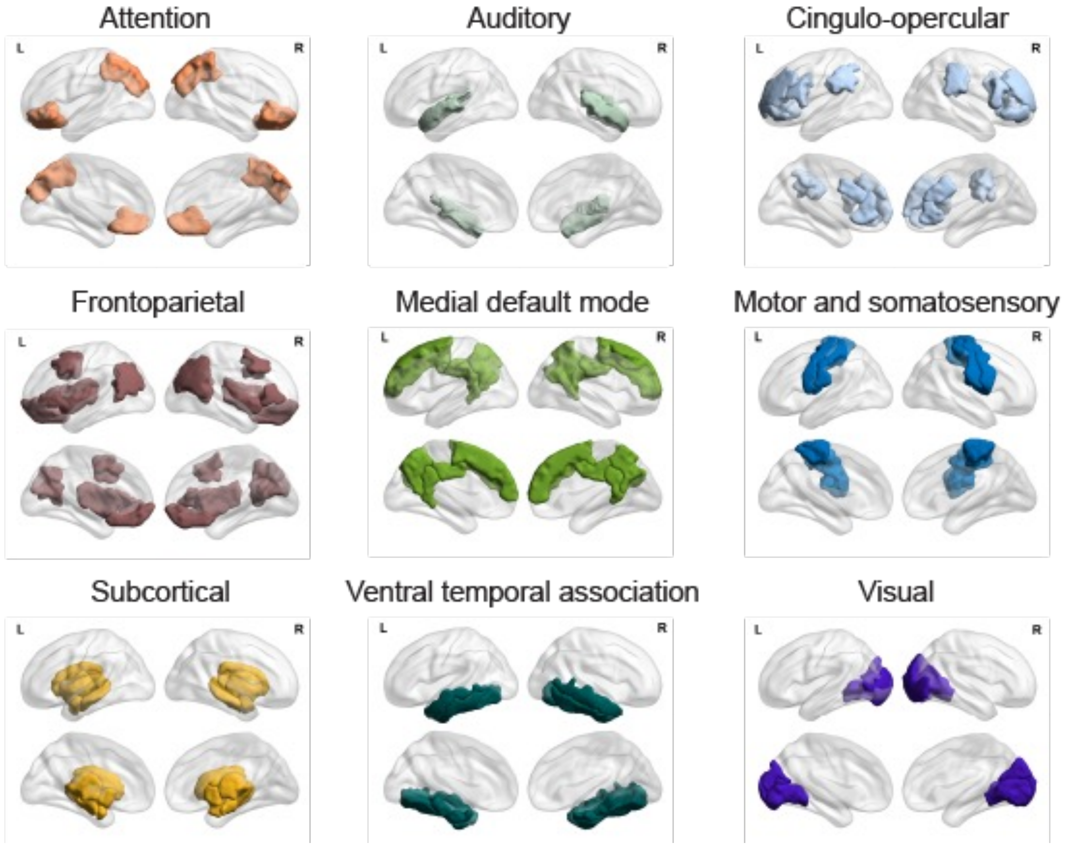
In a system of coupled identical oscillators, a chimera state is a state of partial synchronization where a subset of oscillators become synchronized, while the remainder of the oscillators remain asynchronous



Abrams and Strogatz (2004) PRL

Chimera states in the brain

Combine with a cognitive context

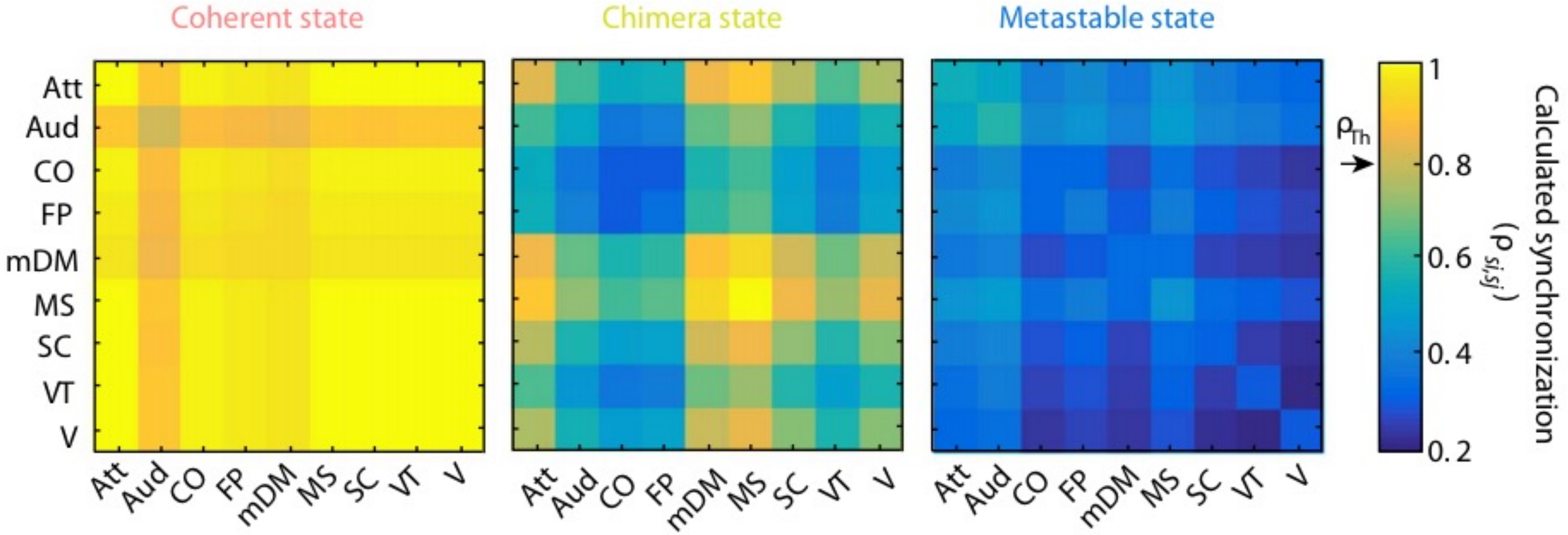


Bansal et al. (2019) Sci Adv

Cognitive chimera states

Measure the pairwise synchronization of brain regions between nodes within cognitive systems

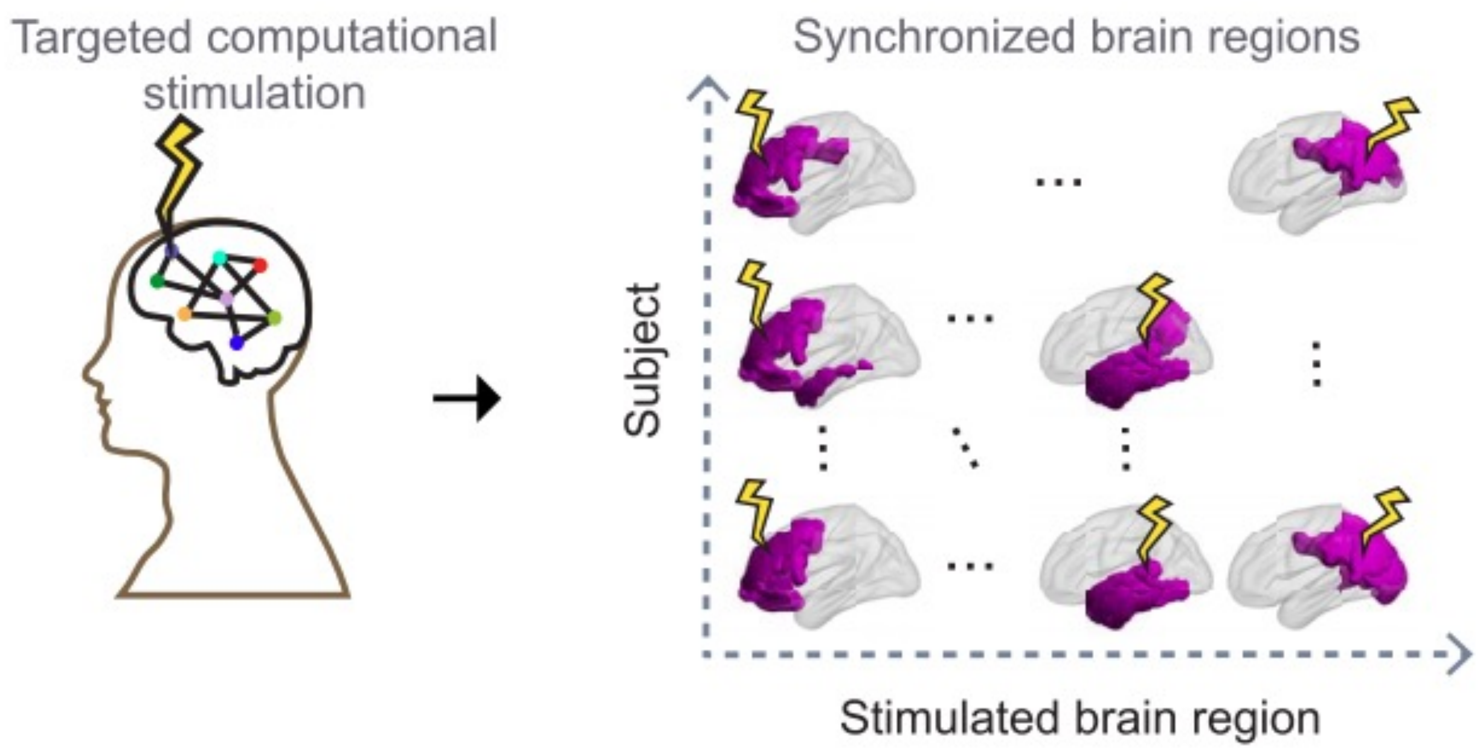
$$\rho_{s_i,s_j} = <\rho_{s_i,s_j}(t)>_T \qquad \rho_{s_i,s_j}(t)e^{i\Theta(t)} = \frac{1}{N_{s_i}+N_{s_j}} \sum_{k\in(s_i\cup s_j)} e^{i\phi_k(t)}$$



Bansal et al. (2019) Sci Adv

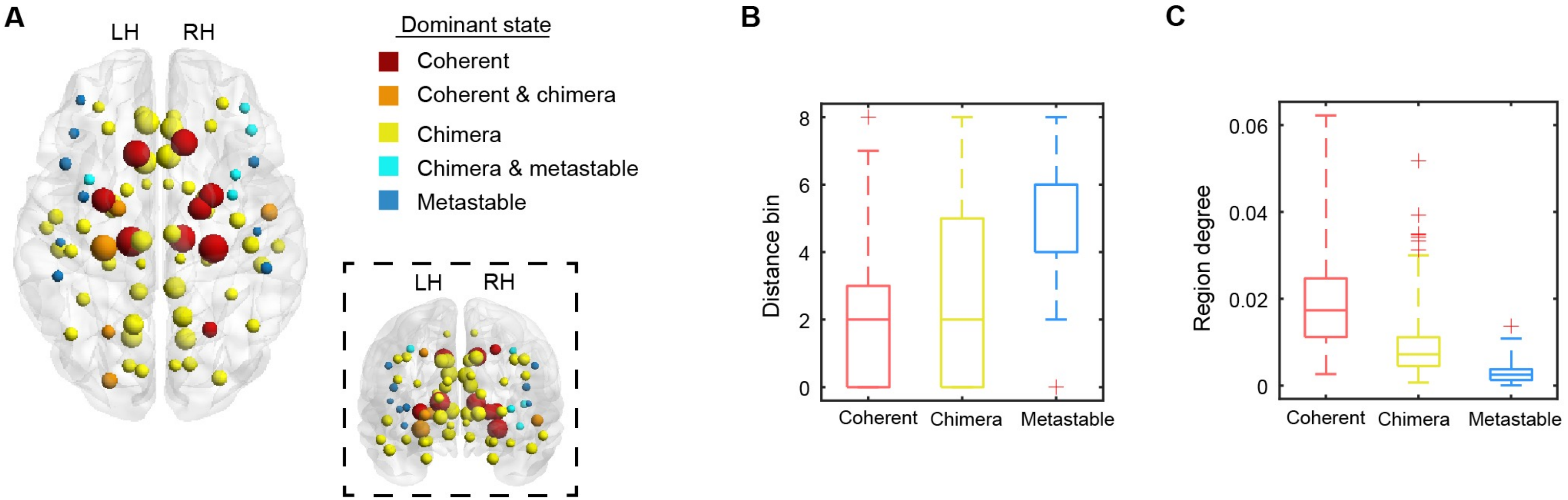
Computational stimulation experiments

Build 30 personalized brain network models

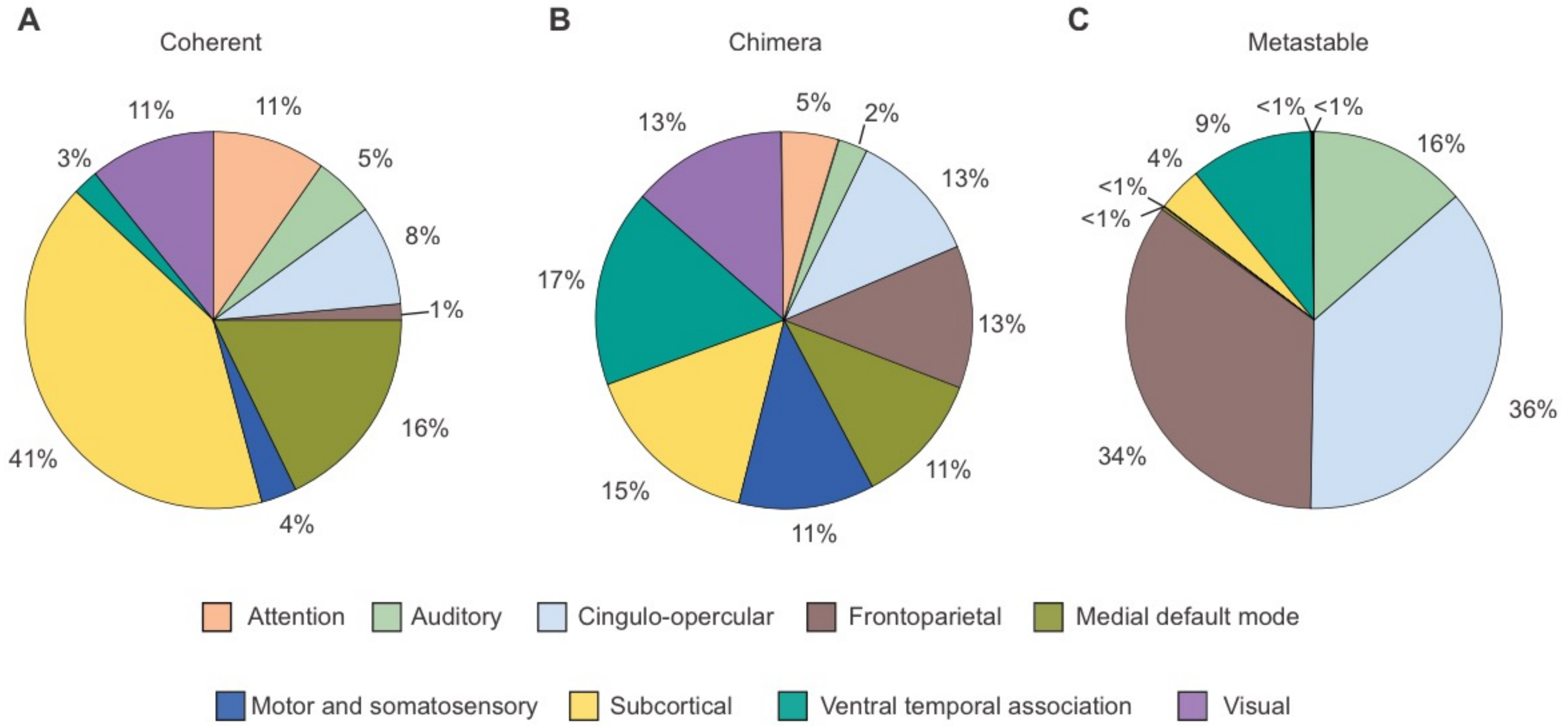


Spatial mapping of activity patterns

Stimulation of different brain regions produces different patterns of activity

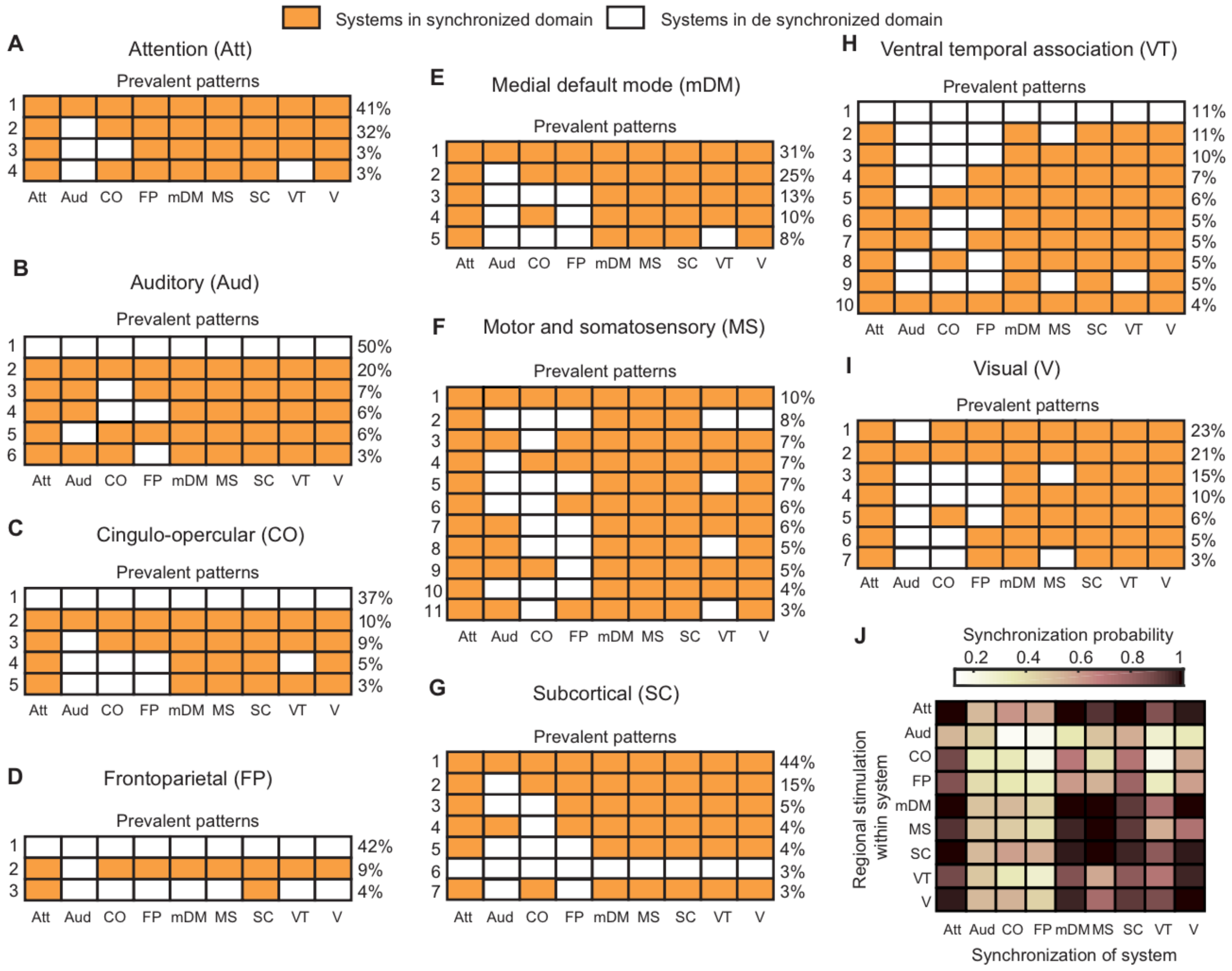


All systems produce chimera states



Bansal et al. (2019) Sci Adv

Chimeras display unique patterning

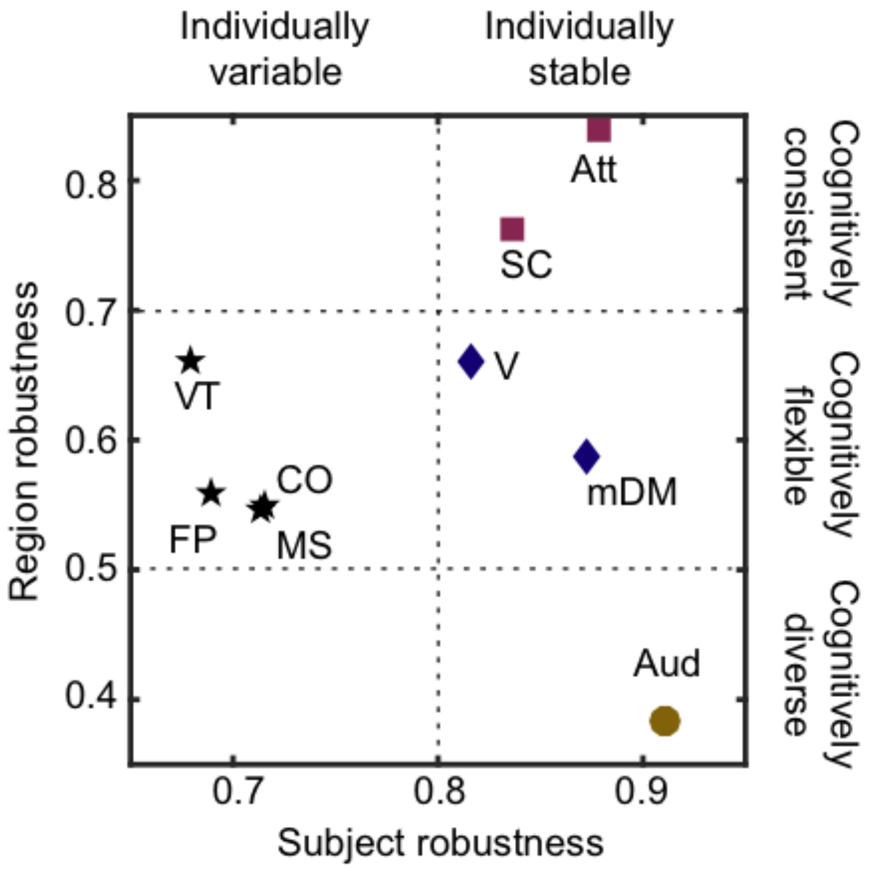


Bansal et al. (2019) Sci Adv

Robustness of chimera patterns

$$R = \frac{1}{p(p-1)} \sum_{i,j=1}^{p} \left(\frac{1}{M} \sum_{s=1}^{M} \delta_{i,j}^{s} \right)$$

p is the total number of patterns in the set – calculate across subjects for simulation of a single node or across nodes within a system for a subject



Bansal et al. (2019) Sci Adv

To summarize

Personalized brain network models accentuate differences in structural variability

Cognitive chimera framework is a novel way for quantifying patterns of brain activity to give insight into variability in cognitive function

Useful for developing personalized medicine treatments

Thanks to…

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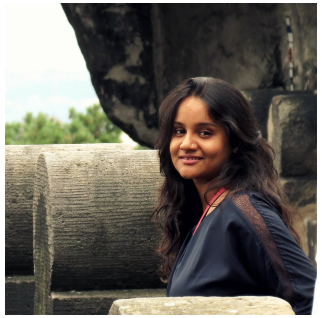
- James Hartz
- Elizabeth Castro



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- Jean Vettel, ARL
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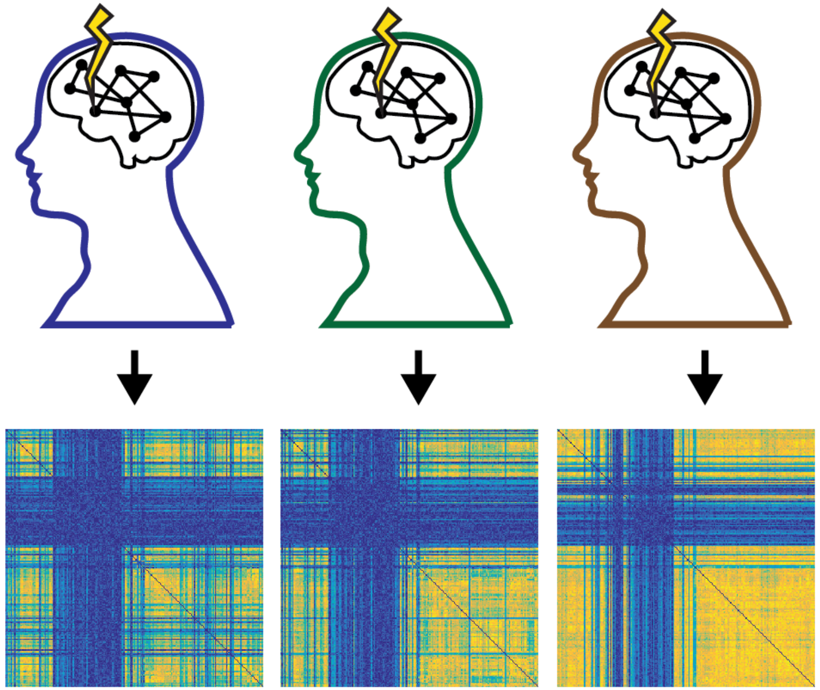
- Dani Bassett, Penn
- Timothy Verstynen, CMU
- Javi Garcia, ARL
- Steven Tompson, ARL

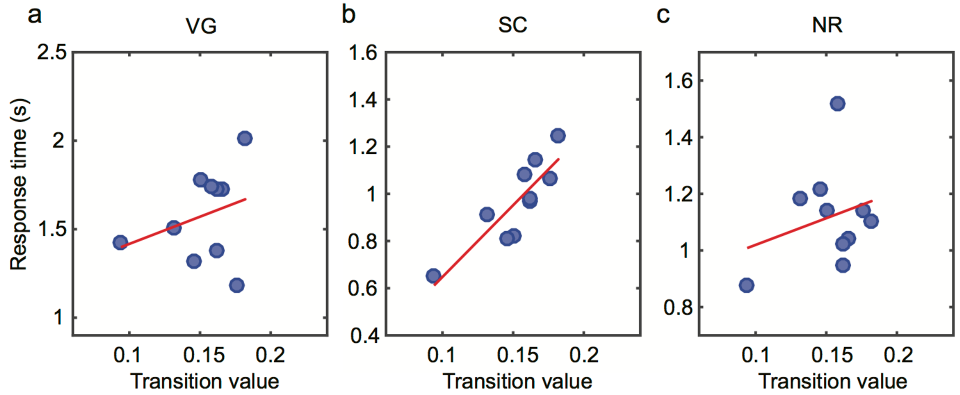


Funding:

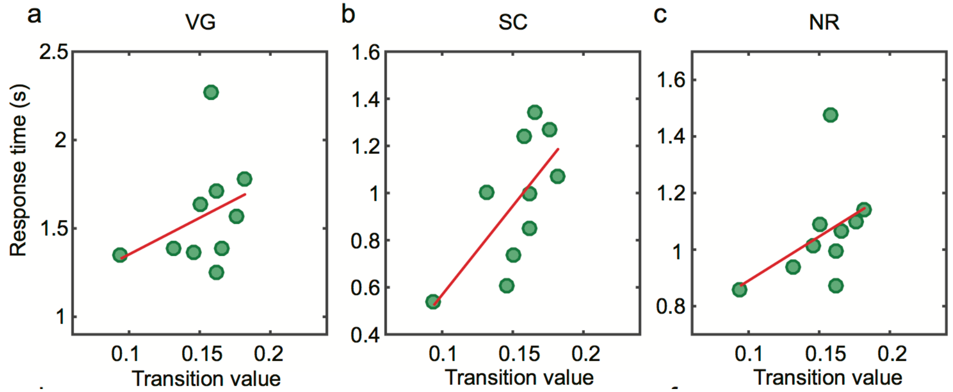
How does stimulation change things?

Weakened correlations – Transition Value

Before Stimulation



After Stimulation

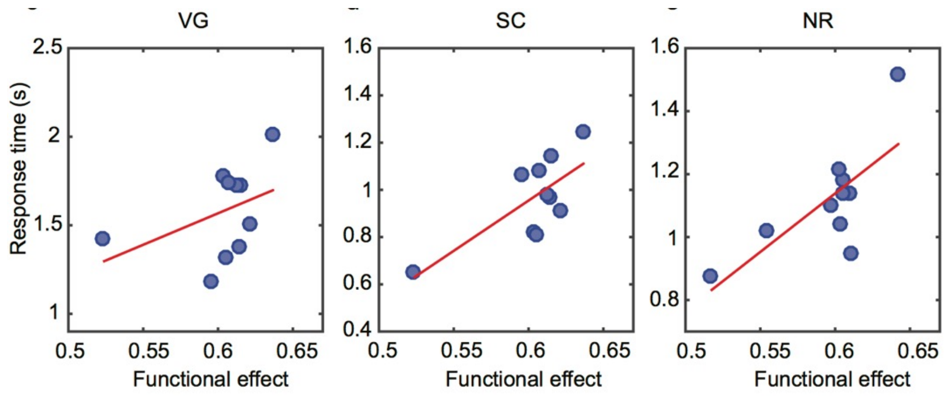


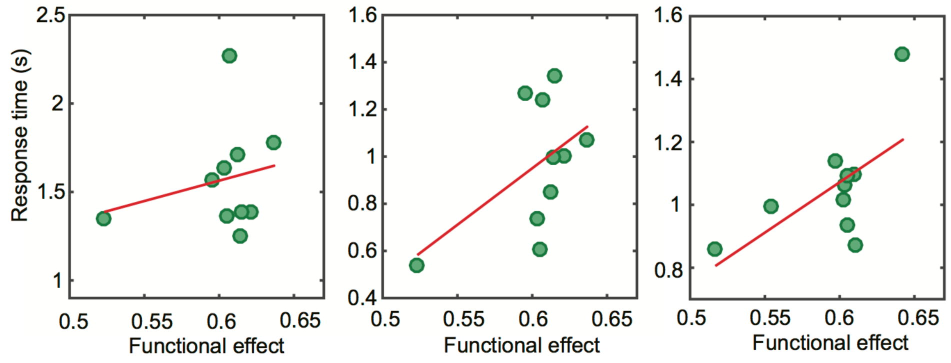
Bansal et al. (2018) PLoS Comp Bio

How does stimulation change things?

Weakened correlations – Functional effect within task circuit Before Stimulation

After Stimulation





Bansal et al. (2018) PLoS Comp Bio

Weakened correlations

Before stimulation

Model feature	VG r	VG p	SC r	SC p	NR r	NR p
Transition value	0.30	0.39	**0.86*•**	**0.001**	0.27	0.45
	[-0.27, 0.80]		[0.68, 0.95]		[-0.52, 0.69]	
Functional effect (global brain)	-0.04	0.91	0.39	0.26	0.23	0.52
	[-0.52, 0.44]		[-0.27, 0.80]		[-0.31, 0.72]	
Functional effect (task circuit)	0.42	0.22	**0.73***	**0.017**	**0.74*•**	**0.016**
	[0.12, 0.82]		[0.01, 0.90]		[0.20, 0.94]	

After Stimulation

Model feature	VG r	VG p	SC r	SC p	NR r	NR p
Transition value	0.35	0.33	**0.68•**	**0.03**	0.45	0.20
	[0.01, 0.70]		[0.32, 0.87]		[0.01, 0.93]	
Functional effect (global brain)	0.19	0.59	0.39	0.27	0.08	0.82
	[-0.18, 0.63]		[-0.22, 0.81]		[-0.43, 0.57]	
Functional effect (task circuit)	0.23	0.52	0.52	0.12	**0.63•**	**0.05**
	[-0.38, 0.57]		[-0.22, 0.79]		[-0.07, 0.88]	

Bansal et al. (2018) PLoS Comp Bio

How does stimulation change things?

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