Multi-layer, Time-varying Brain Networks: Community Structure and Network Flexibility

SIAM CSE – March 1, 2017

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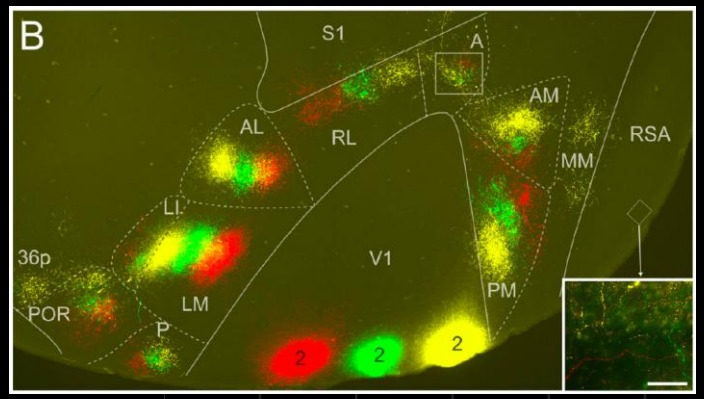
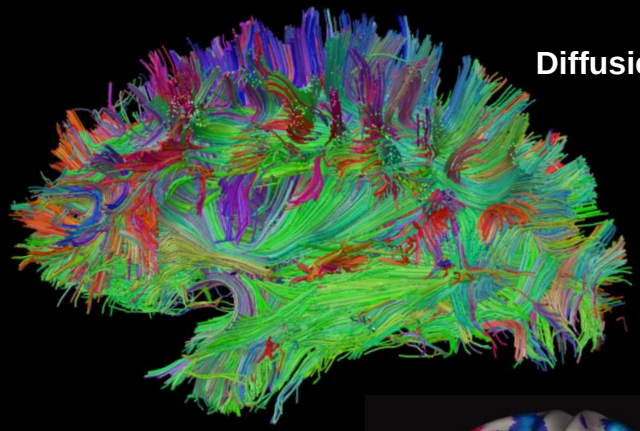
Neural systems are complex networks

Inherently multiscale:
- Micro (neurons, synapses)
- Macro (regions, projections)

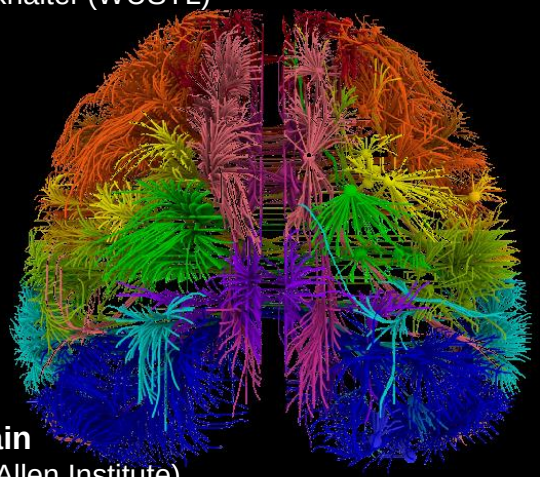
Multiple modes of coupling
- Anatomical (physical projections)
- Functional (dynamic interactions)



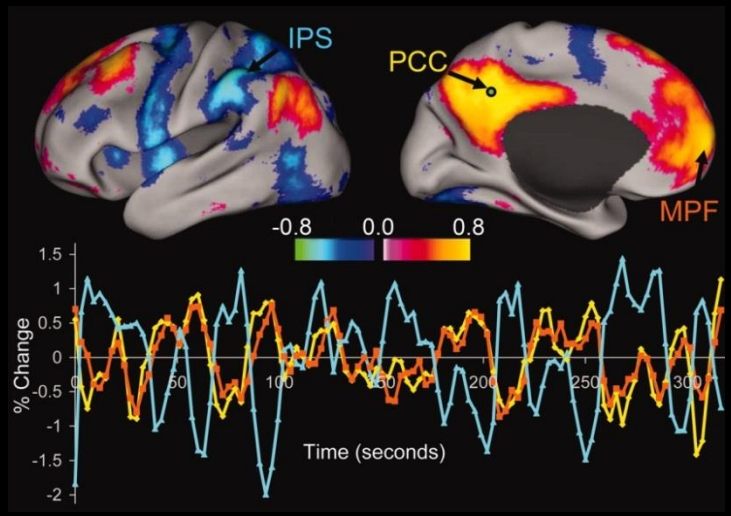
Mouse visual cortex
Andreas Burkhalter (WUSTL)



Diffusion imaging/tractography
Patric Hagmann (EPFL)



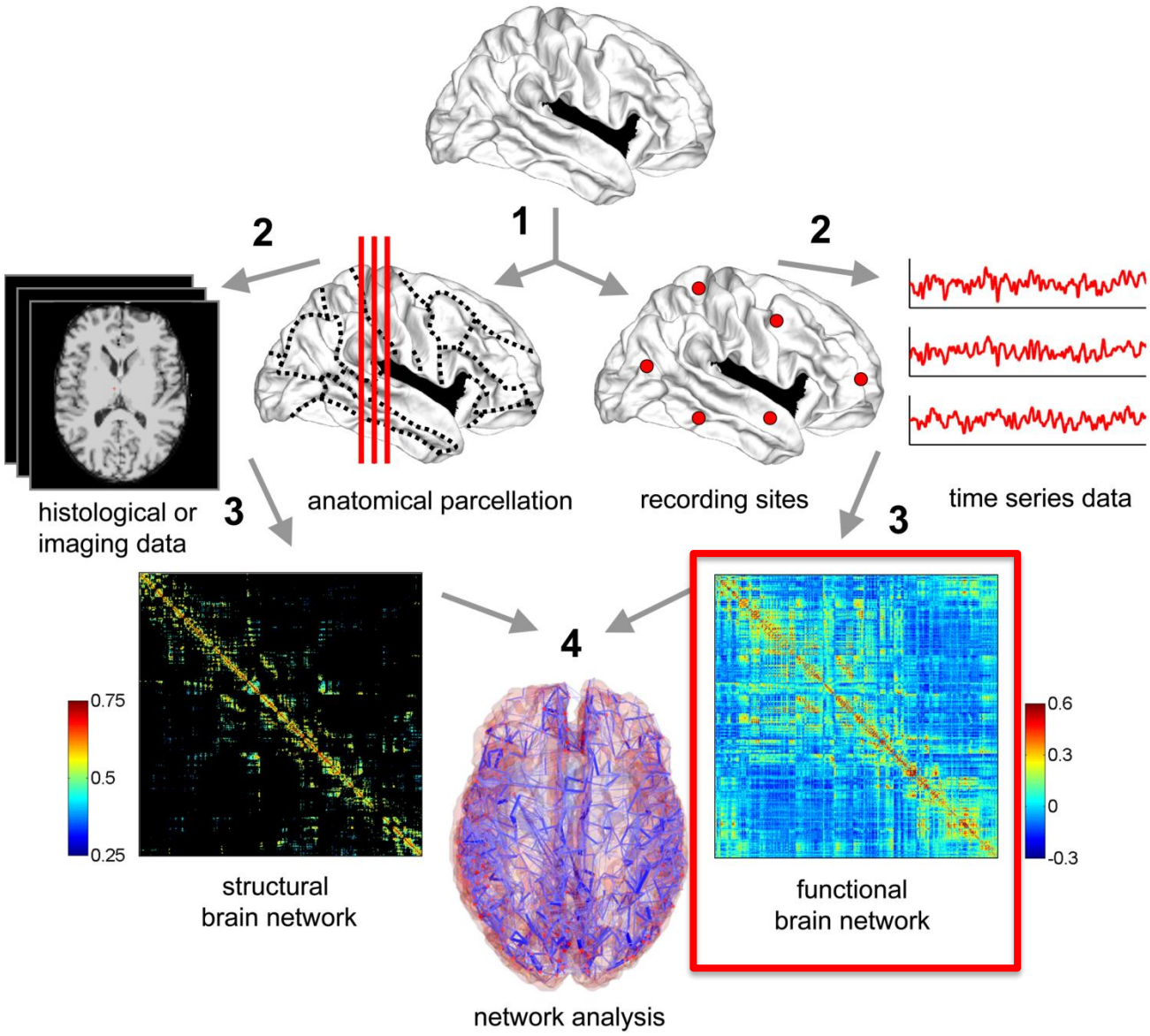
Mouse brain
Oh, Harris (Allen Institute)



Resting-state fMRI
Michael Fox, Marc Raichle (WUSTL)

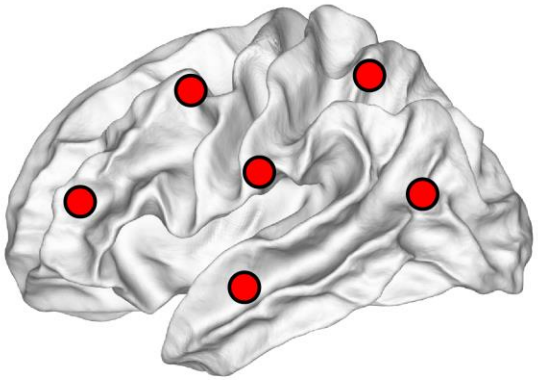
Betzel & Bassett (2016). Multi-scale brain networks. *Neuroimage.*

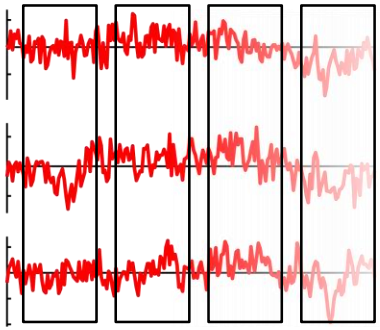
Constructing Brain Networks



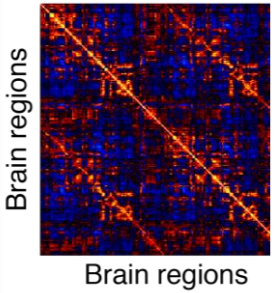
Bullmore & Sporns (2009) *Nature Rev Neurosci* 10, 186.

Time-varying functional brain networks



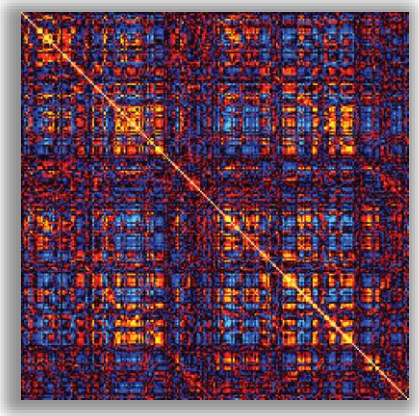


Long-time averaged FC

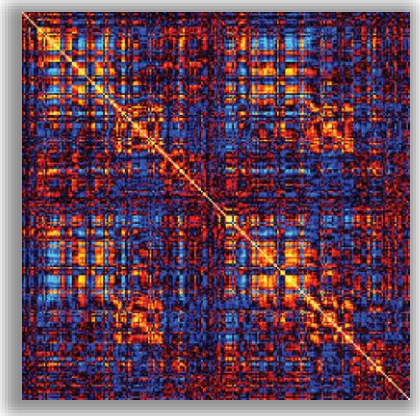


- Neural processes play out at a sub-second scale.
- Cognitive processes at timescales shorter than that of an entire scan session.

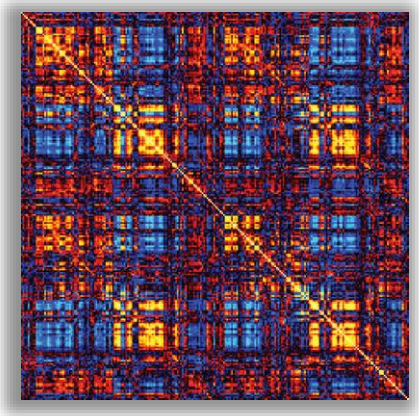
Time 1



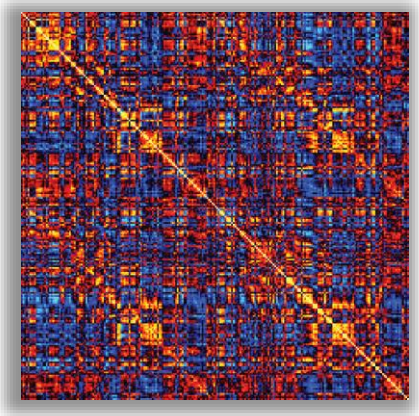
Time 2



Time 3



Time 4



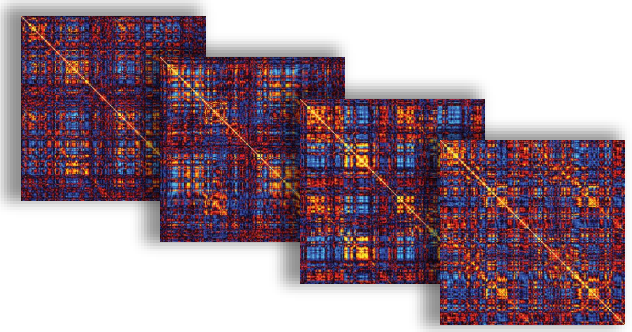
Hutchinson et al (2011). *Neuroimage*, 80, 360.

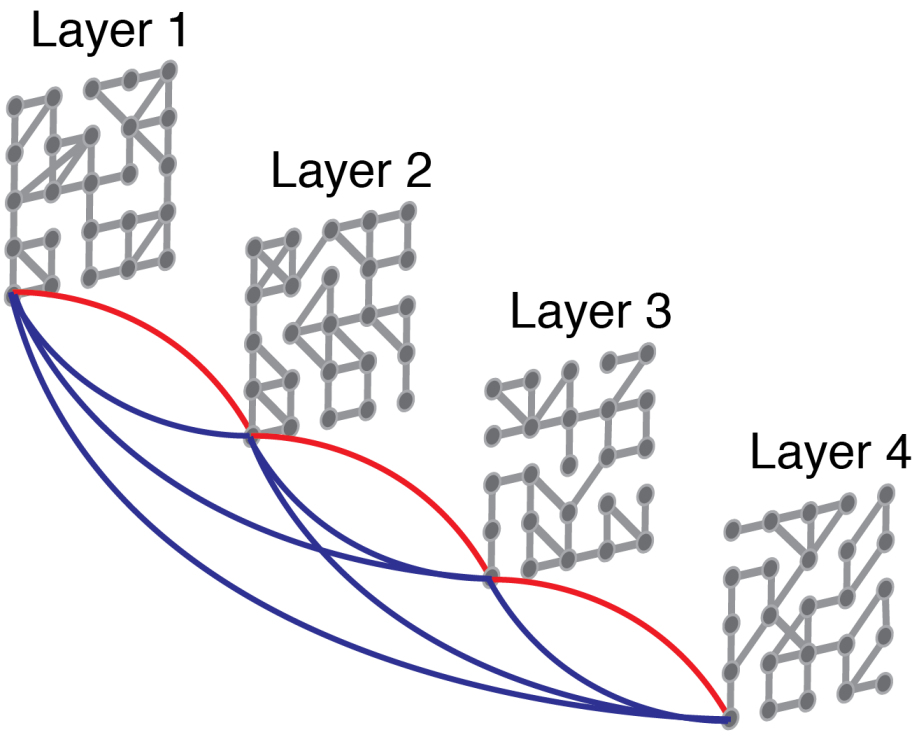
Multi-layer network model

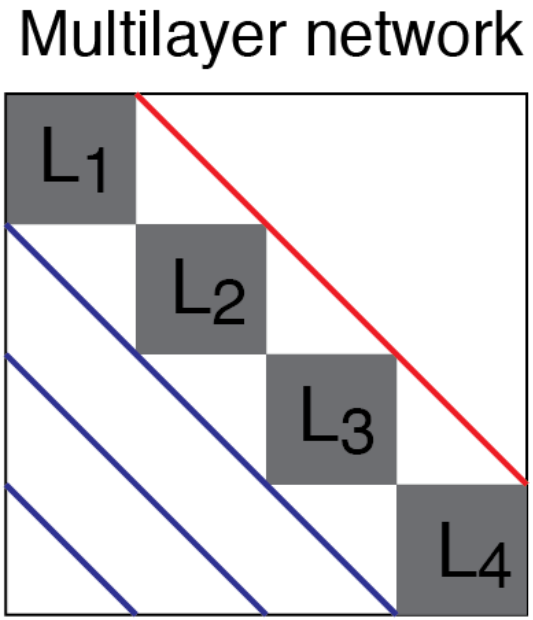
How to analyze a set of networks?

1. Treat each observation as a **layer**.

2. Link each node to itself (identity links) across layers to form a **multi-layer network**.

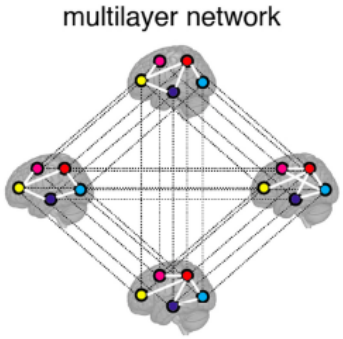






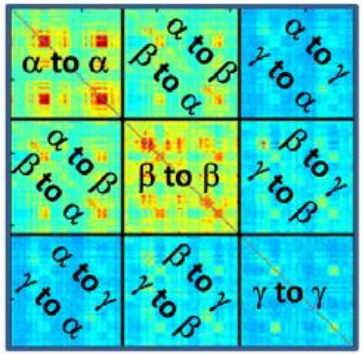
Kivelä et al. (2014). *Journal of complex networks*, 2, 203.

Multi-layer network model in neuroscience



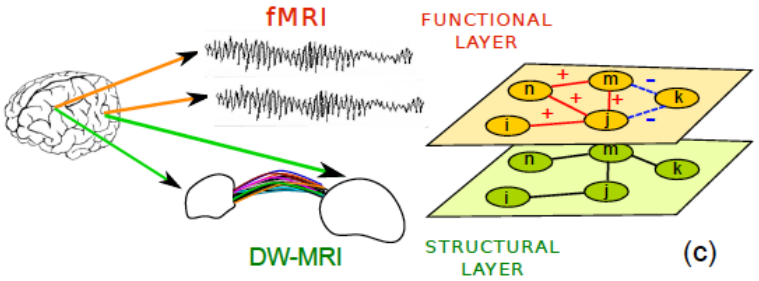
Multi-frequency networks: Layers represent frequency-specific FC

- De Domenico et al (2016). *FINS*.



Multi-frequency networks: Interlayer links represent cross-frequency coupling patterns.

- Brookes et al (2015). *Neuroimage*

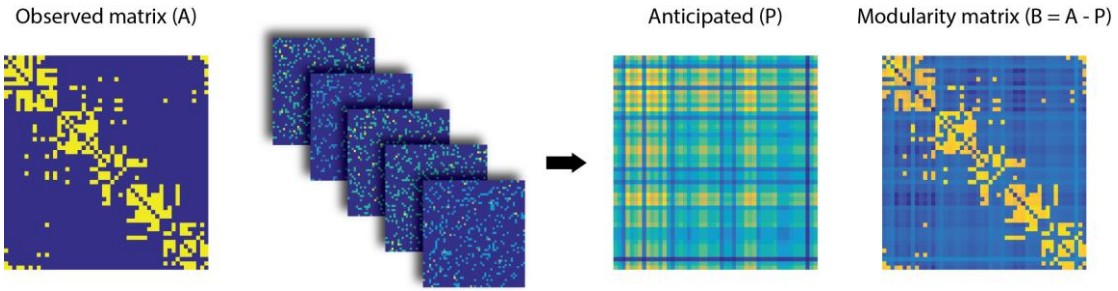


Multi-modal networks: Layers represent different imaging modalities, e.g. fMRI and dMRI

- Battison et al (2016). *arXiv*.

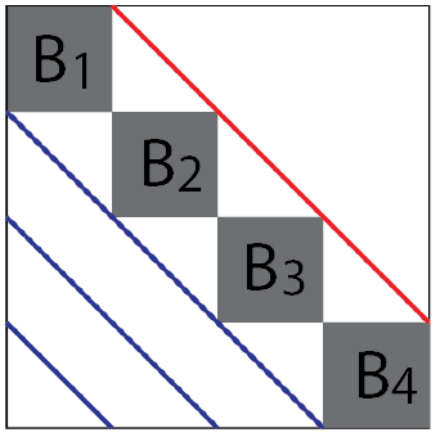
Multi-layer modularity and network flexibility

Community detection algorithms partition network nodes based on topology:

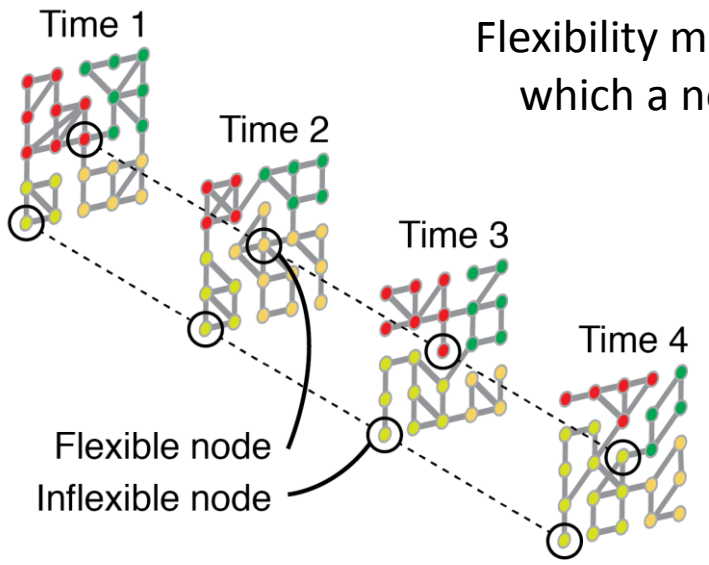


$$Q = \sum_{ij \in C} \left[A_{ij} - P_{ij} \right] \delta(g_i, g_j)$$

- Extended to multi-layer networks (Mucha et al 2011, *Science*)



$$\sum_{ijrs} \left[(A_{ijr} - \gamma_r P_{ijr}) \delta_{rs} + \delta_{ij} C_{jrs} \right] \delta(g_{ir}, g_{js})$$



Flexibility measures the frequency with which a node changes its community assignment across layers.

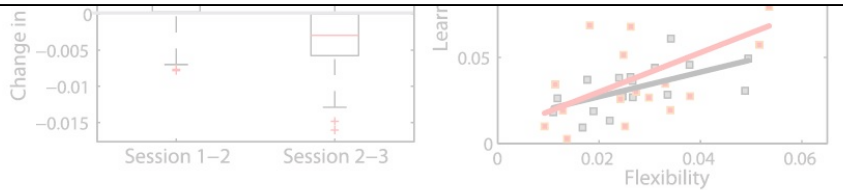
For a review of community detection and brain networks: Sporns & Betzel (2016). Annual Review of Psychology

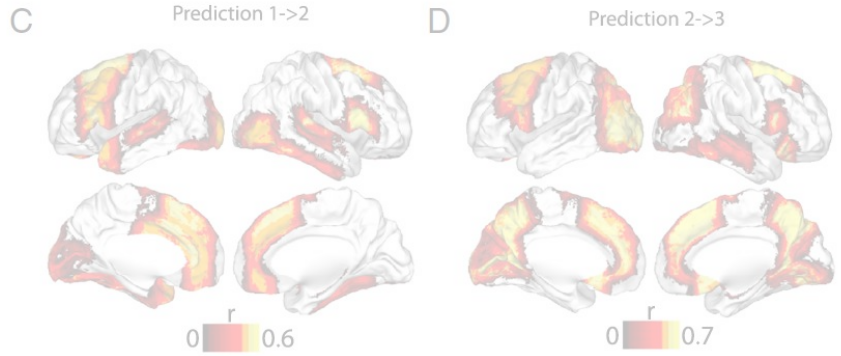
Network flexibility in learning, executive function, disease

Flexibility predicts:

- Executive function (Braun et al 2015, *PNAS*)
- Varies with disease (Braun et al 2015, *PNAS*)
- Varies with age (Betzel et al 2015, *arXiv*)
- Learning rate (Basset et al 2011, *PNAS*; Basset et al 2015, *NatNeuro*)

- Varies day to day
- Associated with cognitive performance
- What exogenous factors influence flexibility?

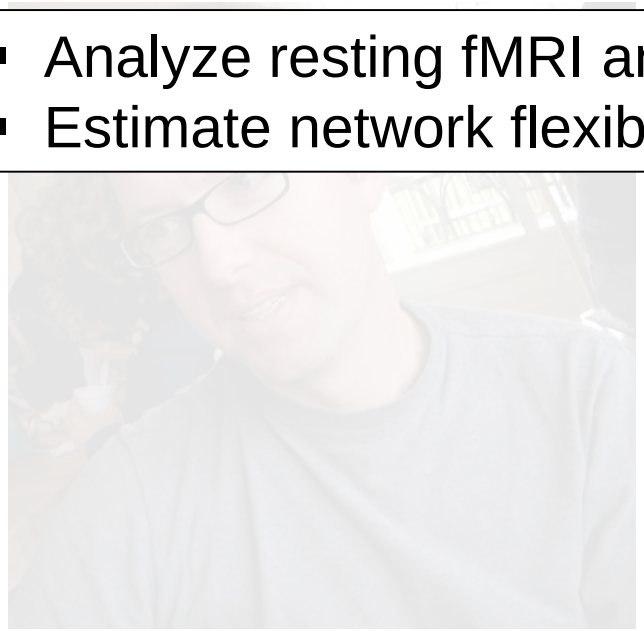




Bassett et al. (2011). *PNAS*, 108(18), 7641-7646.

MyConnectome Project

- Analyze resting fMRI and questionnaire data separately.
- Estimate network flexibility and test for affect-based correlates.



Russ Poldrack

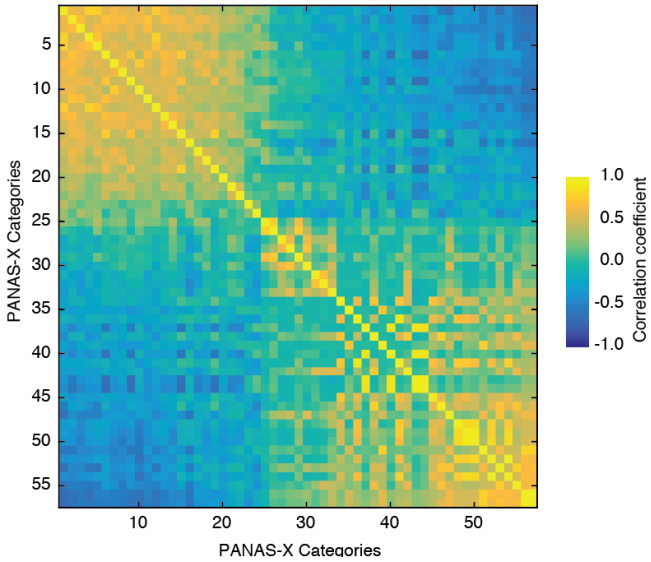
- Rest/task fMRI
- DWI
- Mood questionnaire
- Metabolomics

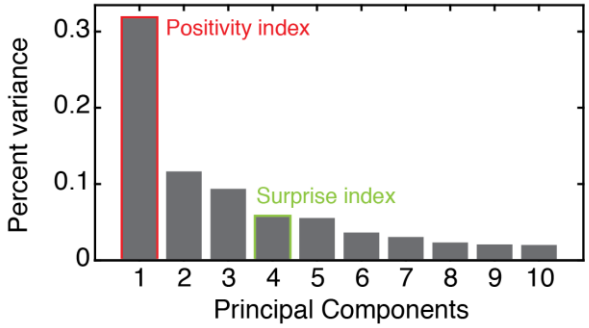
Laumann et al (2015) *Neuron,* 87, 657.

Poldrack et al (2015) *Nat. Comm.* 6.

Quotidian variability in mood questionnaire responses

- 60 questions about mood (PANAS-X)



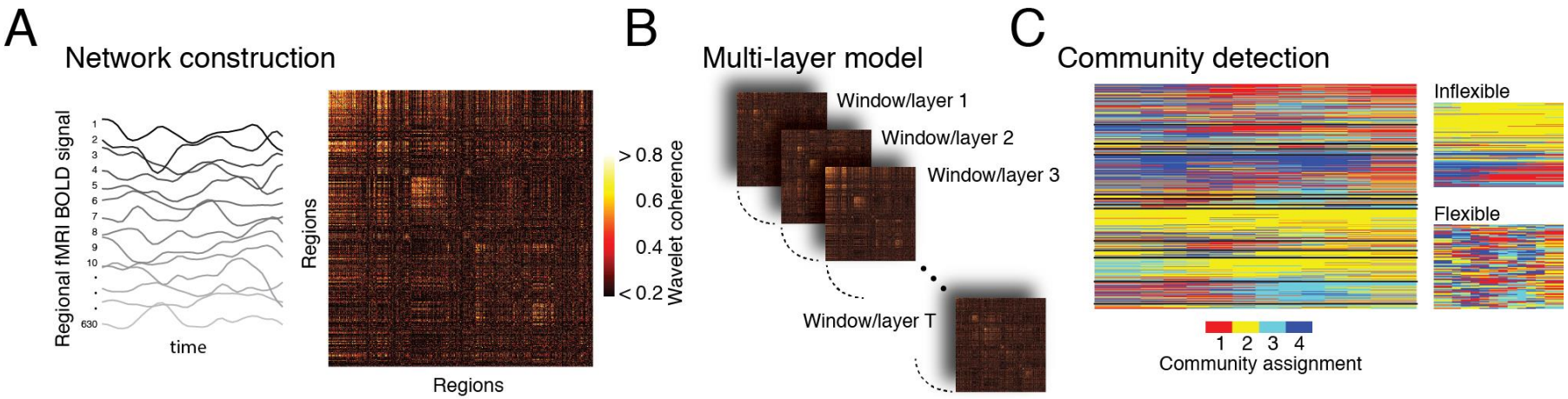


Betzel et al (2016). *Scientific Reports*.

Analysis of resting fMRI data

Analyze 73 recording sessions.

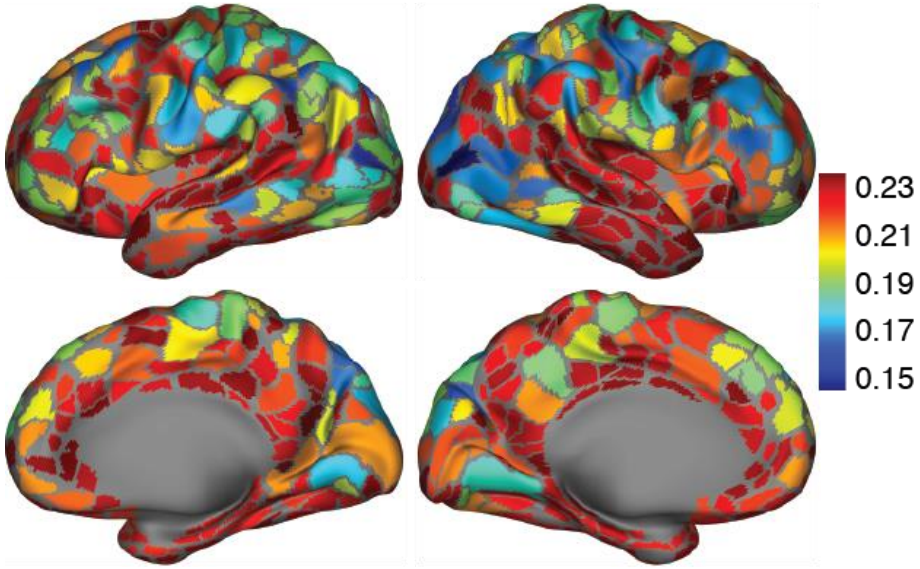
1. Extract fMRI BOLD time series from 630 parcels
2. Divide into 14 non-overlapping windows (37 TR)
3. Construct wavelet coherence matrices within each window
4. Identify communities using multi-layer modularity maximization
5. Compute regional and global flexibility



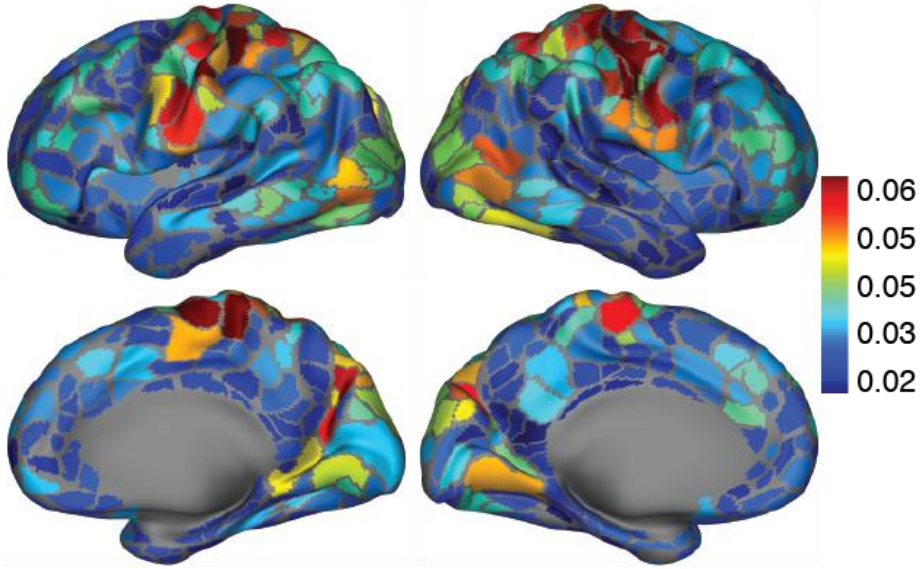
Betzel et al (2016). *Scientific Reports*.

Quotidian variability in regional flexibility

Across scan sessions…



Mean regional flexibility

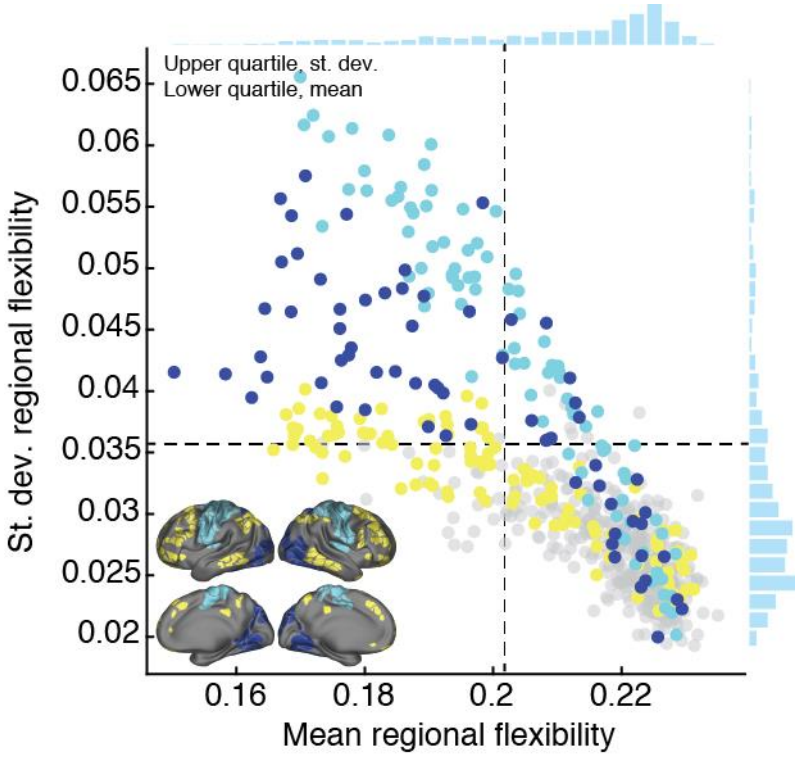


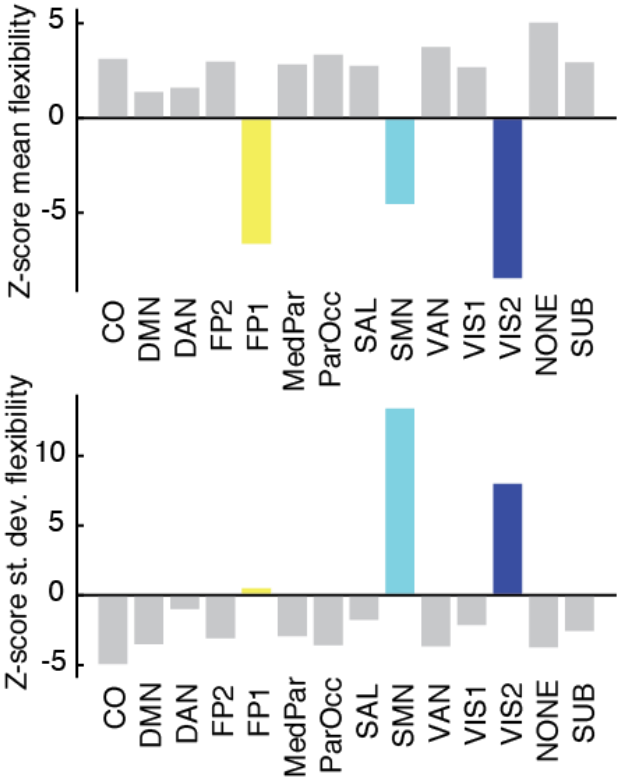
St. dev. regional flexibility

Betzel et al (2016). *Scientific Reports*.

Quotidian variability in regional and global flexibility

Are flexibility patterns uniform or region/system specific?



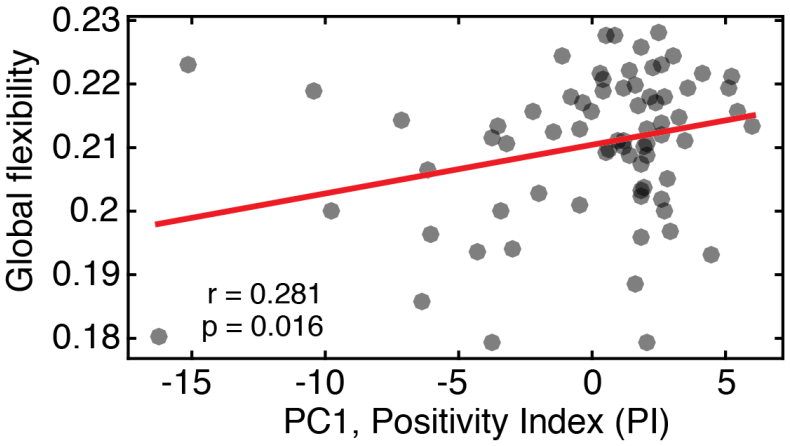


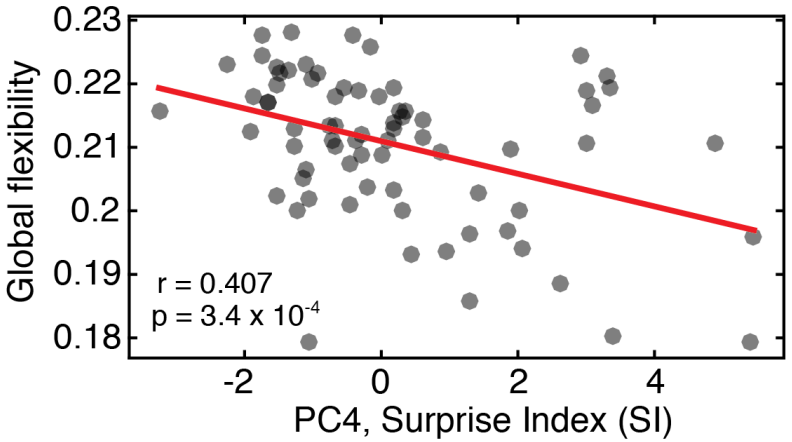
- Fronto-parietal, somatomotor, visual networks least flexible
- Somatomotor and visual networks most variable across sessions

Betzel et al (2016). *Scientific Reports*.

Relating mood indices to flexibility

Test linear relationship of mood indices with **global flexibility** (regional average).



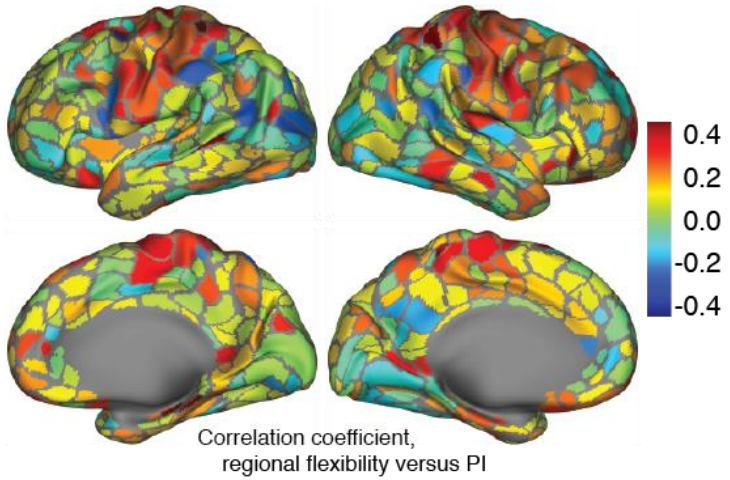


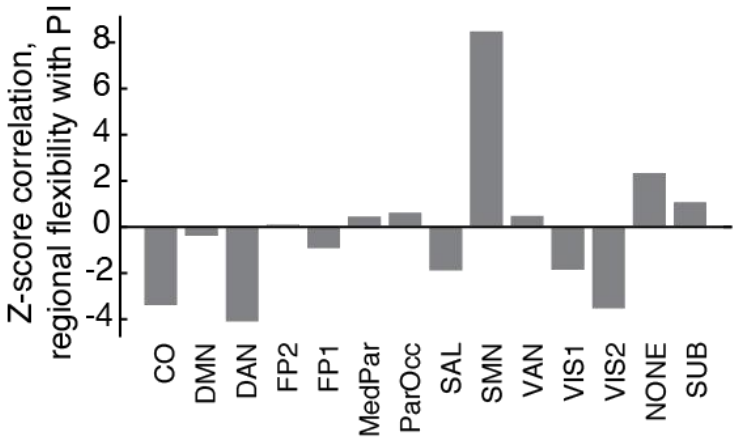
- Self reported positivity implies increased network flexibility
- Self reported surprise implies decreased network flexibility

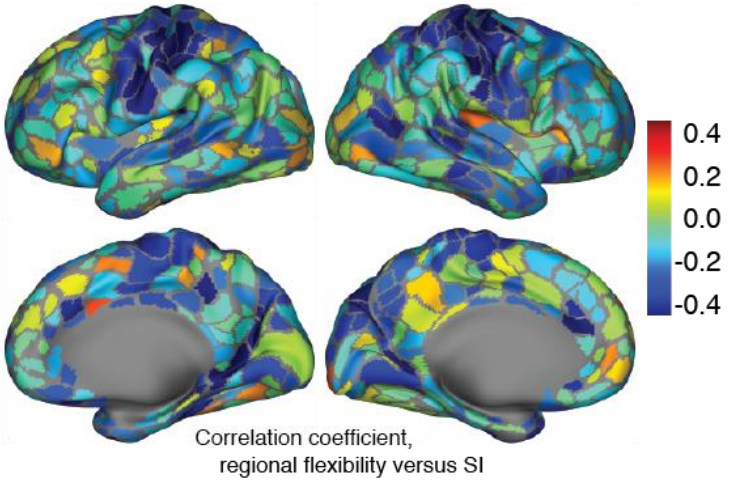
Betzel et al (2016). *Scientific Reports*.

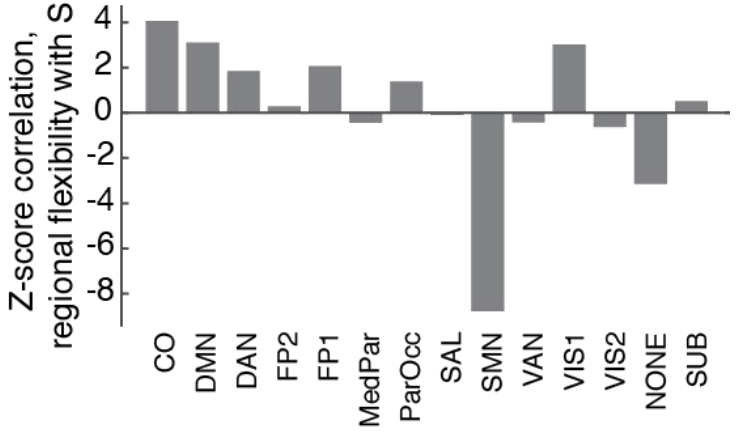
Relating mood indices to flexibility

Relationship is driven by the **regional flexibility** of somatomotor network.









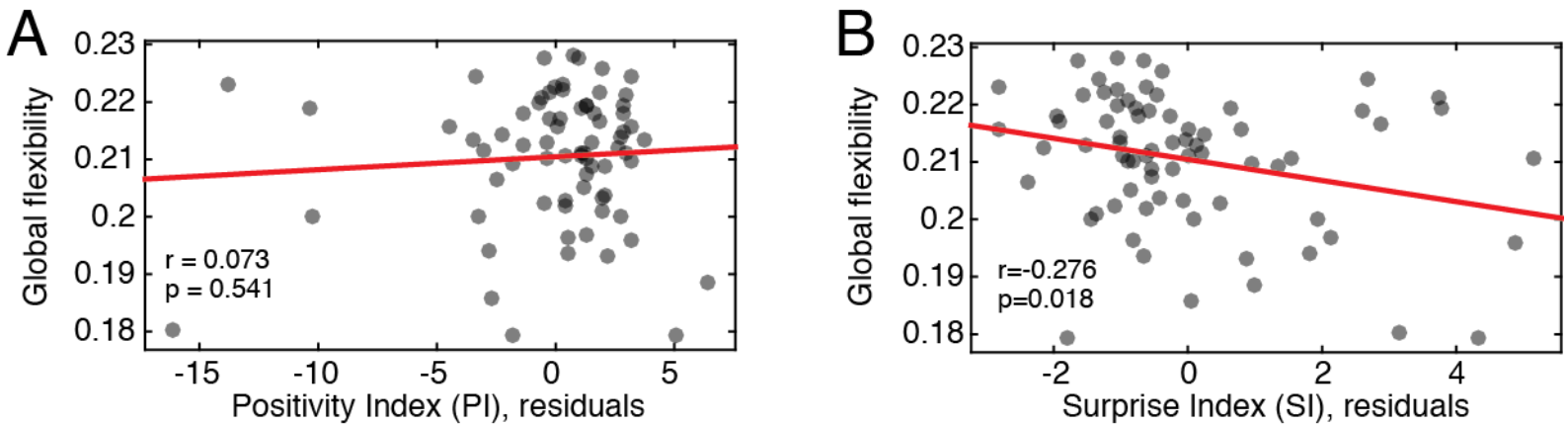
Betzel et al (2016). *Scientific Reports*.

Relating mood indices to flexibility

Possible confounds:

- In-scanner head motion
- Outlying scans/responses
- Non-parametric correlations
- Other psycho-physiological measurements (e.g. sleep, diet, tinnitus, weather)
- Frequency-band specific
- Community detection parameters
- Window length

Self-reported fatigue, however, was correlated with positivity but not surprise.



Betzel et al (2016). *Scientific Reports*.

Summary and outlook

Interested in whether day-to-day variation in flexibility could be explained by behavior/lifestyle.

Remember… *N* = 1

- Suggests a network-level correlate of positive affect and surprise (state of arousal?)
- Flexibility has been associated with NMDA receptor function – suggests pharmacological pathway for modulating mood.
- Flexibility has been associated with learning – suggests that alterations to mood/fatigue/surprise can enhance learning.

Remember… *N* = 1

Betzel et al (2016). *Scientific Reports*.

Acknowledgements

Prof. Danielle Bassett
(Penn)

Prof. Ted Satterthwaite
(Penn)

Prof. Ian Gold
(Penn)

MacArthur Foundation

Alfred P. Sloan Foundation

NIMH National Institute of Mental Health

NSF

Eunice Kennedy Shriver NICHD National Institute of Child Health & Human Development