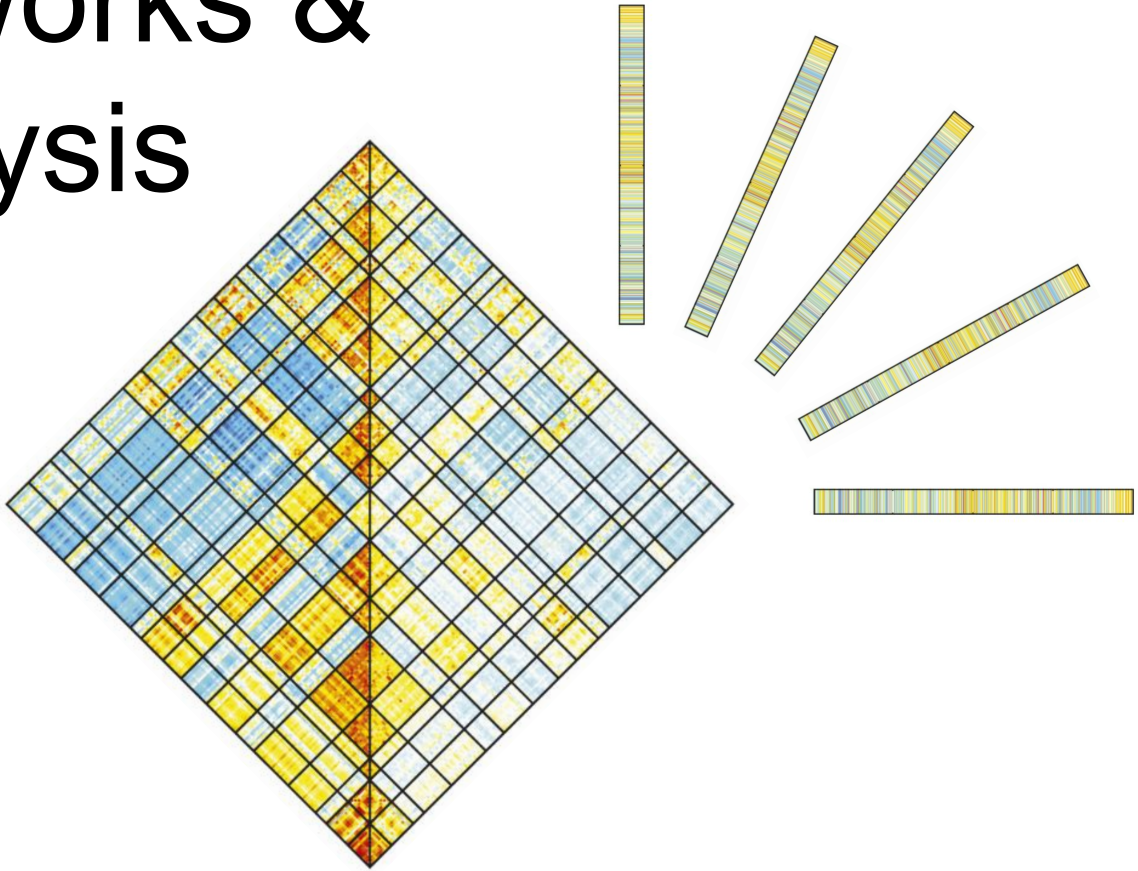
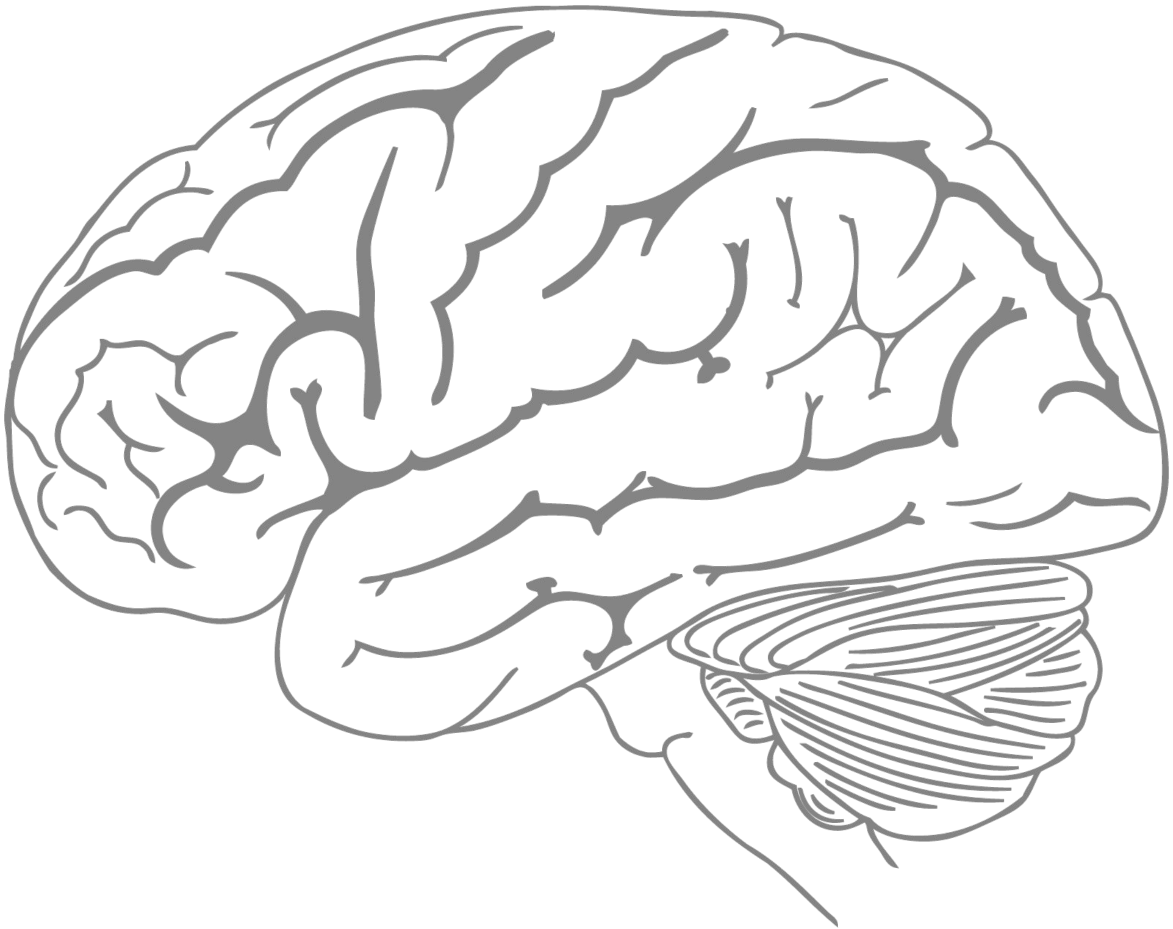
Brain networks & edge analysis



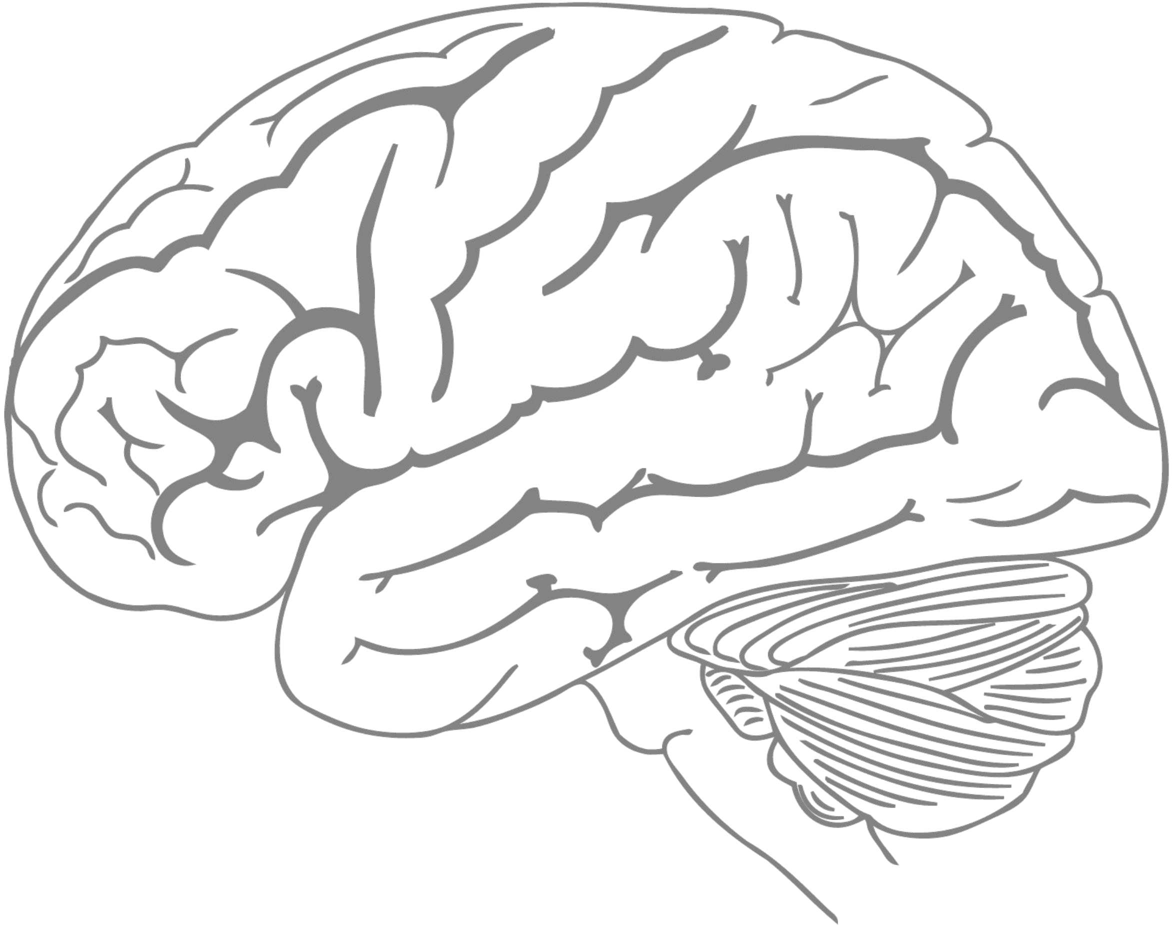
National Institute of Mental Health

Josh Faskowitz

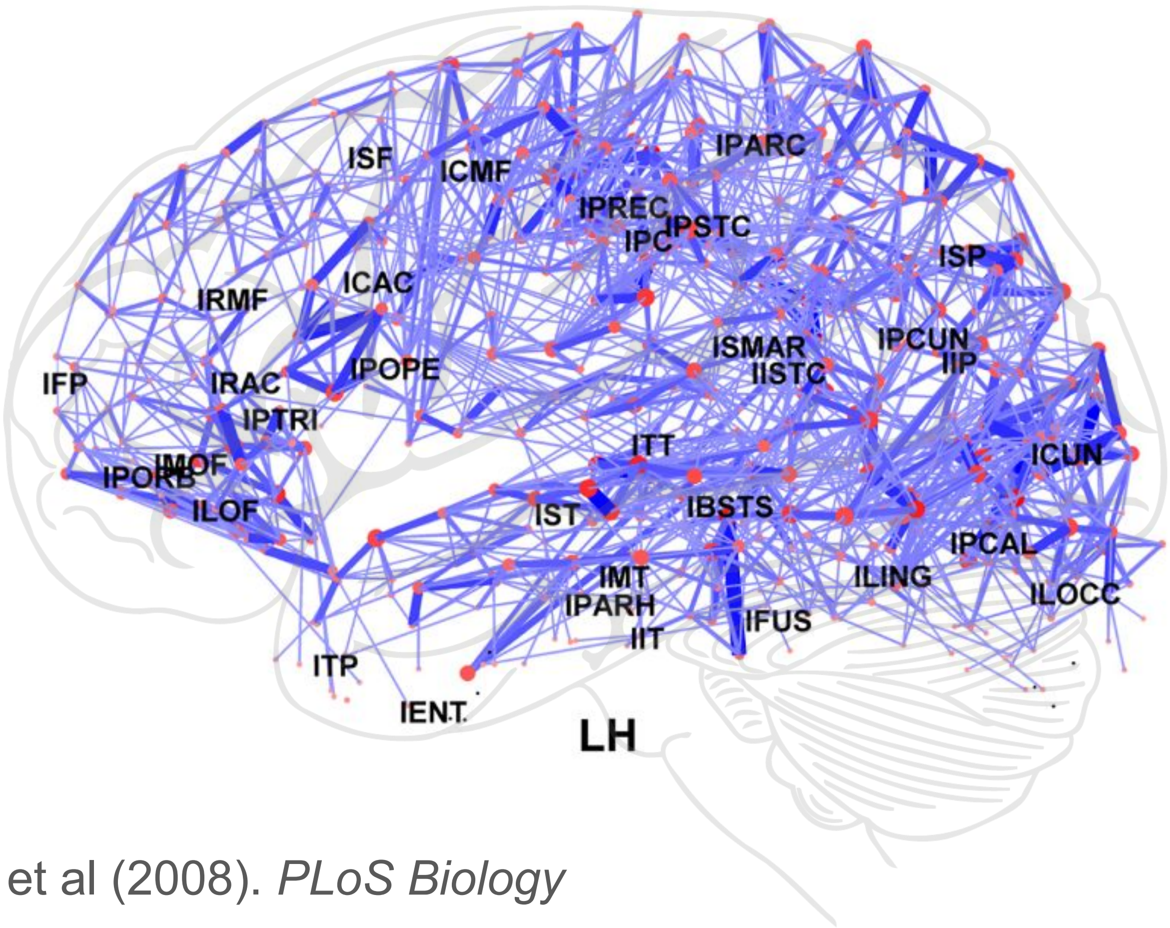


Overview

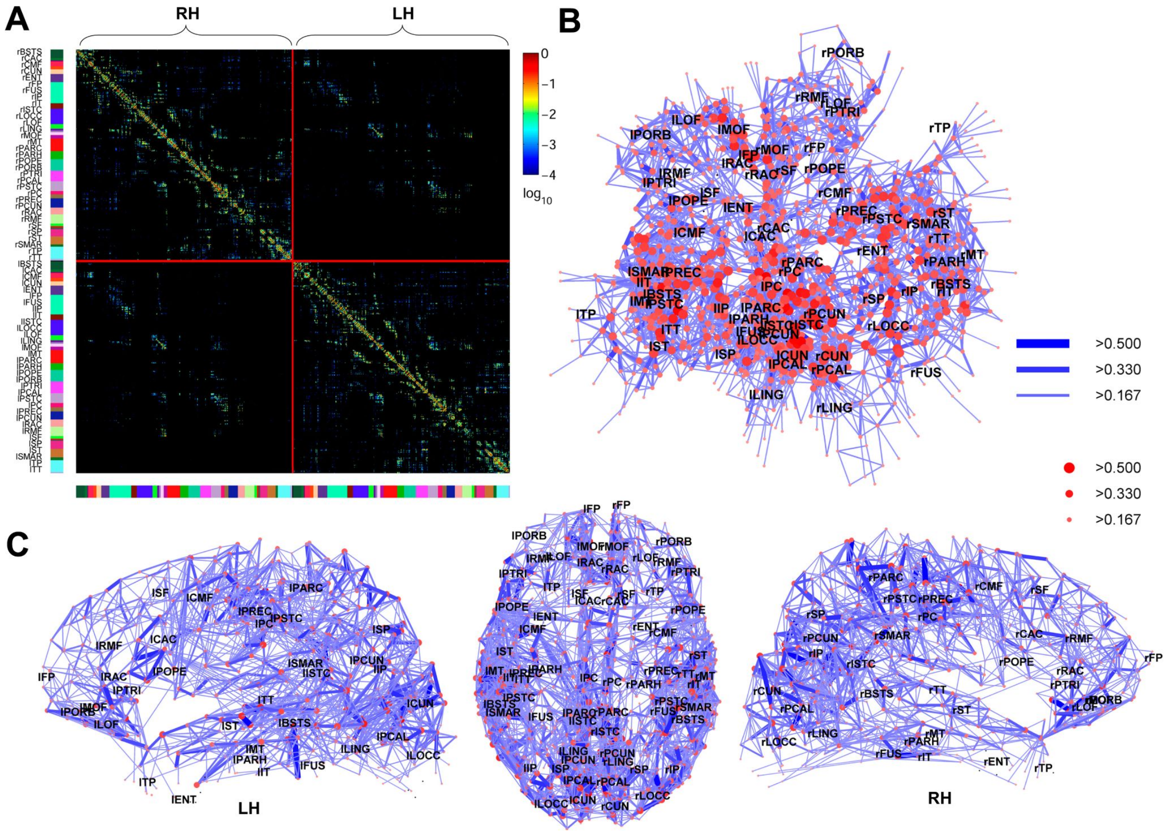
- Brain networks intro
- How we make functional networks
- The edgy approach to functional networks



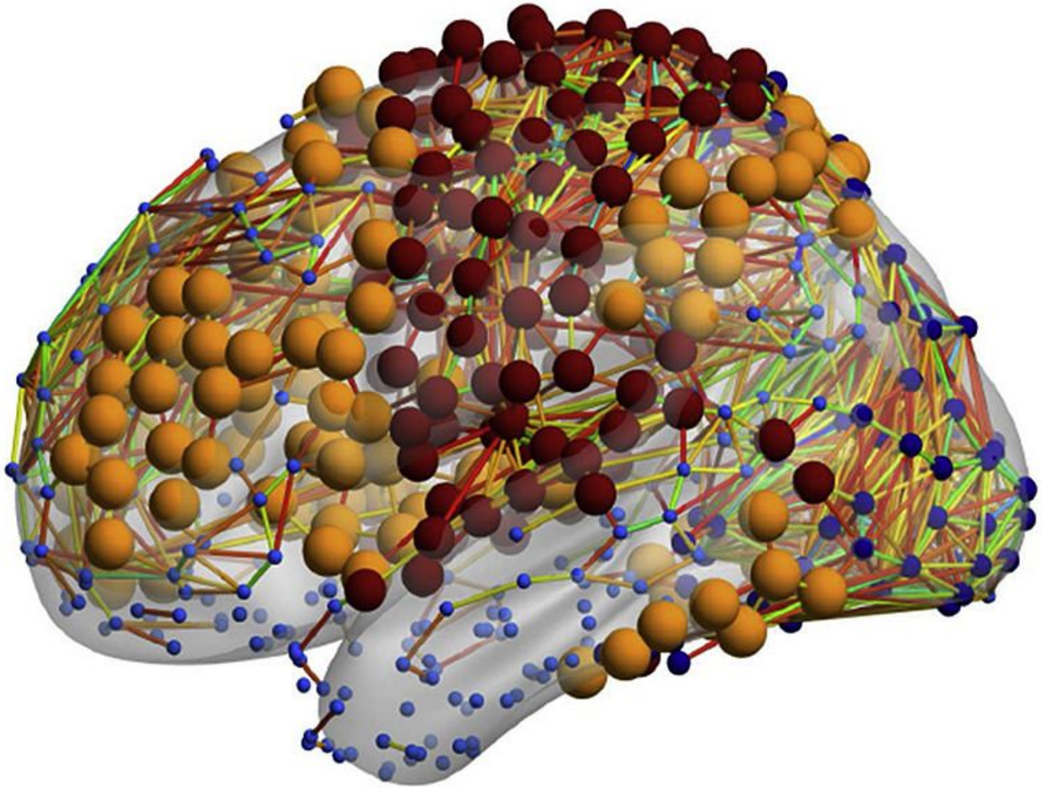
The brain as a networked system



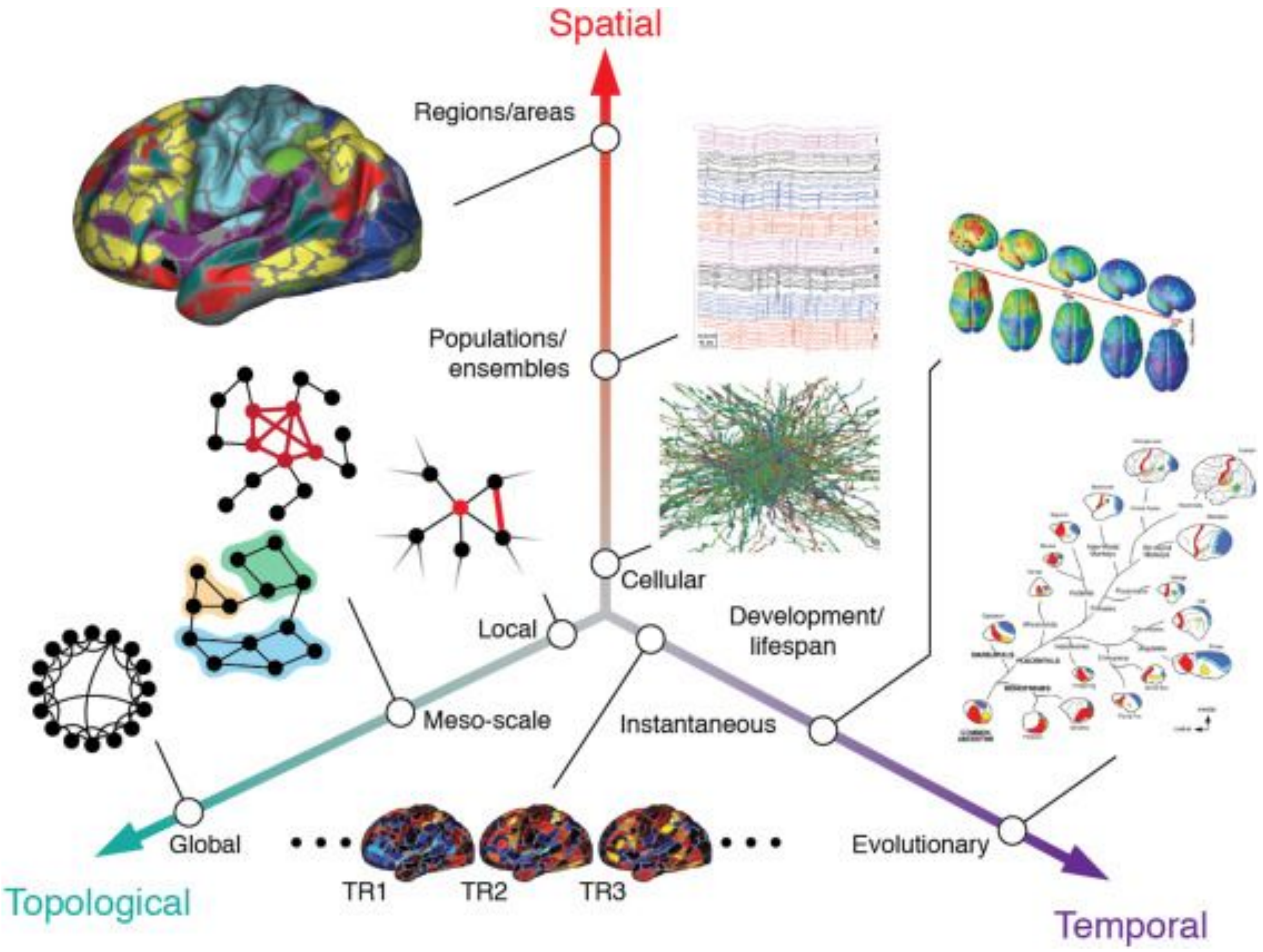
Hagmann et al (2008). *PLoS Biology*



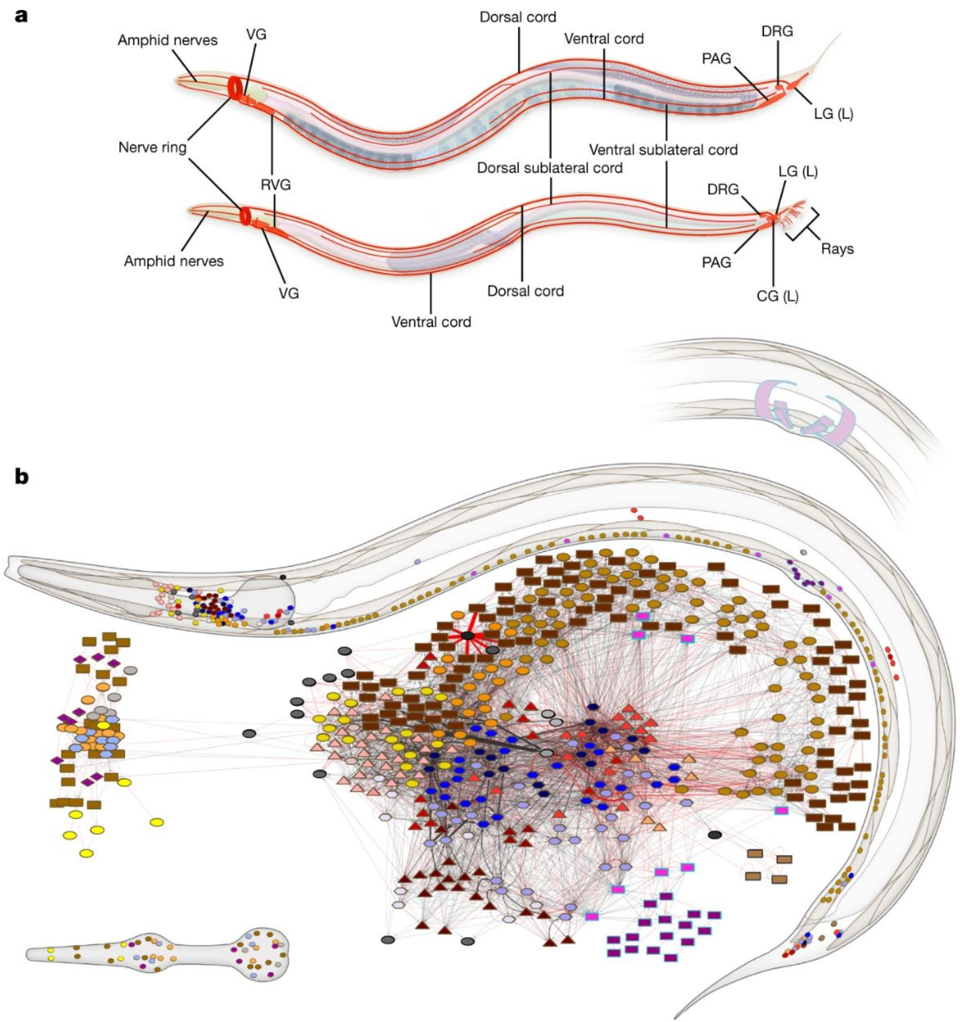
Hagmann et al (2008). *PLoS Biology*



Nicolini et al (2020). *NeuroImage*

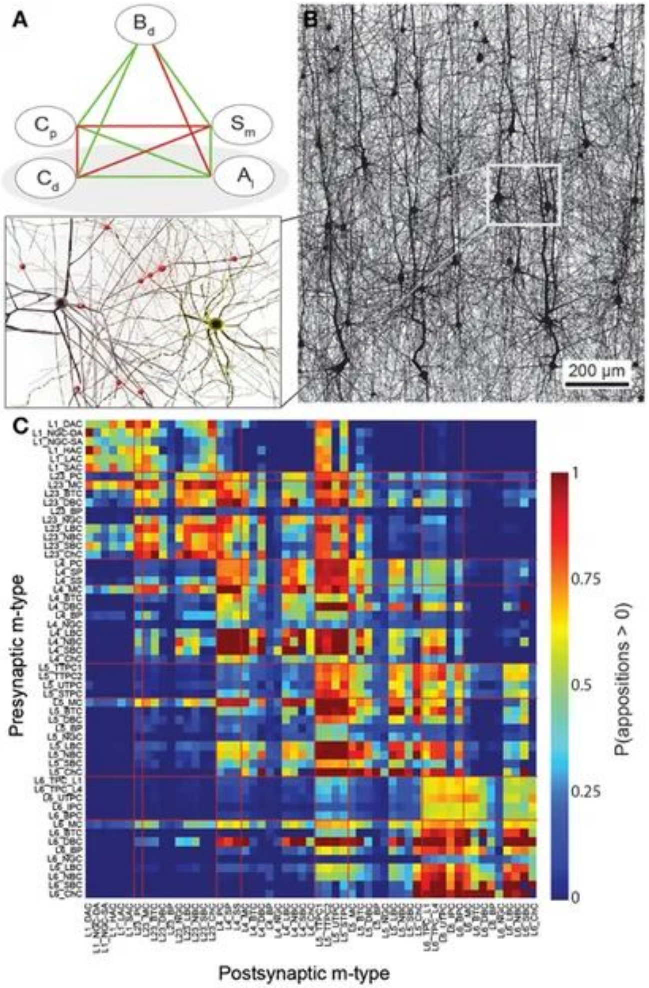


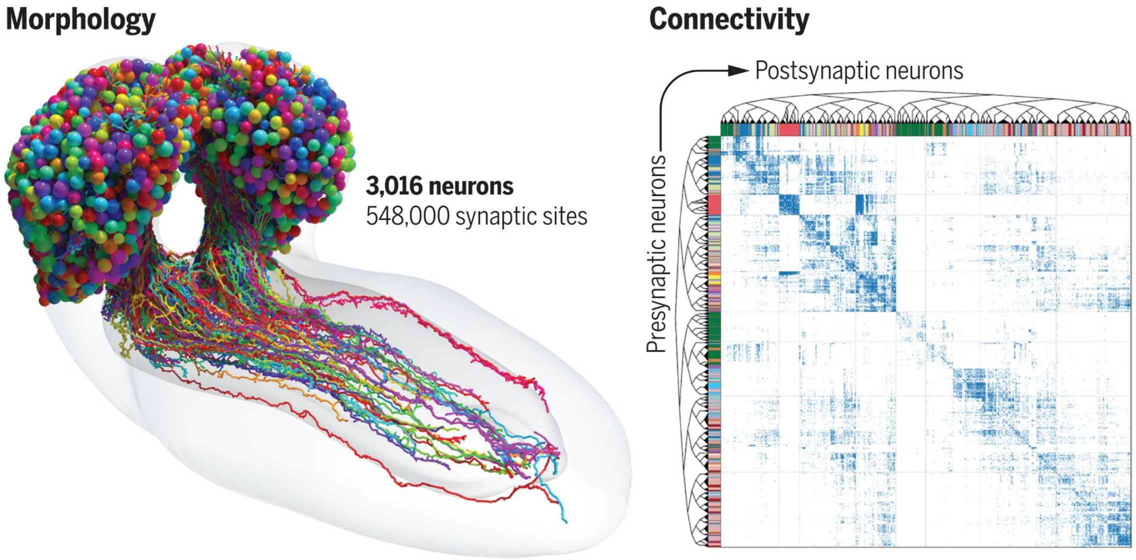
Betzel & Bassett
(2017).
NeuroImage



Cook et al
(2019) *Nature*

Micro

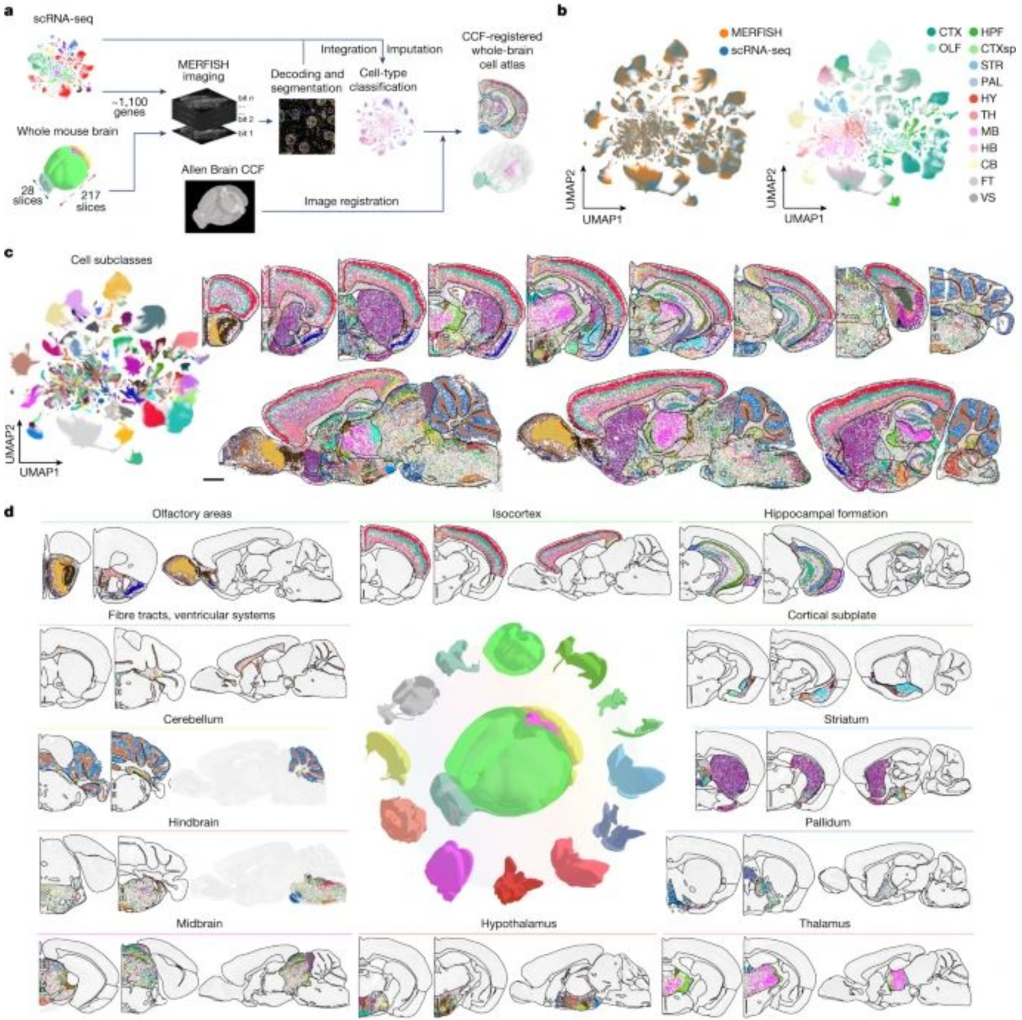




Winding et al. (2023) *Science*

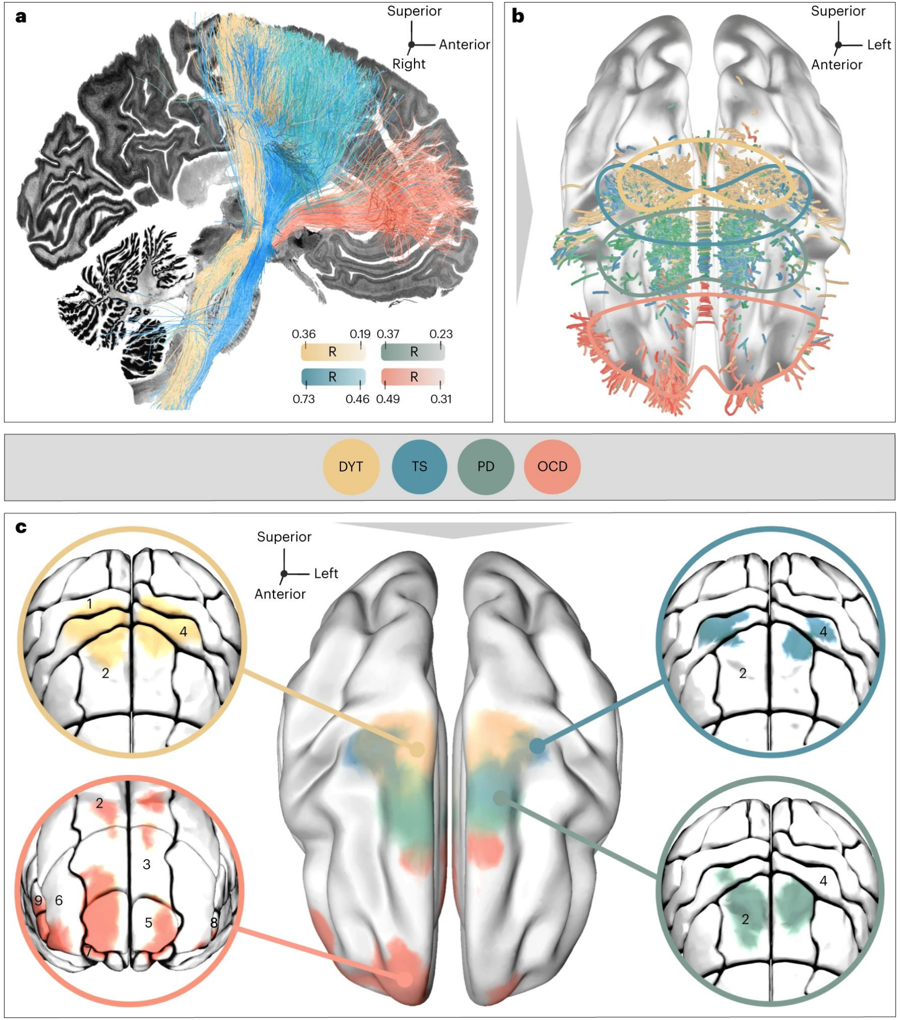
Reimann et al. (2015) *Front. Comp. Neuro*

Micro



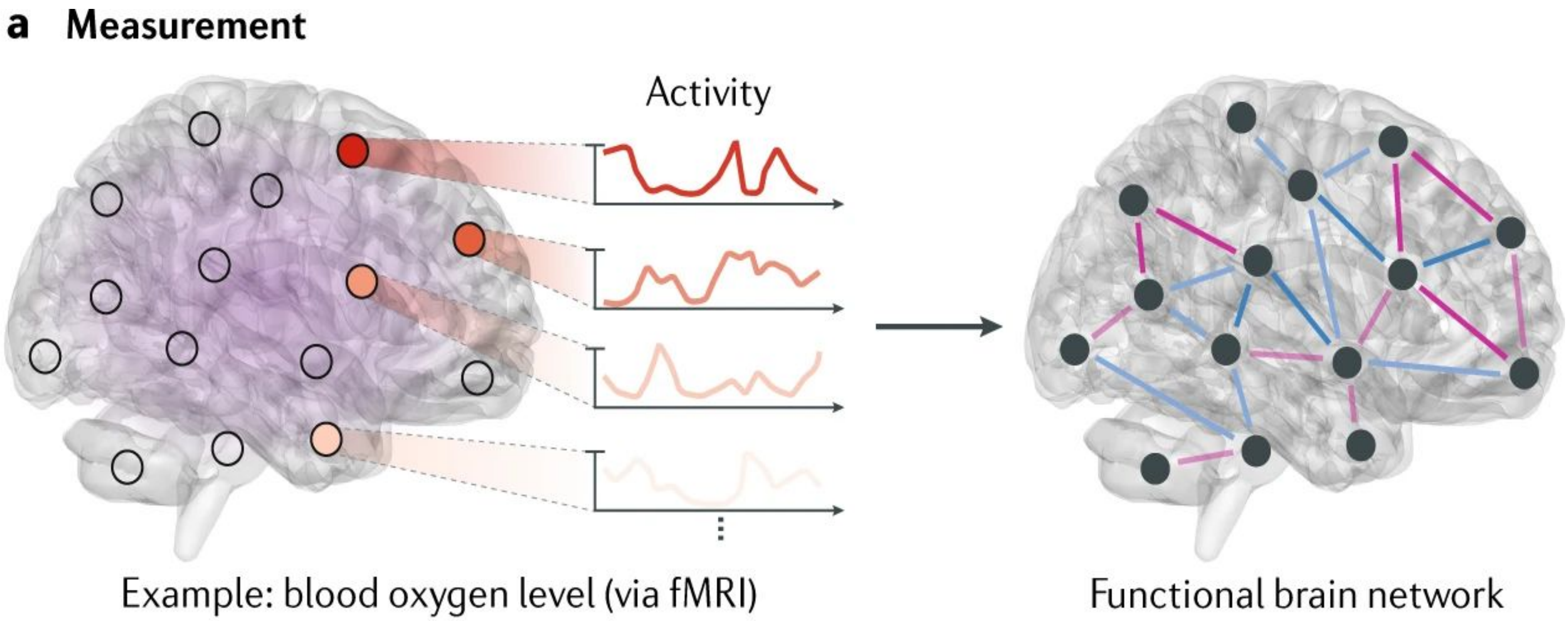
Zhang et al. (2023) *Nature*

Meso



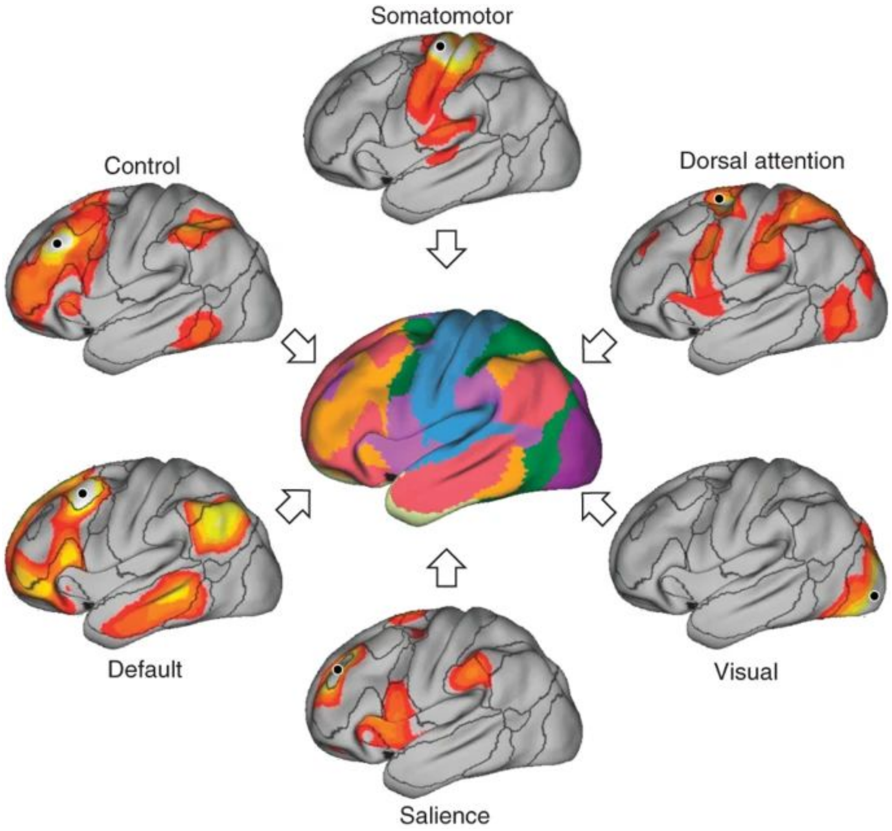
Hollunder et al (2024) *Nat. Neuro.*

Macro



Lynn & Bassett (2019). *Nat. Rev. Physics*

Macro

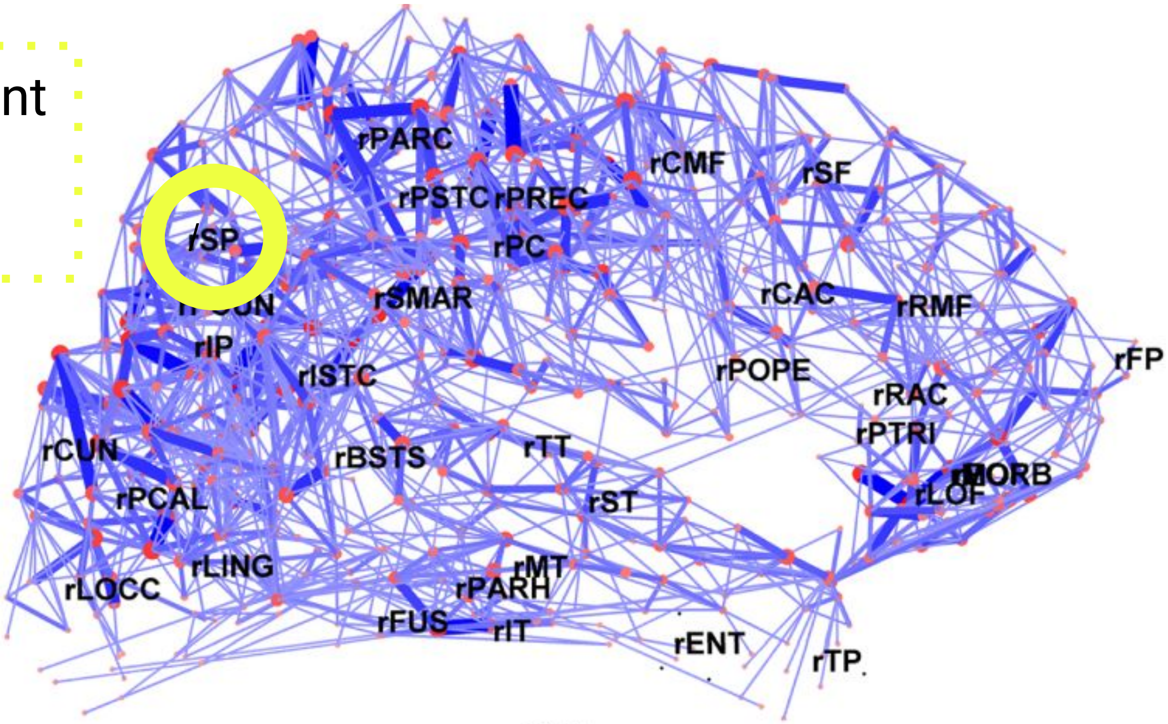


Buckner, Krienen & Yeo (2013). *Nature Rev Neuro*

Macro

Networks of the brain… why?

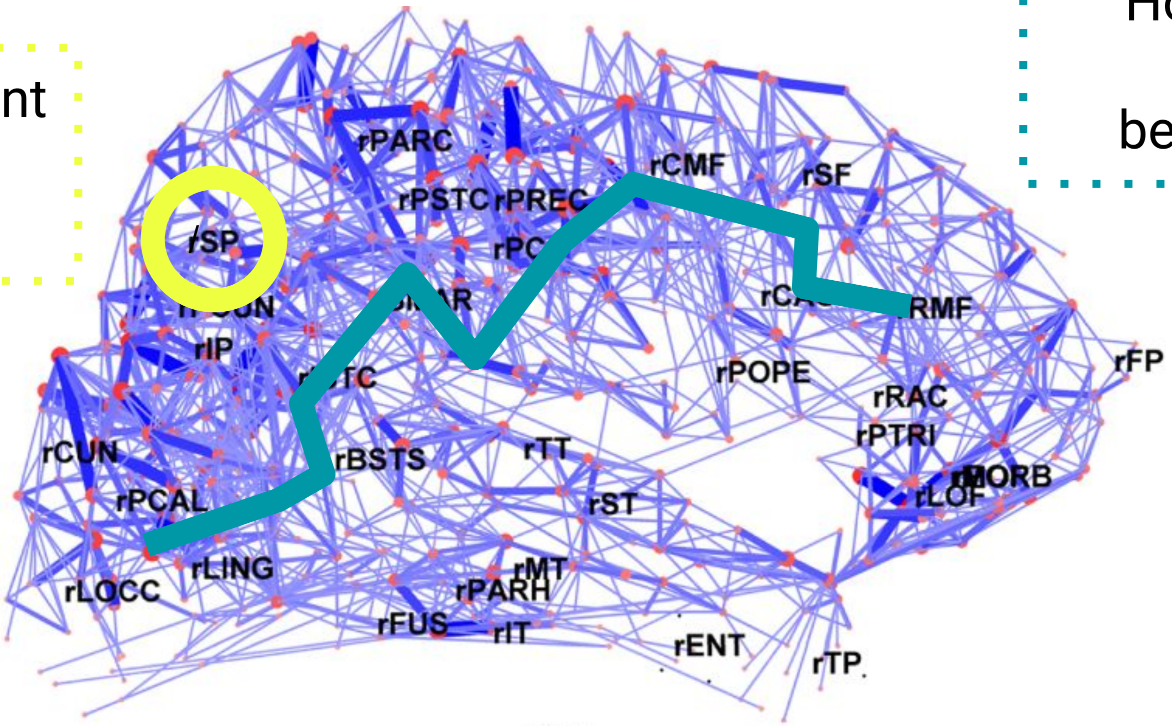
How important are certain nodes?



Hagmann et al (2008). *PLoS Biology*

How important are certain nodes?

How are signals transmitted between nodes?



Hagmann et al (2008). *PLoS Biology*

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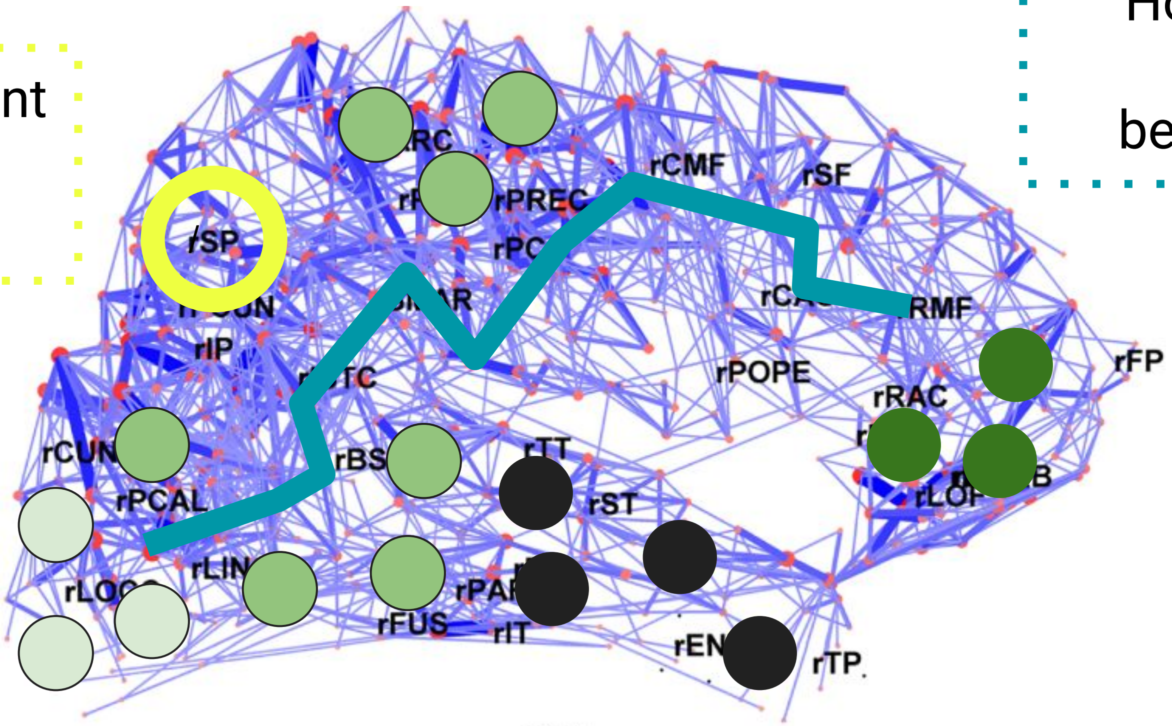


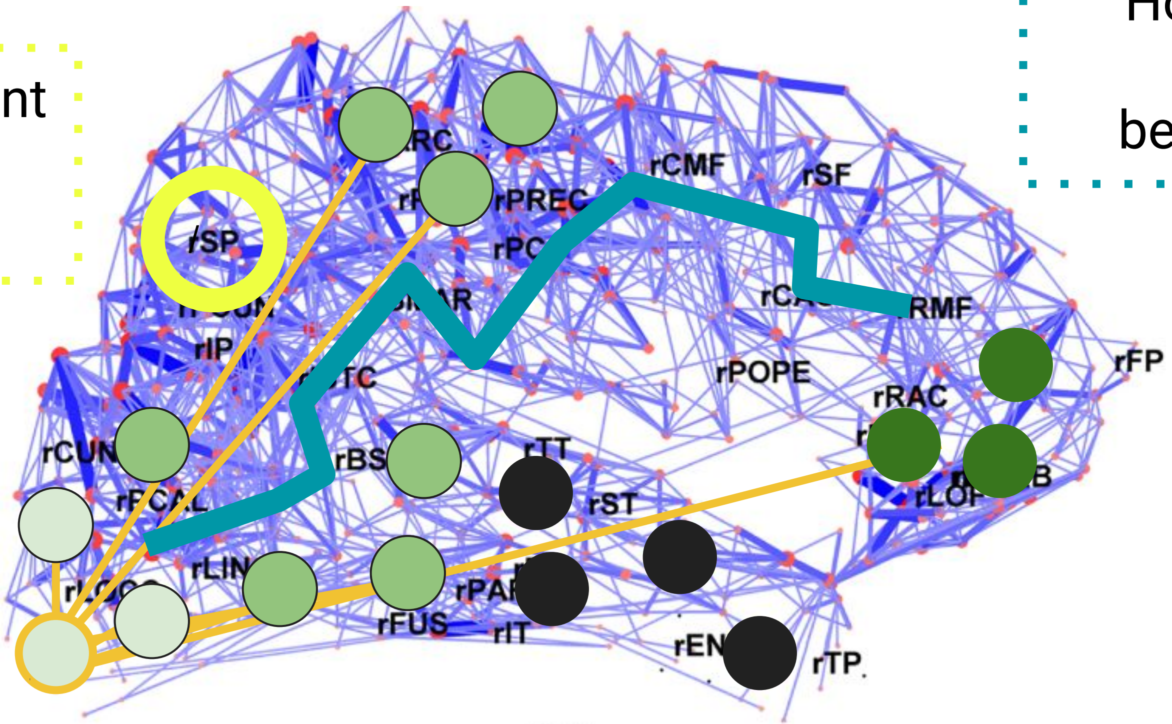
How are signals transmitted between nodes?

Which groups of nodes can be meaningfully grouped?

Hagmann et al (2008). *PLoS Biology*

How important are certain nodes?

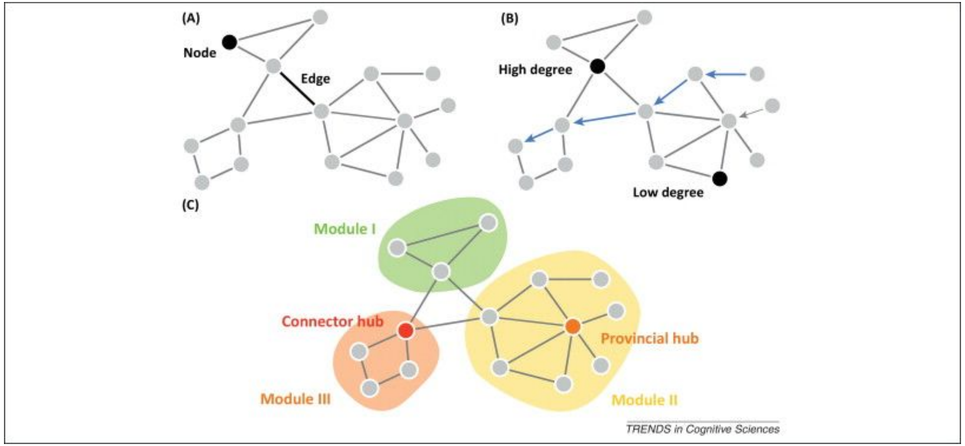
How are signals transmitted between nodes?

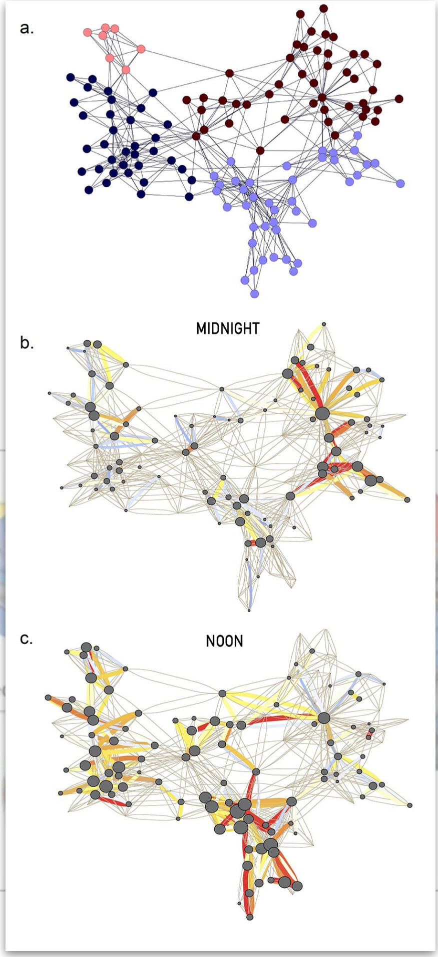


How can we interpret this area of the brain in the context of its connections

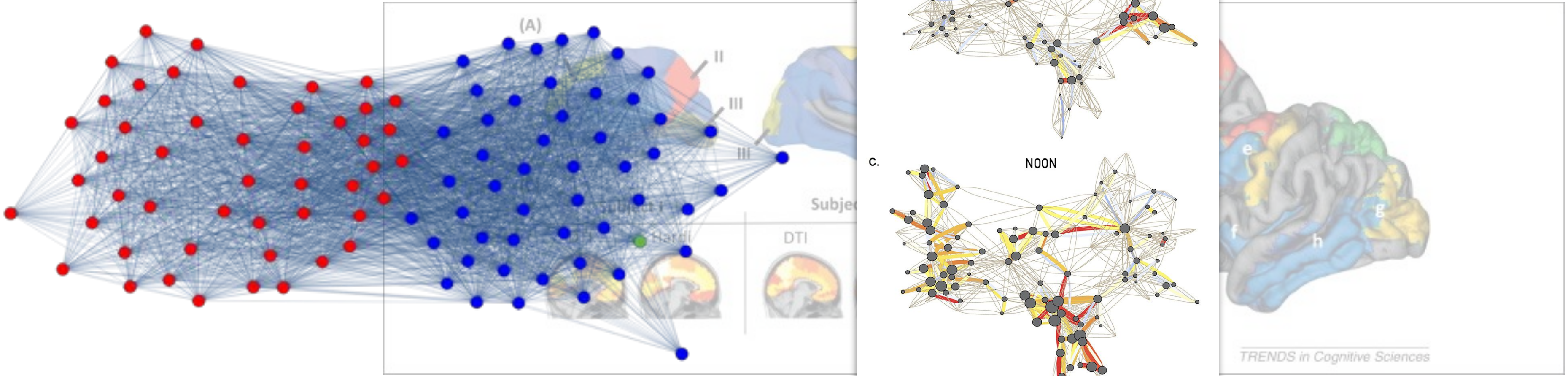
Which groups of nodes can be meaningfully grouped?

Hagmann et al (2008). *PLoS Biology*



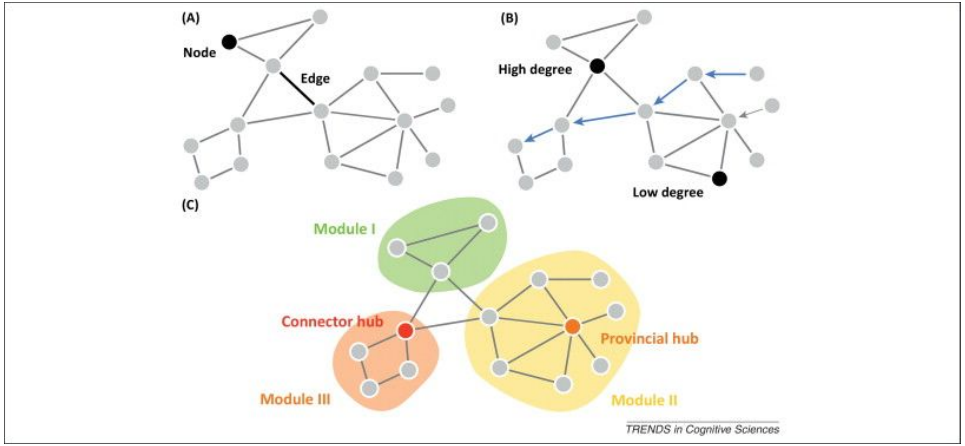


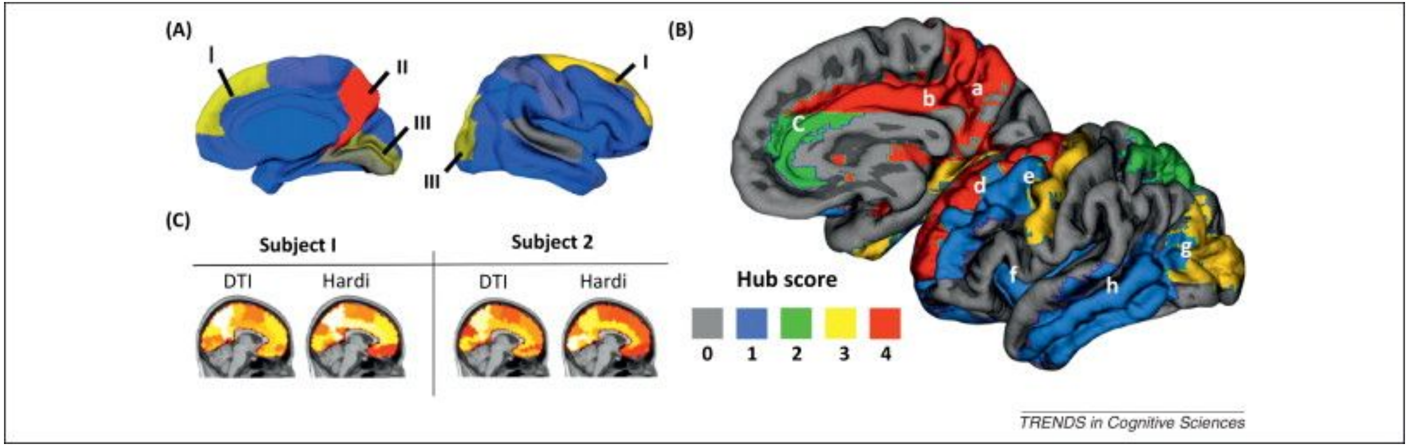
https://networksciencebook.com/chapter/9#summary9



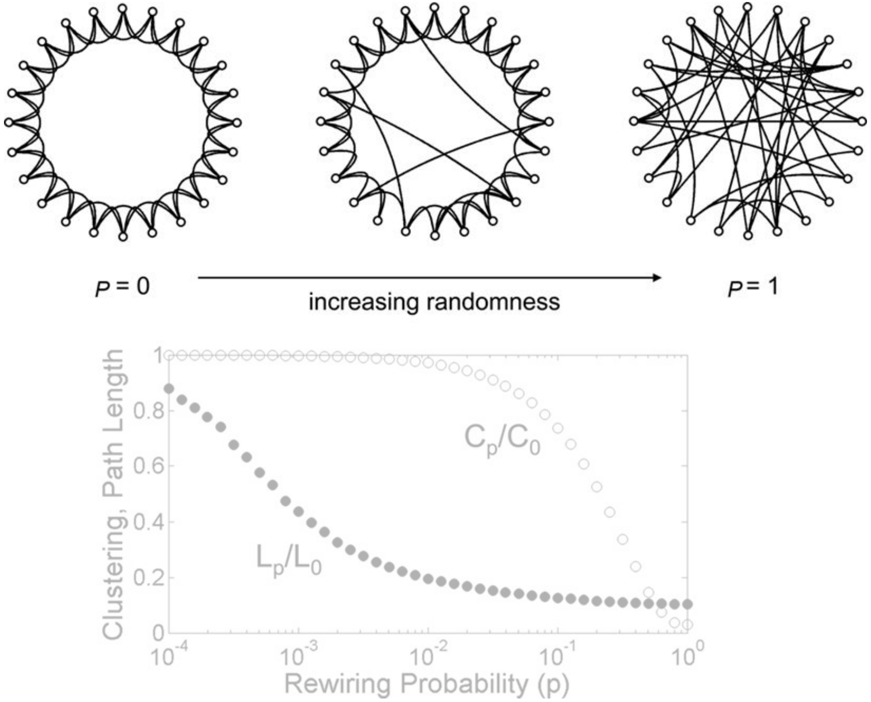
van den Heuvel & Sporns (2013) *TiCS*

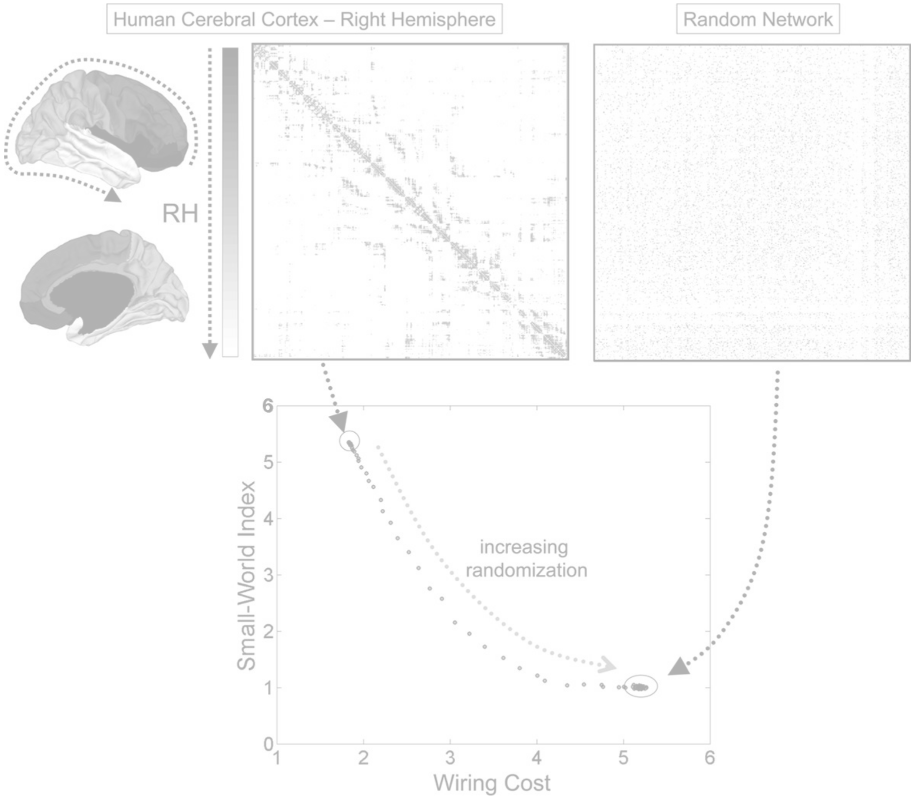
https://christopherwolfram.com/projects/voting-modularity/



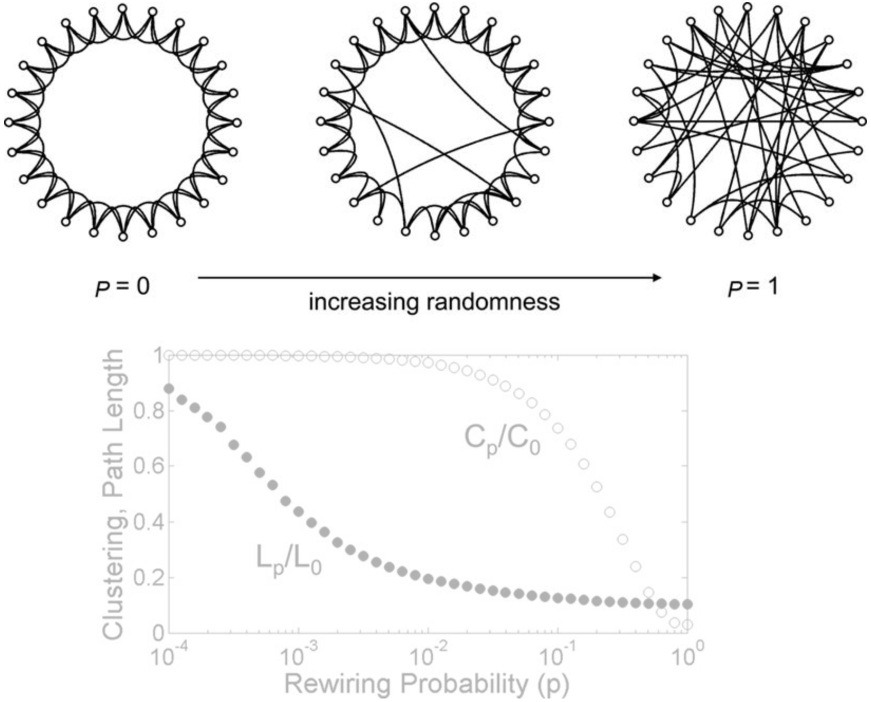


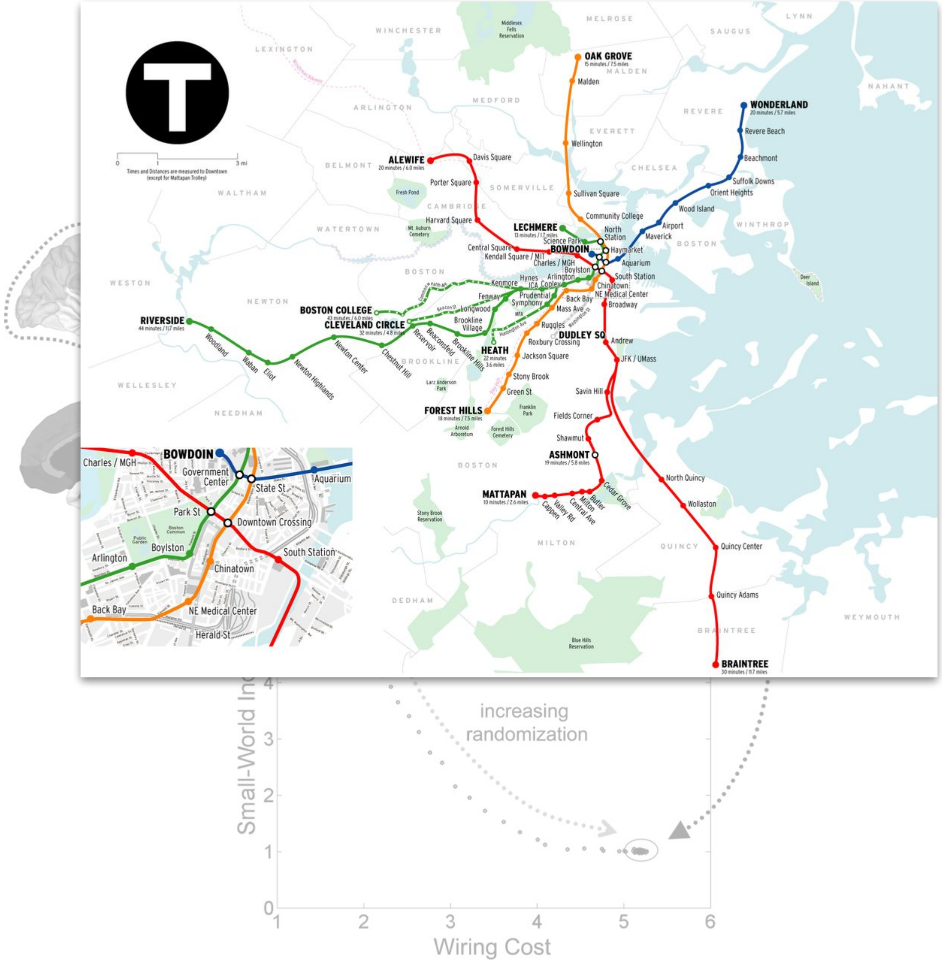
van den Heuvel & Sporns (2013) *TiCS*



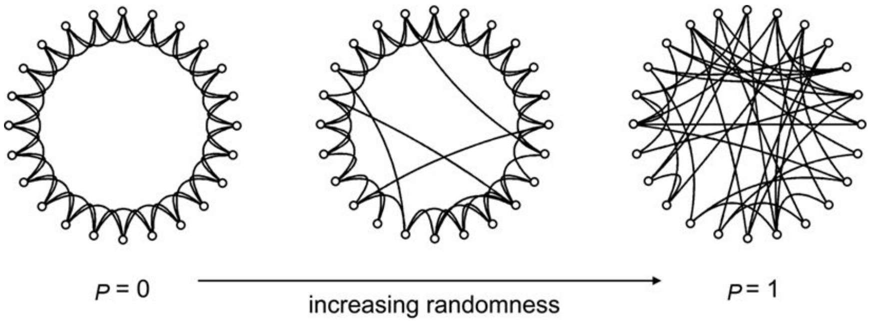


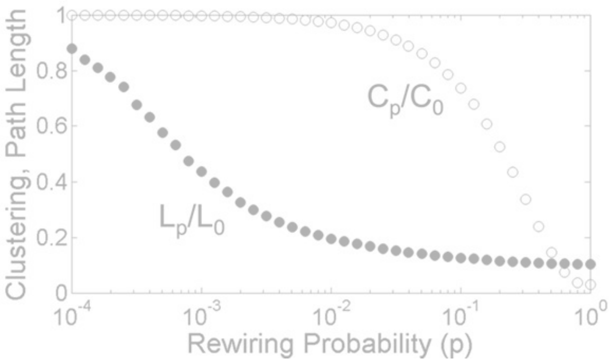
Sporns (2011) *Front. Comp. Neuro.*

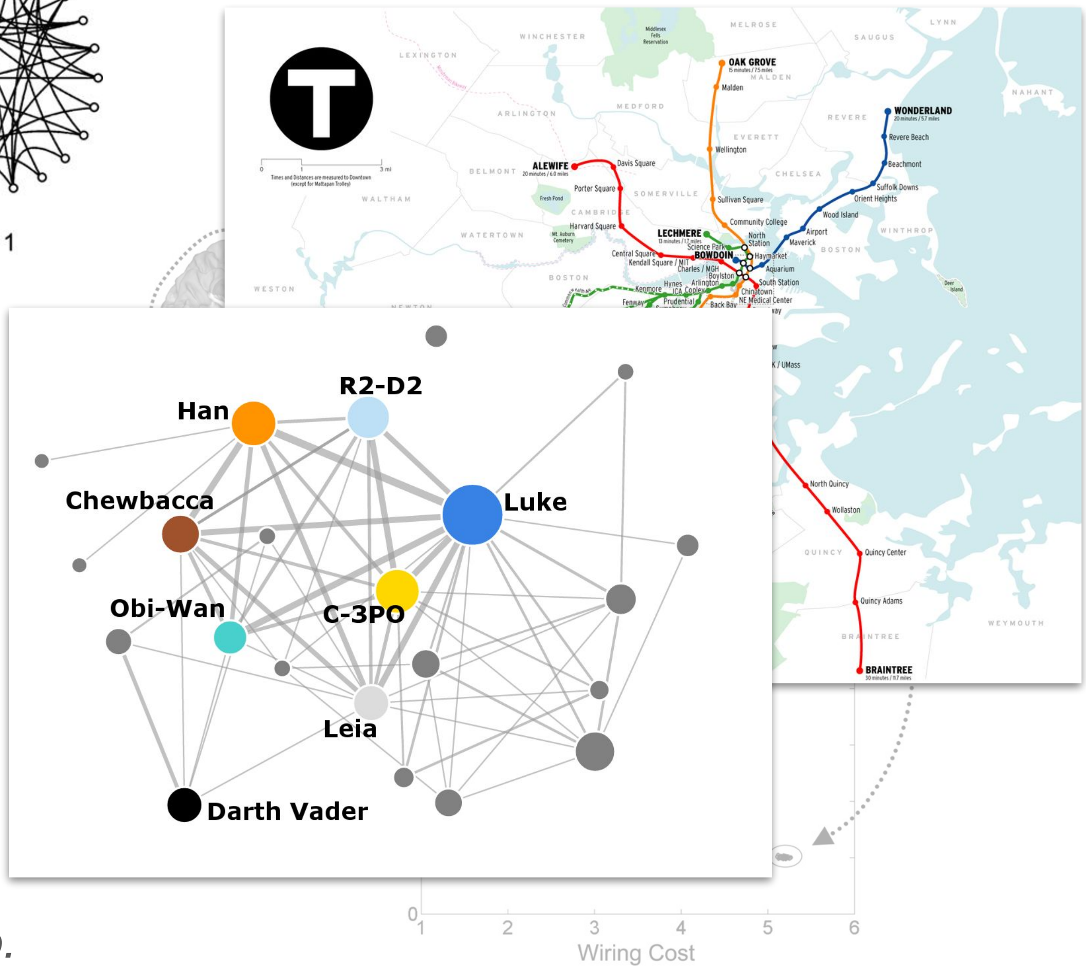




Sporns (2011) *Front. Comp. Neuro.*

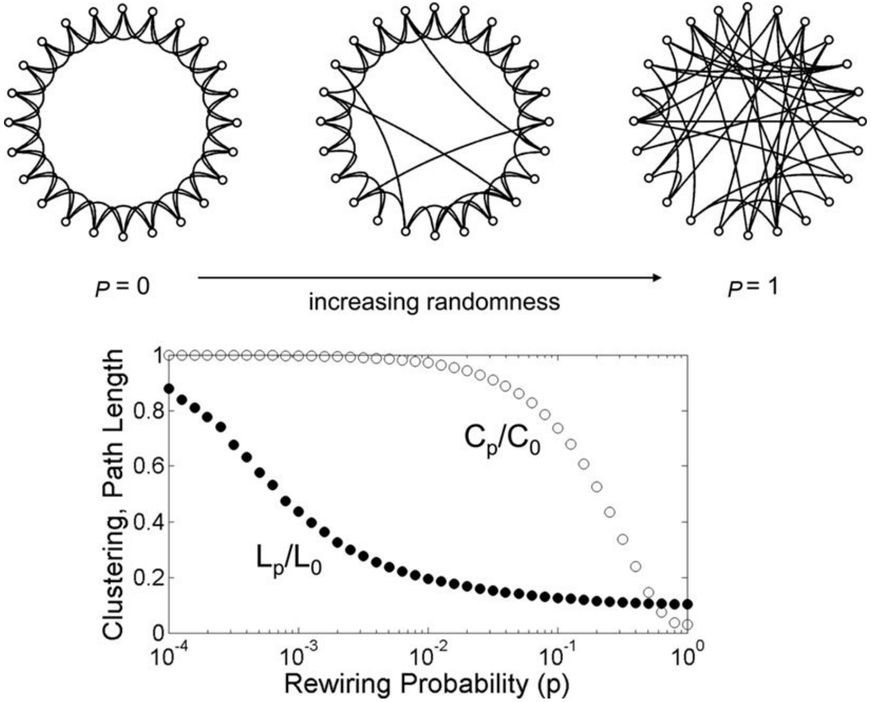


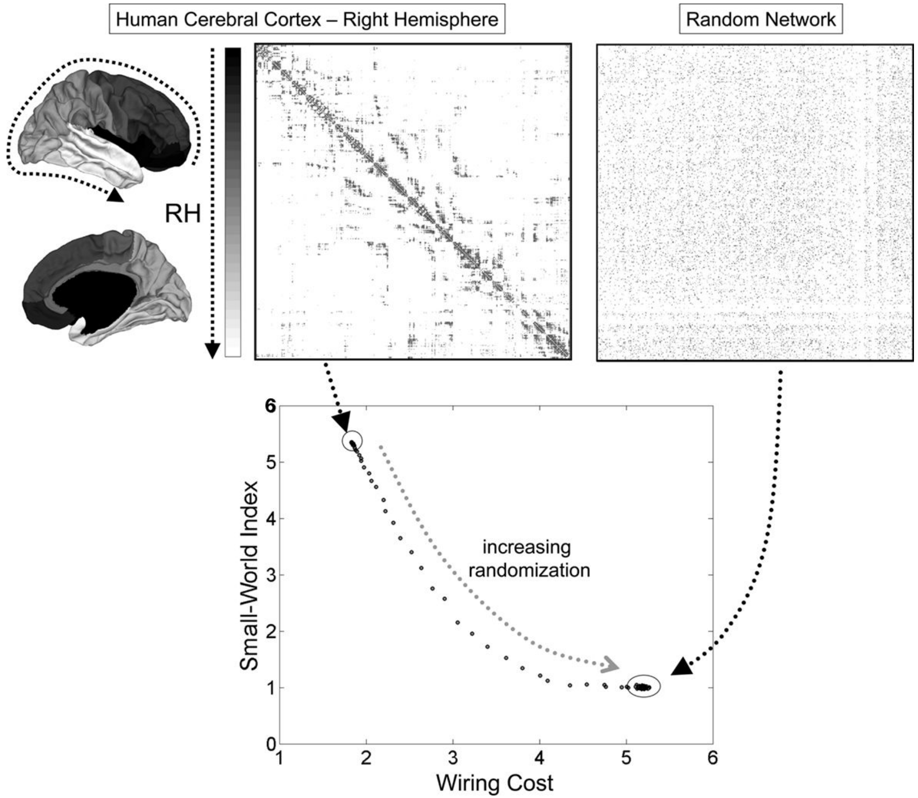




https://evelinag.com/blog/2015/12-15-star-wars-social-network/

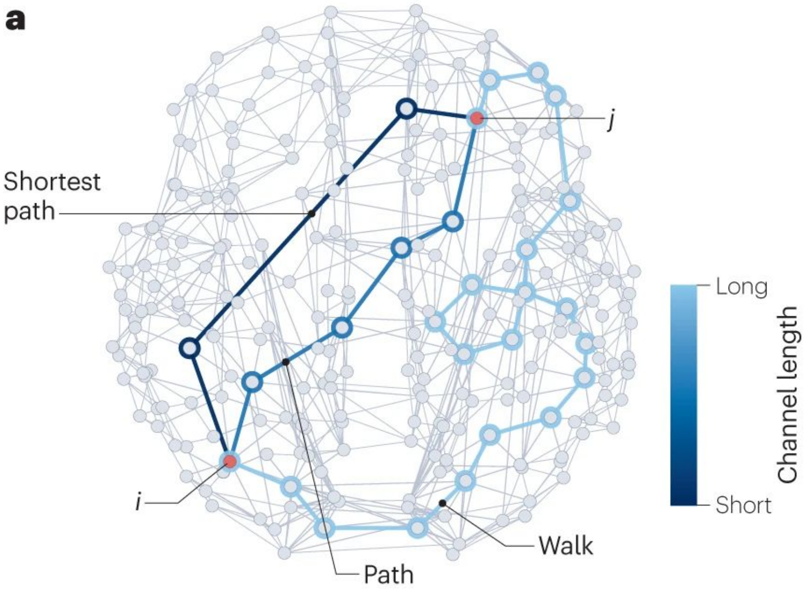
Sporns (2011) *Front. Comp. Neuro.*





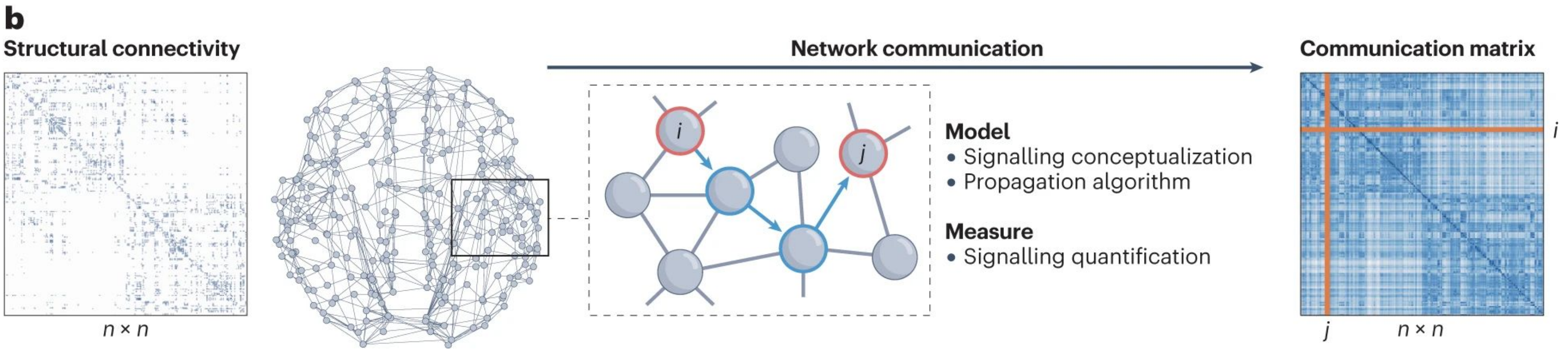
Sporns (2011) *Front. Comp. Neuro.*

Seguin et al (2023) *Nat. Rev. Neuro.*

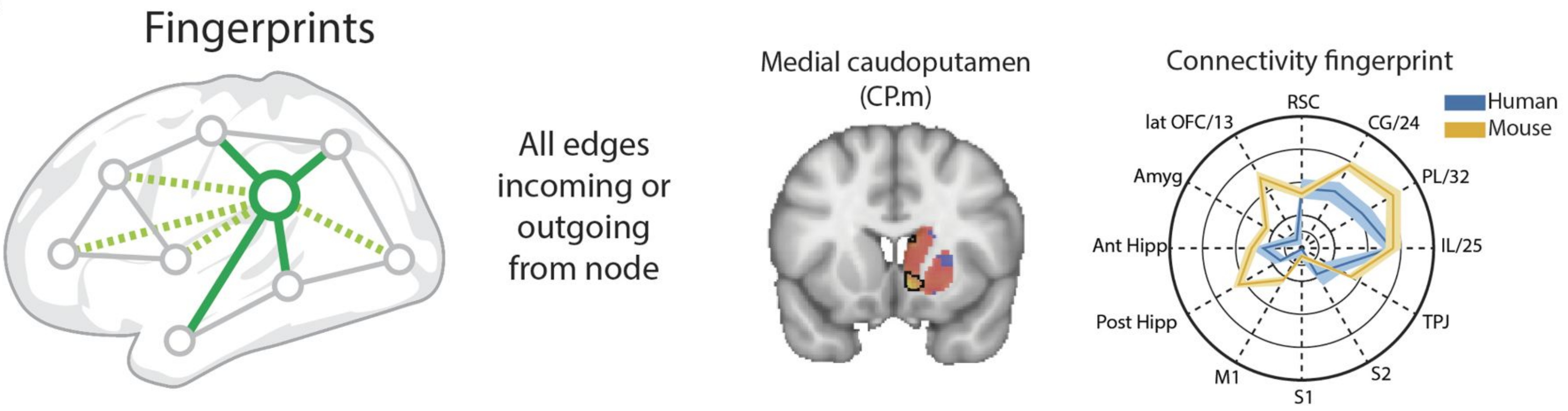


Not only can network measures quantify complex organization, but can make predictions about structure & function relationship

- Models can range from abstract/simple to complicated/biological



Each area of the brain is interpreted in the context of its connections to other areas.



Balsters et al (2020) *Elife*

Why network analysis?

- Quantify “organization” using a variety of descriptors

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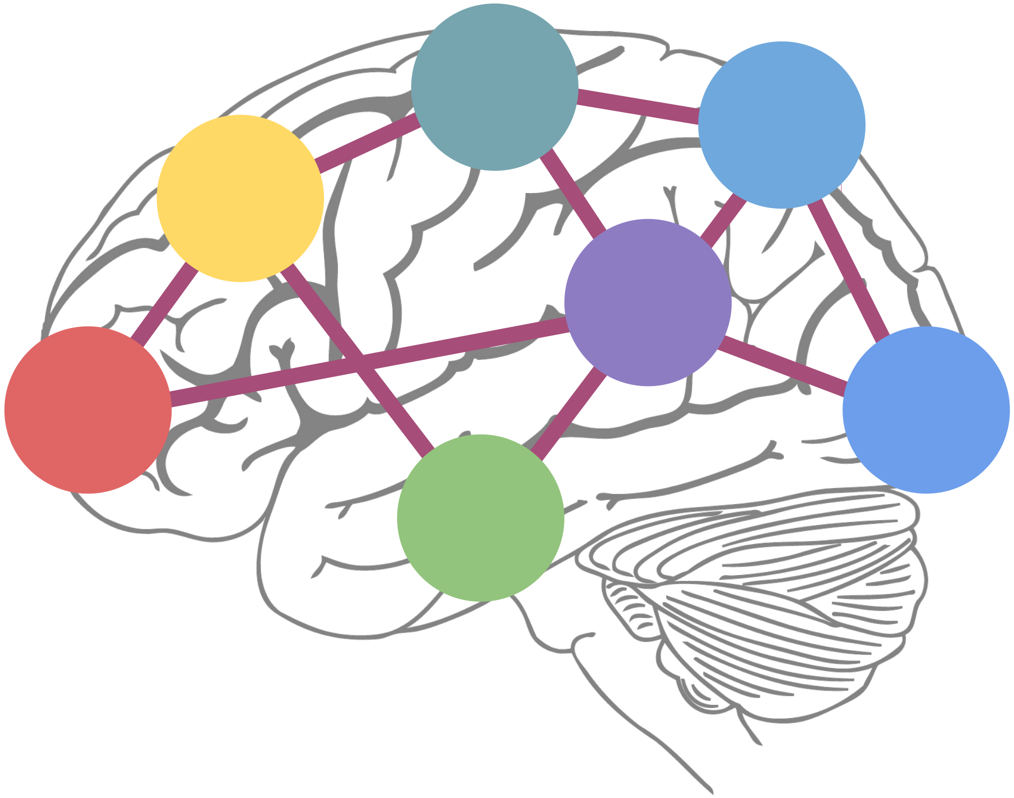
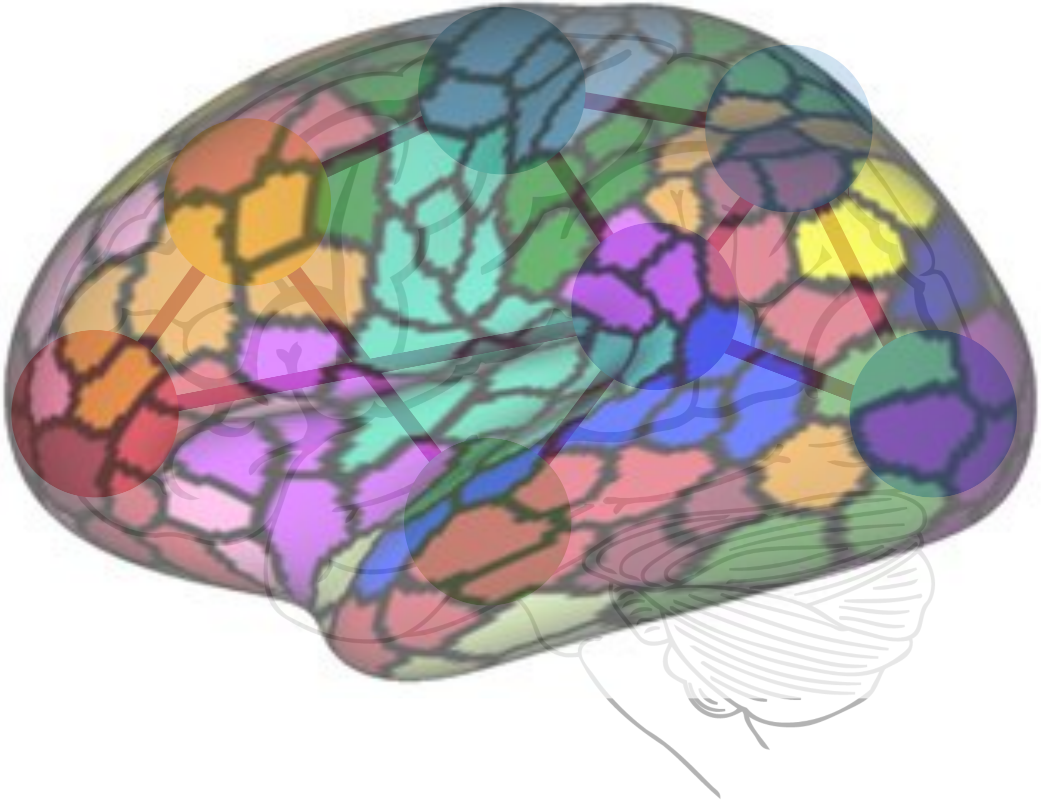
- Capture complexity using a approach amenable to analysis
    - Well developed mathematical underpinnings

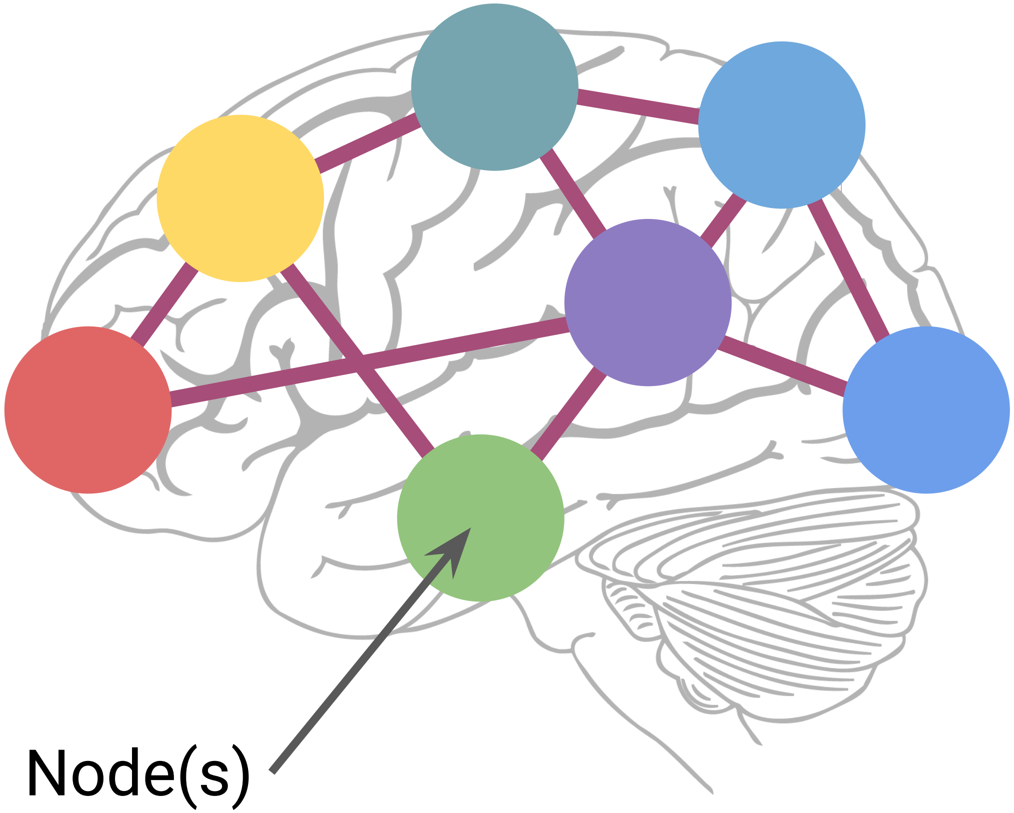
Why network analysis?

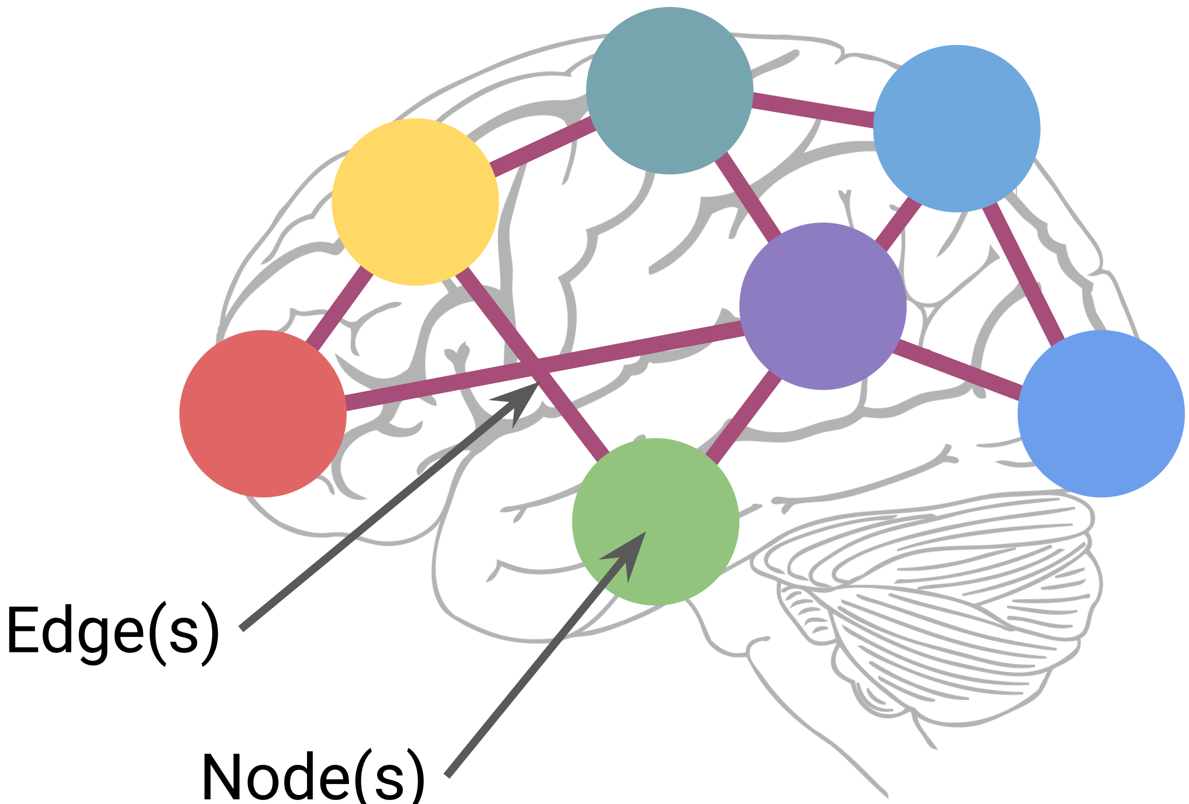
- Quantify “organization” using a variety of descriptors
- Capture complexity using a approach amenable to analysis
  - Well developed mathematical underpinnings
- Data agnostic, even within the realm of neuroscience
  - Big neuroscience data (i.e. millions of voxels, 100’s brain slices, expansive whole brain coverage)
  - Structure / function
  - Can test basic physical principles in neuro contex

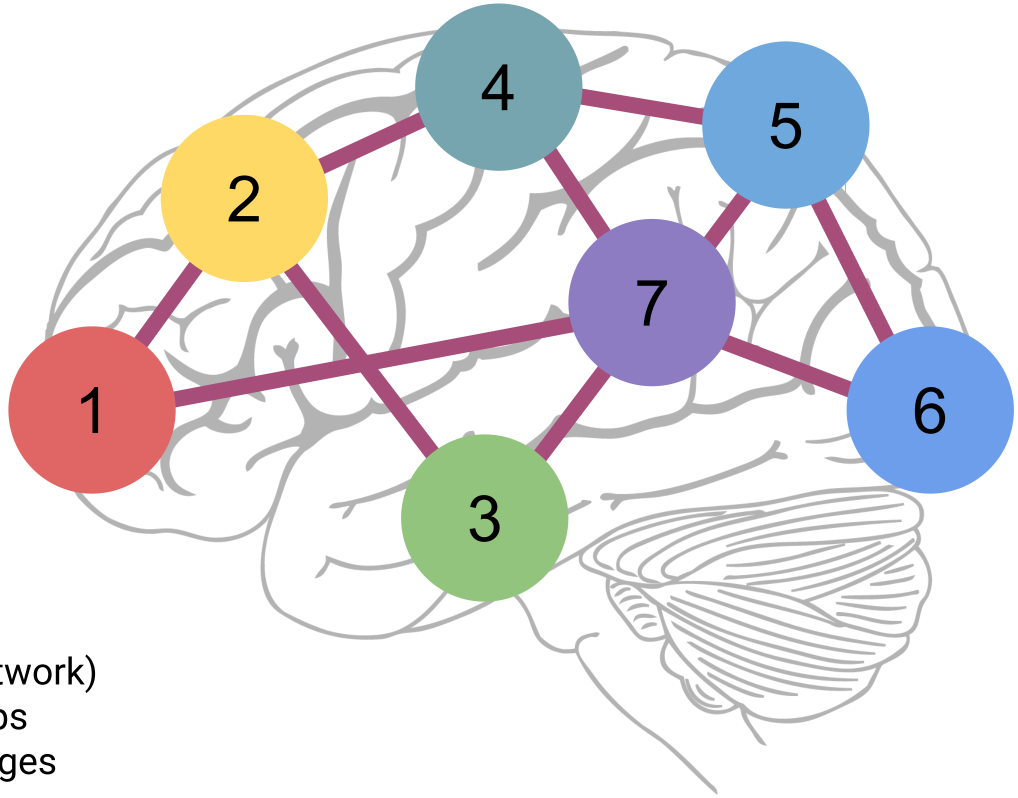


Some basic network *neuro*science



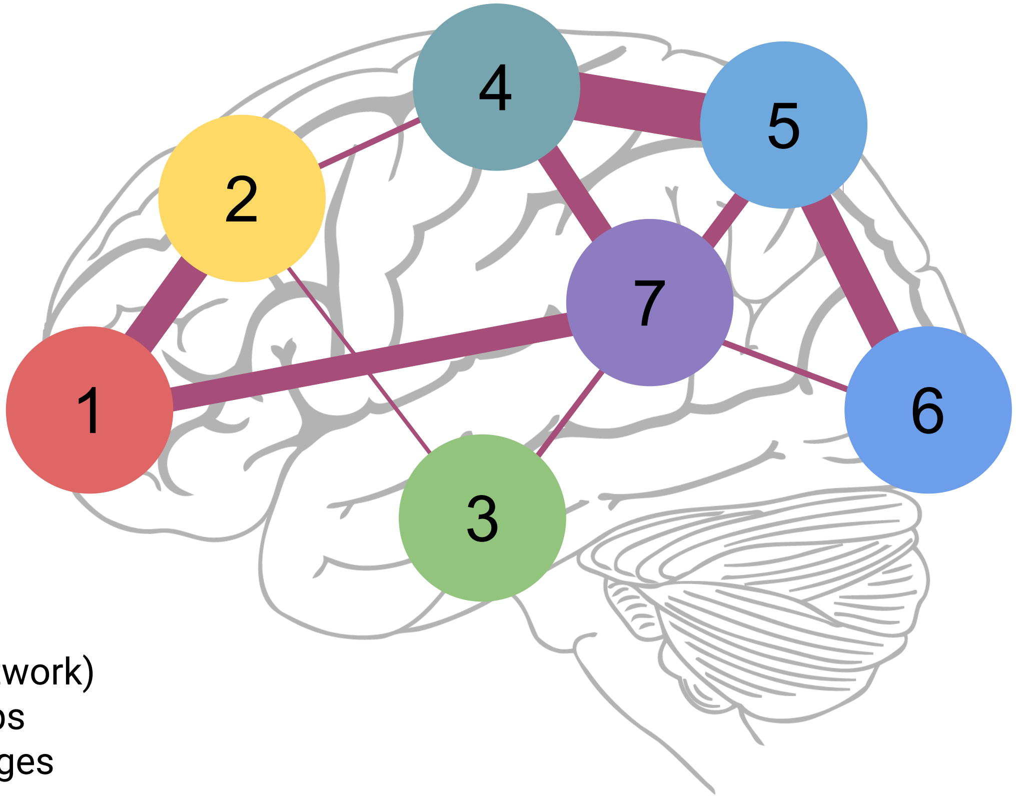

Node(s)


Edge(s)
Node(s)



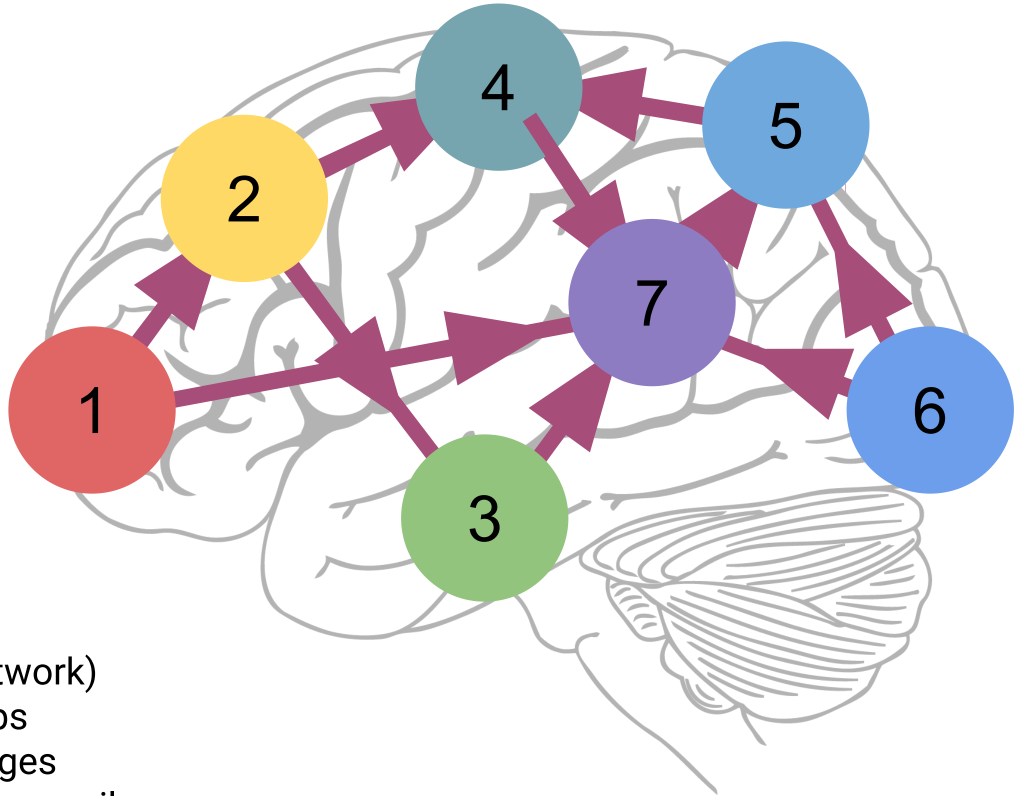
Unweighted

- Simple graph (network)
  - No self-loops
  - No hyperedges
- Binary connections



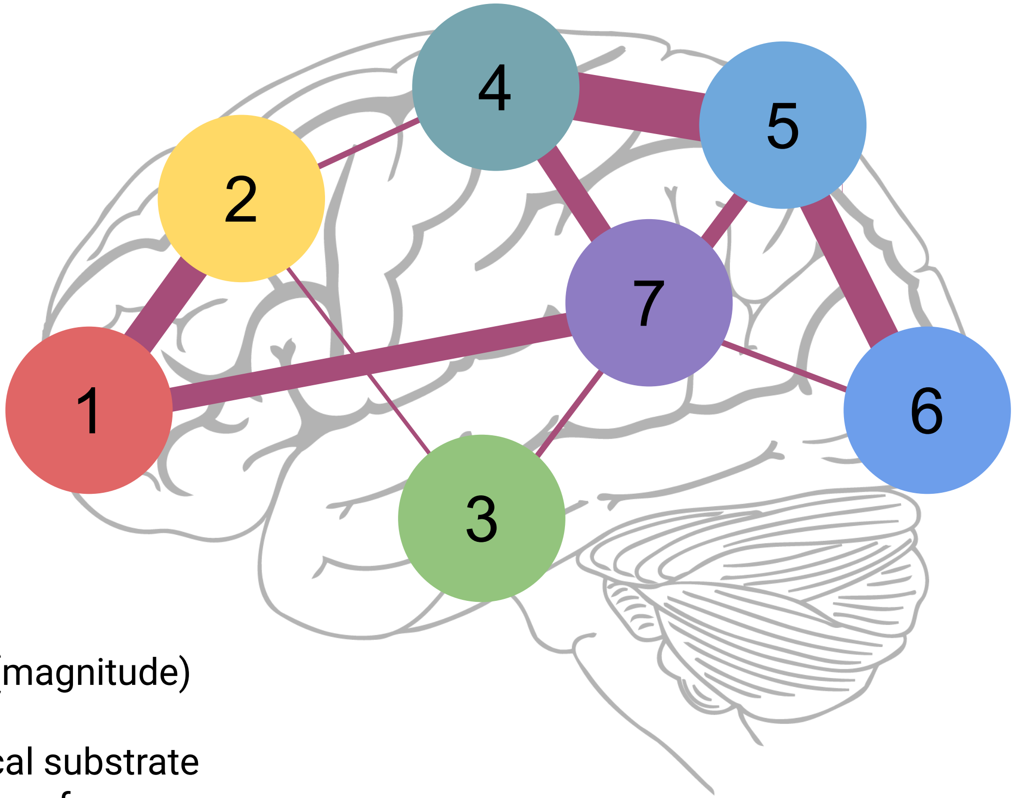
Weighted

- Simple graph (network)
  - No self-loops
  - No hyperedges
- Weighted
  - Could be heavy-tailed
  - Log-normal degree distribution is common



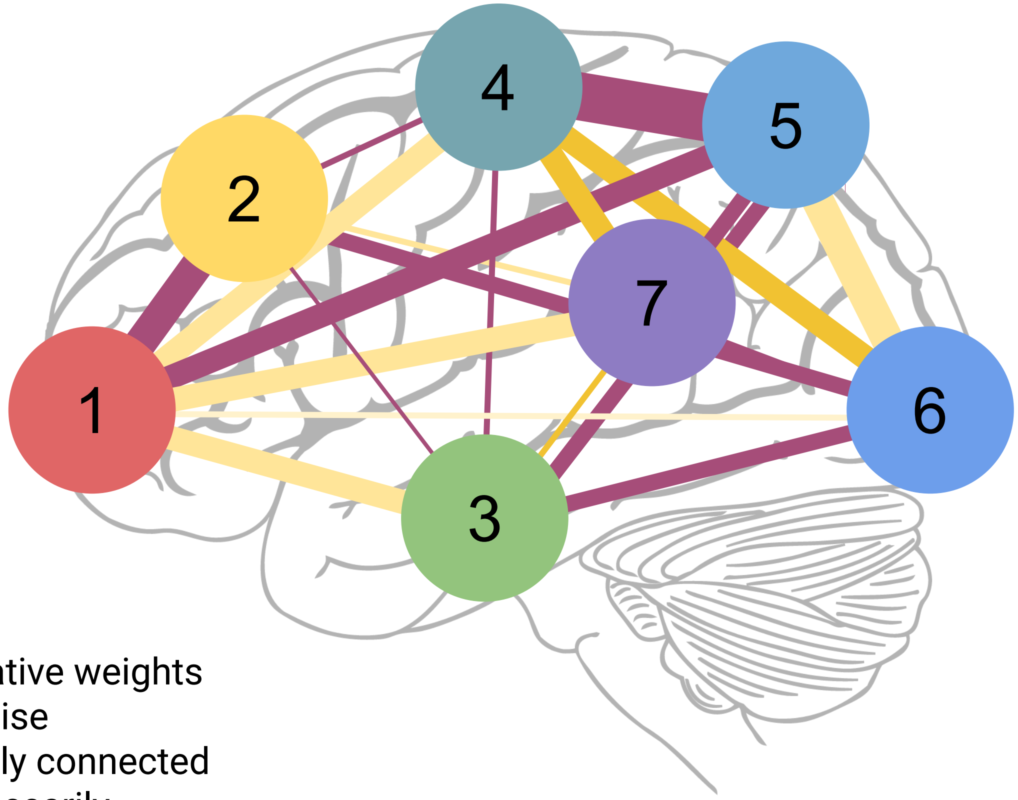
Directed

- Simple graph (network)
  - No self-loops
  - No hyperedges
- Edges are not necessarily reciprocal



Structural

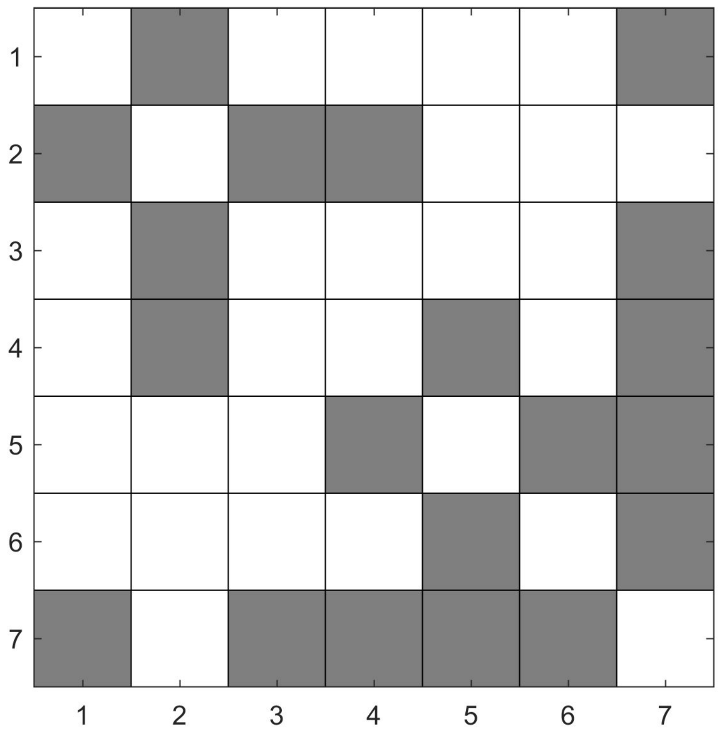
- Positive weights (magnitude)
- Typically sparse
- Commonly physical substrate of edges, challenges for between-hemisphere estimation

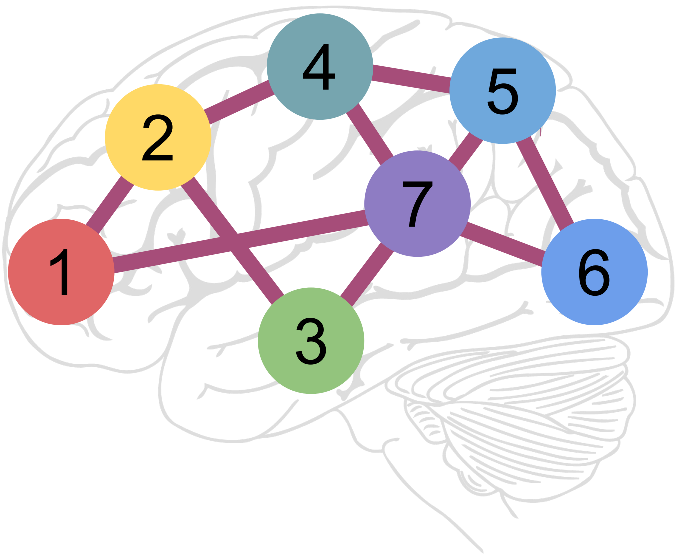


Functional

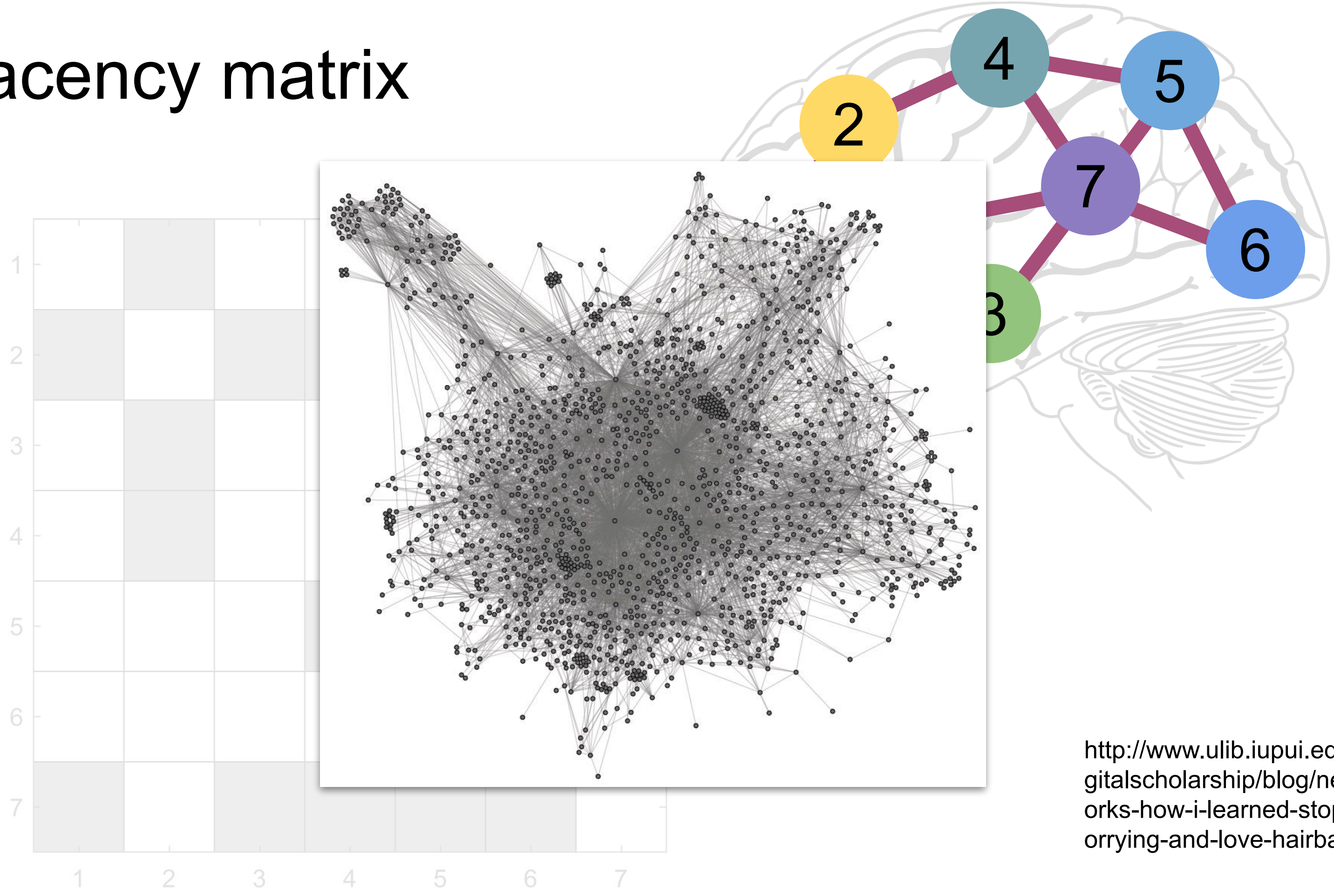
- Positive and negative weights
- Evaluate all pairwise comparisons - fully connected
- Edges aren't necessarily physical

Adjacency matrix



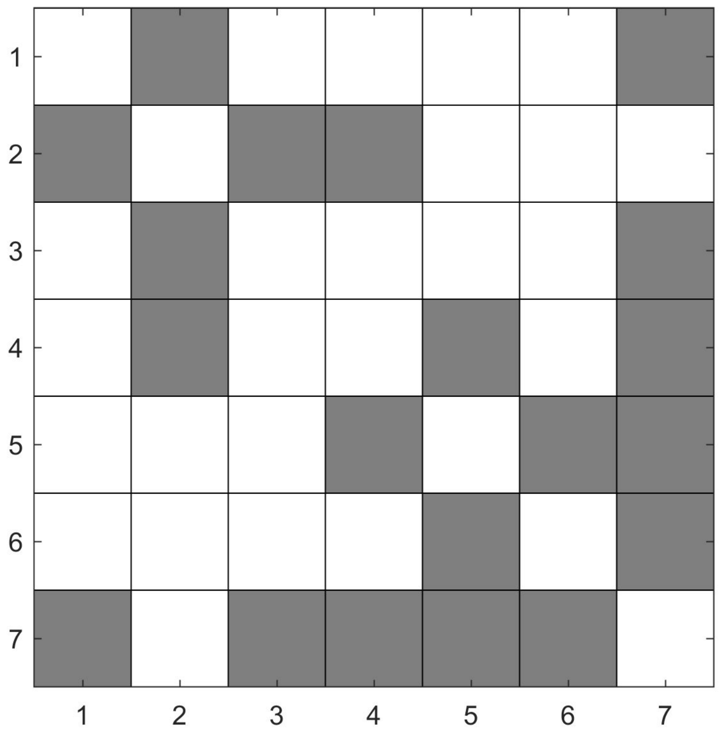


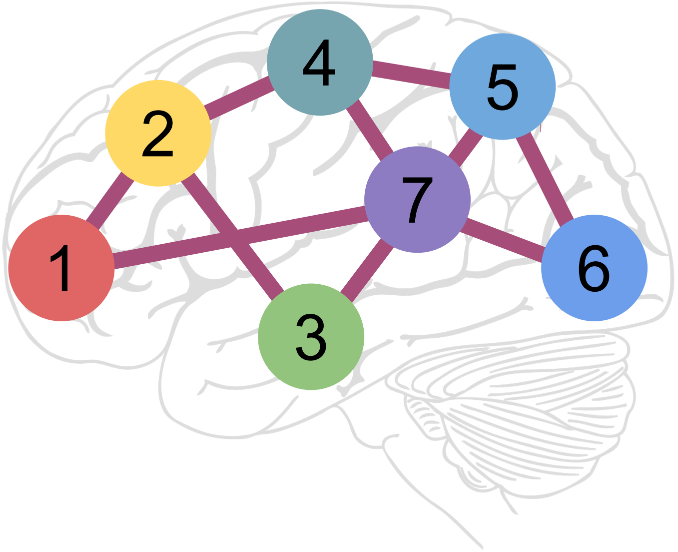
Adjacency matrix



http://www.ulib.iupui.edu/digitalscholarship/blog/networks-how-i-learned-stop-worrying-and-love-hairball

Adjacency matrix





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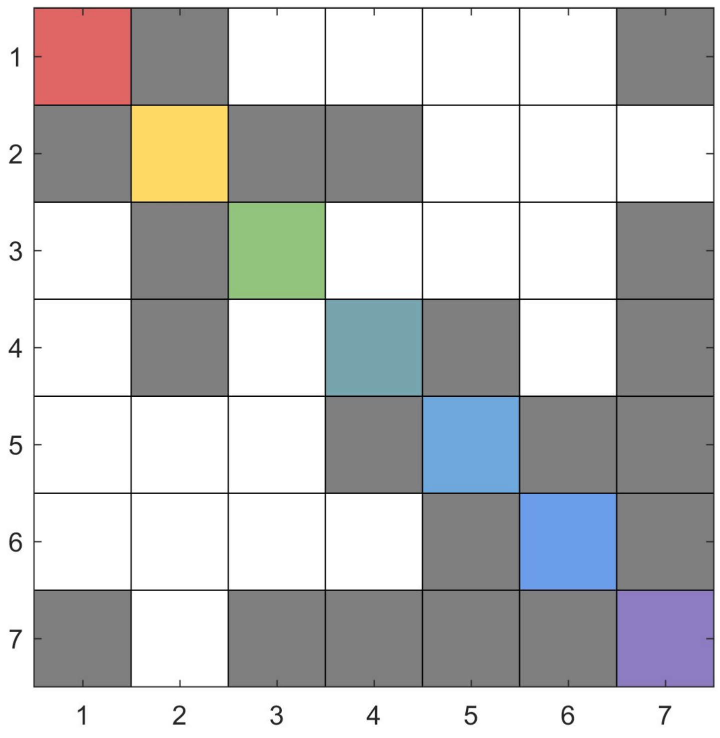

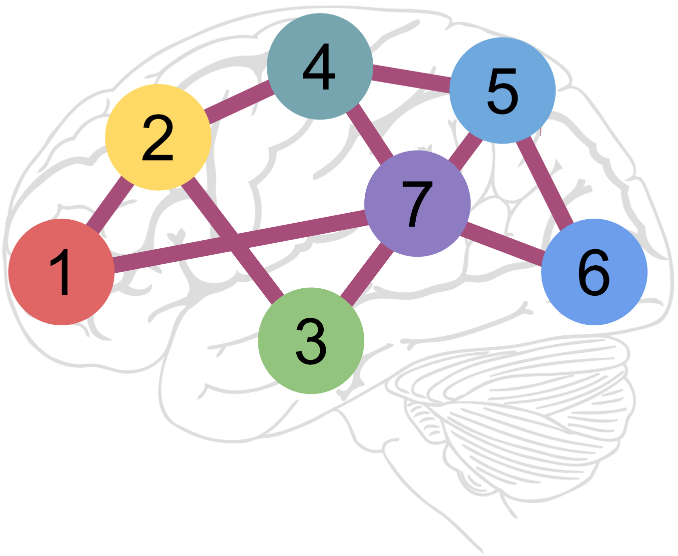

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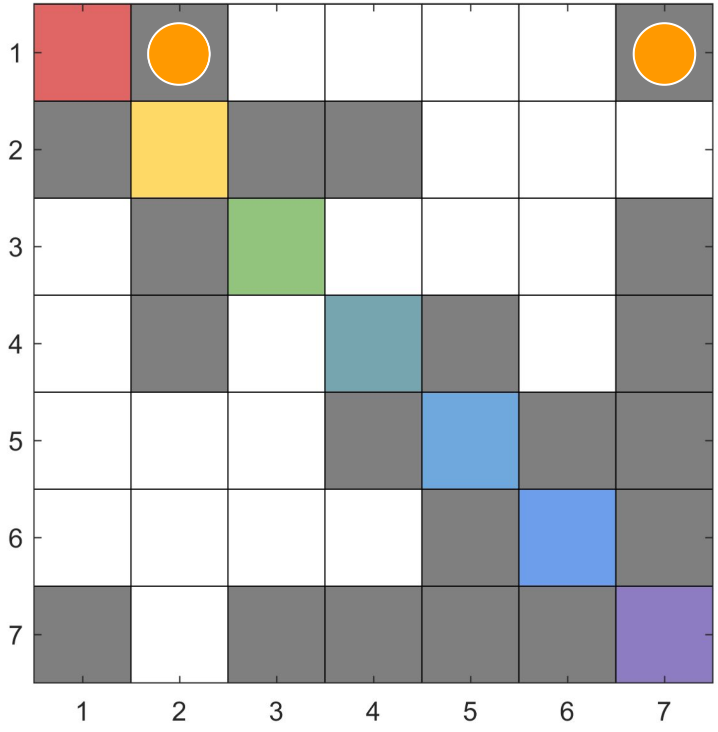

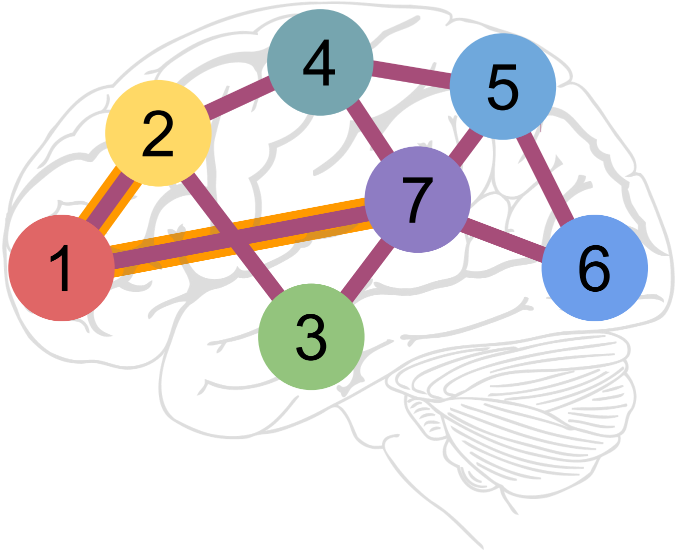

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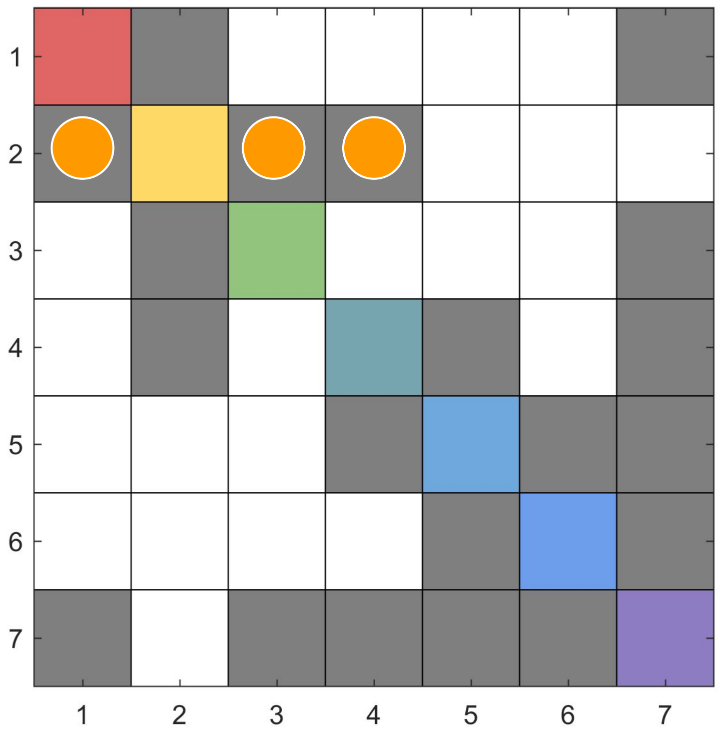

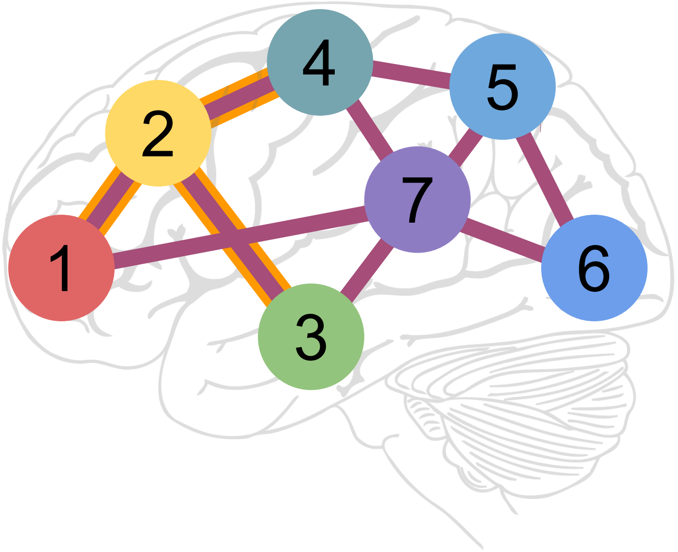

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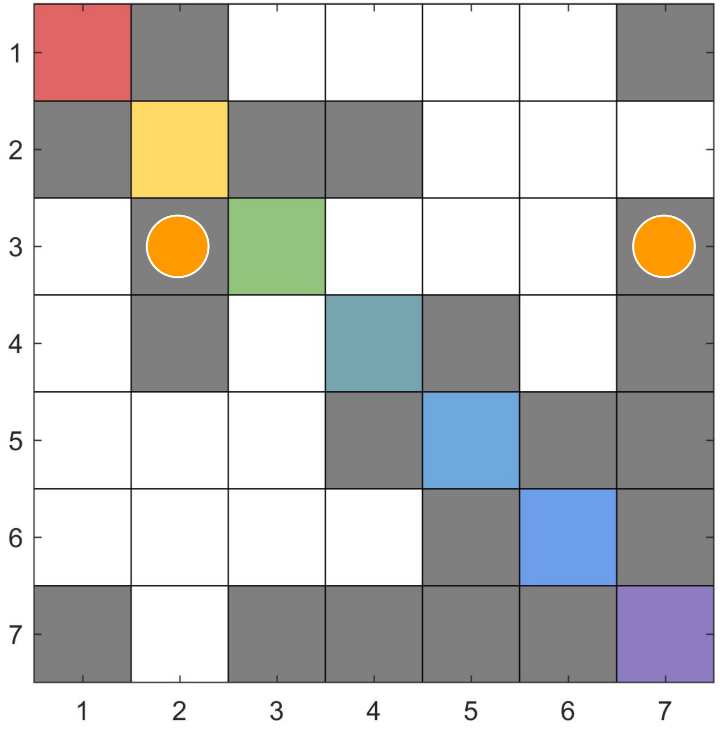

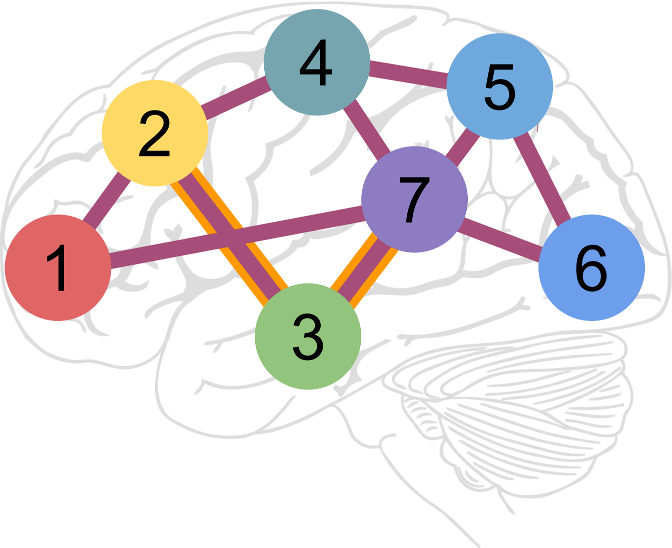

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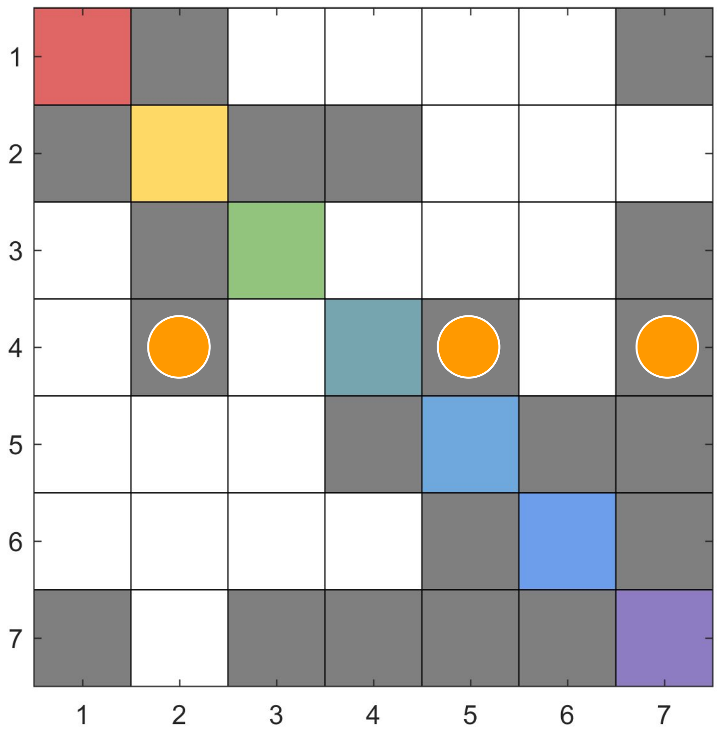

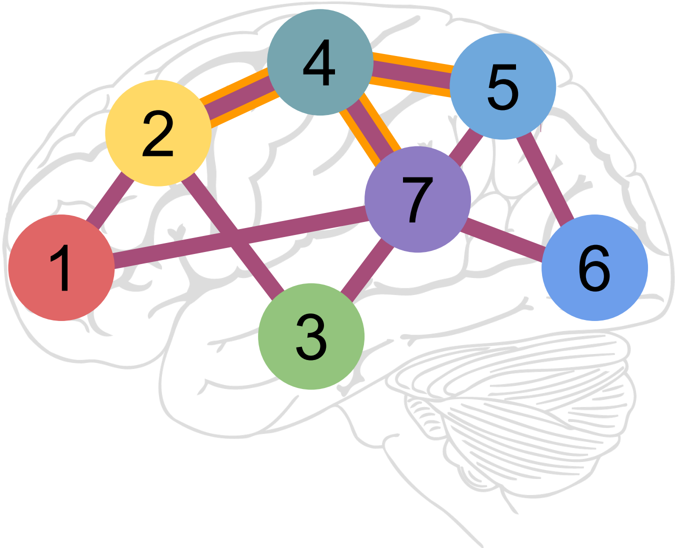

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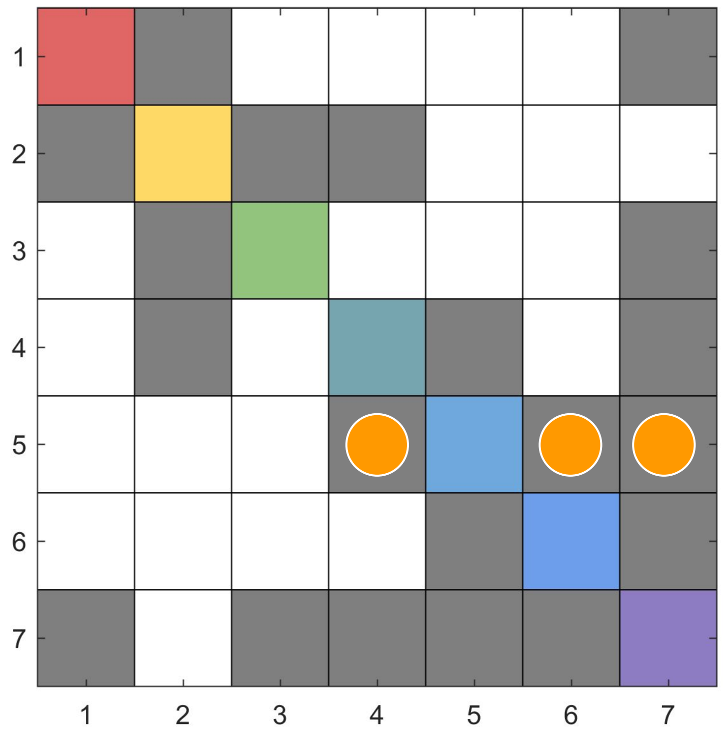

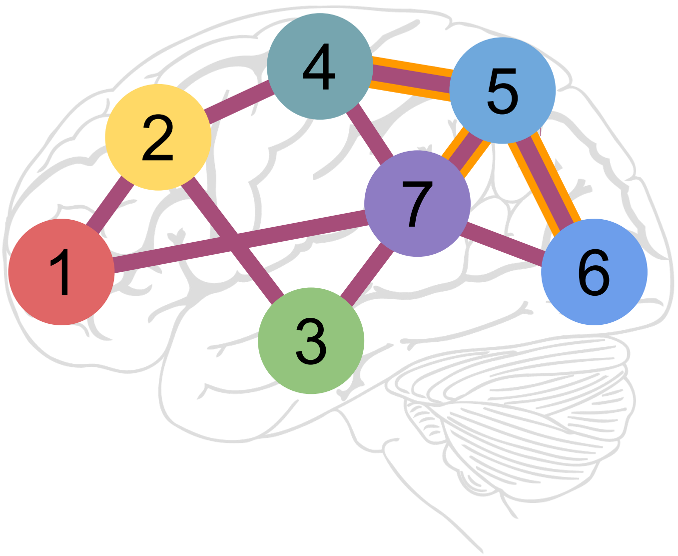

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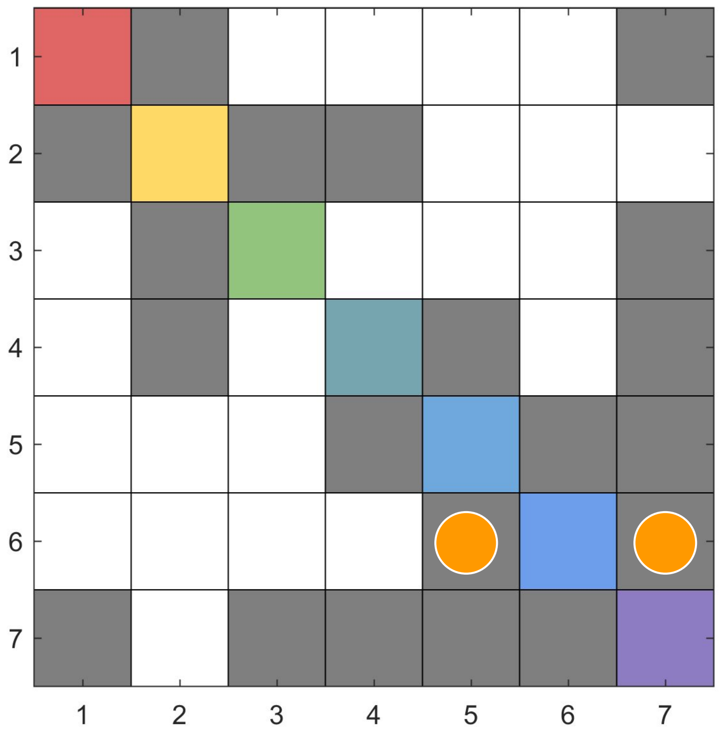

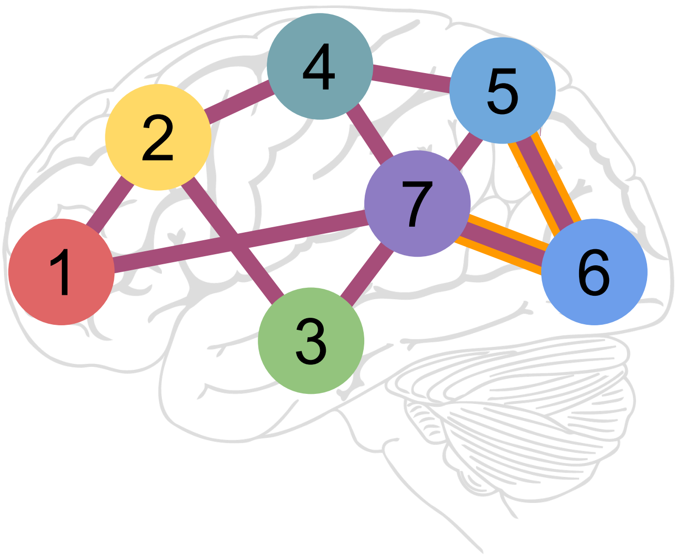

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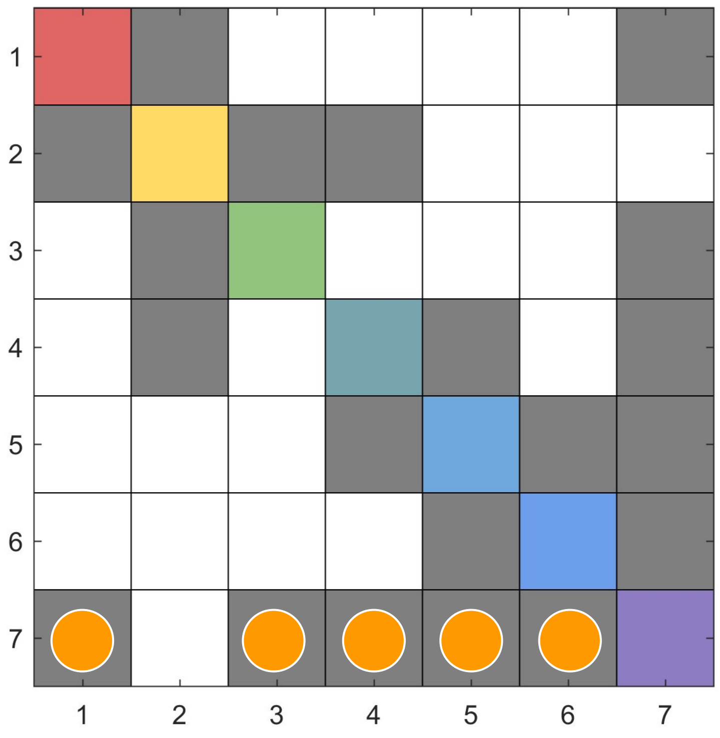

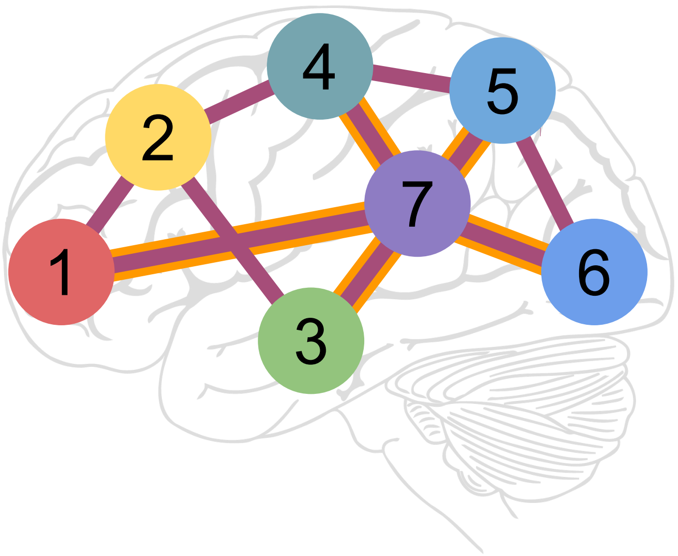

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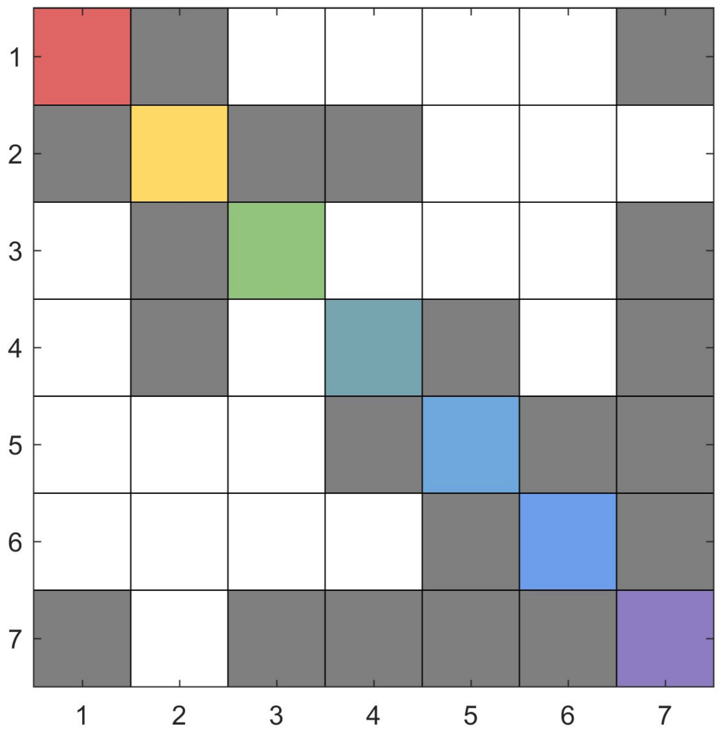
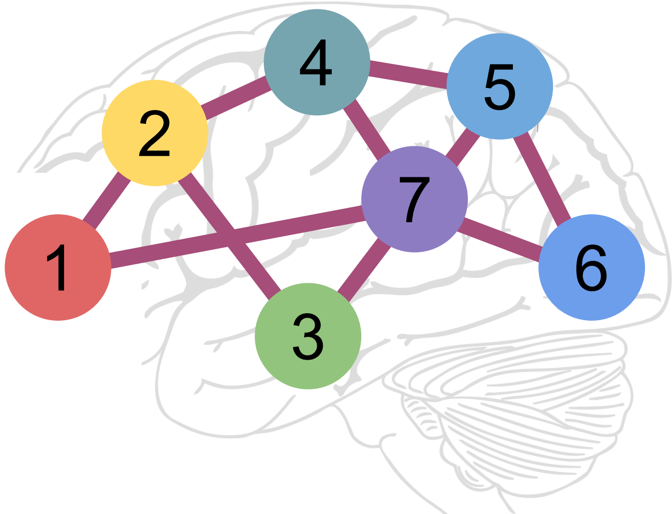
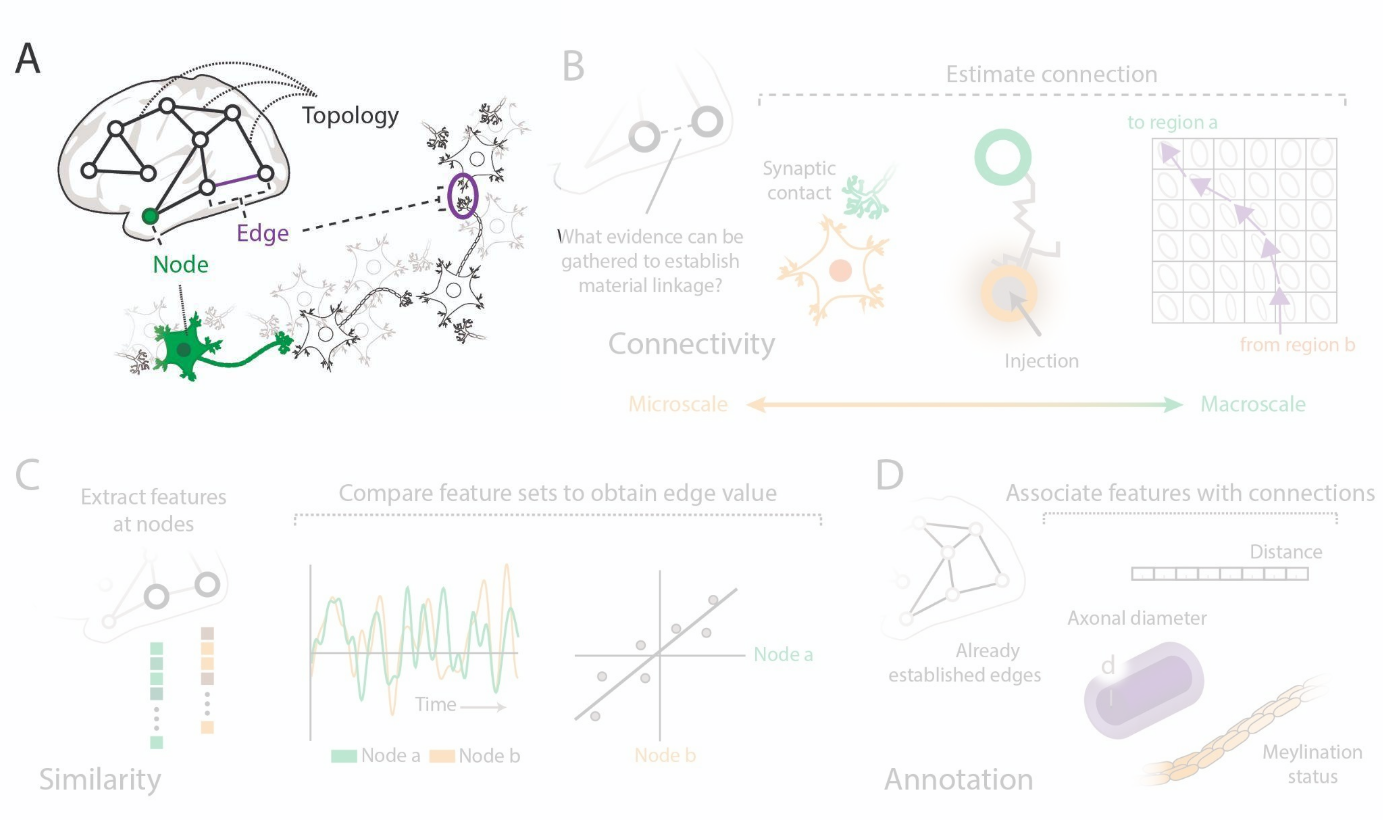




- **Topology**: the pattern of edges/connections that make up the overall structure of the network
- **Density/sparsity**: the fraction of edges present versus all possible edge positions

Types o’ edges



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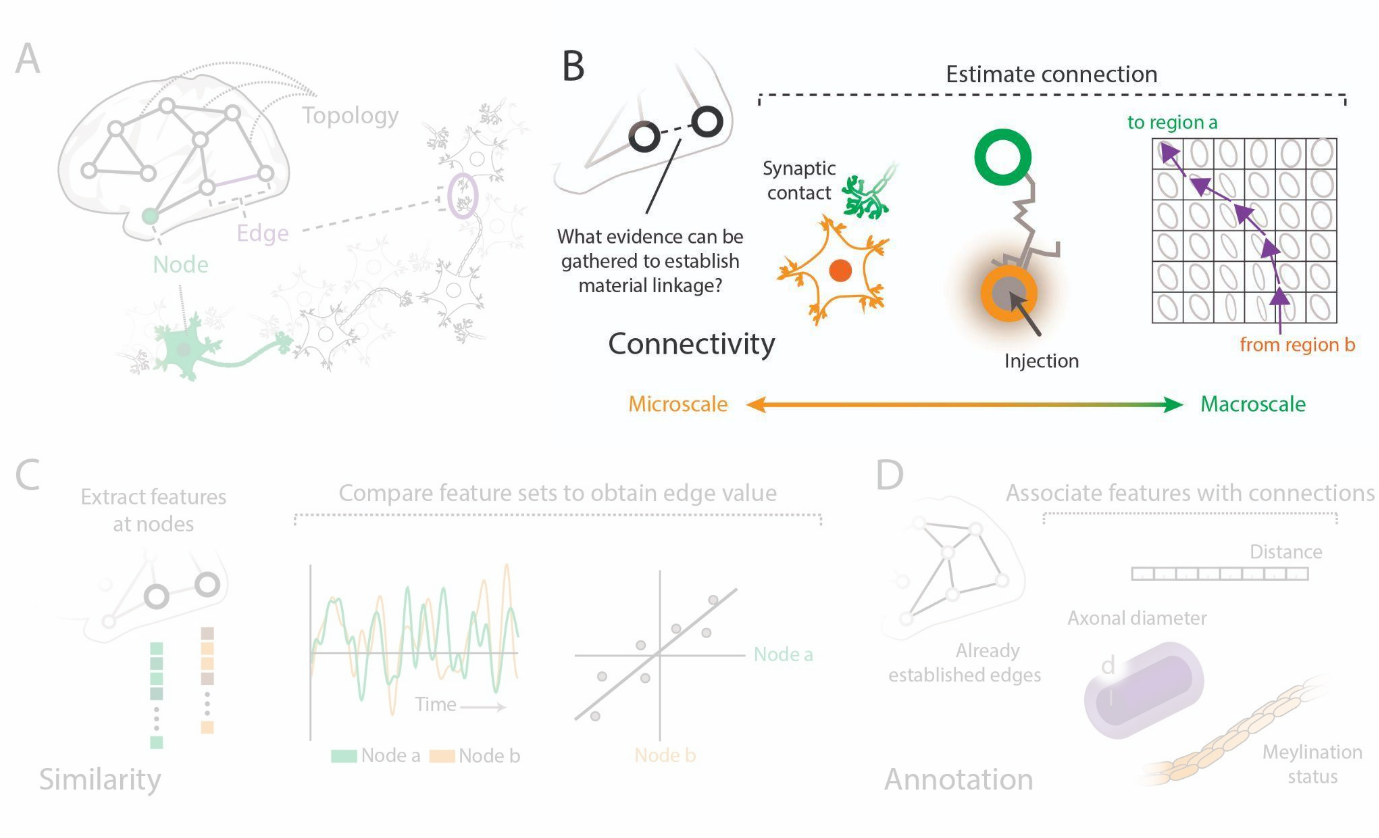

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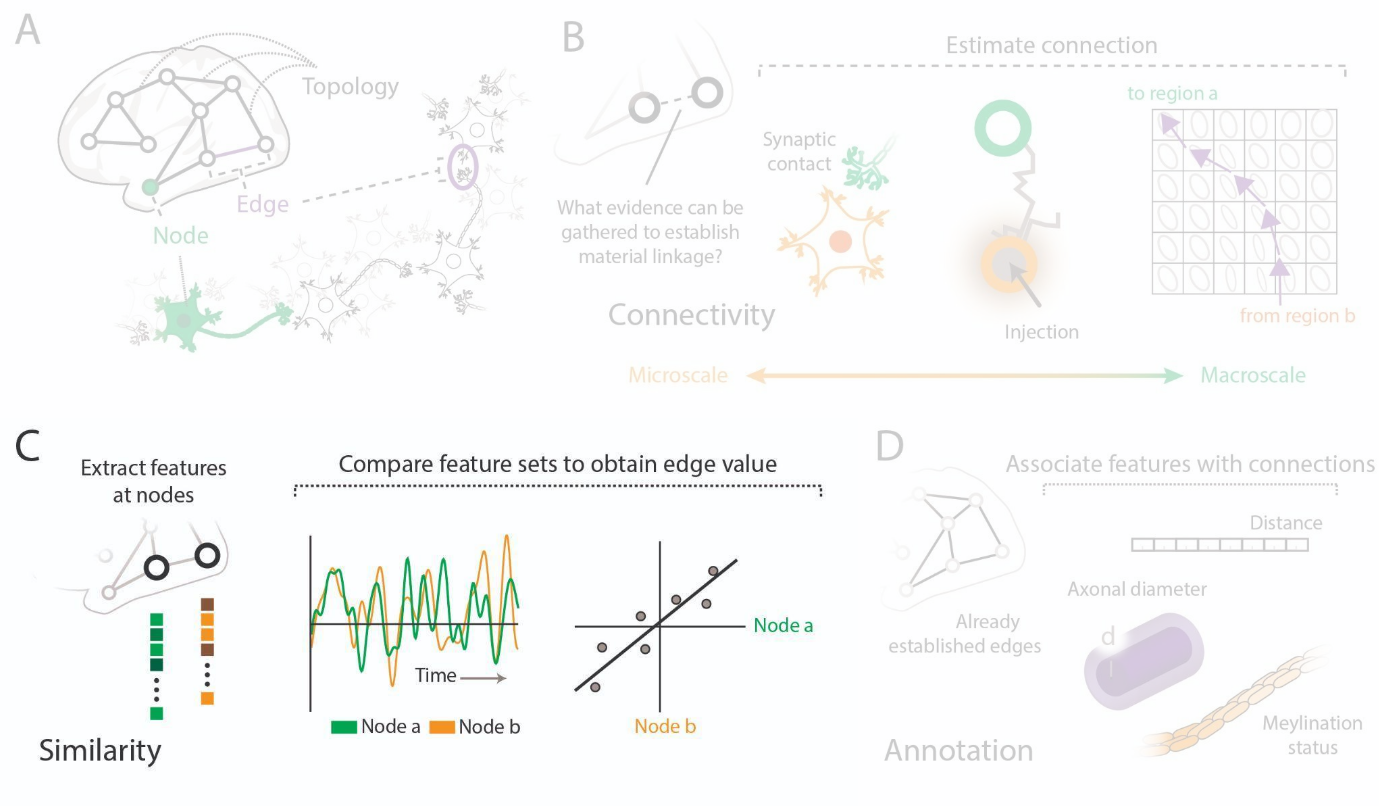

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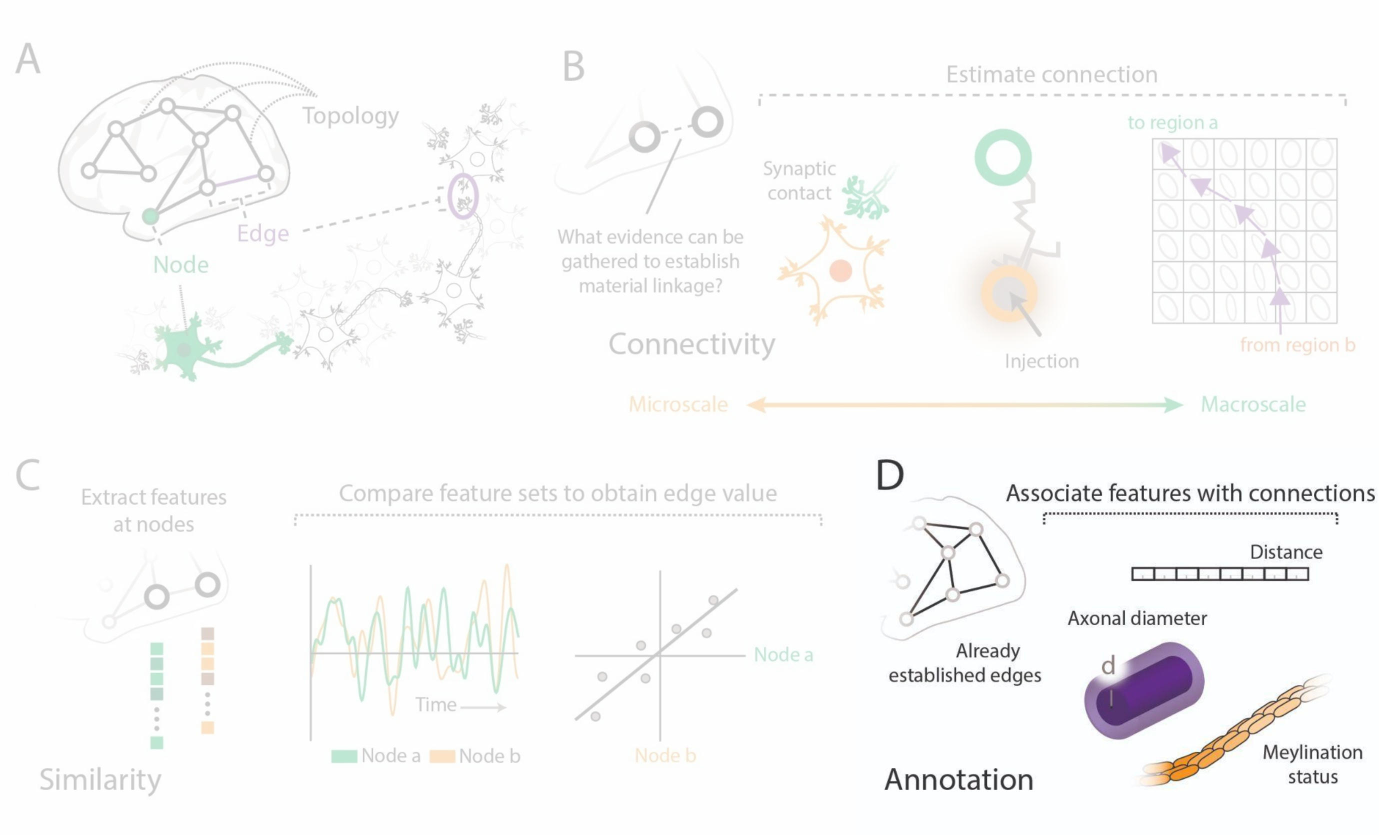
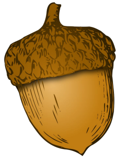
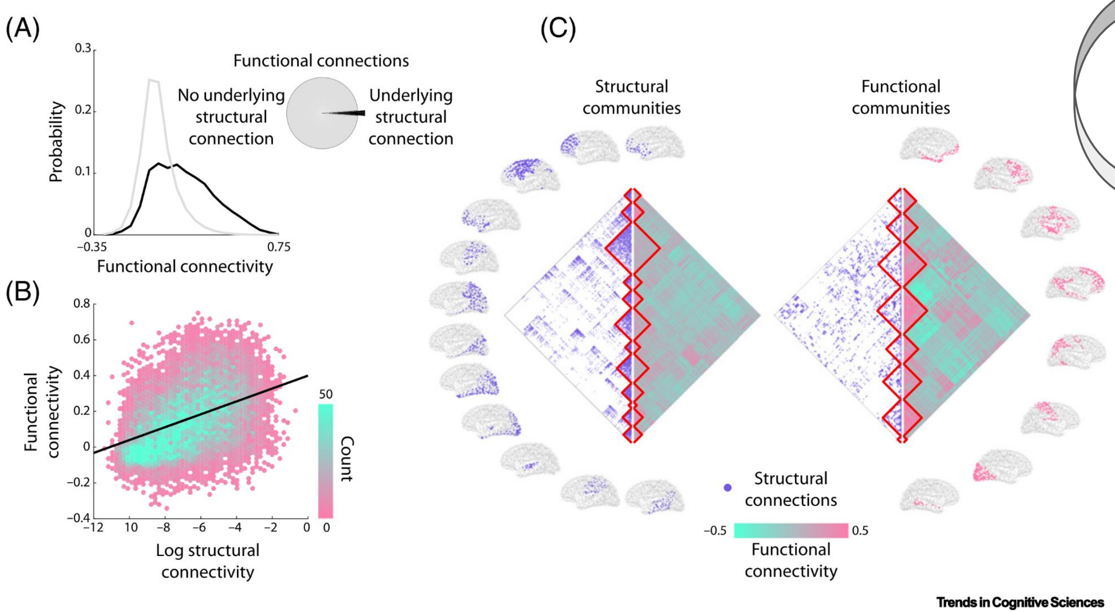


Brain networks in a nutshell





Structural

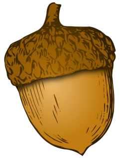
The brain is fundamentally a network at the level of neurons

Functional

Functional networks are not necessarily “real” but the result of taking the similarity of activity

Suarez et al (2022) *TiCS*

Brain networks in a nutshell



Structural

- The brain is fundamentally a network at the level of neurons
- When we think of "wiring" this is a structural network
  - A physical substrate through which communication happens
  - Most commonly associated with white matter functioning
- Data collection:
  - Microscopy recon.
  - Tract tracing
  - Diffusion MRI

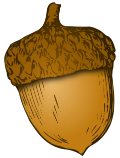
Functional

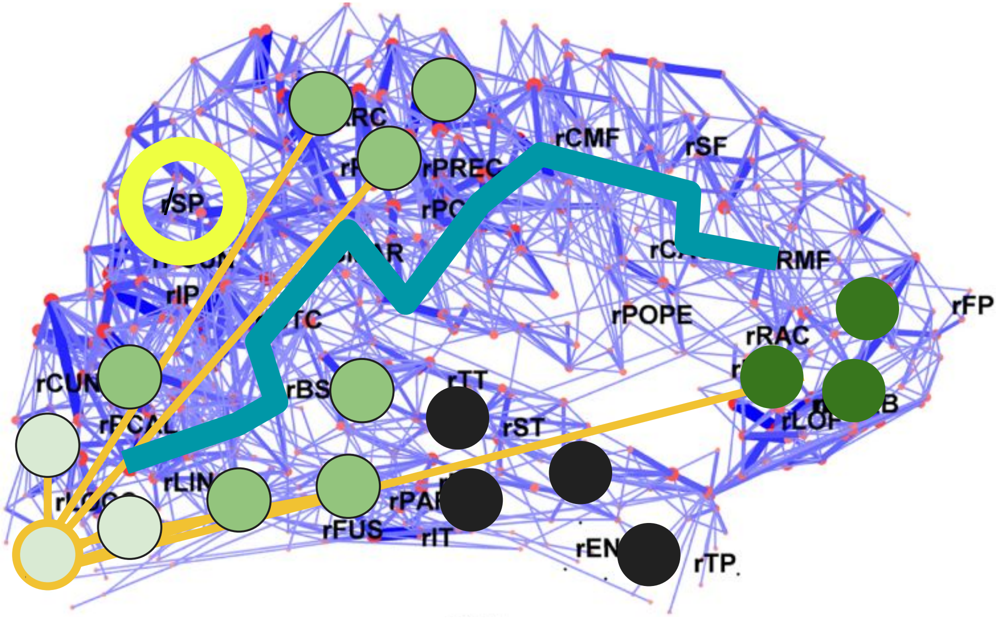
- Functional networks are not necessarily "real" but the result of taking the similarity of activity
- When we think of "communication" even though it's complicated
- Many ways to measure similarity
  - Correlation
  - Mutual information
  - Coherence
- Data collection:
  - Electrophysiology
  - EEG/MEG
  - fMRI

Analysis

- Structure and function result in networks with different features
- Structure / function
  - Sparse / dense
  - Physical / statistical
  - Substrate / similarity
- Node-wise measure to extract features
- Different statistics appropriate for each type
  - Paths-based measures appropriate for struct.
- Func. networks are commonly thresholded to become sparser

Brain networks in a nutshell





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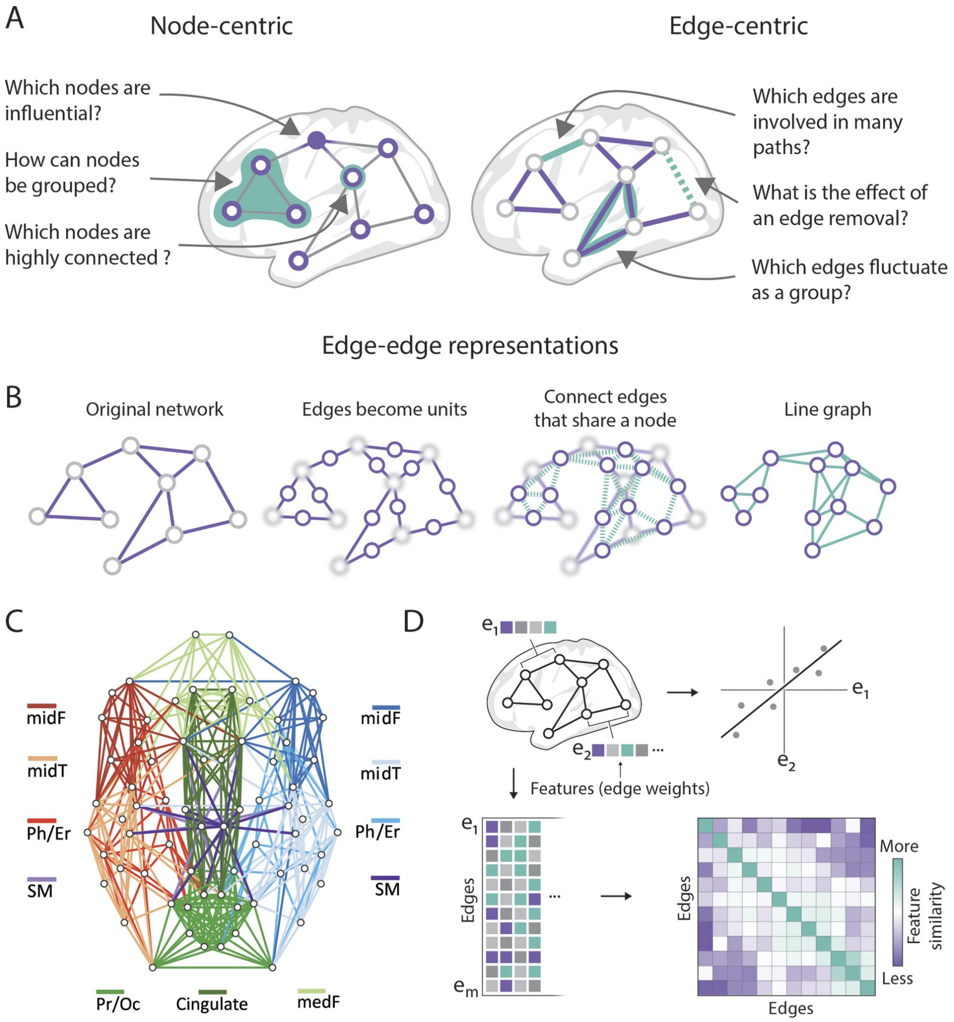

Edges in brain networks: Contributions to models of structure and function

Joshua Faskowitz[1,2], **Richard F. Betzel**[1,2,3,4], **and Olaf Sporns**[1,2,3,4]

[1]Program in Neuroscience, Indiana University, Bloomington, IN, USA
[2]Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA
[3]Indiana University Network Science Institute, Indiana University, Bloomington, IN, USA
[4]Cognitive Science Program, Indiana University, Bloomington, IN, USA

Keywords: Connectome, Network, Edge, Structure function relationship, Connectivity, Network construction, Network communication

Network Neuroscience

From scanner to analysis

Functional brain network journey

Scan your subject!
Get two scans:
anatomical &
functional

Functional brain network journey

Scan your subject!
Get two scans:
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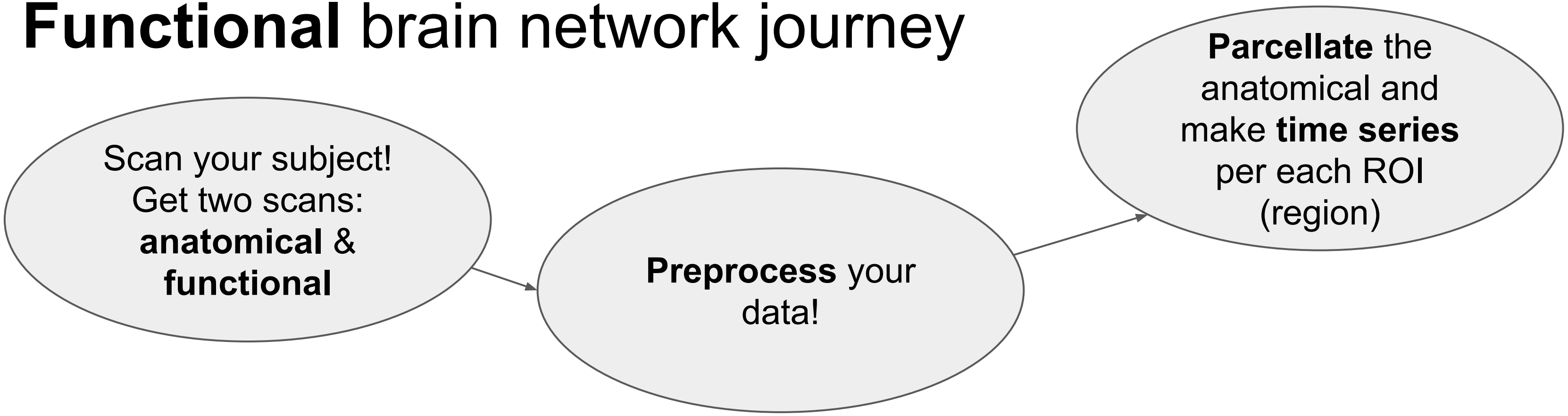
Preprocess your
data!

Functional brain network journey



Functional brain network journey

Scan your subject!
Get two scans:
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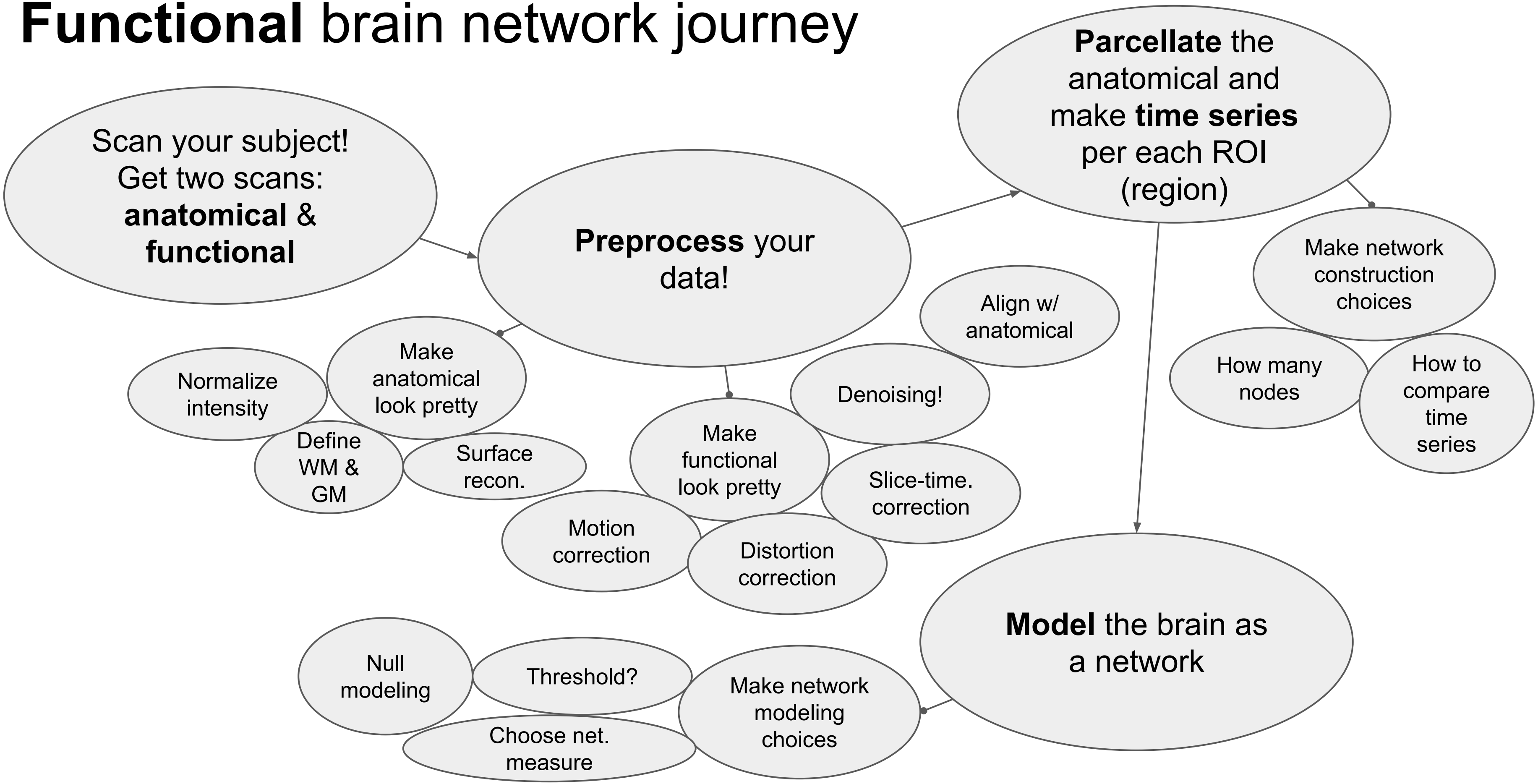
Preprocess your data!

Parcellate the anatomical and make **time series** per each ROI (region)

Model the brain as a network

Functional brain network journey



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Scan your subject! Get two scans: **anatomical & functional**

Preprocess your data!

Normalize intensity

Make anatomical look pretty

Define WM & GM

Surface recon.

Make functional look pretty

Motion correction

Distortion correction

Denoising!

Align w/ anatomical

Slice-time. correction

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Make network construction choices

How many nodes

How to compare time series

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Threshold?

Choose net. measure

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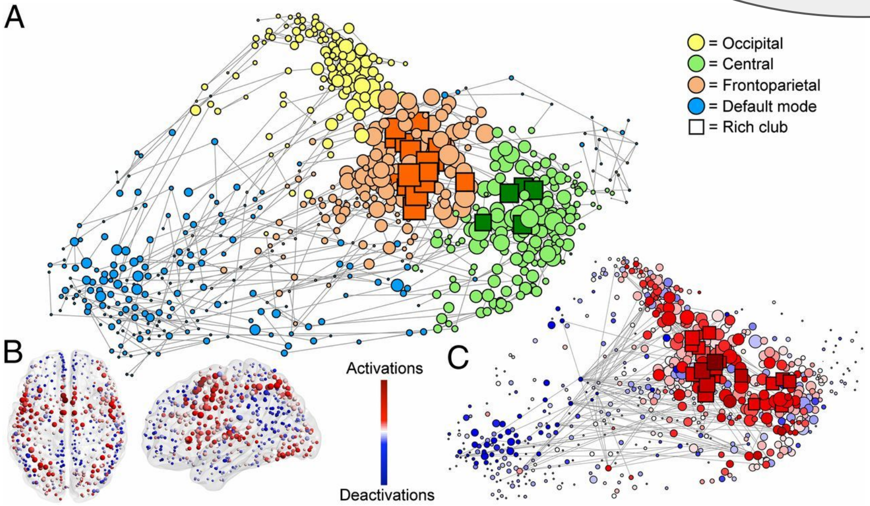
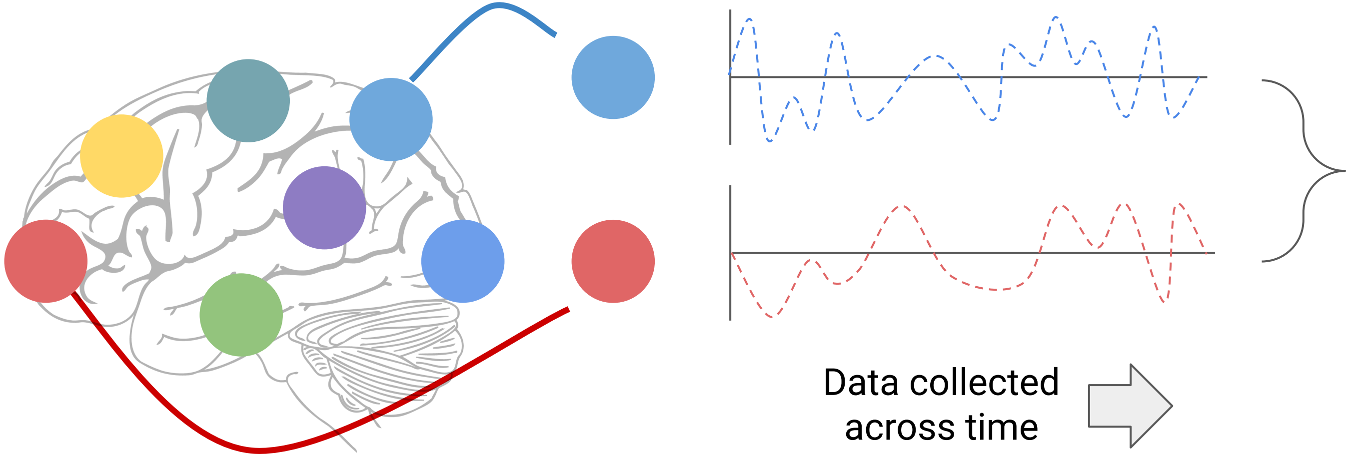


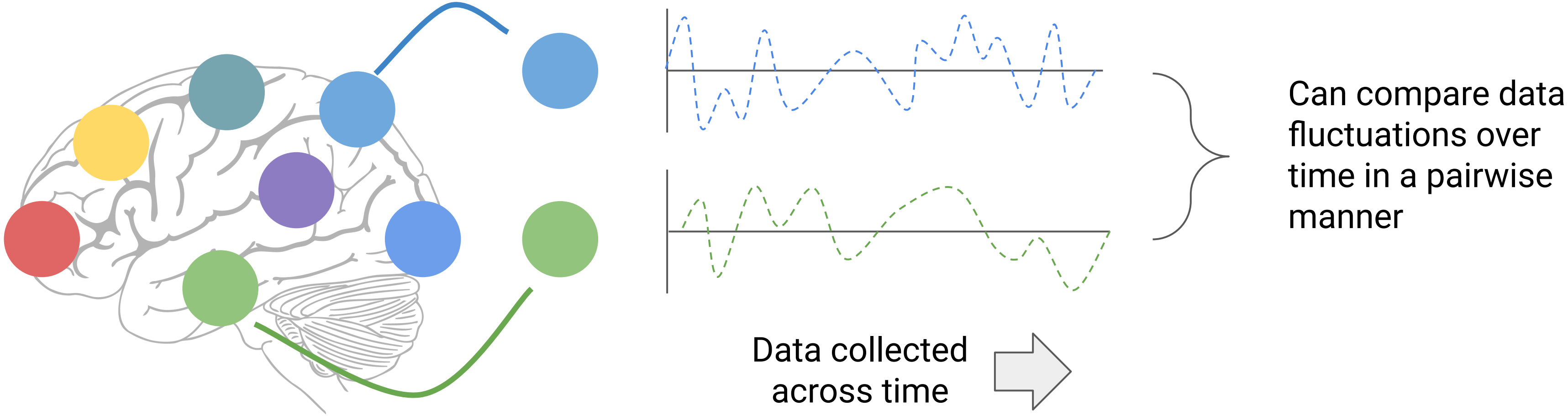
Crossley et al (2013) PNAS

Creating functional networks



Can compare data fluctuations over time in a pairwise manner

Creating functional networks



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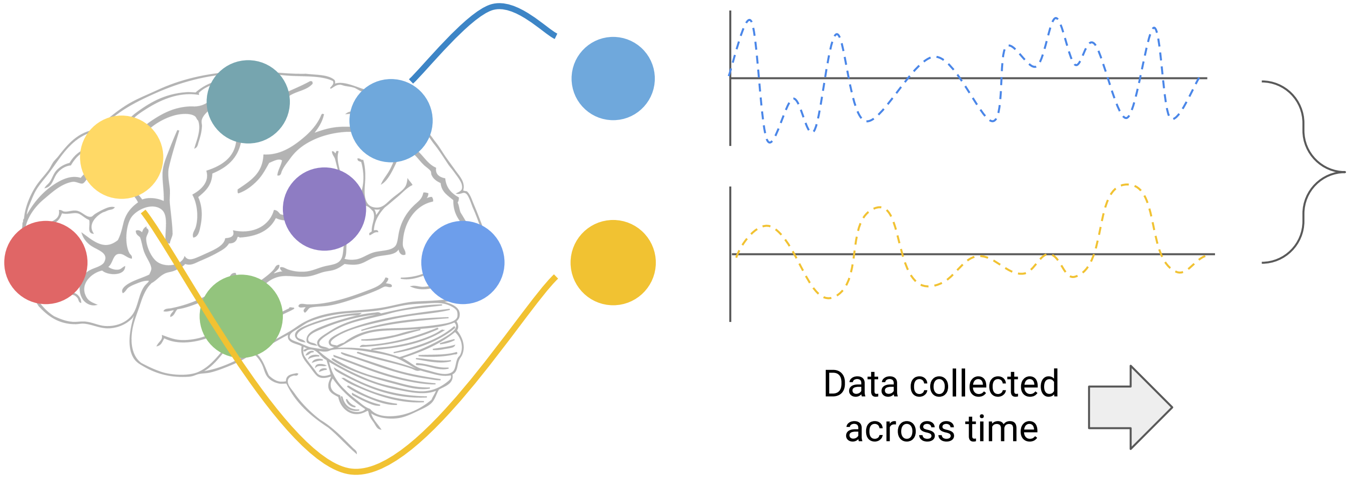

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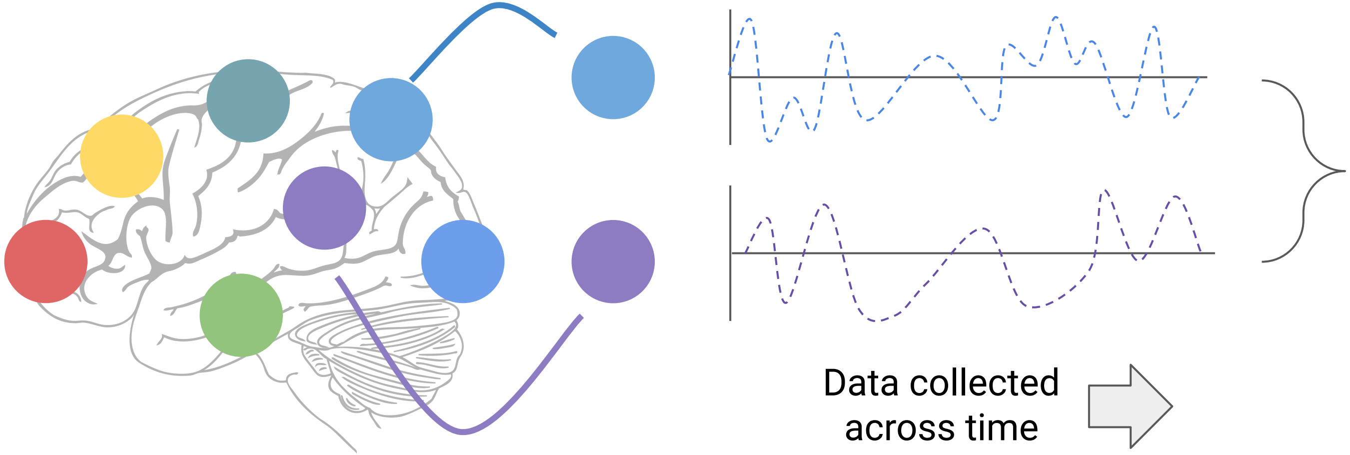

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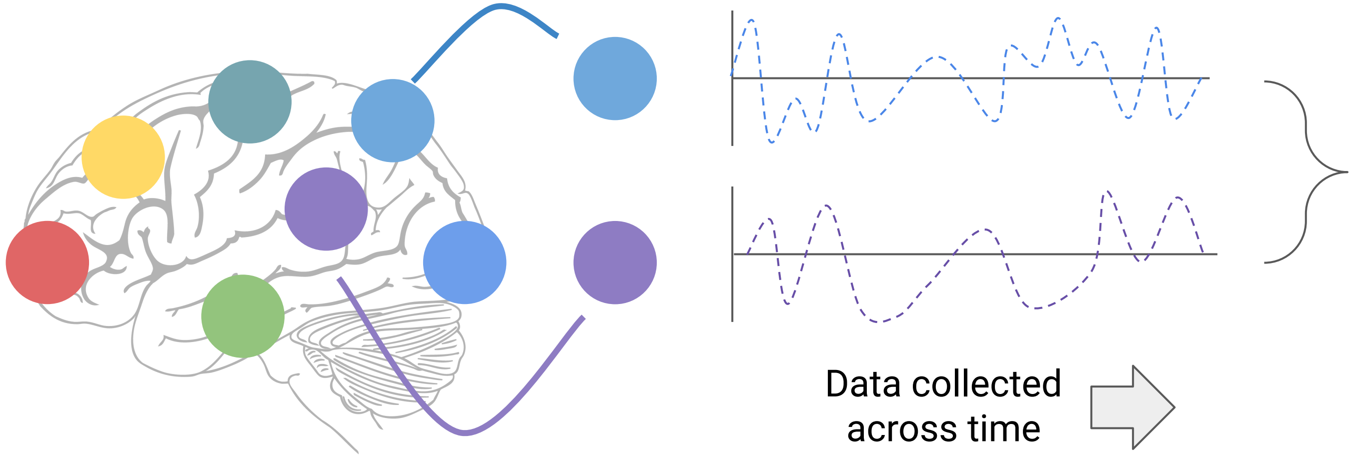
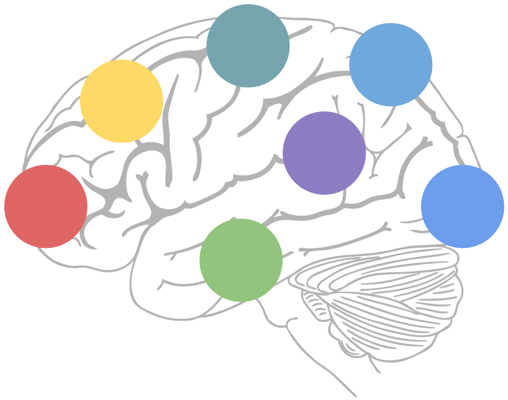


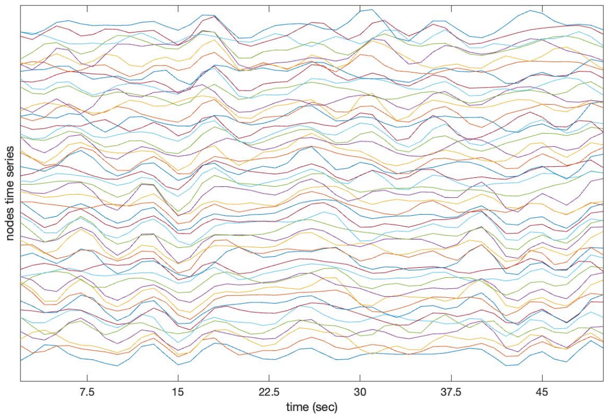
Data collected across time

Can compare data fluctuations over time in a pairwise manner

Until you make all possible pairwise comparisons; giving you a full correlation matrix

Creating functional networks





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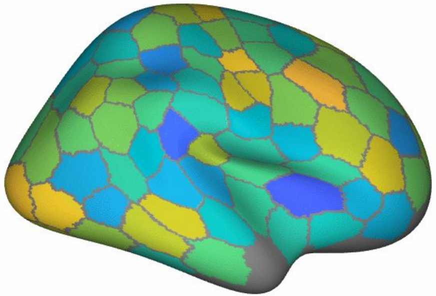
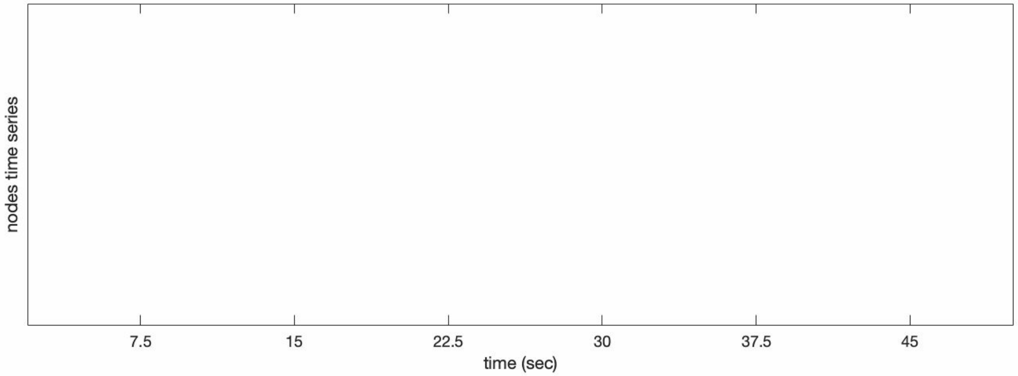
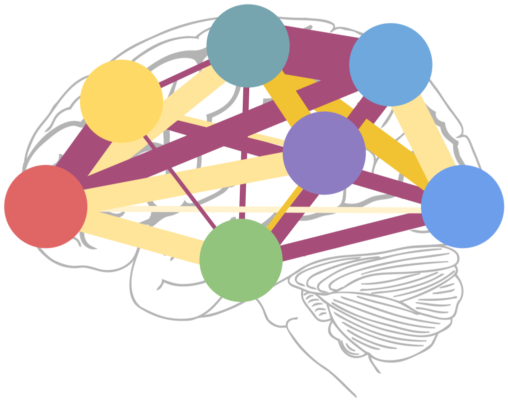
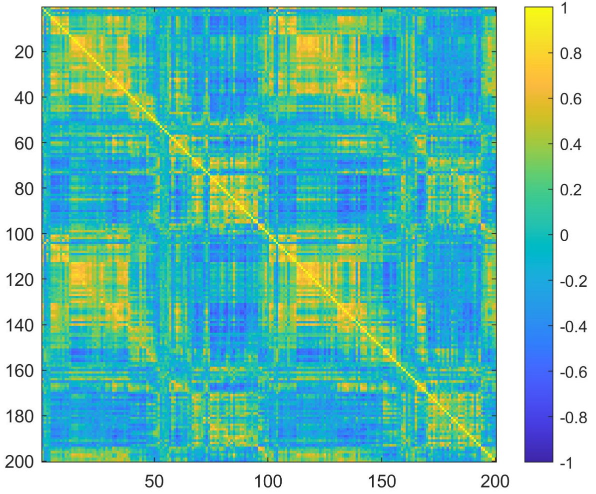




Creating functional networks





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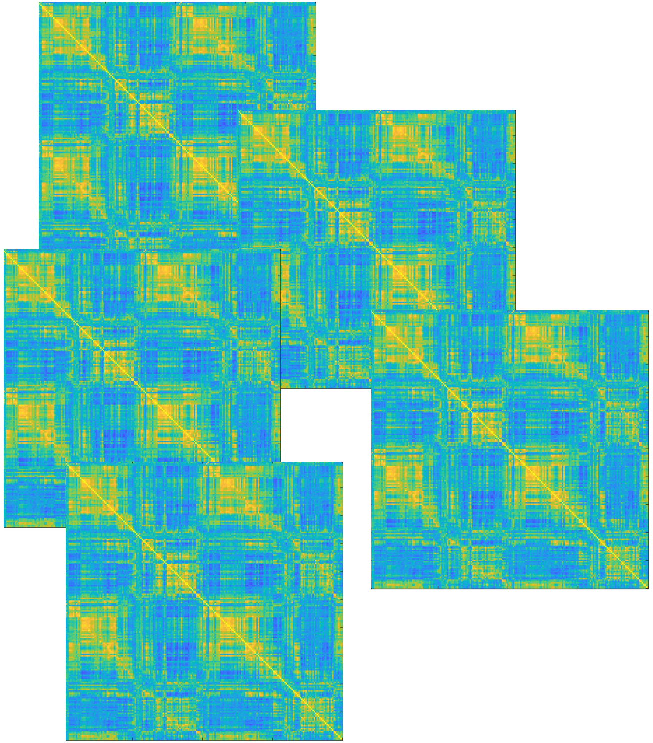
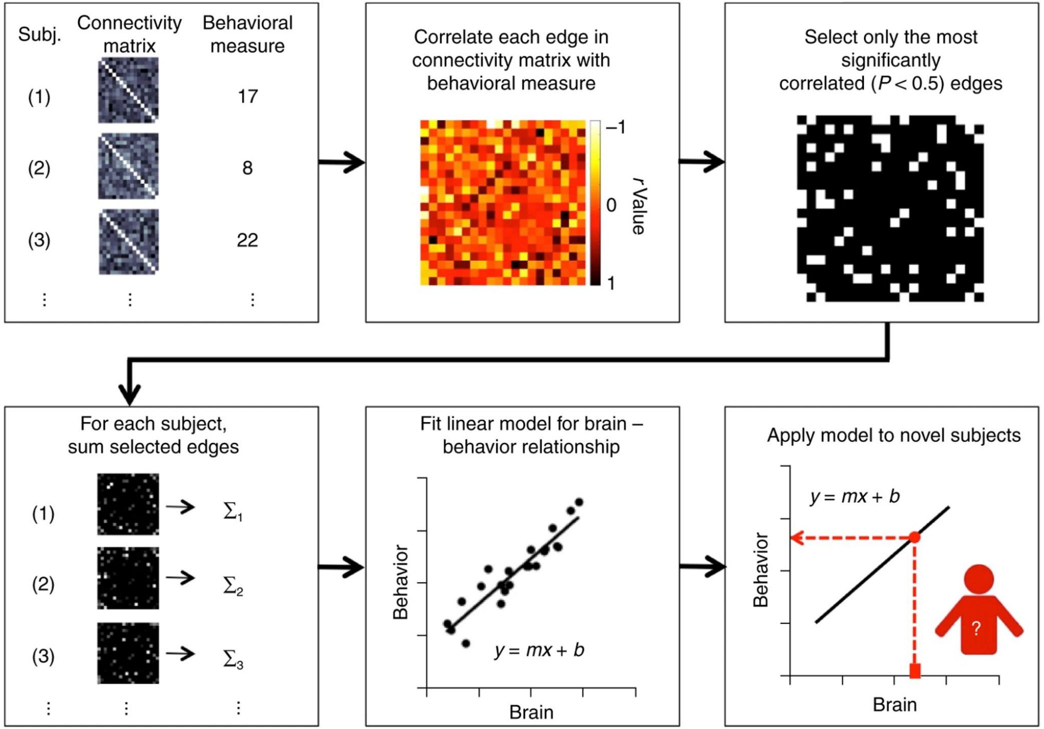
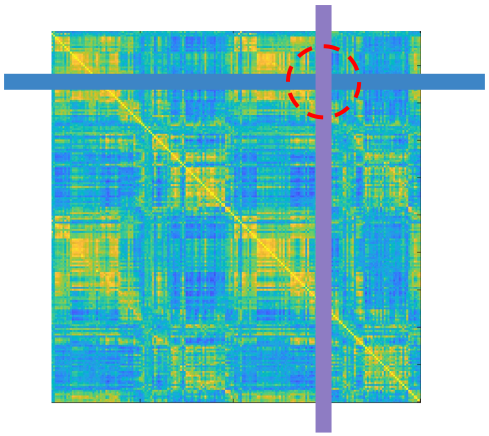
Creating functional networks

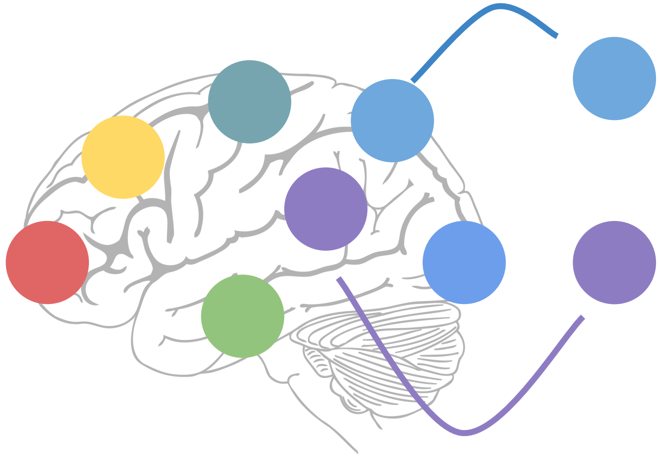


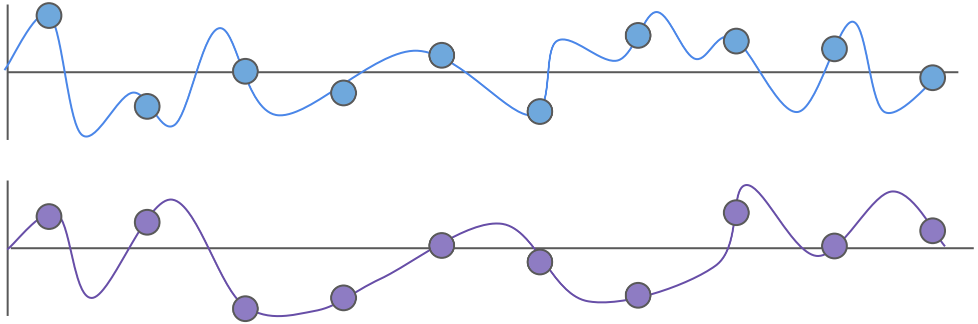


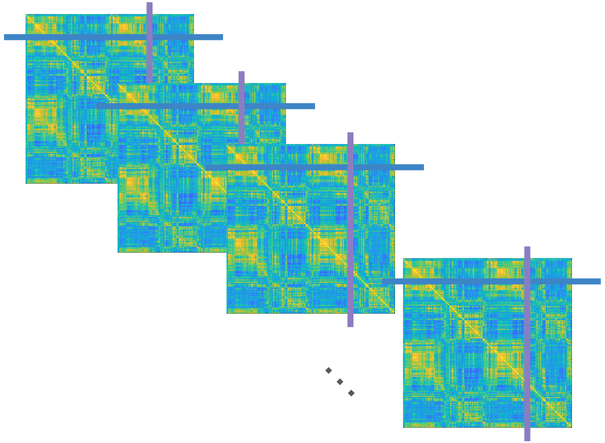
Shen et al (2017) *Nat. Protocols*



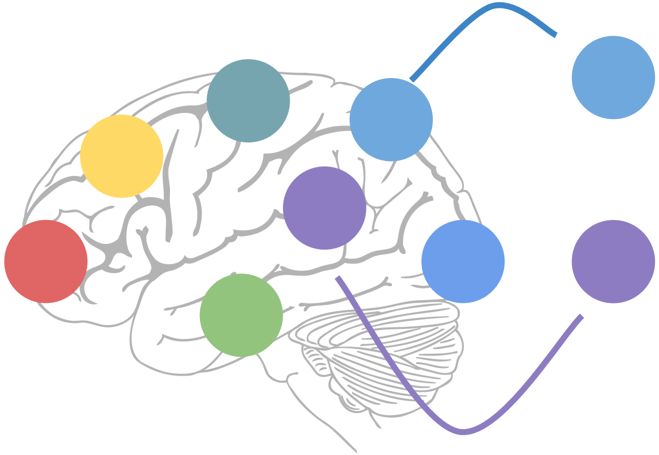
- Time averaged
  - Similarity across your whole acquisition
  - Use all your (good) time points
  - Assess “coupling” between areas or systems
  - “Functional organization” as trait phenotype

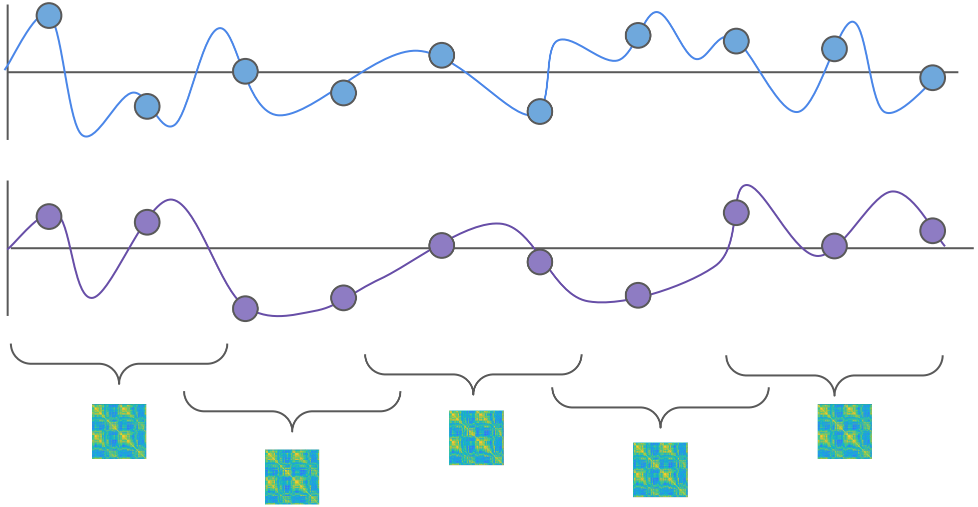


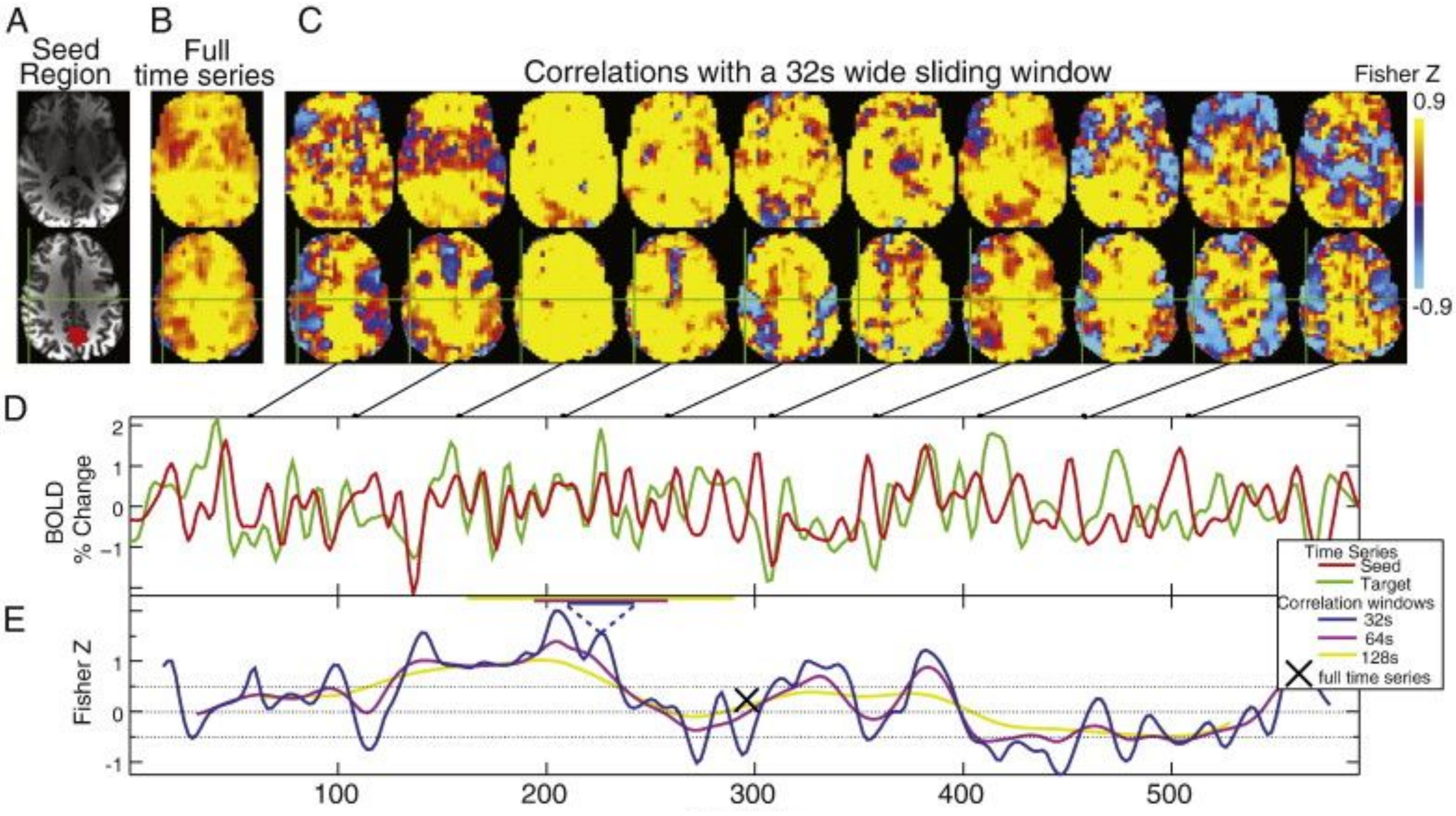




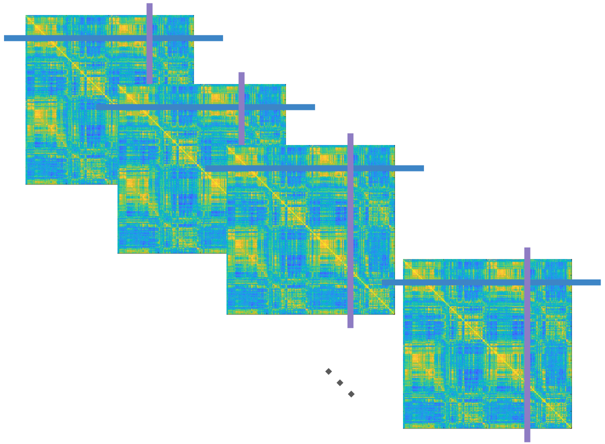
- Time varying
  - Do certain regions go in/out of synchrony?
  - Statistics about these dynamics
    - Variability, state changes, task-response
  - State dependent?







Handwerker et al (2012) *NeuroImage*



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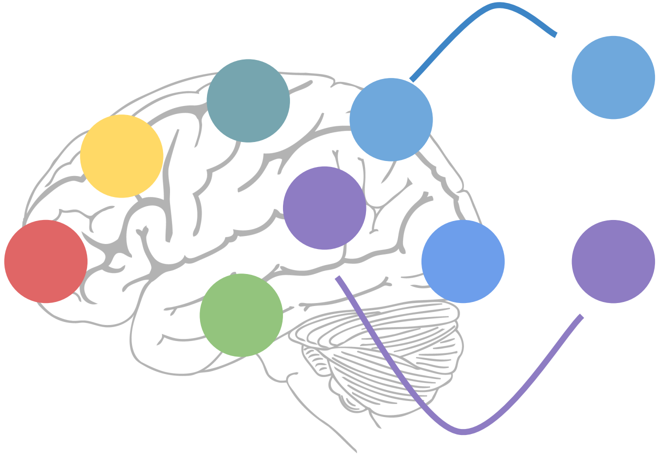
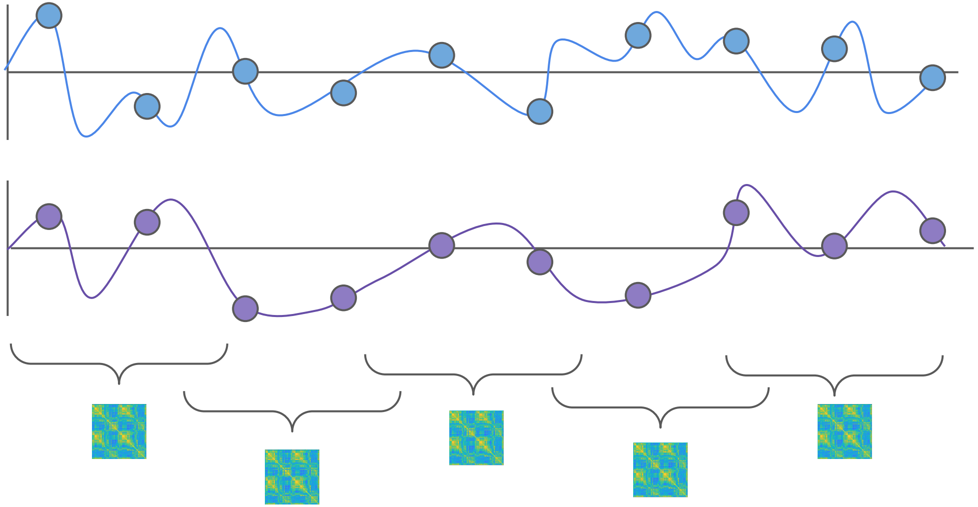
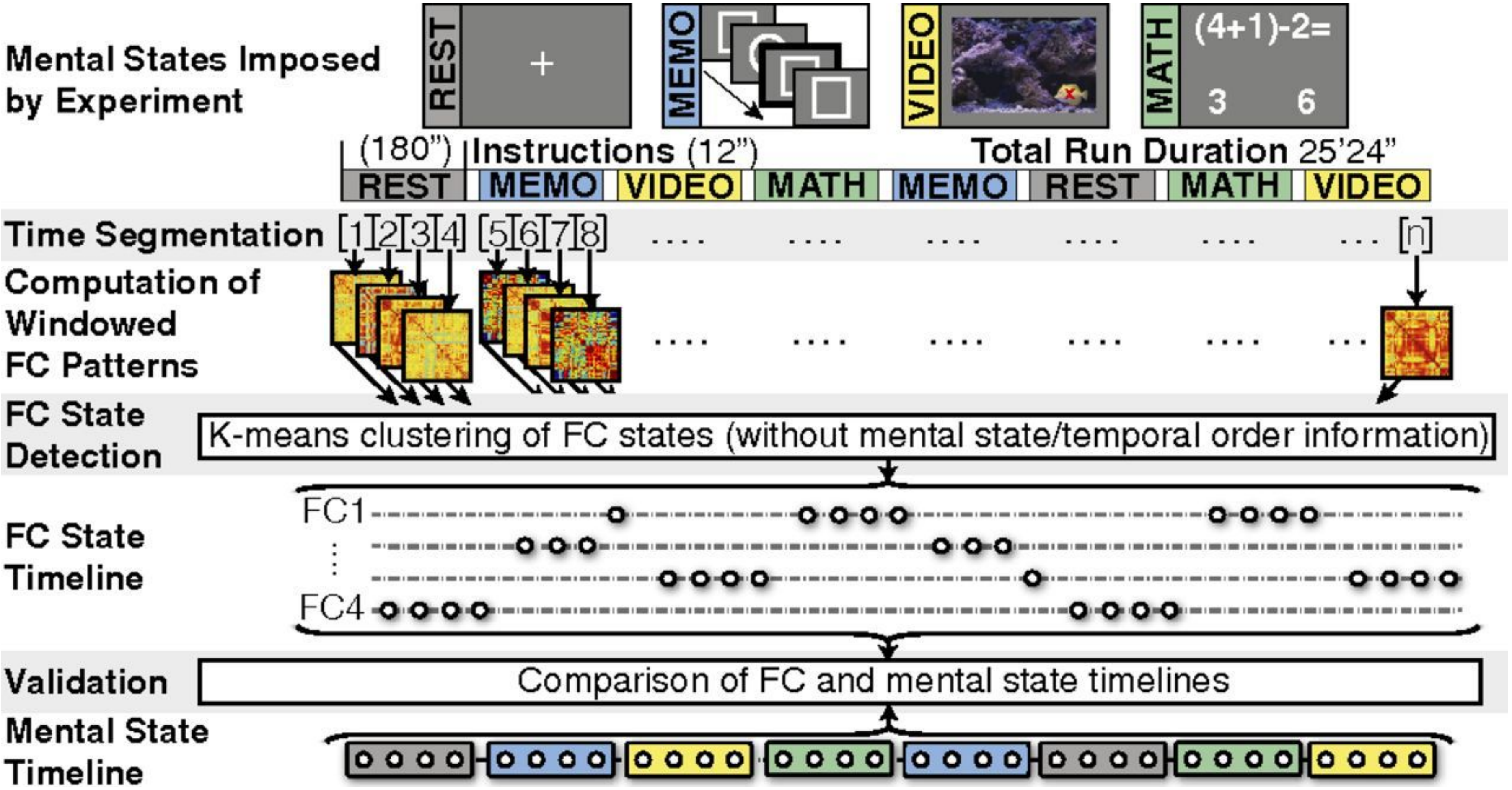
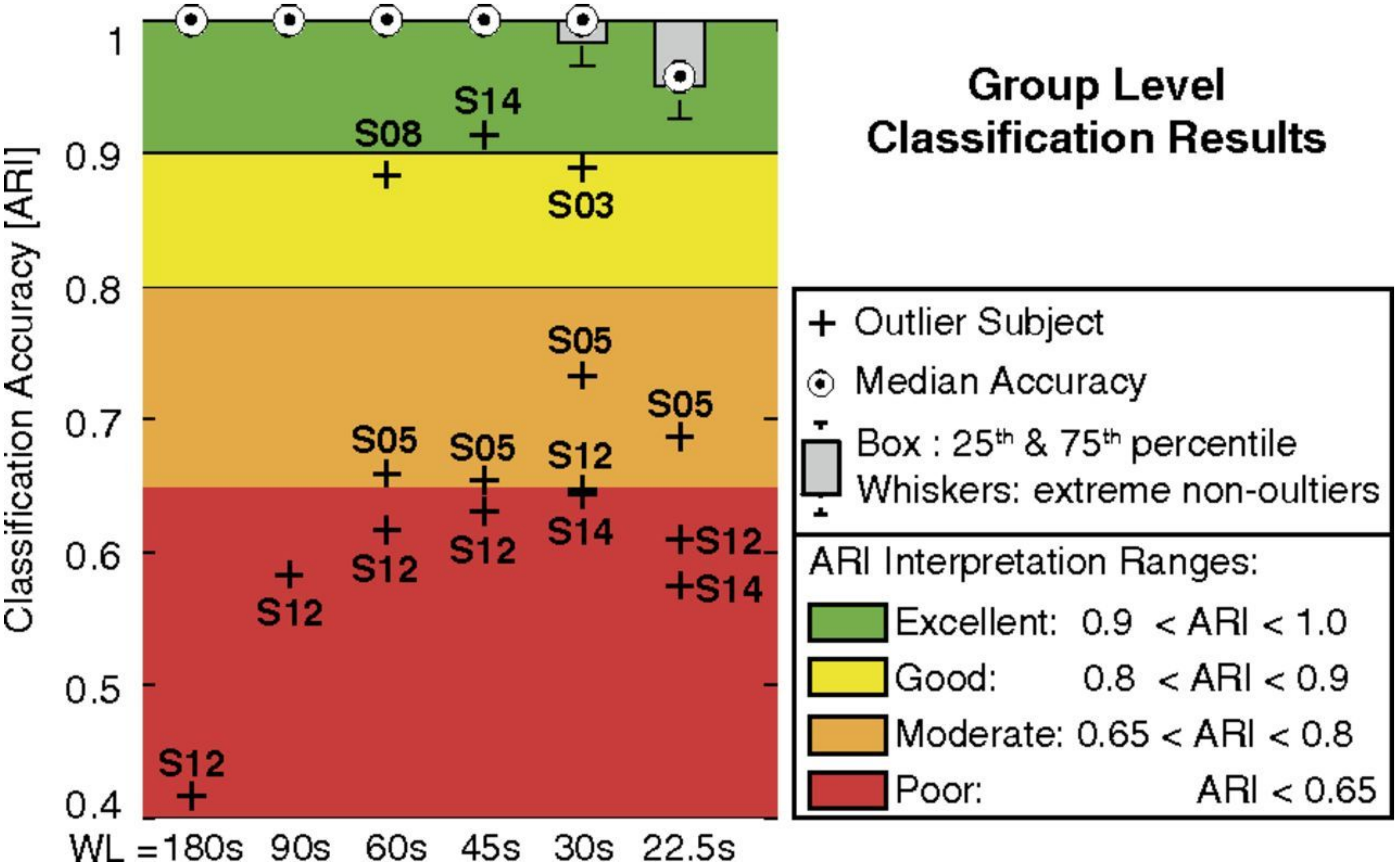




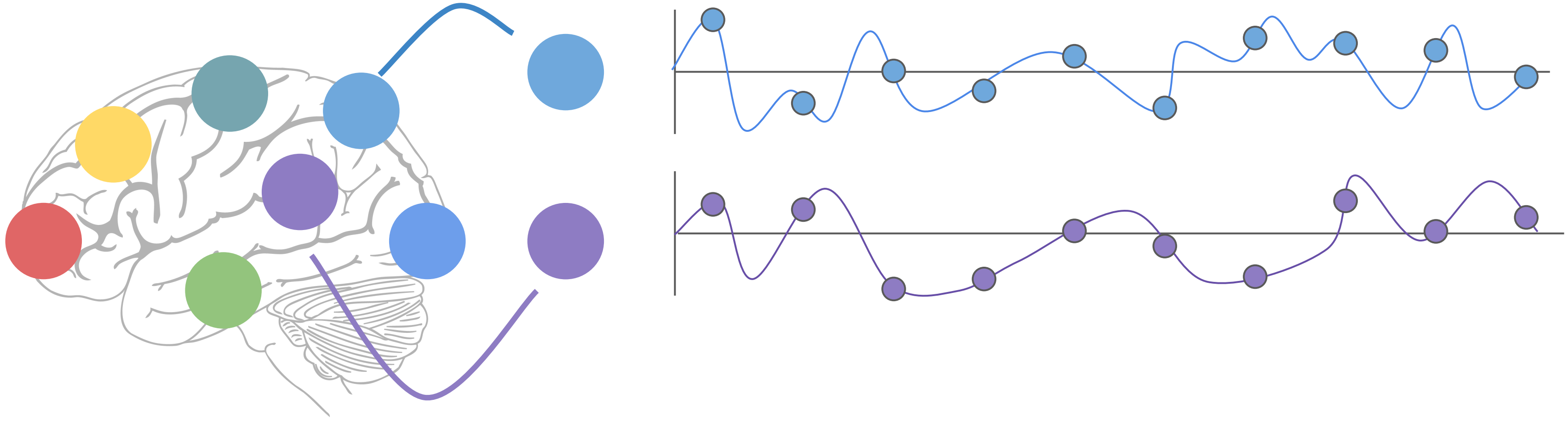


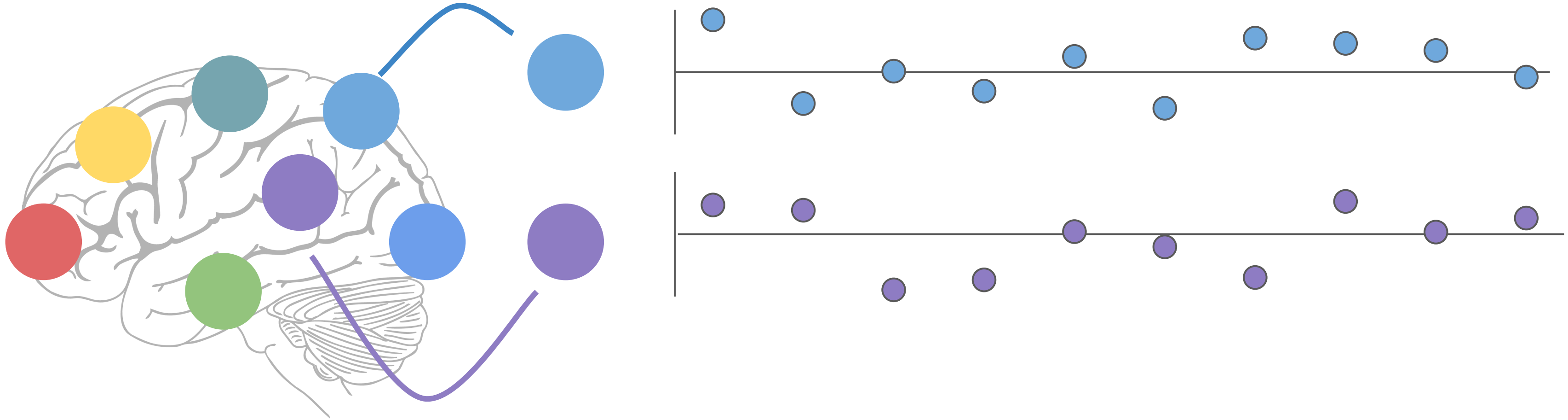
Gonzalez-Castillo et al (2015) *PNAS*

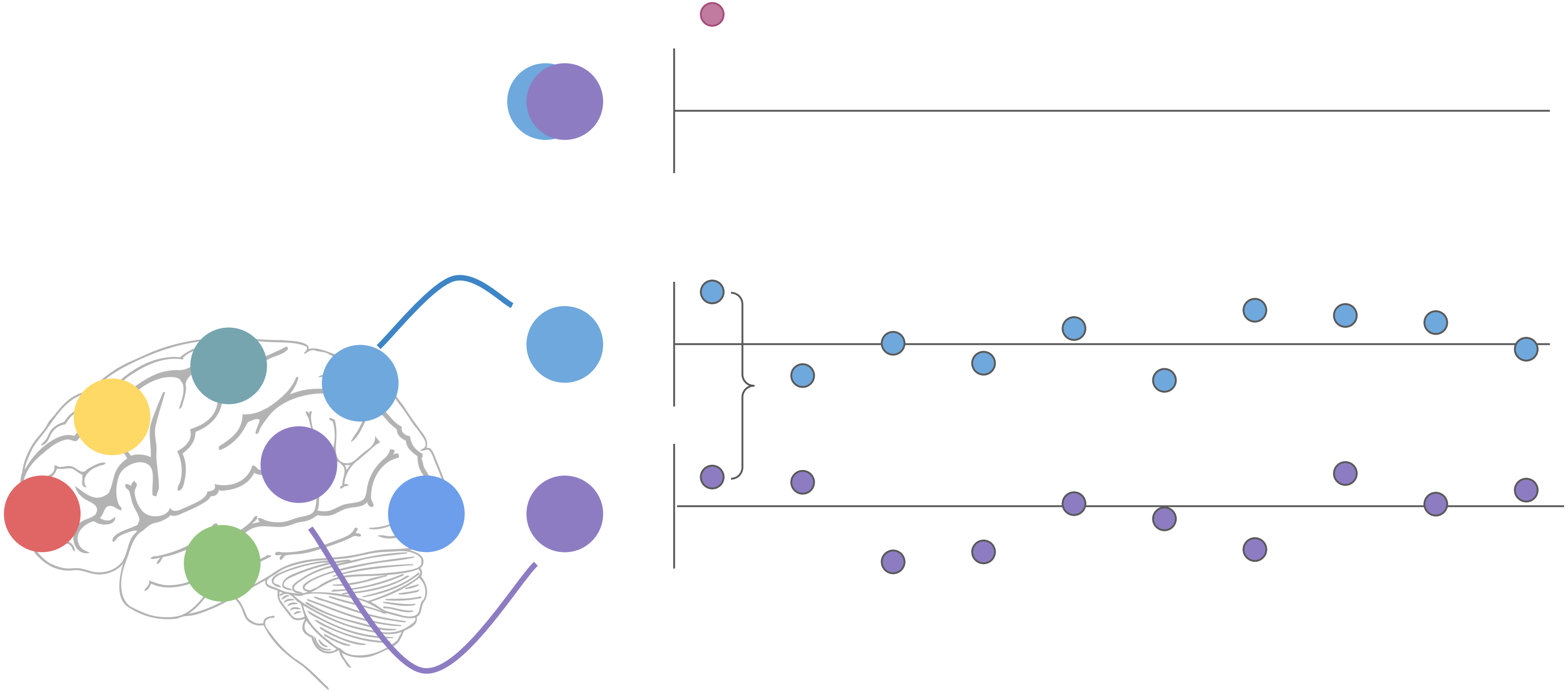


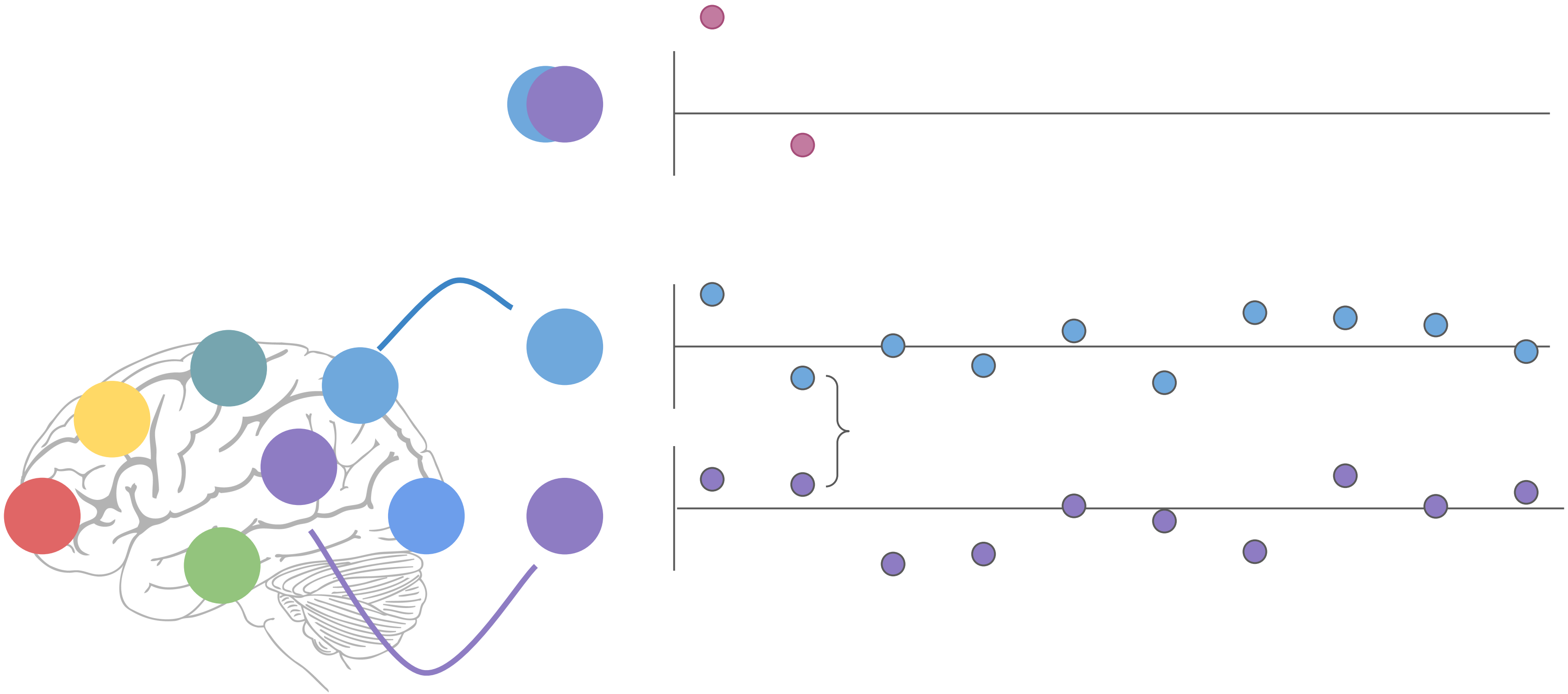
Gonzalez-Castillo et al (2015) *PNAS*

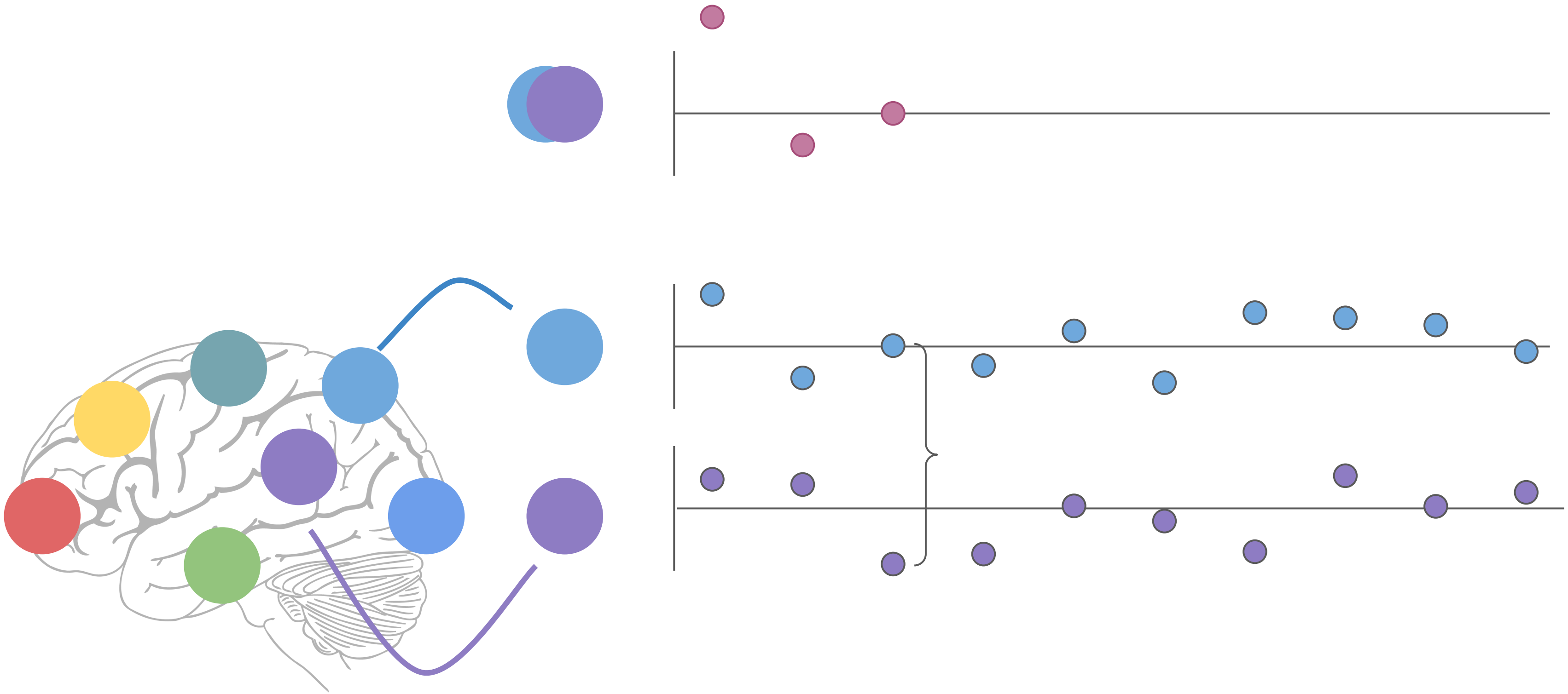
Calculating correlation

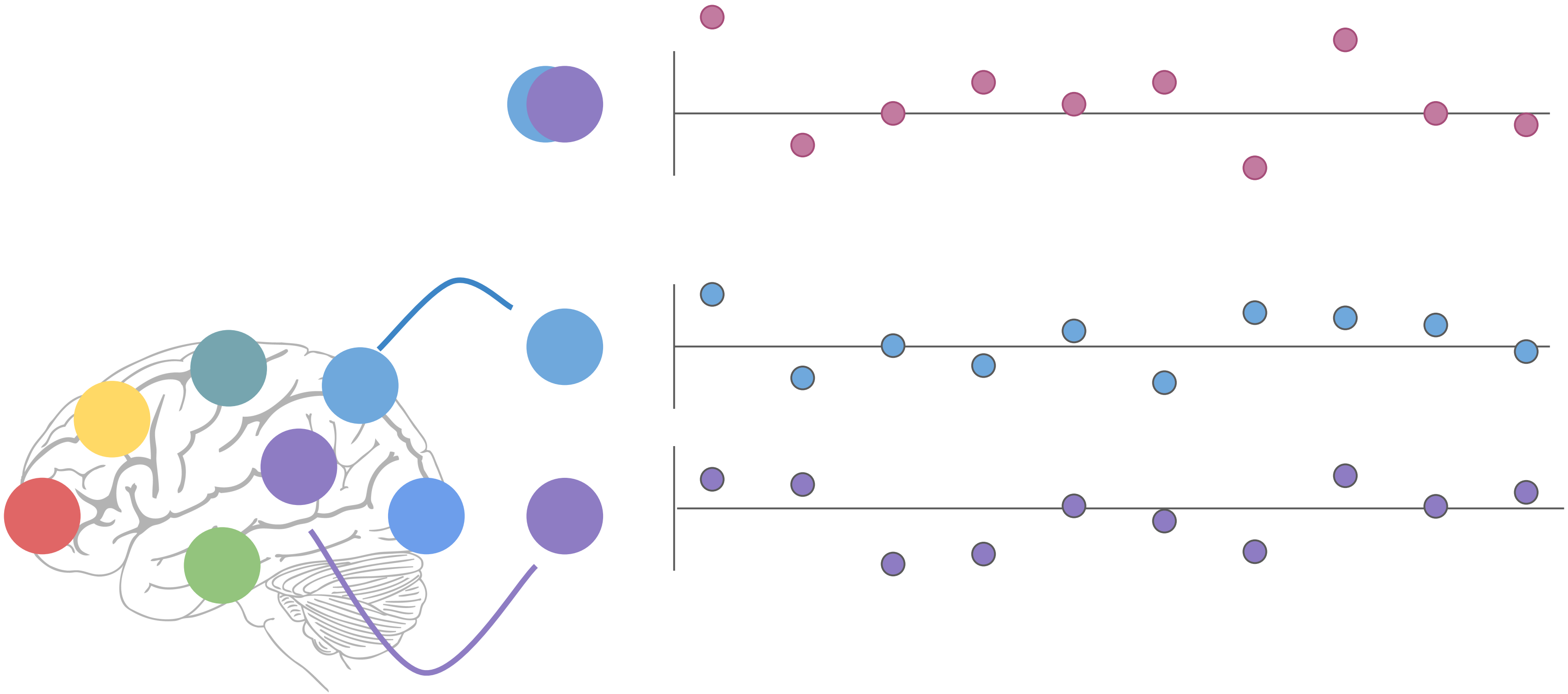












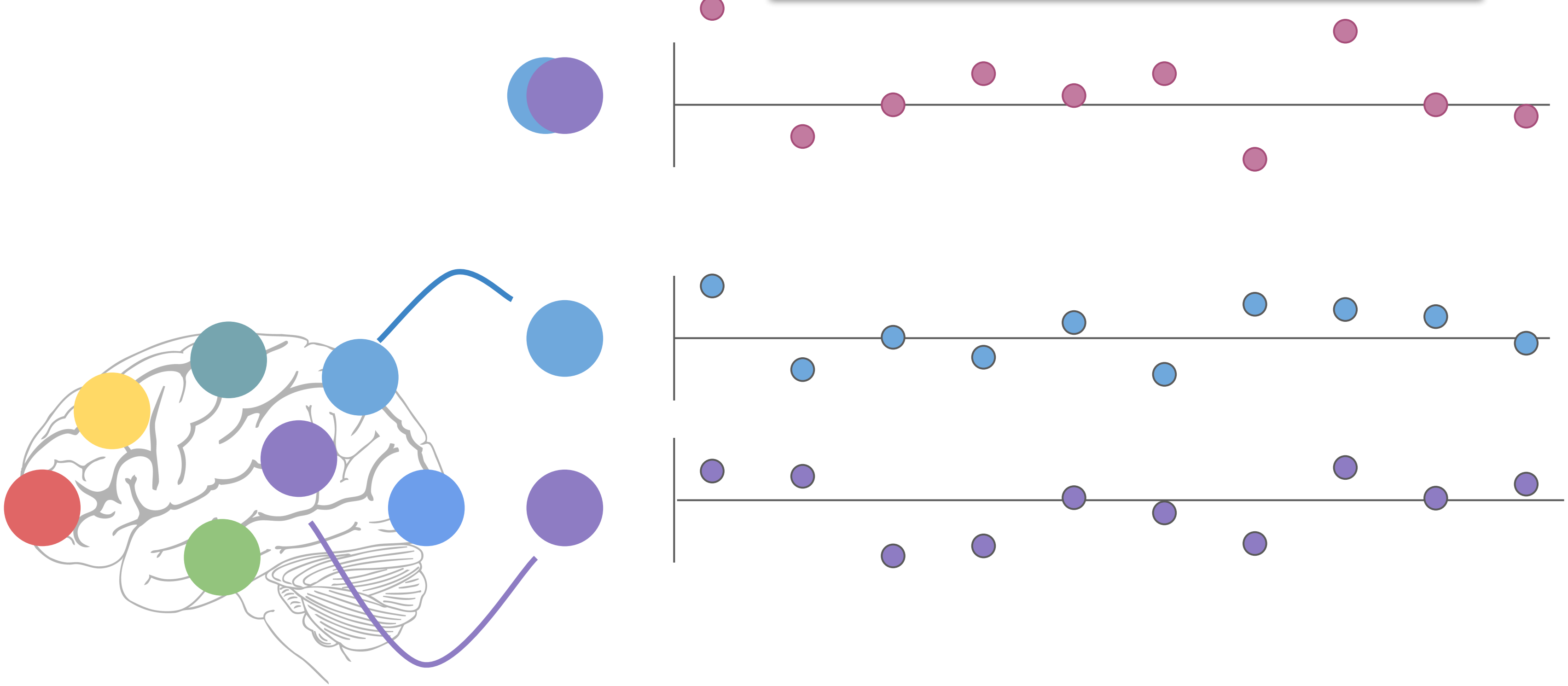
An equivalent expression gives the formula for r_{xy} as the mean of the products of the standard scores as follows:

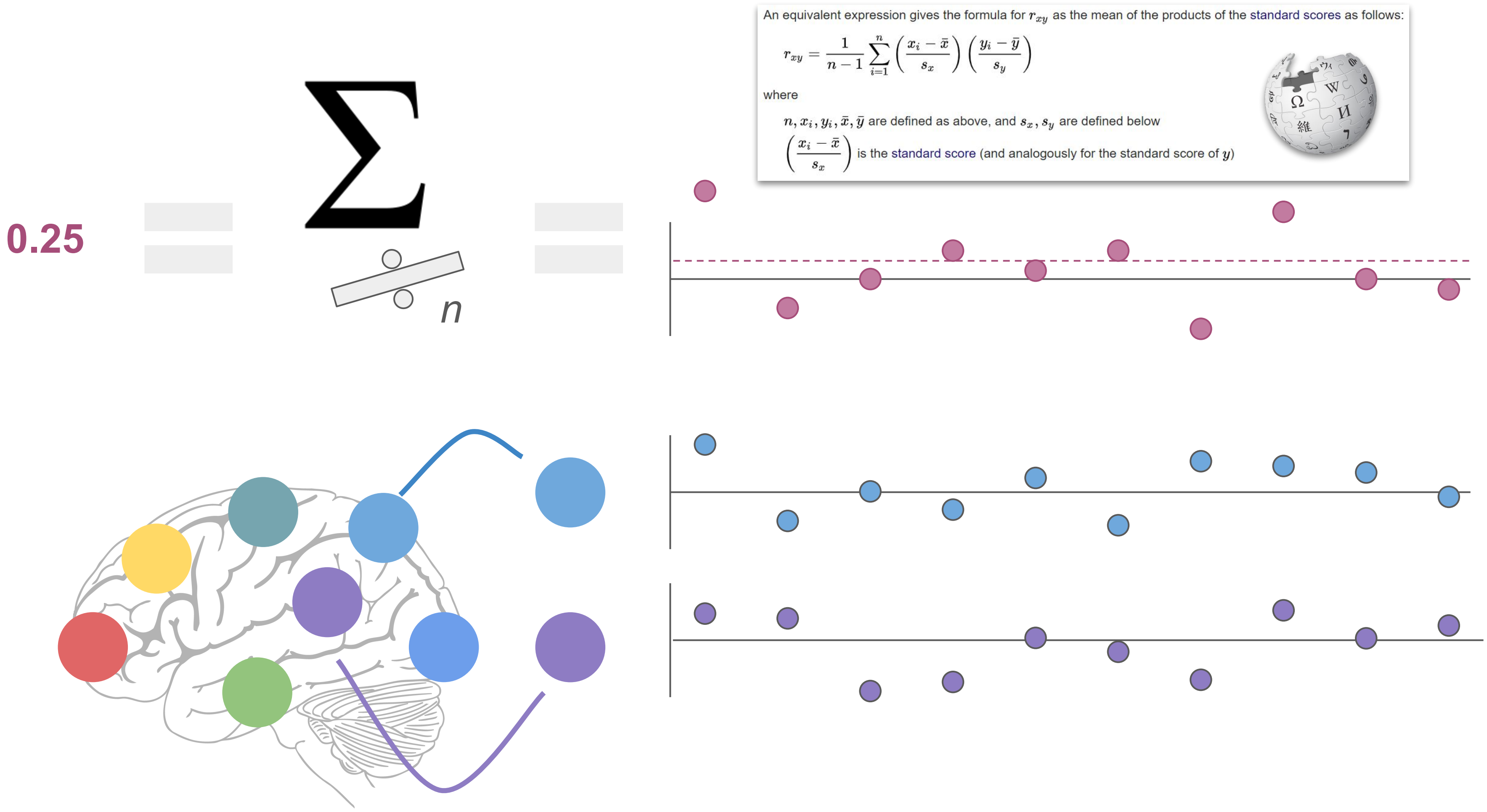
$$r_{xy} = \frac{1}{n-1}\sum_{i=1}^{n}\left(\frac{x_i - \bar{x}}{s_x}\right)\left(\frac{y_i - \bar{y}}{s_y}\right)$$

where

$n, x_i, y_i, \bar{x}, \bar{y}$ are defined as above, and s_x, s_y are defined below

$\left(\frac{x_i - \bar{x}}{s_x}\right)$ is the standard score (and analogously for the standard score of y)





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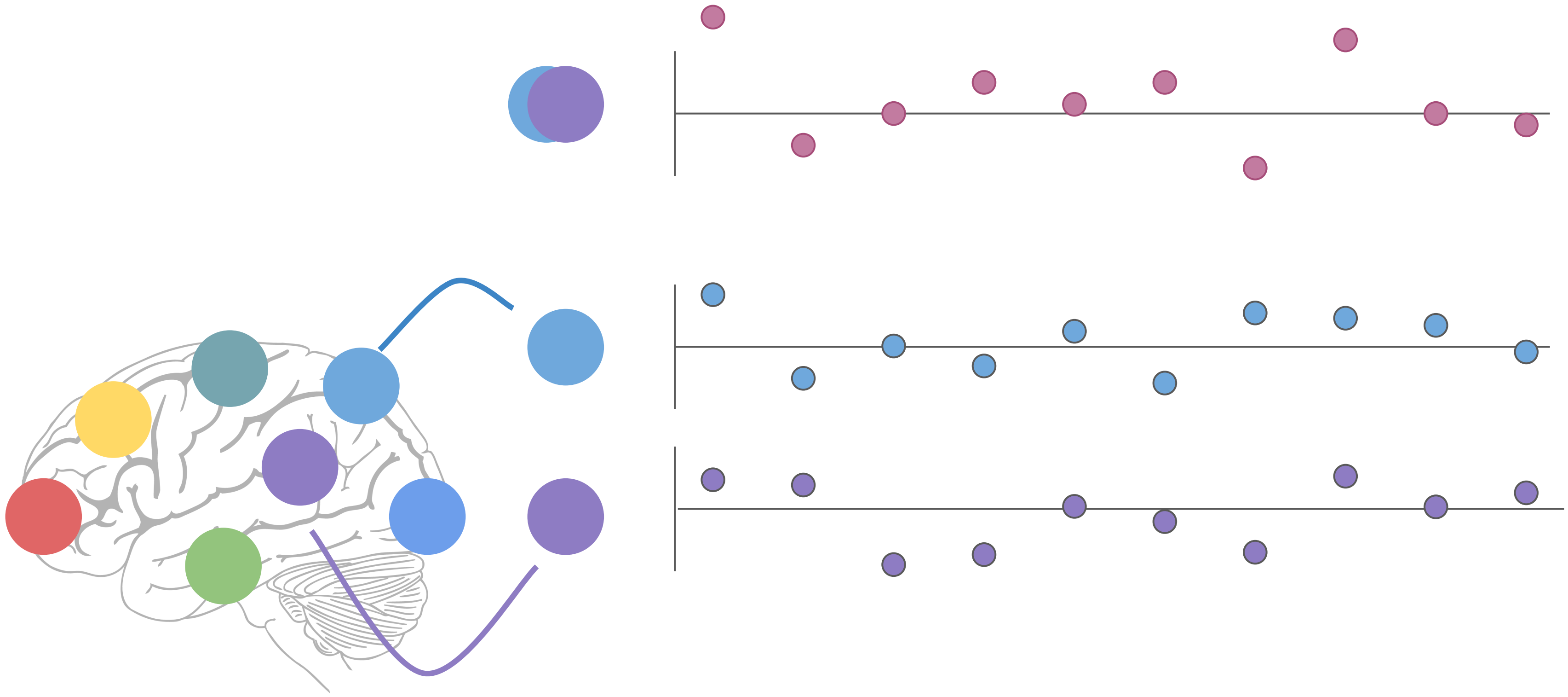
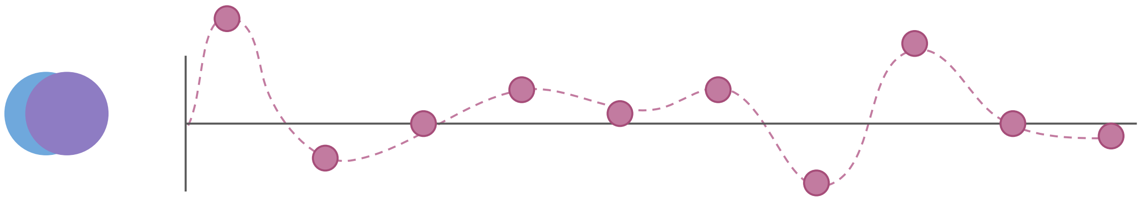
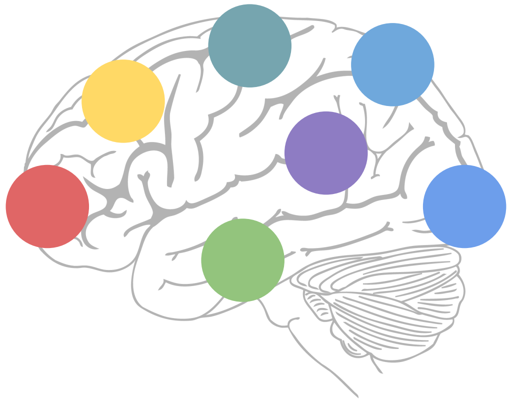
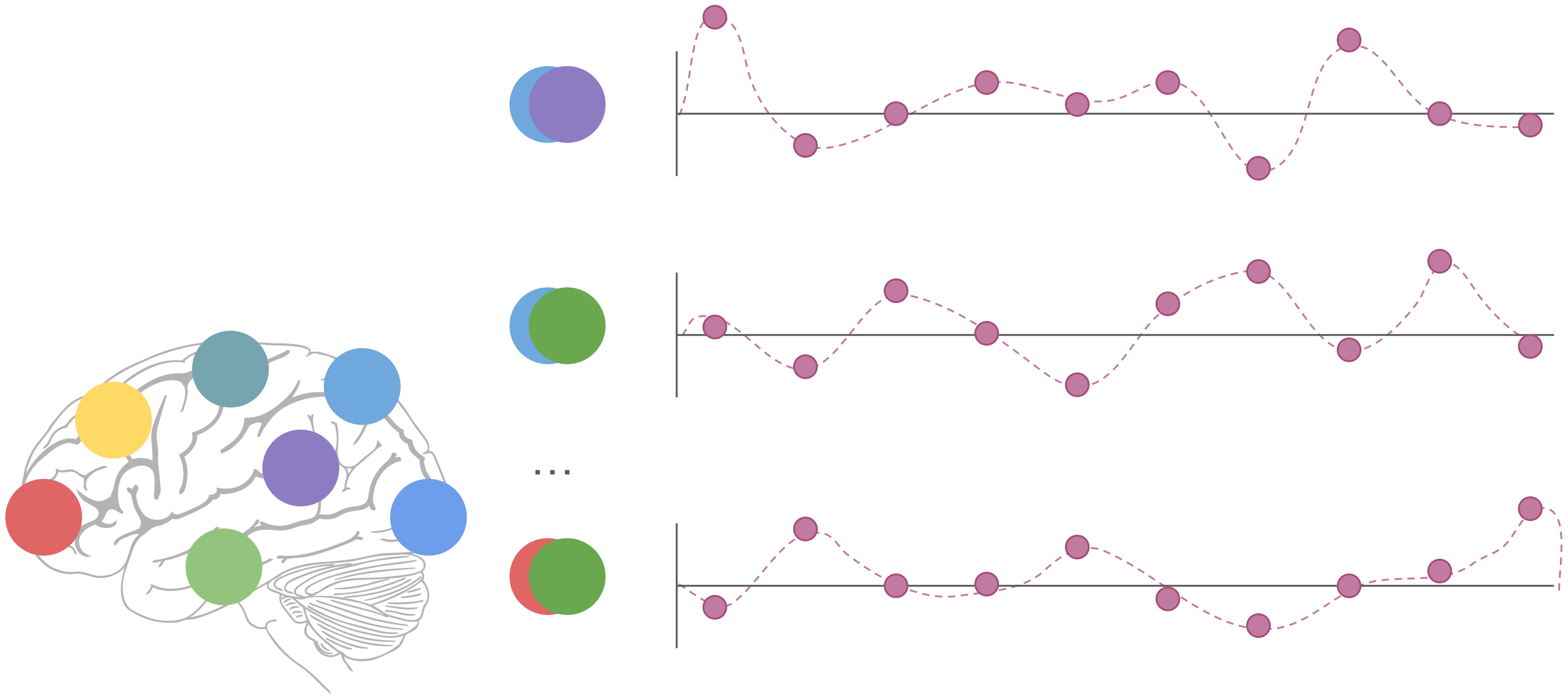
0.25
Σ
n

Time to get edgy







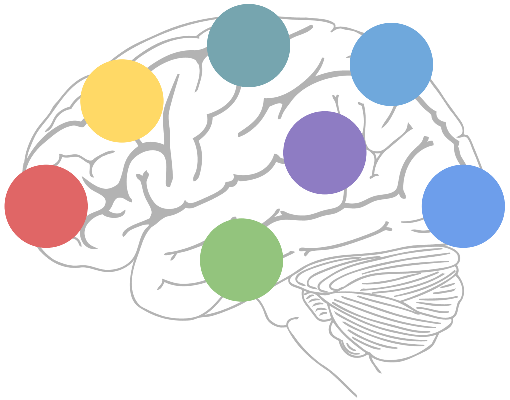


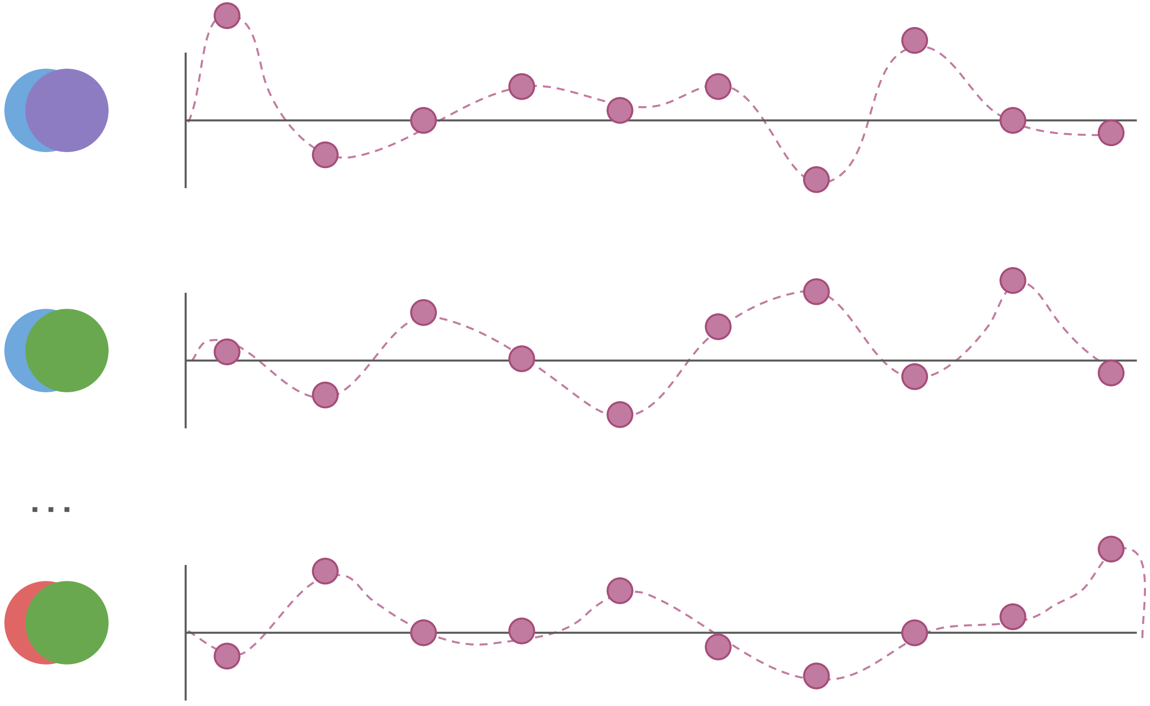
Instantaneous similarity after “unwrapping” the traditional correlation

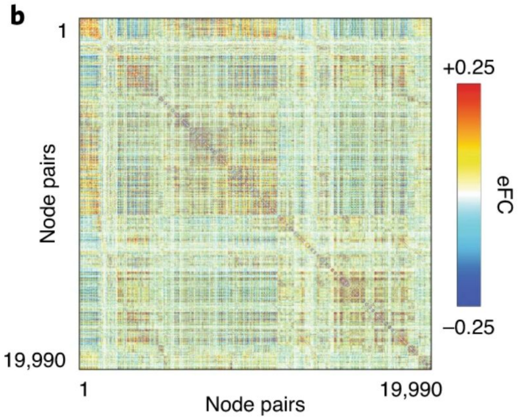
- No sliding step or window parameter
- Time-average is exactly correlation
- Same resolution as data input
  - Single frame information
  - Potential to measure “faster” phenomena

Faskowitz et al (2020) *Nat. Neuro*
Zamani Esfahlani (2020) *PNAS*

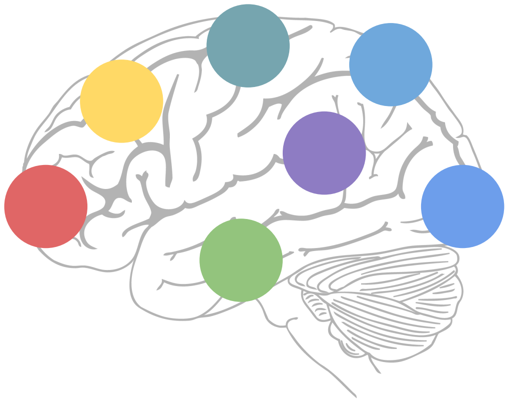
See also! Liu & Duyn (2013) *PNAS*, Lahnakoski et al (2017) *HBM,* van Oort et al (2018) *NeuroImage…*

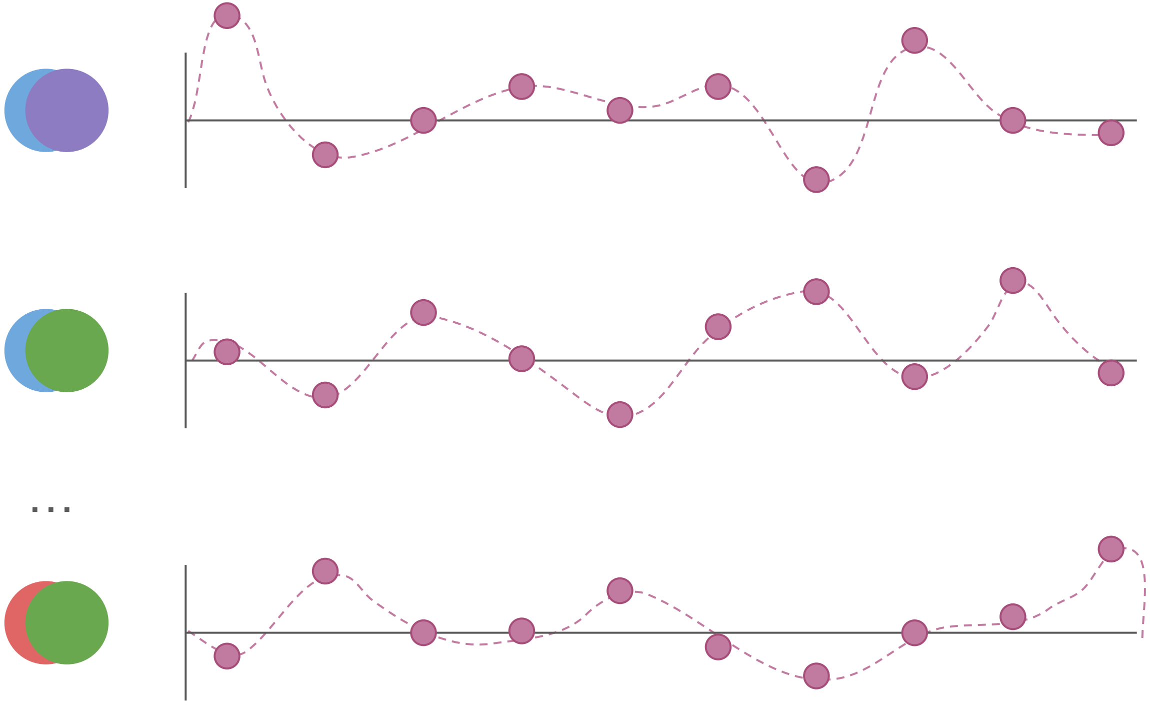


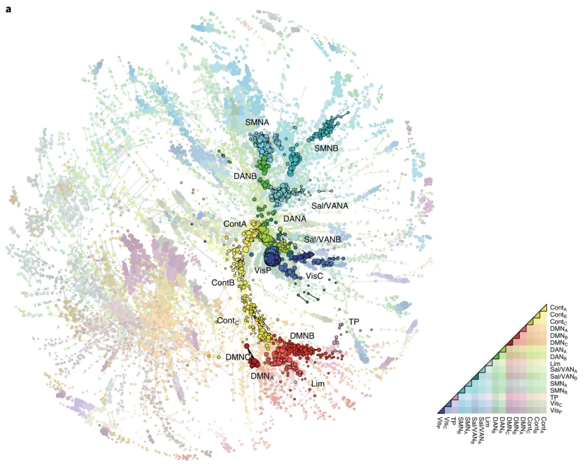




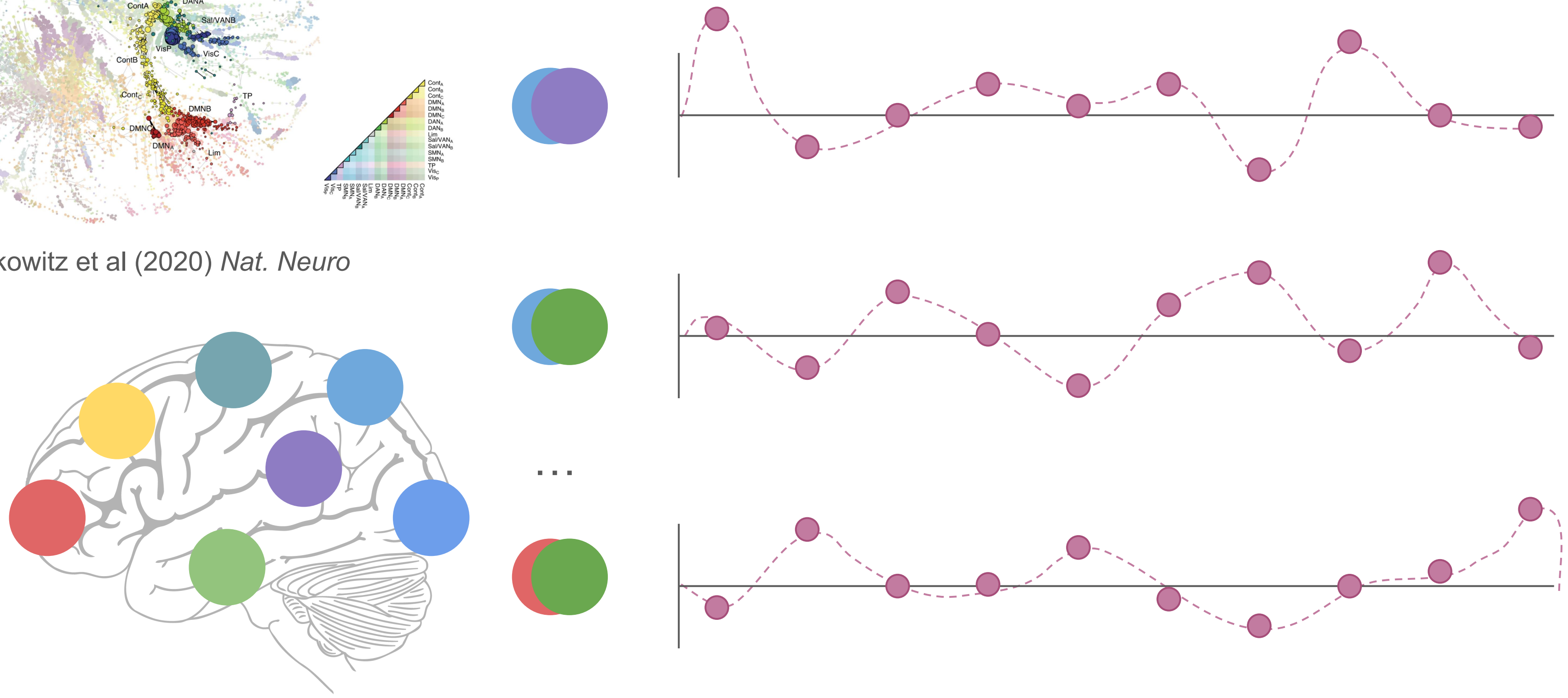
Faskowitz et al (2020) *Nat. Neuro*



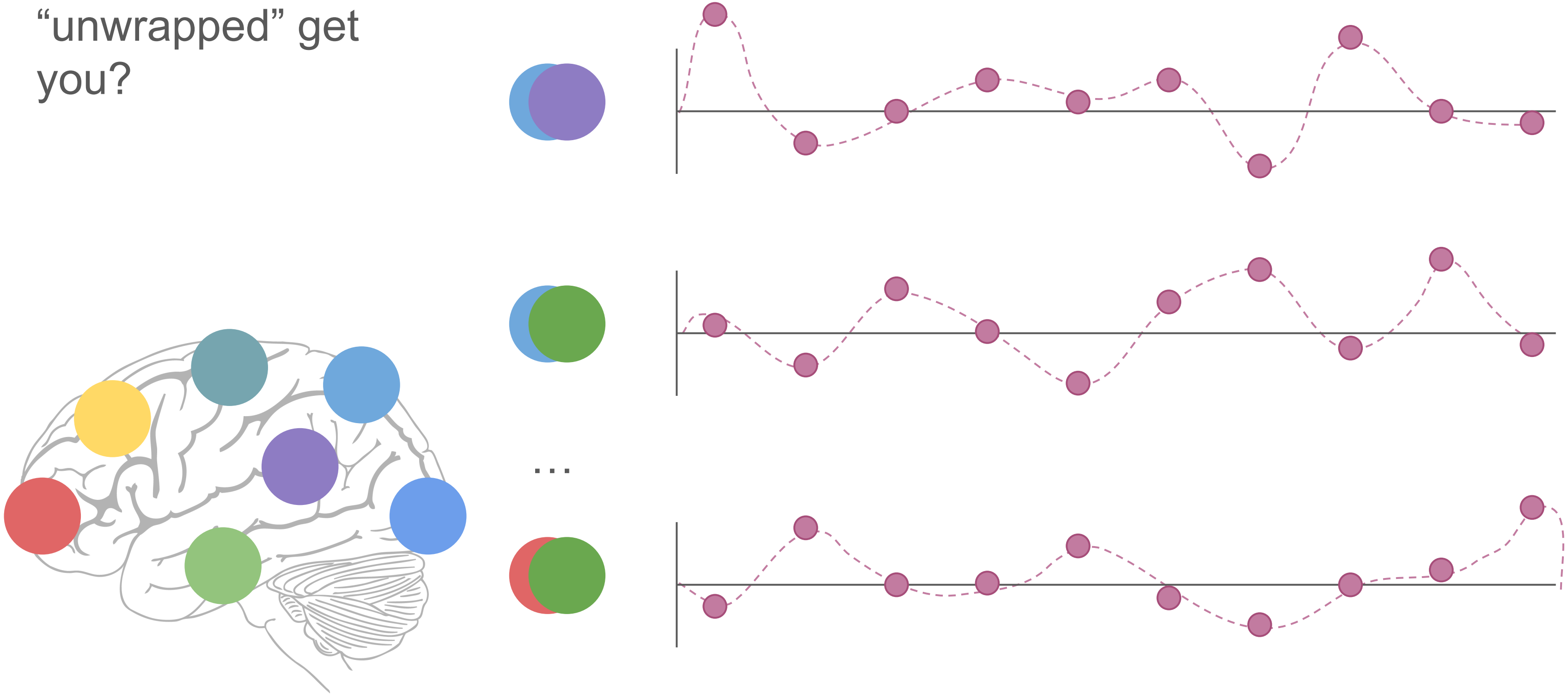




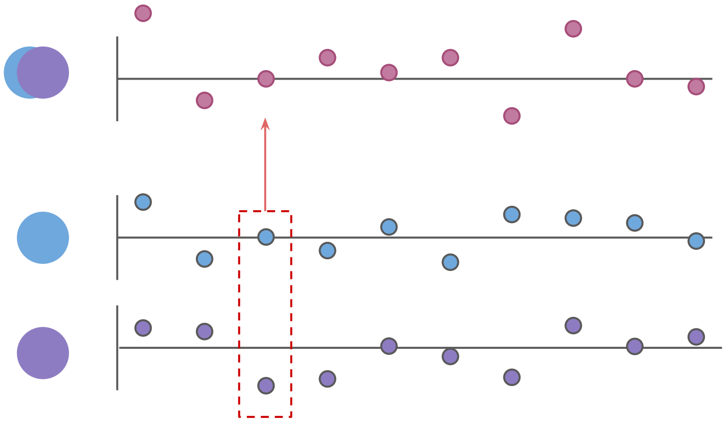
Faskowitz et al (2020) *Nat. Neuro*



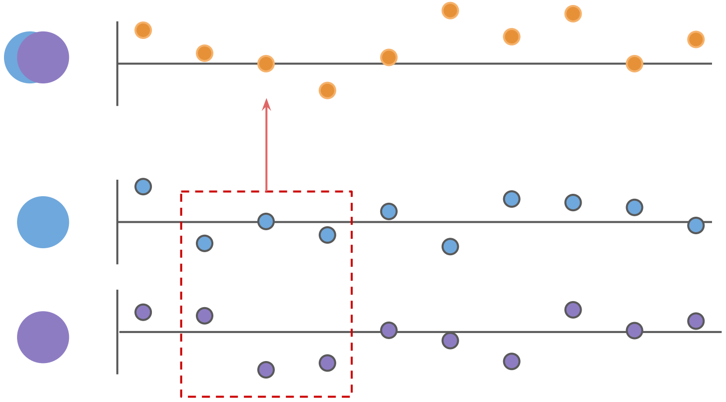
What does the correlation "unwrapped" get you?



- **No sliding step or window parameter**
- Time-average is exactly correlation
- Same resolution as data input
  - Single frame information
  - Potential to measure “faster” phenomena



Edge time series



tv-FC

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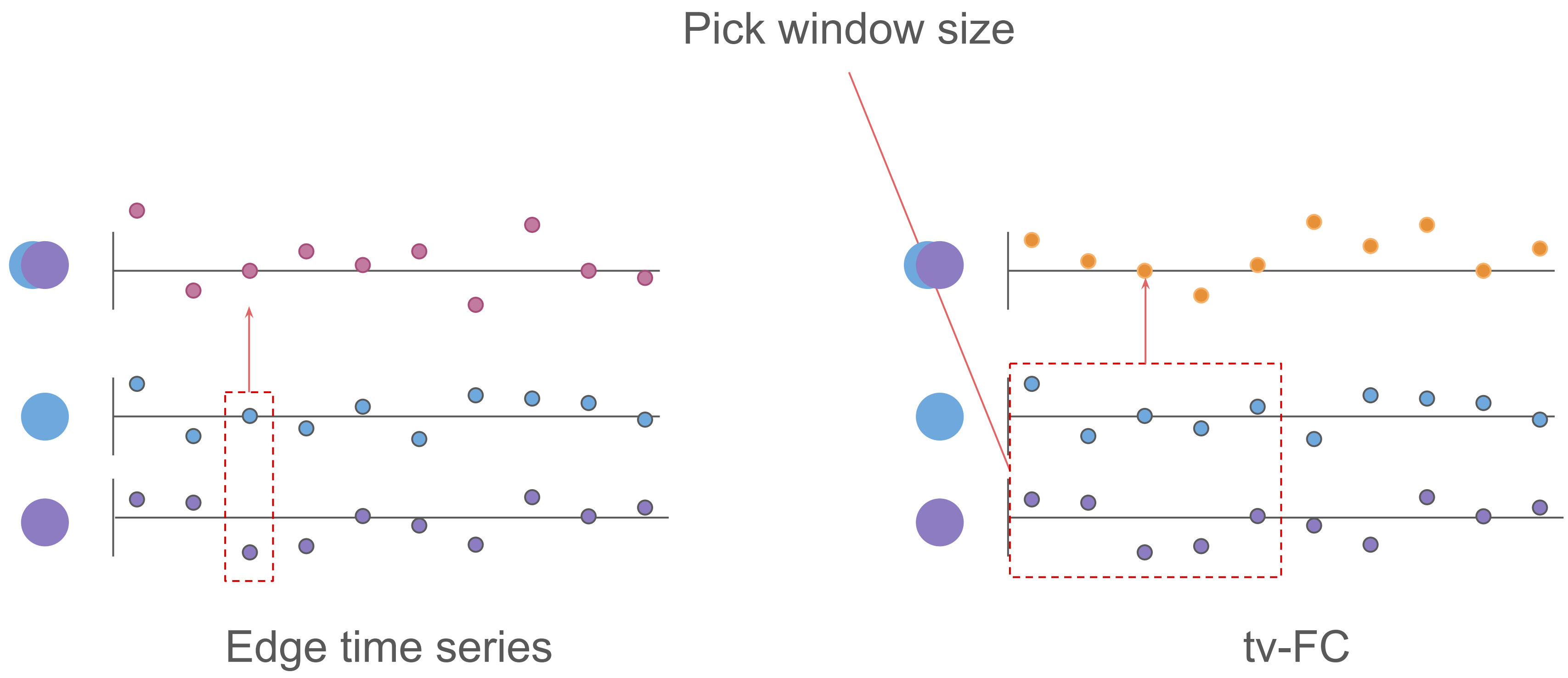

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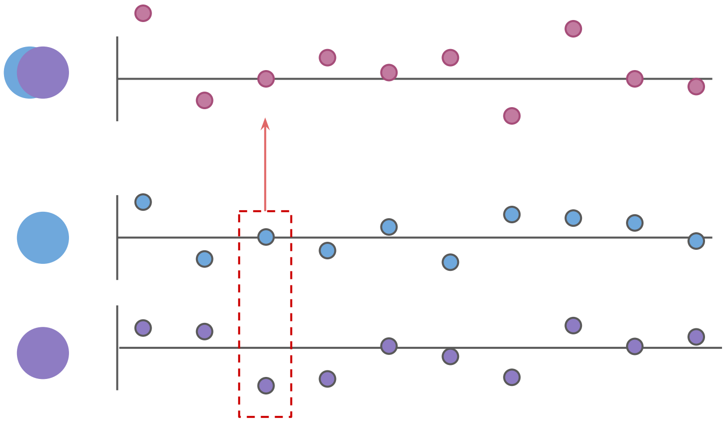
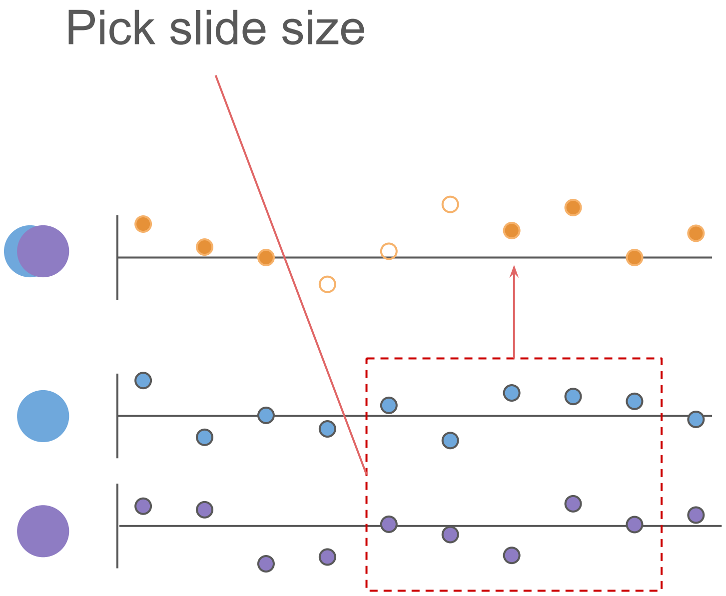


Edge time series



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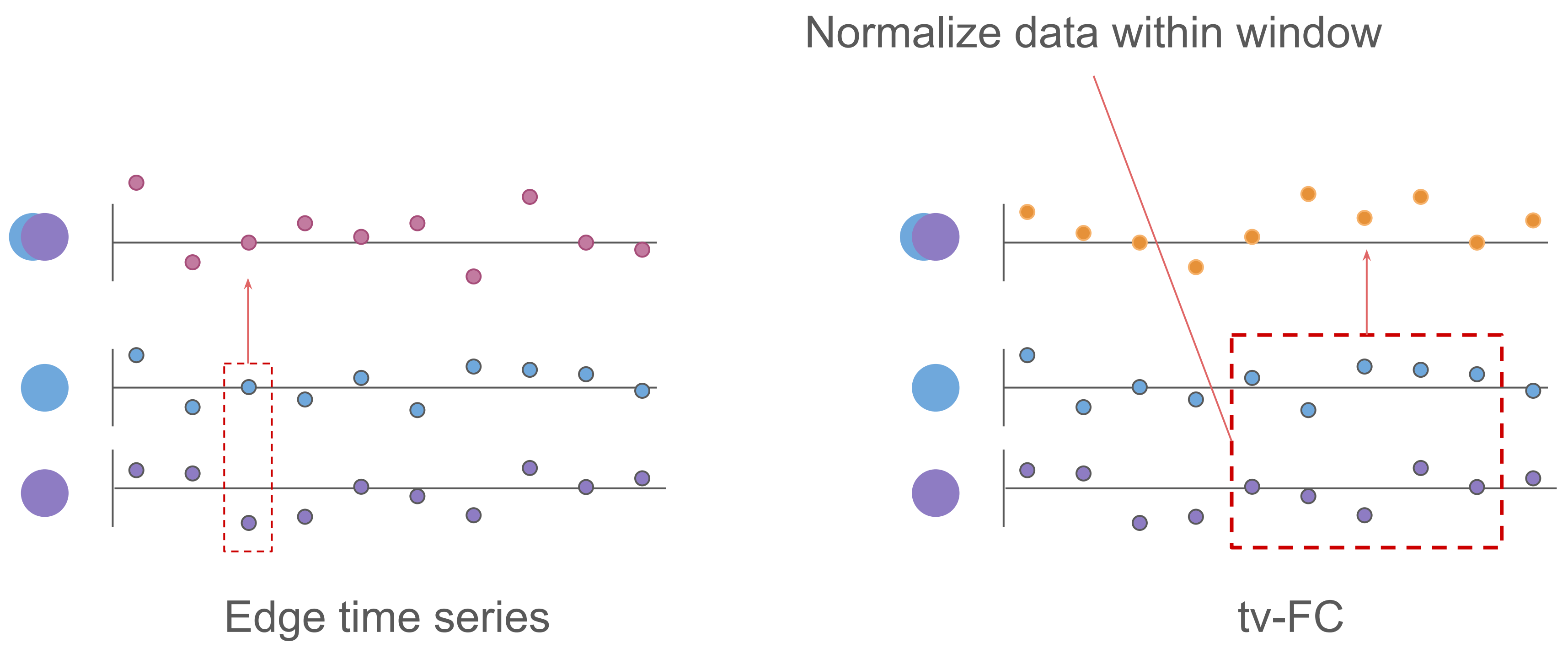

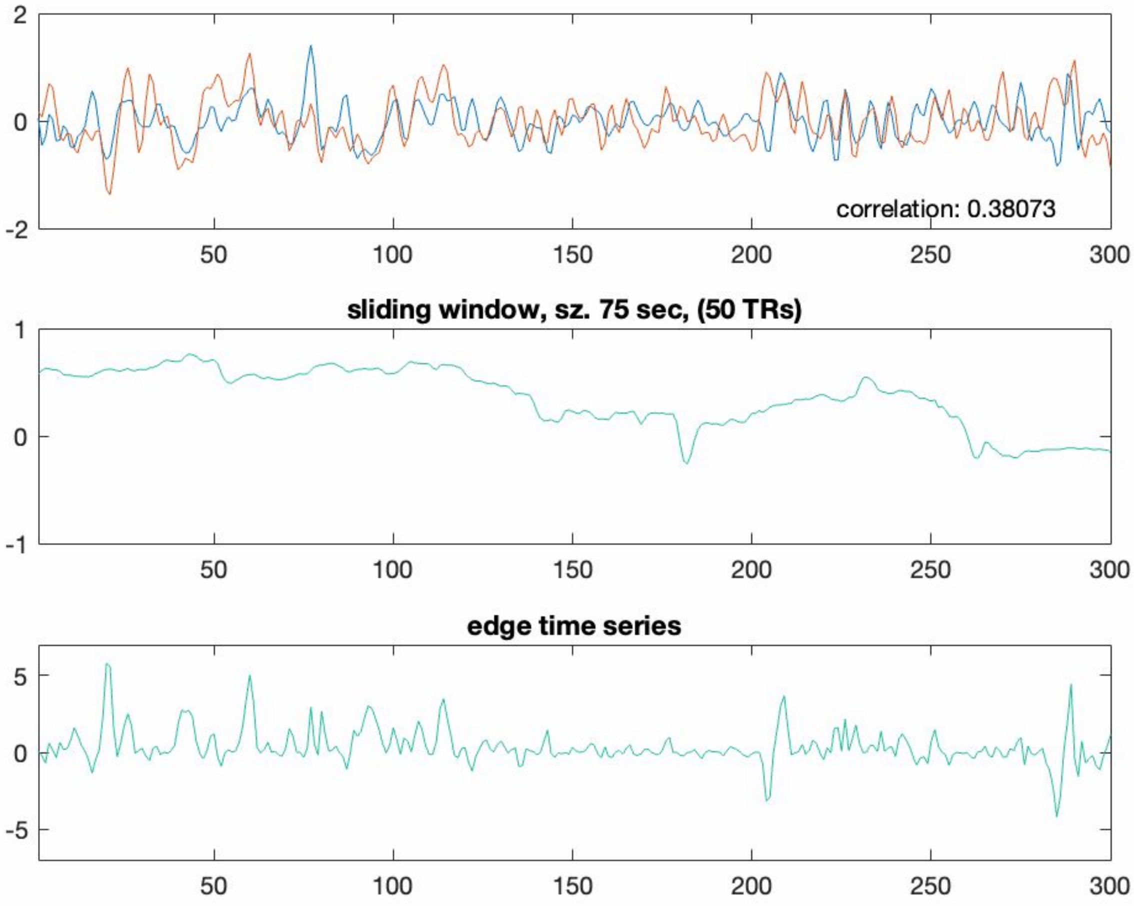

Difference in synchronization timing, variability, shape (but *not* claiming edges are correct vs sliding window)

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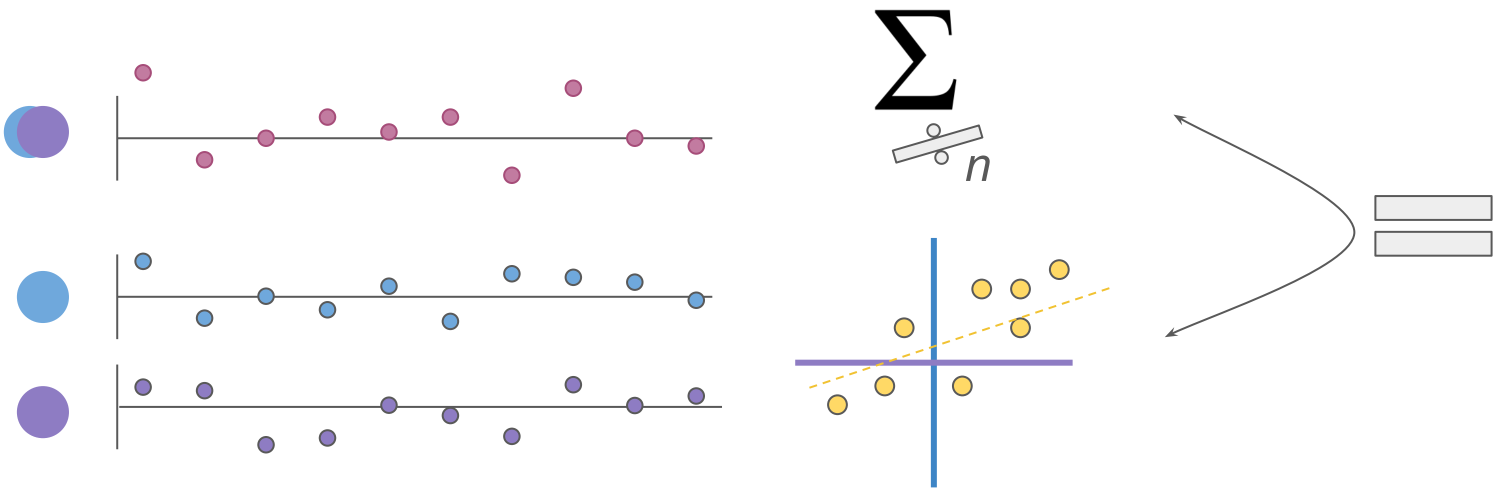

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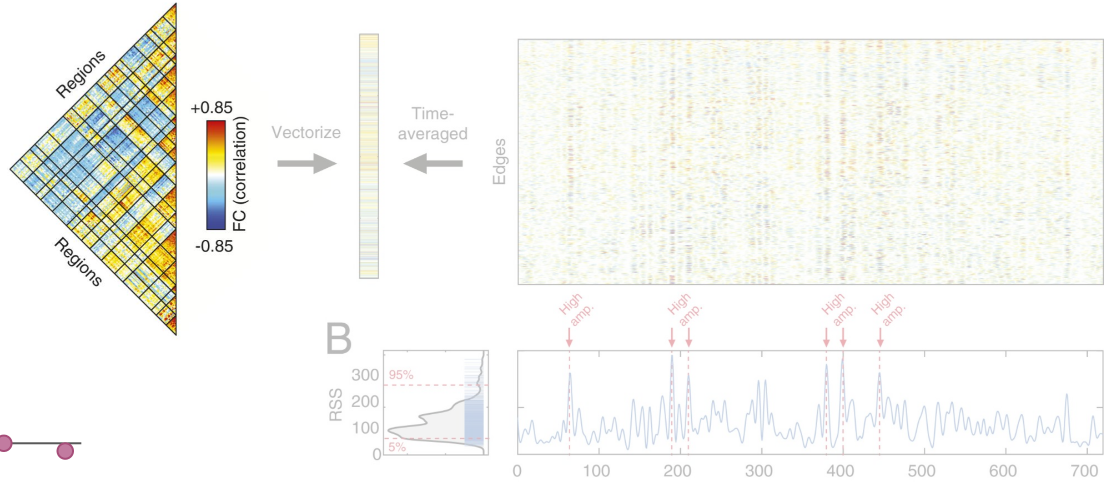

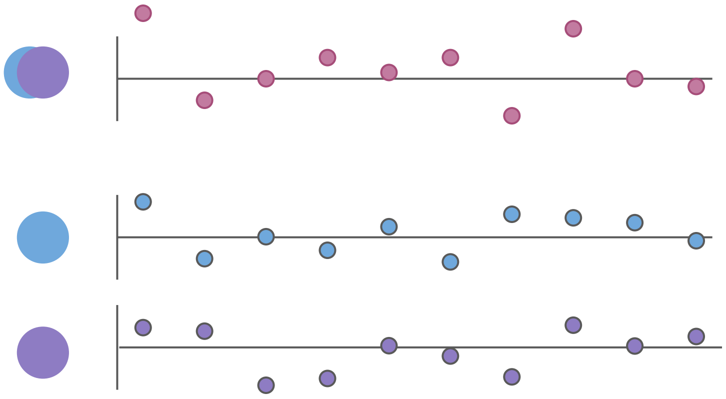

Edge time series

Zamani Esfahlani et al (2020) *PNAS*

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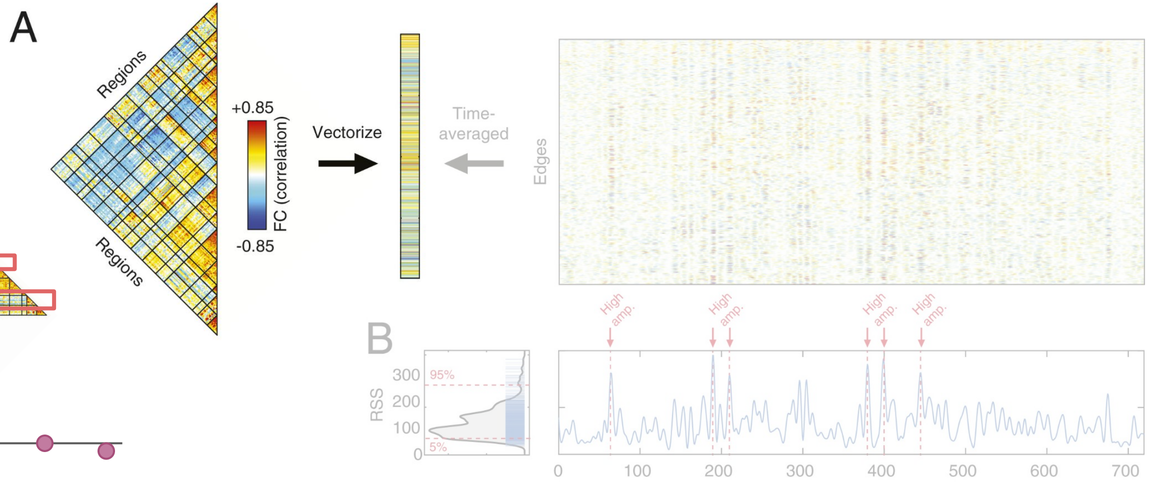

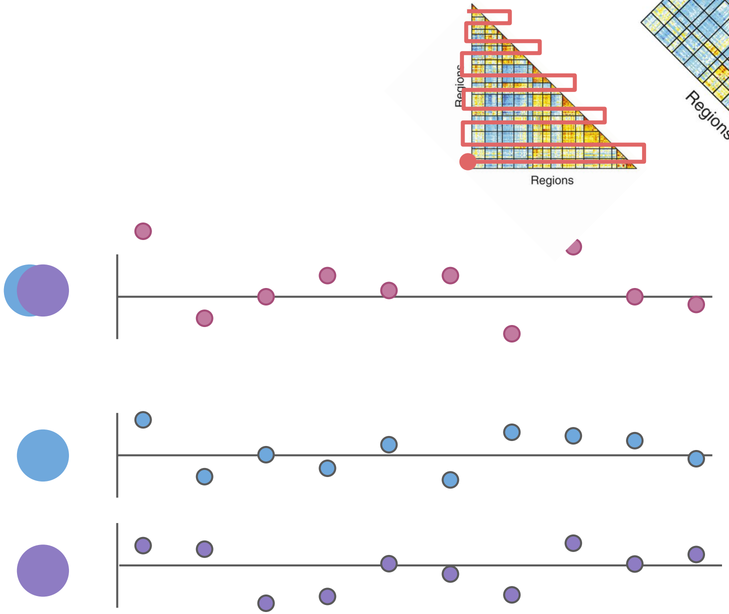

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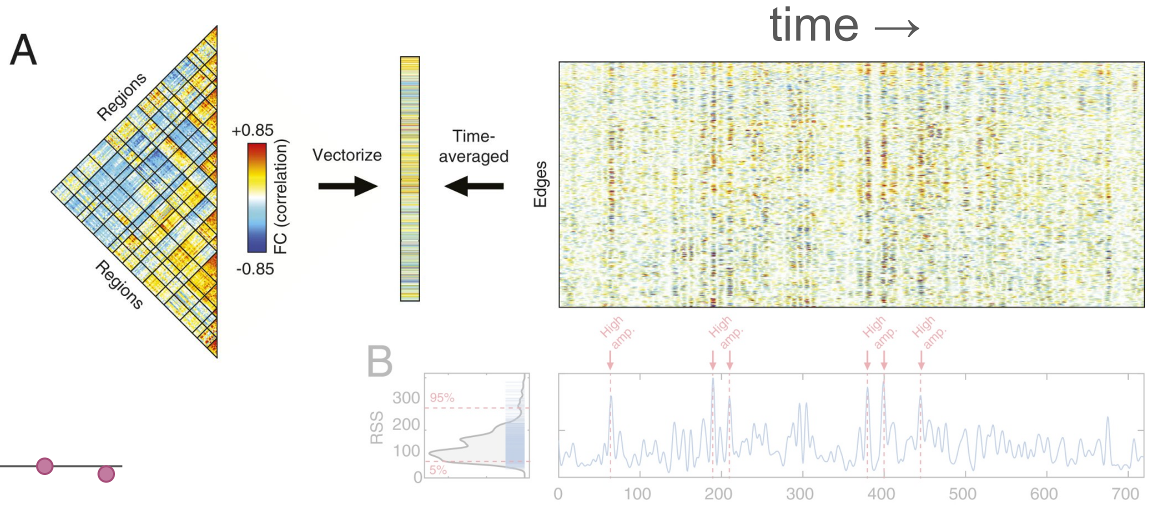

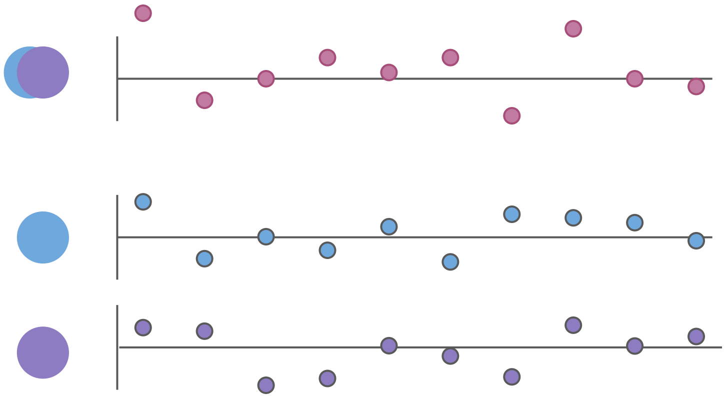

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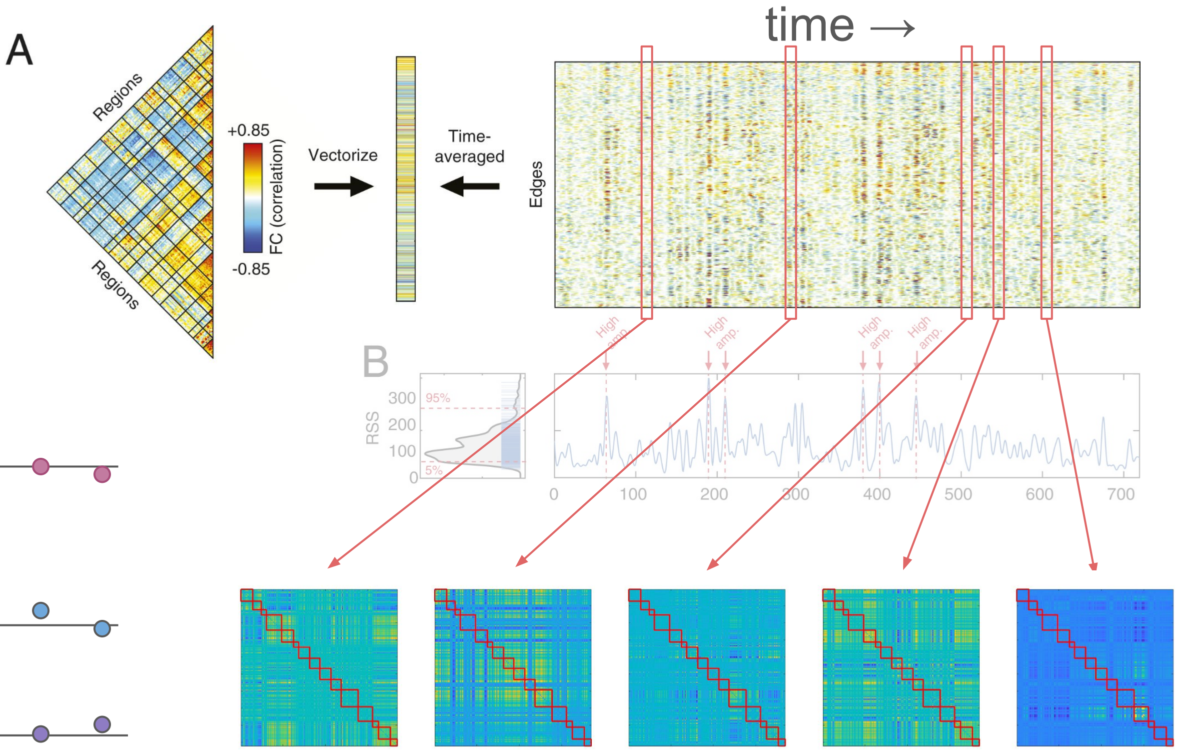
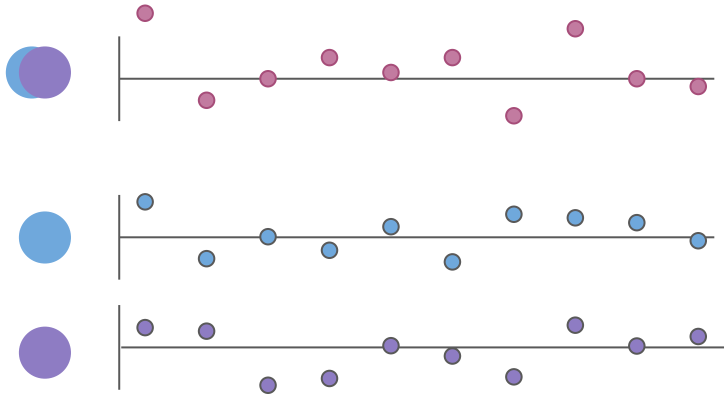
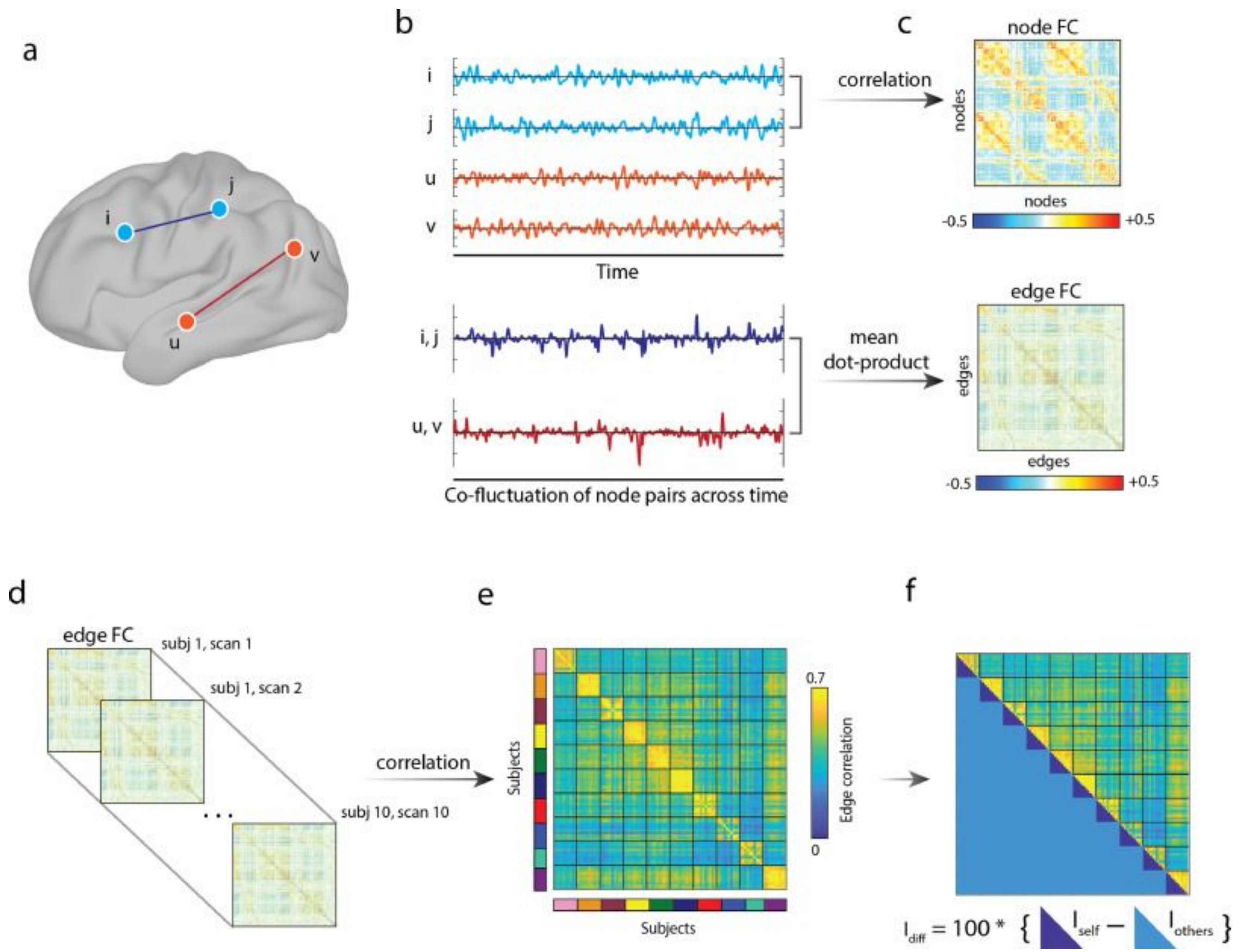




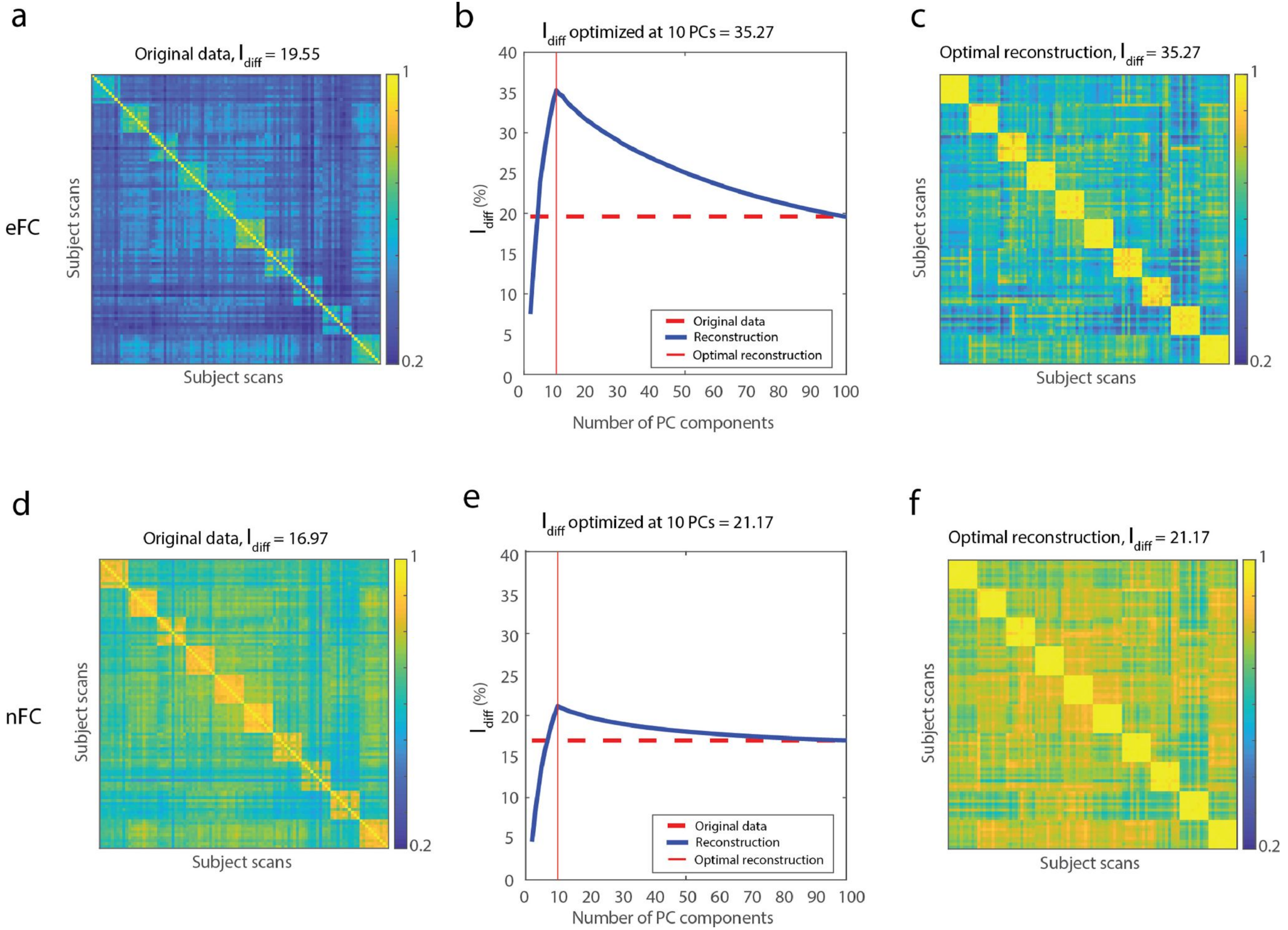
Edge time series

Dataset size explosion! Each column forms an node by node matrix (same size as time FC matrix)

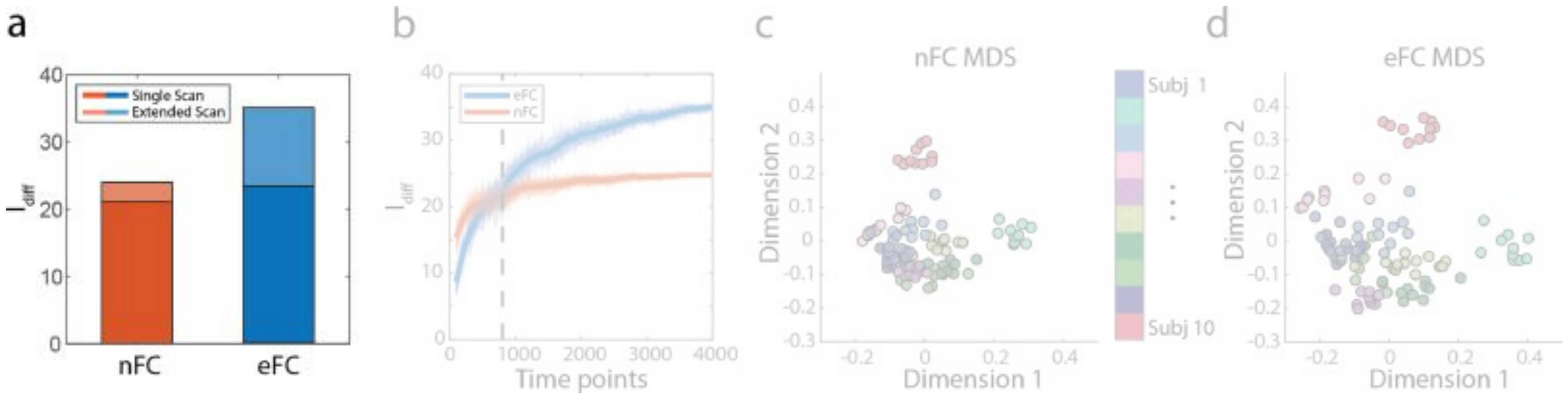
Edge time series matrix = (nodes) x (nodes) x (time)



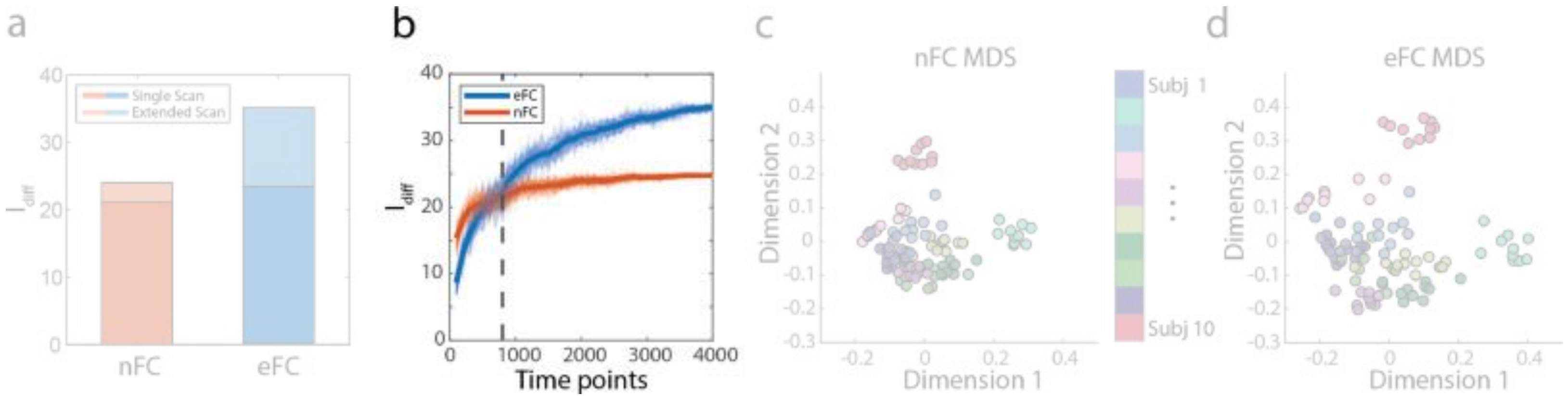
Jo et al (2021) *NeuroImage*



a
Original data, I_{diff} = 19.55
eFC
Subject scans
Subject scans
1
0.2
b
I_{diff} optimized at 10 PCs = 35.27
I_{diff} (%)
Number of PC components
Original data
Reconstruction
Optimal reconstruction
c
Optimal reconstruction, I_{diff} = 35.27
Subject scans
Subject scans
d
Original data, I_{diff} = 16.97
nFC
Subject scans
Subject scans
e
I_{diff} optimized at 10 PCs = 21.17
I_{diff} (%)
Number of PC components
Original data
Reconstruction
Optimal reconstruction
f
Optimal reconstruction, I_{diff} = 21.17
Subject scans
Subject scans



Jo et al (2021) *NeuroImage*



Jo et al (2021) *NeuroImage*

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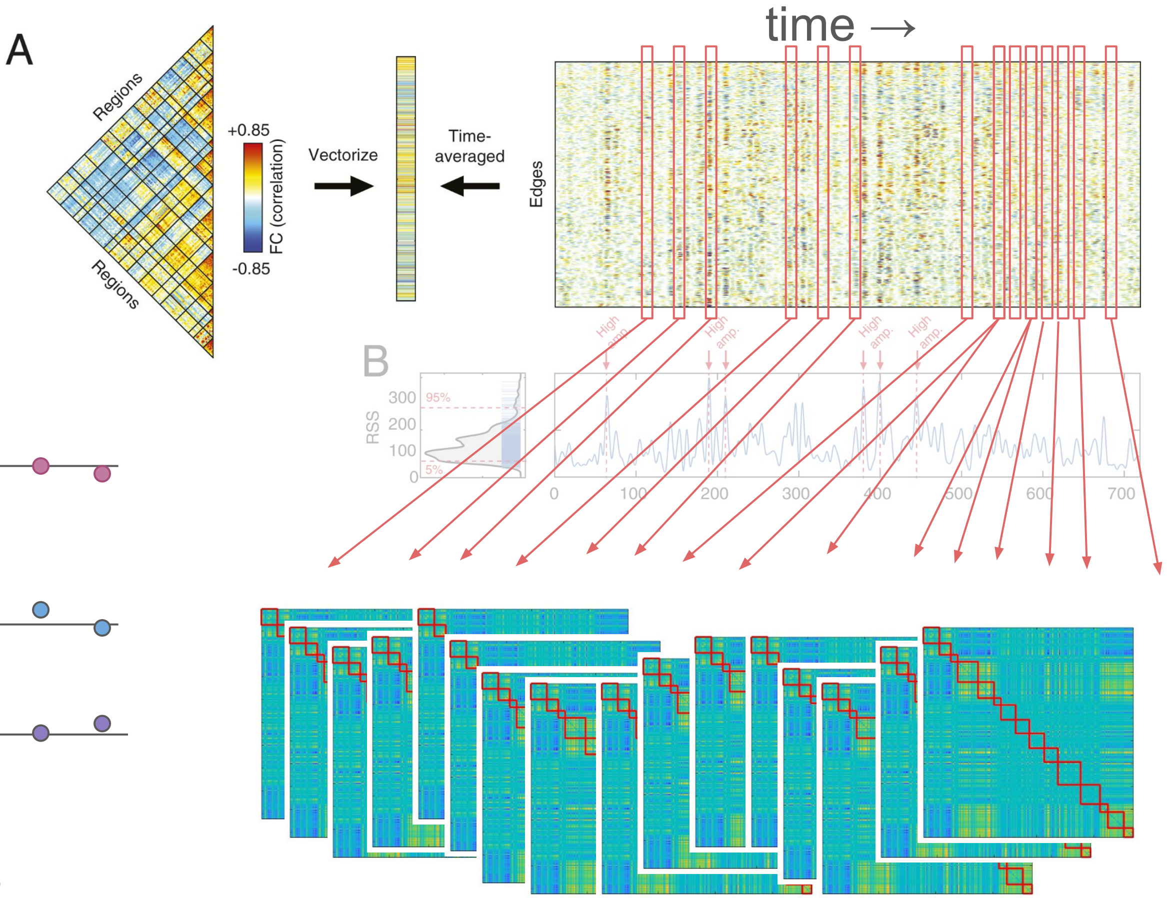

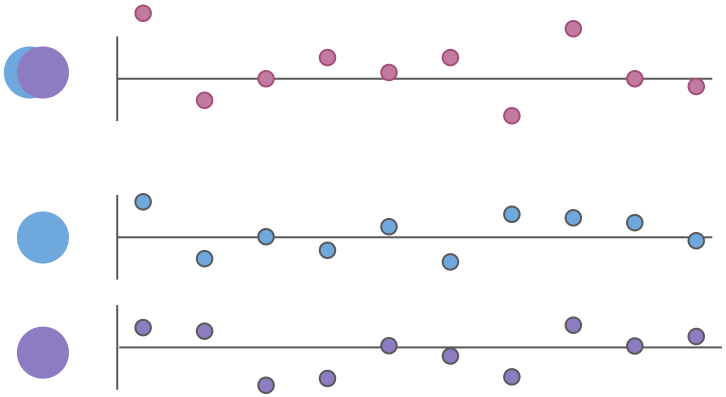

Edge time series

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- **Same resolution as data input**
    - **Single frame information**
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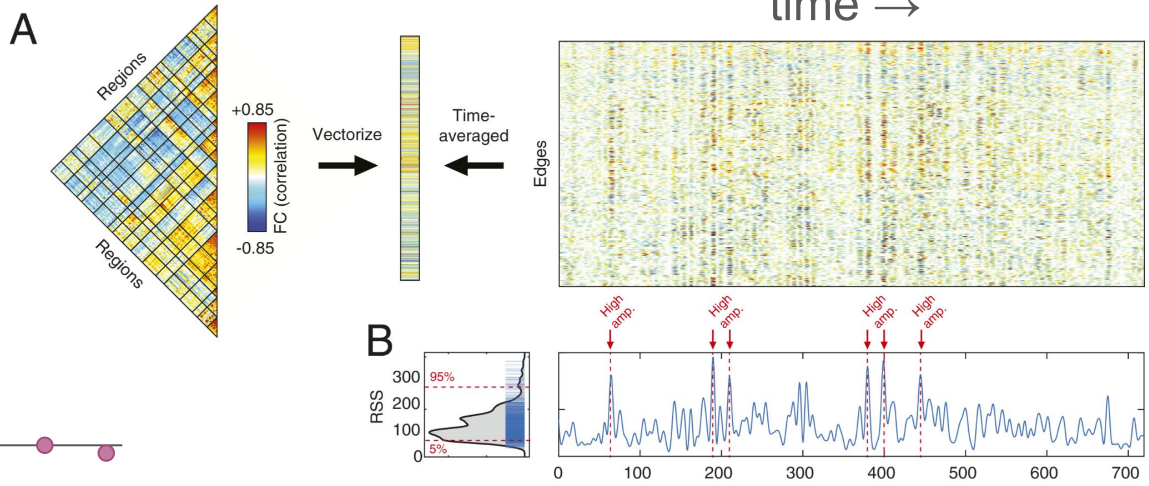
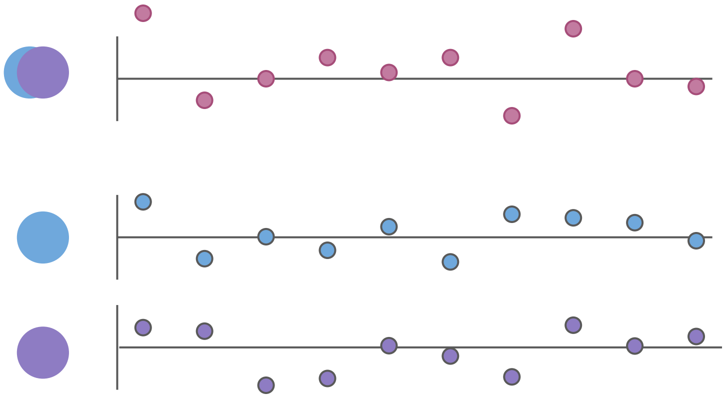
time →





Edge time series

Zamani Esfahlani et al (2020) *PNAS*

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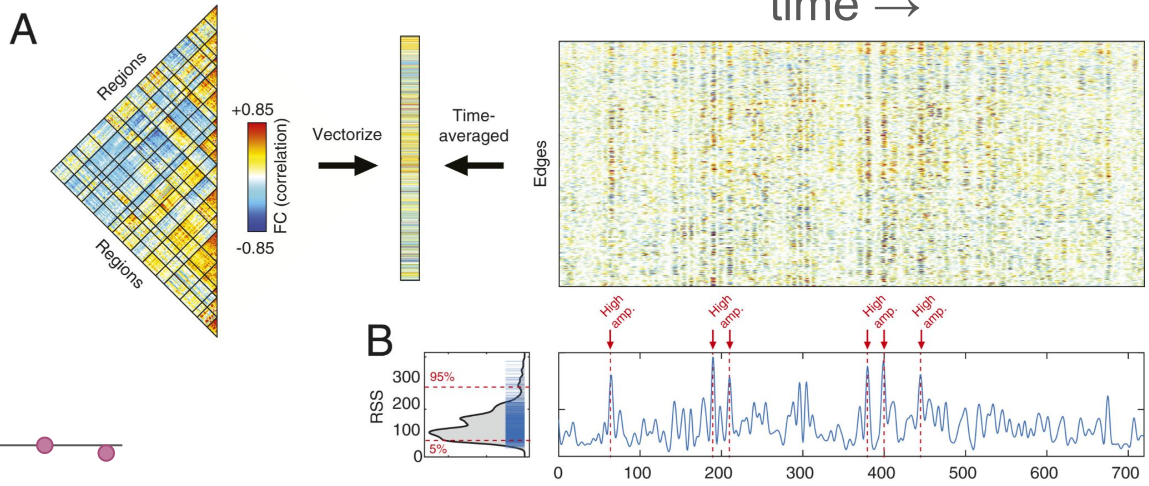
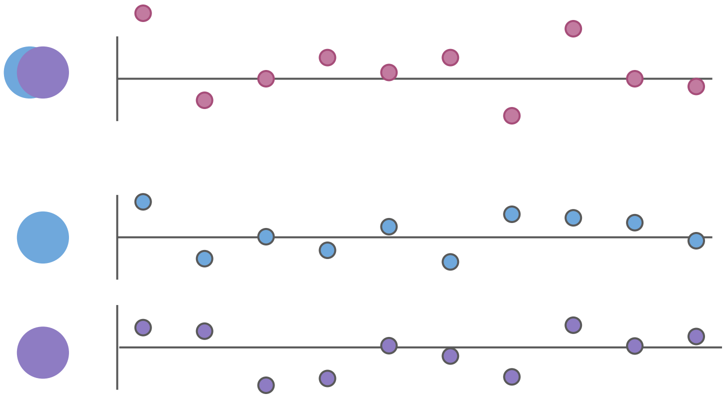
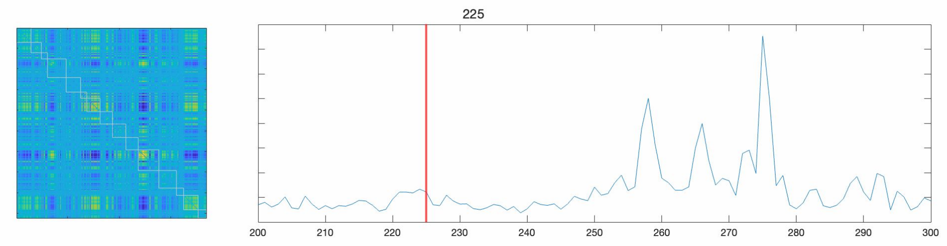
time →





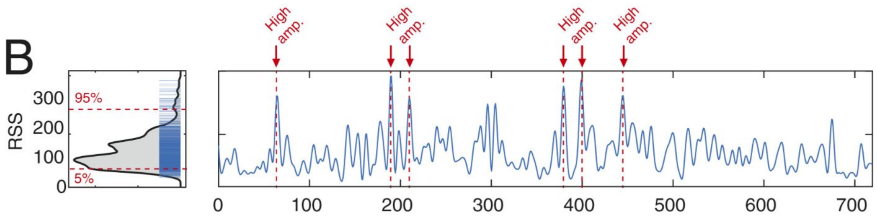


Edge time series

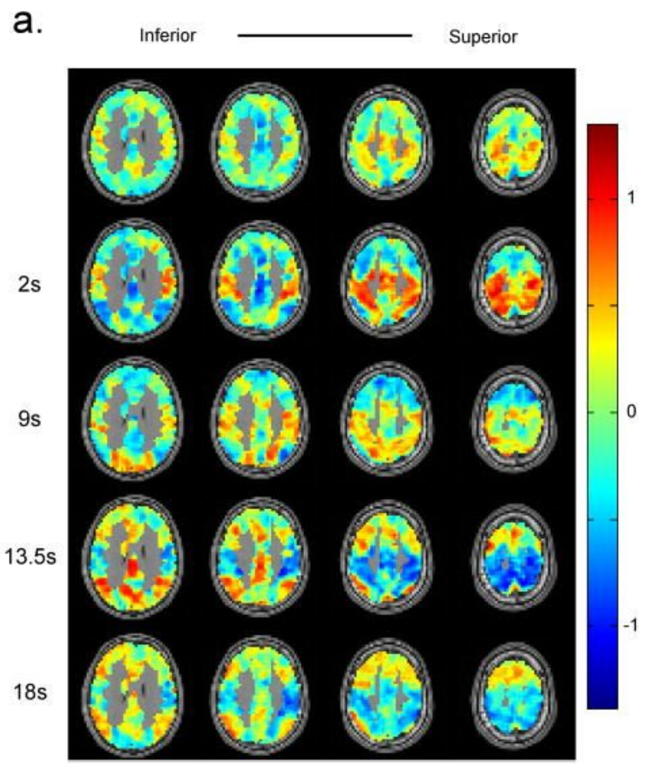
Zamani Esfahlani et al (2020) *PNAS*

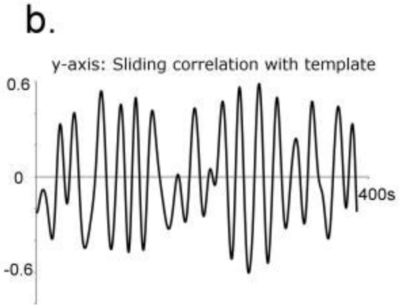
What is the nature of “connectivity” dynamics? Smooth or punctuated?

Zamani Esfahlani et al (2020)
PNAS

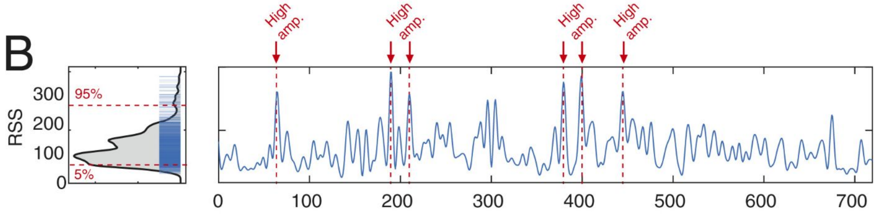


What is the nature of “connectivity” dynamics? Smooth or punctuated?





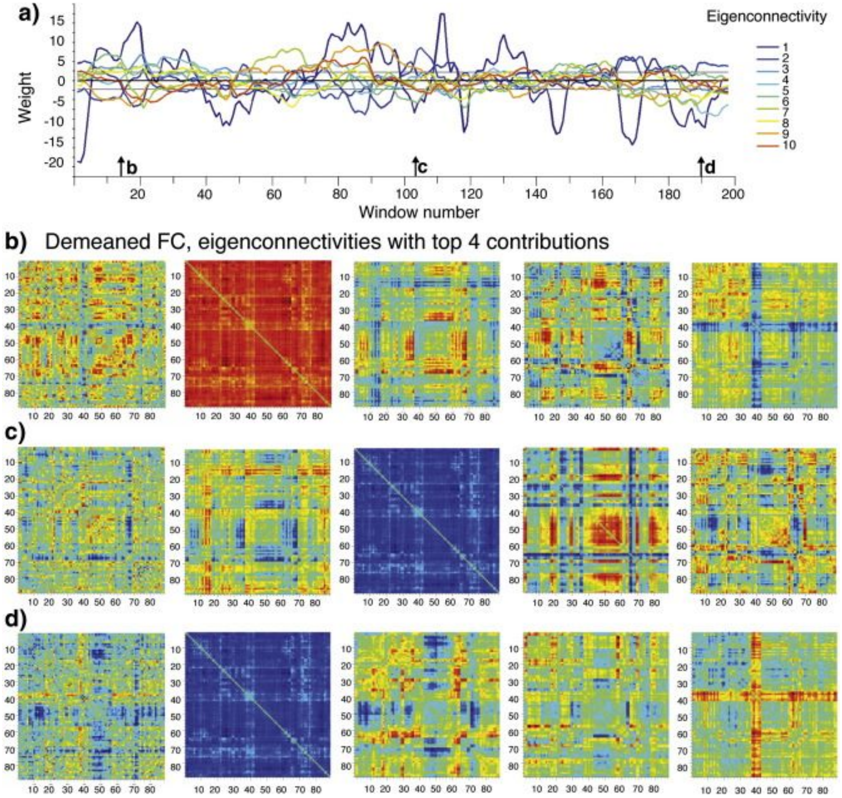
Idea: Compare time series to template across time; events are short temporal patterns



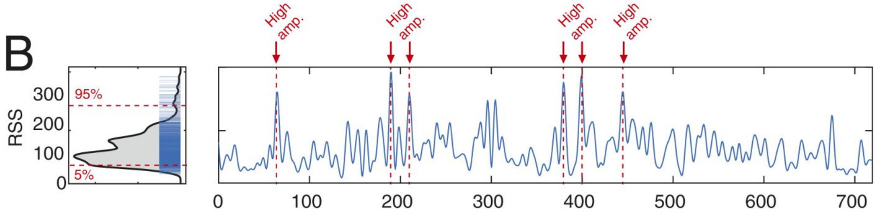
Zamani Esfahlani et al (2020) *PNAS*

Majeed et al. (2011). *NeuroImage*

What is the nature of "connectivity" dynamics? Smooth or punctuated?



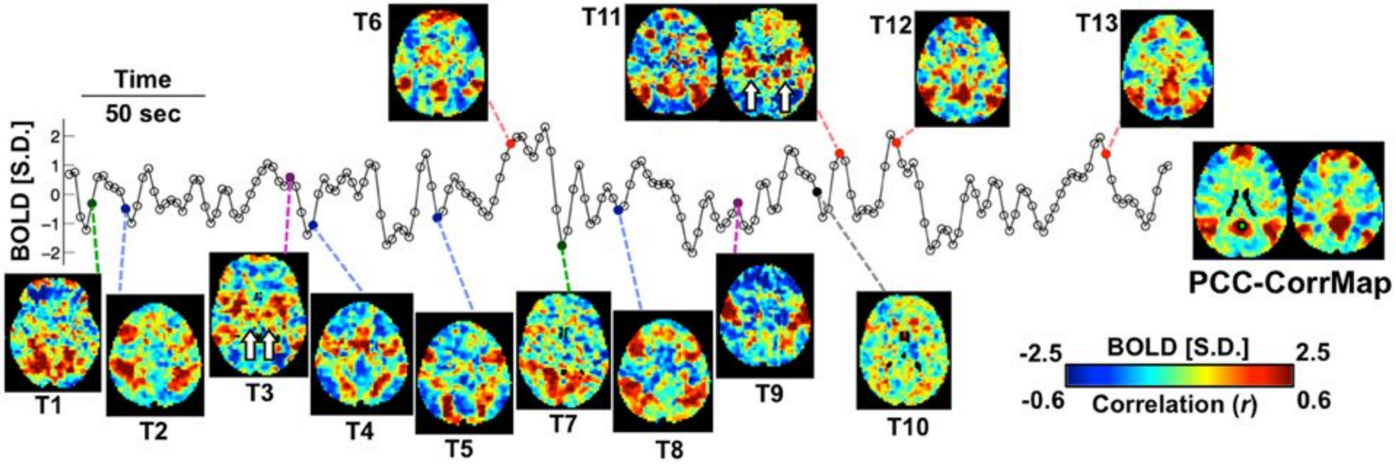
Idea: stack all your data together and run pca; track the expression of modes in your data



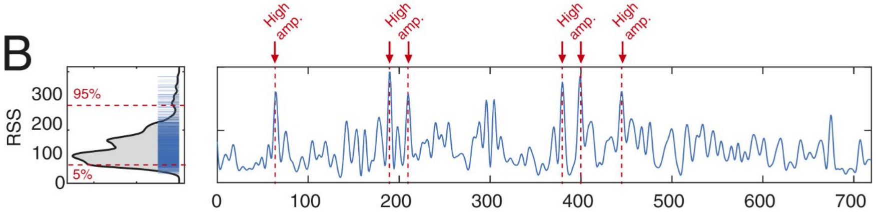
Zamani Esfahlani et al (2020) *PNAS*

Leonardi et al. (2013). *NeuroImage*

What is the nature of “connectivity” dynamics? Smooth or punctuated?



Idea: Look at seed-based correlation to observe different spatial patterns



Zamani Esfahlani et al (2020) *PNAS*

Liu & Duyn (2013) *PNAS*

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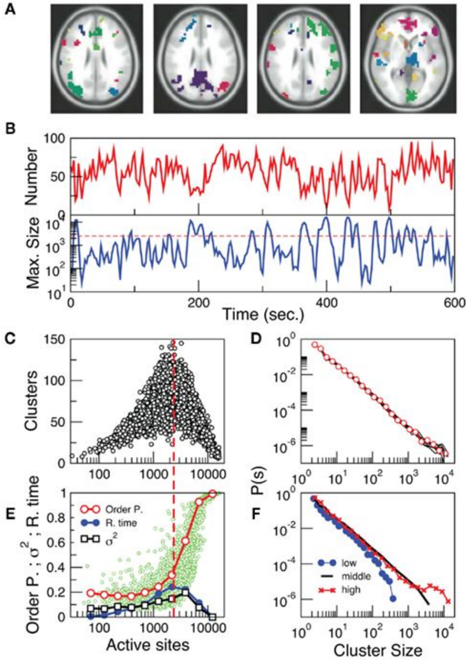
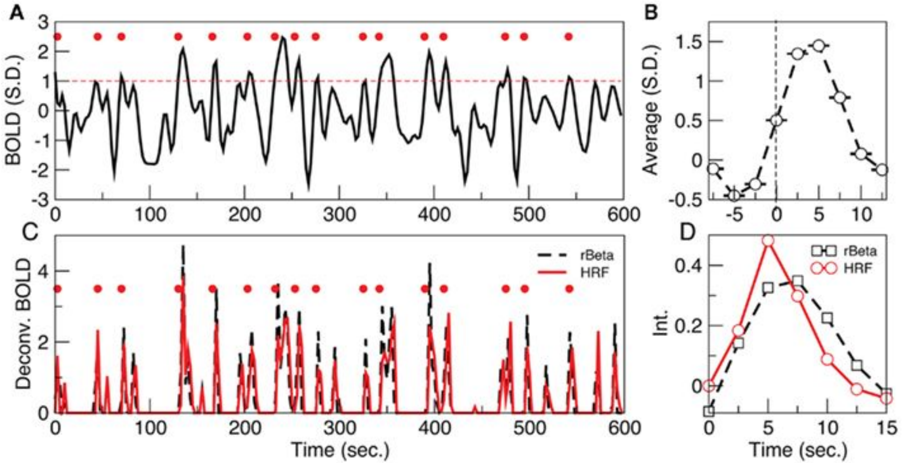
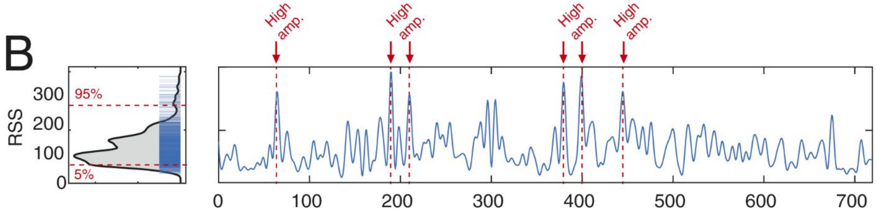


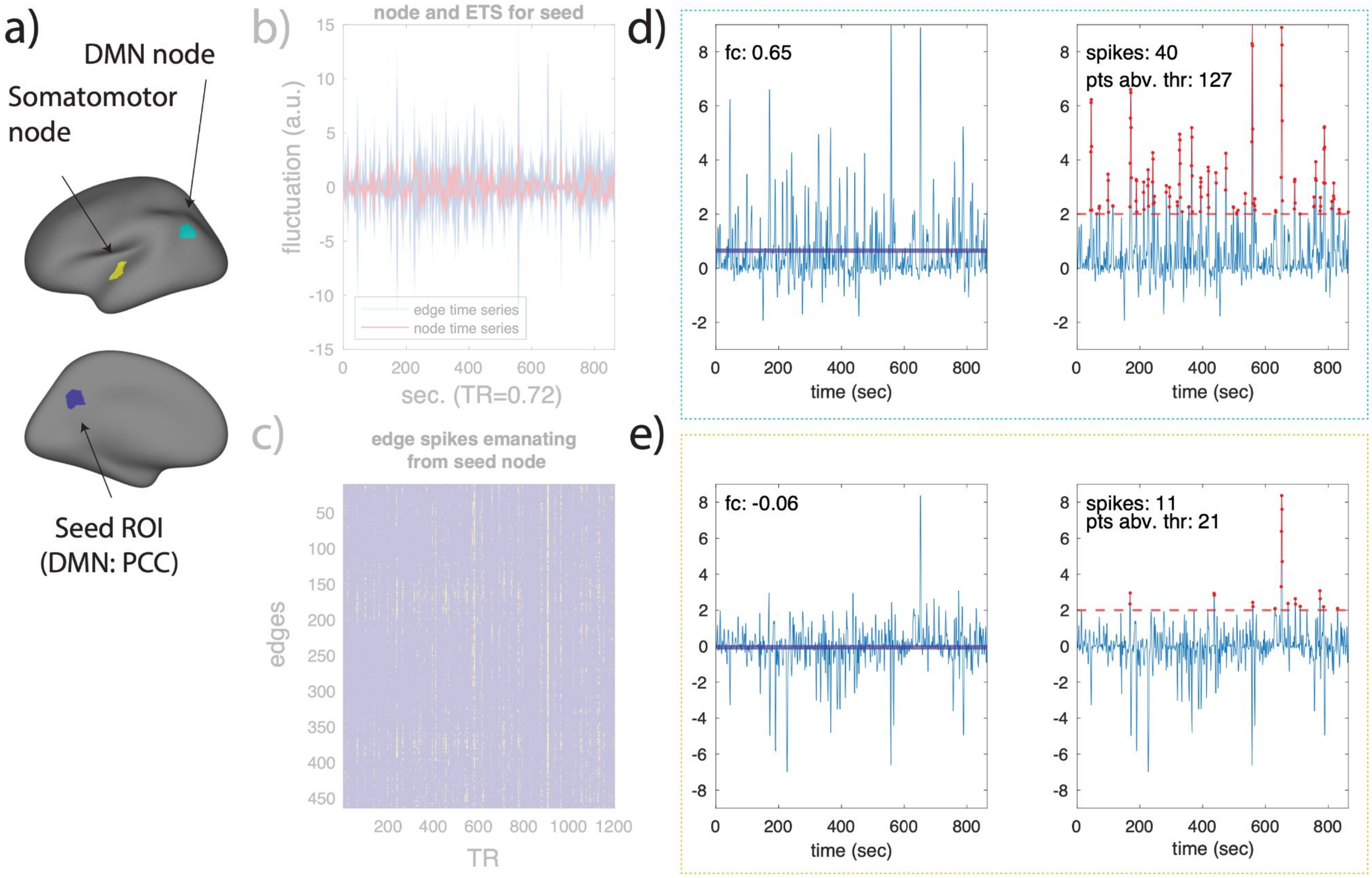


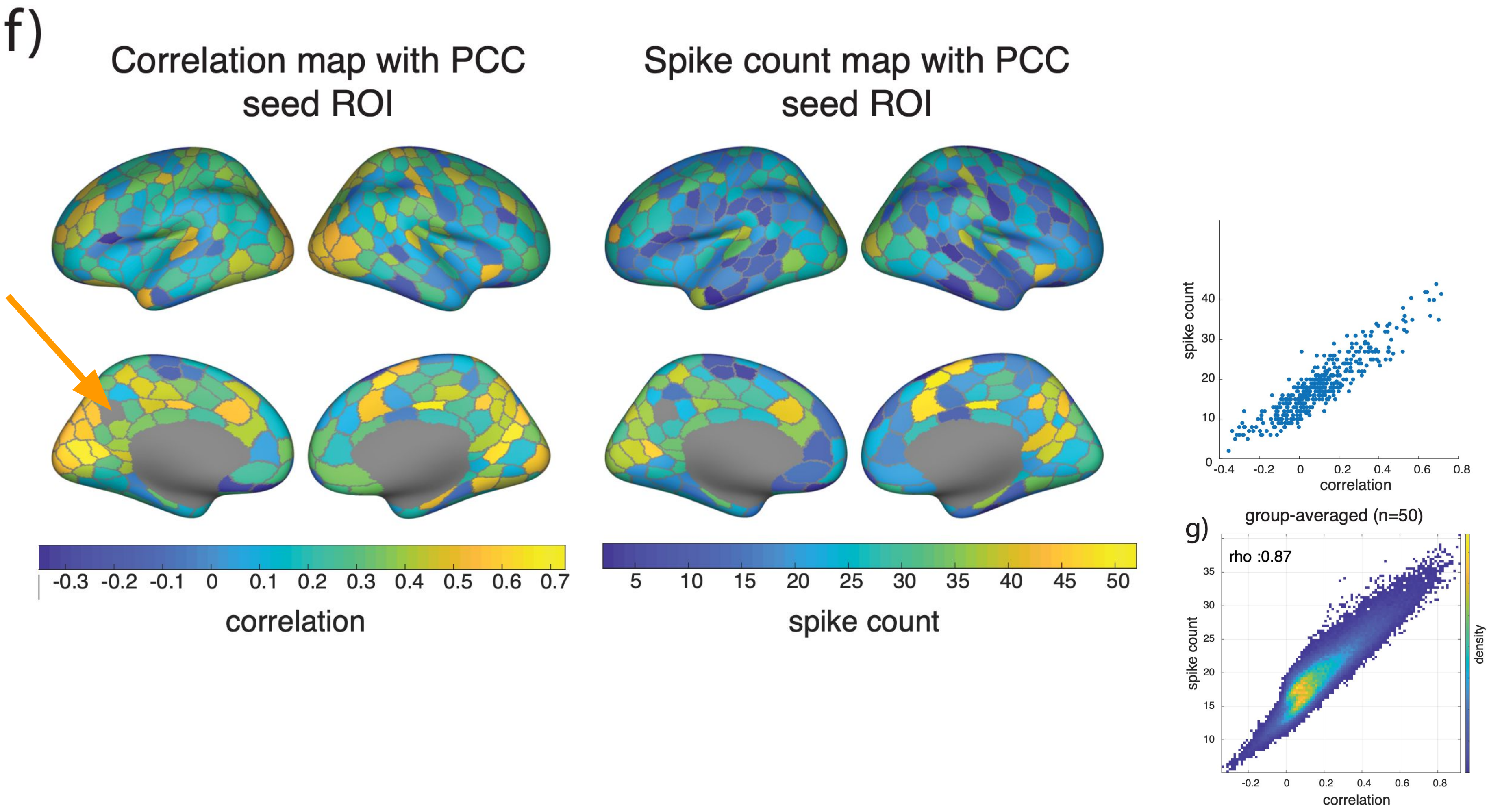
Idea: Reduce ROI time series to 1’s and 0’s by recording above threshold events; measure concurrence



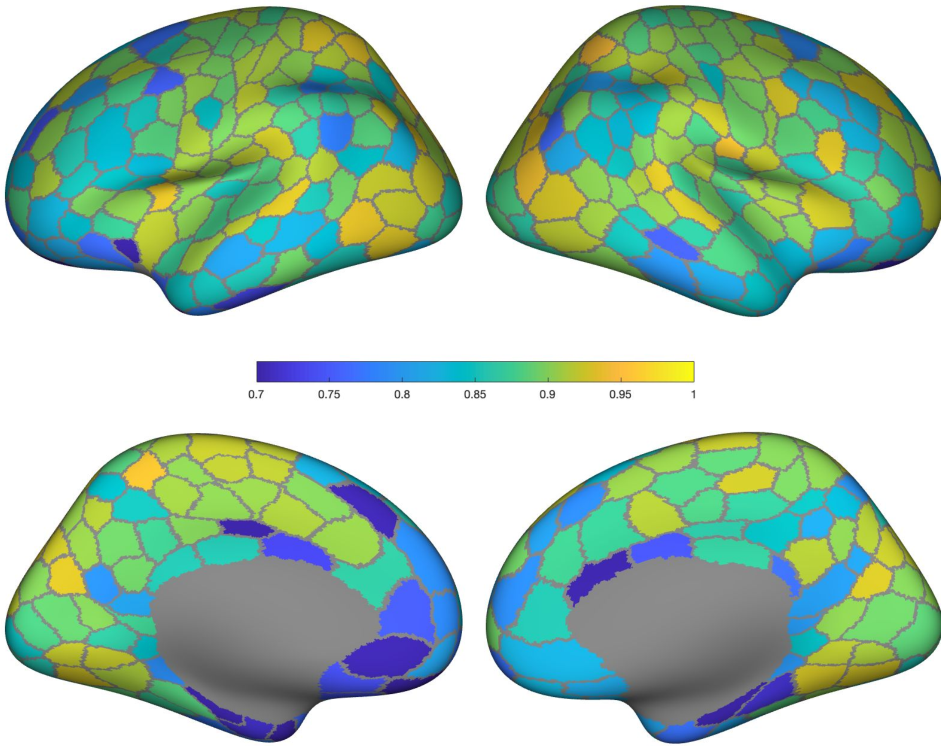
Zamani Esfahlani et al (2020) *PNAS*

Tagliazucchi et al. (2012). *Front. Physiology*


a)
DMN node
Somatomotor node
Seed ROI (DMN: PCC)
b)
node and ETS for seed
fluctuation (a.u.)
sec. (TR=0.72)
edge time series
node time series
c)
edge spikes emanating from seed node
edges
TR
d)
fc: 0.65
spikes: 40
pts abv. thr: 127
time (sec)
e)
fc: -0.06
spikes: 11
pts abv. thr: 21
time (sec)

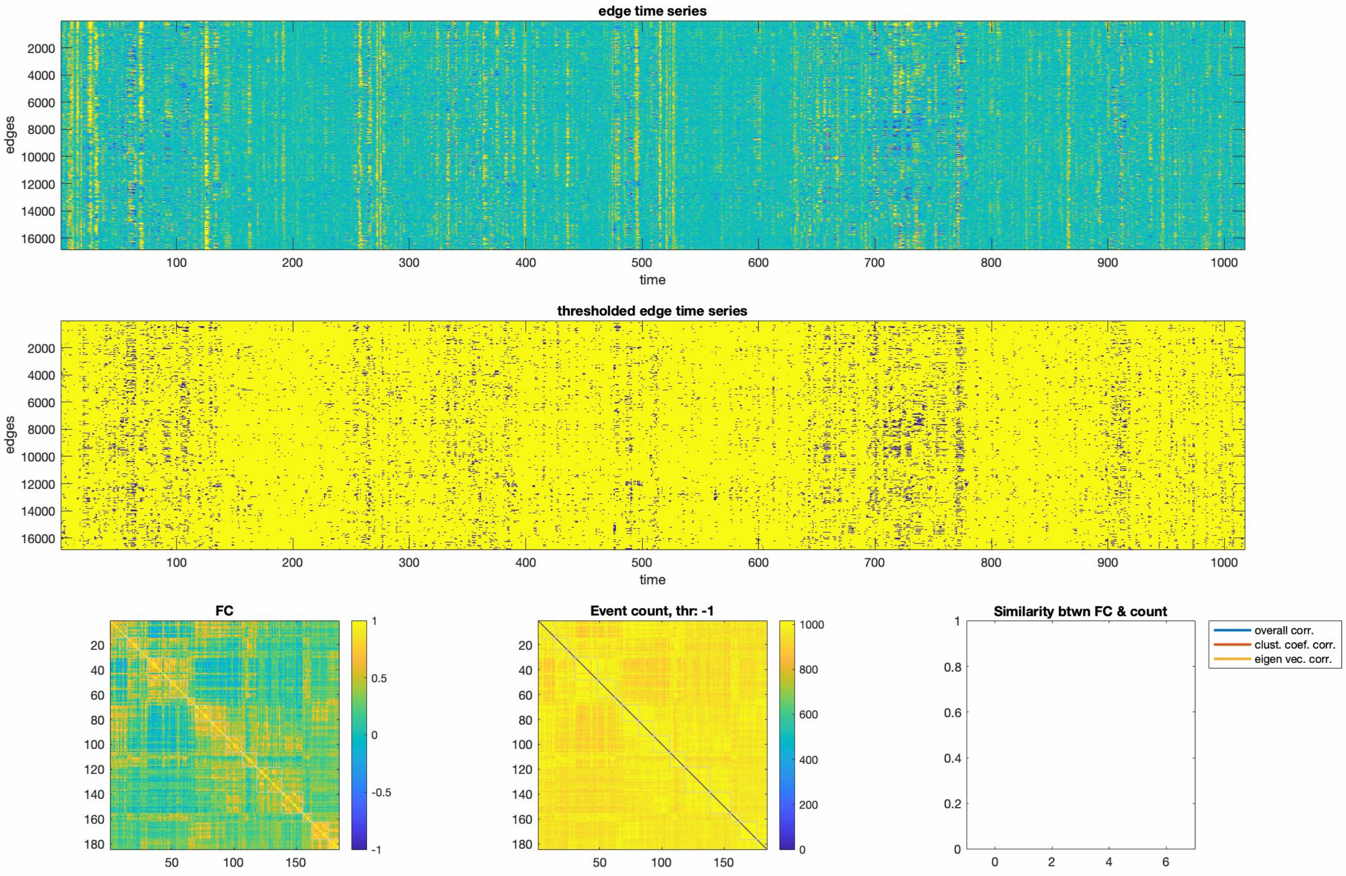


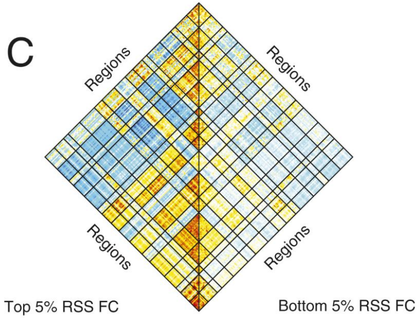
f)
Correlation map with PCC seed ROI
Spike count map with PCC seed ROI
-0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7
correlation
5 10 15 20 25 30 35 40 45 50
spike count
spike count
correlation
g)
group-averaged (n=50)
rho :0.87
spike count
correlation
density



The extent to which this holds true across the cortex

Revisiting an idea related to Tagliazucchi's foundational work on point processes – we ask what happens when we look at the edges time series as points or 'events'





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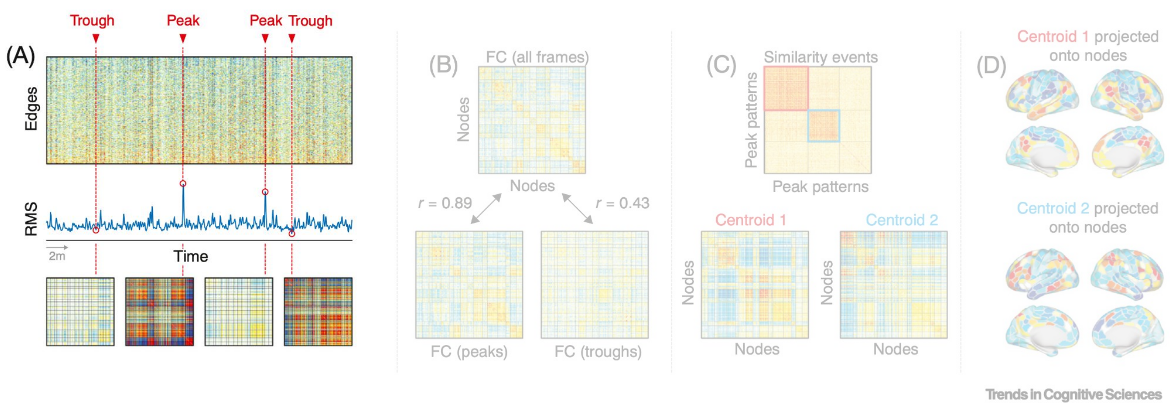

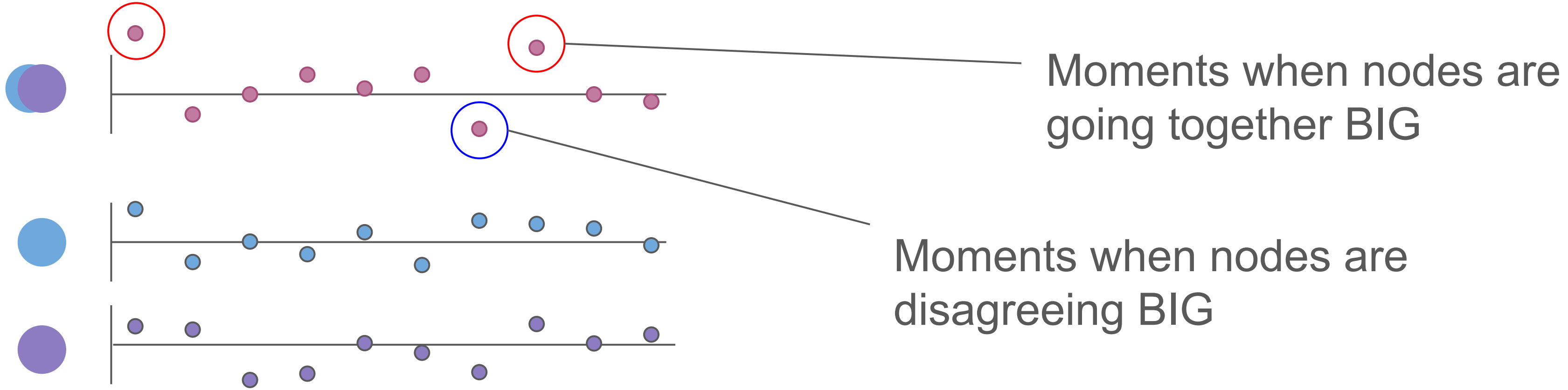

Edge time series

Betzel et al (2023) *TiCS*

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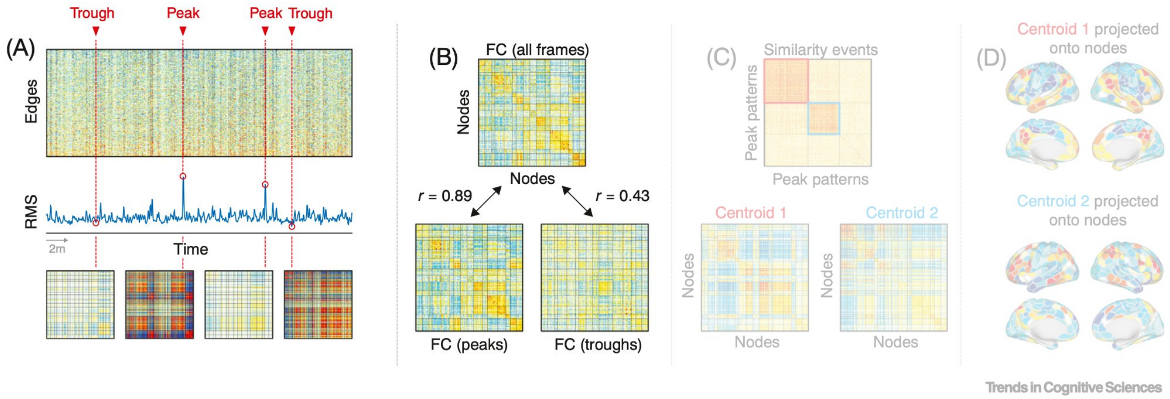

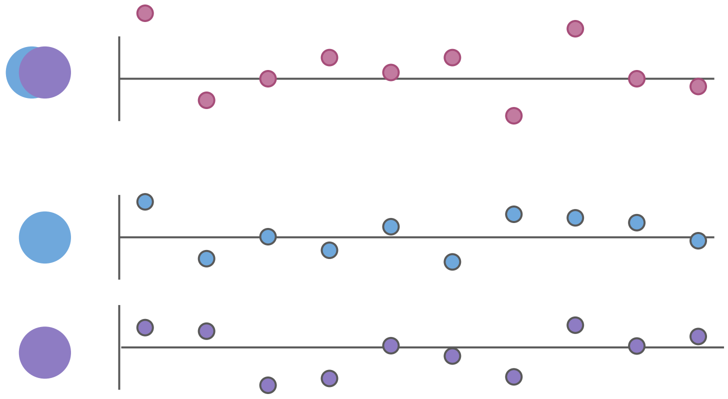

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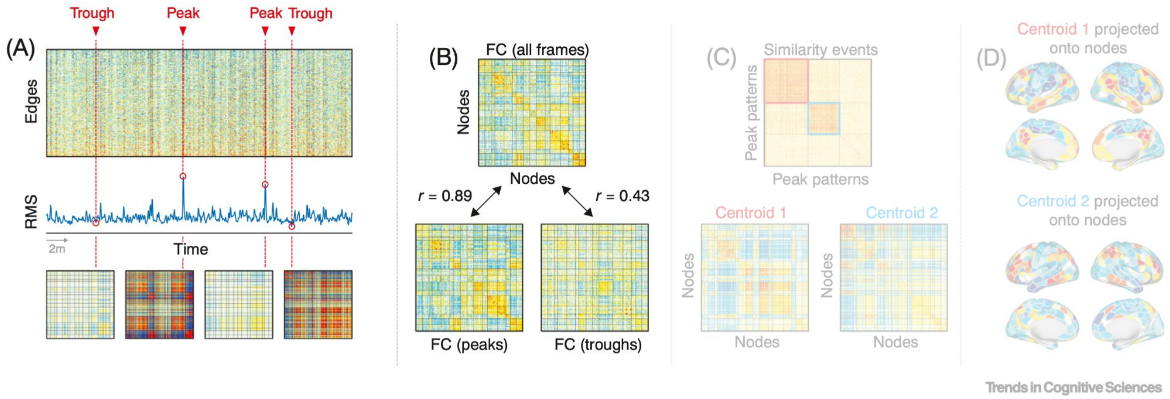

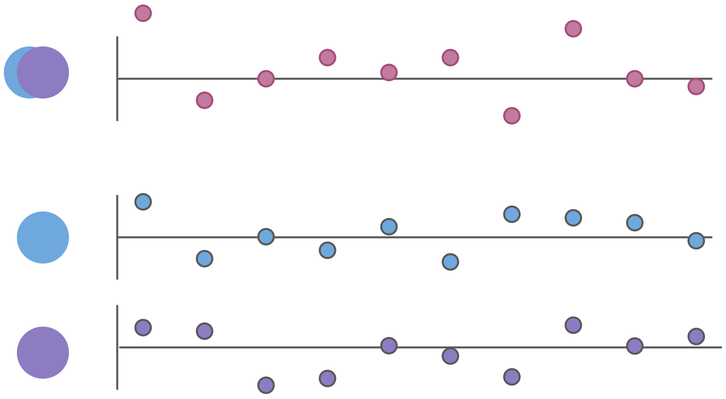

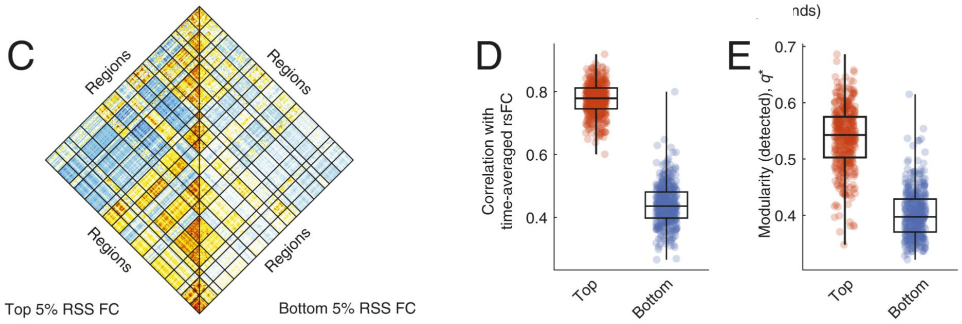

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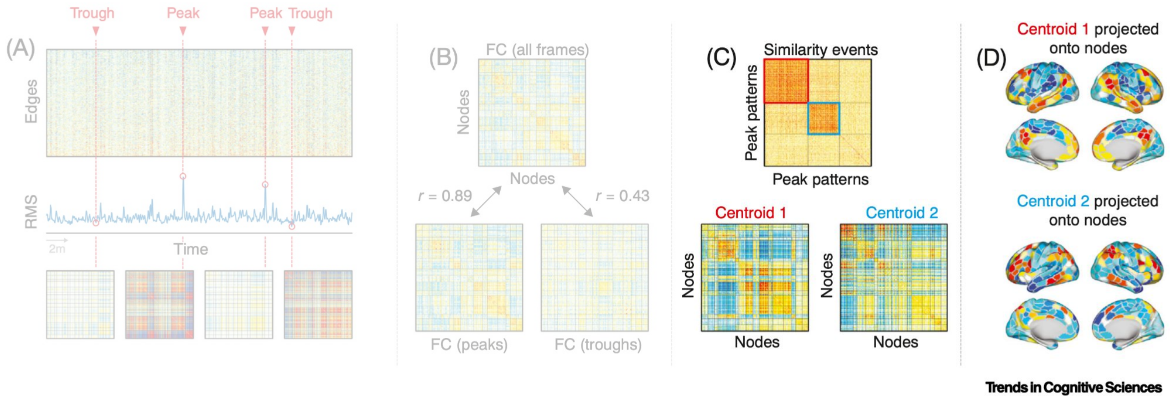

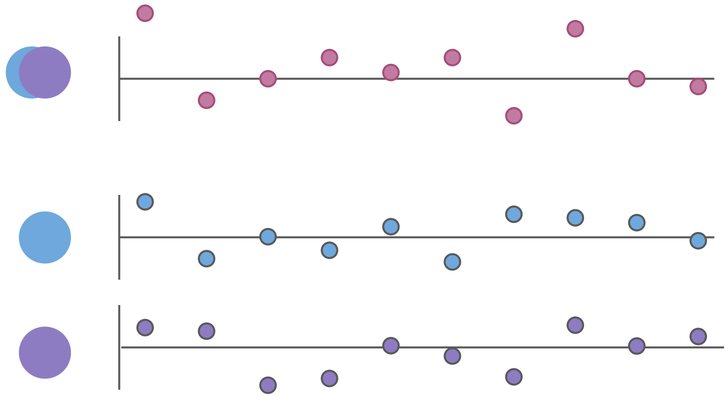

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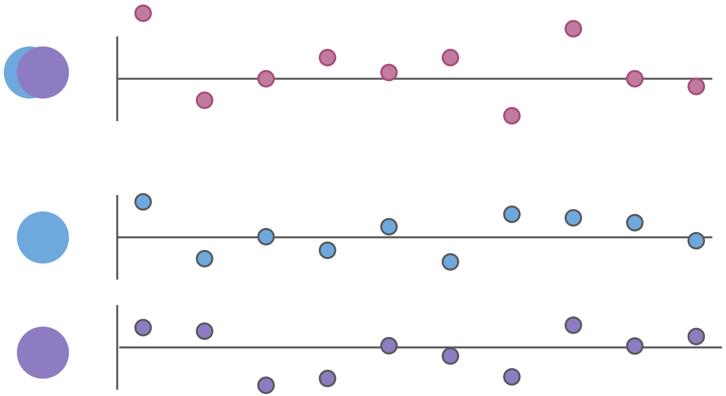
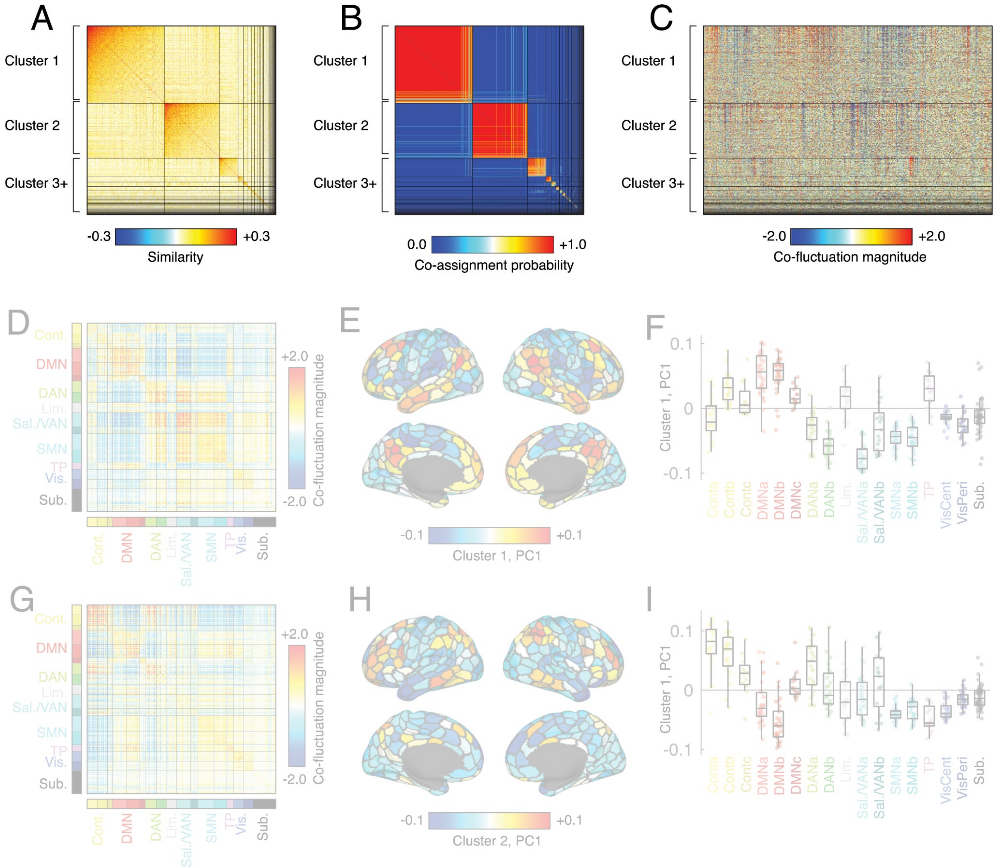
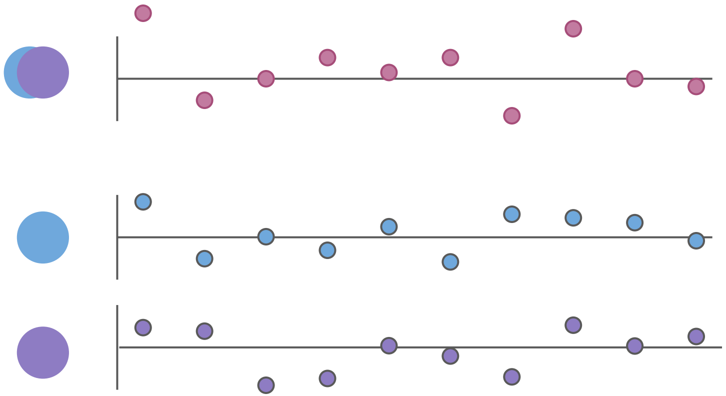


Edge time series

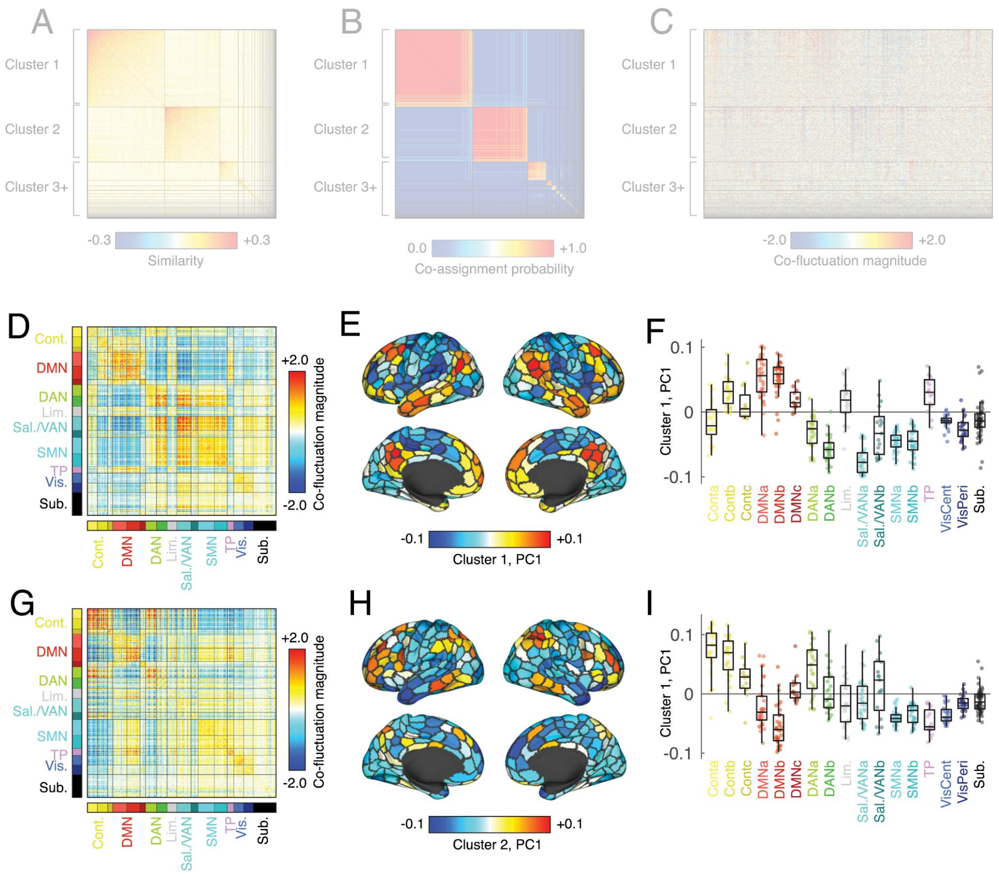


Greenwell et al (2023) *Net. Neuro.*

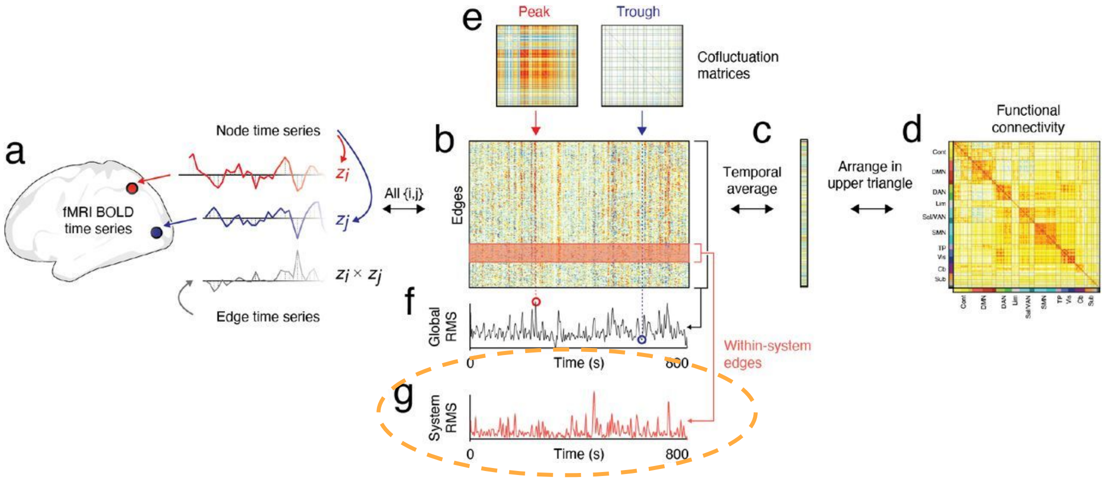
- No sliding step or window parameter
- Time-average is exactly correlation
- **Same resolution as data input**
    - **Single frame information**
    - Potential to measure “faster” phenomena

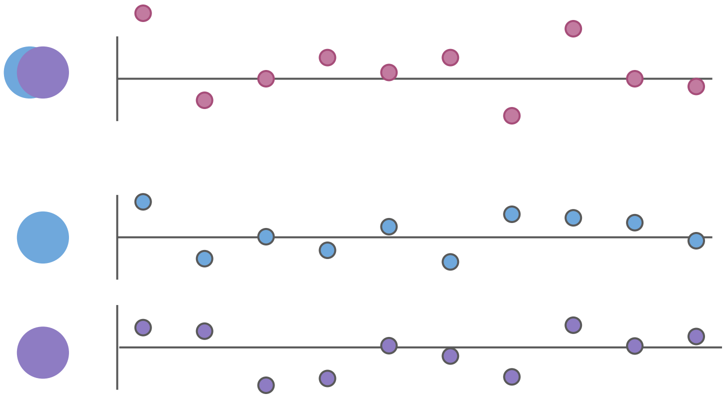


Edge time series



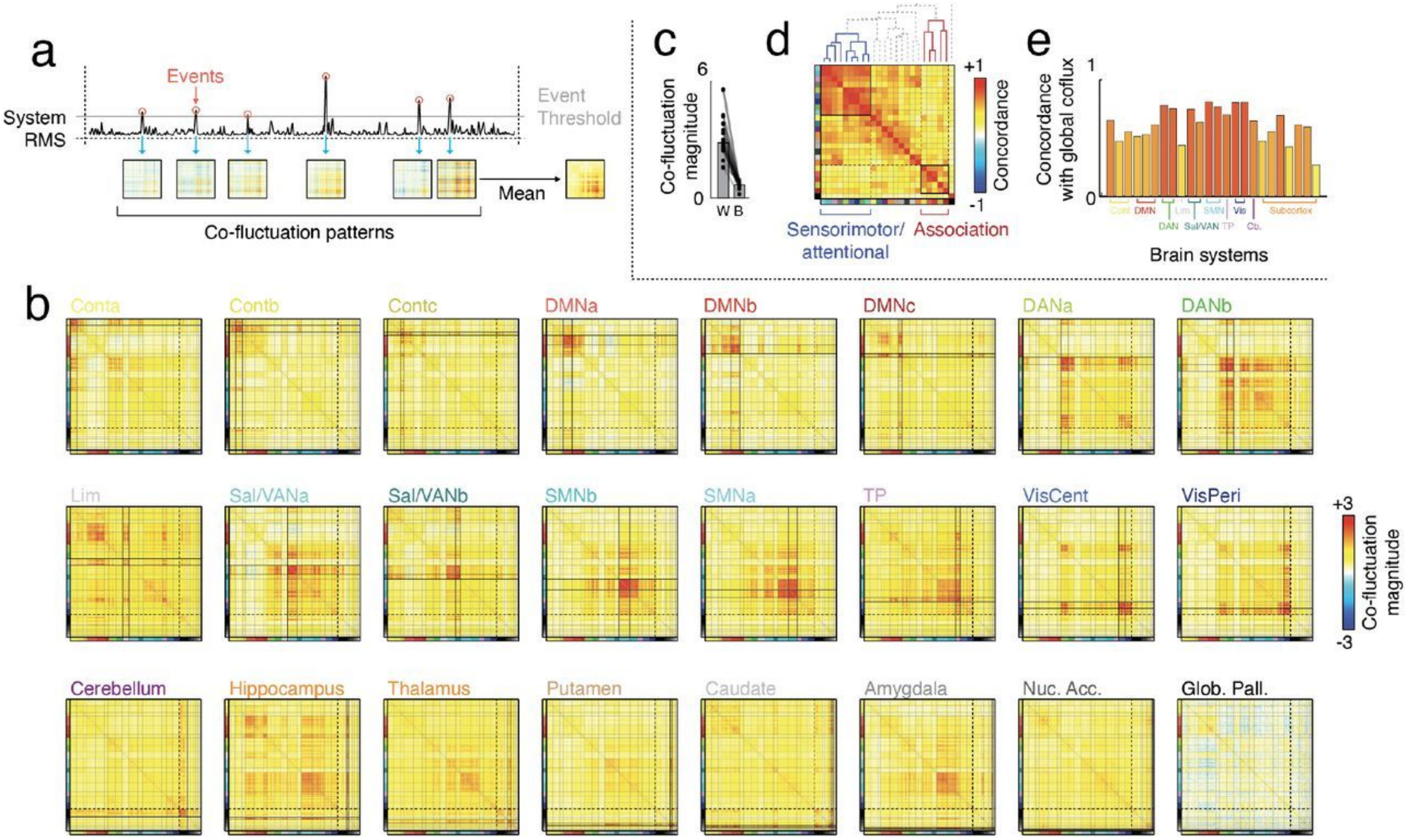
Greenwell et al (2023) *Net. Neuro.*

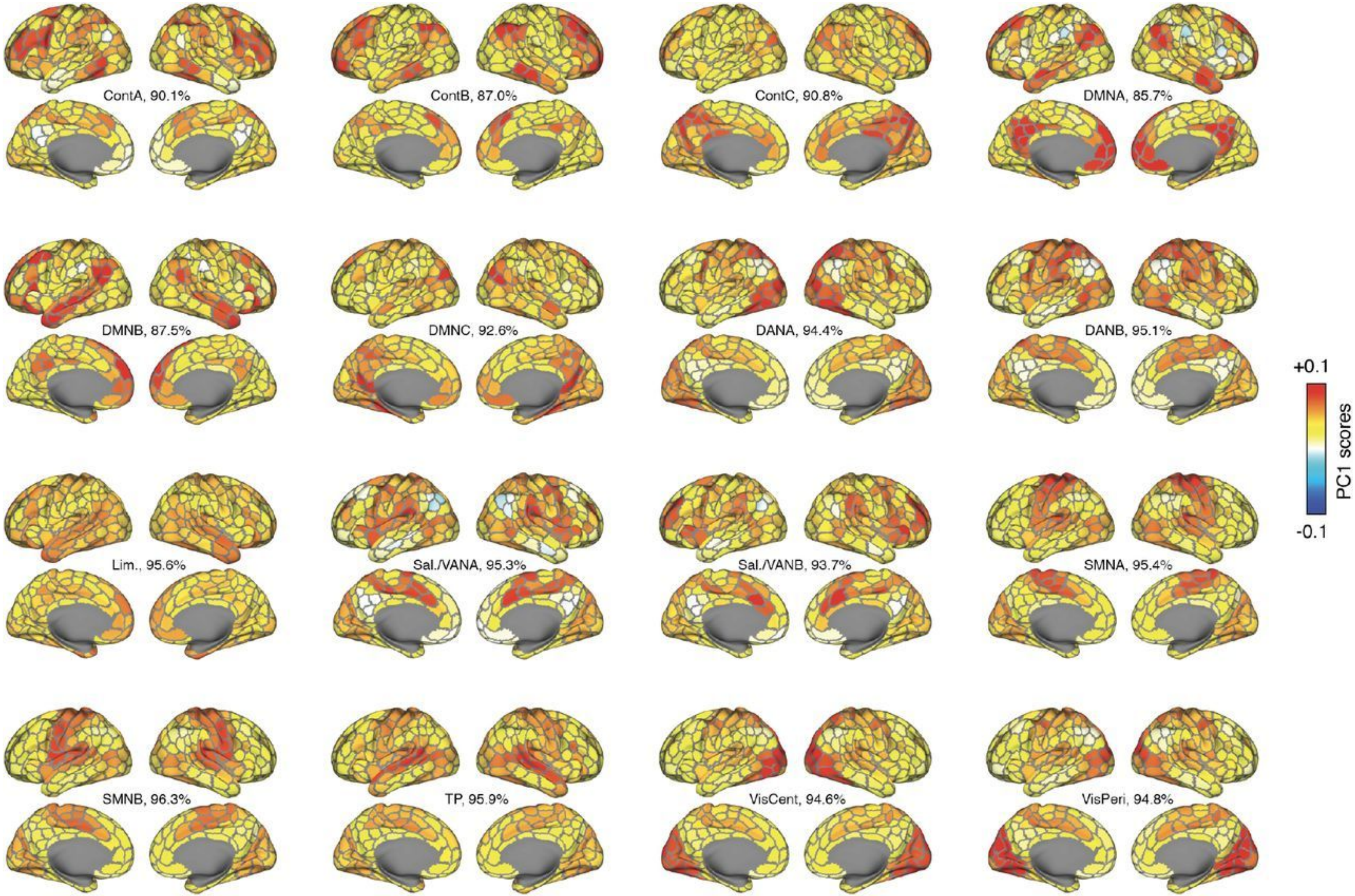




Edge time series

Betzel et al (2022) *BioRxiv*


a
Events
System RMS
Event Threshold
Mean
Co-fluctuation patterns
c
Co-fluctuation magnitude
6
0
W B
d
+1
-1
Concordance
Sensorimotor/ attentional
Association
e
Concordance with global coflux
1
0
Cont DMN Lim SMN Vis Subcortex
DAN Sal/VAN TP Cb.
Brain systems
b
Conta
Contb
Contc
DMNa
DMNb
DMNc
DANa
DANb
Lim
Sal/VANa
Sal/VANb
SMNb
SMNa
TP
VisCent
VisPeri
+3
-3
Co-fluctuation magnitude
Cerebellum
Hippocampus
Thalamus
Putamen
Caudate
Amygdala
Nuc. Acc.
Glob. Pall.


ContA, 90.1%
ContB, 87.0%
ContC, 90.8%
DMNA, 85.7%
DMNB, 87.5%
DMNC, 92.6%
DANA, 94.4%
DANB, 95.1%
Lim., 95.6%
Sal./VANA, 95.3%
Sal./VANB, 93.7%
SMNA, 95.4%
SMNB, 96.3%
TP, 95.9%
VisCent, 94.6%
VisPeri, 94.8%
+0.1
PC1 scores
-0.1

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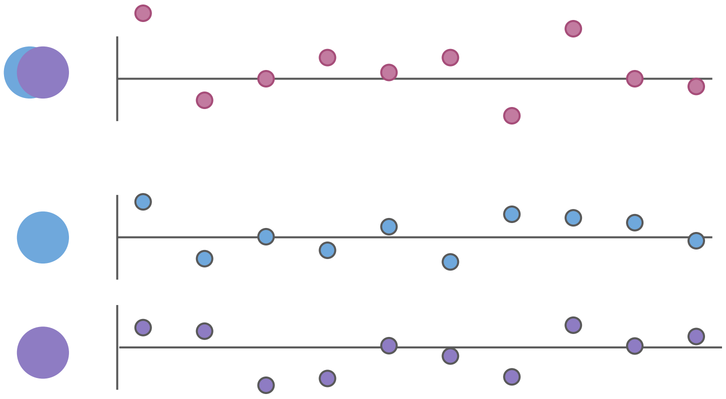
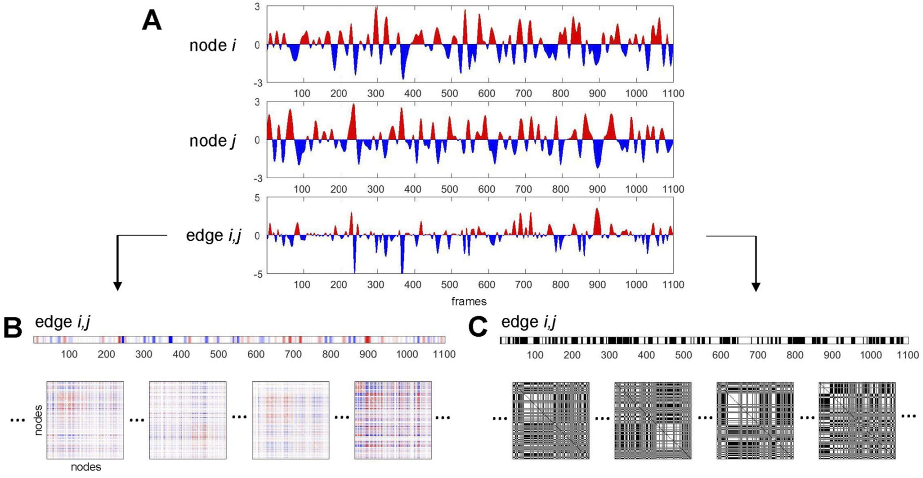
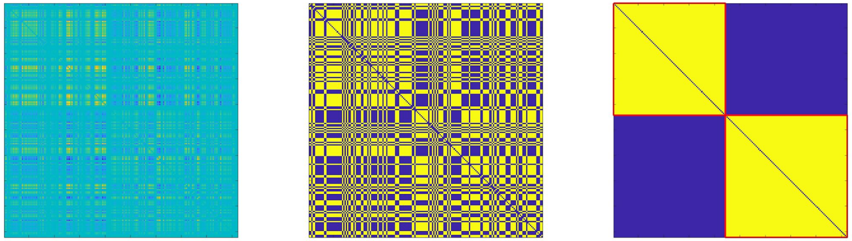


Edge time series





Sporns et al (2022) *Net. Neuro.*

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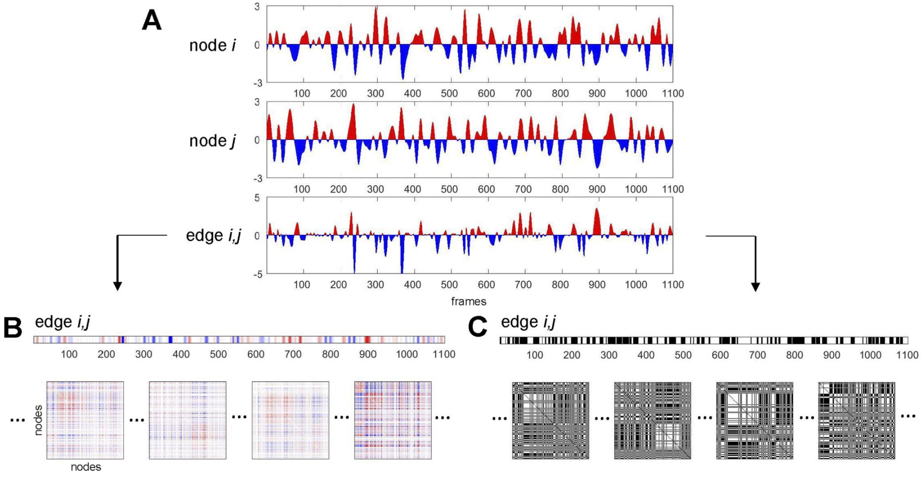

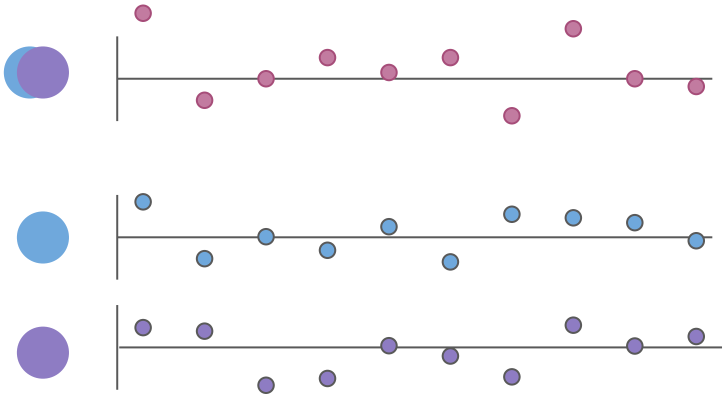

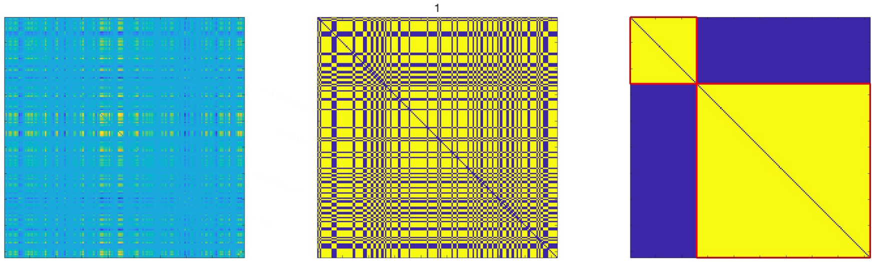

Edge time series

Sporns et al (2022) *Net. Neuro.*

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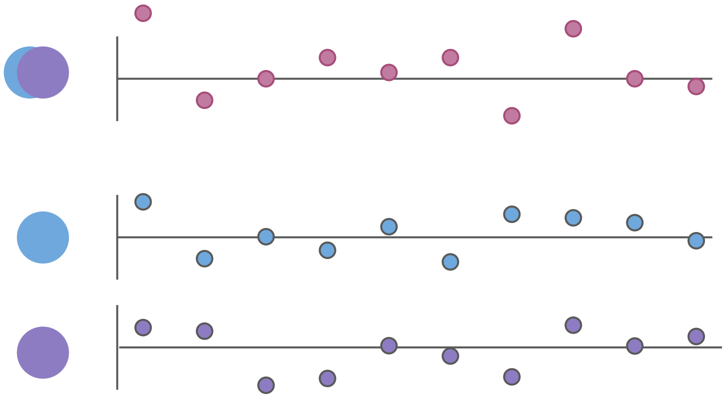

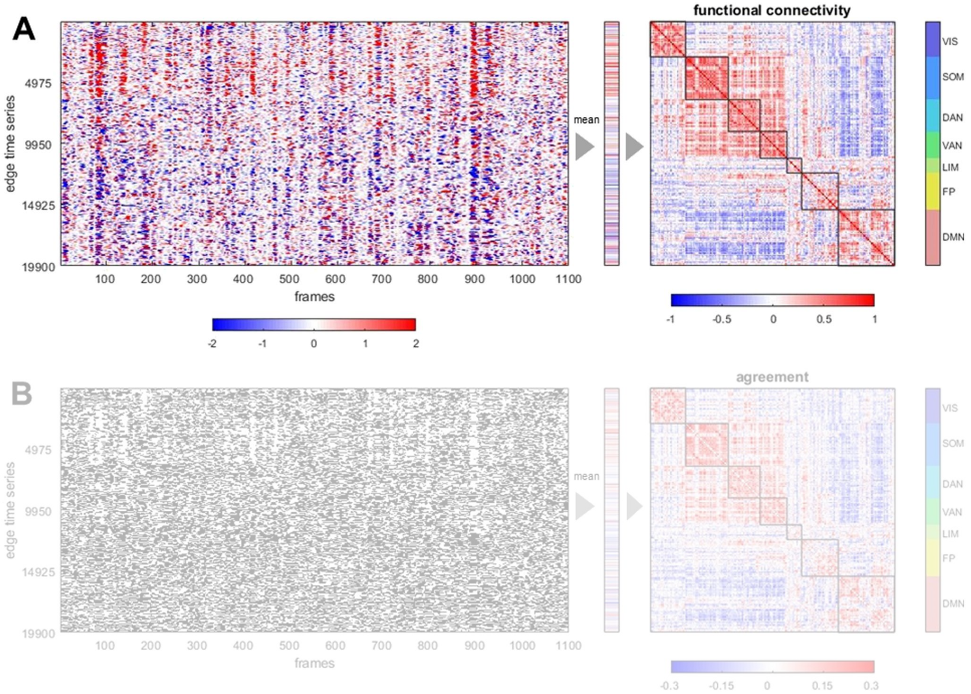

Edge time series

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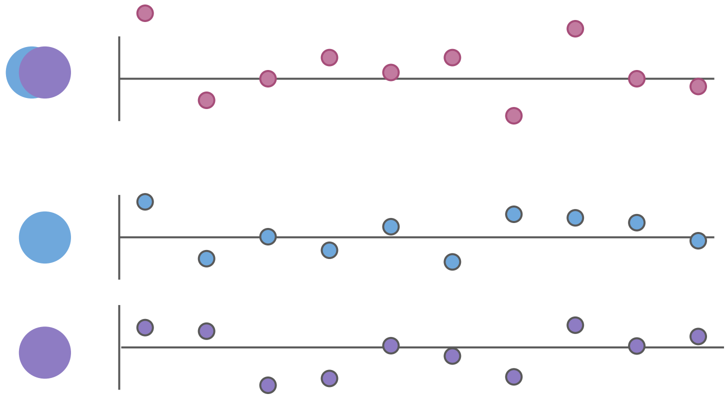
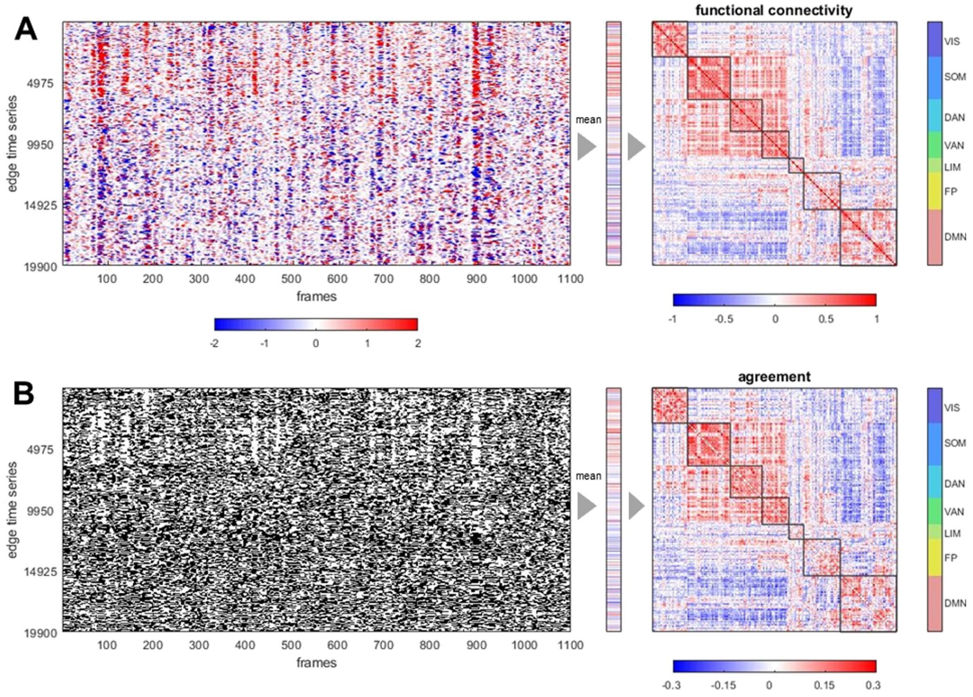


Edge time series



Sporns et al (2022) *Net. Neuro.*

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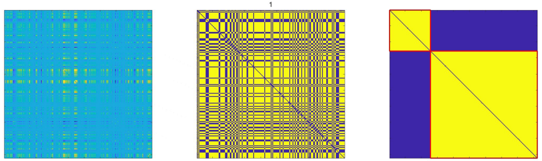
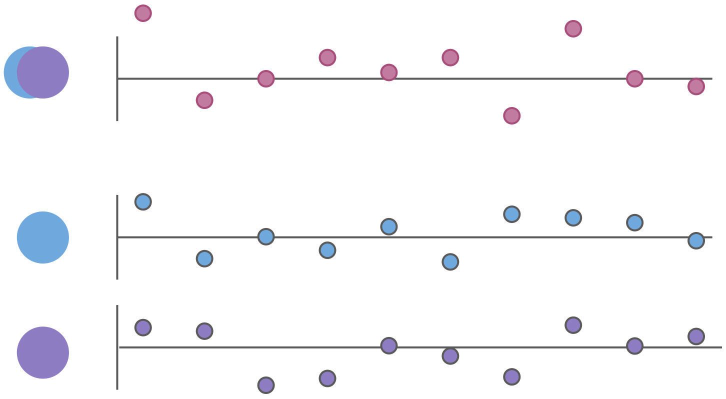
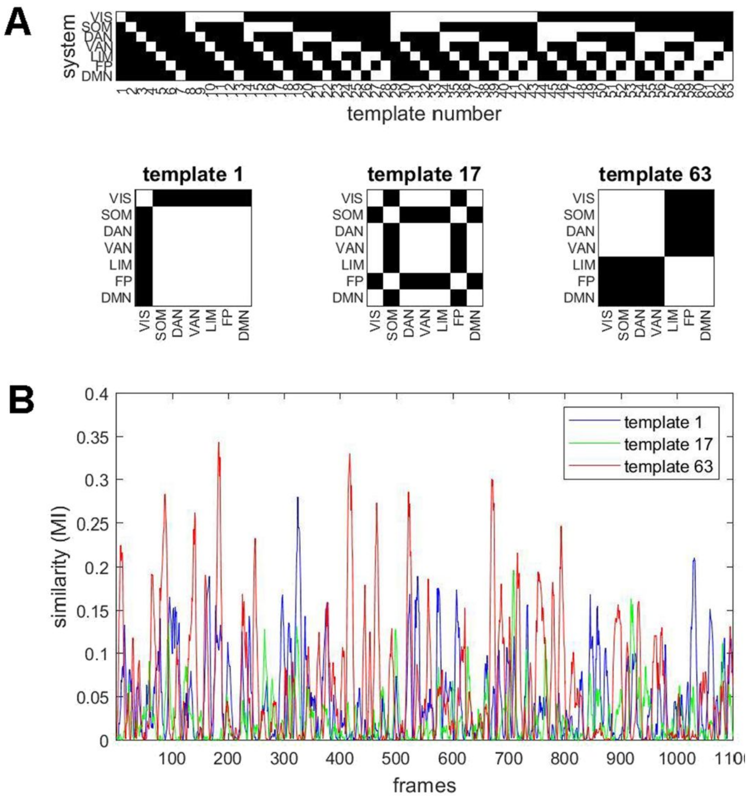




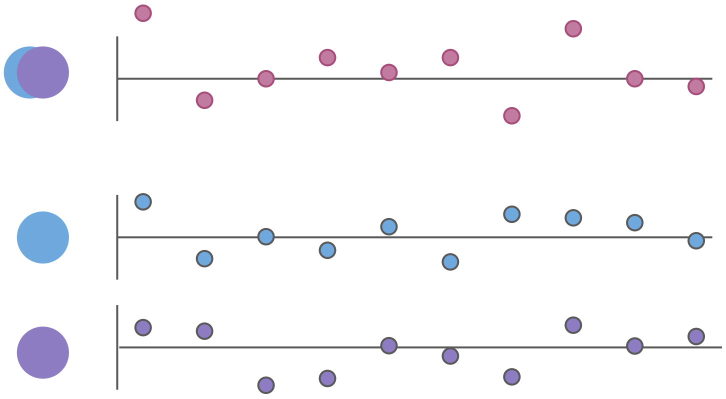
Edge time series



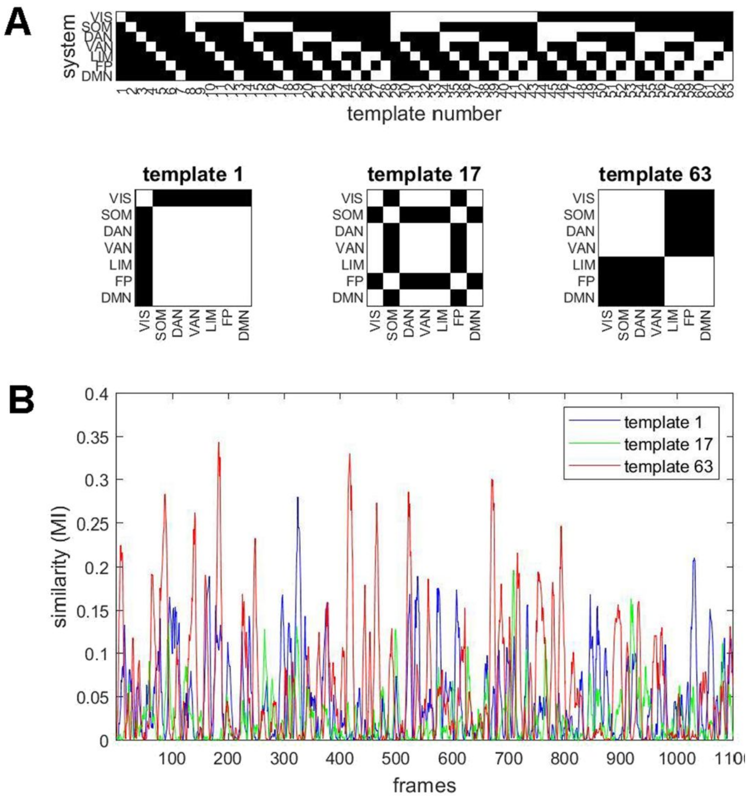
Sporns et al (2022) *Net. Neuro.*

Lots of information from little bits of your data!

Ex. the systems we know and love are expressed briefly and prominently

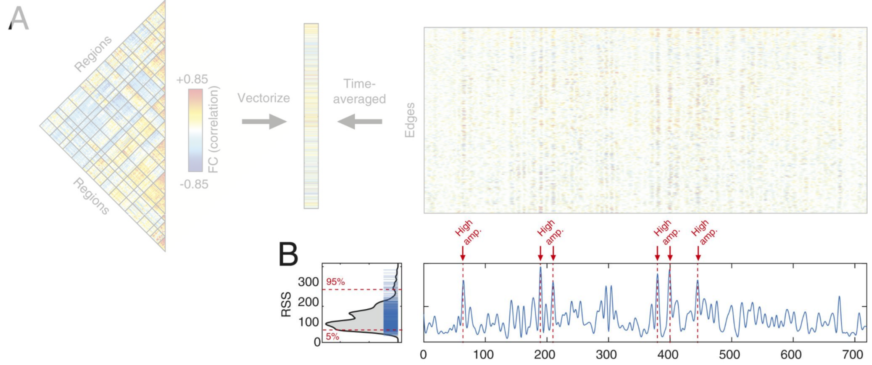


Edge time series

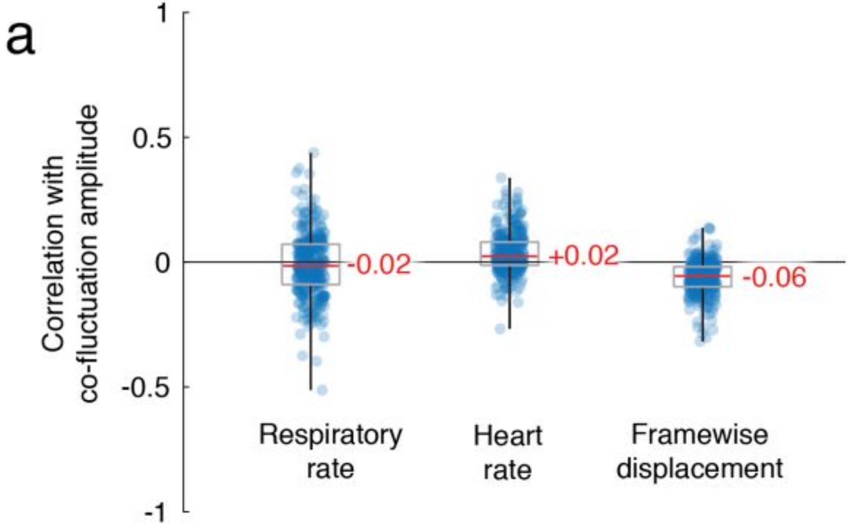


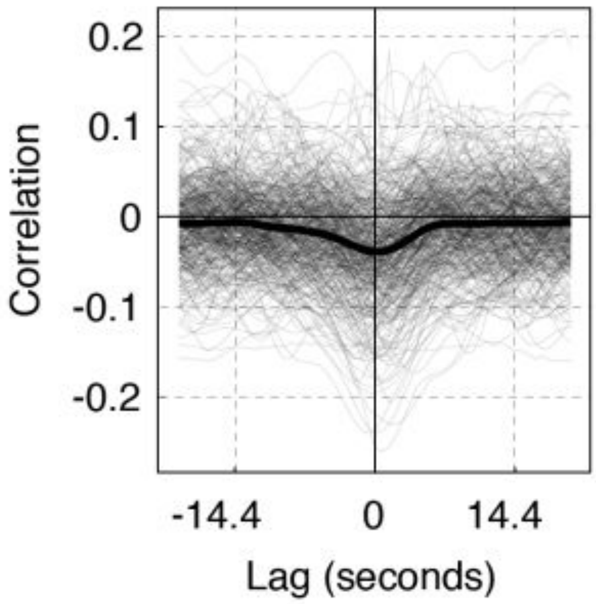
Sporns et al (2022) *Net. Neuro.*

What about motion or other mischievous stuff?

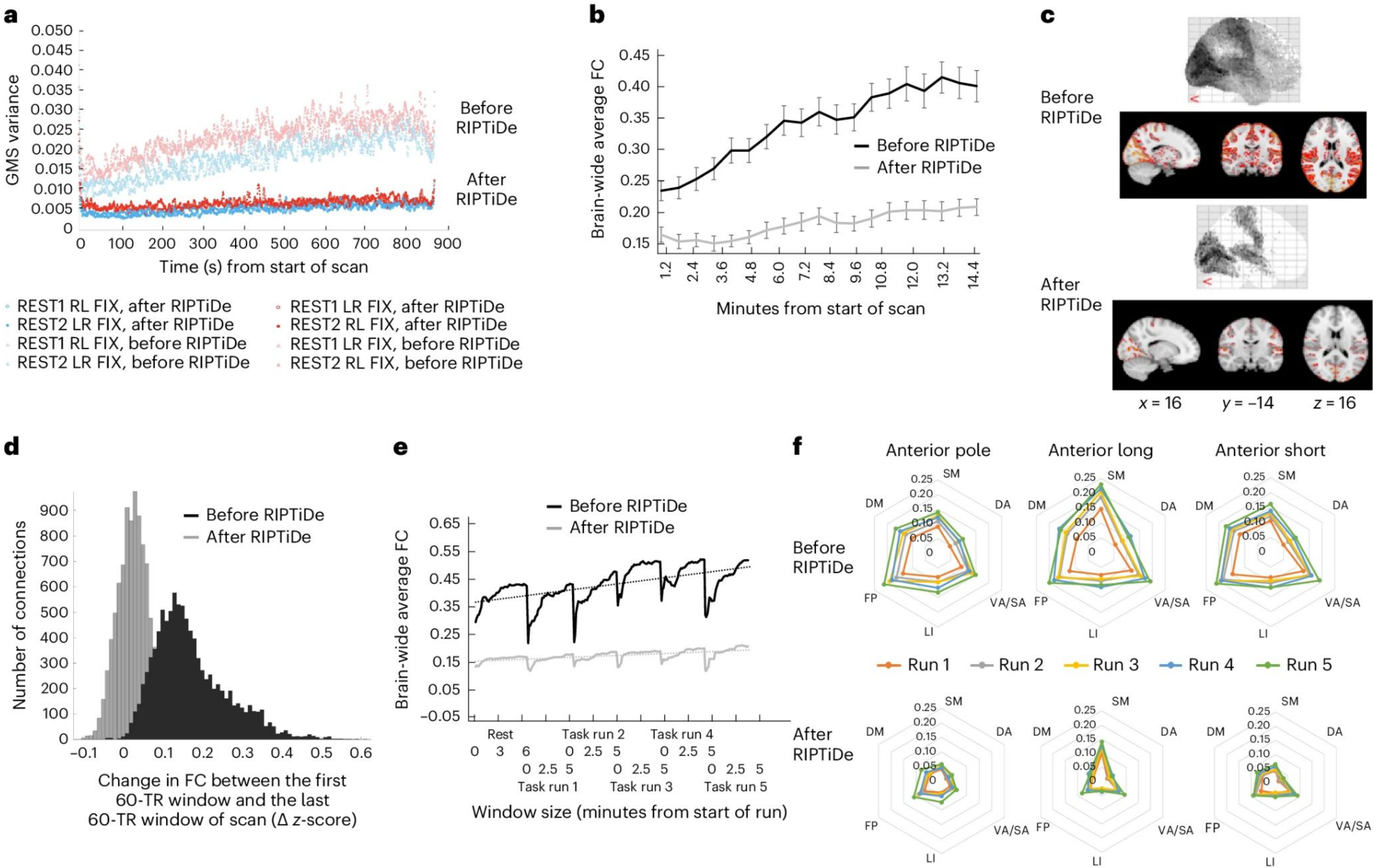


Is it a physiology or motion artifact?

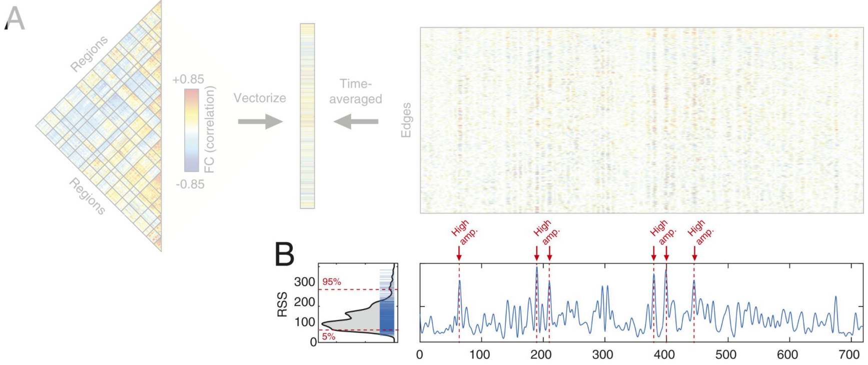




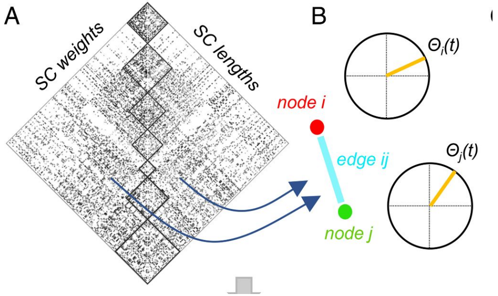
Zamani Esfahlani et al (2020) *PNAS*



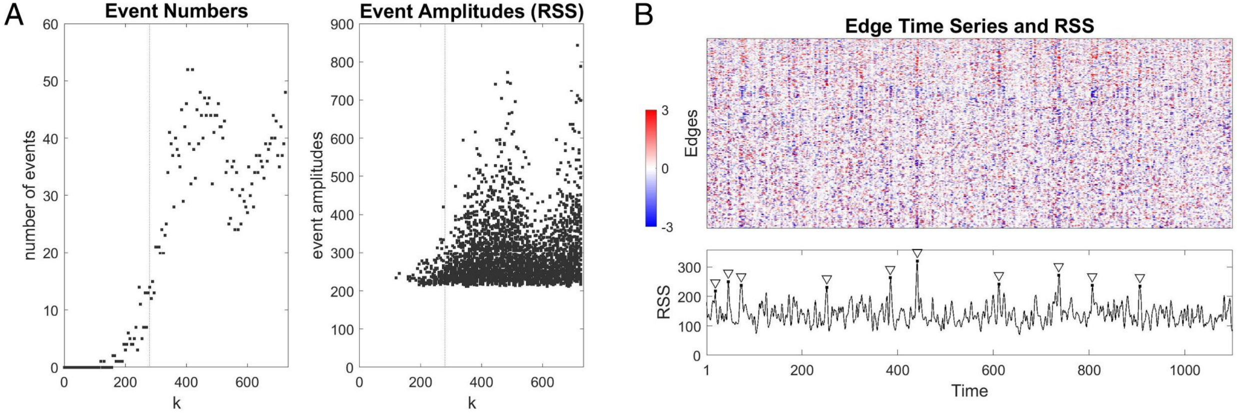
Korpronay et al (2024) *Nat. Hu. Behav.*



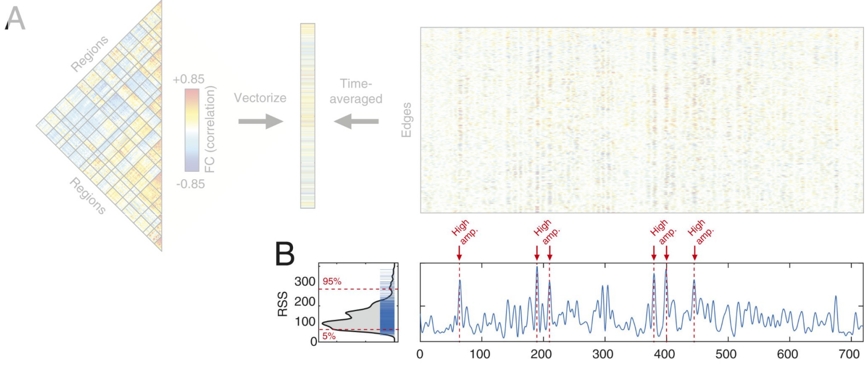
Is it a physiology or motion artifact?



Simulated data using Kuramoto oscillators show same spiky phenomena



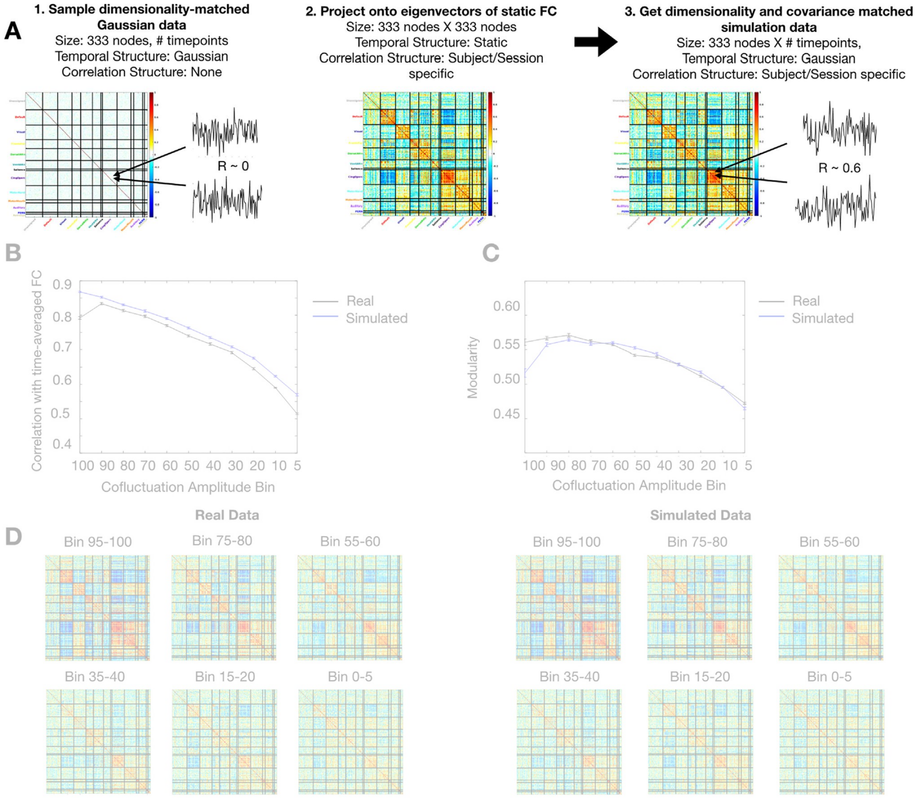
Pope et al (2021) *PNAS*



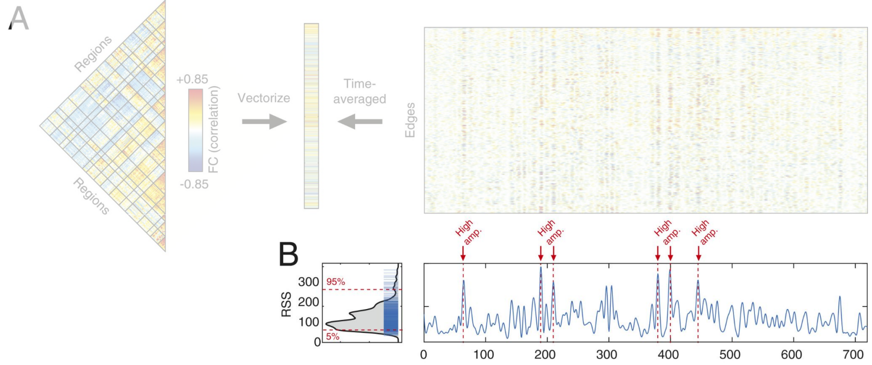
Events could be signatures of modular subsystems

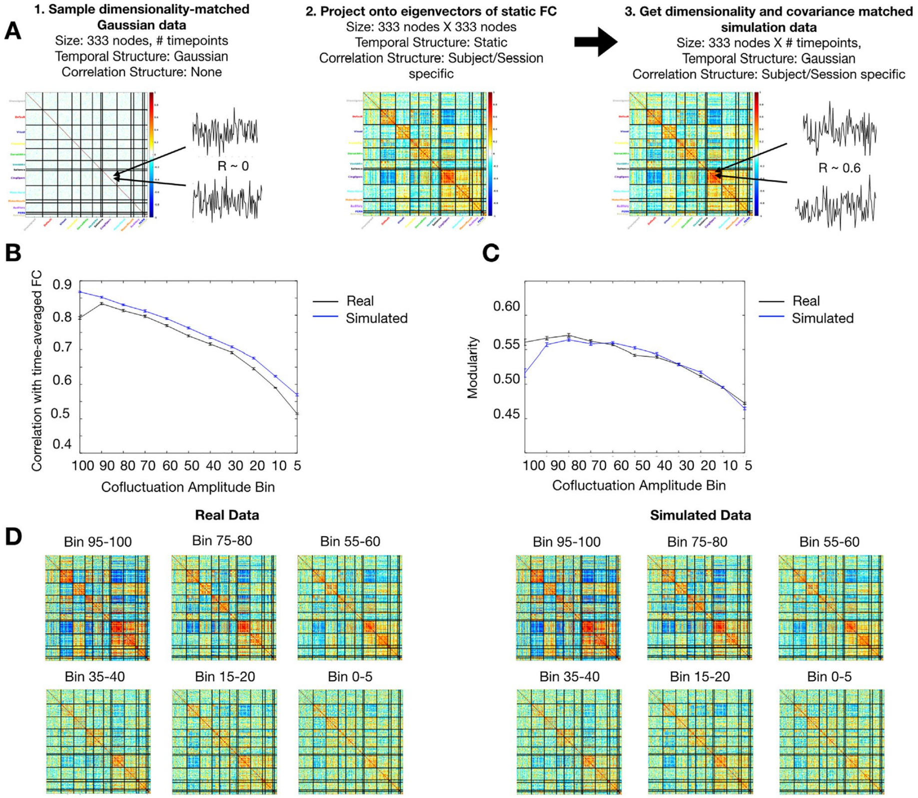
A system with a certain level of modularity/assortativity structure will result (mathematically) in time series with large RSS events

Events themselves are mathematically necessary, but dynamics/timing can't be explained in same manner



Novelli & Razi (2022) Nat. Comms., Ladwig et al (2022) *NeuroImage*





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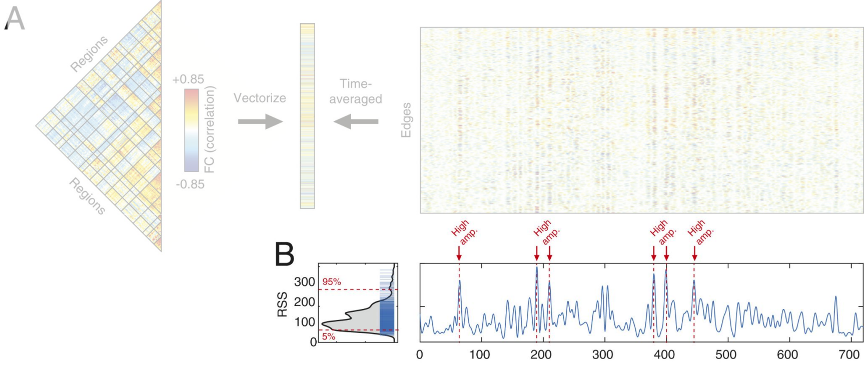

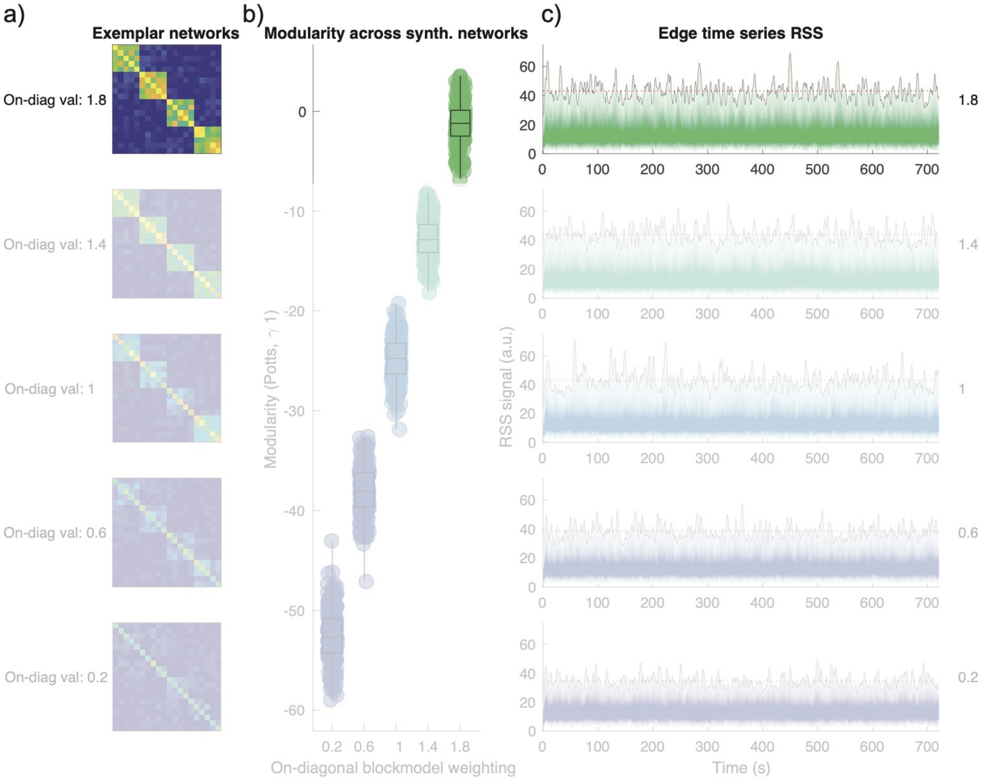

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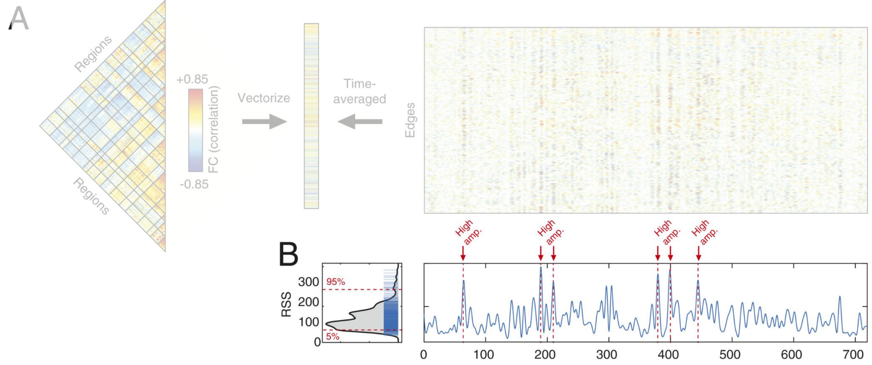
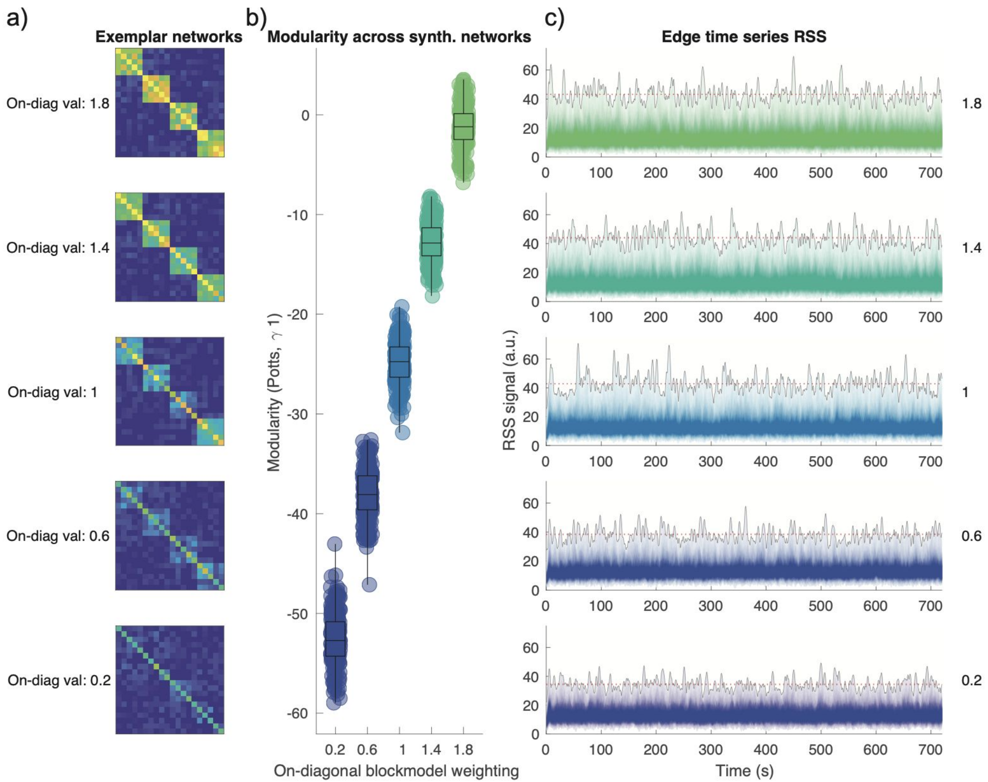
Faskowitz et al (2023). OHBM





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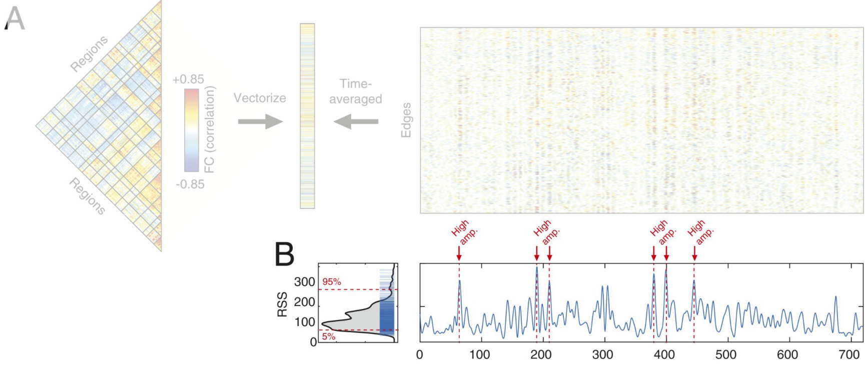

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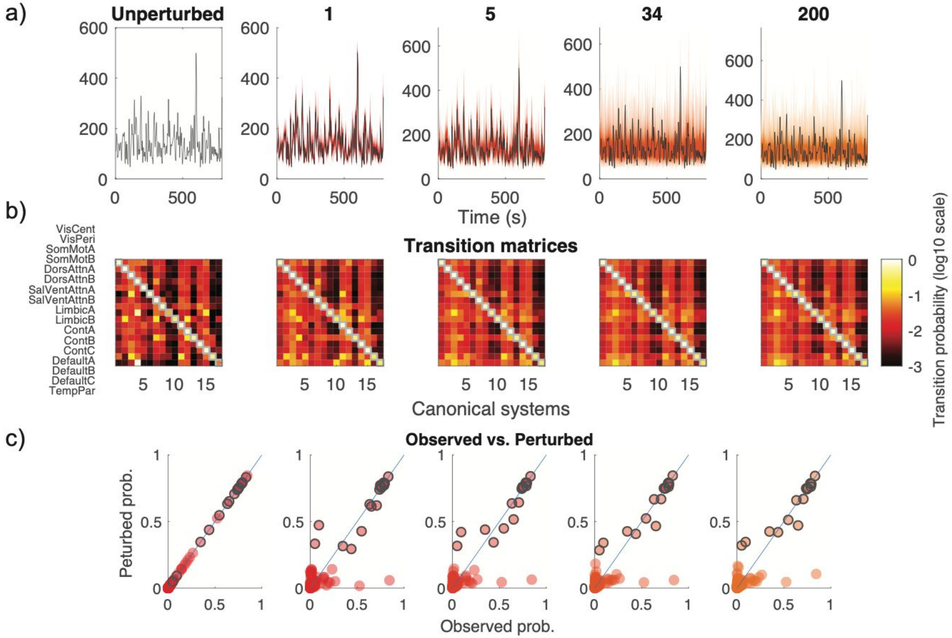
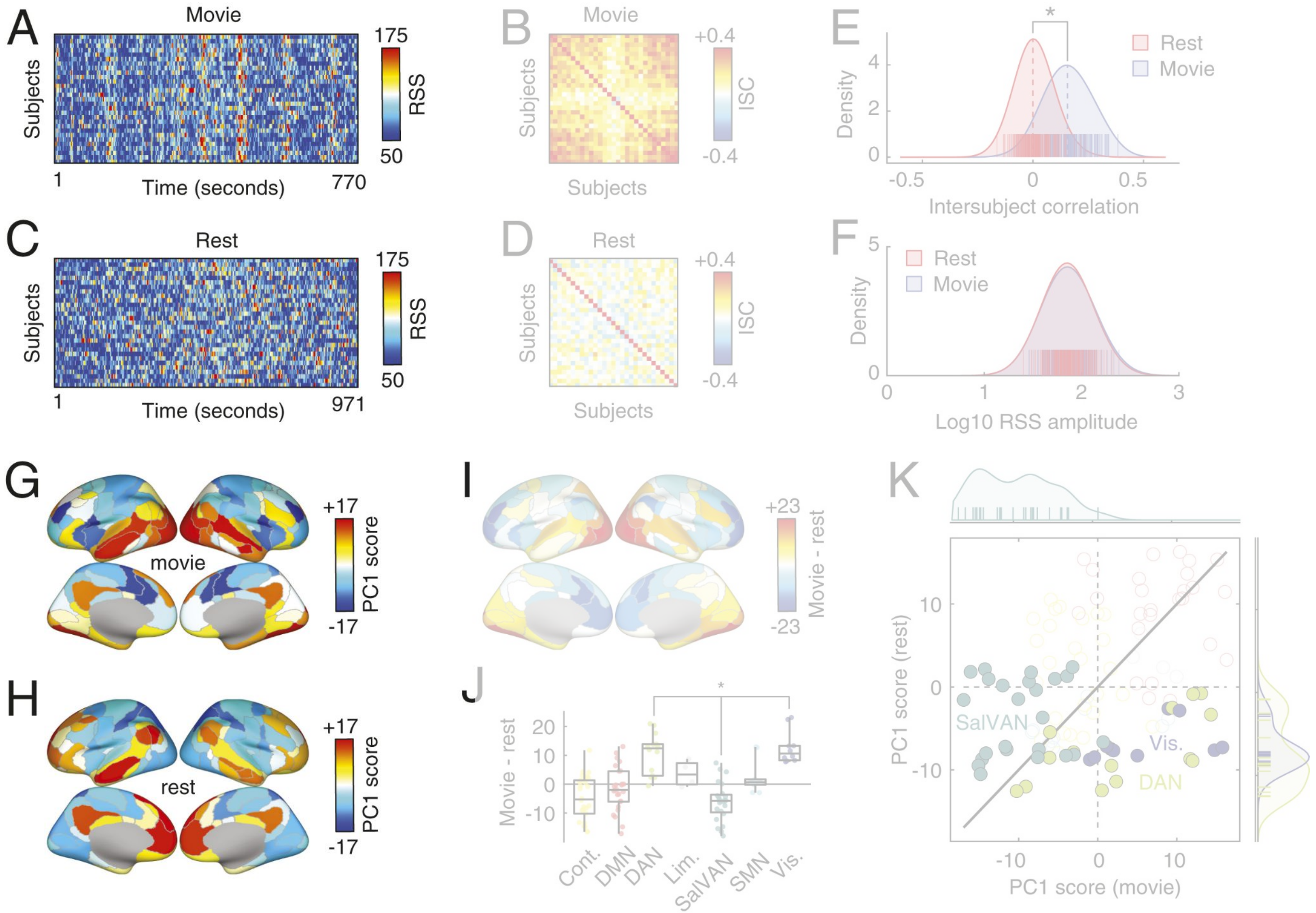


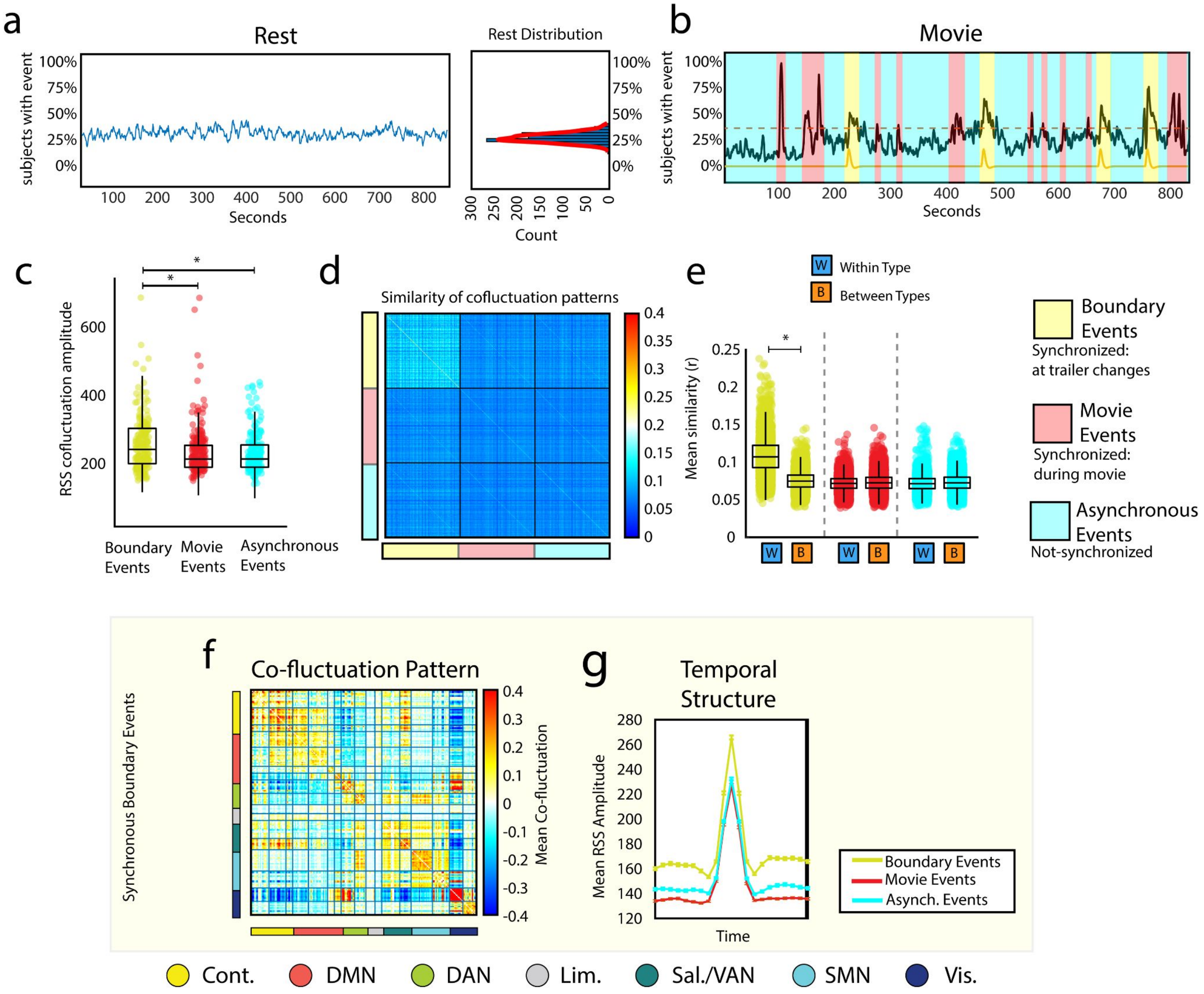
Might there be more information to extract by analyzing the sequence of event patterns? Probably!

Faskowitz et al (2023). OHBM

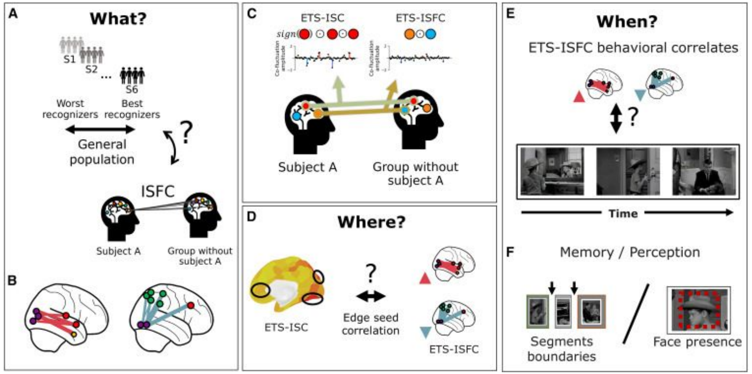
Edges and behavior

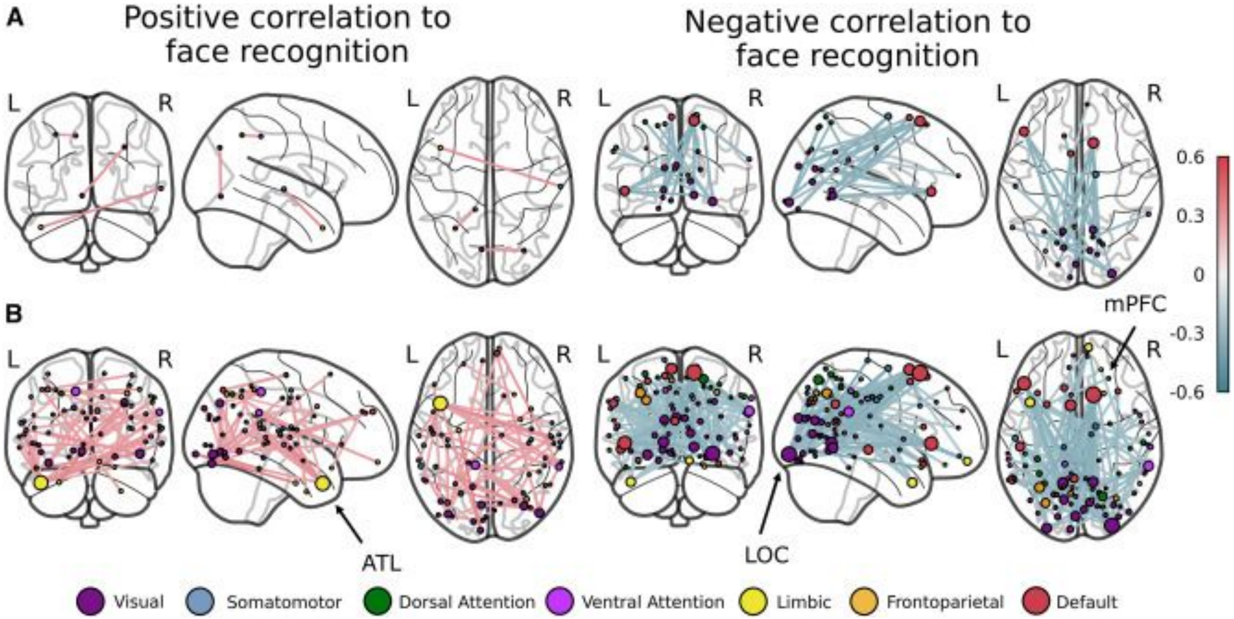


Zamani Esfahlani et al (2020) *PNAS*

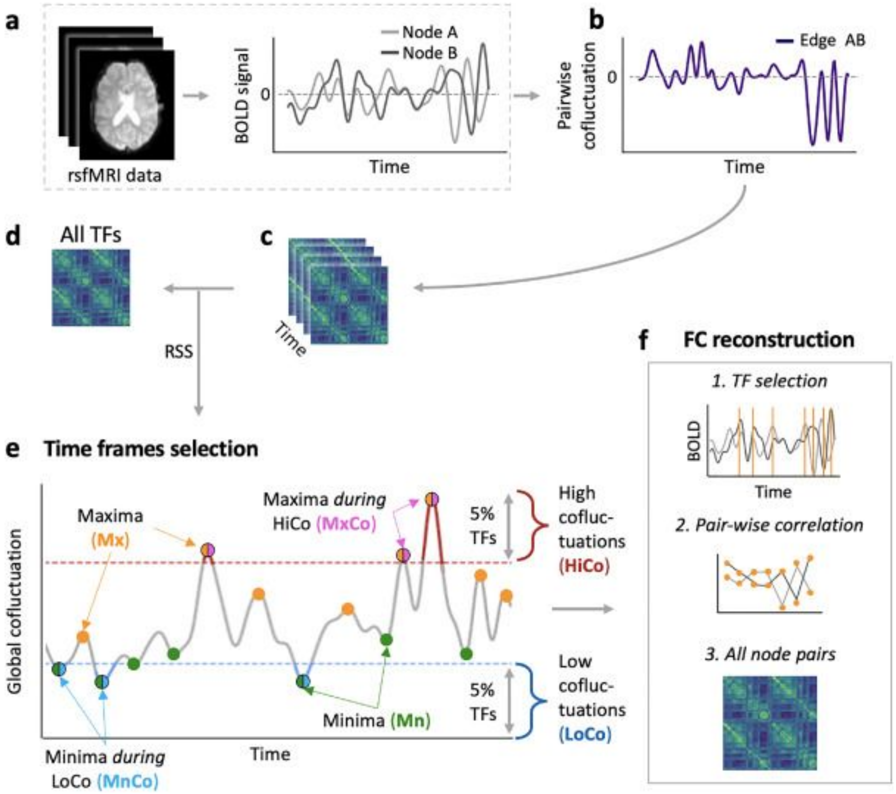


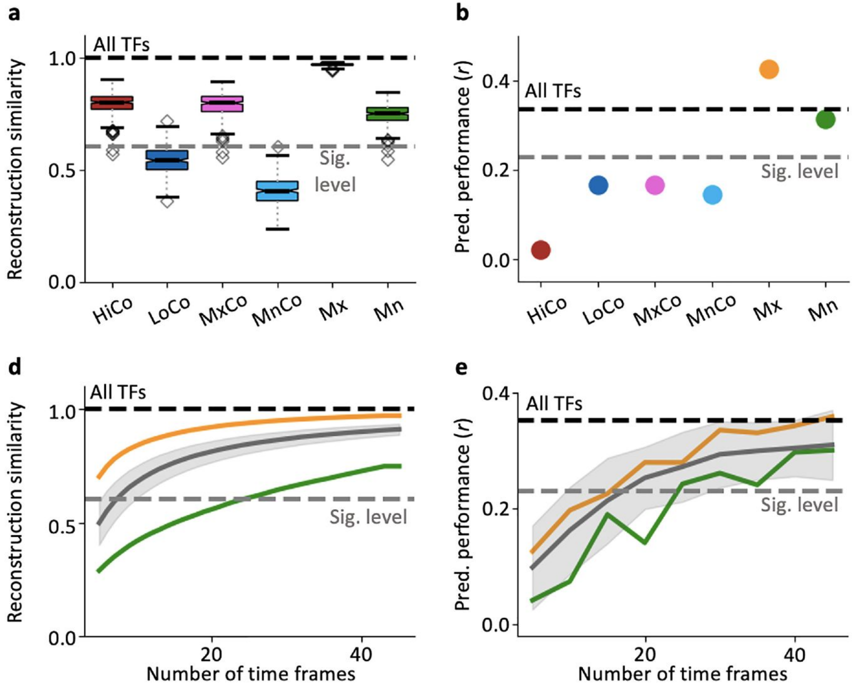
Tanner et al (2023) *Imaging Neuro.*



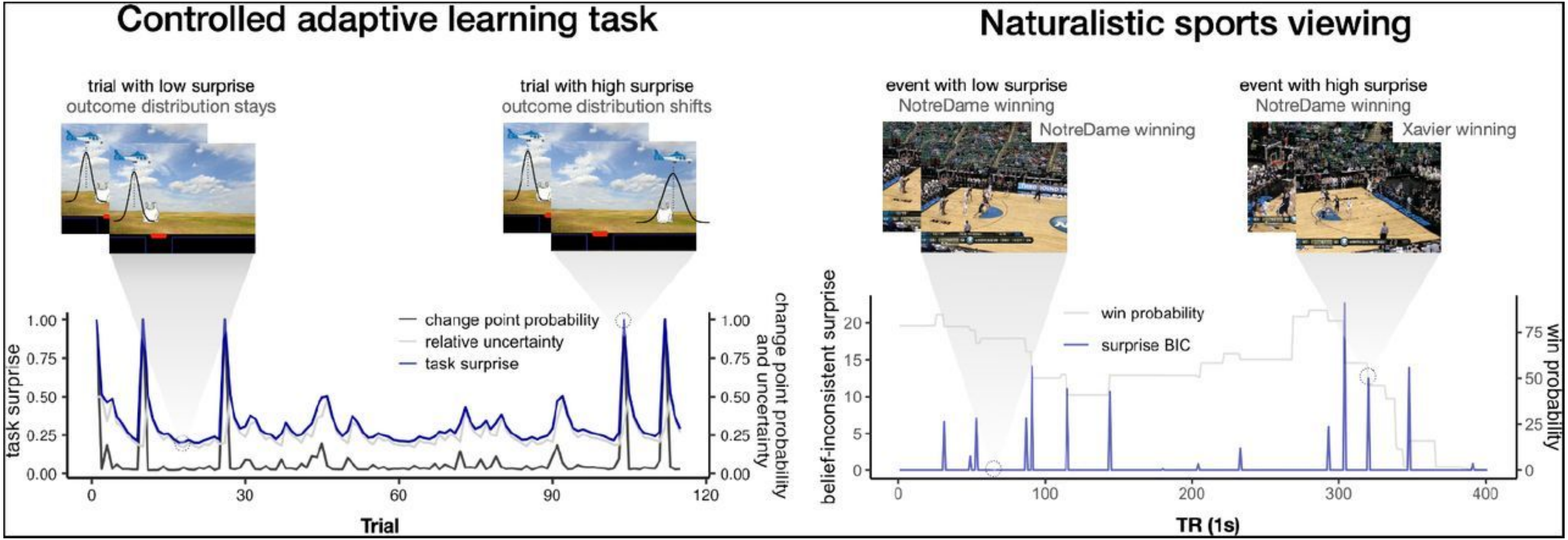


Levakov et al (2023) *Cell Reports*

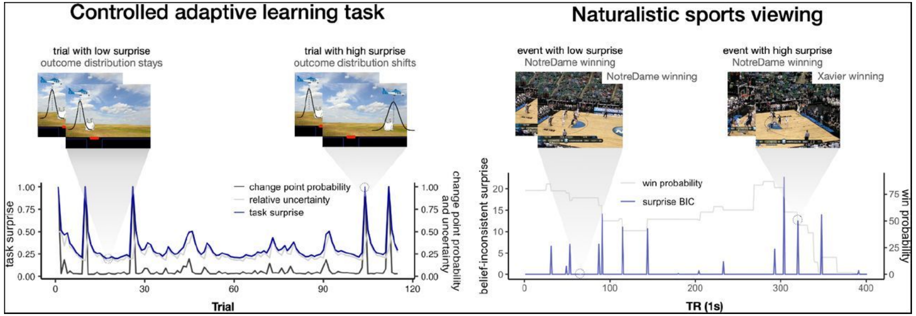


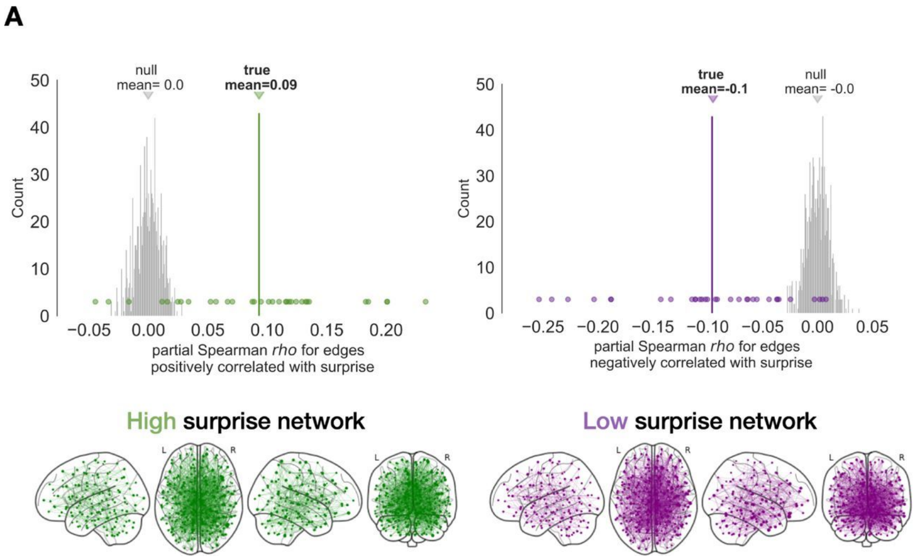


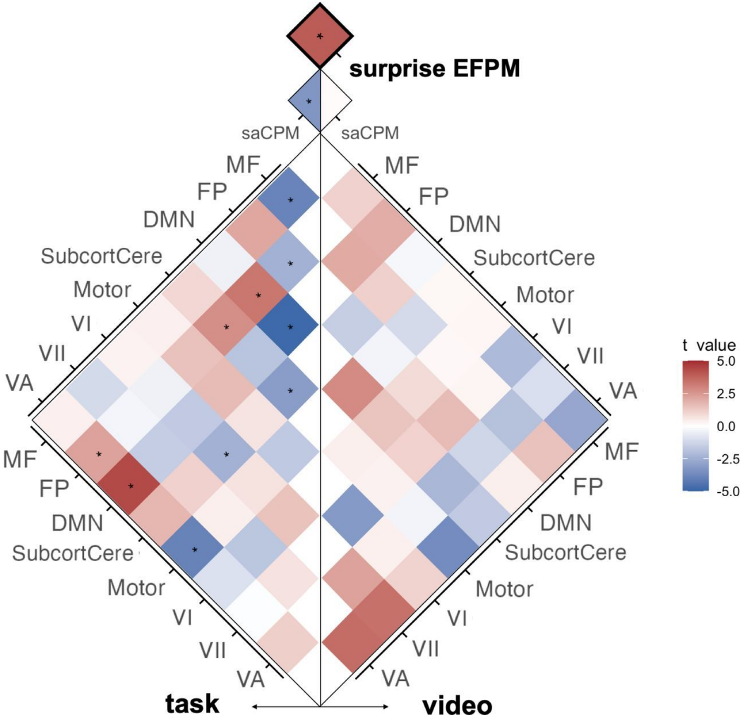
Wehrheim et al (2023) *NeuroImage*



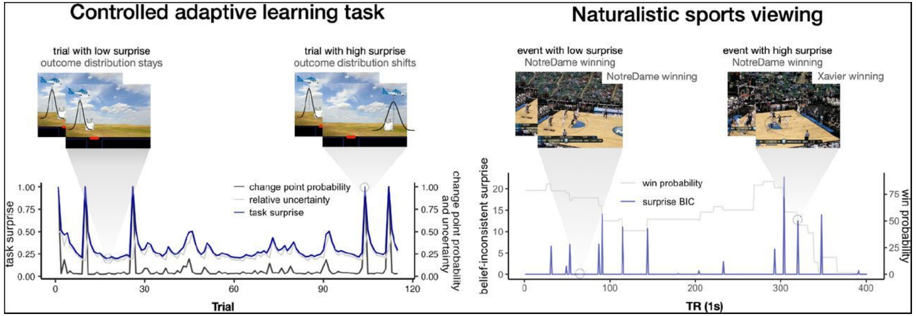
Zhang & Rosenberg (2023) *BioRxiv*



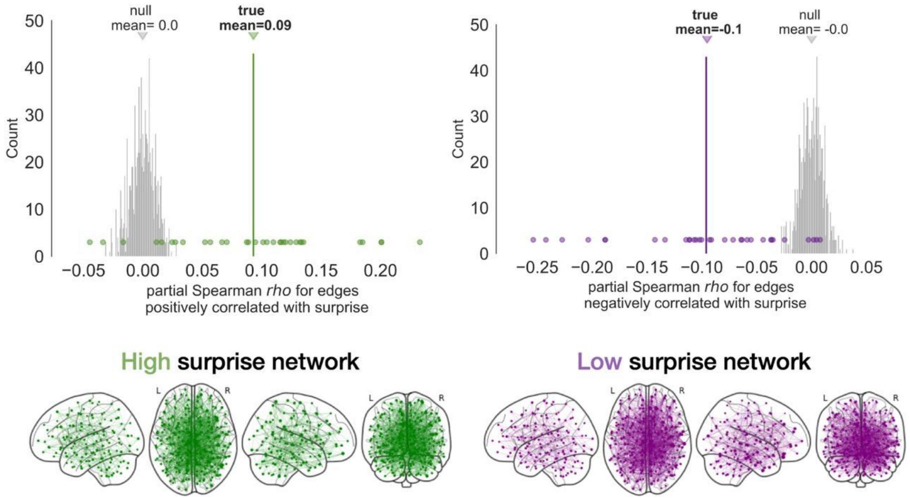


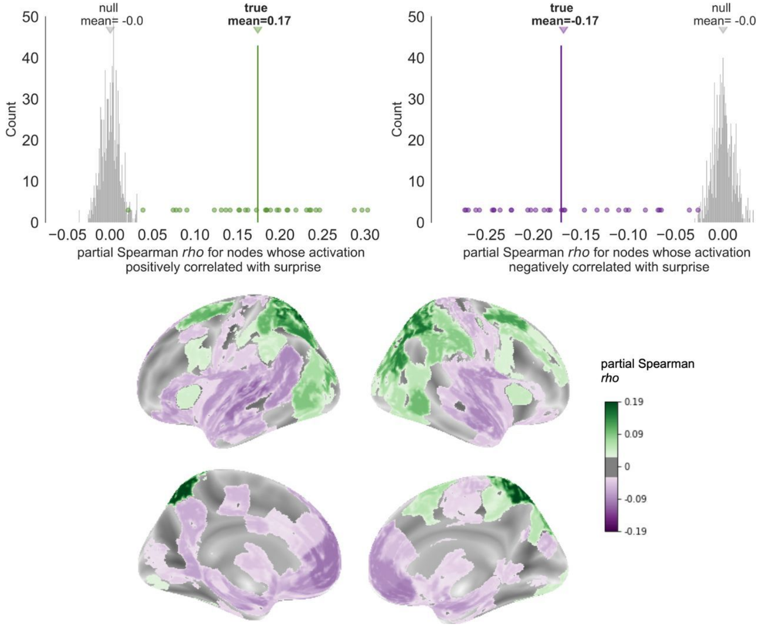


Zhang & Rosenberg (2023) *BioRxiv*

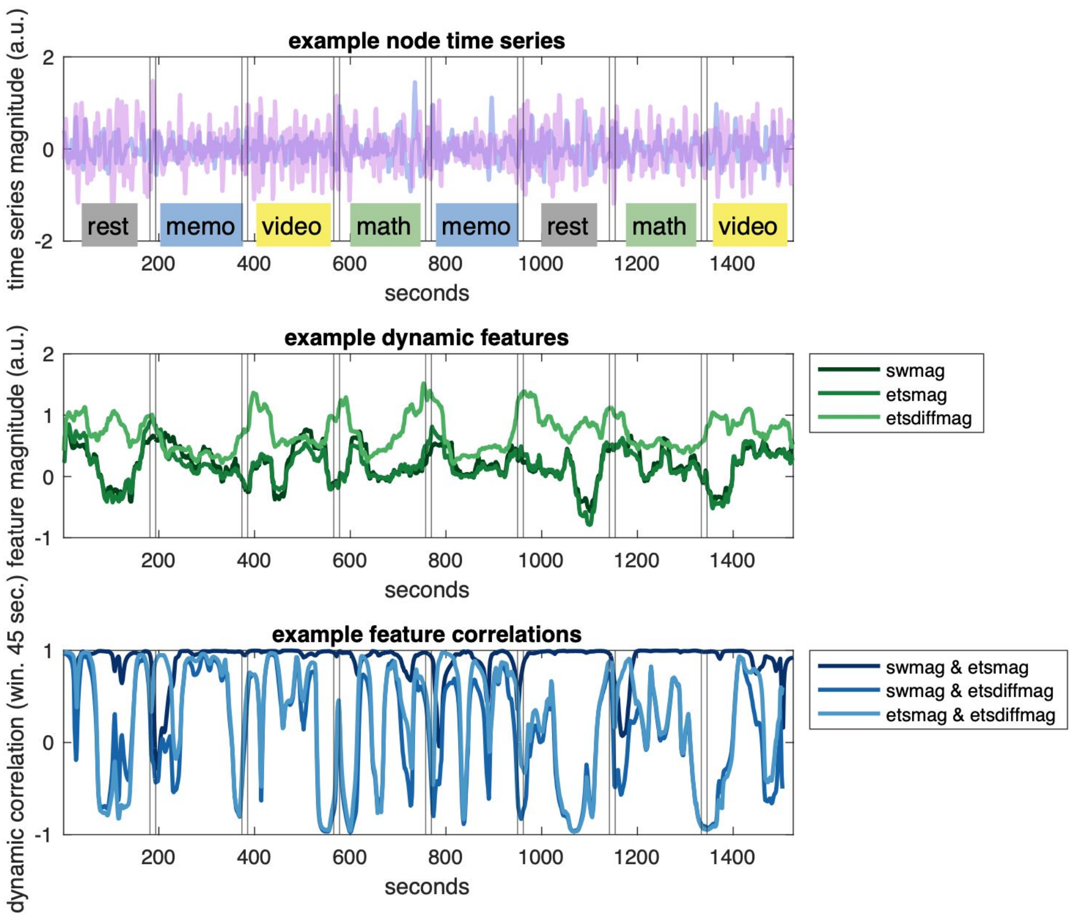


A

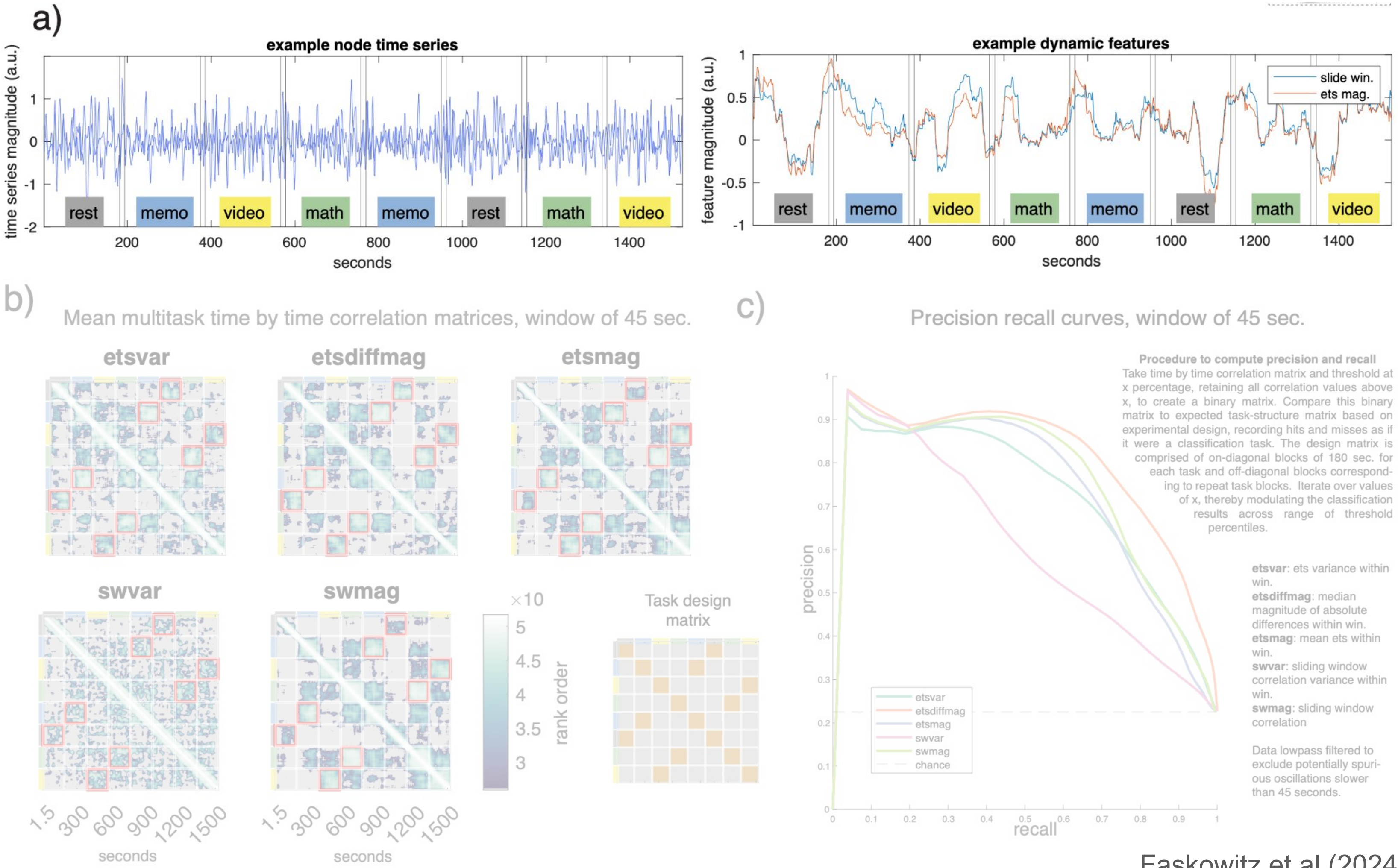




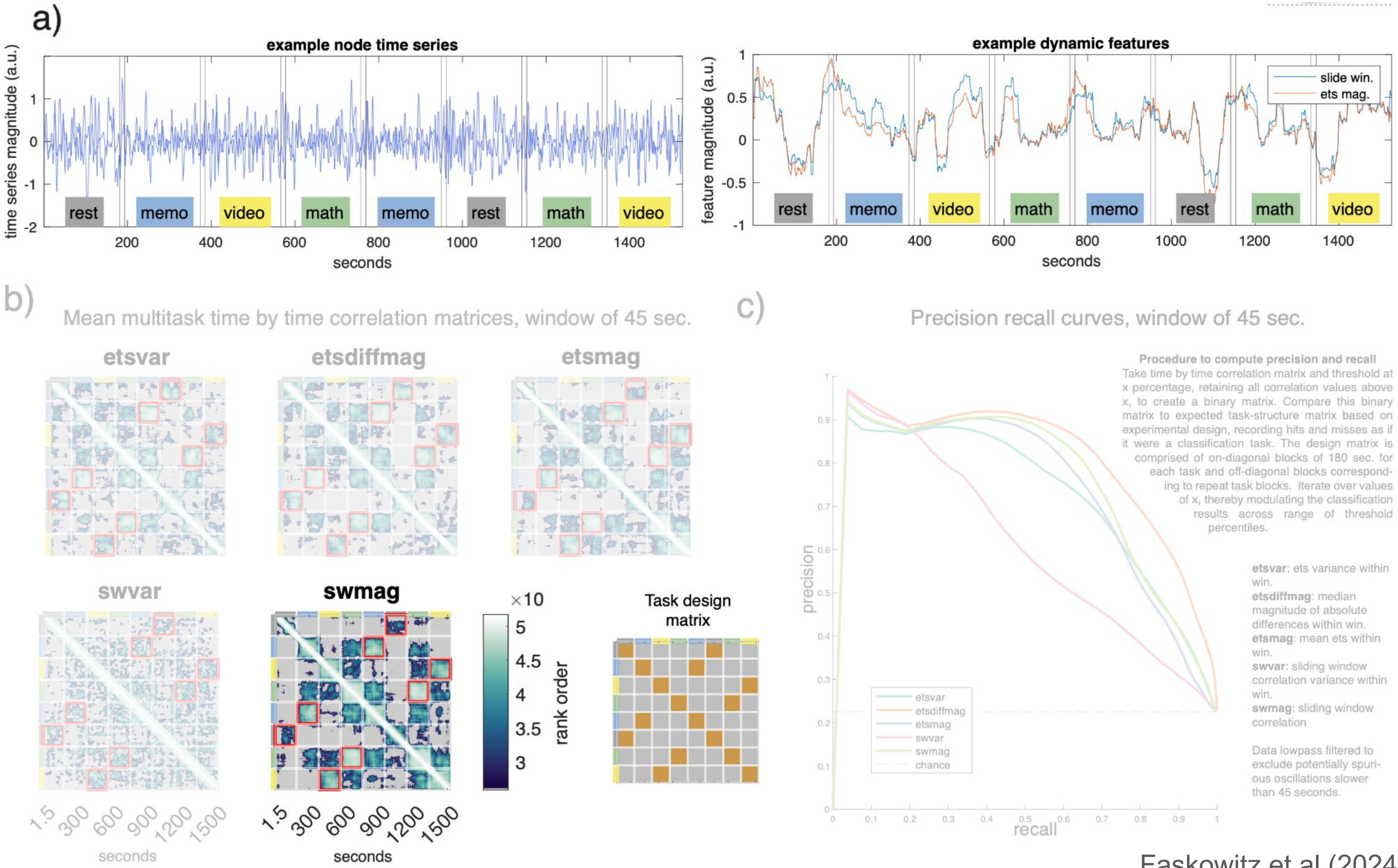
Zhang & Rosenberg (2023) *BioRxiv*



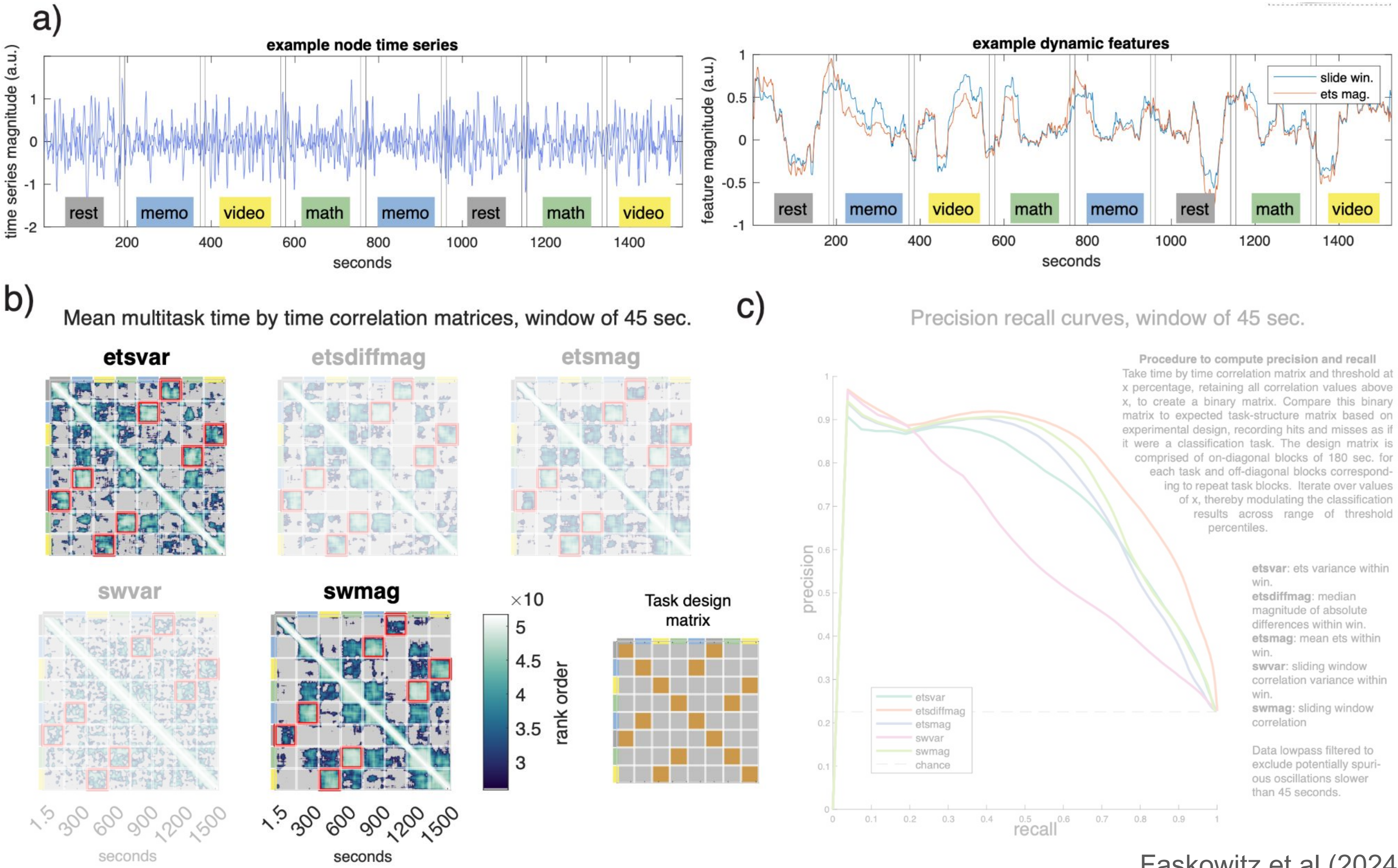
example node time series
time series magnitude (a.u.)
rest
memo
video
math
memo
rest
math
video
seconds
example dynamic features
feature magnitude (a.u.)
swmag
etsmag
etsdiffmag
seconds
example feature correlations
dynamic correlation (win. 45 sec.)
swmag & etsmag
swmag & etsdiffmag
etsmag & etsdiffmag
seconds



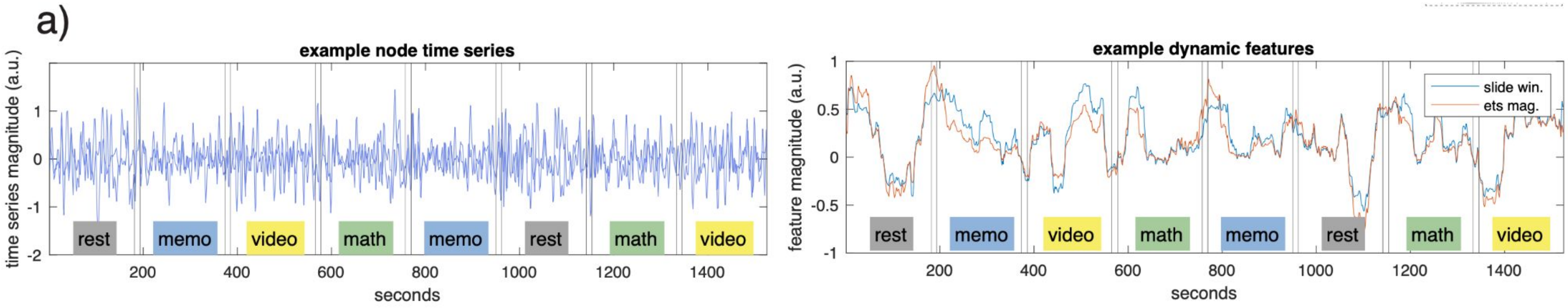
Faskowitz et al (2024). OHBM

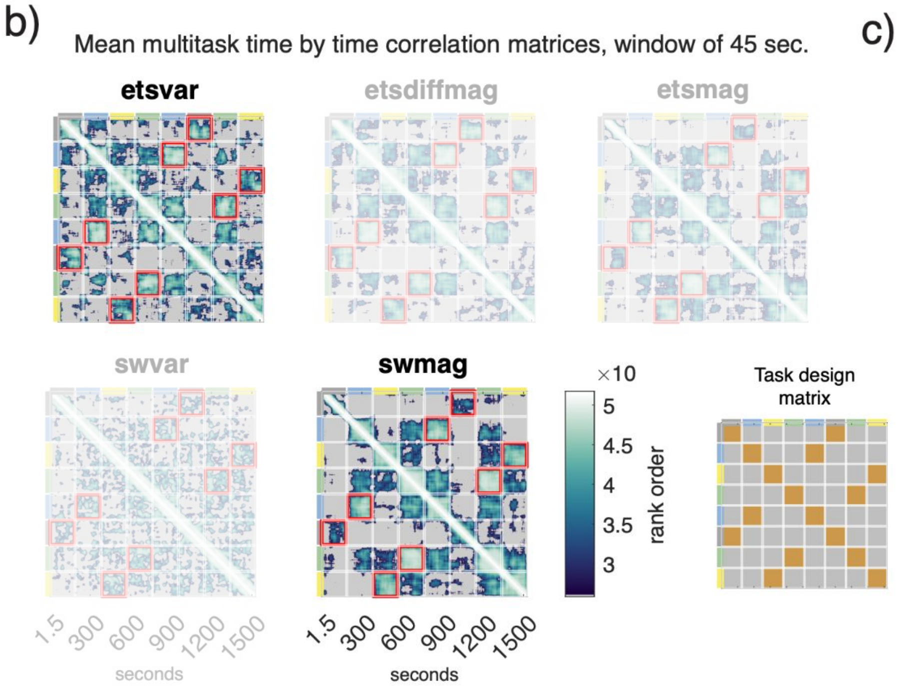


Faskowitz et al (2024). OHBM



Faskowitz et al (2024). OHBM





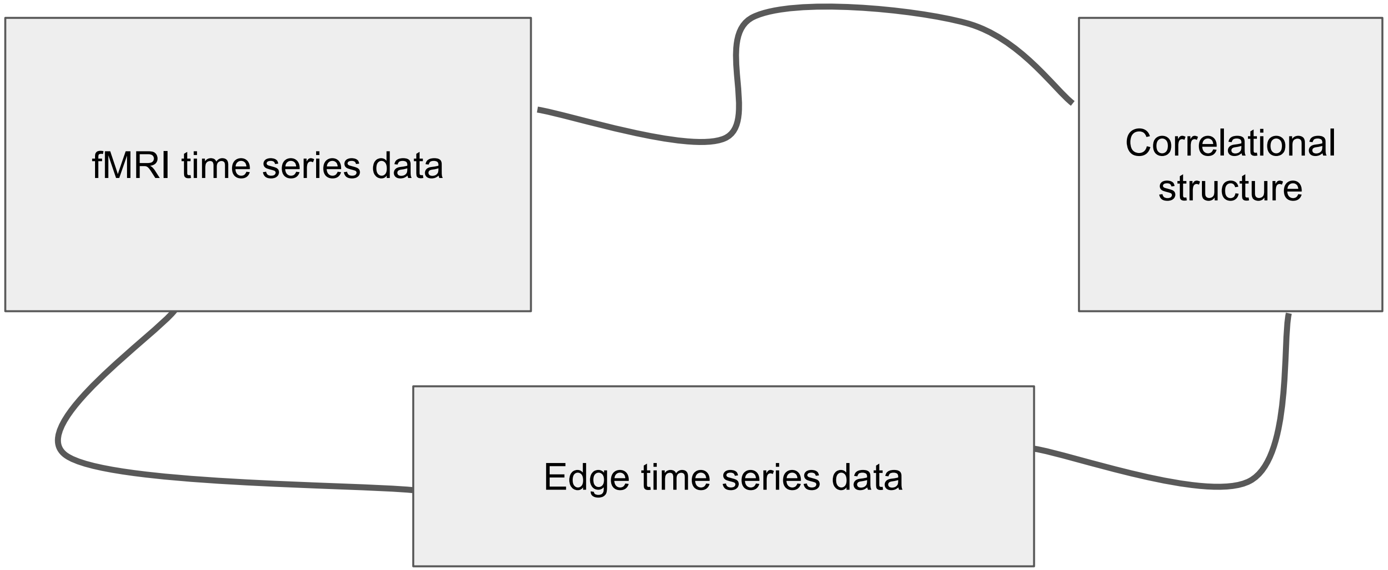
c)

Can we read alternative features from the edge time series to help pick out organization that is predictive of behavior/task?

Faskowitz et al (2024). OHBM

Final thoughts

- Edge time series are a new view of the original data, which put the data in an alternative formation



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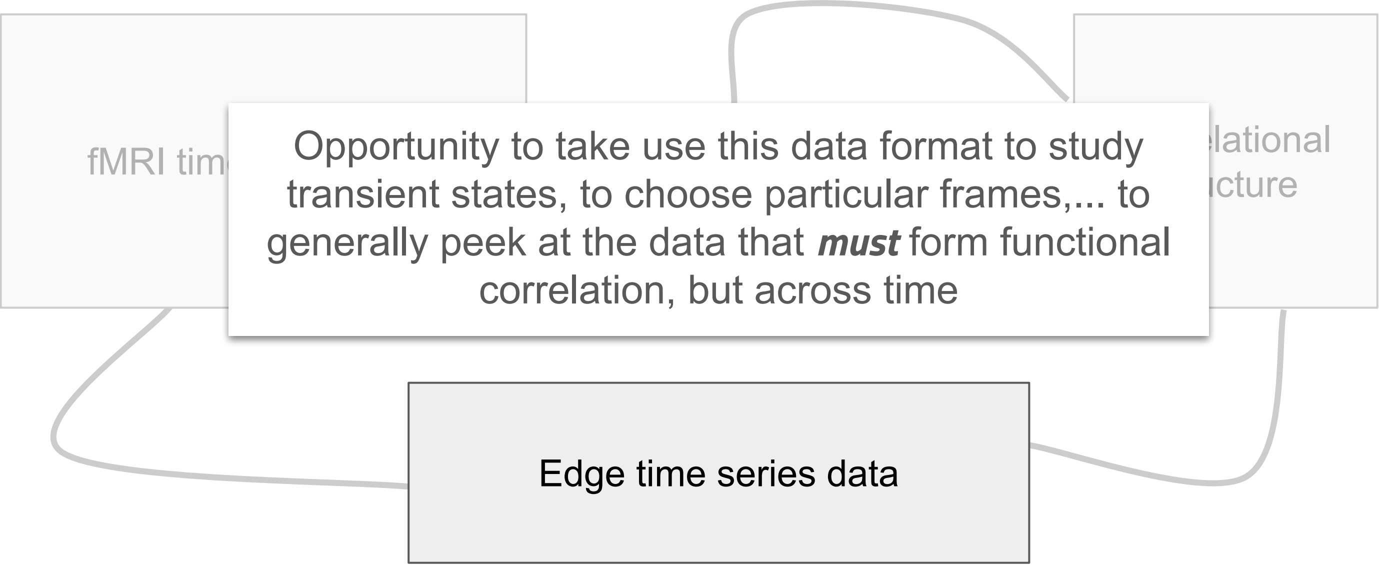
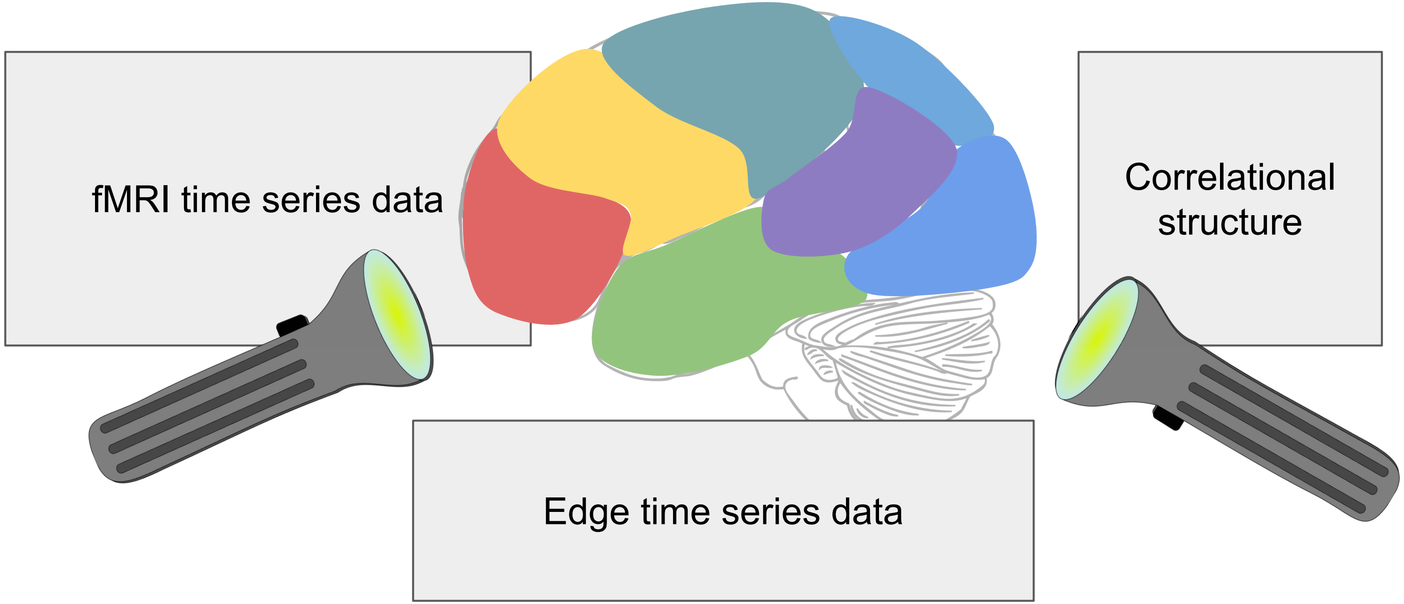
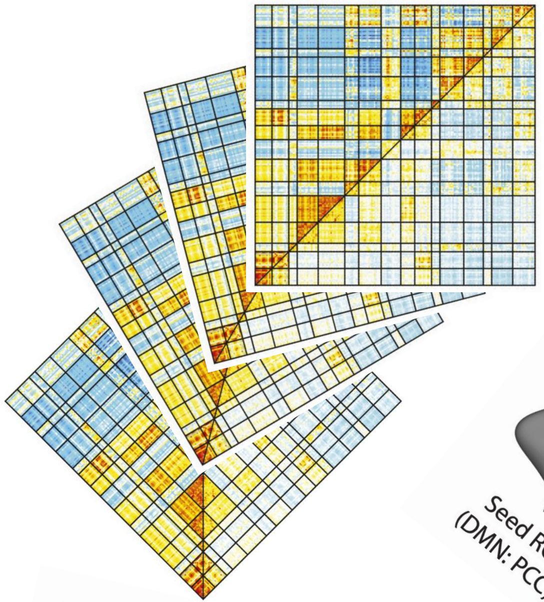
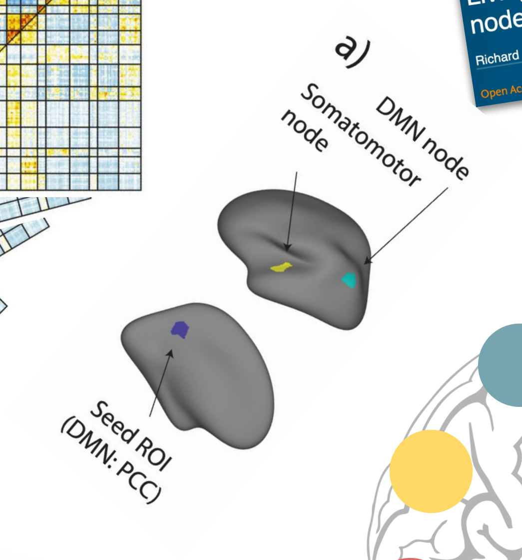
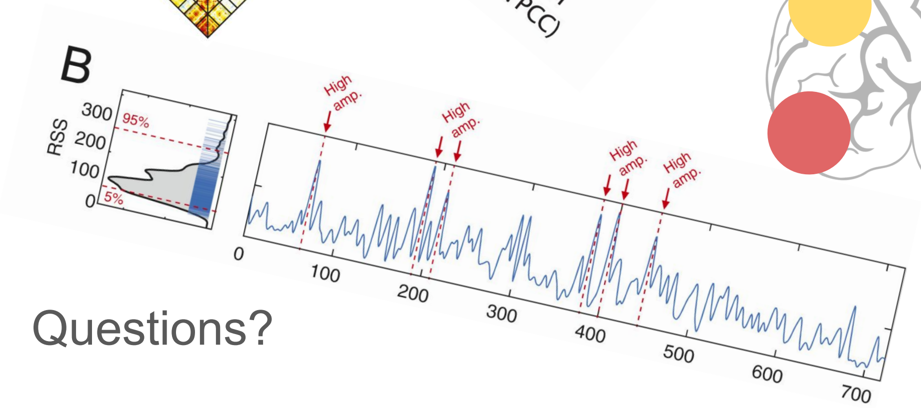


- Edge time series are a new view of the original data, which put the data in an alternative formation







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On the features of spiking connectivity
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On the static and dynamic features of edge time series
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NIH National Institute of Mental Health

FIM

Questions?