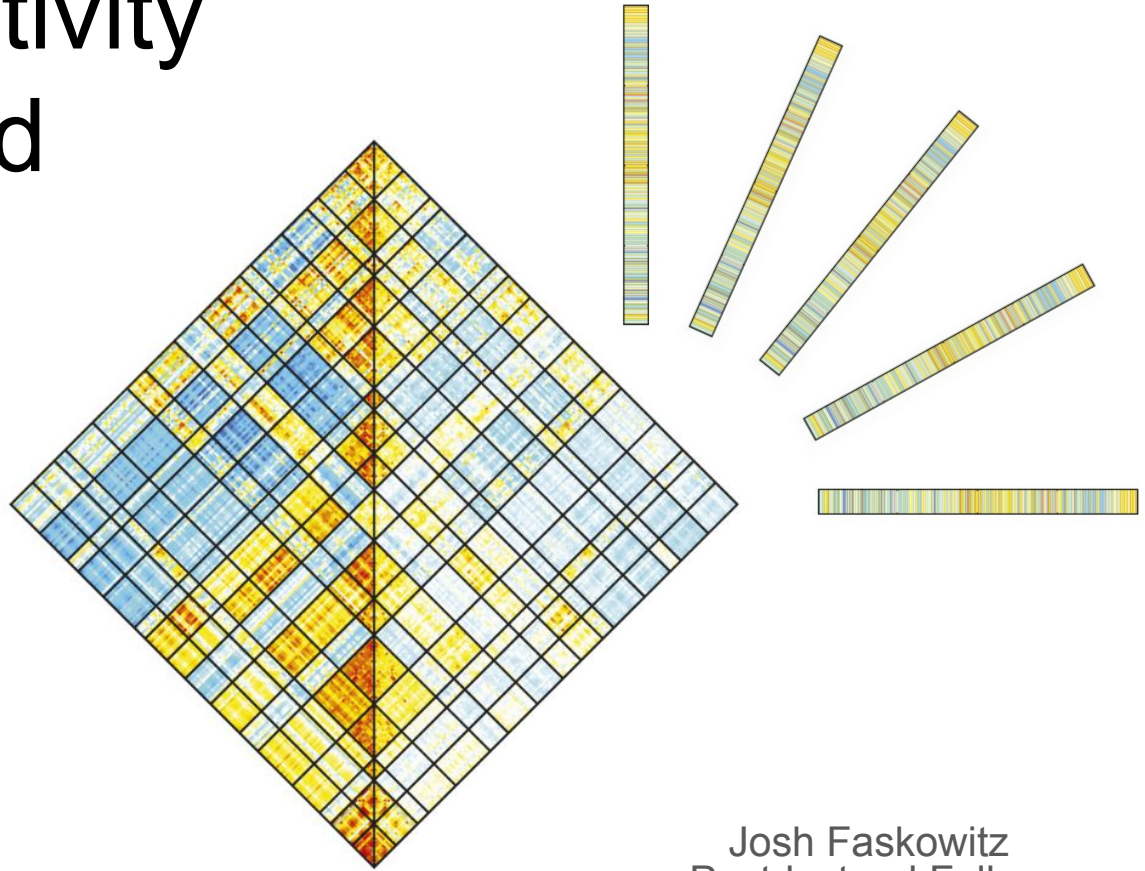
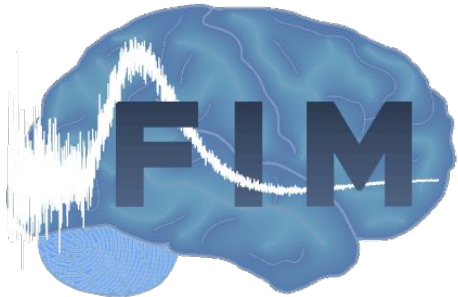


fMRI Connectivity and advanced processing strategies



Josh Faskowitz
Postdoctoral Fellow
Section on Functional Imaging Methods

An fMRI project journey

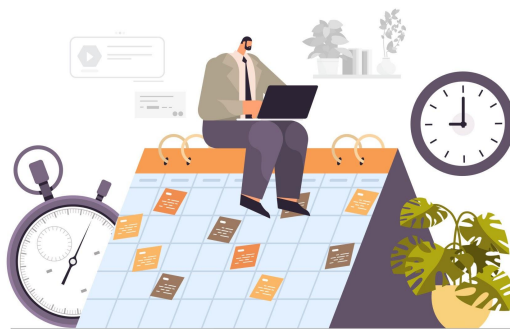
Think up a great idea!

(iterate on that idea)

Hypothesize what you'd like to see

Consult some MRI experts on what images you should collect

Plan for eventually writing your analysis code and sharing your data



An fMRI project journey



Scan your
subjects

An fMRI project journey



Scan your
subjects

Reconstruct
images

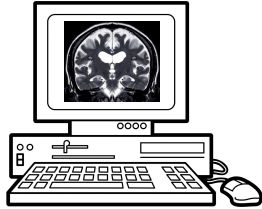
An fMRI project journey



Scan your
subjects

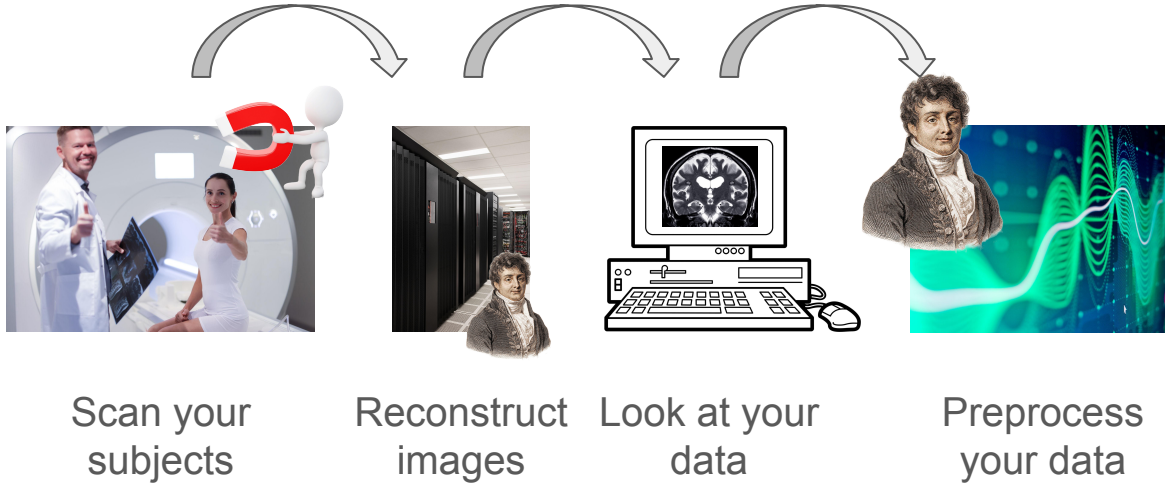


Reconstruct
images

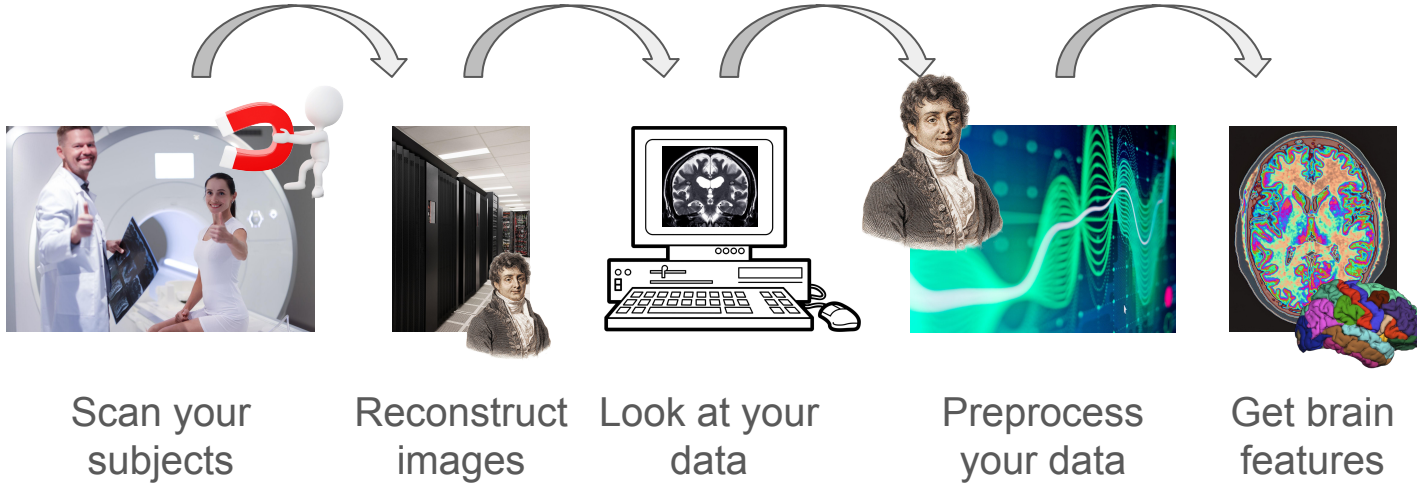


Look at your
data

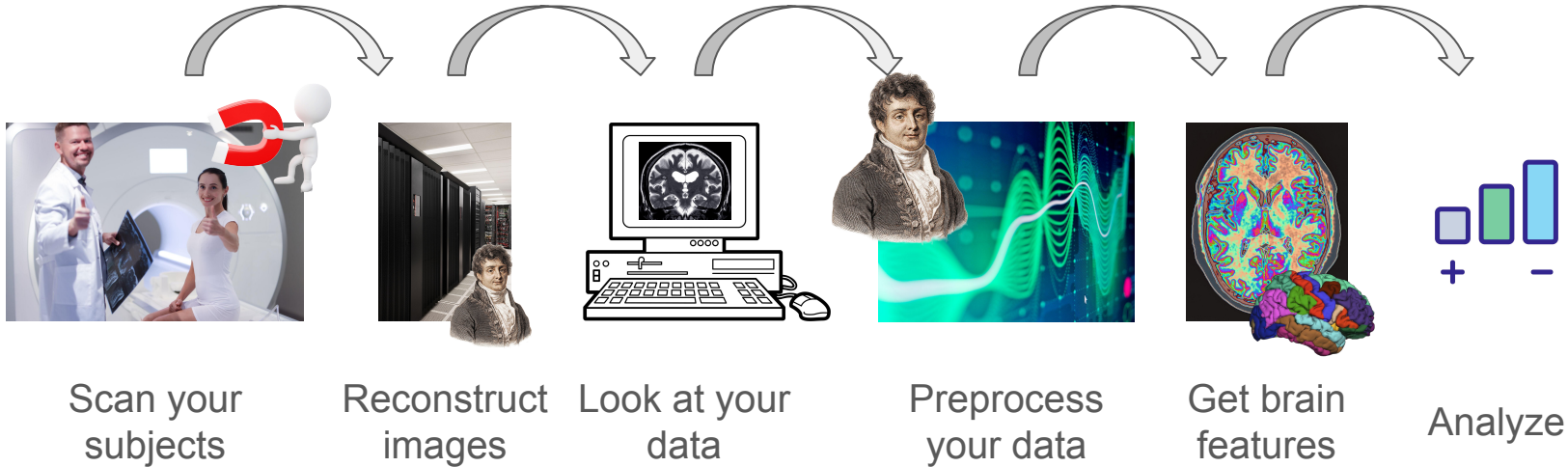
An fMRI project journey



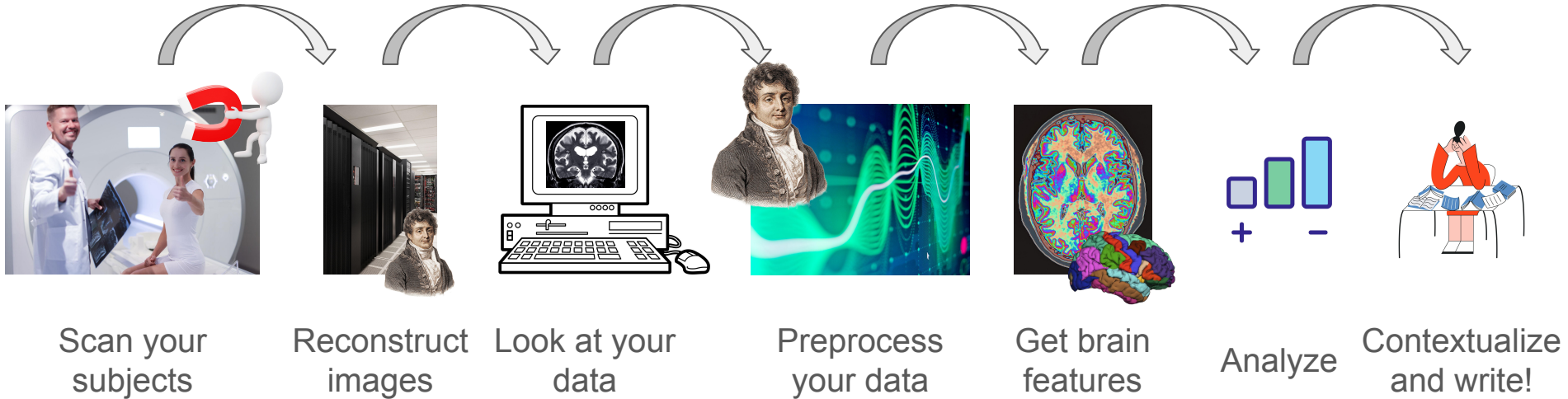
An fMRI project journey



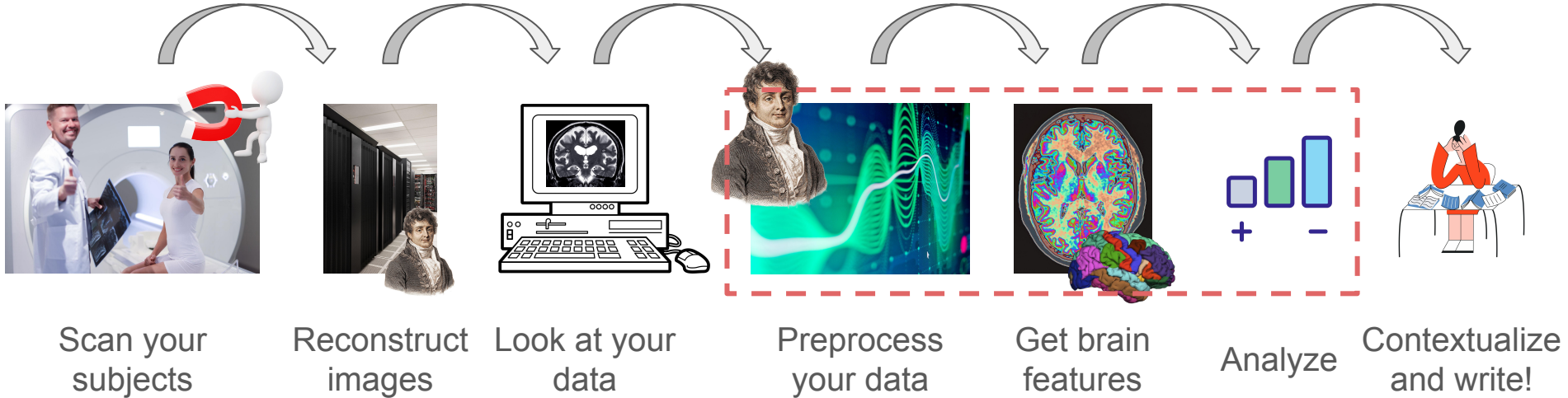
An fMRI project journey



An fMRI project journey



An fMRI project journey



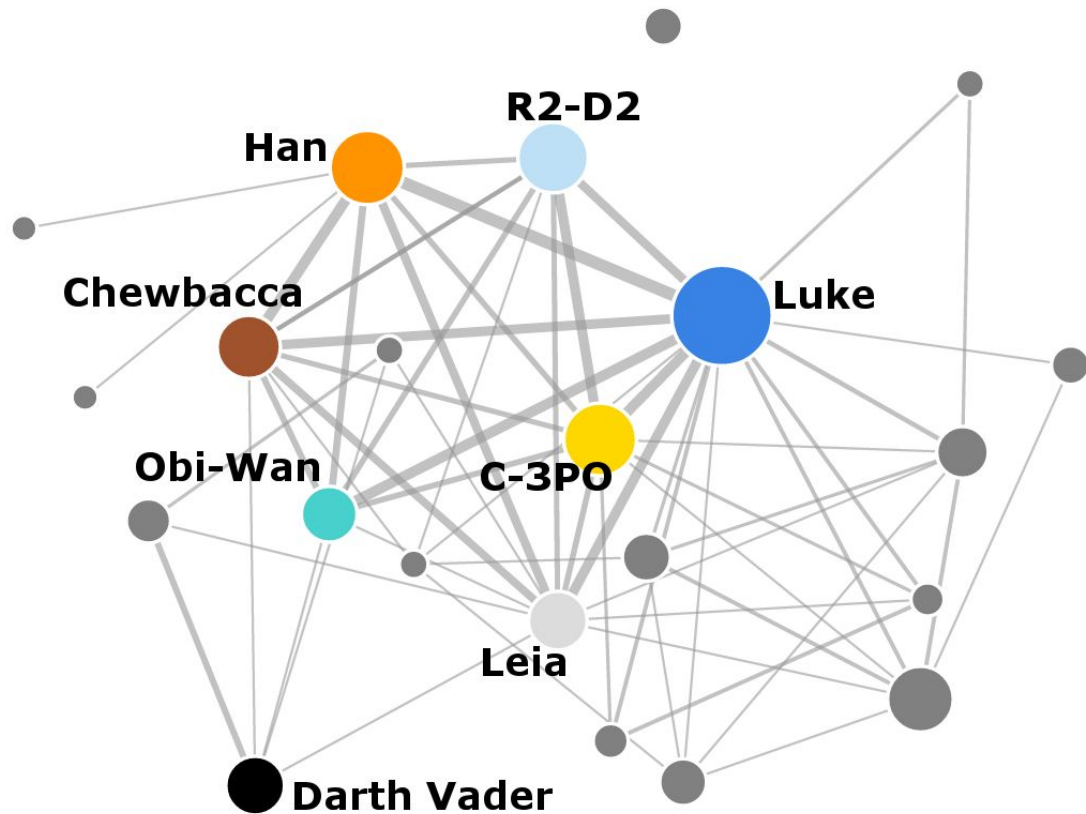
Outline

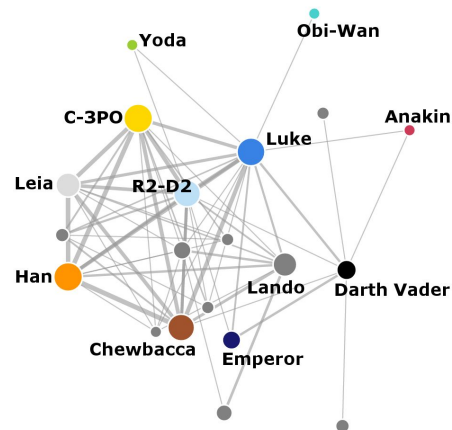
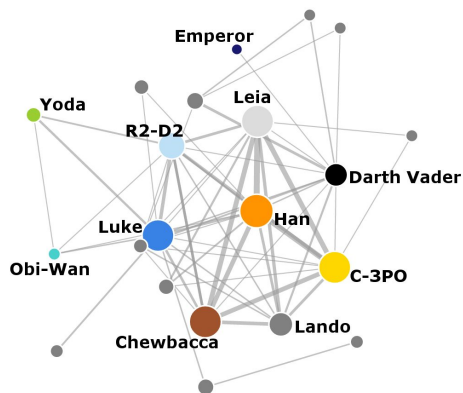
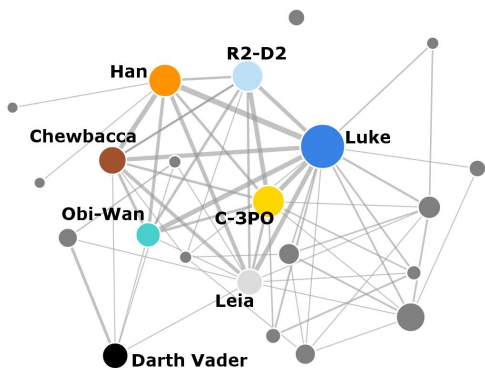
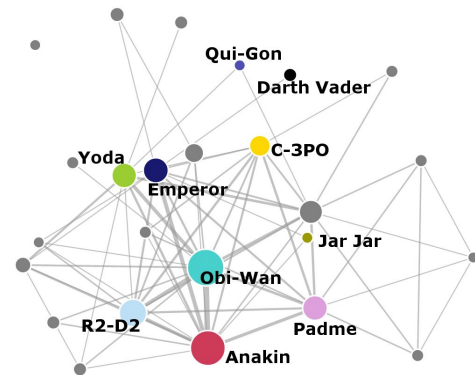
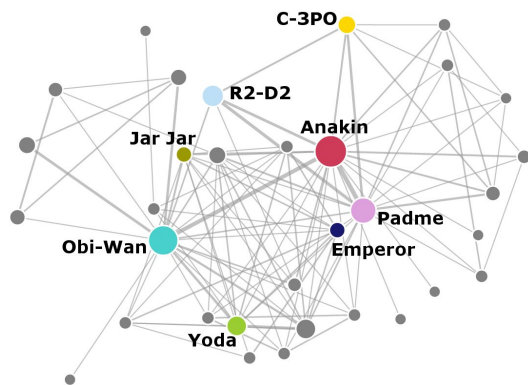
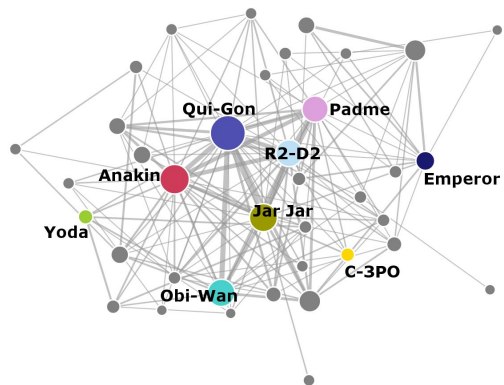
- **Why** study connectivity?
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 - What do we mean by connectivity?
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 - Brain states
 - Dynamic FC
 - Sliding window
 - Edge time series

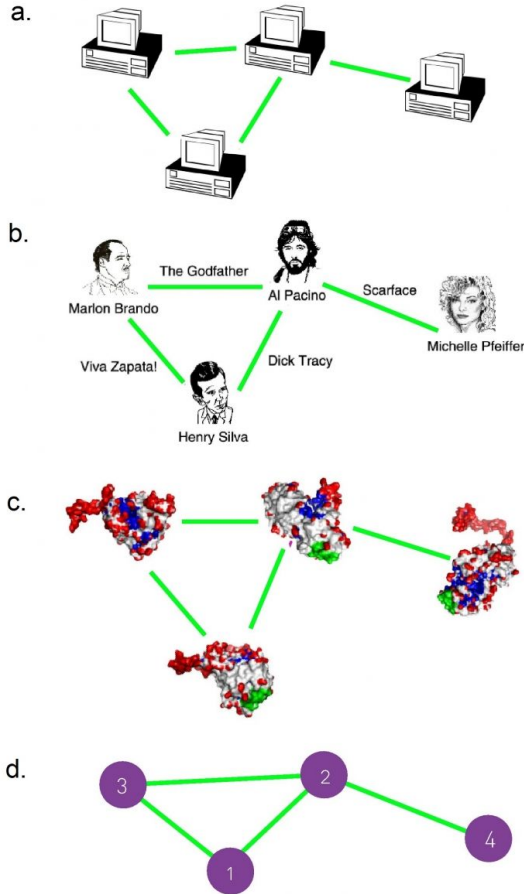
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 - Edge time series

Why study brain connectivity?







Networks describe the interconnected systems we encounter every day.

They provide a **model of these systems** that is suitable for **qualitative and quantitative analysis**.



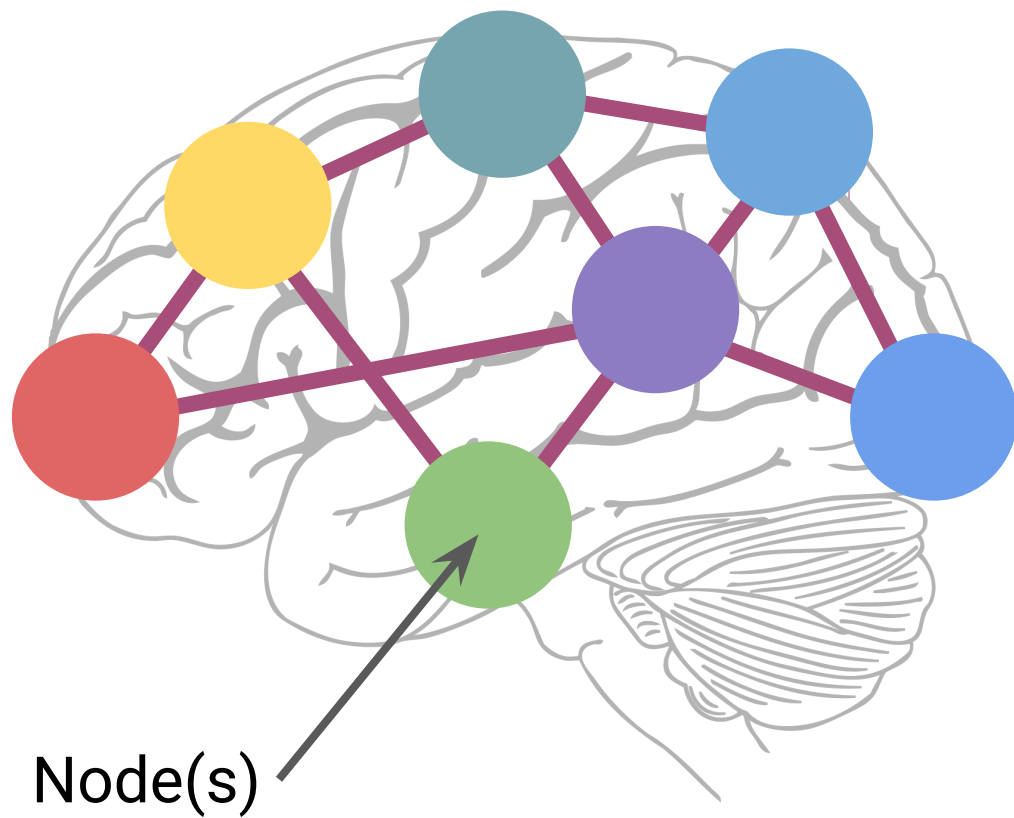
Rush Only Service
Monday-Friday
6:30 AM - 9:00 AM
3:30 PM - 6:00 PM

Network ingredients

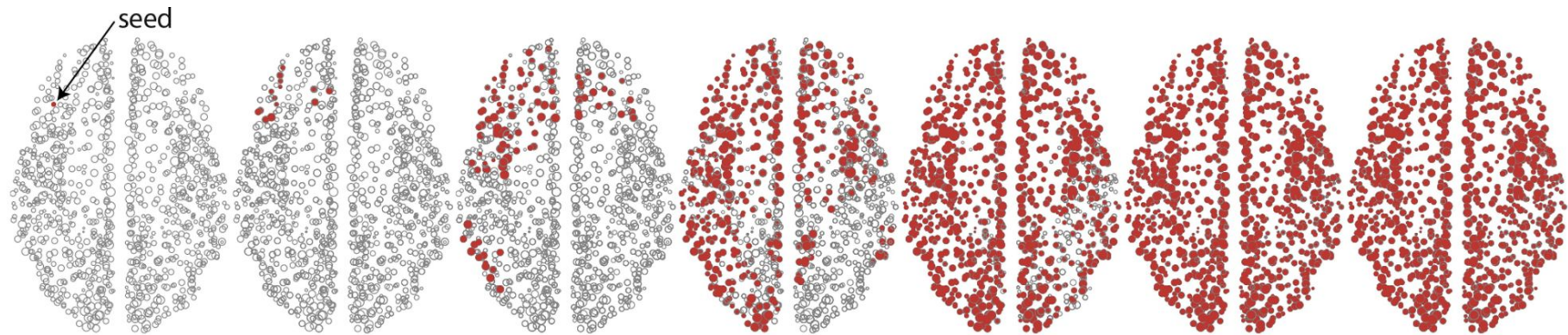
- Node
- Edges

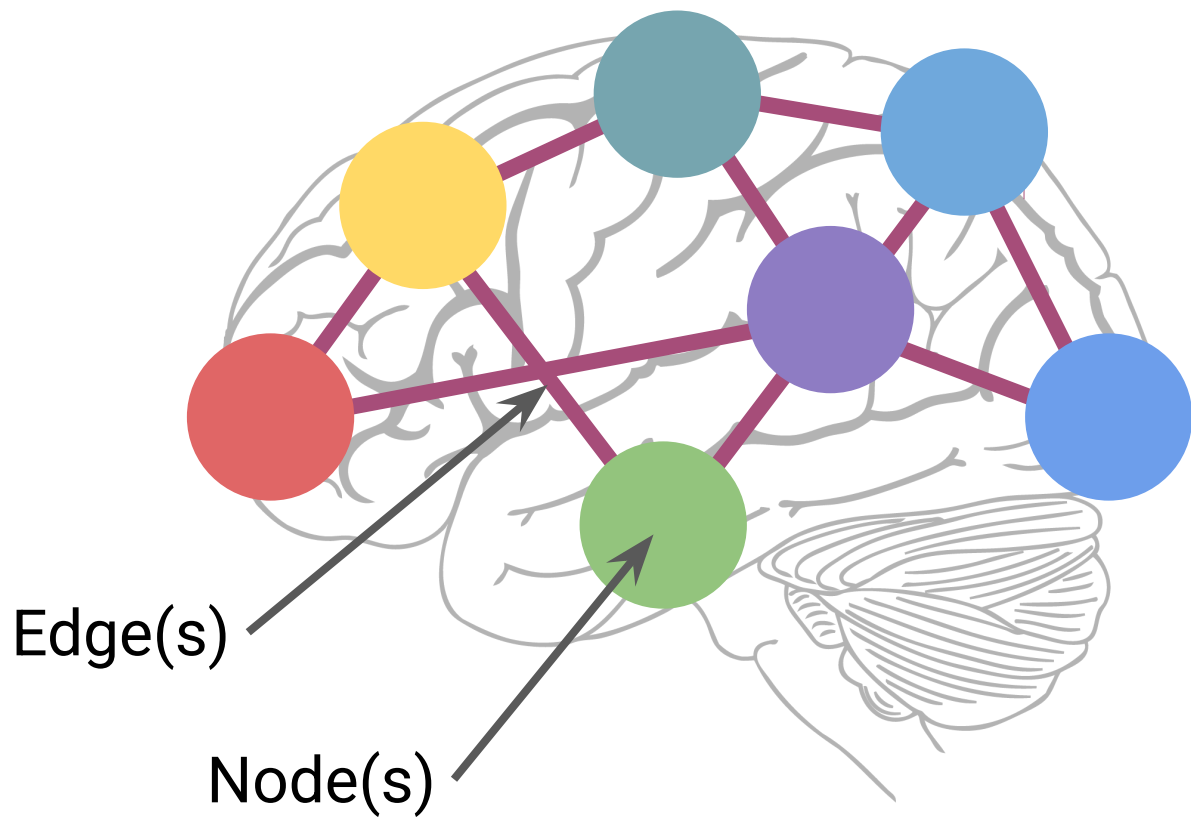
Network ingredients

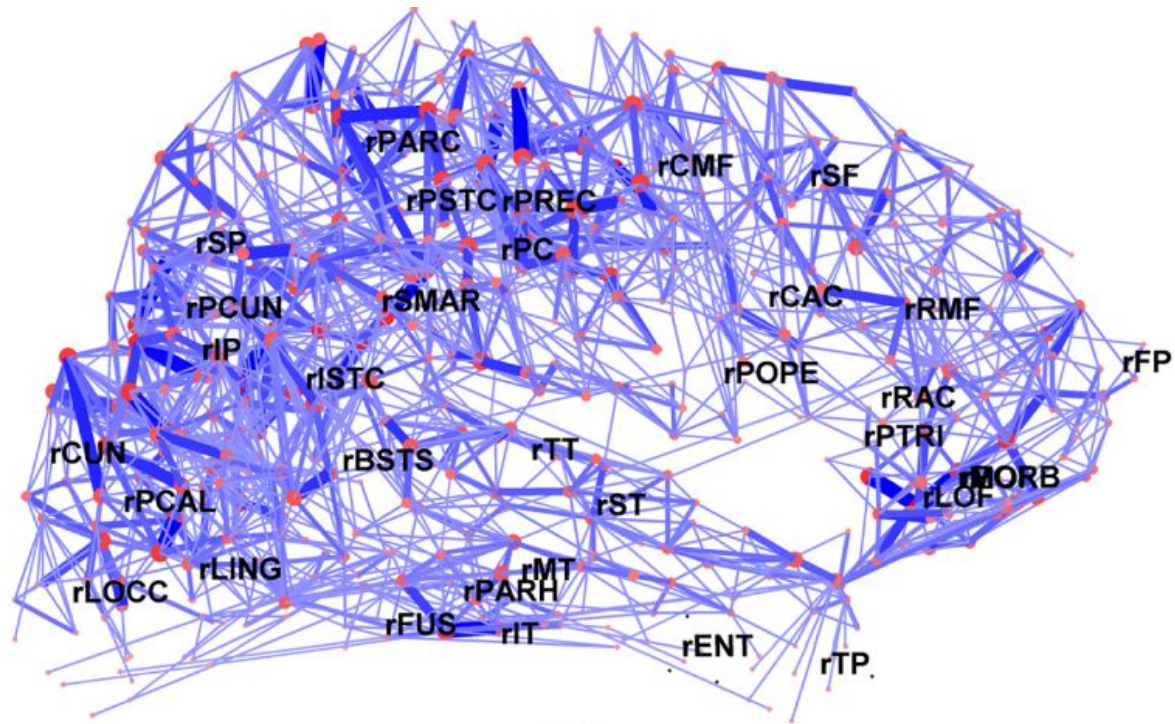
- Node
 - Fundamental elements of your system of interest
- Edges
 - Presence (or quantification) of relationship between pairs of nodes

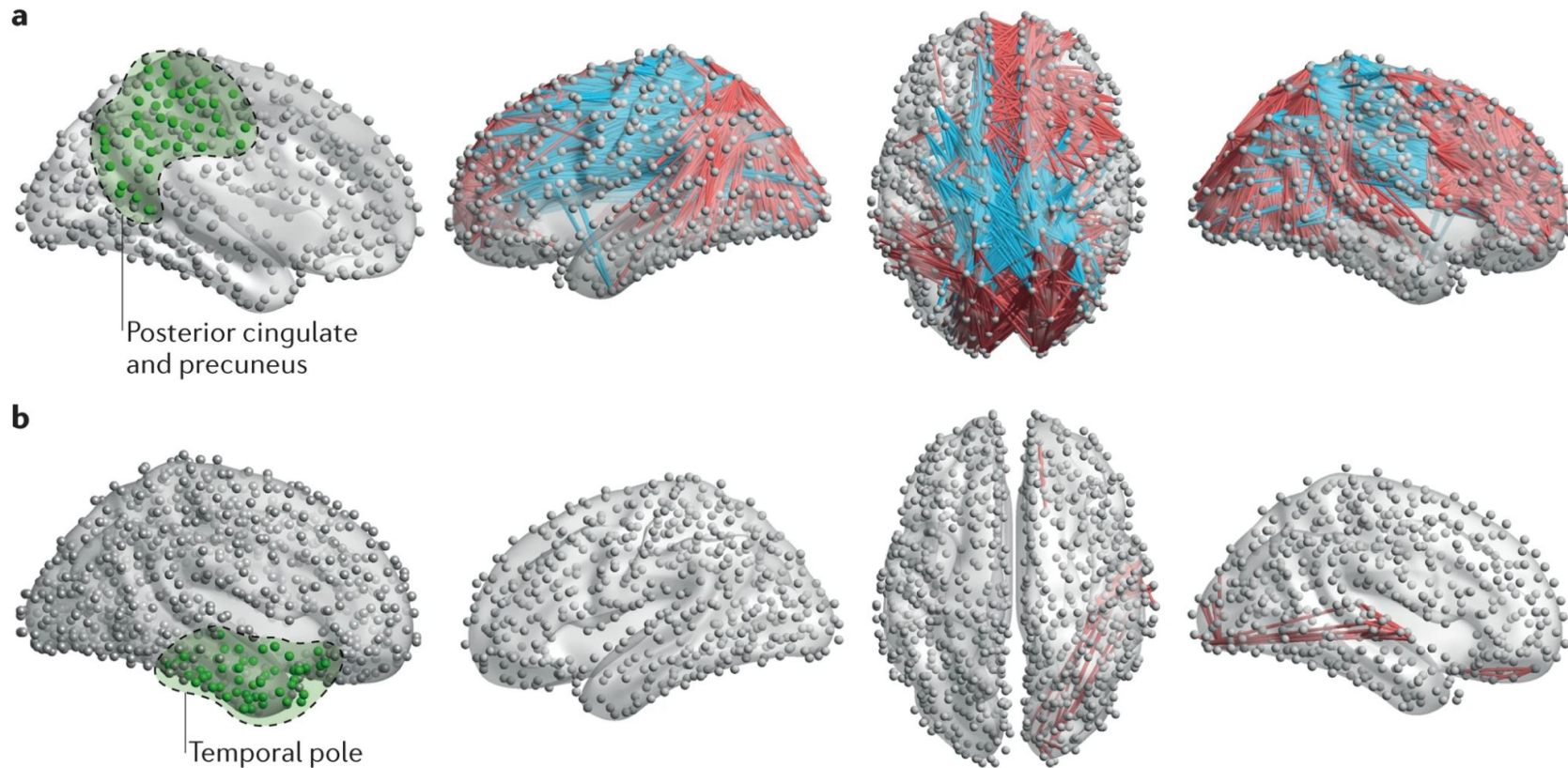


A

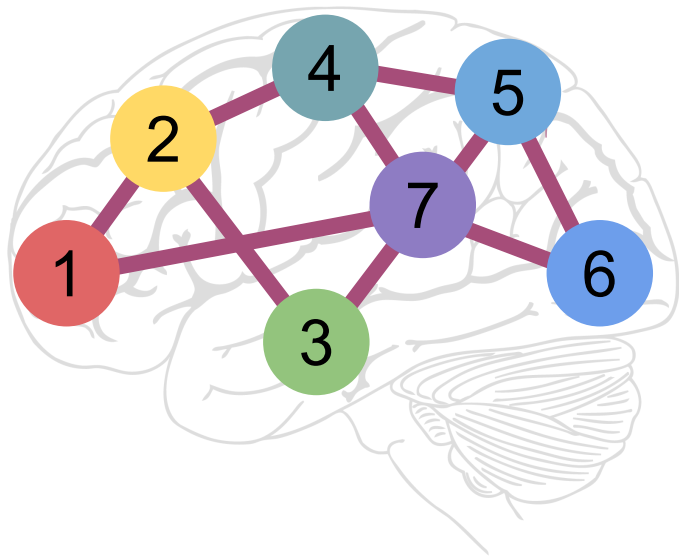
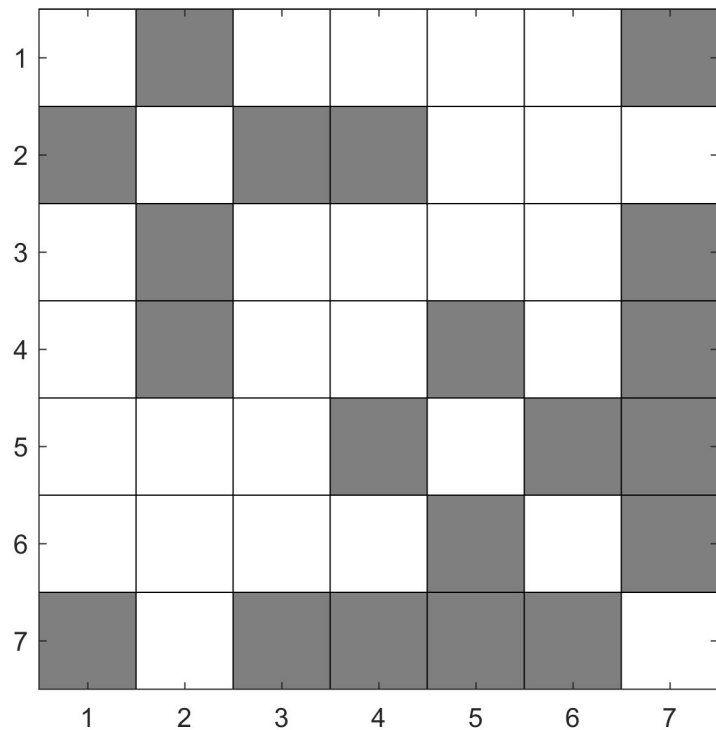




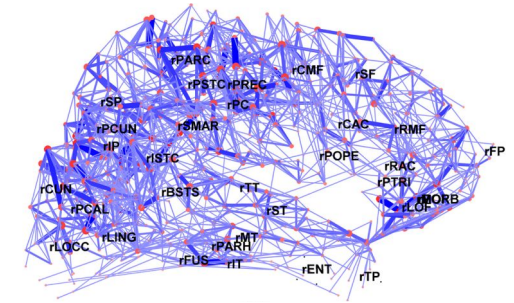
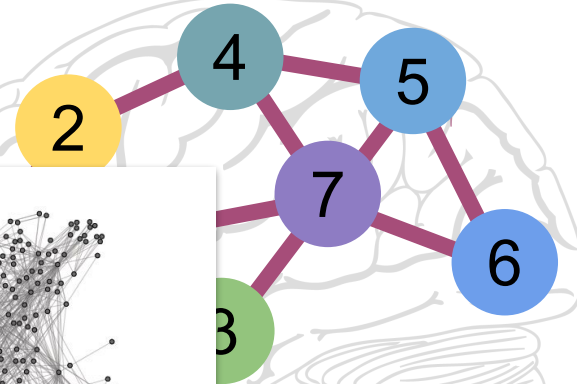
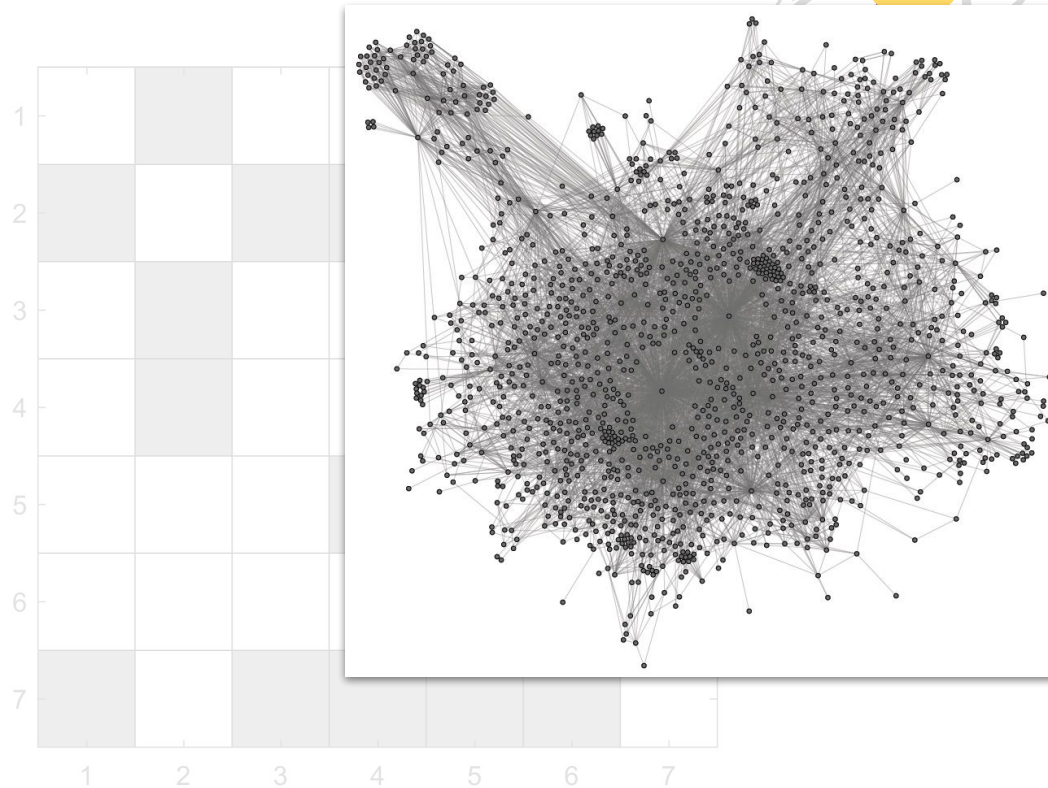




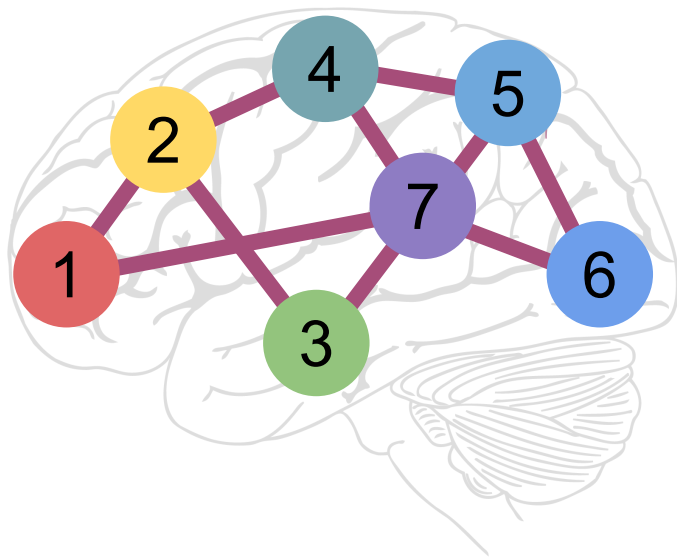
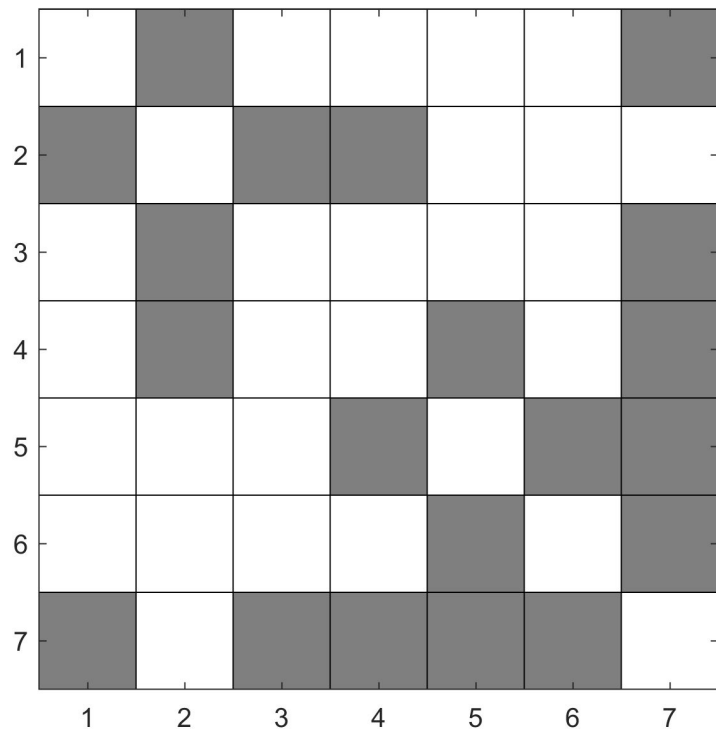
Adjacency matrix



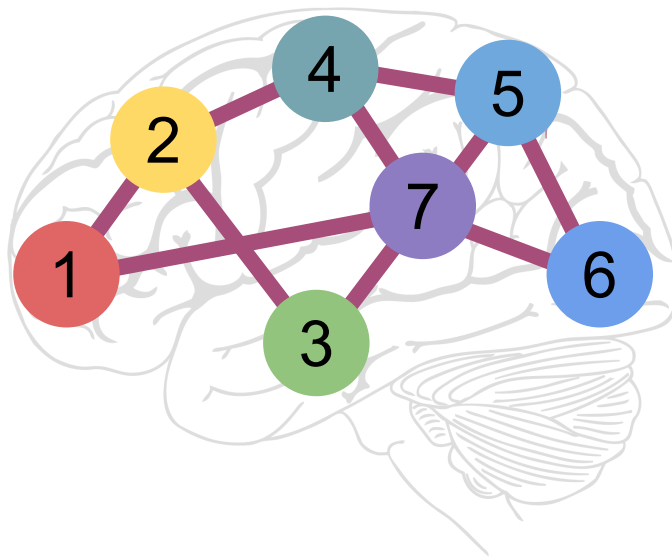
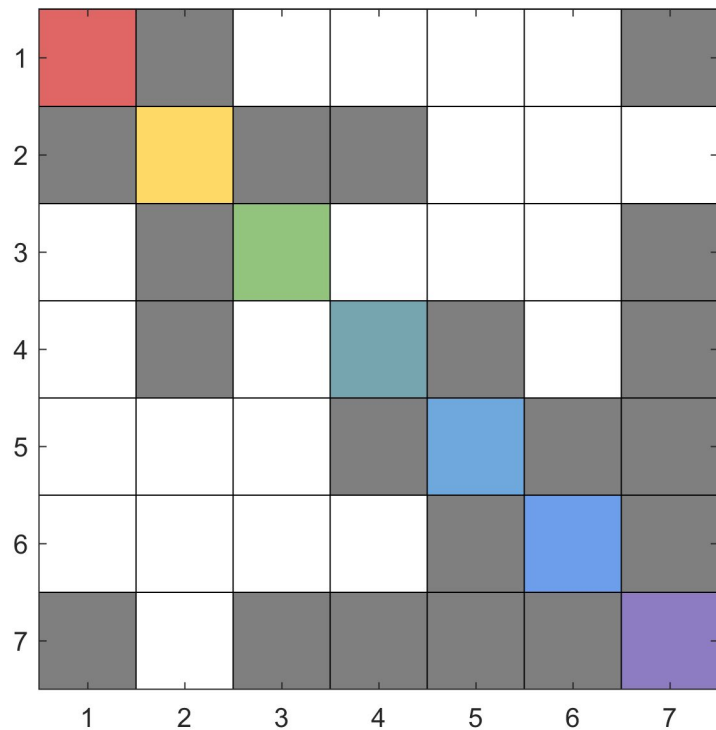
Adjacency matrix



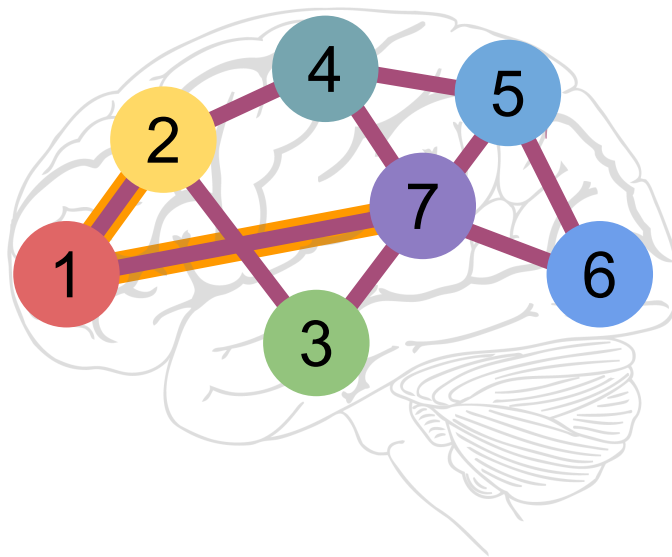
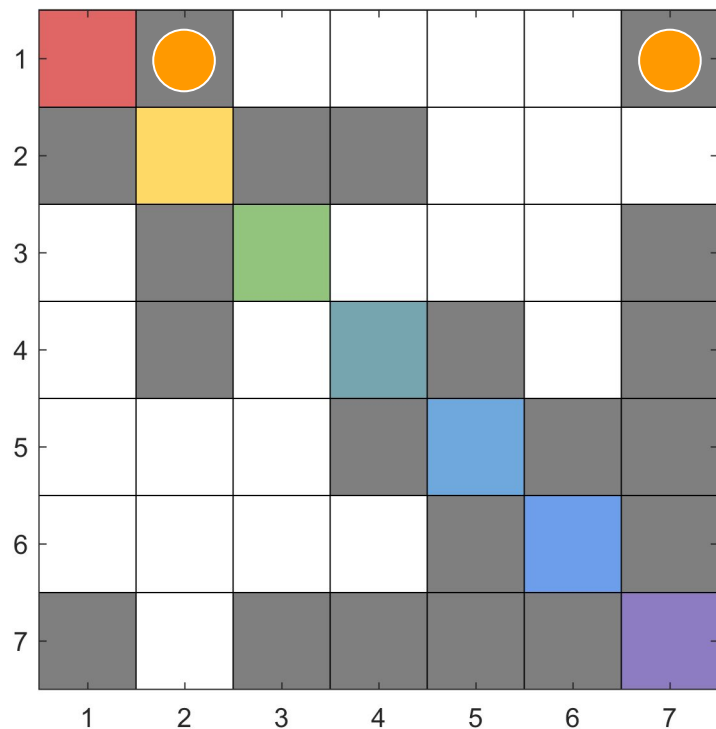
Adjacency matrix



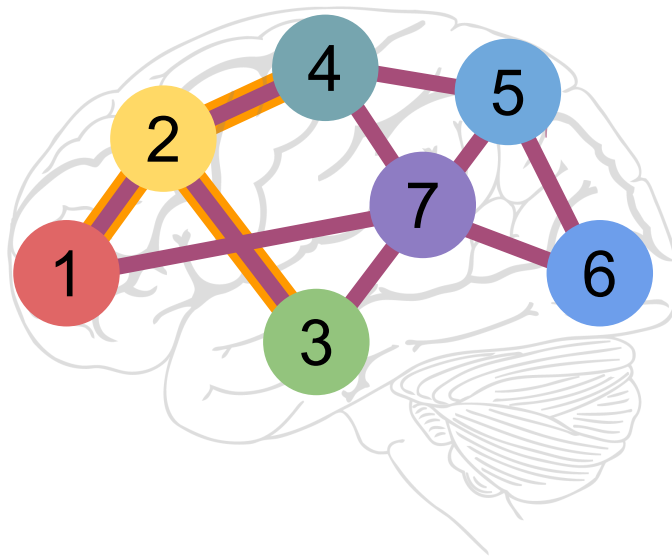
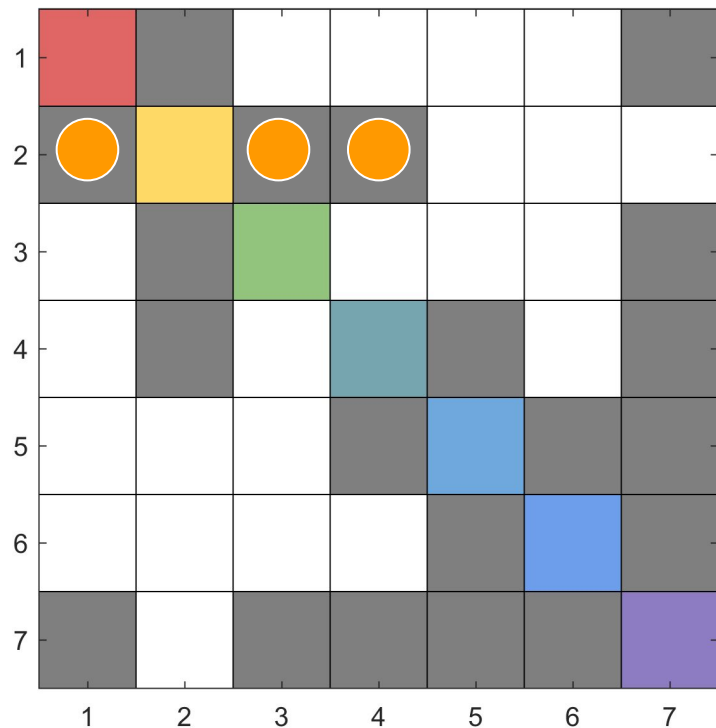
Adjacency matrix



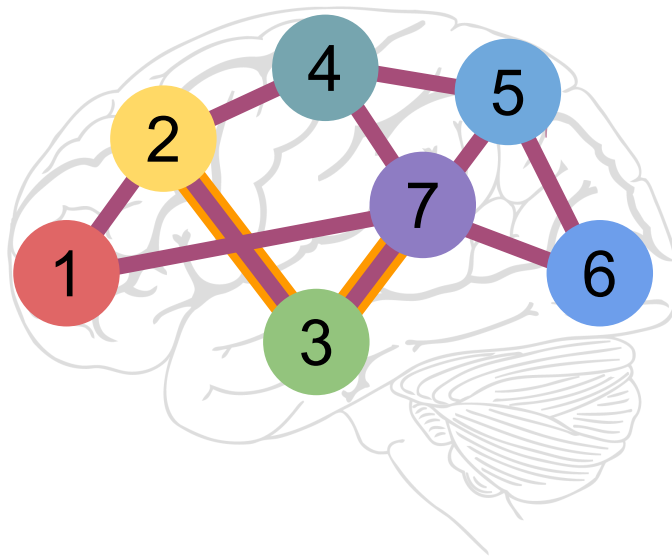
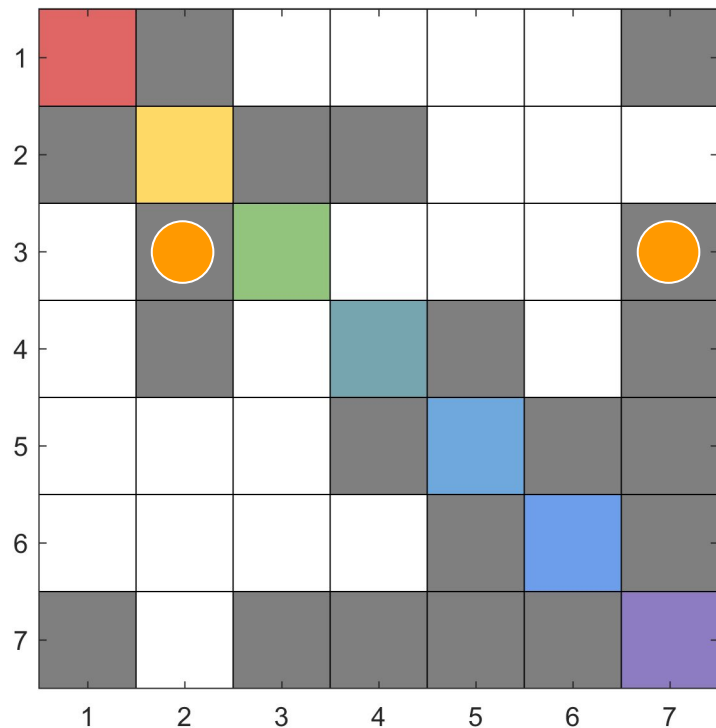
Adjacency matrix



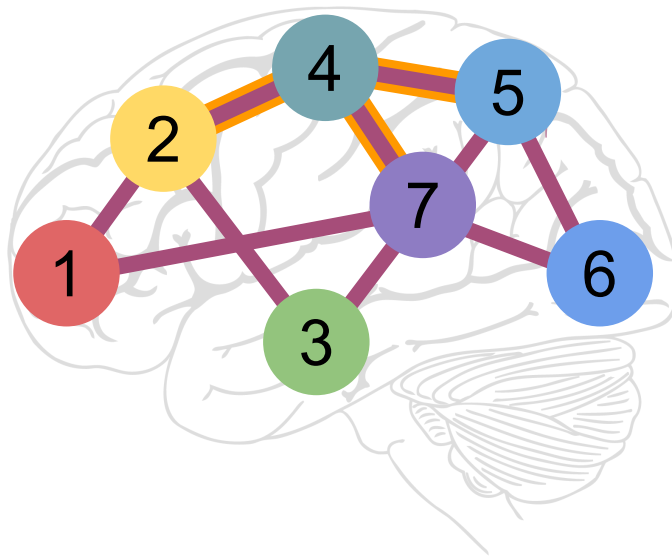
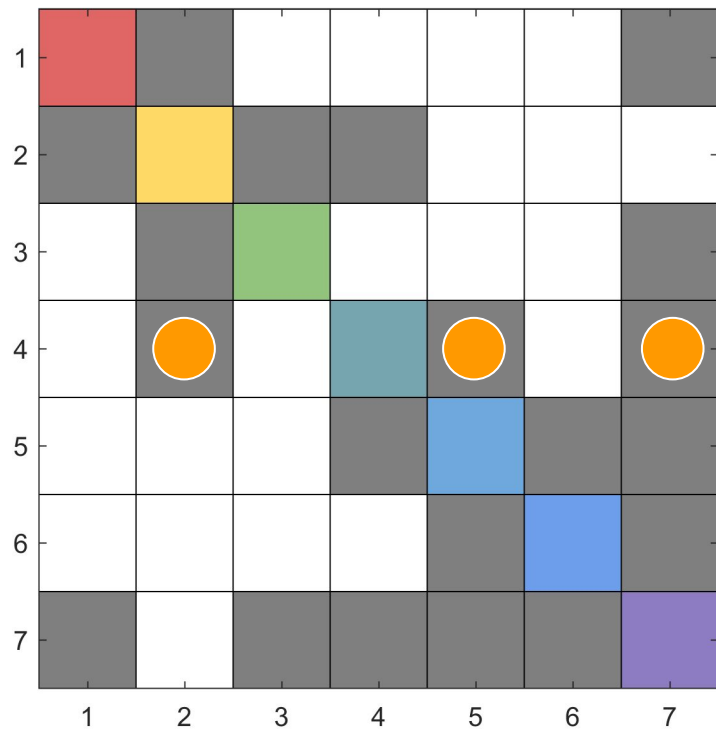
Adjacency matrix



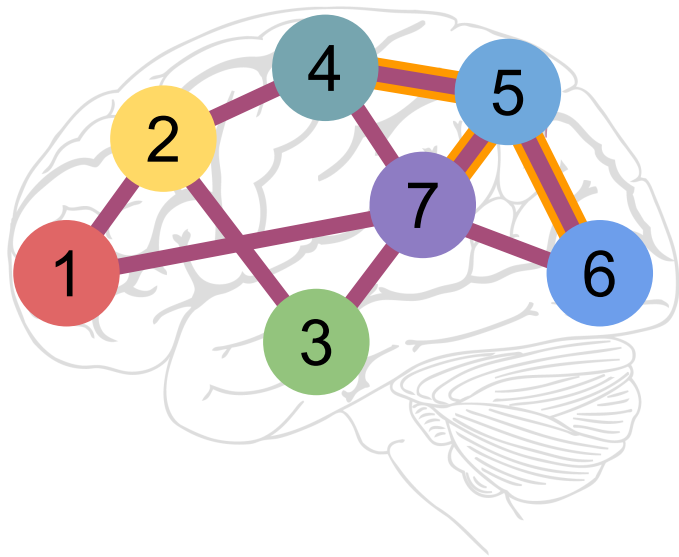
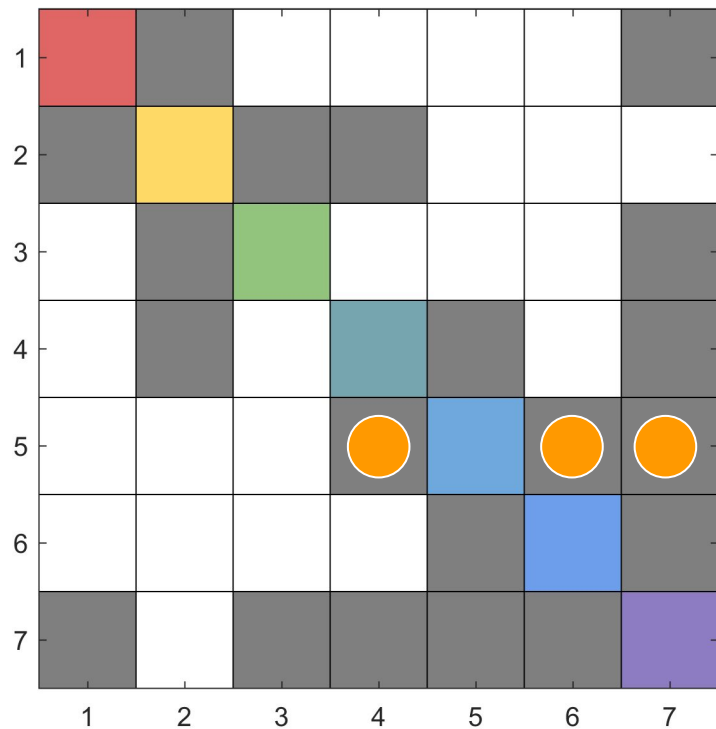
Adjacency matrix



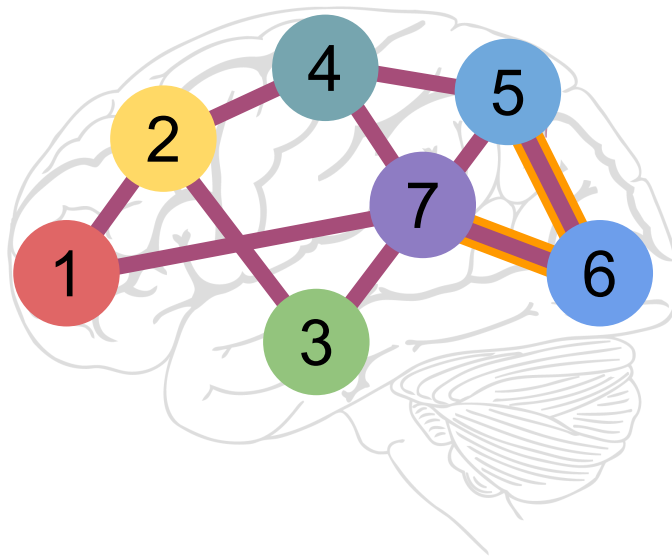
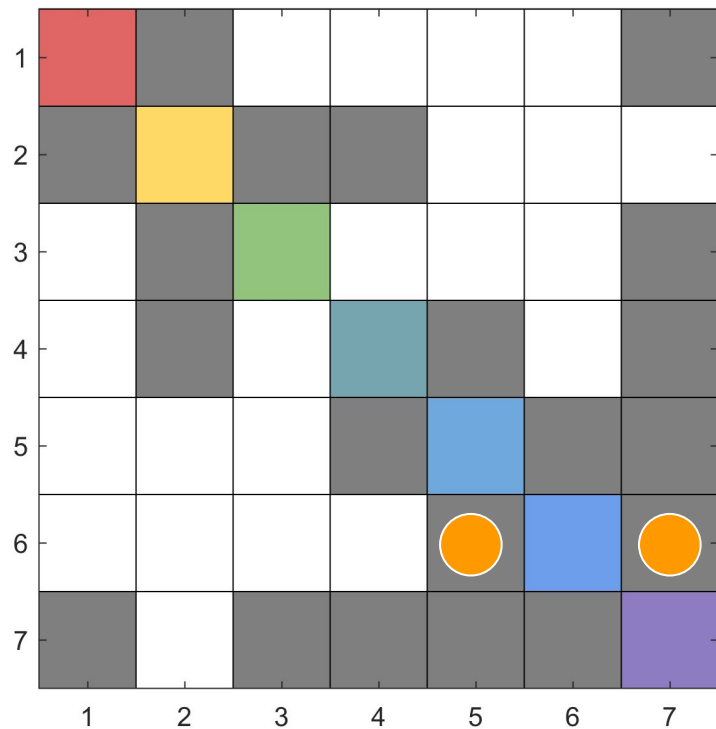
Adjacency matrix



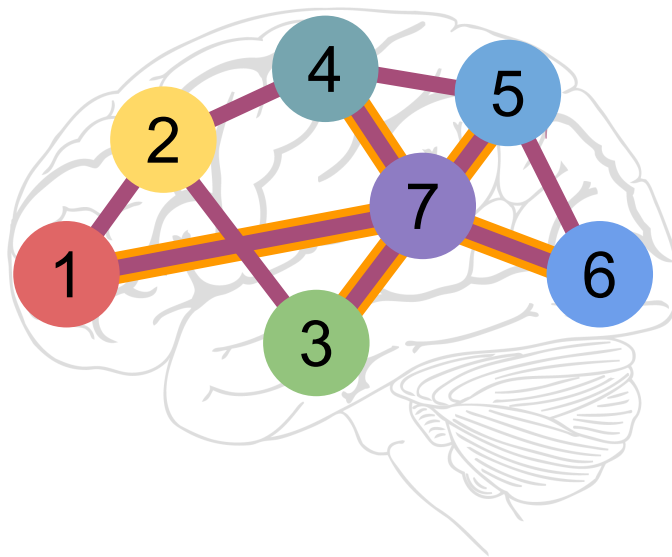
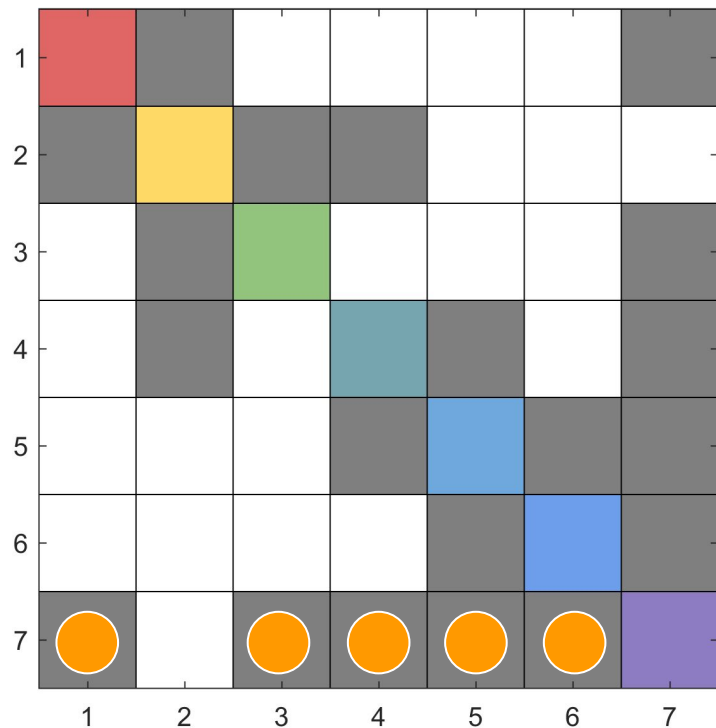
Adjacency matrix



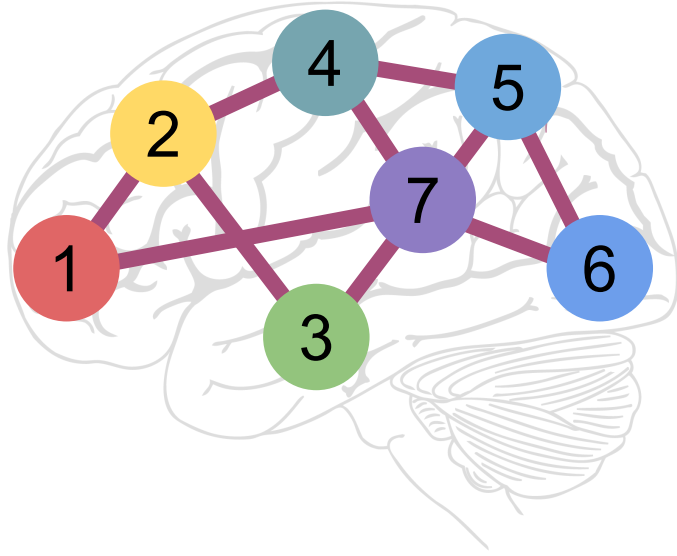
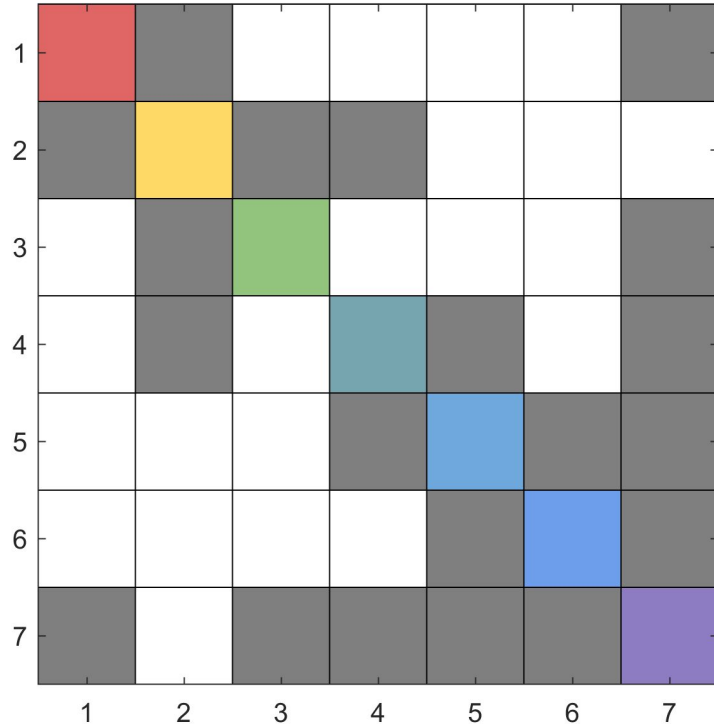
Adjacency matrix



Adjacency matrix

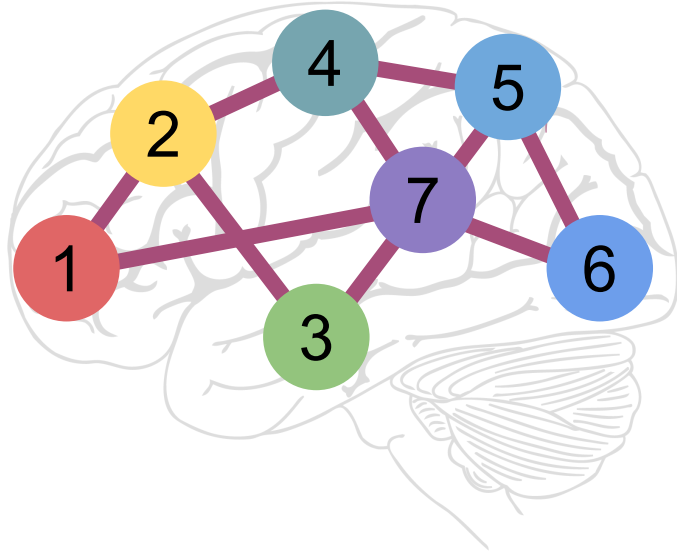
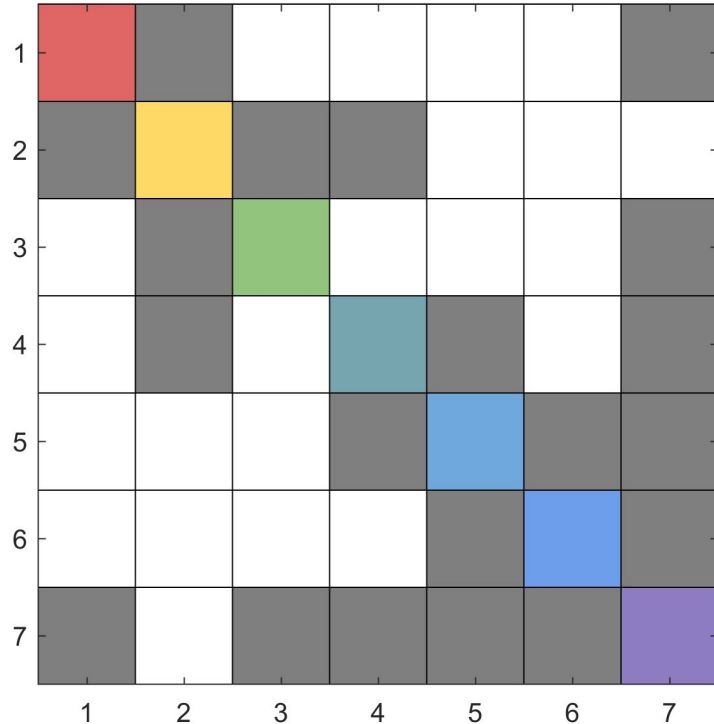


Adjacency matrix



- The adjacency matrix suitable to analyze using computers/code
 - easy to run algorithms on
 - look at the patterns formed by the connections

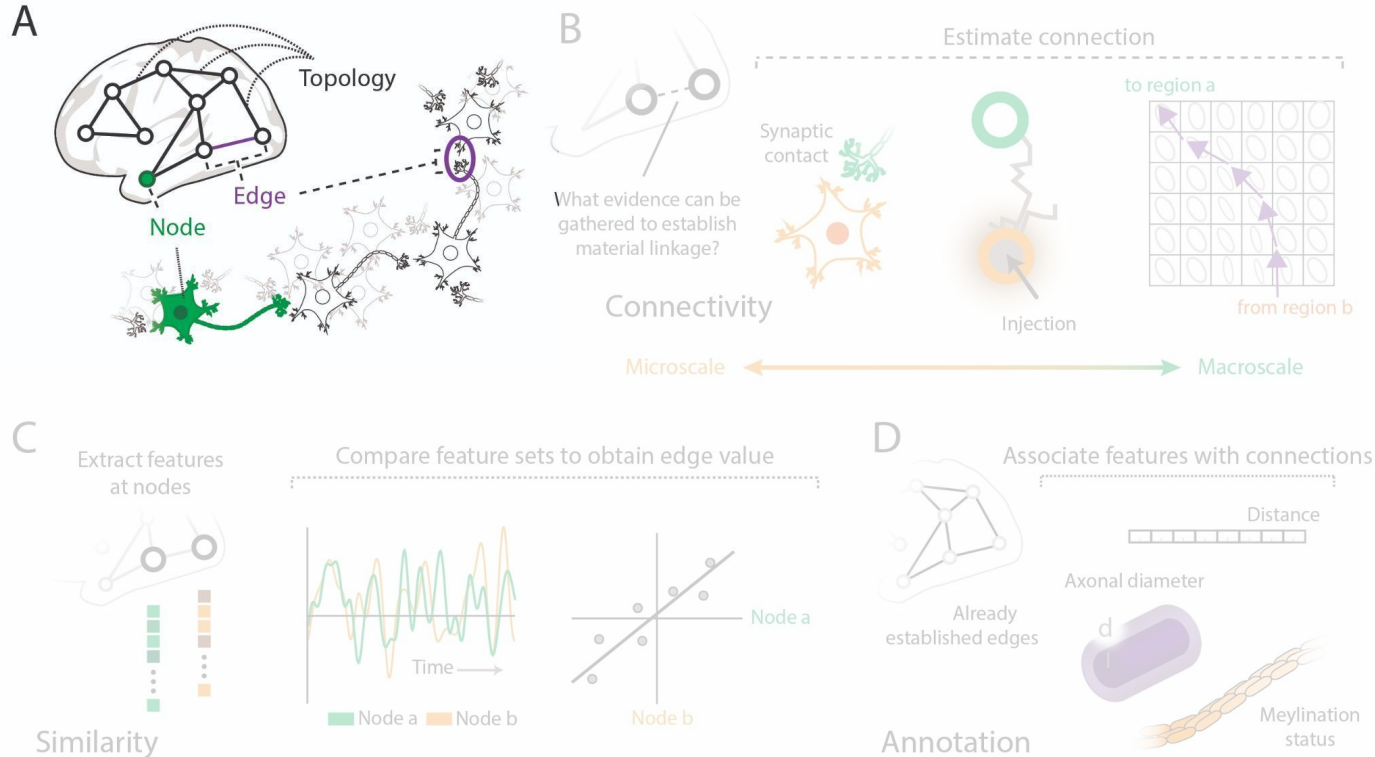
Adjacency matrix



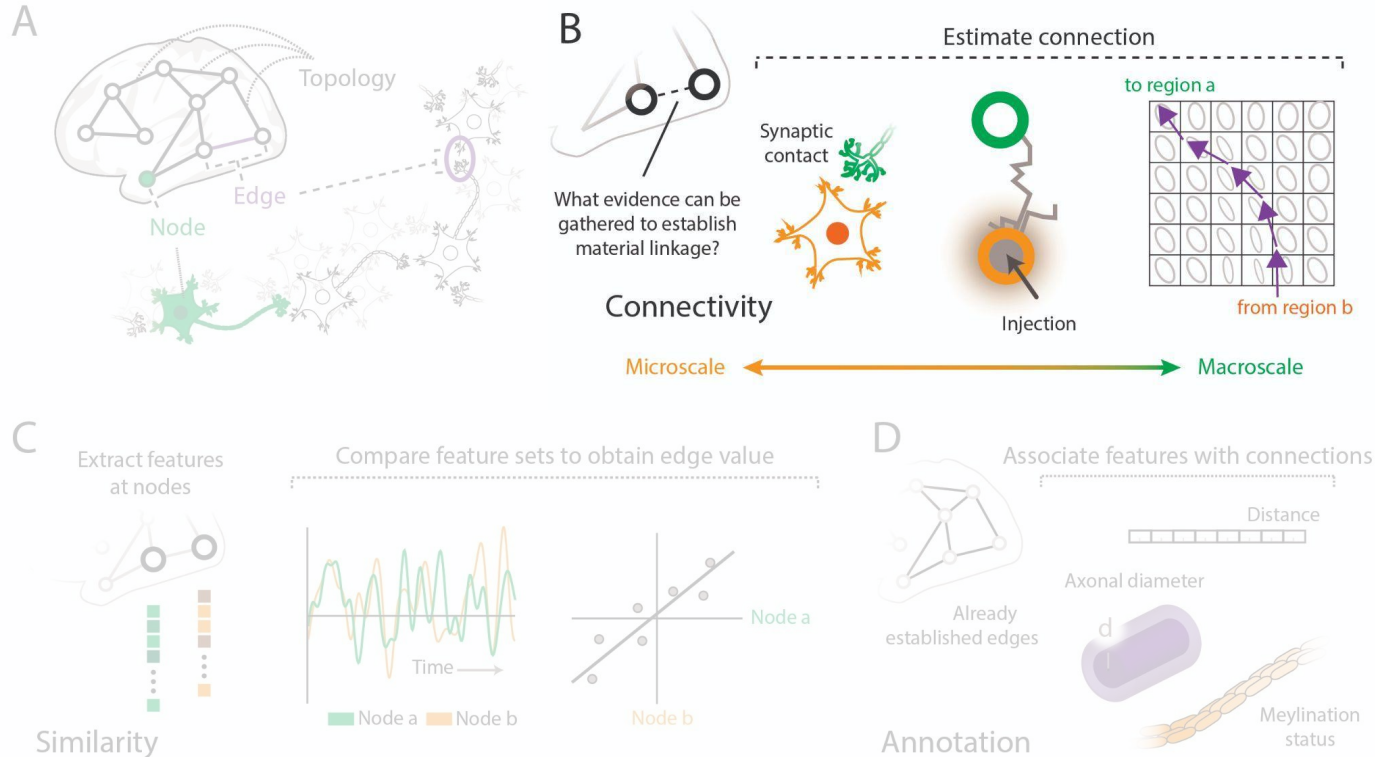
- A model of how system elements connect, in a tidy data structure
- *Lots* of quantitative descriptors developed by the fields of network science and graph theory

What is “connectivity”

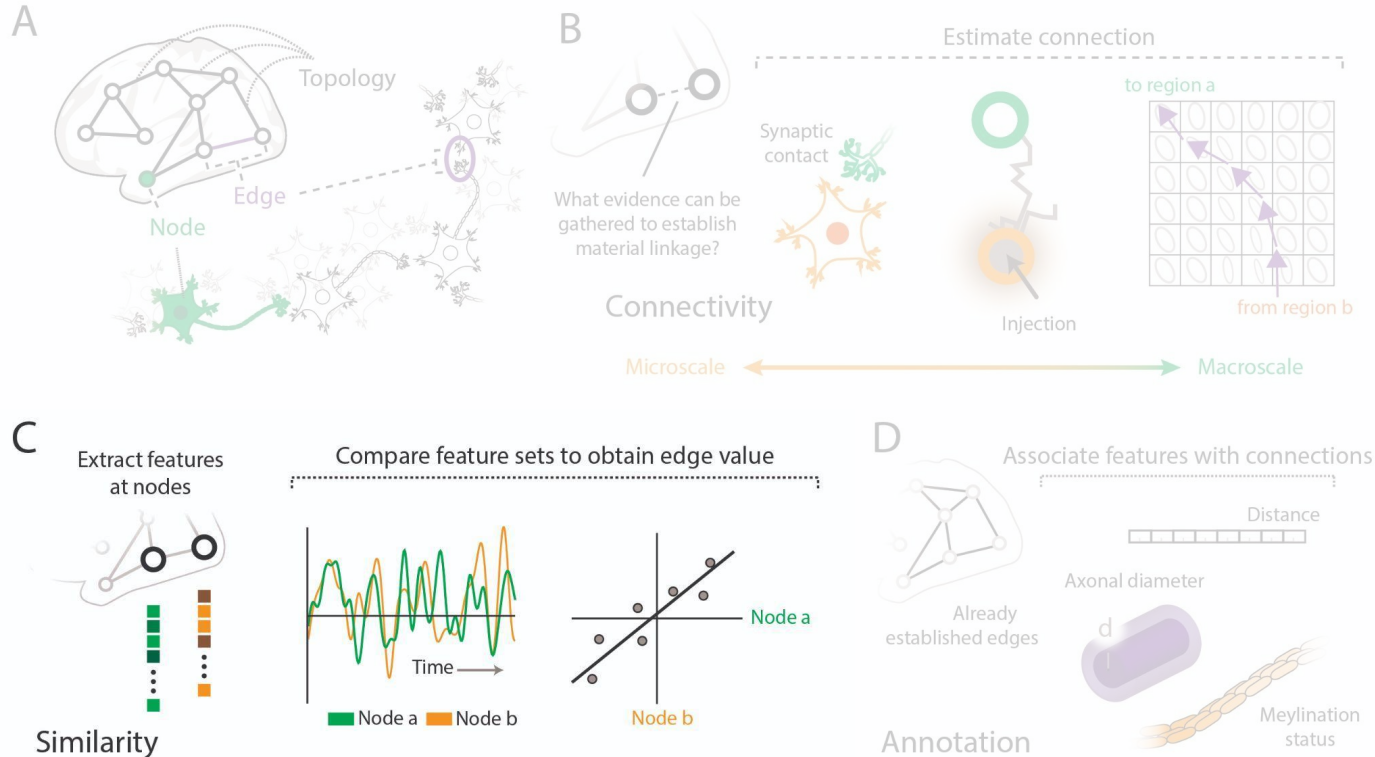
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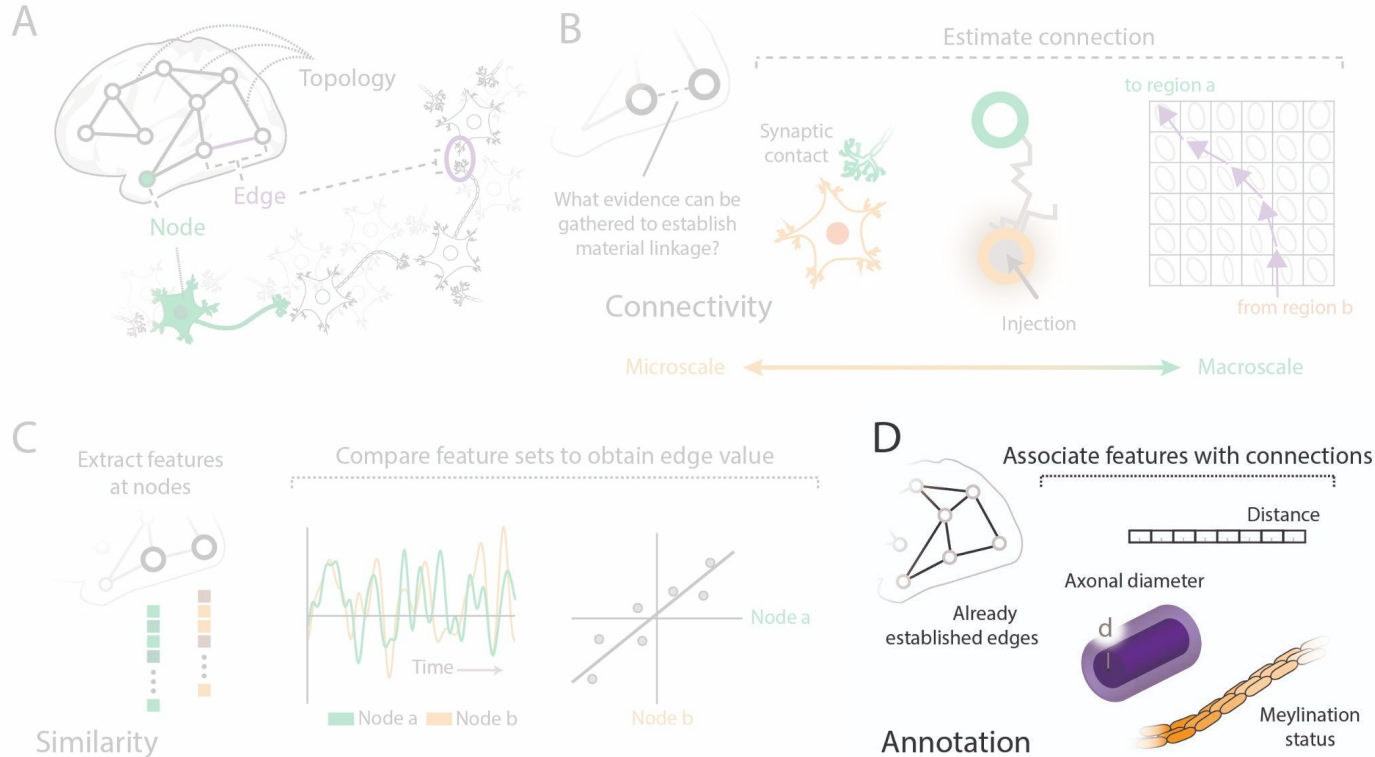
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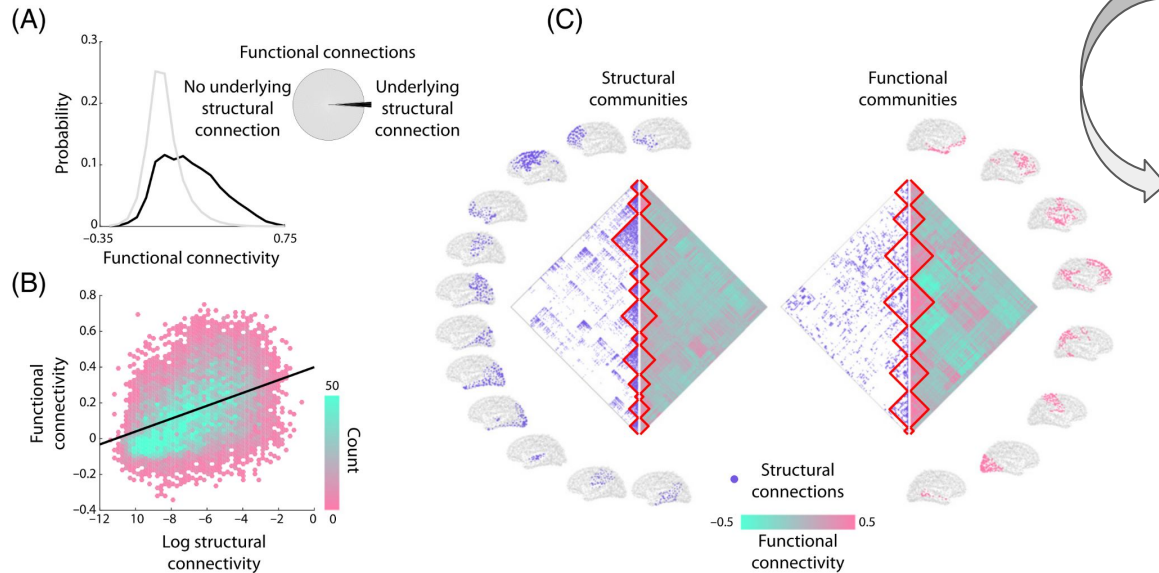
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What is “connectivity”

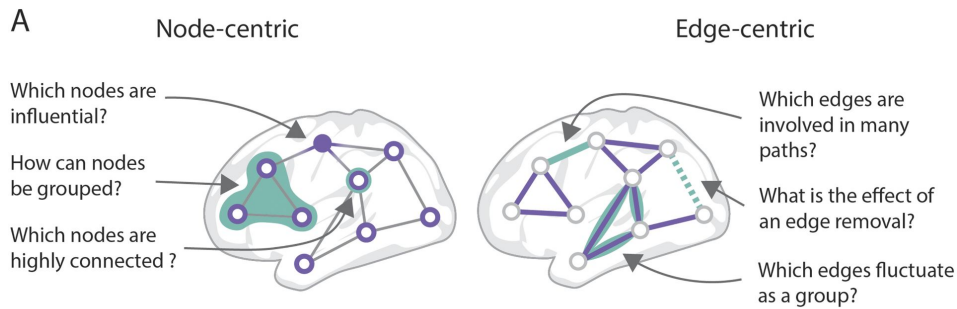


Structural

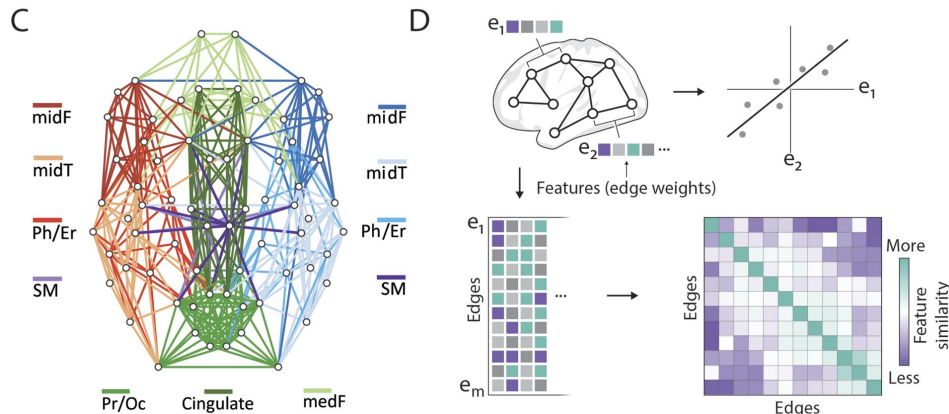
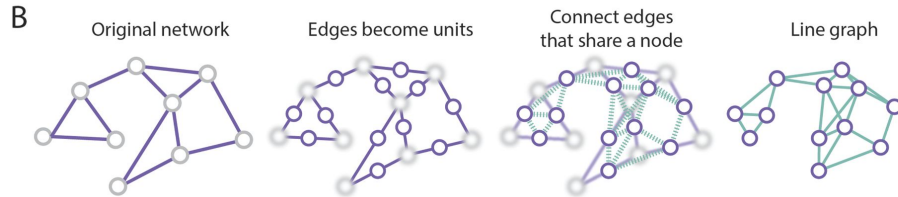
The brain is fundamentally a network at the level of neurons

Functional

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



Edge-edge representations



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}

¹Program in Neuroscience, Indiana University, Bloomington, IN, USA

²Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA

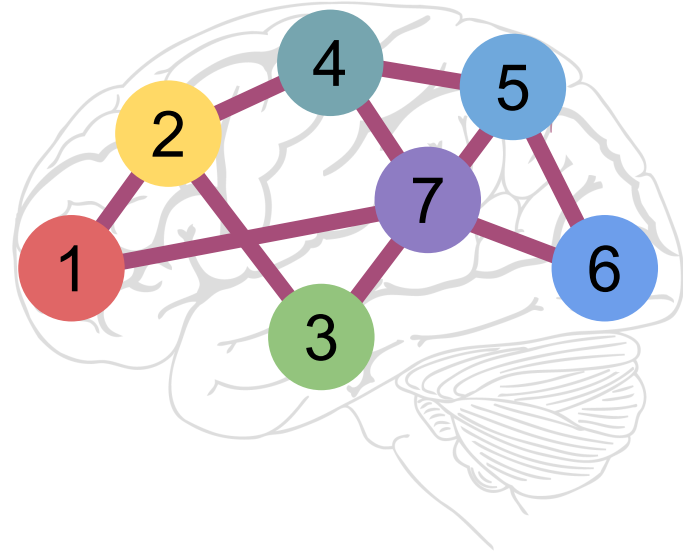
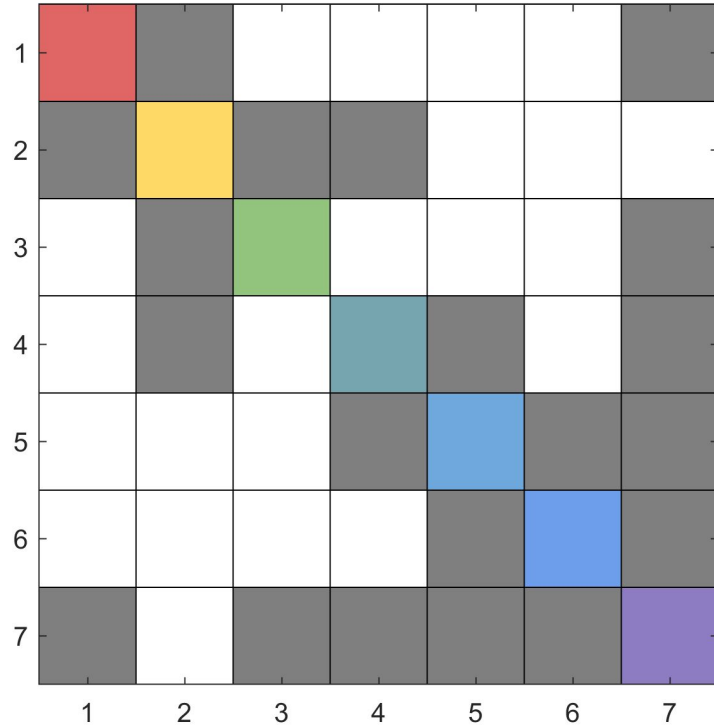
³Indiana University Network Science Institute, Indiana University, Bloomington, IN, USA

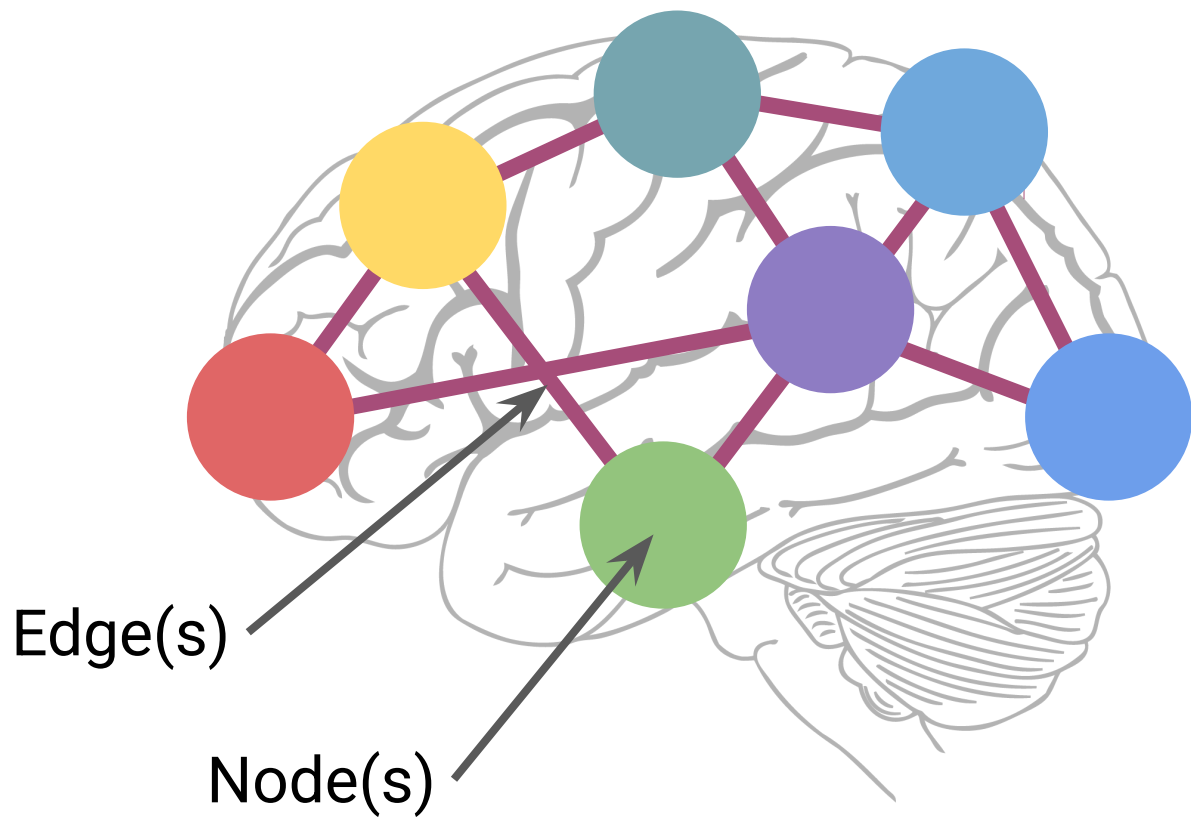
⁴Cognitive Science Program, Indiana University, Bloomington, IN, USA

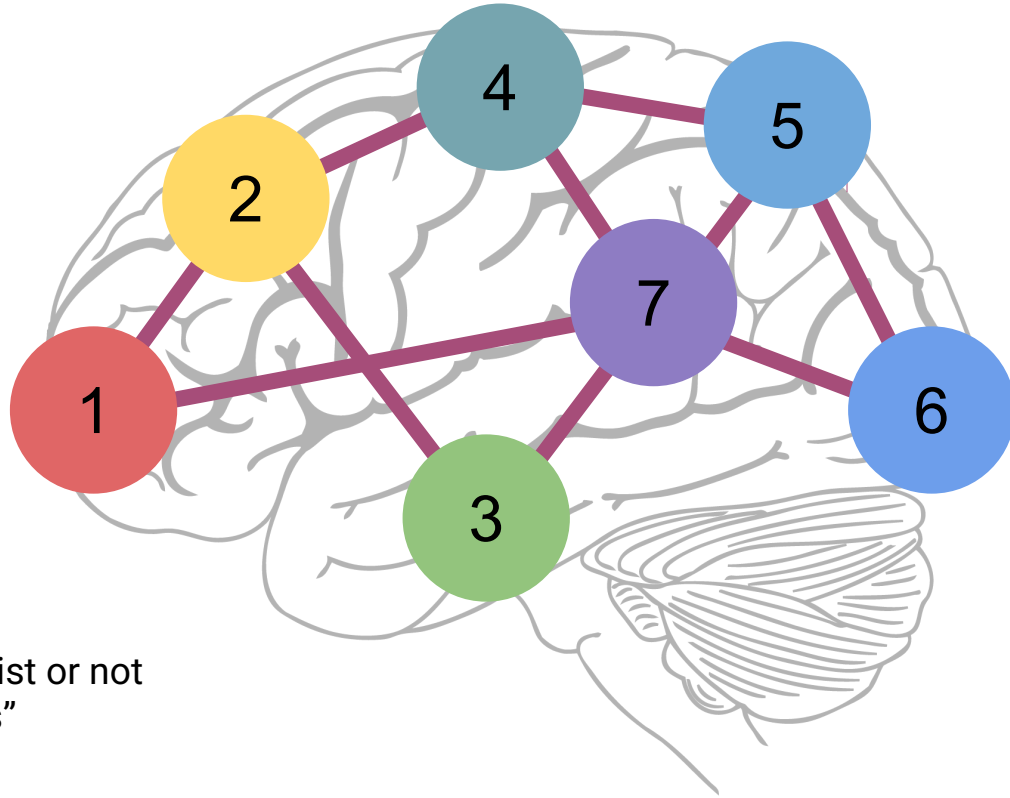
Keywords: Connectome, Network, Edge, Structure function relationship, Connectivity, Network construction, Network communication

Network Neuroscience

Different sorts of brain networks

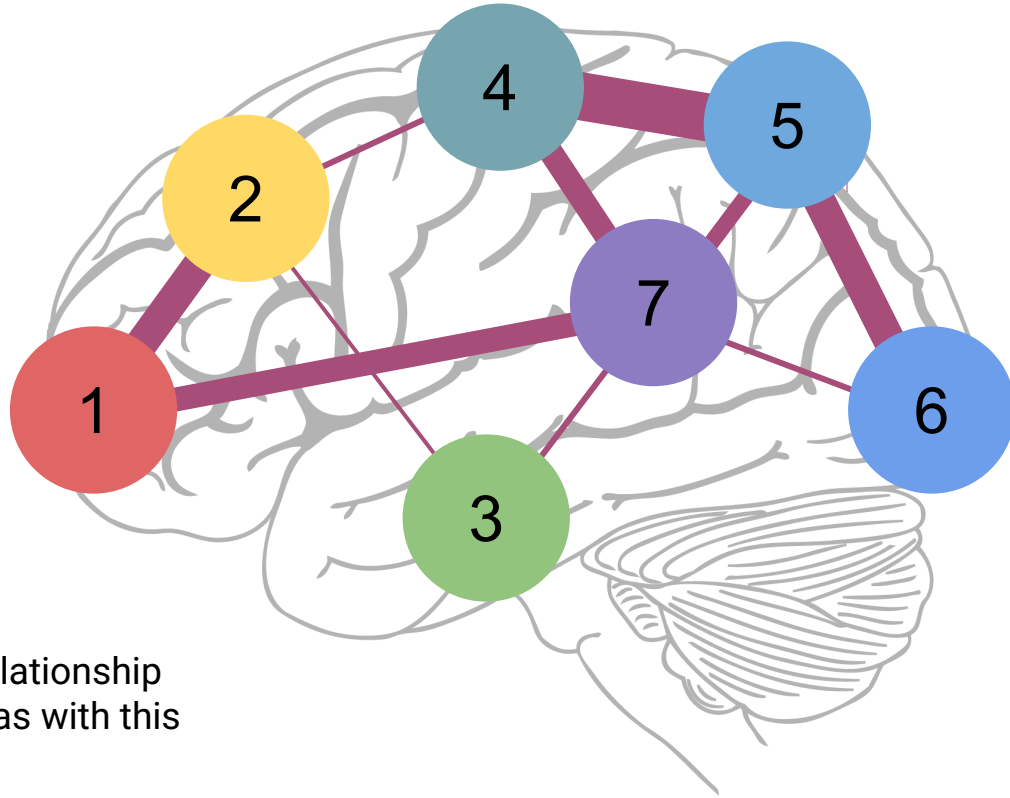






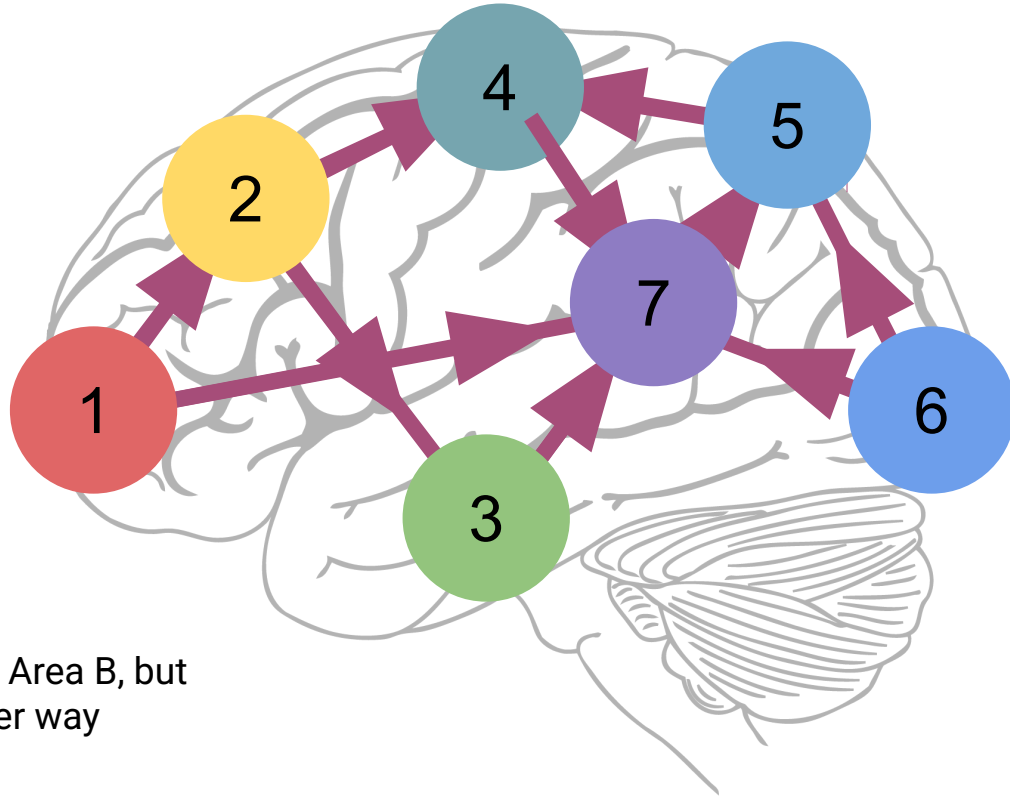
Unweighted

“Does a relationship exist or not
between these two areas”



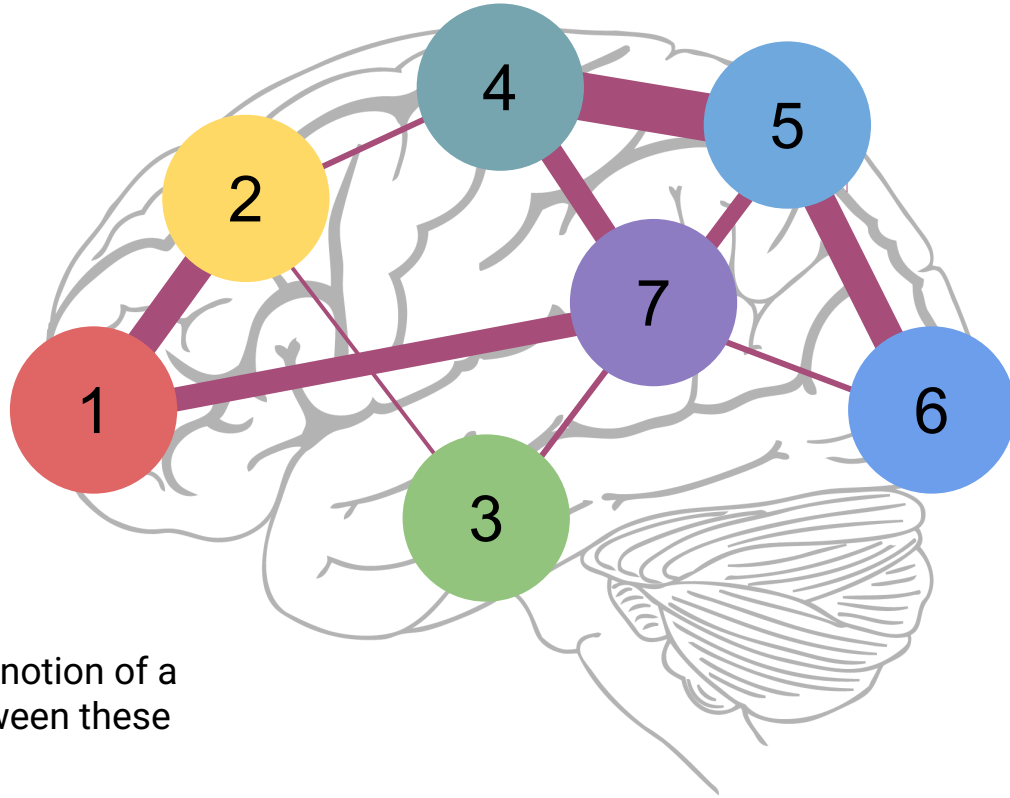
Weighted

“We can quantify the relationship between these two areas with this number”



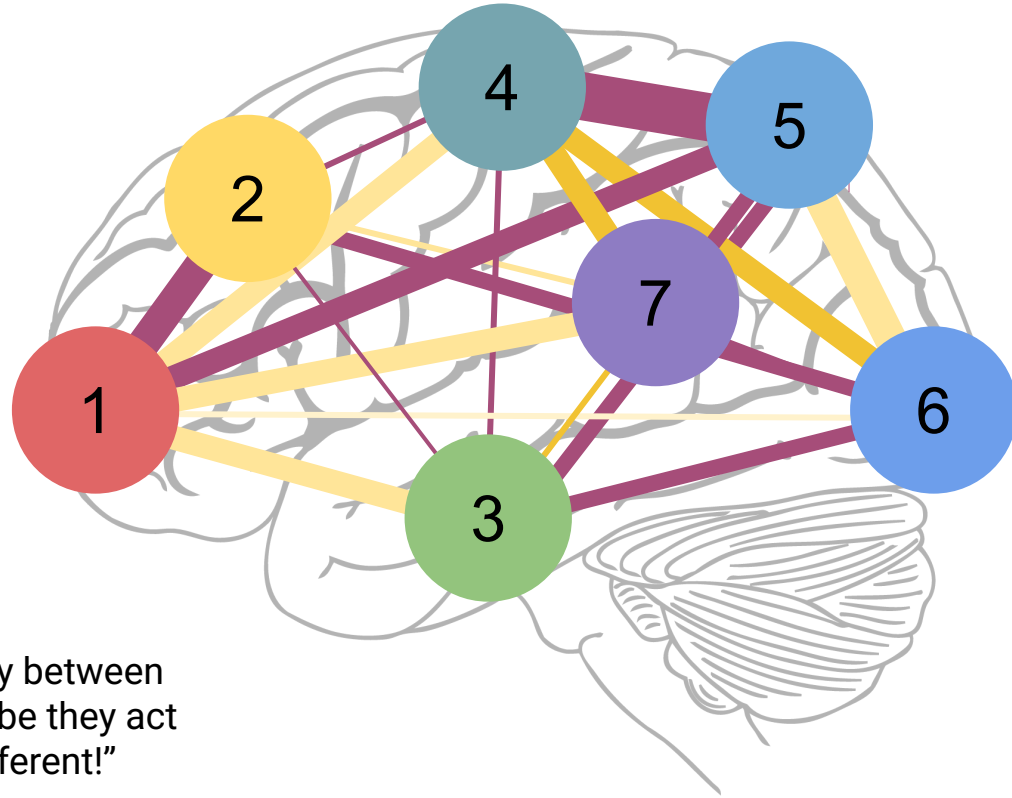
Directed

“Area A sends signal to Area B, but not necessarily the other way around”



Structural

“I am measuring some notion of a physical substrate between these areas”



Functional

“I evaluate the similarity between these two areas – maybe they act the same, or maybe different!”

Why study brain connectivity?

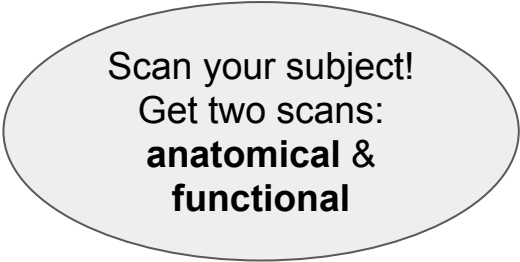
- Networks seem like a nice **intuitive construct**
- The brain is **fundamentally a network** at the neuronal, i.e., microscopic, level
 - But networks are **ALSO** well suited to describe the brain at macro- or mesoscopic level
 - Many ways in which a network model can describe data (e.g. edge patterns, weights); can capture many flavors of brain data
- Lots of angles for analysis (we will get to that 😊)

Outline

- **Why study connectivity?**
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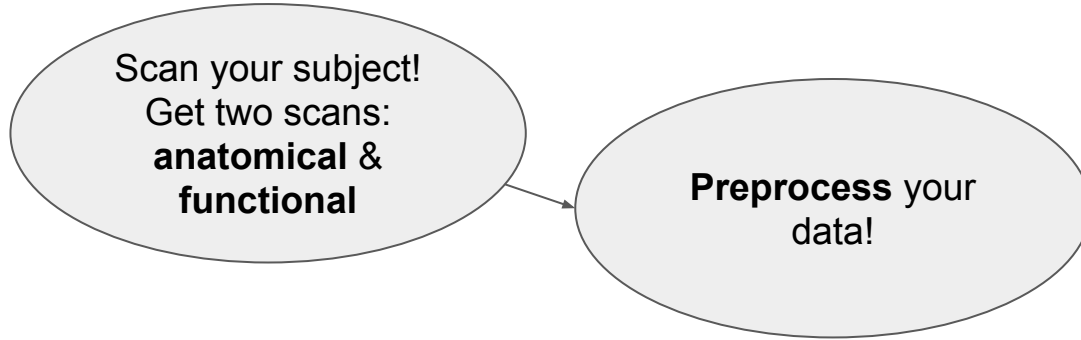
How to get your time series, and an FC matrix

Functional brain network journey

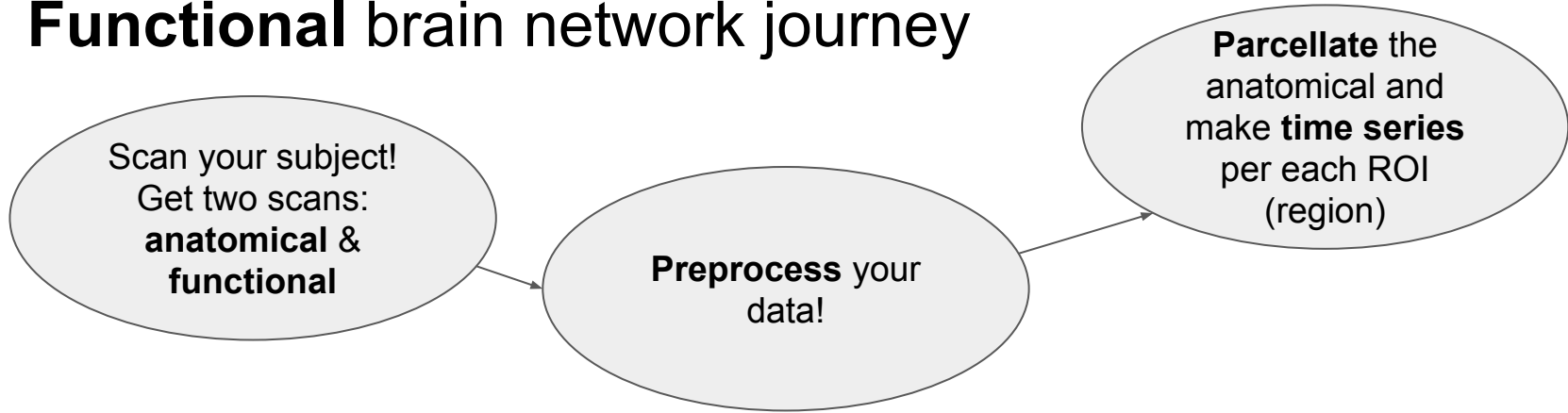


Scan your subject!
Get two scans:
**anatomical &
functional**

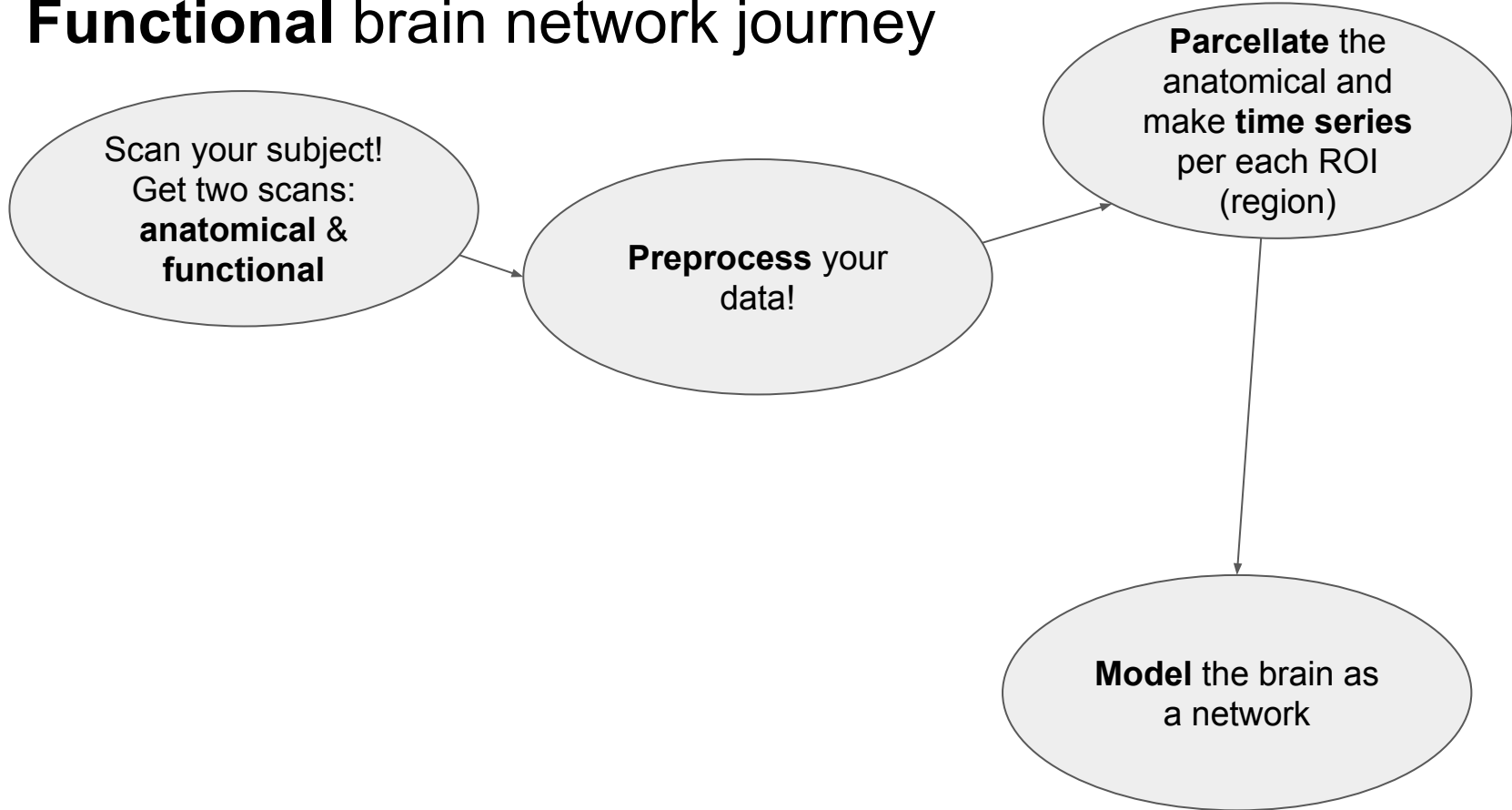
Functional brain network journey



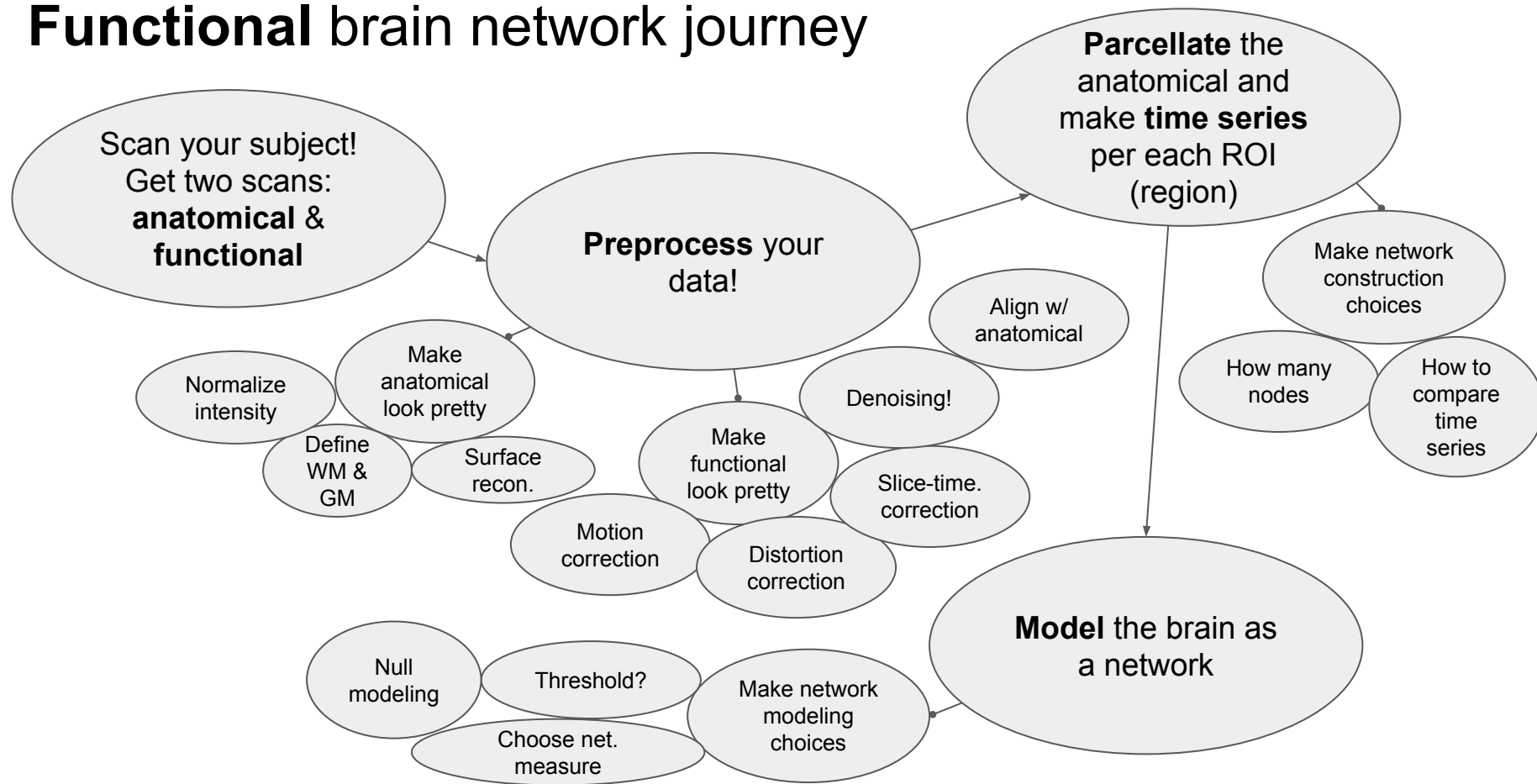
Functional brain network journey



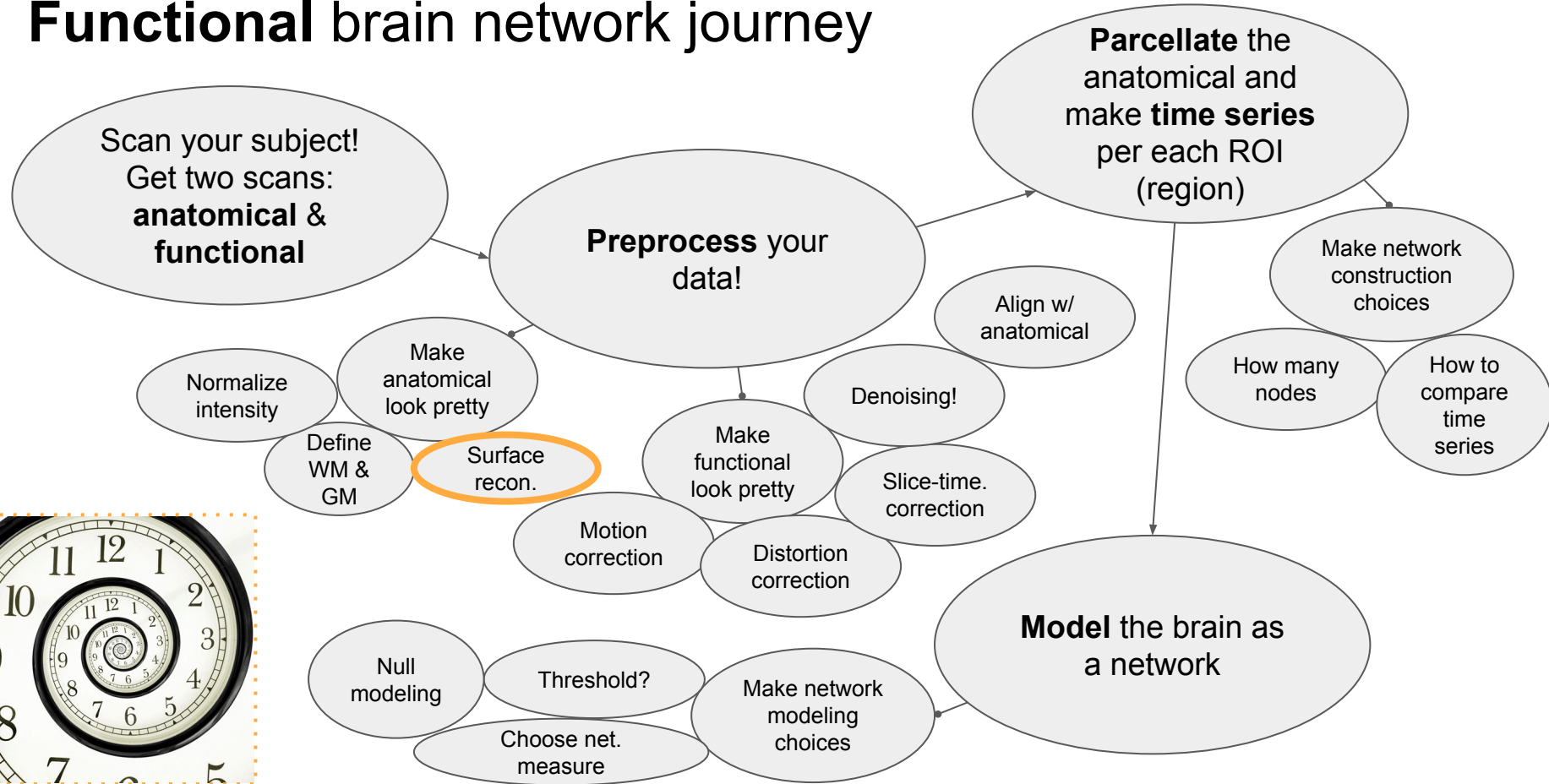
Functional brain network journey



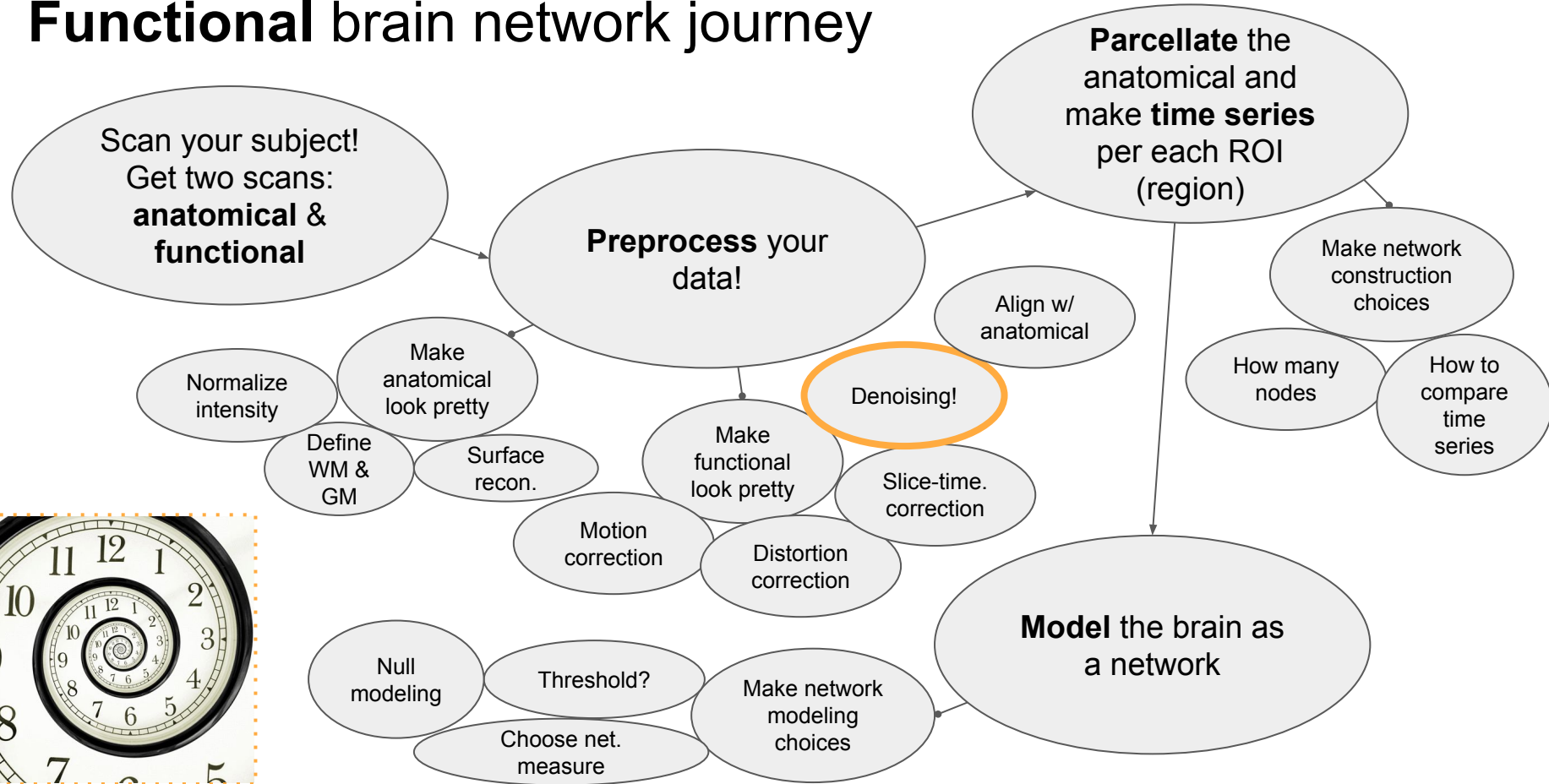
Functional brain network journey



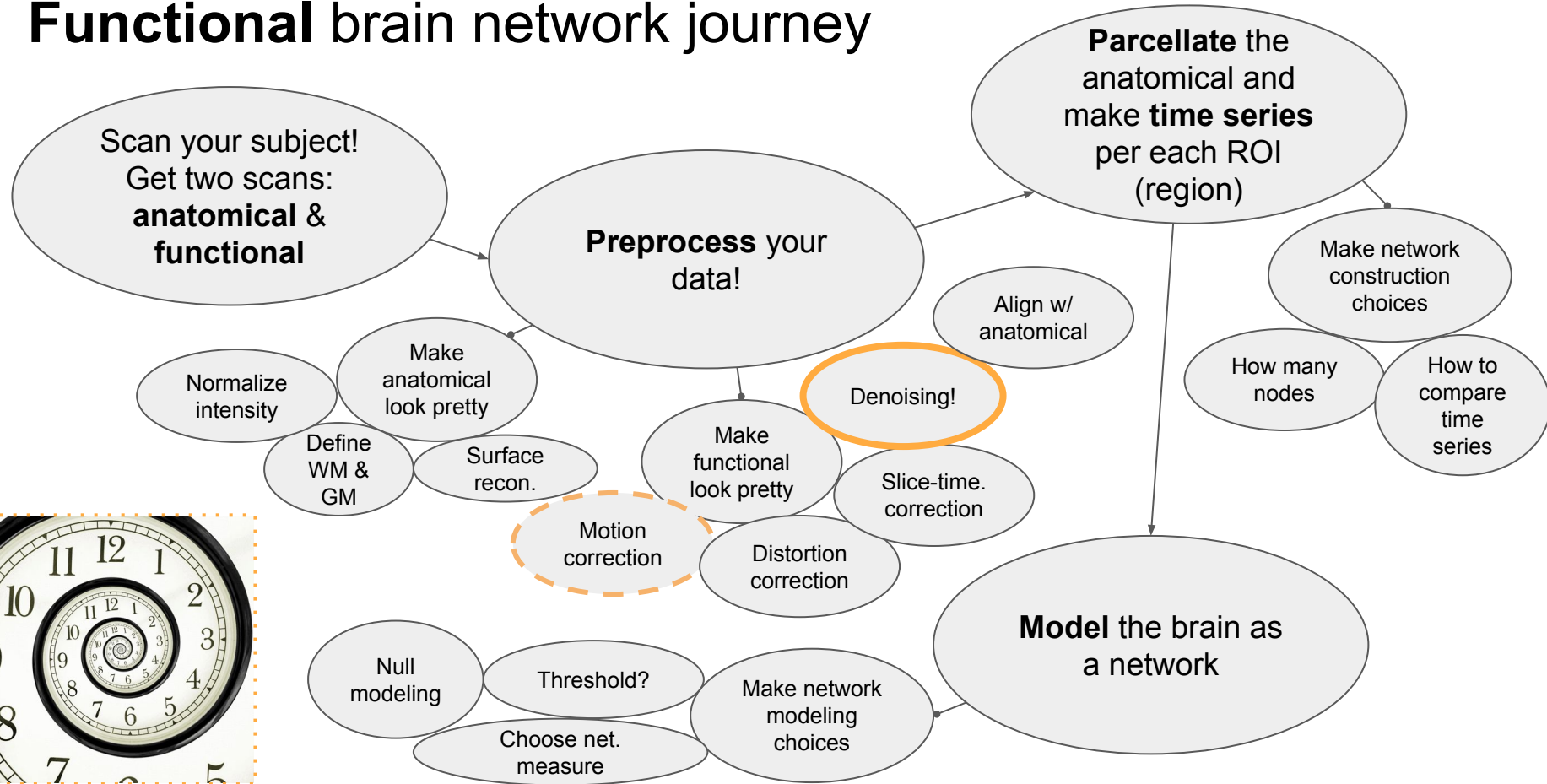
Functional brain network journey



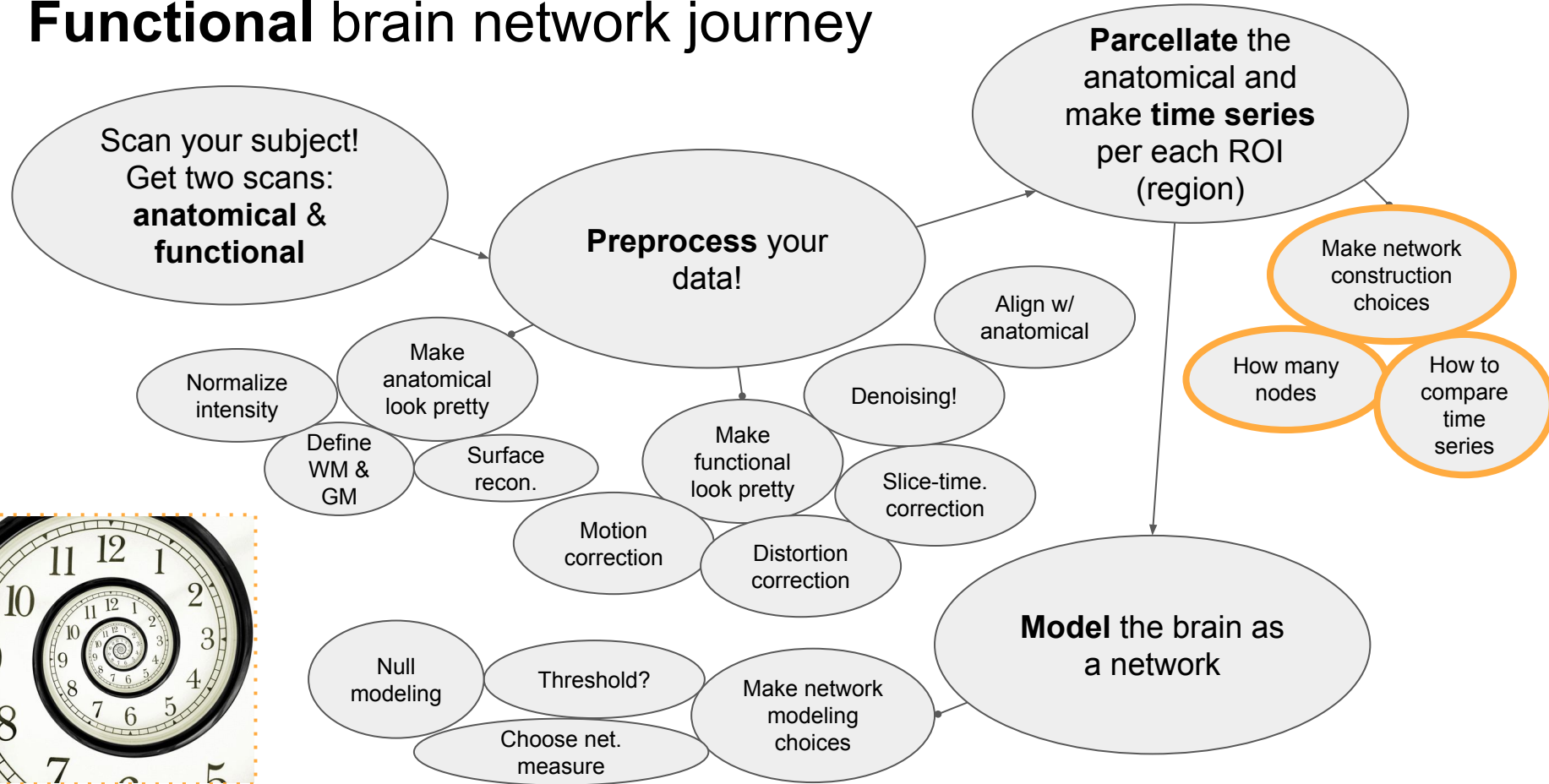
Functional brain network journey



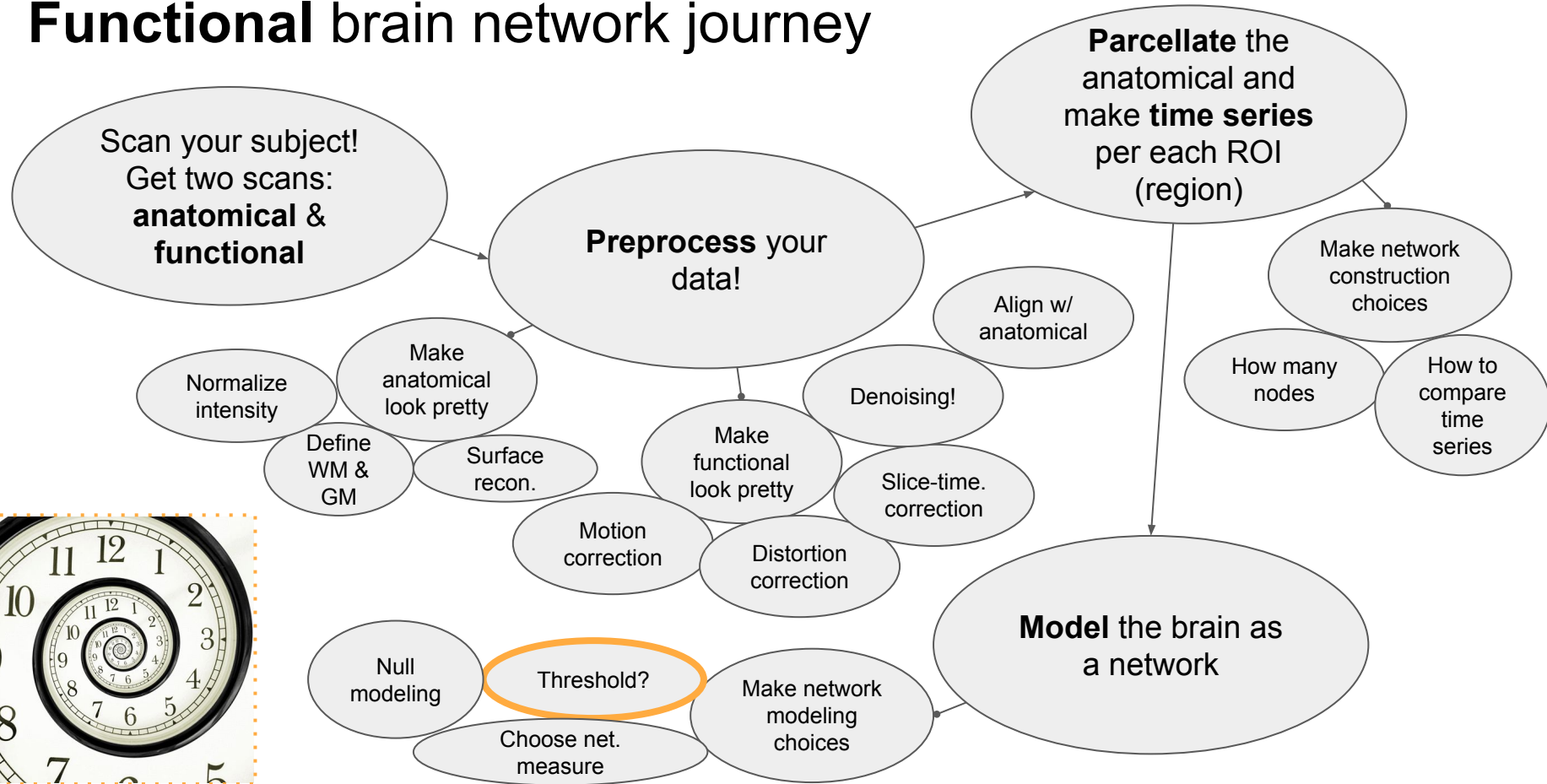
Functional brain network journey



Functional brain network journey



Functional brain network journey

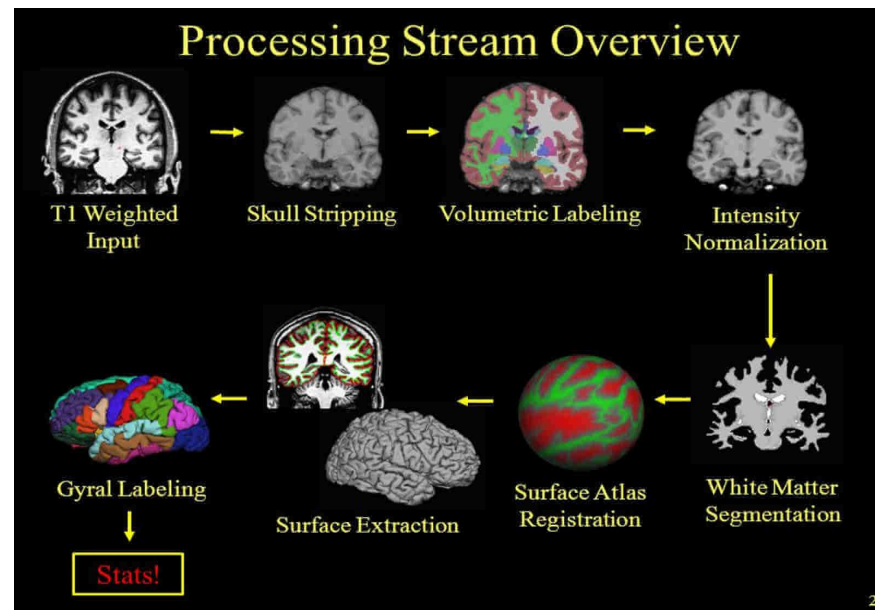
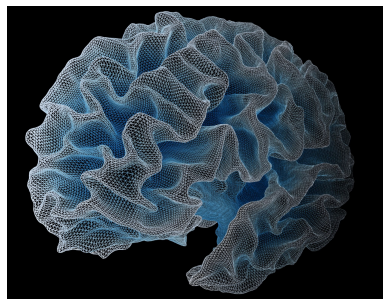


FreeSurfer, FreeSurfer, FreeSurfer

Surface
recon.



- Takes a T1w (and also T2w) anatomical scan and does all sorts of preprocessing
- Results in a surfaces that follow the white matter, gray matter, and pial surfaces
- Segments the cortex and subcortex into anatomical areas
- Helps fitting cortical parcellations later on, based on non-linear surface warp



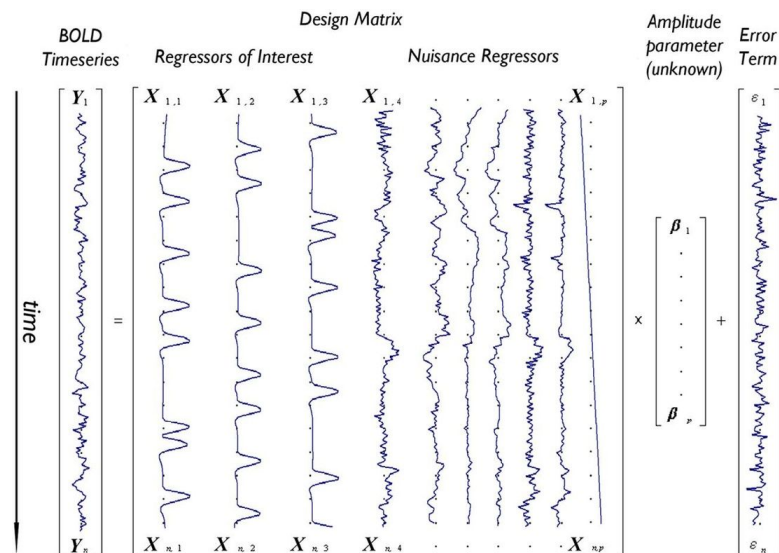
Things that affect FC big time – denoising

Denoising!

Otherwise known as **nuisance regression**

- There is no model of your brain data...but you do model, the **NOISE**
 - The idea is that we want just “brain activity” for our later analysis, so we want to remove as many other sources of variance as possible so we can operate on just “brain activity” in our analyses downstream
- Many different opinions exist about how to do this, and what to include in our noise model

Regular task-design GLM*:



*GLM takes care of noise... unless task is correlated with noise

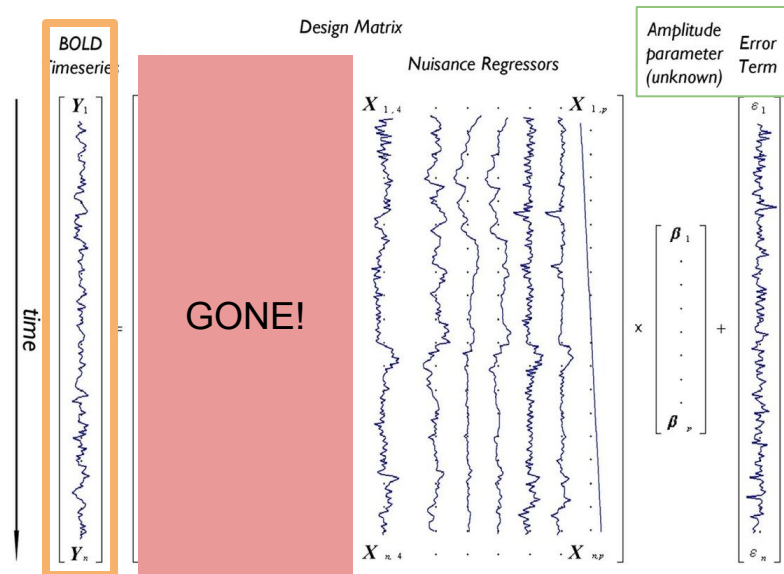
Things that affect FC big time – denoising

Denoising!

Otherwise known as nuisance regression

- There is no model of your brain data...but you do model, the **NOISE**
 - The idea is that we want just “brain activity” for our later analysis, so we want to remove as many other sources of variance as possible so we can operate on just “brain activity” in our analyses downstream
- Many different opinions exist about how to do this, and what to include in our noise model

Resting-state GLM:



Get predicted BOLD time series ($\hat{y}$) and subtract that from actual time series – these residuals are our “brain activity”

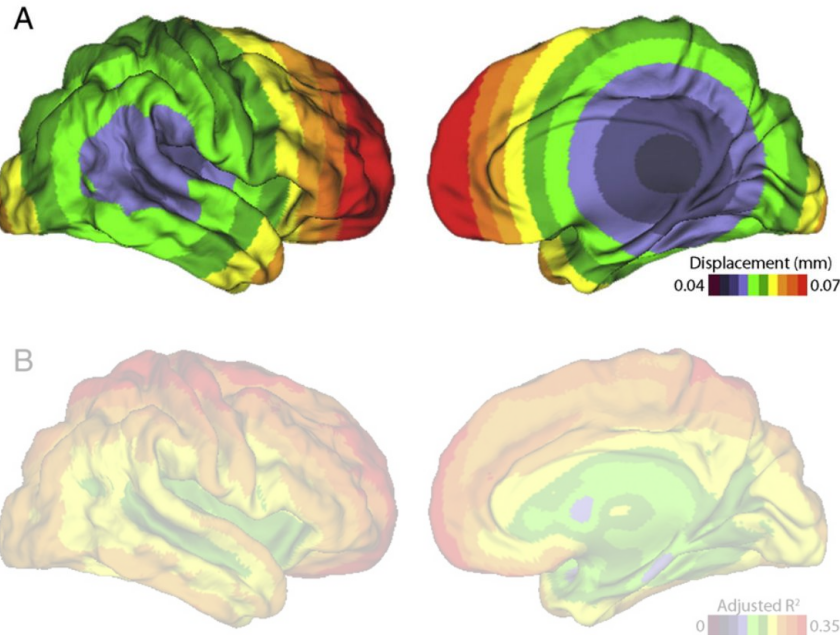
Things that affect FC big time – denoising

Denoising!

Motion correction

244

T.D. Satterthwaite et al. / NeuroImage 64 (2013) 240–256



How much
points in the
brain move
with subject
swiveling their
head

Fig. 1. Spatial distribution of mean relative displacement. A) Average voxelwise displacement across the entire sample as estimated by voxelwise displacement parameters. Displacement is maximal at voxels that are far from the pivot around which rotation occurs. B) Adjusted r^2 maps showing amount of signal variance explained by 6 standard motion parameters.

Things that affect FC big time – denoising

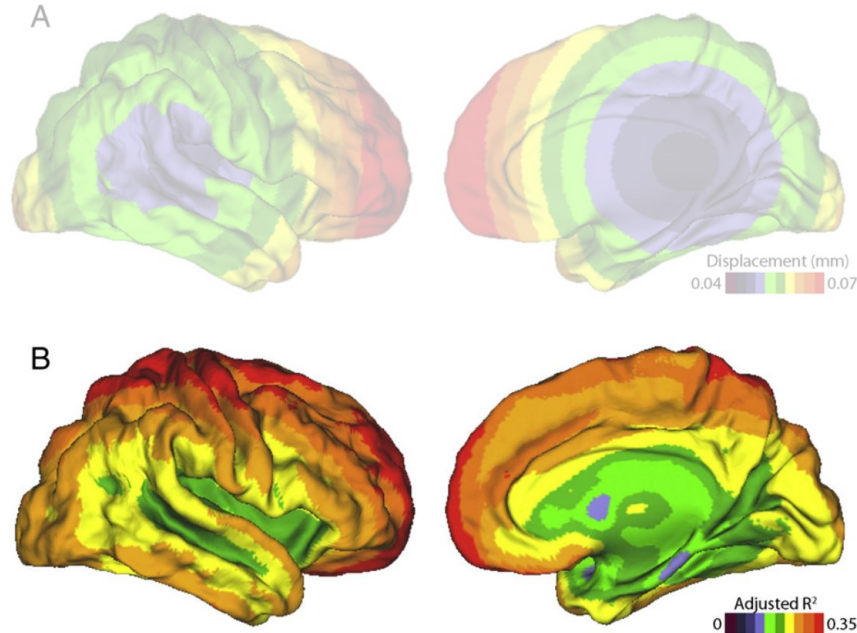
Denoising!

Motion
correction

244

T.D. Satterthwaite et al. / NeuroImage 64 (2013) 240–256

How much
points in the
brain move
with subject
swiveling their
head



Variance of
BOLD
explained by
motion
parameters

Fig. 1. Spatial distribution of mean relative displacement. A) Average voxelwise displacement across the entire sample as estimated by voxelwise displacement parameters. Displacement is maximal at voxels that are far from the pivot around which rotation occurs. B) Adjusted r^2 maps showing amount of signal variance explained by 6 standard motion parameters.

Things that affect FC big time – denoising

Denoising!

Motion correction

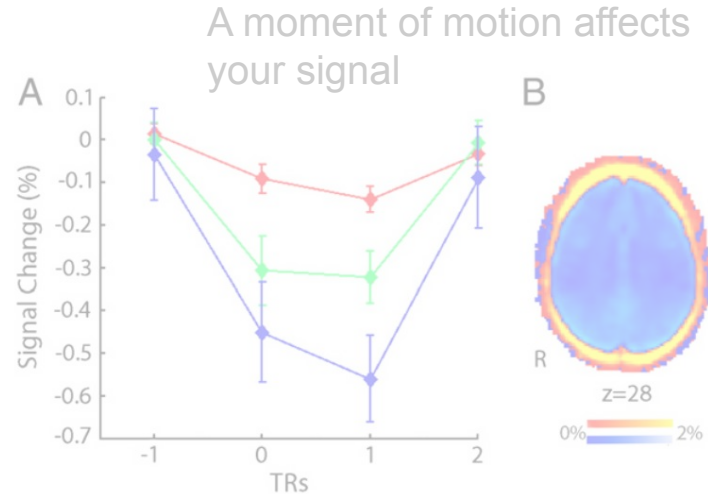


Fig. 3. Timecourse of the motion artifact. A) Motion produces a large reduction in BOLD signal that is maximal in the volume following subject movement. The magnitude of signal reduction increases as motion amplitude increases (red, $> .3$ mm displacements; green, $> .5$ mm, blue $> .7$ mm). Results are from a FIR analysis of the global signal timeseries. B) Motion reduces BOLD signal (blue, negative % signal change) throughout the brain parenchyma, but increases signal around rim of brain (red, positive % signal change). Image is a voxelwise map of timepoint 1 from FIR analysis in (A) using a threshold of 0.7 mm.

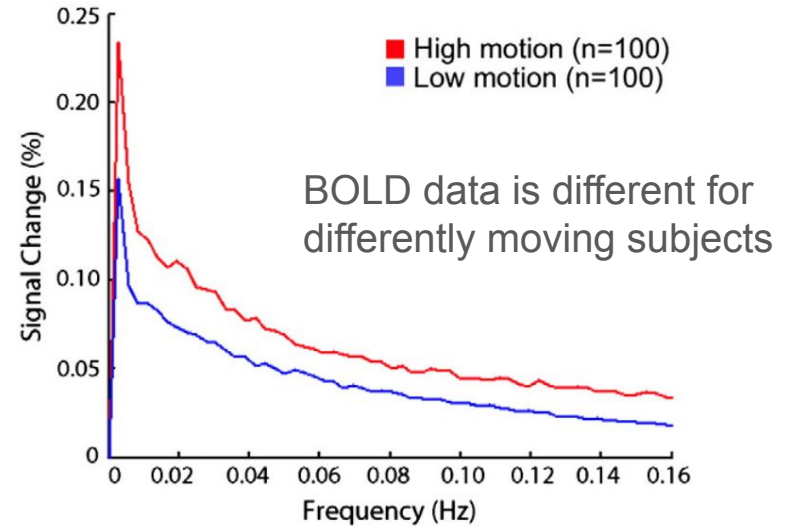


Fig. 4. Magnitude spectra of rsfc-MRI signal among matched groups of high and low motion subjects ($n = 100$ each). The high motion group displays increased magnitude at every frequency. Note that prior to Fourier transform these data have been realigned and spatially smoothed; confound regression has not been applied (see Fig. 9).

Things that affect FC big time – denoising

Denoising!

Motion correction

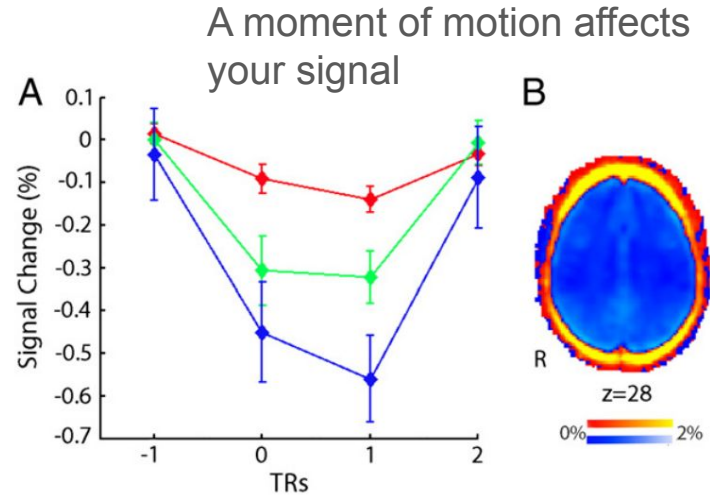


Fig. 3. Timecourse of the motion artifact. A) Motion produces a large reduction in BOLD signal that is maximal in the volume following subject movement. The magnitude of signal reduction increases as motion amplitude increases (red, > .3 mm displacements; green, > .5 mm, blue > .7 mm). Results are from a FIR analysis of the global signal timeseries. B) Motion reduces BOLD signal (blue, negative % signal change) throughout the brain parenchyma, but increases signal around rim of brain (red, positive % signal change). Image is a voxelwise map of timepoint 1 from FIR analysis in (A) using a threshold of 0.7 mm.

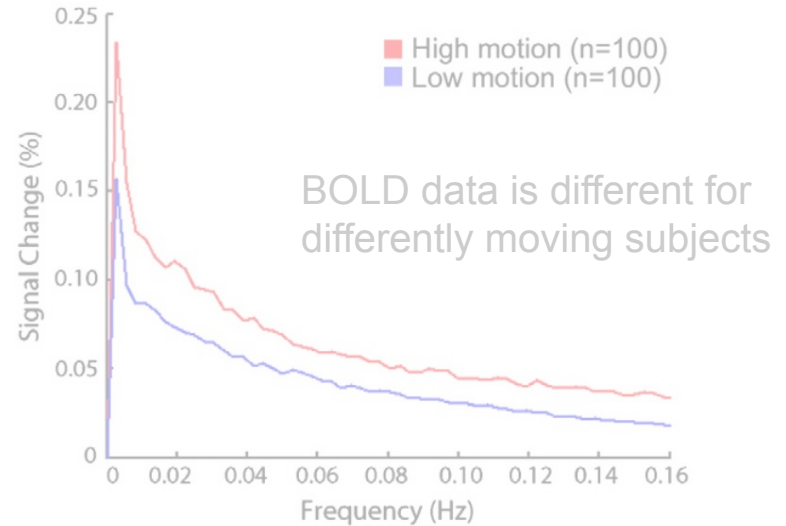
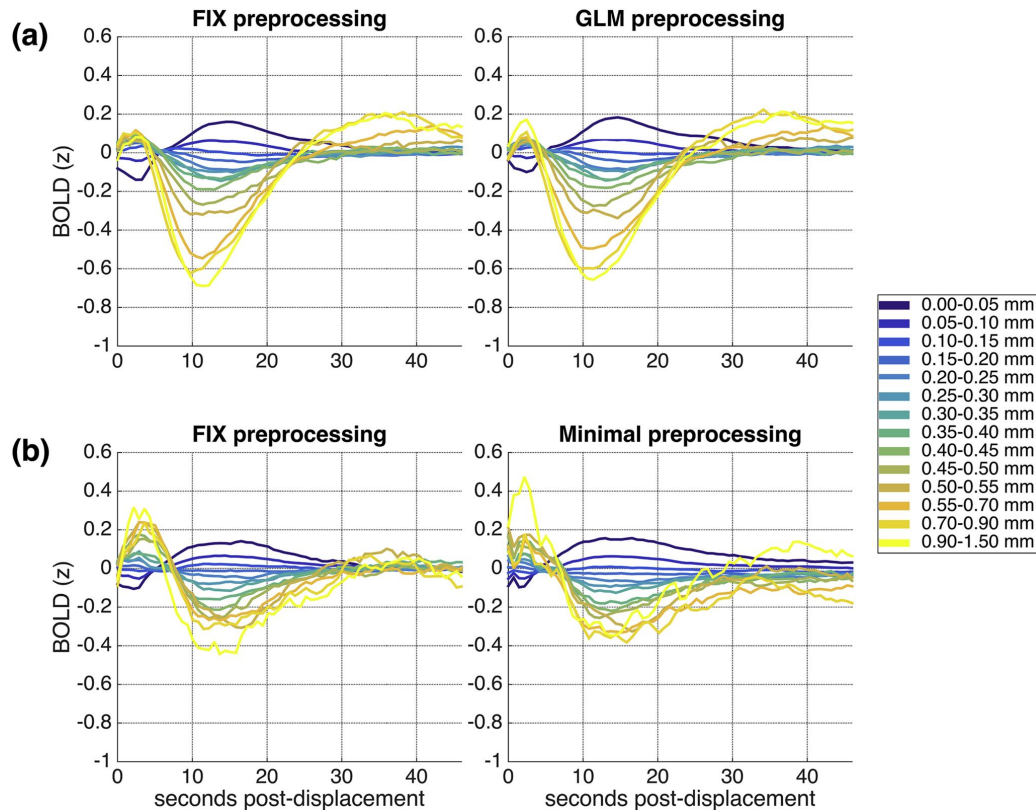


Fig. 4. Magnitude spectra of rsfc-MRI signal among matched groups of high and low motion subjects (n = 100 each). The high motion group displays increased magnitude at every frequency. Note that prior to Fourier transform these data have been realigned and spatially smoothed; confound regression has not been applied (see Fig. 9).

Things that affect FC big time – denoising

Denoising!

Motion
correction



Motion isn't something as simple as an 'event' that can necessarily be regressed or clipped out, as it affects the BOLD signal in nonlinear manner

Things that affect FC big time – denoising

Denoising!

Motion correction

A common way to evaluate your scan's quality/weirdness is to look at a “carpet plot”

326

J.D. Power et al. / NeuroImage 84 (2014) 320–341

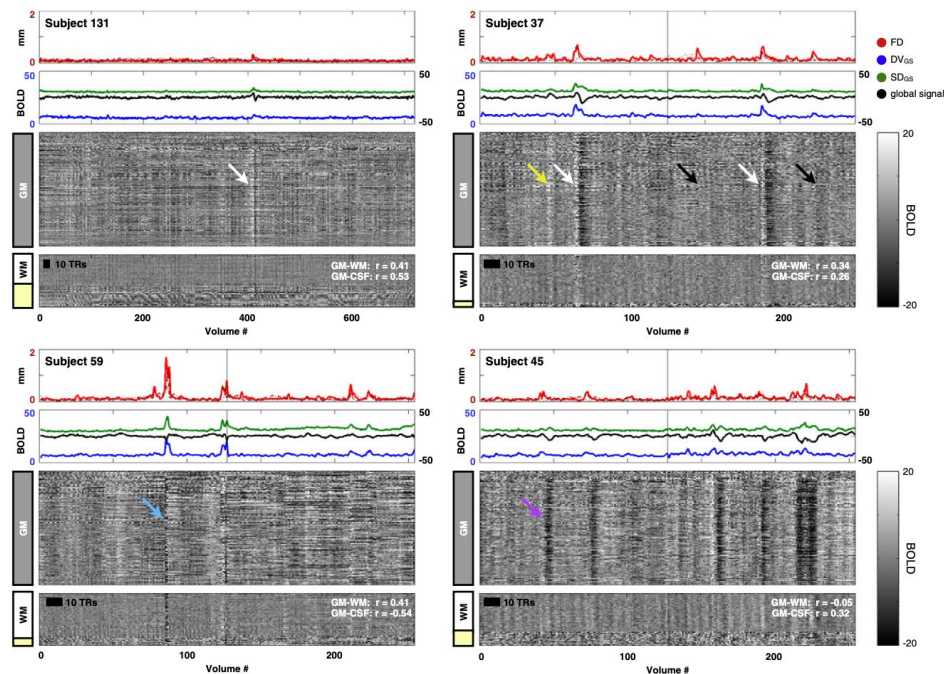


Fig. 4. QC measures and timeseries in subjects with intermittent movements. These subjects exhibit head movements in which the head departs from and returns to positions near the origin (the dotted absolute displacement traces in the upper panels are not elevated). Motion-related signal changes can be brief or long. They can be decreases, increases, or complex waveforms. They are often but not always similar across voxels. Motion-related variance is variably reflected in white matter or CSF voxels.

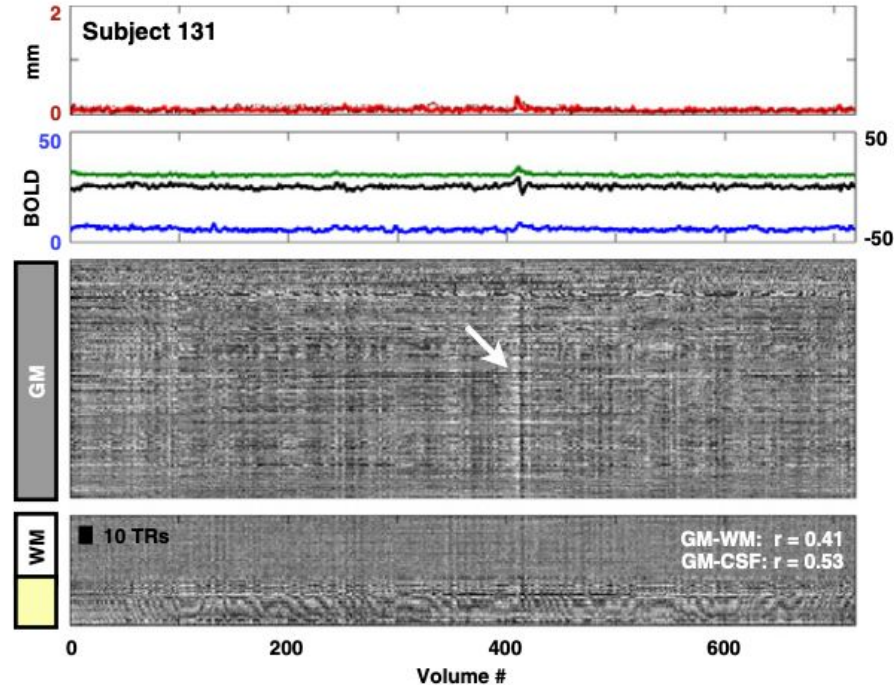
Things that affect FC big time – denoising

Denoising!

Motion correction

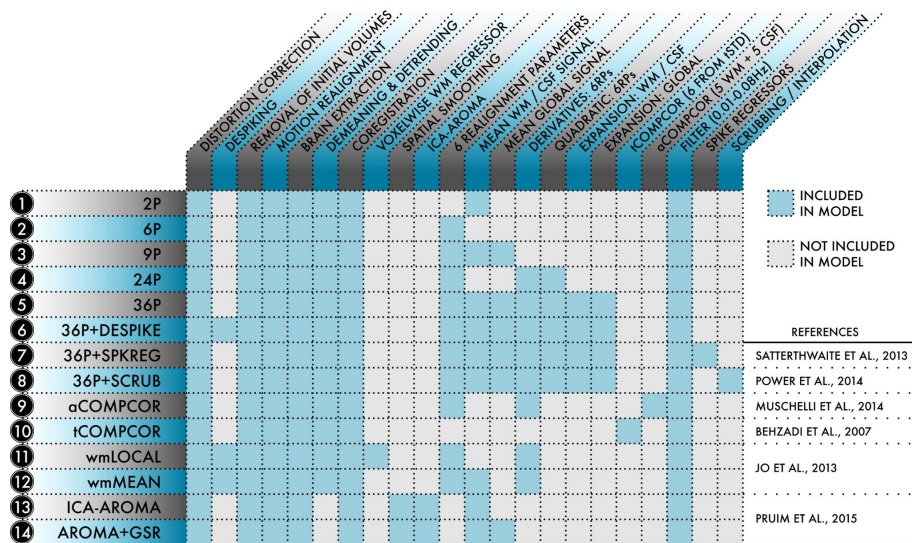
A common way to evaluate your scan's quality/weirdness is to look at a “carpet plot”

Can see how motion (red trace) affects the signal (the grey column artifact)



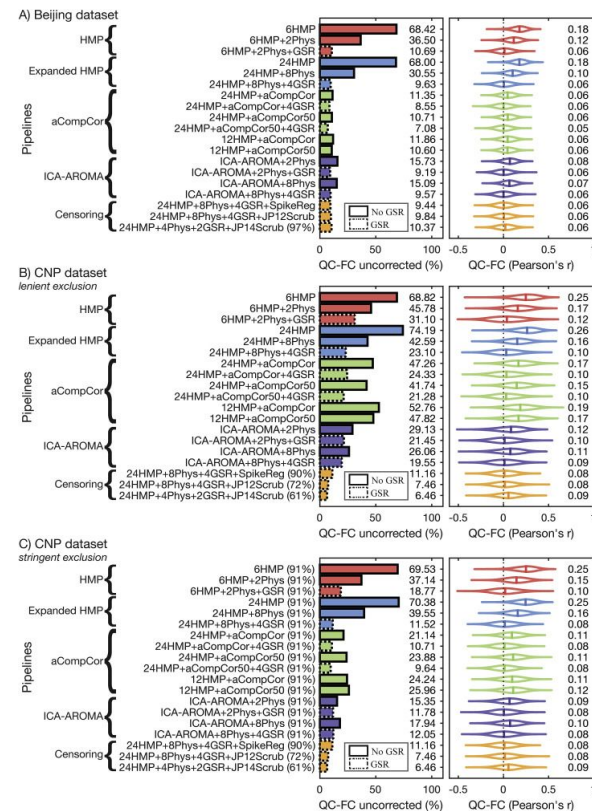
Things that affect FC big time – denoising

Denoising!



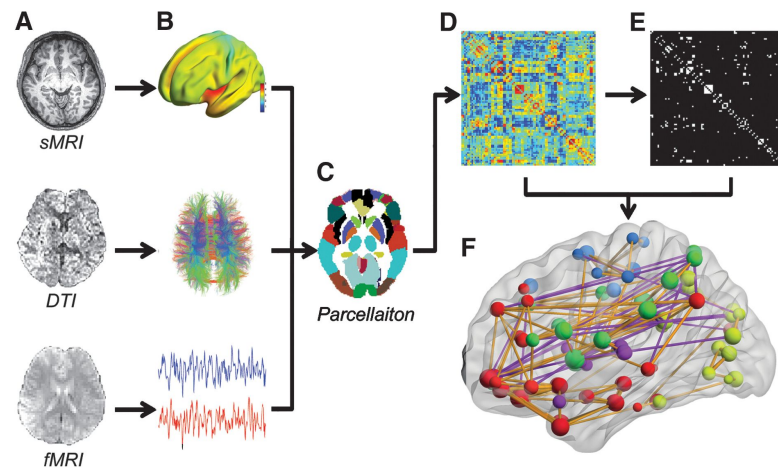
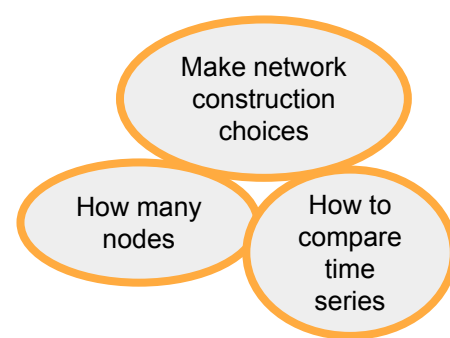
Ciric et al. (2017) *NeuroImage*

Parkes et al. (2017) *NeuroImage*



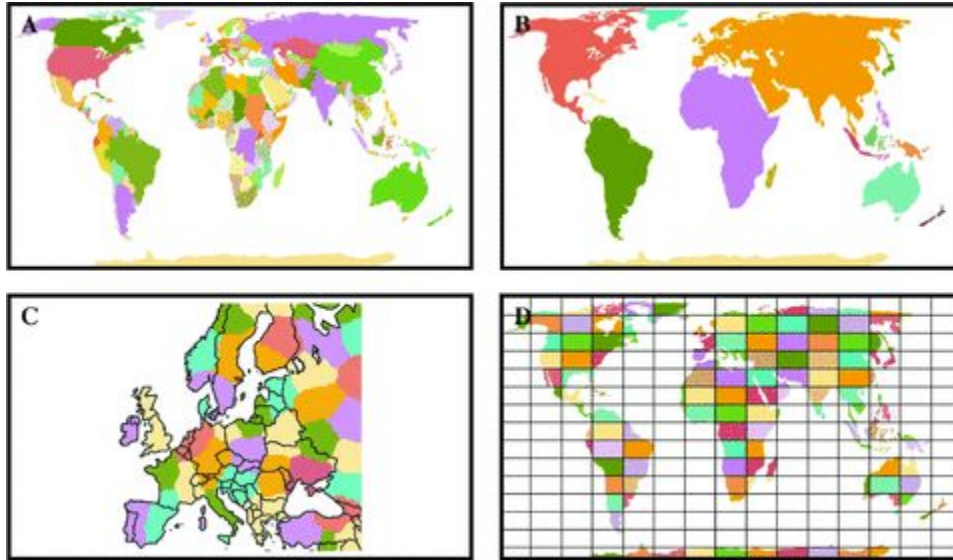
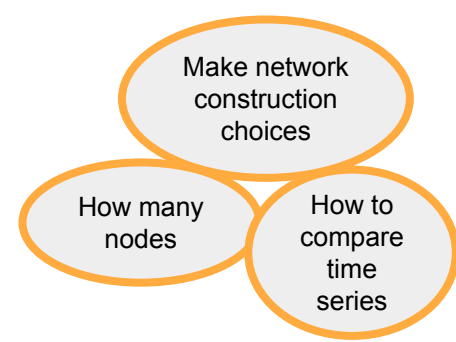
Network construction parameters

- Even if you have just **ONE** anatomical and **ONE** functional scan, you can make **MANY** different sorts of functional networks from these two
 - Differences in these choices will propagate all the way down to your analysis
- Construction choices will have implications for how you analyze the data later on!



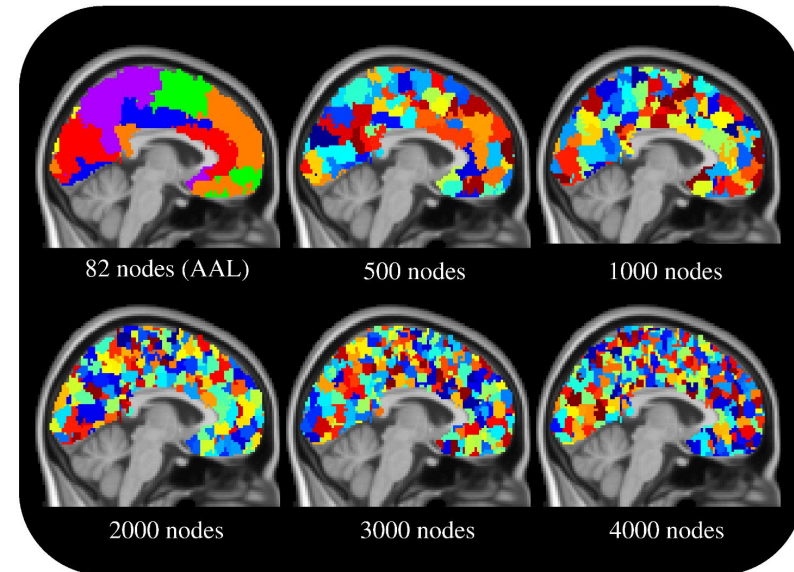
Network construction parameters

How you slice & dice the physical space of the brain



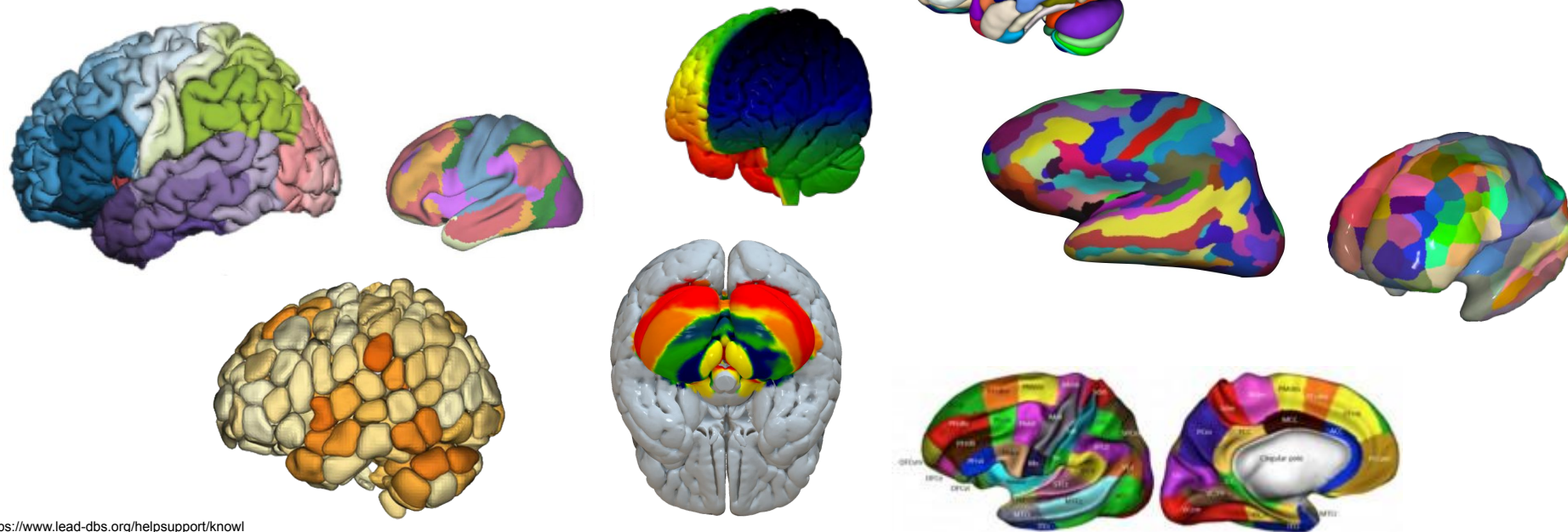
Wig et al. (2016). Ann of NYAS

Zalesky et al (2010). *NeuroImage*



Network construction parameters

How you slice & dice the physical space of the brain



Make network
construction
choices

How many
nodes

How to
compare
time
series

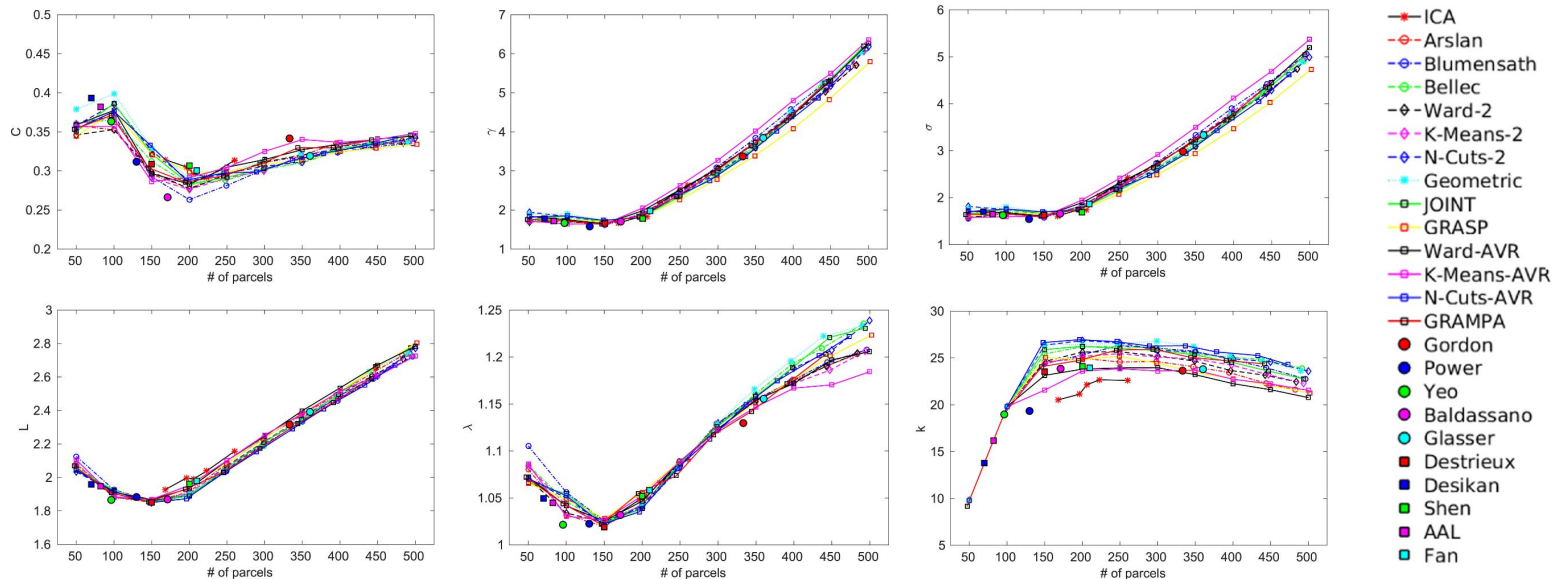
Network construction parameters

How you slice & dice the physical space of the brain

Make network construction choices

How many nodes

How to compare time series

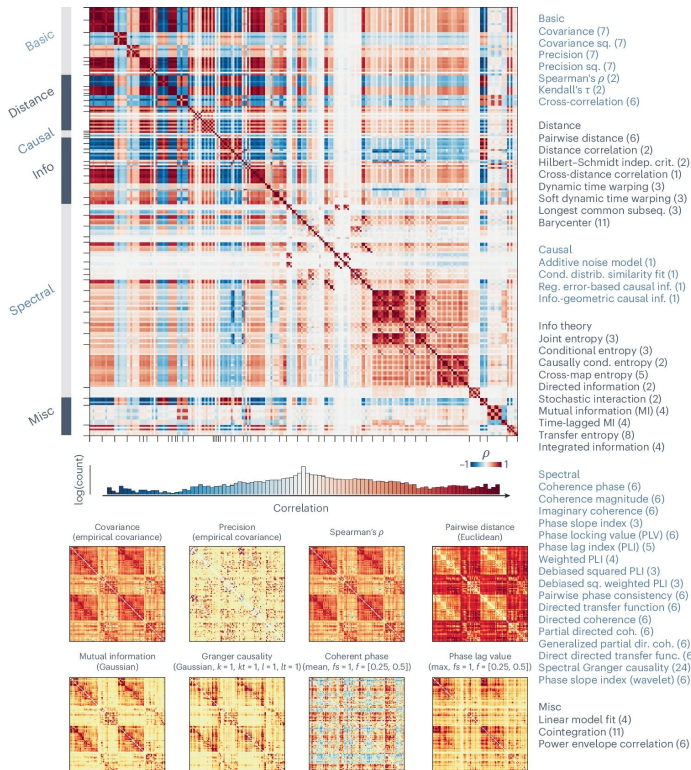


Network construction parameters

Make network construction choices

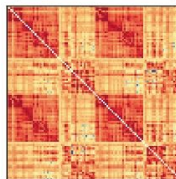
How many nodes

How to compare time series



How you compare two time series changes you idea of the network

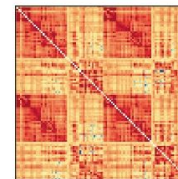
Covariance (empirical covariance)



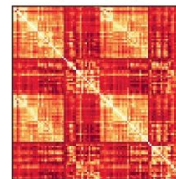
Precision (empirical covariance)



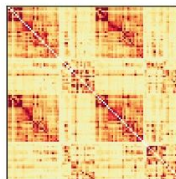
Spearman's ρ



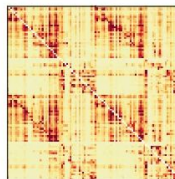
Pairwise distance (Euclidean)



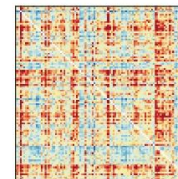
Mutual information (Gaussian)



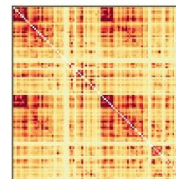
Granger causality (Gaussian, $k=1$, $kt=1$, $l=1$, $lt=1$) (mean, $fs=1$, $f=[0.25, 0.5]$)



Coherent phase (max, $fs=1$, $f=[0.25, 0.5]$)



Phase lag value (max, $fs=1$, $f=[0.25, 0.5]$)



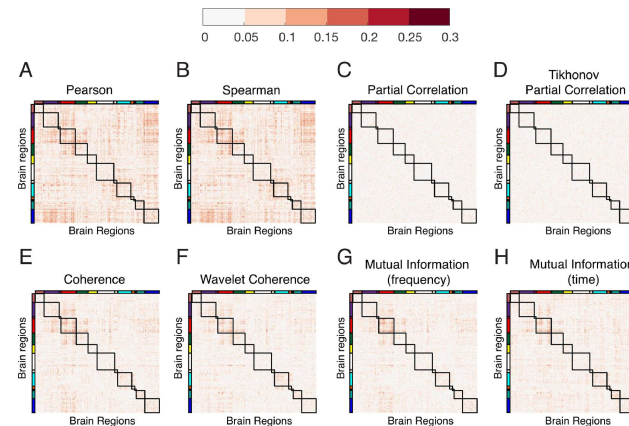
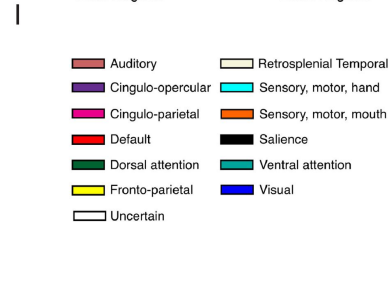
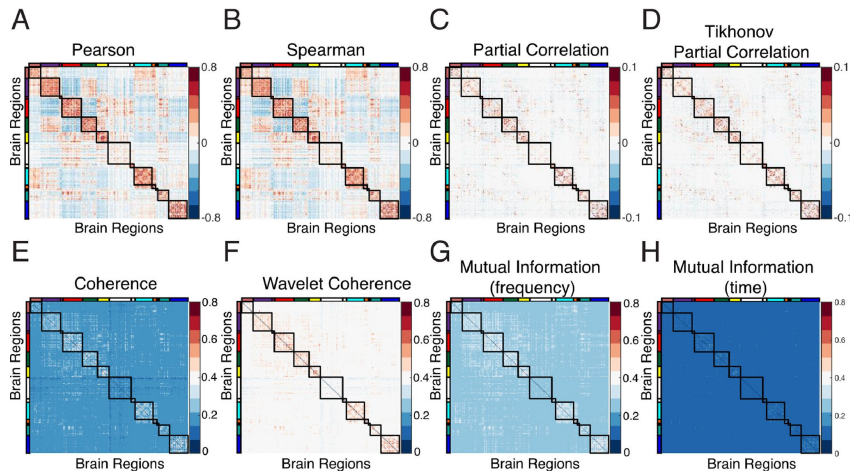
Network construction parameters

Make network construction choices

How many nodes

How to compare time series

How you compare two time series changes your idea of the network



Edge-wise QC-FC correlation

Network construction parameters

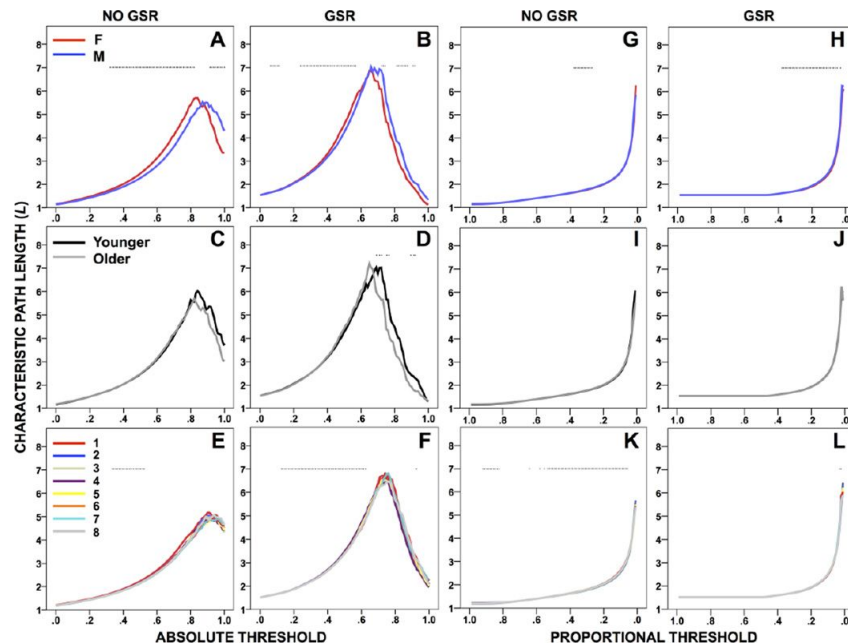
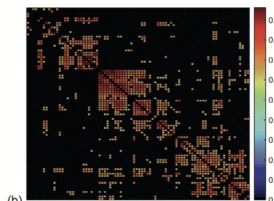
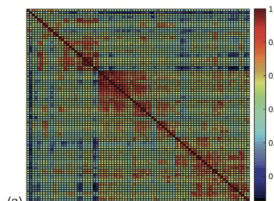
Threshold?

When you compare areas, do you 'zero out' some areas because they are not connected enough?

Full

Threshold w/ weights

Threshold binary

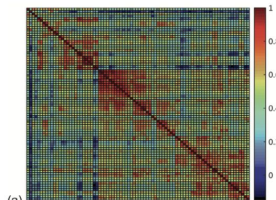


Network construction parameters

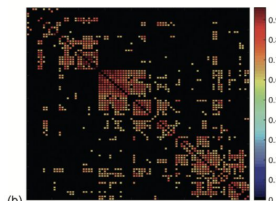
Threshold?

When you compare areas, do you ‘zero out’ some areas because they are not connected enough?

- **Thresholding functional correlation matrix** so as to make it more like a structural matrix (sparse, positive edge weights)
 - If it *must* be done, realize you should:
 - Test different thresholds
 - Explore the effect of retaining the weights vs binarize
 - Threshold in a manner that keeps the network connected (i.e., try not to break in two networks!)



(a)



(b)



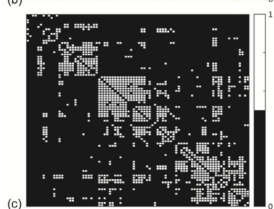
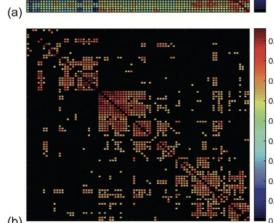
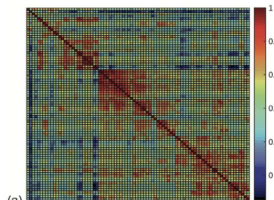
(c)

Network construction parameters

Threshold?

When you compare areas, do you ‘zero out’ some areas because they are not connected enough?

- **Thresholding functional correlation matrix** so as to make it more like a structural matrix (sparse, positive edge weights)
 - If it *must* be done, realize you should:
 - Try minimum (maximum) spanning trees (MST): van Dellen et al. (2018).
 - Giant component threshold: Nicolini et al (2020). Neurolmage.
 - Threshold based on appropriate statistical significance test: Afyouni et al. (2019). Neurolmage.

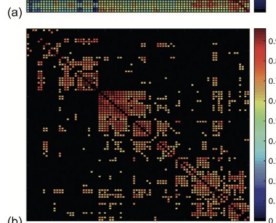
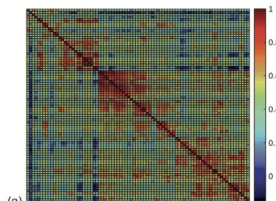


Network construction parameters

Threshold?

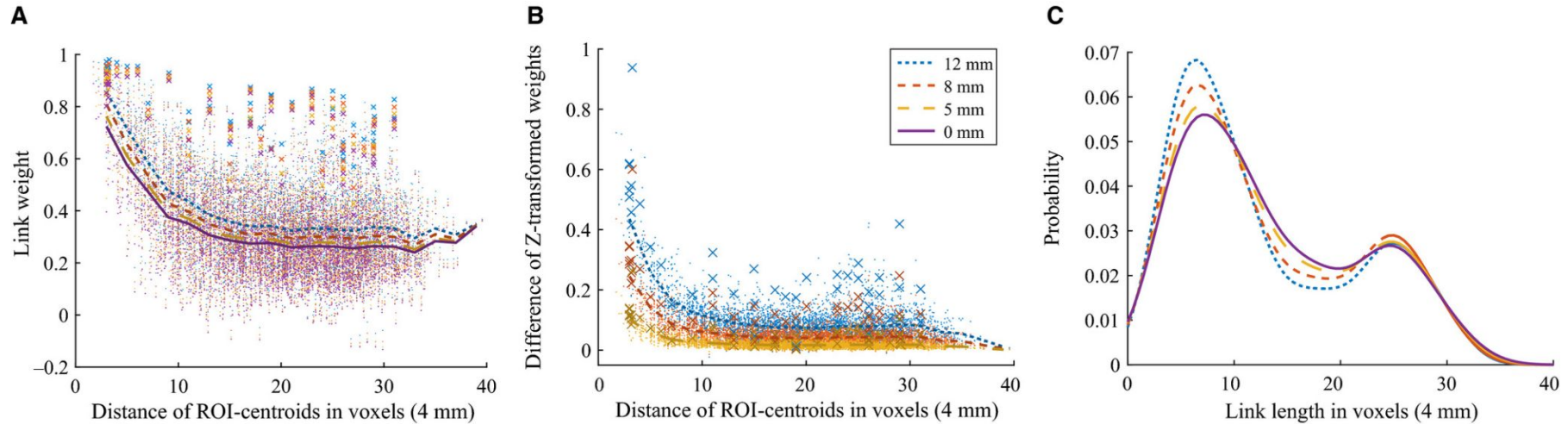
When you compare areas, do you ‘zero out’ some areas because they are not connected enough?

- **Thresholding functional correlation matrix** so as to make it more like a structural matrix (sparse, positive edge weights)
 - If it *must* be done, realize you should:
 - Note that thresholding matrices can introduce bias when doing network group comparisons: van den Heuvel et al. (2017). NeuroImage.



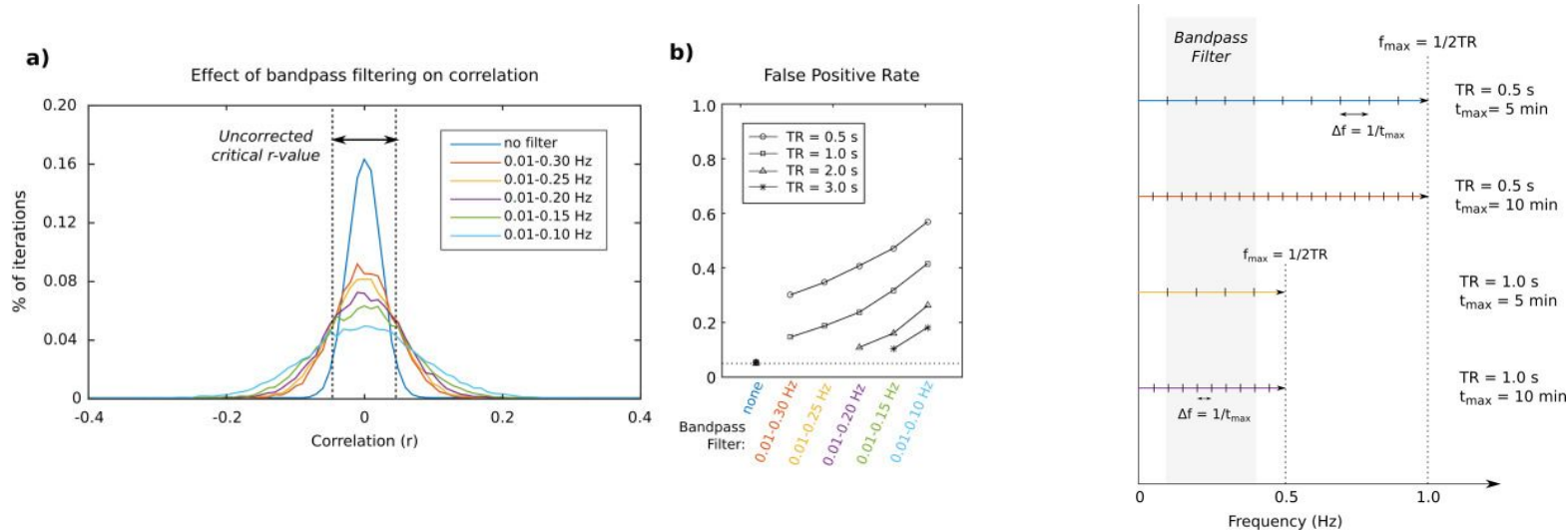
Other things that can influence FC matrix

- Spatially smoothing your data; more smoothing leads to inflated correlations



Other things that can influence FC matrix

- Temporally smoothing your data; more smoothing leads to inflated correlations, again!

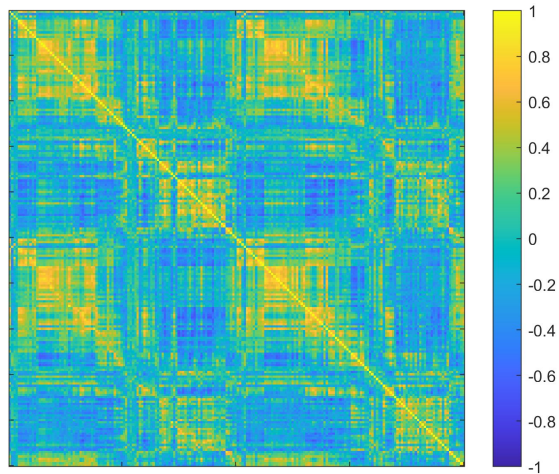
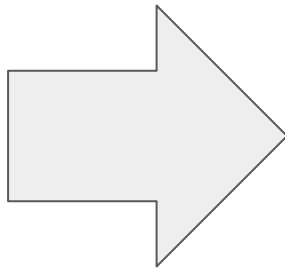


Bright (2017). *NeuroImage*

let's pretend...

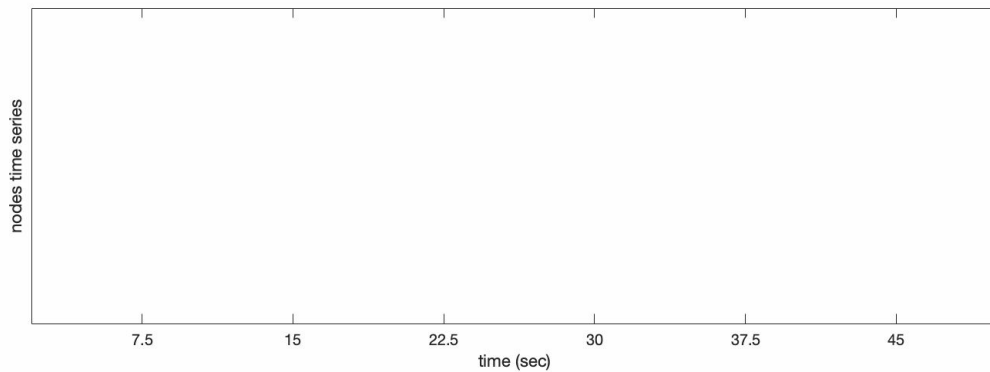
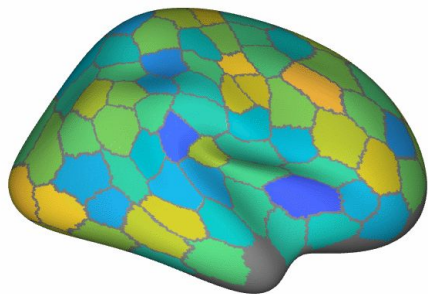
```
# AP Example 1, which was preceded by running:
# + sswwarper2: creates skullstripped anatomical ${anat_cp}, and
# nonlinear warps ${dsets_NL_warp}

afni_proc.py \
  -subj_id          ${subj} \
  -dsets            ${dset_epi} \
  -copy_anat        ${anat_cp} \
  -anat_has_skull    no \
  -anat_follower     anat_w_skull anat ${anat_skull} \
  -blocks            align tlrc volreg regress \
  -blip_forward_dset "${epi_forward}" \
  -blip_reverse_dset "${epi_reverse}" \
  -tcat_remove_first_trs 4 \
  -align_unifize_epi    local \
  -align_opts_aea       -cost lpc+ZZ -giant_move -check_flip \
  -tlrc_base            ${template} \
  -tlrc_NL_warp         \
  -tlrc_NL_warped_dsets ${dsets_NL_warp} \
  -volreg_align_to      MIN_OUTLIER \
  -volreg_align_e2a     \
  -volreg_tlrc_warp     \
  -volreg_warp_dxyz      3
```

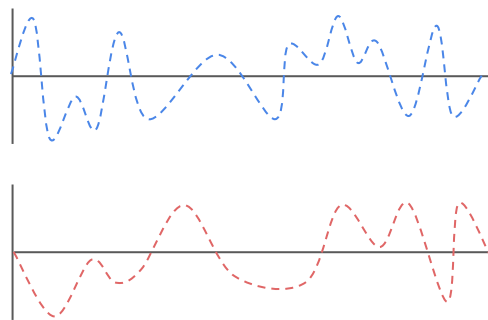
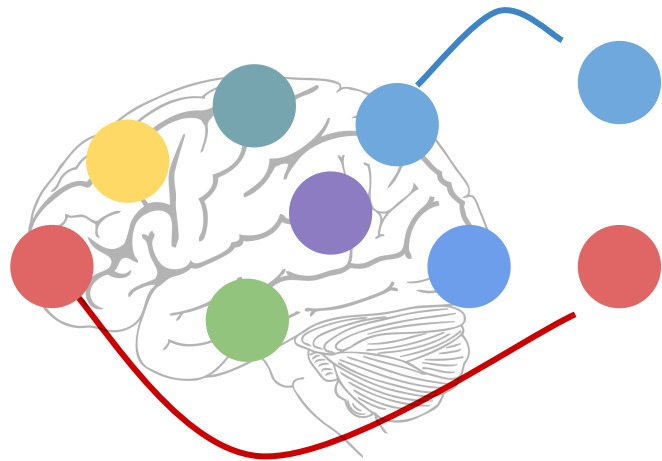


that it's all taken care of

Creating functional networks



Creating functional networks

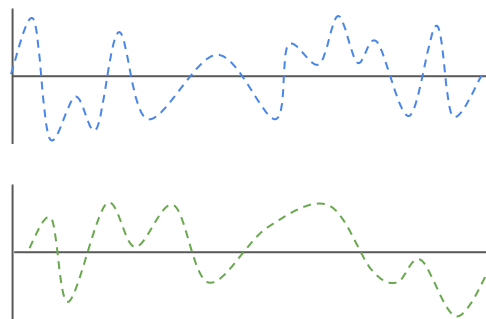
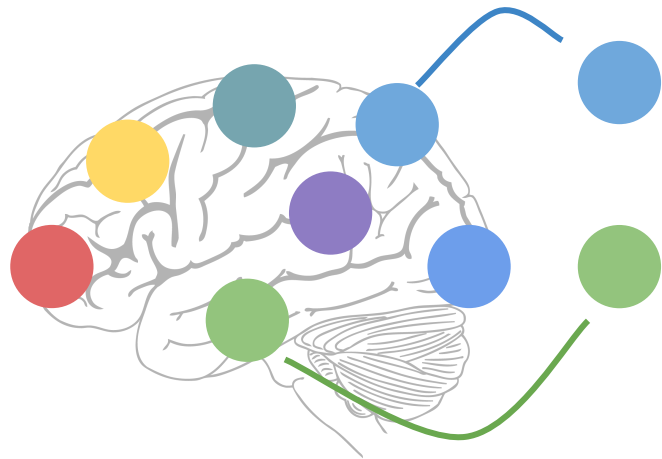


Can compare data
fluctuations over
time in a pairwise
manner

Data collected
across time



Creating functional networks

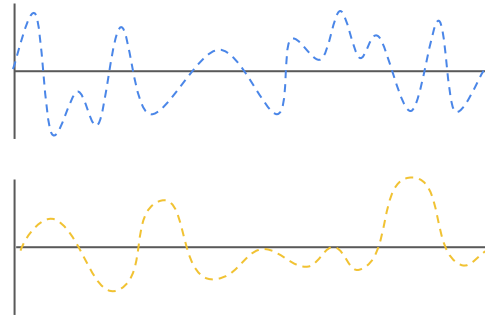
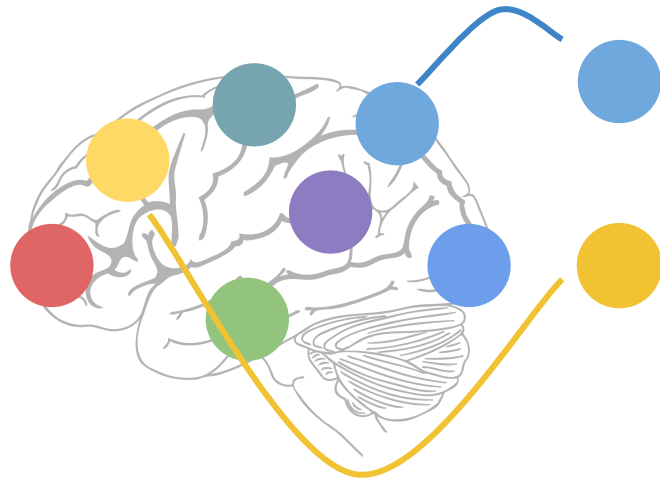


Data collected
across time



Can compare data
fluctuations over
time in a pairwise
manner

Creating functional networks

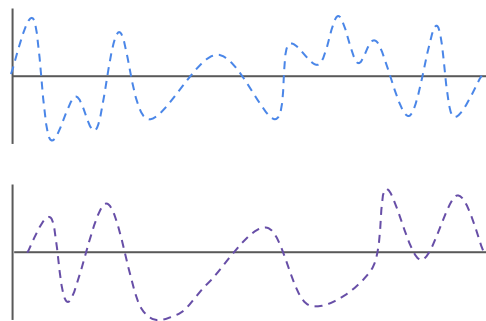
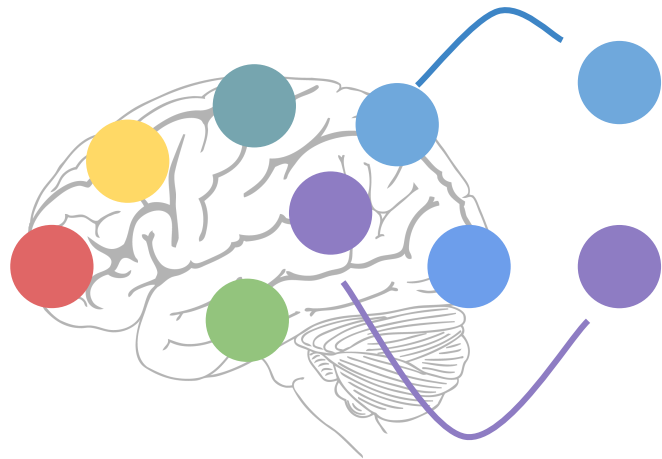


Can compare data fluctuations over time in a pairwise manner

Data collected across time



Creating functional networks

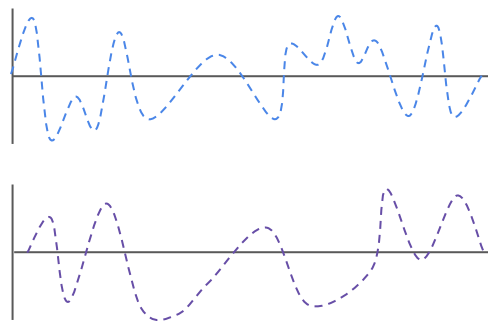
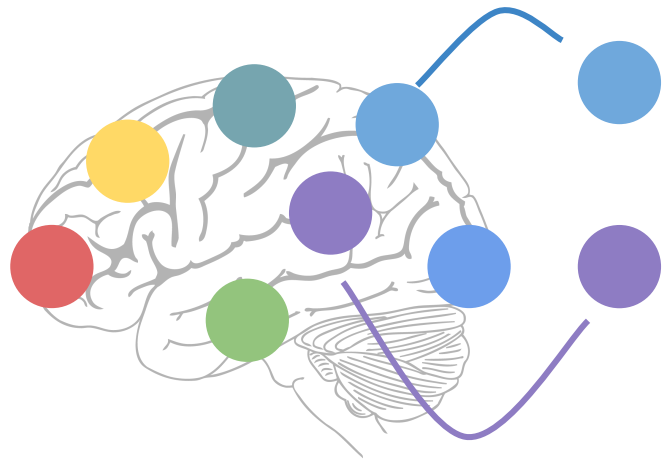


Can compare data fluctuations over time in a pairwise manner

Data collected across time



Creating functional networks



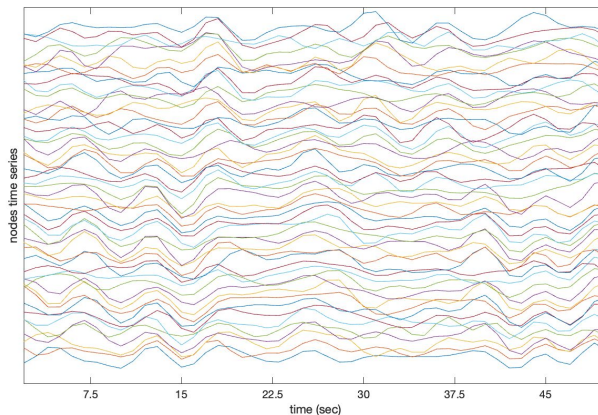
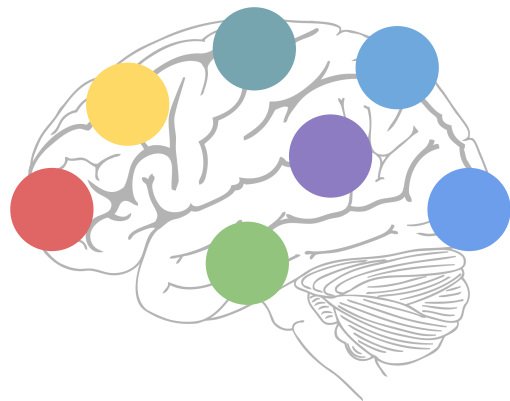
Data collected
across time



Can compare data
fluctuations over
time in a pairwise
manner

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

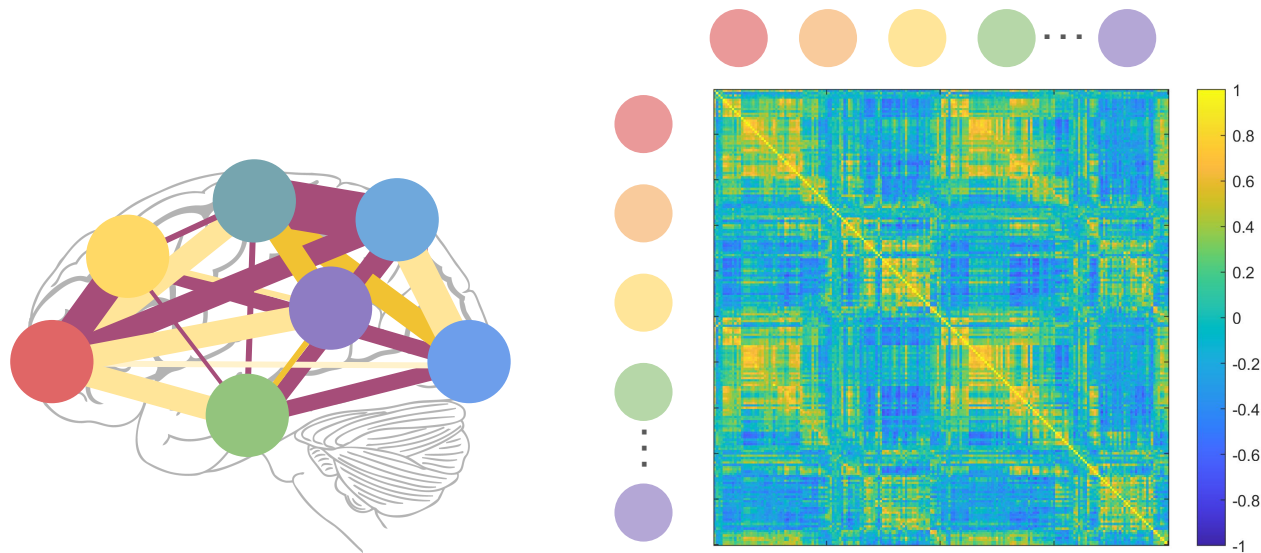
Creating functional networks



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



Can compare data fluctuations over time in a pairwise manner

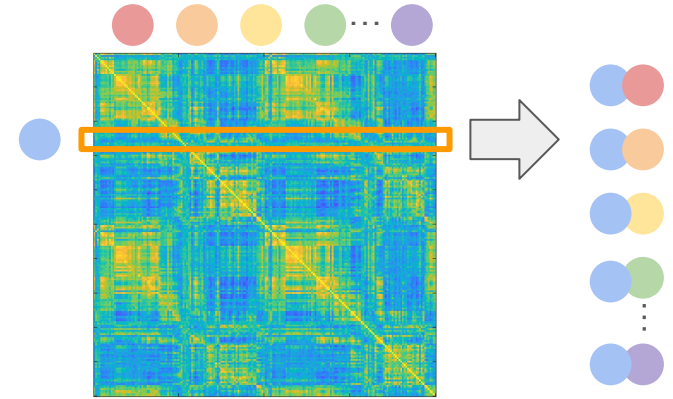
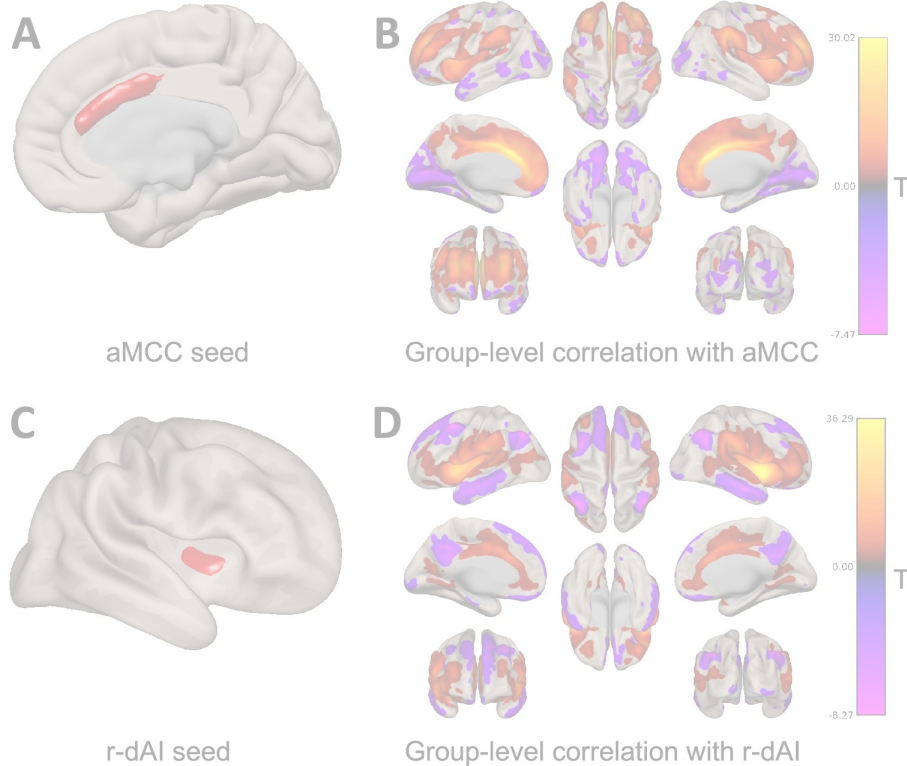
Until you make all possible pairwise comparisons; giving you a full **correlation matrix**

Outline

- **Why** study connectivity?
 - Networks are nice
 - The brain as a network
 - What do we mean by connectivity?
- **How** to get your time series and constructing an FC matrix
 - Preprocessing choices
 - Modeling choices
 - Making an FC matrix
- **Ways to analyze brain connectivity**
 - Seed-based connectivity analysis
 - Time-averaged FC
 - Network-based statistic
 - Connectome predictive modeling (CPM)
 - Clustering / community detection / ICA
 - Network analysis / graph theory
 - Time-varying FC
 - Brain states
 - Dynamic FC
 - Sliding window
 - Edge time series

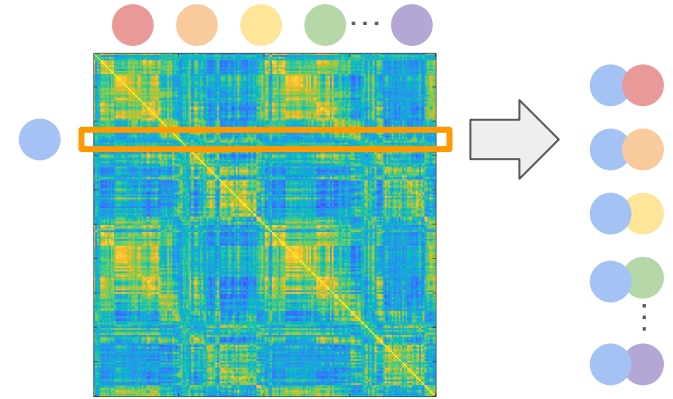
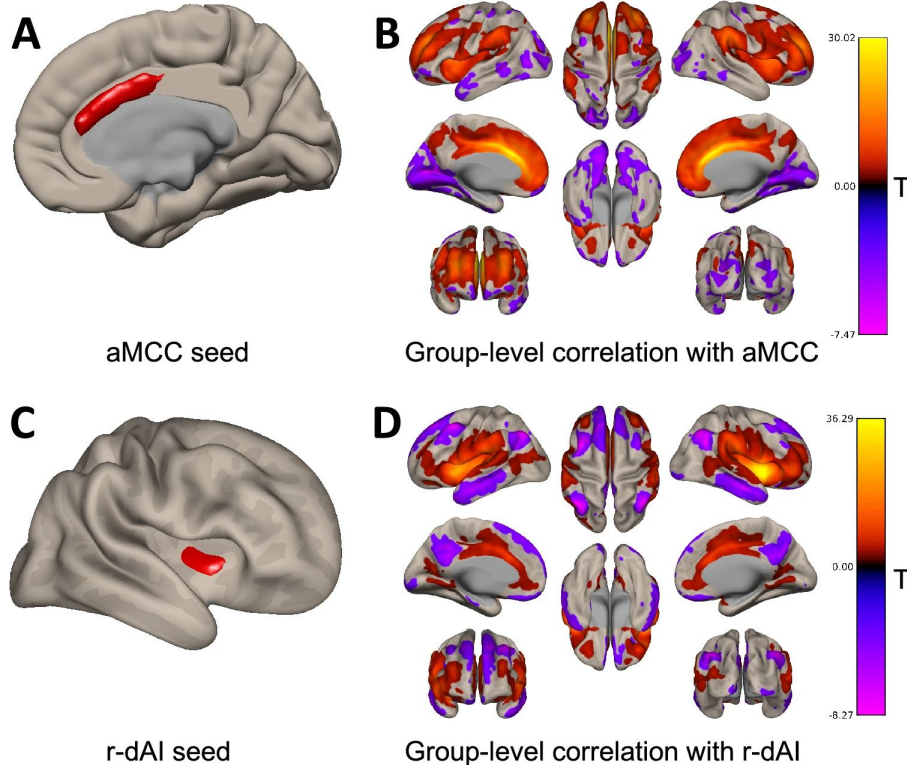
How can I analyze a brain's functional connectivity?

Seed-based correlation



- Like reading a single row of the FC matrix
- Usually a good approach when you have a hypothesis-driven location that you are tied to
- Produces a map that you can analyze like you would other neuro-maps

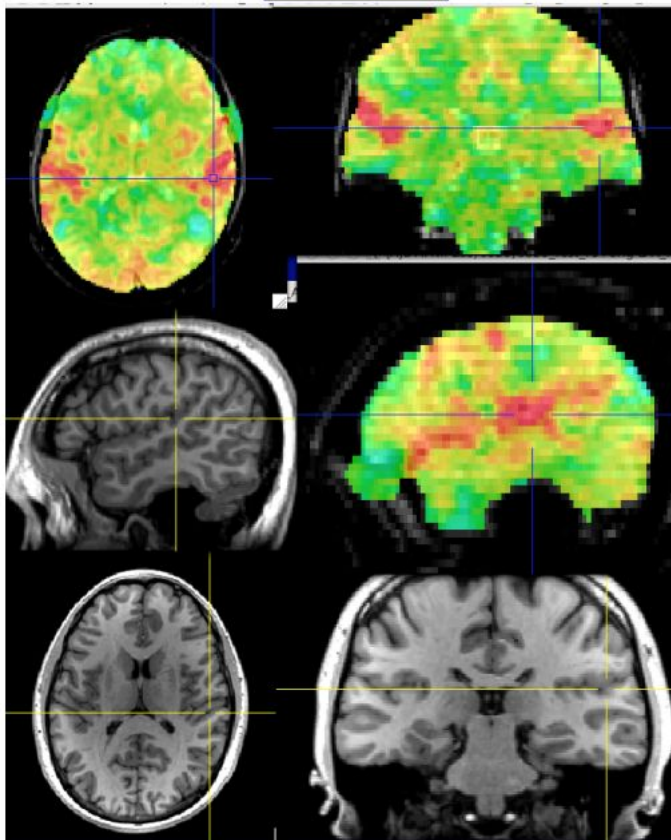
Seed-based correlation



- Like reading a single row of the FC matrix
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AFNI! InstaCorr

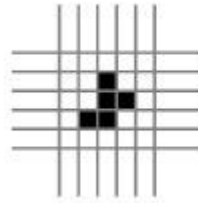
All data herein
from Alex Martin,
et al. [NIMH IRP]



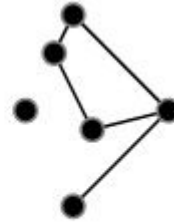
- On-the-fly instantaneous correlation map of resting state data with interactively selected seed voxel
- **Setup phase:** prepares data for correlations (several-to-10+ seconds)
- **Correlation phase:** you select seed voxel, correlation map appears by *magic*

Network-based statistic

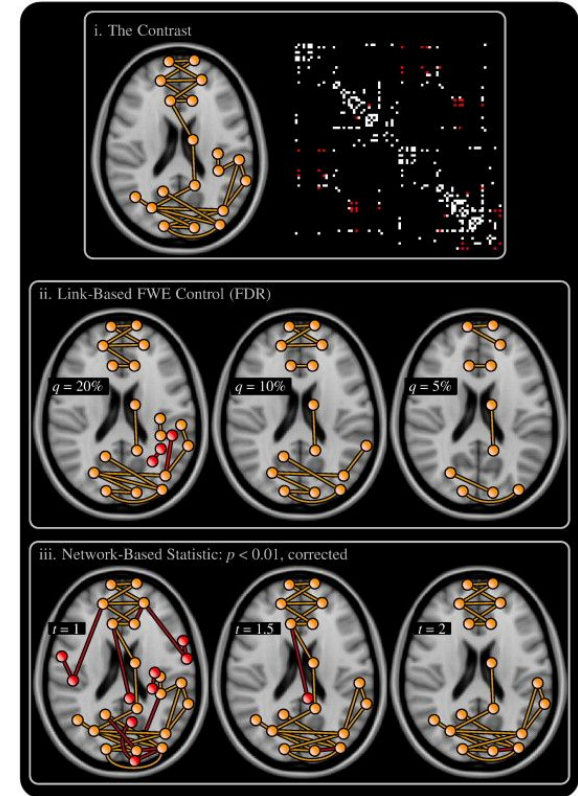
1. Create a test statistic at each edge
2. Identify supra-threshold edges
3. Measure the size of components formed
4. Permute data & recompute statistic, measure largest component size at each null iteration
5. Get p-value of original components given number of null largest components as big



SPM cluster



Graph component



Network-contingency test

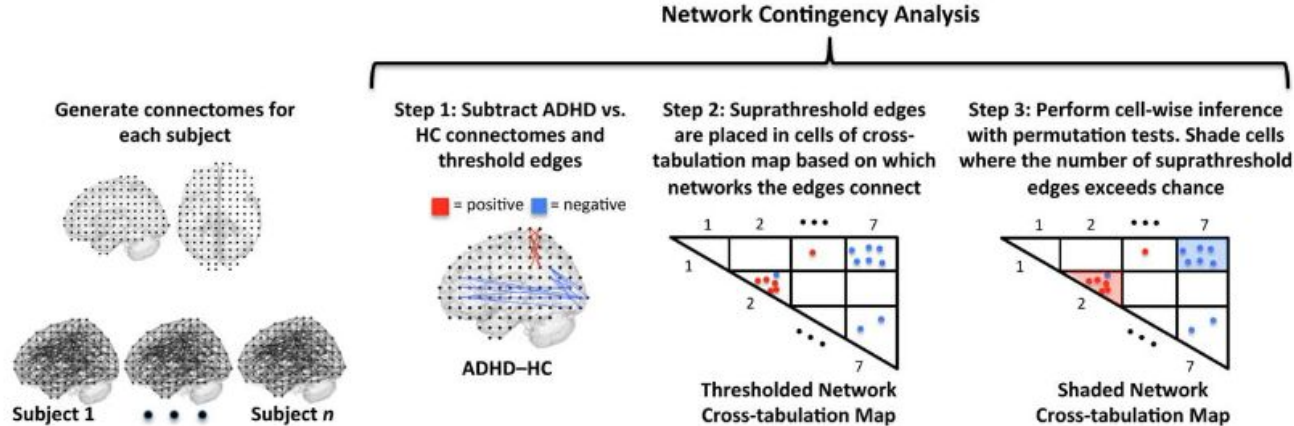
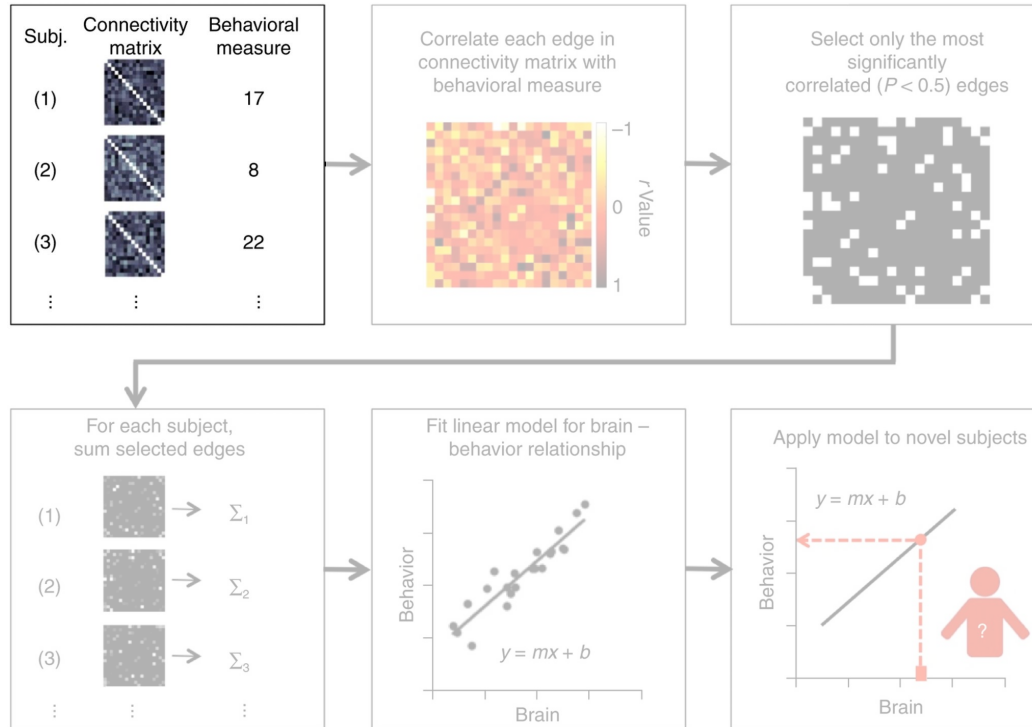


Figure 1.

Steps of the network contingency analysis. All possible interconnections between seven major intrinsic connectivity networks are represented in 28 (nonredundant) cells of a network cross-tabulation map. The network contingency analysis takes a population-based approach to the question of when two networks exhibit disrupted connectivity. For each cell, the analysis

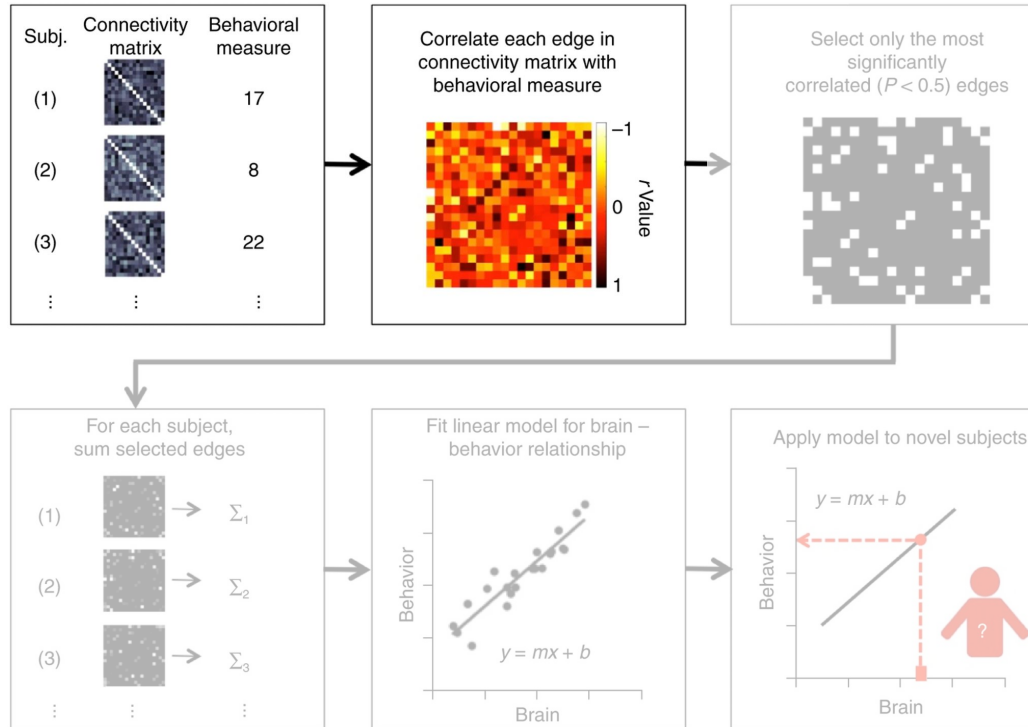
assesses whether the number of disease-modulated edges is greater than would be expected by chance. Each step of the analysis is discussed in greater detail in the main text. ADHD, attention-deficit/hyperactivity disorder; HC, healthy control. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Connectome predictive modeling



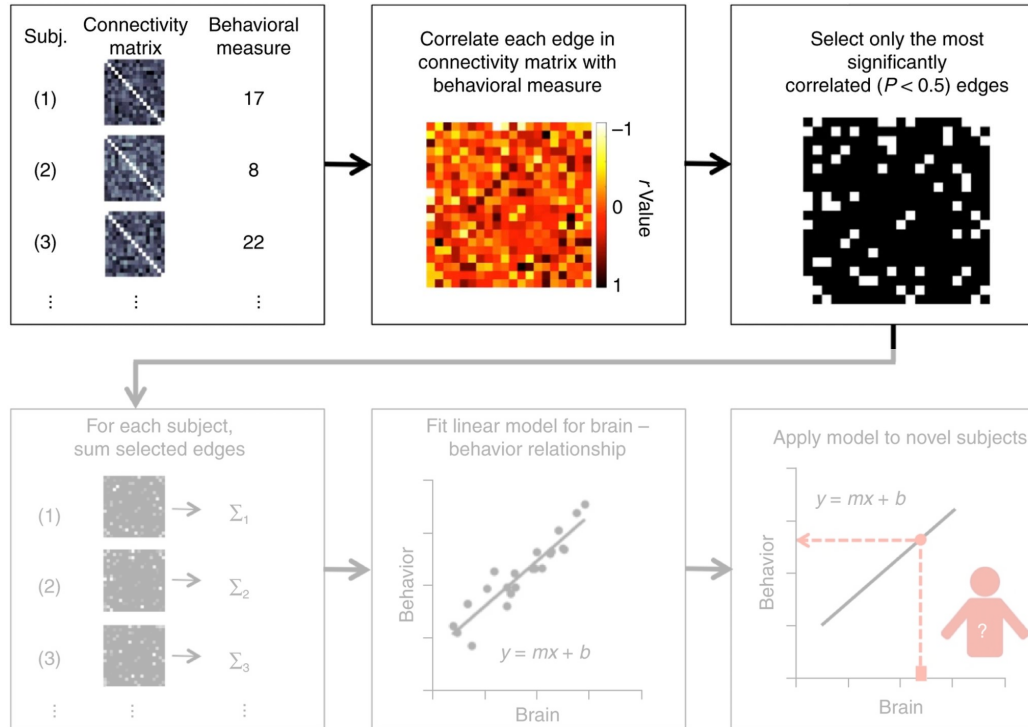
Shen et al (2017) *Nat. Protocols*

Connectome predictive modeling



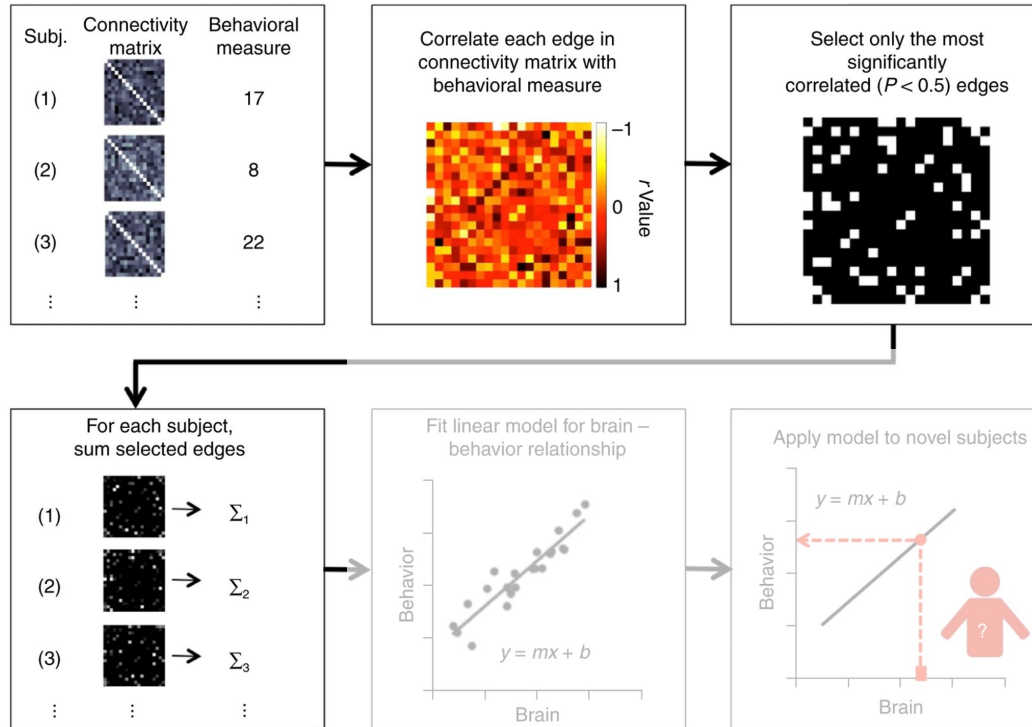
Shen et al (2017) *Nat. Protocols*

Connectome predictive modeling



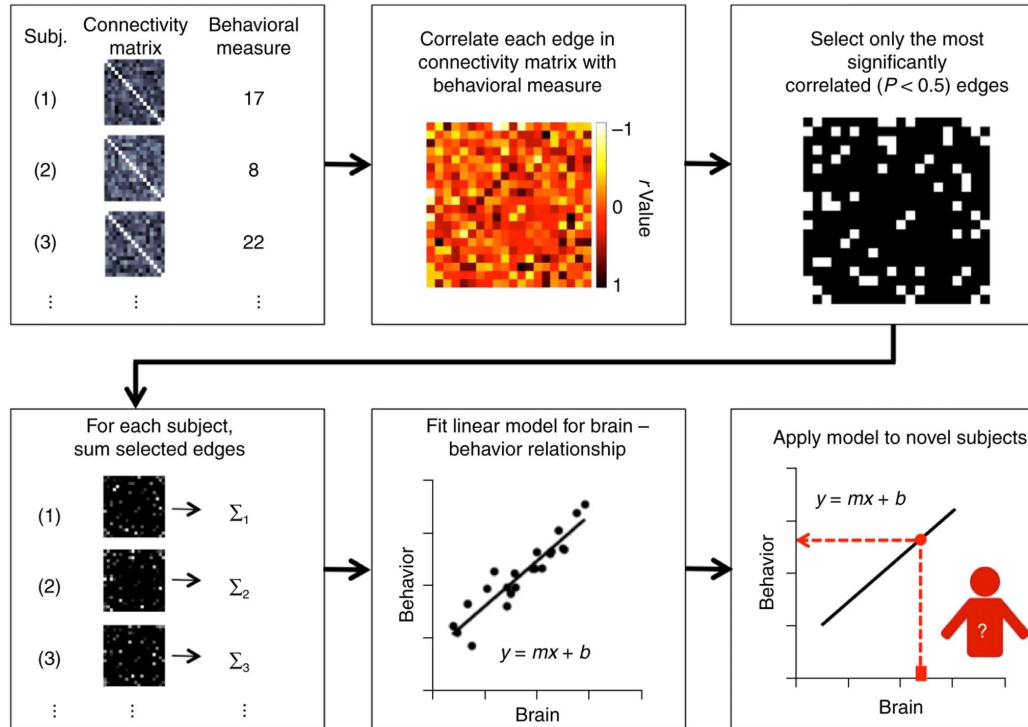
Shen et al (2017) *Nat. Protocols*

Connectome predictive modeling



Shen et al (2017) *Nat. Protocols*

Connectome predictive modeling

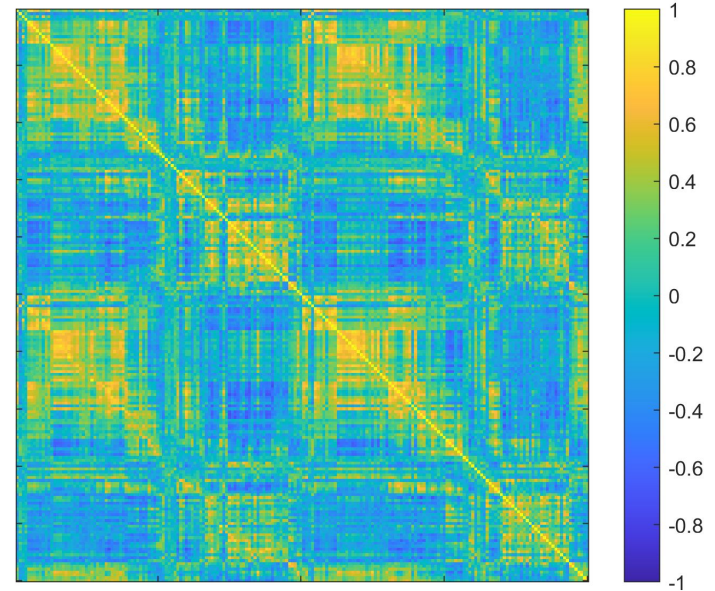


Shen et al (2017) *Nat. Protocols*

Reading direct from the FC matrix

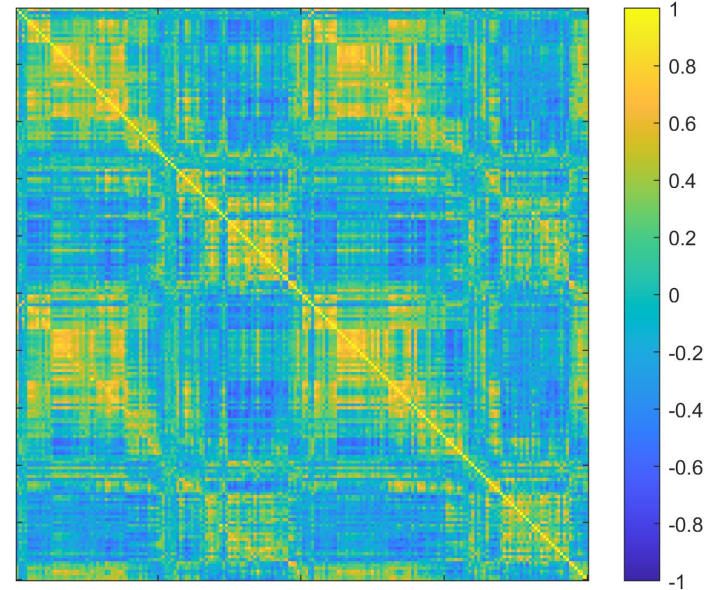
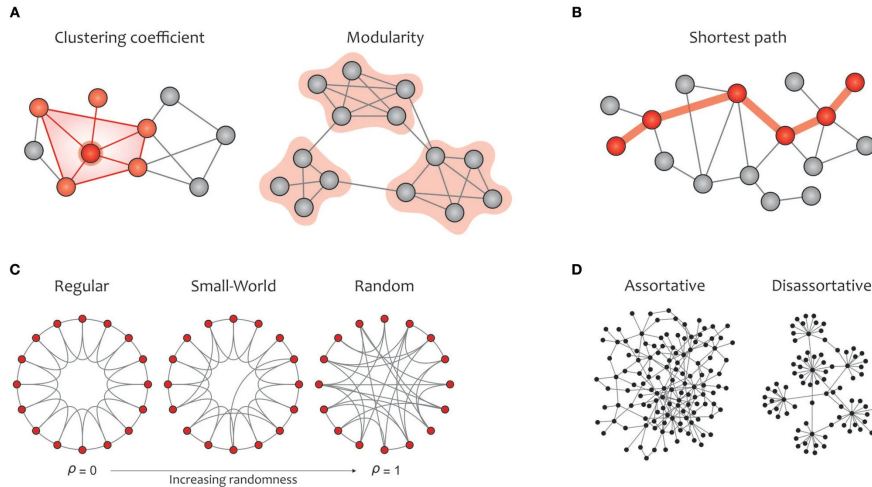
- The covered methods treat the r values contained within the matrix as the construct on which to perform analysis.

“I want to assess the significance, or link my results with, the numbers contained in the matrix”

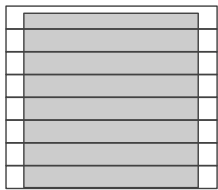
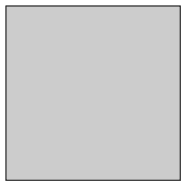


Looking for structure of FC matrix

- Finding **patterns** in this data is the result we are interested in...
- ...Using network algorithms!



Empirical network

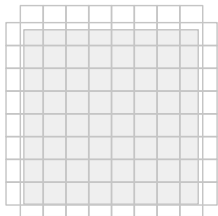
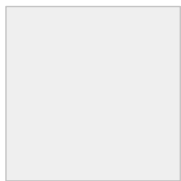


Apply algorithm to
read in data

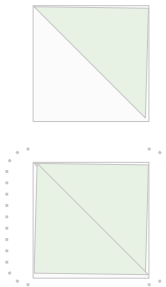


Node-wise
measure

Empirical network

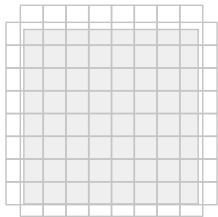
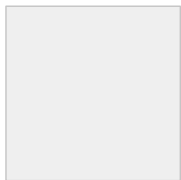


Apply algorithm to
read in data

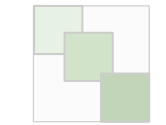


Edge-wise
measure

Empirical network

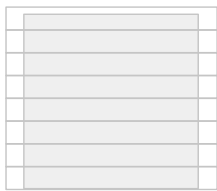
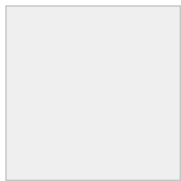


Apply algorithm to
read in data

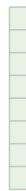


Pattern identification

Empirical network

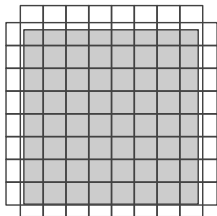
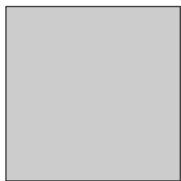


Apply algorithm to
read in data

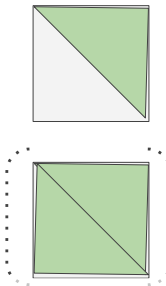


Node-wise
measure

Empirical network

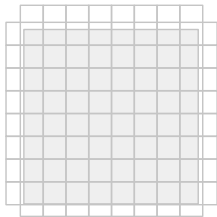
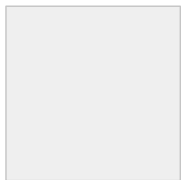


Apply algorithm to
read in data

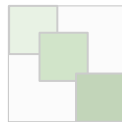


Edge-wise
measure

Empirical network

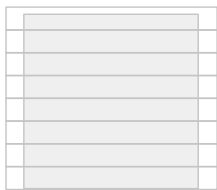
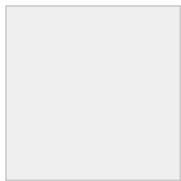


Apply algorithm to
read in data

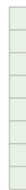


Pattern identification

Empirical network

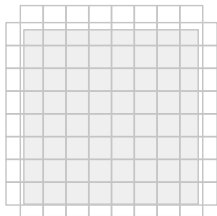
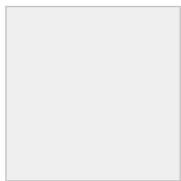


Apply algorithm to
read in data

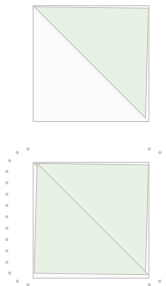


Node-wise
measure

Empirical network

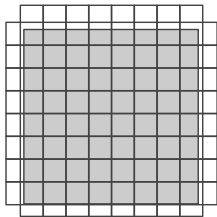
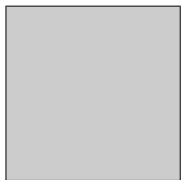


Apply algorithm to
read in data

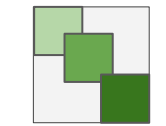


Edge-wise
measure

Empirical network

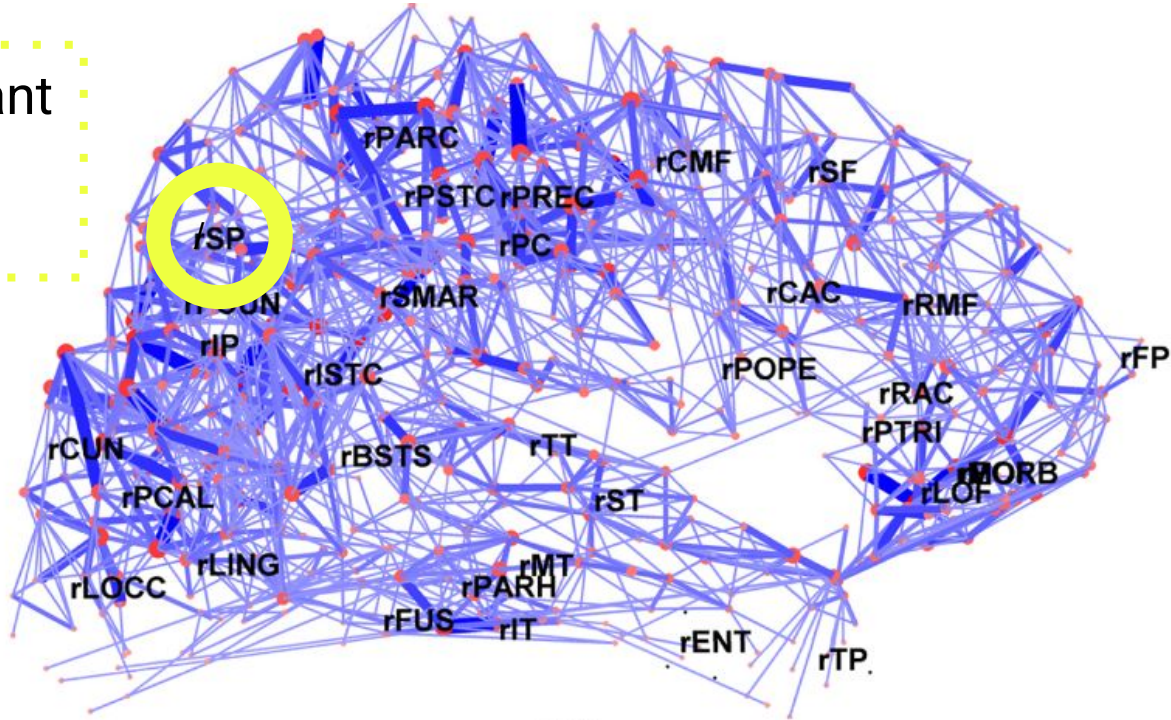


Apply algorithm to
read in data

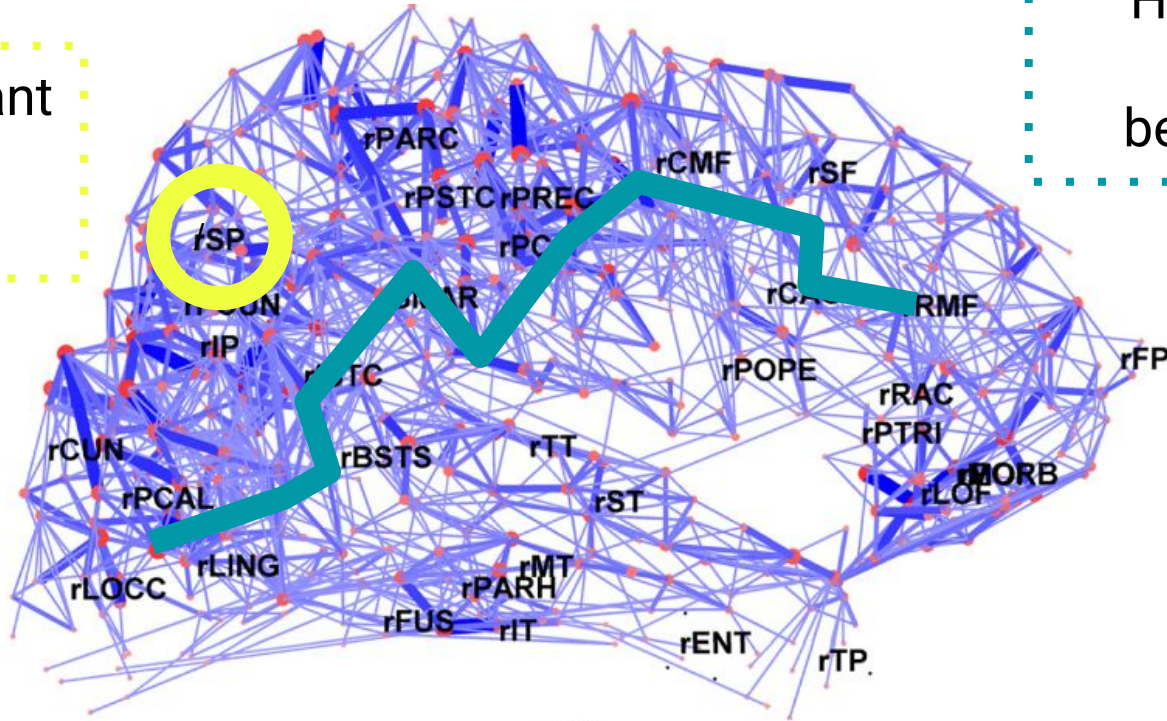


Pattern identification

How important
are certain
nodes?



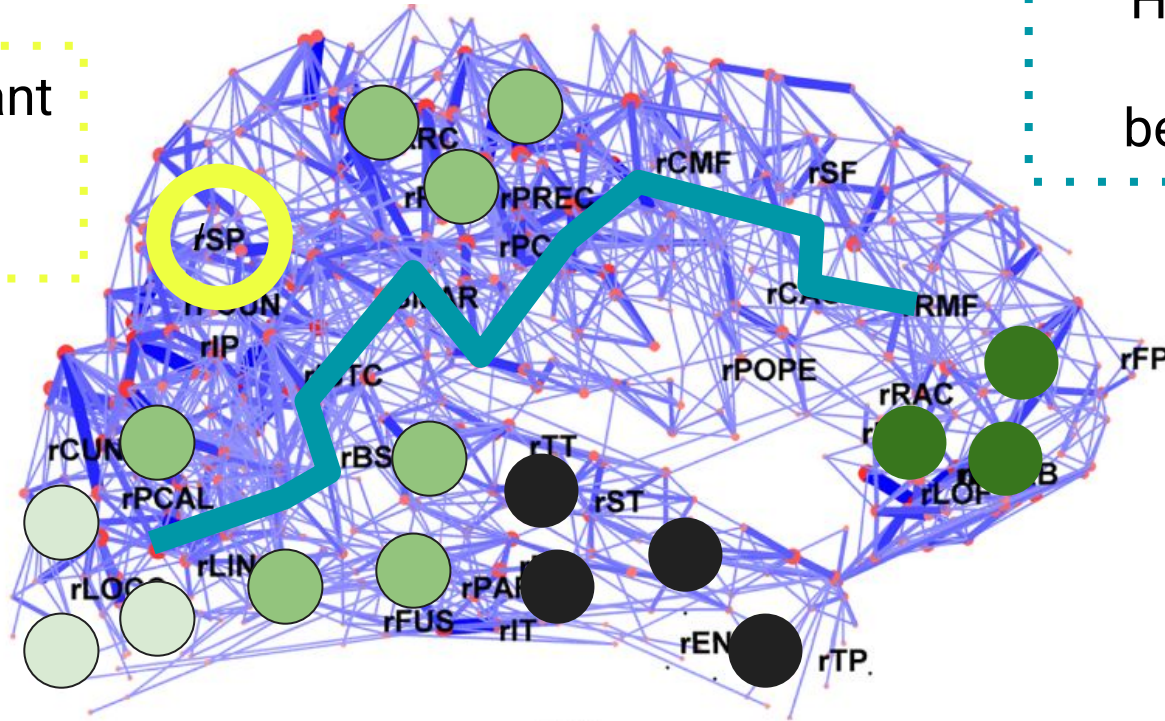
How important
are certain
nodes?



How are signals
transmitted
between nodes?

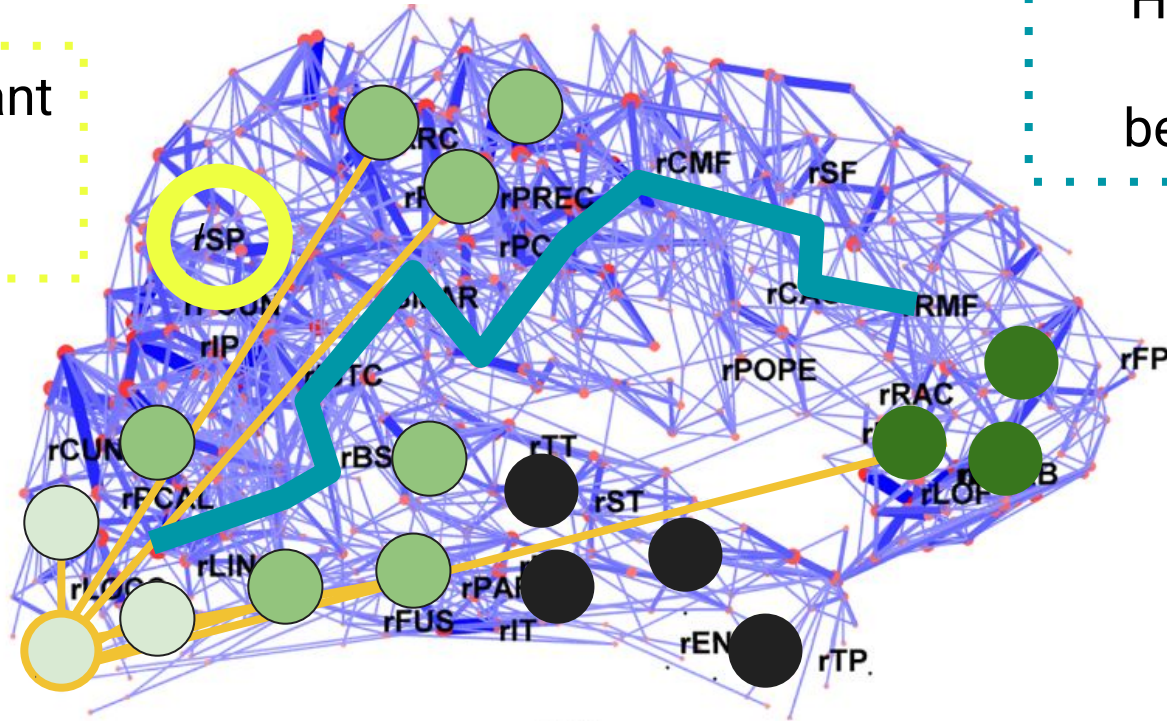
- How important are certain nodes?

How are signals transmitted between nodes?



Which groups of nodes can be meaningfully grouped?

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

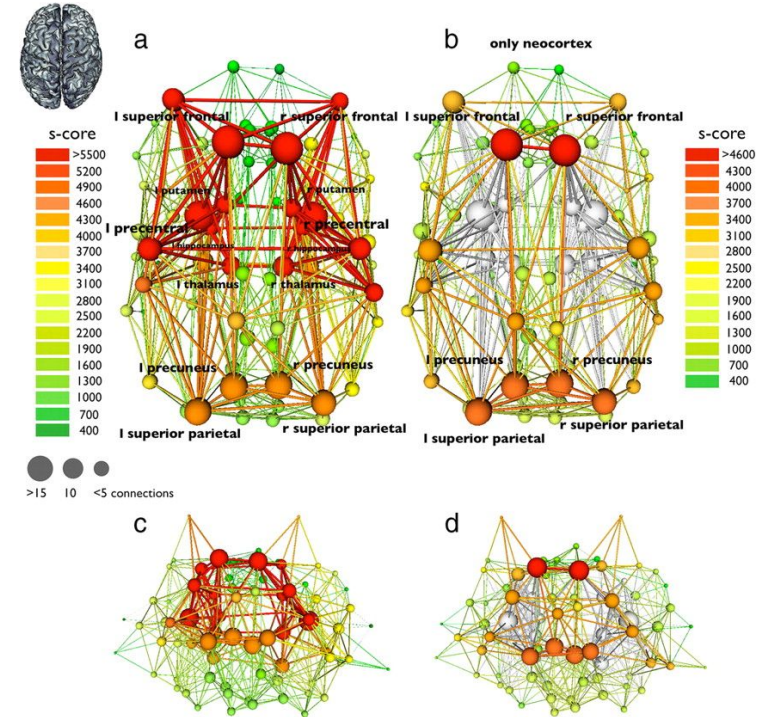
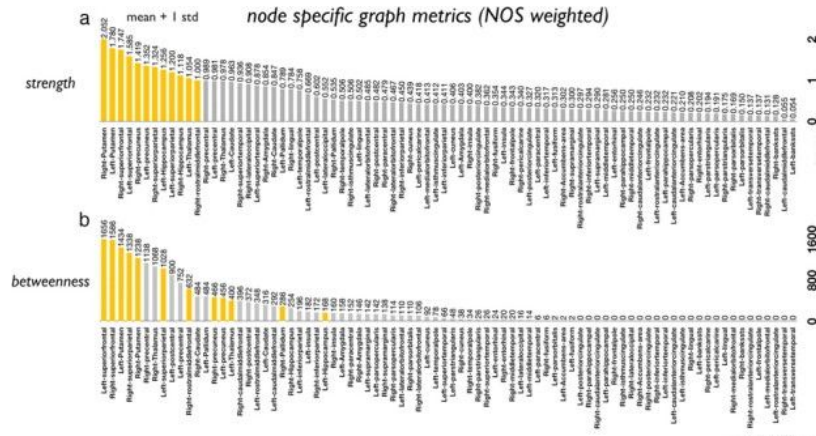
Which groups of nodes can be
meaningfully grouped?

Network approaches

- How important are certain nodes?
- How are signals transmitted between nodes?
- Which groups of nodes can be meaningfully grouped?
- How can we interpret this area of the brain in the context of its connections

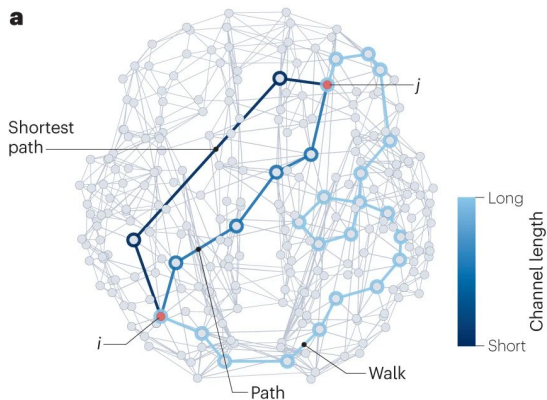
Network approaches

- How important are certain nodes?
 - Measure the degree, strength, centrality of each node

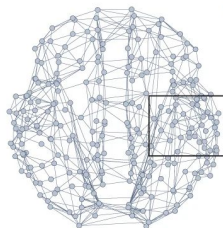
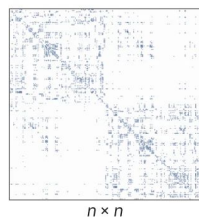


Network approaches

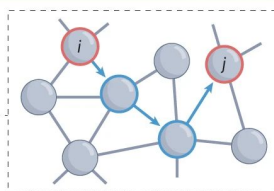
- How are signals transmitted between nodes?



b
Structural connectivity

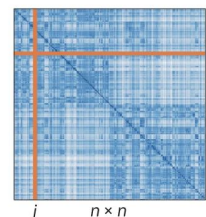


Network communication

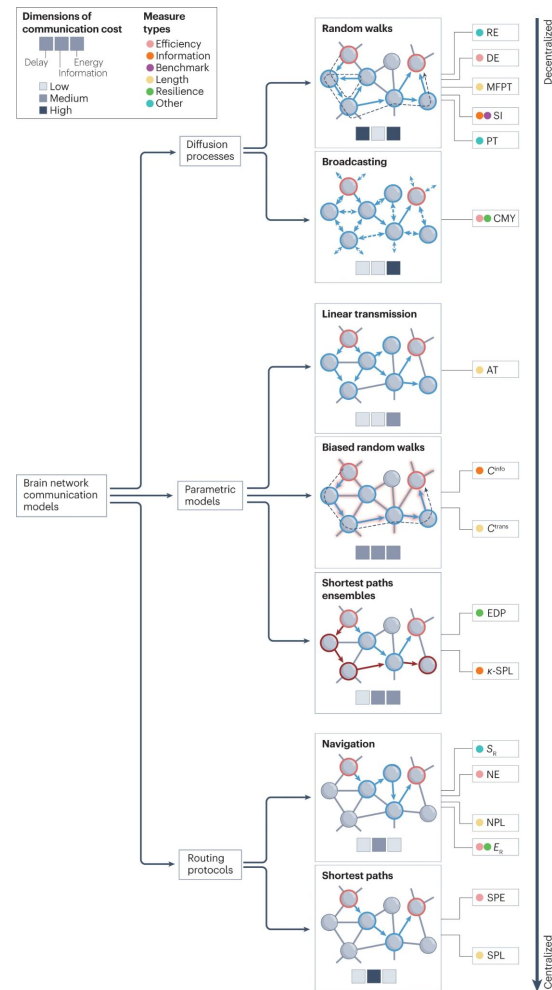


- Model**
- Signalling conceptualization
 - Propagation algorithm
- Measure**
- Signalling quantification

Communication matrix

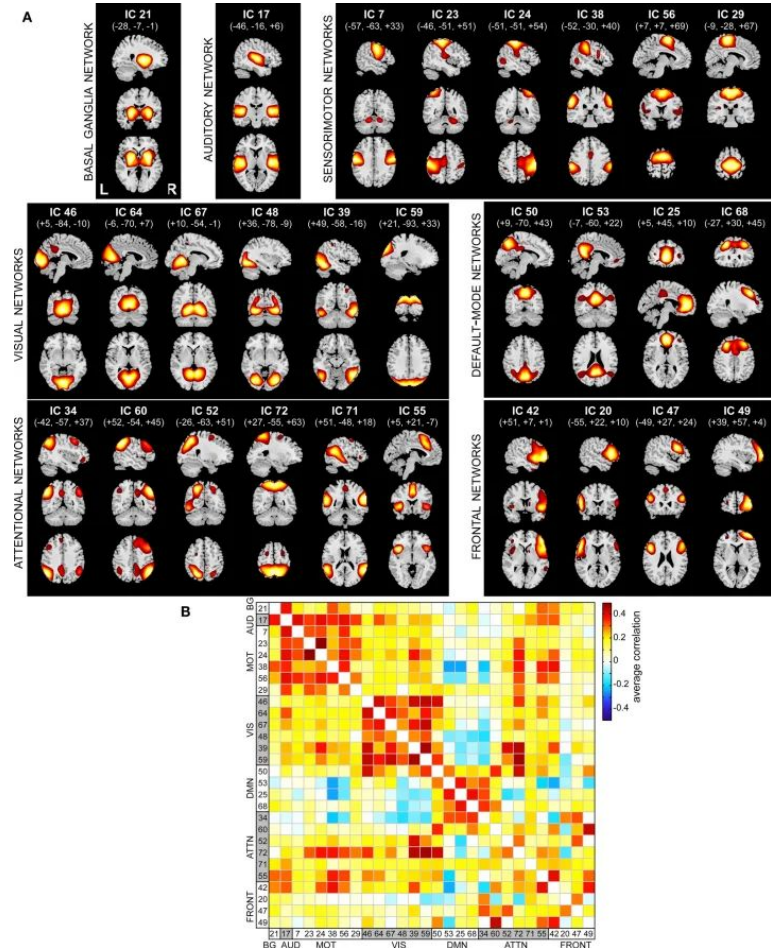


Seguin et al (2023)
Nat. Rev. Neuro.



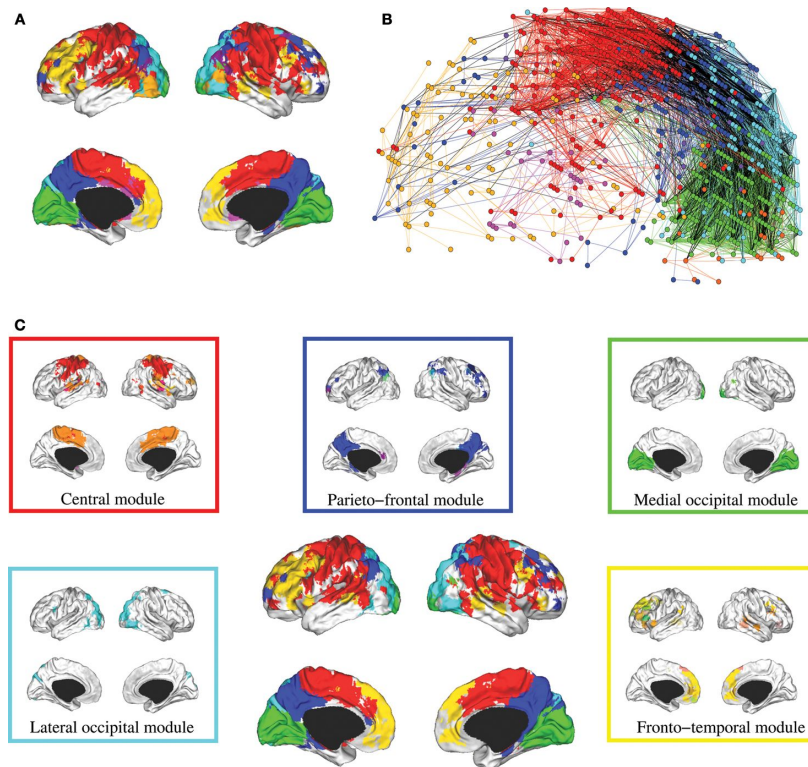
Network approaches

- Which groups of nodes can be meaningfully grouped?
 - Clustering algorithms that seek to bundle nodes (or time series) into coherent groups



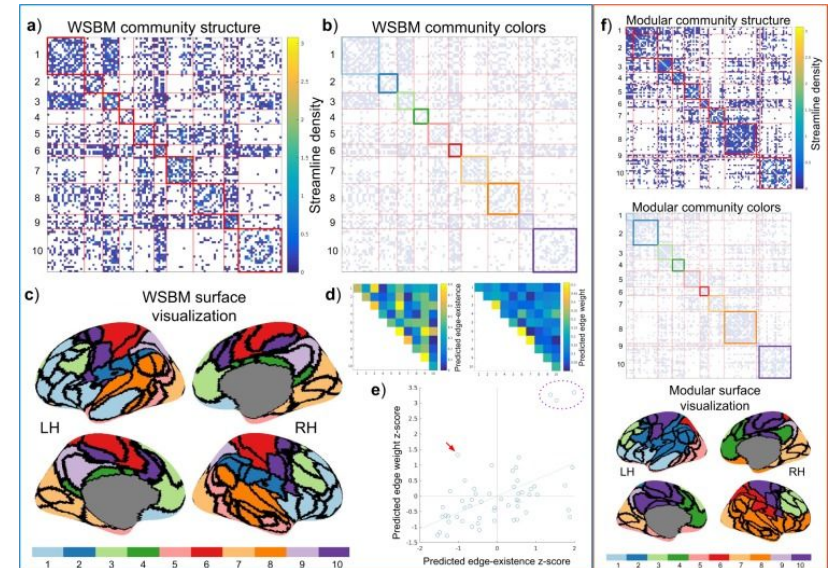
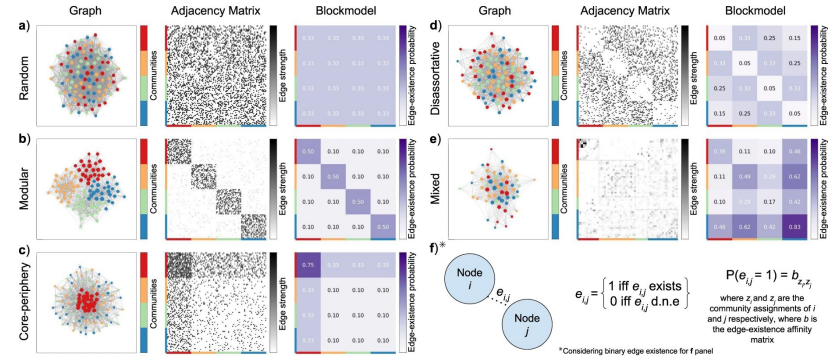
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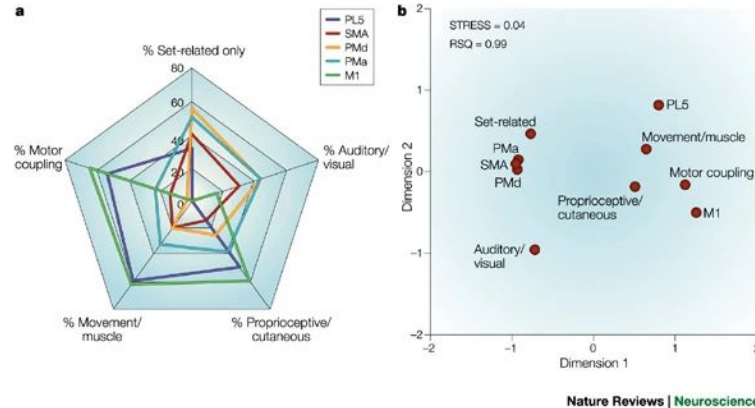
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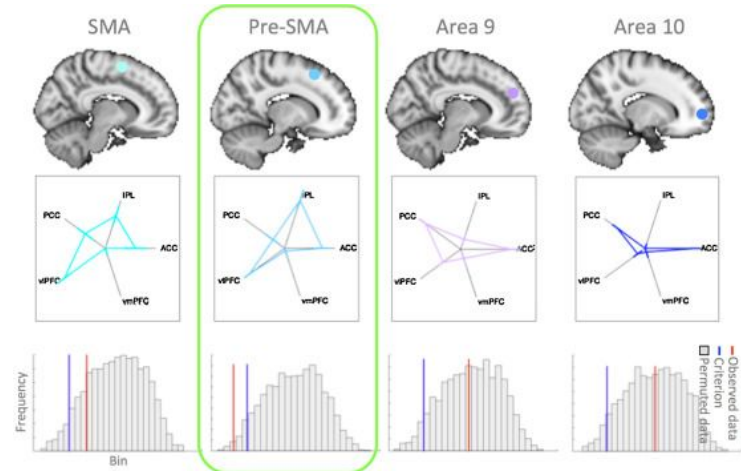


Network approaches

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

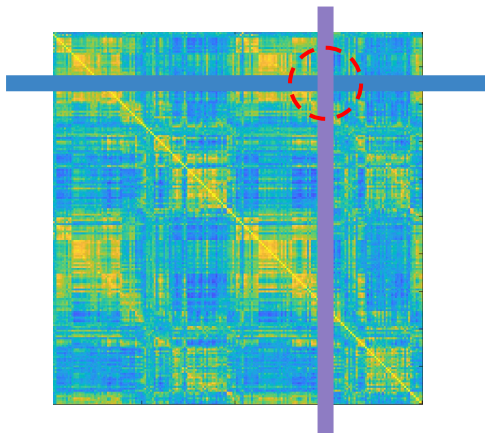


Passingham et al (2002). *Nat. Rev. Neuro*

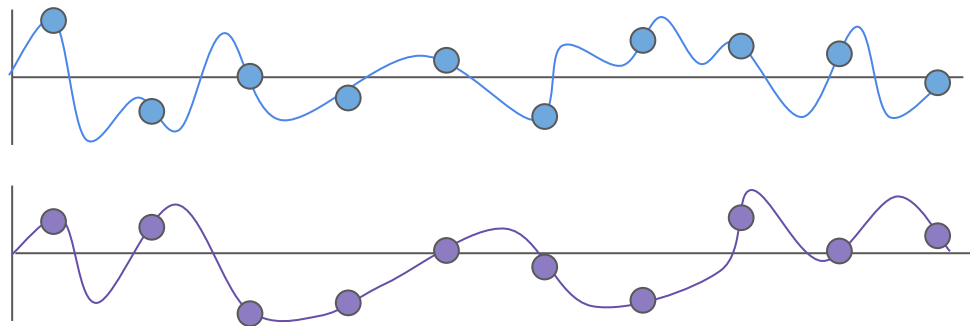
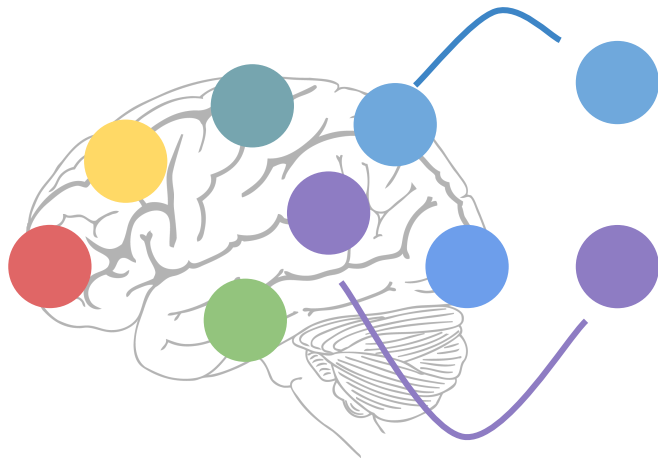


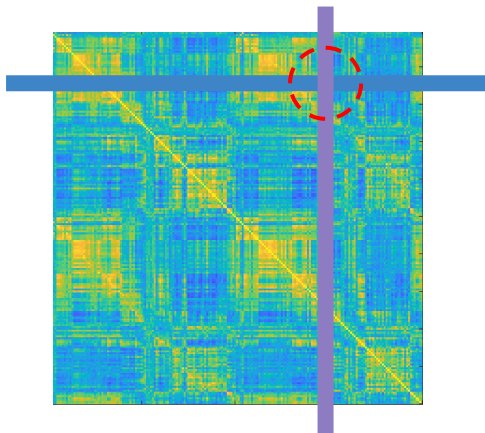
Mars et al (2016). *Neuro. & Biobehav. Rev.*

Let's revisit the FC matrix

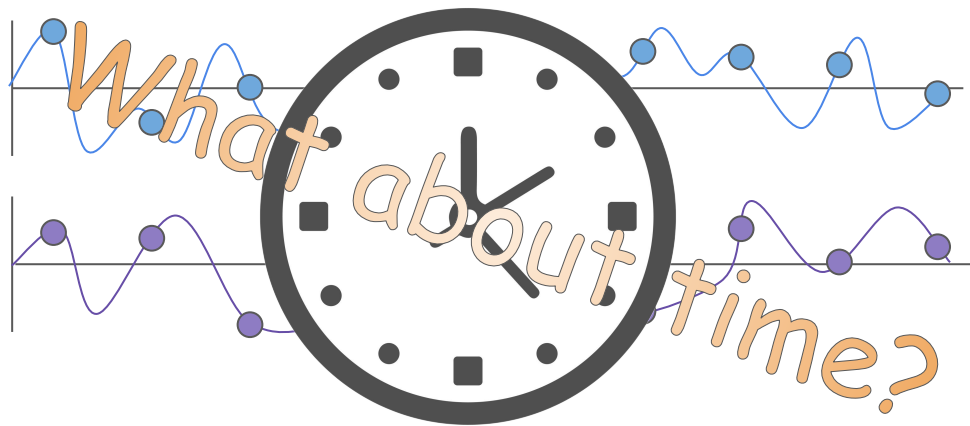
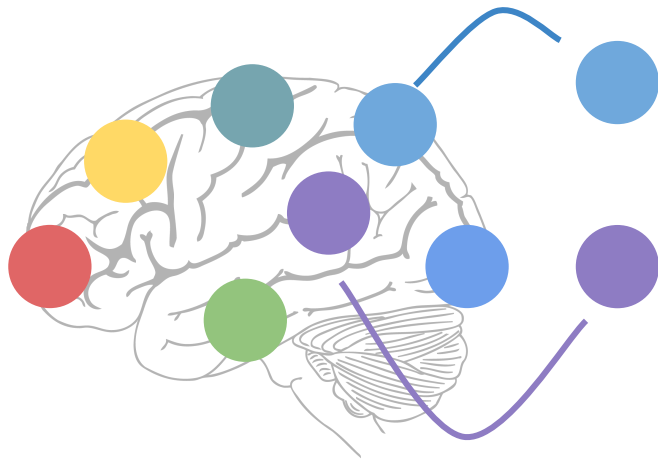


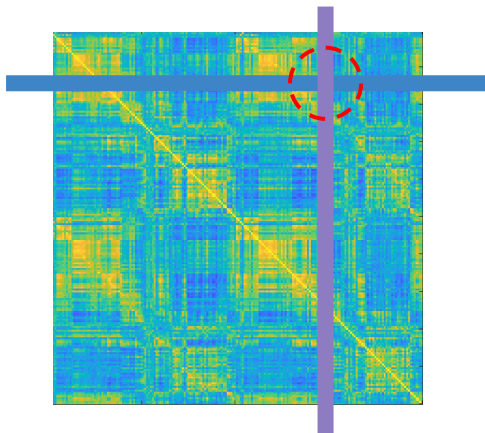
- Time averaged
 - Similarity across your whole acquisition
 - Use all your (good) time points
 - Assess “coupling” between areas or systems
 - “Functional organization” as trait phenotype



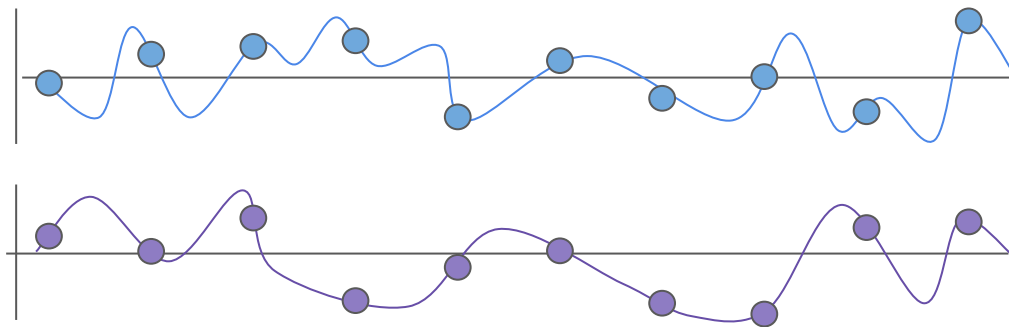
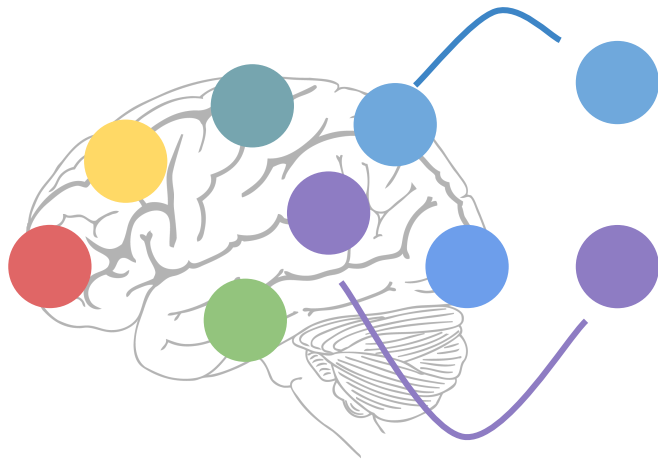


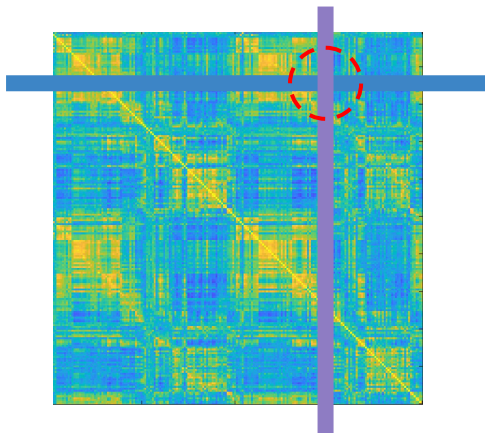
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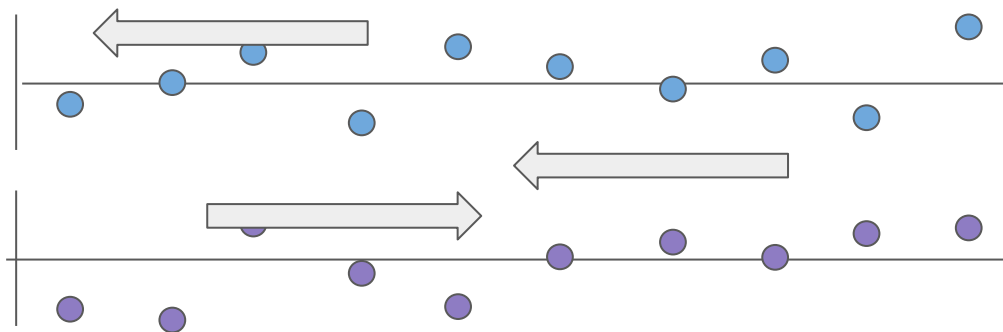
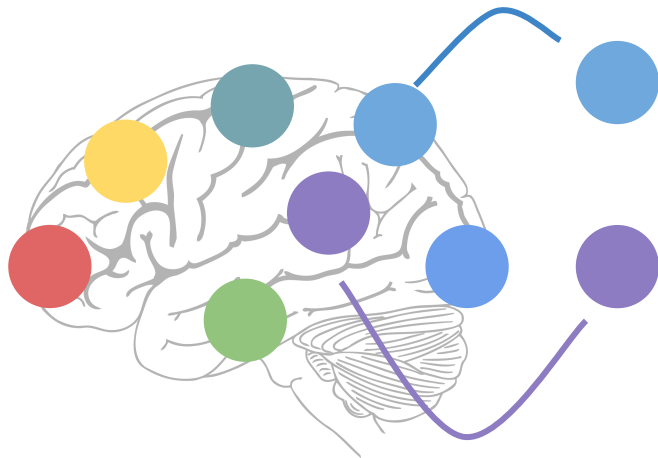


- Time averaged
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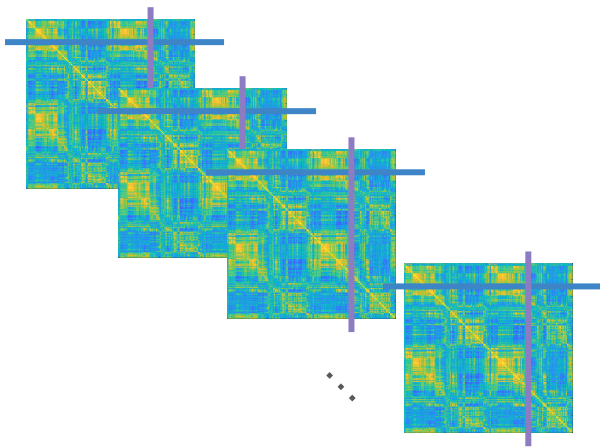




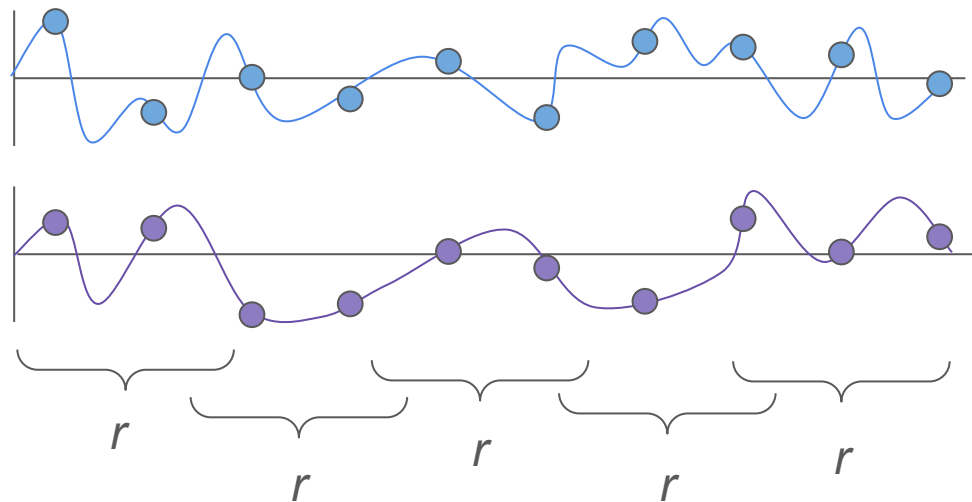
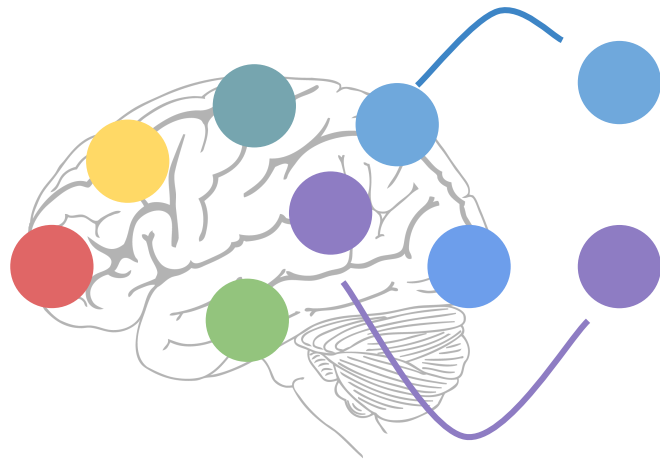
- Time averaged
 - Similarity across your whole acquisition
 - Use all your (good) time points
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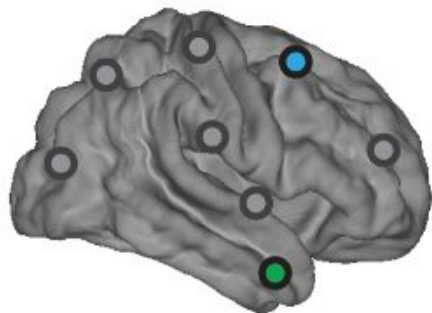
Time averaged FC doesn't care about the temporal succession of datapoints. Therefore, if you scramble the (paired) timepoint, you'll get the same overall r value



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



A



brain network
nodes

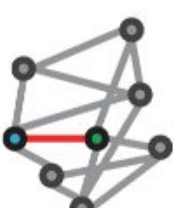
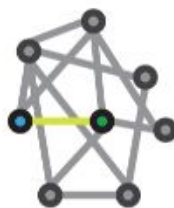


time
windows

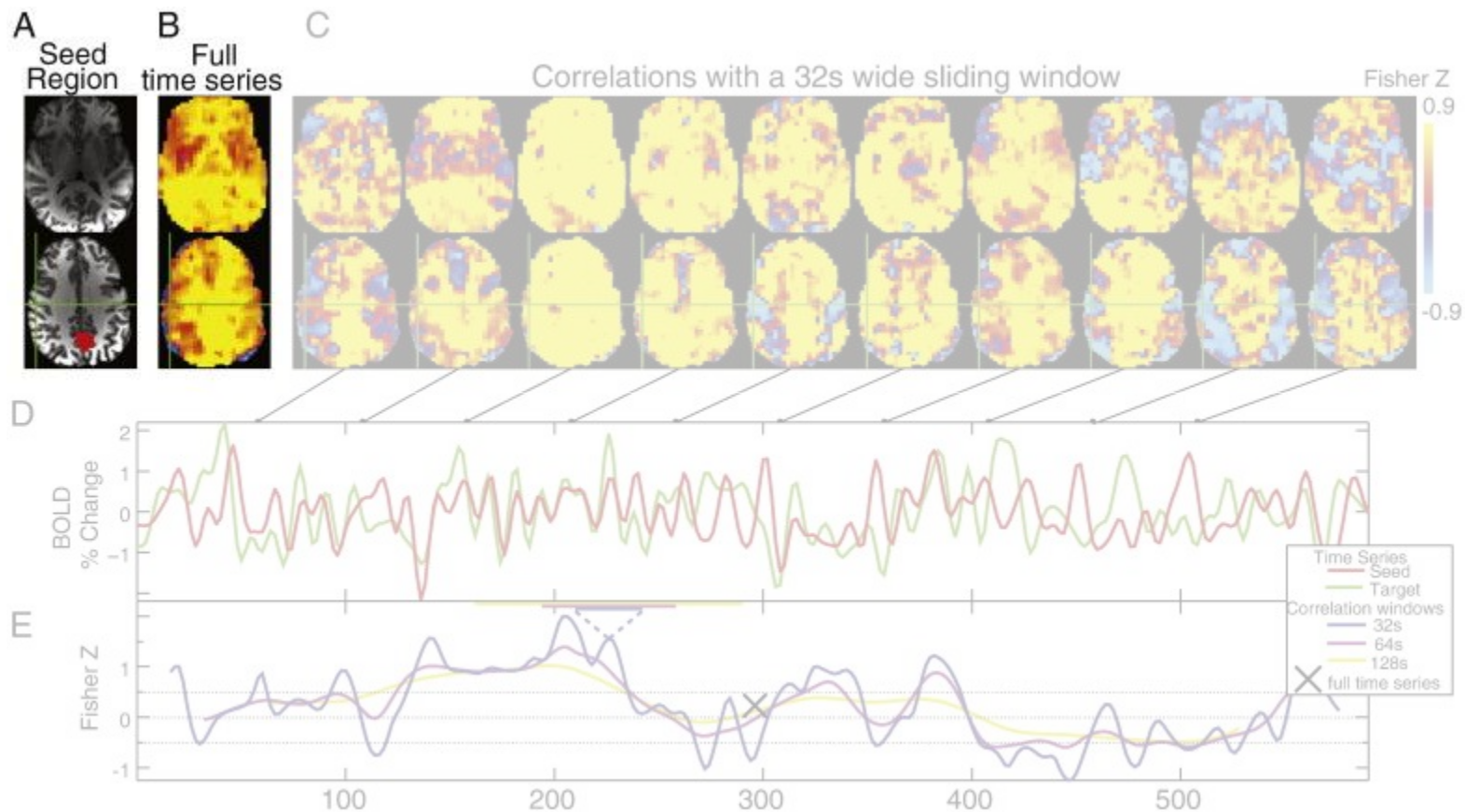
$r \doteq 0.20$ $r \doteq 0.29$ $r \doteq 0.25$ $r \doteq 0.60$

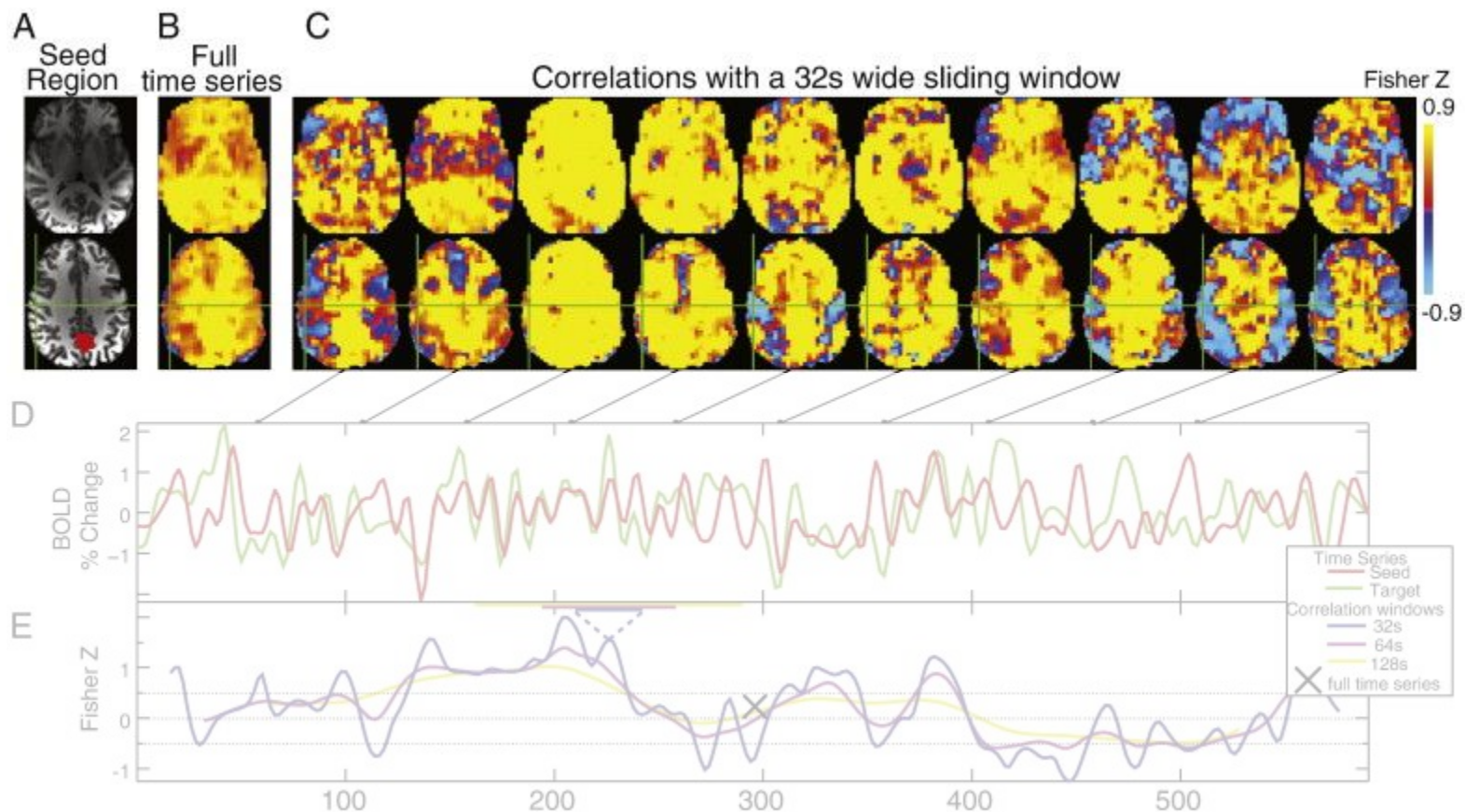


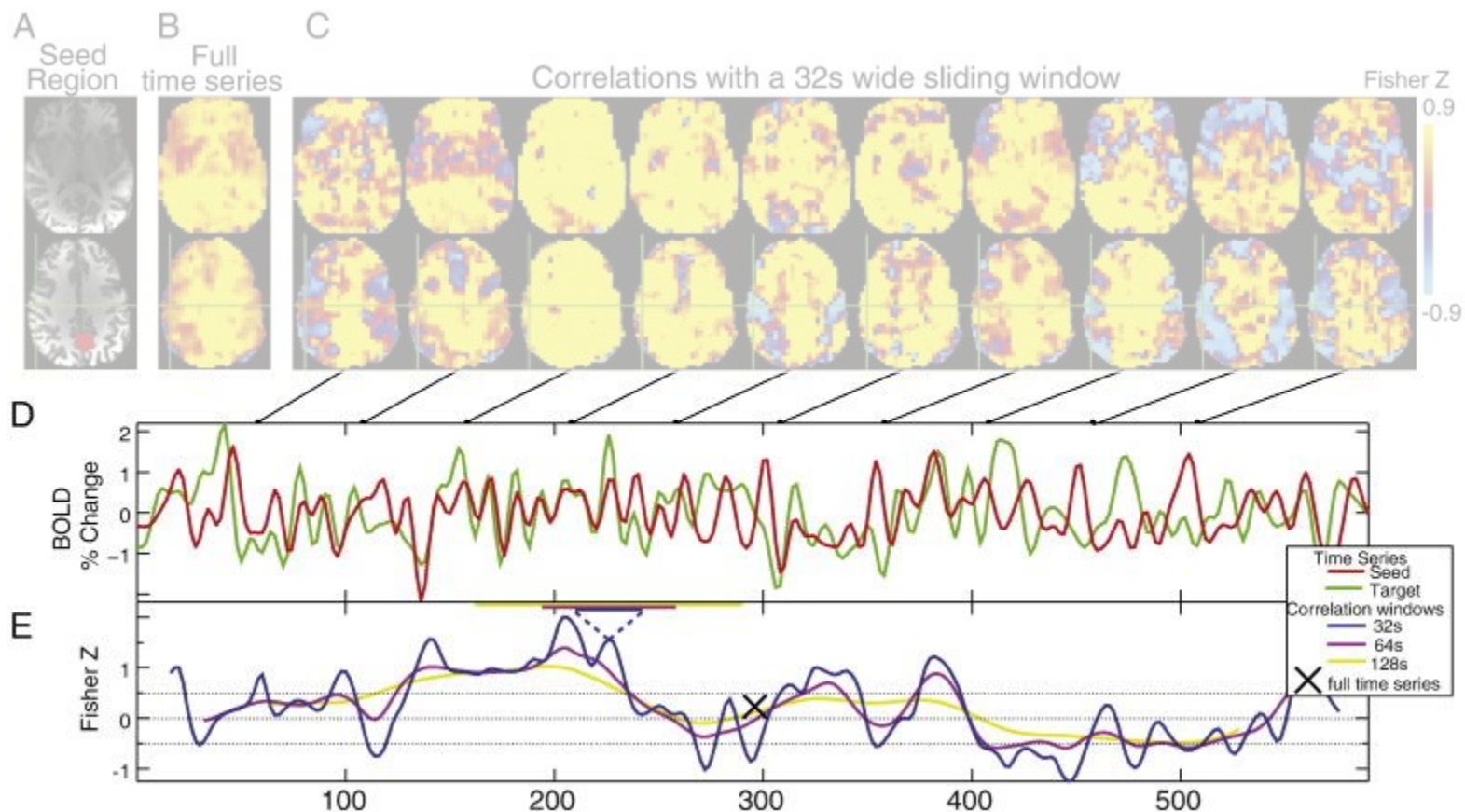
pairwise
coherence



temporal
networks

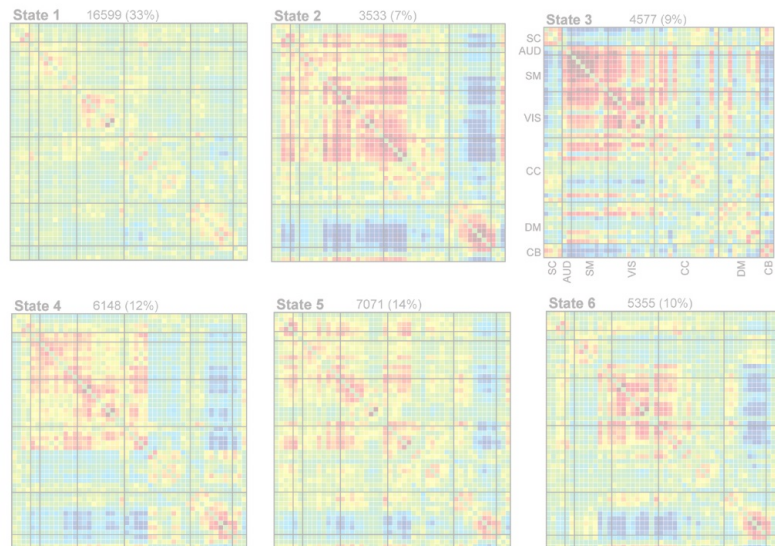
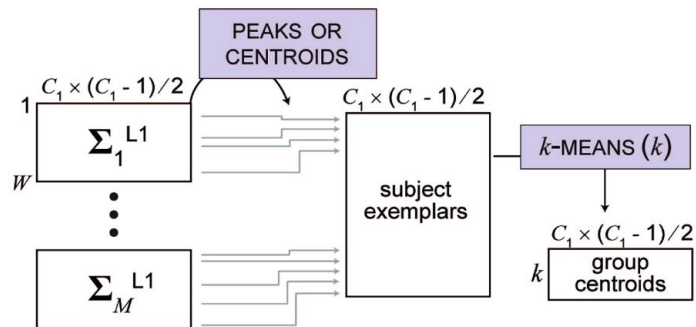






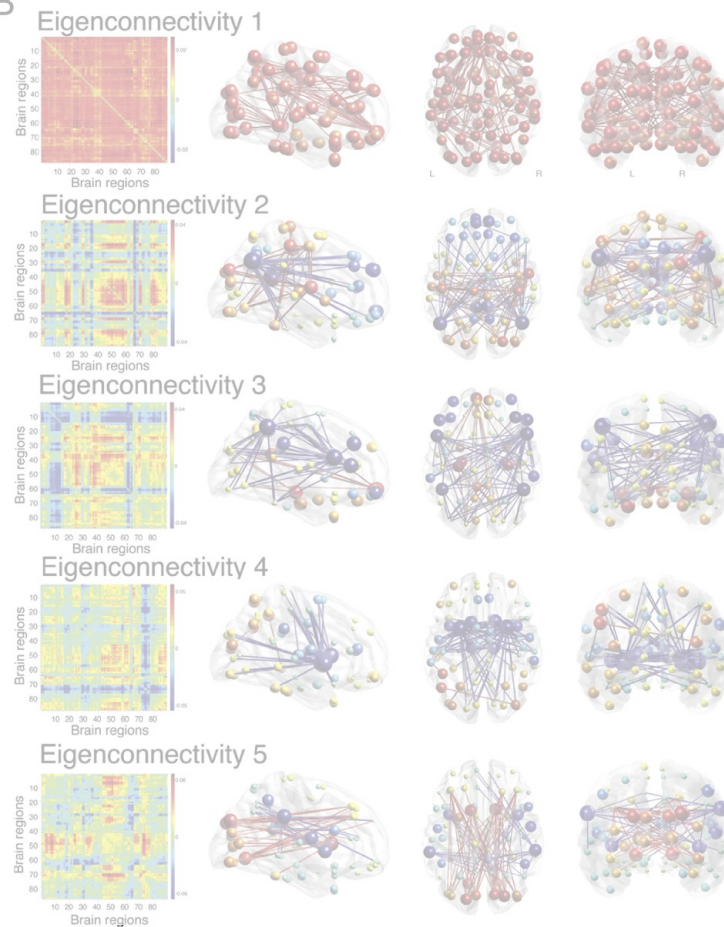
A

CLUSTERING APPROACH



dFC states

B

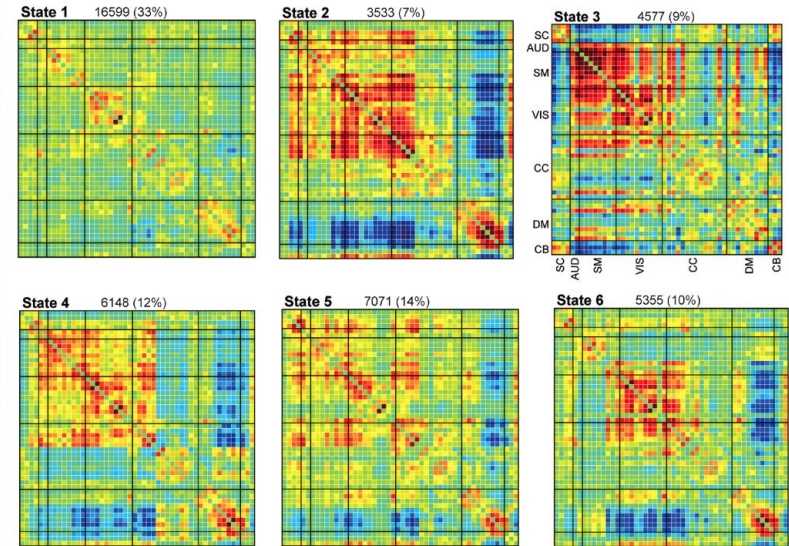


Preti et al. (2016).
NeuroImage

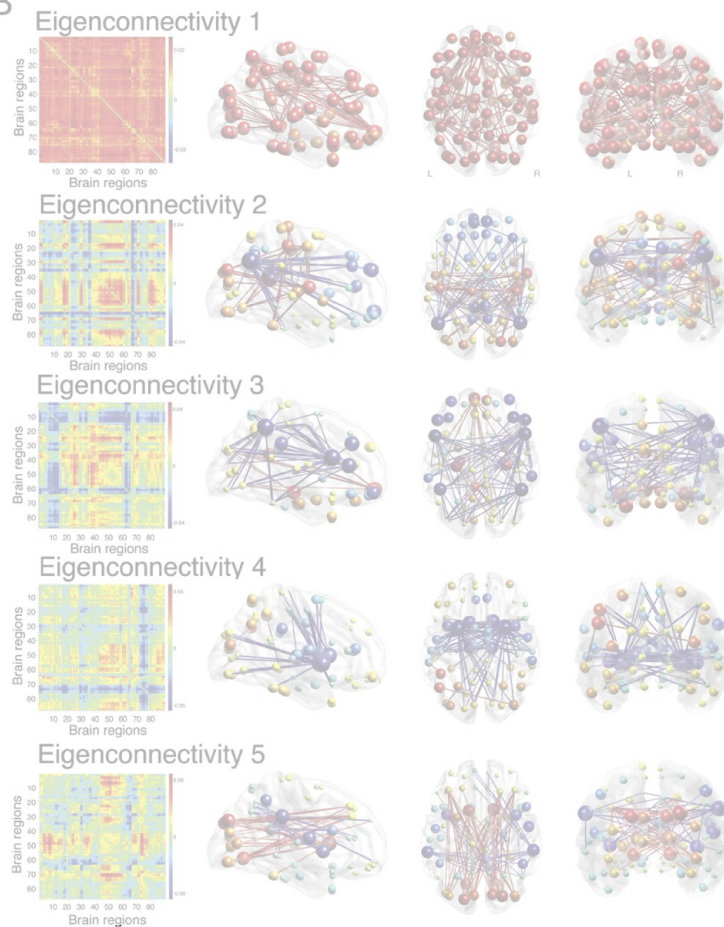
Allen et al. (2014).
Cere. Cor.

Leonardi et al.
(2013). *NeuroImage*.

A



B

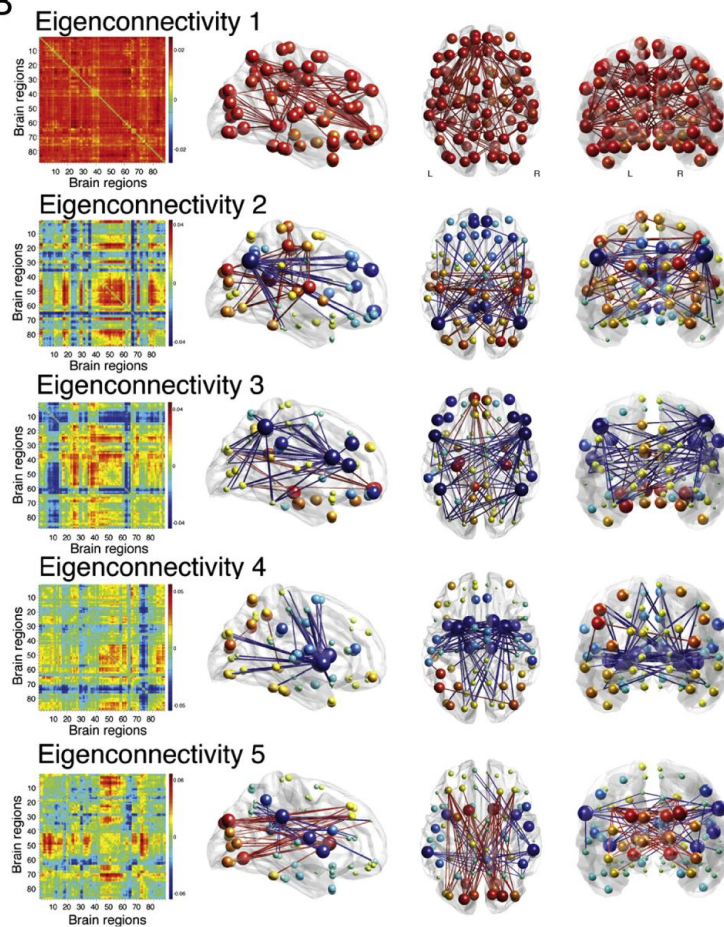


Leonardi et al.
(2013). *NeuroImage*.

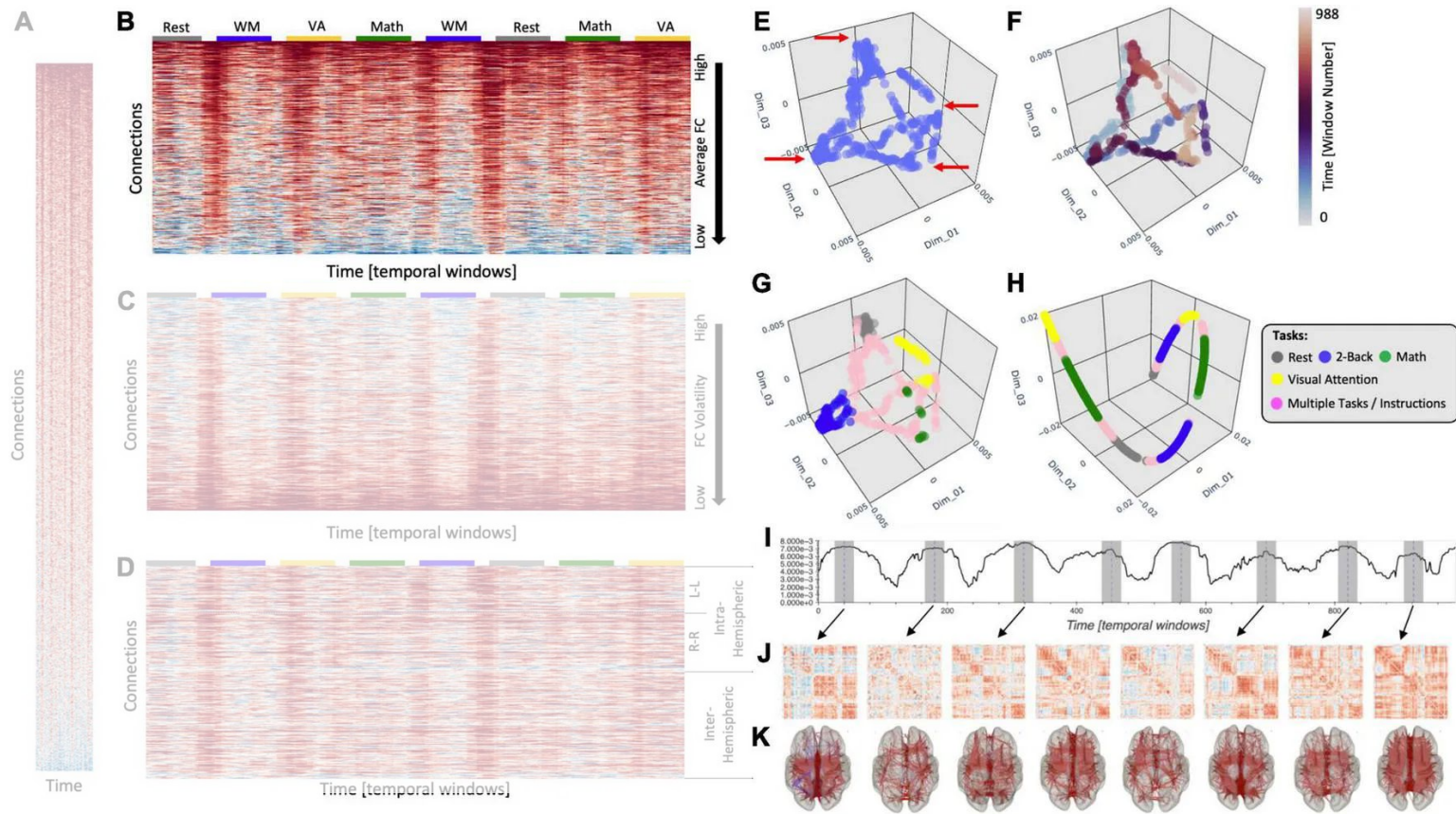
A



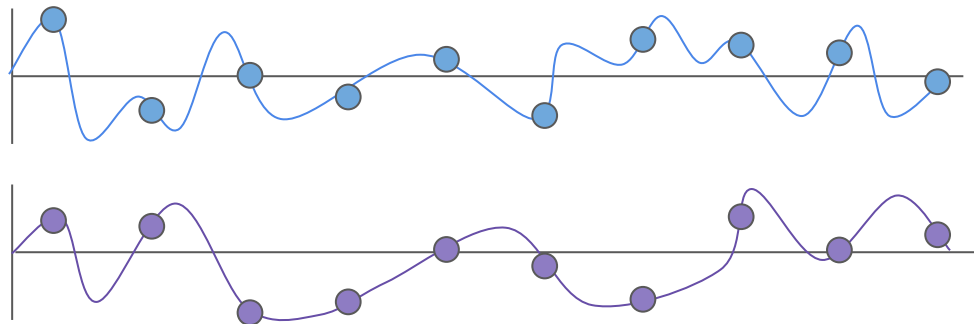
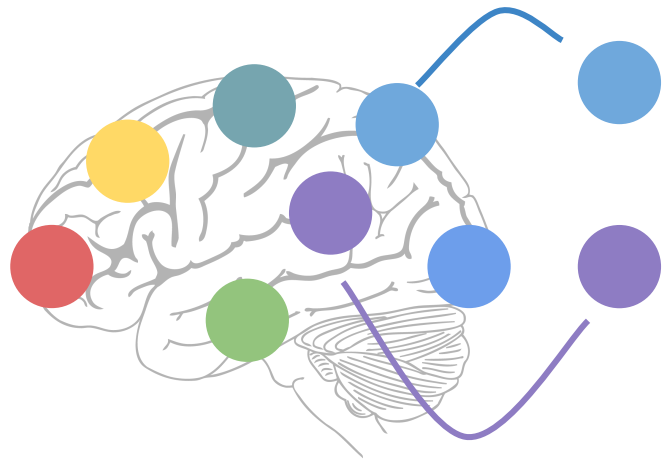
B

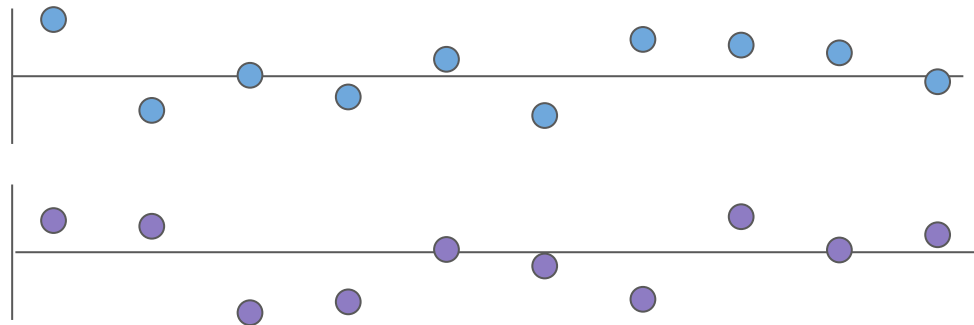
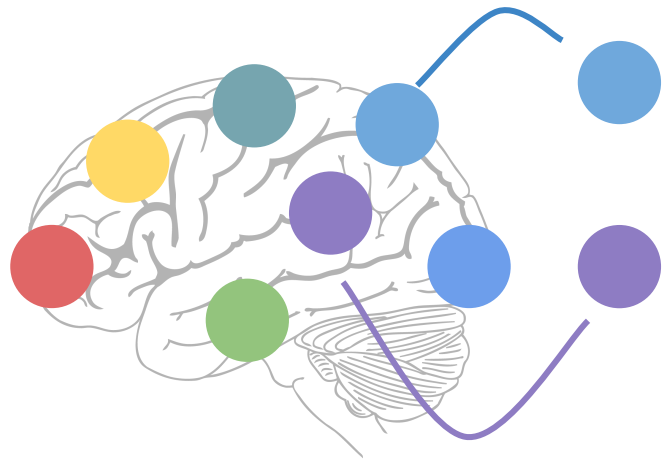


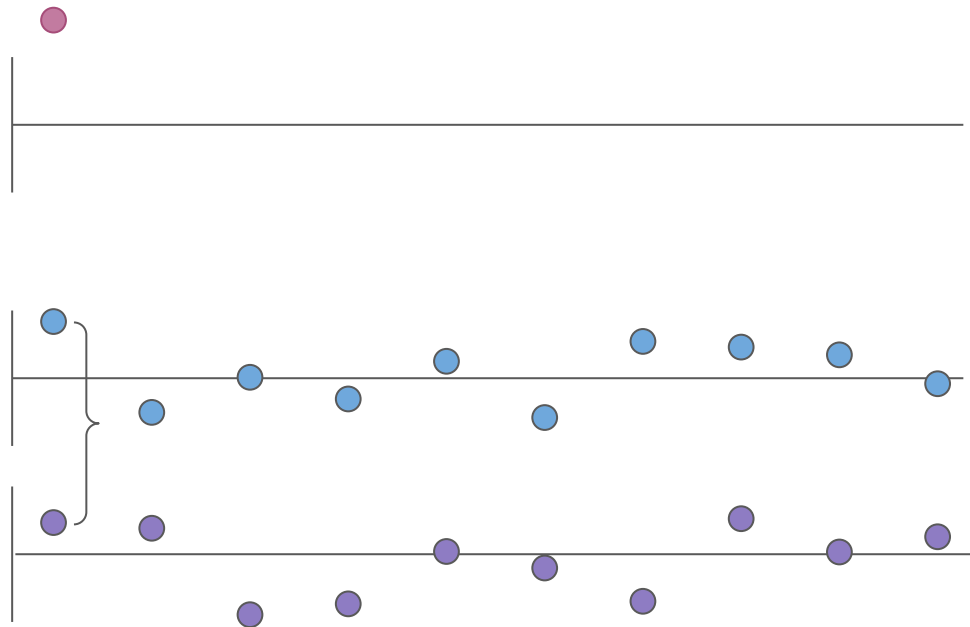
Leonardi et al.
(2013). *NeuroImage*.

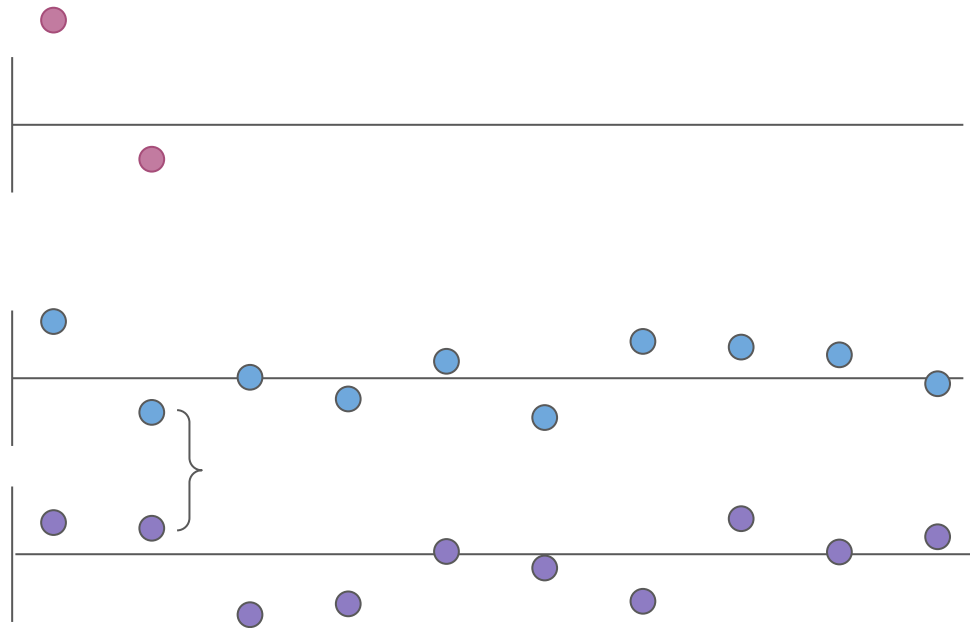


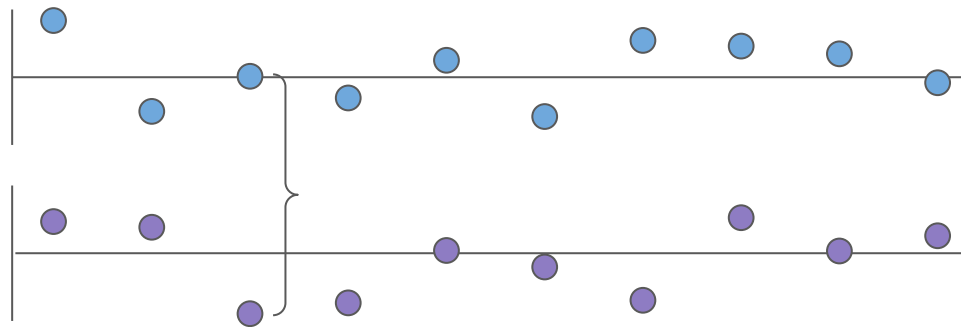
Let's revisit product-moment correlation
(Pearson)

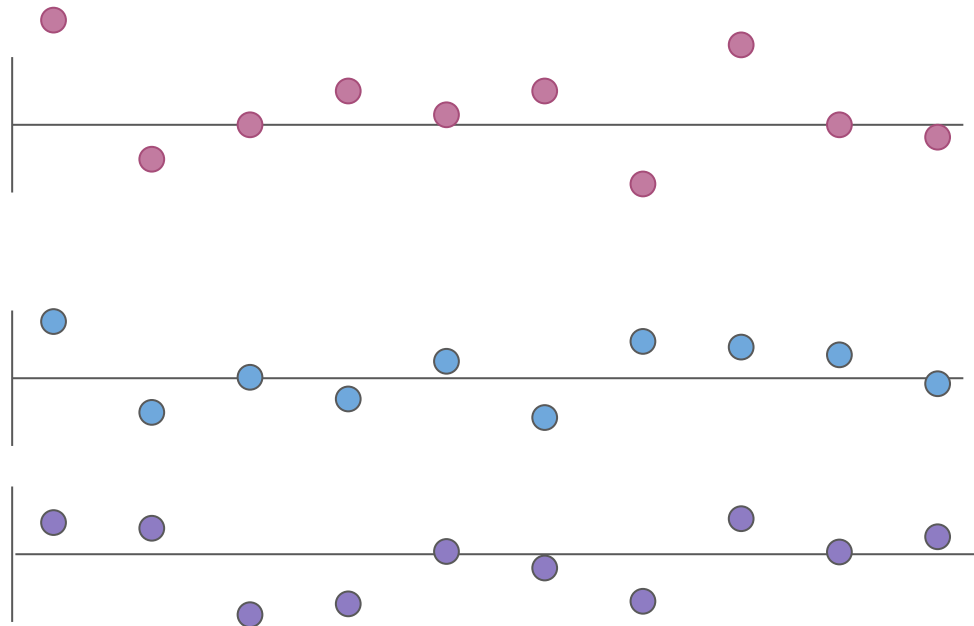


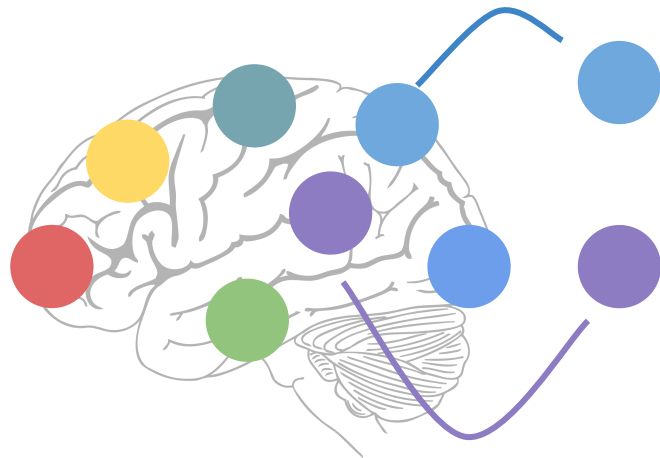












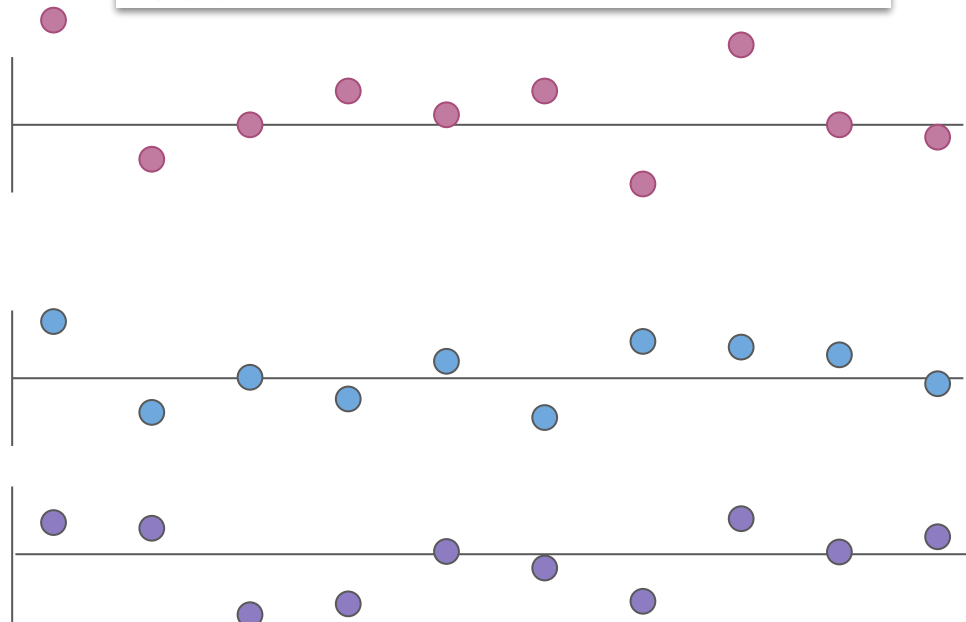
An equivalent expression gives the formula for r_{xy} as the mean of the products of the **standard scores** as follows:

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

where

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

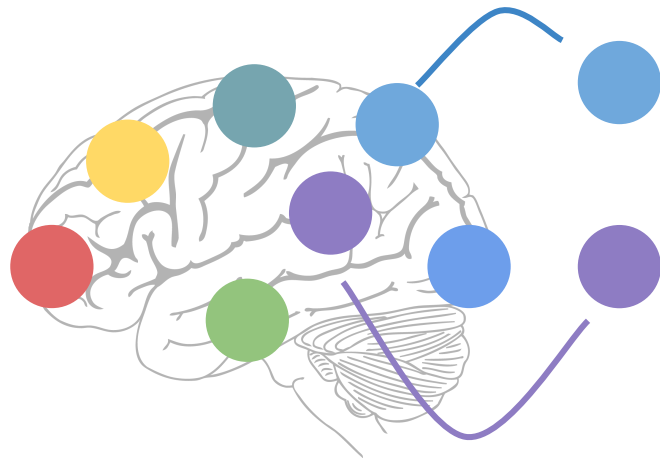
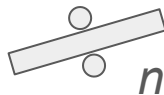
$\left(\frac{x_i - \bar{x}}{s_x} \right)$ is the **standard score** (and analogously for the standard score of y)



0.25



Σ



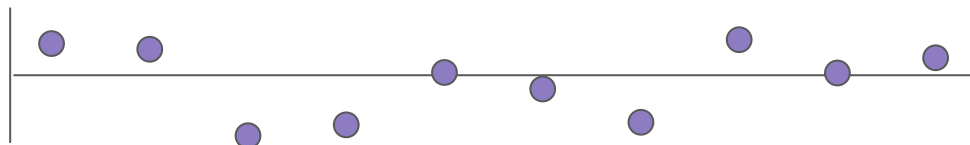
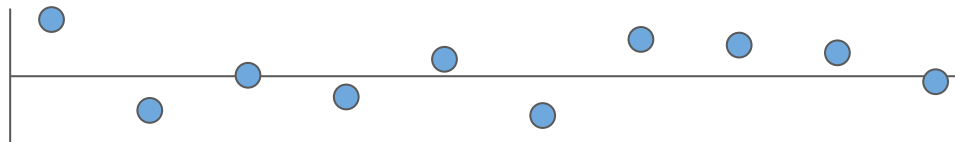
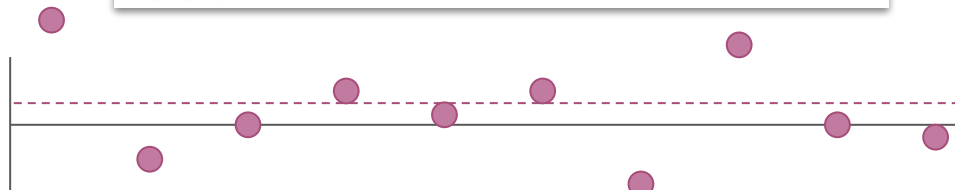
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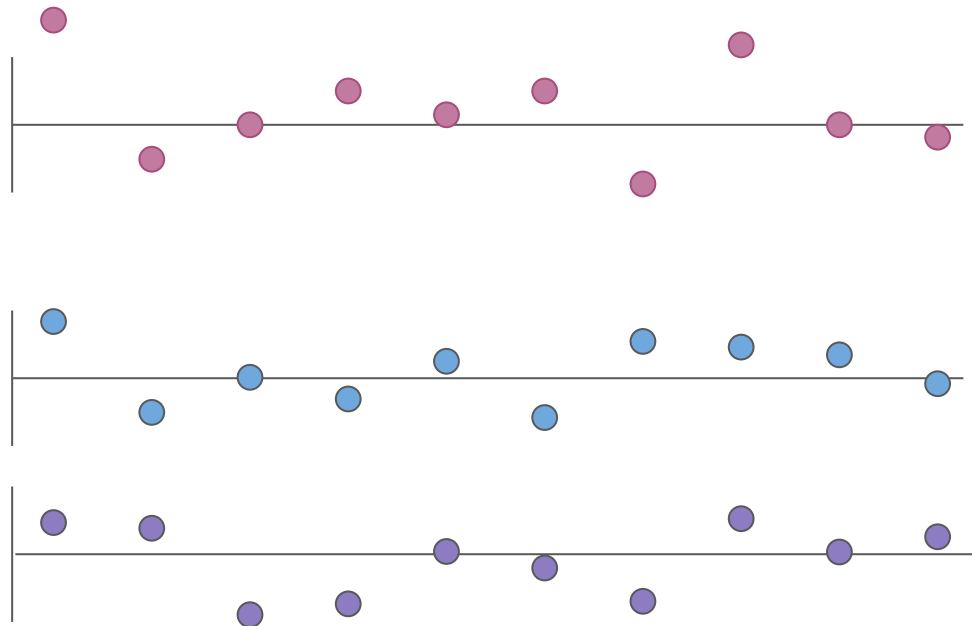
where

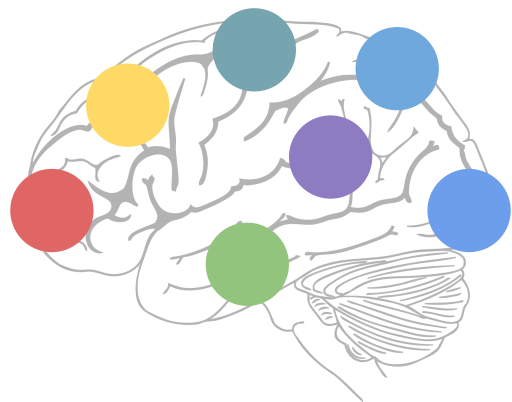
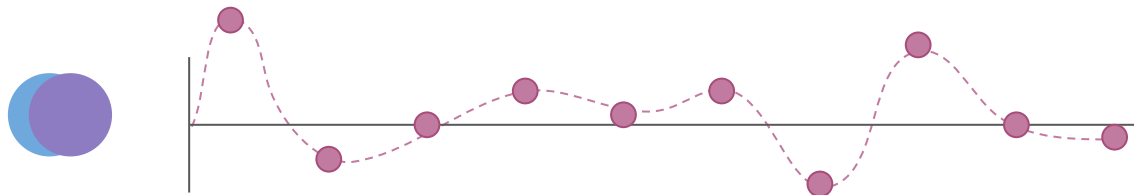
$n, x_i, y_i, \bar{x}, \bar{y}$ are defined as above, and s_x, s_y are defined below

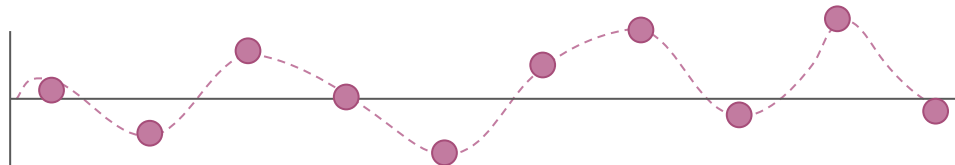
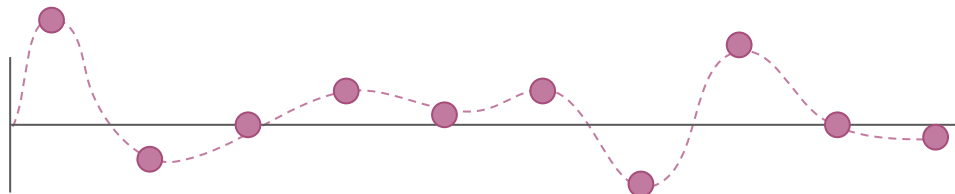
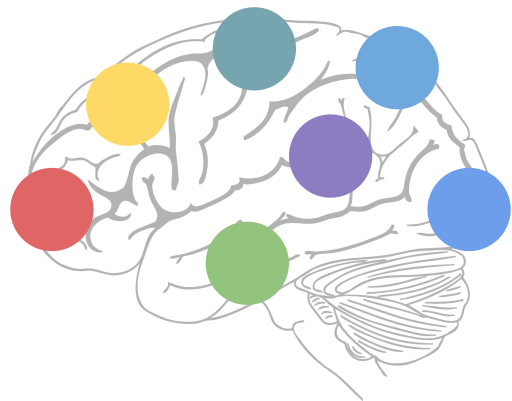
$\left(\frac{x_i - \bar{x}}{s_x} \right)$ is the **standard score** (and analogously for the standard score of y)



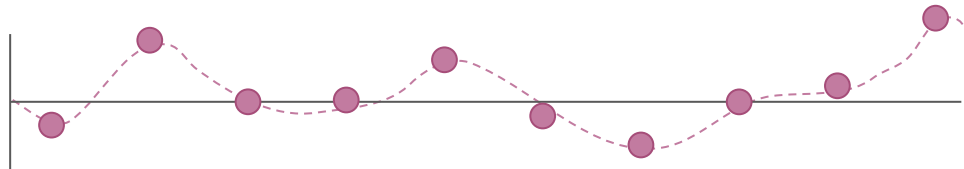
Time to get edgy





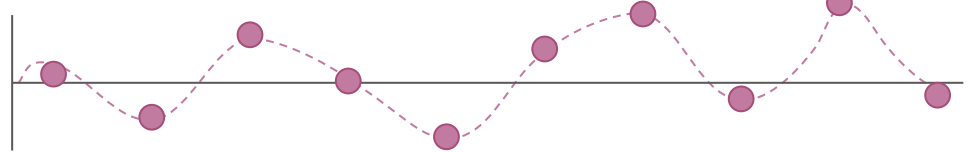
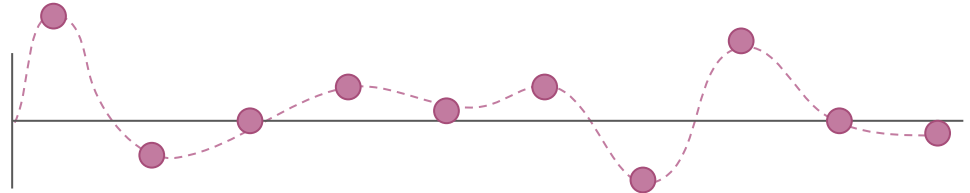
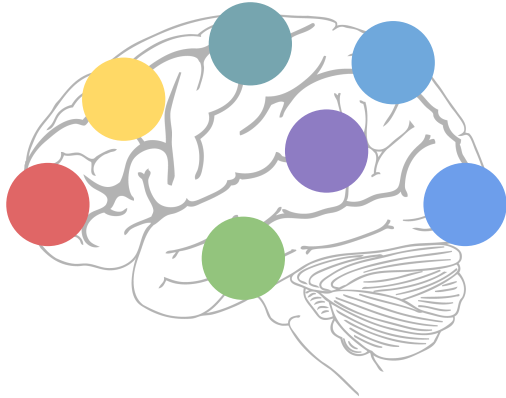


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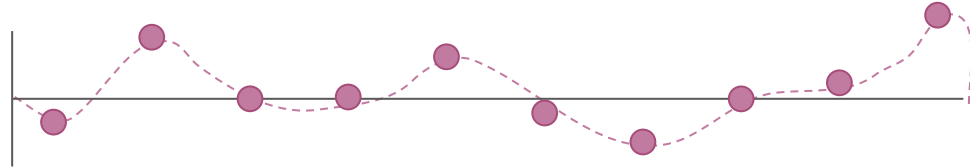


Faskowitz et al (2020) *Nat. Neuro*
Zamani Esfahlani (2020) *PNAS*

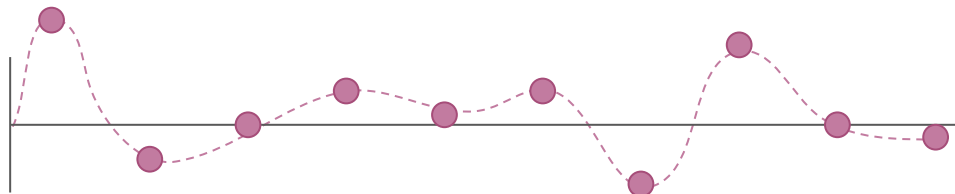
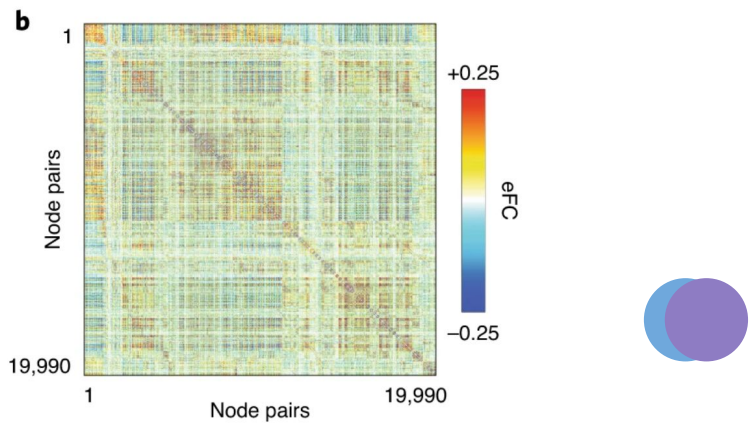
See also! Liu & Duyn (2013) *PNAS*,
Lahnakoski et al (2017) *HBM*, van Oort et
al (2018) *NeuroImage*...



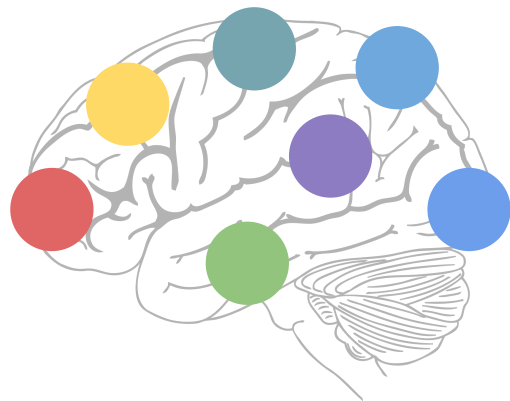
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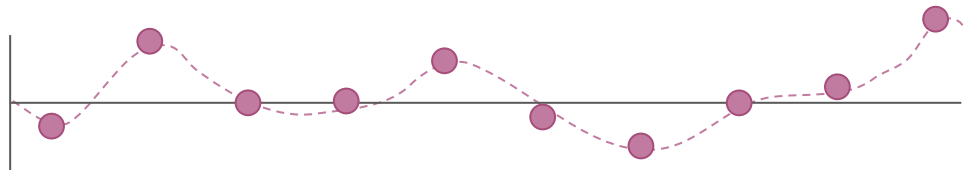
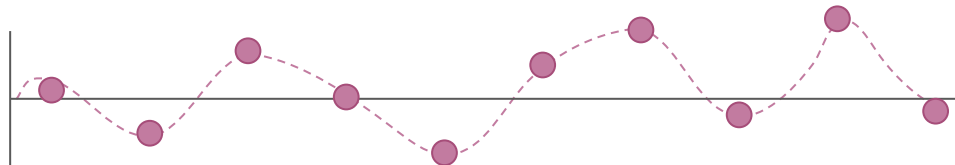
Instantaneous similarity after “unwrapping”
the traditional correlation



Faskowitz et al (2020) *Nat. Neuro*

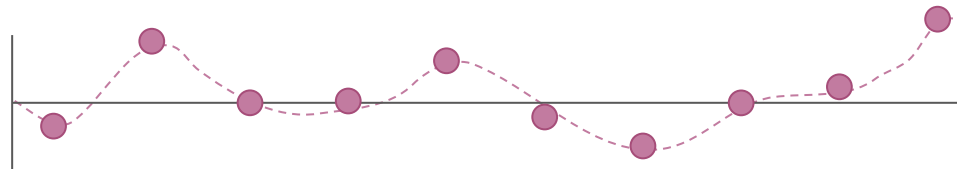
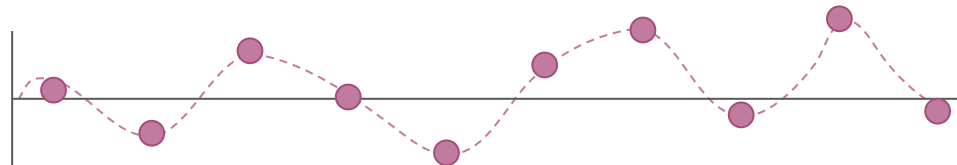
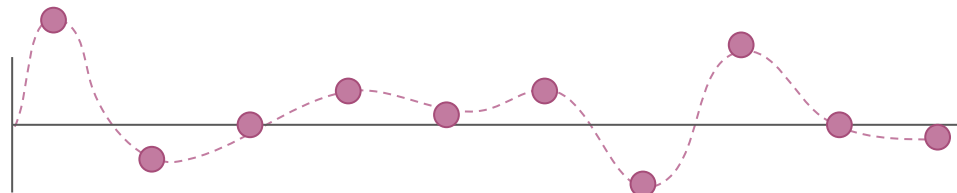


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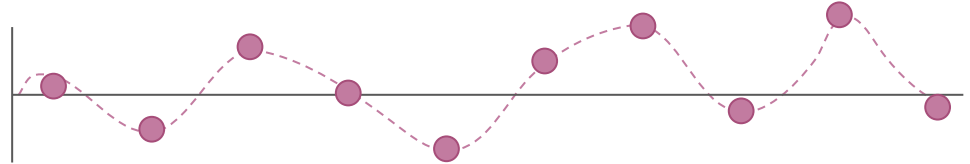
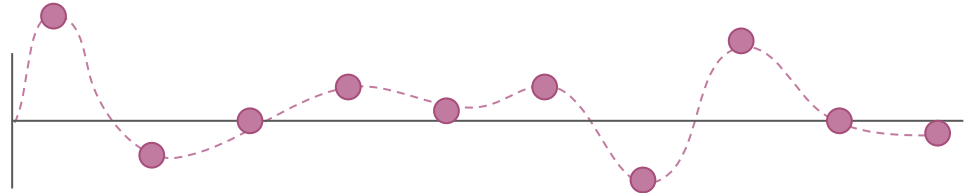
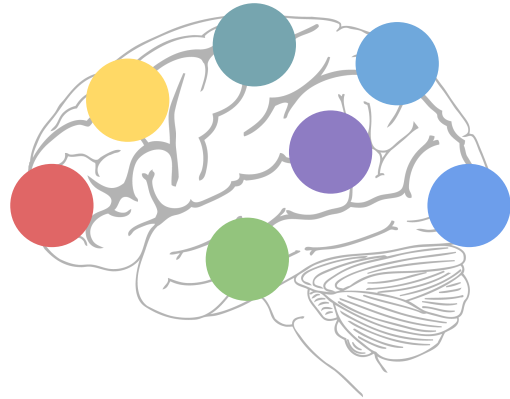




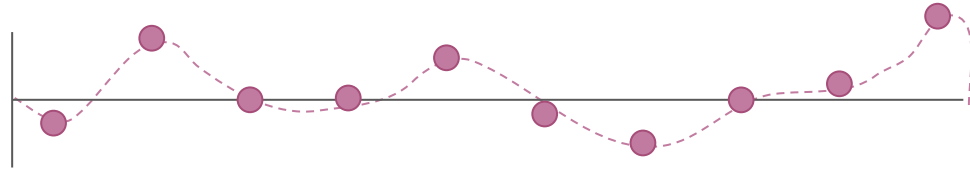
□ □ □



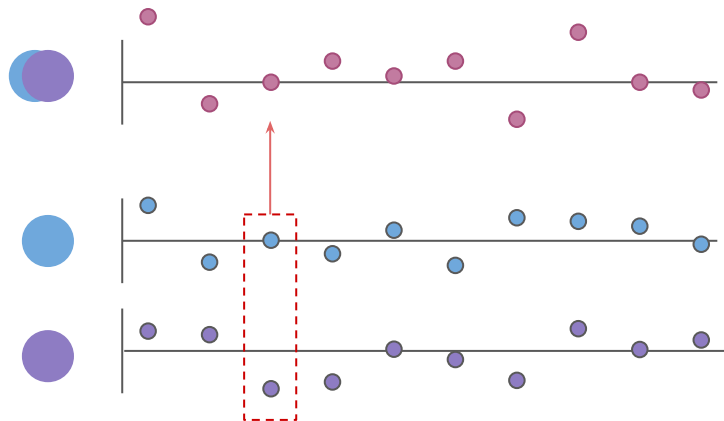
What does the
correlation
“unwrapped” get
you?



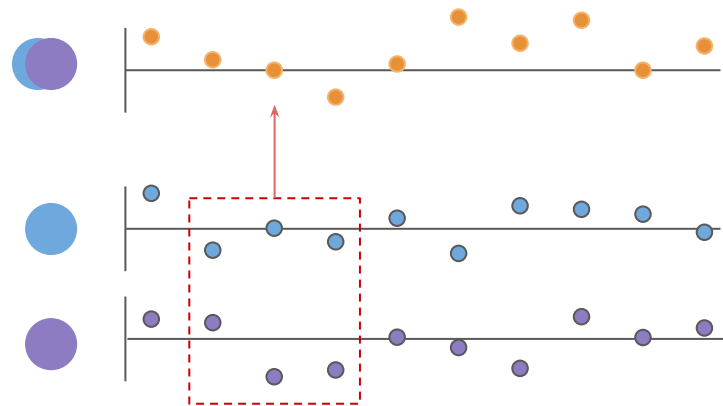
...



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



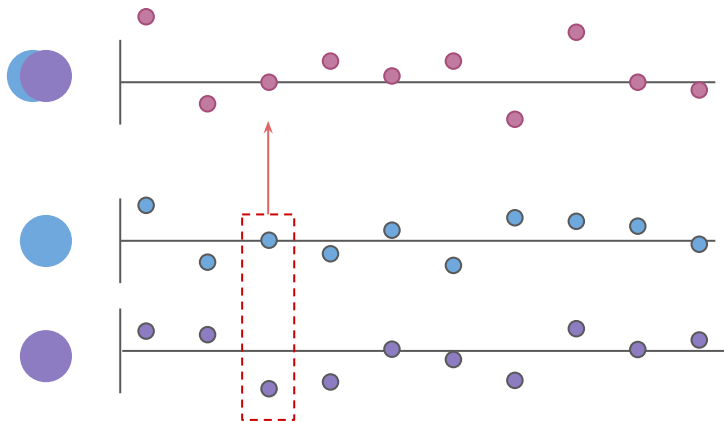
Edge time series



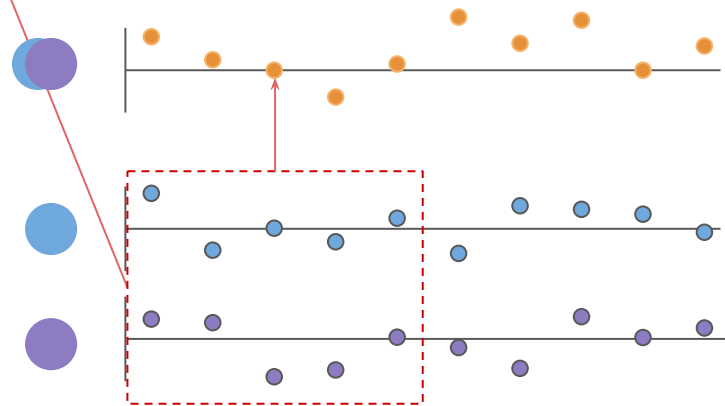
tv-FC

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

Pick window size

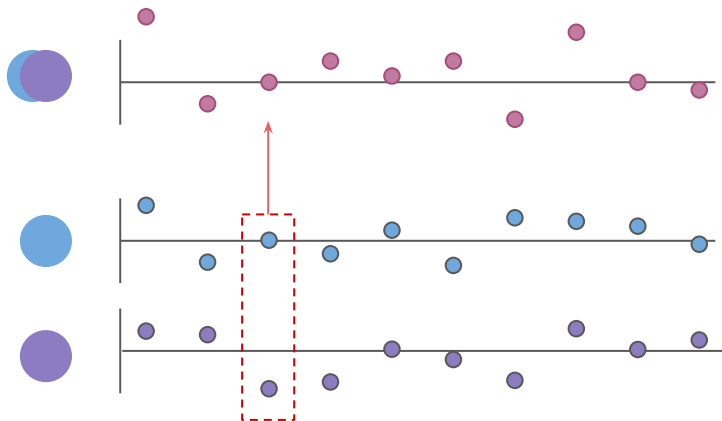


Edge time series



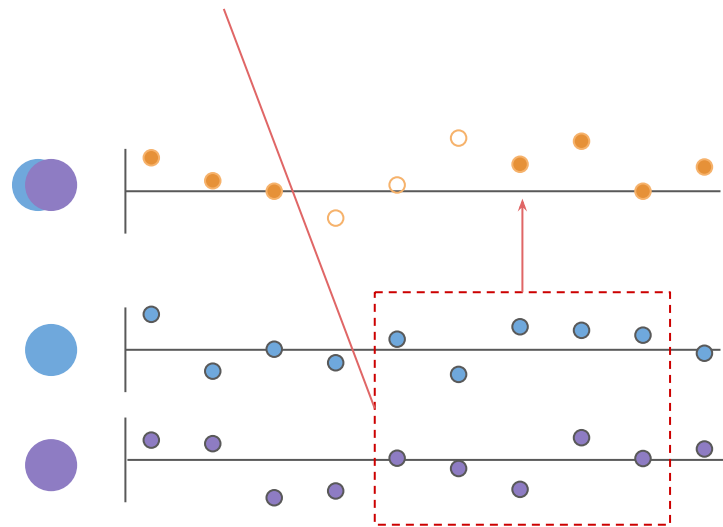
tv-FC

- **No sliding step or window parameter**
- Time-average is exactly correlation
- Same resolution as data input
 - Single frame information
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Edge time series

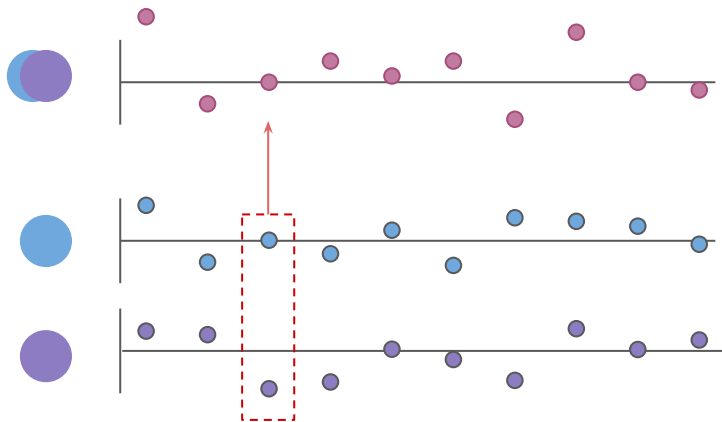
Pick slide size



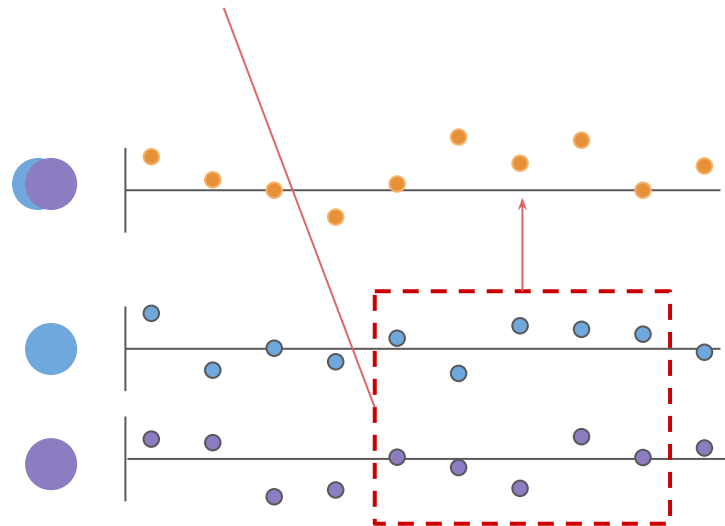
tv-FC

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- Time-average is exactly correlation
- Same resolution as data input
 - Single frame information
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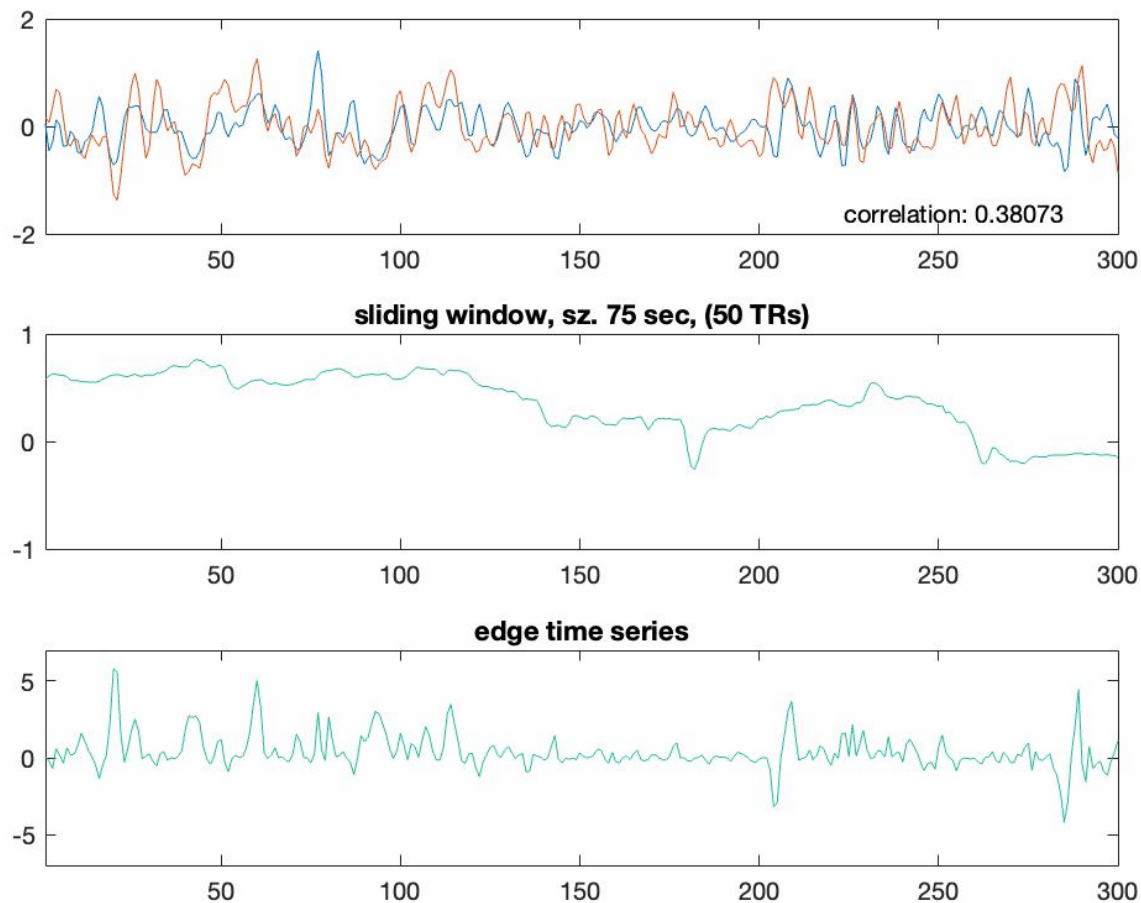
Normalize data within window



Edge time series

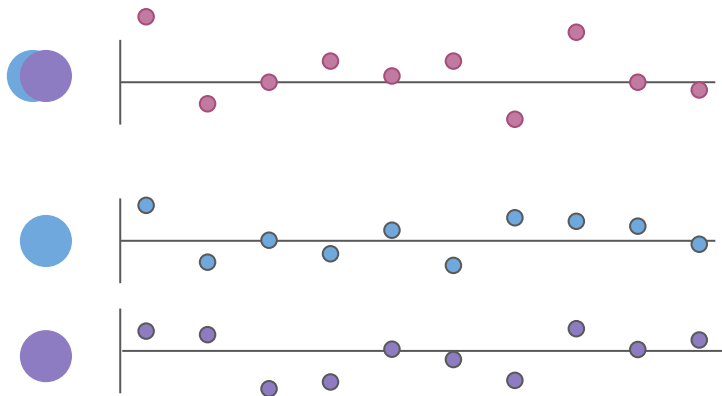


tv-FC

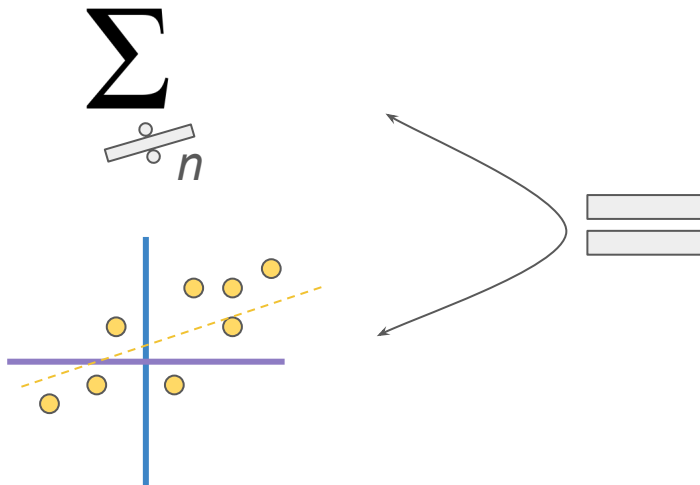


Difference in
synchronization
timing, variability,
shape (but *not*
claiming edges are
correct vs sliding
window)

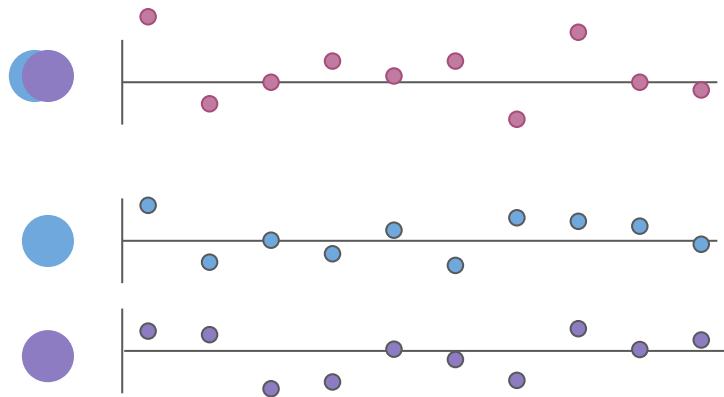
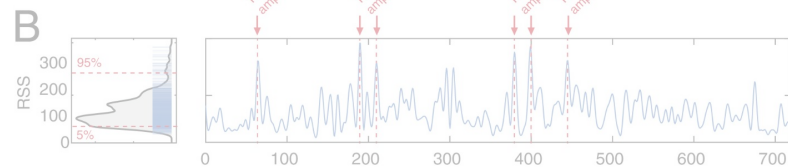
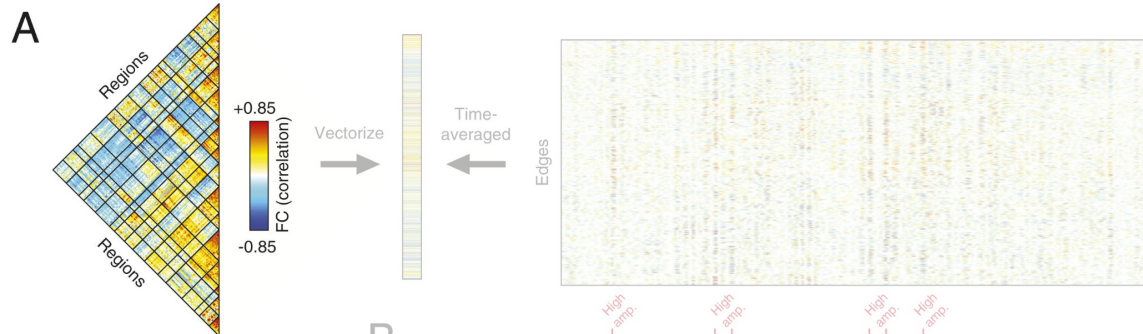
- No sliding step or window parameter
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Edge time series

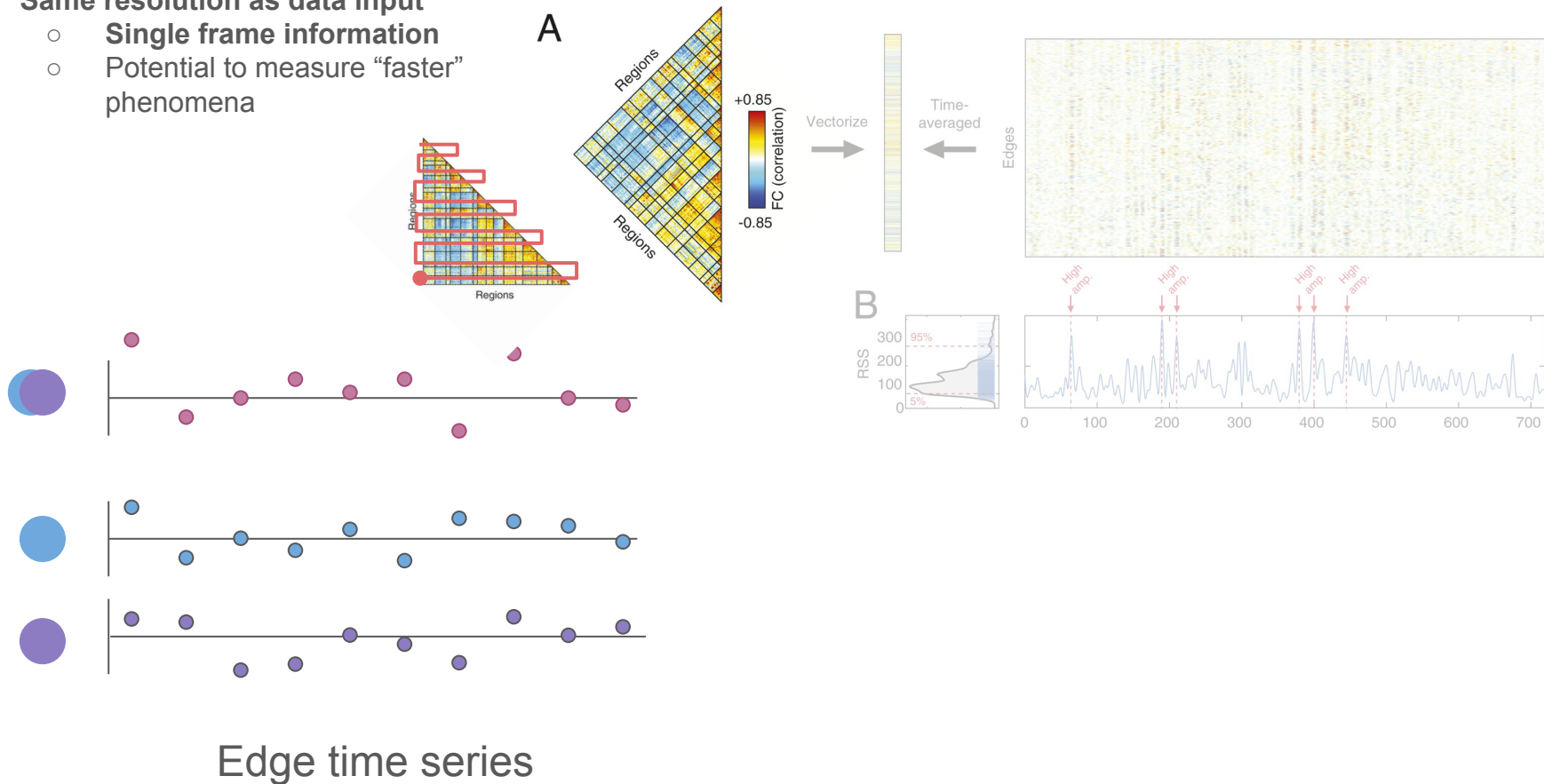


- No sliding step or window parameter
- Time-average is exactly correlation
- **Same resolution as data input**
 - **Single frame information**
 - Potential to measure “faster” phenomena

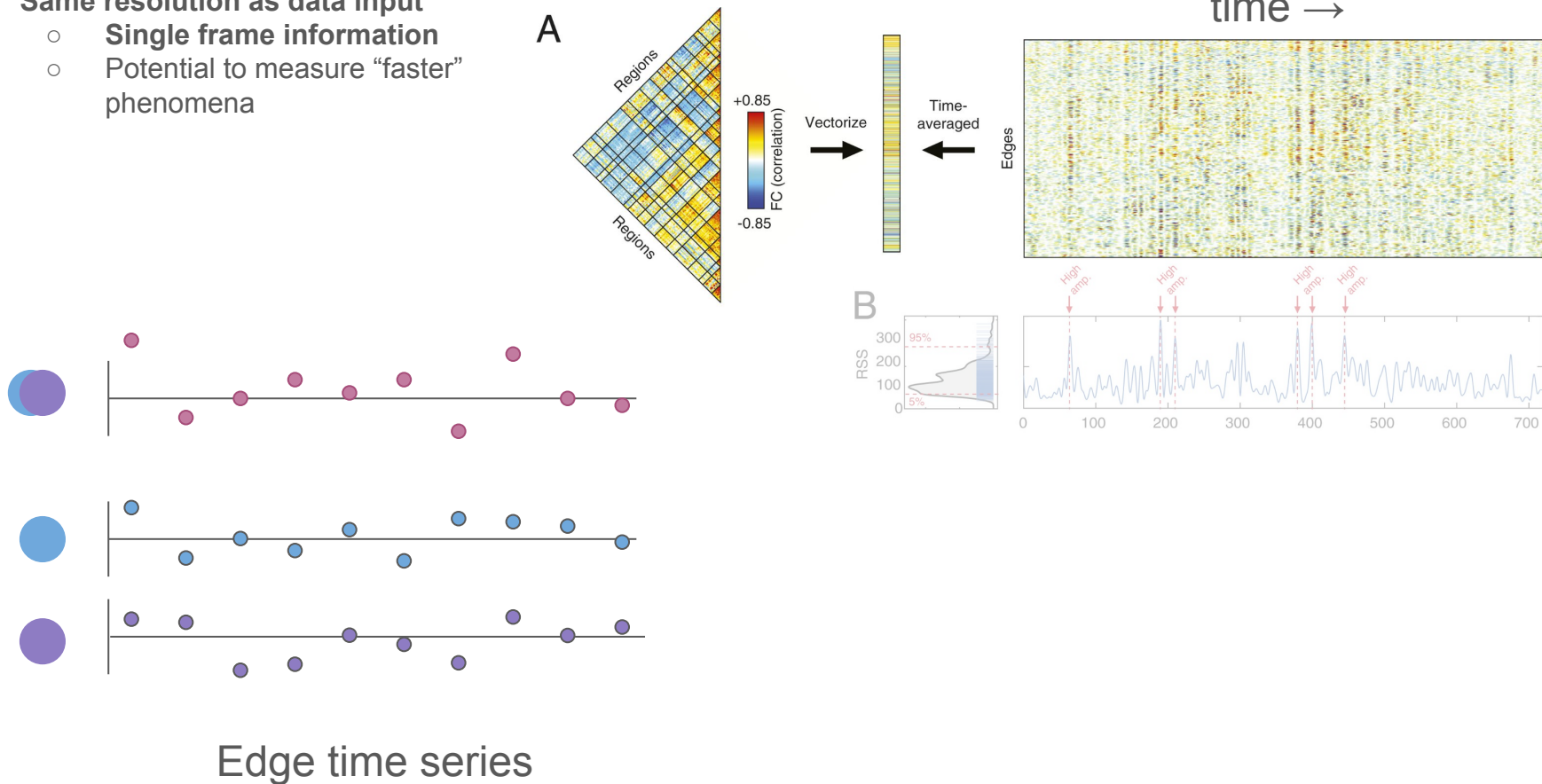


Edge time series

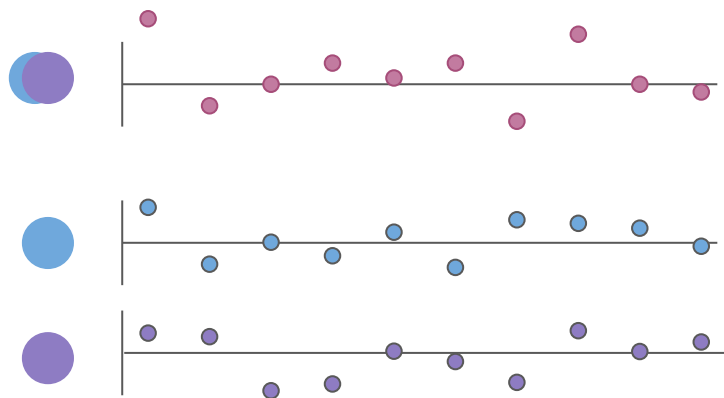
- No sliding step or window parameter
- Time-average is exactly correlation
- **Same resolution as data input**
 - **Single frame information**
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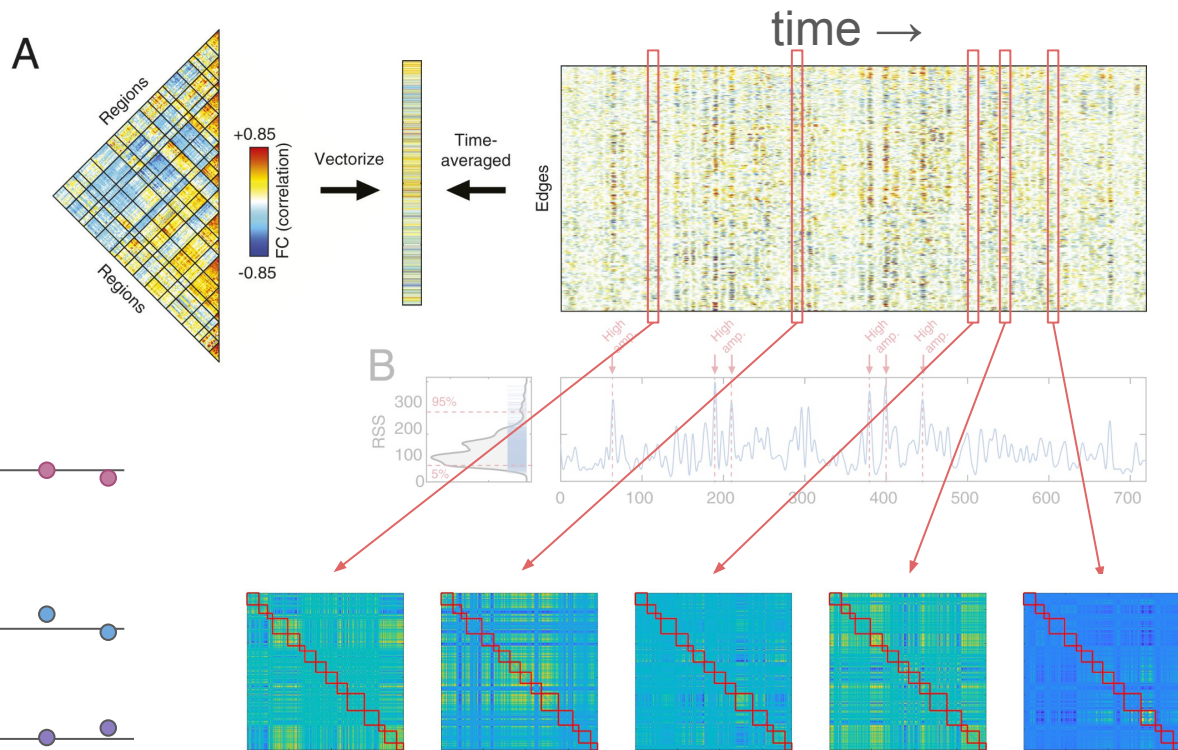
- No sliding step or window parameter
- Time-average is exactly correlation
- **Same resolution as data input**
 - **Single frame information**
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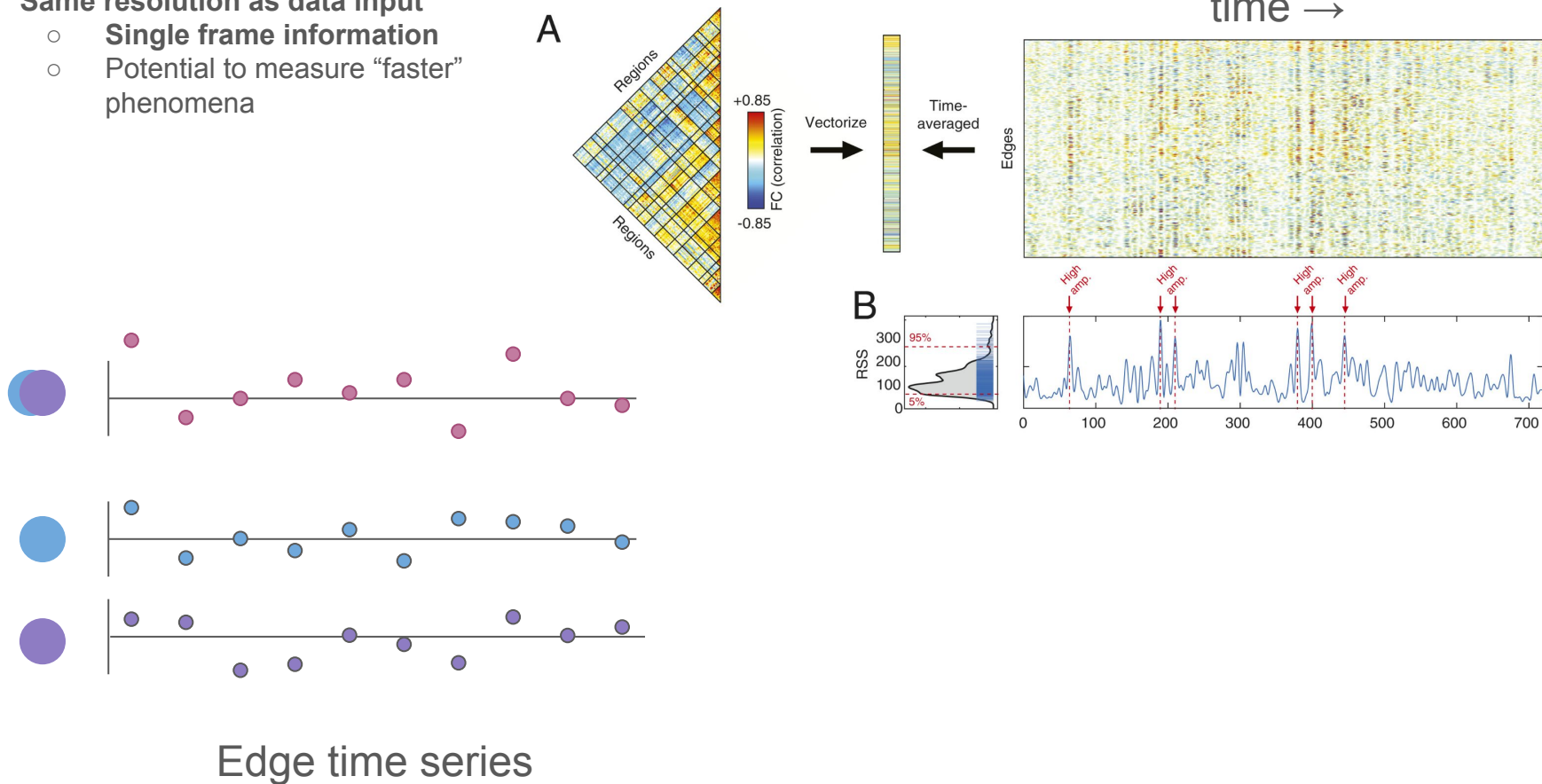


Edge time series

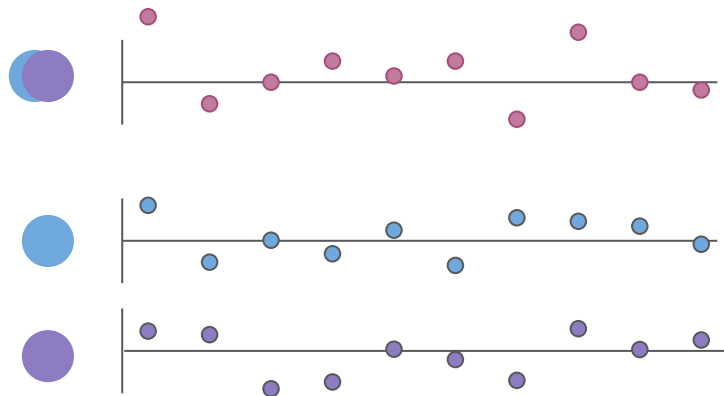


Dataset size explosion! Each column forms an node by node matrix (same size as time FC matrix)
 Edge time series matrix = (nodes) x (nodes) x (time)

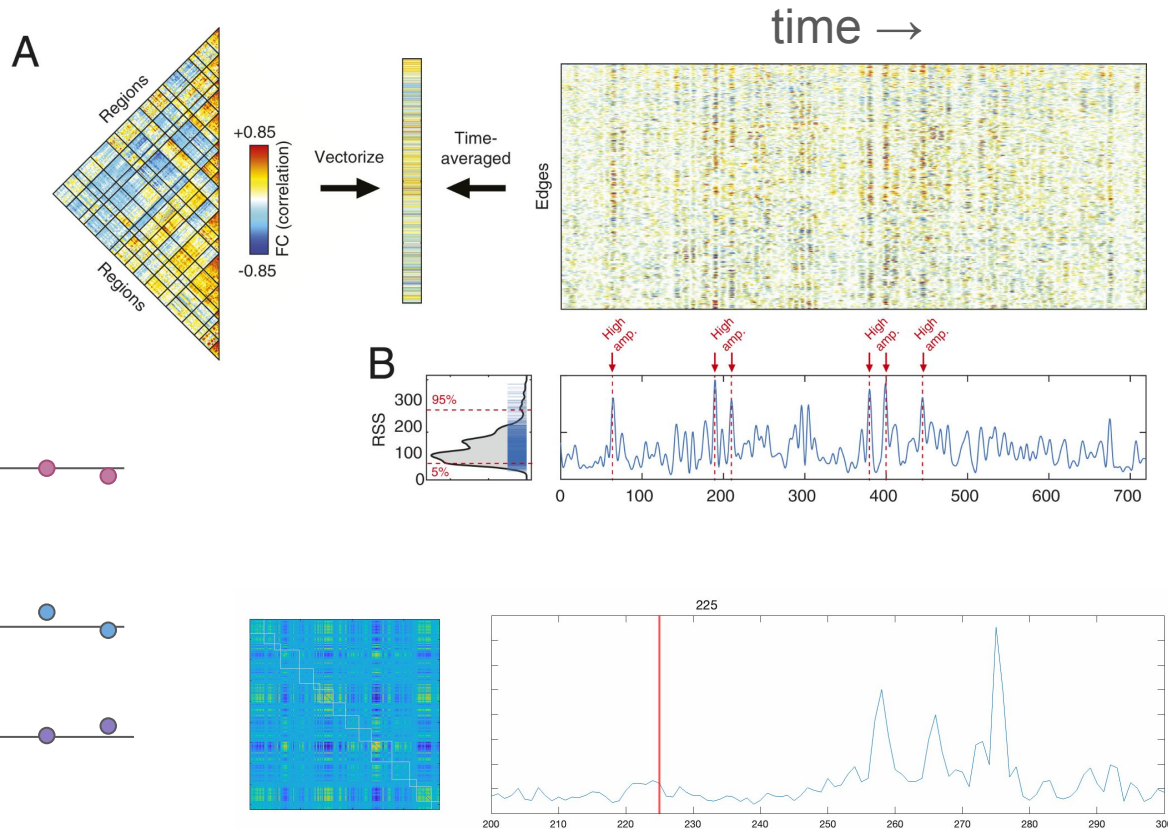
- No sliding step or window parameter
- Time-average is exactly correlation
- **Same resolution as data input**
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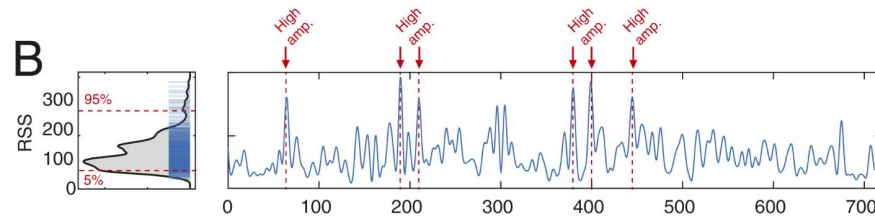


Edge time series

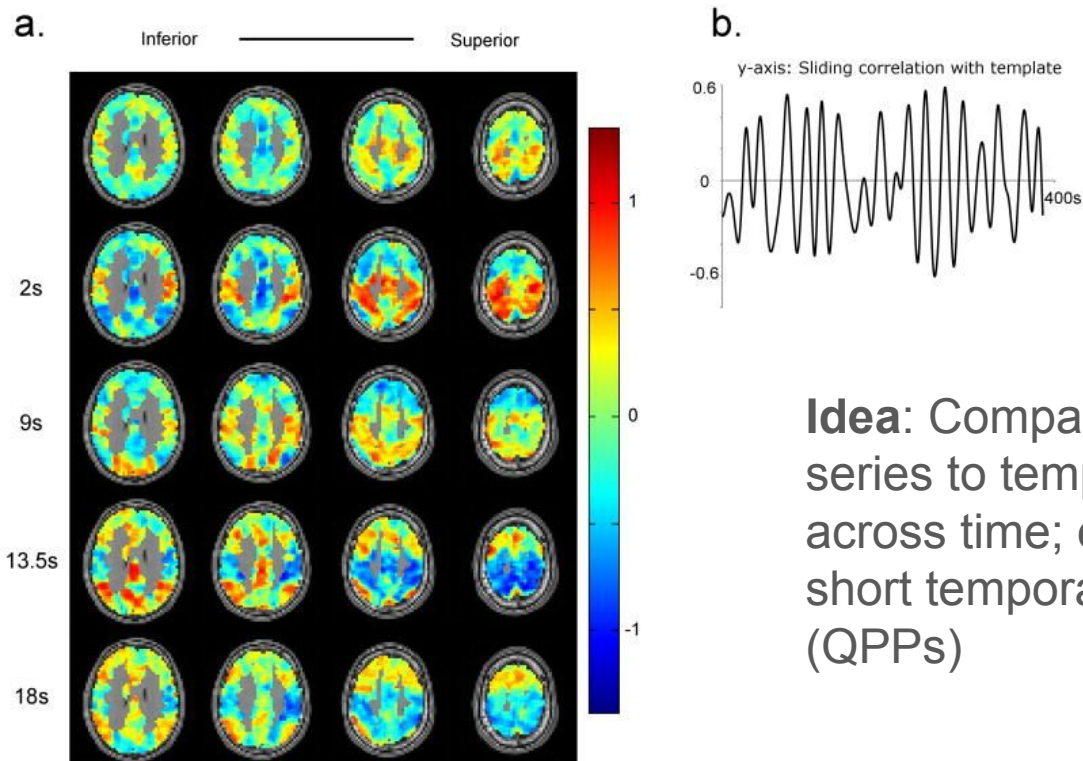


What is the nature of “connectivity” dynamics? Smooth or punctuated?

Zamani Esfahlani et al (2020)
PNAS

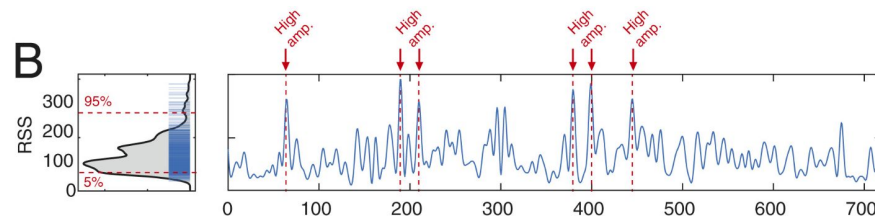


What is the nature of “connectivity” dynamics? Smooth or punctuated?



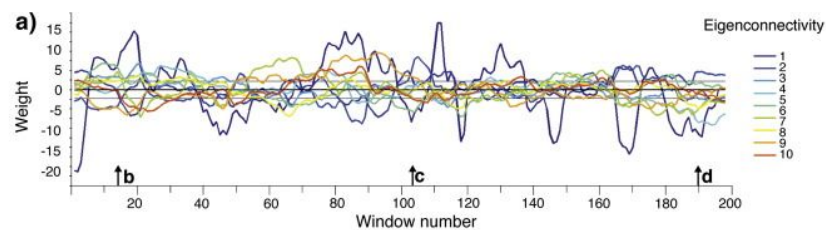
Idea: Compare time series to template across time; events are short temporal patterns (QPPs)

Zamani Esfahlani et al (2020)
PNAS

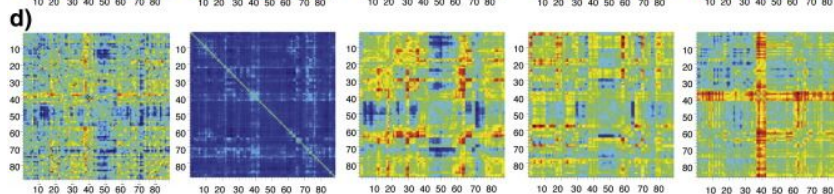
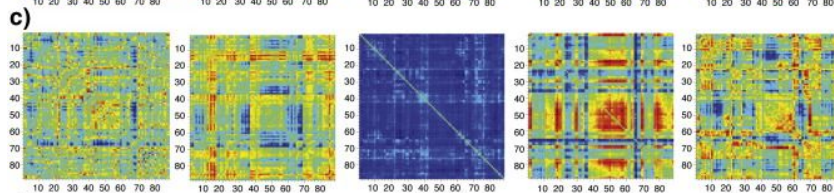
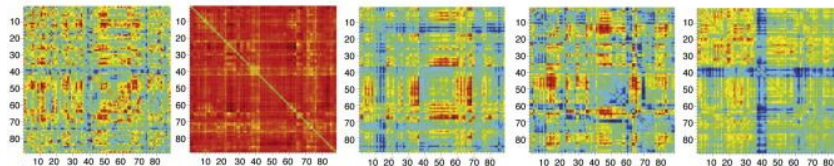


Majeed et al. (2011).
NeuroImage

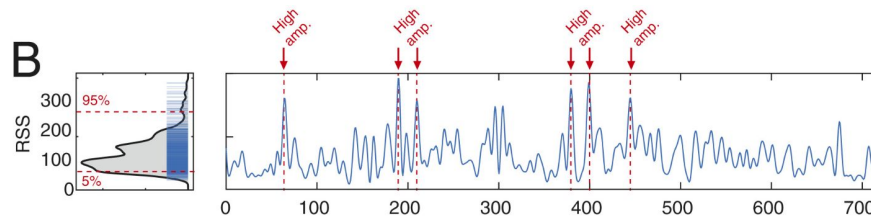
What is the nature of “connectivity” dynamics? Smooth or punctuated?



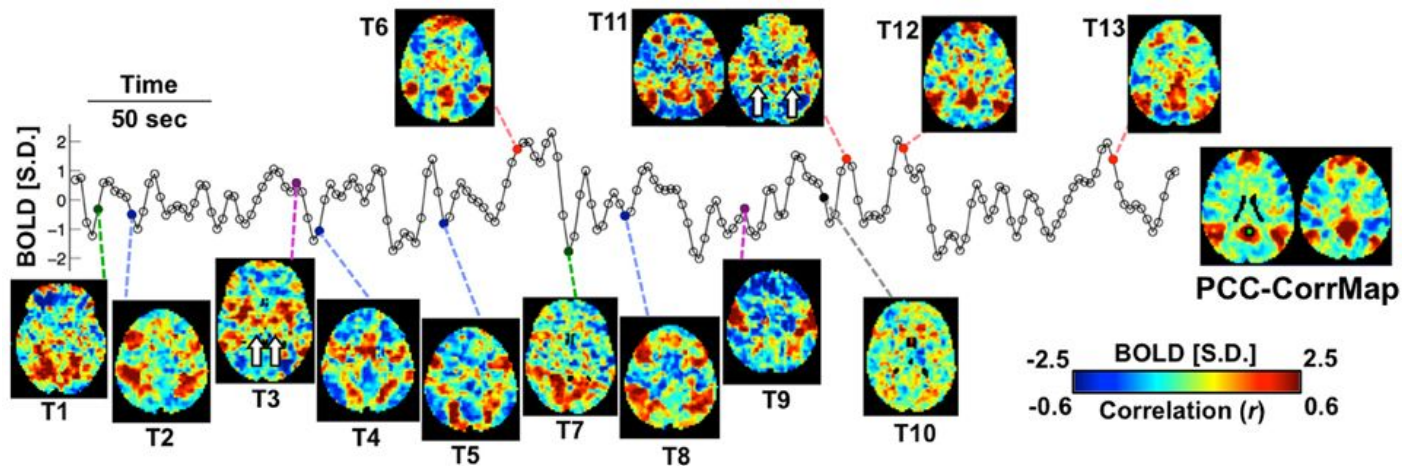
b) Demeaned FC, eigenconnectivities with top 4 contributions



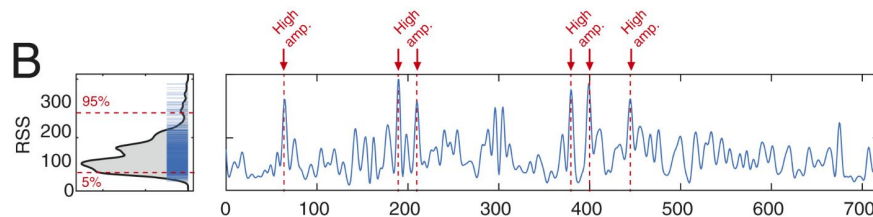
Idea: stack all your data together and run pca; track the expression of modes in your data



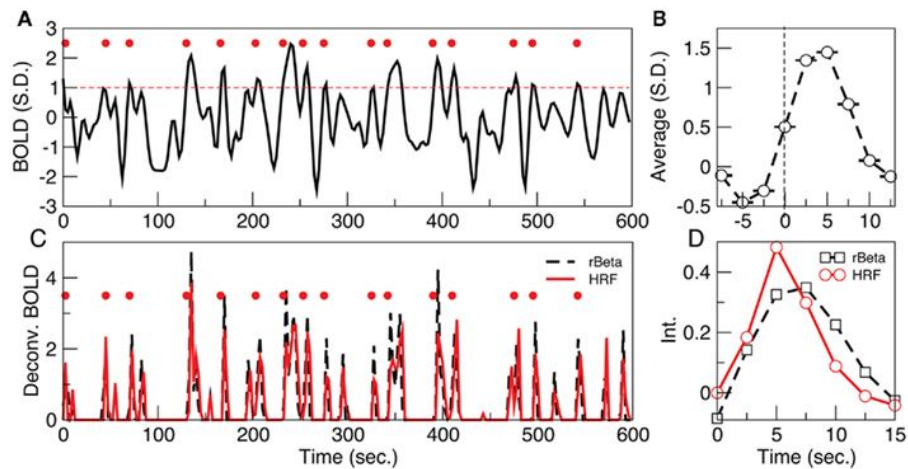
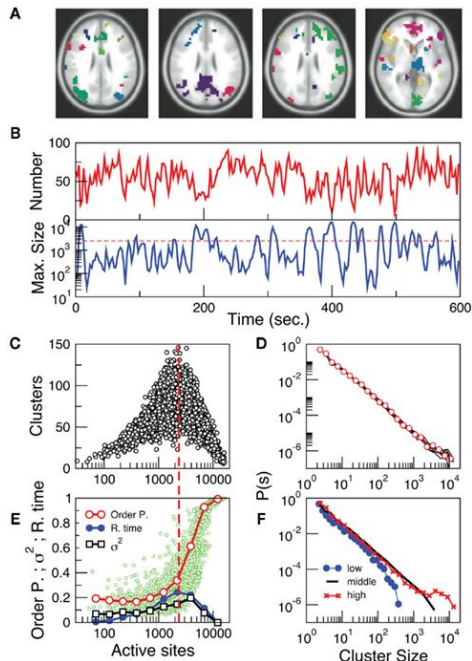
What is the nature of “connectivity” dynamics? Smooth or punctuated?



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

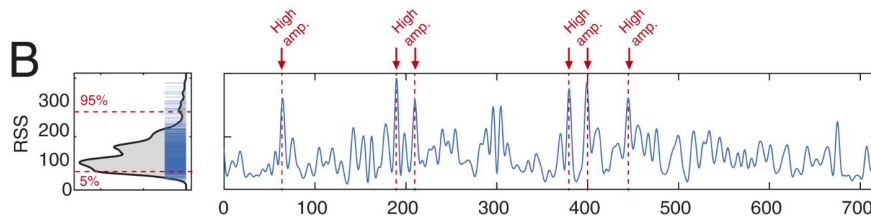


What is the nature of “connectivity” dynamics? Smooth or punctuated?



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

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

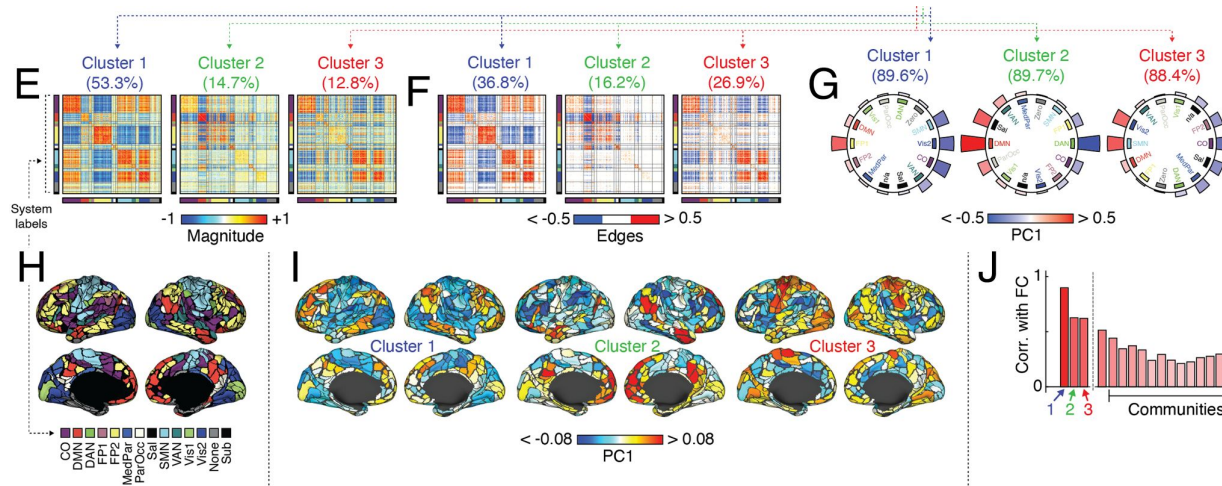
Depending on how the data is processed, it could
look either way!

But without the smoothing that comes with
windowing the data, it is curious that these large
amplitude deflections happen... (even in synthetic
data too)

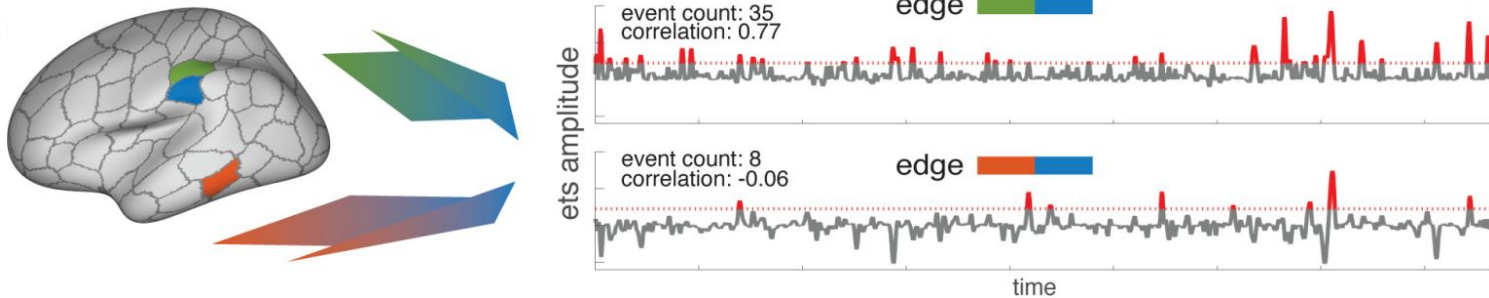
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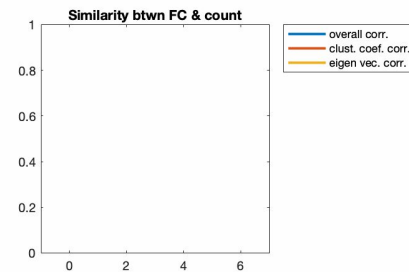
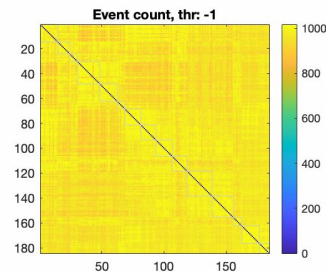
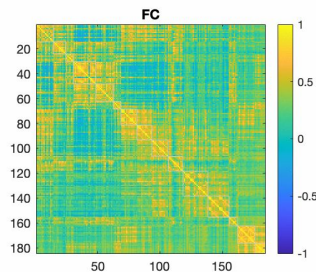
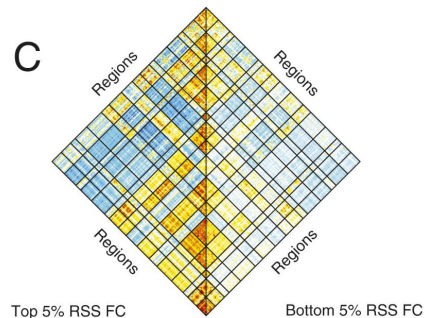
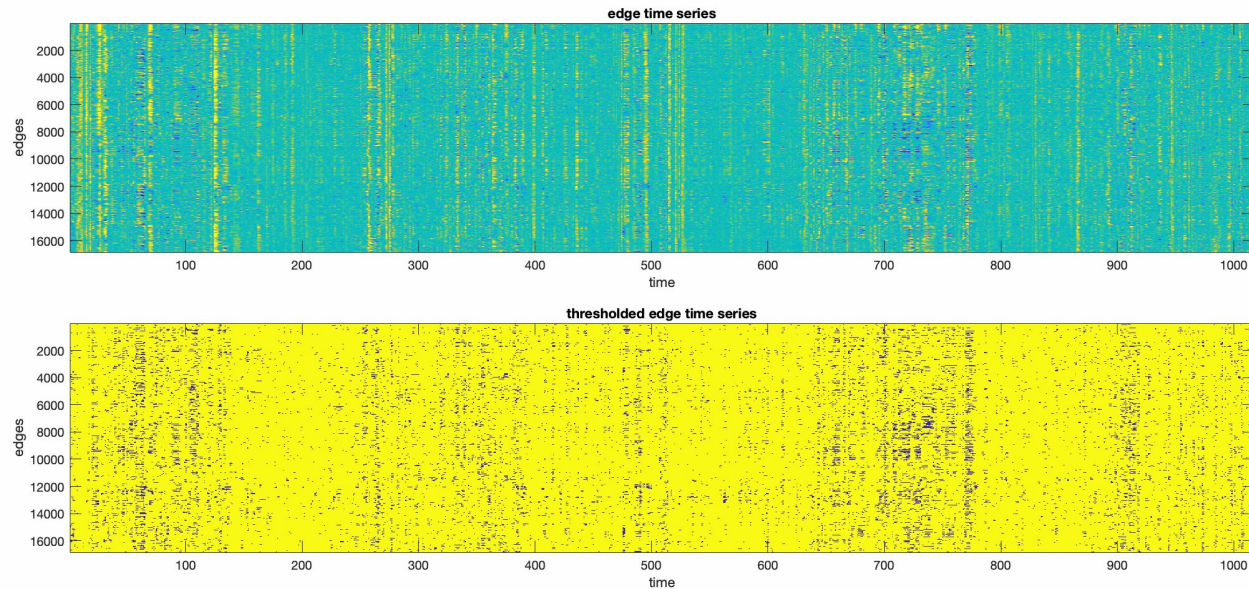


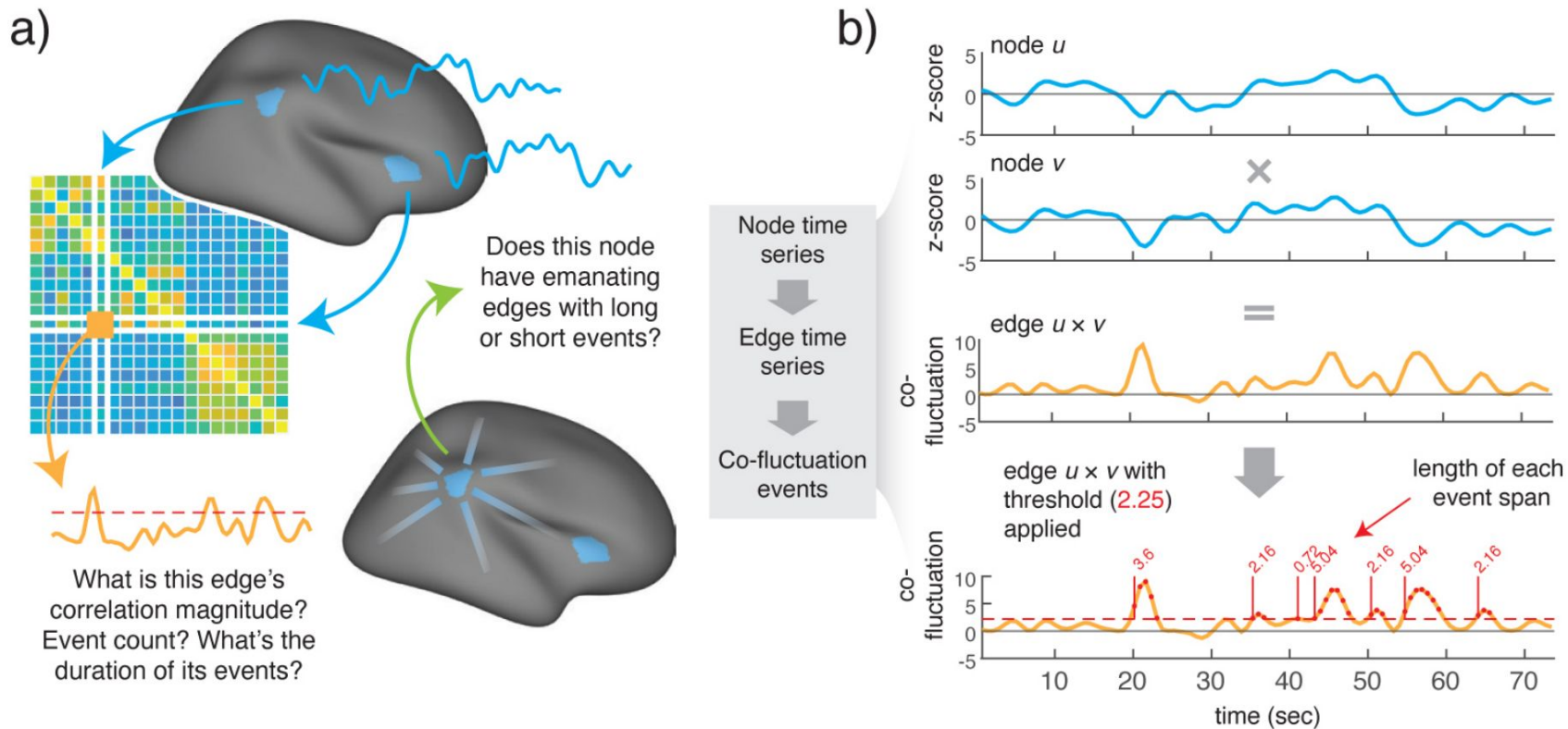
What can we “read out” from the rendering of temporally resolved correlation?



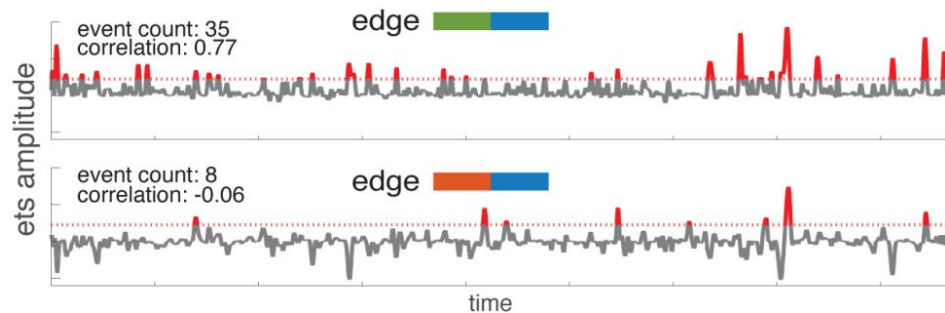
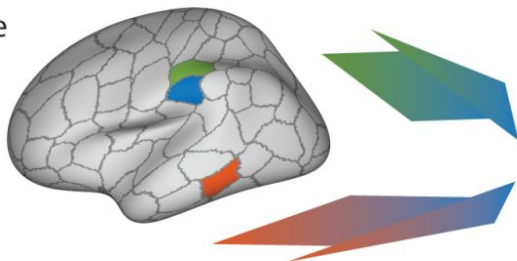
And can extra features be used to further our understanding of the nature of connectivity

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'



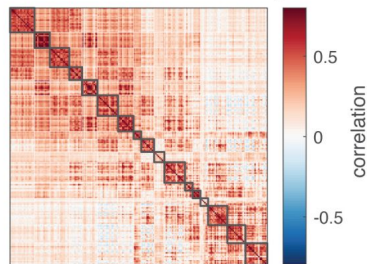


a) What do the edge time series look like for high vs. low correlation edges?

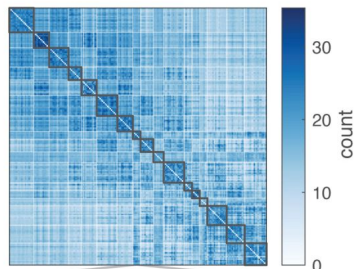


b) **functional connectivity**

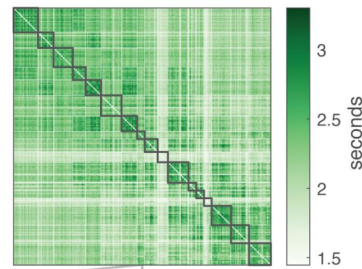
Mean matrices across
N=176 subjects



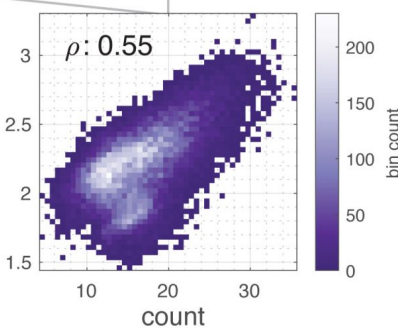
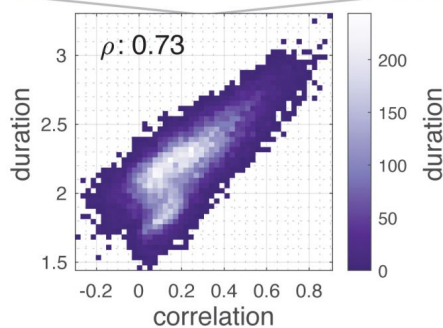
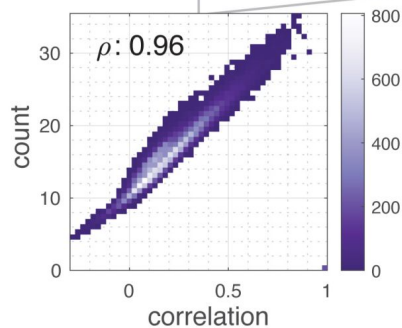
event count



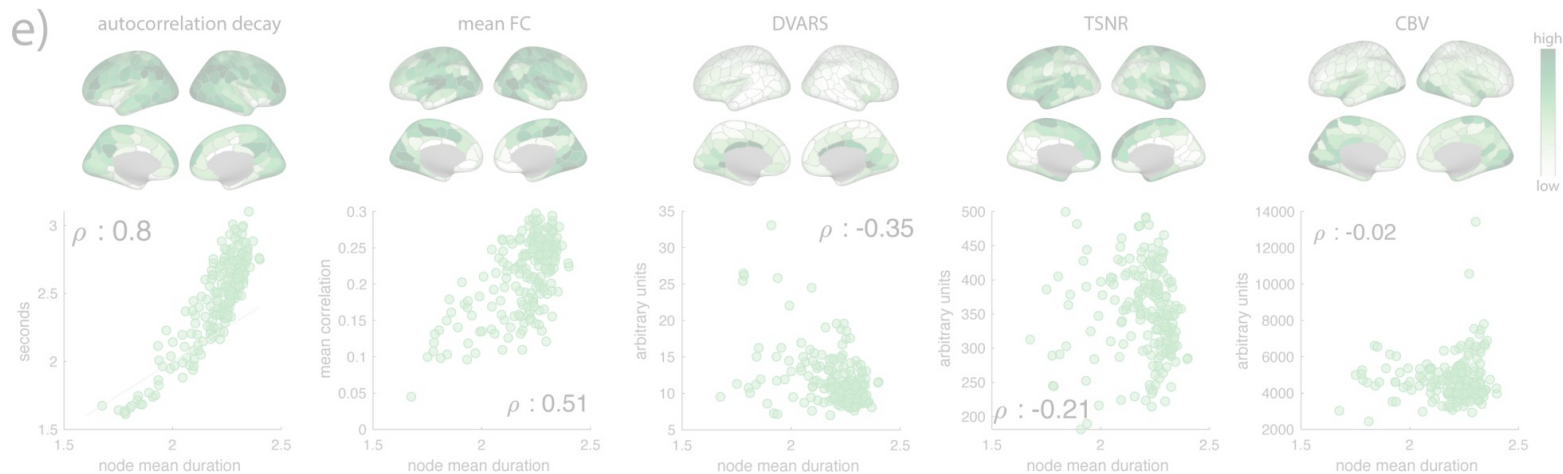
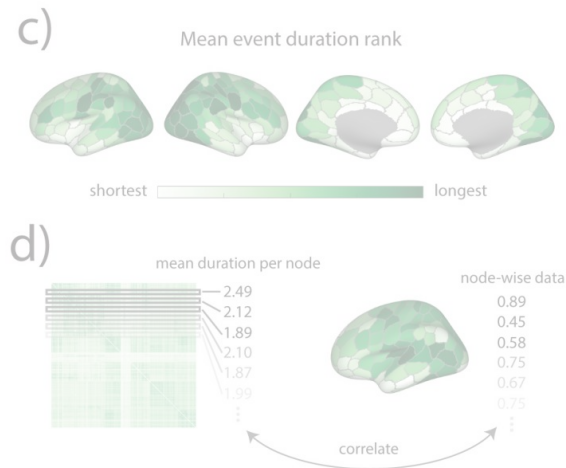
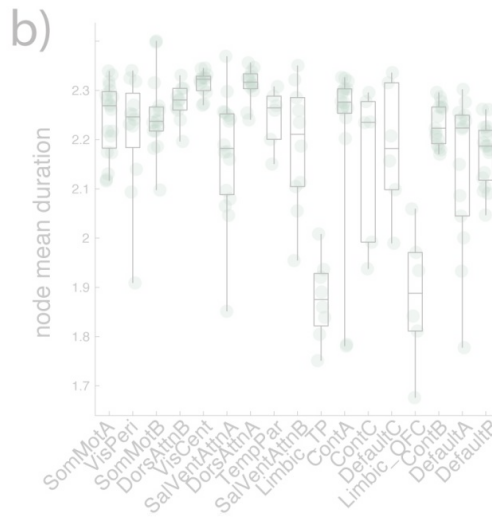
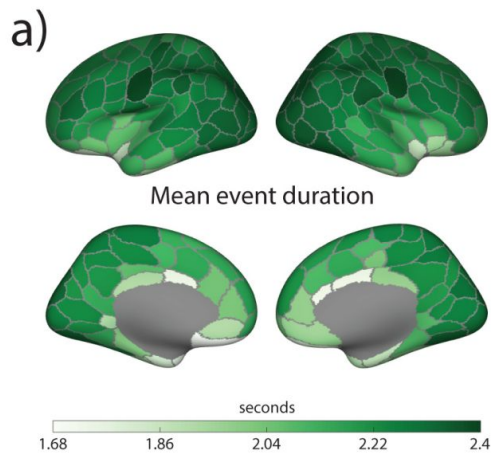
event duration

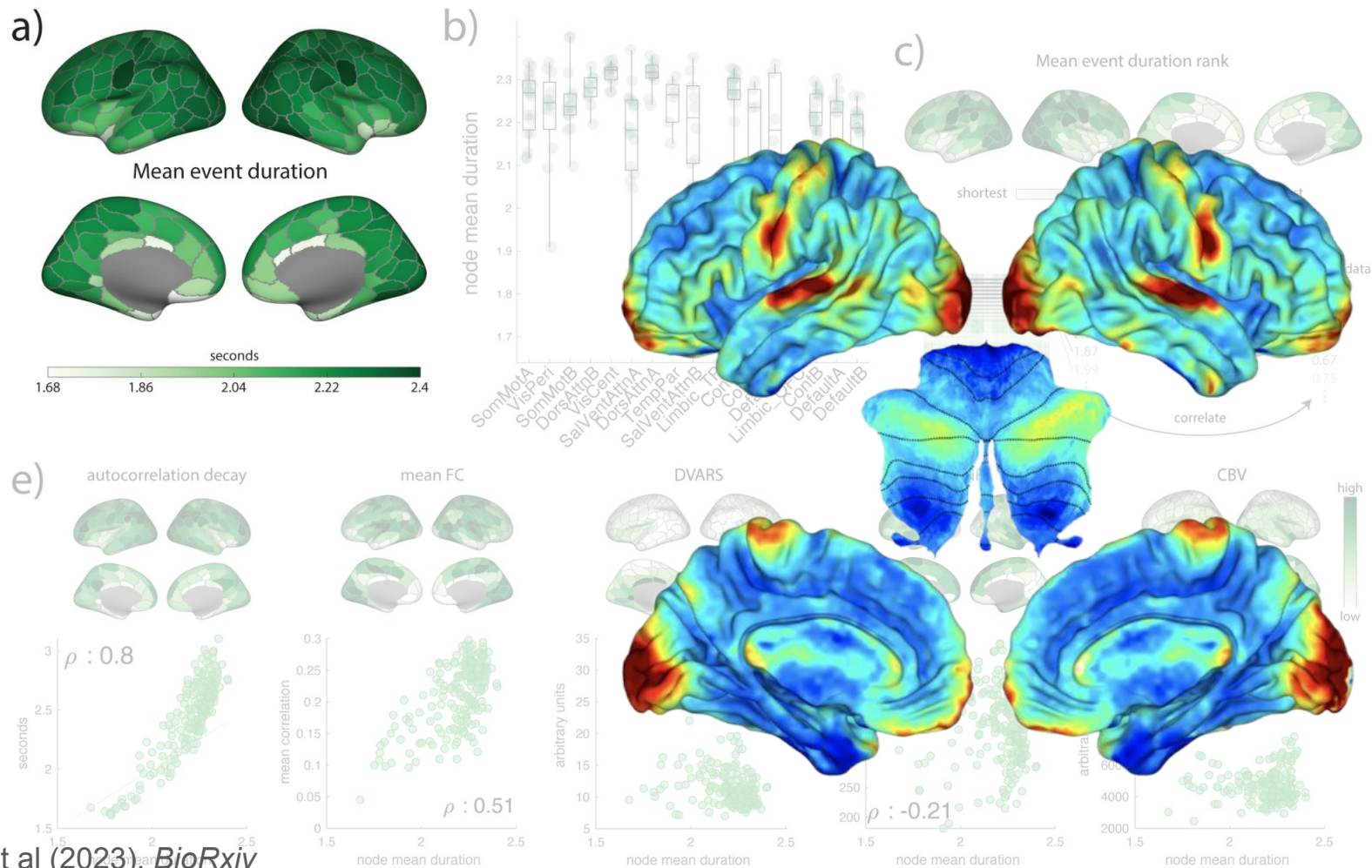


c)

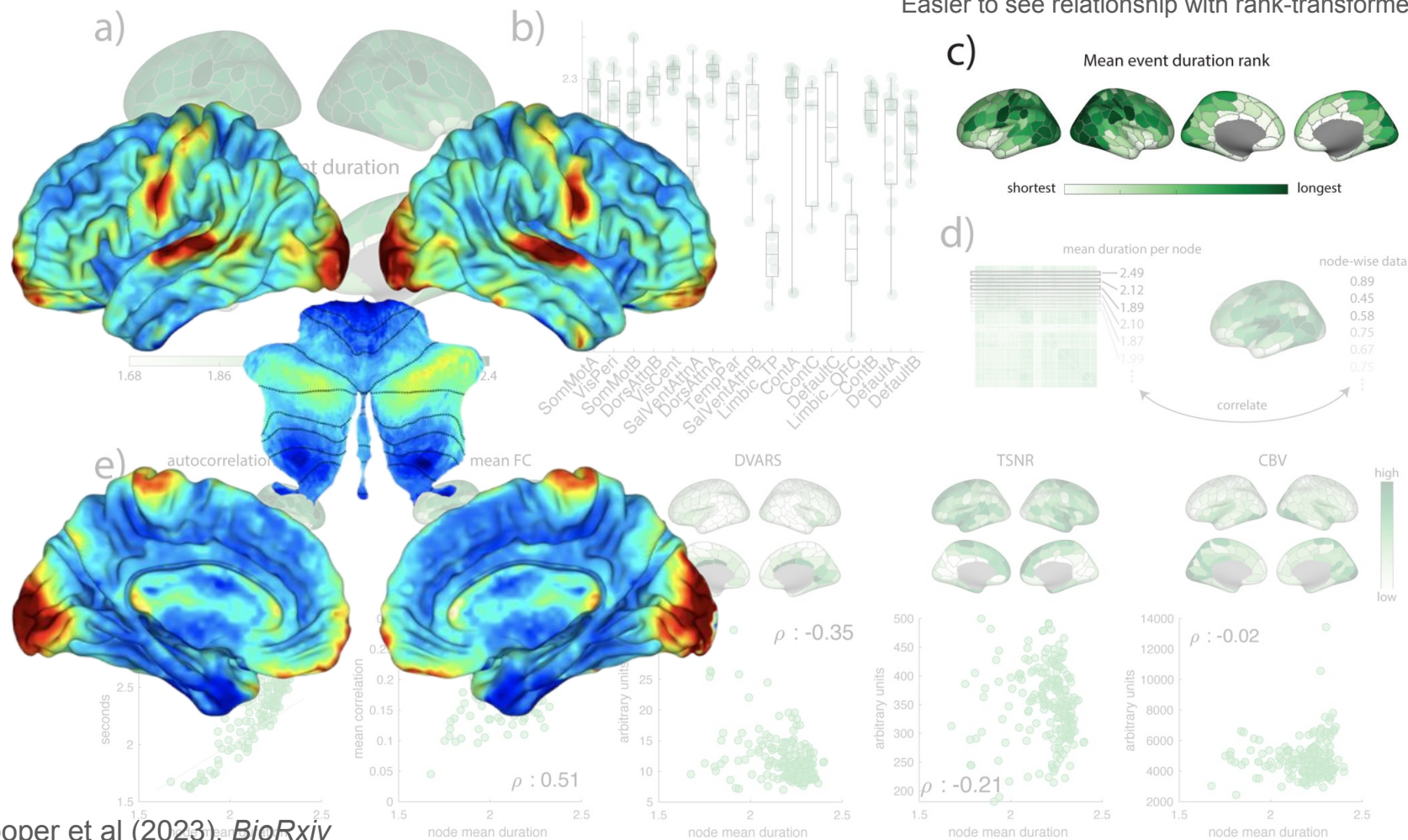


When we look at these discrete events, can we “juice” extra information out of our signal? Adding understanding to our conception of FC.

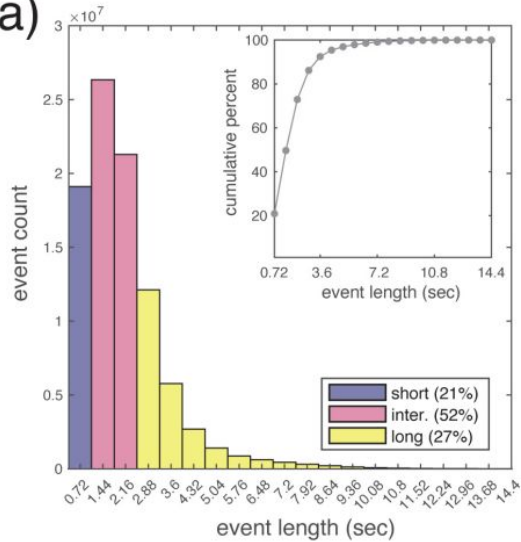




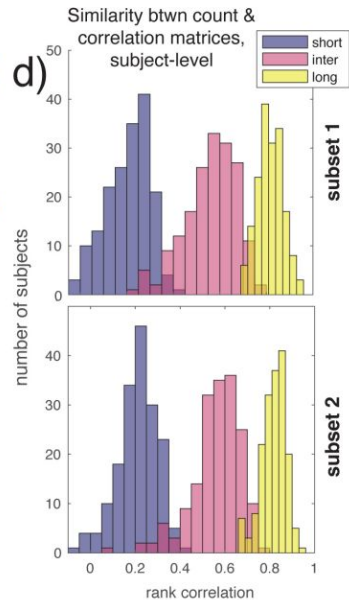
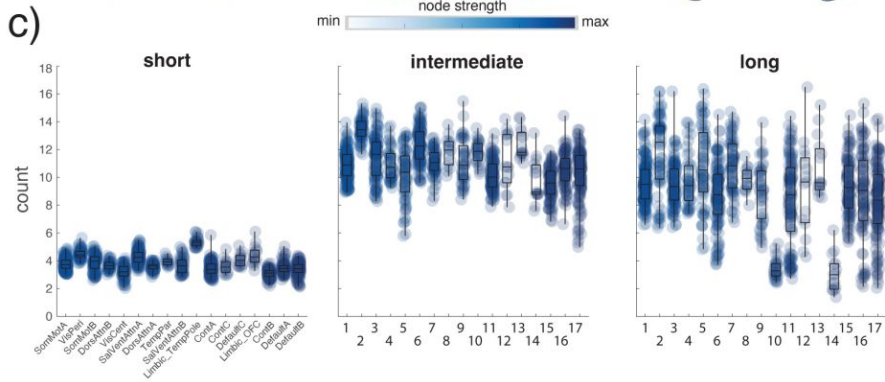
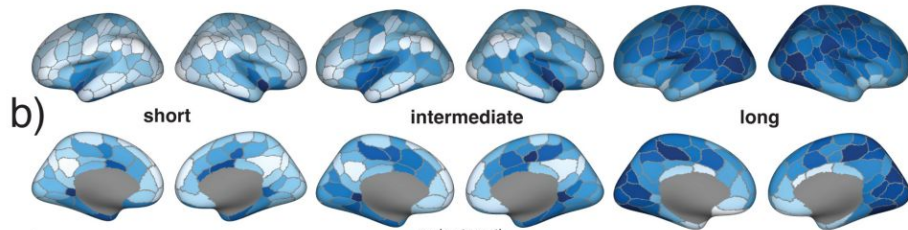
Easier to see relationship with rank-transformed data



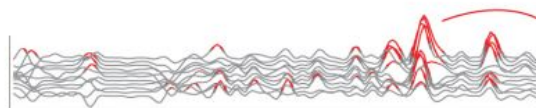
a)



Group events into short, intermediate, and long events, to help separate potentially different 'types' of connectivity transpiring

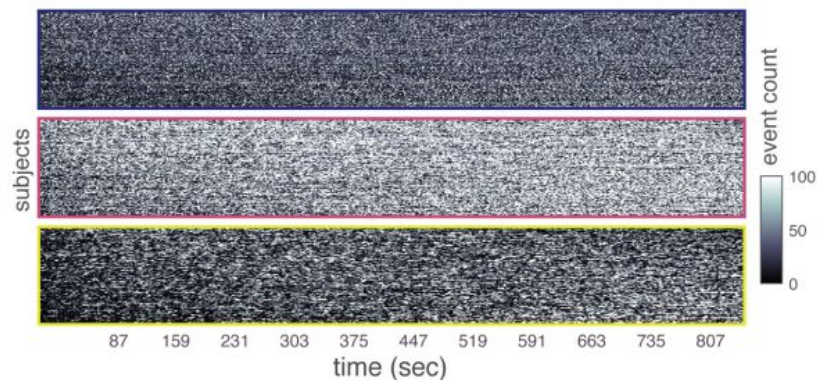


a)

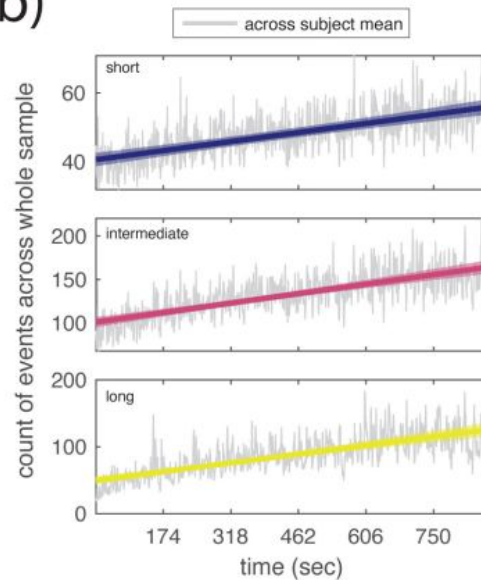


Does event count
increase over time
in the sample?

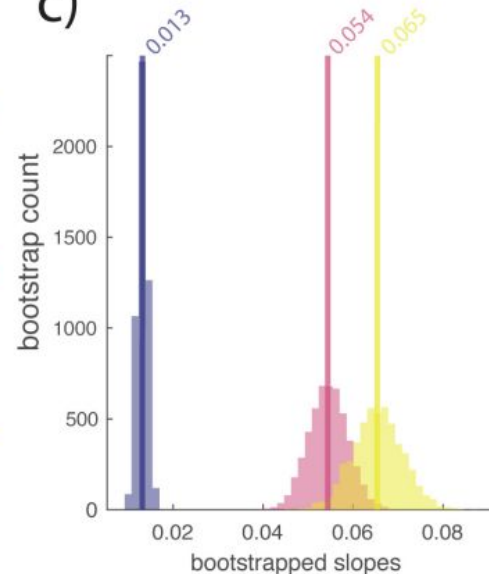
Event data
for all subjects (N=176)



b)



c)

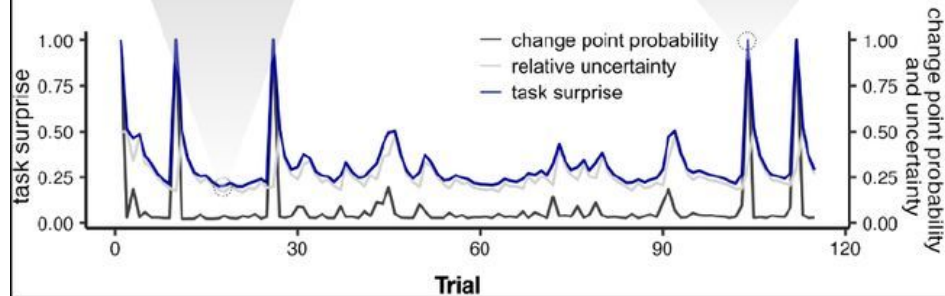


Controlled adaptive learning task

trial with low surprise
outcome distribution stays



trial with high surprise
outcome distribution shifts



Naturalistic sports viewing

event with low surprise

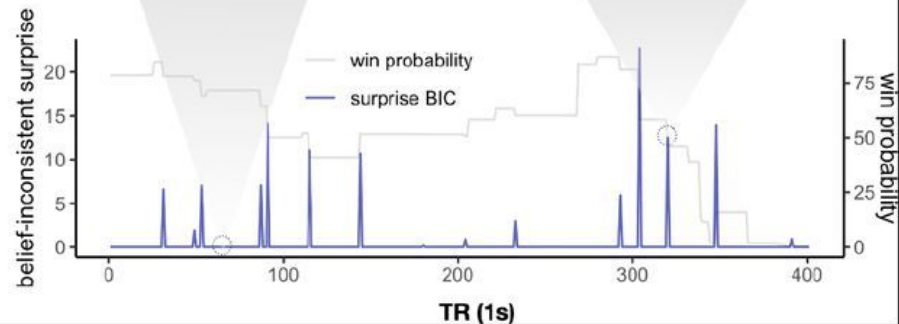
Notre Dame winning

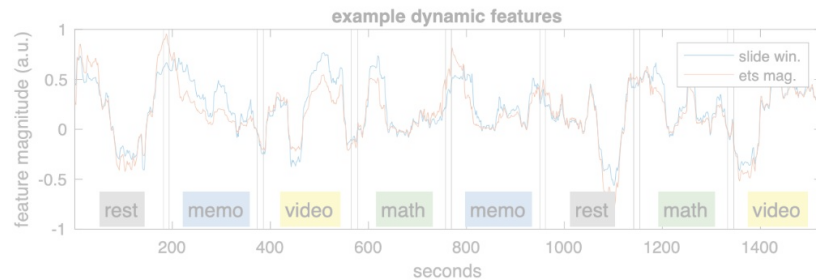
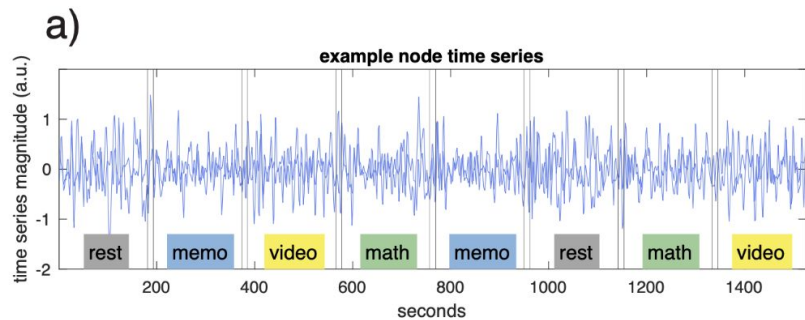


event with high surprise

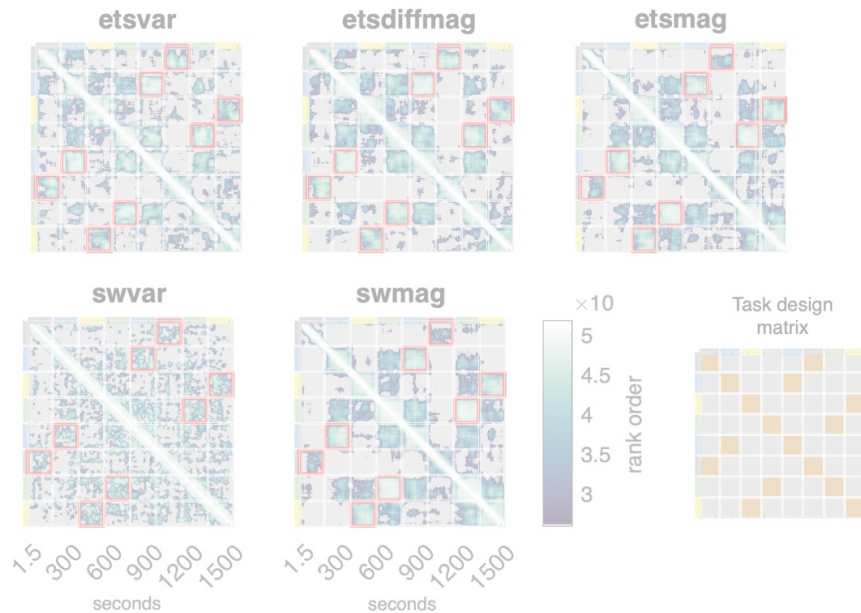
Notre Dame winning

Xavier winning

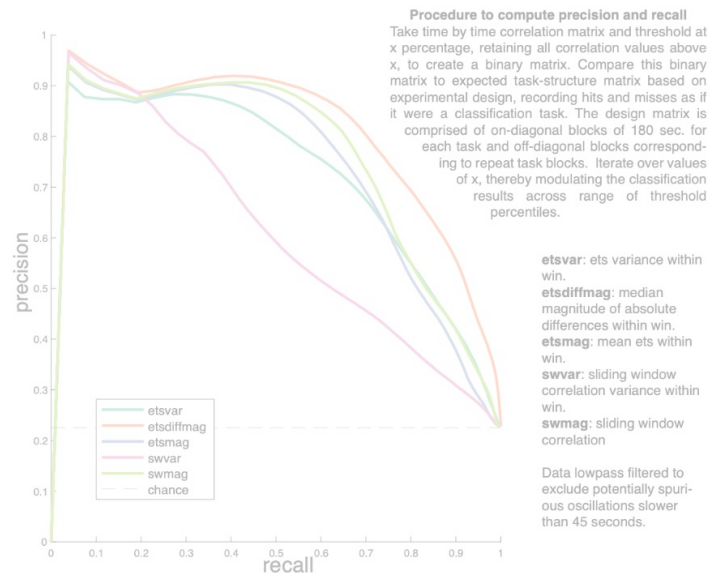


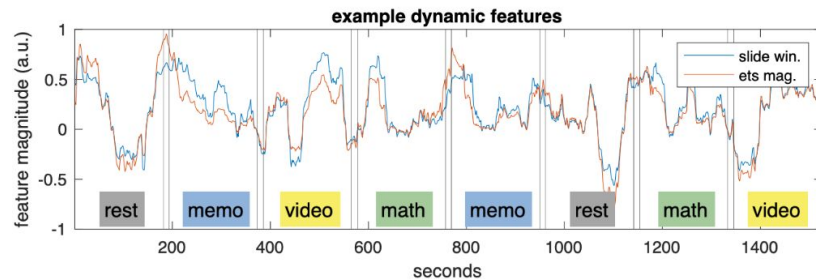
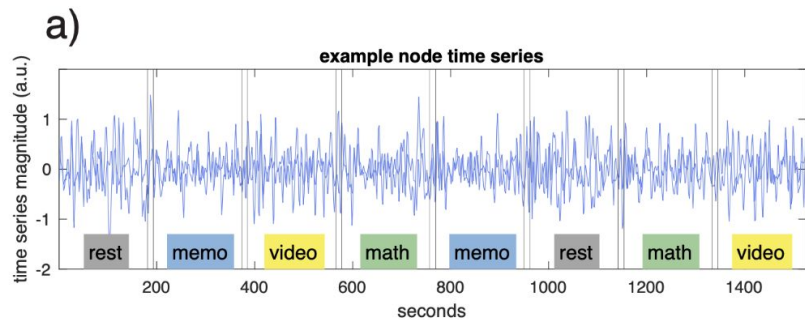


b) Mean multitask time by time correlation matrices, window of 45 sec.

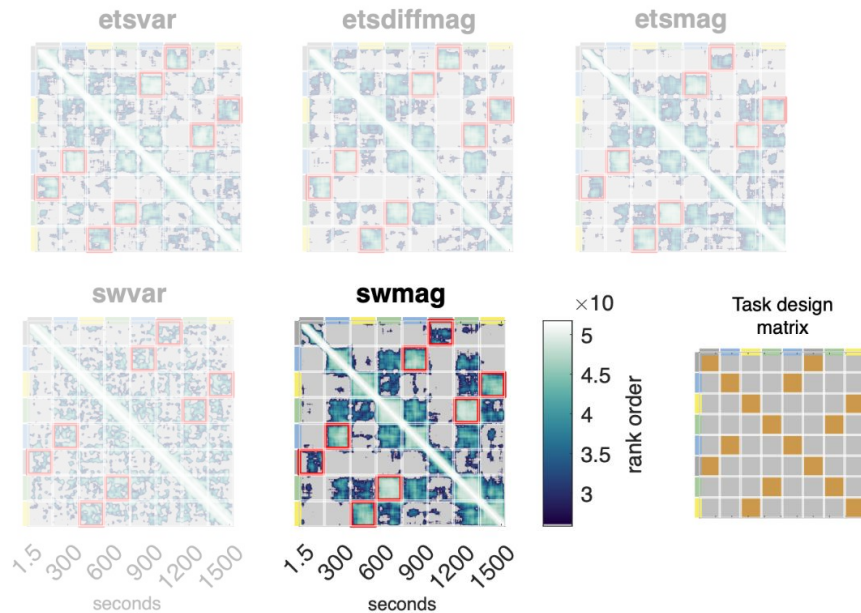


c) Precision recall curves, window of 45 sec.

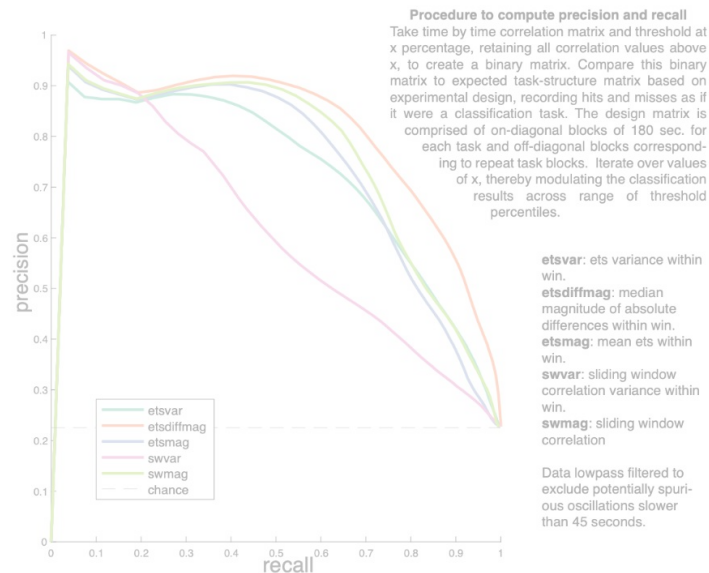


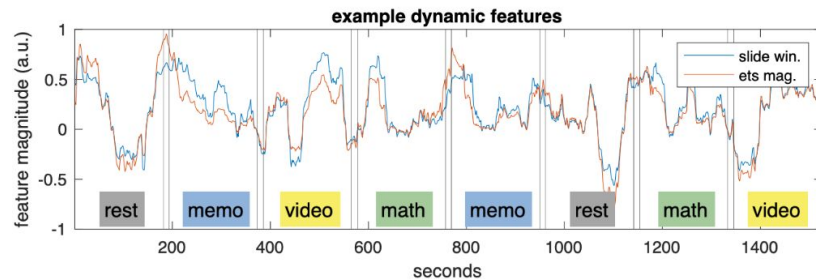
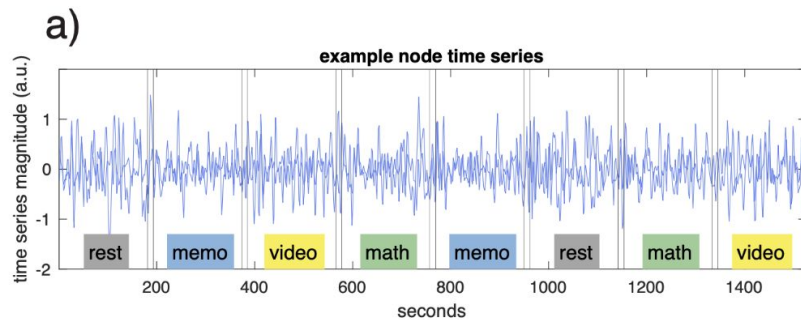


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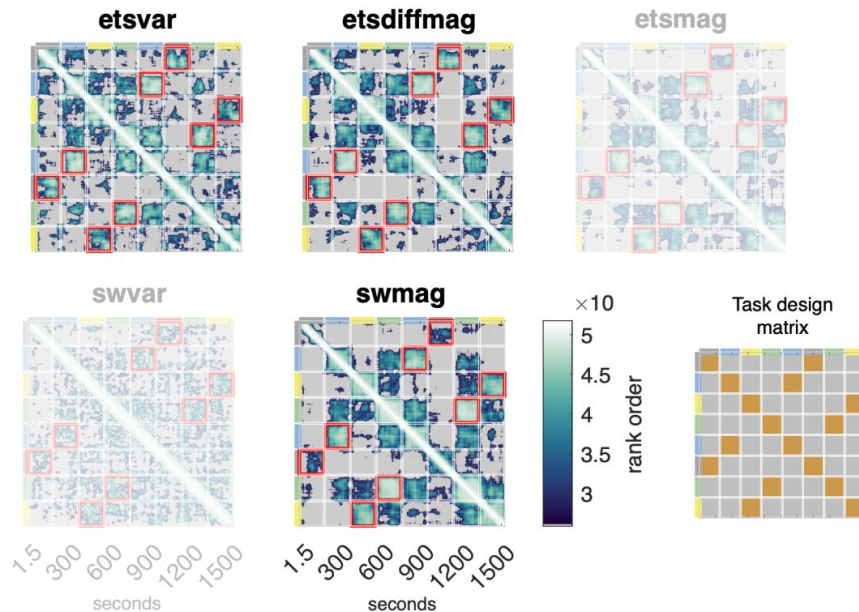


c) Precision recall curves, window of 45 sec.



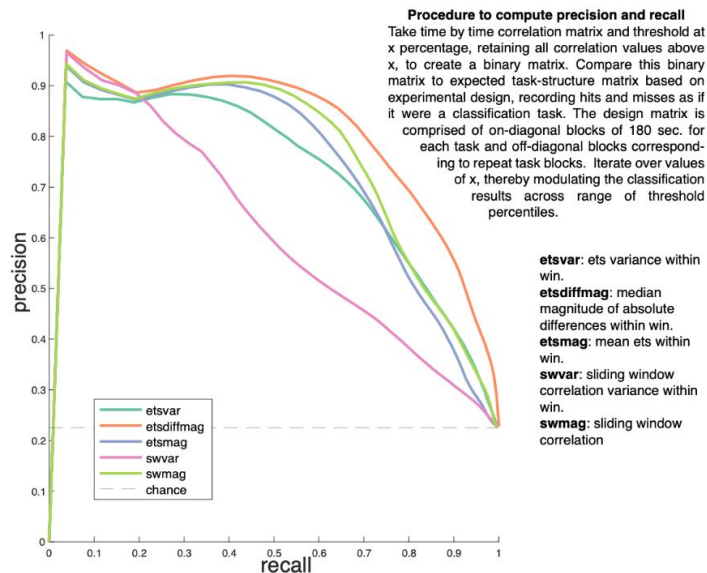
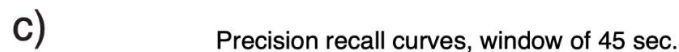
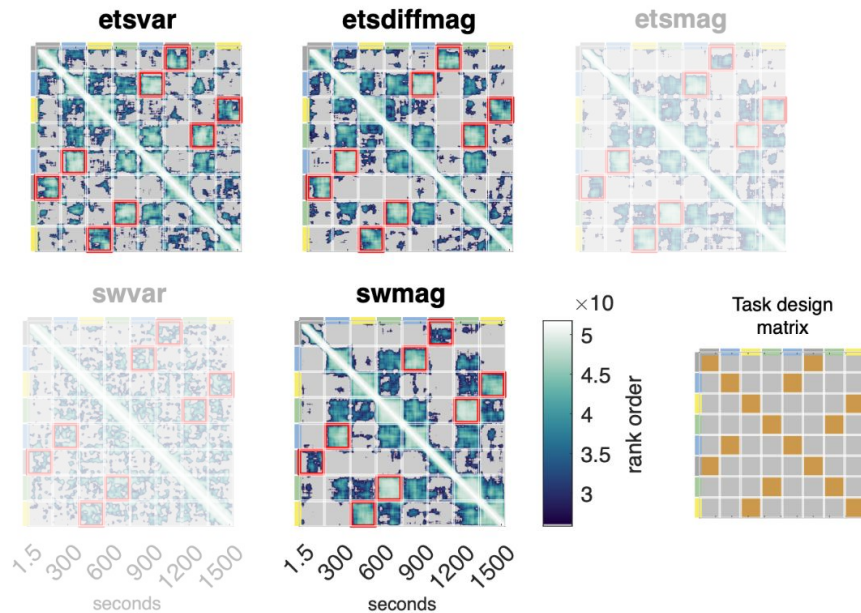
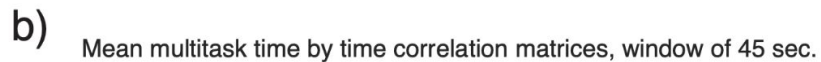
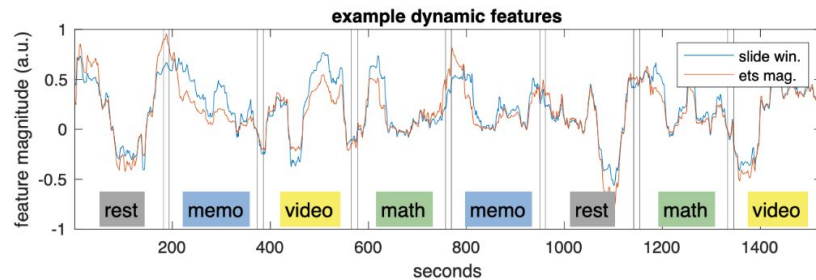
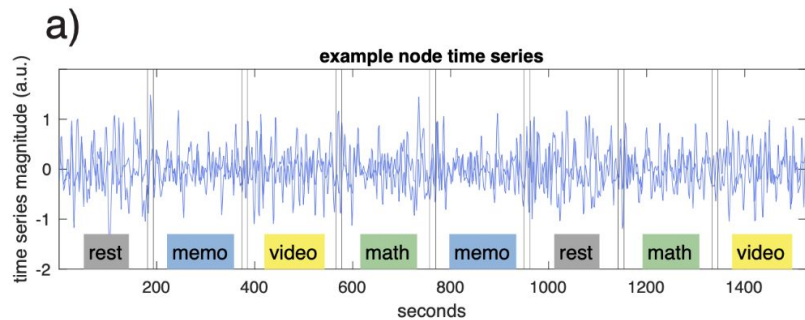


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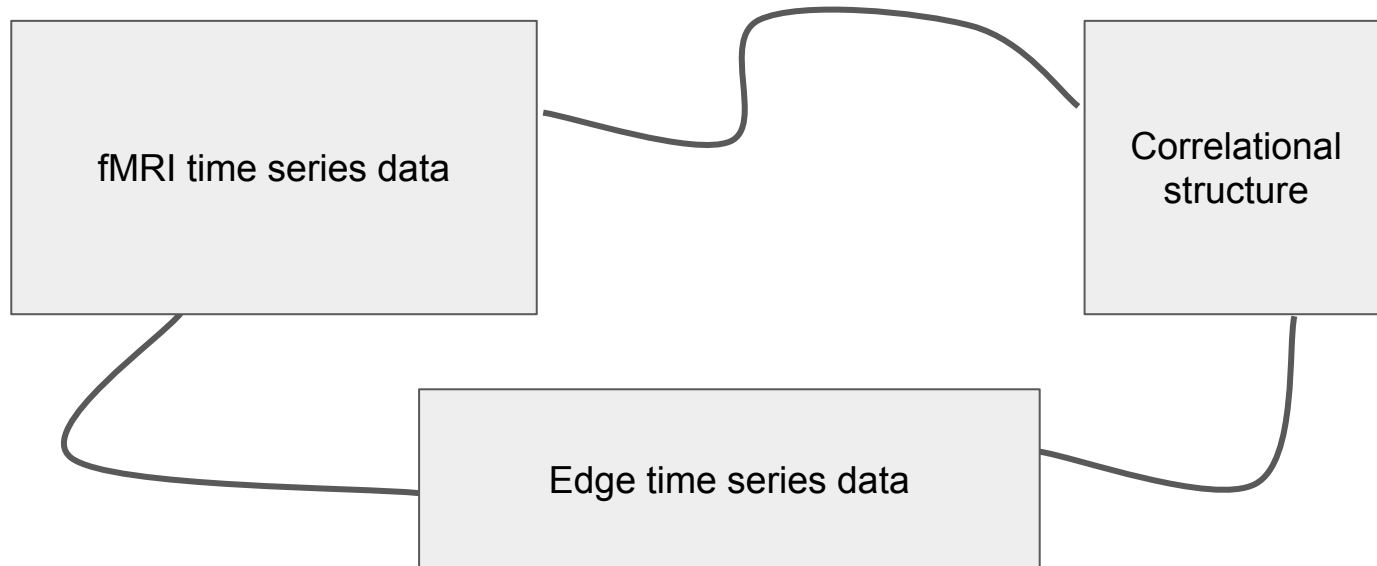
c)

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

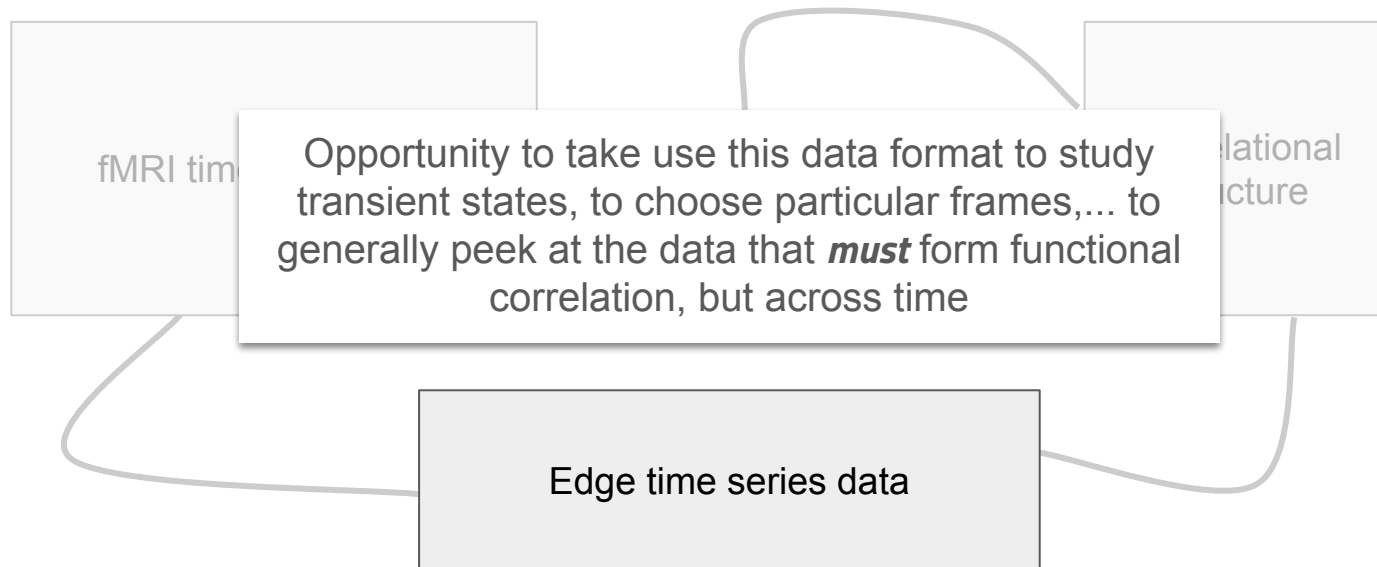


Thoughts on edge time series

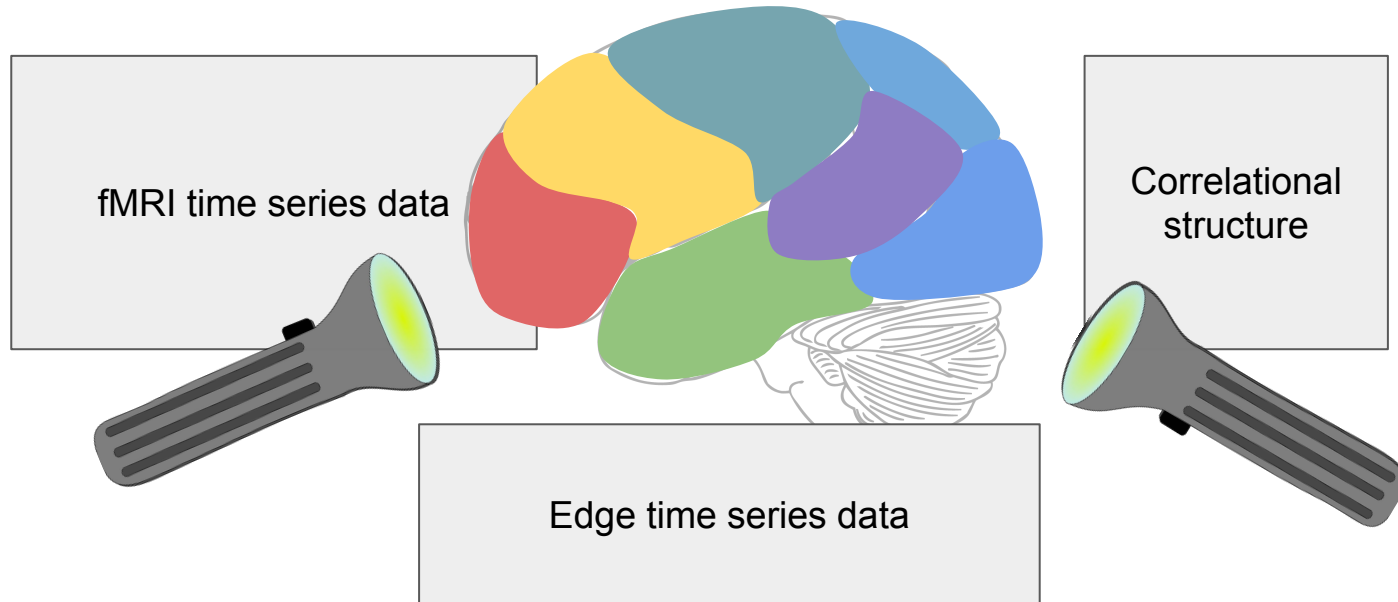
- Edge time series are a new view of the original data, which put the data in an alternative formation



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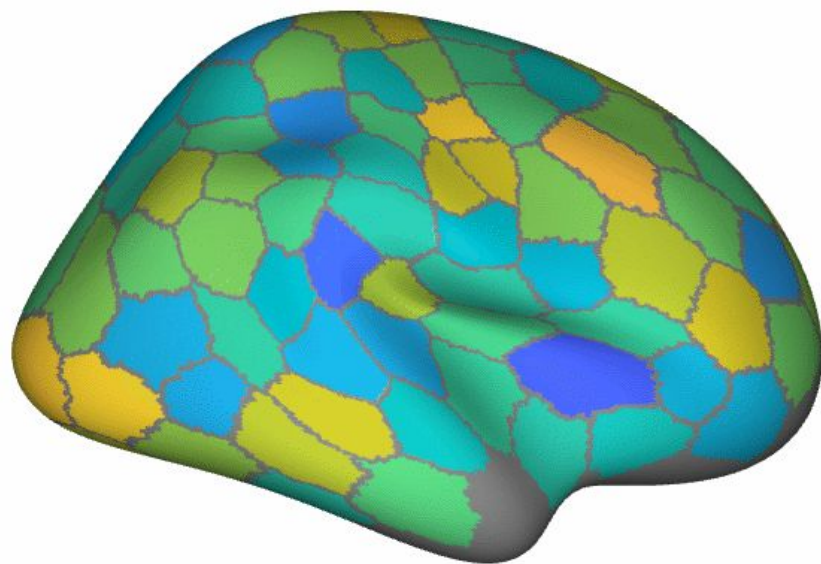


- Edge time series are a new view of the original data, which put the data in an alternative formation



Taking stock

- **Why** study connectivity?
 - Networks are nice
 - The brain as a network
 - What do we mean by connectivity?
- **How** to get your time series and constructing an FC matrix
 - Preprocessing choices
 - Modeling choices
 - Making an FC matrix
- **Ways** to analyze brain connectivity
 - Seed-based connectivity analysis
 - Time-averaged FC
 - Network-based statistic
 - Connectome predictive modeling (CPM)
 - Clustering / community detection / ICA
 - Network analysis / graph theory
 - Time-varying FC
 - Brain states
 - Dynamic FC
 - Sliding window
 - Edge time series



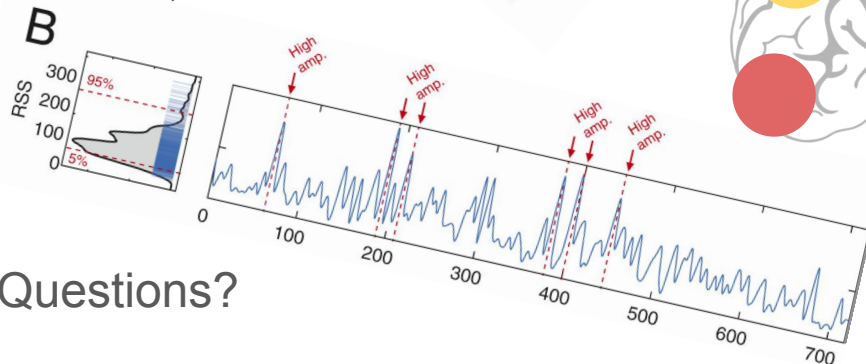
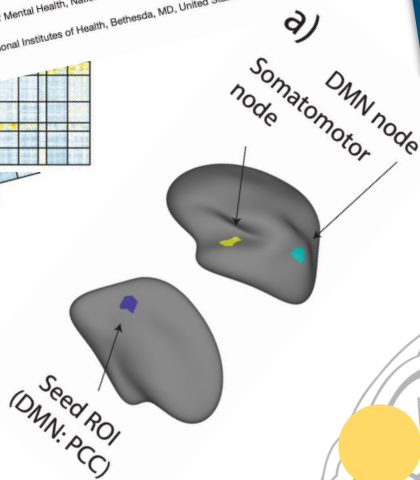
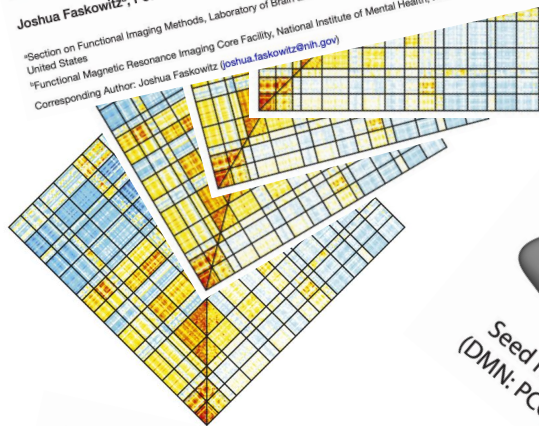
Mapping high-amplitude fMRI edge time series events across space and time

Joshua Faskowitz*, Peter A. Bandettini^{1,2}, Javier Gonzalez-Castillo*

¹Section on Functional Imaging Methods, Laboratory of Brain and Cognition, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, United States

²Functional Magnetic Resonance Imaging Core Facility, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, United States

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Questions?

REVIEW | VOLUME 27, ISSUE 11, P1068-1084, NOVEMBER 2023 [Download Full Issue](#)

Living on the edge: network neuroscience beyond nodes

Richard F. Betzel • Joshua Faskowitz • Olat Sporns • [Show footnote](#)

[Open Access](#) • Published: September 14, 2023 • <https://doi.org/10.1016/j.neuroimage.2023.119844>

On the features of spiking connectivity

Joshua Faskowitz¹, Javier Gonzalez-Castillo¹, Daniel A. Handwerker¹, Peter A. Bandettini^{1,2}

¹ Section on Functional Imaging Methods, National Institute of Mental Health, Bethesda, USA

² Functional Magnetic Resonance Imaging Core Facility, National Institute of Mental Health, Bethesda, USA

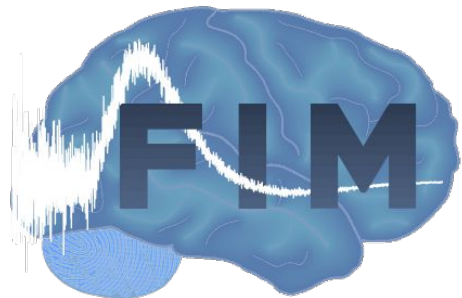
On the static and dynamic features of edge time series

Joshua Faskowitz¹, Tyler Morgan¹, Daniel A. Handwerker¹, Javier Gonzalez-Castillo¹, Peter A. Bandettini^{1,2}

¹ Section on Functional Imaging Methods, ² Functional Magnetic Resonance Imaging Core Facility, National Institute of Mental Health, Bethesda, USA



National Institute of Mental Health

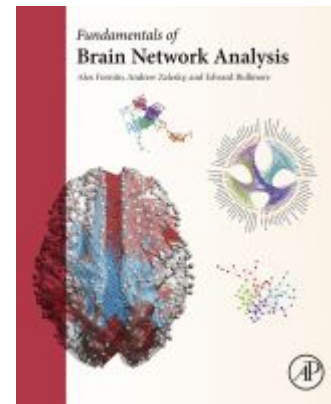


Extra resources

Resources

- Reading

- *Fundamentals of Brain Network Analysis*.
 - **FANTASTIC & Didactic** book, convince lab to obtain a copy
 - [First chapter here for free](#), a good introduction to network neuroscience for new students to get the gist of the field
- [Blog post from OHBM](#) about the network neuroscience educational workshop
- *Discovering the Human Connectome*. A classic!



Resources

- Review Papers

- *Shameless self promotion!!!* [Edges in Brain Networks: Contribution to Models of Structure and Function](#)
- [Linking Structure and Function in Macroscale Brain Networks](#)
- [The road ahead in clinical network neuroscience](#)
- [Network Neuroscience](#)
- [On the nature and use of models in network neuroscience](#)
- [Modular Brain Networks](#)
- [Communication Dynamics in Complex Brain Networks](#)

Resources

- Videos



OHBM network neuroscience educational workshop has videos released:

Part 1 (Alex Fornito) <https://youtu.be/kgUZ1d7JRRY>

Part 2 (Robert Smith) <https://youtu.be/gR6iMuMSuYU>

Part 3 (Petra Ritter) <https://youtu.be/hjZAok-Z-Ps>

Part 4 (Rick Betzel) <https://youtu.be/LkHTFiwzRWY>