Global topology of brain-wide co-fluctuations

Implications on task states, personality, and behavioral symptom dimensions

Chunyin Siu

siuc@Stanford.edu

About me

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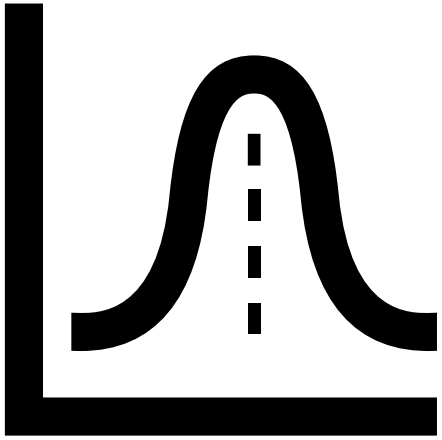

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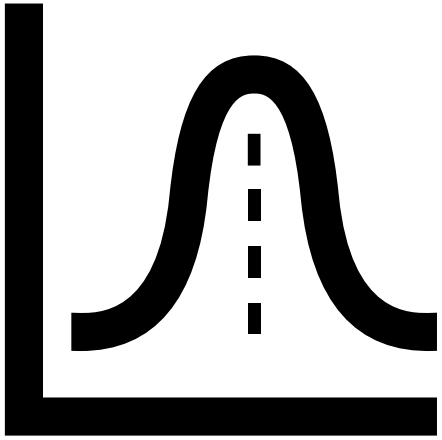

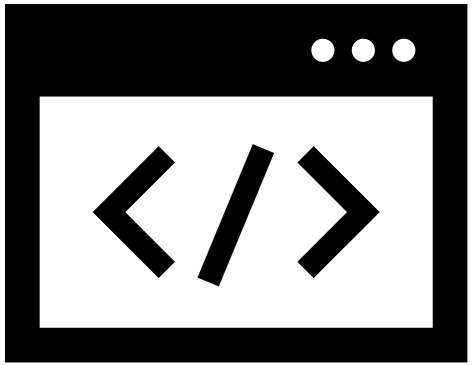

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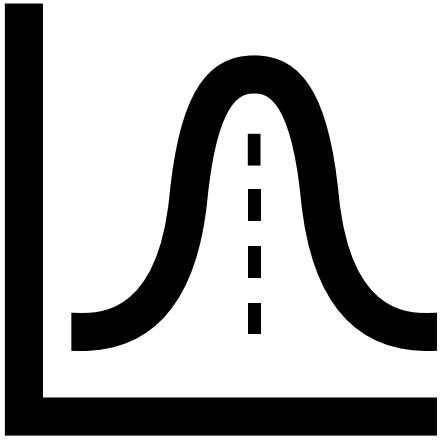

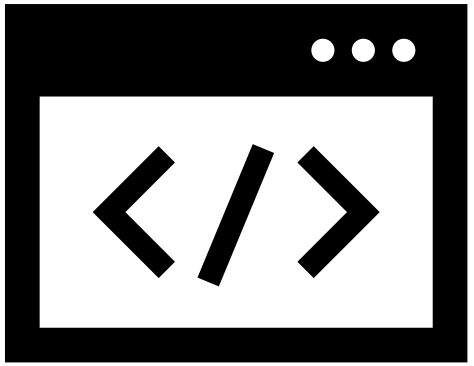

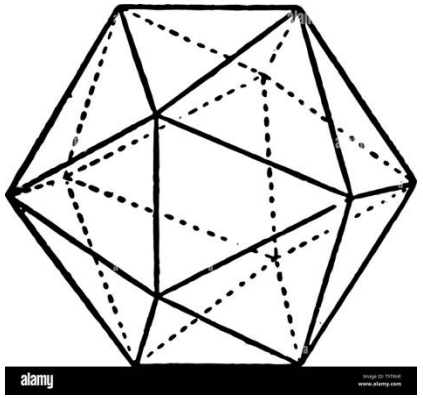

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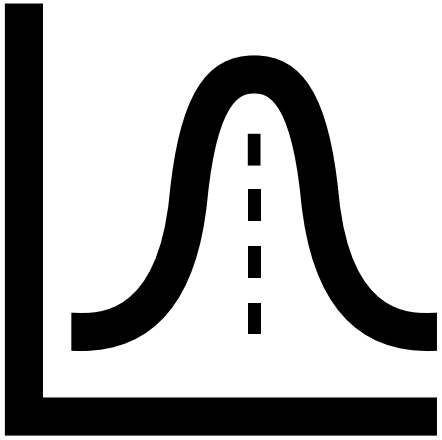
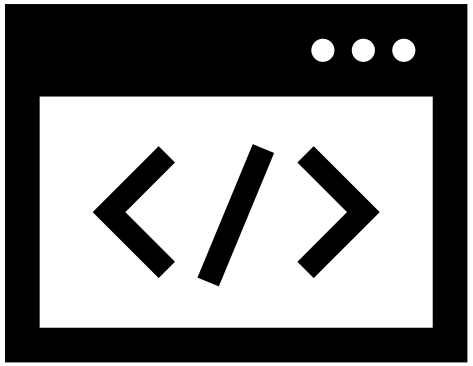
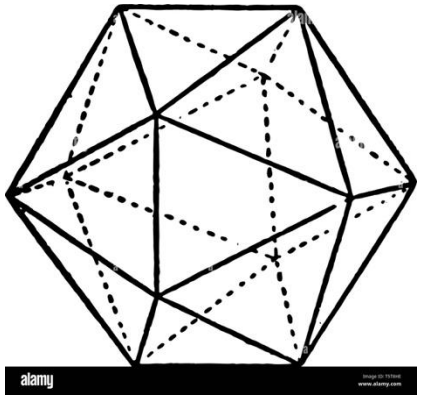
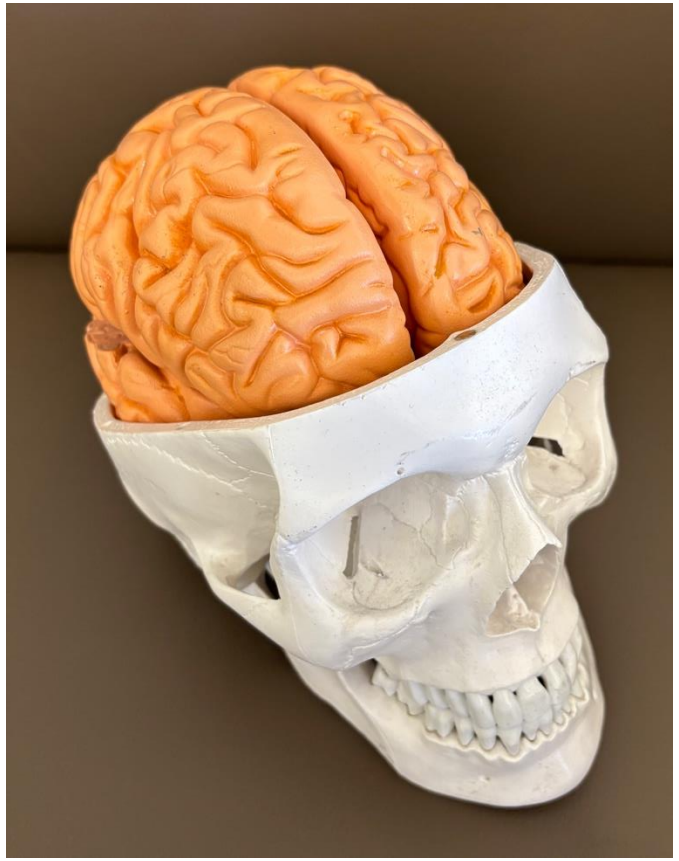






Why mathematics?



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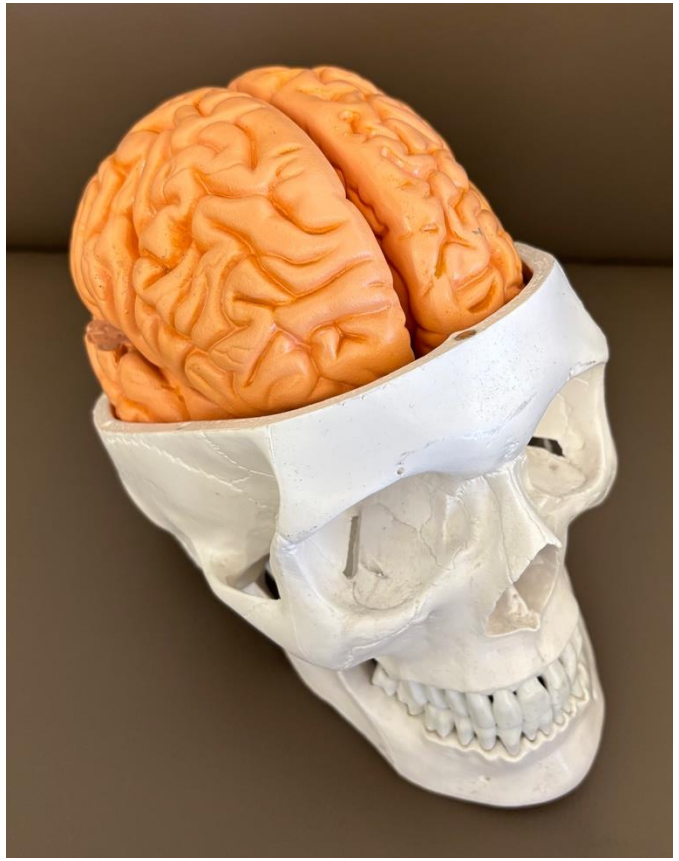
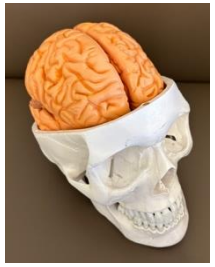


- 3D geometry

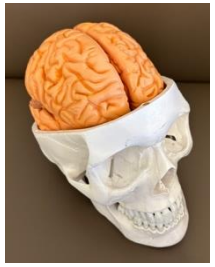
Why mathematics?

- 3D geometry
- Interactions of brain regions



- How to understand the activity of brain regions?

?



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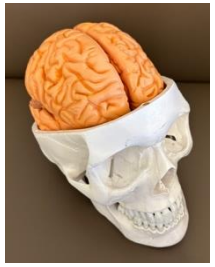
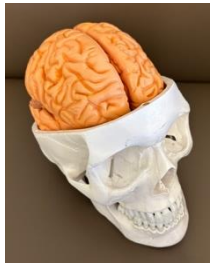
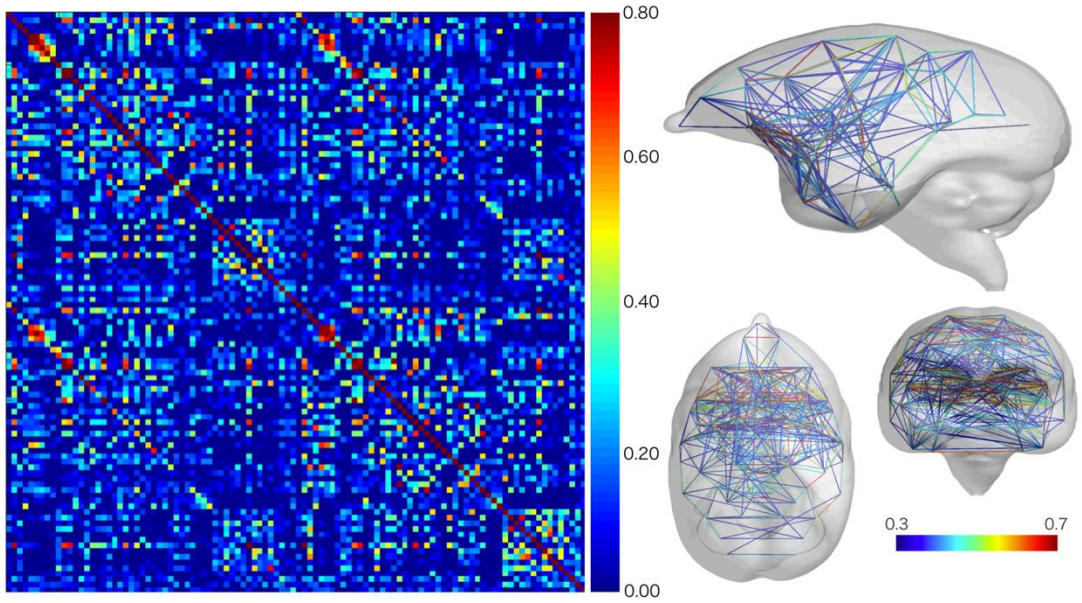


- How to understand the activity of brain regions?
- How to understand the **interactions** of brain regions?
- How to understand their interaction **over time**?



- How to understand the activity of brain regions?
- How to understand the **interactions** of brain regions?
- How to understand their interaction **over time**?
- How to understand how these interactions give rise to **different behavior**?

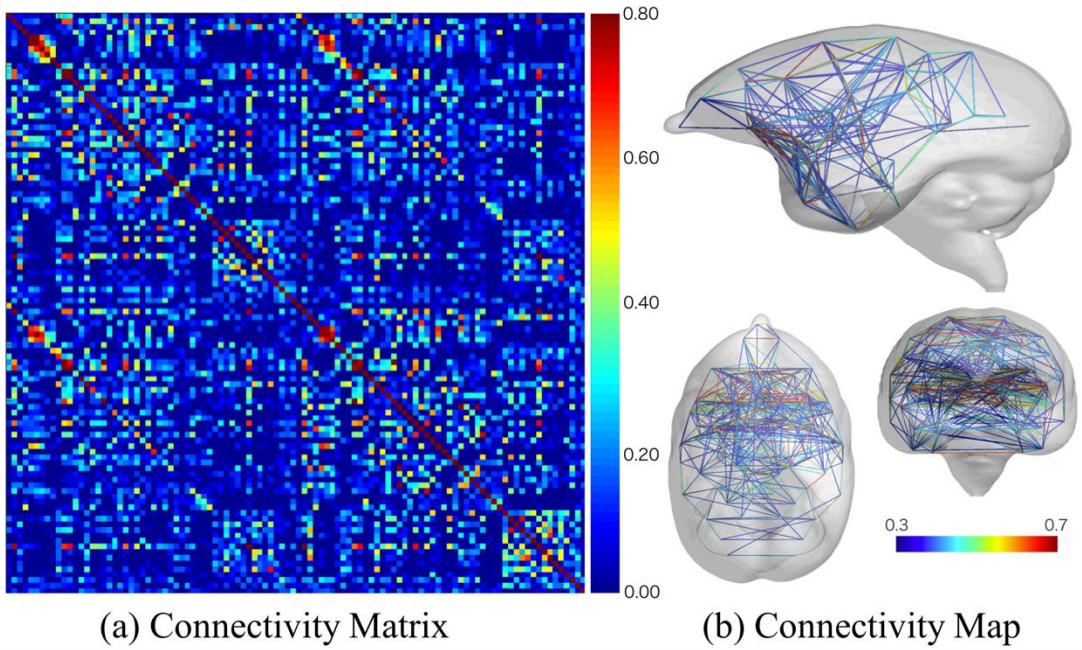
Recap on Functional Connectivity



(a) Connectivity Matrix (b) Connectivity Map

https://cds.ismrm.org/protected/19MProceedings/PDFfiles/3435.html

Recap on Functional Connectivity



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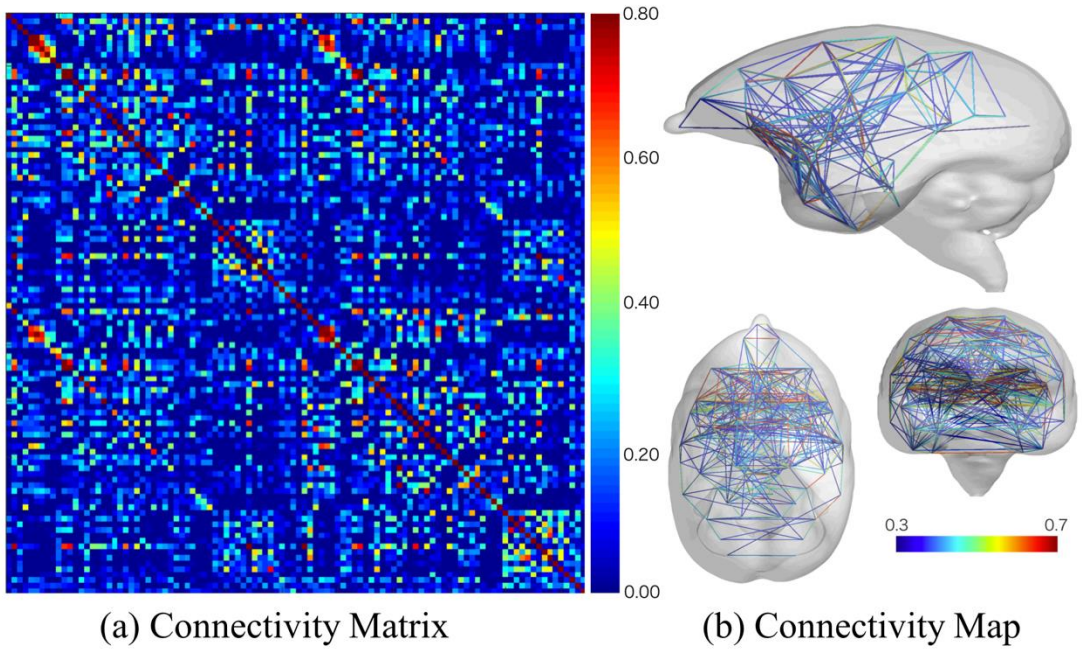
Functional connectivity of two brain regions

Recap on Functional Connectivity



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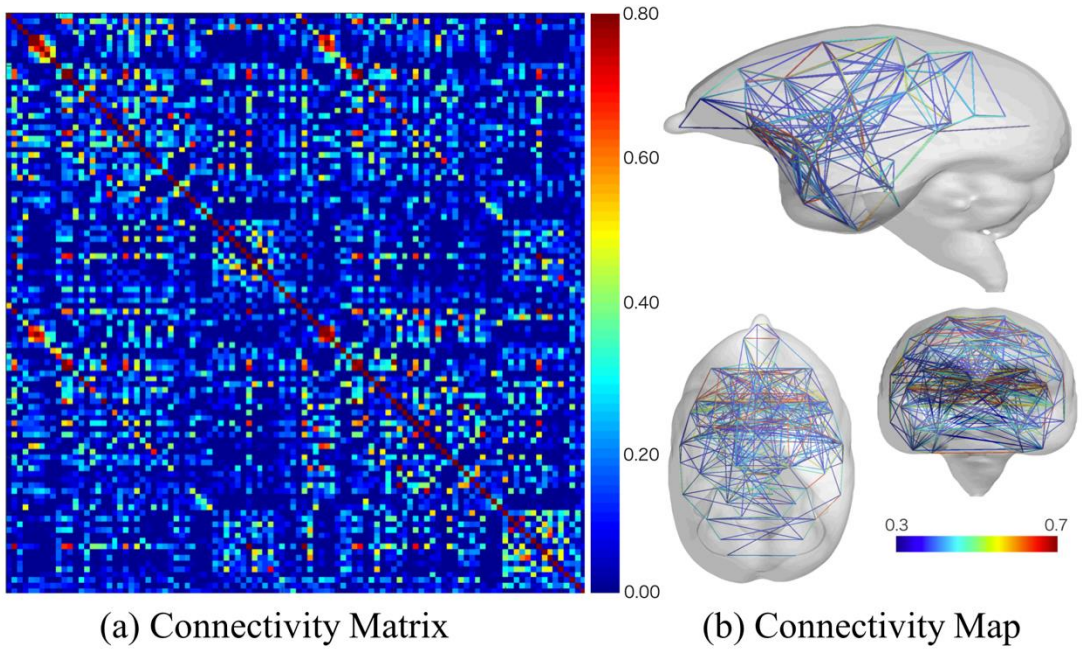
Functional connectivity of two brain regions
= temporal correlation of brain activity of the two regions

Recap on Functional Connectivity



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Functional connectivity of two brain regions
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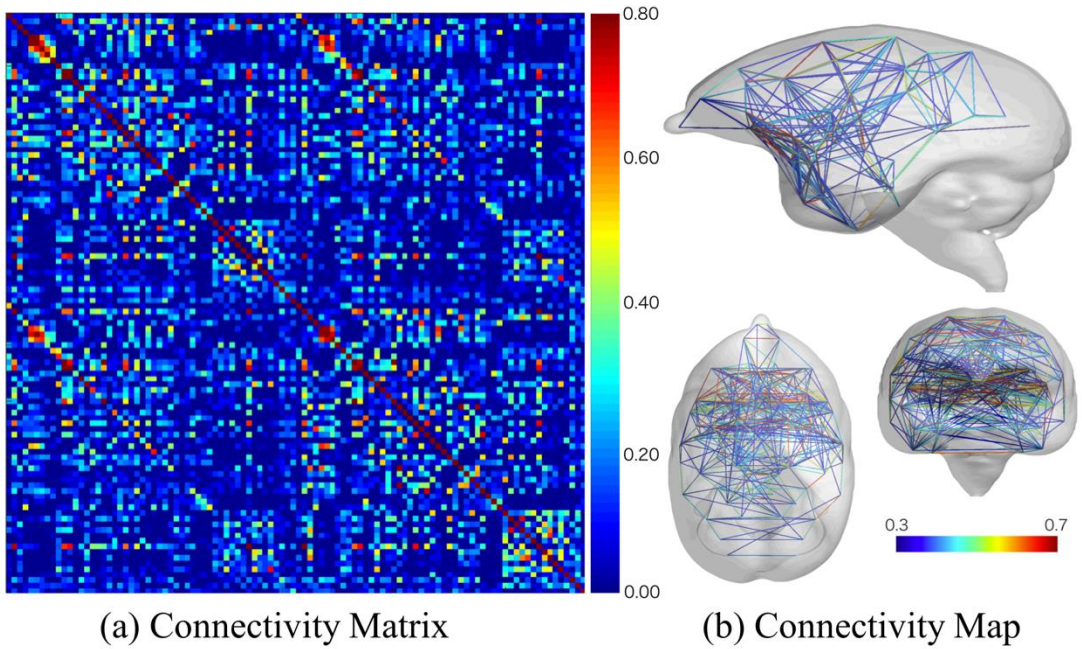

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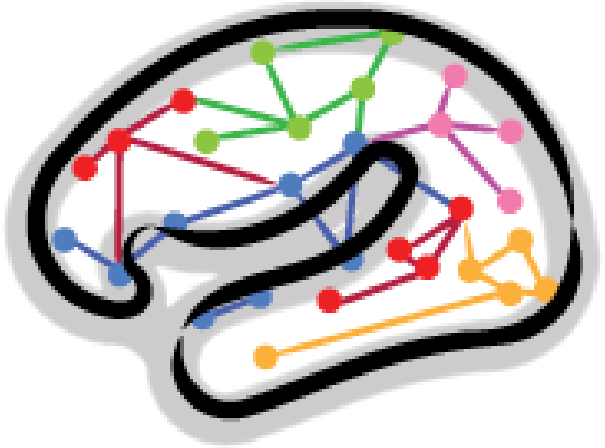
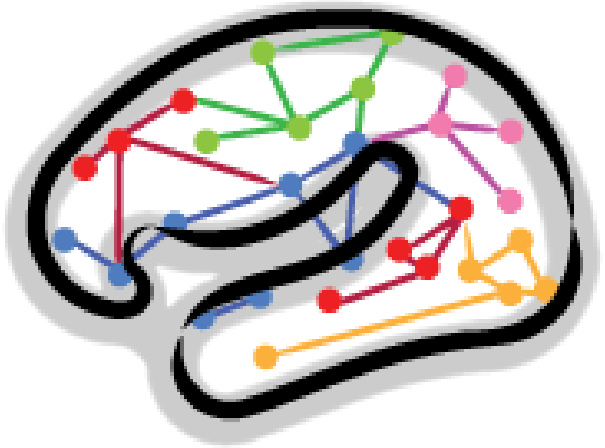
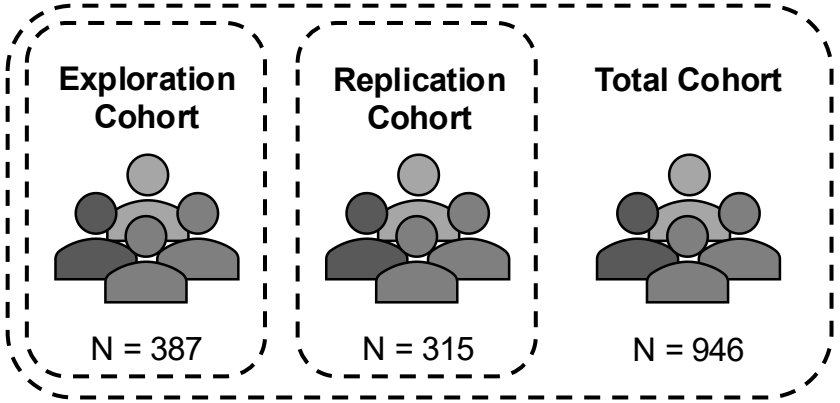
What about brain dynamics?

I. How to represent high-dimensional brain dynamics

Review on brain dynamics Mapper



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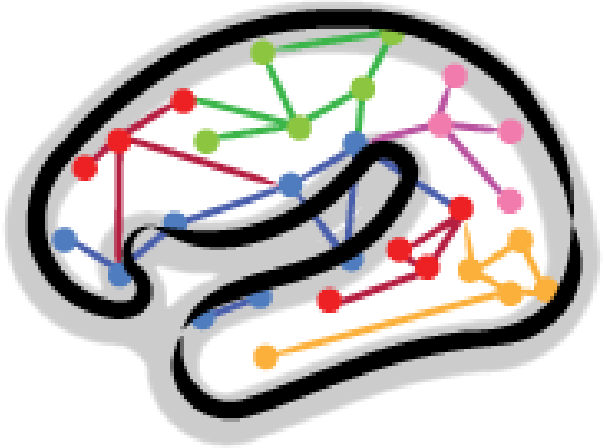
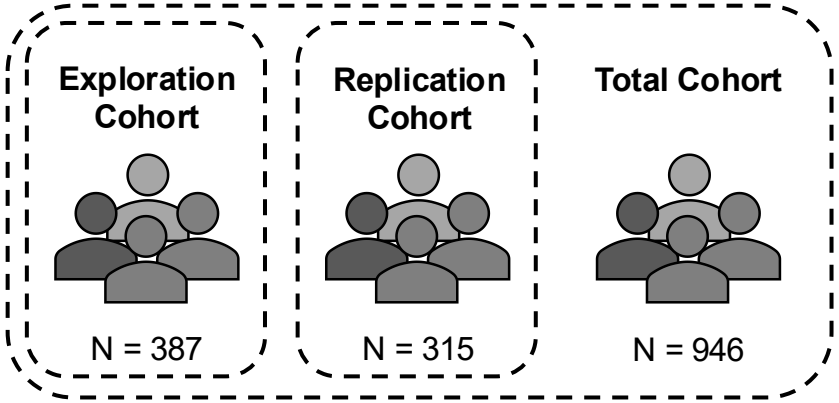
N = 387
Replication Cohort
N = 315
Total Cohort
N = 946

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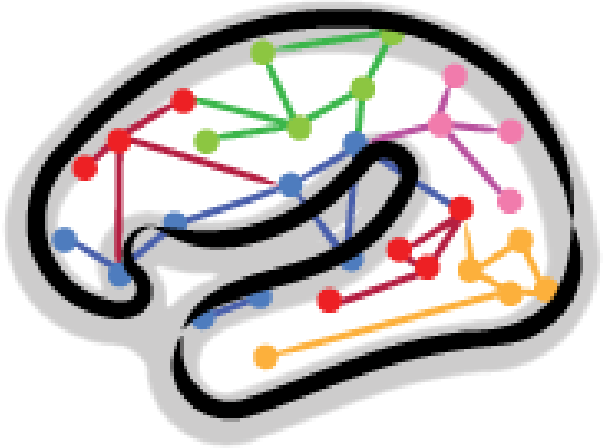

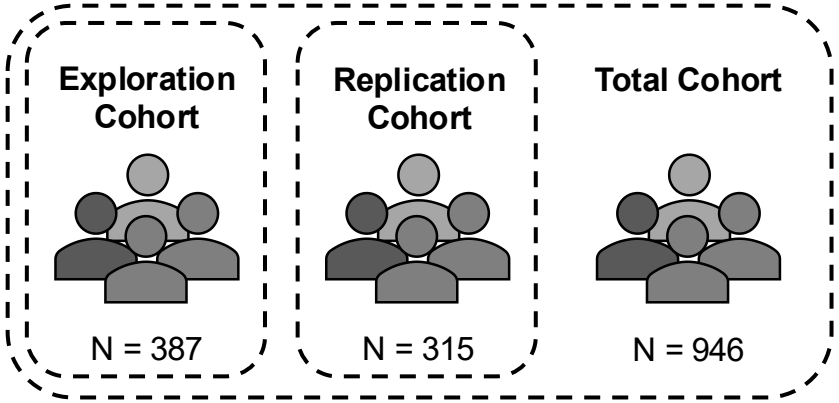
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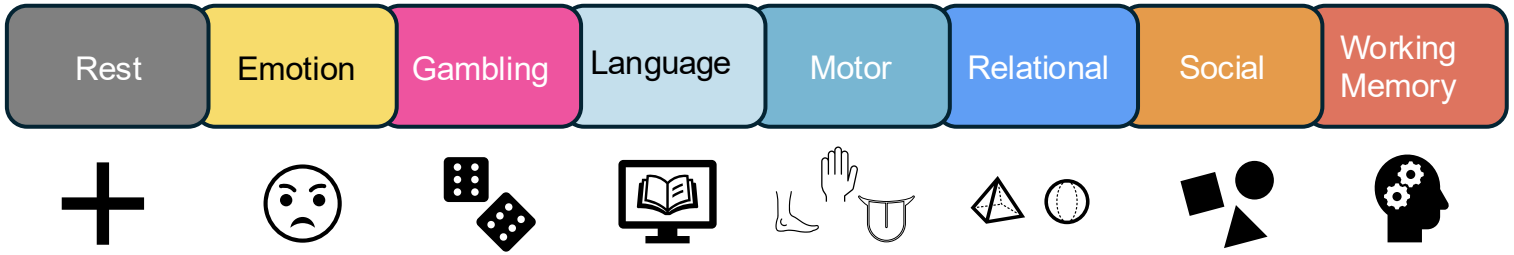
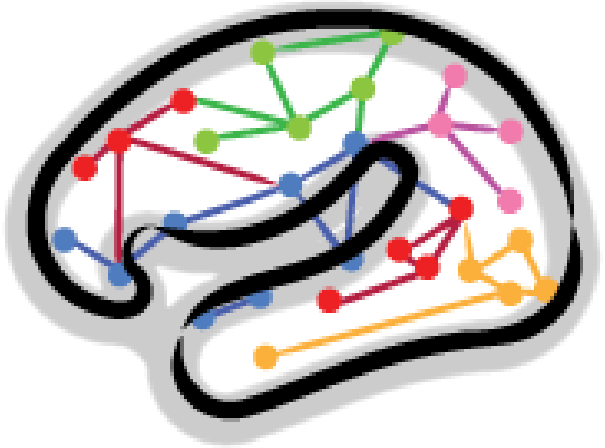
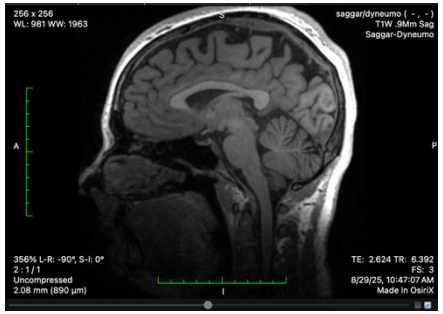
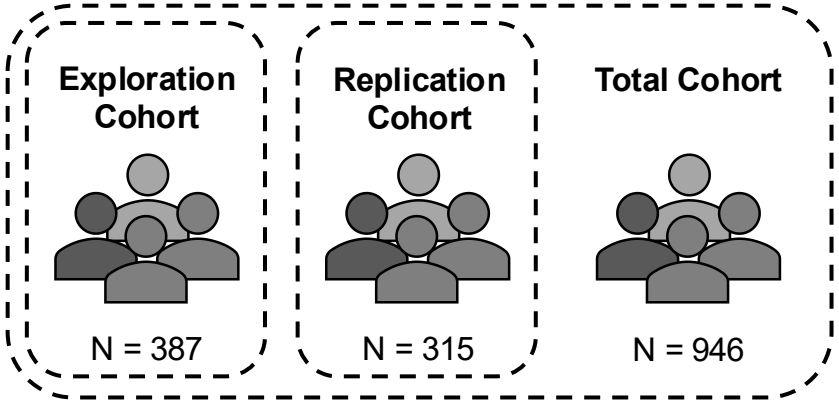

Rest
Emotion
Gambling
Language
Motor
Relational
Social
Working Memory




256 x 256
WL: 981 WW: 1963
saggar/dyneumo (- , -)
T1W .9Mm Sag
Saggar-Dyneumo
A
P
356% L-R: -90°, S-I: 0°
2 : 1 / 1
Uncompressed
2.08 mm (890 µm)
TE: 2.624 TR: 6.392
FS: 3
8/29/25, 10:47:07 AM
Made in OsiriX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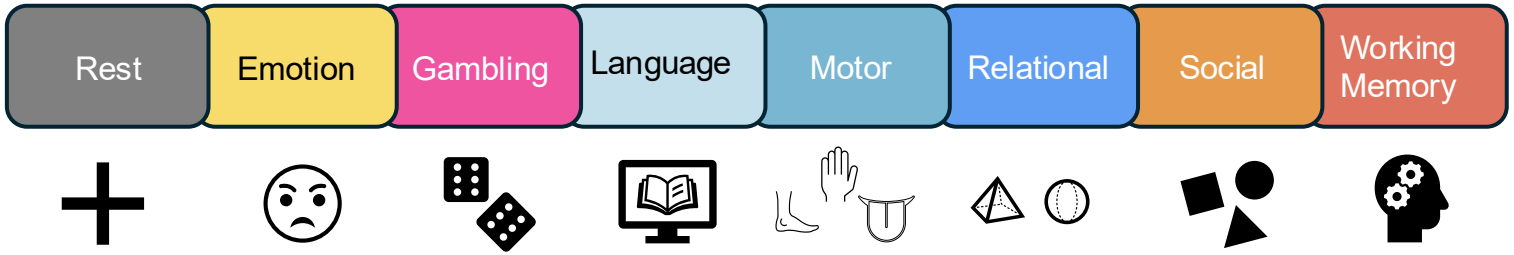
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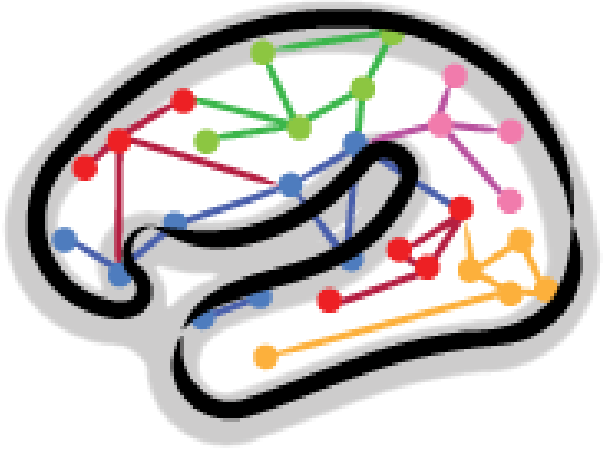

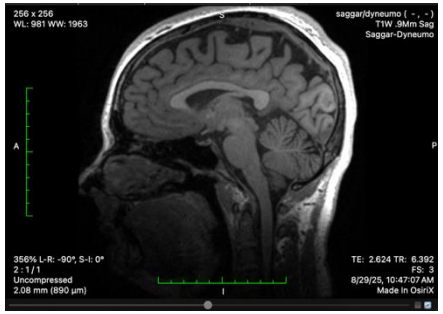
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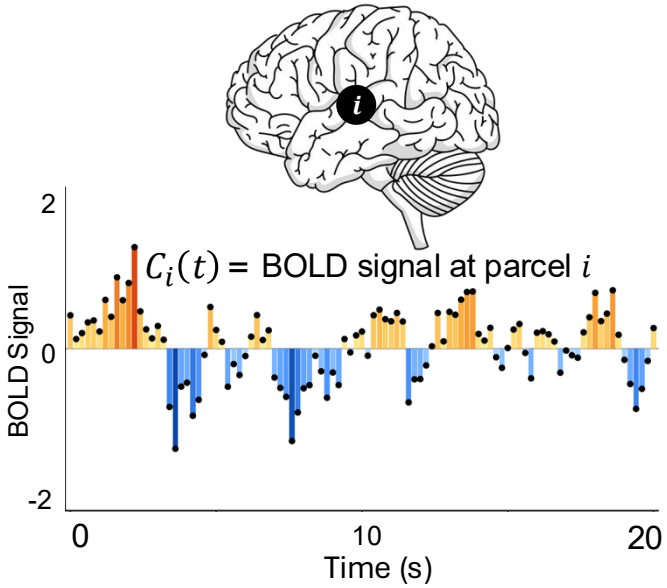
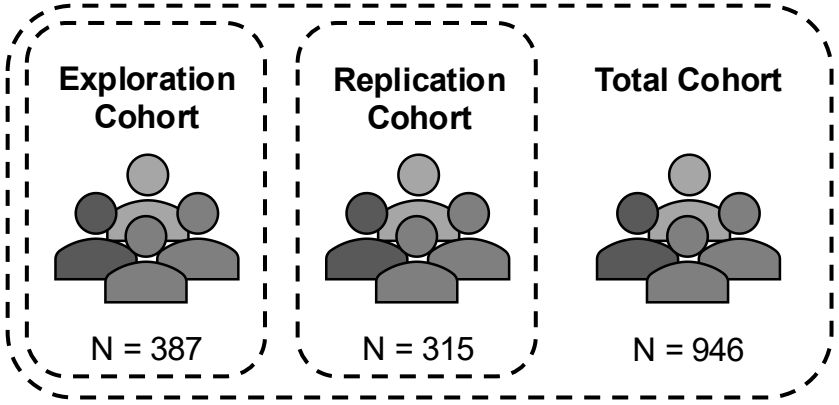

$C_i(t)$ = BOLD signal at parcel i
BOLD Signal
2
0
-2
0
10
20
Time (s)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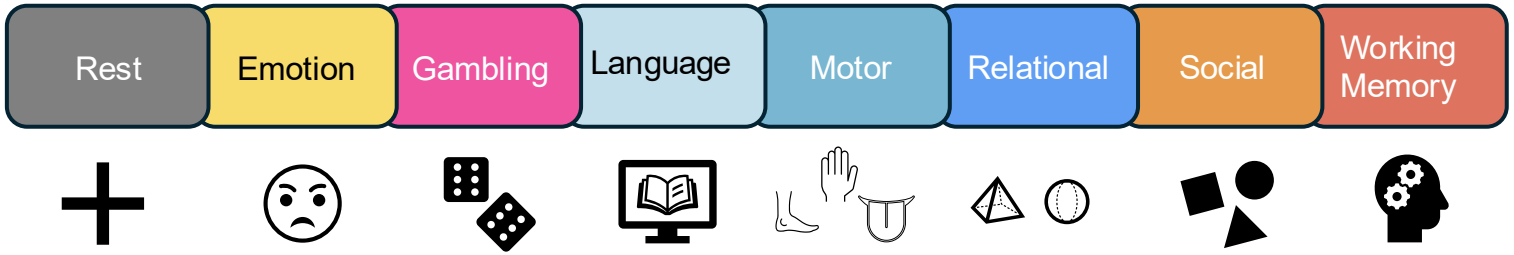
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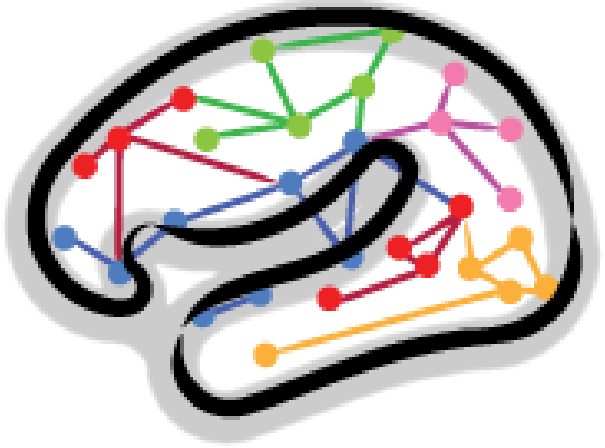

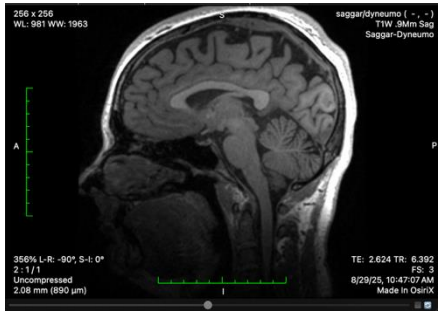

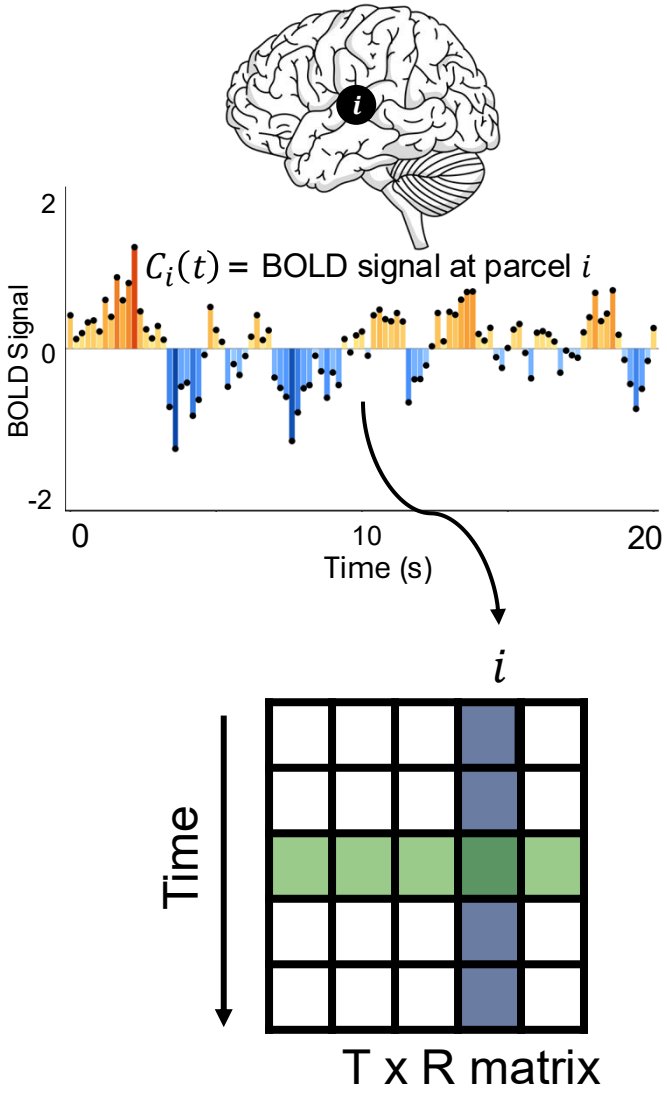

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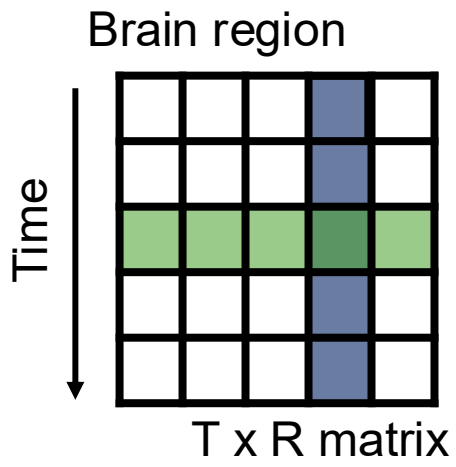
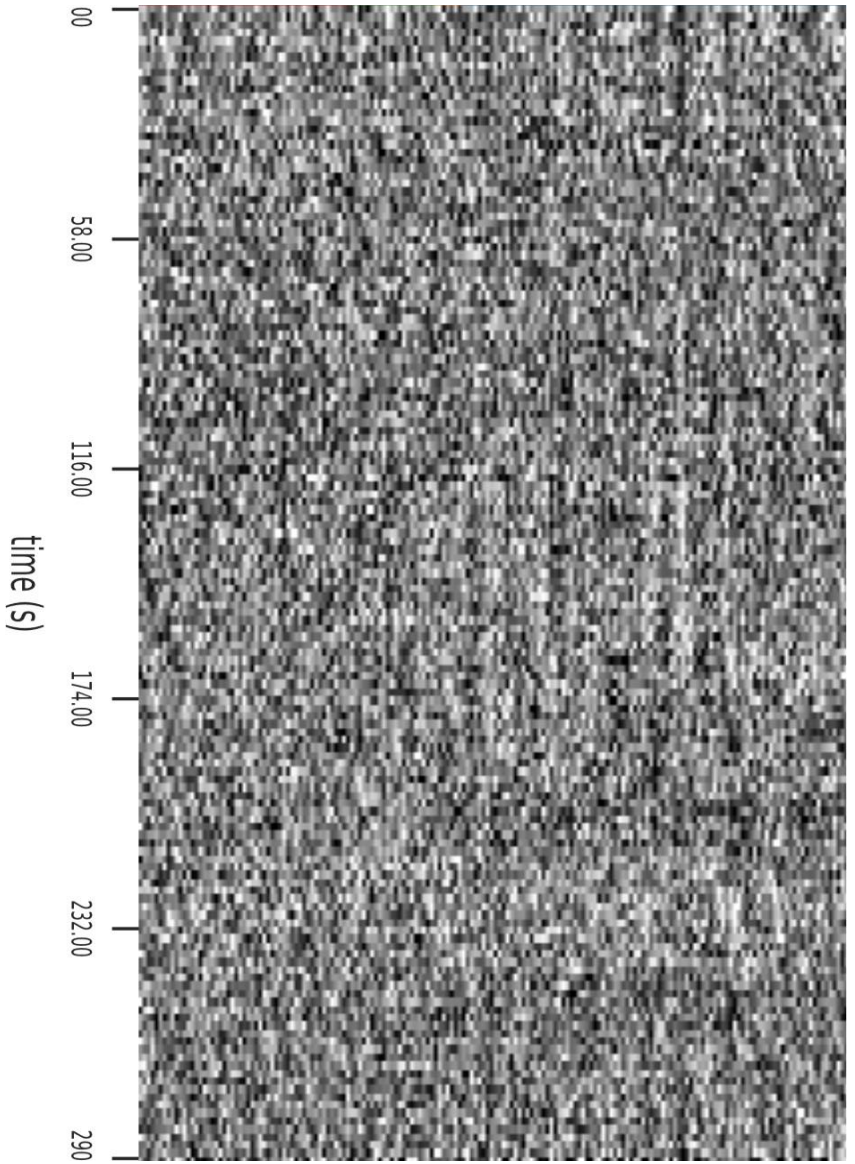
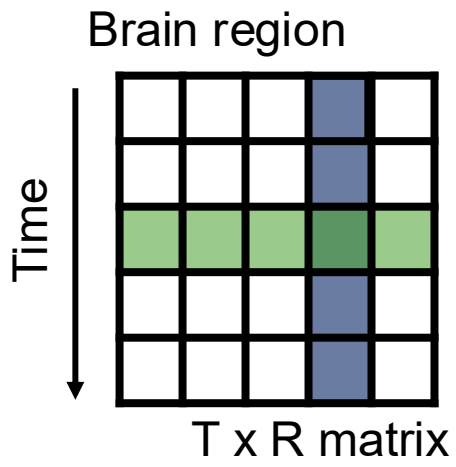
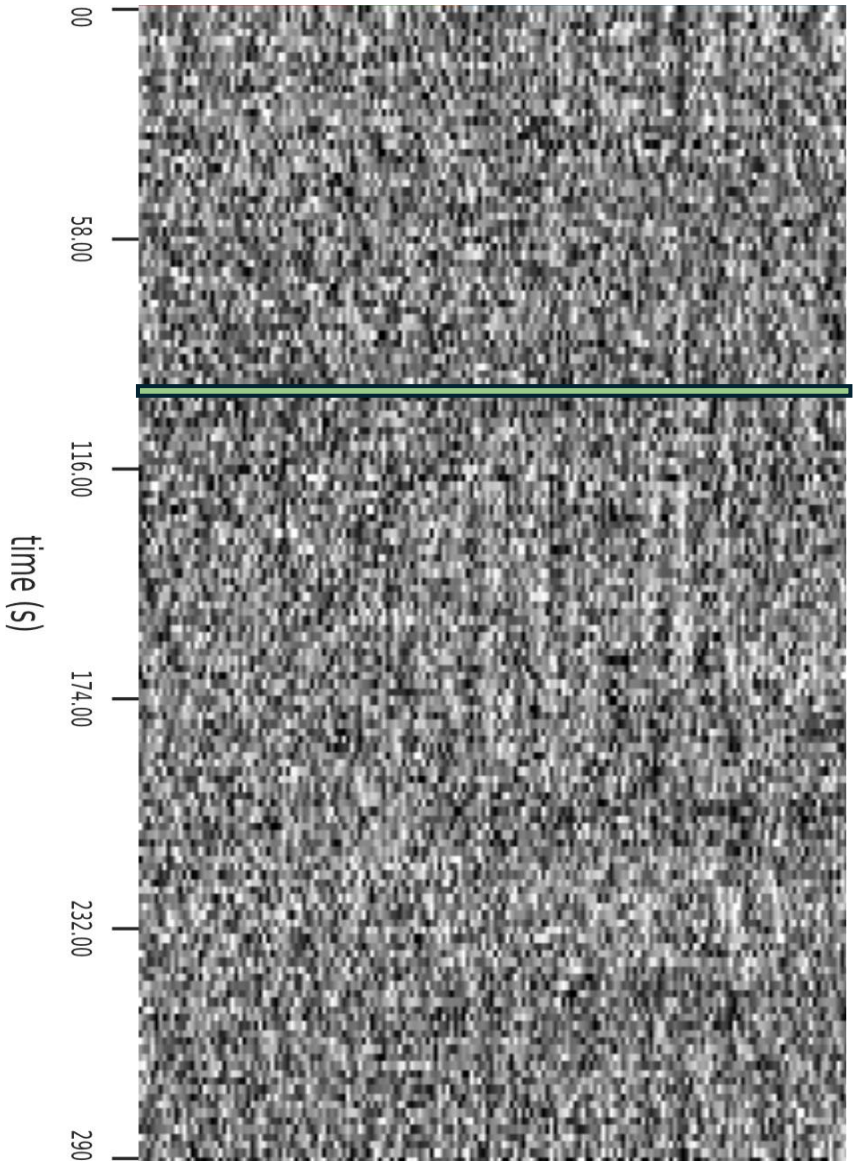




https://andysbrainbook.readthedocs.io/en/latest/OpenScience/OS/fMRIPrep_Demo_3_ExaminingPreprocData.html





Very high-dimensional!

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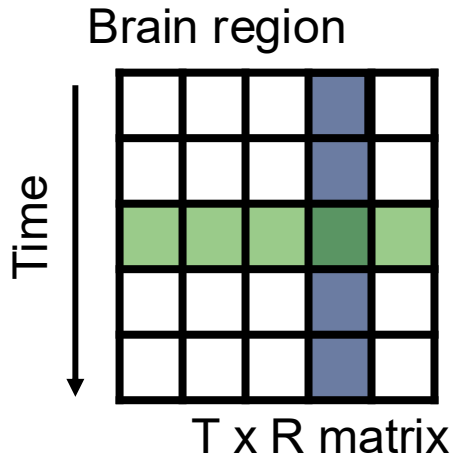
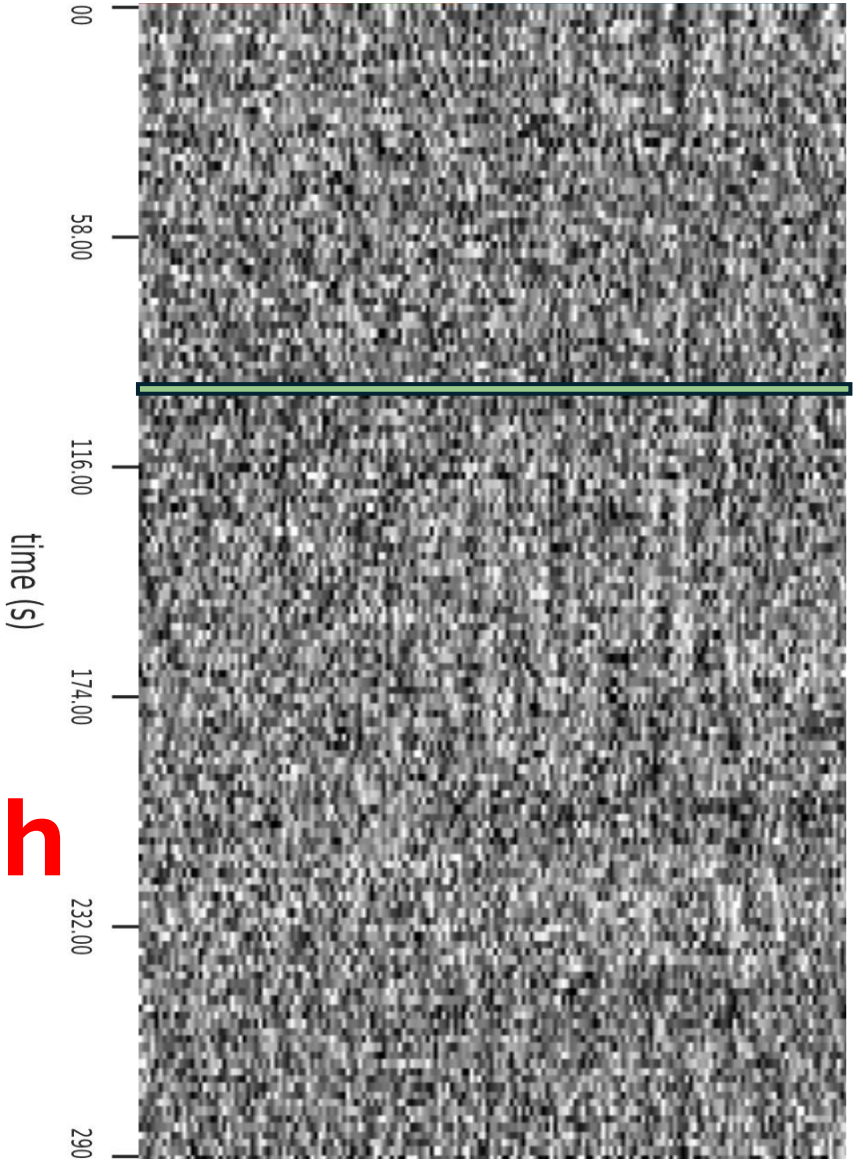


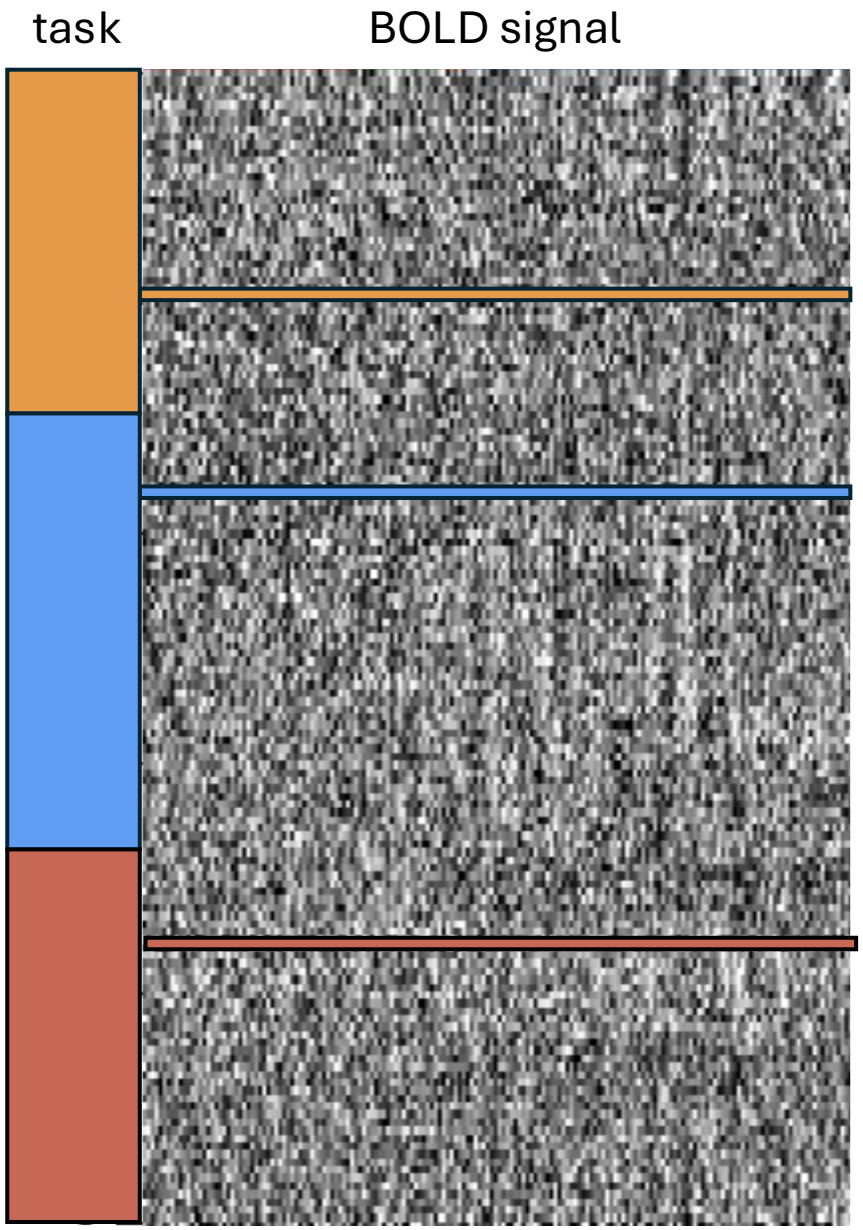


Very high-dimensional!

Solution: Mapper graph

a graphical summary of the distribution of high-dimensional points

https://andysbrainbook.readthedocs.io/en/latest/OpenScience/OS/fMRIPrep_Demo_3_ExaminingPreprocData.html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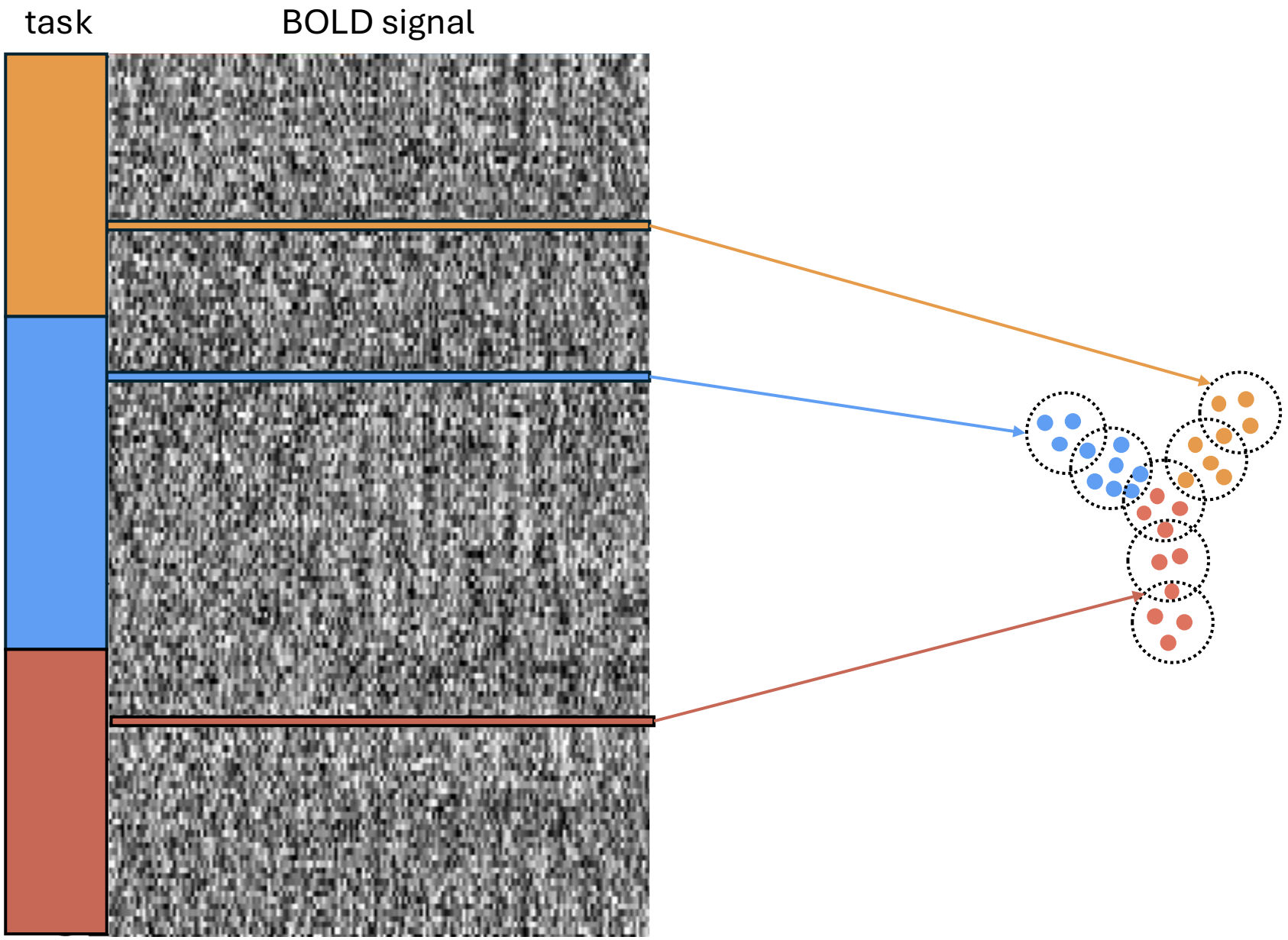
BOLD signal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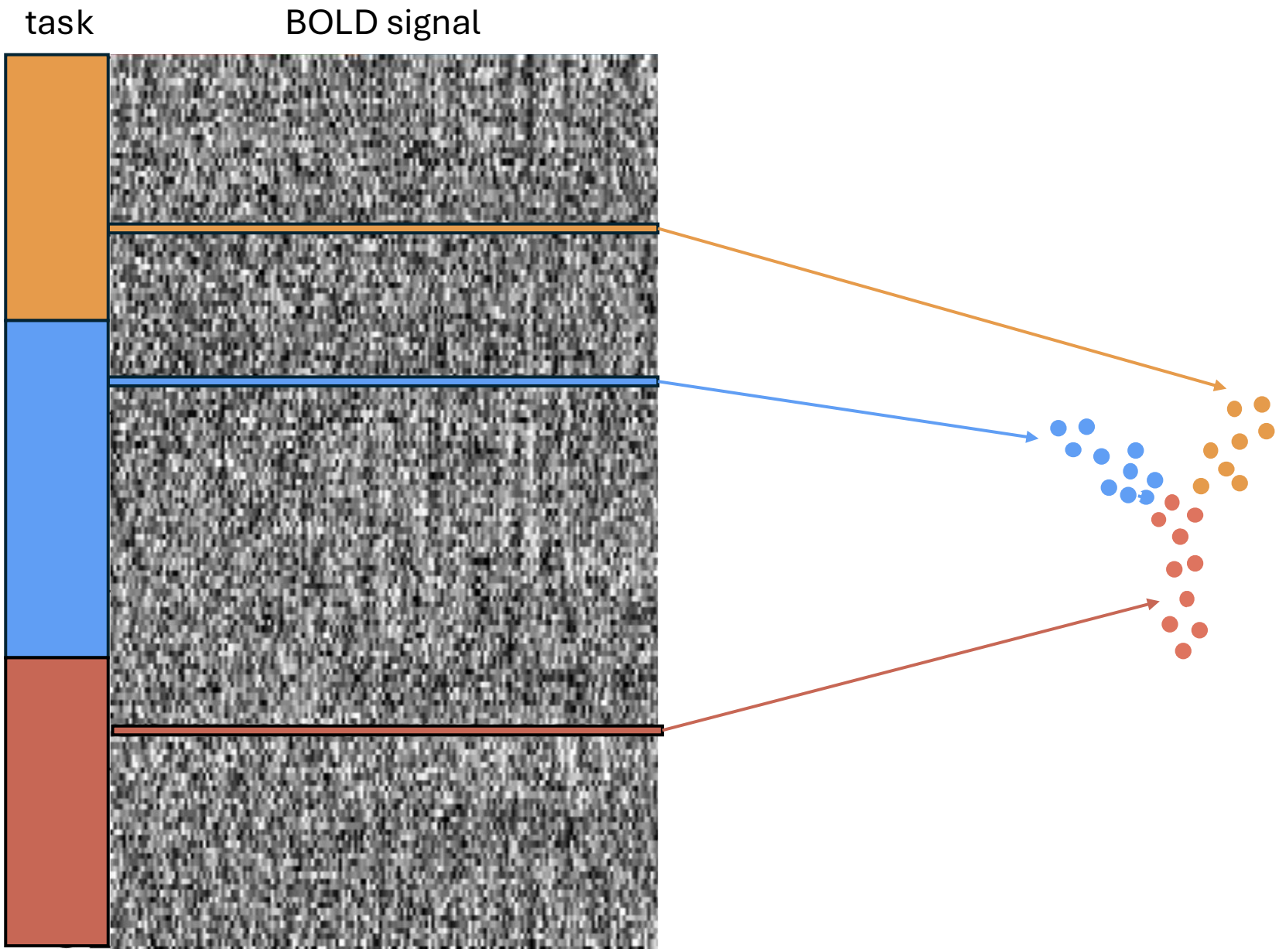
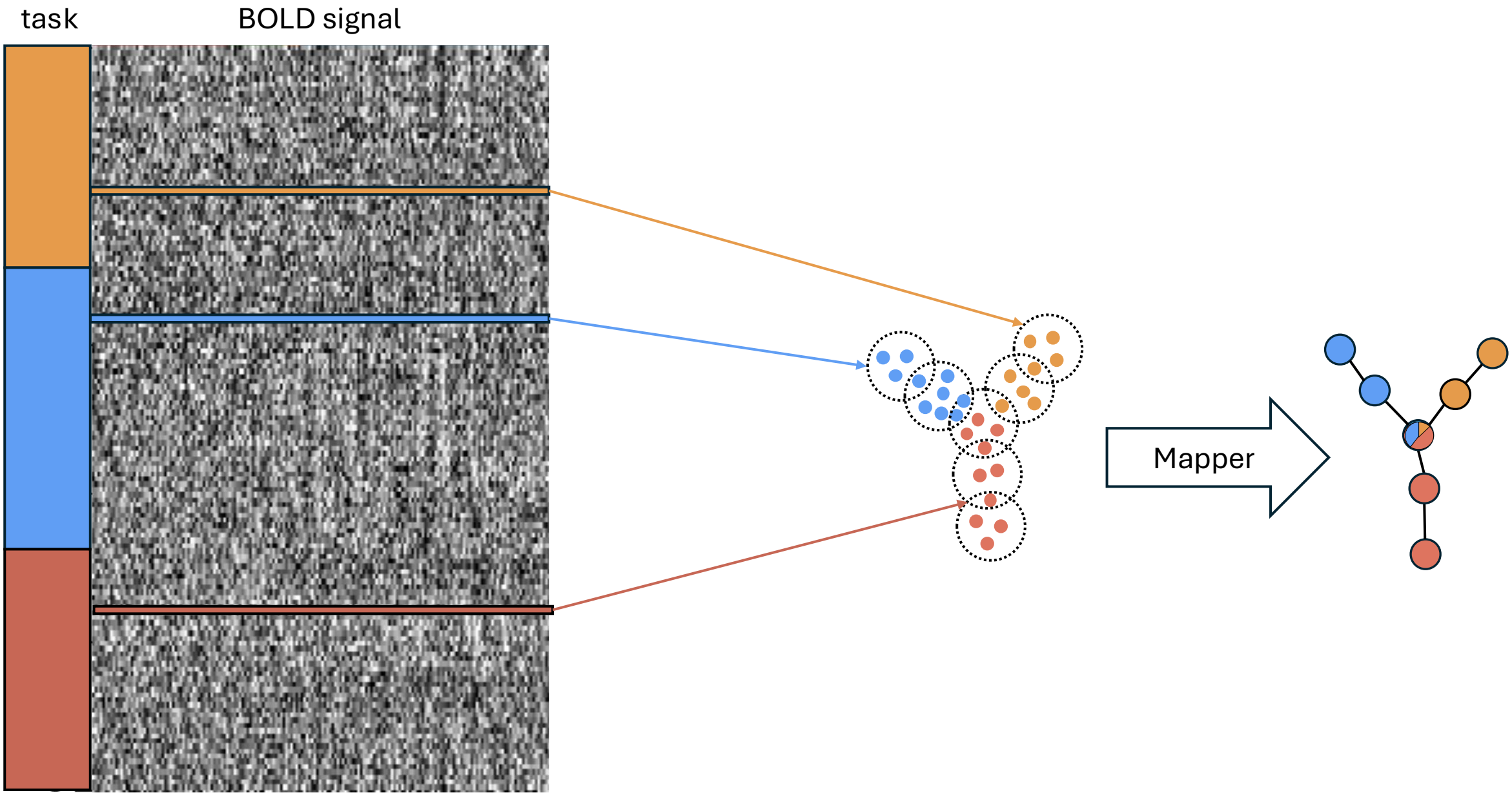

task
BOLD signal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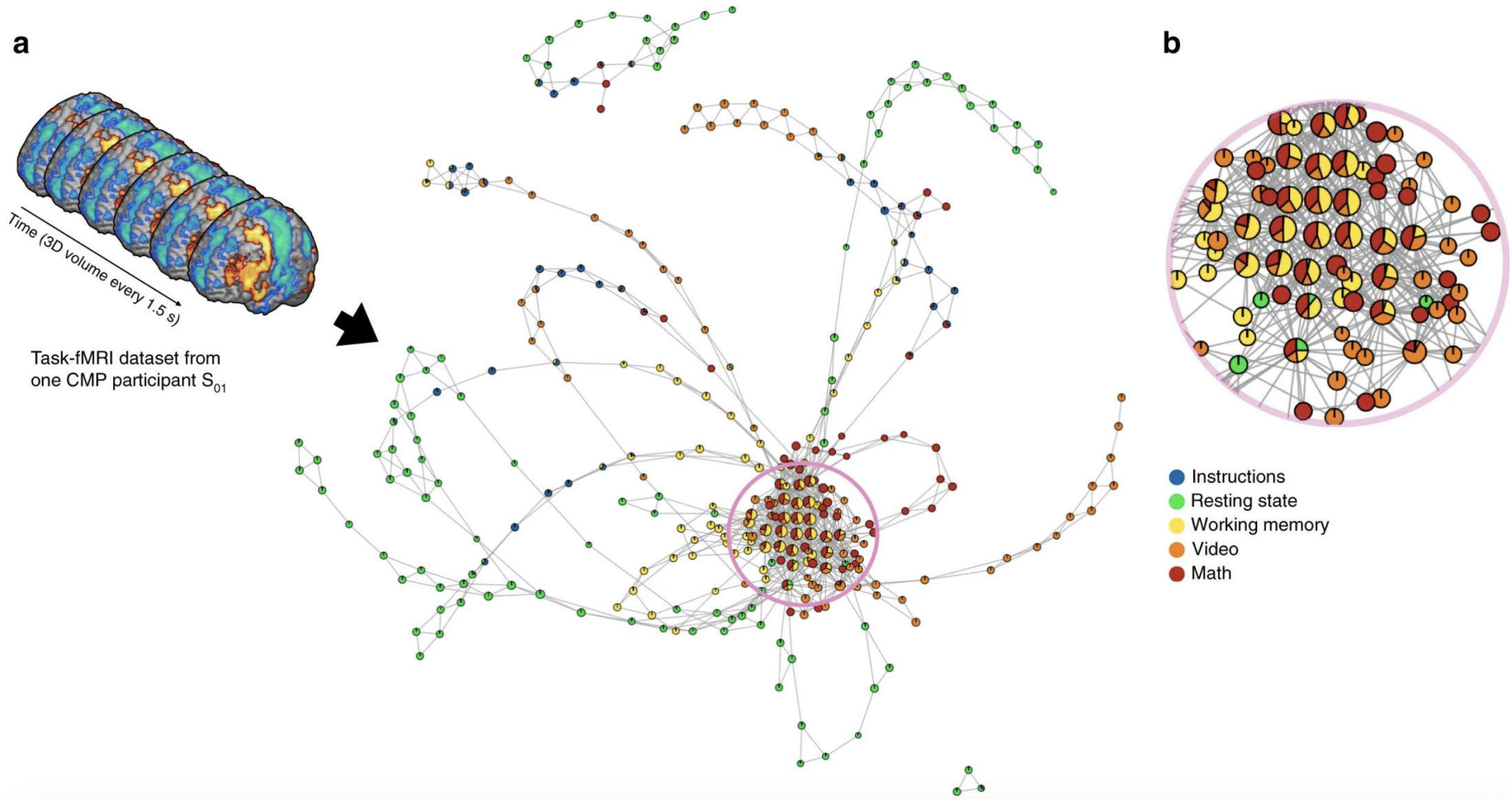
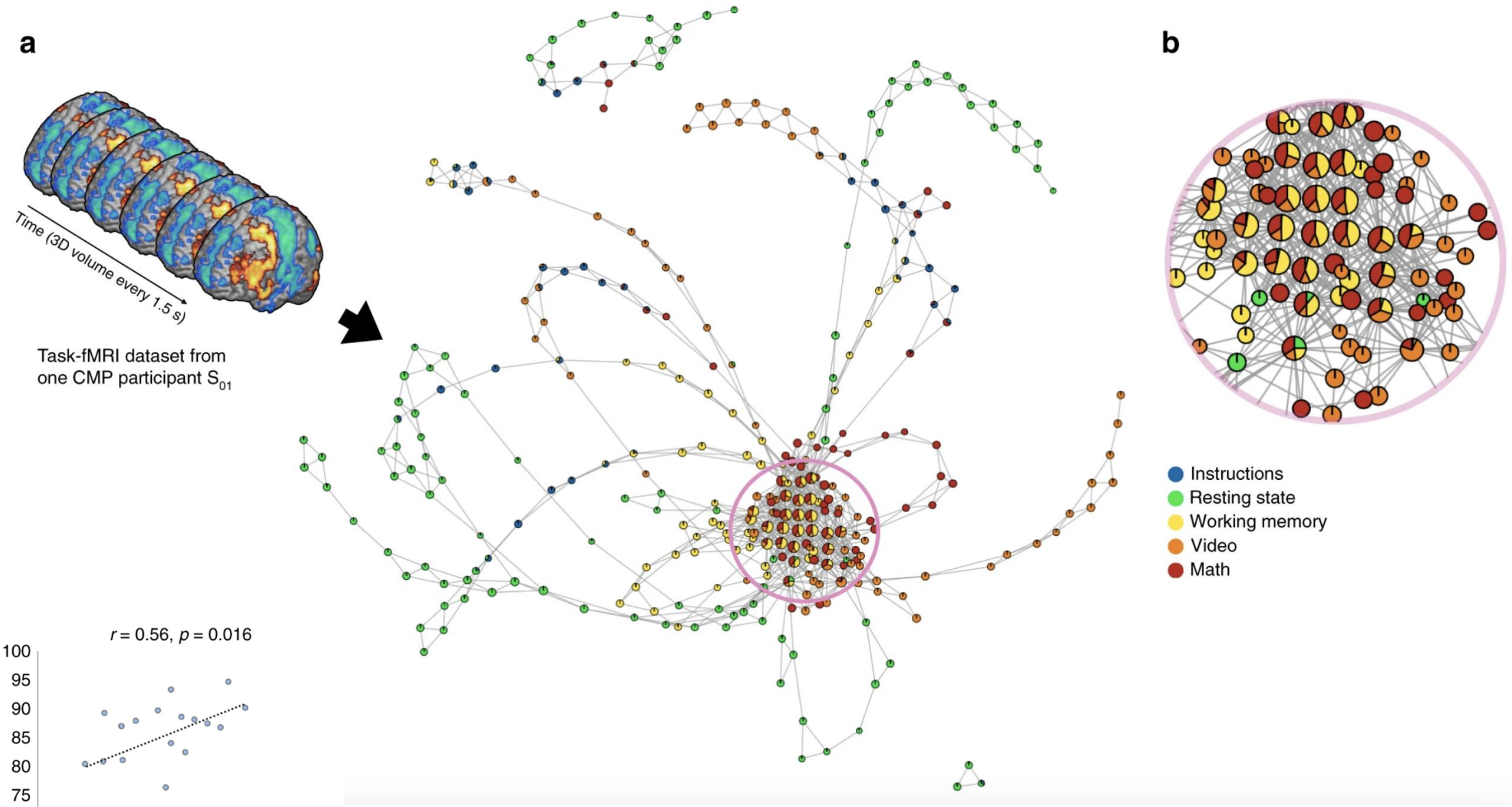
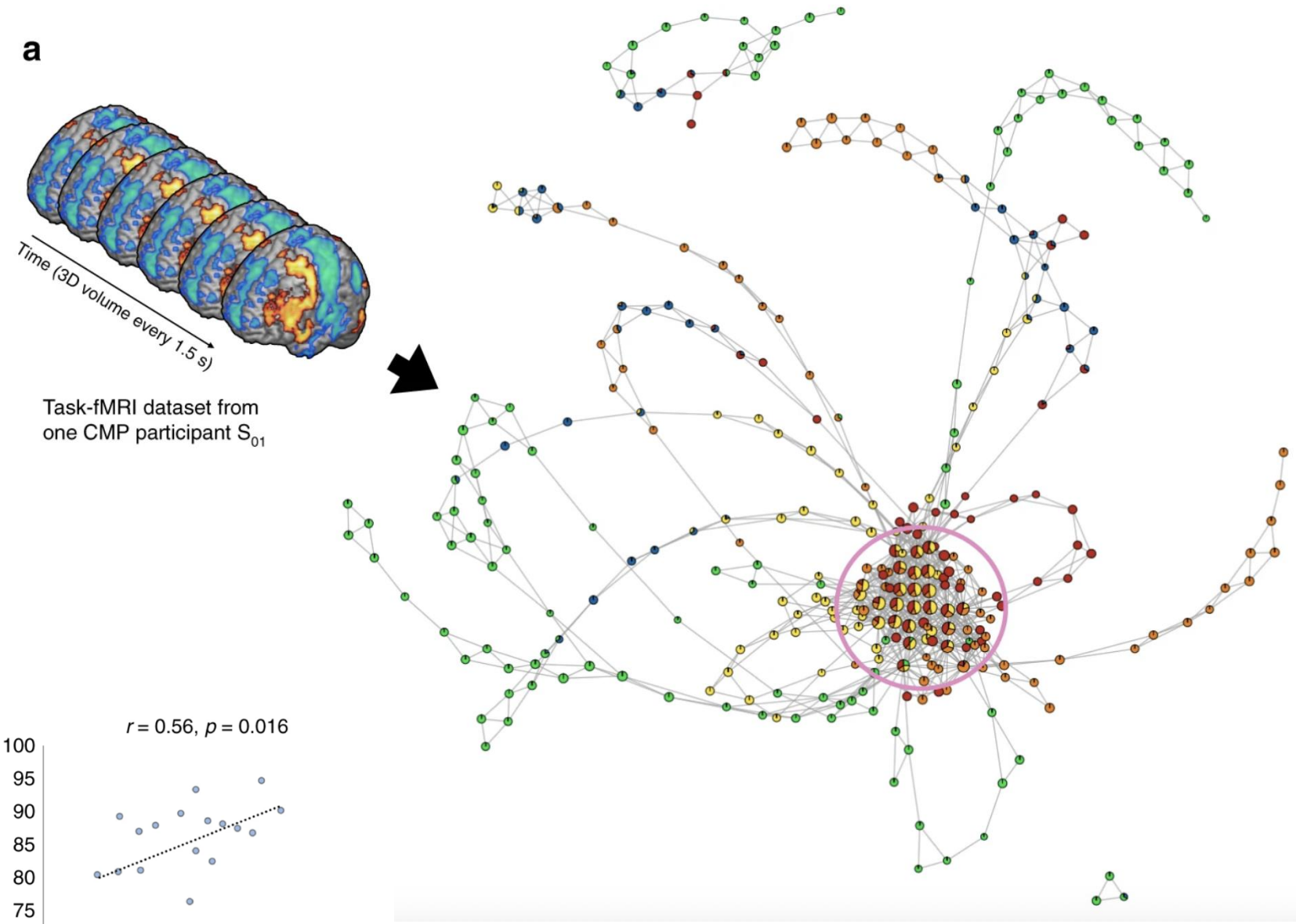
BOLD signal
Mapper

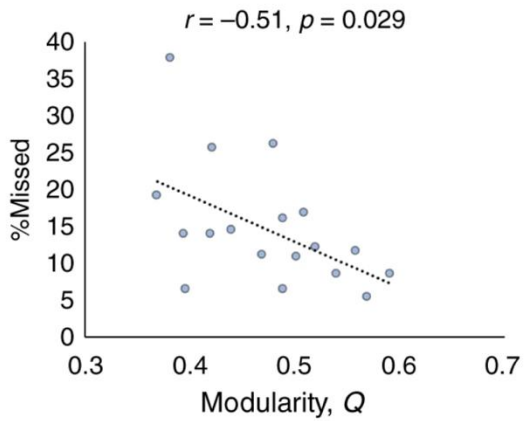


Data from
Gonzalez-Castillo et al's Continuous Multitask Paradigm



Data from
Gonzalez-Castillo et al's Continuous Multitask Paradigm



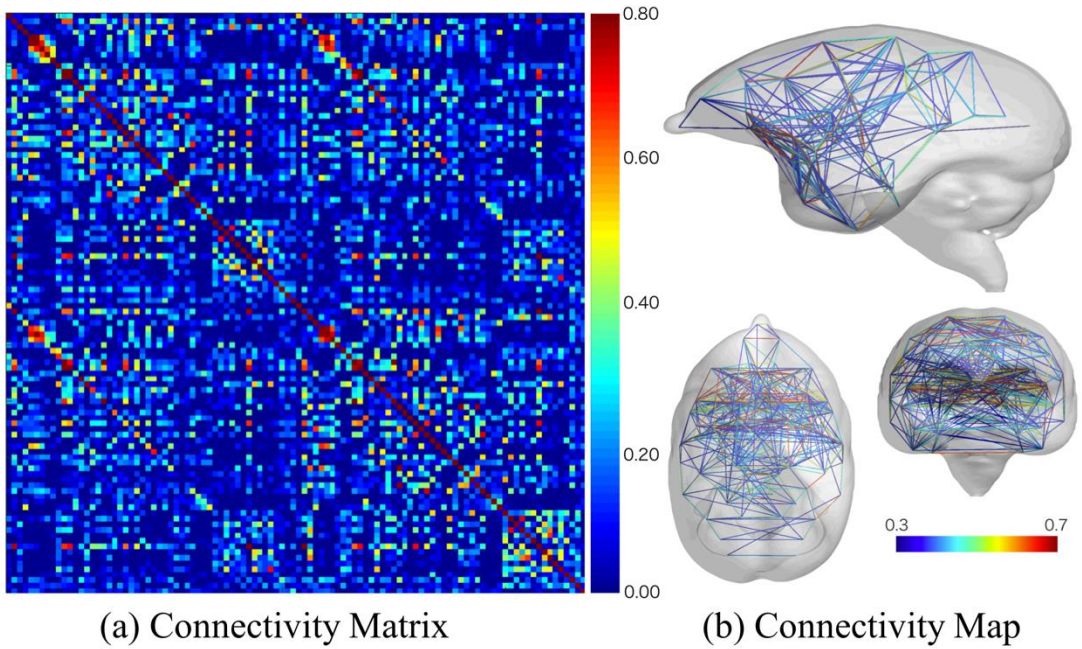


Data from
Gonzalez-Castillo et al's Continuous Multitask Paradigm

	Activation	Connectivity
Temporal Mean	Mean Activation	Functional connectivity
Dynamics	Dynamics Mapper	???

II. How to represent cofluctuation dynamics

Recap on Functional Connectivity



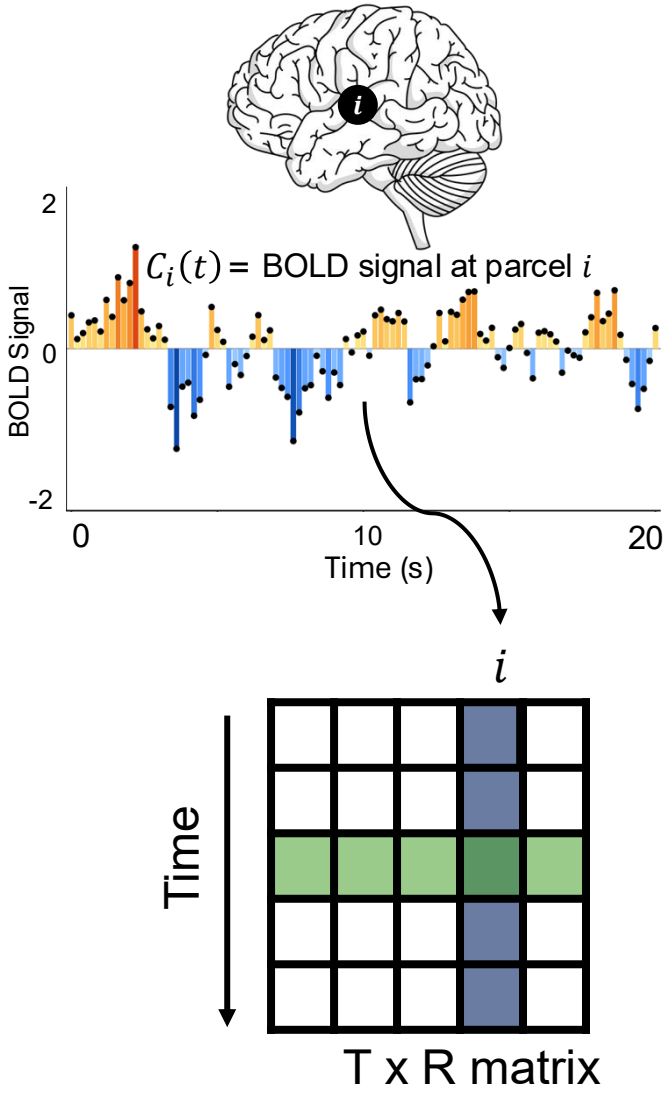
(a) Connectivity Matrix (b) Connectivity Map

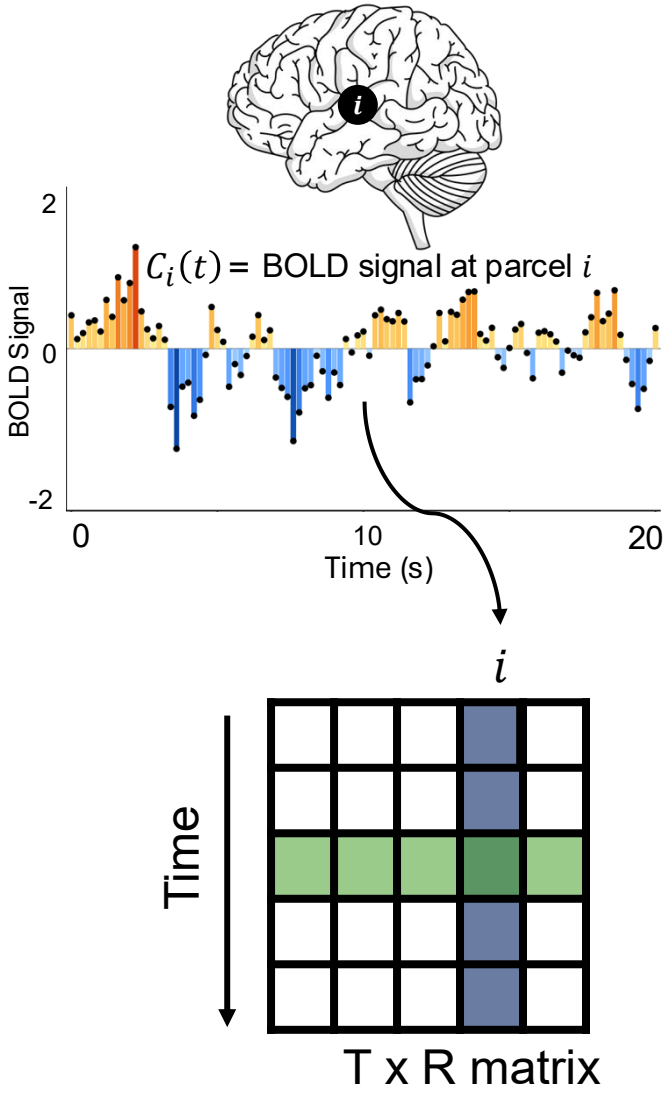
https://cds.ismrm.org/protected/19MProceedings/PDFfiles/3435.html

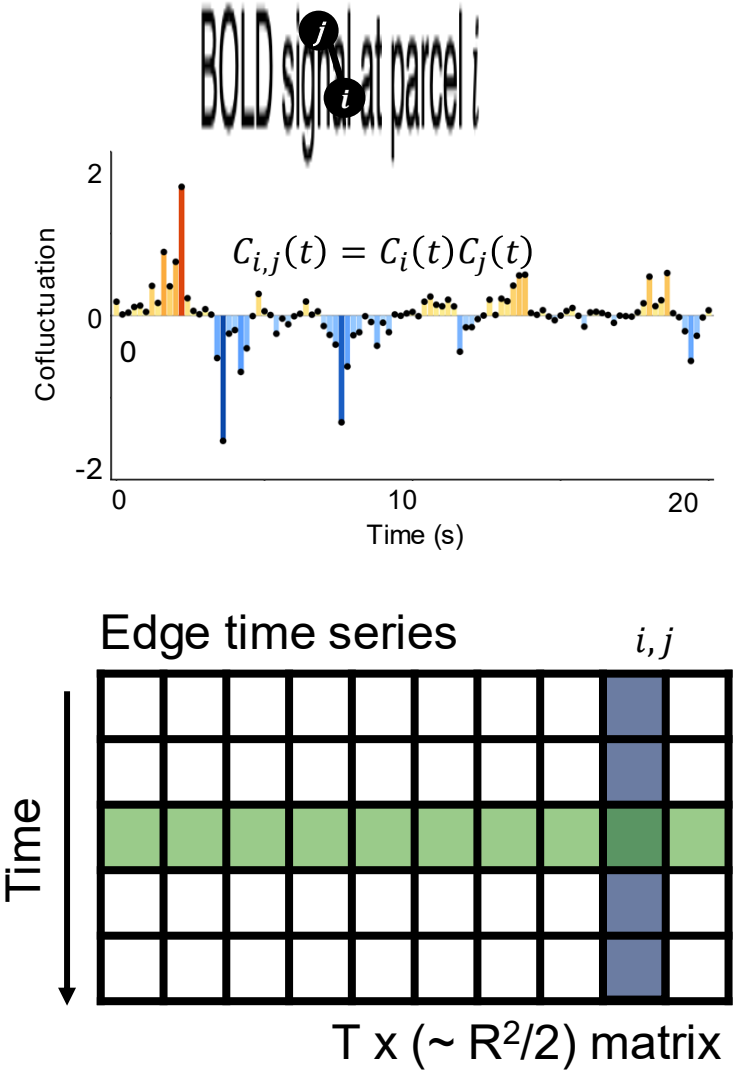
Functional connectivity of two brain regions

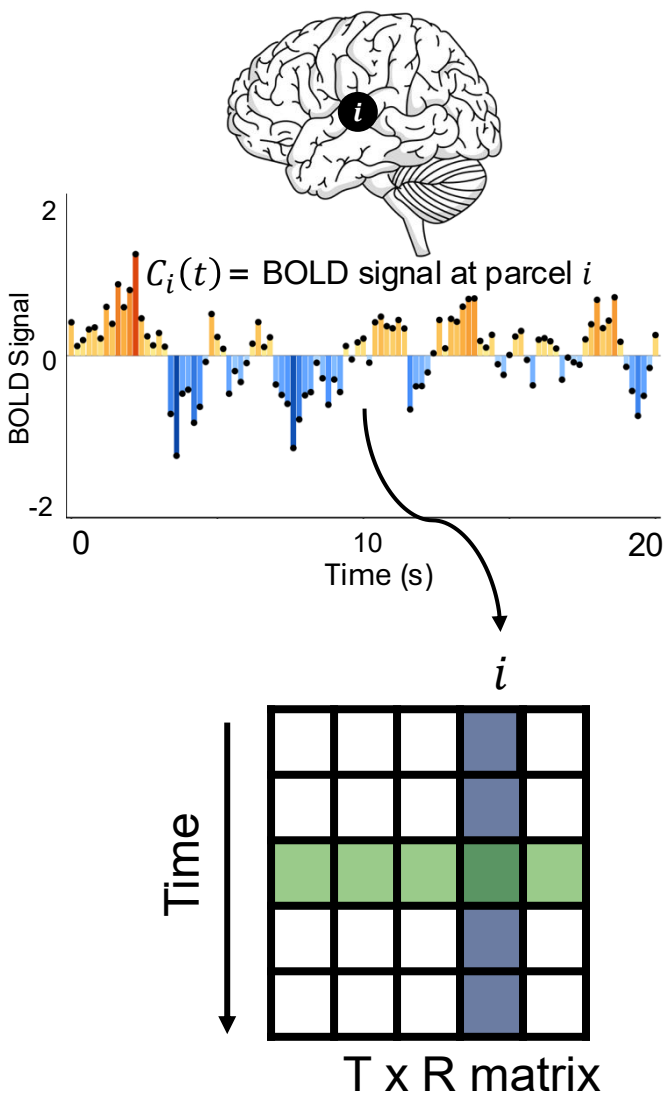
= temporal correlation of brain activity of the two regions

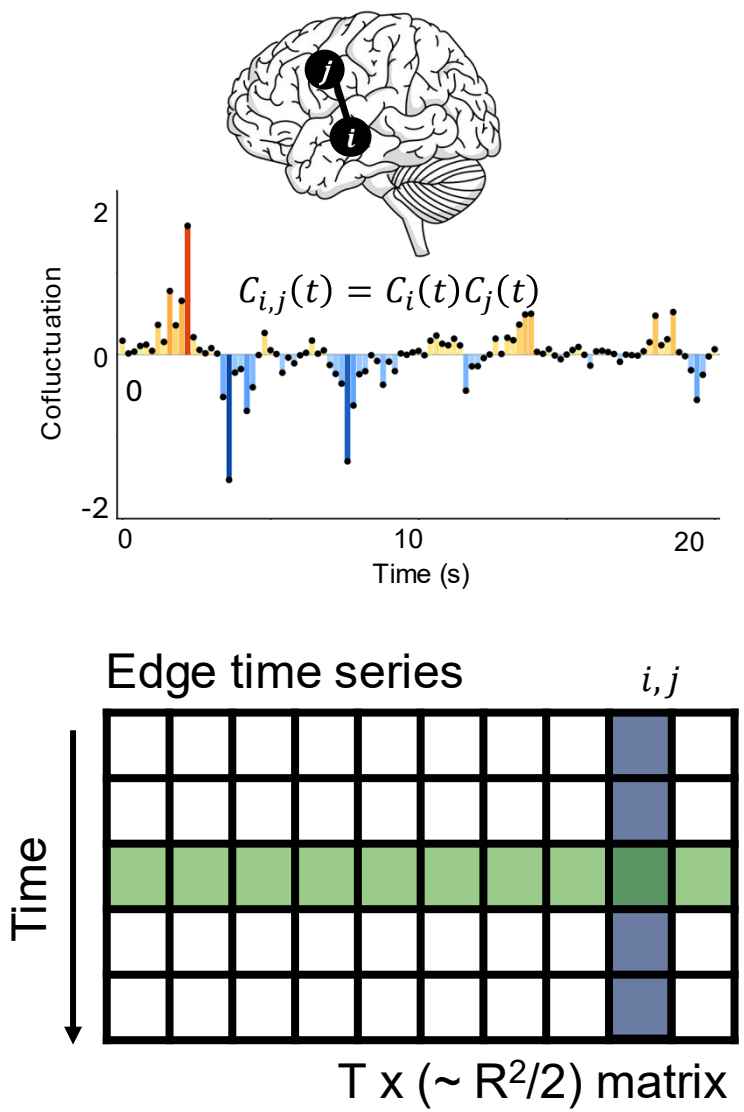
= temporal average of the framewise product of z-scored brain activity of the two regions

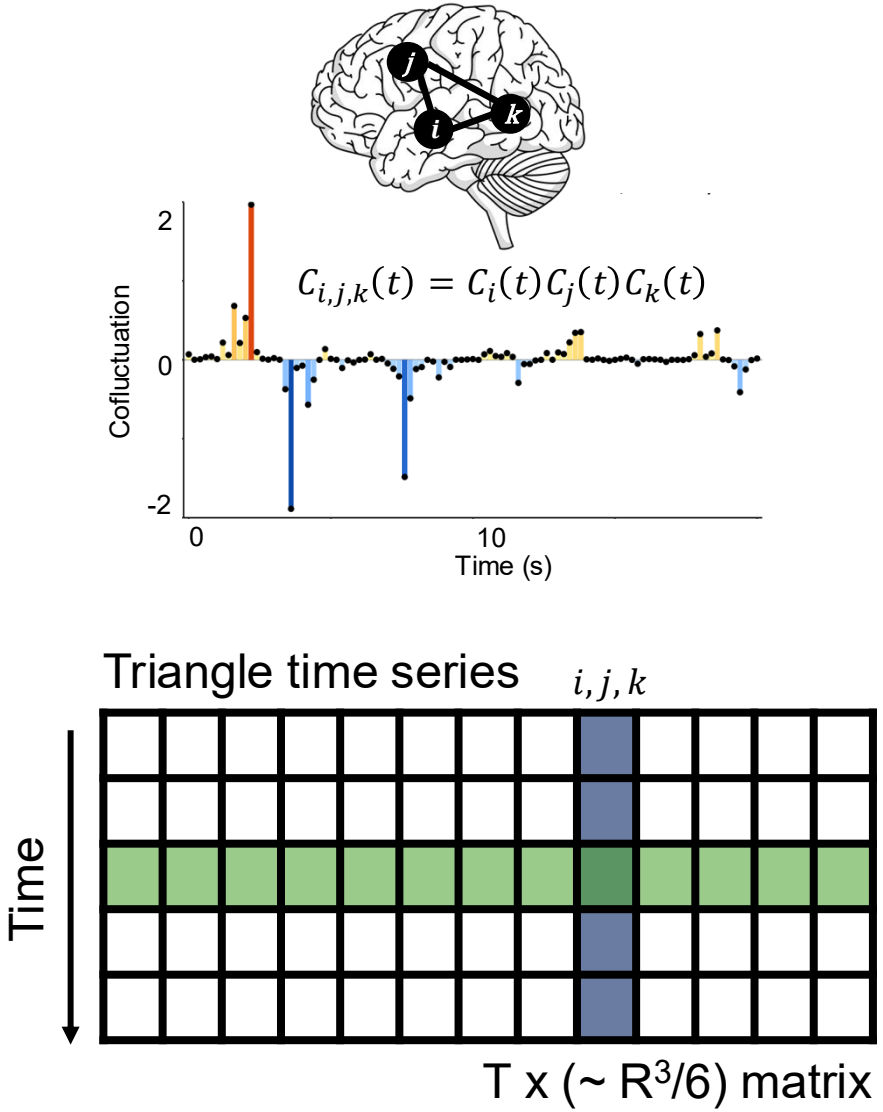

i
2
0
-2
BOLD Signal
$C_i(t)$ = BOLD signal at parcel i
0
10
20
Time (s)
i
Time
T x R matrix

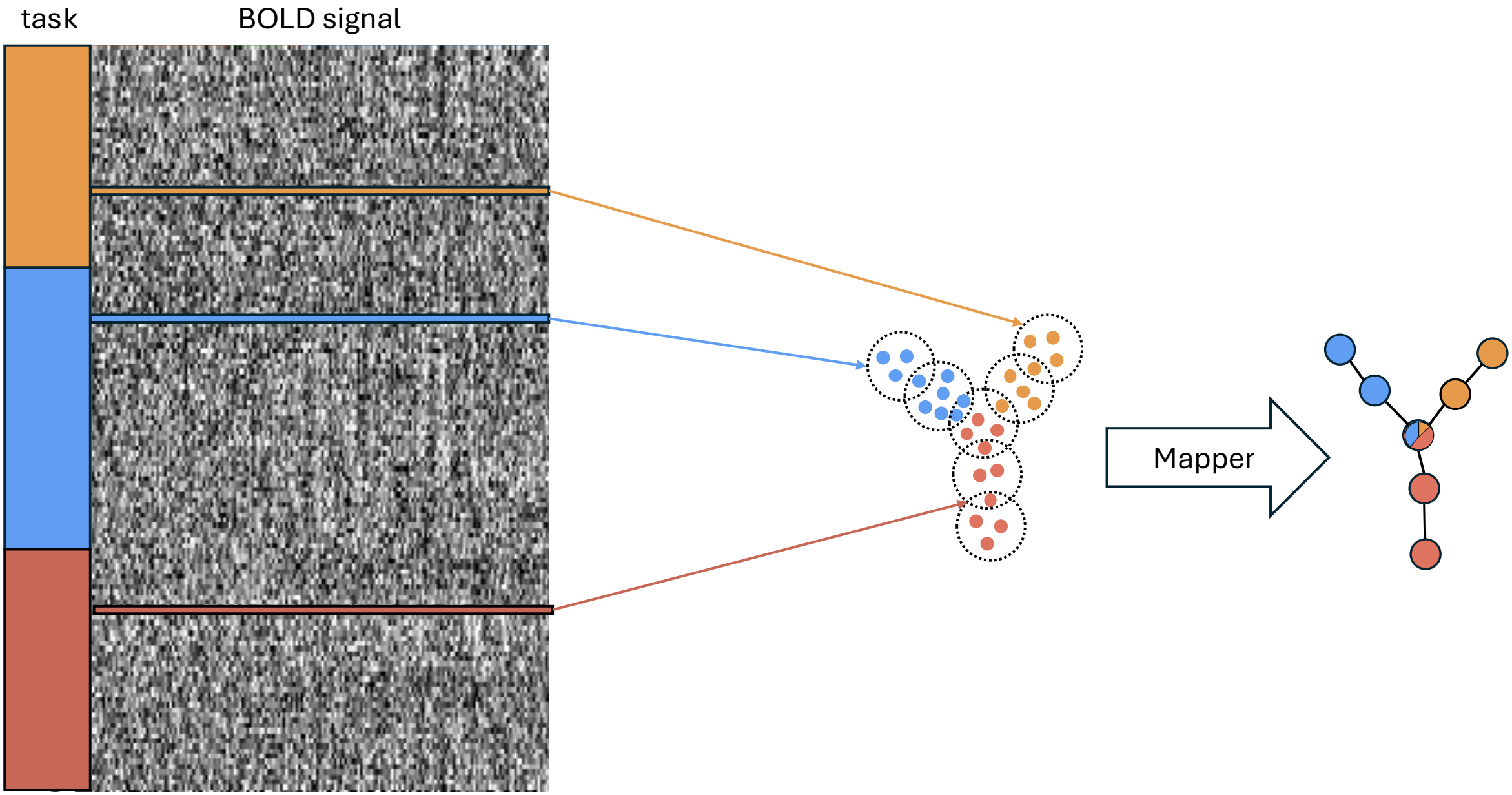

i
$C_i(t)$ = BOLD signal at parcel i
BOLD Signal
2
0
-2
0
10
20
Time (s)
i
Time
T x R matrix


BOLD signal at parcel i
j
i
$C_{i,j}(t) = C_i(t)C_j(t)$
Cofluctuation
2
0
-2
0
10
20
Time (s)
Edge time series
i,j
Time
T x (~ R²/2) matrix

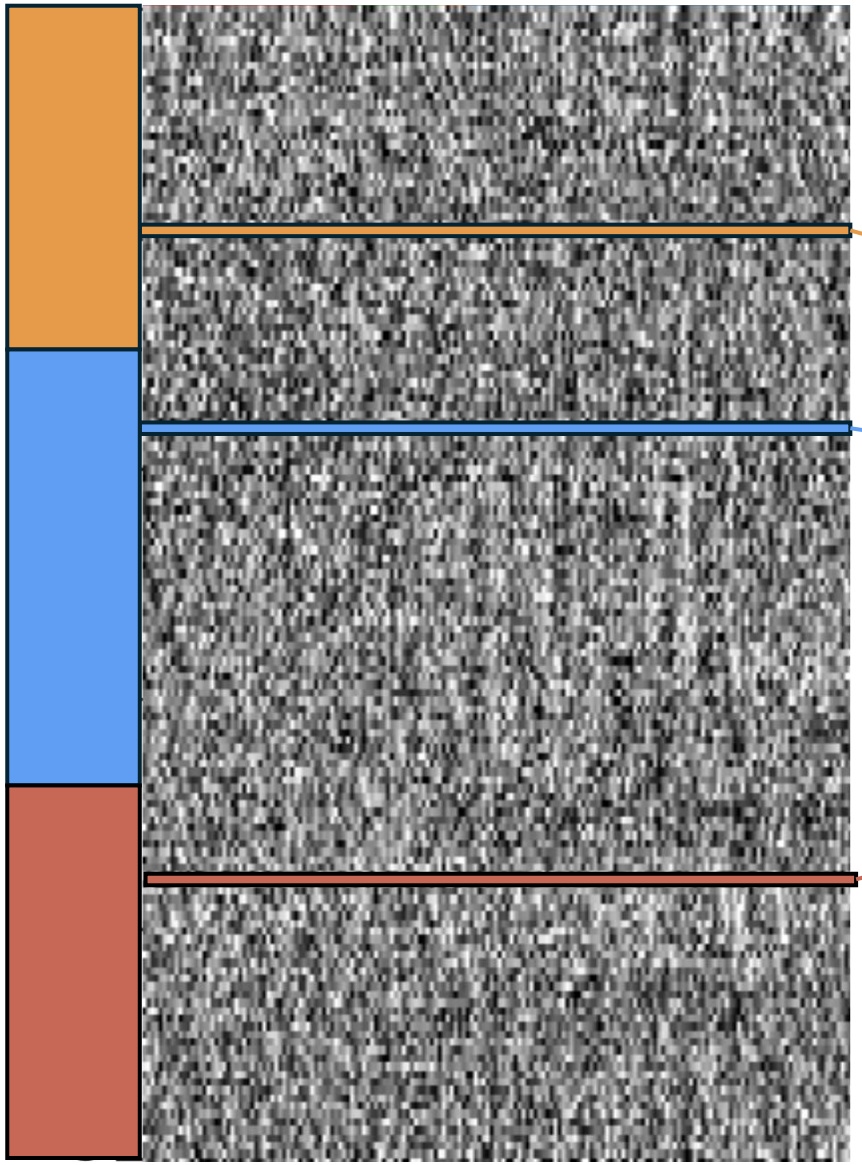

i
$C_i(t)$ = BOLD signal at parcel i
BOLD Signal
2
0
-2
0
10
20
Time (s)
i
Time
T x R matrix

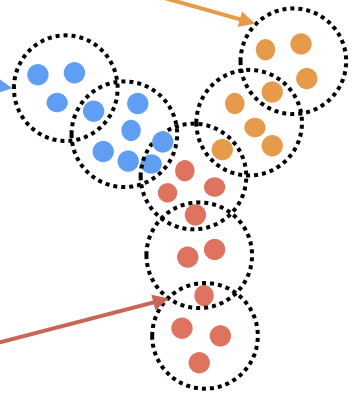

j
i
$C_{i,j}(t) = C_i(t)C_j(t)$
Cofluctuation
2
0
-2
0
10
20
Time (s)
Edge time series
i,j
Time
T x (~ R²/2) matrix


j
i
k
$C_{i,j,k}(t) = C_i(t)C_j(t)C_k(t)$
Cofluctuation
2
0
-2
0
10
Time (s)
Triangle time series
i,j,k
Time
T x (~ R³/6) matrix

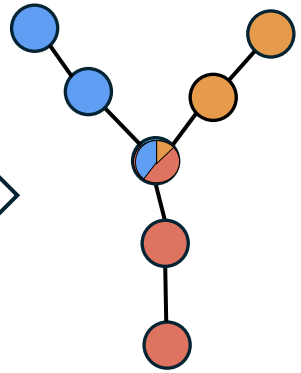

task
BOLD signal
Mapper

task ~~BOLD signal~~ **Edge time series**

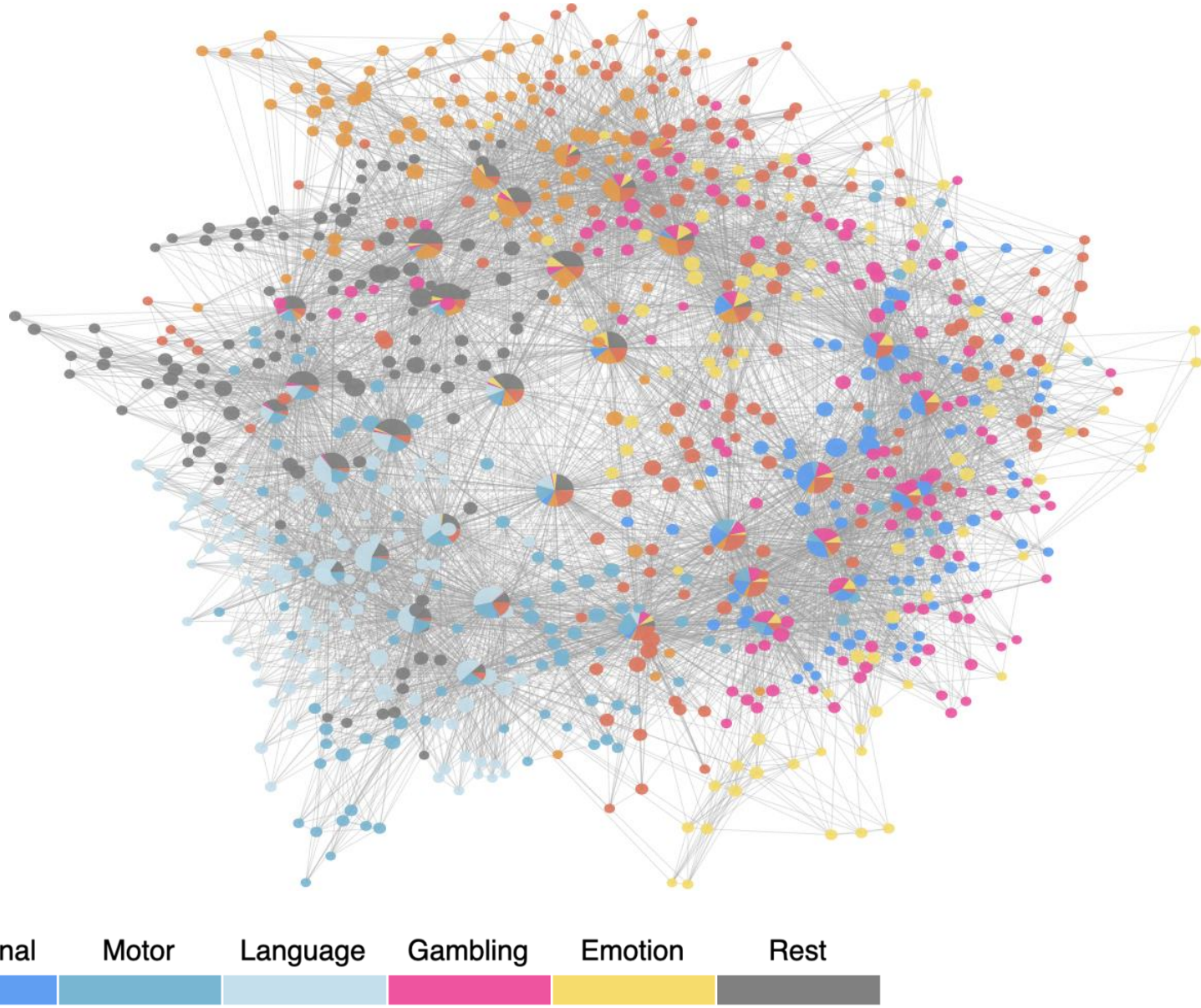




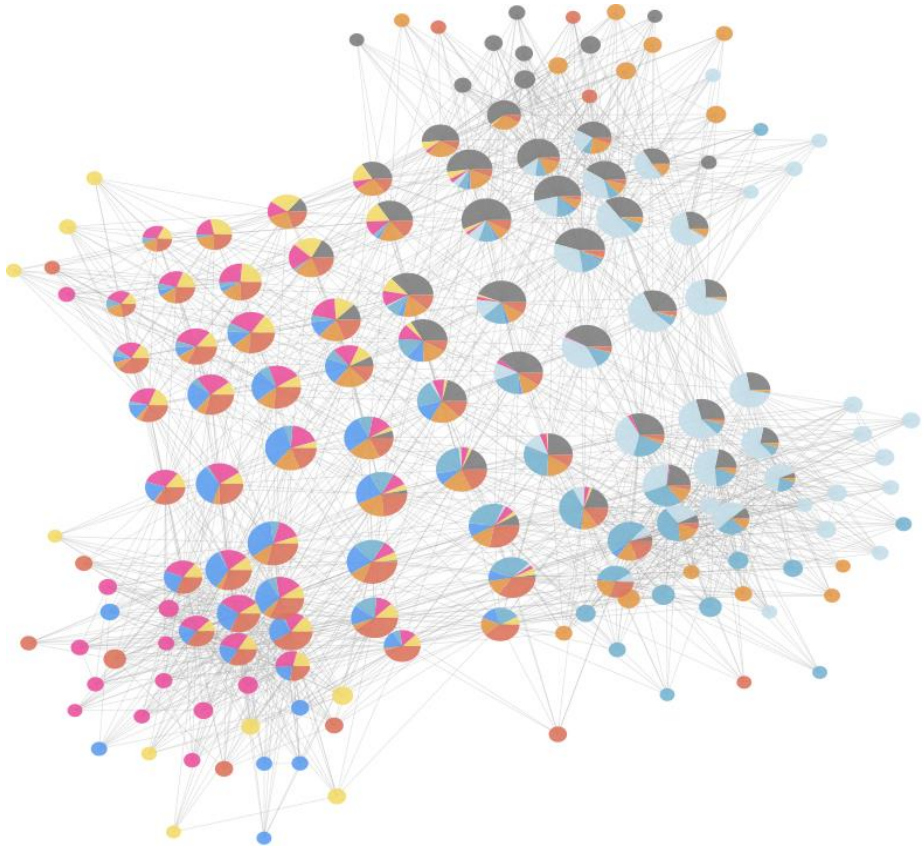
Mapper



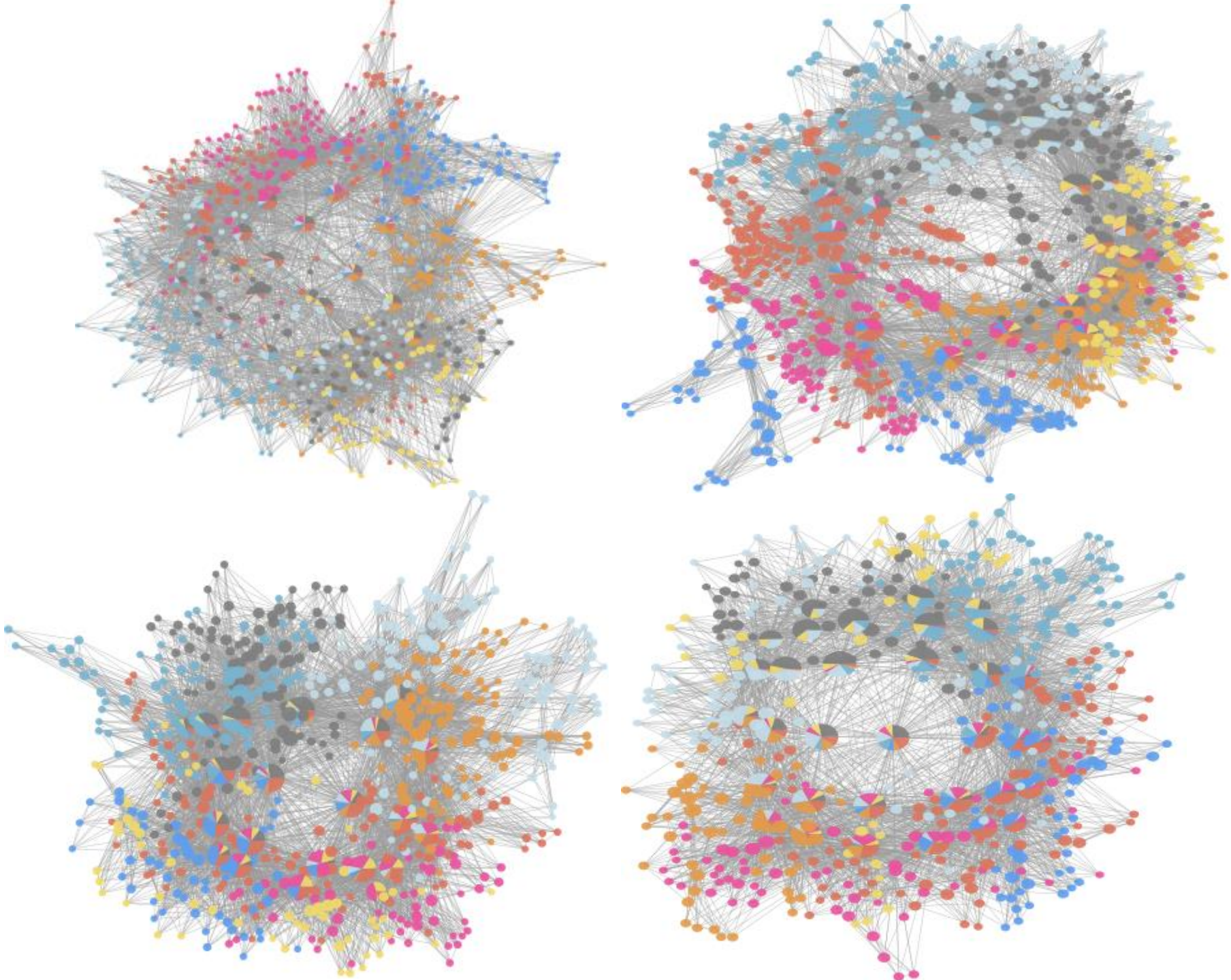
- Data from one subject
- Each node is a cluster of time points
- Pie charts indicate the proportion of tasks at time points in the clusters.

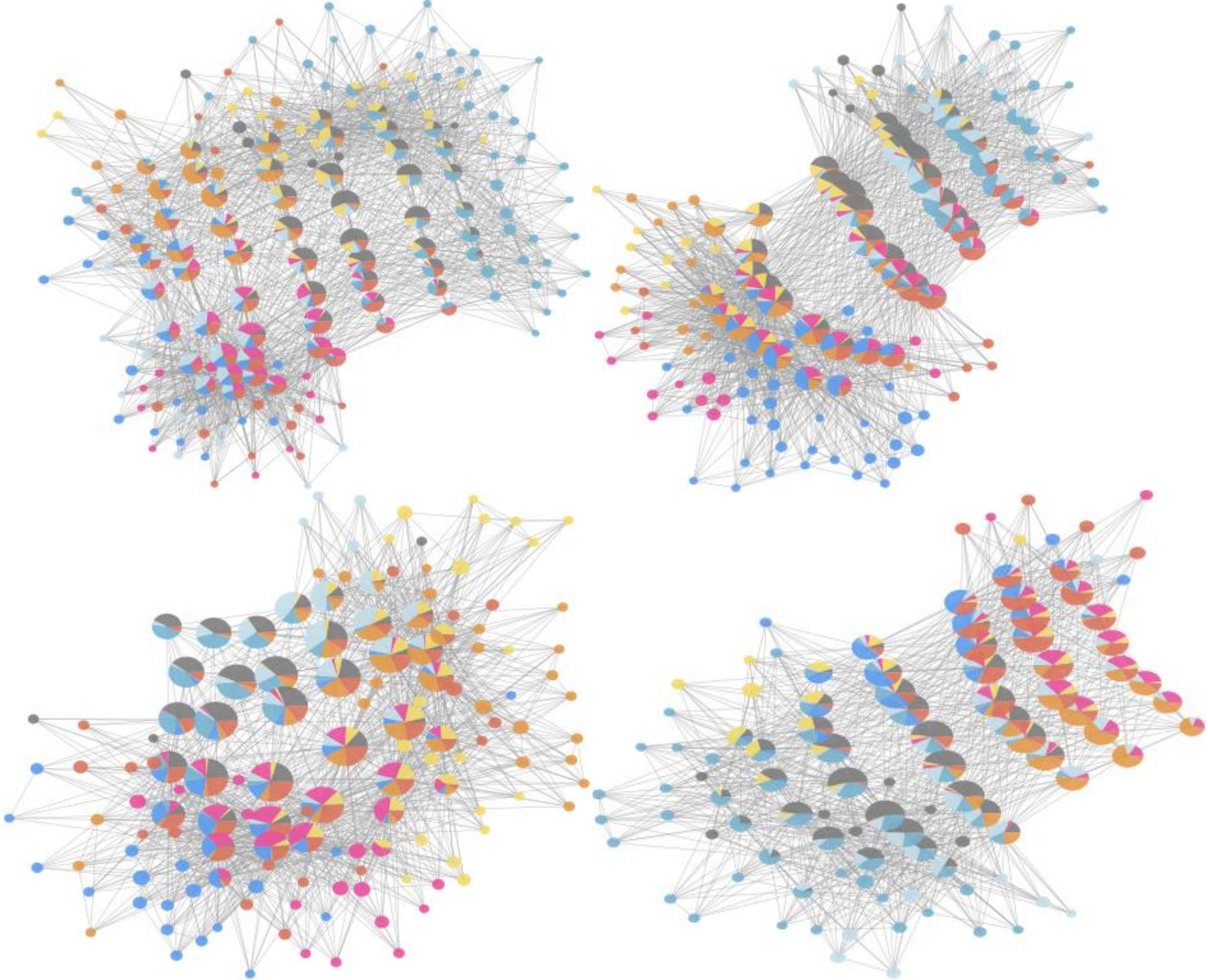


BOLD signal

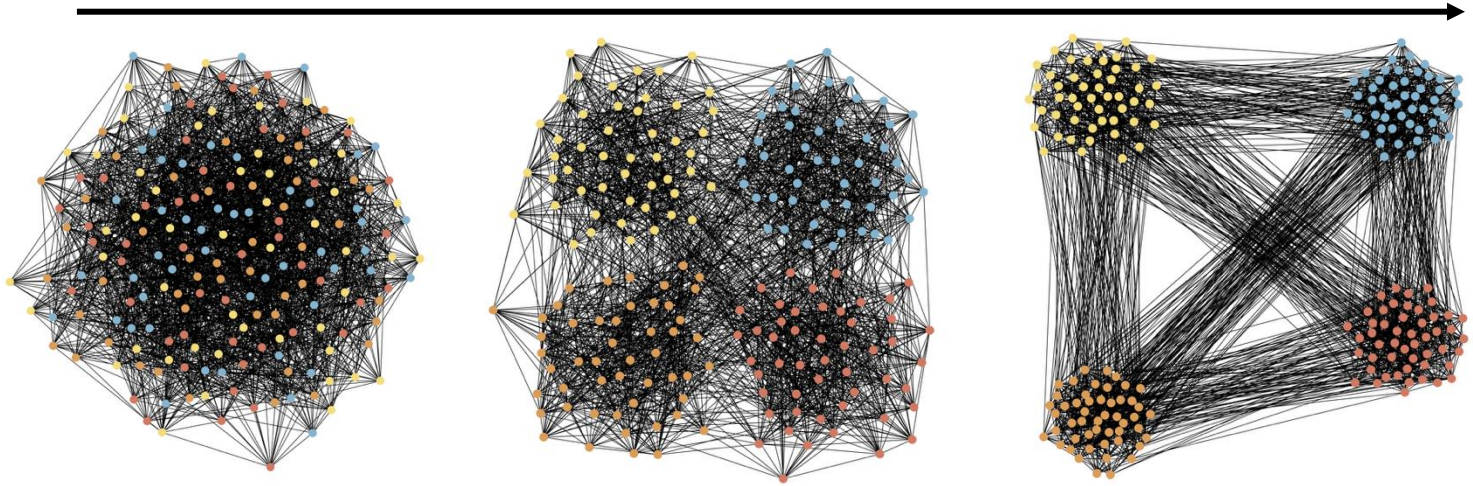


Working Memory Social Relational Motor Language Gambling Emotion Rest

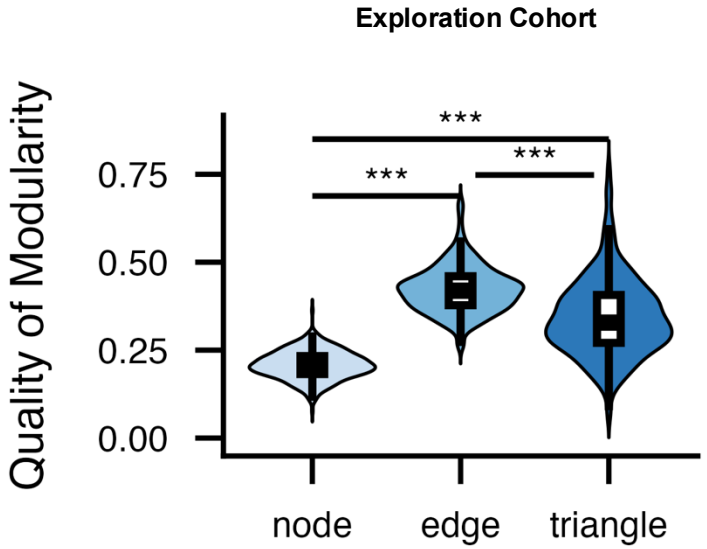




Quantification of Segregation



Edge mapper is better at task profiling.



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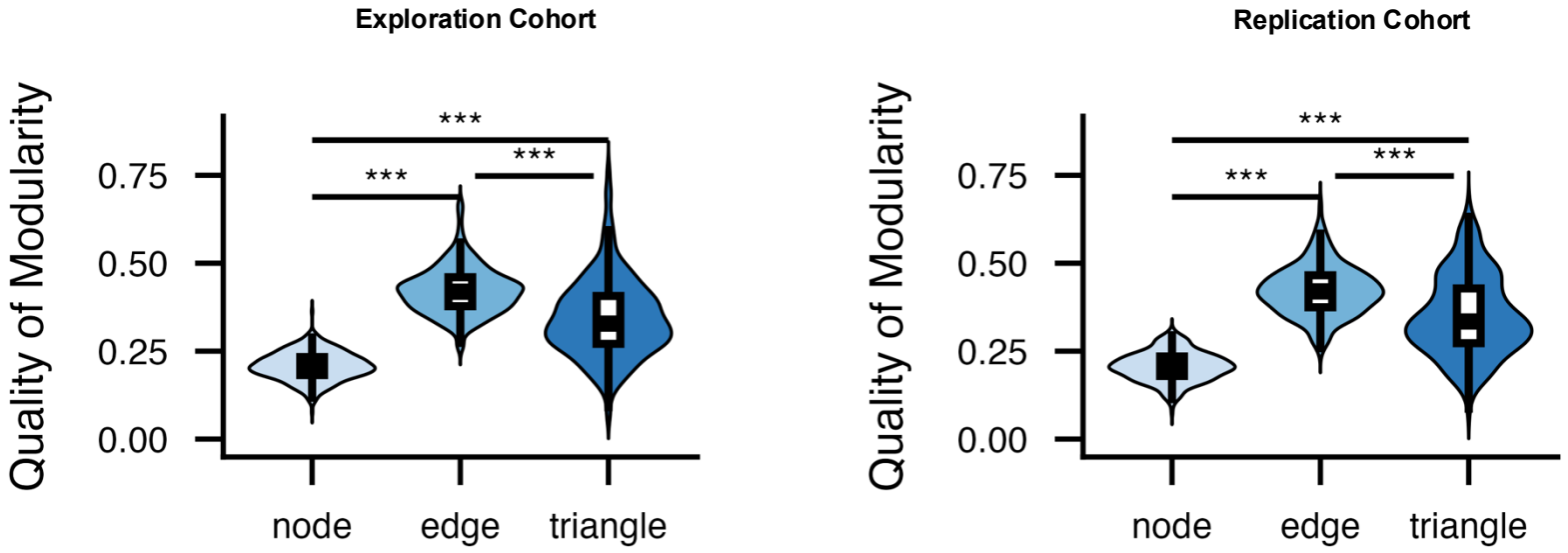
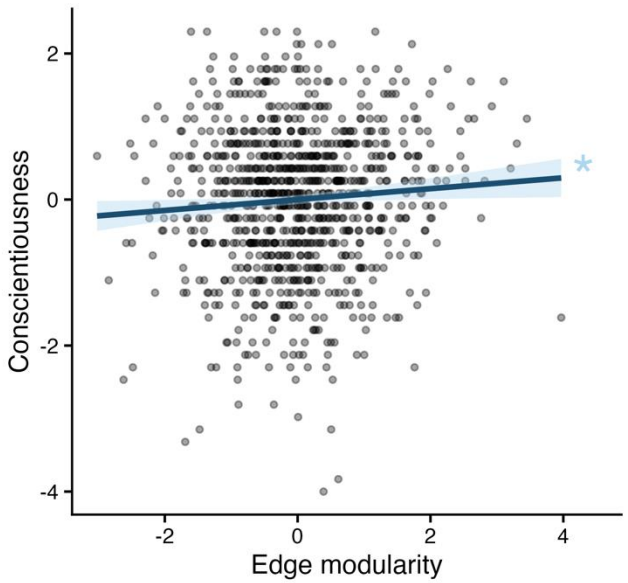
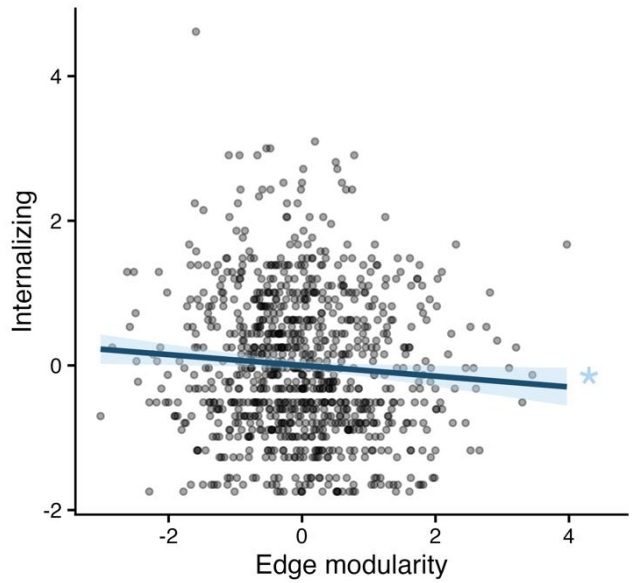
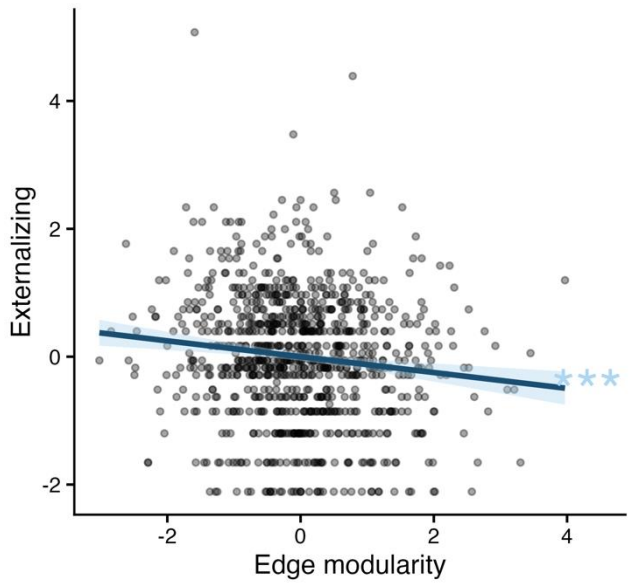


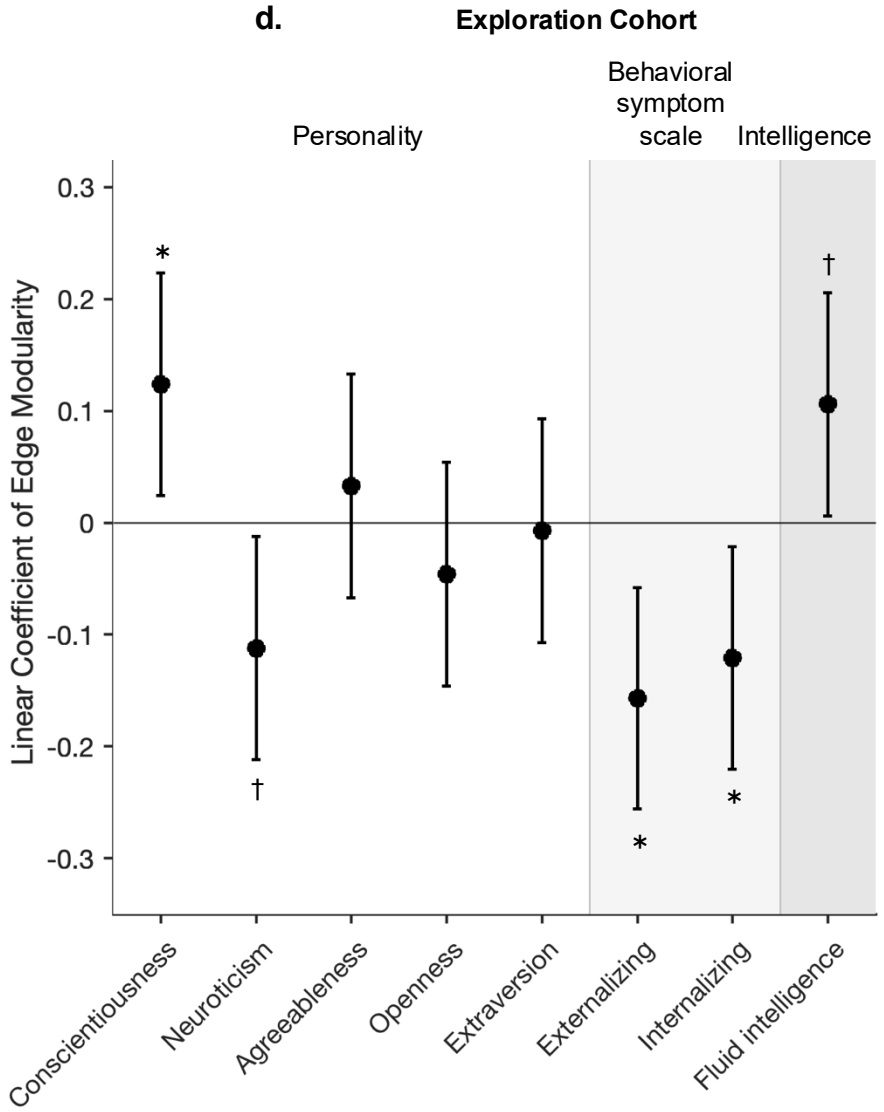
Behavioral implications







Behavioral implications



Legend

† Significance (raw)

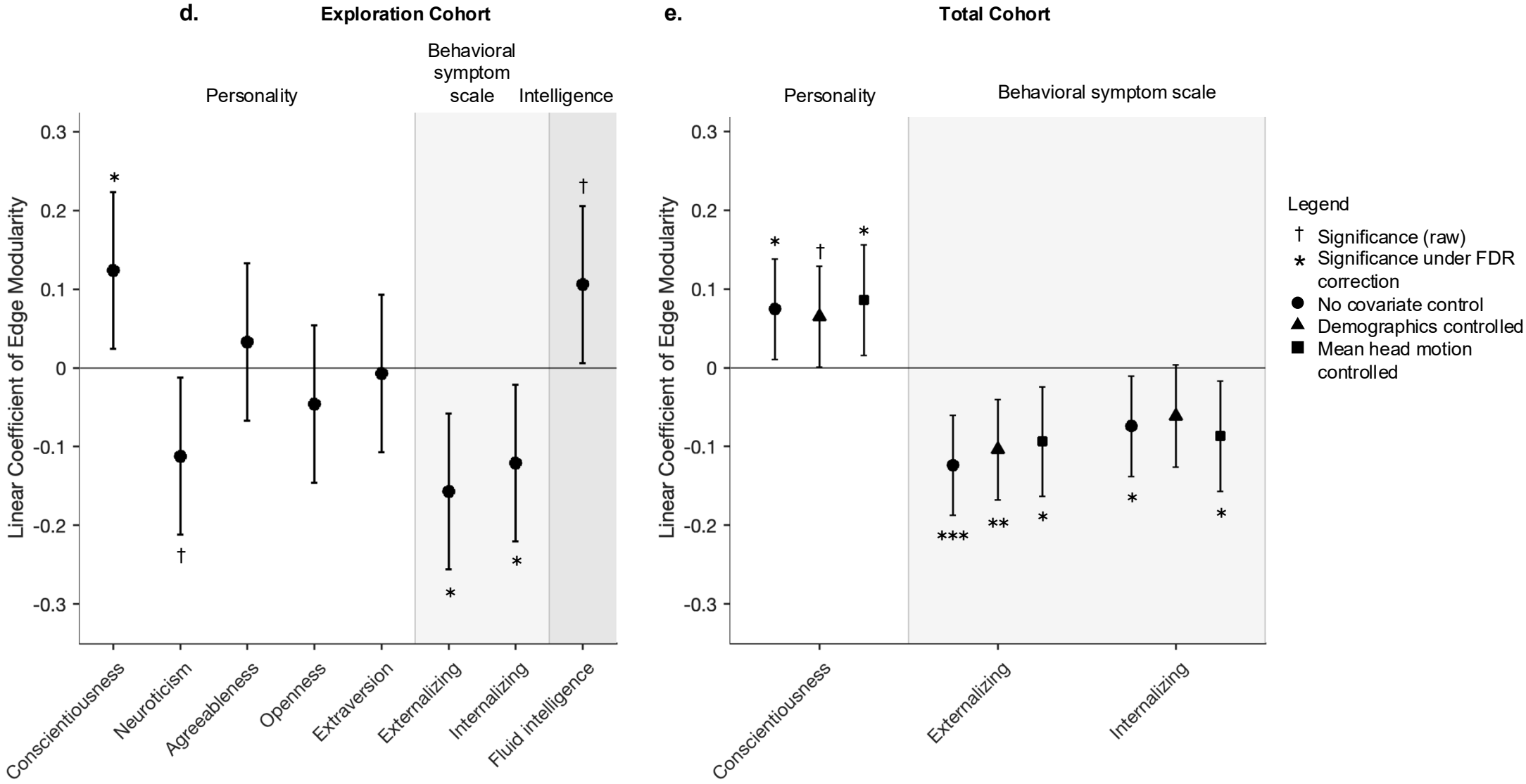
* Significance under FDR correction

● No covariate control

▲ Demographics controlled

■ Mean head motion controlled

Behavioral implications




https://www.dreamstime.com/content-cat-napping-white-bedding-warm-morning-light-happy-long-haired-enjoying-nap-bed-soft-natural-image371898081

Observations

Observations

- Edge Mapper captures the dynamics of cofluctuation.

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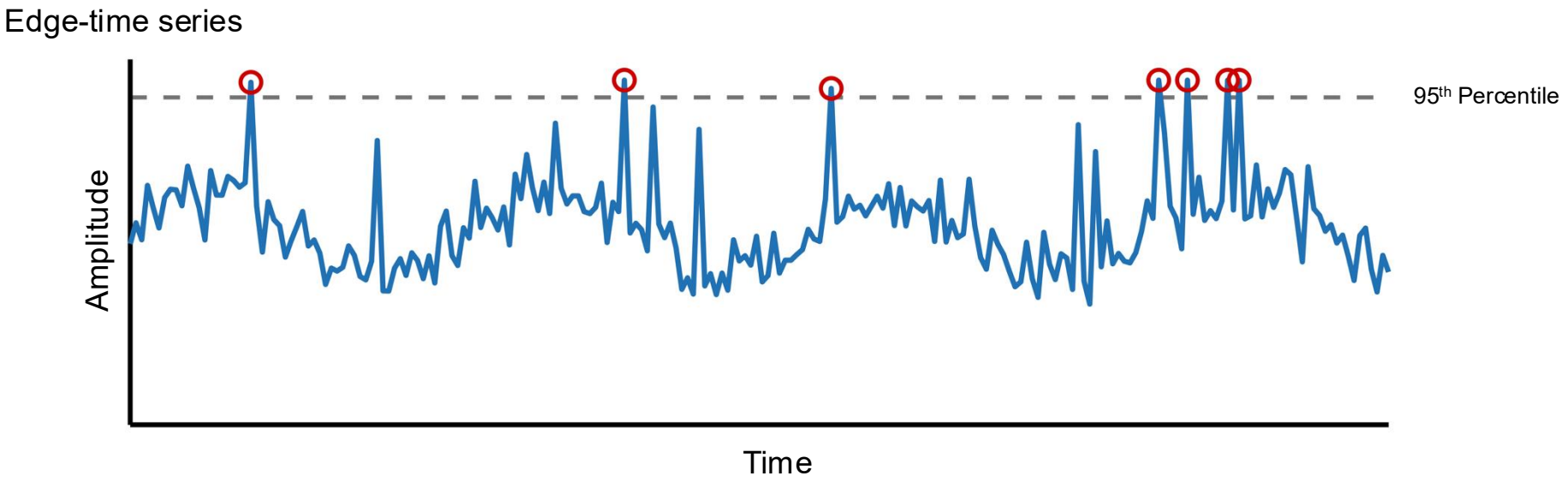
- Why?

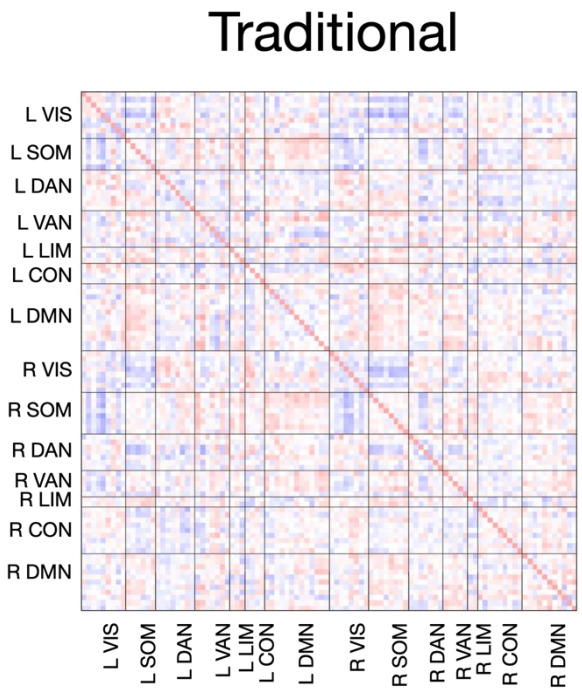
Observations

- Edge Mapper captures the dynamics of cofluctuation.
- Edge Mapper is better at task profiling.
- Better task segregation in edge Mapper is associated with personality and behavioral symptoms.
- Why?
  - Model-driven explanation
  - Data-driven explanation

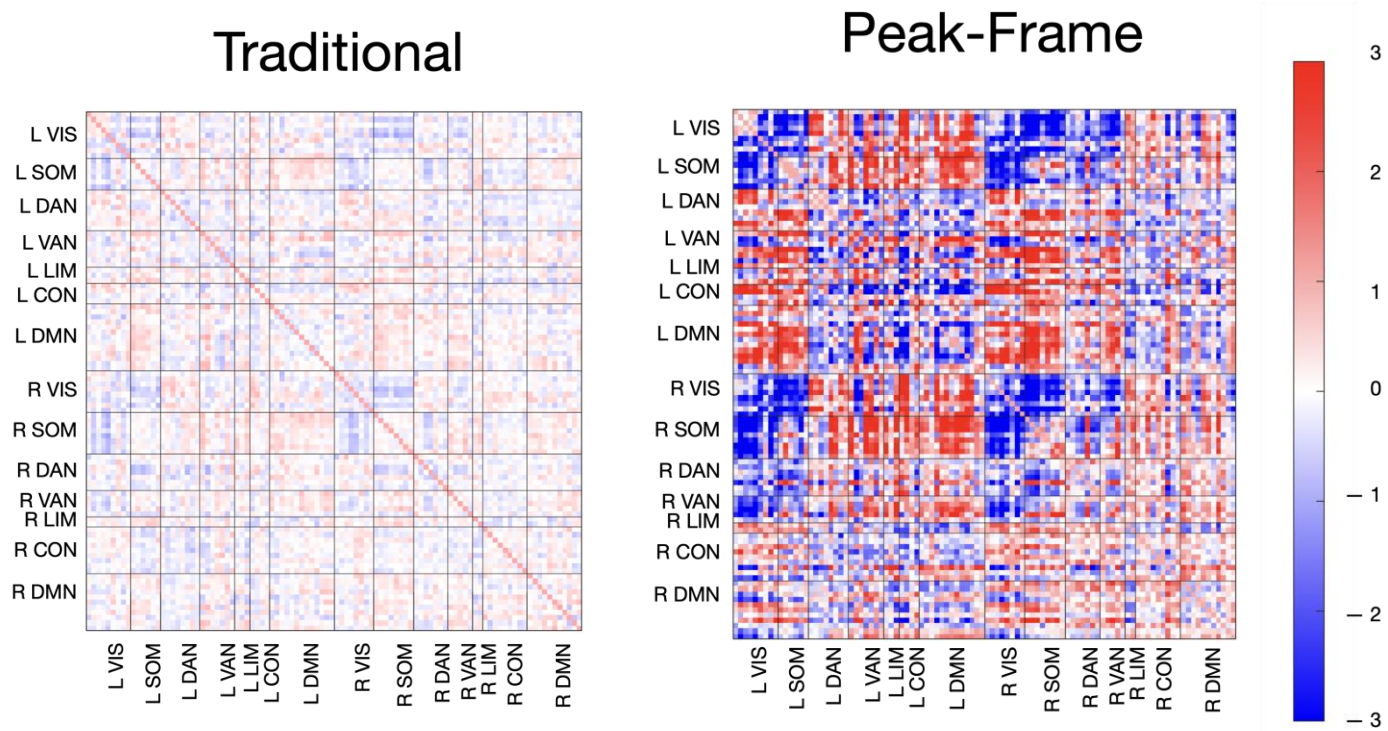
Model: High-amplitude nodes



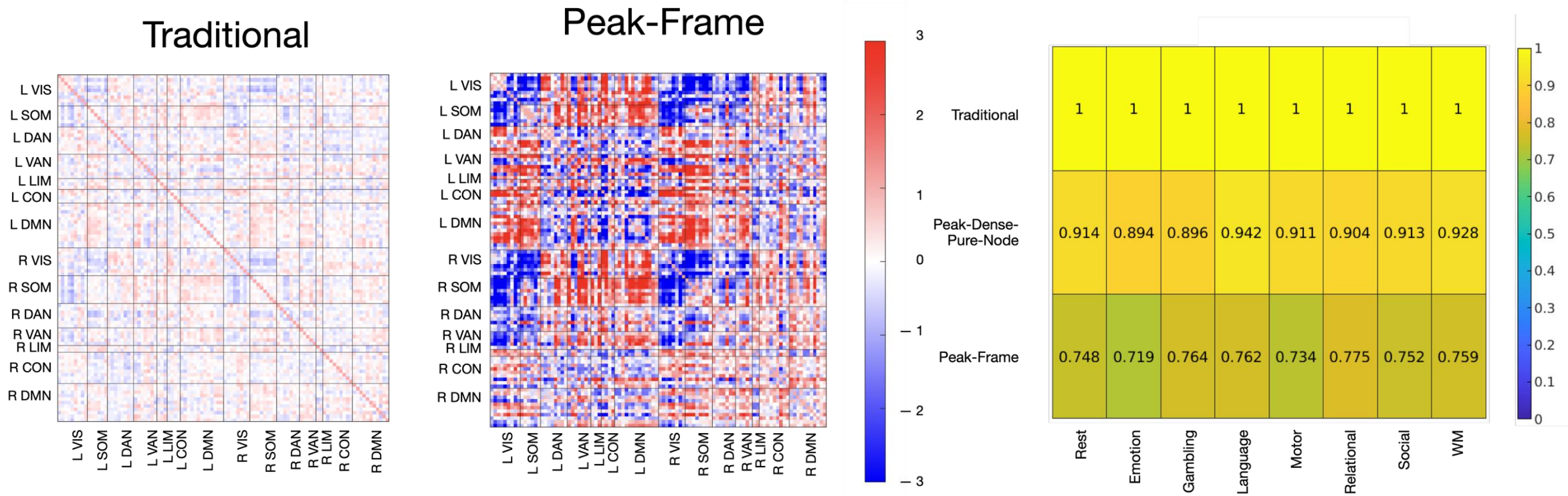
WM – REST contrast



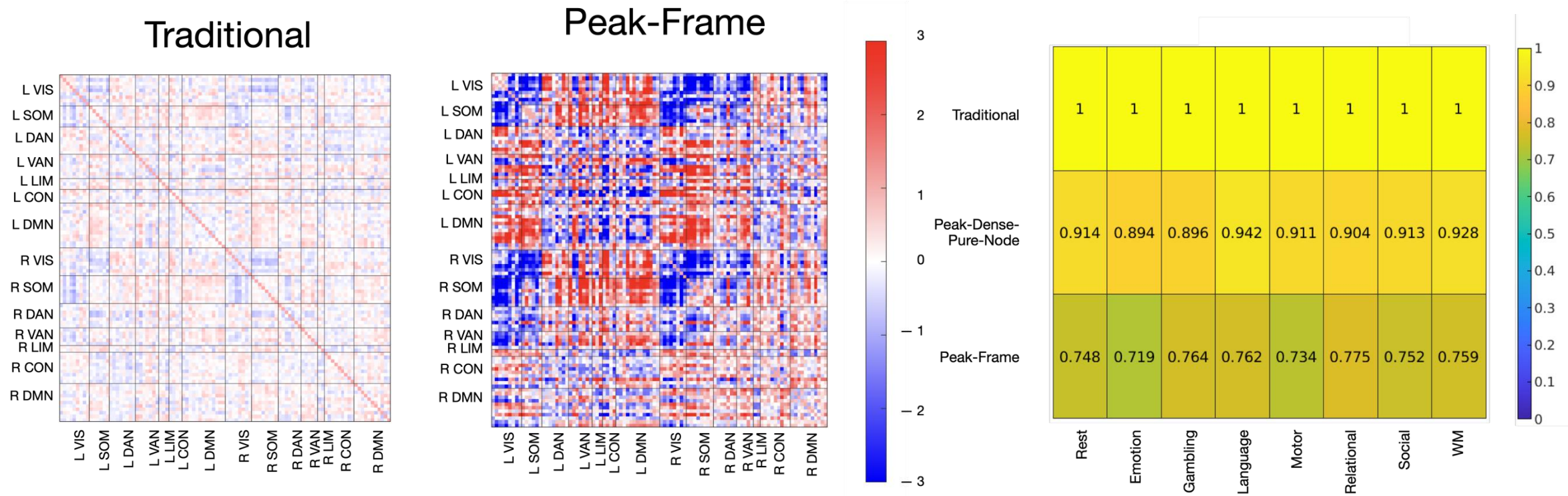
WM – REST contrast



WM – REST contrast



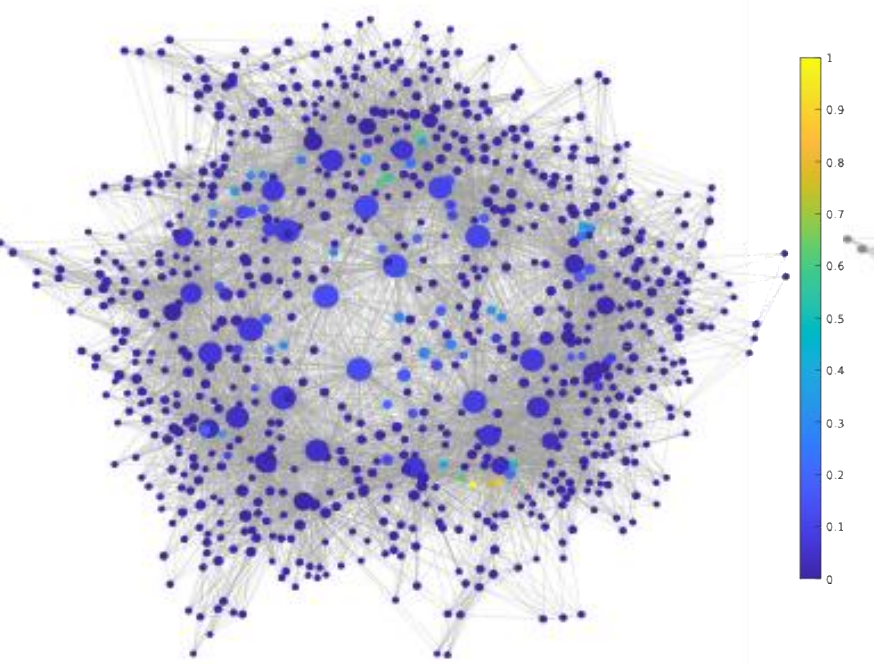
WM – REST contrast



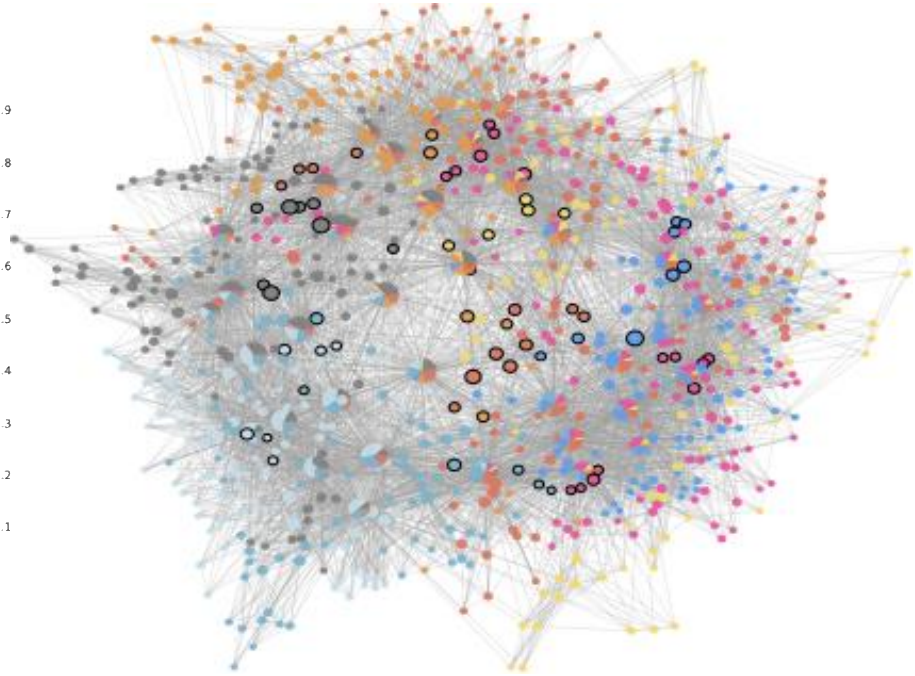
- Do peak frames / nodes drive the task segregation?

Where are the peak frames?

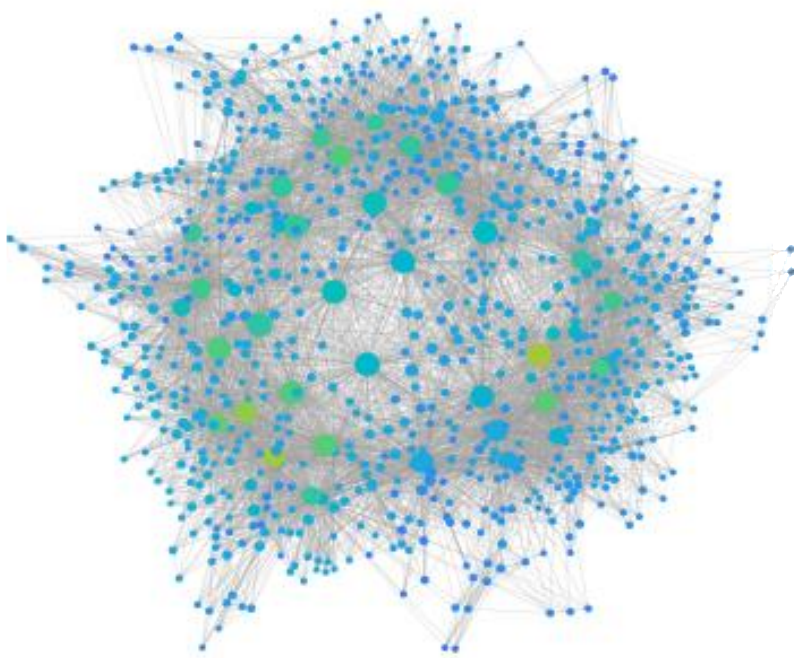
Proportion of peak frames



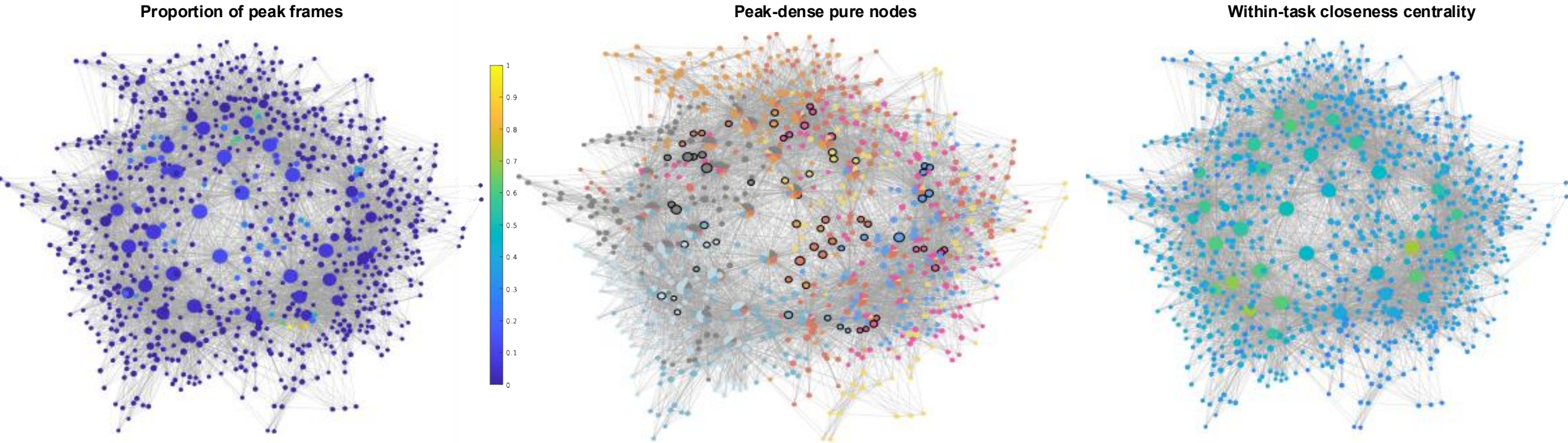
Peak-dense pure nodes



Within-task closeness centrality

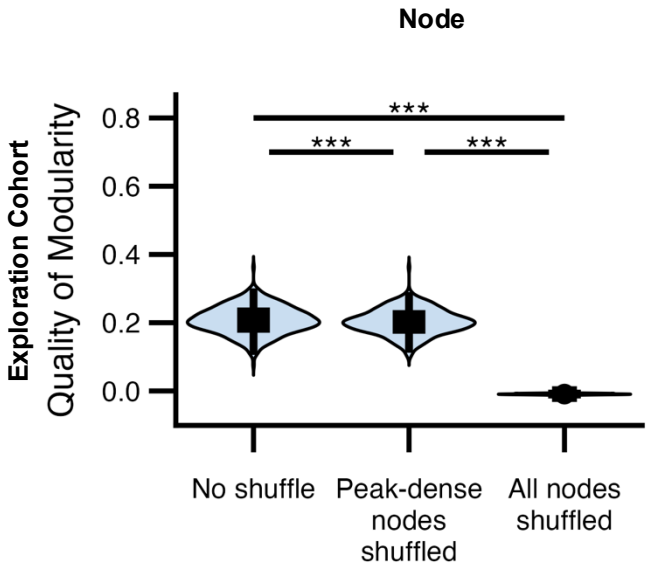


Where are the peak frames?

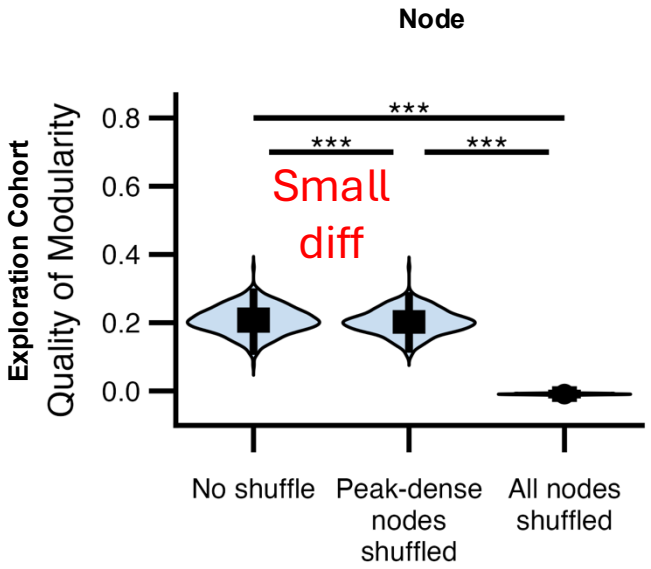


- Do peak frames / nodes drive the task segregation?

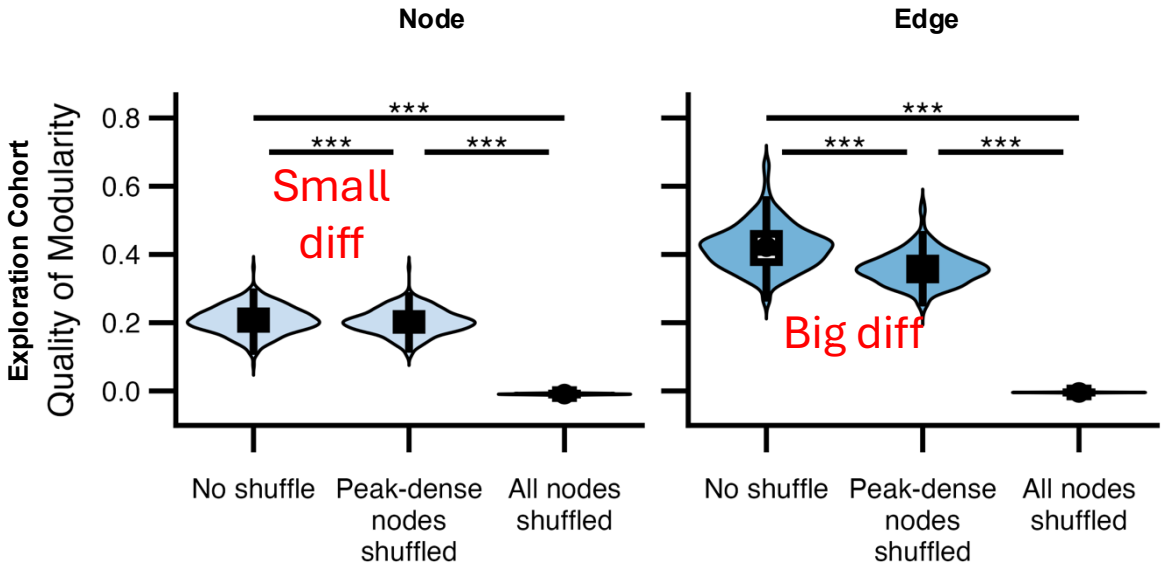
Shuffling


Node
Exploration Cohort
Quality of Modularity
0.8
0.6
0.4
0.2
0.0
***
***
***
No shuffle
Peak-dense nodes shuffled
All nodes shuffled

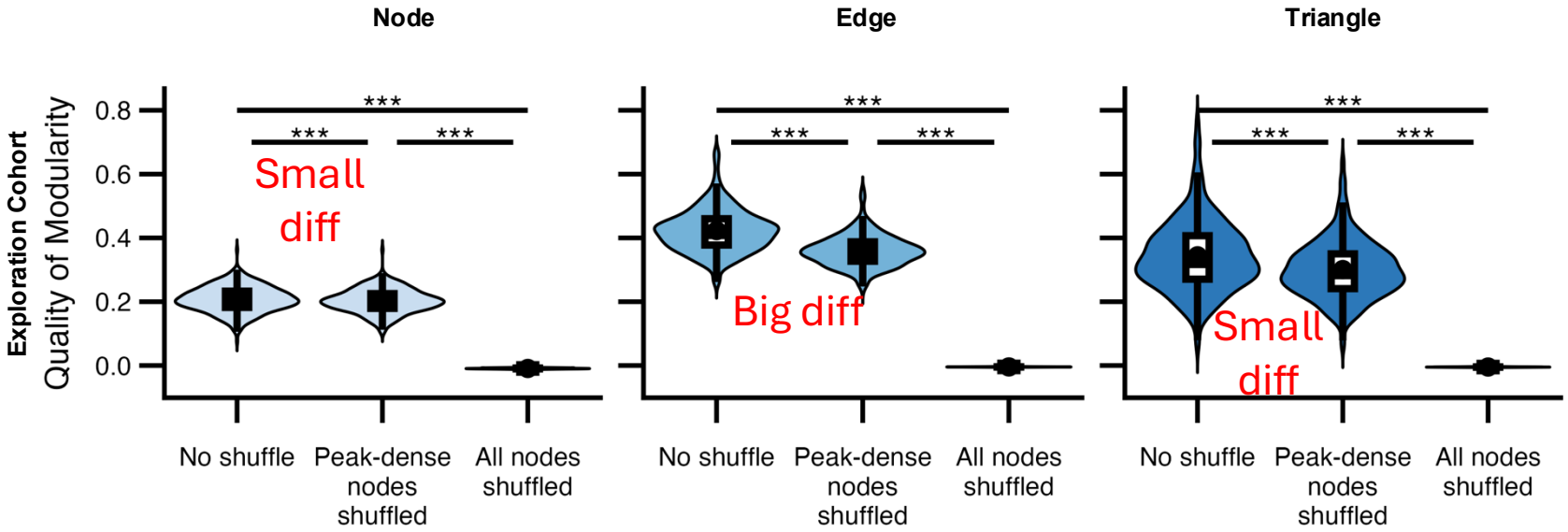
Shuffling


Node
Exploration Cohort
Quality of Modularity
0.8
0.6
0.4
0.2
0.0
***
***
***
Small
diff
No shuffle
Peak-dense
nodes
shuffled
All nodes
shuffled

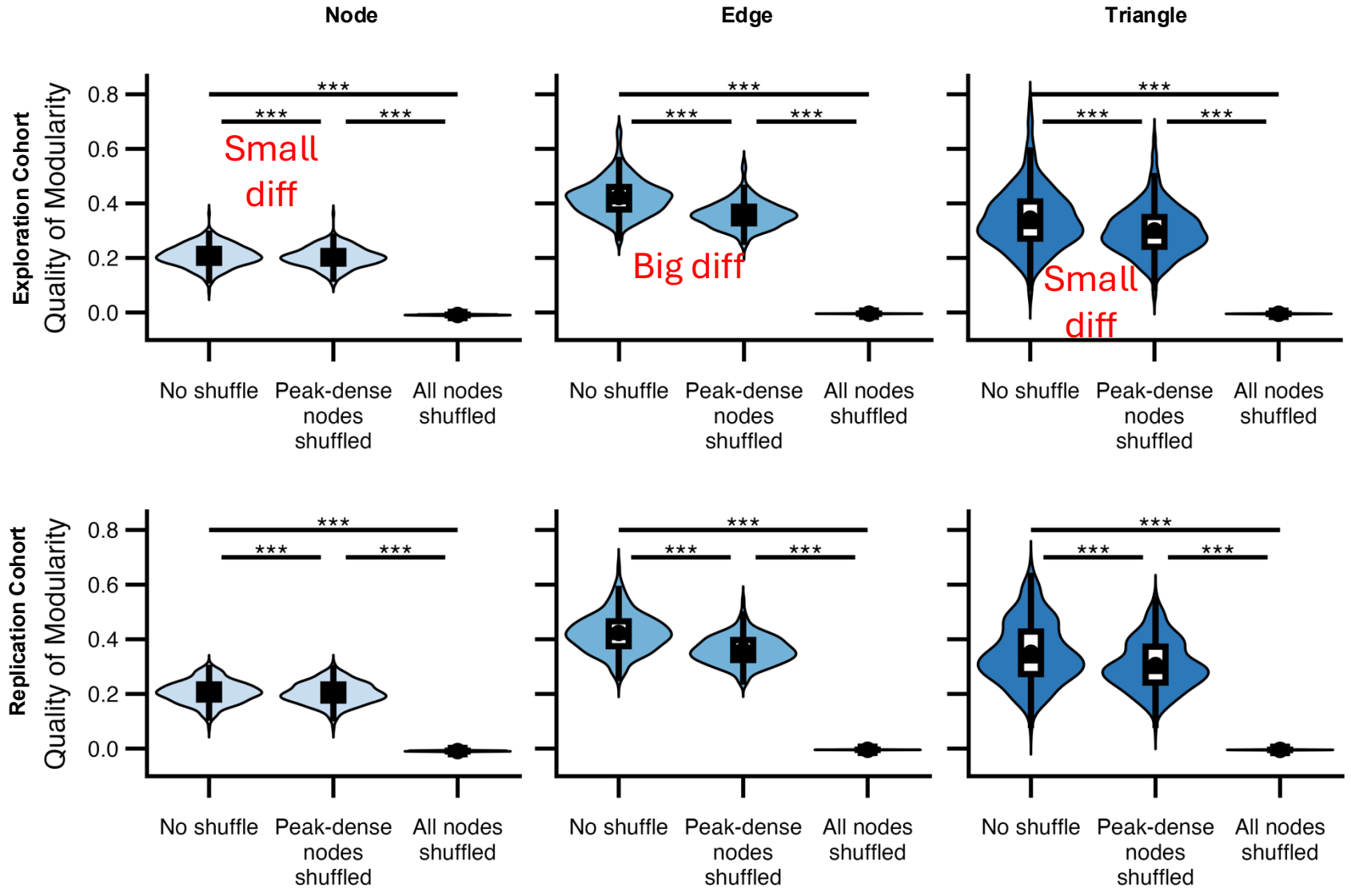
Shuffling


Node
Edge
Exploration Cohort
Quality of Modularity
0.8
0.6
0.4
0.2
0.0
***
***
***
Small diff
Big diff
No shuffle
Peak-dense nodes shuffled
All nodes shuffled

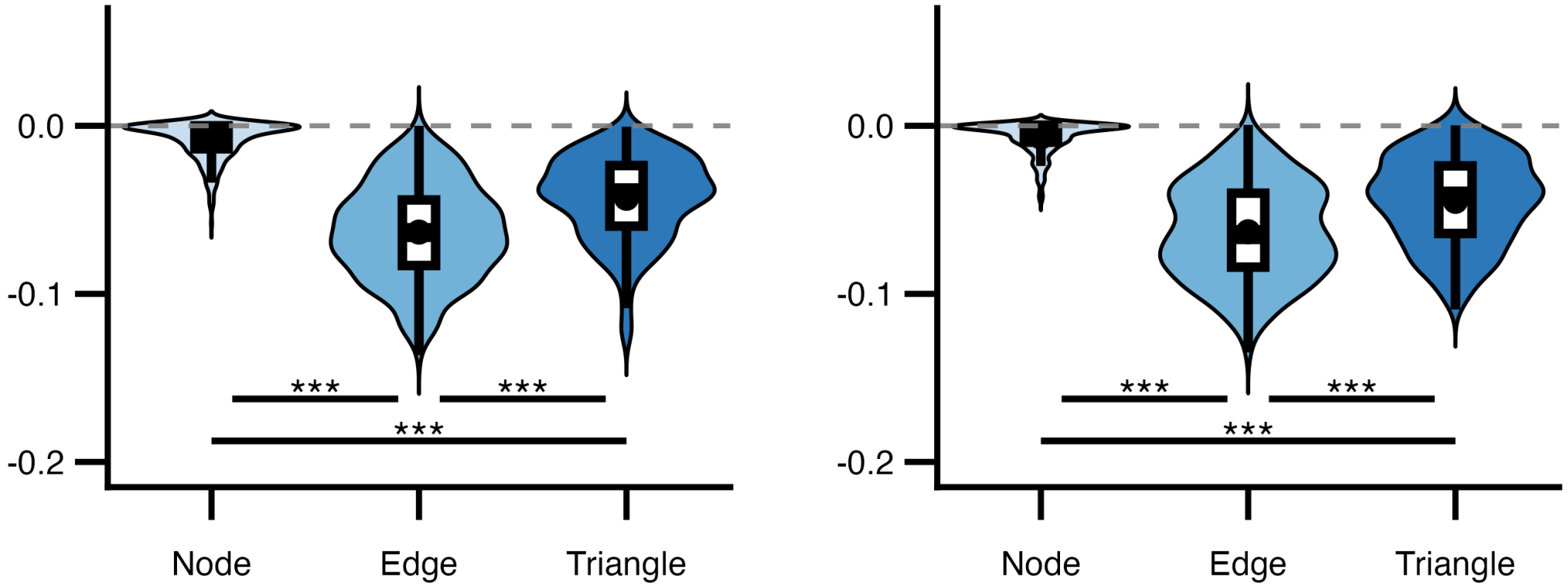
Shuffling


Node
Edge
Triangle
Exploration Cohort
Quality of Modularity
0.8
0.6
0.4
0.2
0.0
***
***
***
Small diff
Big diff
Small diff
No shuffle
Peak-dense nodes shuffled
All nodes shuffled

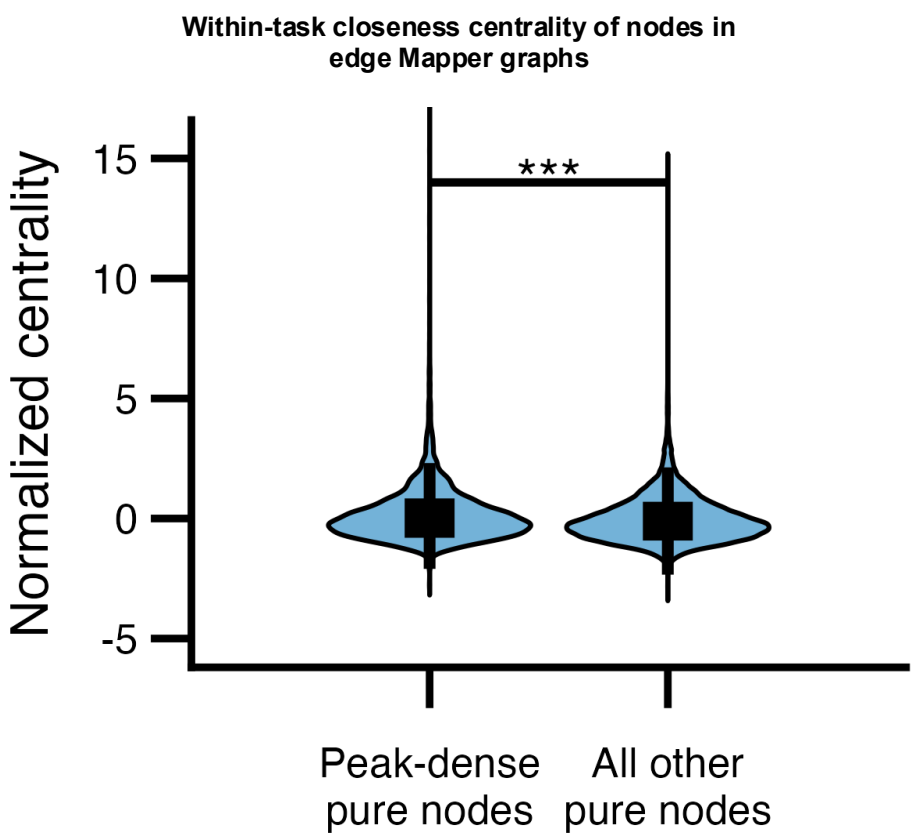
Shuffling

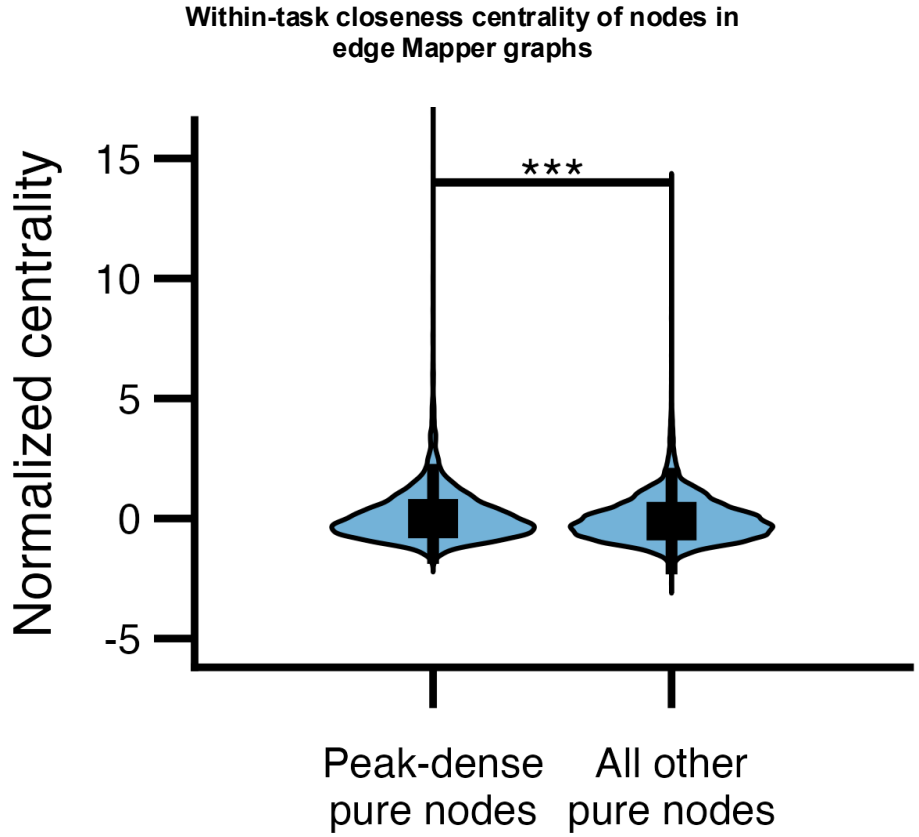

Node
Edge
Triangle
Exploration Cohort
Quality of Modularity
Replication Cohort
0.8
0.6
0.4
0.2
0.0
***
Small diff
Big diff
Small diff
No shuffle
Peak-dense nodes shuffled
All nodes shuffled

The shuffling-no-shuffling delta



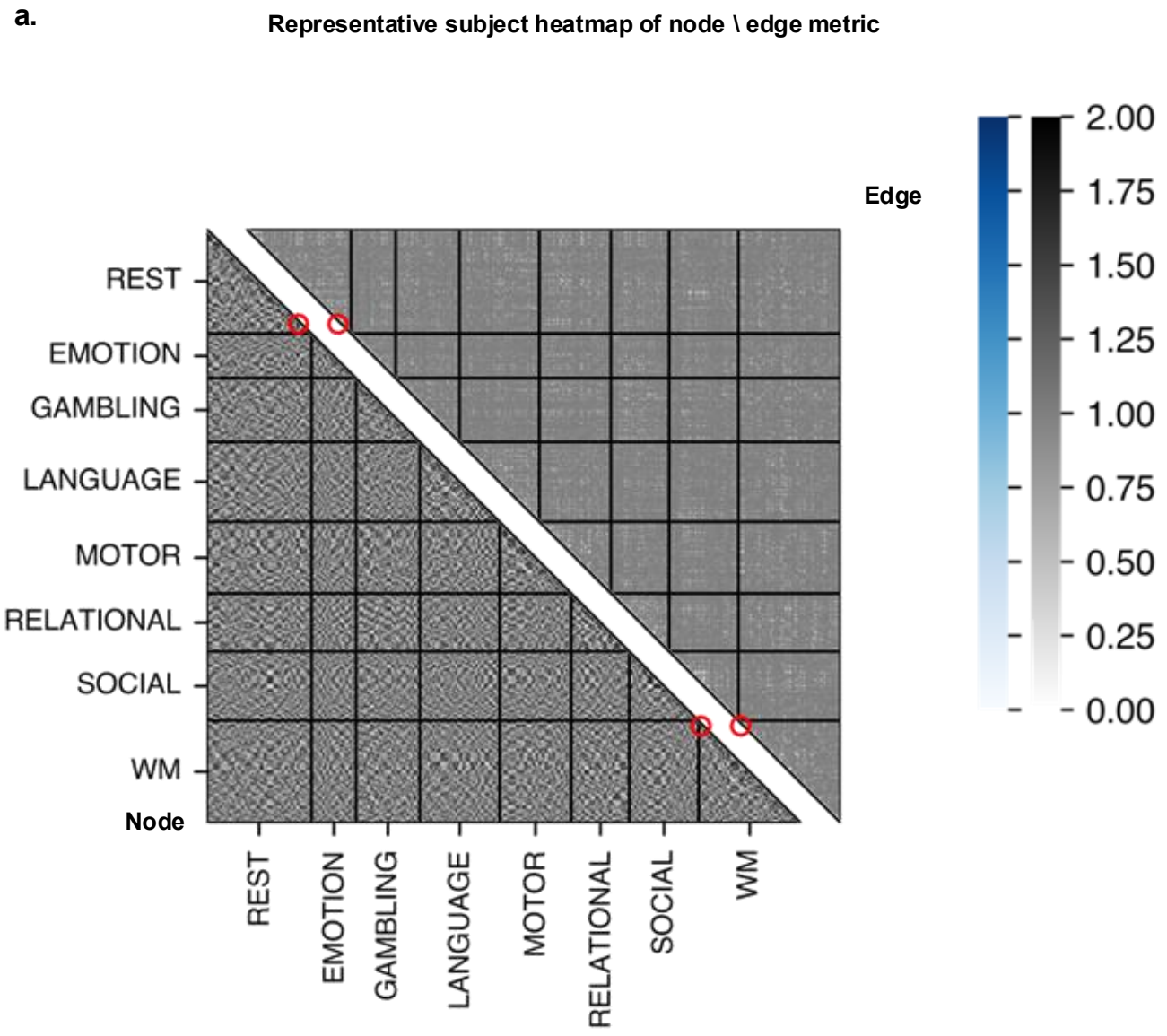
Peak-dense nodes occupy central locations



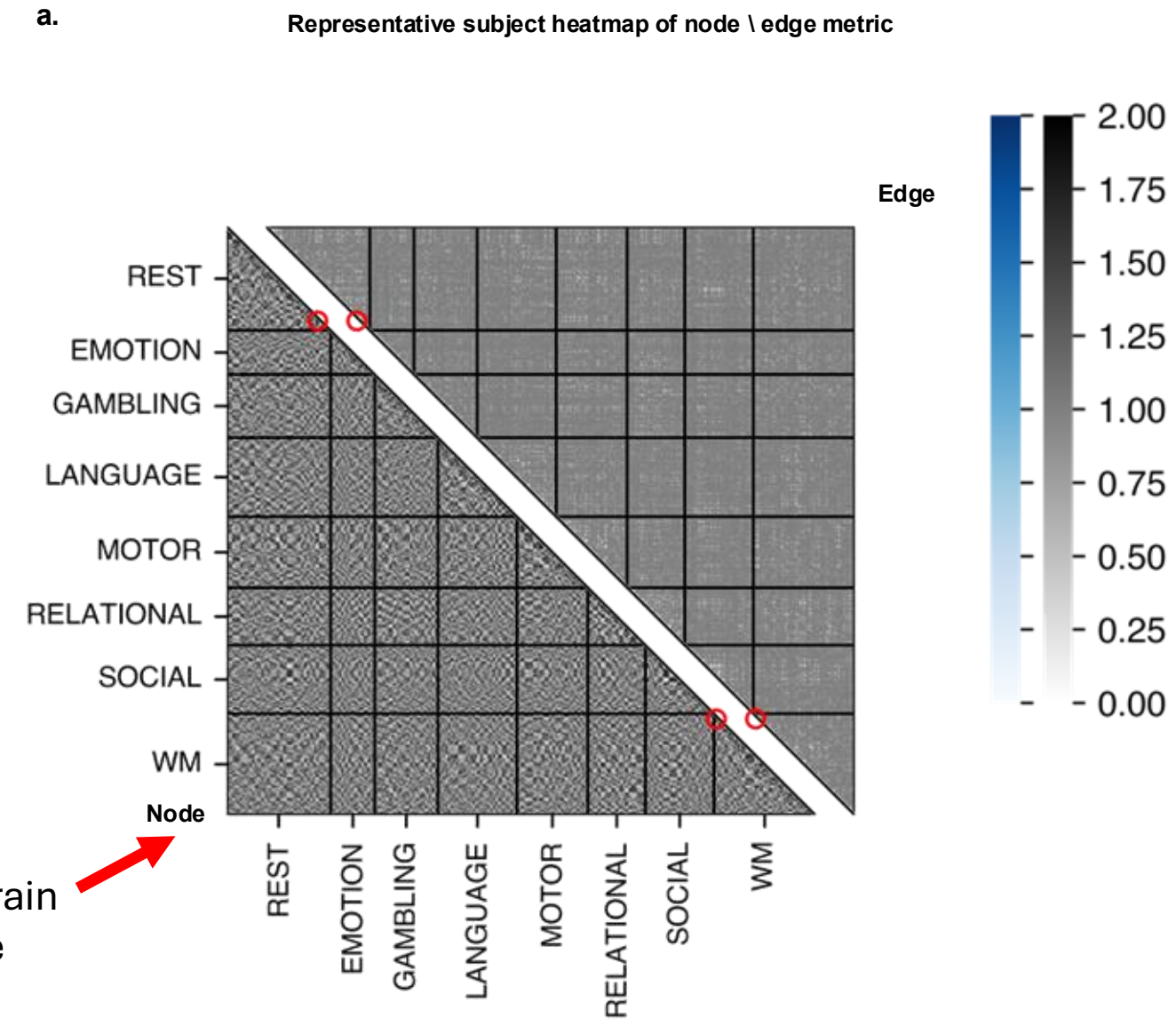


Peak events drive segregation of tasks.

Model-free approach



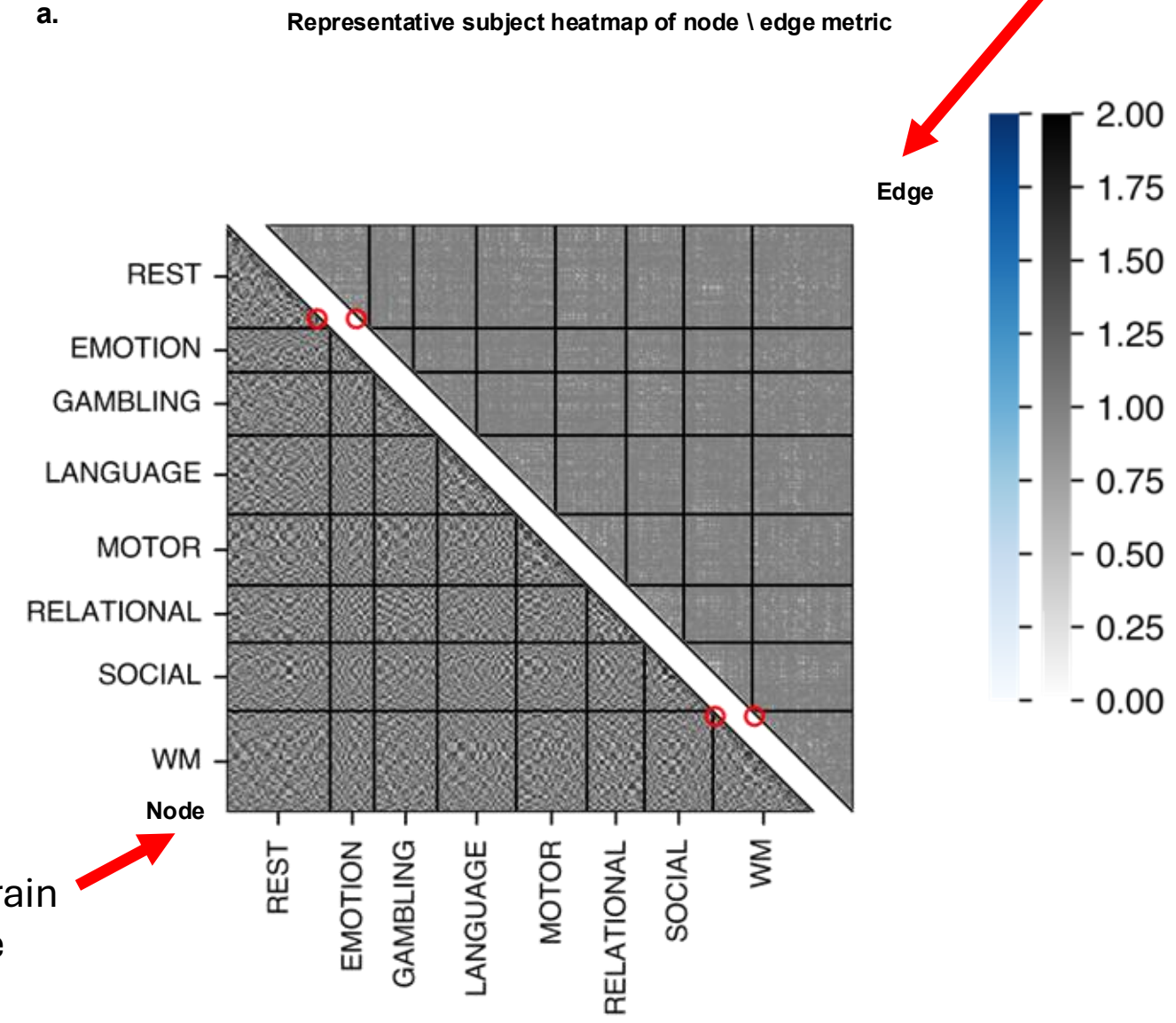
Model-free approach



how far the node-based brain states are at different time

Model-free approach

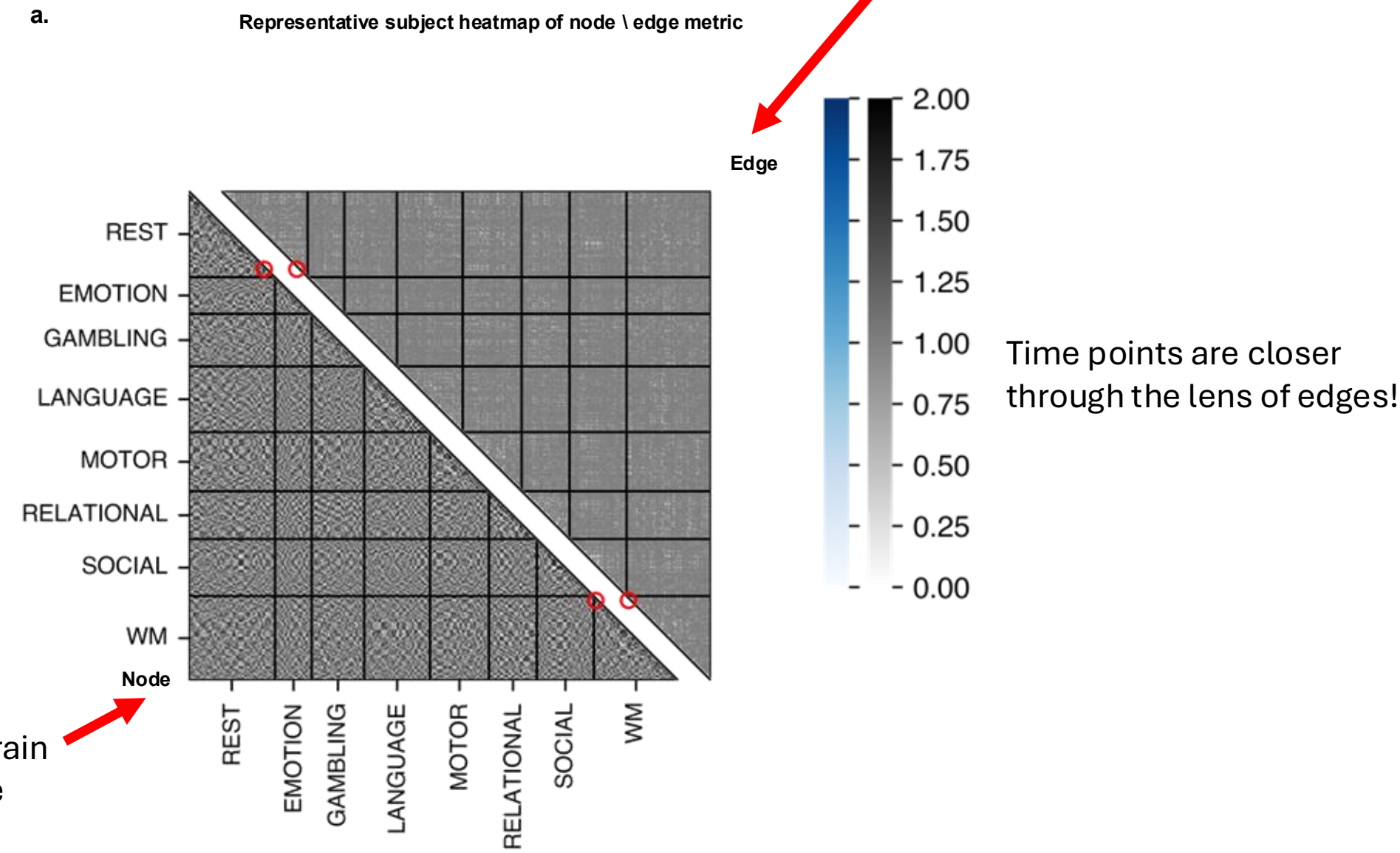
how far the edge-based brain states are at different time



how far the node-based brain states are at different time

Model-free approach

how far the edge-based brain states are at different time

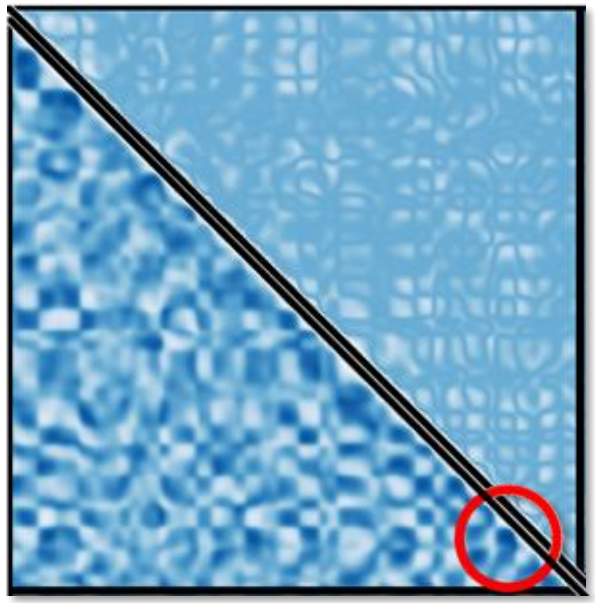


Time points are closer through the lens of edges!

how far the node-based brain states are at different time

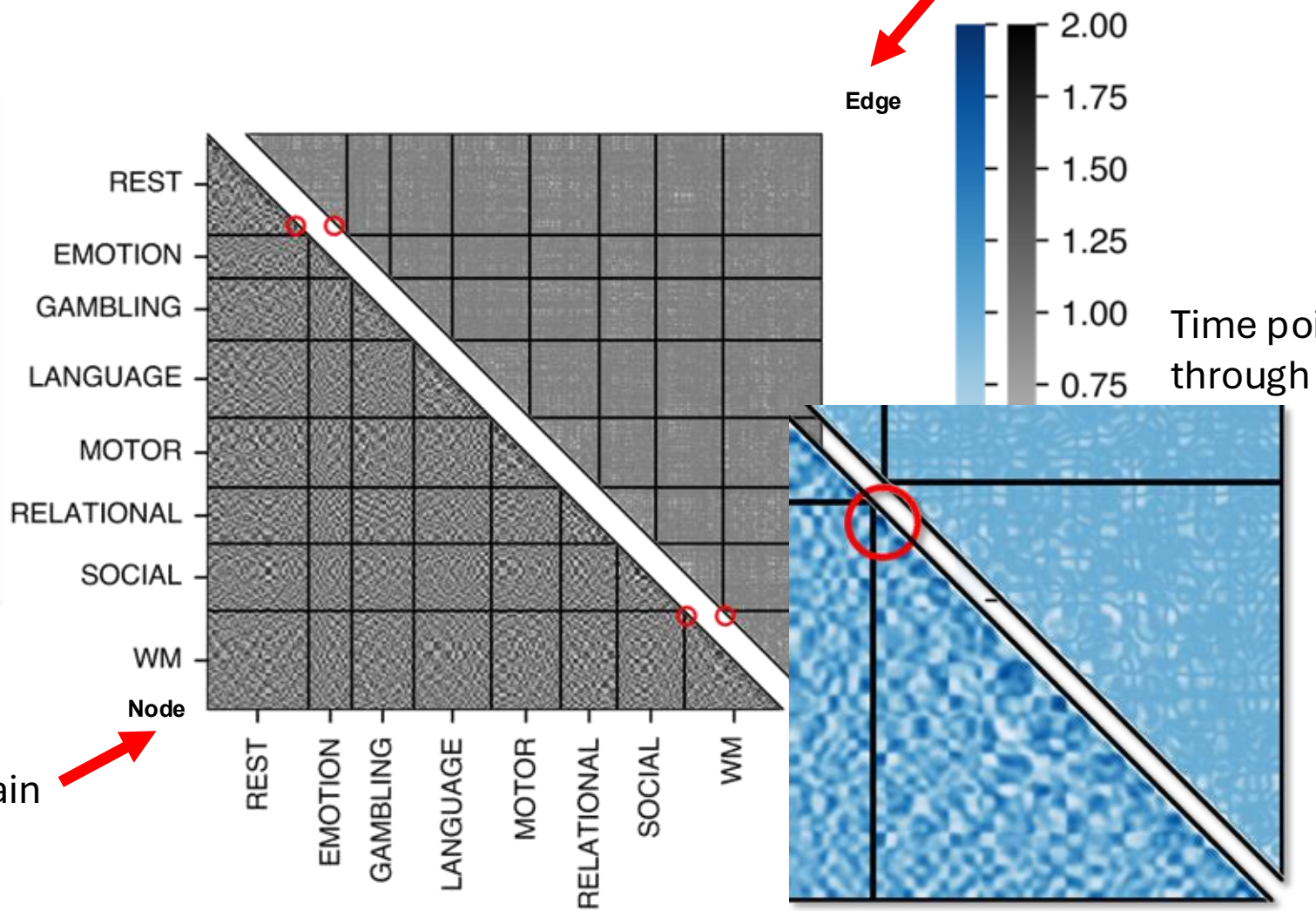
Model-free approach

how far the edge-based brain states are at different time



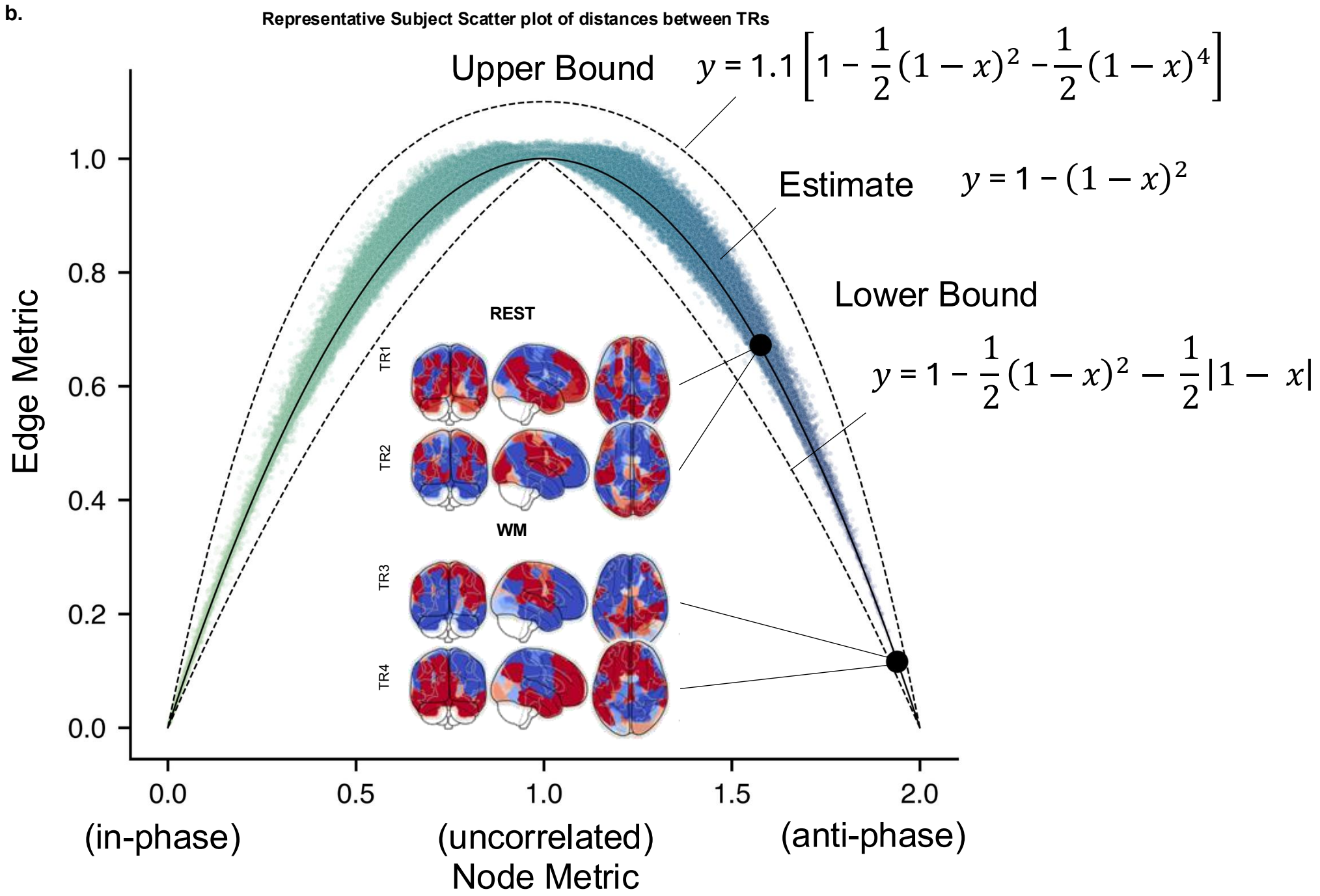
a.

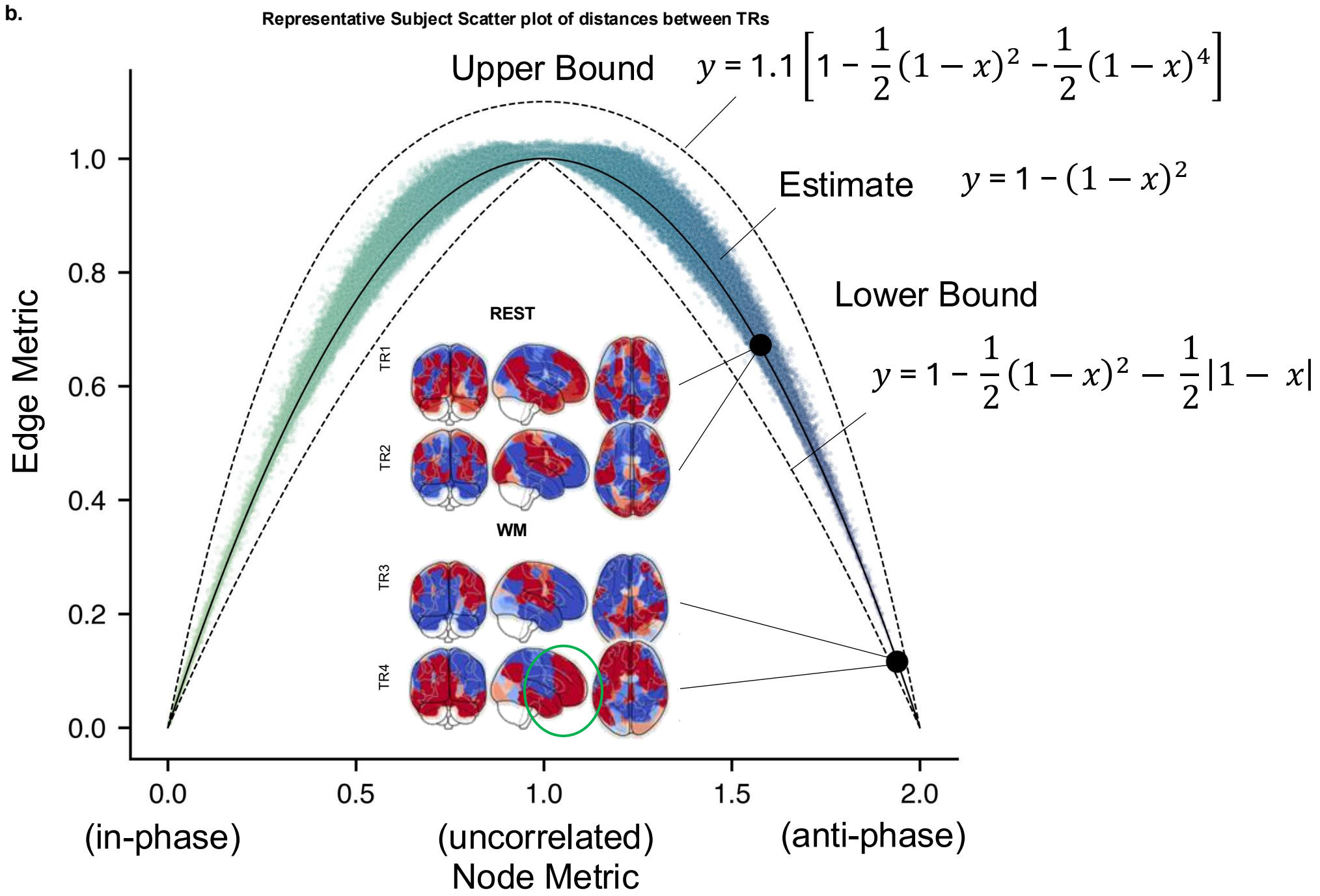
Representative subject heatmap of node \ edge metric



Time points are closer through the lens of edges!

how far the node-based brain states are at different time


b.
Representative Subject Scatter plot of distances between TRs
Upper Bound $y = 1.1\left[1 - \frac{1}{2}(1-x)^2 - \frac{1}{2}(1-x)^4\right]$
Estimate $y = 1 - (1-x)^2$
Lower Bound
$y = 1 - \frac{1}{2}(1-x)^2 - \frac{1}{2}|1-x|$
REST
WM
TR1
TR2
TR3
TR4
Edge Metric
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.5
1.0
1.5
2.0
(in-phase)
(uncorrelated)
(anti-phase)
Node Metric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Upper Bound $y = 1.1\left[1 - \frac{1}{2}(1-x)^2 - \frac{1}{2}(1-x)^4\right]$
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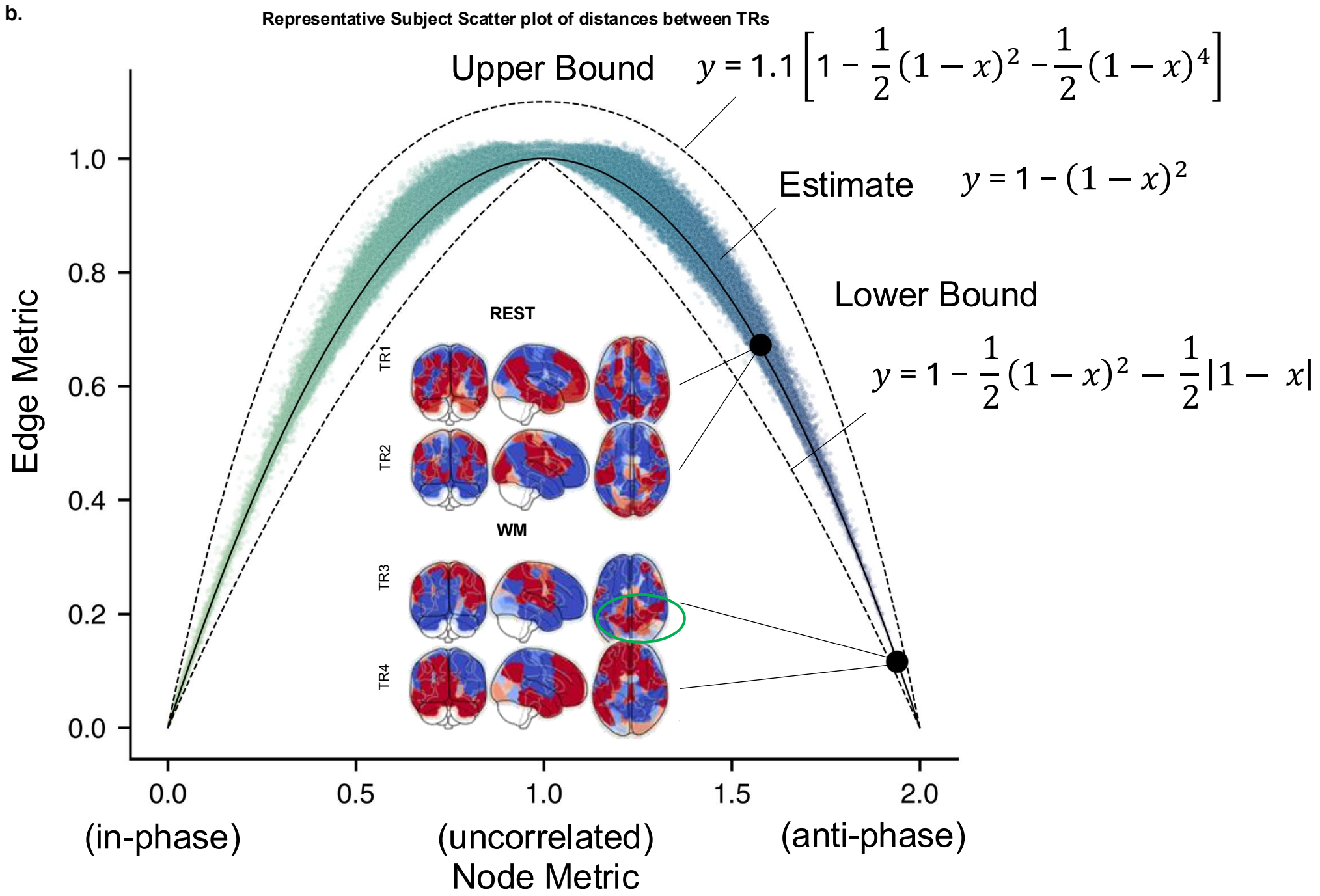
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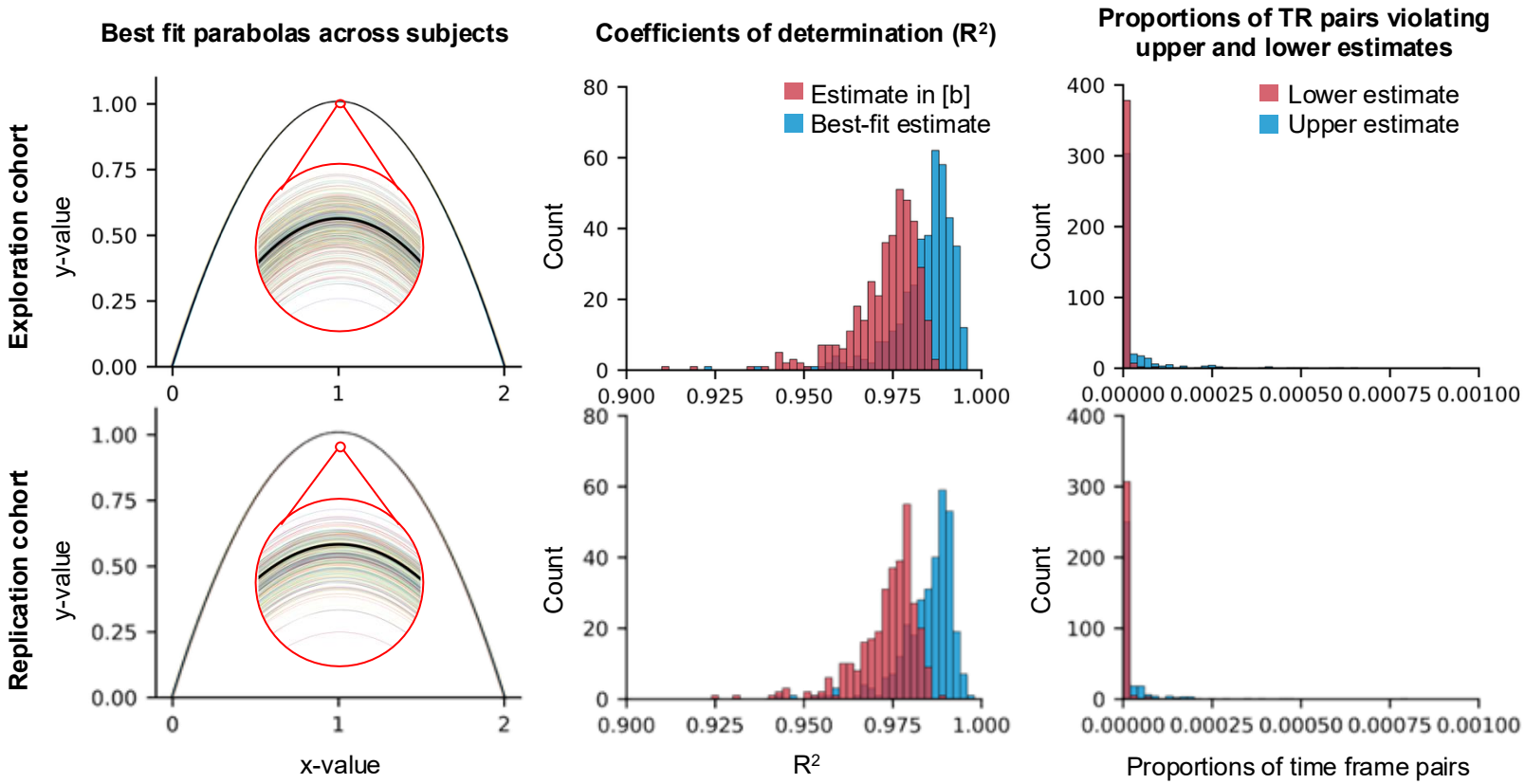
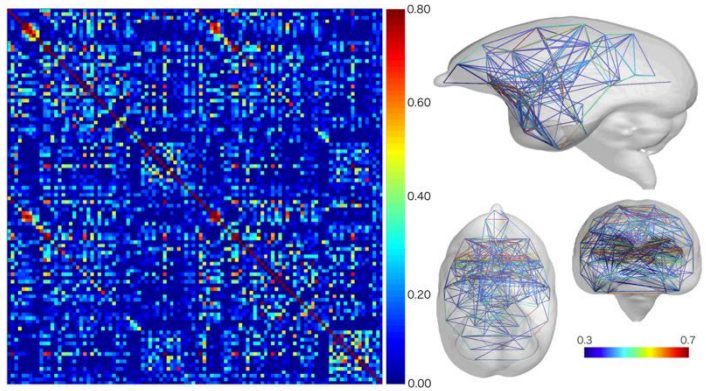

Best fit parabolas across subjects
Coefficients of determination (R^2)
Proportions of TR pairs violating upper and lower estimates
Exploration cohort
Replication cohort
y-value
x-value
Count
R^2
Estimate in [b]
Best-fit estimate
Lower estimate
Upper estimate
Proportions of time frame pairs

Peak events drive segregation of tasks.

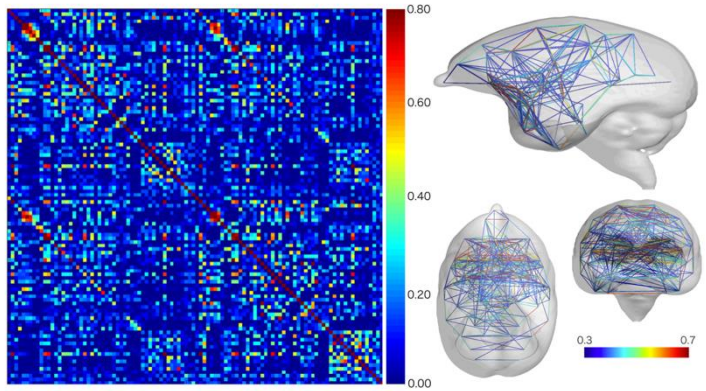
Peak events drive segregation of tasks.

Equating anticorrelated brain states drives segregation for tasks.


https://www.dreamstime.com/content-cat-napping-white-bedding-warm-morning-light-happy-long-haired-enjoying-nap-bed-soft-natural-image371898081



(a) Connectivity Matrix (b) Connectivity Map



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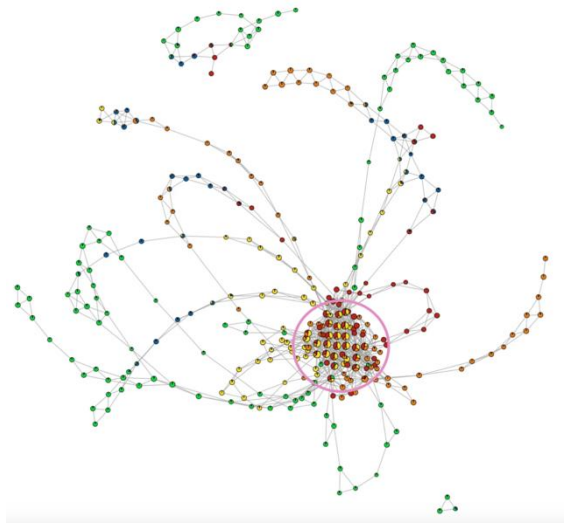

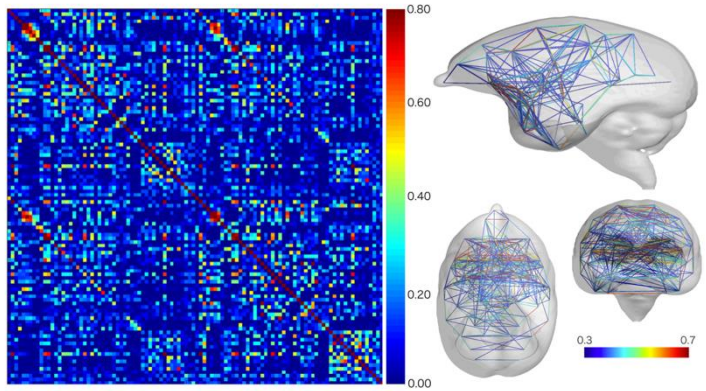

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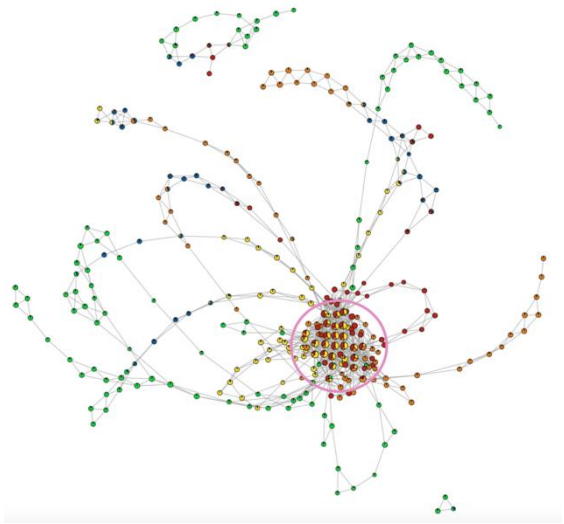

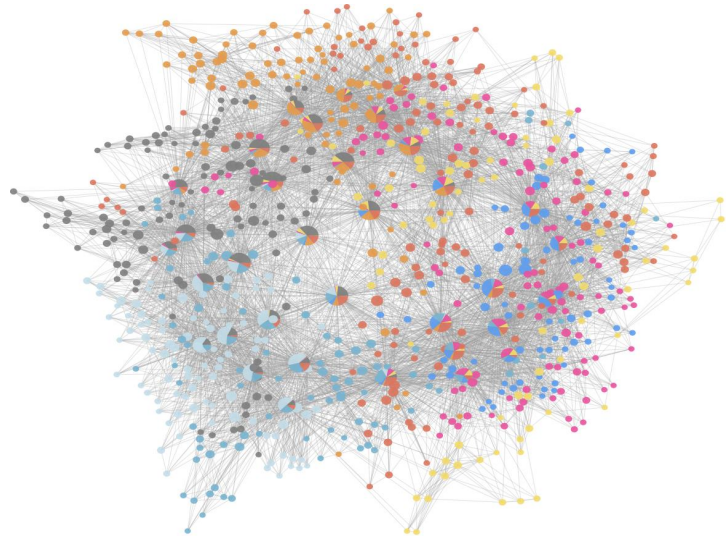

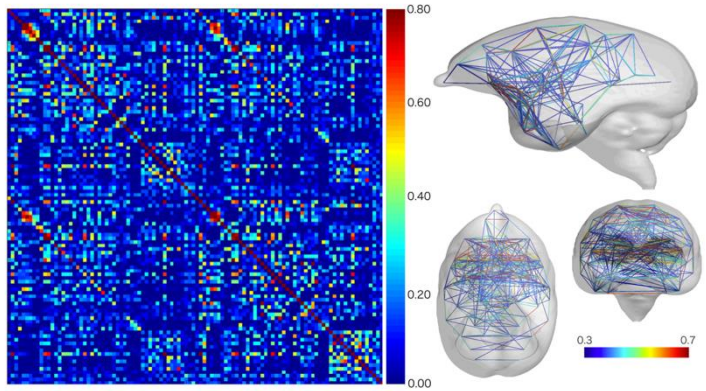

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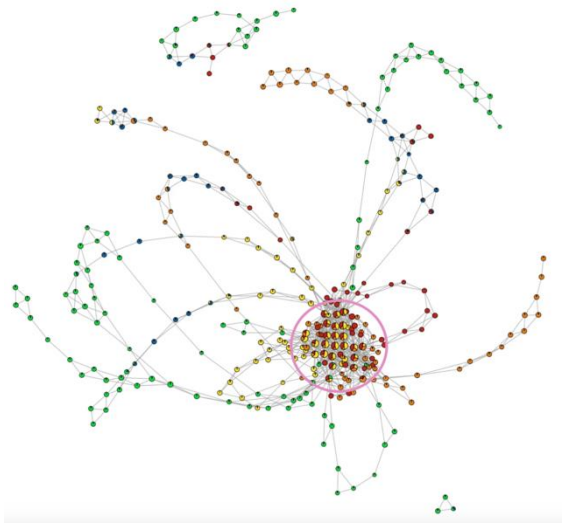

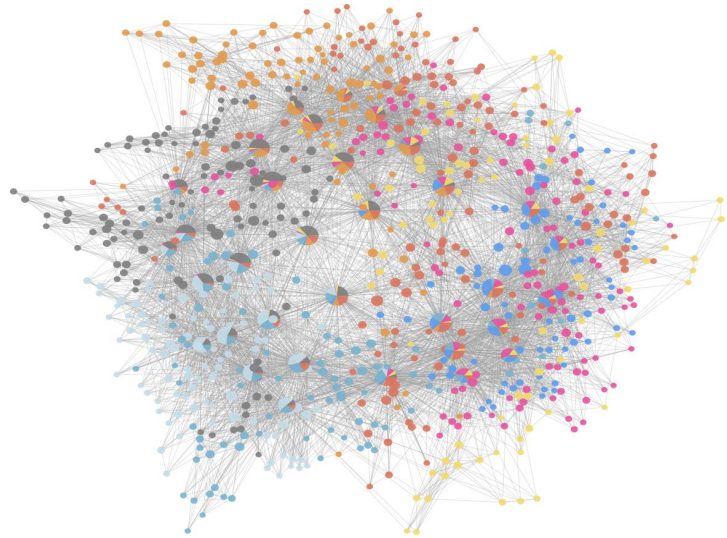

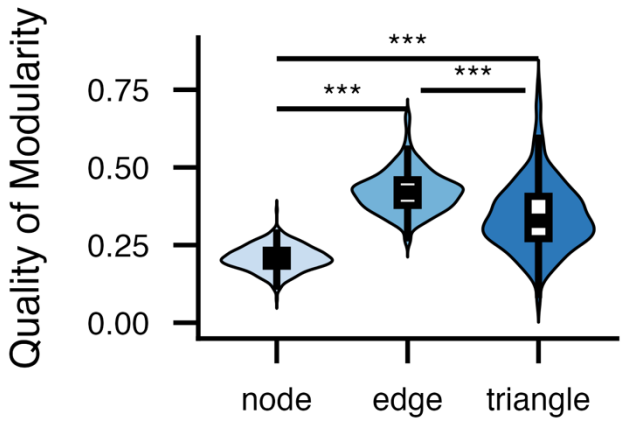

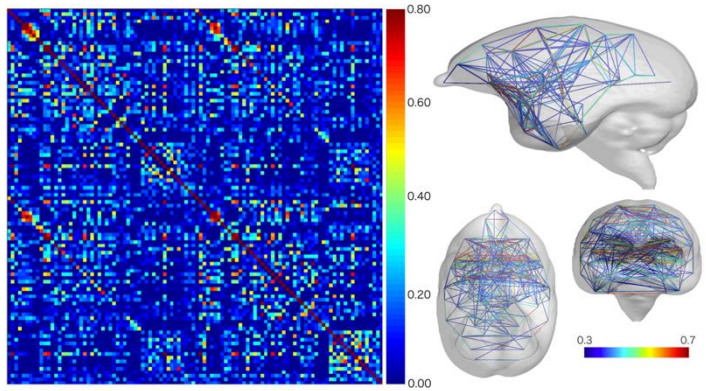

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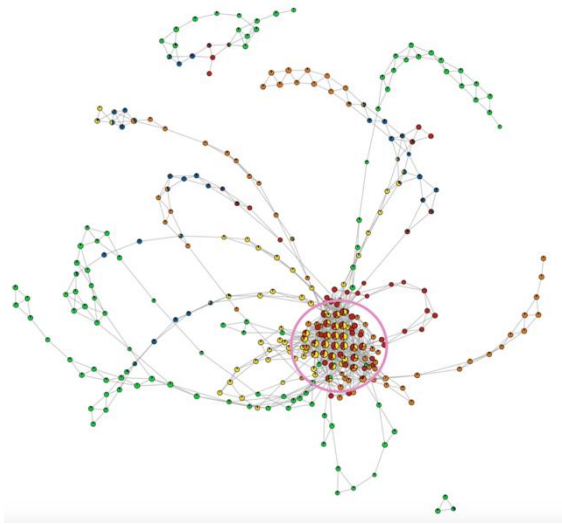

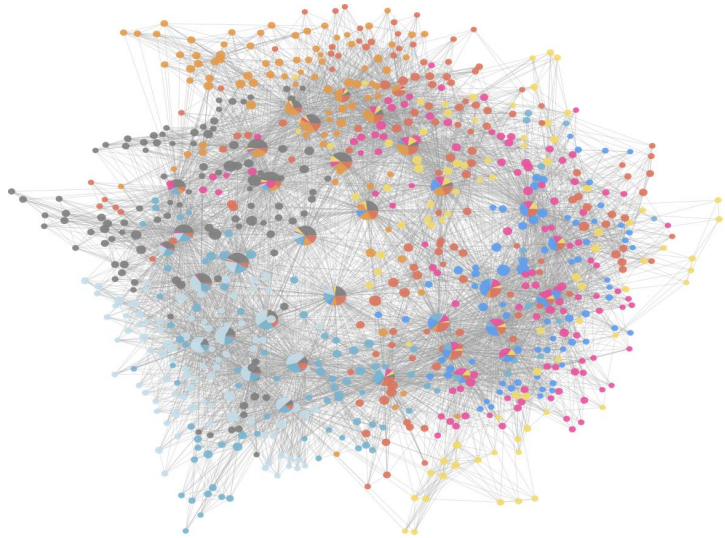

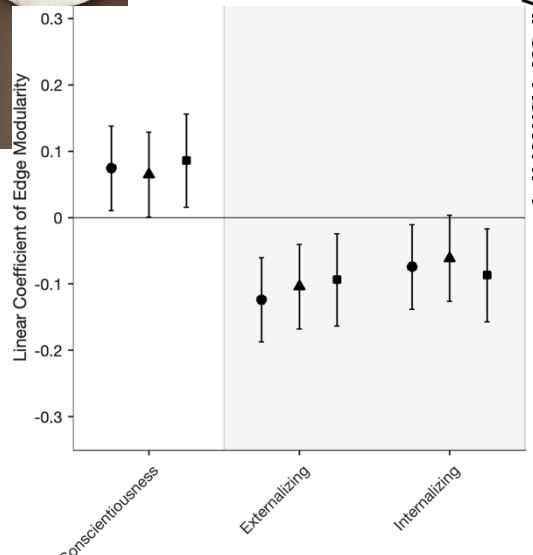

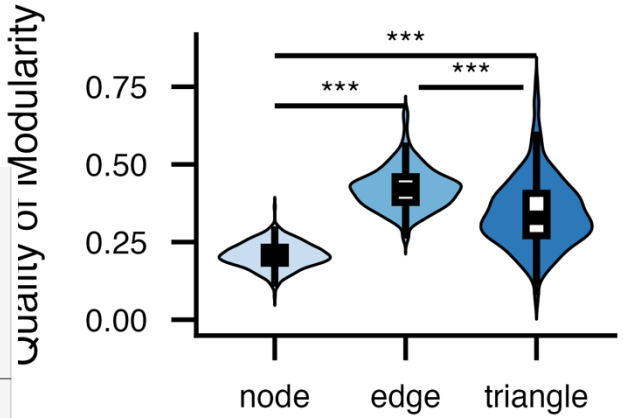

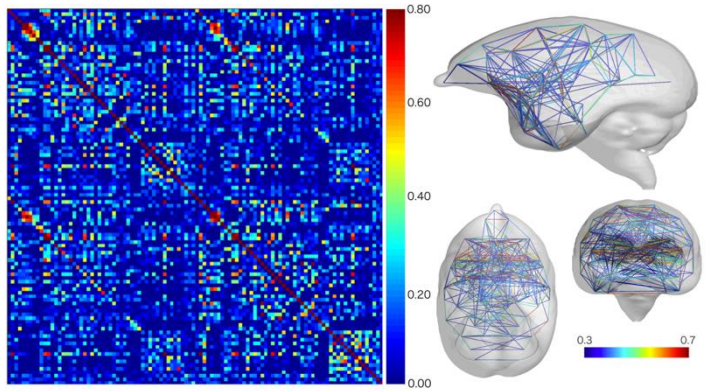

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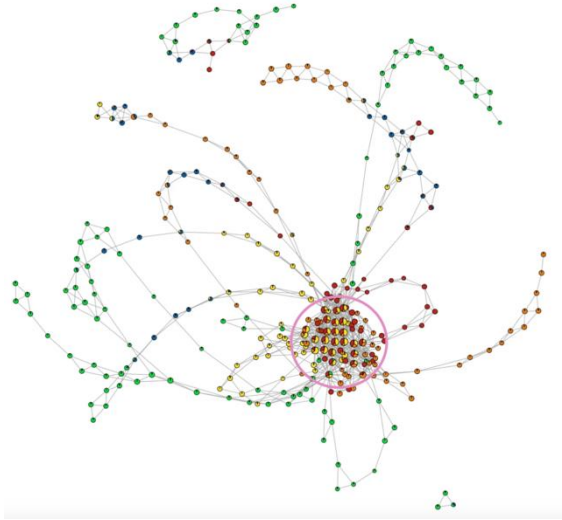

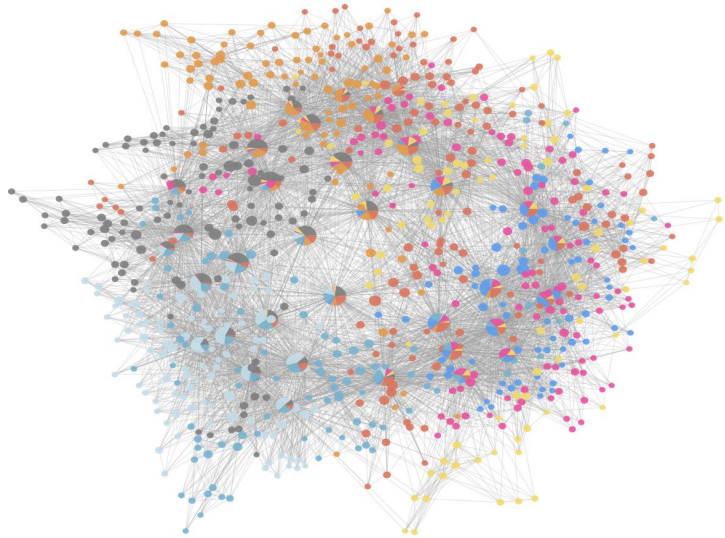

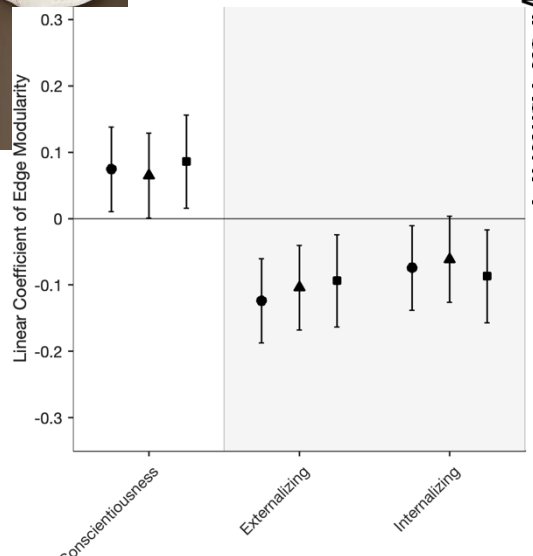

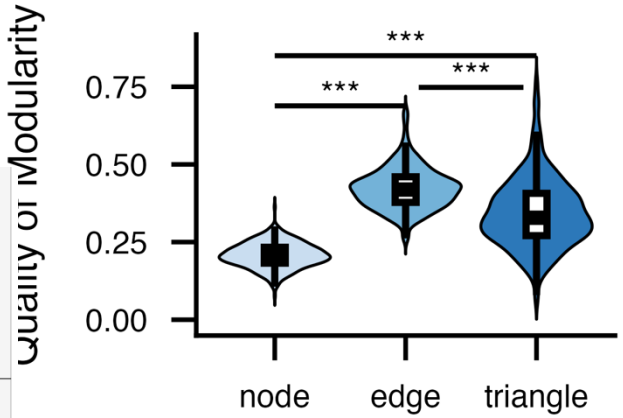

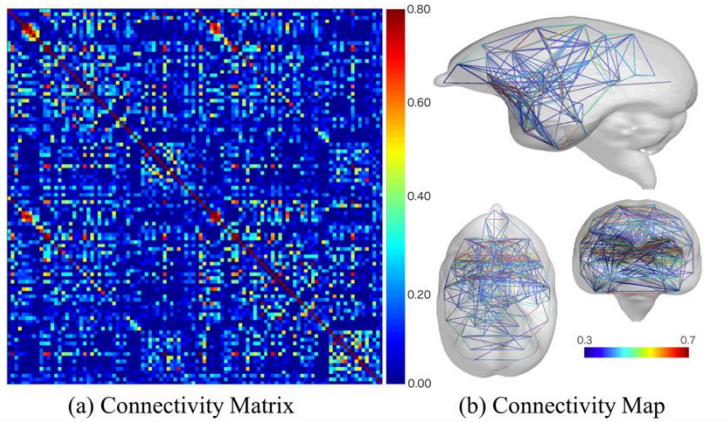

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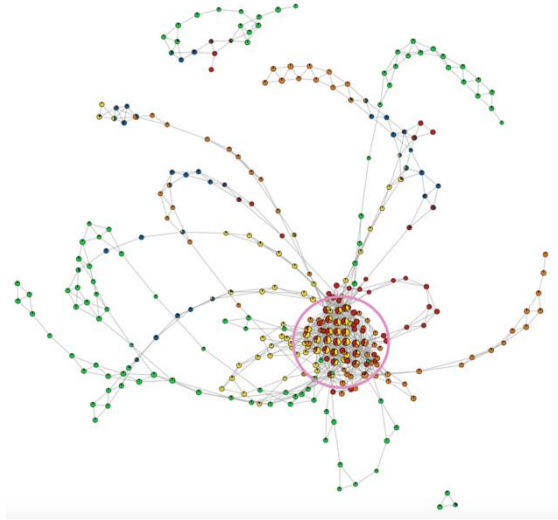

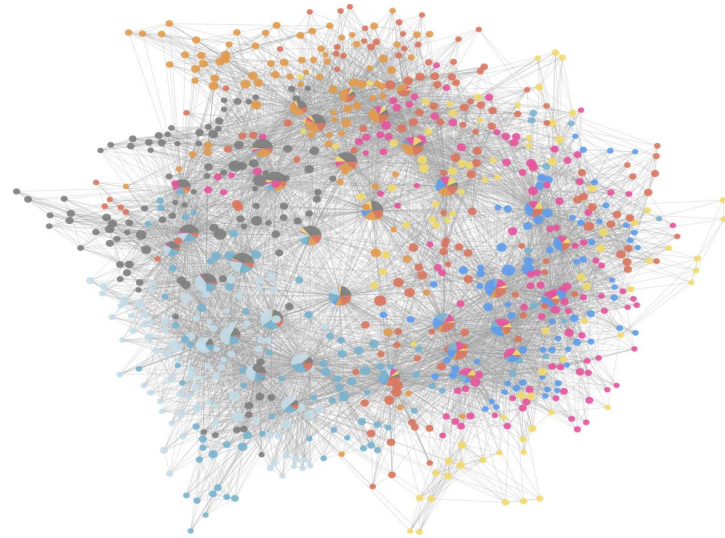

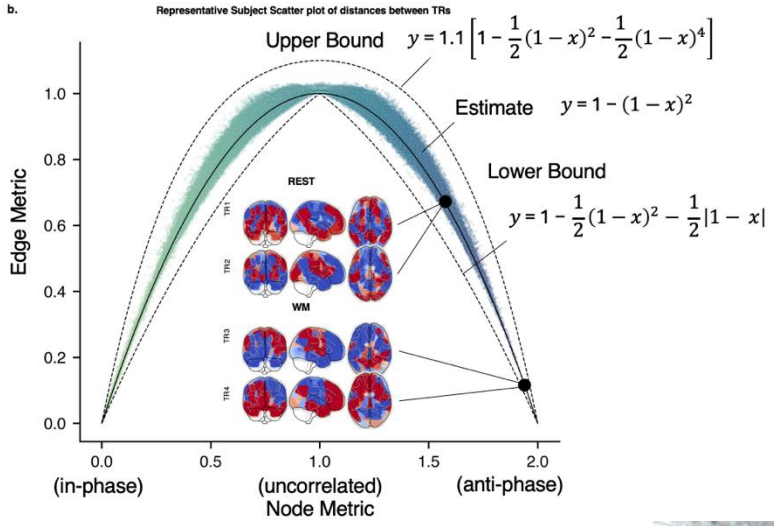

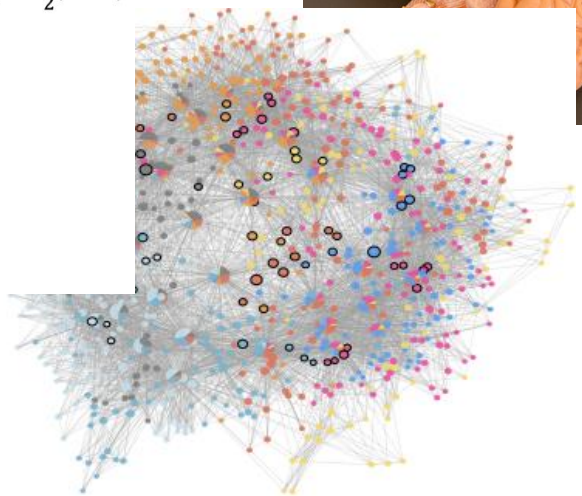

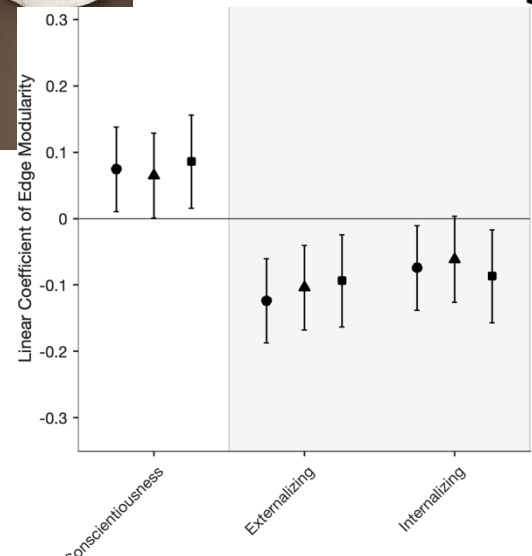

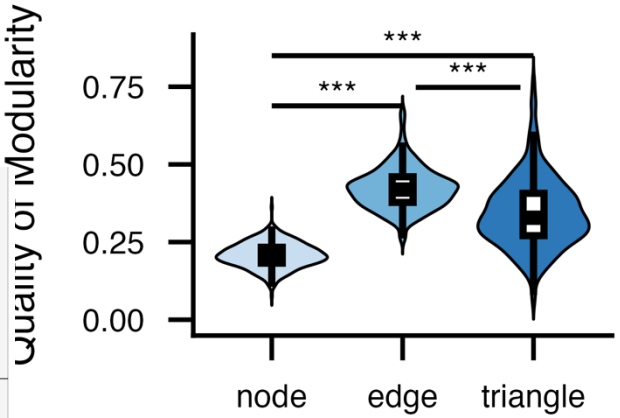

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- The right measurement requires the right mathematical construct.

Thank you!

Croucher Foundation

NIH National Institutes of Health
Turning Discovery Into Health

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