TECHNICAL REPORT
https://doi.org/10.1038/s41593-020-00719-y
nature neuroscience

NATURE NEUROSCIENCE | VOL 23 | DECEMBER 2020 | 1644-1654

Edge-centric functional network representations of human cerebral cortex reveal overlapping system-level architecture

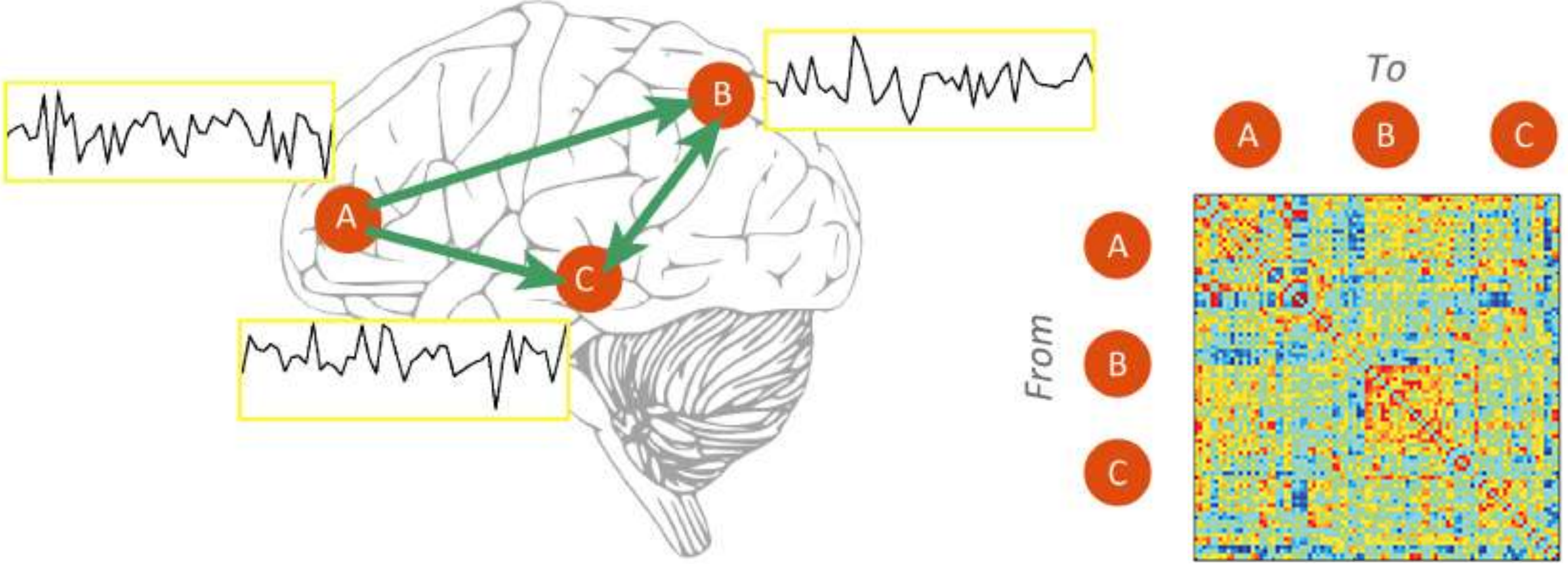
Joshua Faskowitz[1,2], Farnaz Zamani Esfahlani[1], Youngheun Jo[1], Olaf Sporns[1,2,3,4] and Richard F. Betzel[1,2,3,4]

Neuroinformatics Journal Club Discussion

Led by Aaron S. Kemp, MBA – PhD Candidate, UAMS

08/05/22

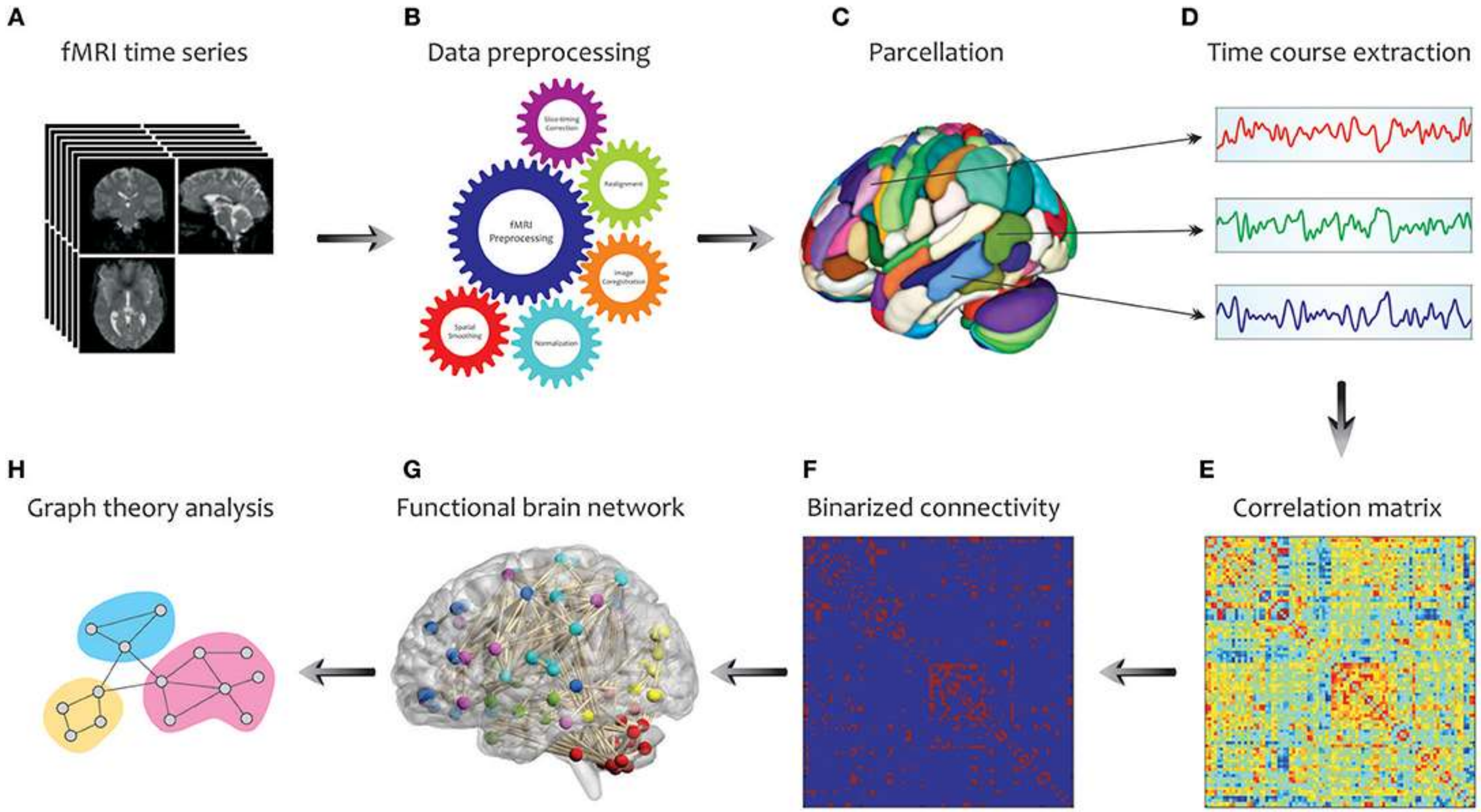
UAMS
Department of
Biomedical Informatics



- Define network *nodes* (spatial coordinates or regions of interest)
- Identify a timeseries associated with each node
- Estimate the *edge strengths*, or connections between the nodes
  - For example, correlate each timeseries with every other timeseries
  - If the data (and method for estimating edges) permits the estimation of causality, the edges may be uni-directional, resulting in an asymmetric network matrix

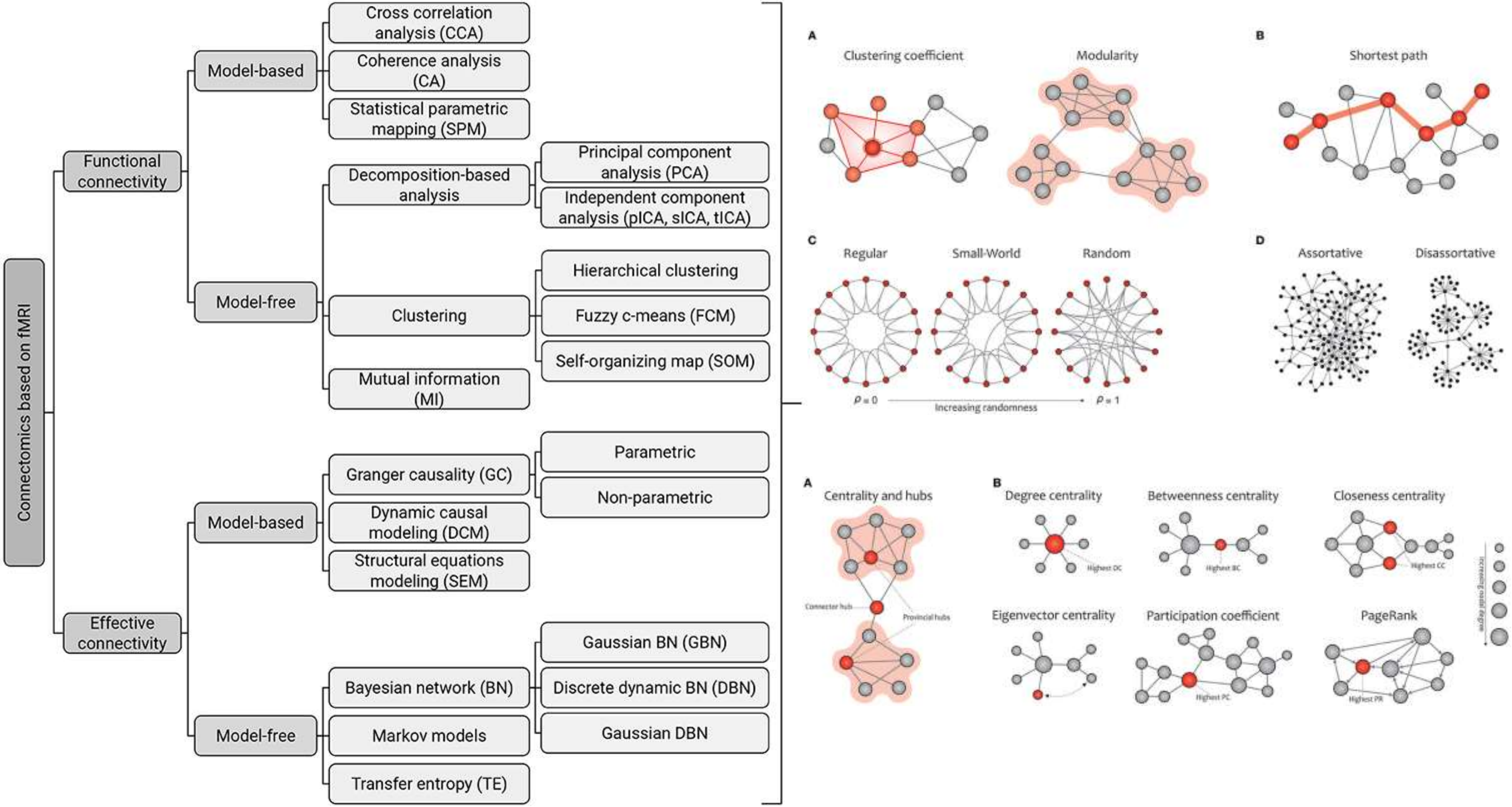
TRENDS in Cognitive Sciences

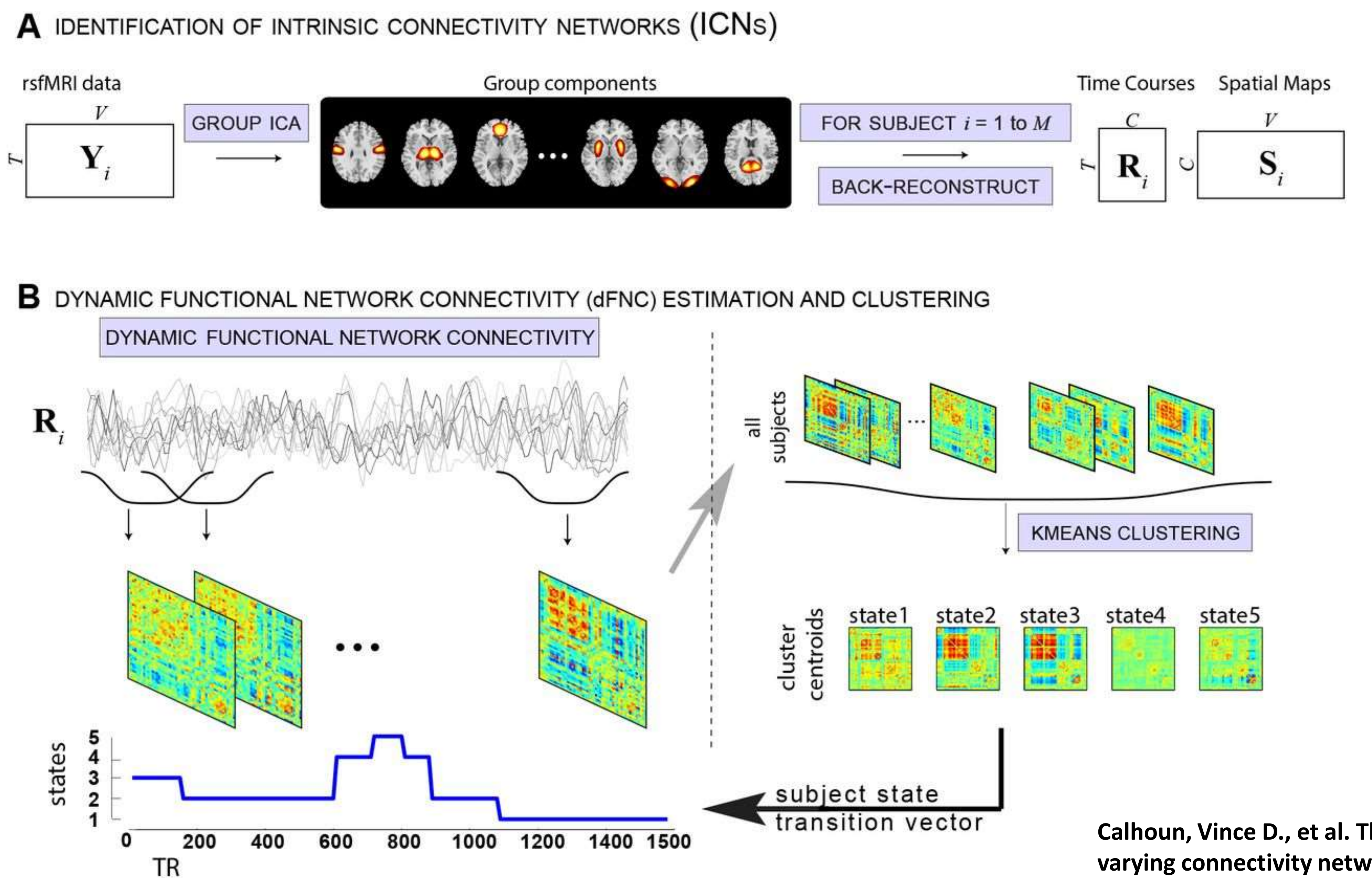
Smith, Stephen M., et al. "Functional connectomics from resting-state fMRI." Trends in cognitive sciences 17.12 (2013): 666-682.



Farahani, Farzad V. (2019). "Application of Graph Theory for Identifying Connectivity Patterns in Human Brain Networks: A Systematic Review". Frontiers in neuroscience (1662-4548), 13 .

Farahani, Farzad V. (2019). "Application of Graph Theory for Identifying Connectivity Patterns in Human Brain Networks: A Systematic Review". Frontiers in neuroscience (1662-4548), 13 .





Calhoun, Vince D., et al. The chronnectome: time-varying connectivity networks as the next frontier in fMRI data discovery. Neuron 84.2 (2014): 262-274.

NETWORK NEUROSCIENCE

NATURE NEUROSCIENCE | VOL 23 | DECEMBER 2020 | 1469-1472

An ‘edgy’ new look

Lucina Q. Uddin

- In traditional graph theoretic analyses of brain networks, functional connectivity (FC) between brain regions—measured as correlation or coherence—is interpreted as an indicator of inter-regional communication[3].
- Strong node FC is observed between two brain regions if they exhibit a high level of instantaneous co-fluctuation in their signals and reflects temporally correlated activity between brain regions.
- Faskowitz and colleagues[4] introduced a new metric they call edge FC (eFC) to capture a different aspect of inter-regional communication: the dynamics of edges themselves.
- If two sets of edges or connections co-fluctuate in concert, they exhibit strong eFC in this new framework.
- The added benefits of tracking eFC across the brain are that it permits analysis of how communication patterns evolve over time and can reveal whether similar patterns of communication are occurring across different parts of the brain simultaneously.

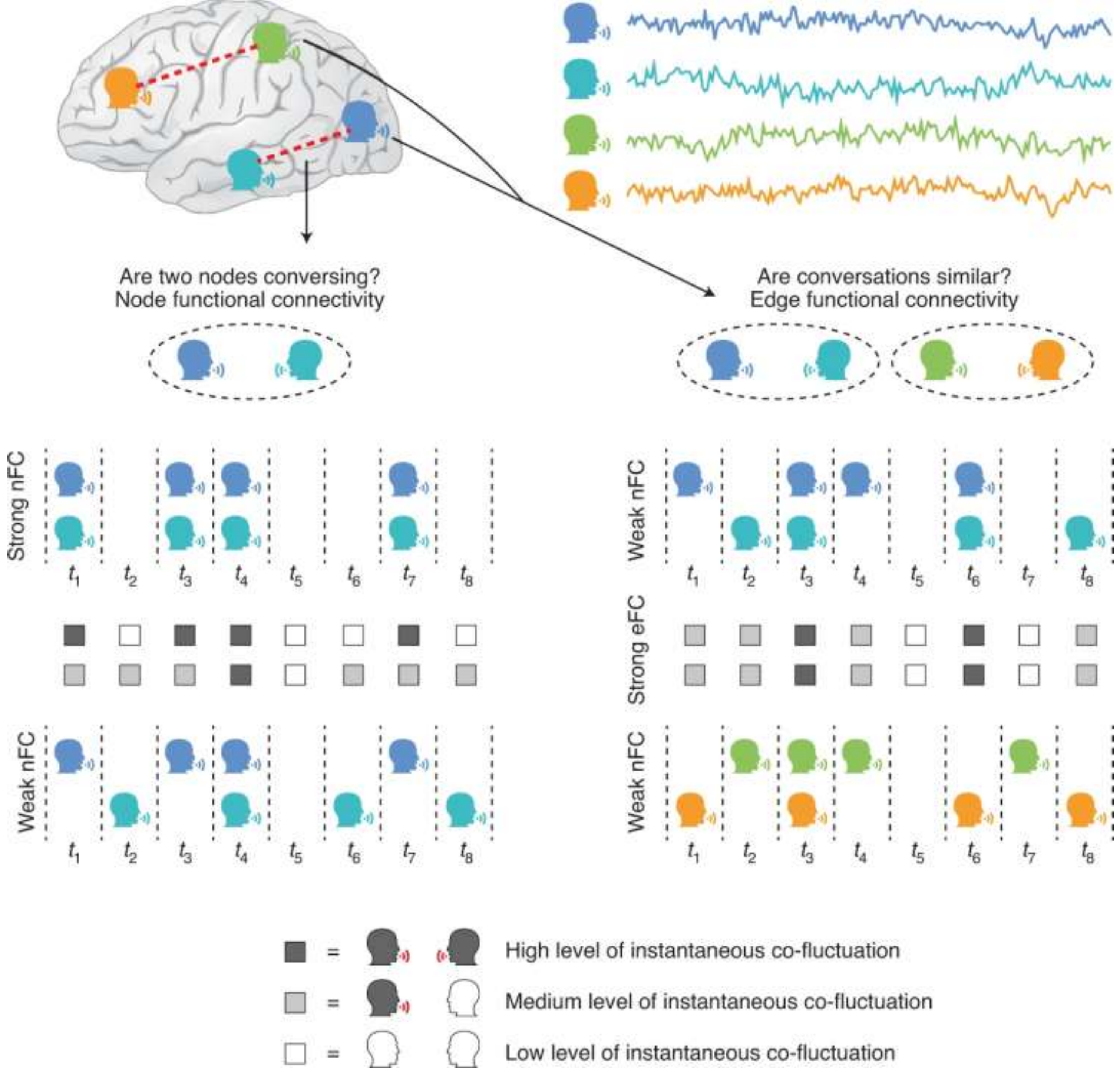
NETWORK NEUROSCIENCE

NATURE NEUROSCIENCE | VOL 23 | DECEMBER 2020 | 1469-1472

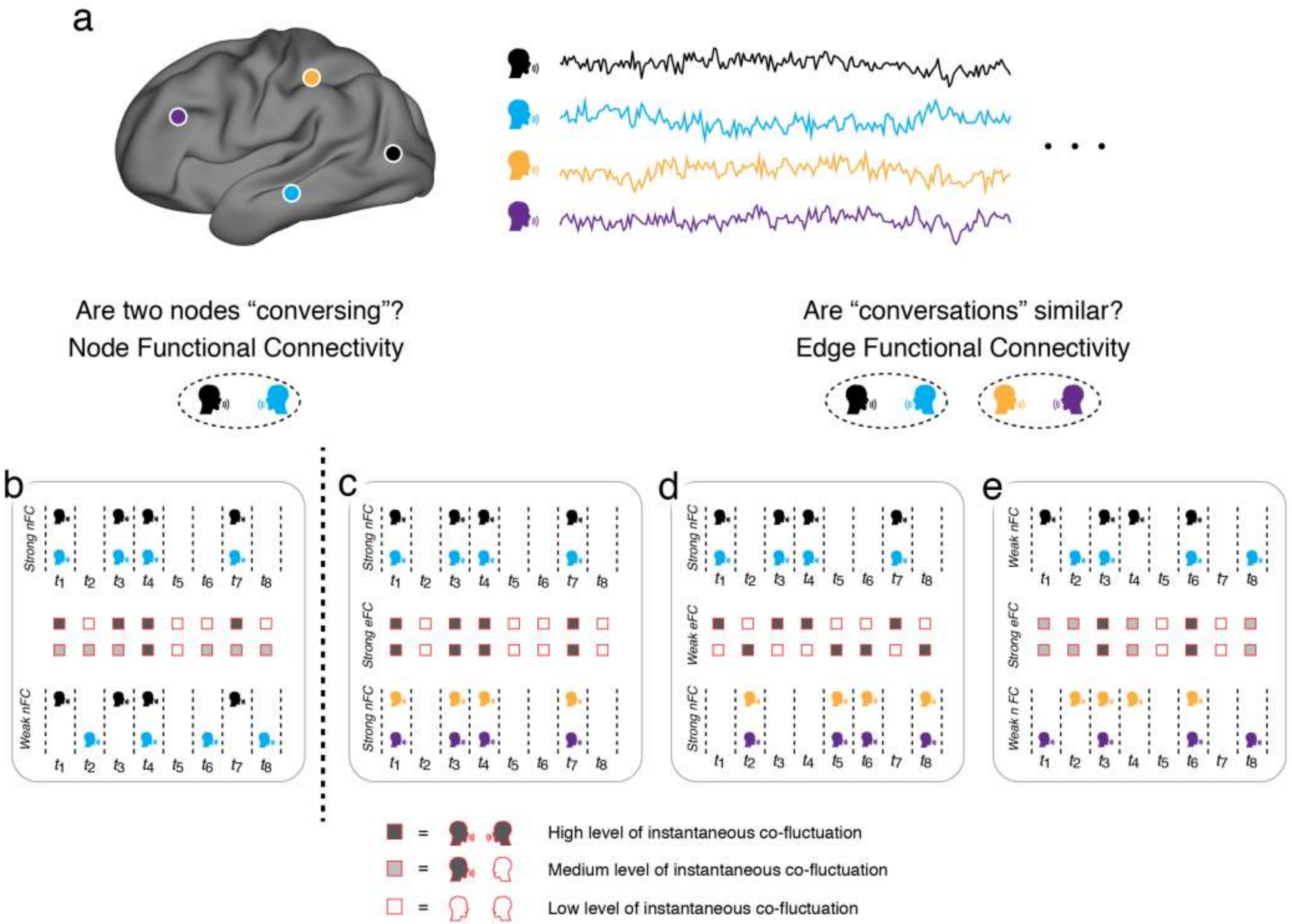
An 'edgy' new look

Lucina Q. Uddin

- There were **three main goals** of the work aiming to introduce eFC to the network neuroscience community:
  - Develop a framework for analyzing eFC using three large, publicly available neuroimaging datasets, the **Human Connectome Project**, **Midnight Scan Club** and **Healthy Brain Network**, to establish feasibility and evaluate the stability of the metric.
  - Partition **eFC networks** to explore **community** structures derived from this novel metric.
  - Assess how eFC can be **modulated** during brain states characterized by changes in **sensory input** during passive viewing of movies.

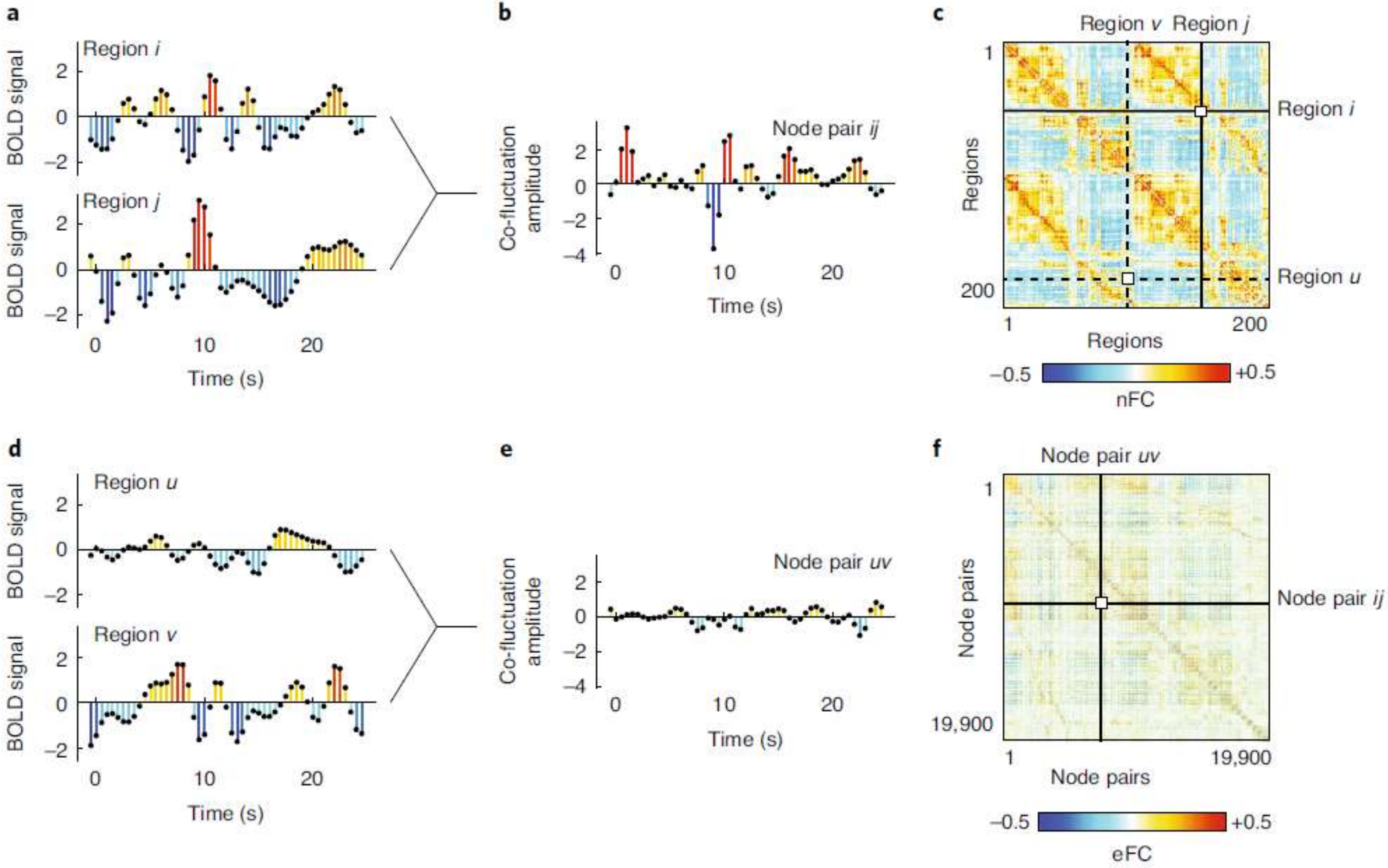


Are two nodes conversing?
Node functional connectivity
Are conversations similar?
Edge functional connectivity
Strong nFC
Weak nFC
Weak nFC
Strong eFC
Weak nFC
t_1 t_2 t_3 t_4 t_5 t_6 t_7 t_8
= High level of instantaneous co-fluctuation
= Medium level of instantaneous co-fluctuation
= Low level of instantaneous co-fluctuation

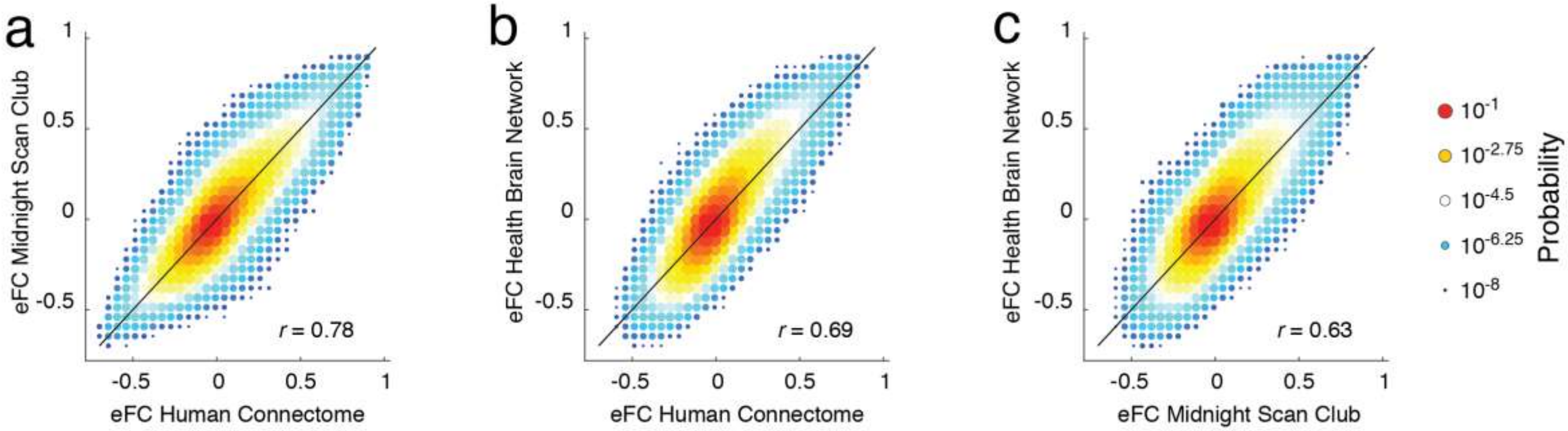

a
Are two nodes "conversing"?
Node Functional Connectivity
Are "conversations" similar?
Edge Functional Connectivity
b
Strong nFC
Weak nFC
c
Strong nFC
Strong eFC
Strong nFC
d
Strong nFC
Weak eFC
Strong nFC
e
Weak nFC
Strong eFC
Weak n FC
t_1 t_2 t_3 t_4 t_5 t_6 t_7 t_8
High level of instantaneous co-fluctuation
Medium level of instantaneous co-fluctuation
Low level of instantaneous co-fluctuation

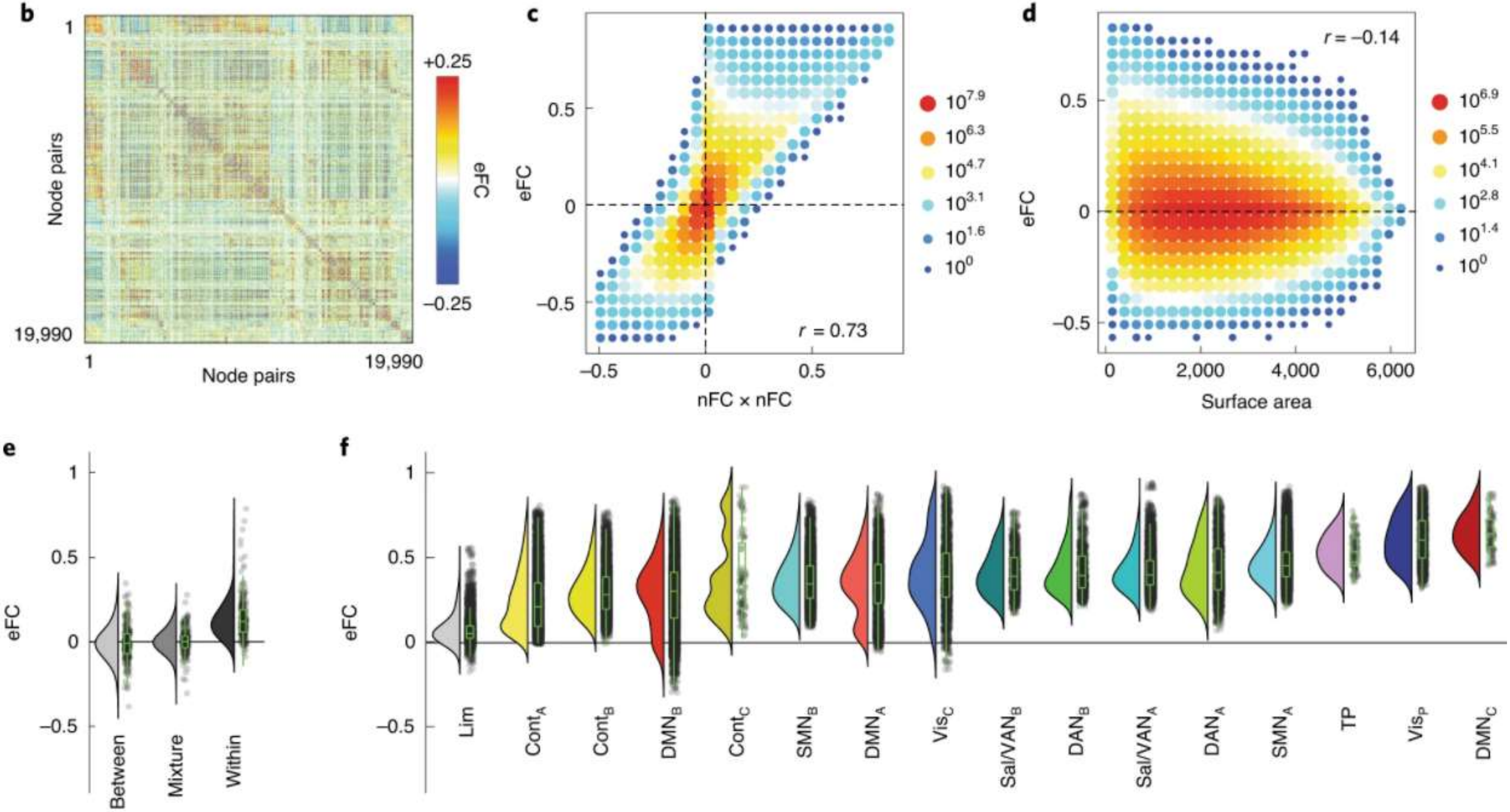
Overview

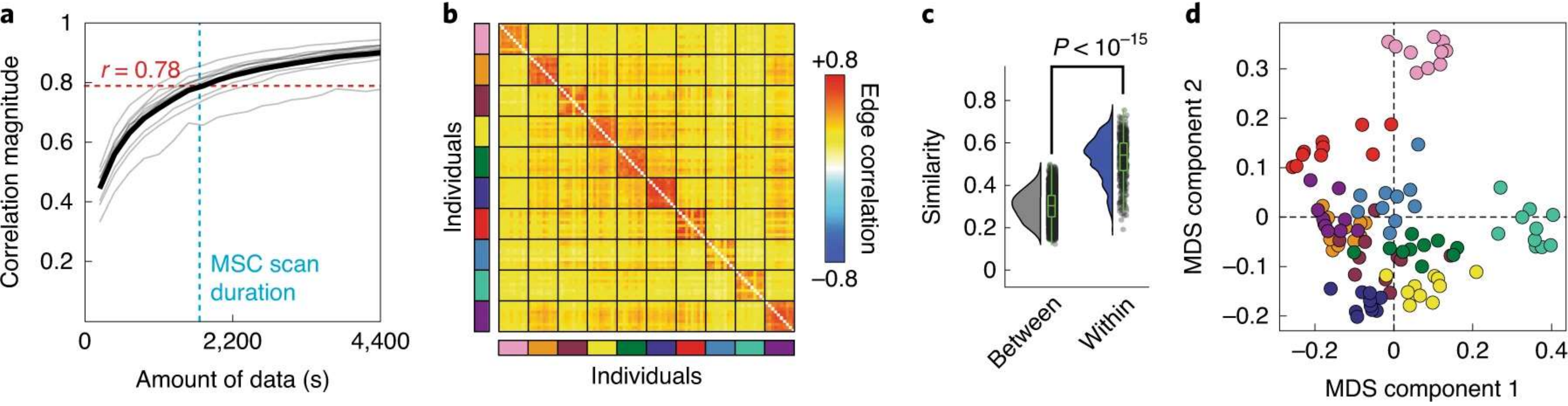
- Network neuroscience has relied on a **node-centric network model** in which cells, populations and regions are linked to one another via anatomical or functional connections. This model cannot account for interactions of edges with one another.
- This study introduces an **edge-centric network model** that generates constructs '**edge time series**' and '**edge functional connectivity**' (eFC).
- Using network analysis, this study shows that, at rest, eFC is **consistent** across datasets and **reproducible** within the same individual over multiple scan sessions.
- Clustering eFC yields **communities of edges** that naturally divide the brain into overlapping clusters, with regions in **sensorimotor** and **attentional** networks exhibiting the **greatest levels of overlap**.
- Demonstrate that eFC is systematically **modulated** by variation in **sensory input**. In future work, the edge-centric approach could be useful for identifying novel biomarkers of disease, characterizing individual variation and mapping the architecture of highly resolved neural circuits.


a
Region i
Region j
BOLD signal
Time (s)
b
Node pair ij
Co-fluctuation amplitude
Time (s)
c
Region v
Region j
Region i
Region u
Regions
−0.5
+0.5
nFC
d
Region u
Region v
BOLD signal
Time (s)
e
Node pair uv
Co-fluctuation amplitude
Time (s)
f
Node pair uv
Node pair ij
Node pairs
19,900
−0.5
+0.5
eFC

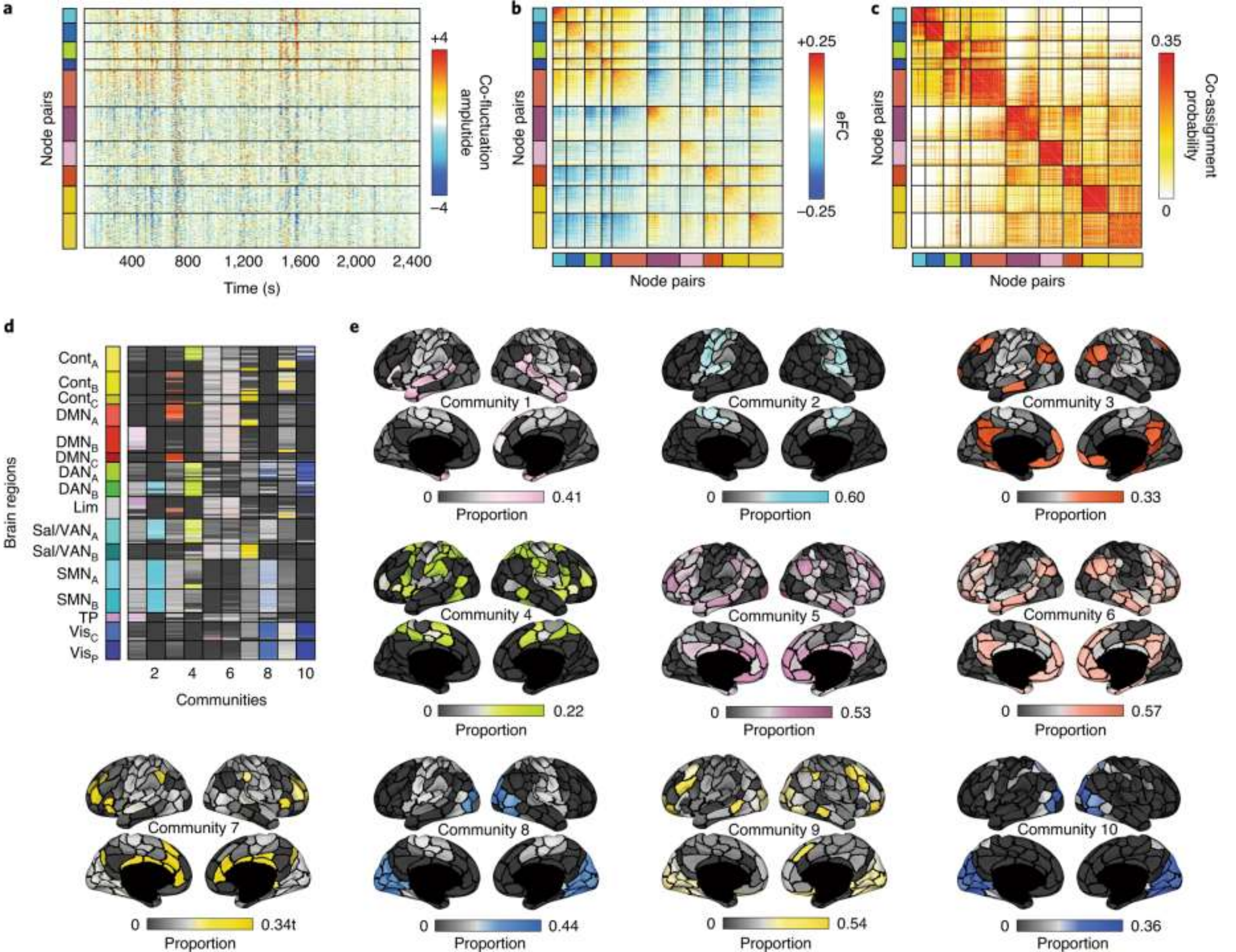
Stability of eFC across datasets

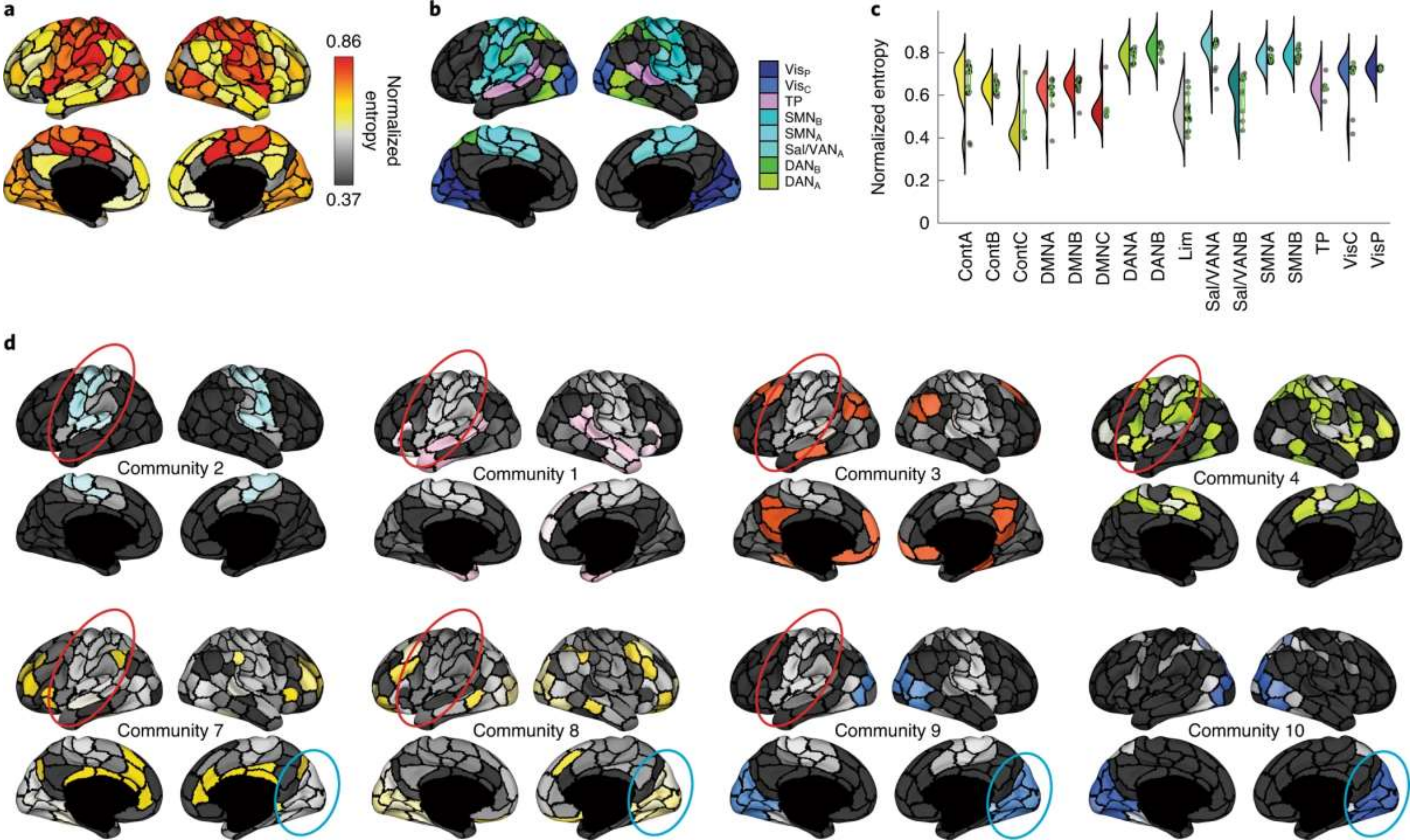



b
Node pairs
1
19,990
+0.25
−0.25
eFC
c
eFC
nFC × nFC
r = 0.73
$10^{7.9}$
$10^{6.3}$
$10^{4.7}$
$10^{3.1}$
$10^{1.6}$
10^{0}
d
eFC
Surface area
r = −0.14
$10^{6.9}$
$10^{5.5}$
$10^{4.1}$
$10^{2.8}$
$10^{1.4}$
10^{0}
e
eFC
Between
Mixture
Within
f
eFC
Lim
$Cont_A$
$Cont_B$
DMN_B
$Cont_C$
SMN_B
DMN_A
Vis_C
Sal/VAN_B
DAN_B
Sal/VAN_A
DAN_A
SMN_A
TP
Vis_P
DMN_C

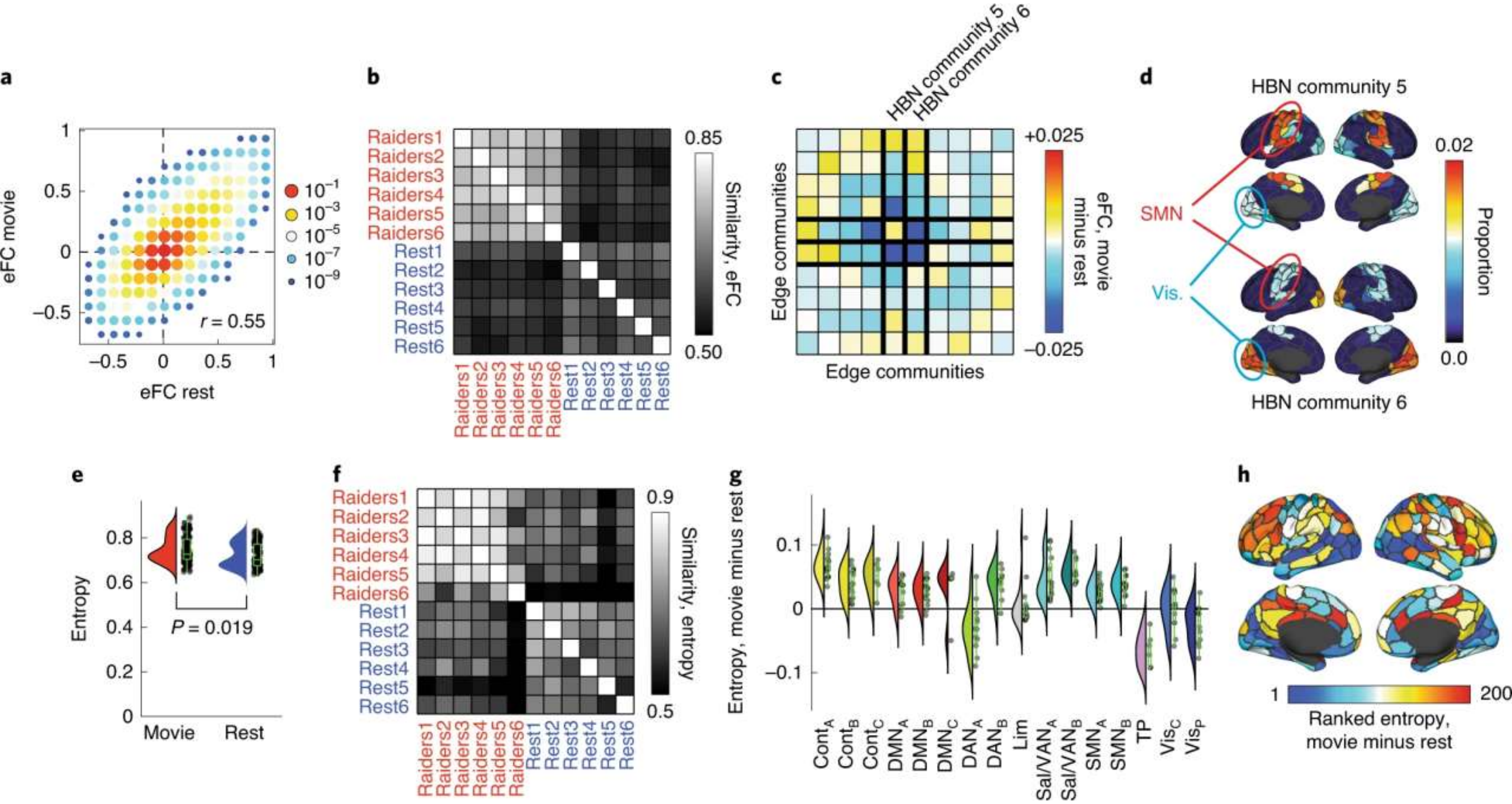


a
Correlation magnitude
1
0.8
0.6
0.4
0.2
r = 0.78
MSC scan duration
0
2,200
4,400
Amount of data (s)
b
Individuals
+0.8
Edge correlation
–0.8
Individuals
c
P < 10^−15
Similarity
0.8
0.6
0.4
0.2
0
Between
Within
d
MDS component 2
0.3
0.2
0.1
0
–0.1
–0.2
–0.2
0
0.2
0.4
MDS component 1


a
Node pairs
+4
−4
Co-fluctuation amplitude
400
800
1,200
1,600
2,000
2,400
Time (s)
b
Node pairs
+0.25
eFC
−0.25
Node pairs
c
Node pairs
0.35
Co-assignment probability
0
Node pairs
d
Cont$_A$
Cont$_B$
Cont$_C$
DMN$_A$
DMN$_B$
DMN$_C$
DAN$_A$
DAN$_B$
Lim
Sal/VAN$_A$
Sal/VAN$_B$
SMN$_A$
SMN$_B$
TP
Vis$_C$
Vis$_P$
Brain regions
2
4
6
8
10
Communities
e
Community 1
0
0.41
Proportion
Community 2
0
0.60
Proportion
Community 3
0
0.33
Proportion
Community 4
0
0.22
Proportion
Community 5
0
0.53
Proportion
Community 6
0
0.57
Proportion
Community 7
0
0.34t
Proportion
Community 8
0
0.44
Proportion
Community 9
0
0.54
Proportion
Community 10
0
0.36
Proportion



a
0.86
Normalized entropy
0.37
b
Vis_P
Vis_C
TP
SMN_B
SMN_A
Sal/VAN_A
DAN_B
DAN_A
c
Normalized entropy
0
0.2
0.4
0.6
0.8
ContA
ContB
ContC
DMNA
DMNB
DMNC
DANA
DANB
Lim
Sal/VANA
Sal/VANB
SMNA
SMNB
TP
VisC
VisP
d
Community 2
Community 1
Community 3
Community 4
Community 7
Community 8
Community 9
Community 10



a
eFC movie
eFC rest
r = 0.55
10^-1
10^-3
10^-5
10^-7
10^-9
b
Raiders1
Raiders2
Raiders3
Raiders4
Raiders5
Raiders6
Rest1
Rest2
Rest3
Rest4
Rest5
Rest6
Similarity, eFC
0.85
0.50
c
HBN community 5
HBN community 6
Edge communities
Edge communities
eFC, movie minus rest
+0.025
−0.025
d
HBN community 5
HBN community 6
SMN
Vis.
Proportion
0.02
0.0
e
Entropy
Movie
Rest
P = 0.019
f
Similarity, entropy
0.9
0.5
g
Entropy, movie minus rest
Cont_A
Cont_B
Cont_C
DMN_A
DMN_B
DMN_C
DAN_A
DAN_B
Lim
Sal/VAN_A
Sal/VAN_B
SMN_A
SMN_B
TP
Vis_C
Vis_P
h
Ranked entropy, movie minus rest
1
200

Key Results (selected quotes from article)

- "Here we presented a network model of human cerebral cortex that focused on edge–edge interactions.
- The network formed by these interactions—a construct we referred to as eFC—was similar across datasets and more similar within individuals than between them.
- When clustered, eFC provided a natural estimate of pervasively overlapping community structure.
- We found that the amount of overlap varied across the cortex but peaked in sensorimotor and attention networks.
- We found that brain regions associated with sensorimotor and attention networks participated in disproportionately many communities compared to other brain systems, but that, relative to one another, those same regions participated in similar sets of communities.
- Lastly, we showed that eFC and community overlap varied systematically during passive viewing of movies."

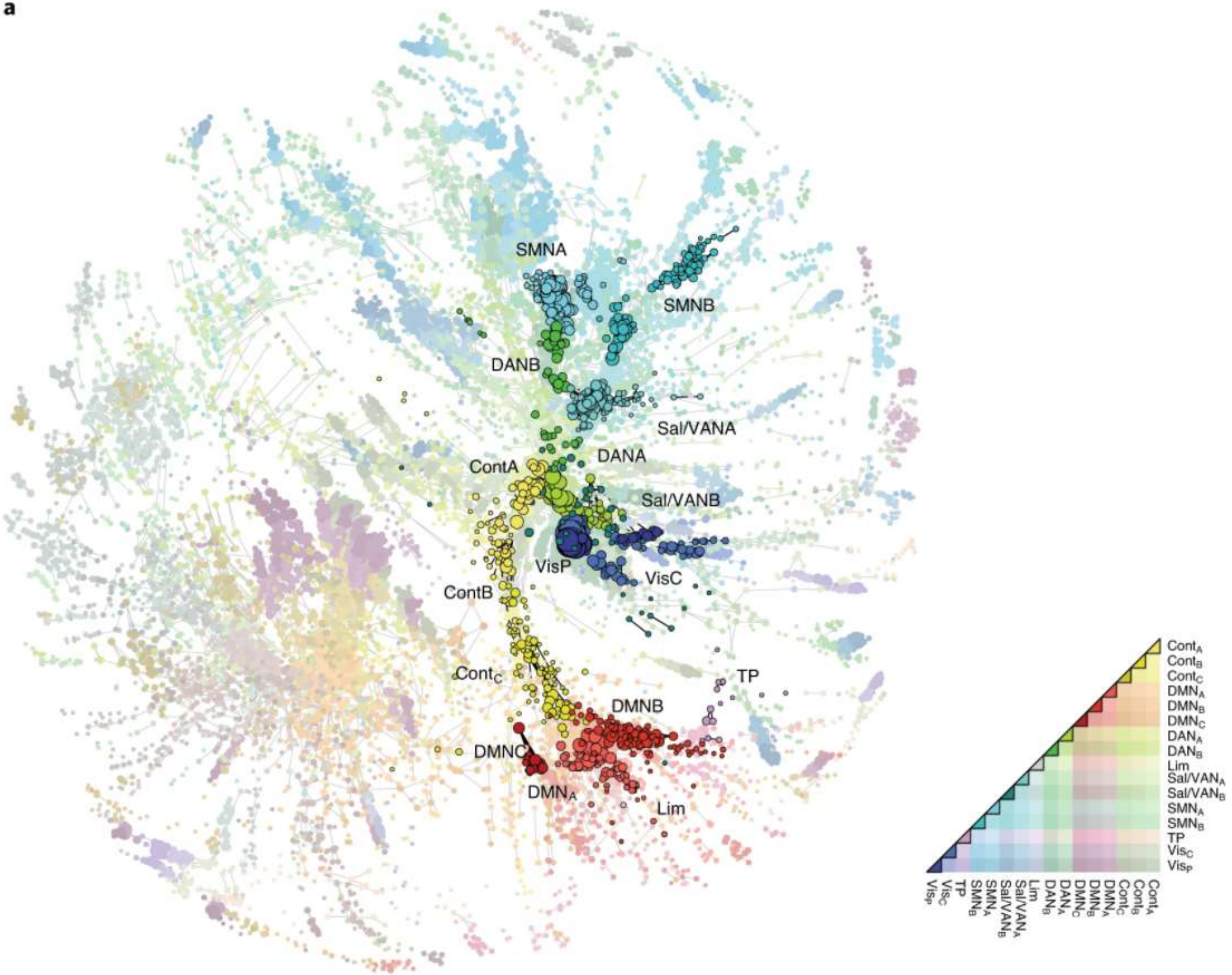
Conclusions (quotes from article)

- "In this study, we developed a novel **edge-centric representation** of functional neuroimaging data that operates directly on observed time series.
- Our method for estimating connection weights between edges can be viewed as a **temporal 'unwrapping' of the familiar Pearson correlation**—the measure frequently used to estimate the magnitude of nFC between pairs of brain regions.
- Whereas the Pearson correlation coefficient calculates the time-averaged co-fluctuation magnitude for node pairs, we simply omit the averaging step, yielding **'edge time series',** which represent the **co-fluctuation magnitude** between two nodes at every instant in time.
- This simple step enables us to track fluctuations in edge weight across time and, critically, allow for **dyadic relationships between edges**, creating an edge-centric representation of nervous system architecture.
- If we interpret edge time series as a temporal unwrapping of nFC, which is thought to reflect the aggregate effect of communication processes between neural elements, then edge times series track, with high temporal resolution, the communication patterns between distributed neural elements."

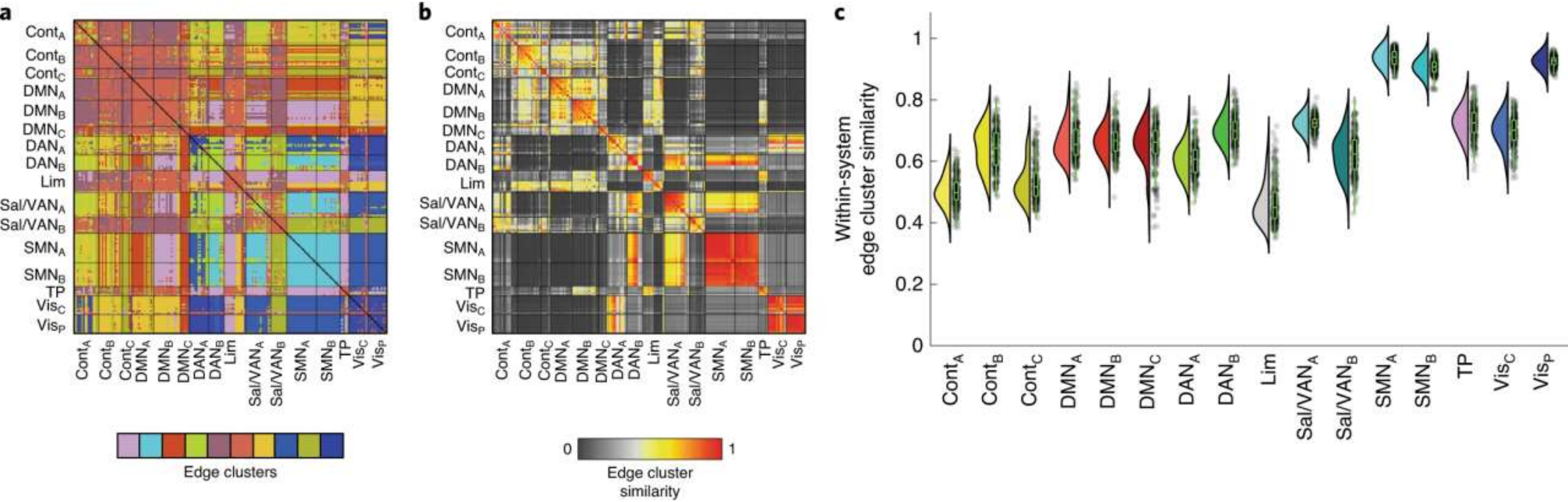
Future Directions

- eFC might be useful in applications of machine learning and classification of neuroimaging data
- Essentially, eFC time series offer a moment-to-moment assessment of how strongly two nodes (brain regions) co-fluctuate with one another, providing an estimate of **time-varying nFC without the requirement that we specify a window**.
- This overcomes one of the main limitations of sliding window estimates of time-varying nFC, namely that the use of a window leads to a ‘blurring’ of events across time

a



SMNA
SMNB
DANB
Sal/VANA
DANA
ContA
Sal/VANB
VisP
VisC
ContB
ContC
TP
DMNB
DMNC
DMNA
Lim
ContA
ContB
ContC
DMNA
DMNB
DMNC
DANA
DANB
Lim
Sal/VANA
Sal/VANB
SMNA
SMNB
TP
VisC
VisP


a
b
c
Cont_A
Cont_B
Cont_C
DMN_A
DMN_B
DMN_C
DAN_A
DAN_B
Lim
Sal/VAN_A
Sal/VAN_B
SMN_A
SMN_B
TP
Vis_C
Vis_P
Edge clusters
0
1
Edge cluster similarity
Within-system edge cluster similarity
0
0.2
0.4
0.6
0.8
1