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Estimating the impact of structural directionality:

How reliable are undirected connectomes?

NETWORK NEURO SCIENCE

Leonardo L. Gollo (Penelope Kale)

Citations	2019	1728
h-index	20	18

Computational & theoretical neuroscience

University of Queensland, Australia

Andrew Zalesky

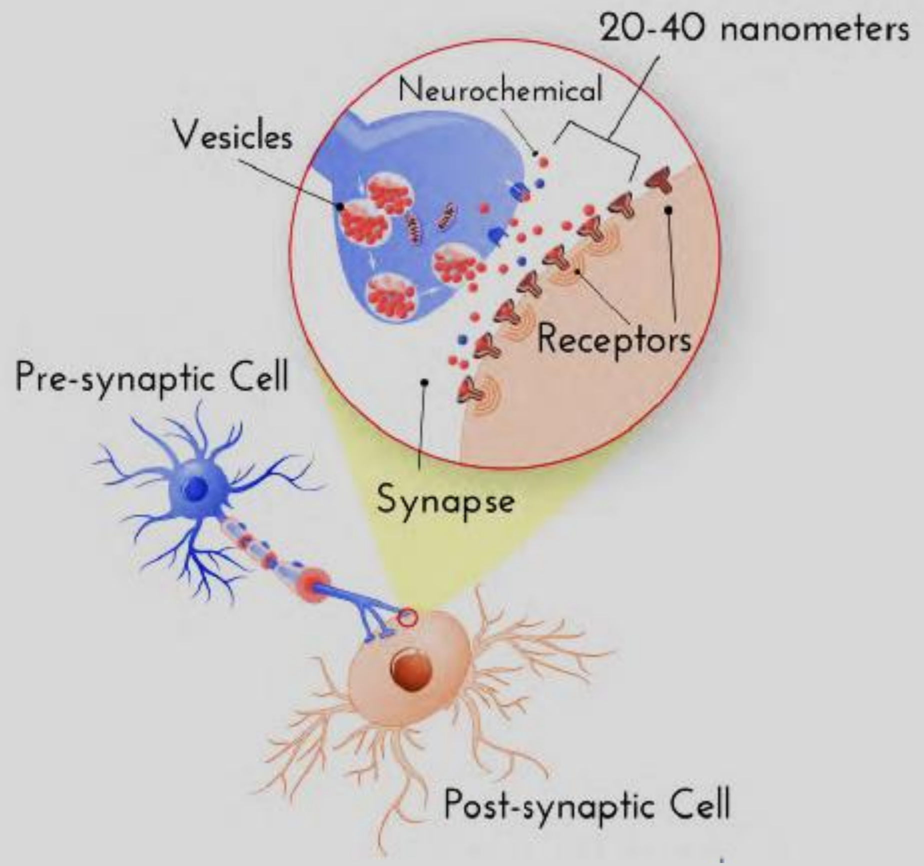
Citaties	13168	10646
h-index	51	46

Neuroimaging

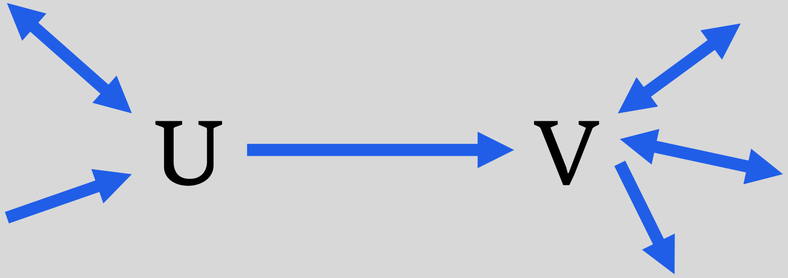
University of Melbourne, Australia

2018 Jun 1

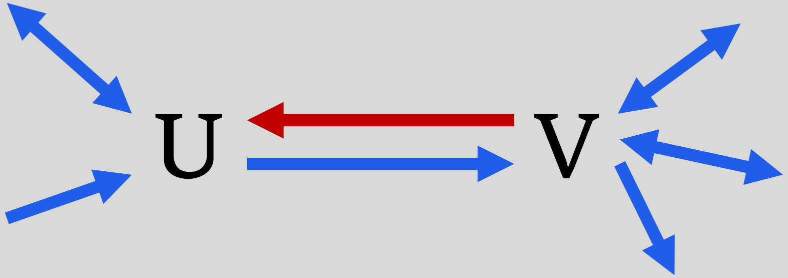
OUTLINE


20-40 nanometers
Neurochemical
Vesicles
Receptors
Pre-synaptic Cell
Synapse
Post-synaptic Cell

Directed connectomes

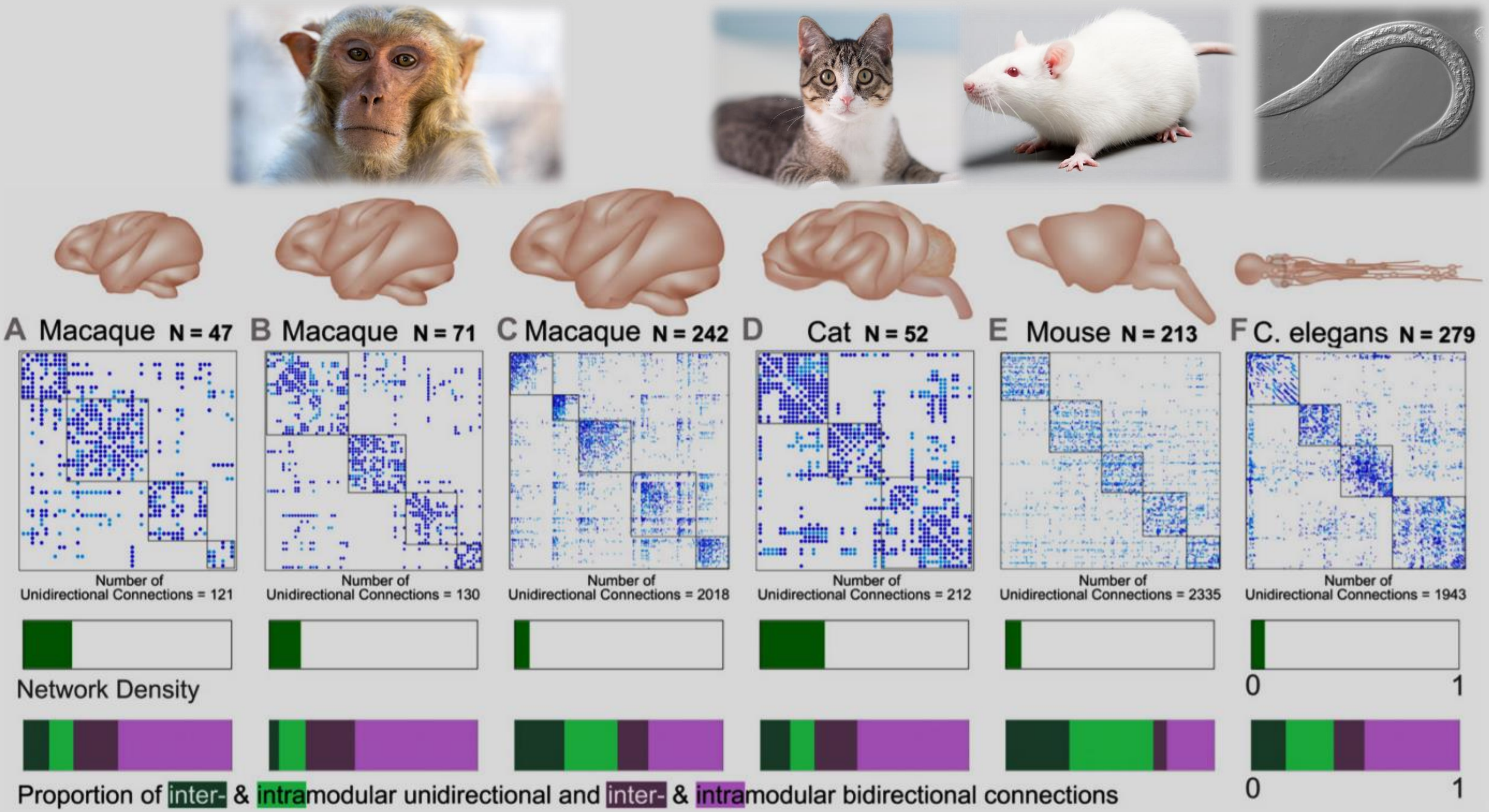


Bidirectional connection

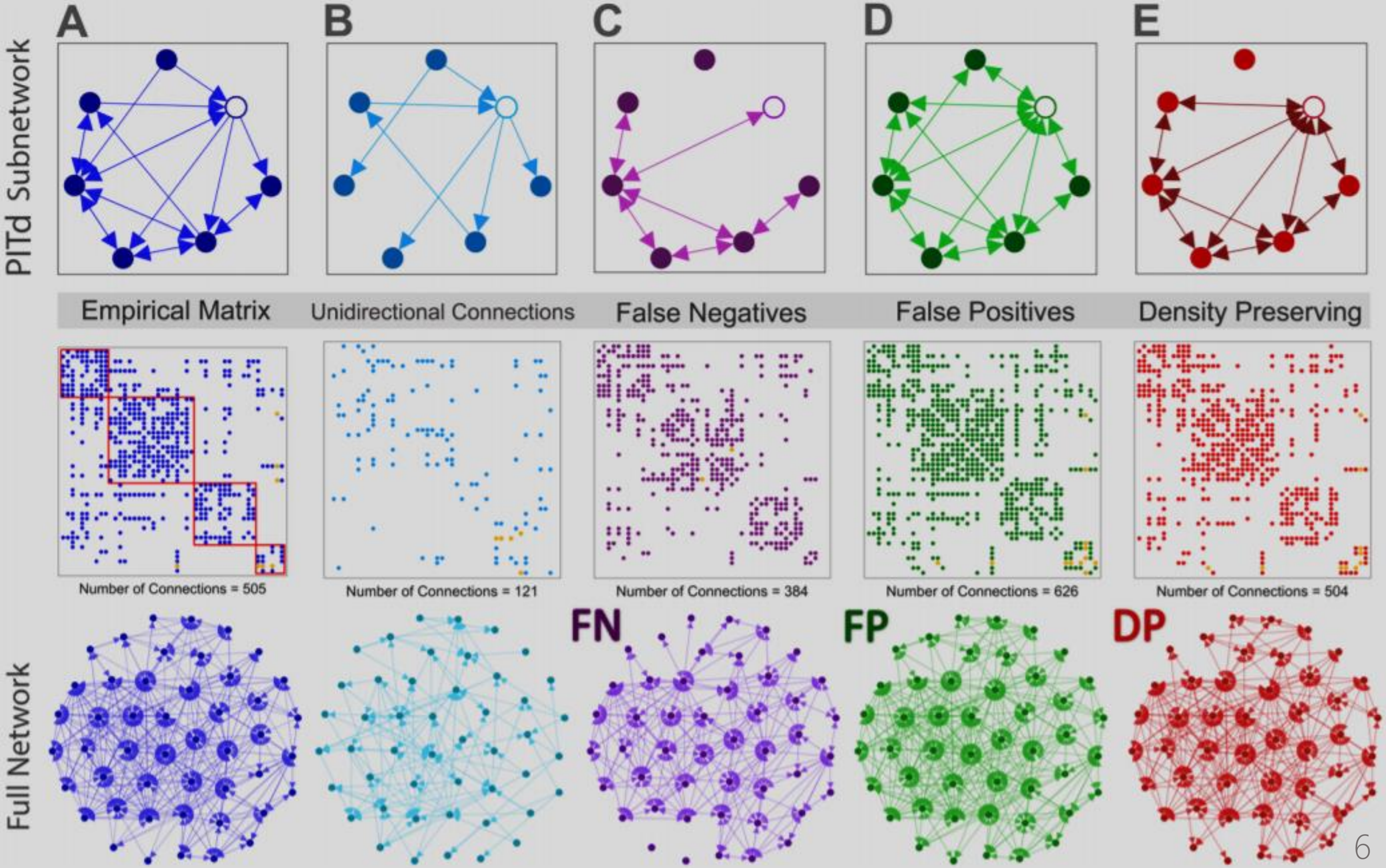


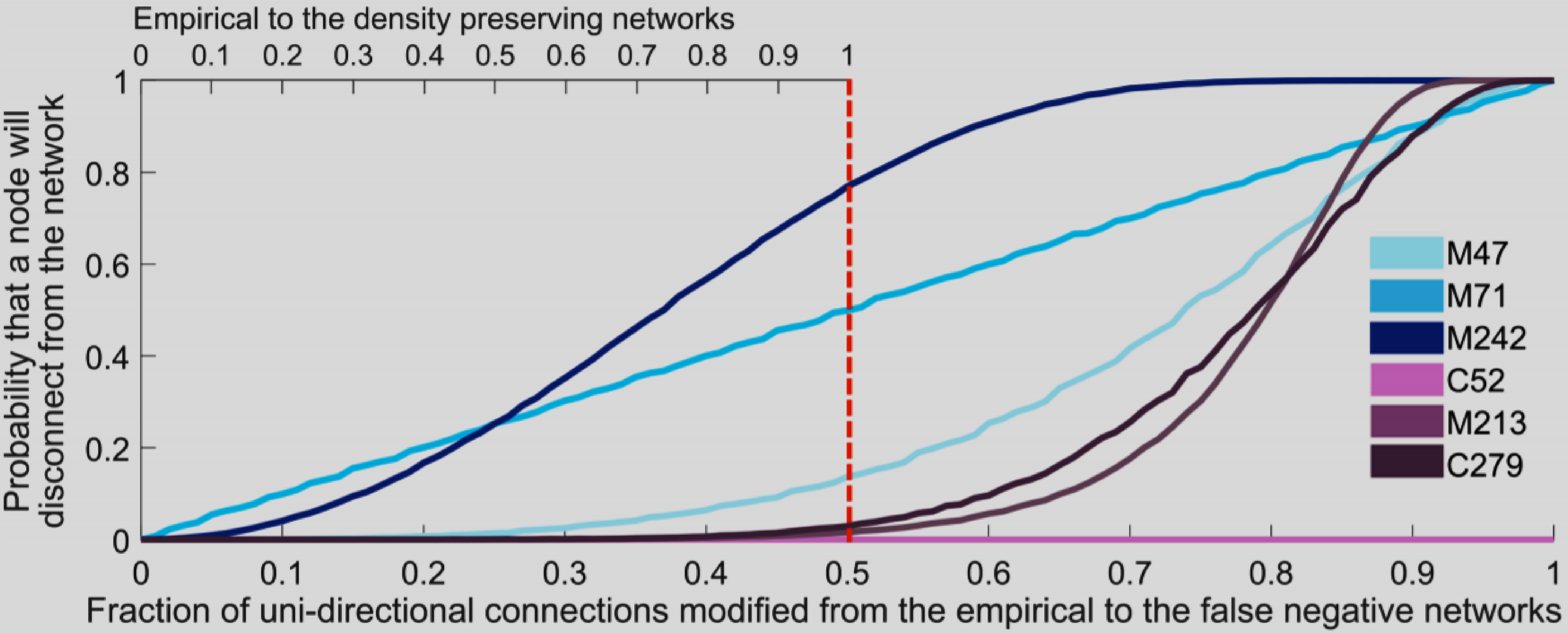
False positive connection

False negative connection



A Macaque N = 47
B Macaque N = 71
C Macaque N = 242
D Cat N = 52
E Mouse N = 213
F C. elegans N = 279
Number of Unidirectional Connections = 121
Number of Unidirectional Connections = 130
Number of Unidirectional Connections = 2018
Number of Unidirectional Connections = 212
Number of Unidirectional Connections = 2335
Number of Unidirectional Connections = 1943
Network Density
0
1
0
1
Proportion of inter- & intramodular unidirectional and inter- & intramodular bidirectional connections


A
B
C
D
E
PITd Subnetwork
Empirical Matrix
Unidirectional Connections
False Negatives
False Positives
Density Preserving
Number of Connections = 505
Number of Connections = 121
Number of Connections = 384
Number of Connections = 626
Number of Connections = 504
FN
FP
DP
Full Network

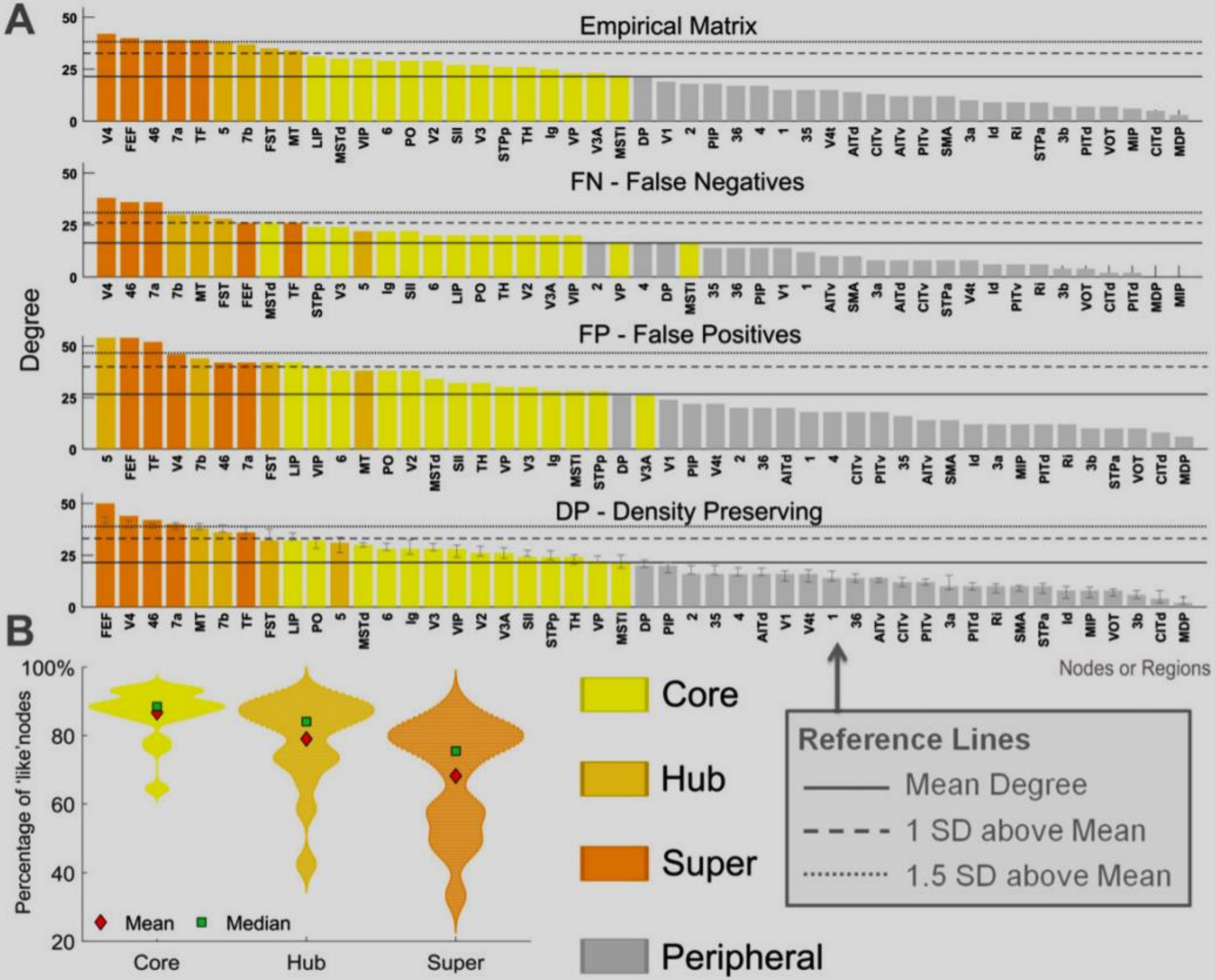

Empirical to the density preserving networks
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Probability that a node will disconnect from the network
1 0.8 0.6 0.4 0.2 0
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
Fraction of uni-directional connections modified from the empirical to the false negative networks
M47
M71
M242
C52
M213
C279

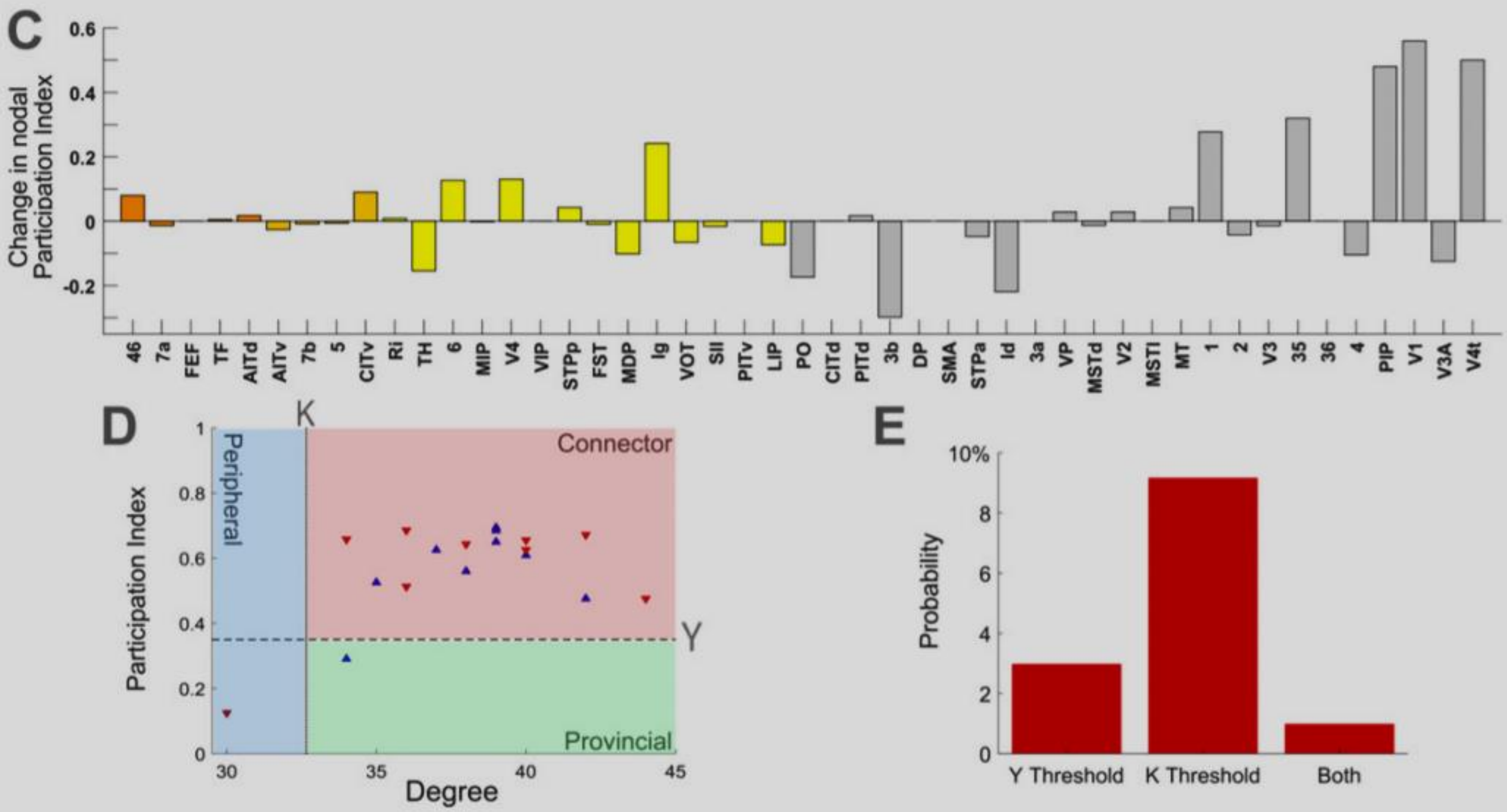
Network Measures

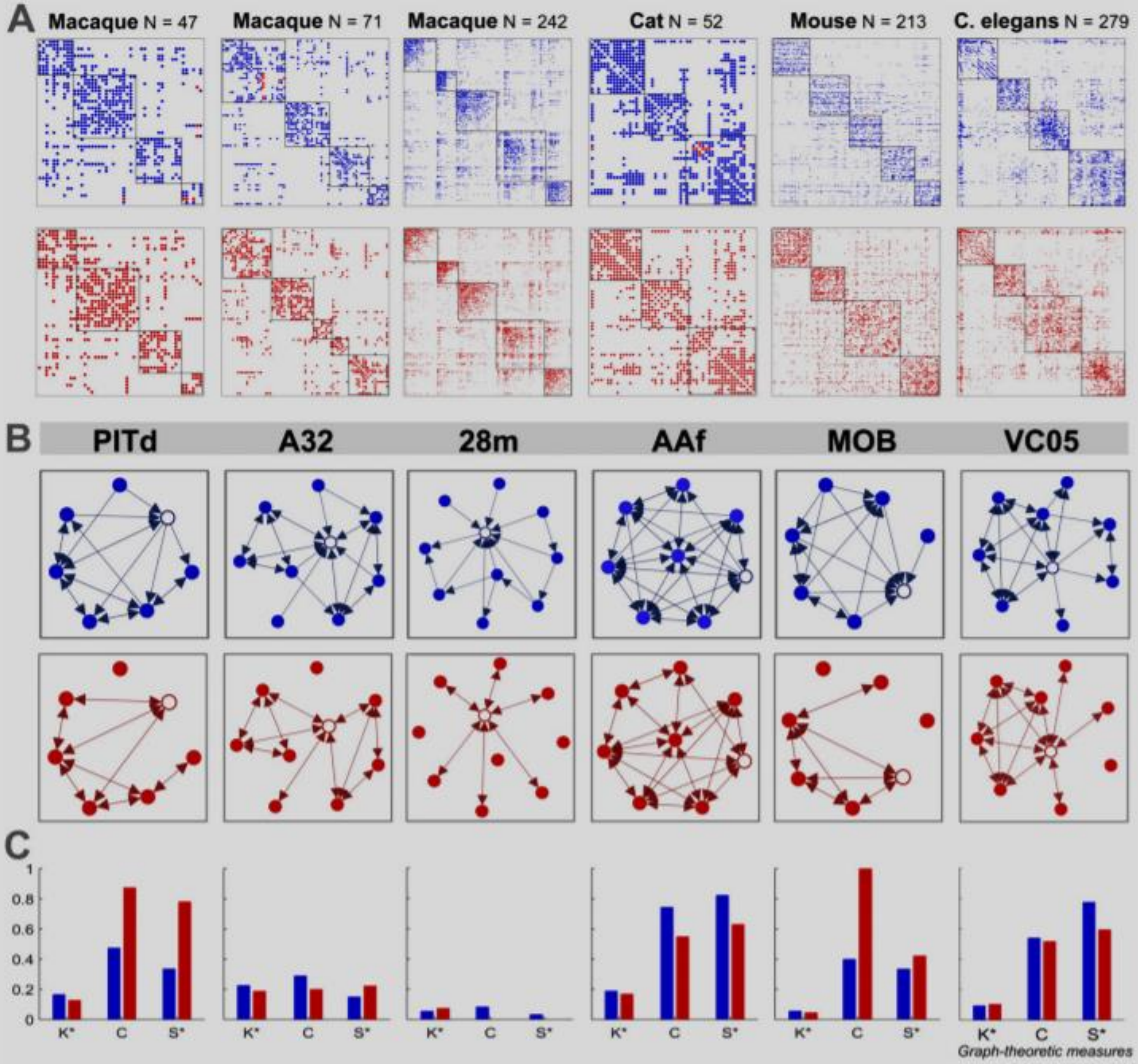
- Degree
- Betweenness Centrality
- Number of Triangles
- Clustering Coefficient
- Shortest Path Length
- Characteristic Path Length
- Global Efficiency
- Participation Index
- Small Worldness

Graph-theoretic Measure	Formula	
Degree (Rubinov and Sporns, 2010)	K_i = degree of node *i* (sum of directed in- and out-degree)	(both) $K_i = \sum_{j \in N} a_{ij}$ $K_i^{in} = \sum_{j \in N} a_{ji}\ K_i^{out} = \sum_{j \in N} a_{ij}$
Betweenness Centrality (Freeman, 1978)	B_i = betweenness centrality of node *i*, $B_{hj}(i)$ = number of shortest paths between *h* & *j* passing through *i*, B_{hj} = number of shortest paths between *h* & *j*	$B_i = \frac{1}{(n-1)(n-2)} \sum_{\substack{h,j \in N \\ h \neq j, h \neq i, j \neq i}} \frac{B_{hj}(i)}{B_{hj}}$
Number of Triangles (Rubinov and Sporns, 2010)	$t_i^{\rightarrow}$ = number of triangles around node *i* $t_i^{\rightarrow} = \frac{1}{2} \sum_{j,h \in N} (a_{ij} + a_{ji})(a_{ih} + a_{hi})(a_{jh} + a_{hj})$	
Clustering Coefficient (Fagiolo, 2007)	$C_i^{\rightarrow}$ = clustering coefficient of node *i* $C_i^{\rightarrow} = \frac{1}{n} \sum_{i \in N} \frac{t_i^{\rightarrow}}{(K_i^{out} + K_i^{in})(K_i^{out} + K_i^{in} - 1) - 2 \sum_{i \in N} a_{ij} a_{ji}}$ $C^{\rightarrow}$ = mean clustering coefficient of the network $C^{\rightarrow} = \sum_{i=1}^{N} \frac{C_i^{\rightarrow}}{N}$	

Shortest Path Length (Rubinov and Sporns, 2010)	$d_{ij}^{\rightarrow}$ = shortest path length between nodes *i* & *j*, where $g_{i\rightarrow j}$ is the shortest path between *i* & *j*	$d_{ij}^{\rightarrow} = \sum_{a_{ij} \in g_{i\rightarrow j}} a_{ij}$
Characteristic Path Length (Watts and Strogatz, 1998)	$L^{\rightarrow}$ = average distance between all nodes	$L^{\rightarrow} = \frac{1}{n} \sum_{i \in N} \frac{\sum_{j \in N, j \neq i} d_{ij}^{\rightarrow}}{n-1}$
Global Efficiency (Latora and Marchiori, 2001)	$G^{\rightarrow}$ = global efficiency of the network	$G^{\rightarrow} = \frac{1}{n} \sum_{i \in N} \frac{\sum_{j \in N, j \neq i} (d_{ij}^{\rightarrow})^{-1}}{n-1}$
Participation Index (Guimera and Amaral, 2005)	Y_i^{out}=out-participation index, M= set of modules, $K_i^{out}(m)$ = number of out-connections between *i* & all nodes in module *m*	$Y_i^{out} = 1 - \sum_{m \in M} \left(\frac{K_i^{out}(m)}{K_i^{out}} \right)^2$
Small Worldness (Humphries and Gurney, 2008)	$S_i^{\rightarrow}$ = small worldness of node *i* $S^{\rightarrow}$ = small world index of network $C_i{}^{\rightarrow}{}_{rand}$ = clustering of a random network, $L_{rand}^{\rightarrow}$ = path length of a random network	$S_i^{\rightarrow} = \frac{C_i^{\rightarrow} / C_{i\,rand}^{\rightarrow}}{L^{\rightarrow} / L_{rand}^{\rightarrow}}$ $S^{\rightarrow} = \frac{C^{\rightarrow} / C_{rand}^{\rightarrow}}{L^{\rightarrow} / L_{rand}^{\rightarrow}}$


A
Empirical Matrix
V4 FEF 46 7a TF 5 7b FST MT LIP MSTd VIP 6 PO V2 SII V3 STPp TH Ig VP V3A MSTl DP V1 2 PIP 36 4 1 35 V4t AITd CITv AITv PITv SMA 3a Id Ri STPa 3b PITd VOT MIP CITd MDP
FN - False Negatives
V4 46 7a 7b MT FST FEF MSTd TF STPp V3 5 Ig SII 6 LIP PO TH V2 V3A VIP 2 VP 4 DP MSTl 35 36 PIP V1 1 AITv SMA 3a AITd CITv STPa V4t Id PITv Ri 3b VOT CITd PITd MDP MIP
FP - False Positives
5 FEF TF V4 7b 46 7a FST LIP VIP 6 MT PO V2 MSTd SII TH VP V3 Ig MSTl STPp DP V3A V1 PIP V4t 2 36 AITd 1 4 CITv PITv 35 AITv SMA Id 3a MIP PITd Ri 3b STPa VOT CITd MDP
DP - Density Preserving
FEF V4 46 7a MT 7b TF FST LIP PO 5 MSTd 6 Ig V3 VIP V2 V3A SII STPp TH VP MSTl DP PIP 2 35 4 AITd V1 V4t 1 36 AITv CITv PITv 3a PITd Ri SMA STPa Id MIP VOT 3b CITd MDP
Degree
0
25
50
Nodes or Regions
B
Percentage of 'like' nodes
100%
80
60
40
20
Mean
Median
Core
Hub
Super
Core
Hub
Super
Peripheral
Reference Lines
Mean Degree
1 SD above Mean
1.5 SD above Mean


C
Change in nodal Participation Index
0.6
0.4
0.2
0
-0.2
46
7a
FEF
TF
AITd
AITv
7b
5
CITv
Ri
TH
6
MIP
V4
VIP
STPp
FST
MDP
Ig
VOT
SII
PITv
LIP
PO
CITd
PITd
3b
DP
SMA
STPa
Id
3a
VP
MSTd
V2
MSTl
MT
1
2
V3
35
36
4
PIP
V1
V3A
V4t
D
K
Y
Peripheral
Connector
Provincial
Participation Index
Degree
E
10%
Probability
Y Threshold
K Threshold
Both



A
Macaque N = 47
Macaque N = 71
Macaque N = 242
Cat N = 52
Mouse N = 213
C. elegans N = 279
B
PITd
A32
28m
AAf
MOB
VC05
C
1
0.8
0.6
0.4
0.2
0
K*
C
S*
Graph-theoretic measures

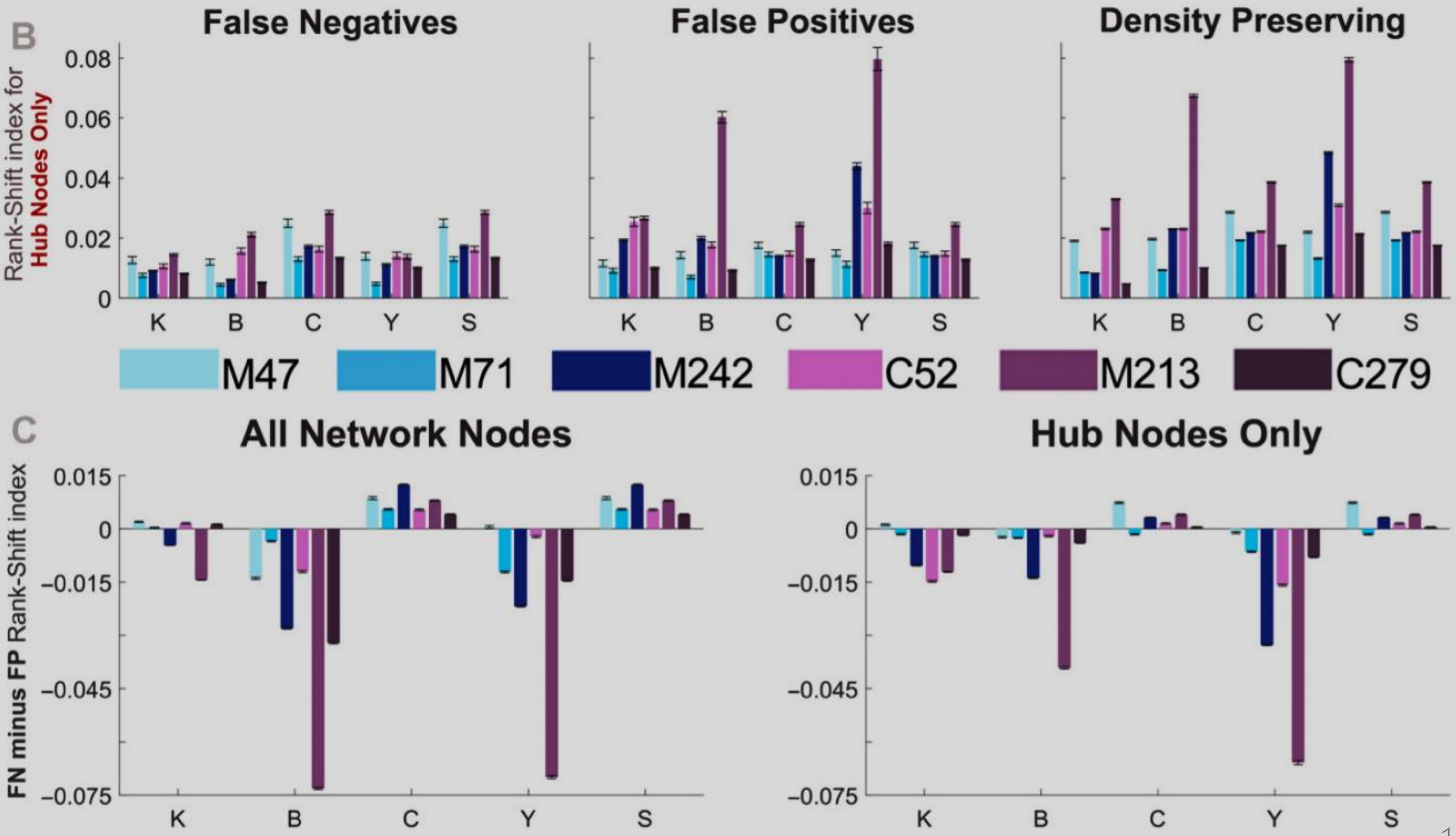
Rank-shift index (RSI)

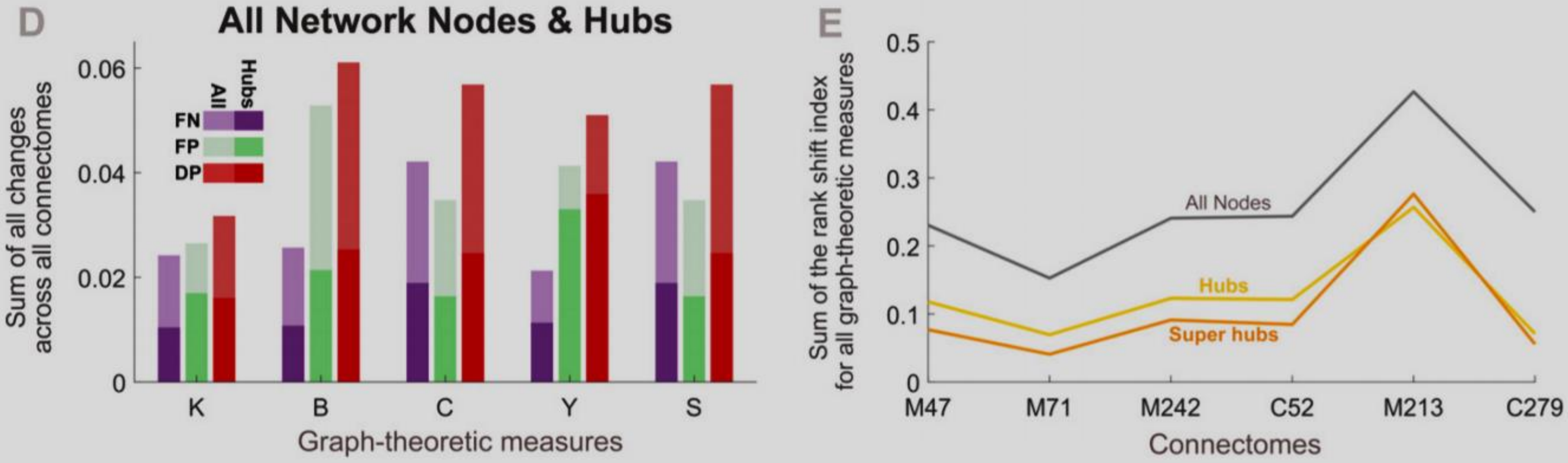
ranking of the empirical (E) for each node

ranking of the perturbed (B) for each node

$$RSI = \sum_{i=1}^{N} \frac{|E_i - B_i|}{D}.$$

the maximum possible difference (D) in which the ranks of the network are reversed


B
False Negatives
False Positives
Density Preserving
Rank-Shift index for Hub Nodes Only
0.08
0.06
0.04
0.02
0
K B C Y S
M47
M71
M242
C52
M213
C279
C
All Network Nodes
Hub Nodes Only
FN minus FP Rank-Shift index
0.015
0
−0.015
−0.045
−0.075


D
All Network Nodes & Hubs
Sum of all changes
across all connectomes
0.06
0.04
0.02
0
All
Hubs
FN
FP
DP
K
B
C
Y
S
Graph-theoretic measures
E
Sum of the rank shift index
for all graph-theoretic measures
0.5
0.4
0.3
0.2
0.1
0
All Nodes
Hubs
Super hubs
M47
M71
M242
C52
M213
C279
Connectomes


Leonardo L. Gollo
I am a Senior Research Fellow with training in Physics and Neuroscience. I design simple computational and mathematical models aiming to understand how the brain works.
Michael Breakspear
I am Group Leader of the Systems Neuroscience Group at Hunter Medical Research Institute.