Decoding Connectomes: Insights From The Network Theory

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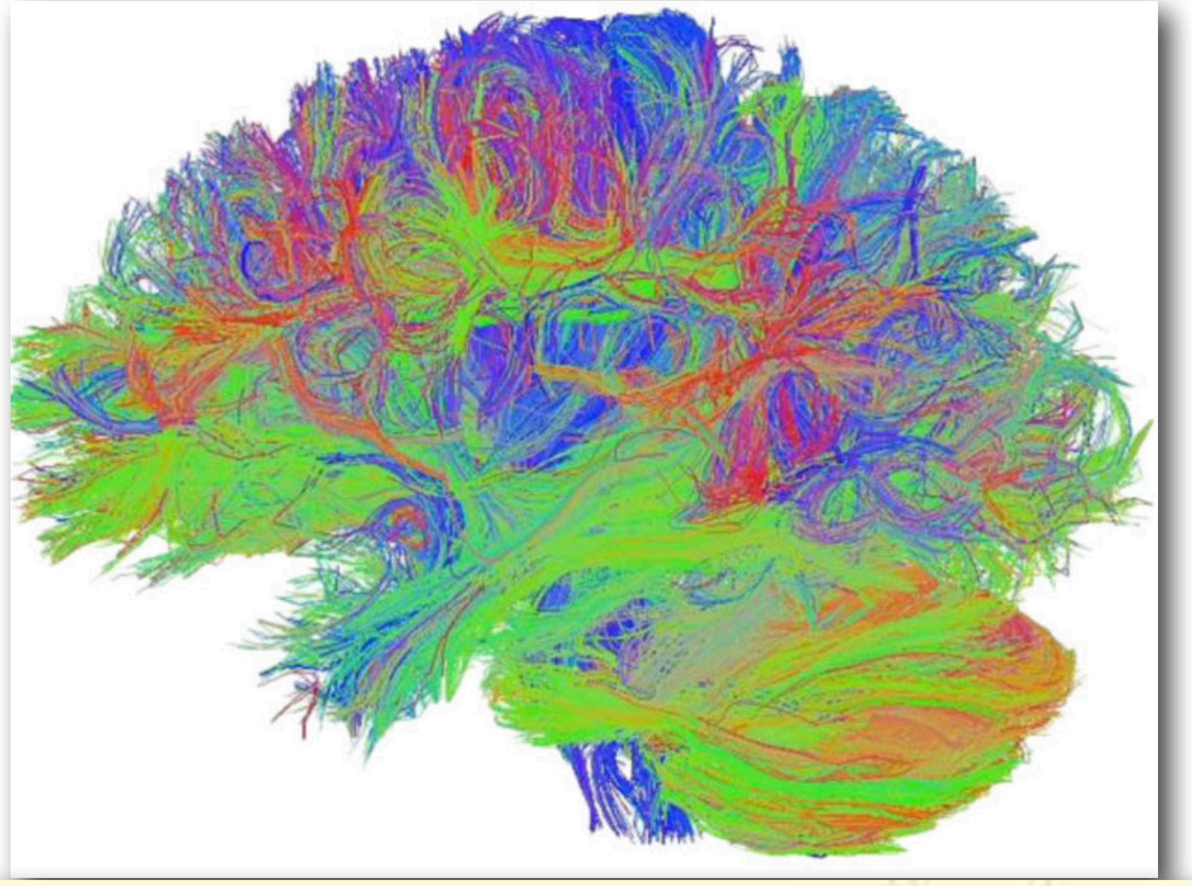
20th December 2024

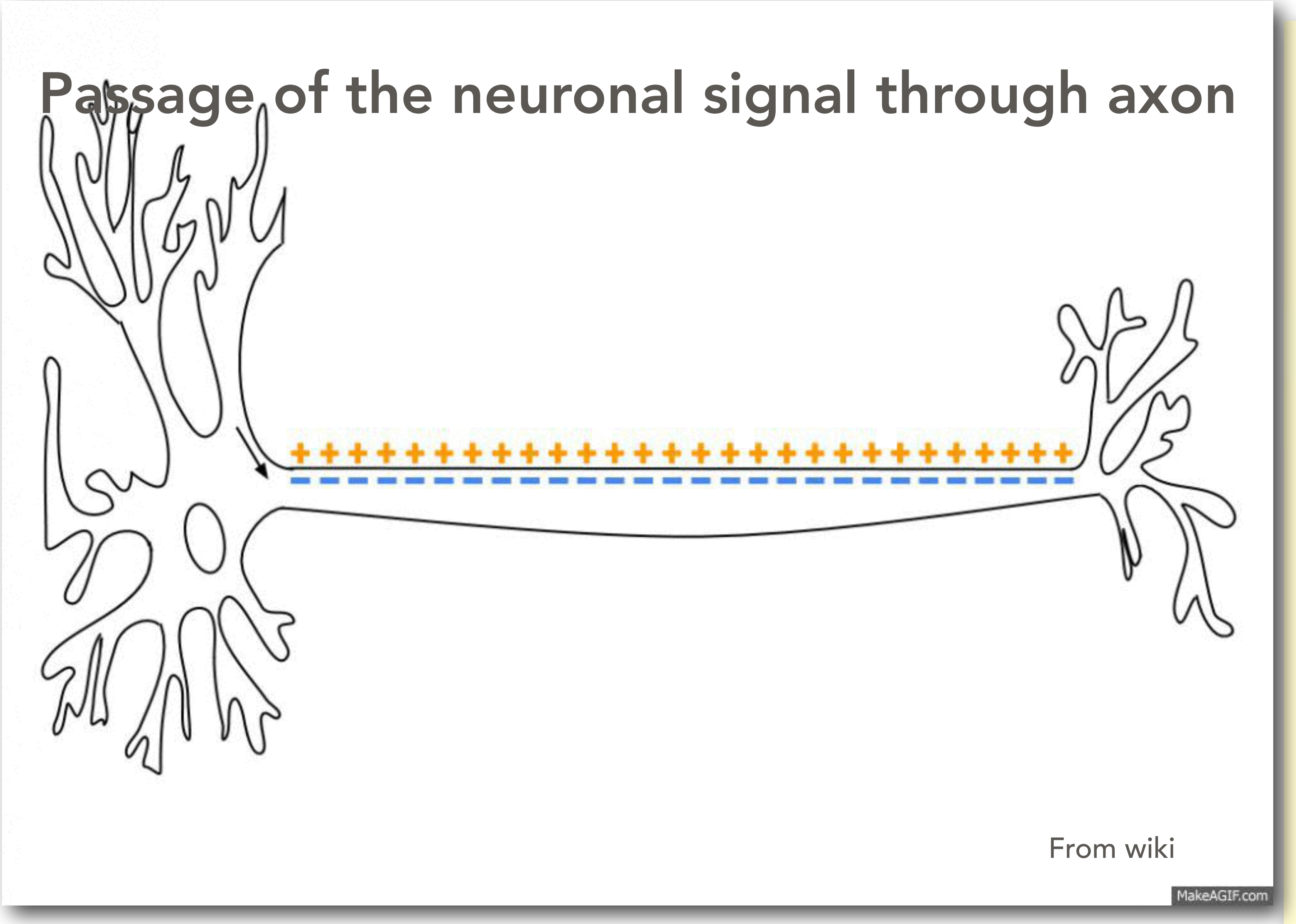
What is Connectome?

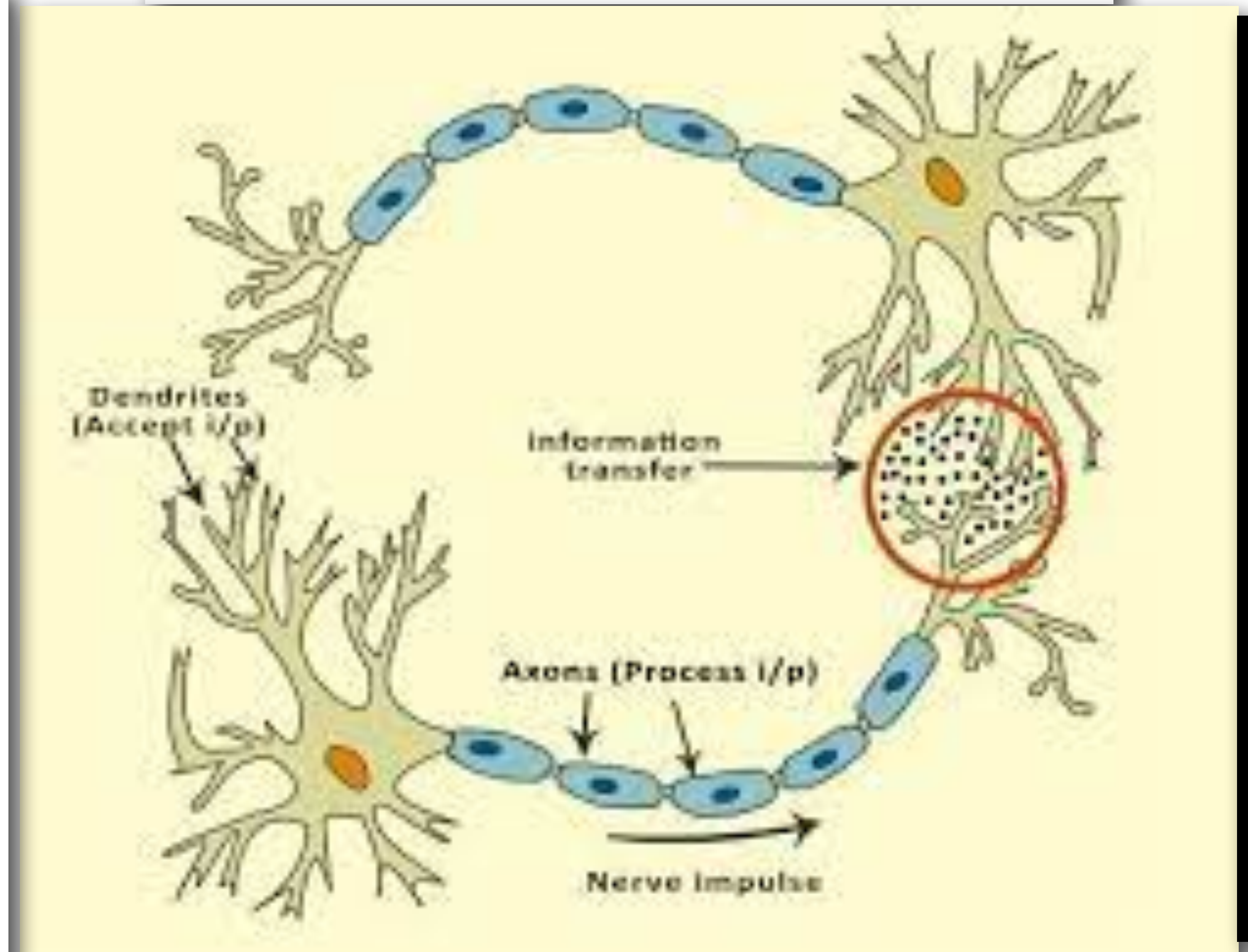
Connectome is a map of the nerve-cell connections in the Brain



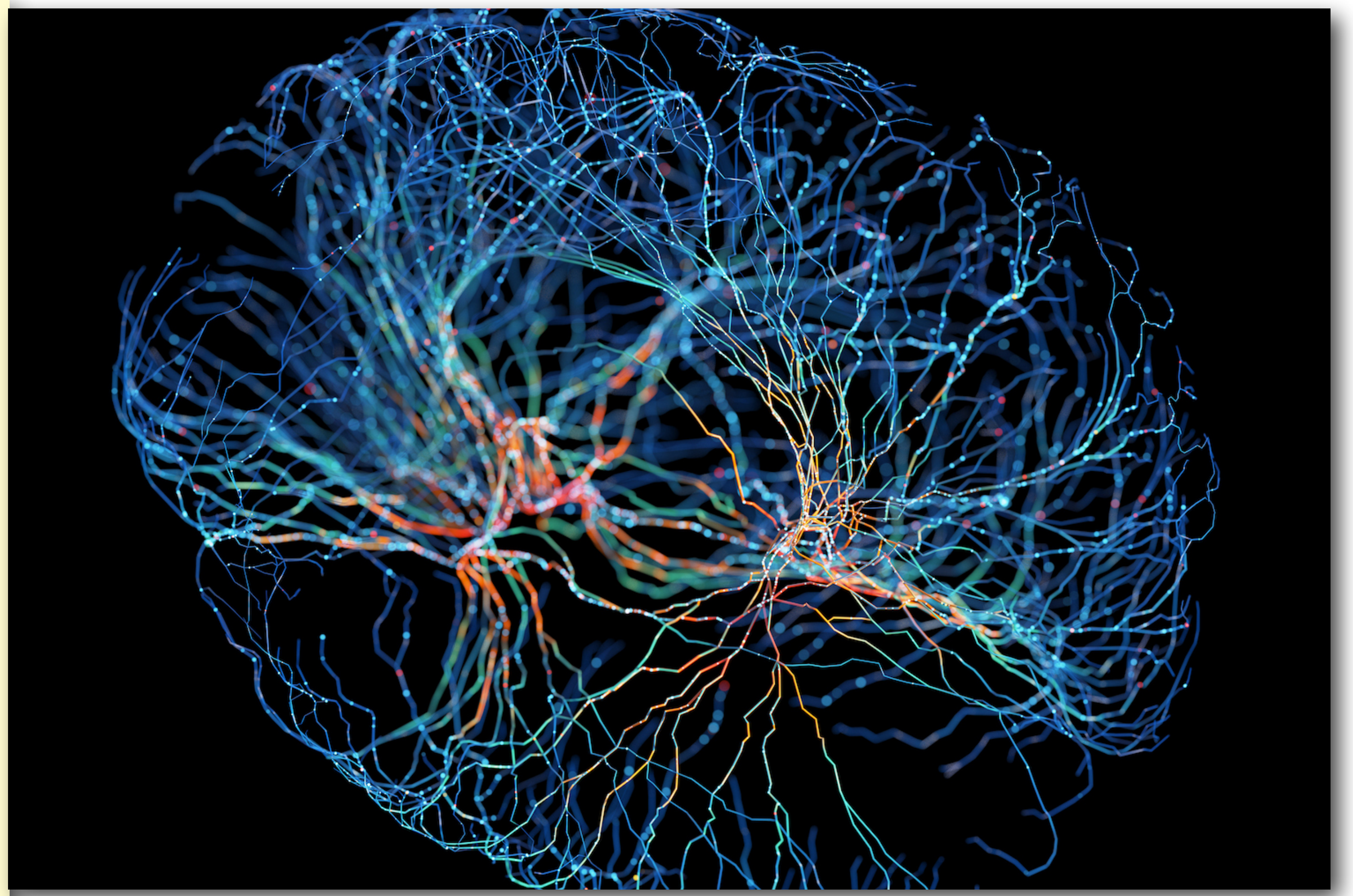
Brain Network

(https://www.genengnews.com/topics/translational-medicine/brain-network-mapping-study-challenges-basis-for-psychiatric-distinctions/





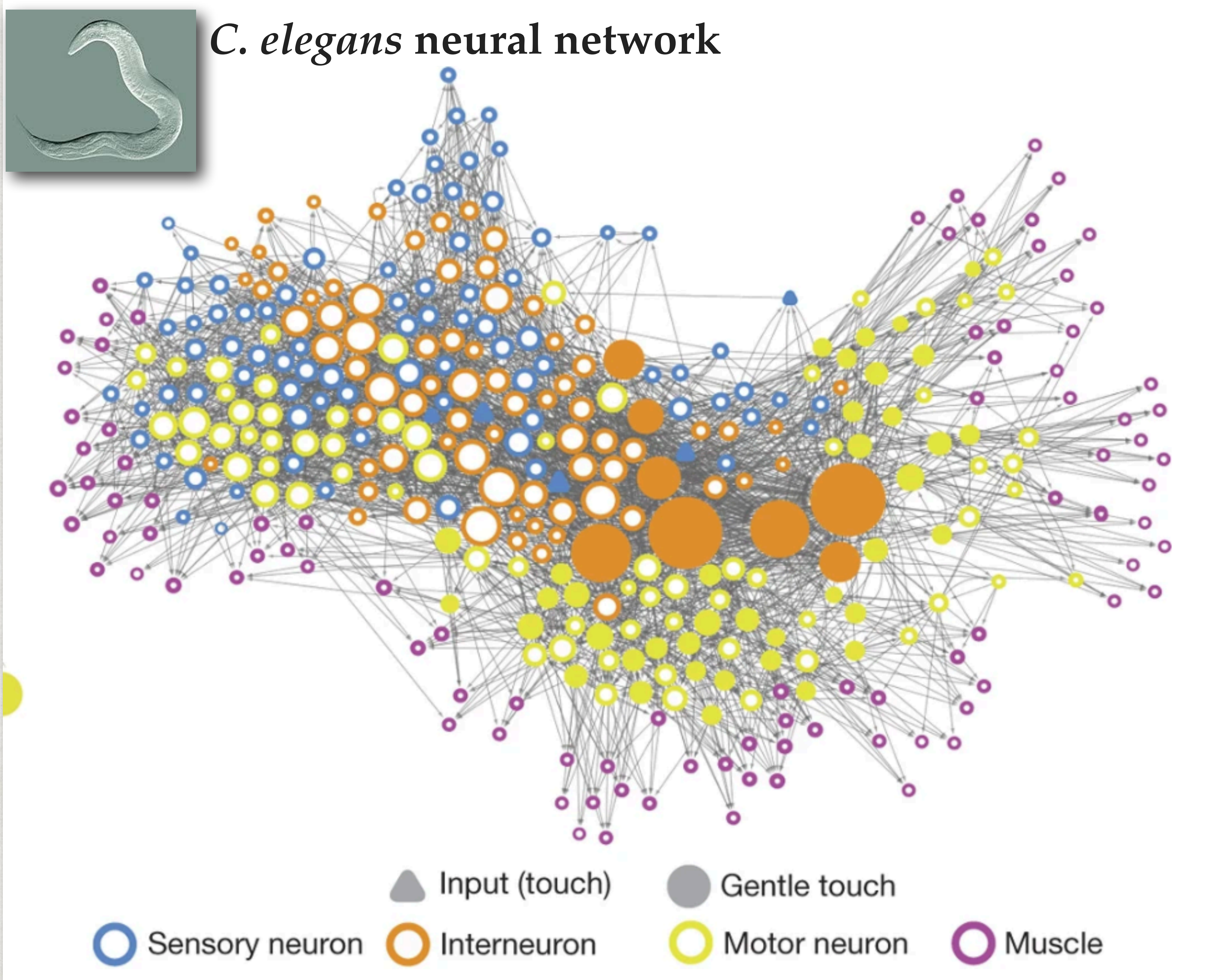
Communication between the cells



https://www.google.com/imgres?q=network%20of%20neurons&imgurl=https%3A%2F%2Fdata-flair.training%2Fblogs%2Fwp-content%2Fuploads%2Fsites%2F2%2F2018%2F01%2Fimage-2.png&imgrefurl=https%3A%2F%2Fdata-flair.training%2Fblogs%2Fartificial-neural-network%2F&docid=PGbbtfFtsrWlCM&tbnid=58b-lPSFSlWmgM&vet=12ahUKEwiuuKeR1auKAxXa1jgGHQyFCDQQM3oECEkQAA..i&w=652&h=531&hcb=2&ved=2ahUKEwiuuKeR1auKAxXa1jgGHQyFCDQQM3oECEkQAA

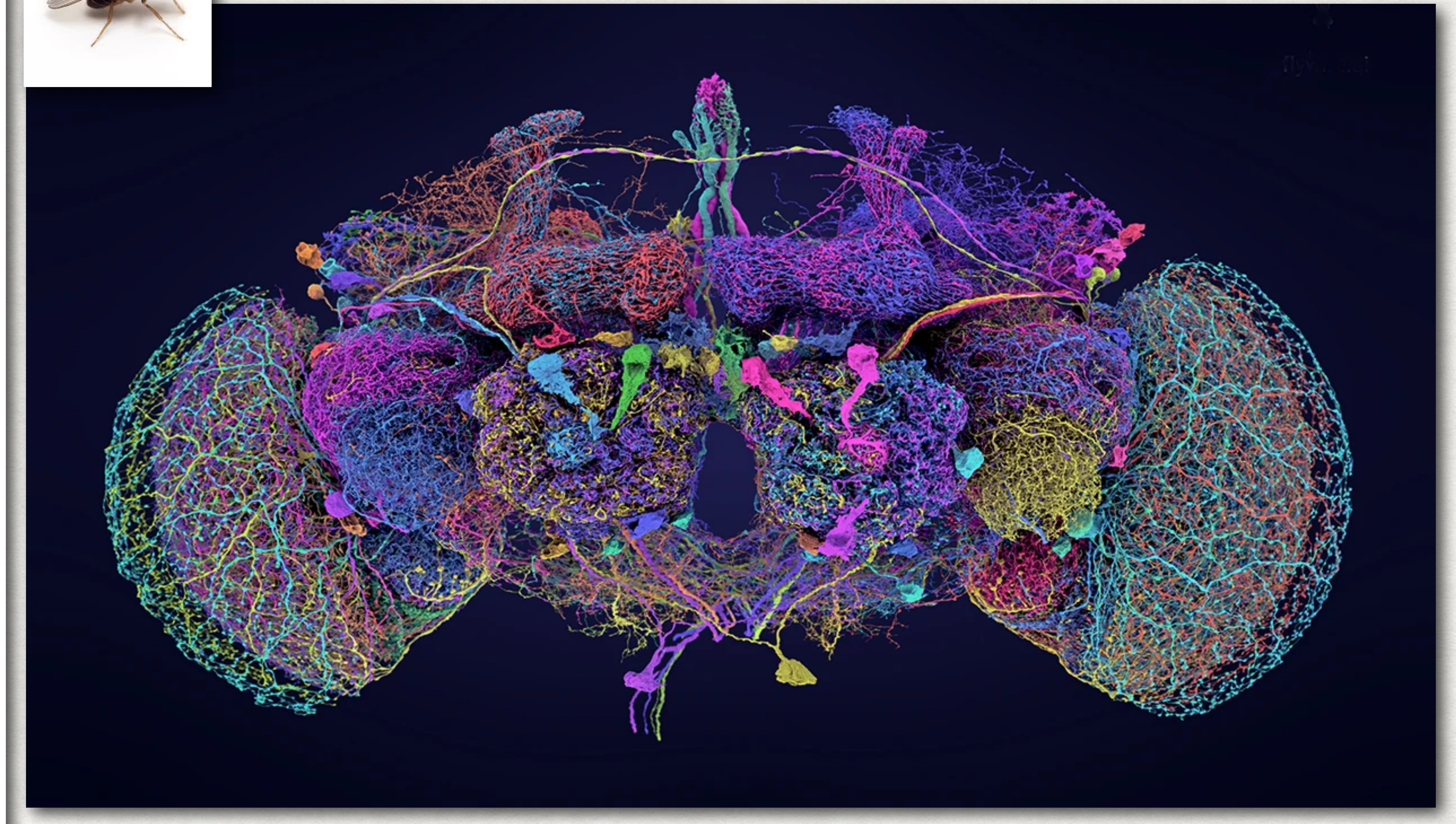
Fundamentals of Brain Network Analysis Edited by: Alex Fornito, Andrew Zalesky and Edward T. Bullmore

COMPLETE CELL-LEVEL CONNECTOMES



G. Yan, *et al.* Network control principles predict neuron function in the Caenorhabditis elegans connectome, Nature 2017

fruit-fly brain

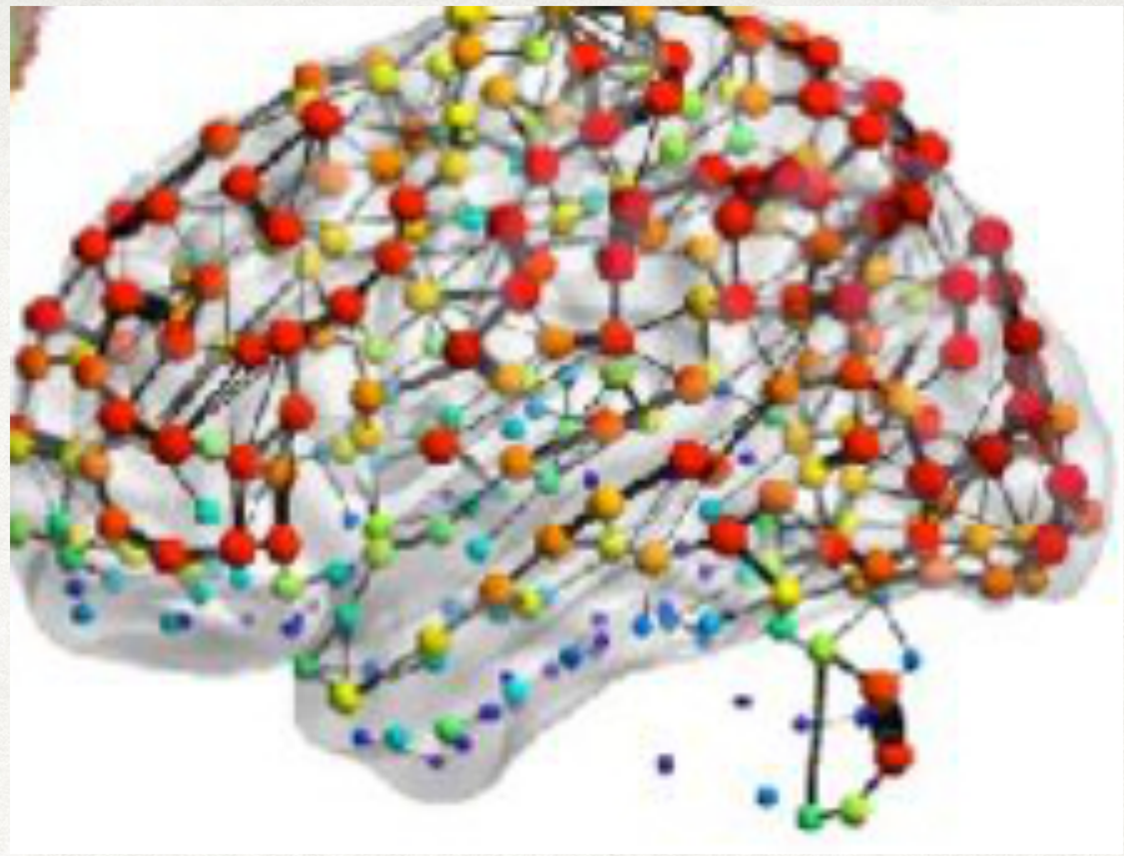


140,000 neurons in the fruit-fly brain

https://www.science.org/content/article/complete-map-fruit-fly-brain-circuitry-unveiled

Brain networks

- Human Brain: 86 billion neurons

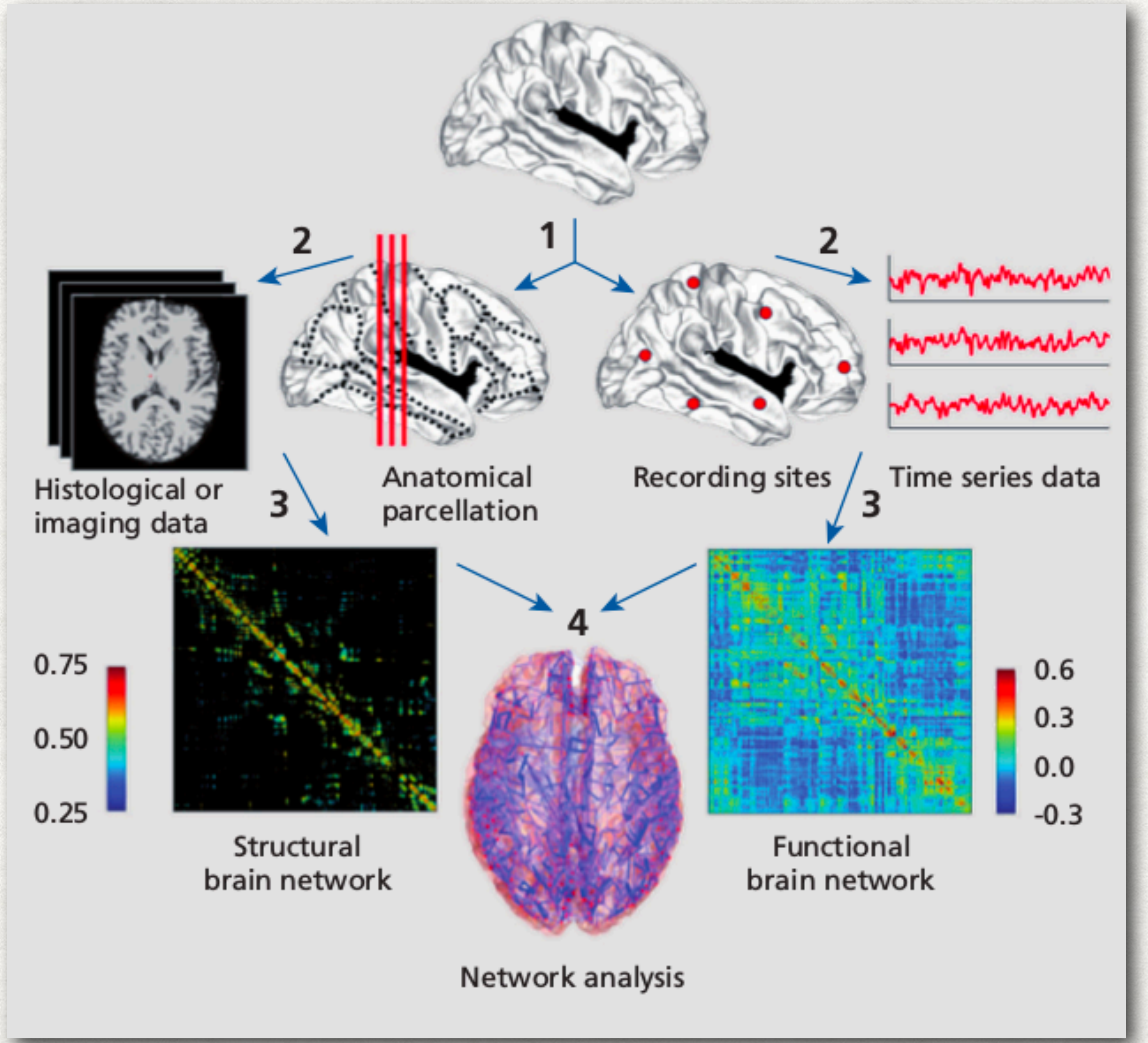


doi: https://doi.org/10.1101/743245

Fig. Brain network

1 Structural Connectome

Nodes: Different Brain Regions
Connections: Density of the white matter tracts between these regions
Method: Parcellation of the brain volume (left in the figure) or DTI



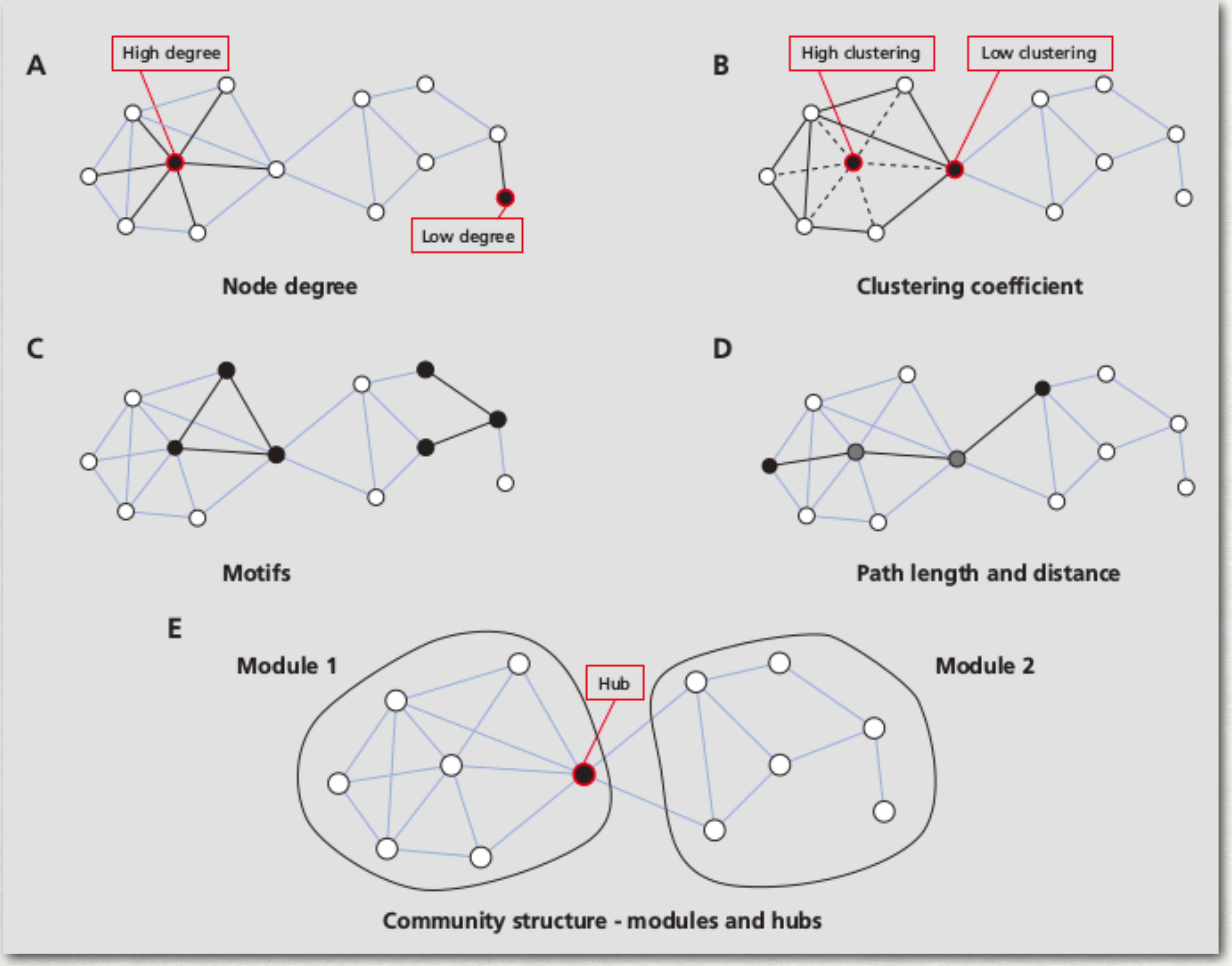
Olaf Sporns, Dialogues in Clinical Neuroscience - Vol 15 . No. 3 . 2013

2 Functional Connectome

Nodes: Different Brain Regions
Connections: Functional coherence between the brain regions
Method: On the basis of time series obtained from the sensors and/or recording sites (right), EEG/MEG

Pre-processing involves, applying the bandpass filter with a desired cutoff frequencies and then removing the artifacts using infomax Independent Component Analysis (ICA)

DECODING THE BRAIN: A NETWORK THEORY APPROACH



Olaf Sporns, Dialogues in Clinical Neuroscience - Vol 15 . No. 3 . 2013

1 **SEGREGATION**
CLUSTERING, MOTIFS, MODULARITY

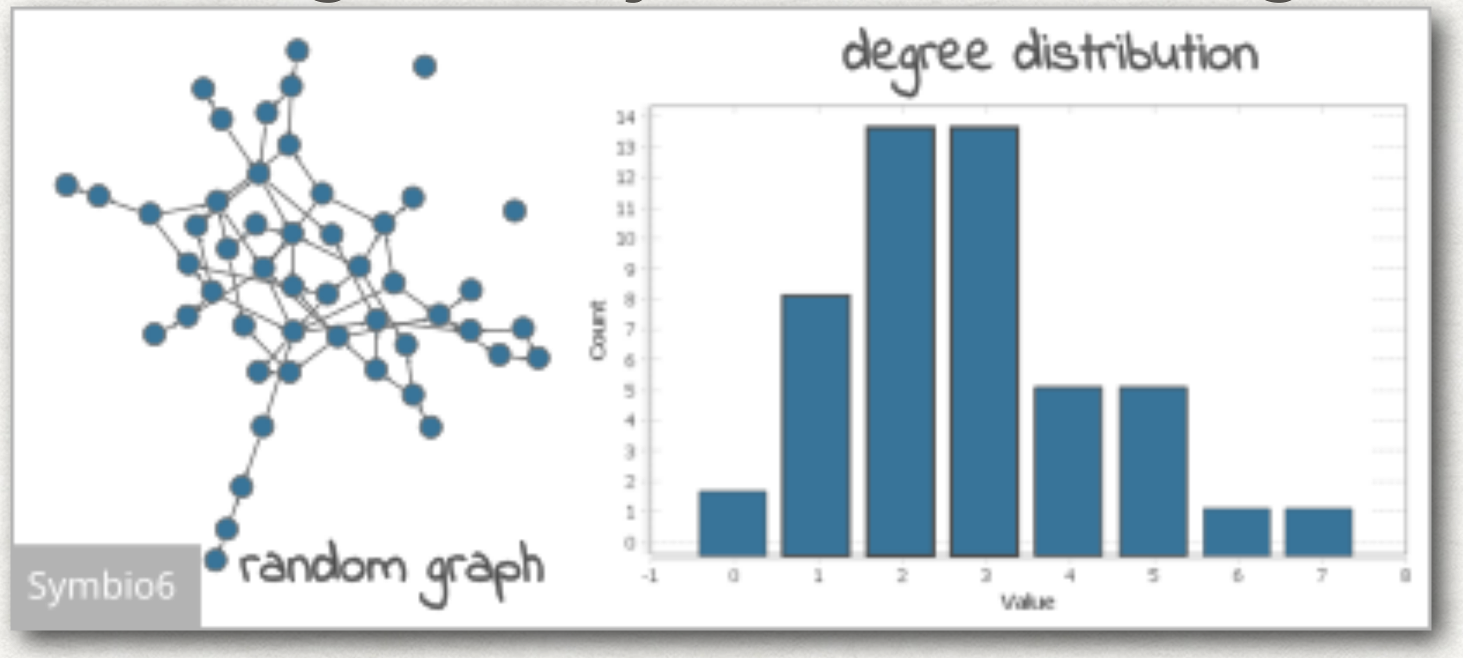
2 **INTEGRATION**
DISTANCE, PATH LENGTH, EFFICIENCY

3 **INFLUENCE**
DEGREE, PARTICIPATION, BETWEENNESS

DECODING THE BRAIN: A NETWORK THEORY APPROACH

Degree Distribution

https://symbio6.nl/en/blog/theory/definition/degree-distribution

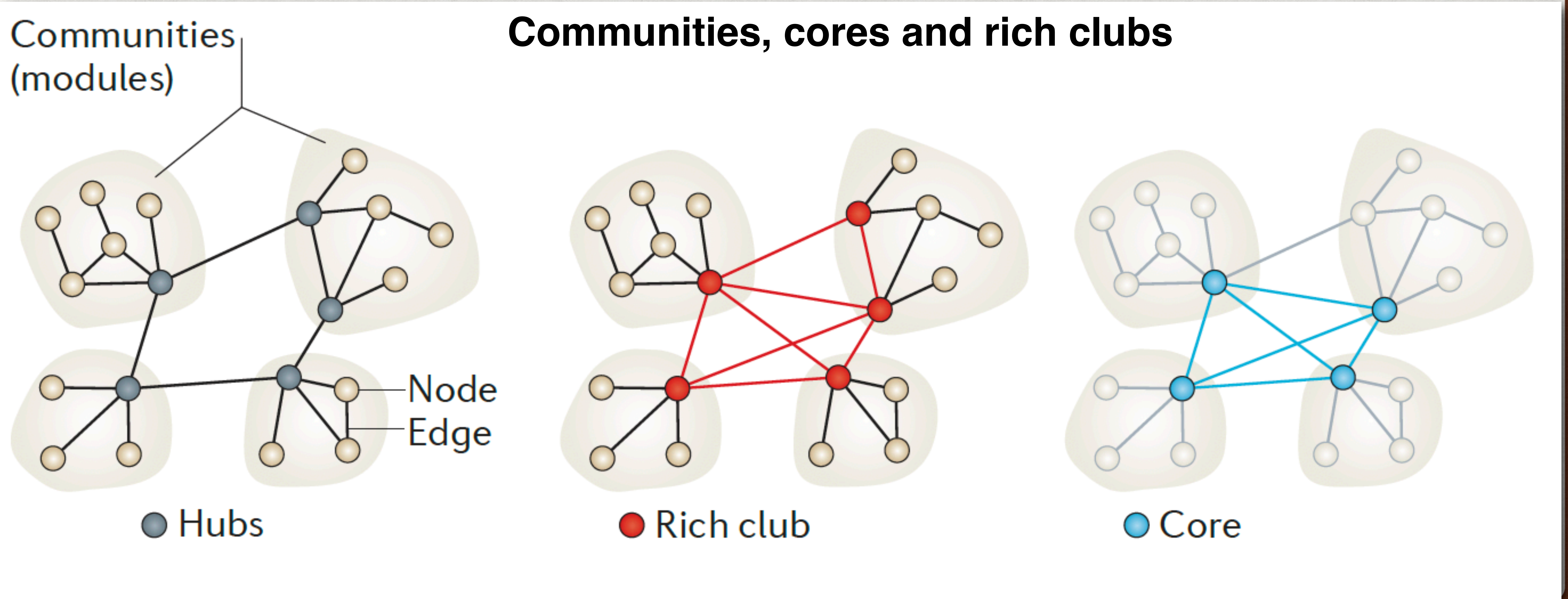


4 TOPOLOGY

DEGREE DISTRIBUTION, COMMUNITIES, RICHCLUB, CORE, FRACTAL DIMENSION INDEX...

5 ROBUSTNESS

PERCOLATION, DEGREE DISTRIBUTION



Olaf Sporns, Dialogues in Clinical Neuroscience - Vol 15 . No. 3 . 2013

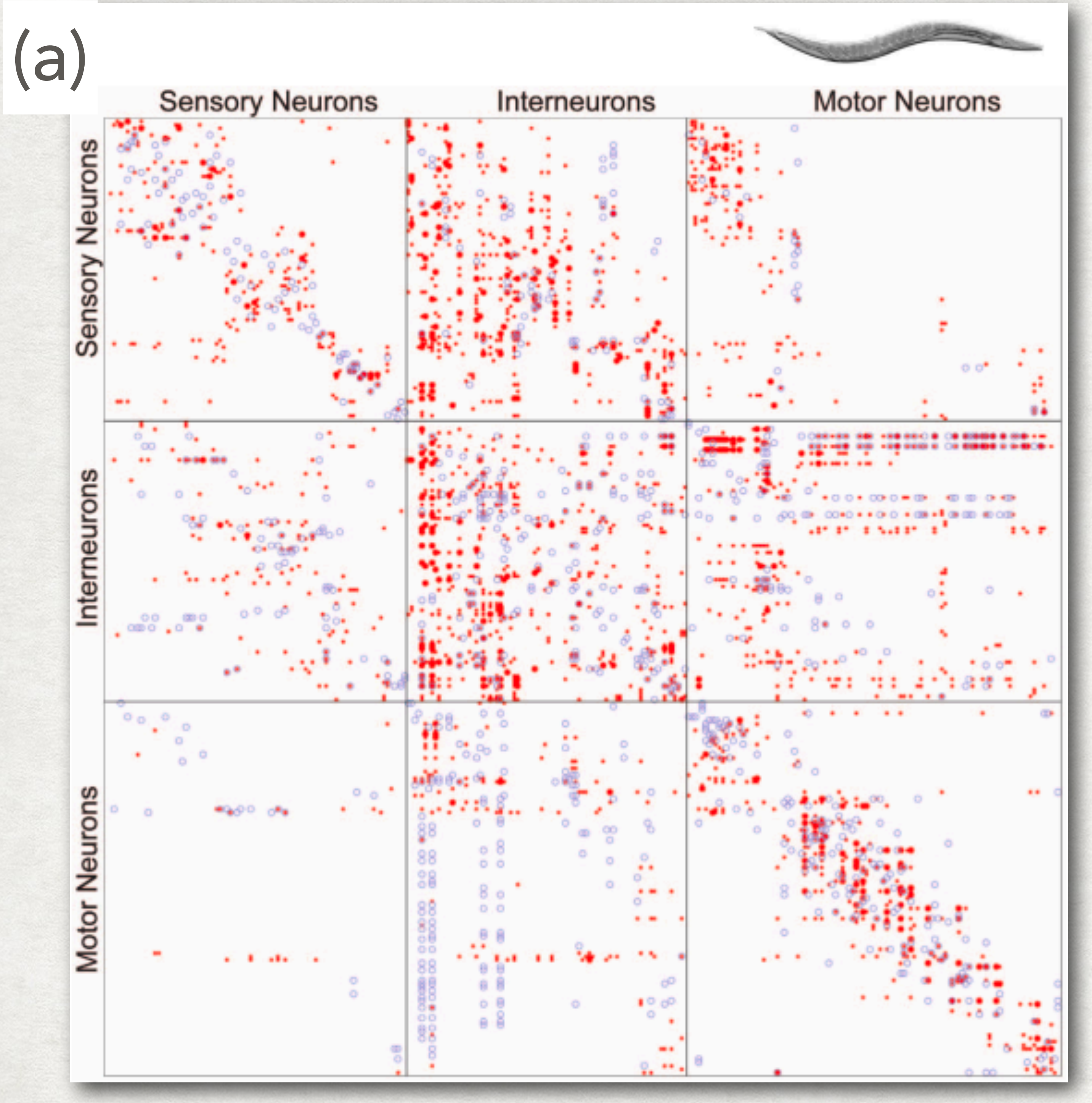
WHAT WE KNOW ABOUT THE BRAIN NETWORKS

Brain networks are modular: Seggregation

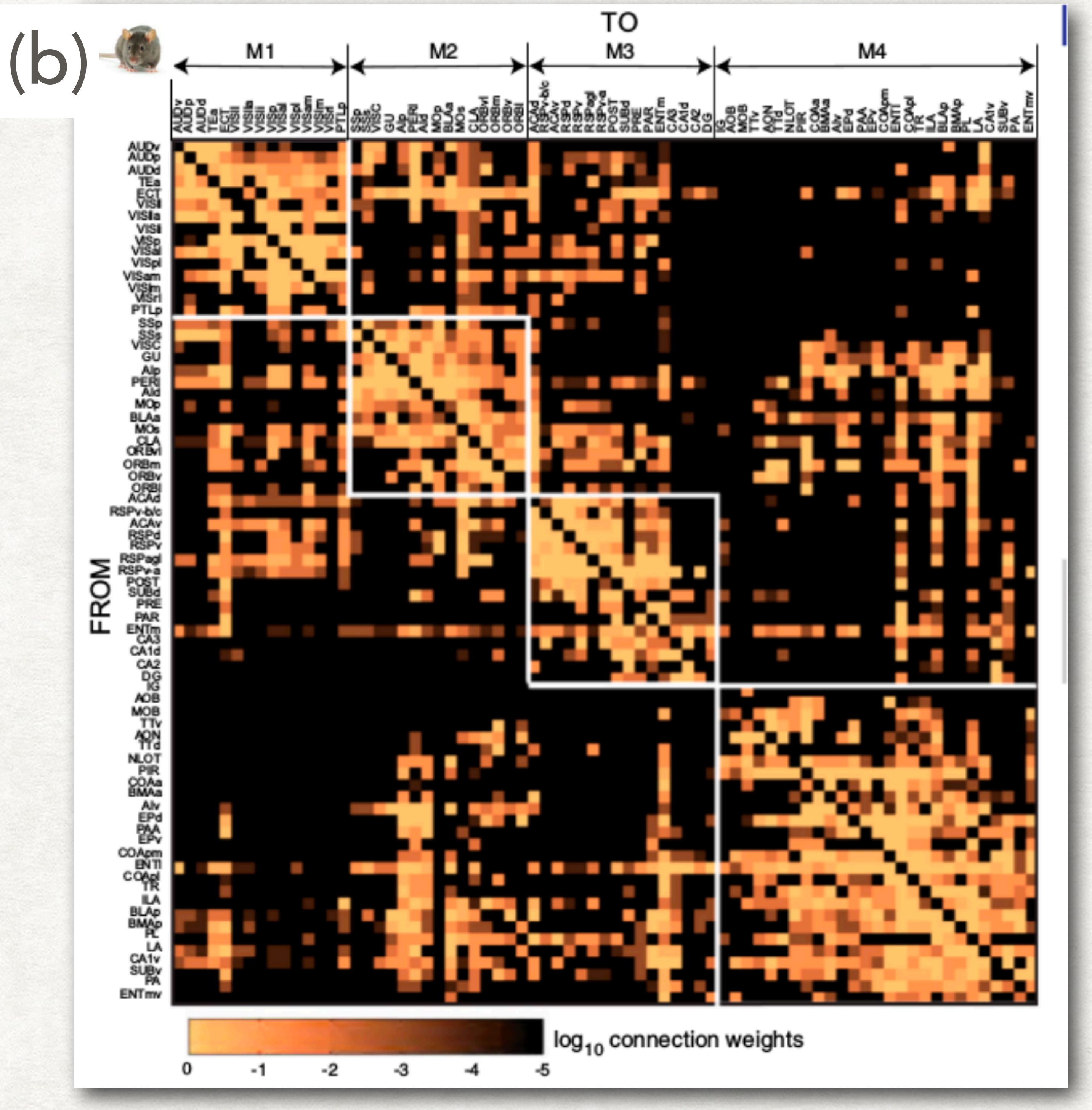
Modules in brain consist of a number of densely **intraconnected regional nodes**, and each node often sharing functional specializations and/or anatomical locations with the other nodes in the same module.

ALMOST ALL THE STUDIED SPECIES HAVE BEEN STUDEIED SO FAR HAVE MODULAR STRUCTURE

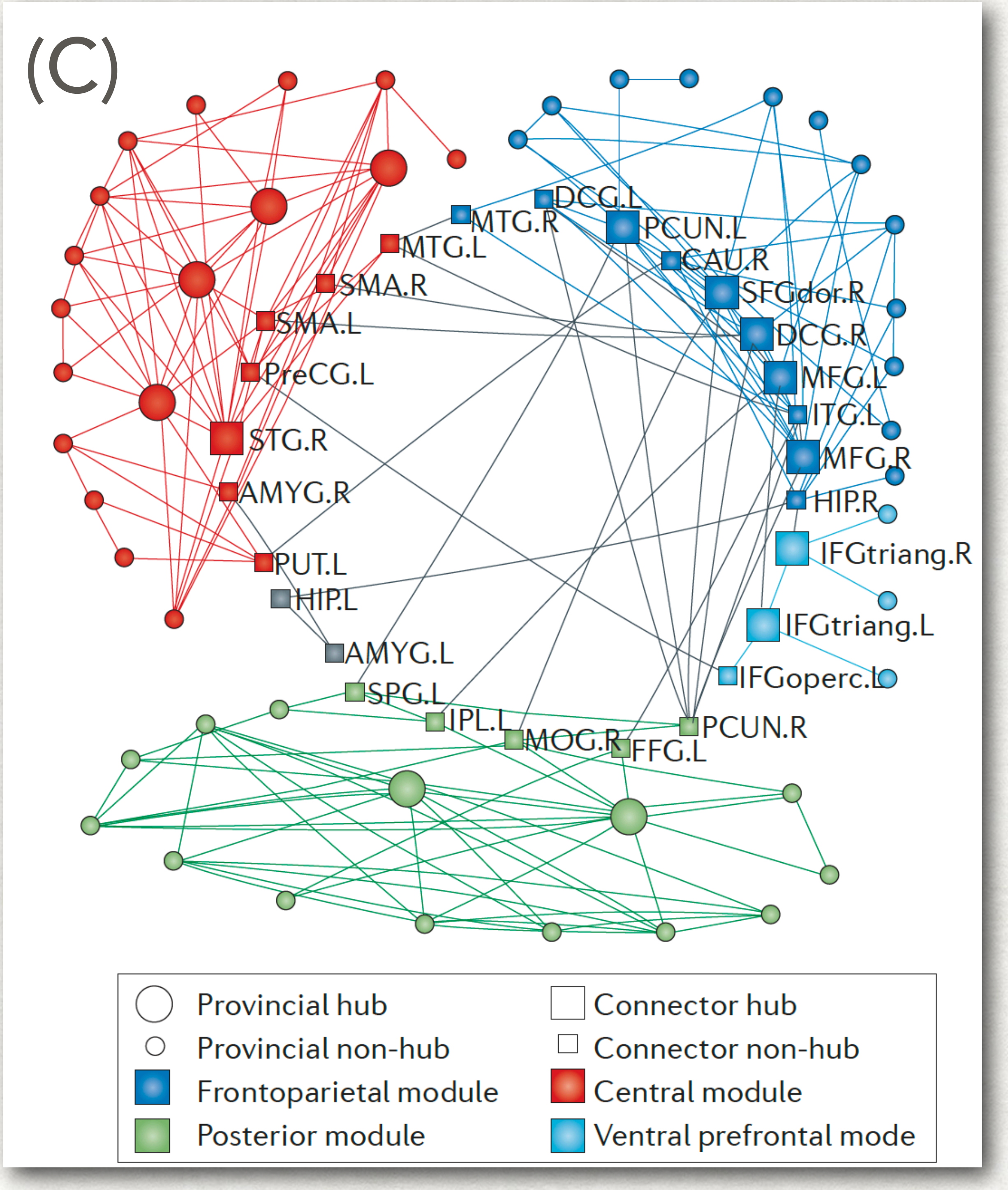
Cerebral cortex of Caenorhabditis elegans



Cerebral cortex of Rat



Hubs and modules in the Human brain



(a) Adjacency matrices for the gap junction network (blue circles) and the chemical synapse network (red points) with Neurons are grouped by category (sensory neurons, interneurons, motor neurons). No. of nodes=279, connections 2990 (chemicals). [L. R. Varshney el., 2011] (b) Modular Struture of the rat brain [M. Bota. O. Sporns, L. W. Swanson, PNAS 2015; (c) Modular Human Brain Network [The economy of brain network organization (2012)].

Why Modular Structure?

1 **Independent specialized subnetworks:** One of the earliest and most influential ideas was formulated by Simon (1962, 1995), who argued that a "**nearly decomposable**" system built of multiple, sparsely inter-connected modules **allow faster adaptation or evolution of the system in response to changing environmental conditions**. Modular systems can evolve by change in one module at a time or by duplication and mutation of modules without risking loss of function in modules that are already well adapted (David Meunier, Renaud Lambiotte, Edward T. Bullmore 2010)

2 **Time-scale seperation:** Modular networks tend to produce time-scale separation, i.e., fast intra-modular processes and slow inter-modular processes (Pan and Sinha, 2009)

3 **Robustness:** The presence of modules allows some neuronal activity to remain locally encapsulated and to maintain dynamical balance (Kaiser et al., 2007; Kaiser and Hilgetag, 2010), So, the **errors may remain localized to one module**.

4 **Co-existence of segregation and integration:** It is advantageous for nervous system design because the high clustering of connections between nodes in the same module will favor locally segregated processing (with low wiring cost) of specialized functions such as visual motion detection, while the short path length will support globally integrated processing of more generic functions such as working memory (Sporns et al., 2004).

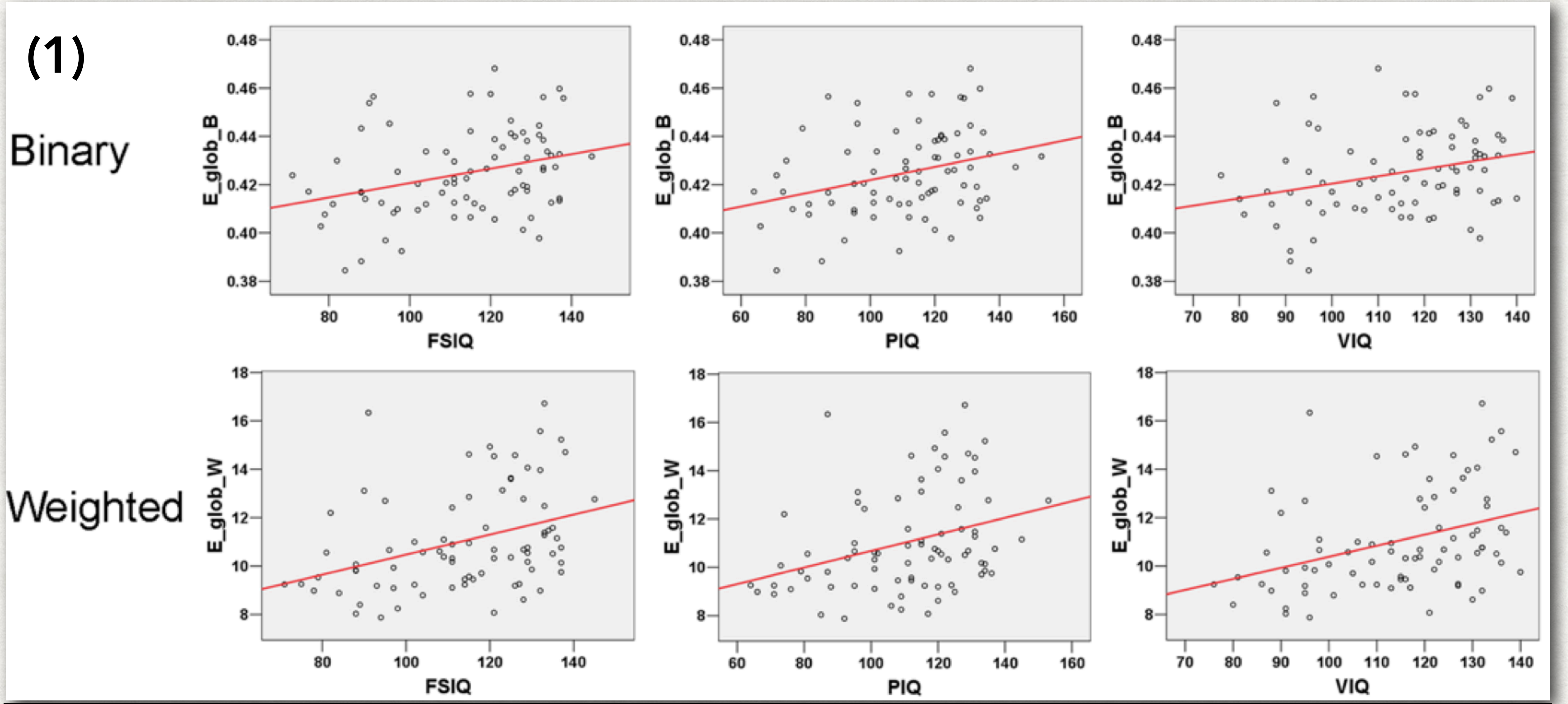
https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2010.00200/full

Efficiency matters: Insights from Network Science

Higher the efficiecny, higher IQ

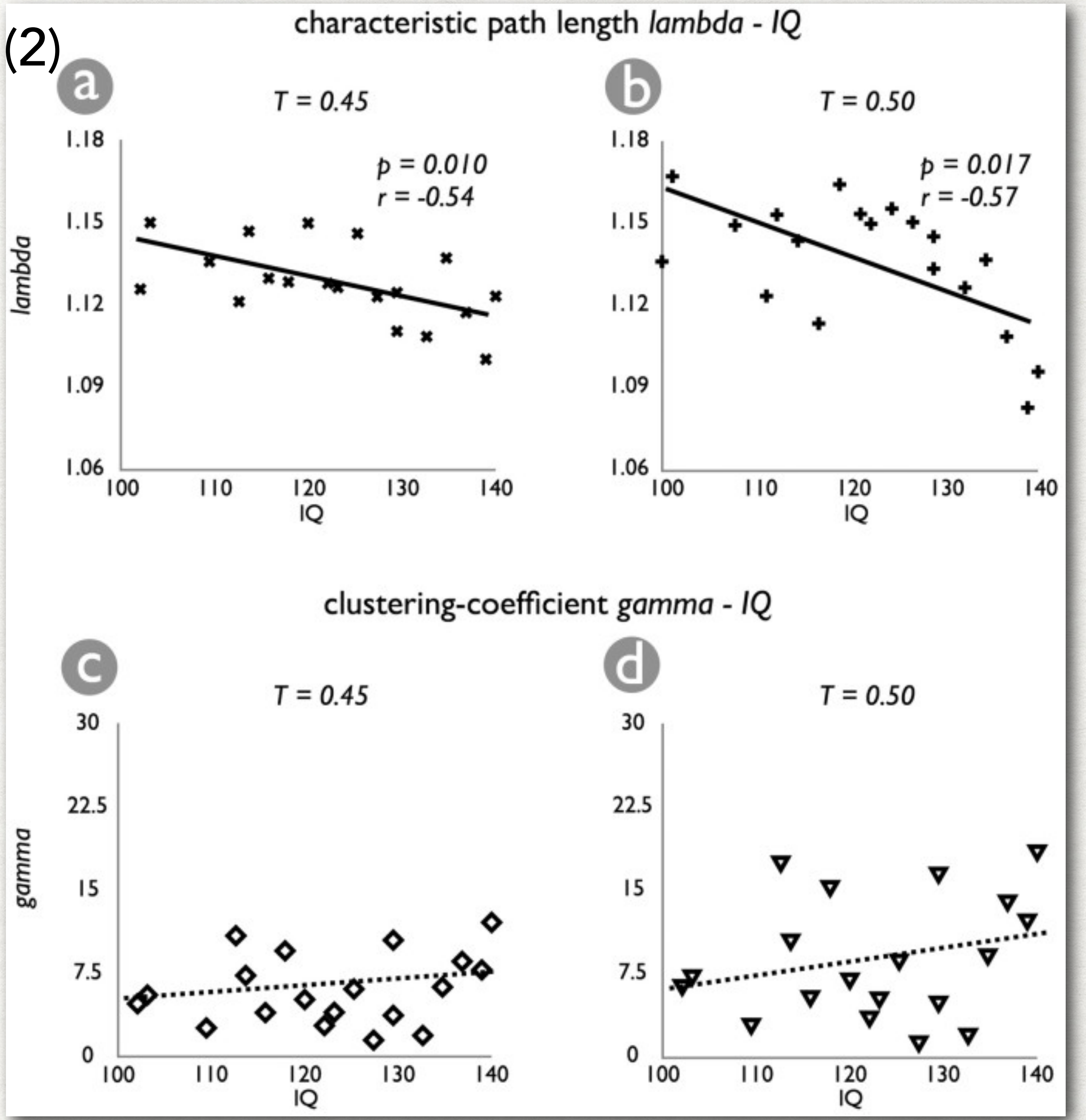
The IQ scores of healthy volunteers were negatively correlated with the characteristic path-lengths of structural and functional networks among regions of the cerebral cortex (**1.** Yonghui Li et al. 2009; **2.** Martijn P van den Heuvel et al. 2009).

For structural connectome



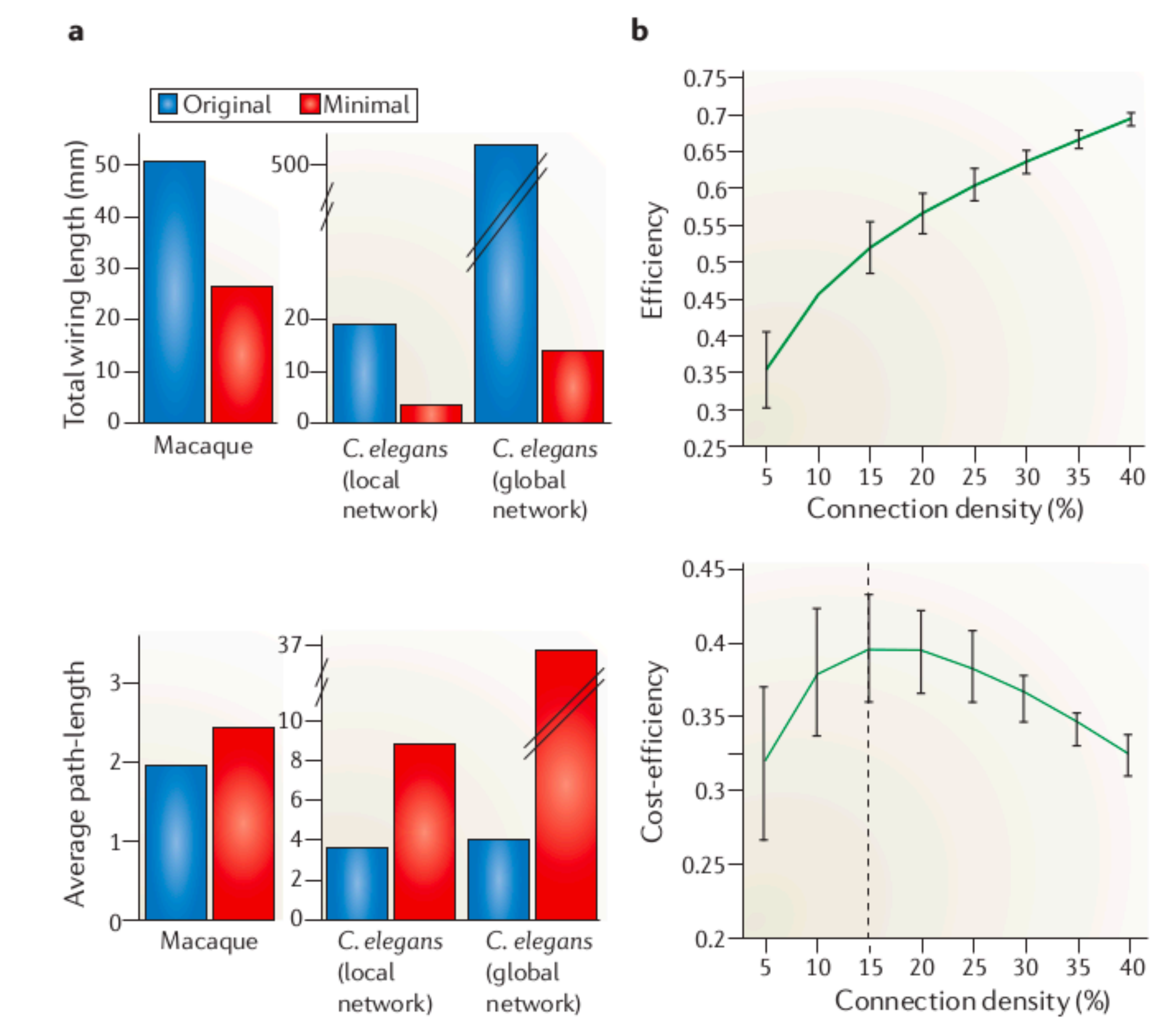
Brain Anatomical Network and Intelligence (2009): Study of the full scale IQ (FSIQ), performance IQ (PIQ) and verbal IQ (VIQ). Significant partial correlation between E_glob and intelligence tests scores. Eglob was found to be positively correlated to FSIQ, PIQ and VIQ in both the binary and weighted networks.

For functional connectome



Efficiency of Functional Brain Networks and Intellectual Performance (2009): λ (L/L^{random}) and γ (C/C^{random}) Versus IQ versus IQ. The normalized characteristic path length λ was found to be negatively correlated with IQ, as shown in a and b. IQ was not significantly associated with the normalized clustering coefficient γ. The negative association between λ and IQ suggests a strong positive association between the level of global communication efficiency within the brain network and intelligence.

Economical trade-offs between wiring cost and topological efficiency in Brain

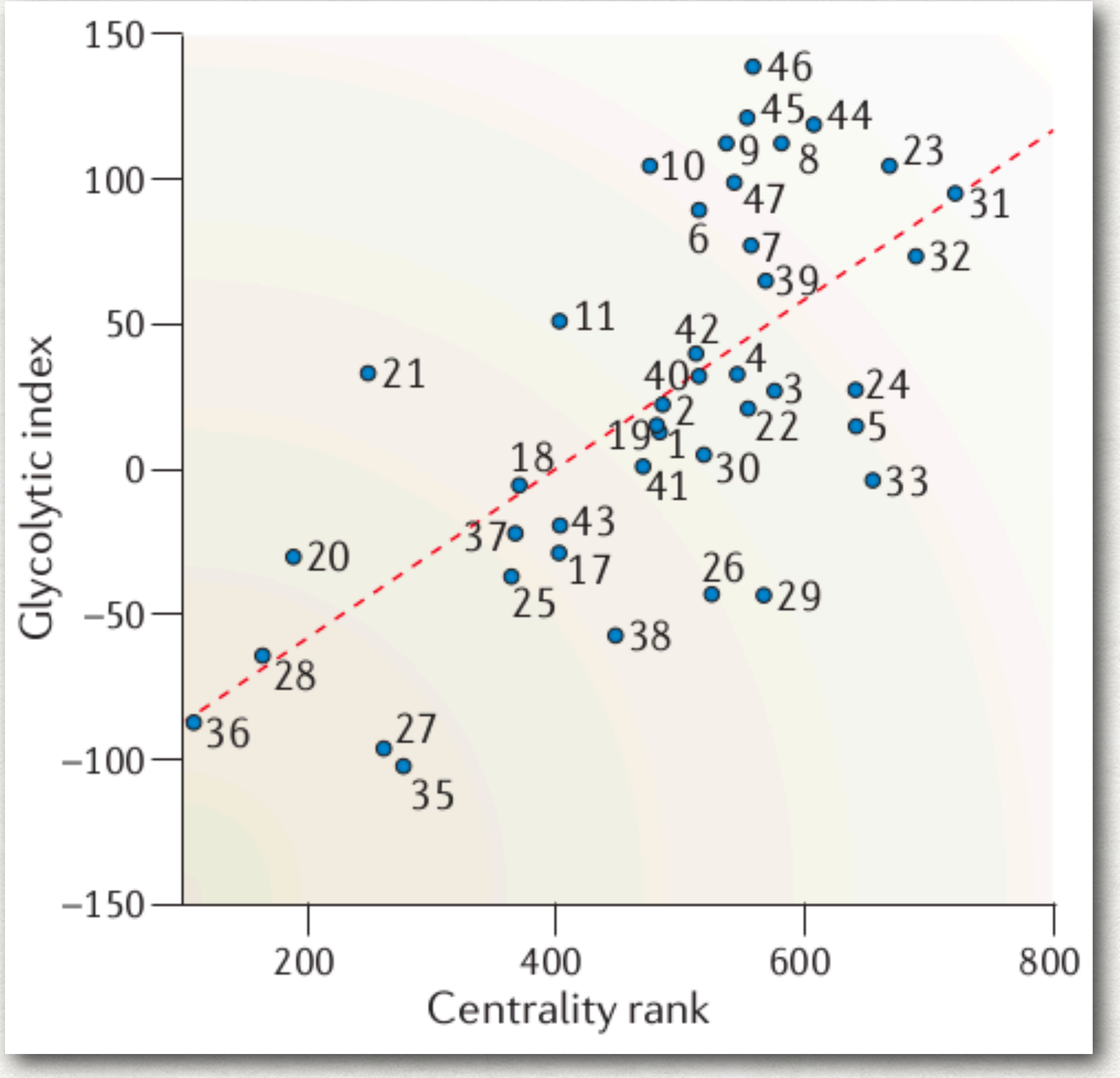


[Bullmore and Sporns, Nat. Rev. 2012]

The empirical networks can not be modified to gain better efficiency at lesser cost. The large-scale anatomical network of the macaque monkey can be computationally re-wired to minimize wiring cost but at the cost of efficiency. Similar is the case with the connectome of C. elegans.

Higher centrality comes with a cost!

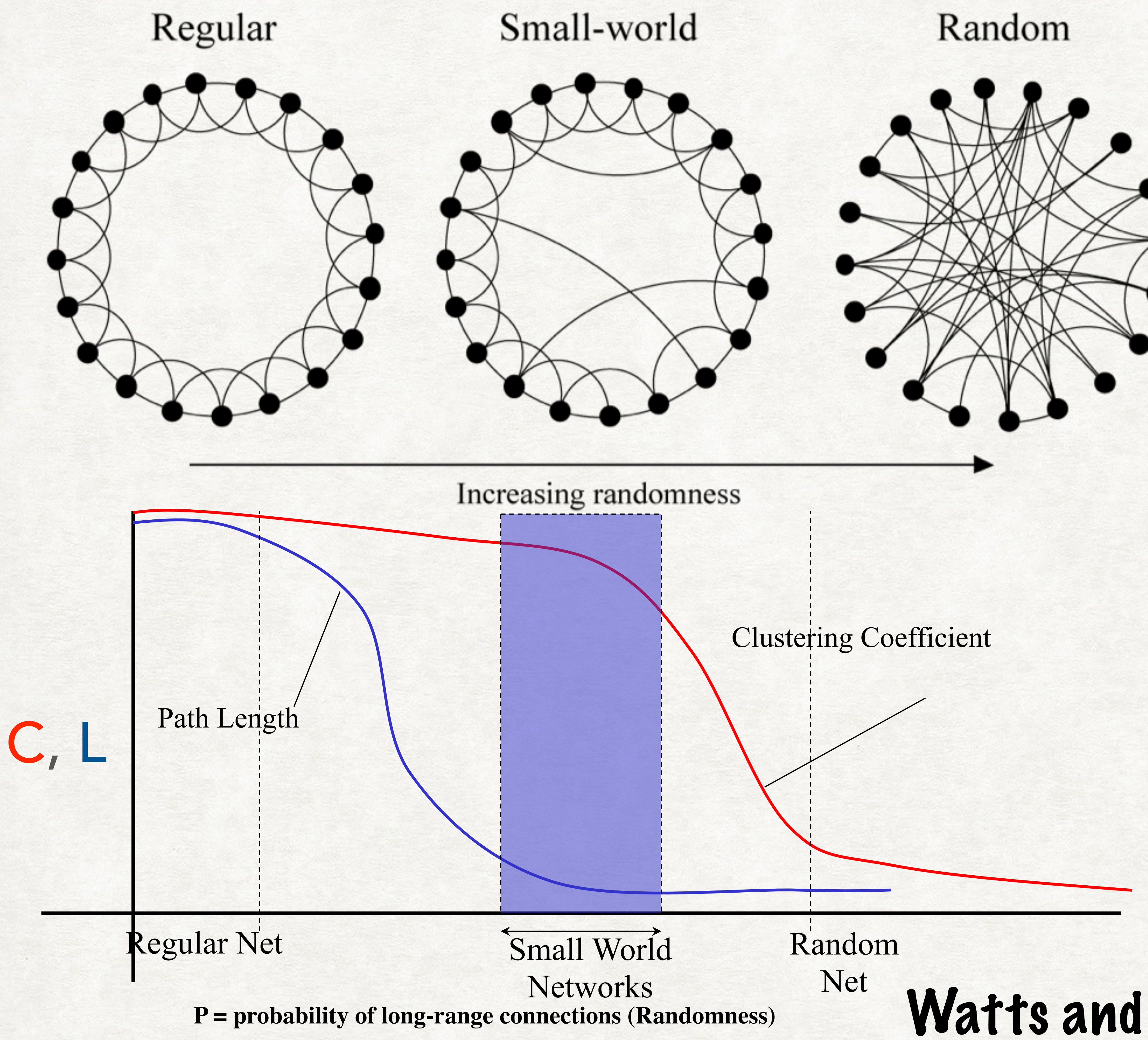
Brain areas with high centrality have a high glycolytic index.



The figure shows a scatter plot of the centrality rank (estimated from the betweenness centrality of the connectomes of ve participants) and the glycolytic index for 41 Brodmann areas of the cerebral cortex. The correlation indicates that areas with high centrality have a high glycolytic index. Mapped Using Resting-State Functional MRI (fMRI).

From: Fundamentals of Brain Network Analysis Edited by: Alex Fornito, Andrew Zalesky and Edward T. Bullmore

Economical Small-World Brain: Insights from Network Science



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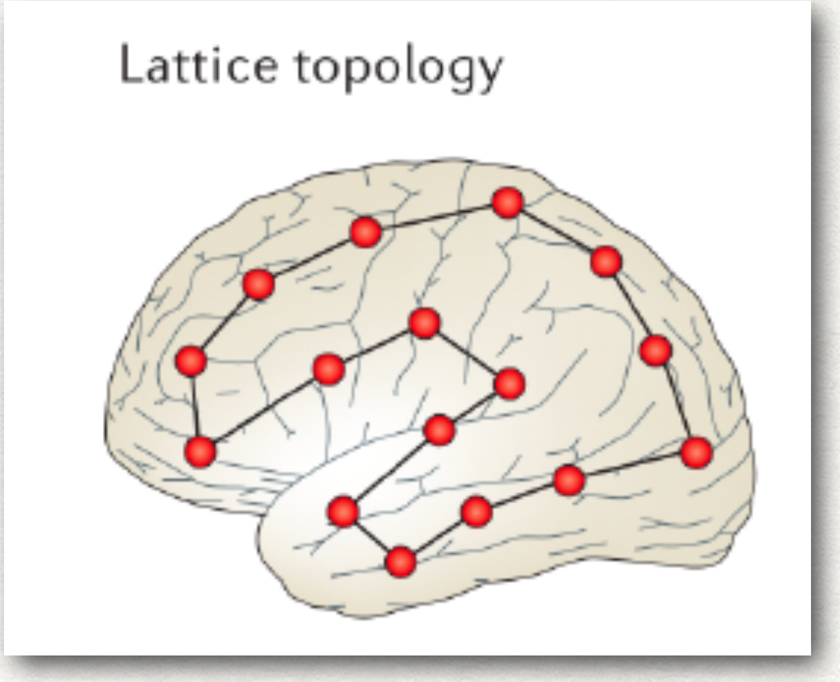
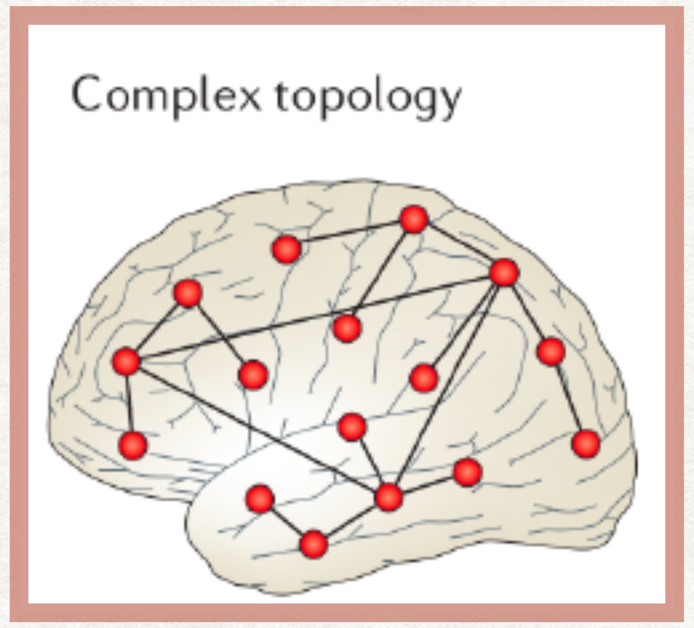
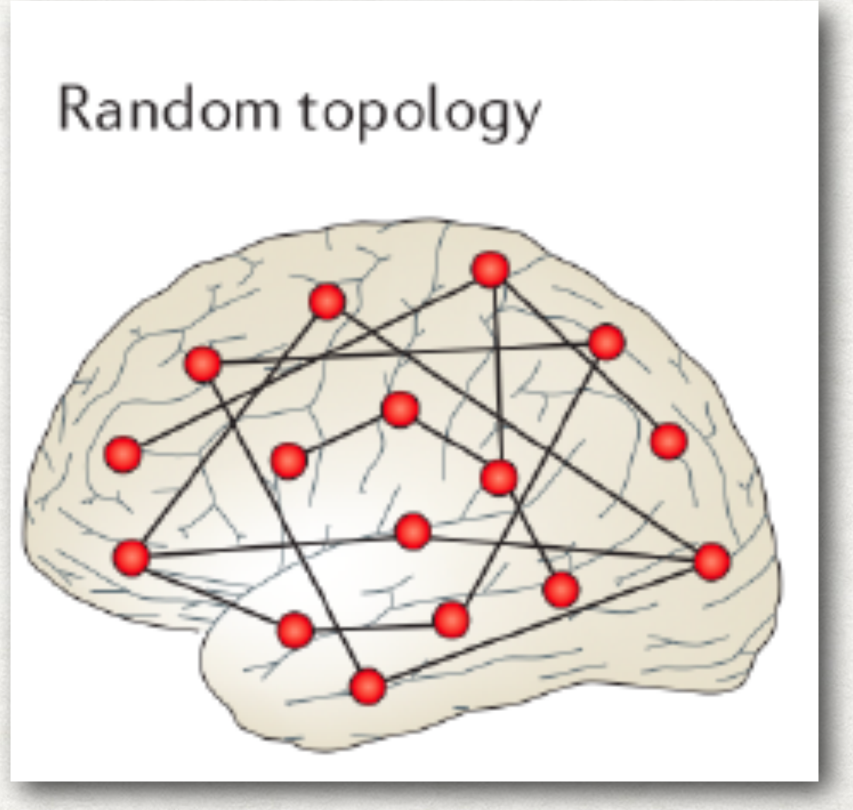


Segrregation: High clustering, and low cost, but low efficiency

Segrregation + Integration



High clustering, and efficiency, and low cost



Integration: Higher efficiency, low clustering, high cost

Watts and Strogatz, Nature 1998

Randomness	Type of Graph	Clustering	Path Length
$p=0$	Regular	Highly clustered	High diameter: $L_{max} \simeq \frac{N}{\langle k \rangle}$
$p=1$	Random (~Erdos-Renyi)	Low clustering: $C \approx \langle k \rangle / N$	Low diameter : $L_{max} \simeq \frac{ln(N)}{lnk}$

Fractal topology, of the brain networks

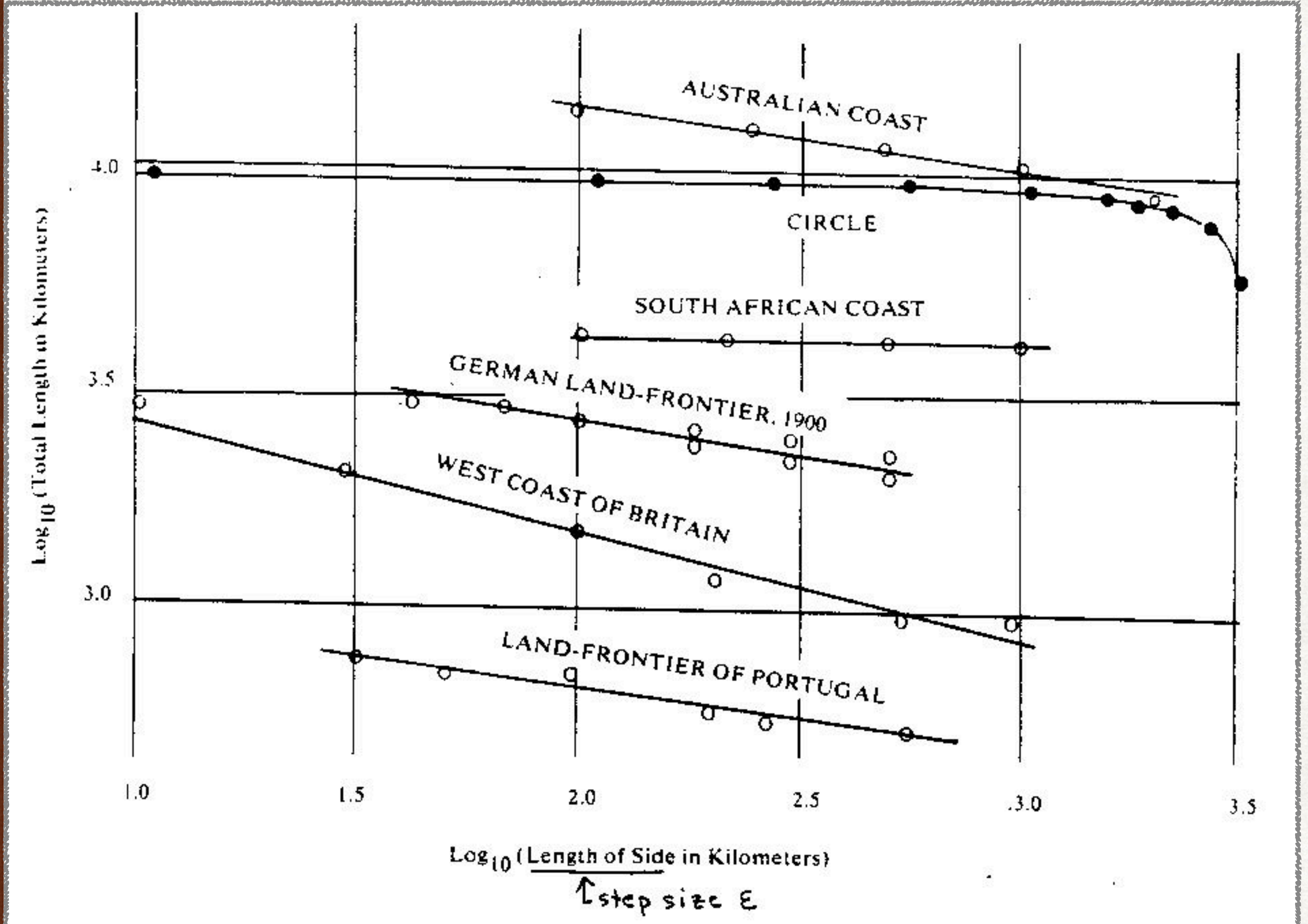


Plate 33 ¤ RICHARDSON'S EMPIRICAL DATA CONCERNING THE RATE OF INCREASE OF COASTLINES' LENGTHS

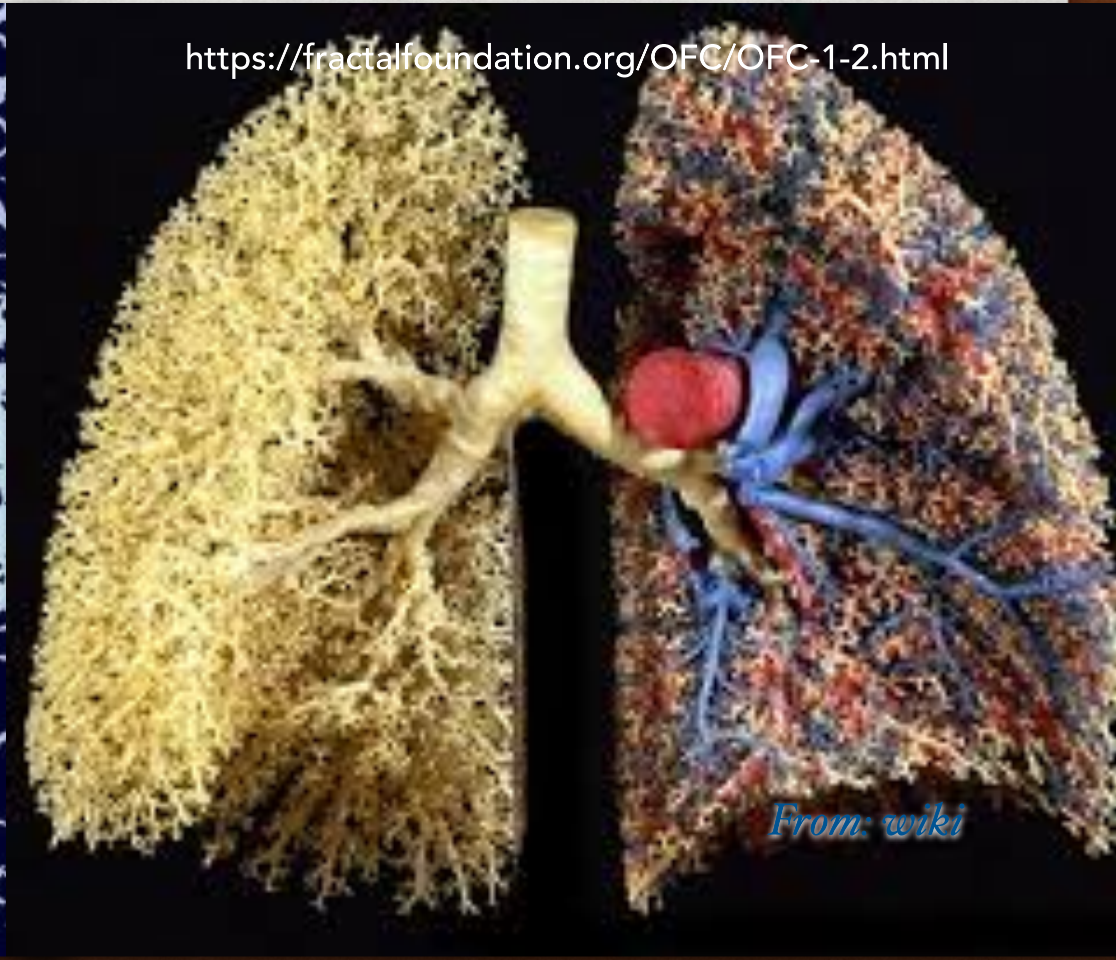
Fractals in Nature

Benoit Mandelbrot: Coastline does not have length, then what property does it have?

$$L(\varepsilon) \sim F\varepsilon^{1-D},$$

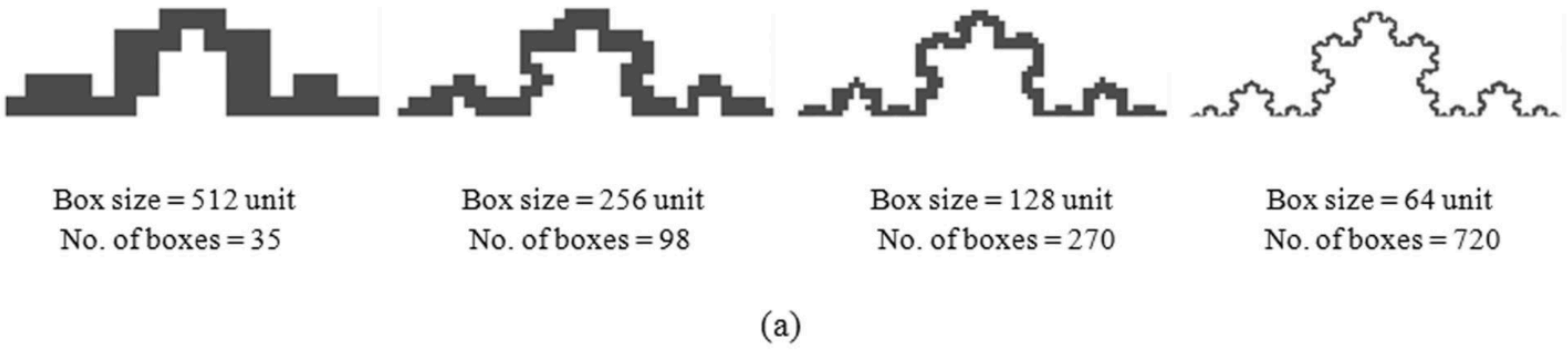
Dimension (D) of the coaslines are in between 1 and 2.

Self-similarity	Irregularity	Infinite Detail	Fractional Dimension



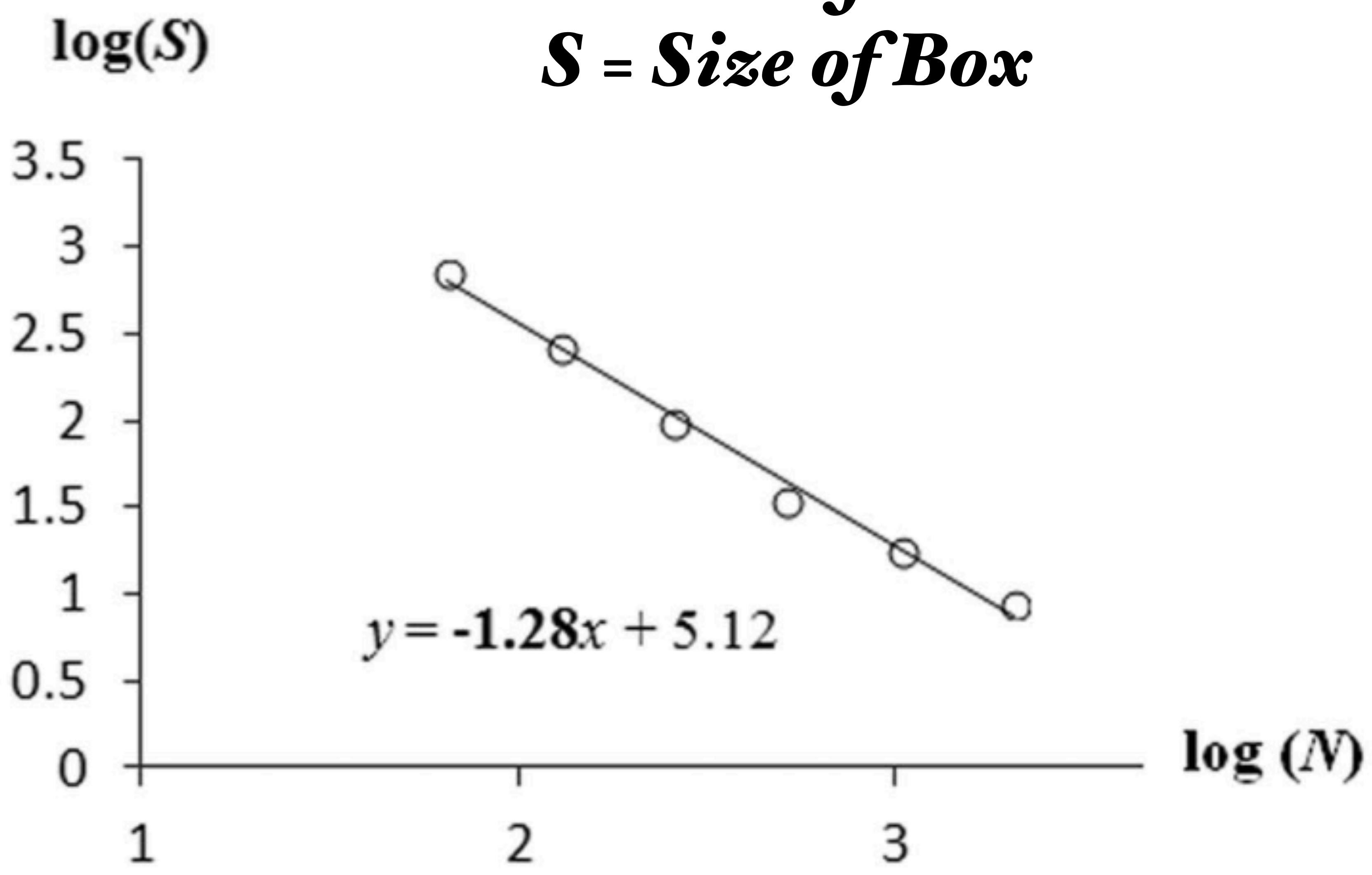
Calculating the dimension (D)

Box-Counting Method (Russell et al. 1980)



N* = *No. of Boxes
S* = *Size of Box

S	N	log (S)	log (N)
2048	9	3.31	0.95
1024	18	3.01	1.26
512	35	2.71	1.55
256	98	2.41	1.99
128	270	2.11	2.43
64	720	1.81	2.86

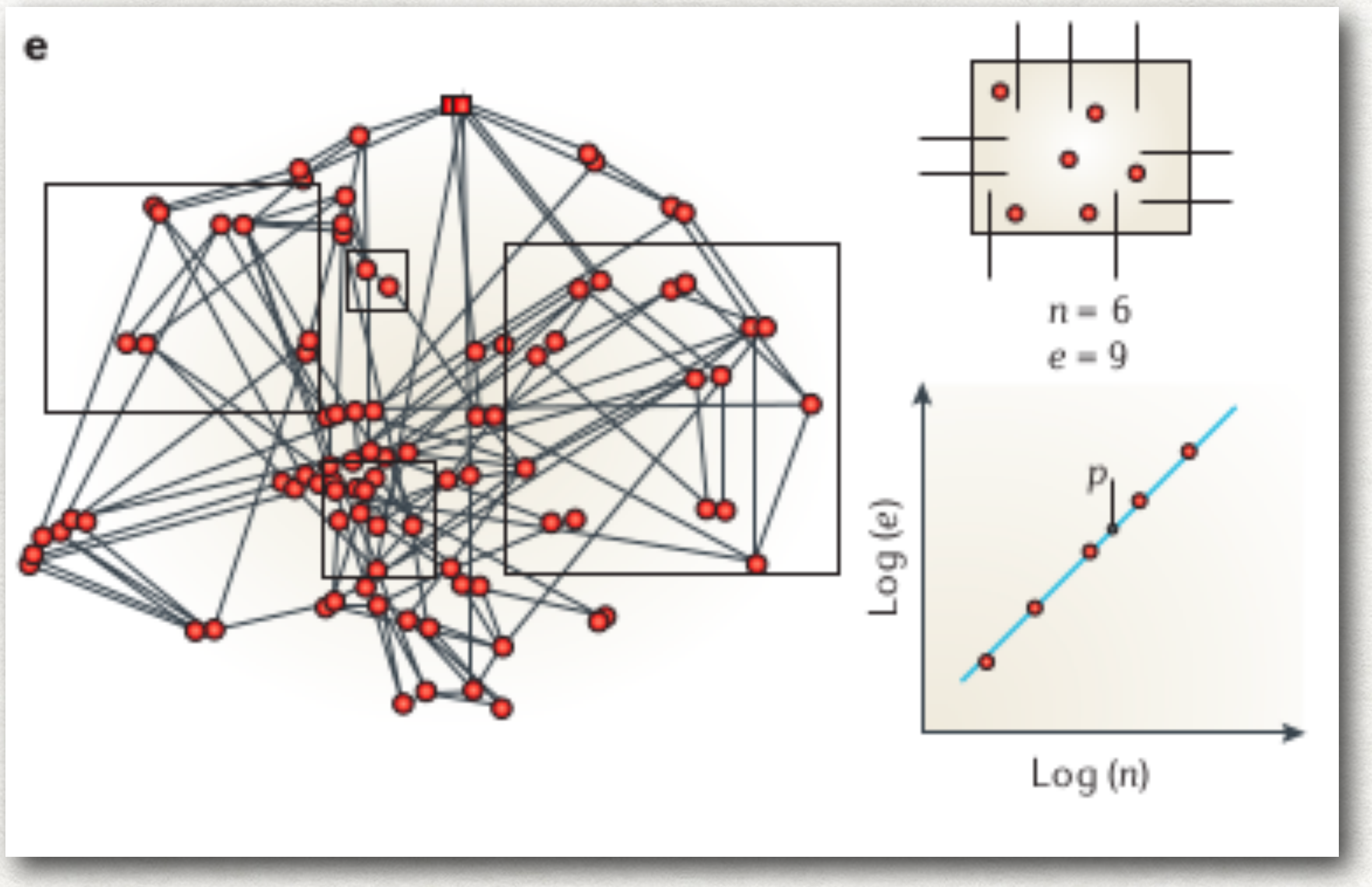


Calculation of Box Counting dimension of Koch curve using the ‘Fractalyse’ program. (a) Boxes that cover the any part Koch curve; (b) Number of covered boxes having with respect to different sizes; (c) Log-log graph that shows the slope of resulting line is 1.28, i.e. the Box Counting dimension of Koch curve is 1.28. https://www.researchgate.net/publication/271197420_Fractal-Based_Generative_Design_of_Structural_Trusses_Using_Iterated_Function_System [accessed Mar 14 2024].

Fractal topology of the Brain networks

In the 1960s, E. F. Rent, an IBM employee, found a remarkable trend between the number of pins (terminals, T) at the boundaries of integrated circuit designs at IBM and the number of internal components (g), such as logic gates or standard cells, now it's famous as the rent's rule $T = t * g^p$, p is Rent's exponent

Topological Rentian scaling in Brain: scaling of the number of nodes within a topological partition with the number of connections or edges, crossing the boundary of that topological partition.



$$e = k * n^p,$$

where, e is number of connection going out from n no of nodes, and $0 \leq p \leq 1$ and k are Rent exponent and coefficient respectively.

(Danielle S. Bassett et al. 2010, PLoS Comp. Bio.)

Fractal topology of the Brain networks

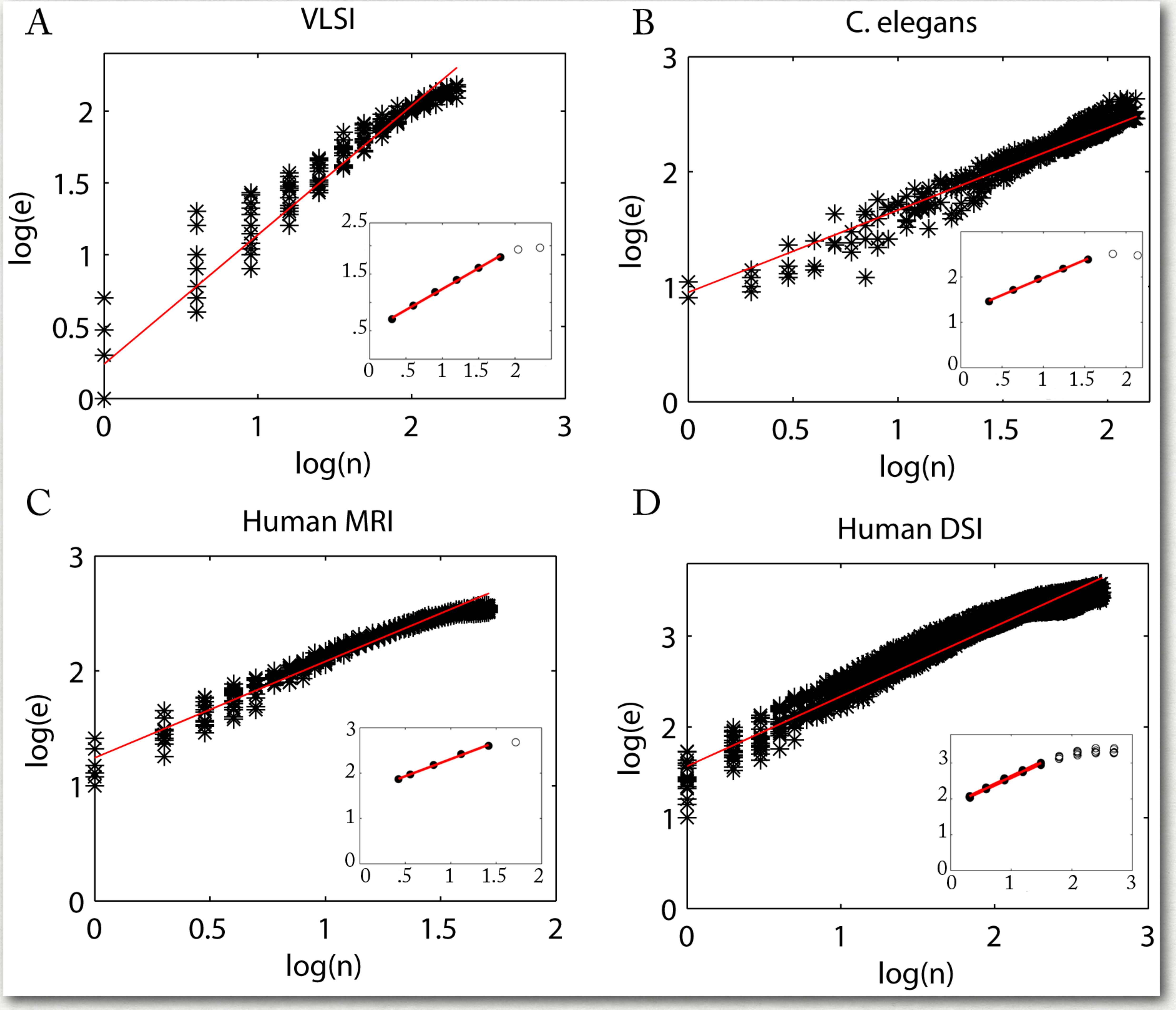


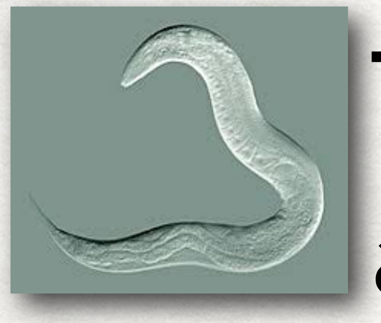
Fig. Topological and physical Rentian scaling in nervous and computational systems.

(Danielle S. Bassett et al. 2010, PLoS Comp. Bio.)

Insights from Core Analysis

✓ **Why Core?**

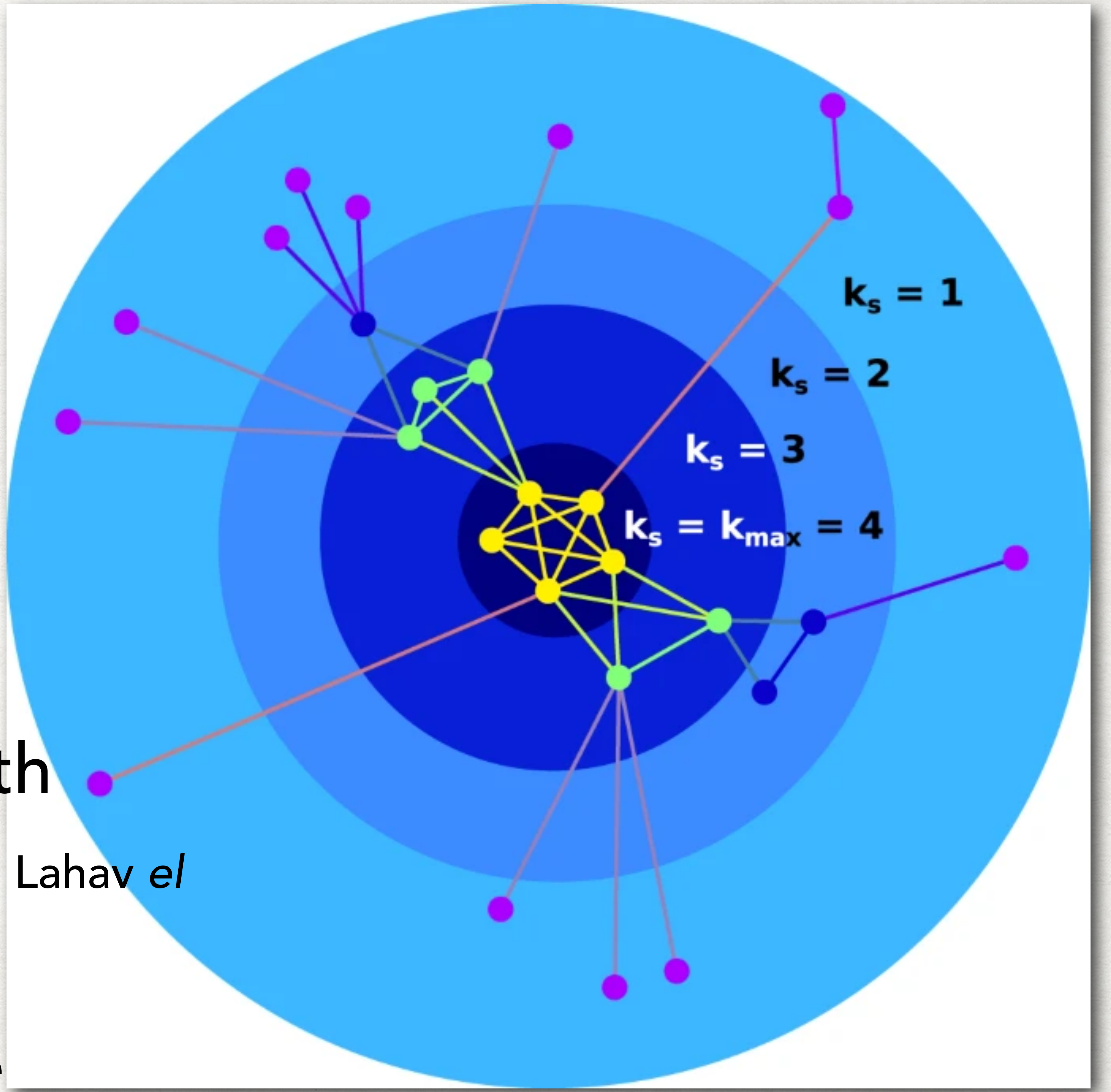
Core act as a crucial hub that integrates the more loosely connected peripheral nodes, ensuring efficient network functionality



The core of the C-elegans brain comprises sensory and motor neurons [N. Chatterjee and S. Sinha]

✓ In the human cortex, the core regions are associated with consciousness, providing a platform for its emergence [Nir Lahav *el al.* 2016]

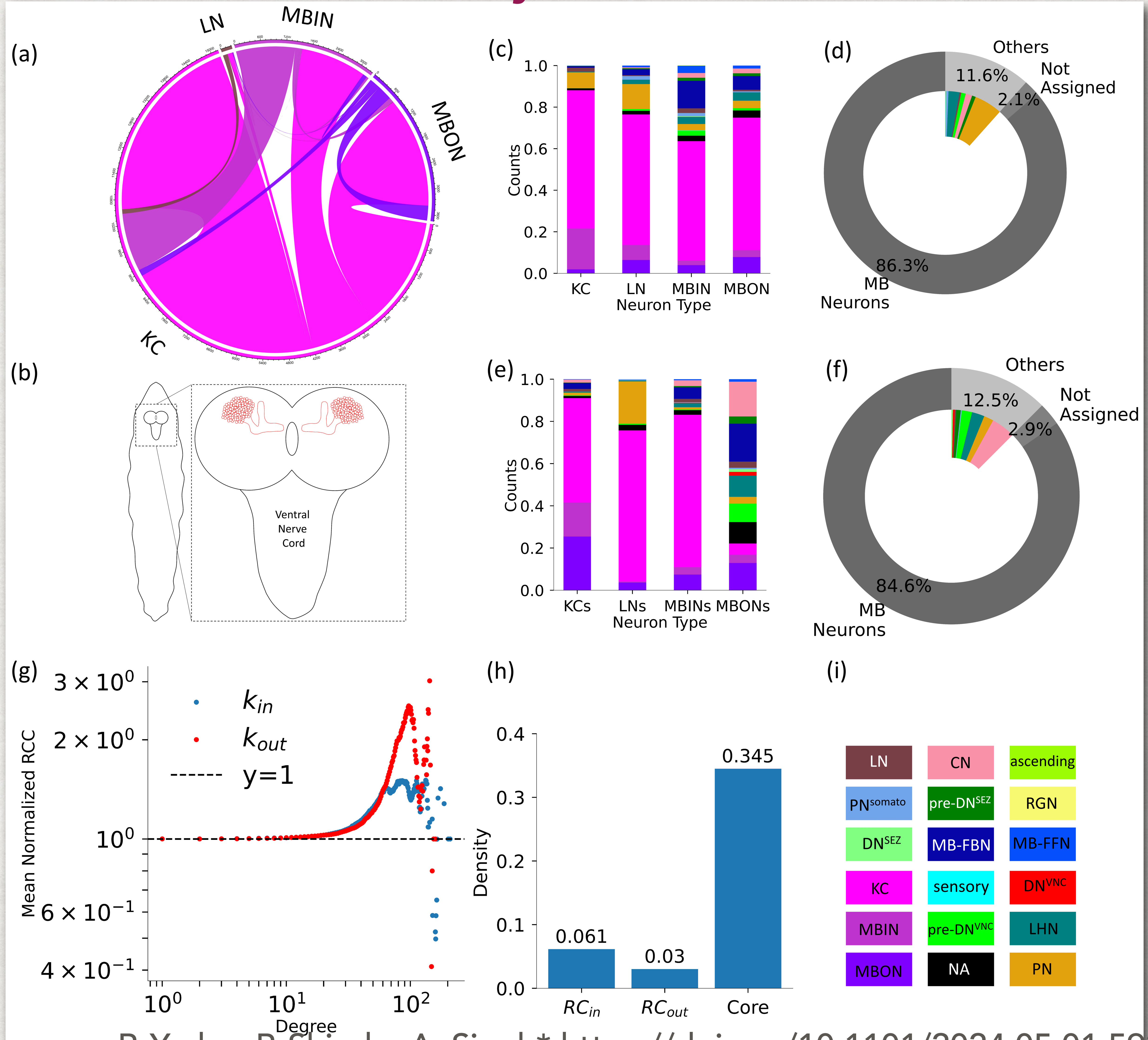
✓ Core topology has been found to be important for the resilience in human brain networks for cognitive function in healthy middle- and old-aged adults. The Presence of Robustly Connected Core Nodes Is Negatively Related to Age [https://doi.org/10.1073/pnas.2203682119].



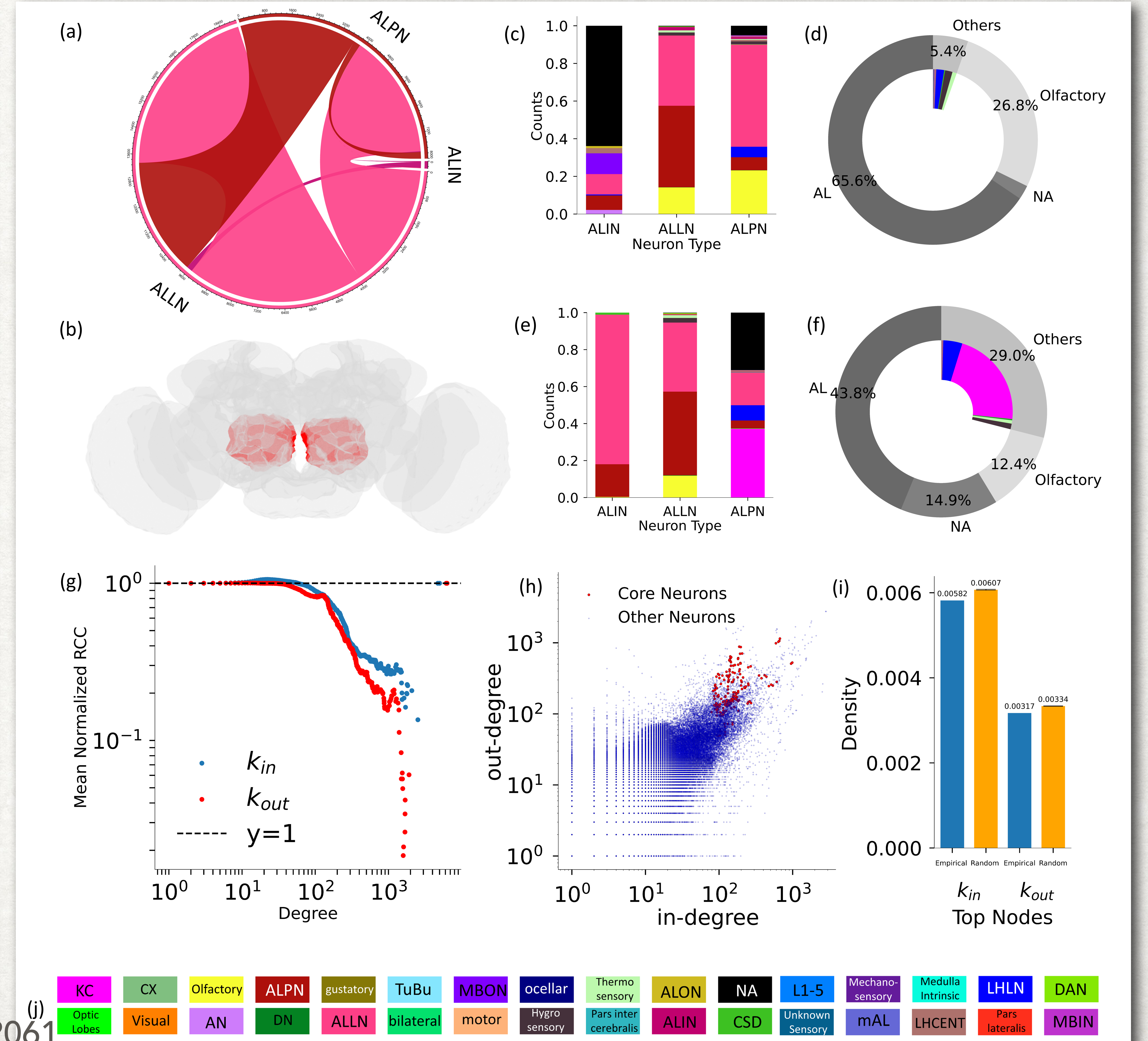
K-shell decomposition of an example network. At each step of the algorithm, nodes with degree equal to or less than k are removed iteratively until none remain. Kate Burleson-Lesser et al. 2020

Core Organization in the different developmental stages of the Fruit Fly

Larval Brain: No. Of Neurons = 2952
Mashroom Body Neurons form core



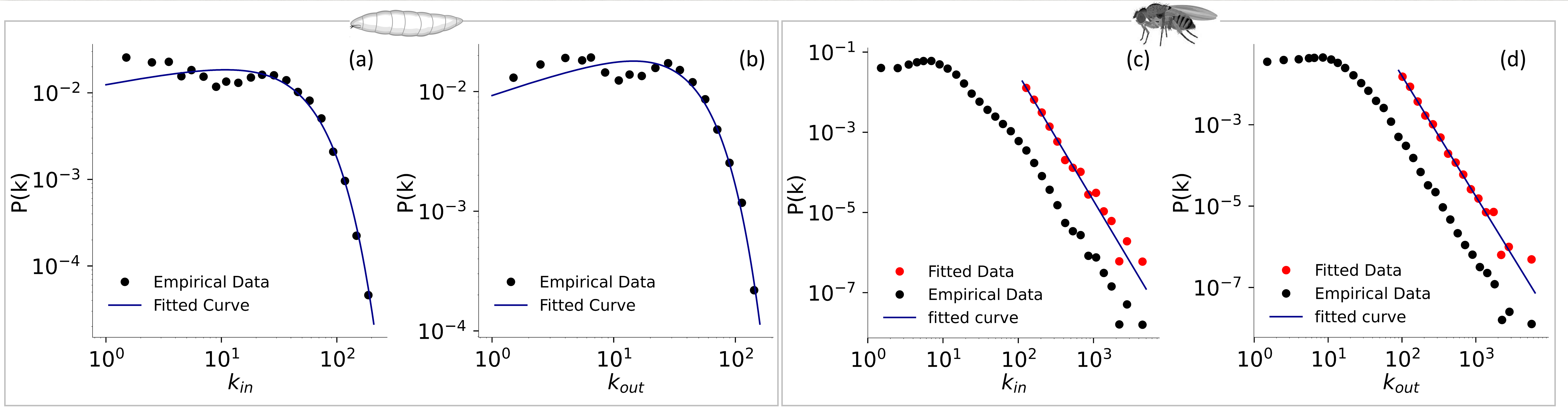
Adult Brain:No. Of Neurons = 124891
Antennal Lobe Neurons form core



P. Yadav, P. Shinde, A. Singh* https://doi.org/10.1101/2024.05.01.592061

Brain Topology: Insights from Degree Distribution Analysis

Distinct topology across Drosophila developmental stages



P. Yadav, P. Shinde, A. Singh https://doi.org/10.1101/2024.05.01.592061

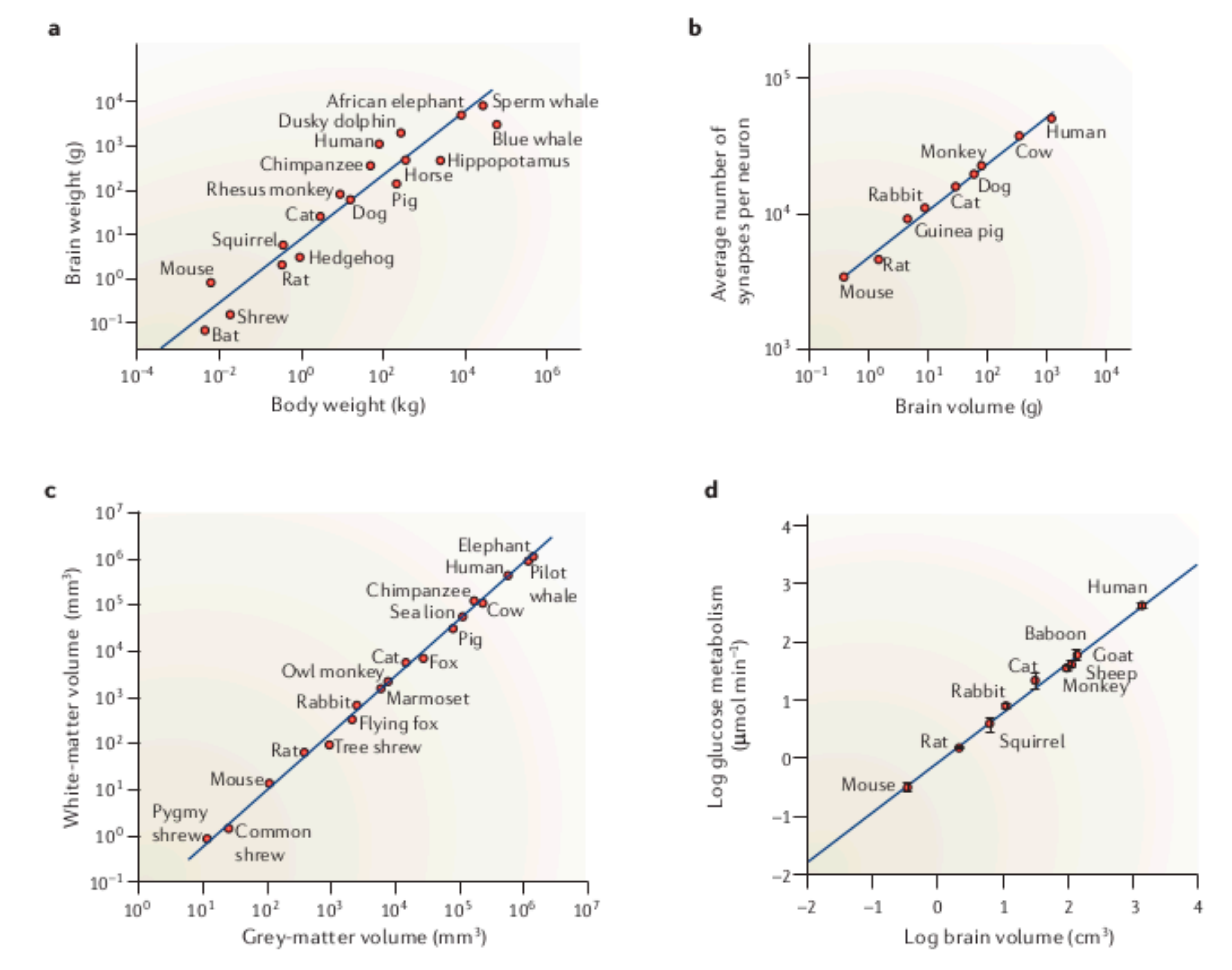
For the larval brain: $P(k) \propto k^{\beta-1}e^{-\lambda k^{\beta}}$

λ and β are determined to be 0.0247 and 1.2409 for in-degree and 0.0244 and 1.3348 for the out-degree

For the Adult brain: $P(k) \propto k^{-\beta}$

Power-law for the out-degree of the adult brain is in the scale-free regime ($\beta = 2.96$), and for the in-degree, it is very close to the scale-free regime ($\beta = 3.15$)

ALLOMETRIC SCALING OF THE BRAINS



The economy of brain network organization (E. Bullmore and O. Sporns, Nat. Rev. 2012)

Brain Size Affects:

(a) The larger organism has a larger brain,

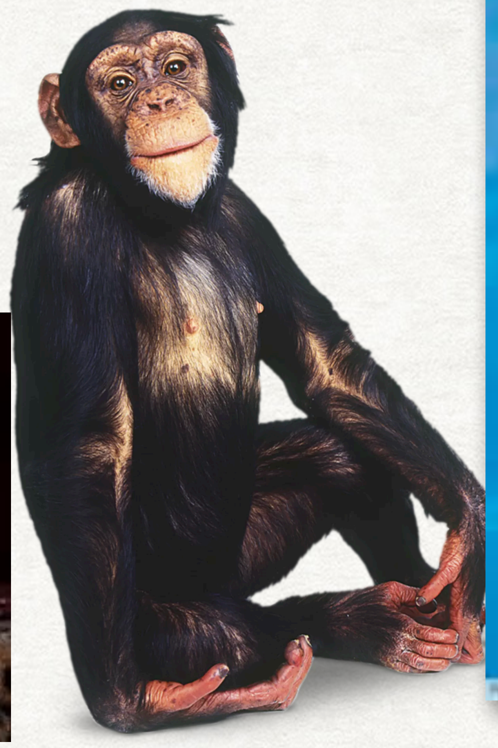
(b) larger brains have more synapses per neuron,

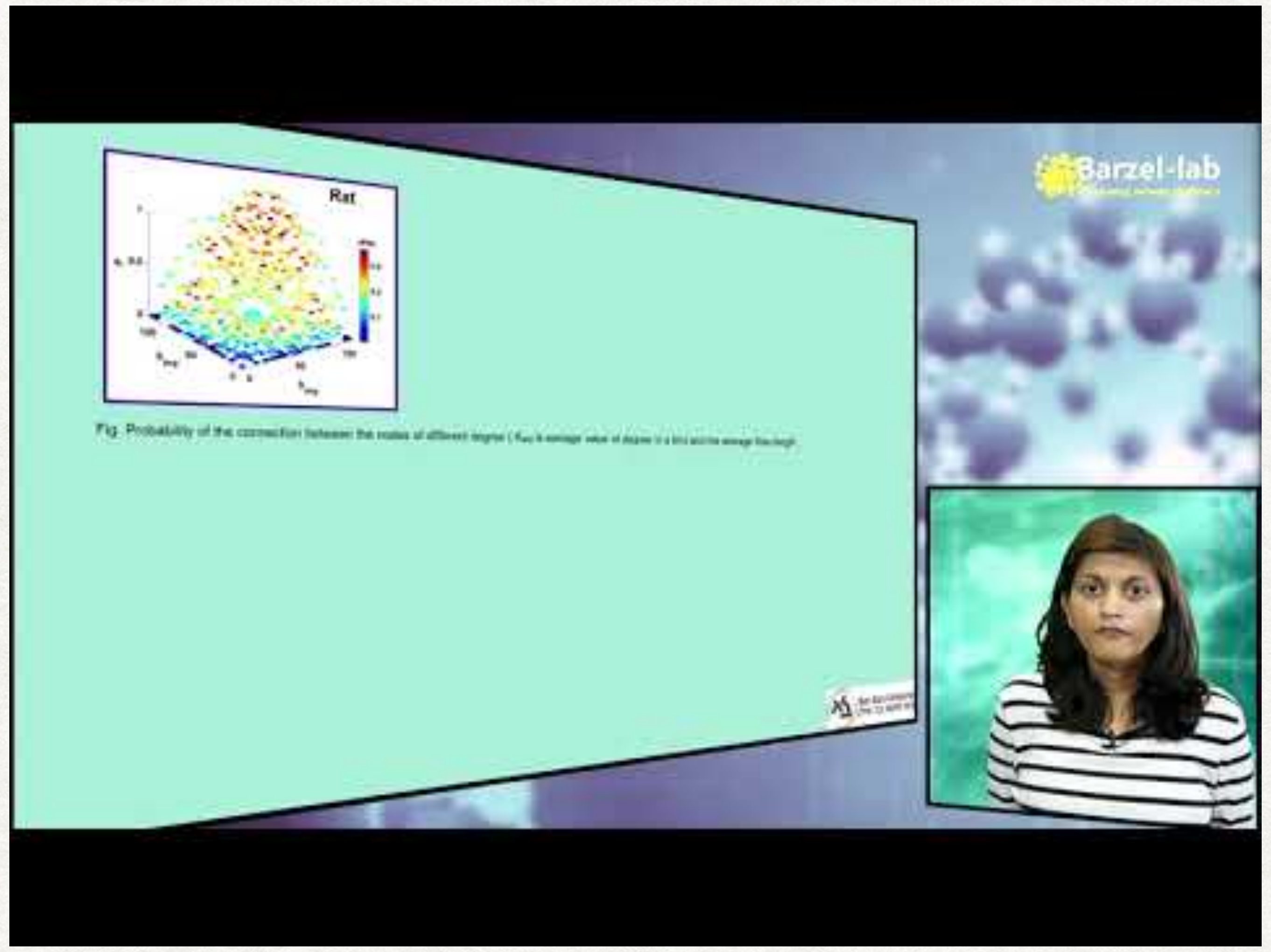
(c) Gray matter volume and white matter volume are correlated

(d) larger brains are metabolically more expensive.

Does Size Affect
Topology of Brain?





Click for More Details!

A. Singh, Rotem G., B. Barzel, et. al.

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All the group members of Complex Systems Lab @ IISER Tirupati

Clockwise from left: Prateek Yadav (iPhD), Kartik Dahake (PhD), Amod Rai (PhD), Ritish Khetrapal (DST-Project associate-I), Sheksha (BS-MS thesis student)

Thanks!