Neuroinformatics

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Week 6: Brain Connectivity Analysis (I)

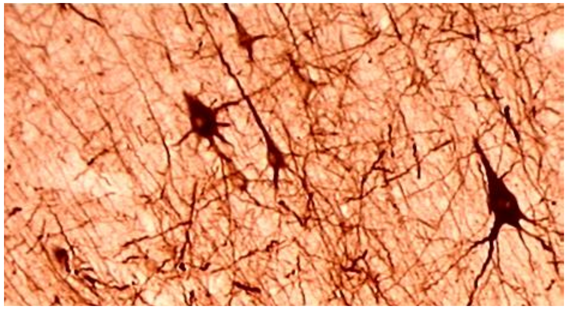
Outline

- What are neural networks?
- Introduction to network analysis
- How can the fibre tract network structure be examined?

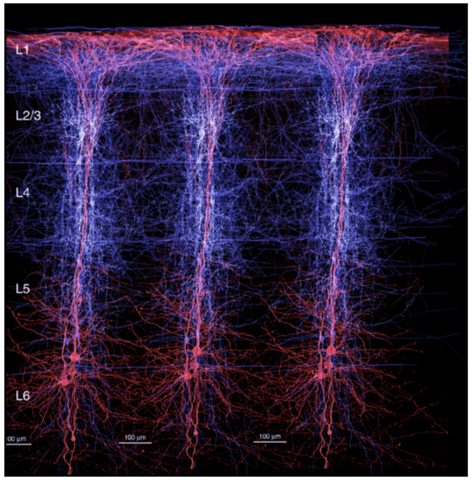
- Topological network organisation
- Spatial network organisation
- Linking structure and function

What are neural networks?

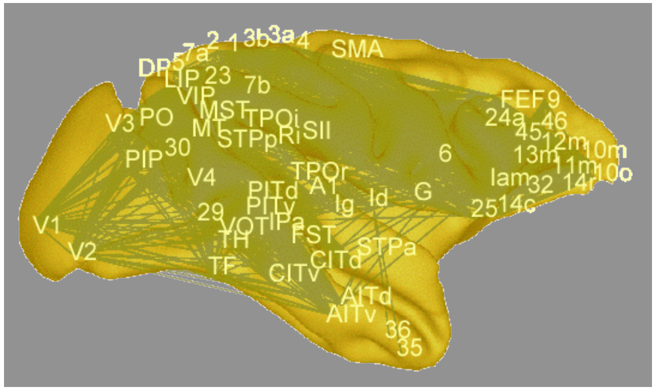
Levels of connectivity



Axons between neurons



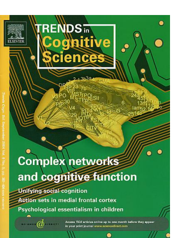
Links between cortical columns



Fibre tracts between brain areas

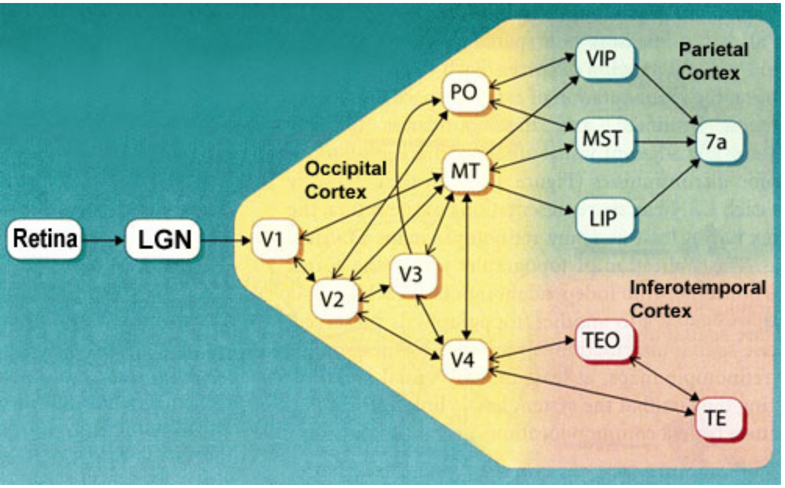
Types of connectivity

- Structural / Anatomical (connection):
  two regions are connected by a fibre tract
- Functional (correlation):
  two regions are active at the same time
- Effective (causation):
  region A modulates activity in region B

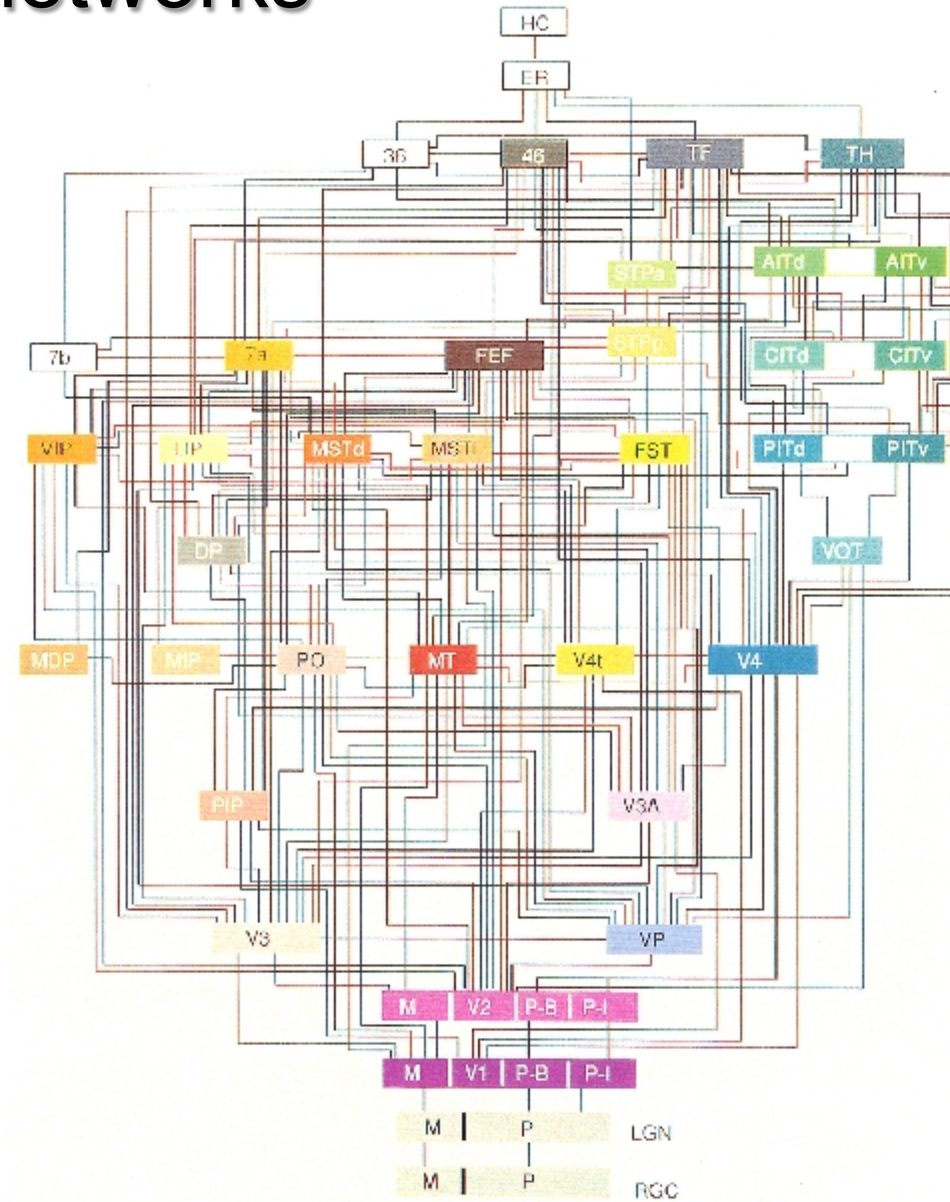


Sporns, Chialvo, Kaiser, Hilgetag.Trends in Cognitive Sciences, 2004

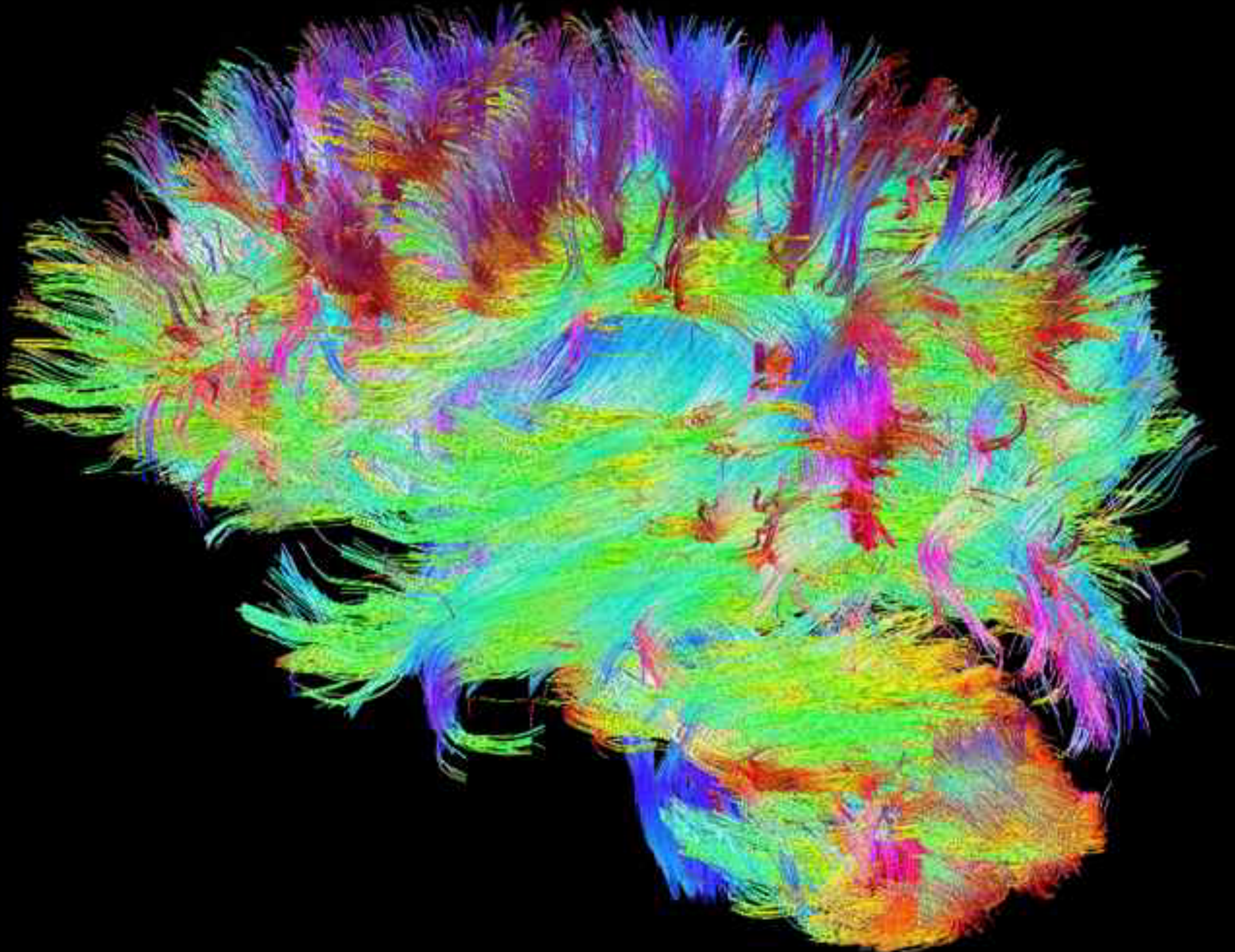
Cortical networks



Dorsal and ventral visual pathway



Visual system



Introduction to network analysis

Network Science

Rapidly expanding field:

Watts & Strogatz, *Nature* (June 1998) cited 4,000+ times

Barabasi & Albert, *Science* (October 1999) cited 4,000+ times

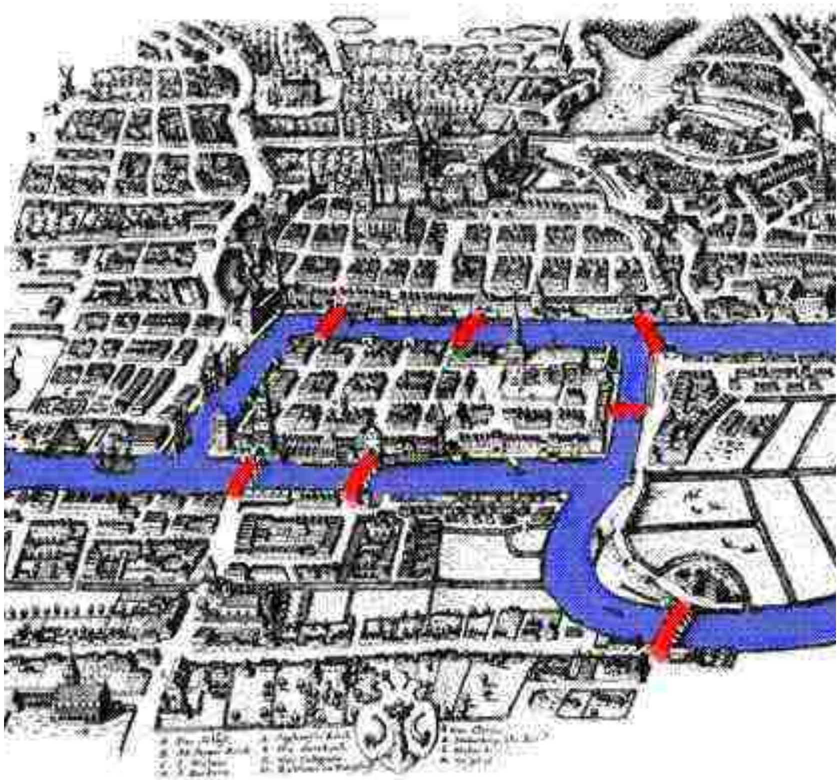
Modelling of SARS spreading over the airline network
(Hufnagel, *PNAS*, 2004)

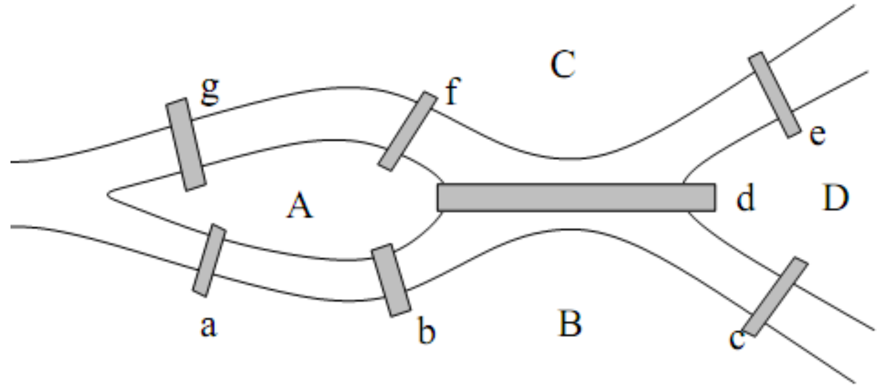
Identity and Search in Social Networks
(Watts et al., *Science*, 2002)

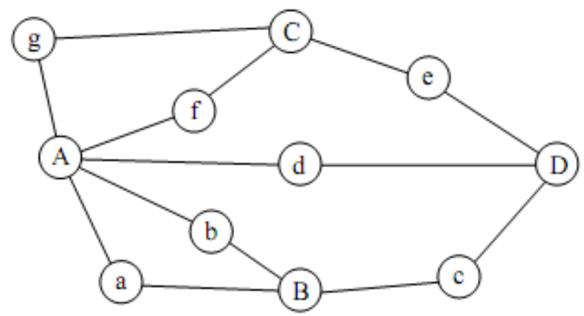
The Large-Scale Organization of Metabolic Networks.
(Jeong et al., *Nature*, 2000)

First textbook on brain connectivity
(Sporns, ‘Networks of the Brain’, MIT Press, October 2010)

Origin of graph theory: Leonhard Euler, 1736







Bridges over the river Pregel in Königsberg (now Kaliningrad)
Euler tour: path that visits each edge and returns to the origin

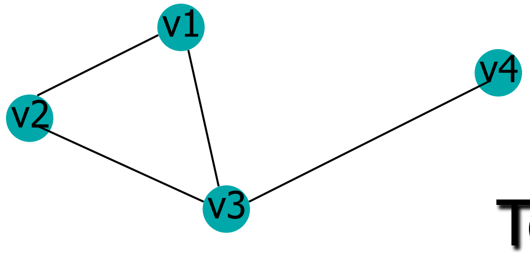
Graphs

- Graph: set of nodes and edges (non-directed)

  $$G = (V,E)$$

- Set of nodes: V (singular: vertex; plural: vertices)
- Set of edges: $E \subseteq V \times V$
- E.g., V={v1,v2,v3,v4},

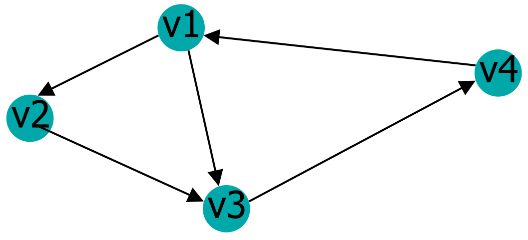
  E={(v1,v2), (v1,v3), (v2,v3), (v3,v4)}



Topology

Directed graphs (Digraphs)

- Graph: set of nodes and *arcs* (directed)
- Set of nodes (vertices): V
- Set of edges: $E \subseteq V \times V$, the order matters
- E.g., V={v1,v2,v3,v4},
  E={(v1,v2), (v1,v3), (v2,v3), (v3,v4), (v4,v1)}



Graphs and Networks

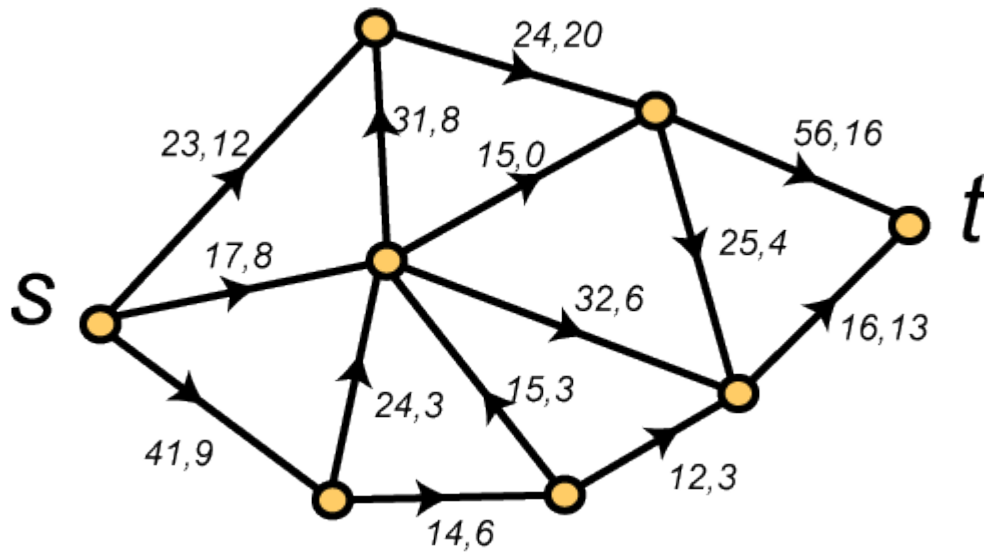
In theory (mathematics)

Graph: G=(V,E)

Network: N=(G, s, t, c)

defined by graph G with source s, sink t, and edge capacity c

(examples: electricity/power grid, water flow, metabolic flux)



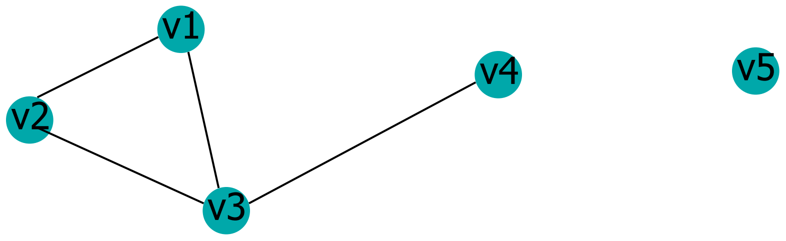
In reality (CS, engineering, economics, life and social sciences):

term network used throughout (as in this course)

Nodes in graphs

- Isolated nodes
- Degree of a node
- Connected graph
- Average degree of a graph
- Edge density: probability that any two nodes are connected
  d= ____E_ __
  (N*N-1) /2)

- Isolated node: v5
- Degree of a node:
  d(v1)=2, d(v4)=1
- Average degree of a graph:
  D = (2+2+3+1+0)/5 = 1.6
- Edge density
  d=4/(5*4/2) = 0.4



Examples: edge density

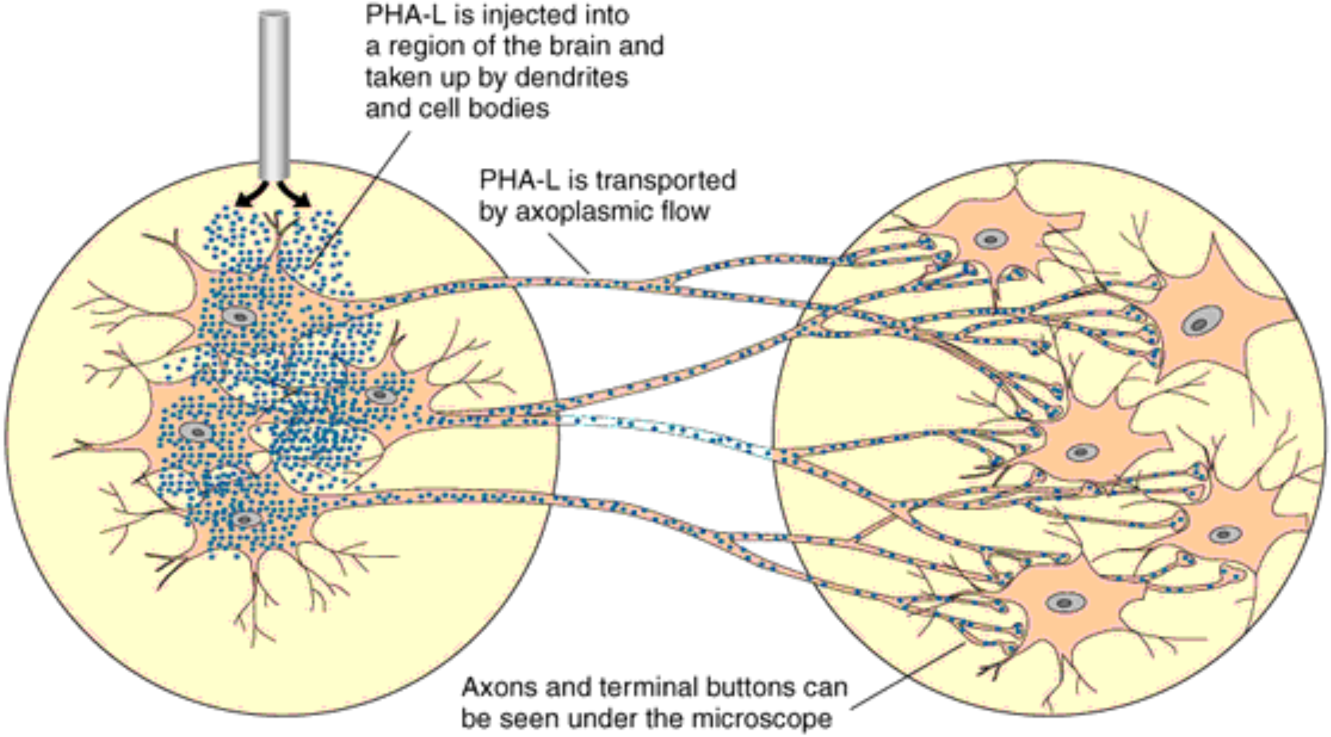
	nodes	edges	density [%]
Autobahnen	1 168	2 486	0.18
Internet	6 524	29 629	0.0696
www	325 729	1 497 135	0.0014
Power Grid	4 677	12 500	0.0572
metabolic	422	1 972	1.3
C. Elegans	202	2 540	6.3
(partial network)			
macaque	73	835	16

sparse network
(density ~ 1%)

dense network
(density > 5%)

How can the fibre tract network structure be examined?

Tract tracing with dyes*



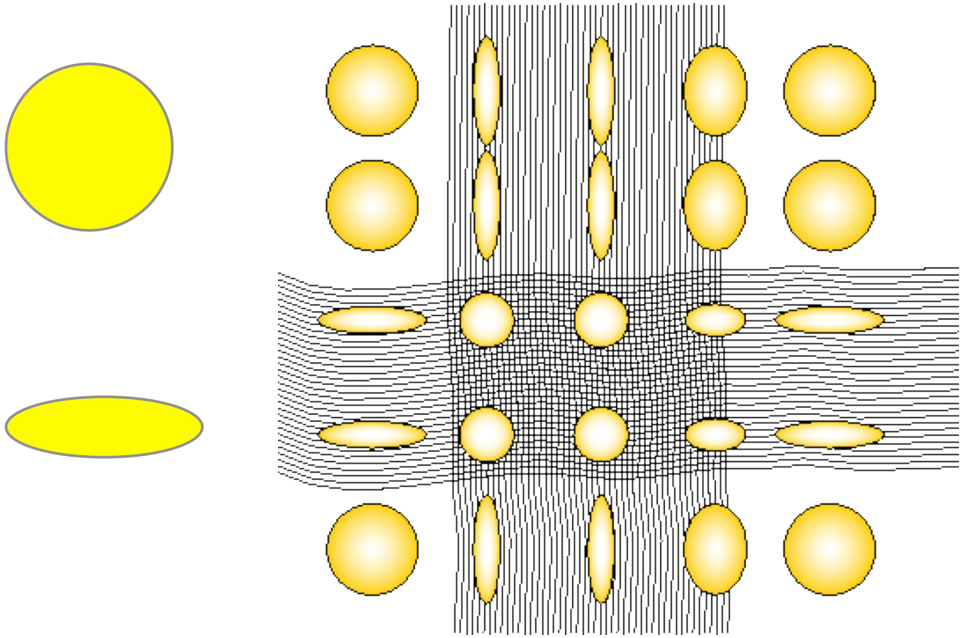
PHA-L: Phaseolus vulgaris-leucoagglutinin

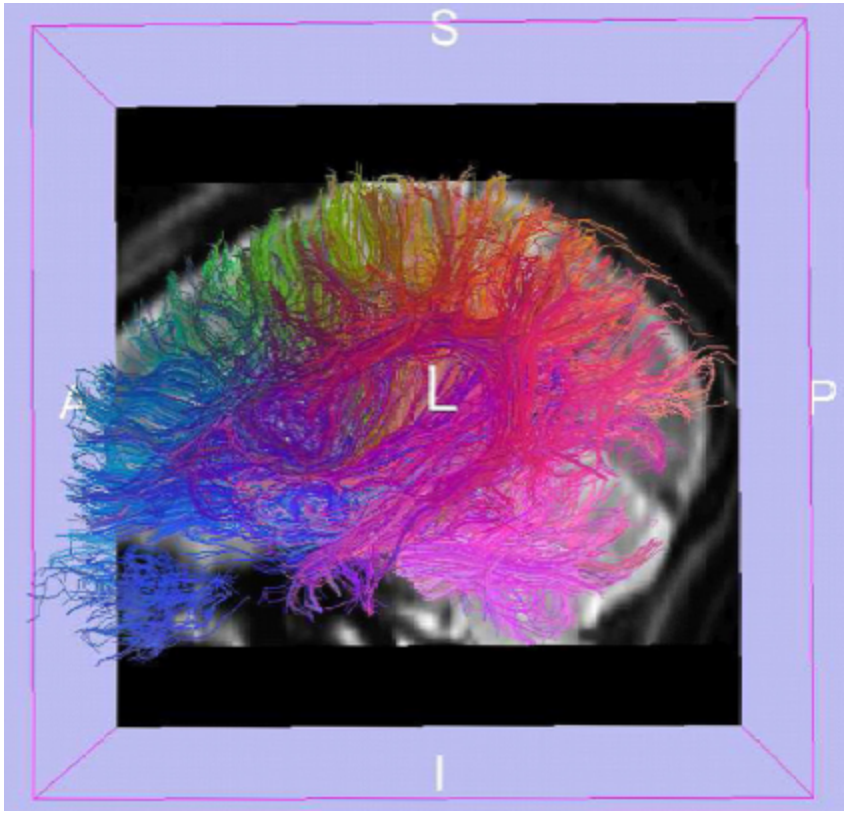
Anterograde: soma → synapse
Retrograde: soma ← synapse

* Horseradish peroxidase (HRP) method; fluorescent microspheres; Phaseolus vulgaris-leucoagglutinin (PHA-L) method; Fluoro-Gold; Cholera B-toxin; DiI; tritiated amino acids

Diffusion Tensor Imaging (DTI)

New
Est. 1994



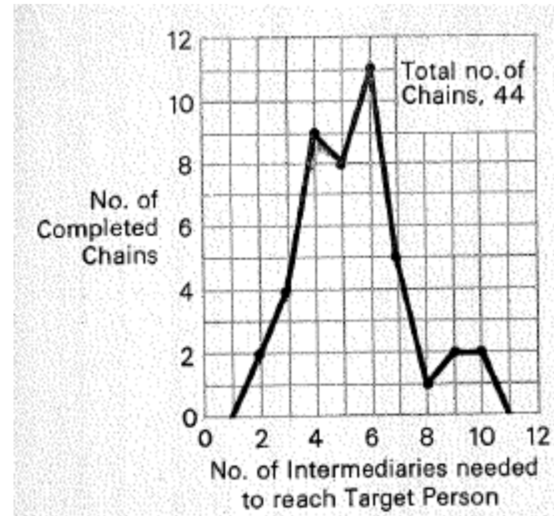


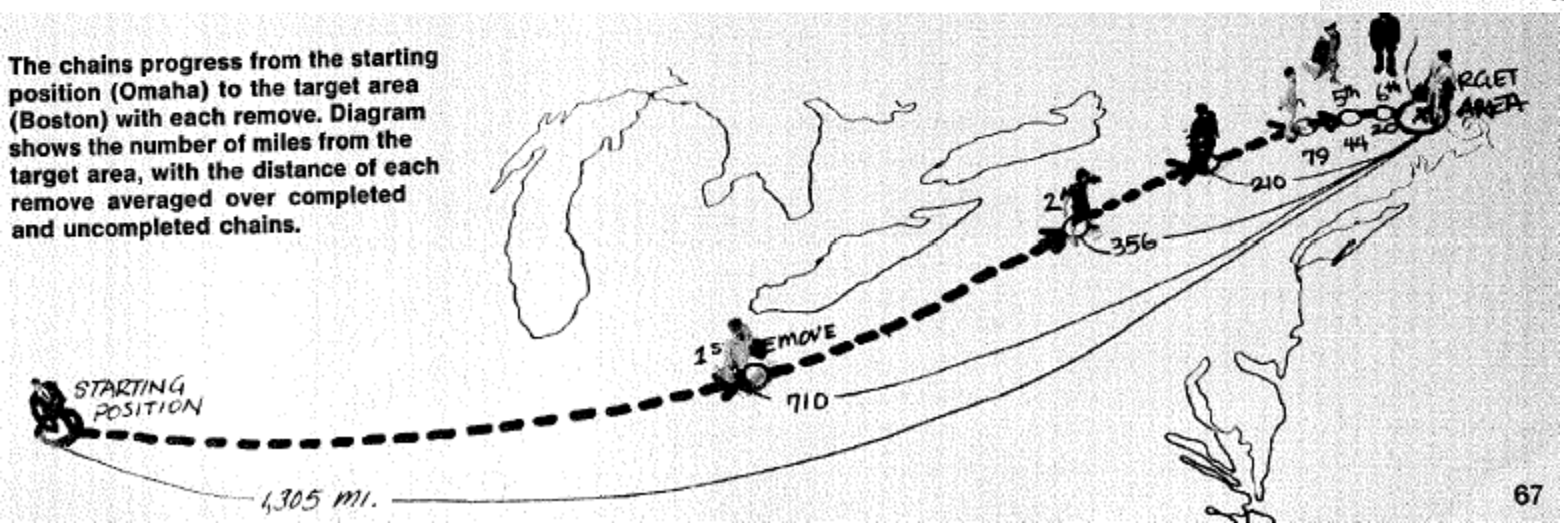
Topological network organisation

It’s a small world

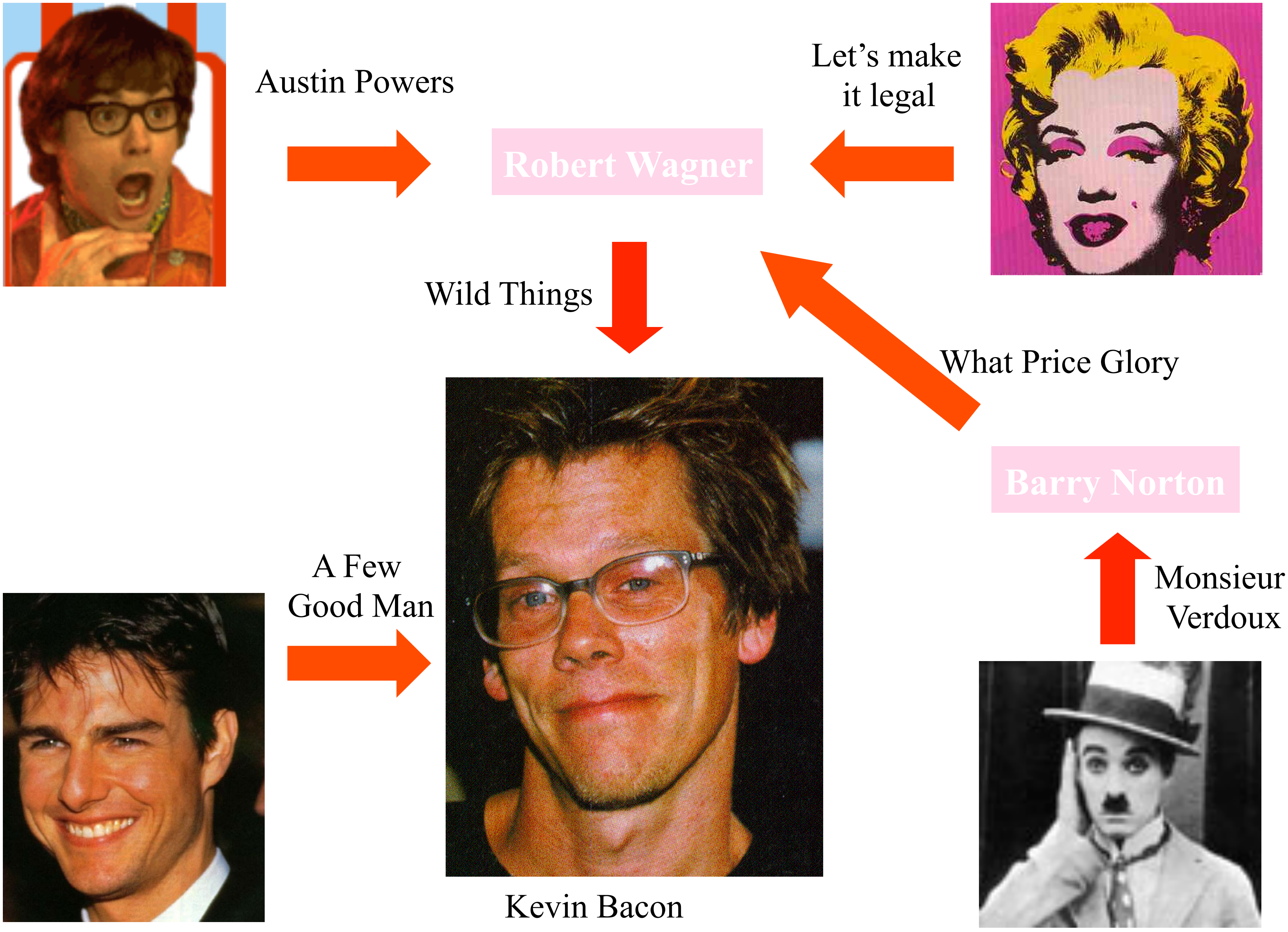
Nodes: individuals

Links: social relationship



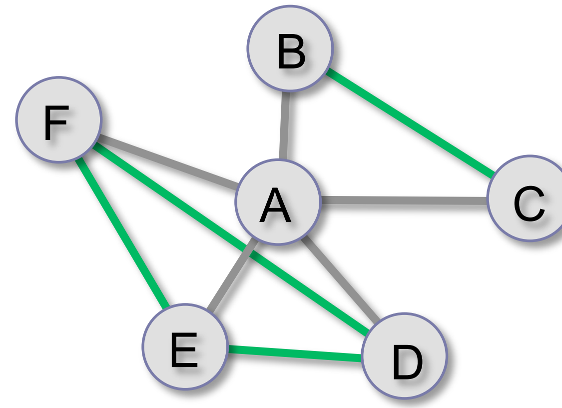


S. Milgram. *Psychology Today* (1967)


Austin Powers
Robert Wagner
Let's make it legal
Wild Things
What Price Glory
Barry Norton
A Few Good Man
Monsieur Verdoux
Kevin Bacon

Network properties

<u>Clustering coefficient</u>
Neighbours = nodes that are directly connected



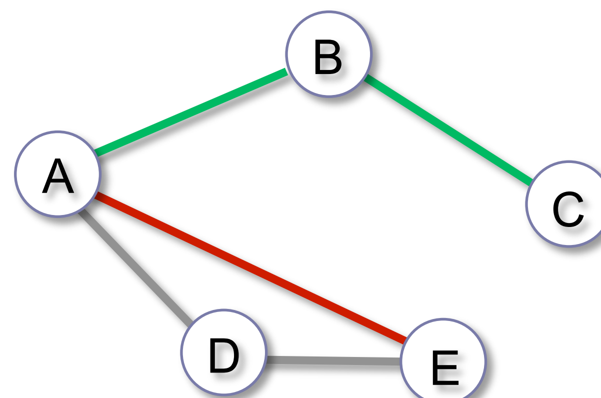
local clustering coefficient
C_{local}= average connectivity between neighbours
C_{local}=1 -> all neighbours are connected

C_A=4/10=0.4

C : global clustering coefficient (average over all nodes)

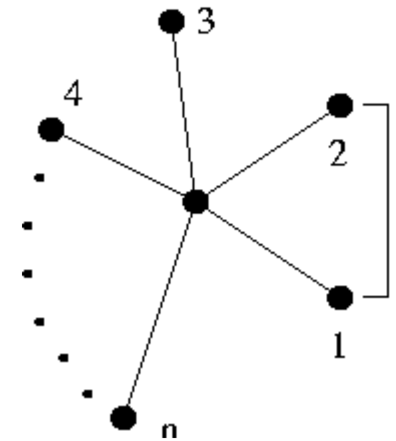
<u>Characteristic path length</u>
Shortest path between nodes *i* and *j*:
L_{ij} = minimum number of connections to cross to go from one node to the other node

Characteristic path length L = average of shortest path lengths for all pairs of nodes



Shortest path lengths:
A -> C : 2
A -> E : 1

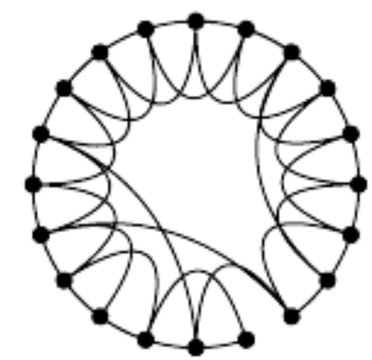
Small-world networks



Clustering coefficient is higher than in random networks

(e.g. 40% compared to 15% for the macaque monkey)

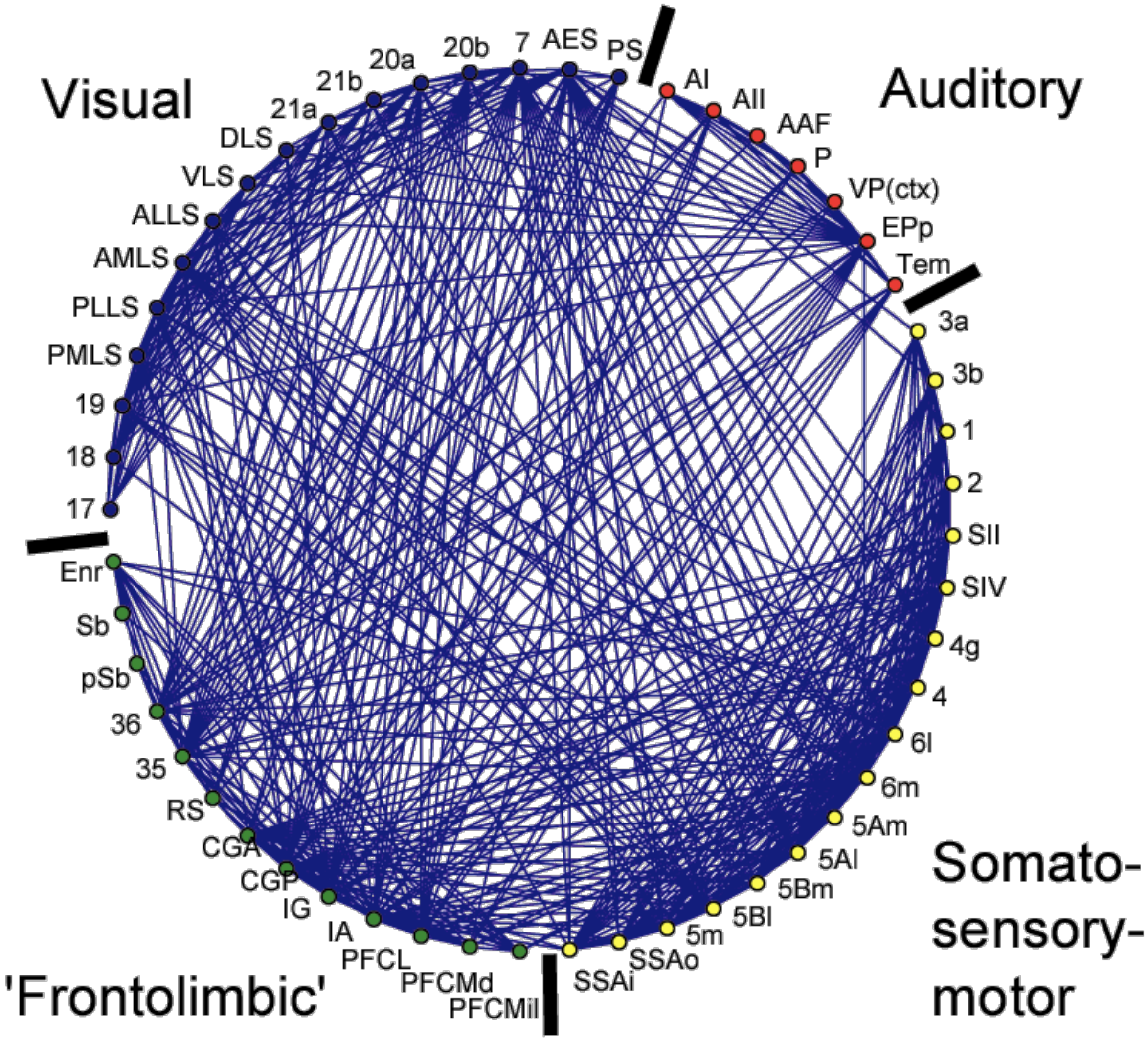
Small-world



Characteristic Path Length is comparable to random networks

Watts & Strogatz, Nature, 1998

Modular small-world connectivity



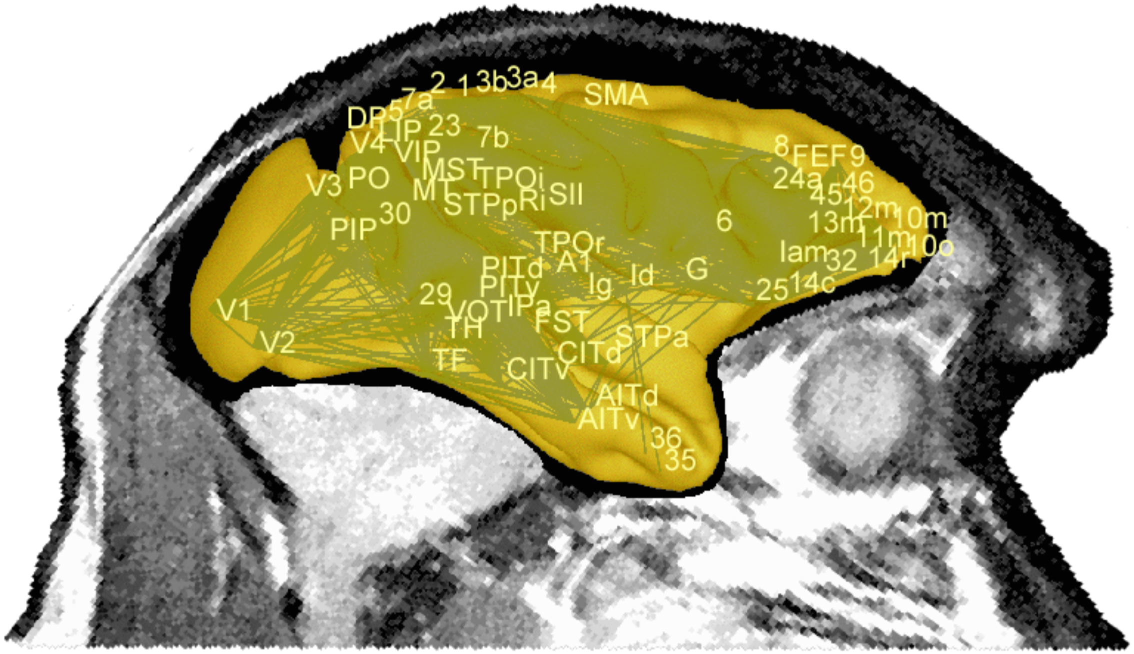
Small-world
Neighbours are well connected; short characteristic path length (~2)

Modular
Clusters: relatively more connections within the cluster than between clusters

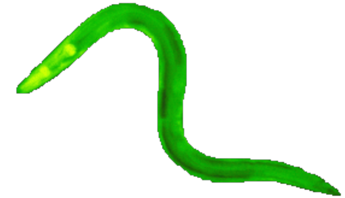
Hilgetag & Kaiser (2004) *Neuroinformatics* **2**: 353

Spatial network arrangement

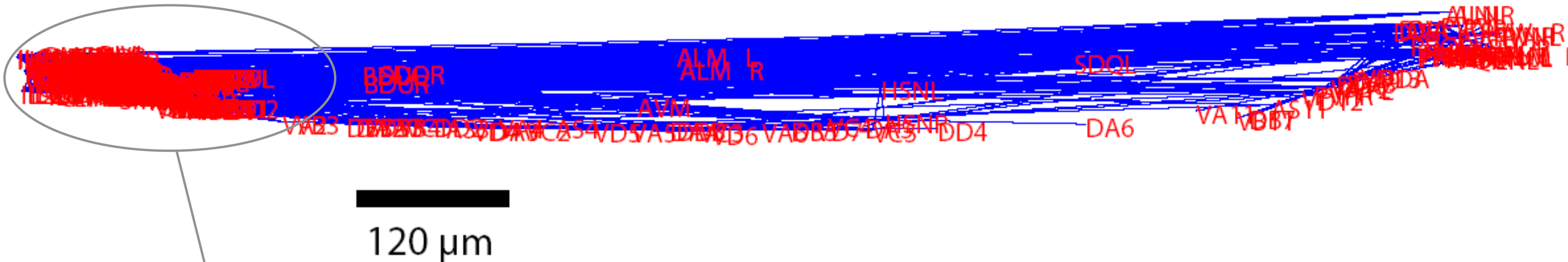
Macaque (rhesus monkey) cortical network

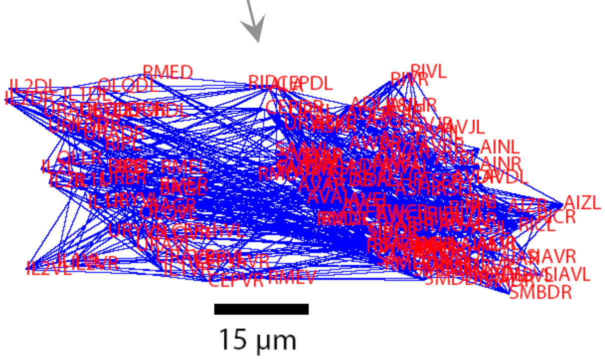


C. elegans neural network



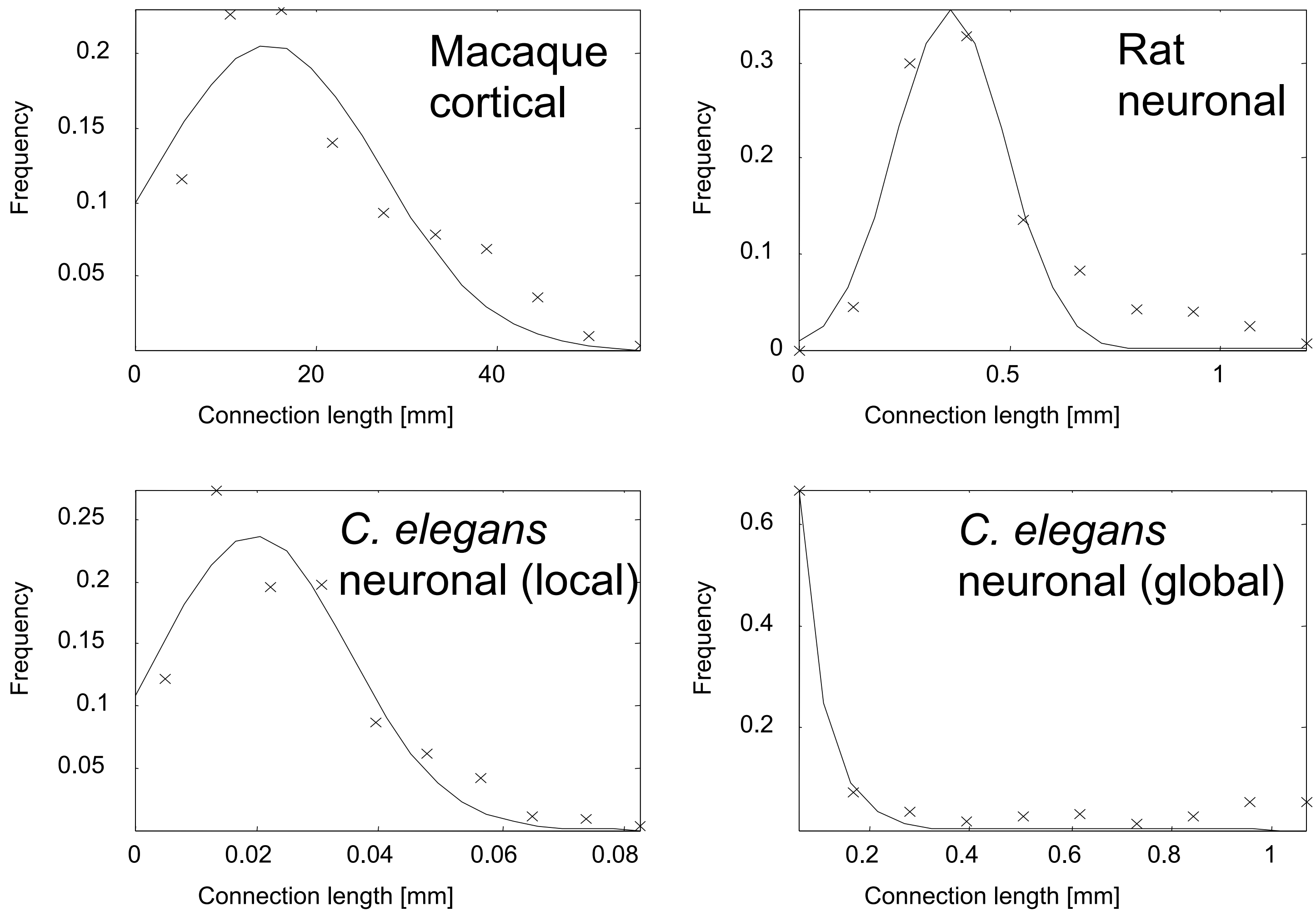
Global level (277 neurons)





Local level (131 neurons)

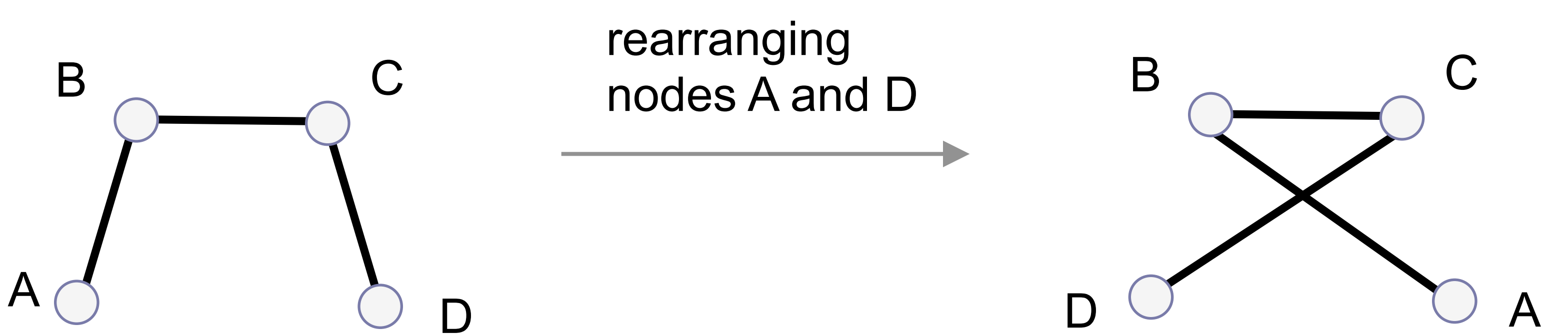
Most projections connect adjacent neurons



Kaiser et al. (2009) *Cerebral Cortex*

Reducing neural wiring costs

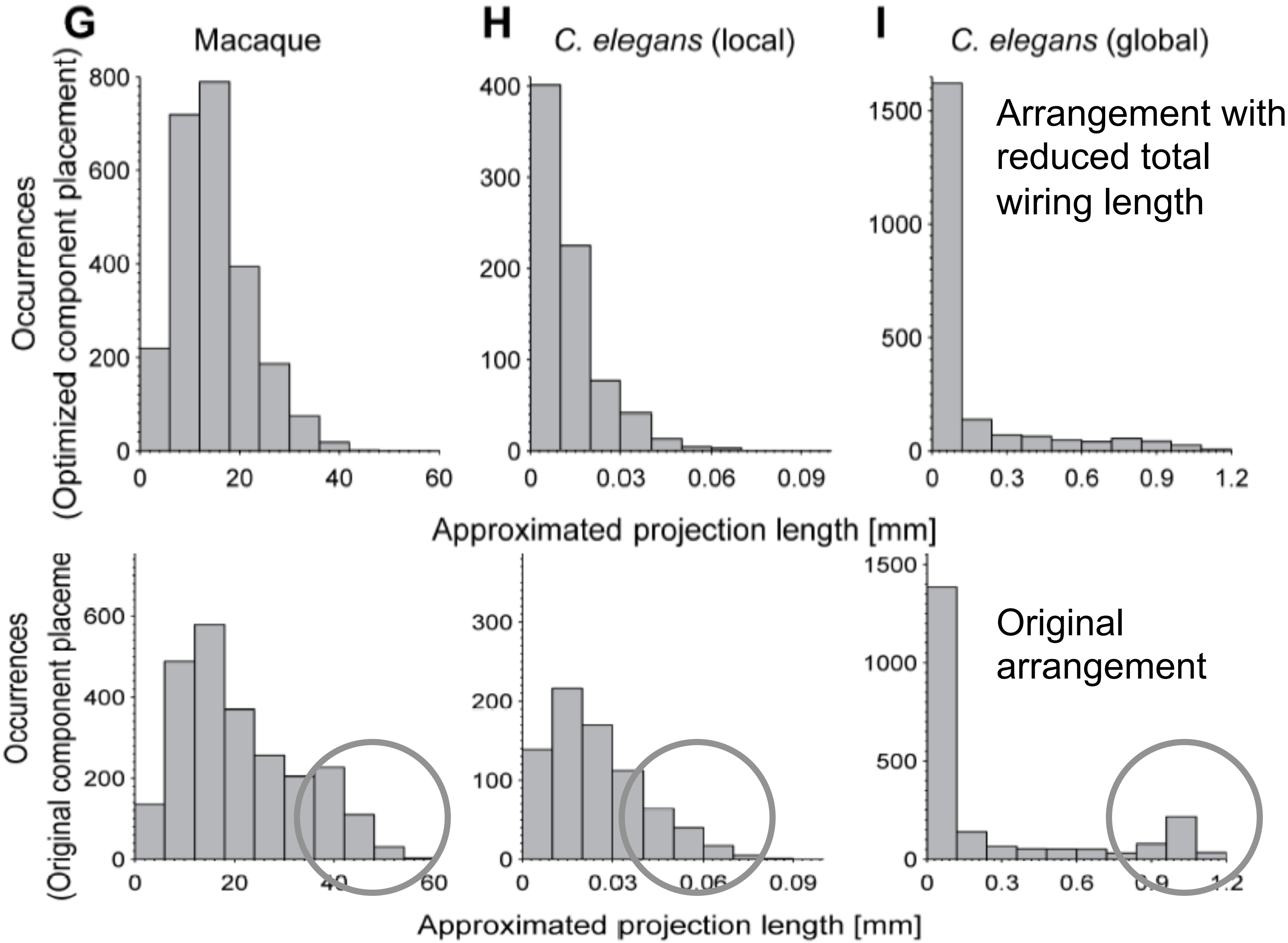
- Minimizing total wire length reduces metabolic costs for connection establishment and signal propagation
- *Component Placement Optimization, CPO*
  Every alternative arrangement of network nodes will lead to a higher total wiring length



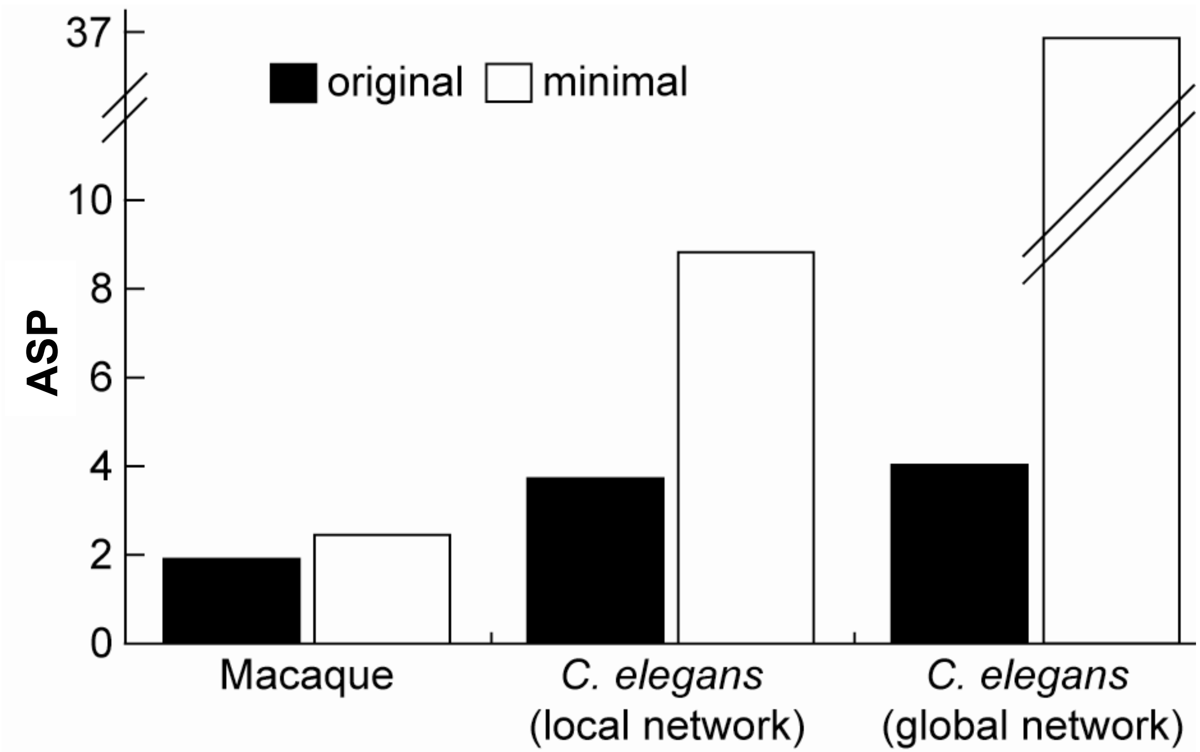
- Not the case! Reductions by 30-50% possible

Kaiser & Hilgetag (2006) *PLoS Computational Biology*, 7:e95

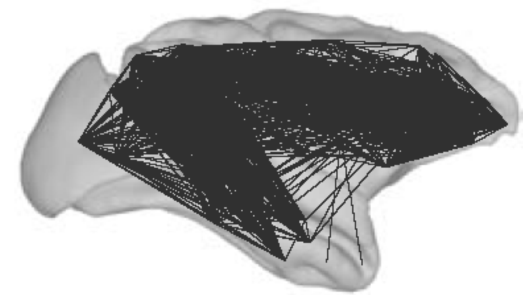
More long-distance projections than expected



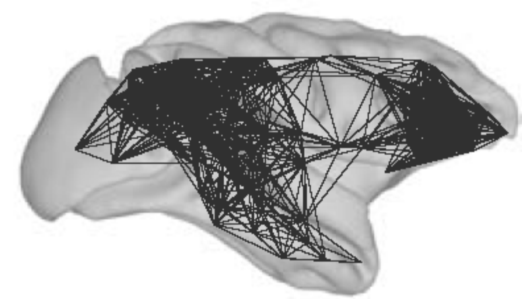
When long-distance fibers are missing (minimal):



original



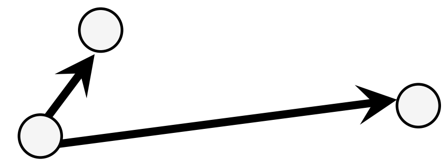
minimal



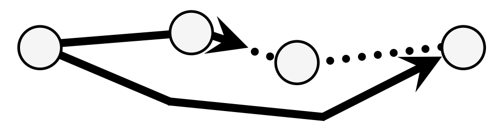
Long-distance connections are short-cuts that help to reduce the characteristic path length (or average shortets path, ASP): Less long-distance connections -> longer path lengths

Low path lengths = few intermediate processing steps are beneficial

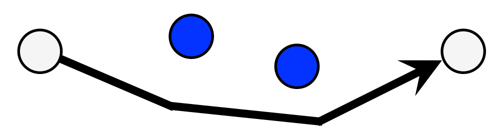
- **Synchrony of near and distant regions**



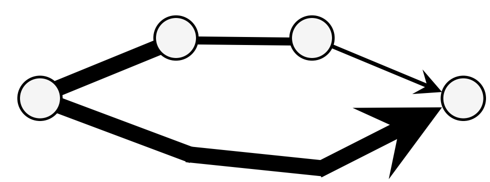
- **Reduced transmission delays**



- **Less (cross-modal) interference**

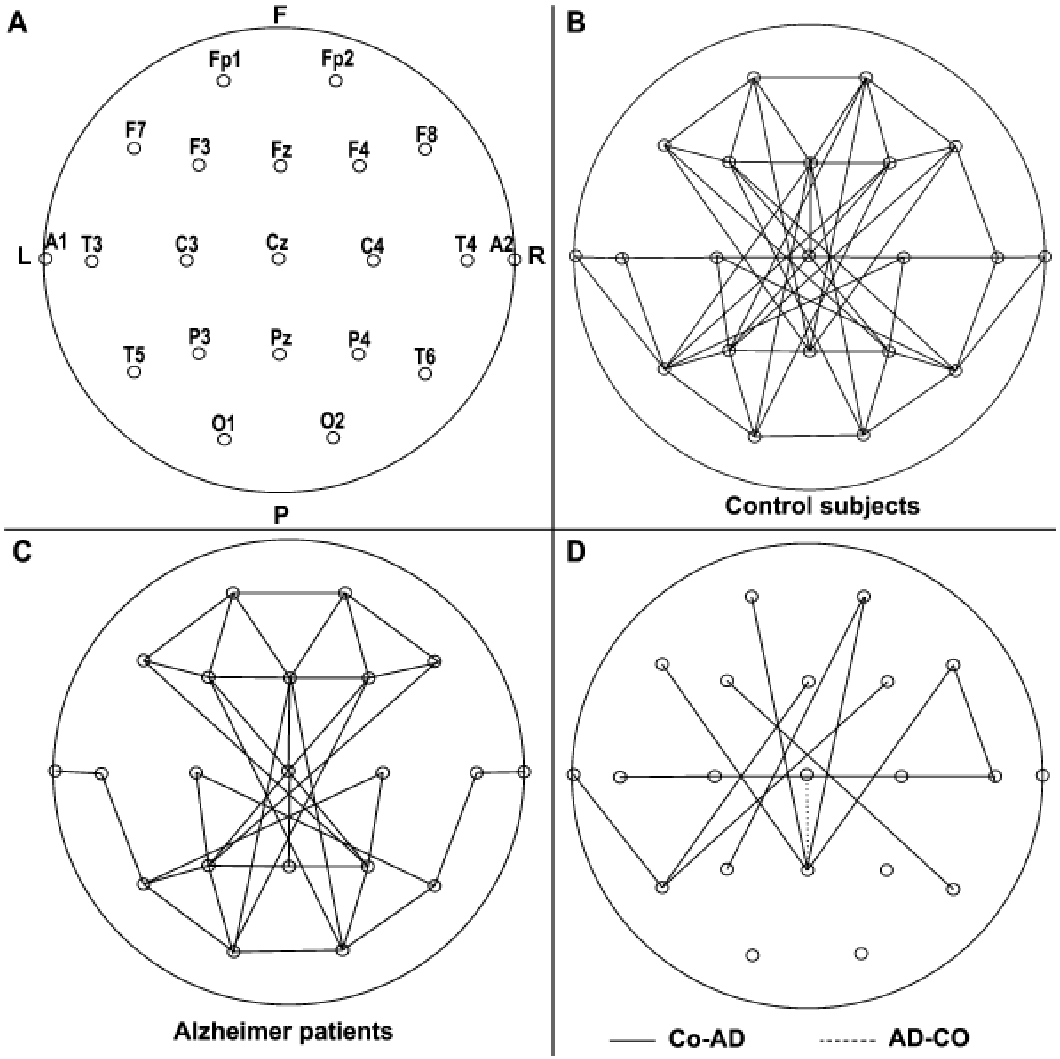


- **Higher reliability of transmission**



Linking structure and function

Small-world properties



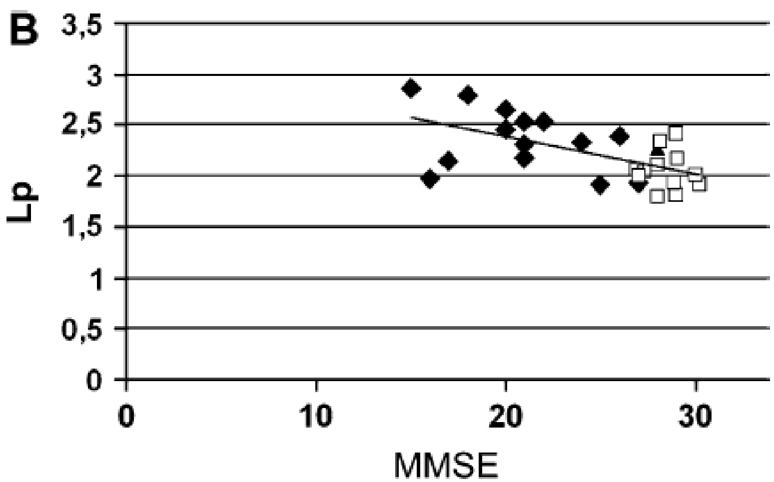
EEG synchronization Network (functional connectivity)

in Alzheimer's patients and control group

Stam et al. *Cerebral Cortex* (2007)

Alzheimer: Path length vs. task performance

Mini Mental State Examination
(attention, memory, language)

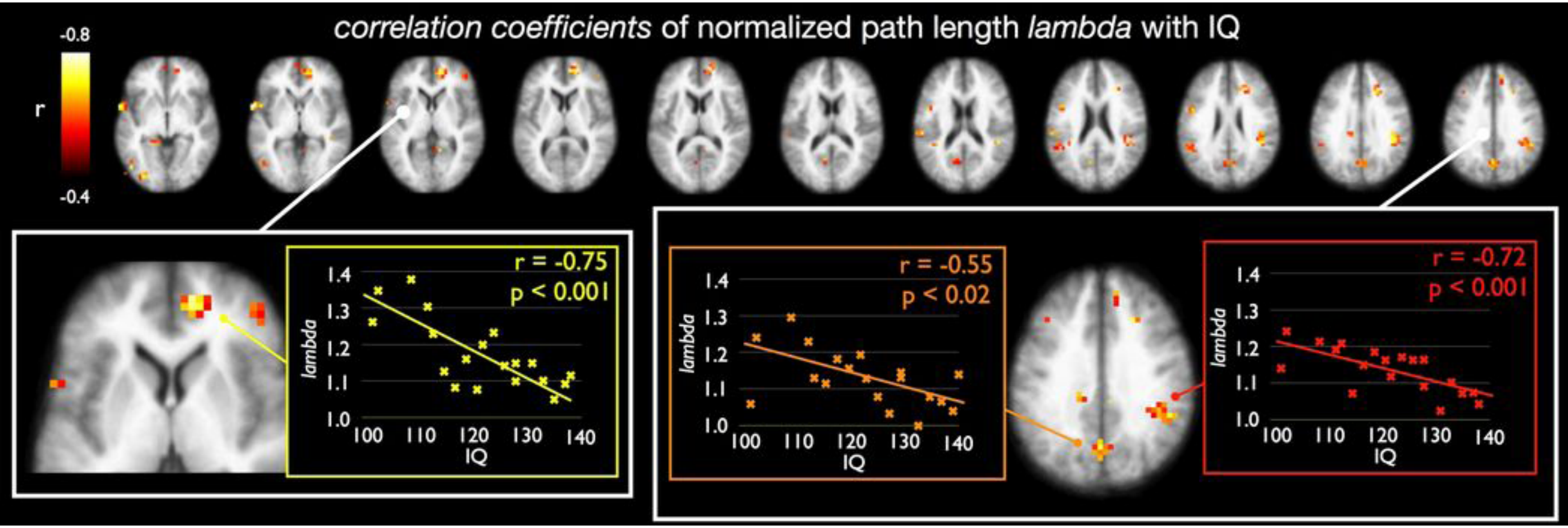


Diamonds:
Alzheimer patients

Empty squares:
Control

Cognition: Path length vs. IQ

Resting state fMRI in 19 subjects (functional connectivity based on coherence)



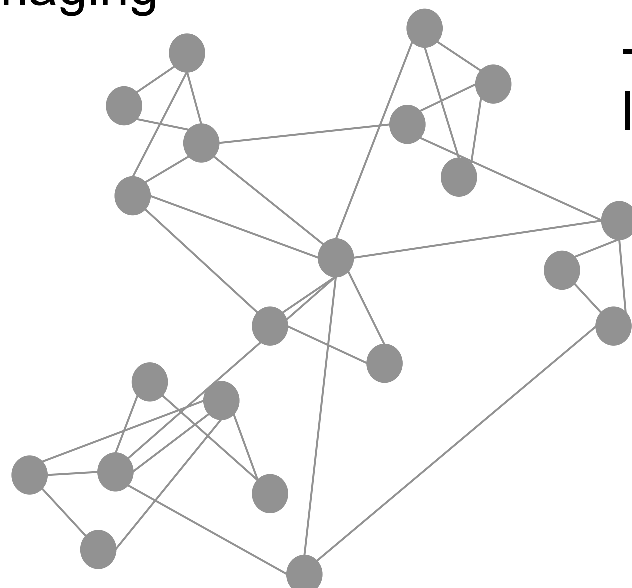
Correlations between local path length lambda (shortest path length from one node to any other node) and IQ (Intelligence Quotient) for medial prefrontal cortex, bilateral inferior parietal cortex and precuneus / posterior cingulate regions ($p < 0.05$, corrected for age).

Van den Heuvel (2009) *J. Neurosci.* 29: 7619

Summary

2. Finding structural fibre tract connectivity:
- Diffusion tensor imaging
- Tract tracing

3. Topological properties:
- multiple clusters/ modularity
- small-world: path lengths and local neighbourhood clustering

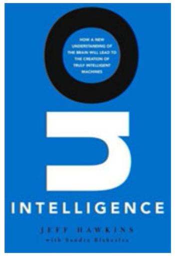


4. Spatial properties:
- Preference for connections to neighbours
- Fast processing due to long-distance connections

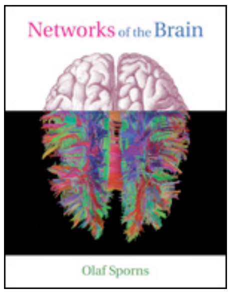
1. Types of connections:
- Structural
- Functional
- Effective

5. Linking structure and function:
- Alzheimer's disease: path lengths
- IQ: path lengths

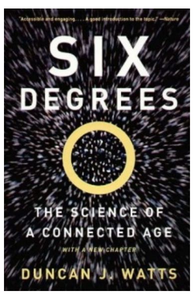
Further readings



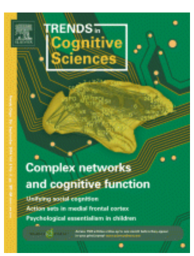
Jeff Hawkins with Sandra Blakeslee. *On Intelligence*. Henry Holt and Company, 2004



Olaf Sporns. *Networks of the Brain*. MIT Press, 2010



Duncan J. Watts. *Six Degrees: The Science of a Connected Age*. Norton & Company, 2004



Sporns, Chialvo, Kaiser, Hilgetag. Trends in Cognitive Sciences (September 2004) www.dynamic-connectome.org

Kaiser, Neuroimage, 2011