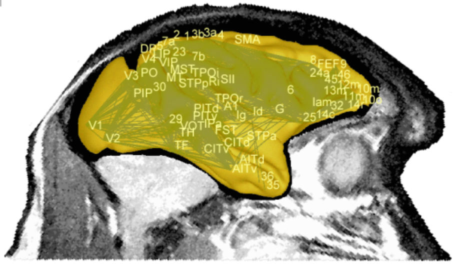

A Tutorial in Connectome Analysis (I): Topological and Spatial Features of Brain Networks

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http://www.biological-networks.org

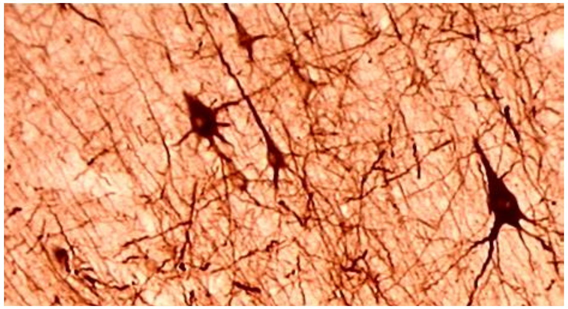
Outline

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

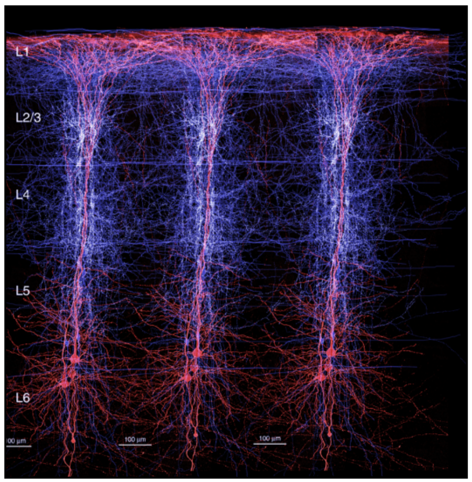
- Topological network organisation

What are neural networks?

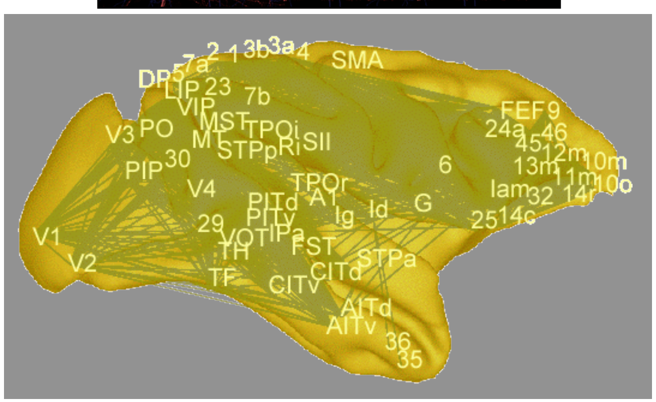
Levels of connectivity



Axons between neurons



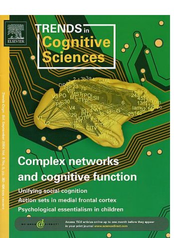
Links between cortical columns



Fibre tracts between brain areas

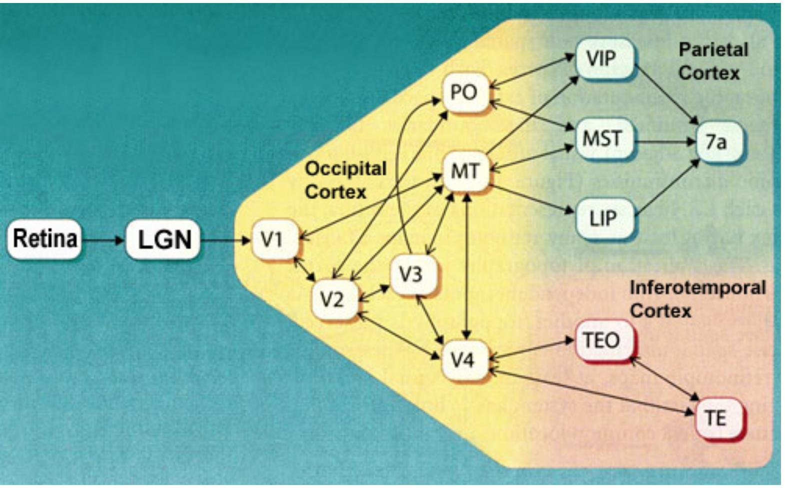
Types of connectivity

- 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

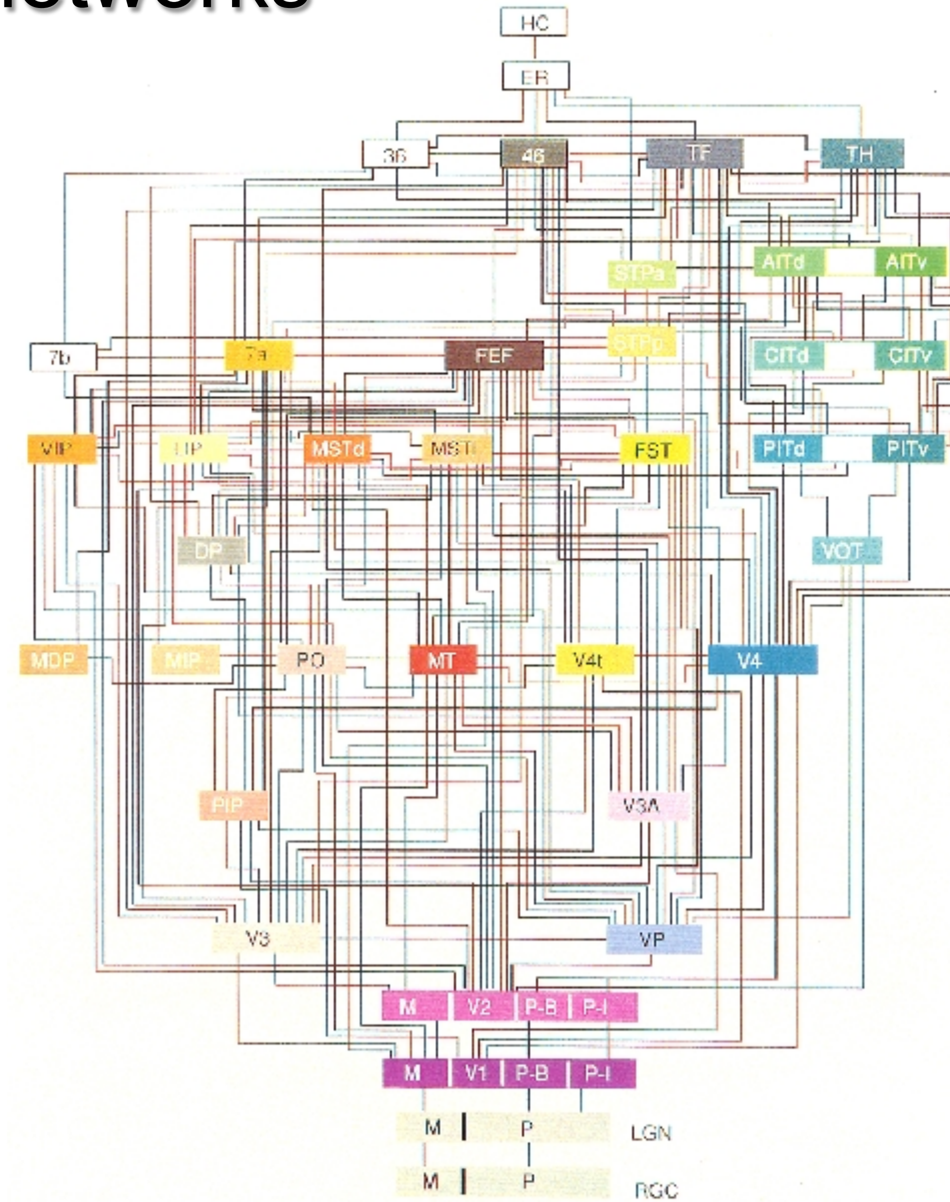


Sporns, Chialvo, Kaiser, Hilgetag. Trends in Cognitive Sciences, 2004

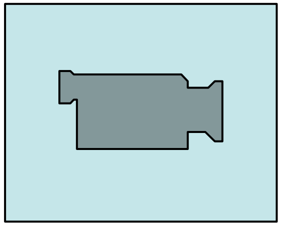
Cortical networks



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

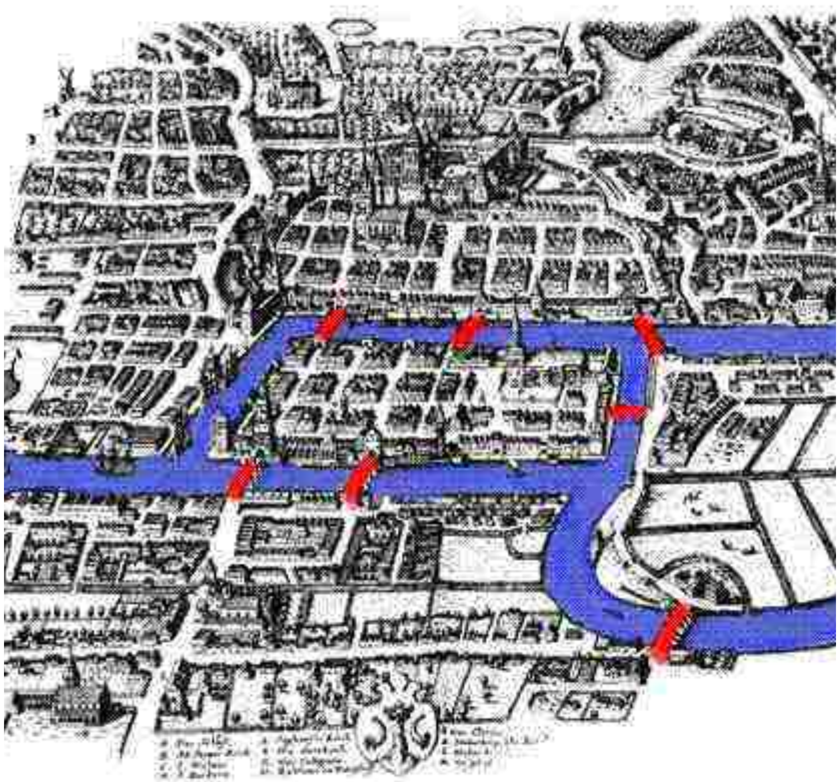
Modelling of SARS spreading over the airline network
(Hufnagel, *PNAS*, 2004)

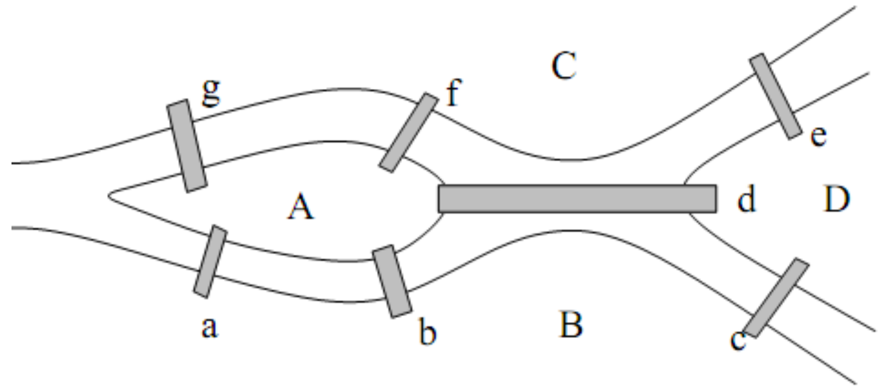
Identity and Search in Social Networks
(Watts et al., *Science*, 2002)

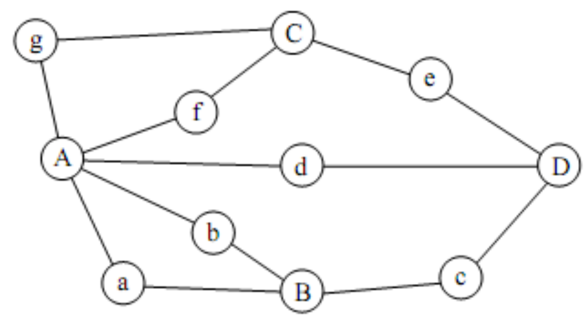
The Large-Scale Organization of Metabolic Networks.
(Jeong et al., *Nature*, 2000)

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

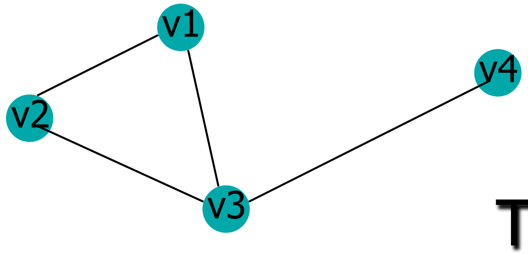
Graphs

- 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},

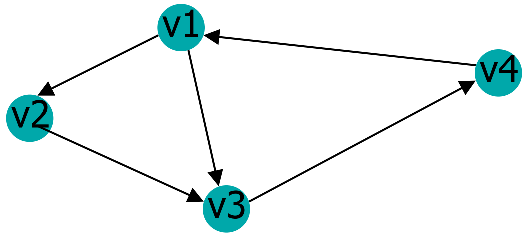
  E={(v1,v2), (v1,v3), (v2,v3), (v3,v4)}



Topology

Directed graphs (Digraphs)

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



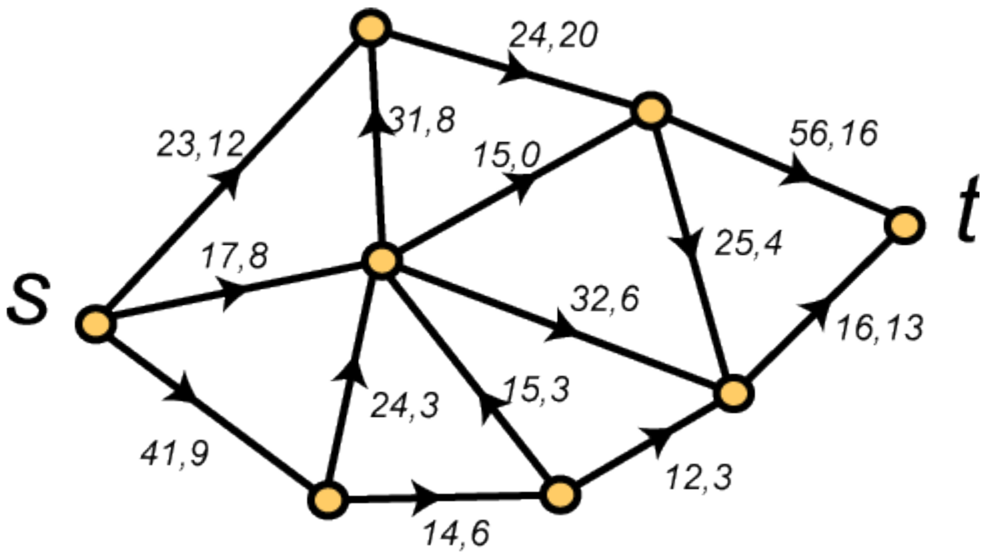
Graphs and Networks

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)

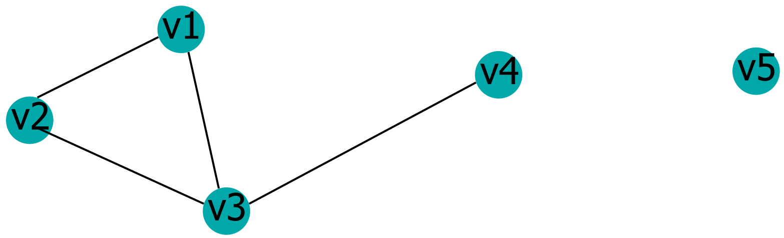


In reality (CS, engineering, economics, life and social sciences):
term network used throughout (as in this course)

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
  $$d = \frac{E}{(N*N-1)/2)}$$

- Isolated node: v5
- Degree of a node:
  d(v1)=2, d(v4)=1
- Average degree of a graph:
  D = (2+2+2+1+0)/5 = 1.4
- Edge density
  d=4/(5*4/2) = 0.4



Examples: edge density

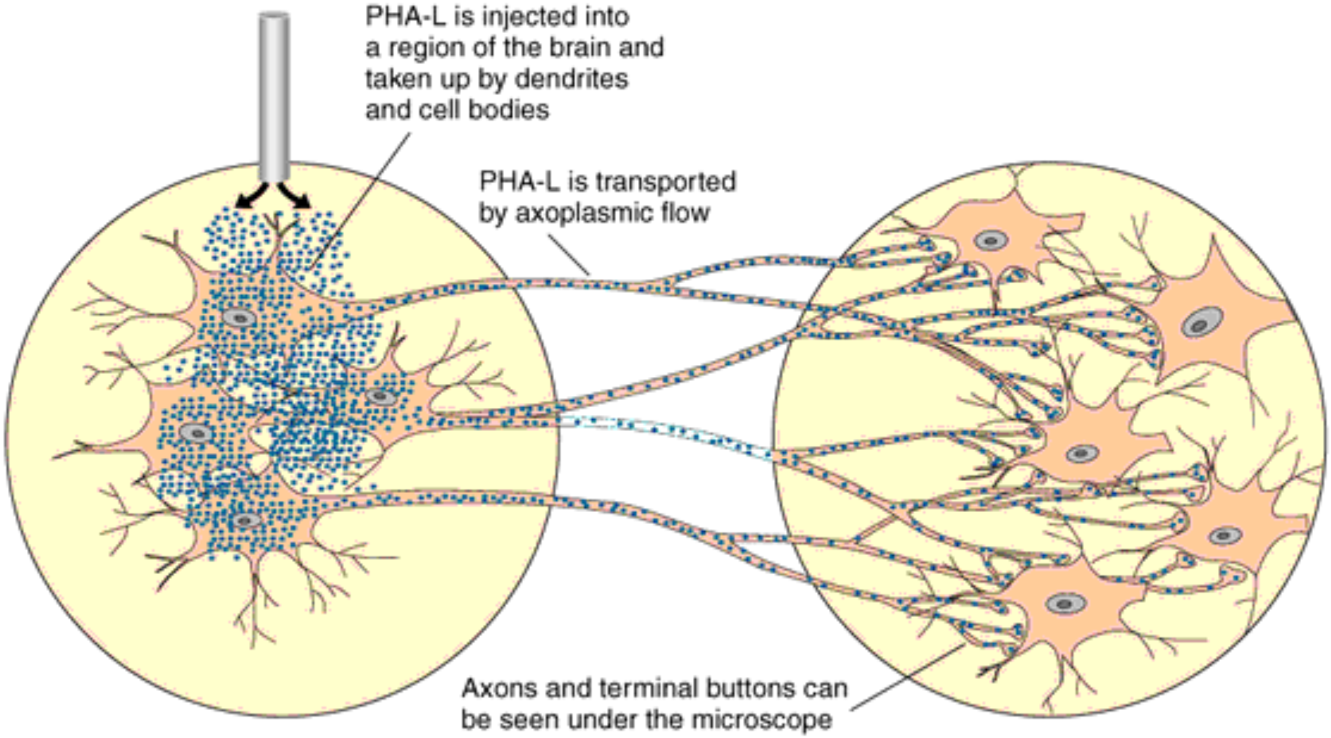
	nodes	edges	density [%]
Autobahnen	1 168	2 486	0.18
Internet	6 524	29 629	0.0696
www	325 729	1 497 135	0.0014
Power Grid	4 677	12 500	0.0572
metabolic	422	1 972	1.3
C. Elegans	202	2 540	6.3
(partial network)			
macaque	73	835	16

sparse network
(density ~ 1%)

dense network
(density > 5%)

How can the fibre tract network structure be examined?

Tract tracing with dyes*



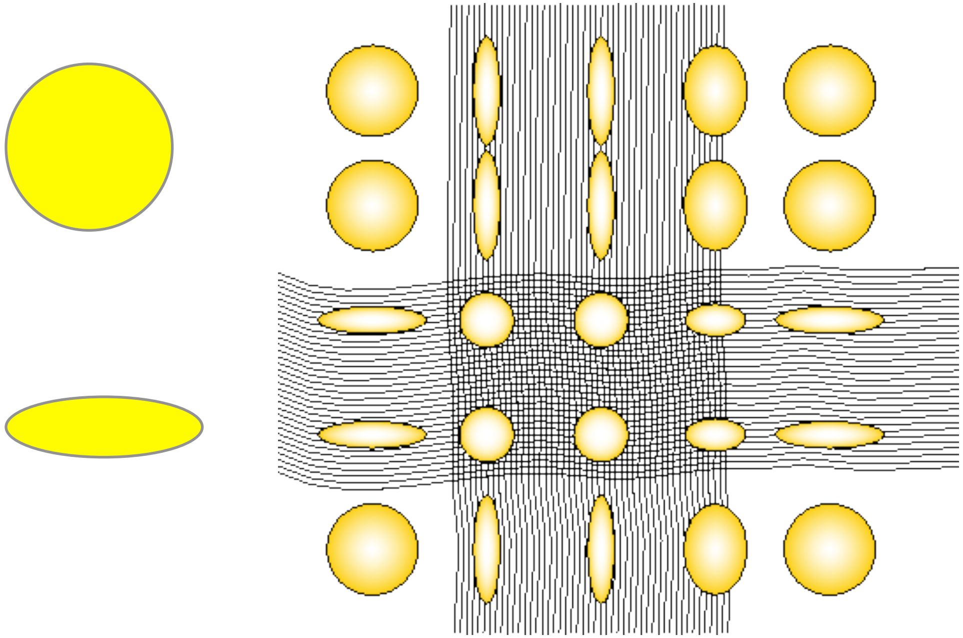
PHA-L: Phaseolus vulgaris-leucoagglutinin

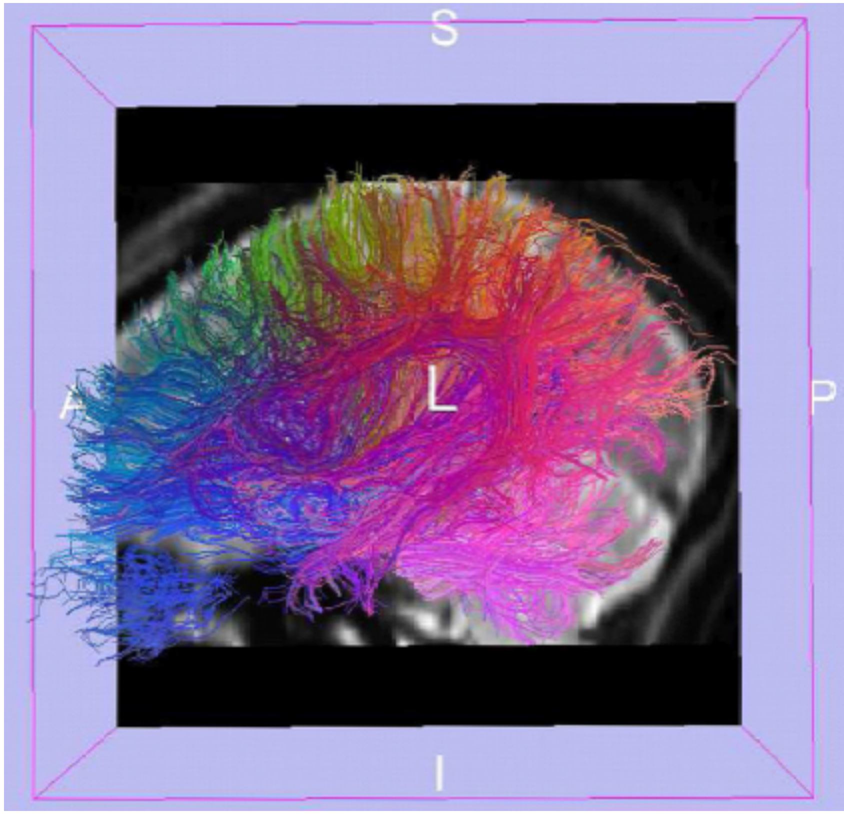
Anterograde: soma → synapse
Retrograde: soma ← synapse

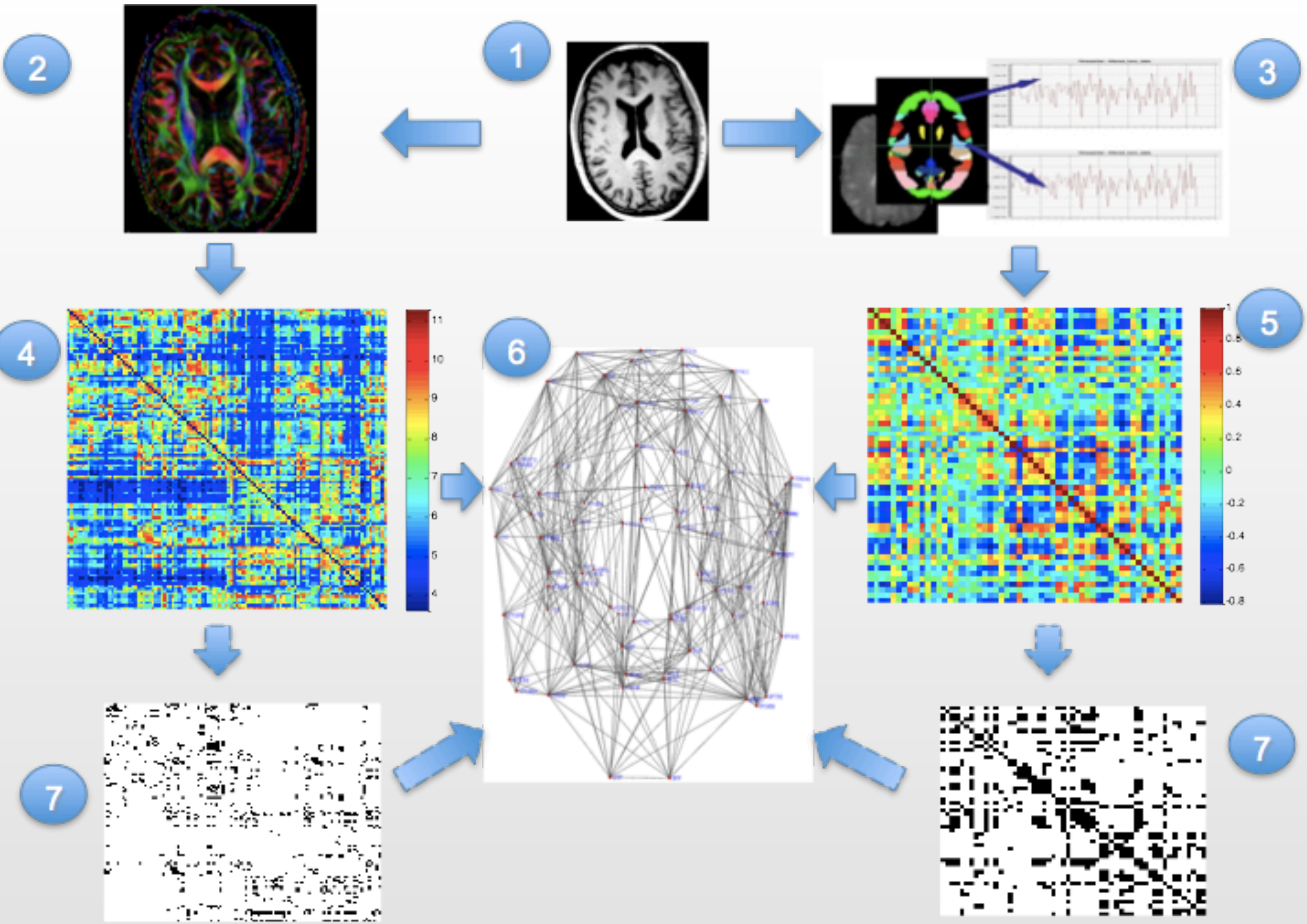
* Horseradish peroxidase (HRP) method; fluorescent microspheres; Phaseolus vulgaris-leucoagglutinin (PHA-L) method; Fluoro-Gold; Cholera B-toxin; DiI; tritiated amino acids

Diffusion Tensor Imaging (DTI)

New
Est. 1994

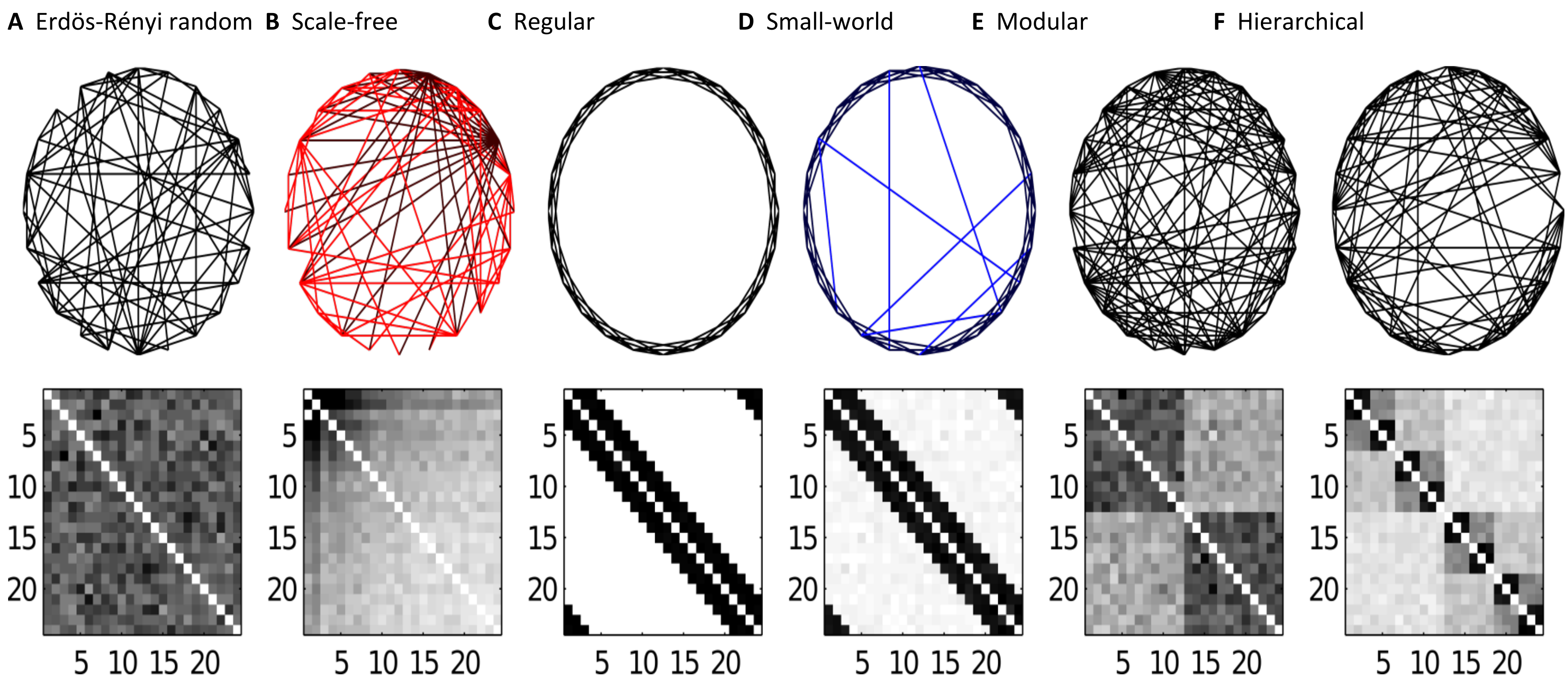





1
2
3
4
5
6
7
7
11
10
9
8
7
6
5
4
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8

Topological network organisation

Archetypes of complex networks



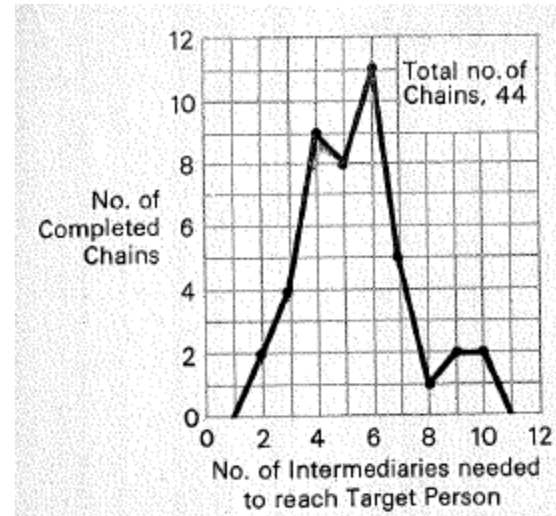
Note: real complex networks show a *combination* of these types!

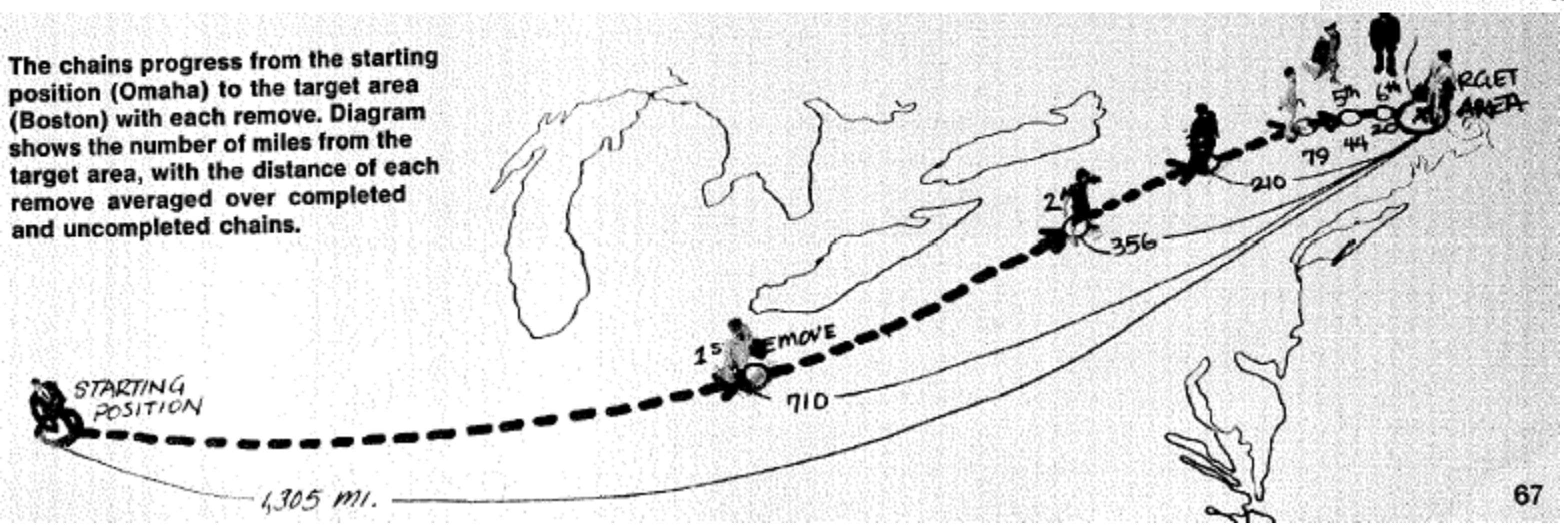
Kaiser (2011) *Neuroimage*

It's a small world

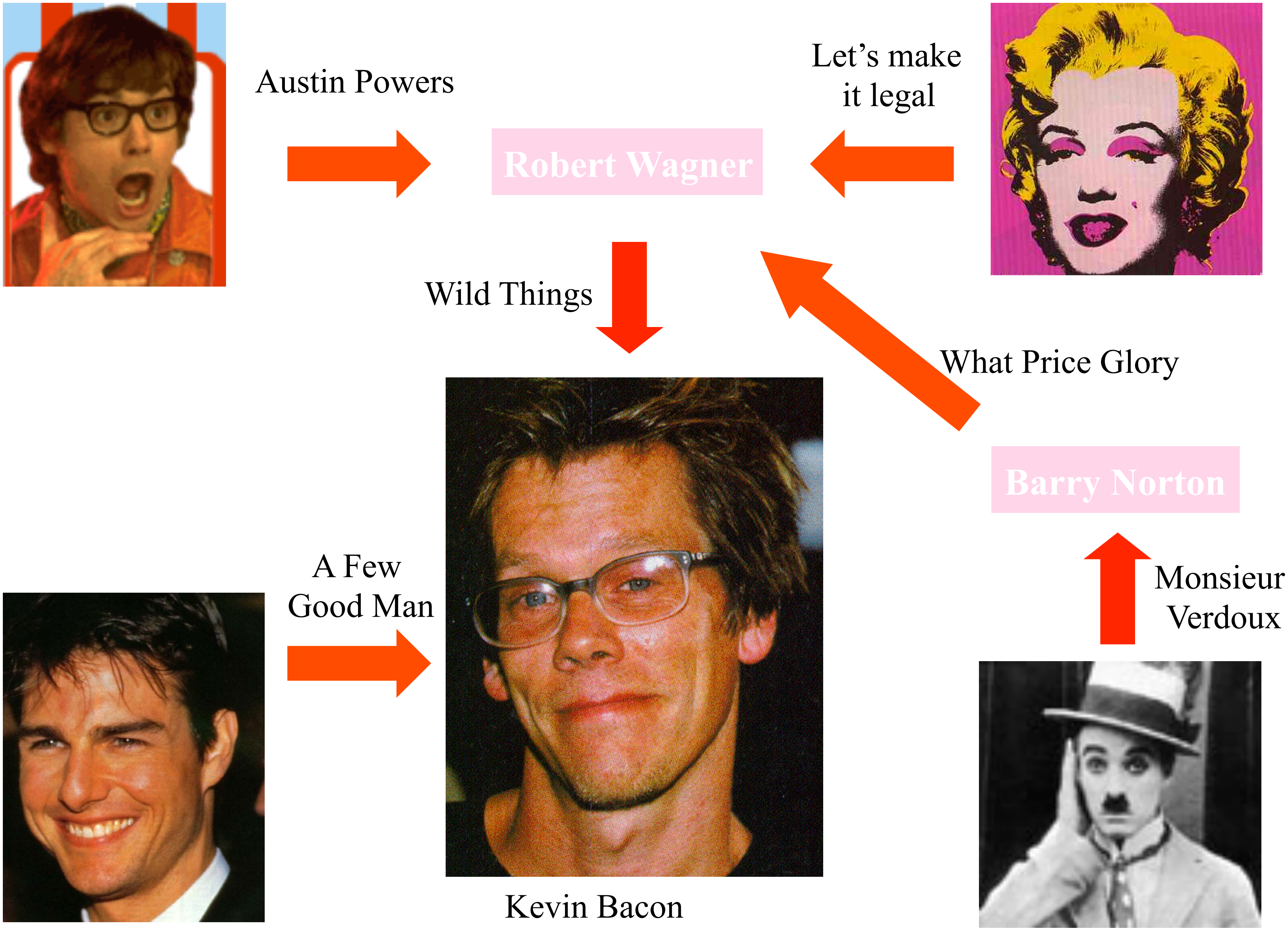
Nodes: individuals

Links: social relationship





S. Milgram. *Psychology Today* (1967)

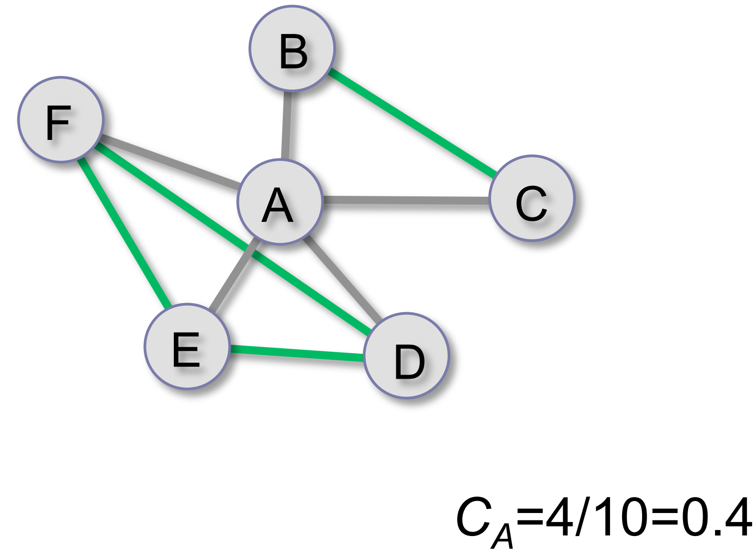

Austin Powers
Let's make it legal
Robert Wagner
Wild Things
What Price Glory
Barry Norton
A Few Good Man
Monsieur Verdoux
Kevin Bacon

Network properties

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

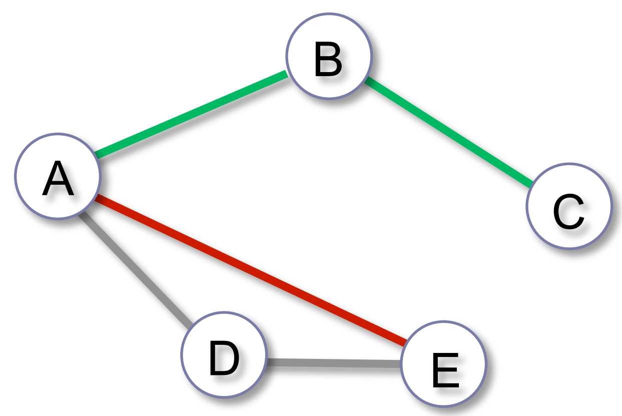
local clustering coefficient
C_{local}= average connectivity between neighbours
C_{local}=1 -> all neighbours are connected

C : global clustering coefficient (average over all nodes)



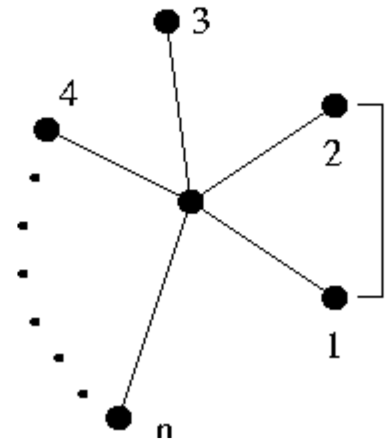
<u>Characteristic path length</u>
Shortest path between nodes *i* and *j*:
L_{ij} = minimum number of connections to cross to go from one node to the other node

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



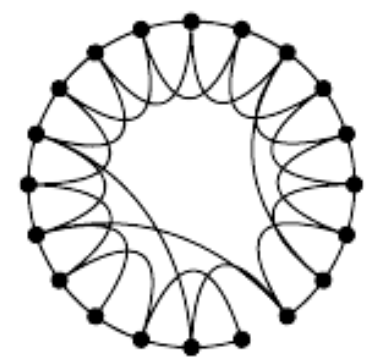
Shortest path lengths:
A -> C : 2
A -> E : 1

Small-world networks



Clustering coefficient is higher than in random networks

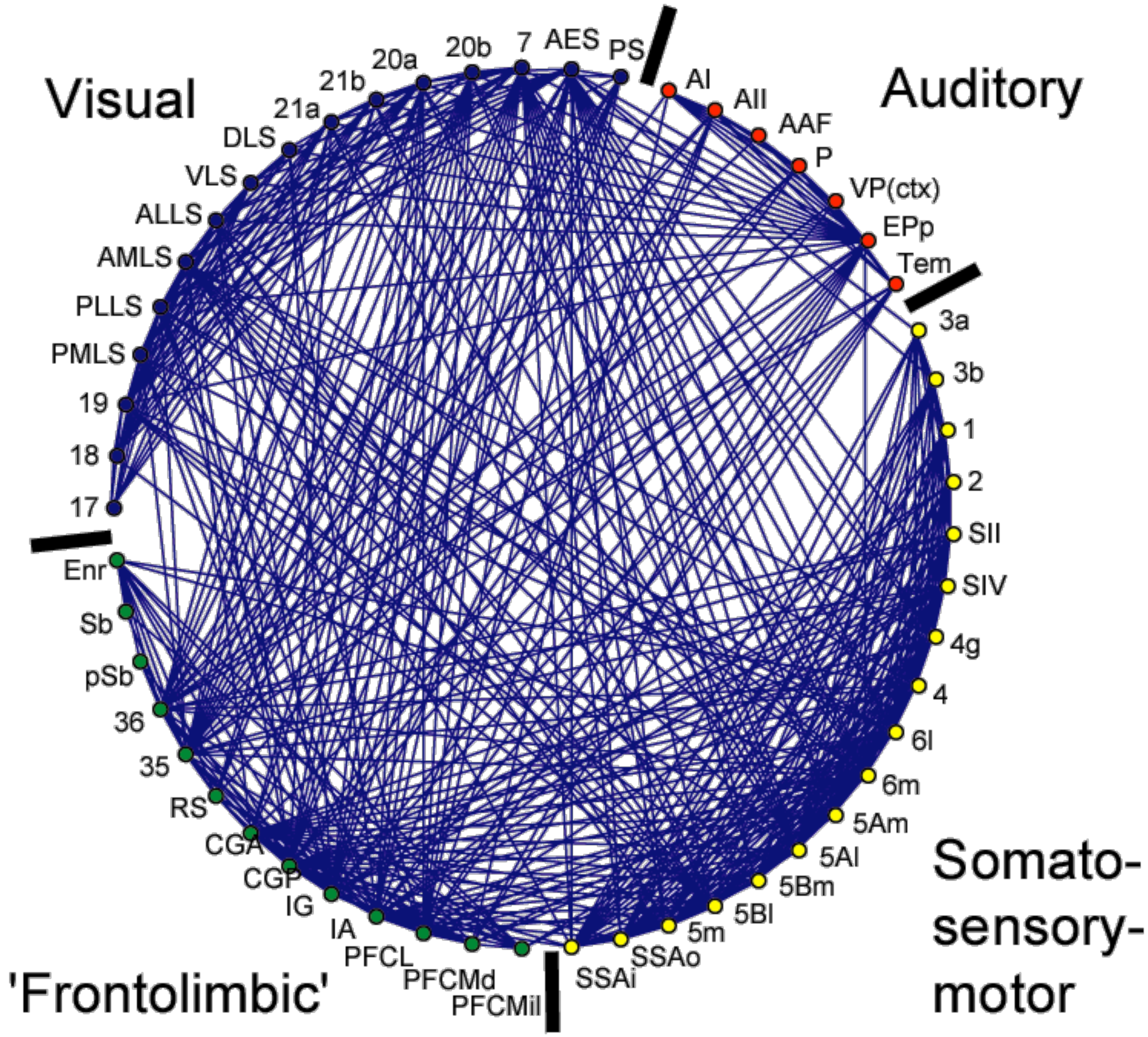
(e.g. 40% compared to 15% for the macaque monkey)



Characteristic Path Length is comparable to random networks

Watts & Strogatz, Nature, 1998

Modular small-world connectivity



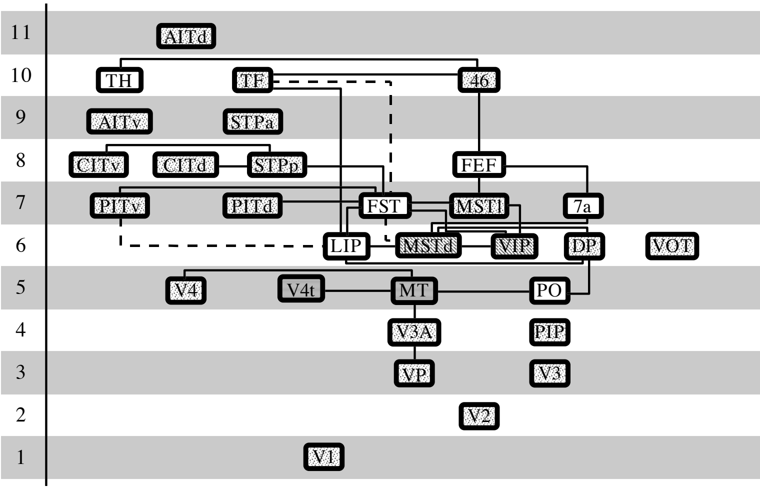
<u>Small-world</u>
Neighbours are well connected; short characteristic path length (~2)

<u>Modular</u>
Clusters: relatively more connections within the cluster than between clusters

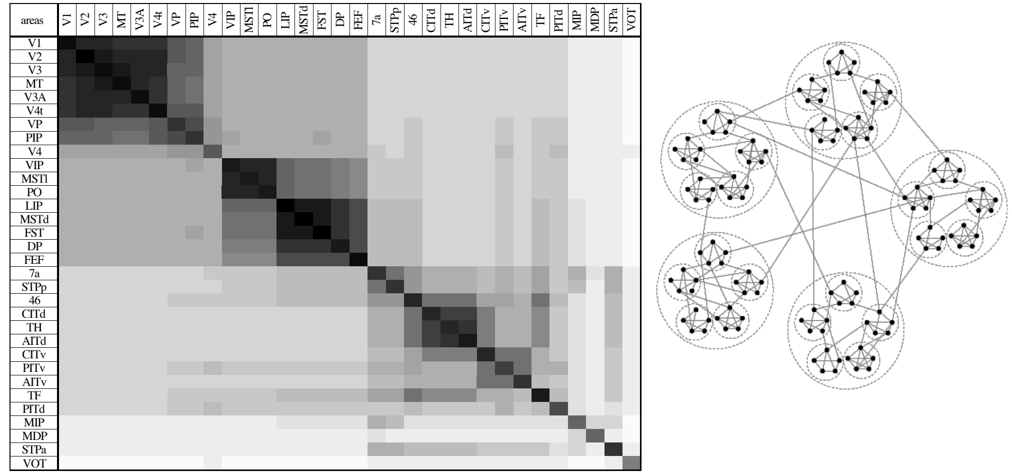
Hilgetag & Kaiser (2004) *Neuroinformatics* **2**: 353

Hierarchy

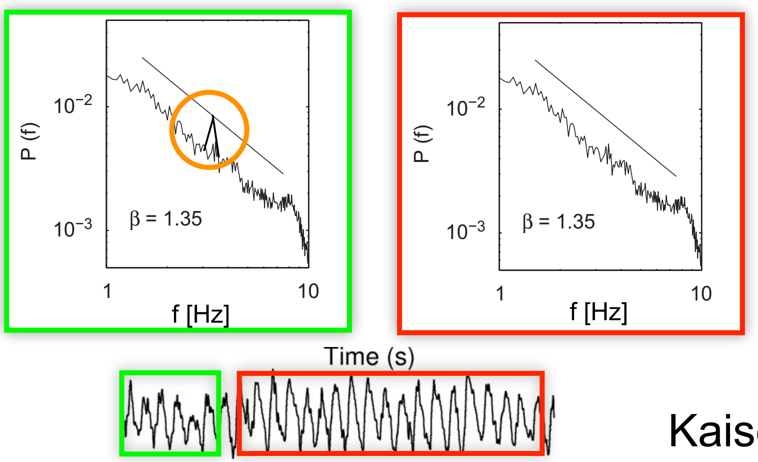
Sequential



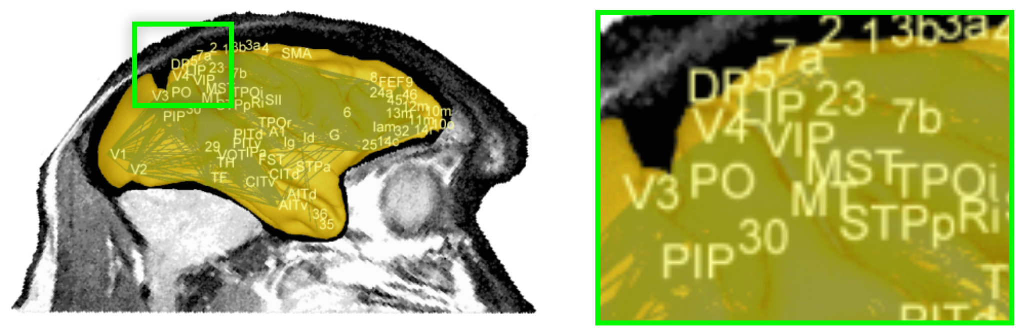
Topological



Temporal



Spatial

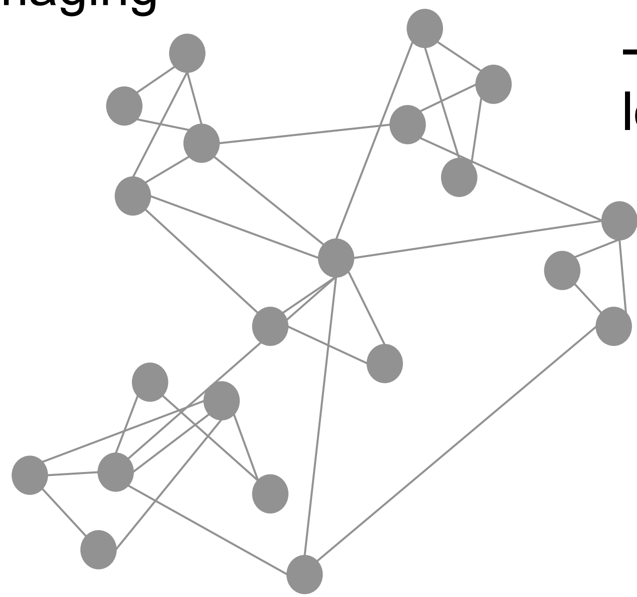


Kaiser et al. (2010) *Frontiers in Neuroinformatics*
Hilgetag & Kaiser *PLoS Comput. Biol.* (in preparation)

Summary

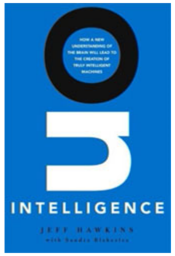
2. Finding structural fibre tract connectivity:
- Diffusion tensor imaging
- Tract tracing

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

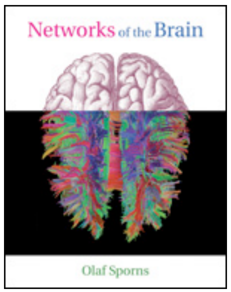


1. Types of connections:
- Structural
- Functional
- Effective

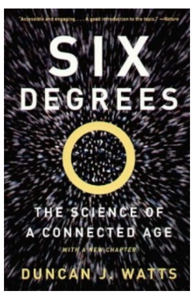
Further readings



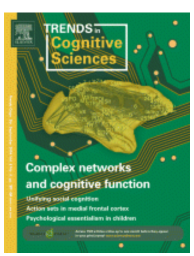
Jeff Hawkins with Sandra Blakeslee. *On Intelligence*. Henry Holt and Company, 2004



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.biological-networks.org