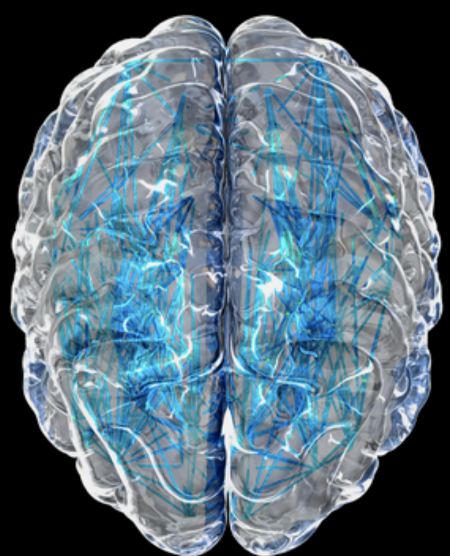
A Tutorial in Connectome Analysis (I): Topological and Spatial Features of Brain Networks



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United Kingdom

http://www.dynamic-connectome.org

http://neuroinformatics.ncl.ac.uk/

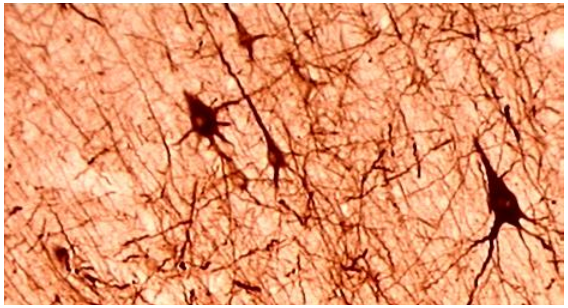
@ConnectomeLab

Outline

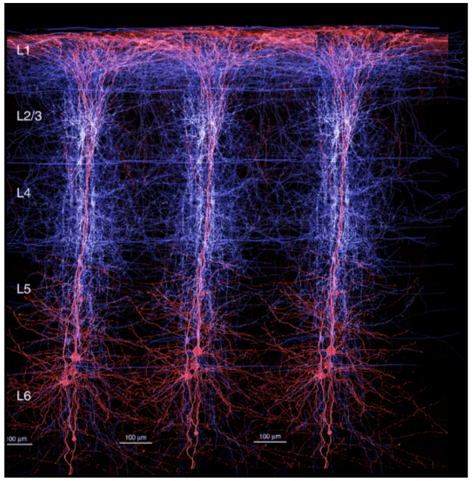
- What are neural networks?
- Introduction to network analysis
- How can the fibre tract network structure be examined?
- Topological network organisation

What are neural networks?

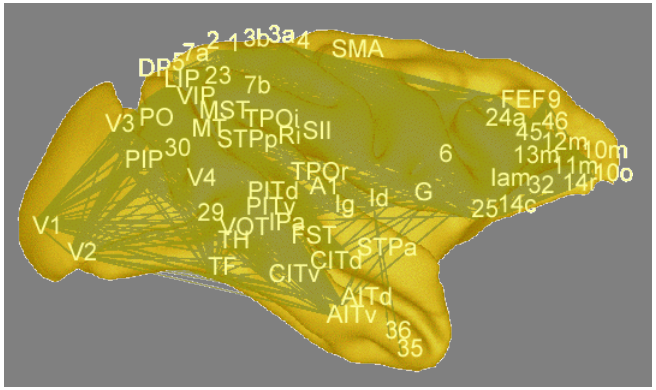
Levels of connectivity



Axons between neurons



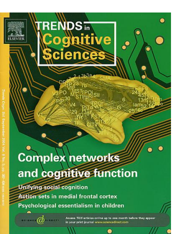
Links between cortical columns



Fibre tracts between brain areas

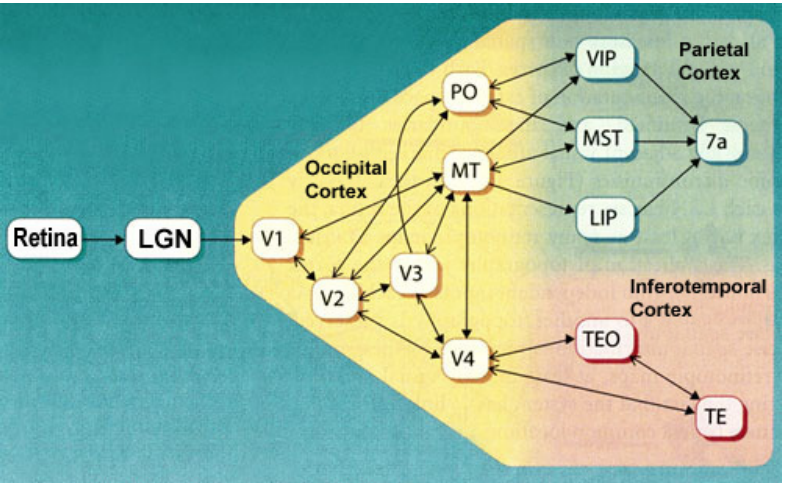
Types of connectivity

- 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

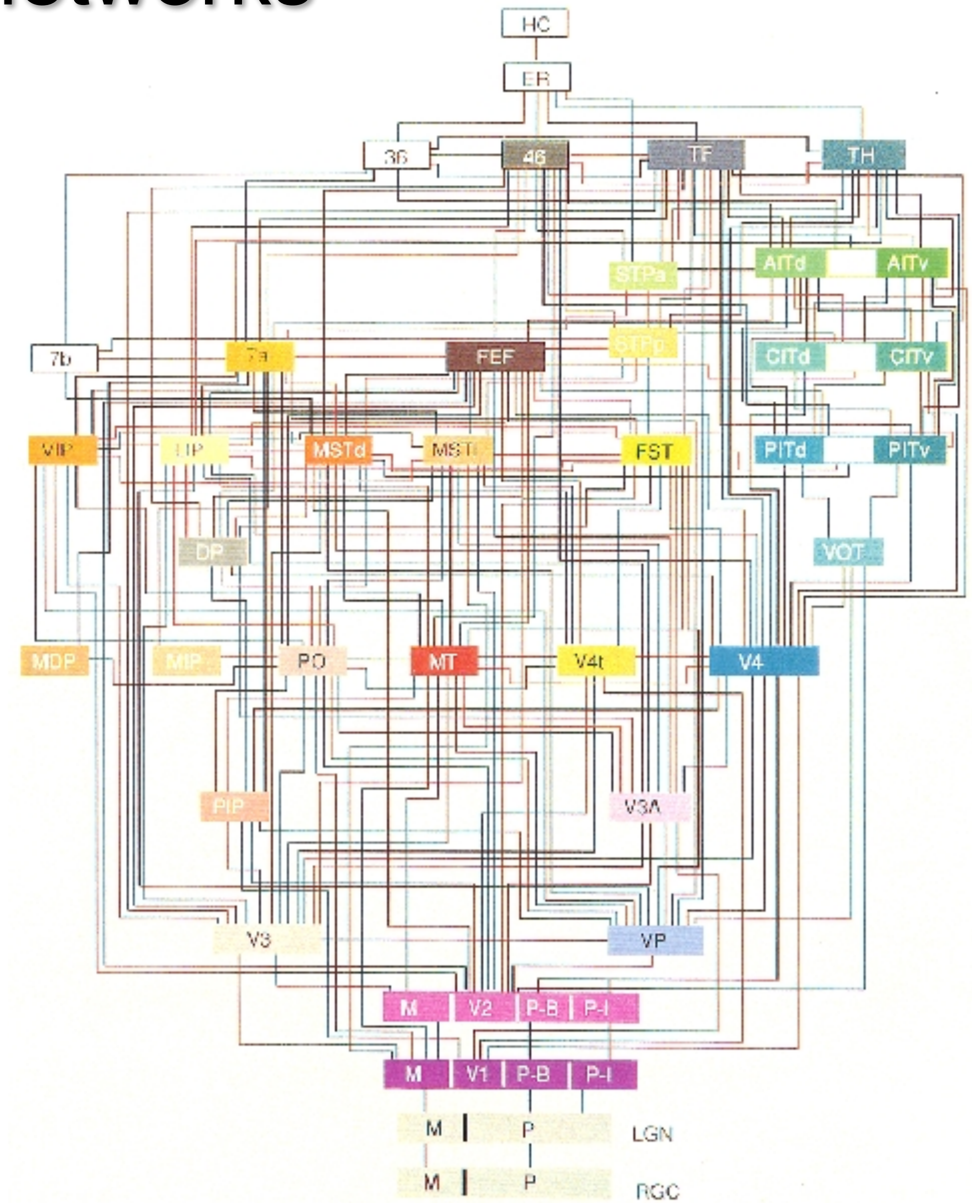


Sporns, Chialvo, Kaiser, Hilgetag. Trends in Cognitive Sciences, 2004

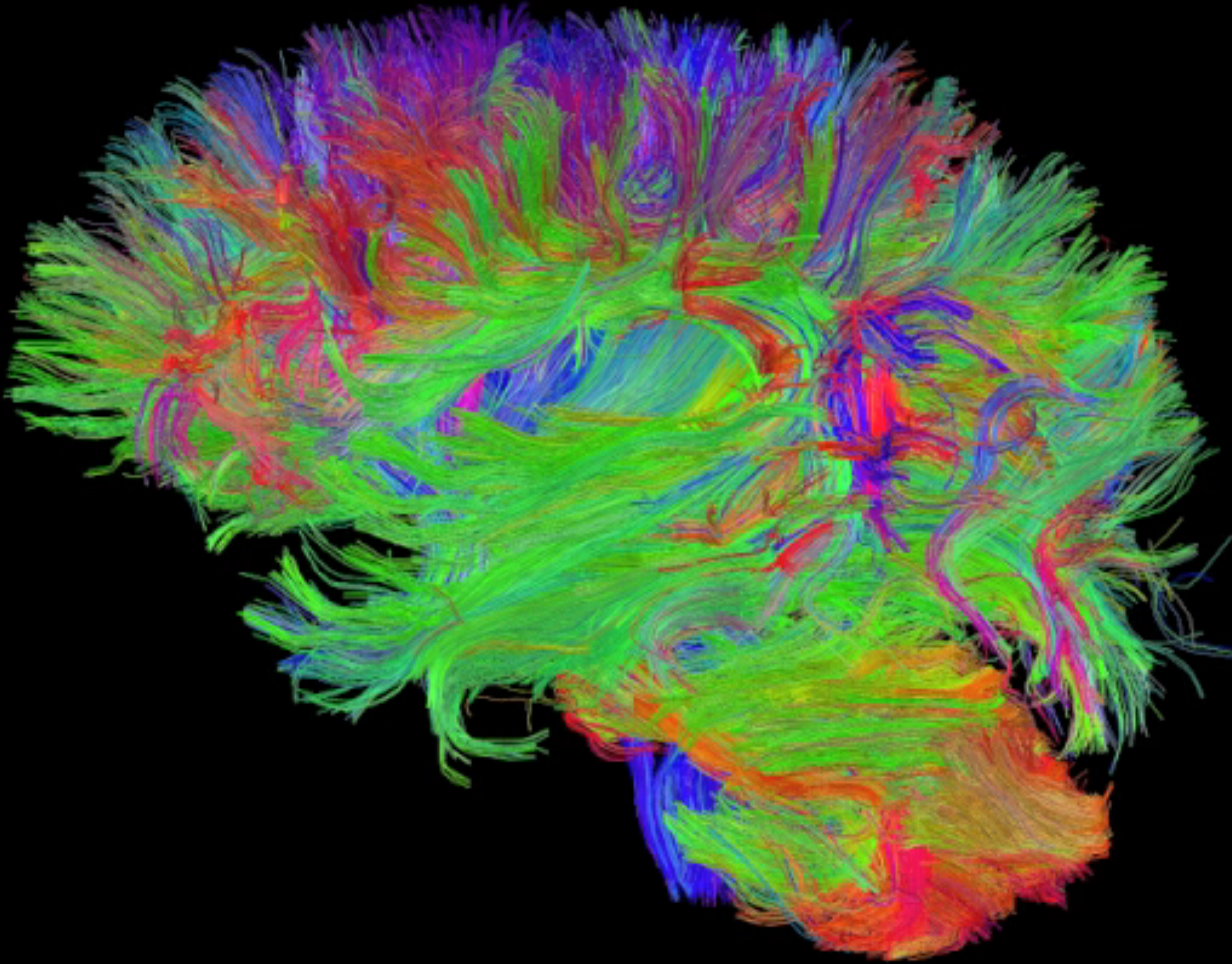
Cortical networks



Dorsal and ventral visual pathway



Visual system



Introduction to network analysis

Network Science

Rapidly expanding field:

Watts & Strogatz, *Nature* (June 1998)

Barabasi & Albert, *Science* (October 1999)

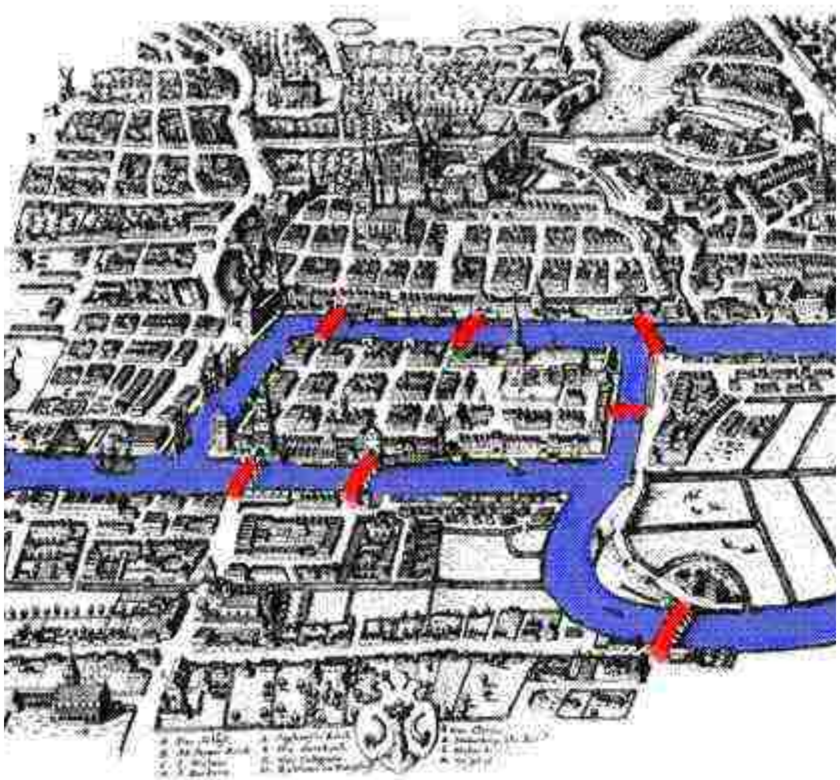
Modelling of SARS spreading over the airline network
(Hufnagel, *PNAS*, 2004)

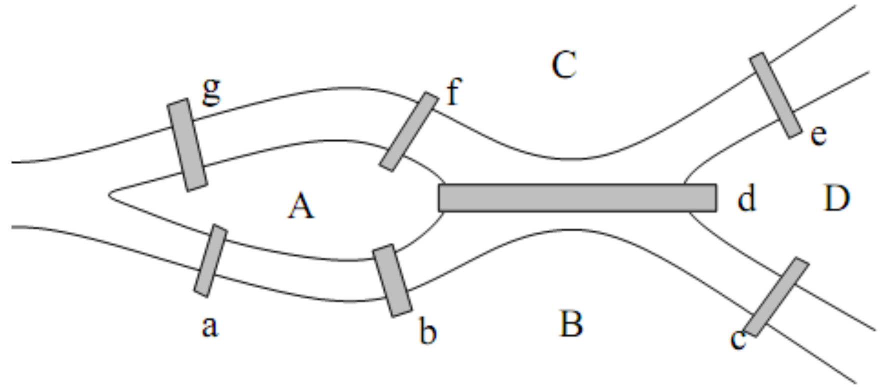
Identity and Search in Social Networks
(Watts et al., *Science*, 2002)

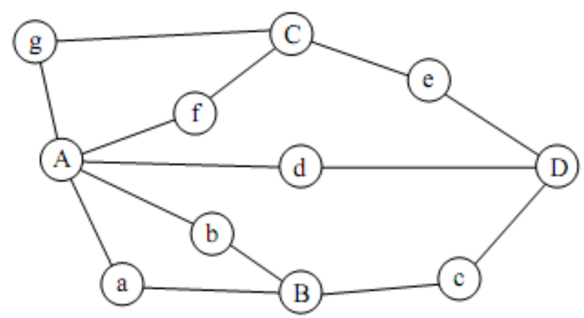
The Large-Scale Organization of Metabolic Networks.
(Jeong et al., *Nature*, 2000)

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

Nodes in graphs

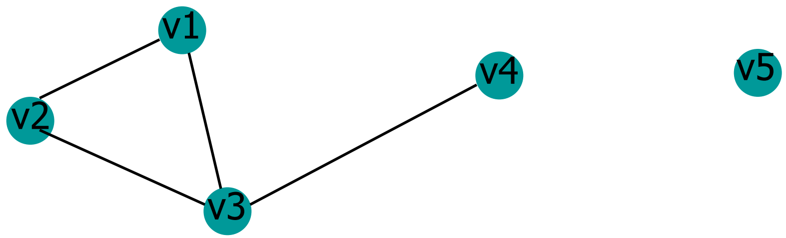
- Isolated nodes
- Degree of a node
- Connected graph
- Average degree of a graph
- Edge density: probability that any two nodes are connected
  $d = \dfrac{E}{(N*N-1)/2)}$

➢ 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

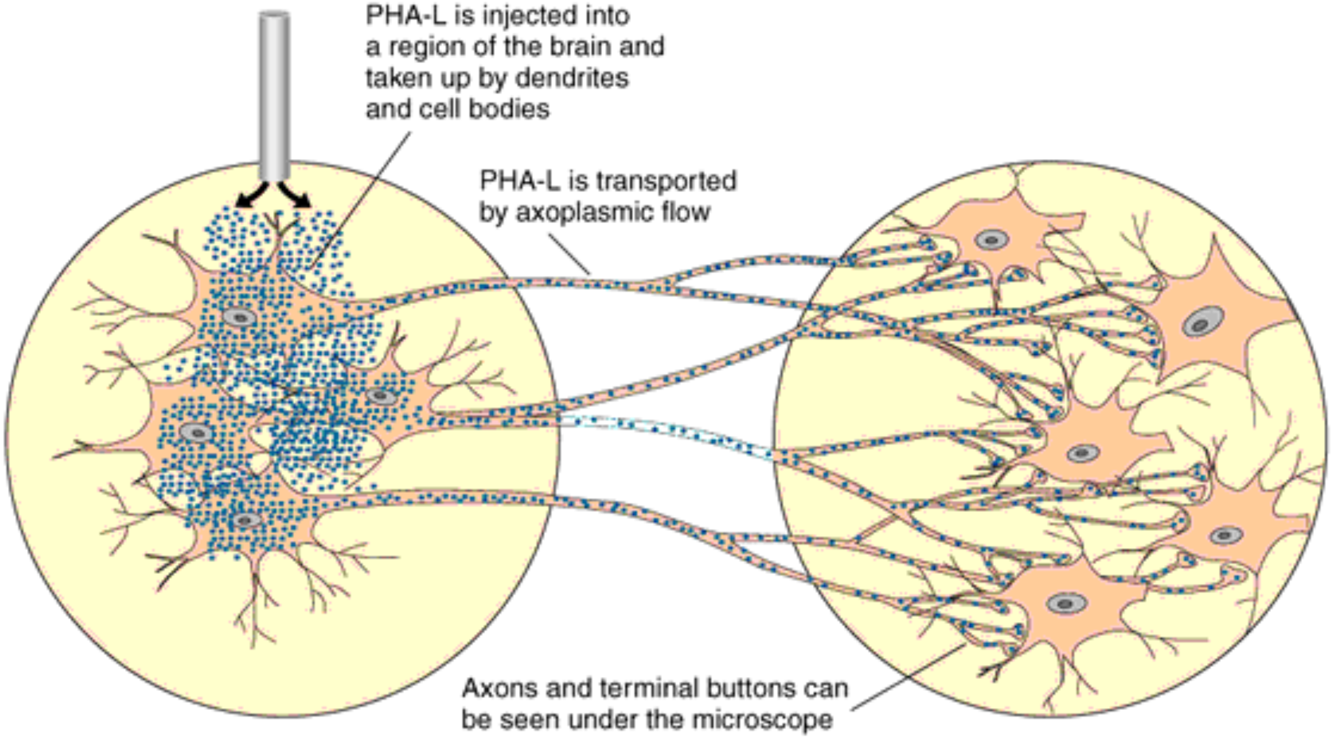
	nodes	edges	density [%]
Autobahnen	1 168	2 486	0.18
Internet	6 524	29 629	0.0696
www	325 729	1 497 135	0.0014
Power Grid	4 677	12 500	0.0572
metabolic	422	1 972	1.3
C. Elegans	202	2 540	6.3
(partial network)			
macaque	73	835	16

sparse network
(density ~ 1%)

dense network
(density > 5%)

How can the fibre tract network structure be examined?

Tract tracing with dyes*



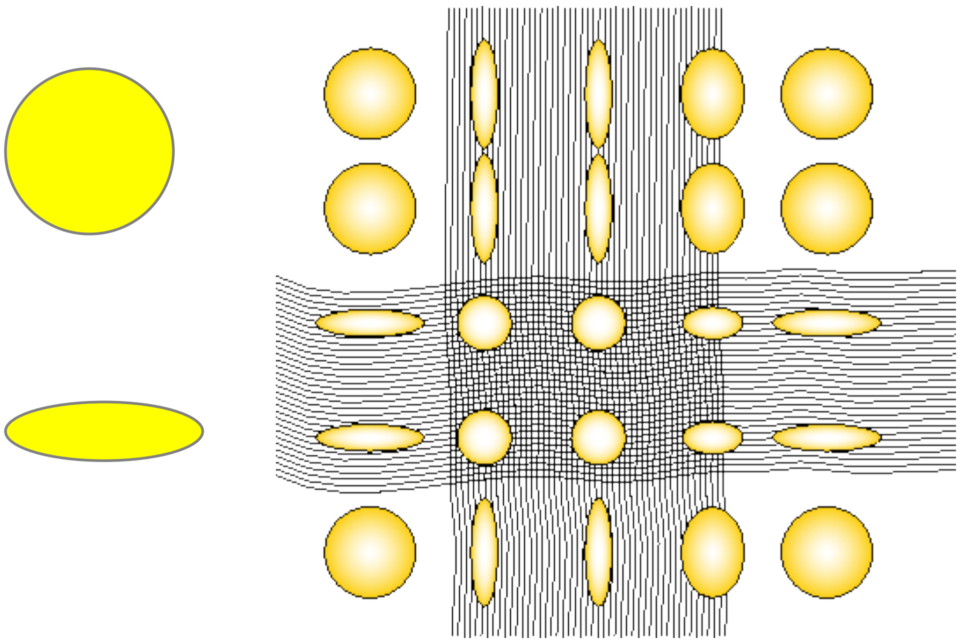
PHA-L: Phaseolus vulgaris-leucoagglutinin

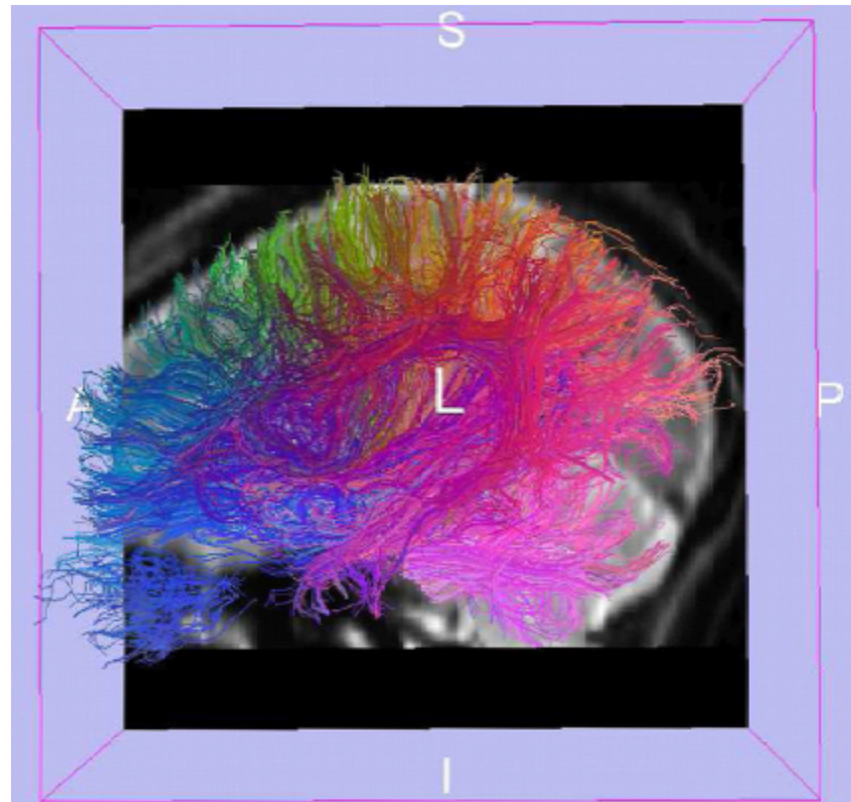
Anterograde: soma → synapse
Retrograde: soma ← synapse

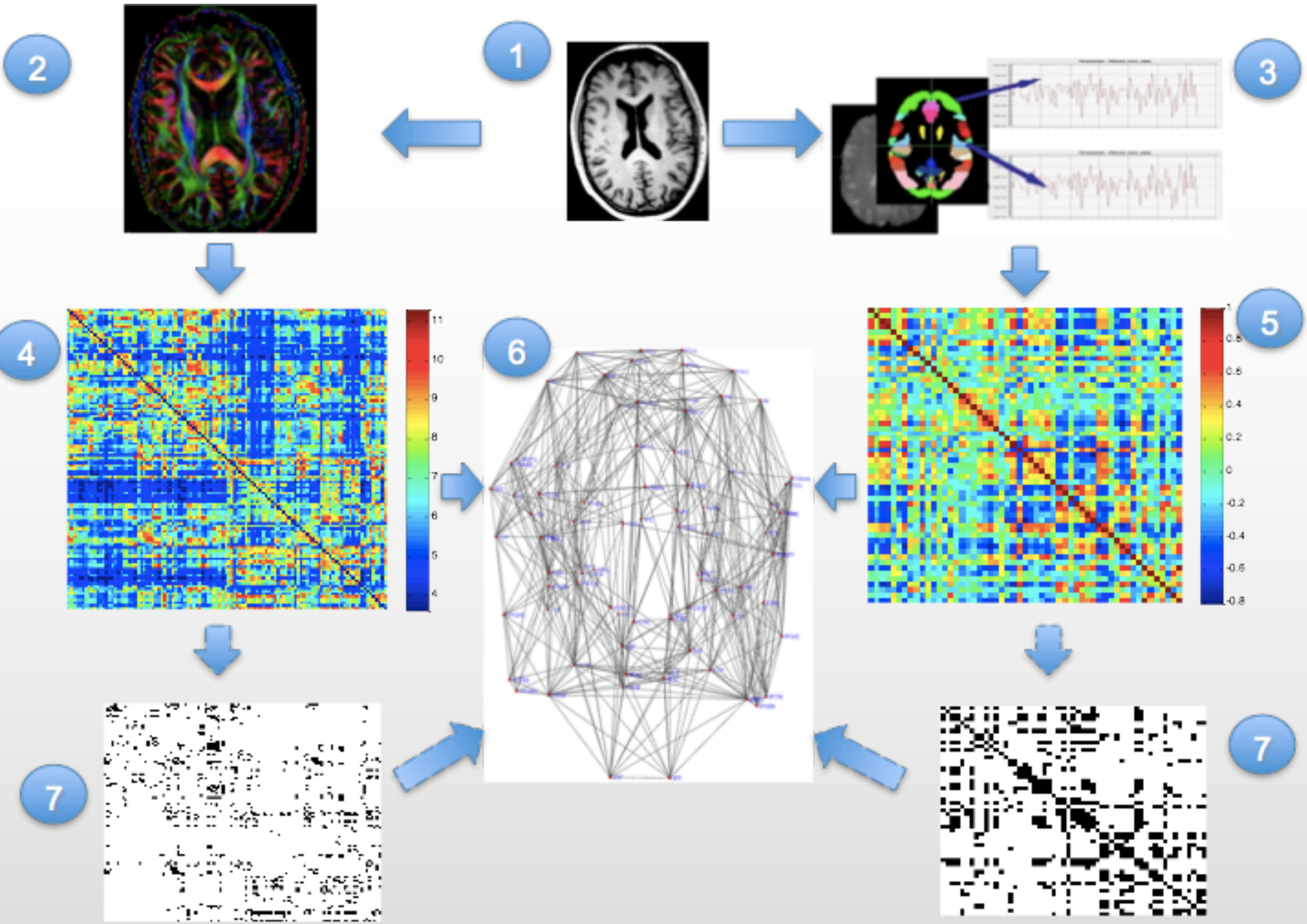
* Horseradish peroxidase (HRP) method; fluorescent microspheres; Phaseolus vulgaris-leucoagglutinin (PHA-L) method; Fluoro-Gold; Cholera B-toxin; DiI; tritiated amino acids

Diffusion Tensor Imaging (DTI)

New
Est. 1994

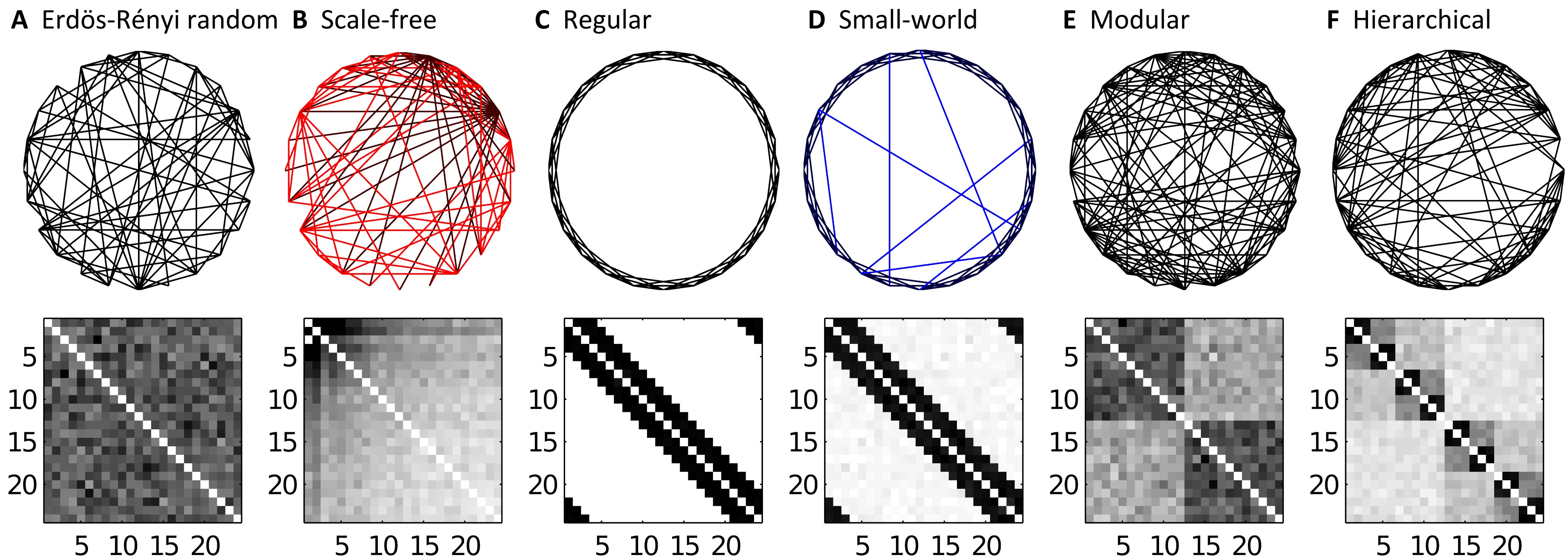





1
2
3
4
5
6
7
7
11
10
9
8
7
6
5
4
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8

Topological network organisation

Archetypes of complex networks



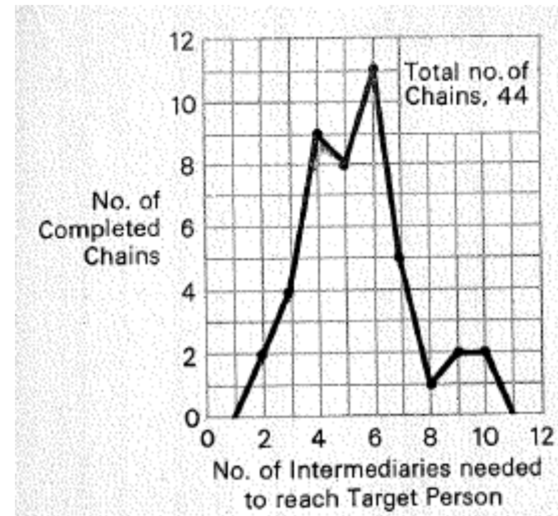
Note: real complex networks show a *combination* of these types!

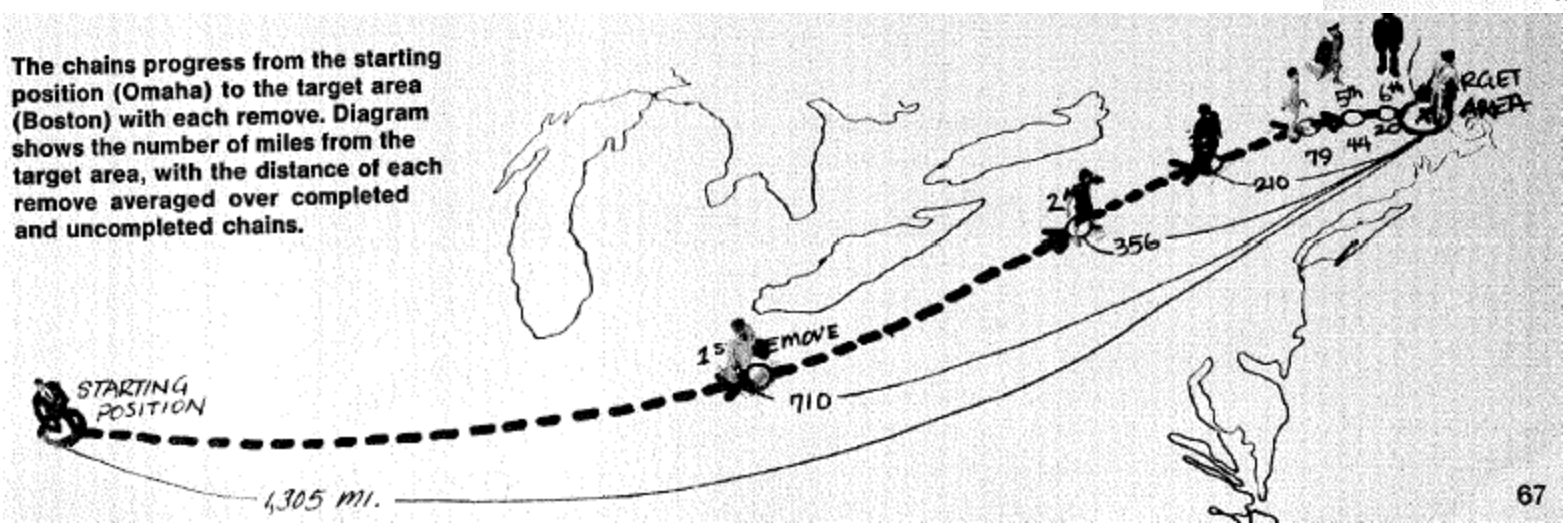
Kaiser (2011) *Neuroimage*

It’s a small world

Nodes: individuals

Links: social relationship





S. Milgram. *Psychology Today* (1967)

Austin Powers

Robert Wagner

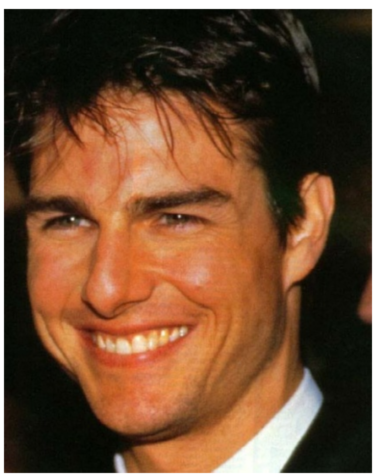
Let's make it legal

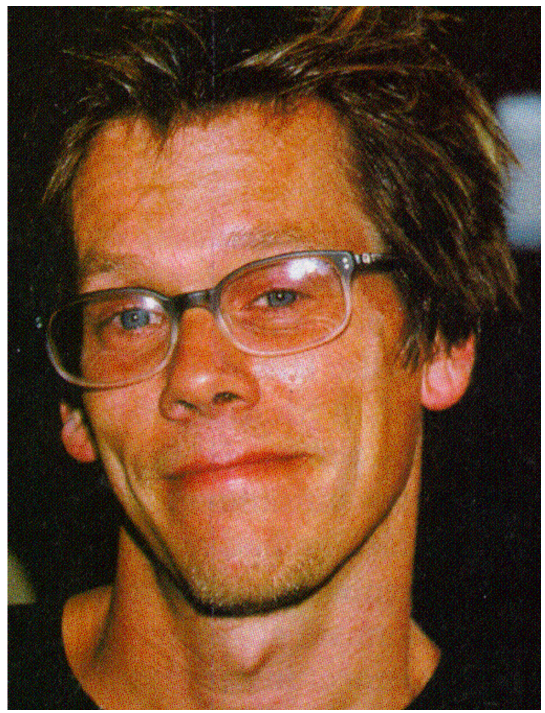
Wild Things

What Price Glory

Barry Norton

A Few Good Man





Kevin Bacon

Monsieur Verdoux

Network properties

<u>Clustering coefficient</u>

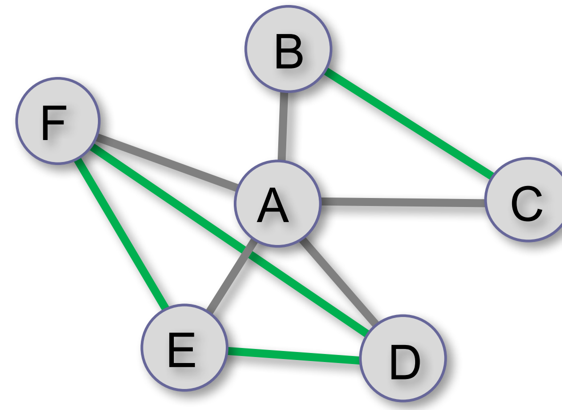
Neighbours = nodes that are directly connected

local clustering coefficient

C_{local}= average connectivity between neighbours

C_{local}=1 -> all neighbours are connected

C : global clustering coefficient (average over all nodes)



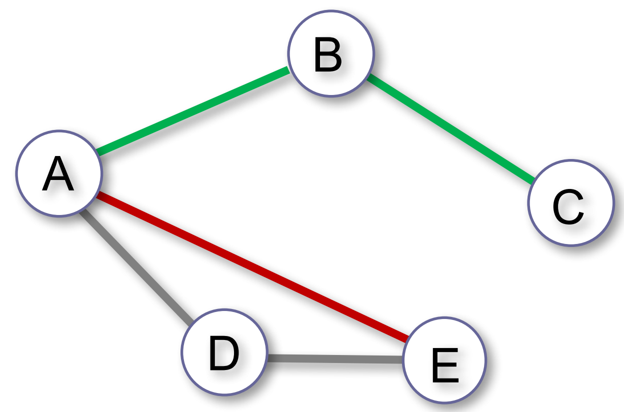
C_A=4/10=0.4

<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

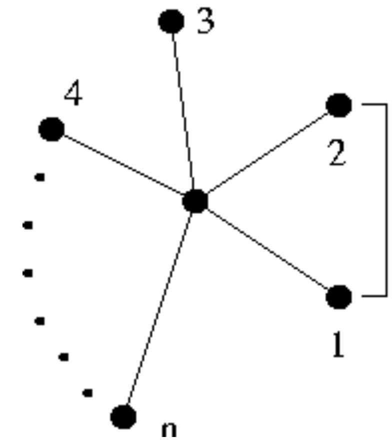


Shortest path lengths:

A -> C : 2

A -> E : 1

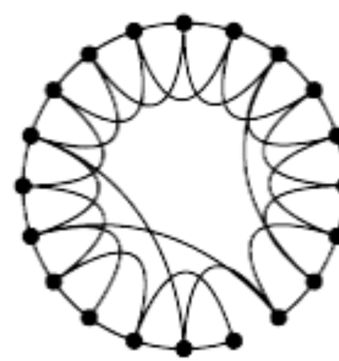
Small-world networks



Clustering coefficient is higher than in random networks

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

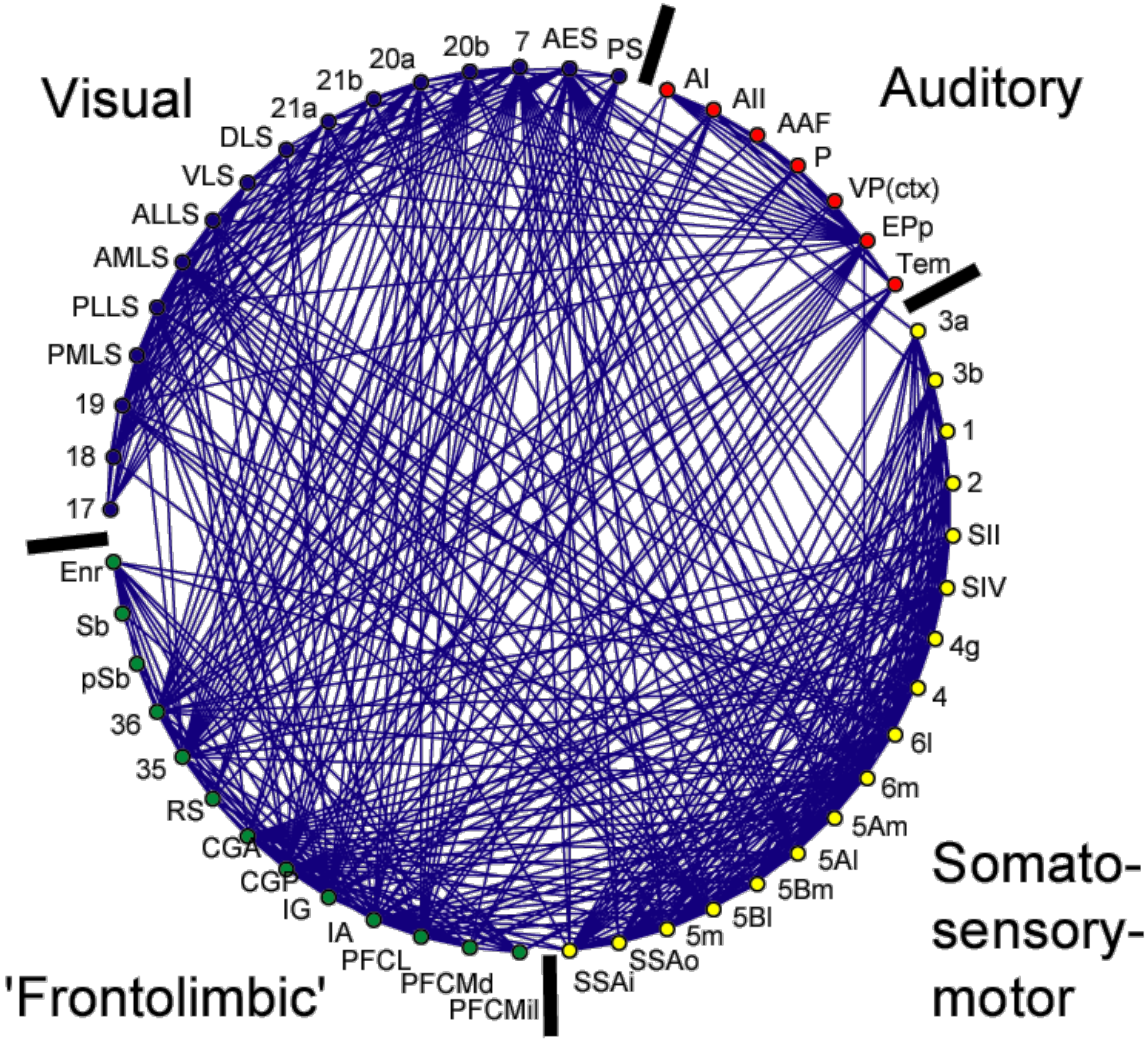
Small-world



Characteristic Path Length is comparable to random networks

Watts & Strogatz, Nature, 1998

Modular small-world connectivity



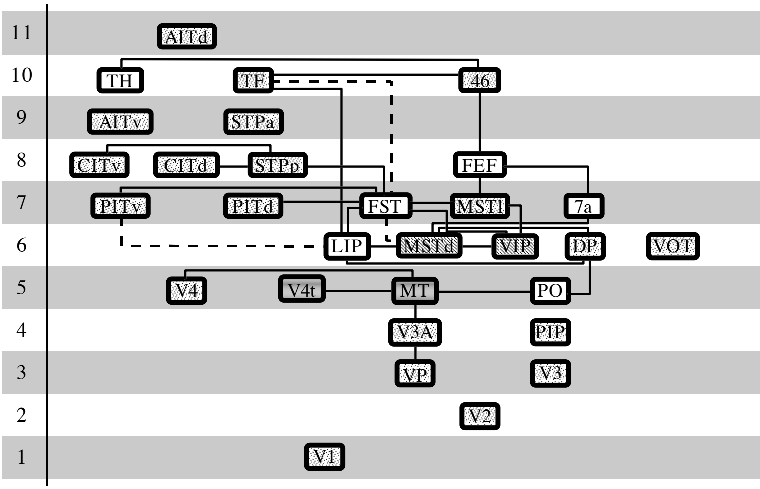
Small-world
Neighbours are well connected; short characteristic path length (~2)

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

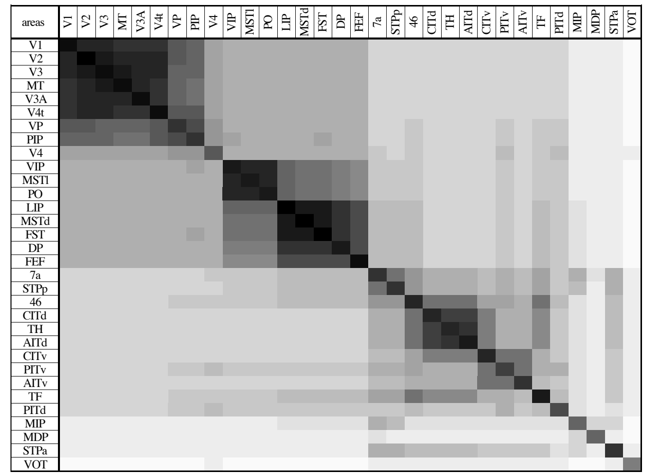
Hilgetag & Kaiser (2004) *Neuroinformatics* **2**: 353

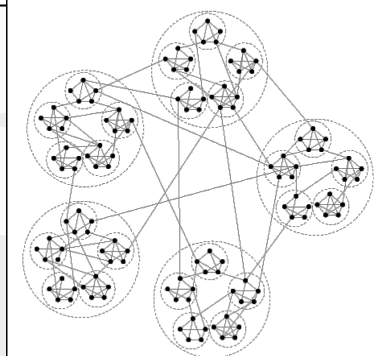
Hierarchy

Sequential

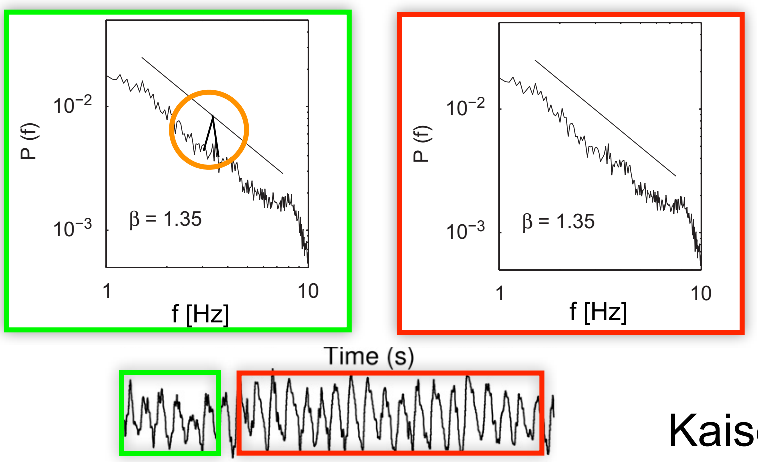


Topological

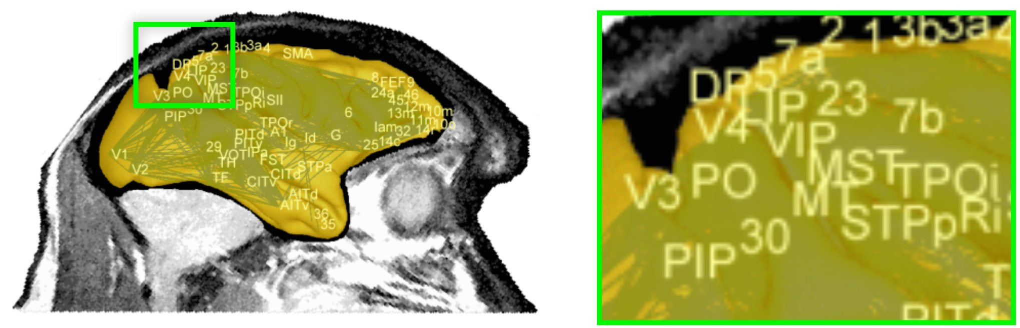




Temporal



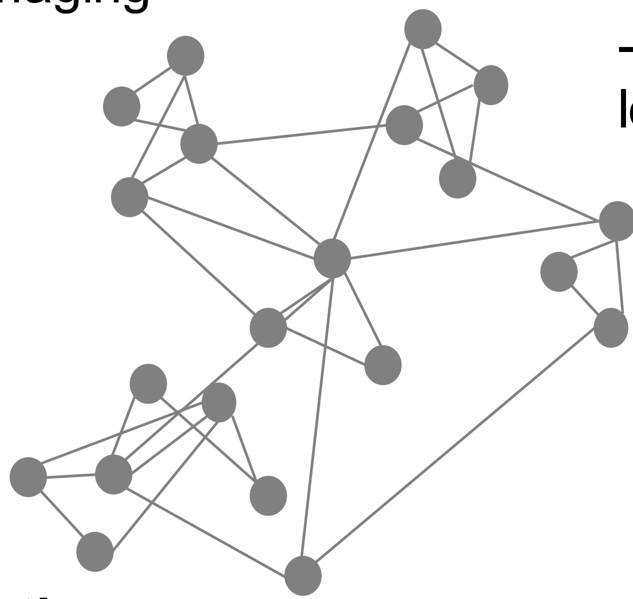
Spatial



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

Summary

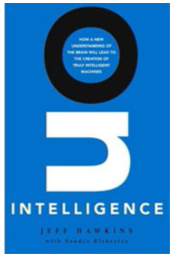
2. Finding structural fibre tract connectivity:
- Diffusion tensor imaging
- Tract tracing



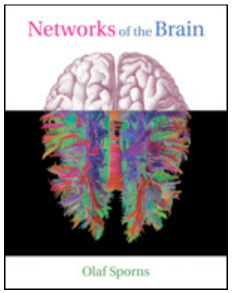
3. Topological properties:
- multiple clusters/ modularity
- small-world: path lengths and local neighbourhood clustering

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

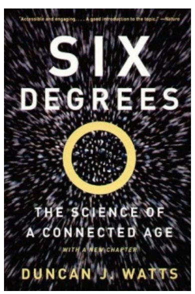
Further readings



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.dynamic-connectome.org

Practical

use Matlab or Octave

- Measures for brain connectivity structure and development (including data for the macaque and cat):
  http://www.dynamic-connectome.org
  http://www.dynamic-connectome.org/t/tutorial/honey.mat

- Brain Connectivity Toolbox: http://www.brain-connectivity-toolbox.net/

- Connectome Viewer: http://www.connectomeviewer.org/

Matlab analysis - topology

```
%% Network features using adjacency matrix matrix
%% see networks under the resources link at
%% http://www.dynamic-connectome.org/
%% for example, cat55.mat or mac95.mat

% how many nodes are there?
N = length(matrix)

% how many edges are there (i.e. non-zero matrix elements)?
E = nnz(matrix)

% what is the edge density (likelihood that any two nodes are connected?
d = E / (N * (N-1))

% are there any loops (connections from node to itself)?
min(min(matrix))  % any negative value out there?
trace(matrix)     % any non-zero diagonal elements (aka self-loops)
```

Matlab analysis – spatial organisation

```
% network with 3D coordinates in variable pos e.g. using
% http://www.dynamic-connectome.org/t/tutorial/honey.mat

%% visualize network
spy(matrix)       % binary view
pcolor(matrix)    % view of values for weighted networks

hist(nonzeros(matrix))
unique(nonzeros(matrix))

%% Spatial Network visualisation
% view from top
subplot(1,3,1); gplot(pos(:, [1,2])); axis equal

% view from side
subplot(1,3,2); gplot(pos(:, [1,3])); axis equal

% view from back
subplot(1,3,3); gplot(pos(:, [2,3])); axis equal
```