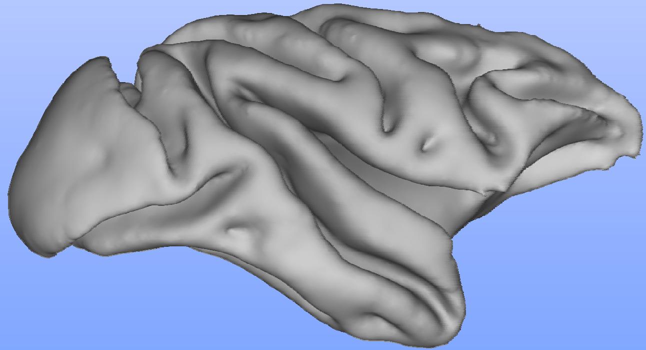
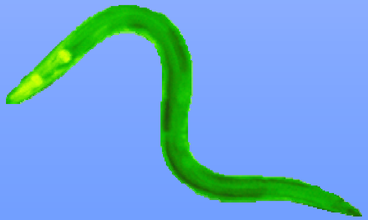
The Institute of Neuroscience

Spatial and modular organisation of brain networks prevents large-scale activation





Marcus Kaiser

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Institute of Neuroscience
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United Kingdom

http://www.biological-networks.org

Network Science

Rapidly expanding field:

Watts & Strogatz, *Nature* (June 1998) cited 2,255 times

Barabasi & Albert, *Science* (October 1999) cited 2,122 times

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

Identity and Search in Social Networks

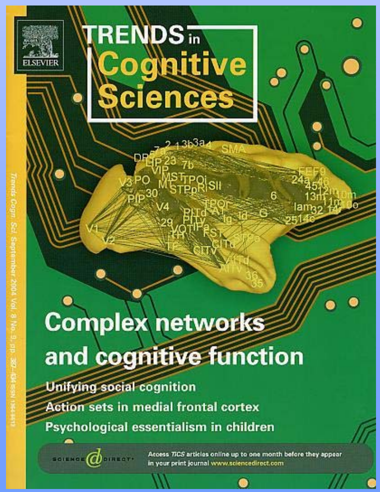
(Watts et al., *Science*, 2002)

The Large-Scale Organization of Metabolic Networks.

(Jeong et al., *Nature*, 2000)

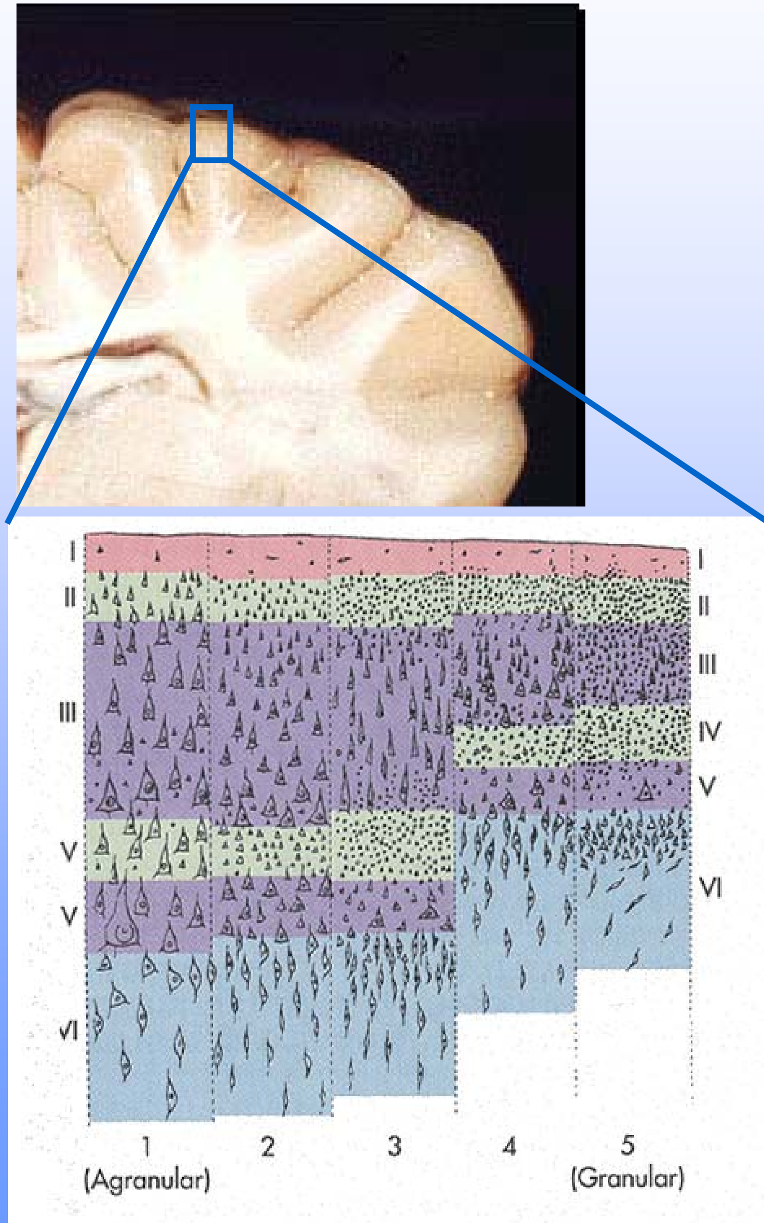
Types of neural/cortical connectivity

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



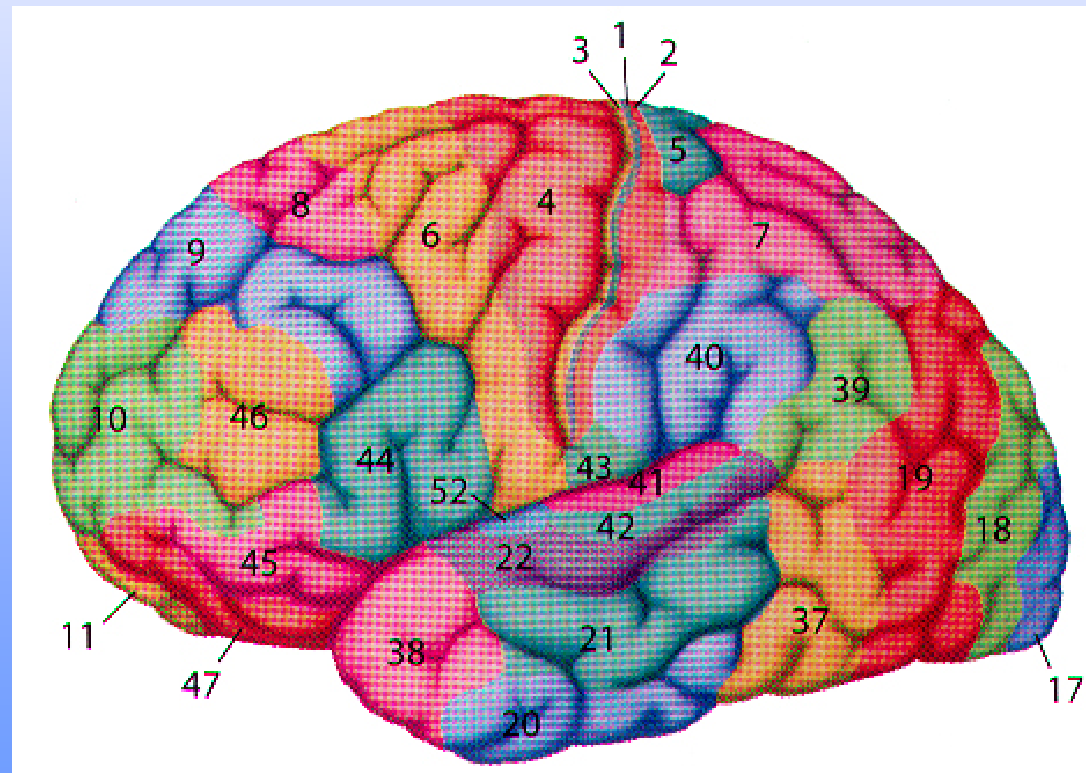
Sporns, Chialvo, Kaiser, *Hilgetag.Trends in Cognitive Sciences*, 2004

Cortical networks



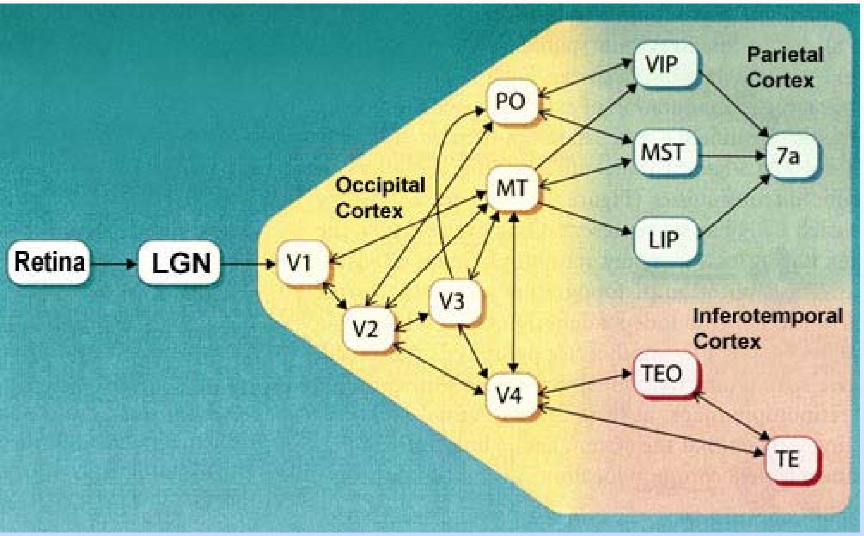
Nodes: cortical areas

Edges: fiber tracts between areas

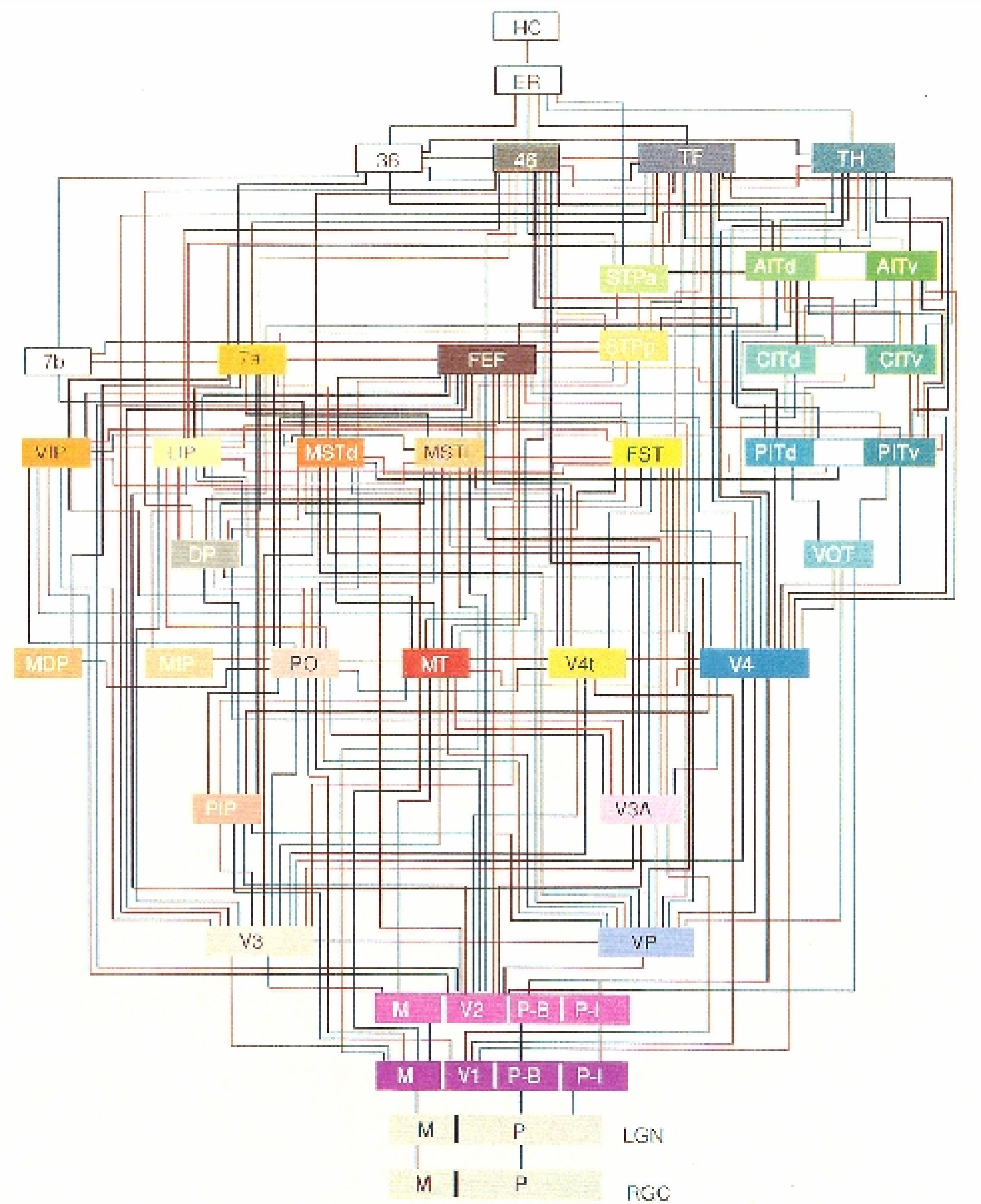


Human cortical areas (after Brodmann, 1909)

Cortical networks



Visual pathways



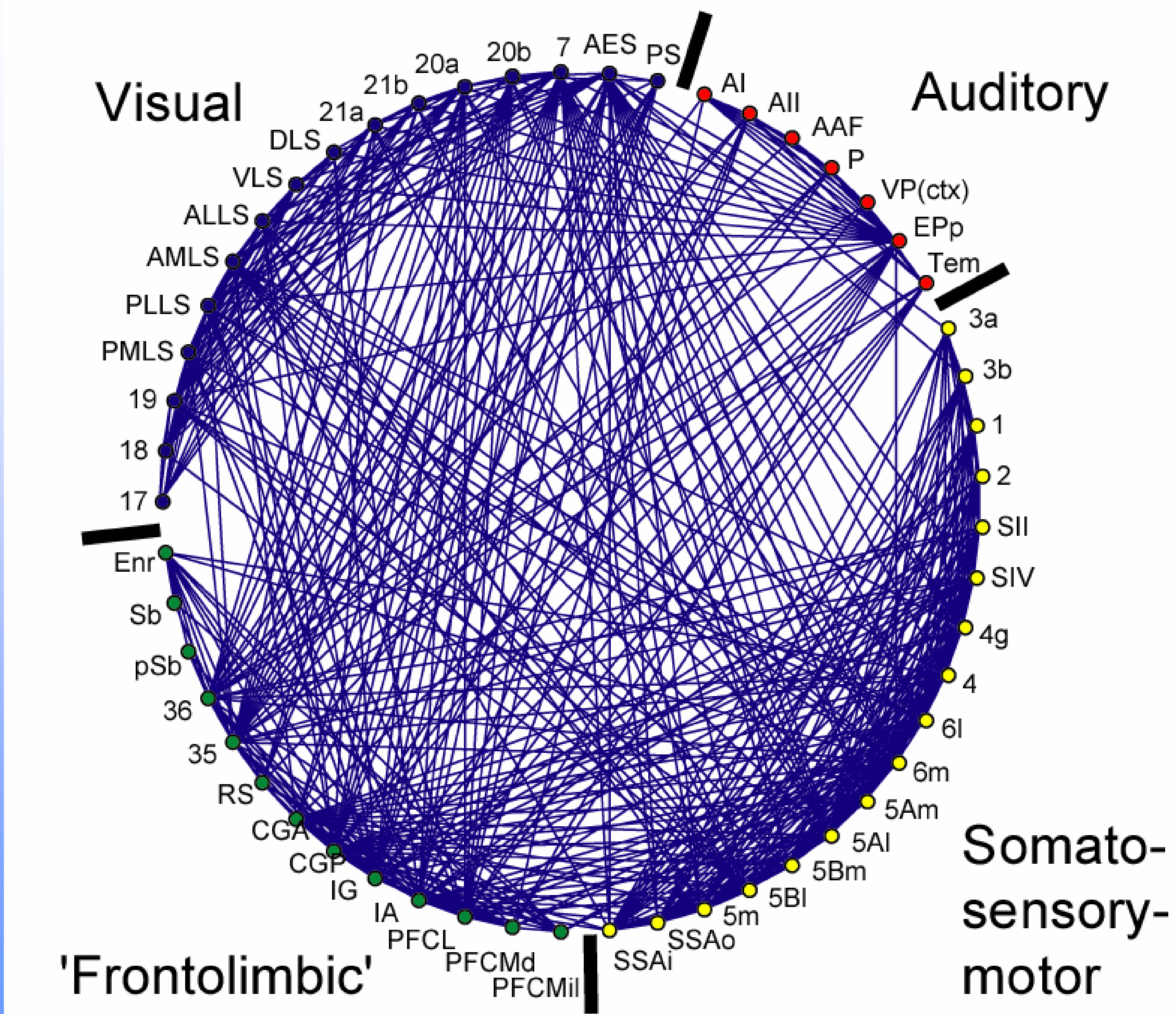
Visual system

Structure and Function in Neural Systems

- **Multiple clusters**
- **Small-world architecture**
- **Scale-free organisation**
- **Spatial arrangement**

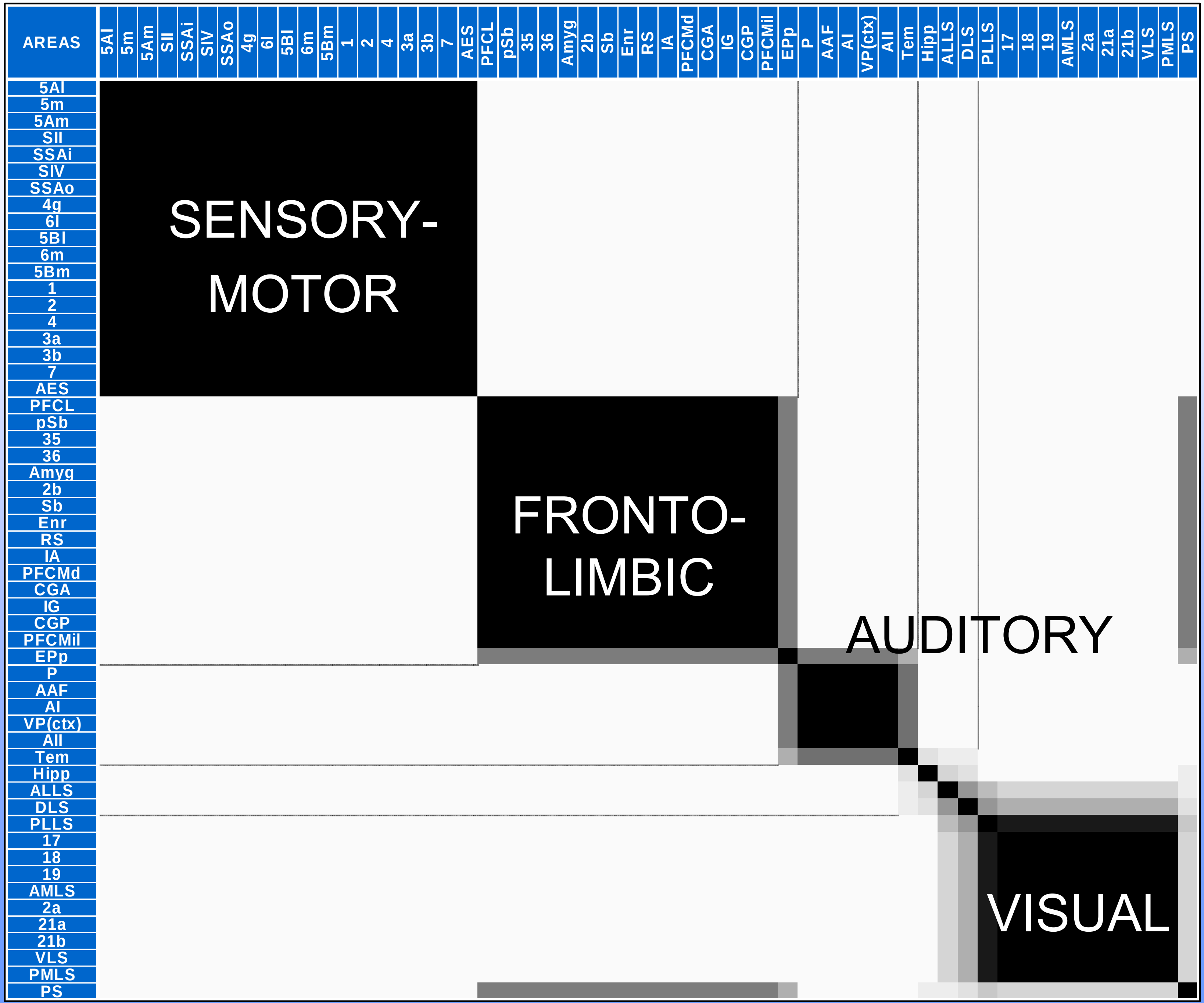
- **Development of spatial networks**
- **Hierarchy and critical activation**

Cat cortical network



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

Multiple clusters/communities



Hilgetag et al. (2000) *Phil Trans R Soc* **355**: 91

Reconstructing connectivity

Macaque visual cortex (31 nodes)

	V1	V2	V3	PIP	V3A	V4	PO	MT	V4t	DP	VOT	LIP	VIP	MIP	MDP	MSTd	MSTl	PITd	PITv	7a	STPp	CITd	CITv	STPa	AITv	FEF	TF	46	FST	TH	AITd
V1		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	0	1	1	0	1	1
V2	0		1	0	1	1	1	1	1	1	0	1	1	0	0	1	1	0	1	1	1	0	1	0	0	1	1	1	1	0	0
V3	0	1		0	1	1	1	1	1	1	0	1	1	0	0	1	1	0	1	1	0	0	0	0	0	1	1	1	1	0	0
PIP	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
V3A	0	1	1	0		1	0	1	1	1	0	1	1	0	0	1	1	0	1	1	0	0	0	0	0	1	1	1	1	0	0
V4	1	1	1	0	1		0	1	1	1	0	1	1	0	0	1	1	1	1	1	1	1	1	0	0	1	1	1	0	1	1
PO	0	1	1	0	0	0		0	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
MT	0	1	1	0	1	1	0		1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	0	0	1	0	1	1	0	0
V4t	0	1	1	0	1	1	1	1		1	0	1	1	0	0	1	1	0	1	1	1	0	1	0	0	1	1	1	1	0	0
DP	0	1	1	0	1	1	1	1	1		0	1	1	0	0	1	1	0	1	1	1	0	1	0	0	1	1	1	1	0	0
VOT	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LIP	0	1	1	0	1	1	0	1	1	1	0		1	0	0	1	1	0	0	0	0	0	0	0	0	1	0	1	1	0	0
VIP	0	1	1	0	1	1	1	1	1	1	0	1		0	0	1	1	0	1	1	1	0	1	0	0	1	1	1	1	0	0
MIP	0	0	0	0	0	0	0	0	0	0	0	0	0		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MDP	0	0	0	0	0	0	0	0	0	0	0	0	0	1		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MSTd	0	1	1	0	1	1	0	1	1	1	0	1	1	0	0		1	0	1	1	0	0	0	0	0	1	1	1	1	0	0
MSTl	0	1	1	0	1	1	1	1	1	1	0	1	1	0	0	1		0	1	1	1	0	1	0	0	1	1	1	1	0	1
PITd	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0		1	1	1	1	1	1	1	0	1	1	0	1	1
PITv	1	1	1	0	1	1	0	0	1	1	0	0	1	0	0	1	1	1		1	1	1	1	0	0	0	1	1	0	1	1
7a	1	1	1	0	1	1	0	0	1	1	0	0	1	0	0	1	1	1	1		1	1	1	0	0	0	1	1	0	1	1
STPp	1	1	0	0	0	1	0	0	1	1	0	0	1	0	0	0	1	1	1	1		1	1	1	1	0	1	1	0	1	1
CITd	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1		1	1	1	0	1	1	0	1	1
CITv	1	1	0	0	0	1	0	0	1	1	0	0	1	0	0	0	1	1	1	1	1	1		1	1	0	1	1	0	1	1
STPa	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1		1	0	0	0	0	1	1
AITv	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	1		0	0	0	0	1	1
FEF	0	1	1	0	1	1	0	1	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	0	0		1	1	0	0	0
TF	1	1	1	0	1	1	0	0	1	1	0	0	1	0	0	1	1	1	1	1	1	1	1	0	0	1		1	0	1	1
46	1	1	1	0	1	1	0	1	1	1	0	1	1	0	0	1	1	1	1	1	1	1	1	0	0	1	1		0	1	1
FST	0	1	1	0	1	0	1	1	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0		0	0
TH	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	0	1	1	0		1
AITd	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	0	1	1	0	1	

Figure 8

Green: **correct** prediction

Red: **wrong** prediction

Yellow: prediction of **untested** connectivity

Node degree
- Clustering coefficient

Avg. shortest path distance
- Matching index
- *Local density*

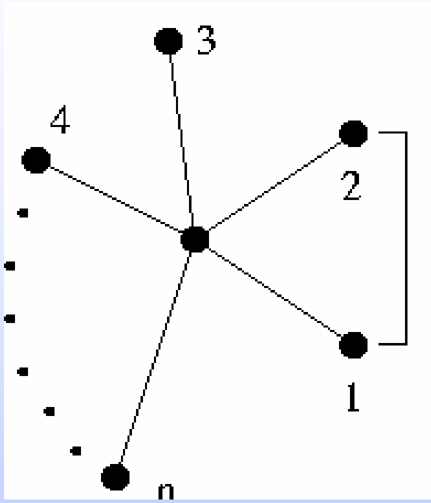
Standard deviation of nearest distances
- *Area size*

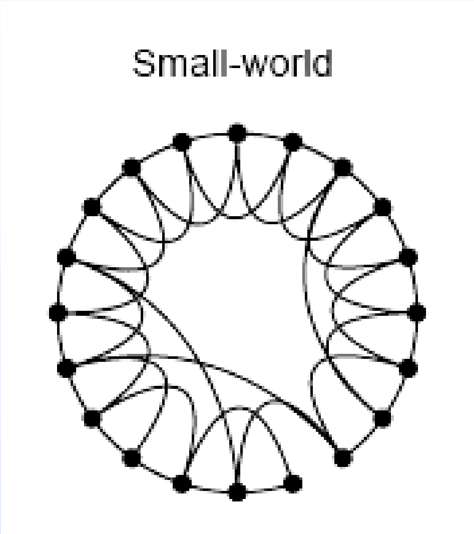
Cartesian coordinates (x, y, z)

Costa LdF, Kaiser M, Hilgetag CC (2007) *BMC Systems Biology* 1:16

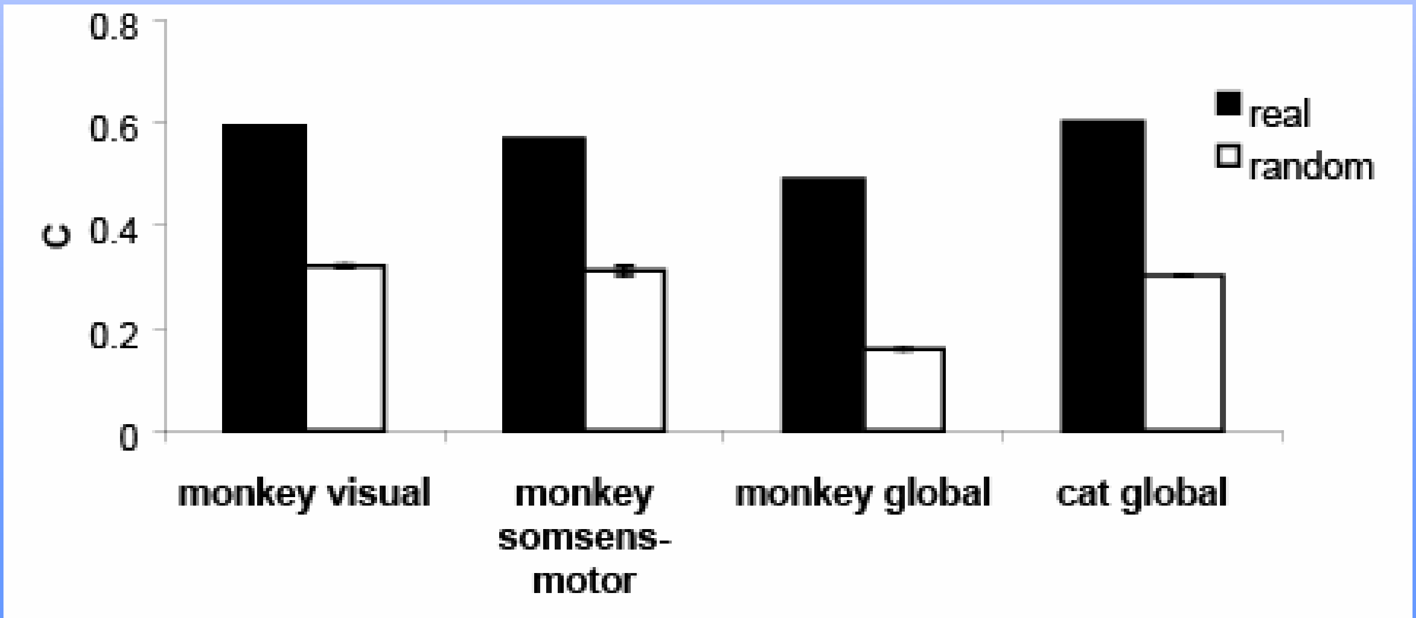
Small-world architecture

Small-world features





- Average clustering coefficient



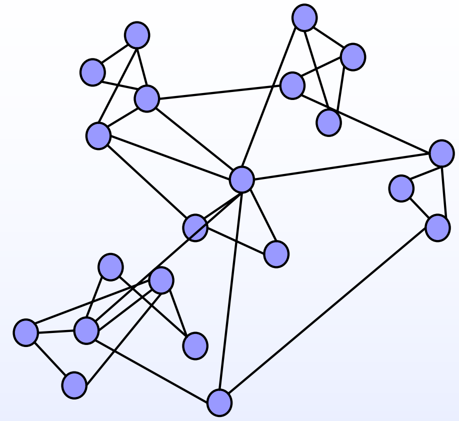
path length ~2

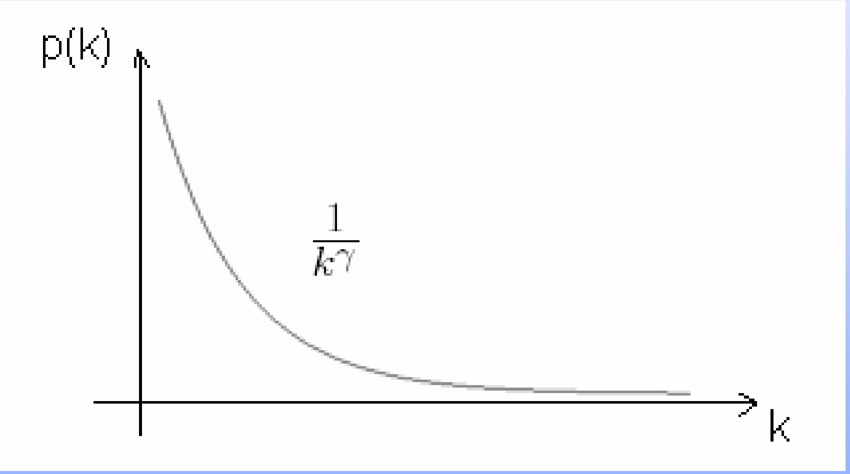
→

One degree of separation

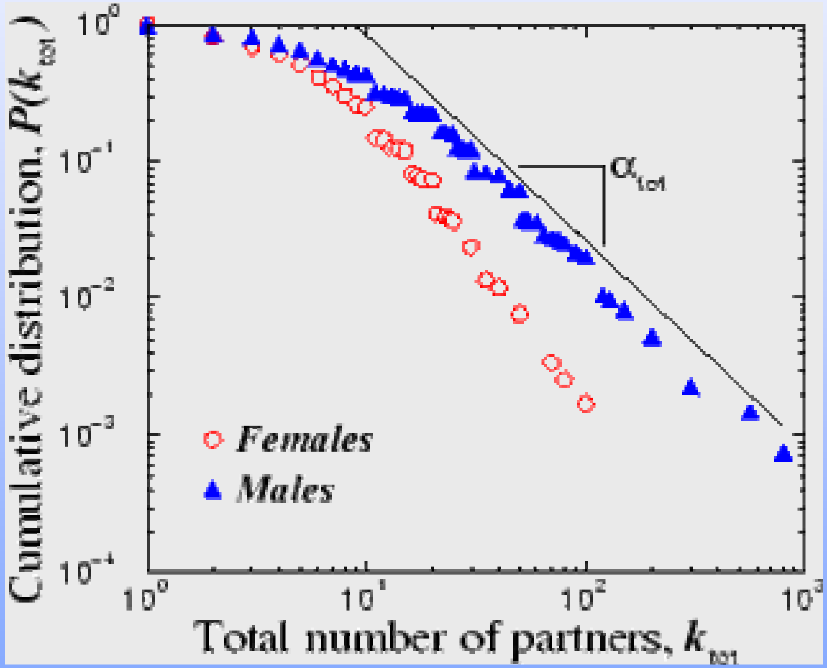
Scale-free organization

Scale-free networks





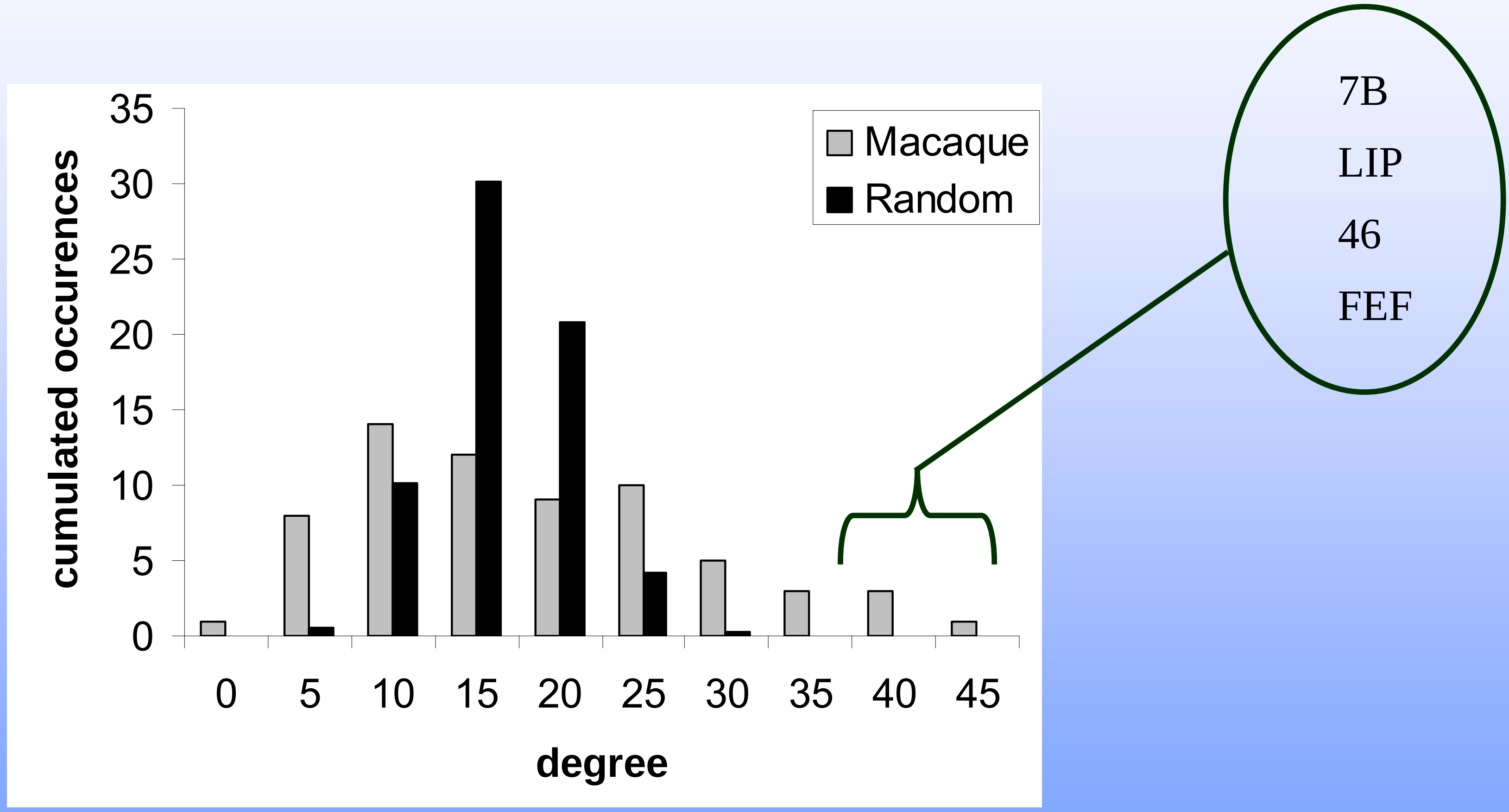
Log-log plot



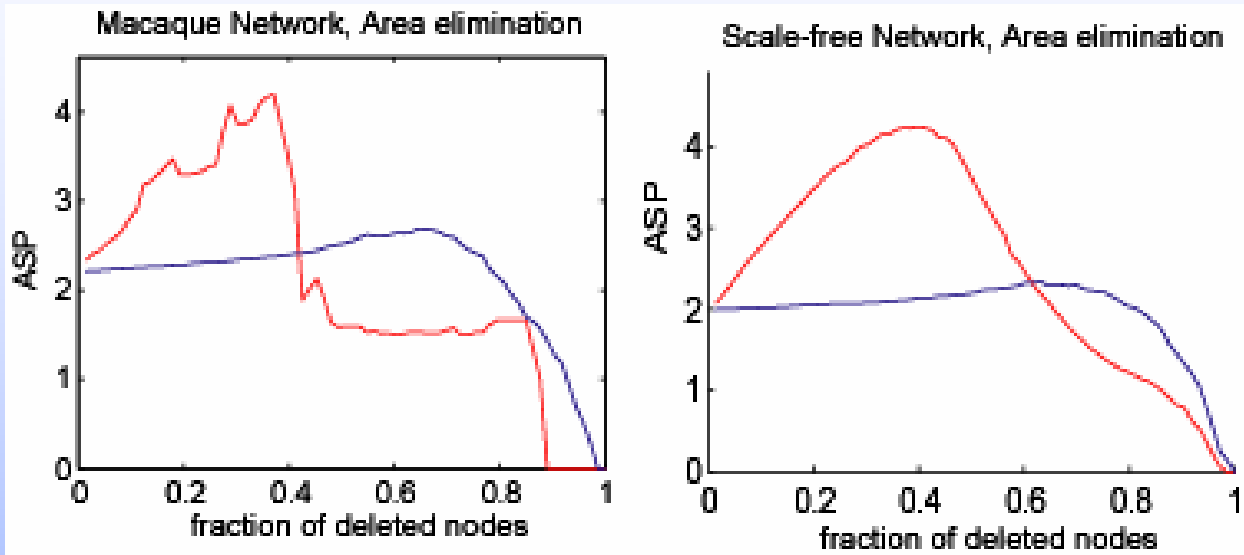
(Barabasi & Albert, Science, 1999)

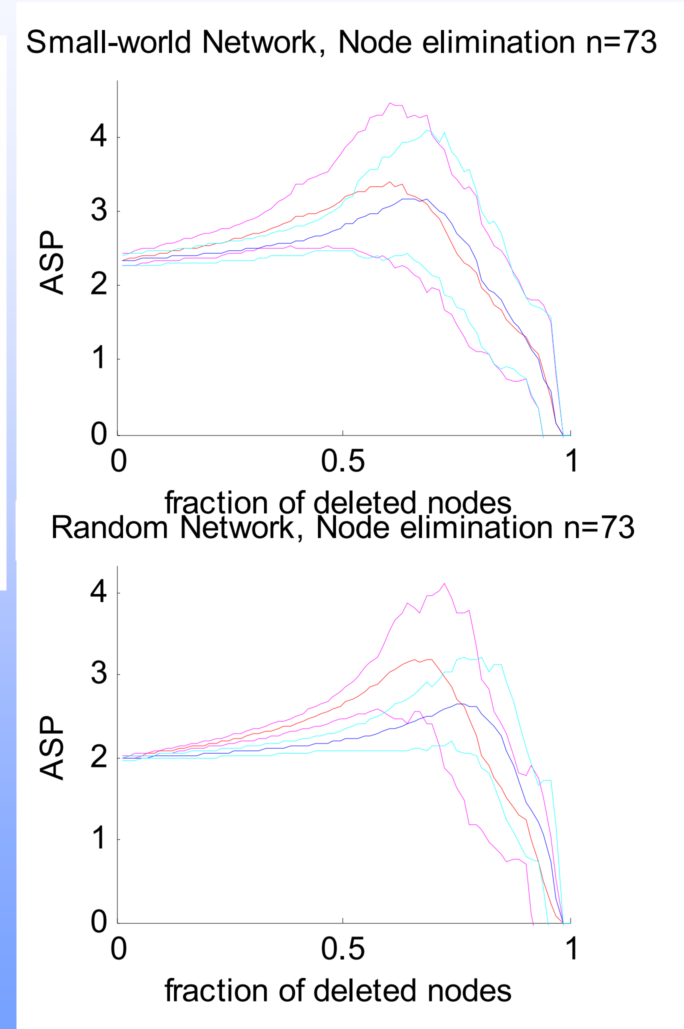
(Liljeros, Nature, 2001)

Is the brain similar to scale-free networks?



Sequential node removal





randomly = irrespective of degree

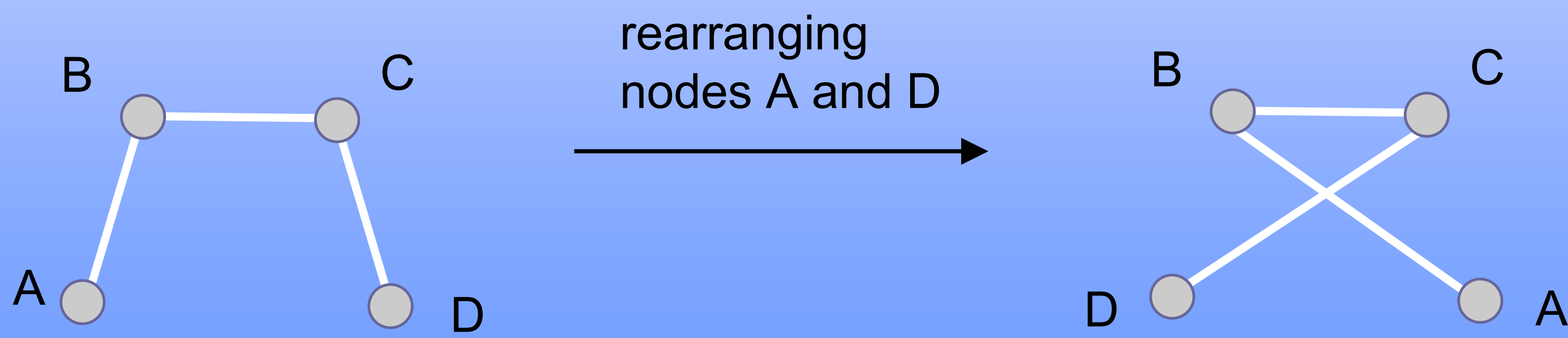
targeted = highly-connected nodes first

Kaiser et al. (2007) *European Journal of Neuroscience* 25:3185-3192

Spatial arrangement

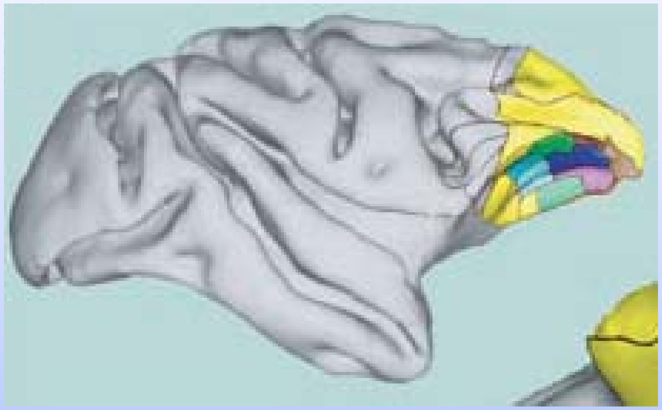
Reducing neural wiring costs

- **Minimizing total wire length reduces metabolic costs for connection establishment and signal propagation**
- **Every alternative arrangement of network nodes will lead to a higher total wiring length (Component Placement Optimization, CPO)**
  (Cherniak, *J. Neurosci*., 1994)

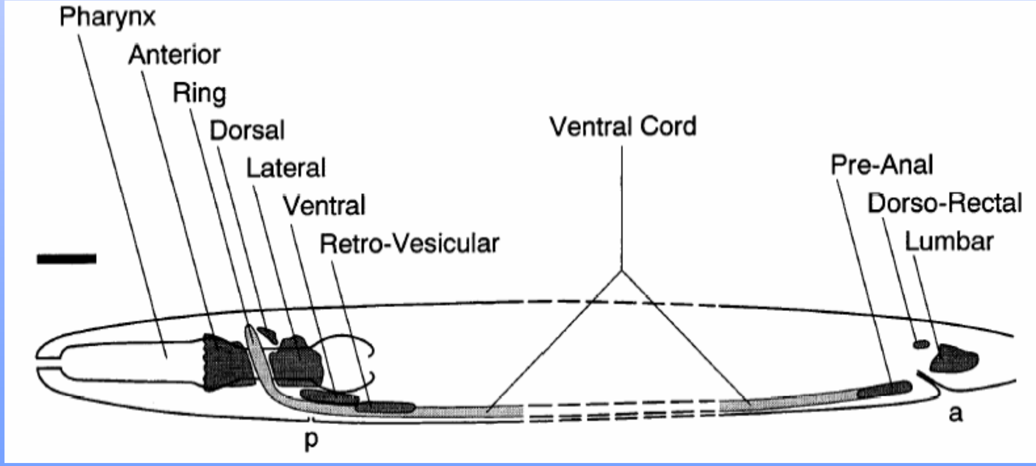


Previous results supporting CPO

- **Macaque: layout of cortical prefrontal areas**
  (Klyachko & Stevens, *PNAS*, 2003)

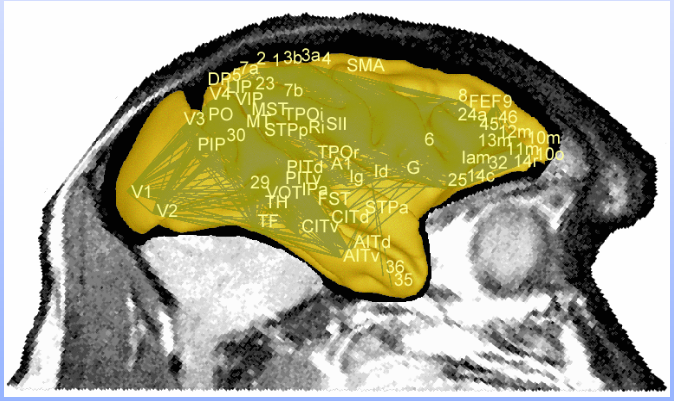


- ***C. elegans*:**
  layout of ganglia
  (Cherniak, *J. Neurosci*., 1994)

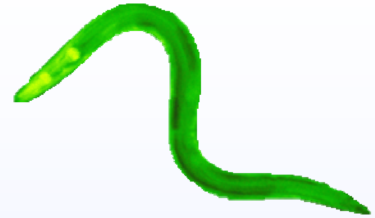


Rhesus monkey cortical network

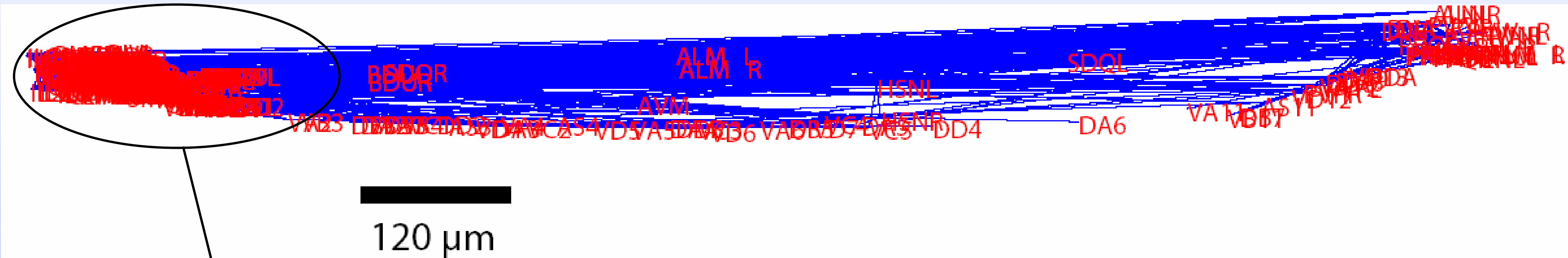
	V1	V2	V3	VP	V3A	V4	VOT
V1	N	1	1	0	1	1	0
V2	1	N	1	1	1	1	1
V3	1	1	N	1	1	1	0
VP	0	1	0	N	1	1	1
V3A	1	1	1	1	N	1	0
V4	1	1	1	1	1	N	1
VOT	0	1	0	1	0	0	N

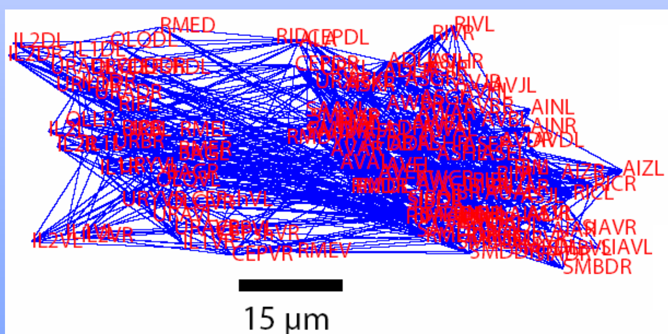


C. elegans neural network



Global level (277 neurons with 2105 connections)

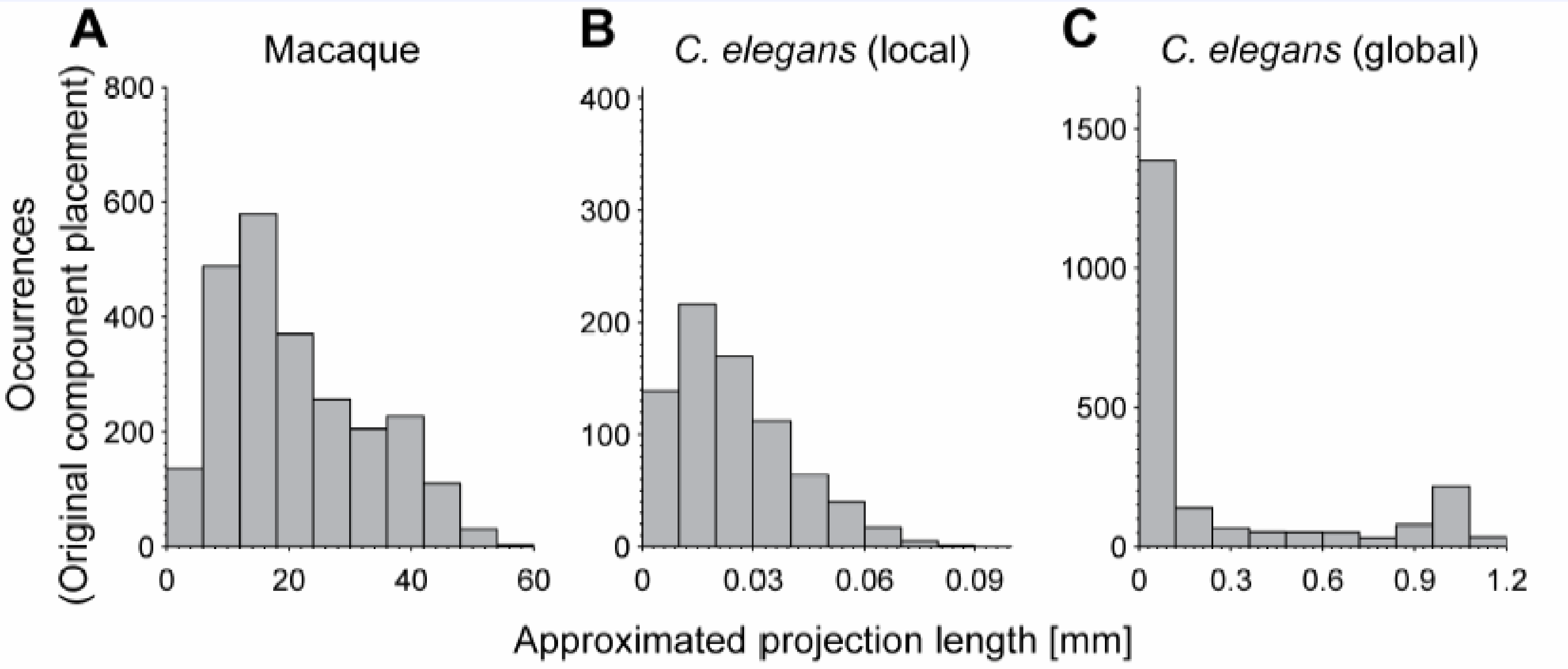




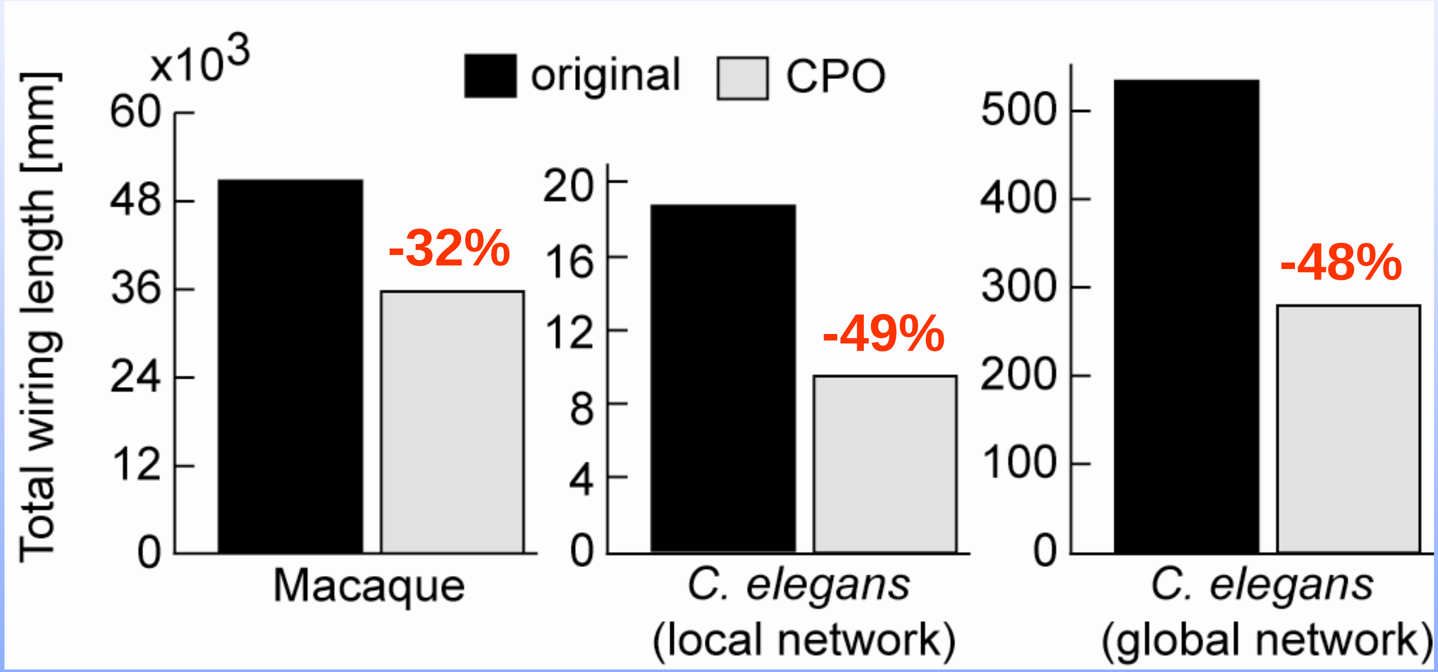
Local level (rostral ganglia, 131 neurons, 764 connections)

(White et al., 1986; Choe et al., 2004)

Wiring length distribution

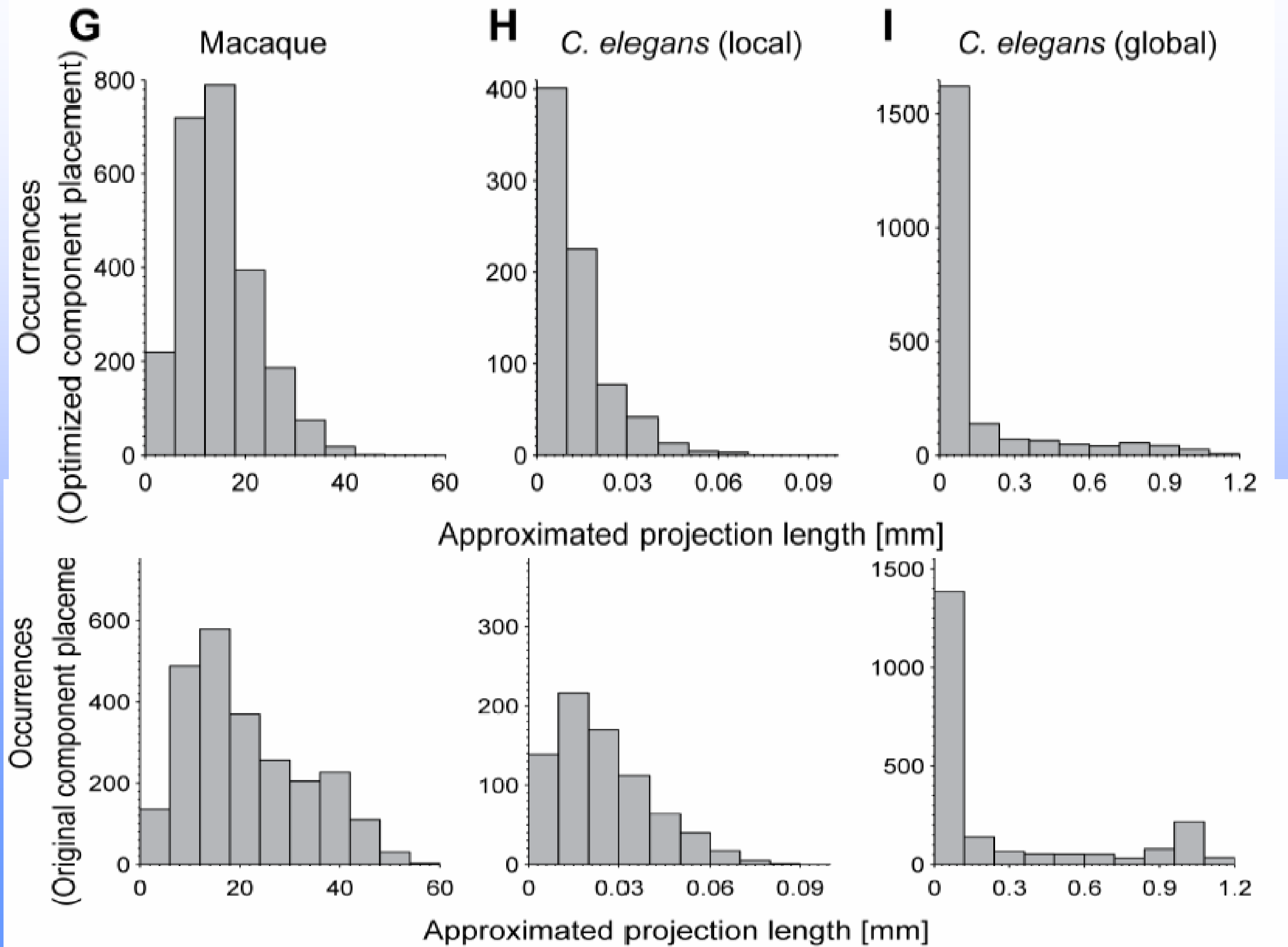


Reduced wiring length for alternative placements



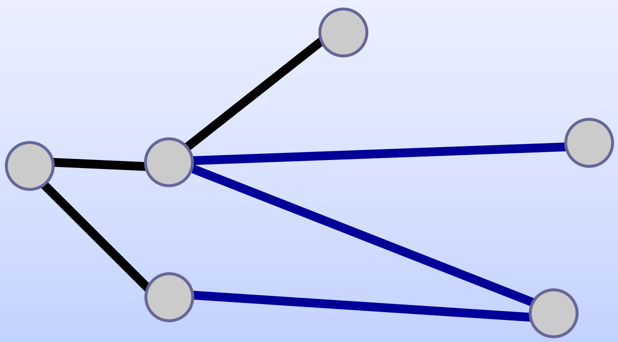
Kaiser & Hilgetag (2006) *PLoS Computational Biology*, 7:e95

Fewer long-distance projections for optimized placement

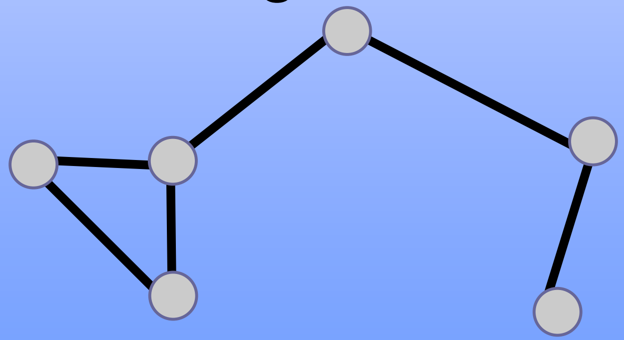


Networks without long-distance connections

Original network

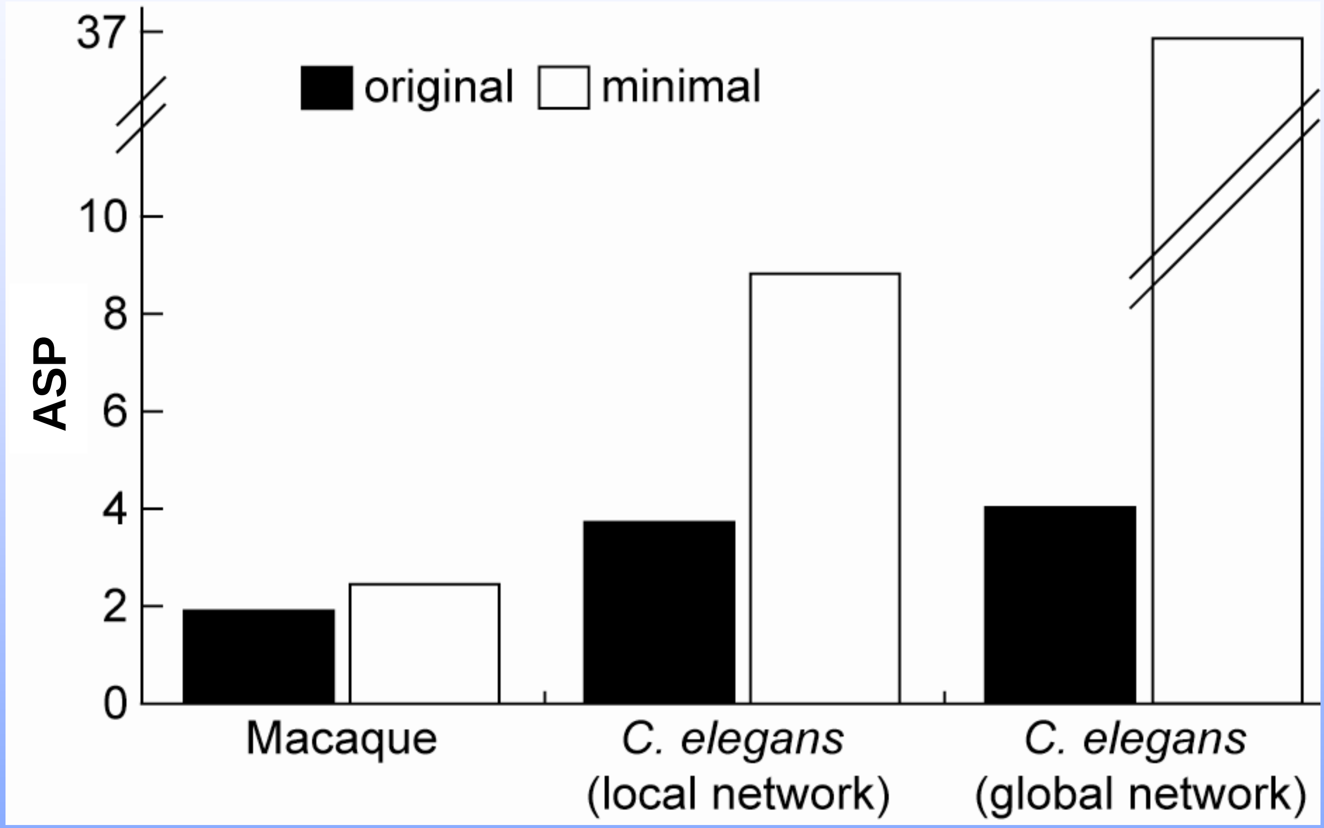


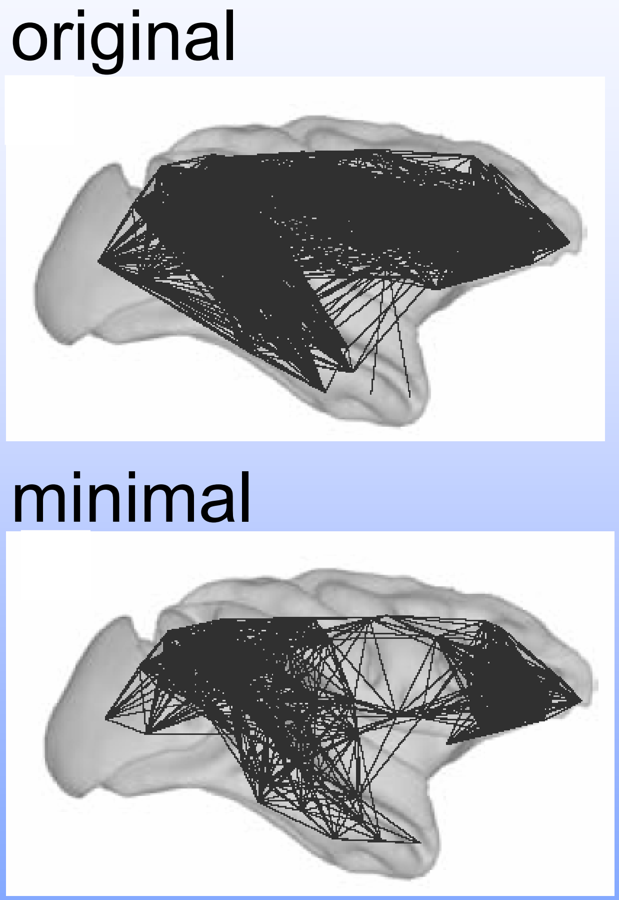
Minimal wiring



same number of connections
preference for short-distance

Why are there long-distance connections?





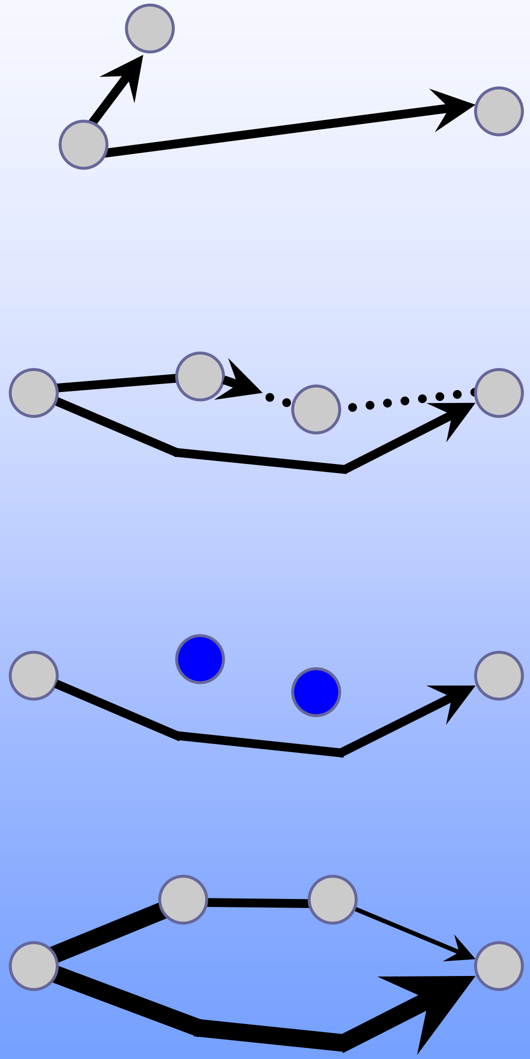
Benefits of fewer processing steps

- **Synchrony of near and distant regions**

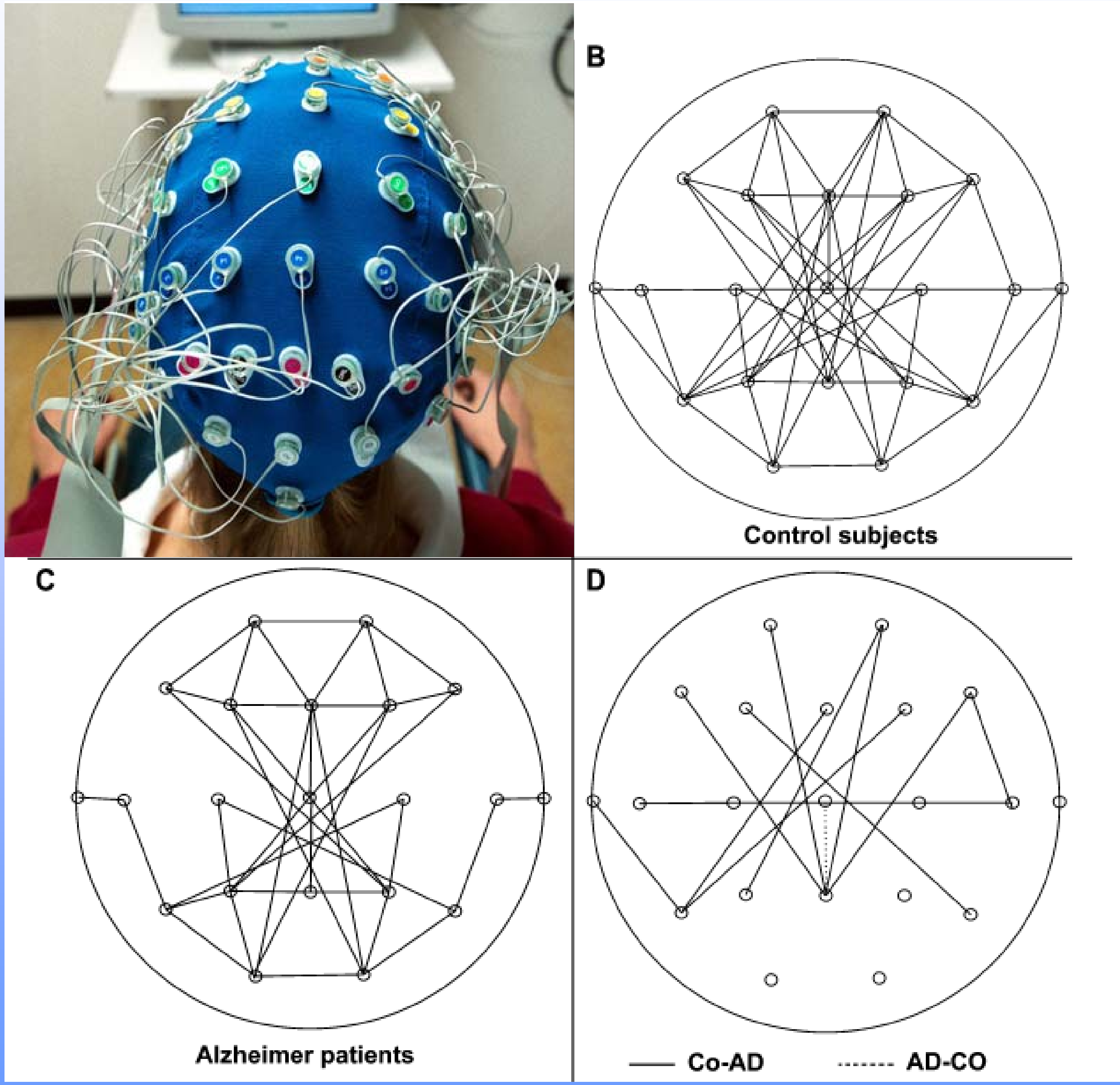
- **Reduced transmission delays**

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

- **Higher reliability of transmission**



Altered Connectivity in Alzheimer patients

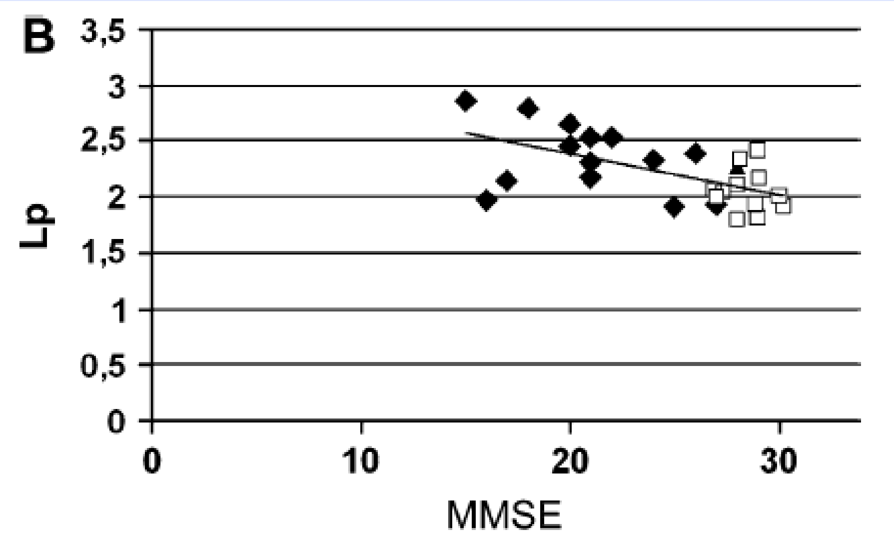


EEG
synchronization
Network

Stam et al. (2007) Cerebral Cortex, 17:92

Path length and task performance

Mini Mental State Examination
(attention, memory, language)

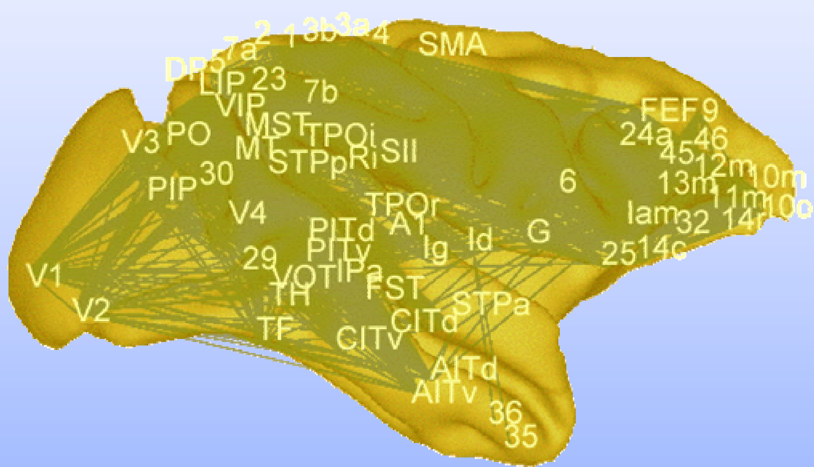


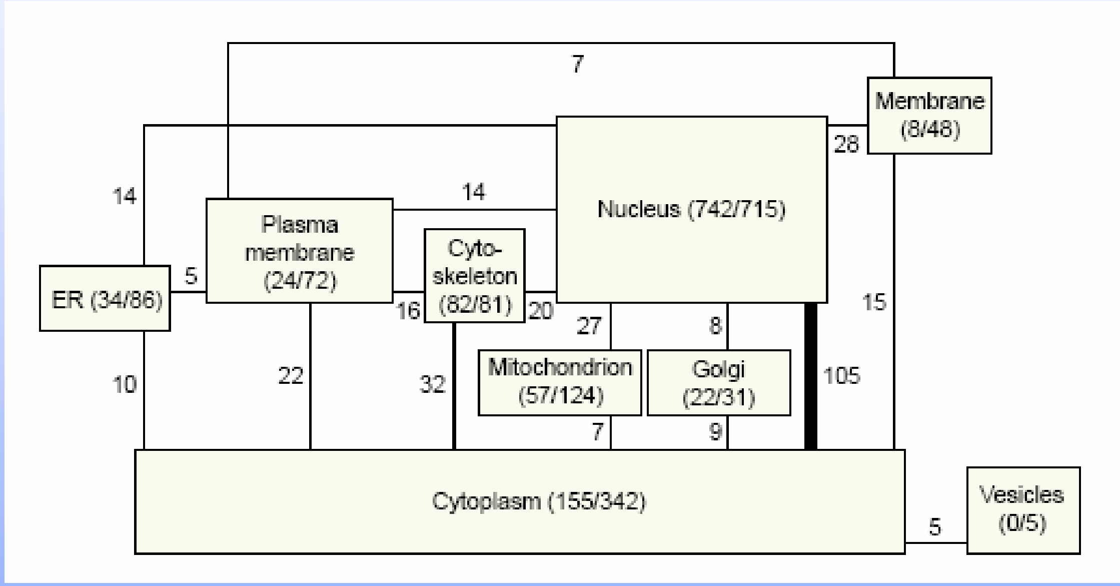
Diamonds:
Alzheimer patients

Empty squares:
Control

Development

Real-world networks extend in space!





References

Kaiser & Hilgetag (2004). *Physical Review E* 69:036103

Kaiser & Hilgetag (2007). *Neurocomputing*, 70:1829-1832

Nisbach & Kaiser (2007). *European Physical Journal B*, 58:185–191

Topological and spatial organization

(1) Preference for short-distance connections

(2) Existence of long-distance connections

(3) Small-world properties

Spatial growth

(4) Spatial and topological clusters

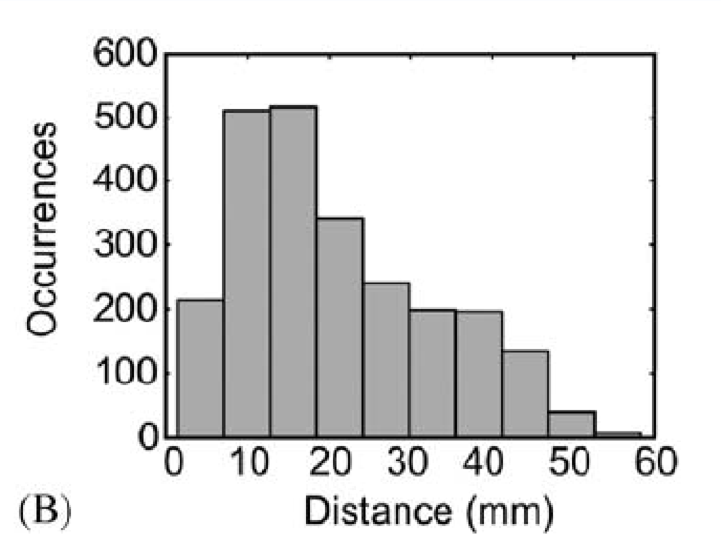
Time windows

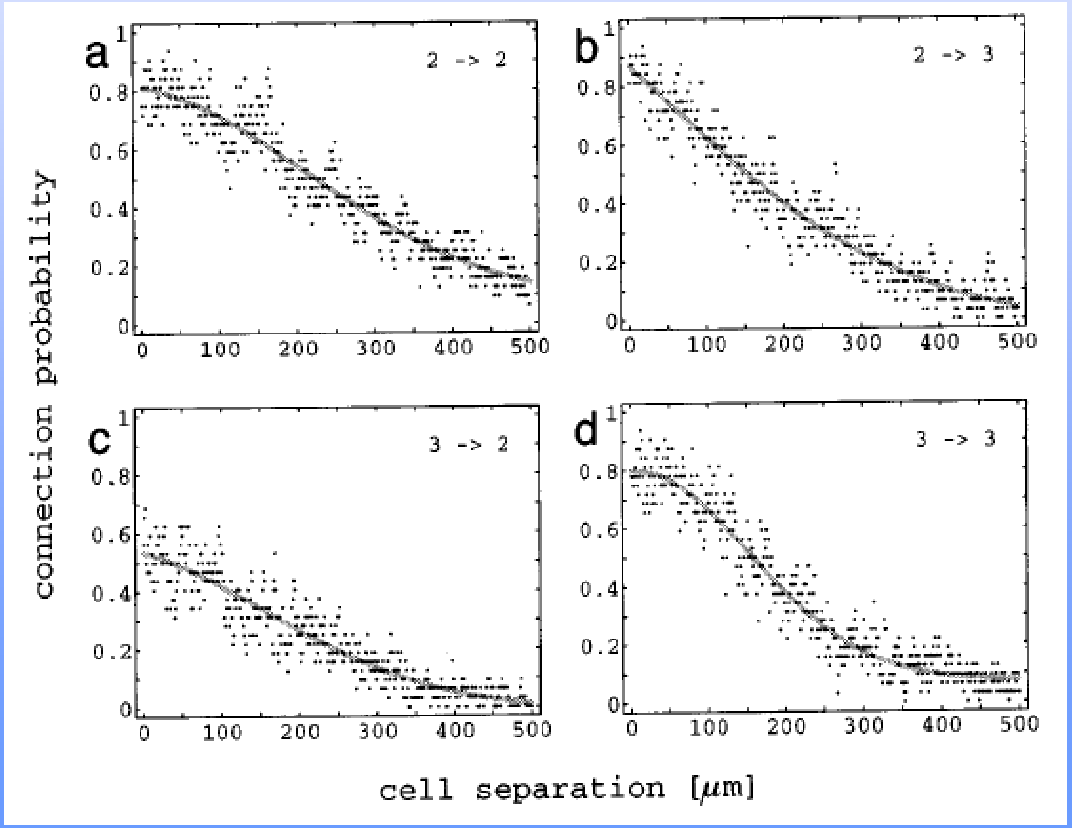
Distance dependence

Global connectivity (between areas)

Kaiser & Hilgetag, 2004

Macaque
(one hemisphere)





Local connectivity

Braitenberg & Schuez, 1998

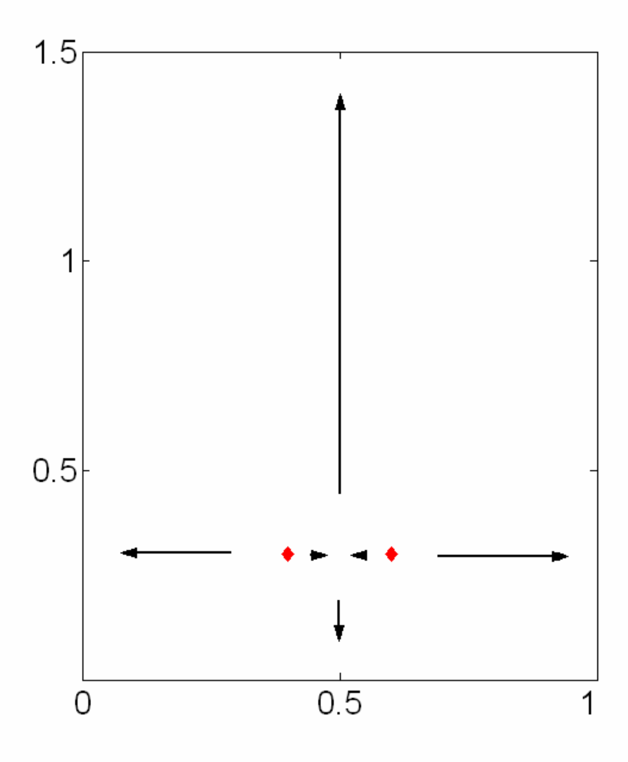
Hellwig, 2000

Rat visual cortex
(layers 2, 3)

Spatial growth

Edge formation probability depends on spatial distance *d* between nodes *u* and *v*

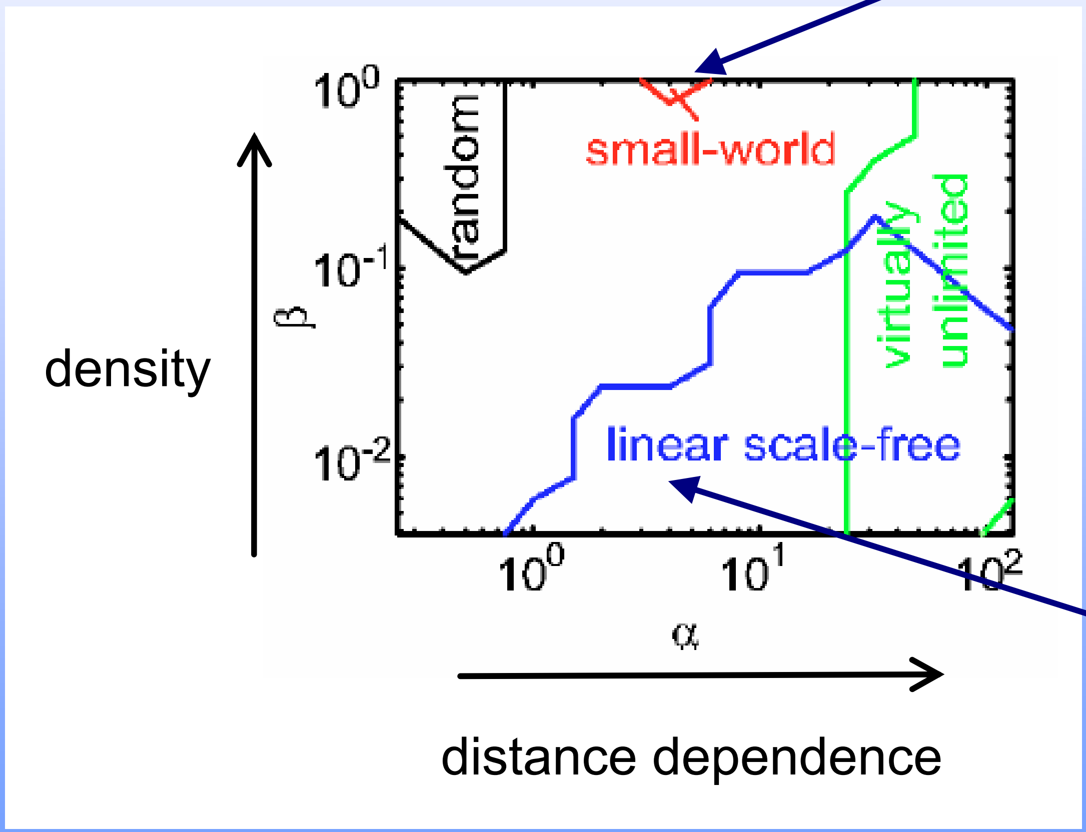
$$P(u, v) = \beta \; e^{-\alpha \; d(u,v)}$$



Kaiser & Hilgetag, Physical Review E, 2004

Resulting network topology

Cortical Networks



- German highway system
- Yeast Protein-Protein Interaction Network

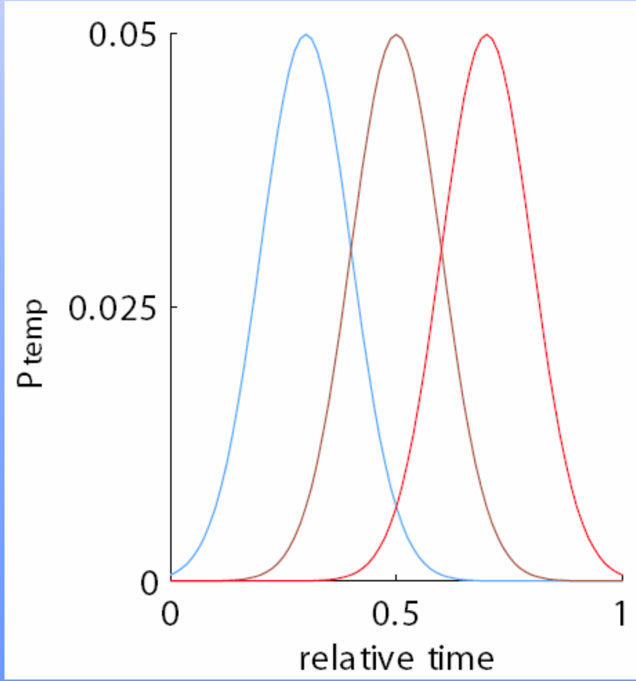
Spatial growth and time windows

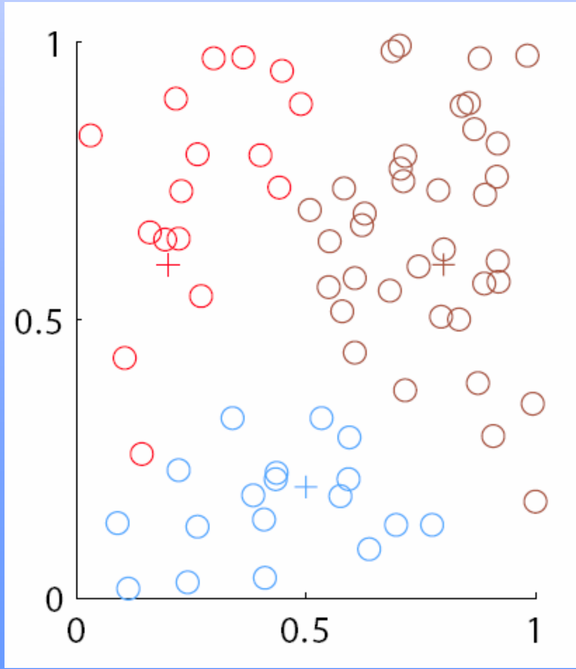
Spatial component:

$P_{dist}(u,v) = c * e^{-a\, d(u,v)}$

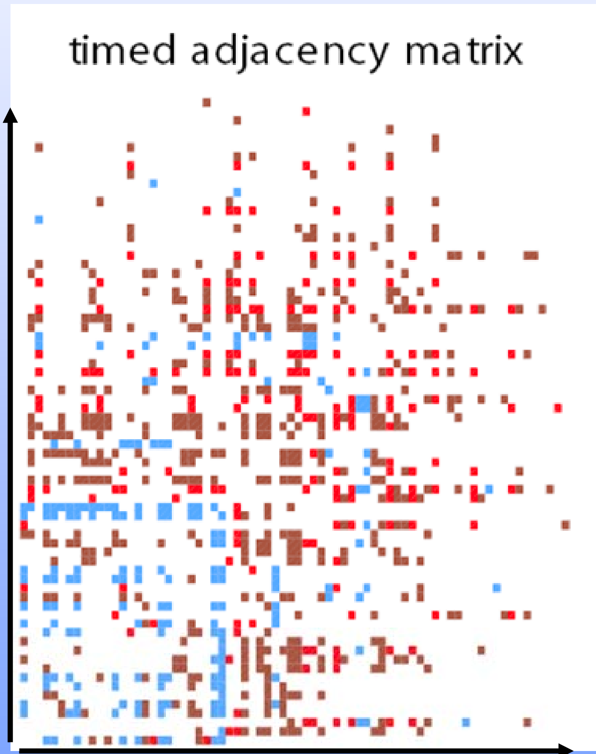
Time-window dependance:

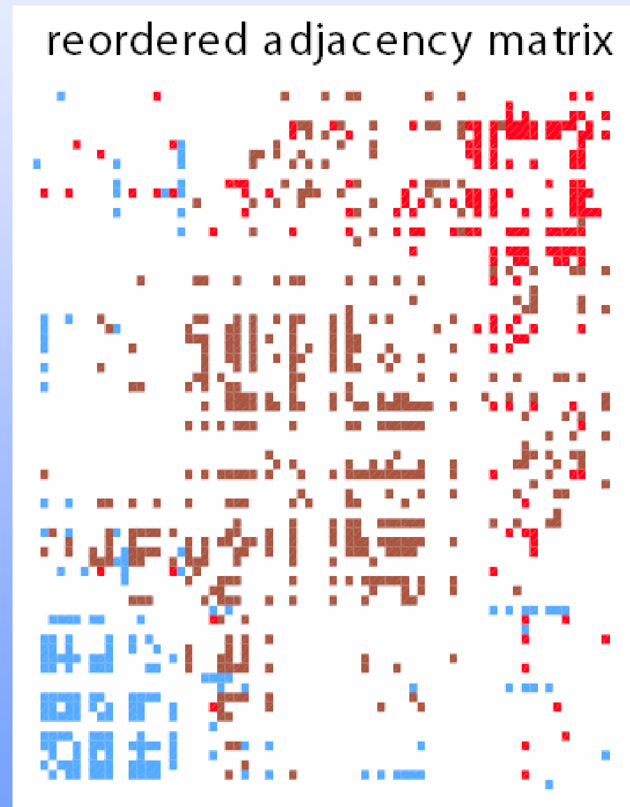
$P(u,v) = P_{temp}(u) * P_{temp}(v) * P_{dist}(u,v)$





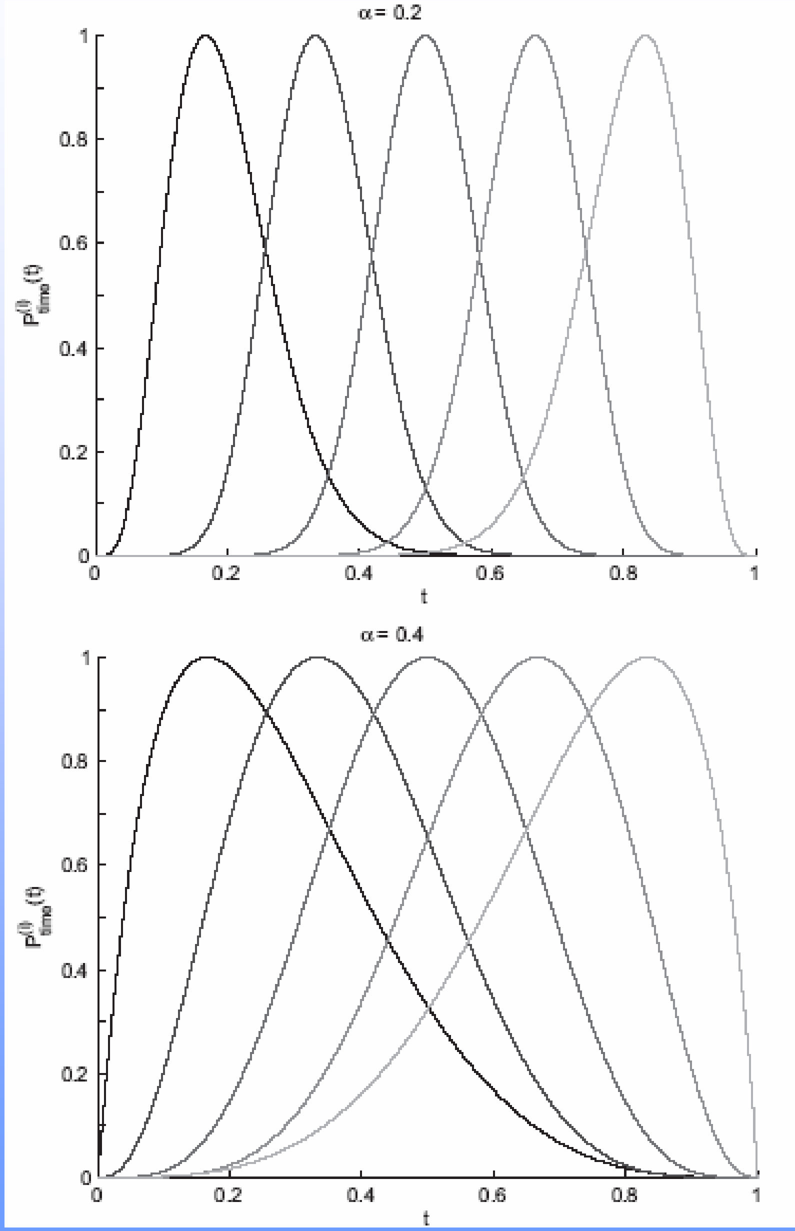
Development of Clusters

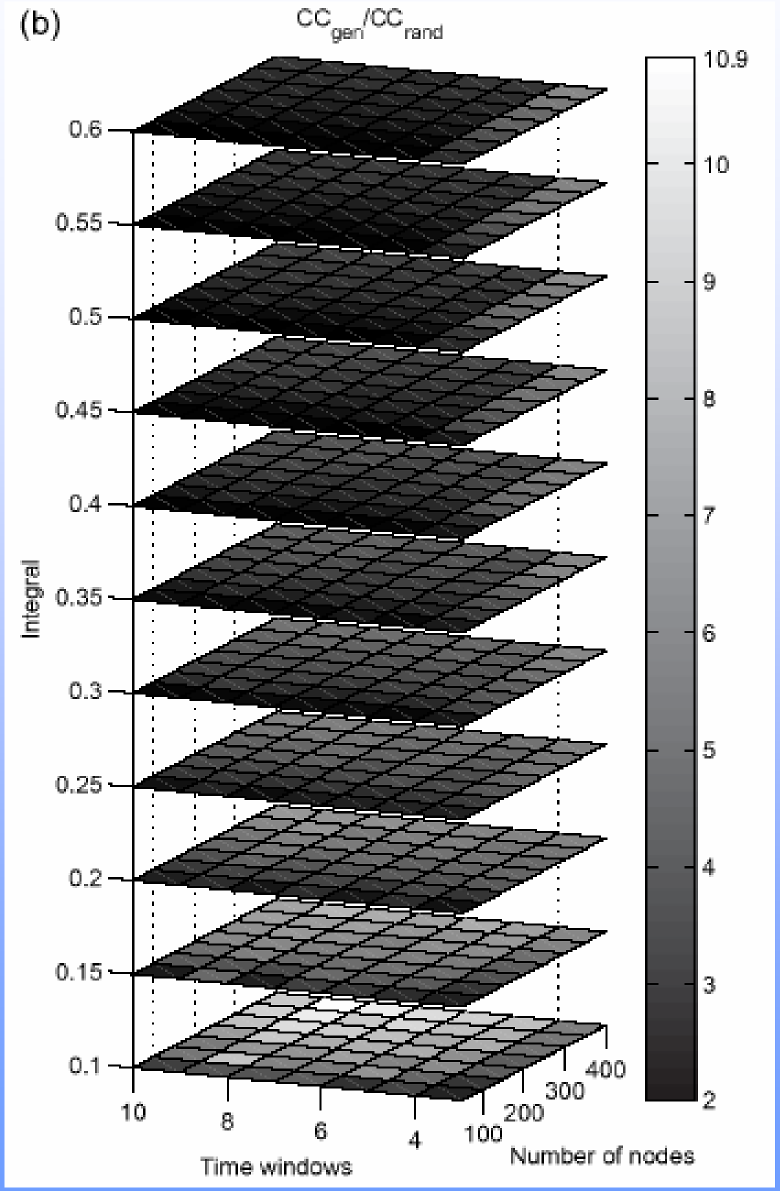




Kaiser & Hilgetag (2007). *Neurocomputing*, 70:1829-1832

Robustness of small-world properties





Nisbach & Kaiser (2007). *European Physical Journal B*, 58:185–191

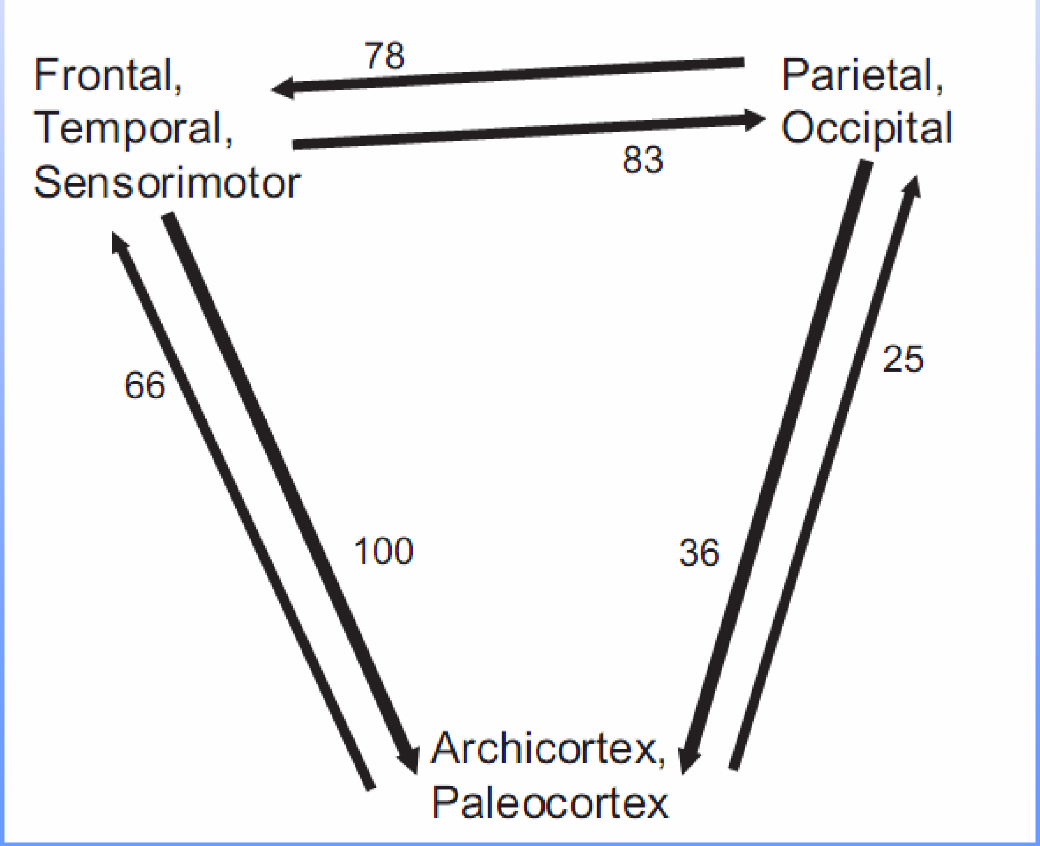
Is this model implemented in the brain?

Experimentally testable predictions:

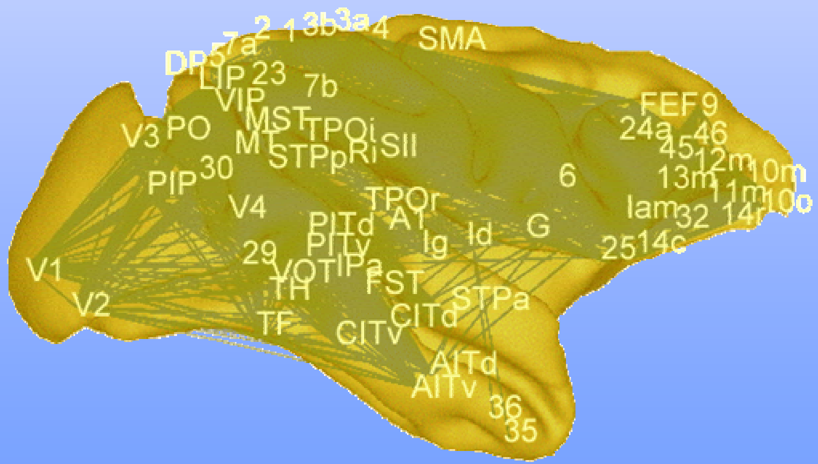
(1) A small overlap of the time windows of two regions should result in fewer fibre tracts between those regions.

(2) Regions with wider time windows should (a) have a larger number of connections and (b) be part of a larger cluster.

(3) Older regions should get more connections than newer regions.



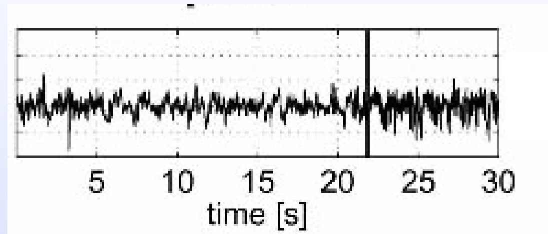
Hierarchy and critical activation



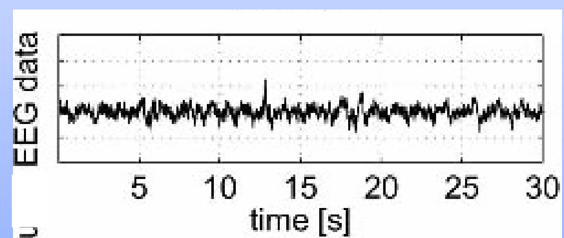
One degree of separation

Critical range of cortical function

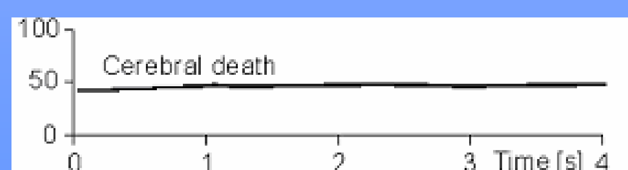
High level of activation



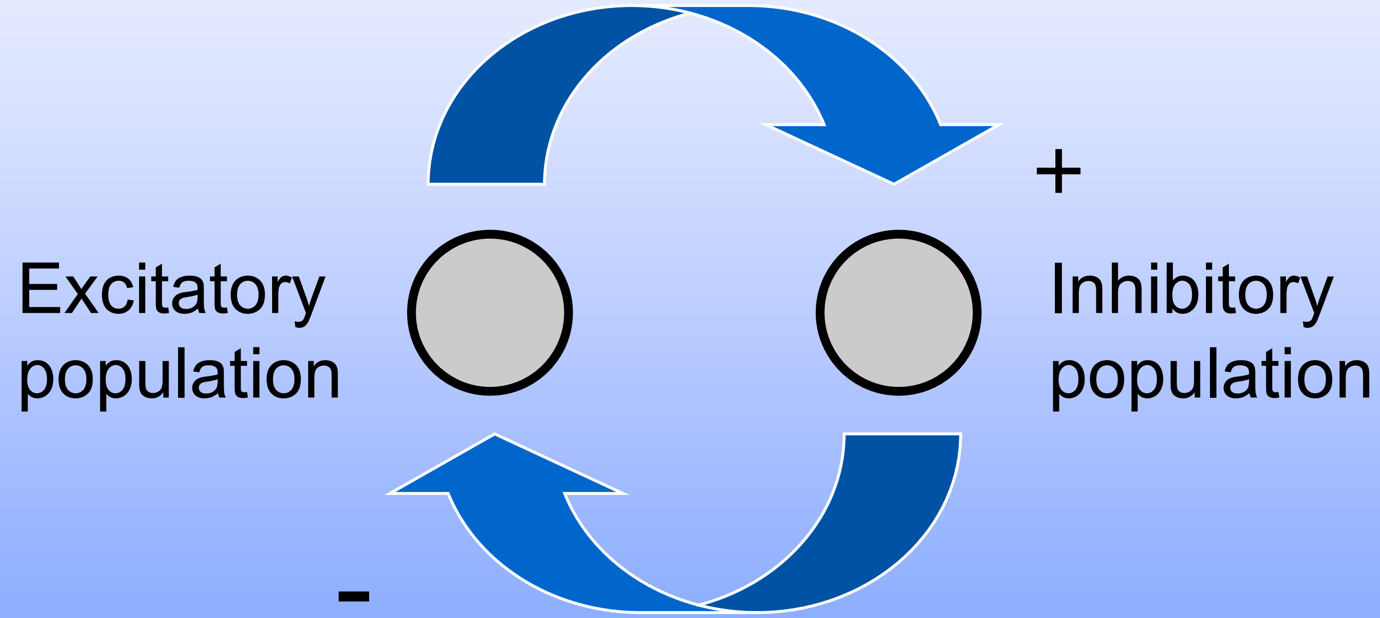
Epileptic seizure



Low activation

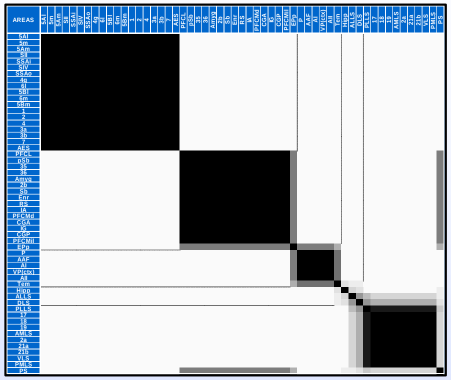


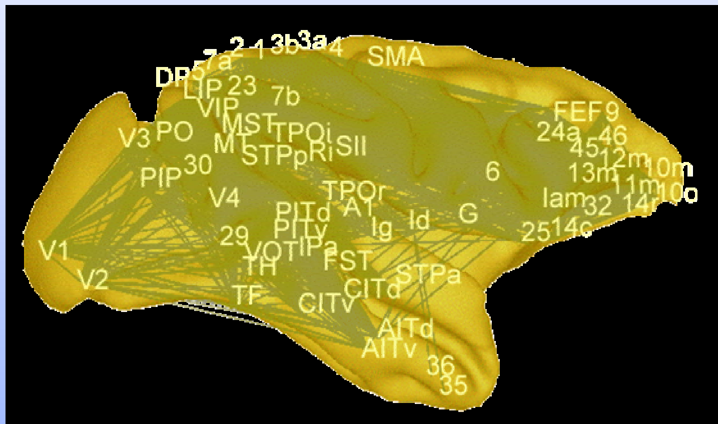
Standard model:
Balance between inhibition and excitation

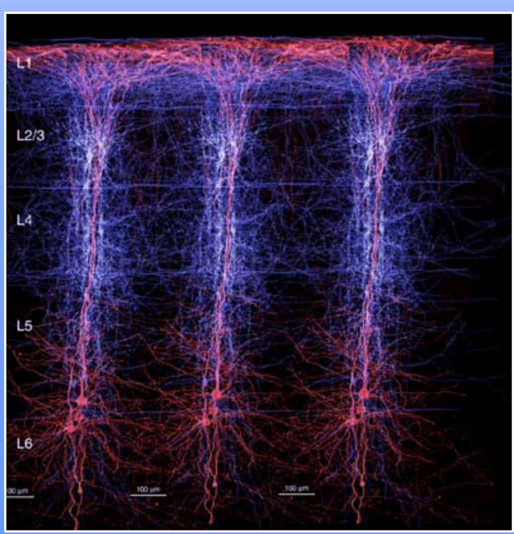


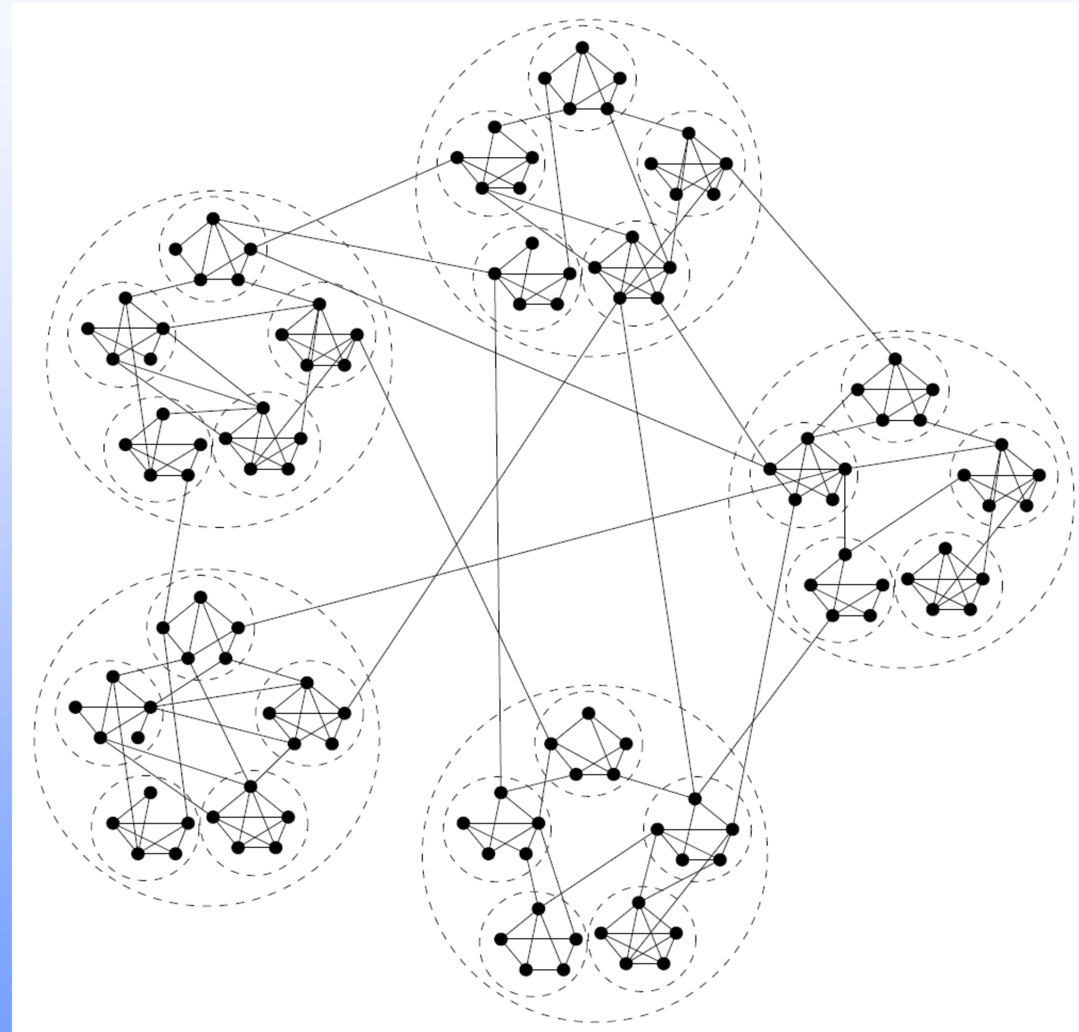
Soltesz & Staley. *Computational Neuroscience of Epilepsy*. Academic Press, to appear in Nov.

Topological model: Hierarchical modular network





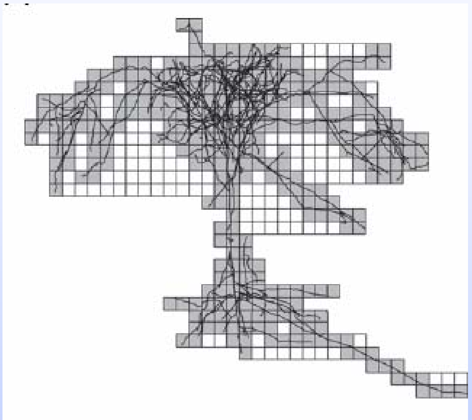


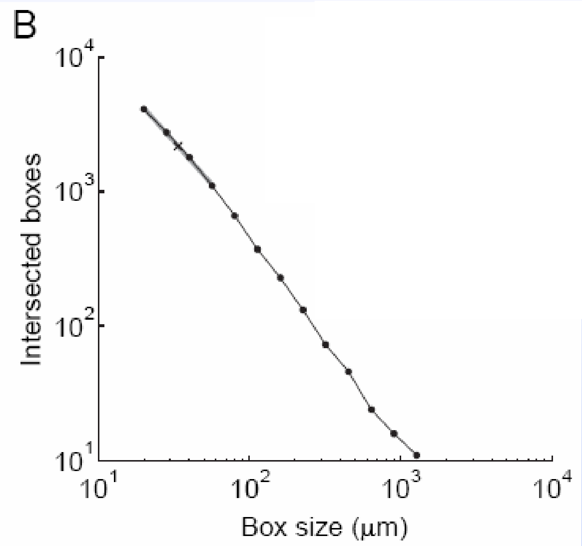


- clusters of sub-clusters of nodes

Spatial self-similarity

Neuron

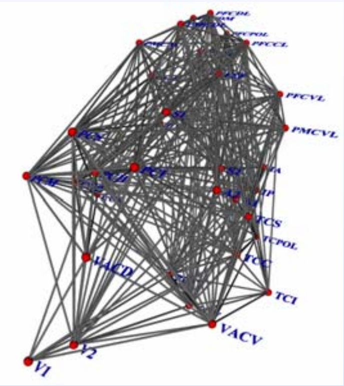


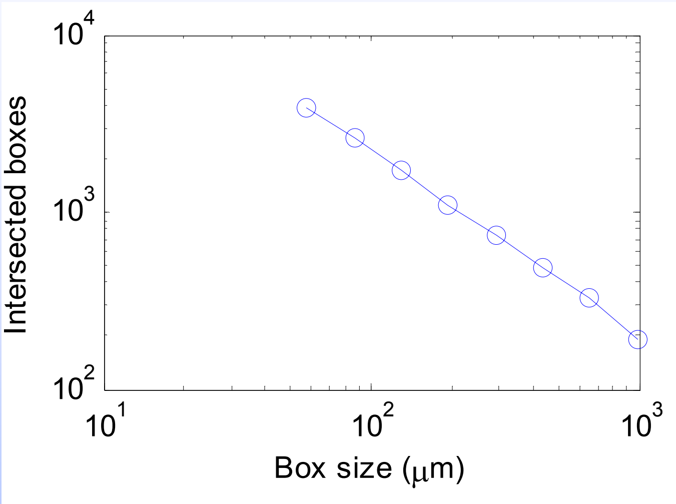


Box counting dimension:
1.5-1.7

Binzegger et al. (2005), Cerebral Cortex

Cortical network



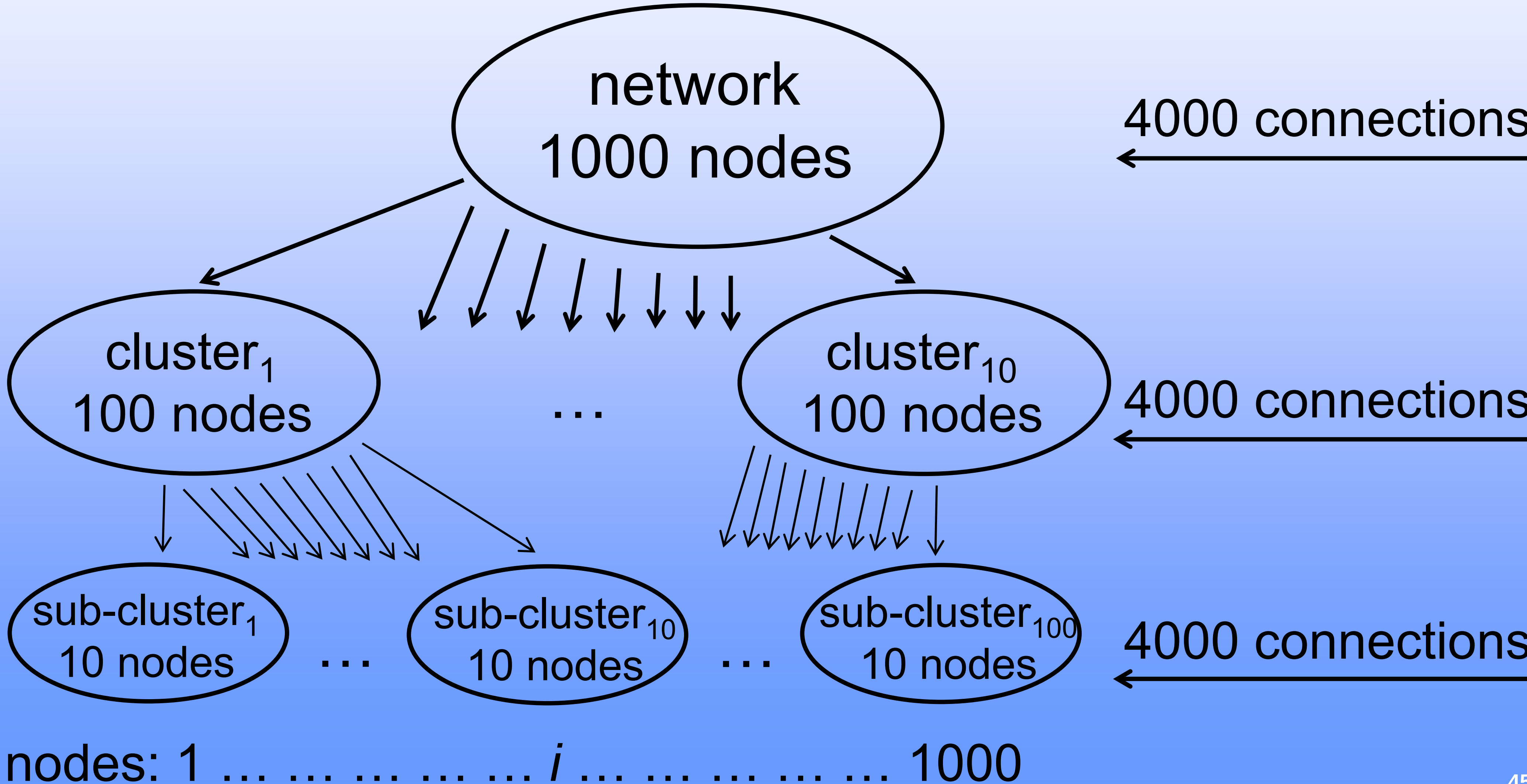


Box counting dimension:
1.39-1.42

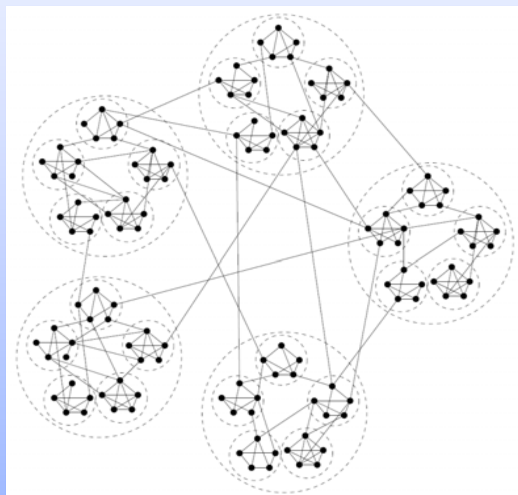
(Kaiser, unpublished)

Hierarchical cluster network model

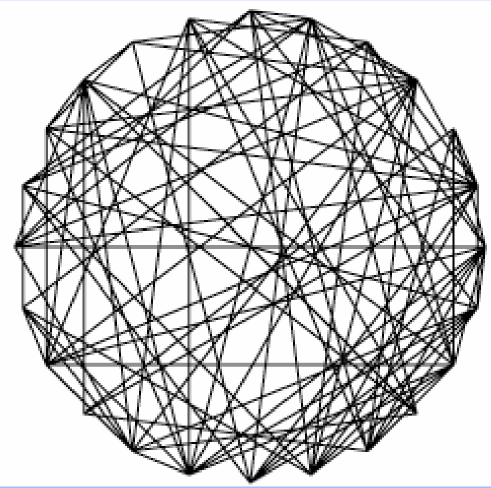
- 1,000 nodes; 12,000 bidirectional connections
- activation threshold: >6 presynaptic neurons, stochastic deactivation, *p*=0.3



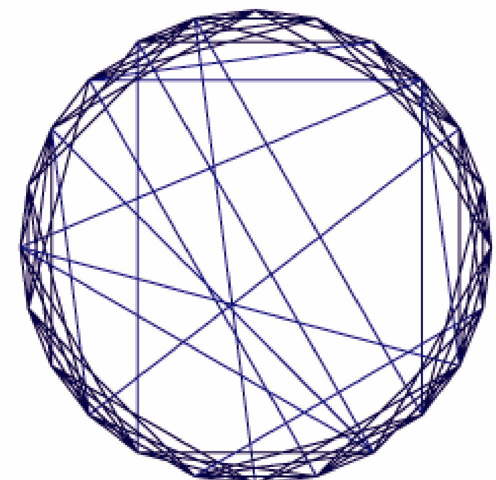
Comparison networks



hierarchical cluster



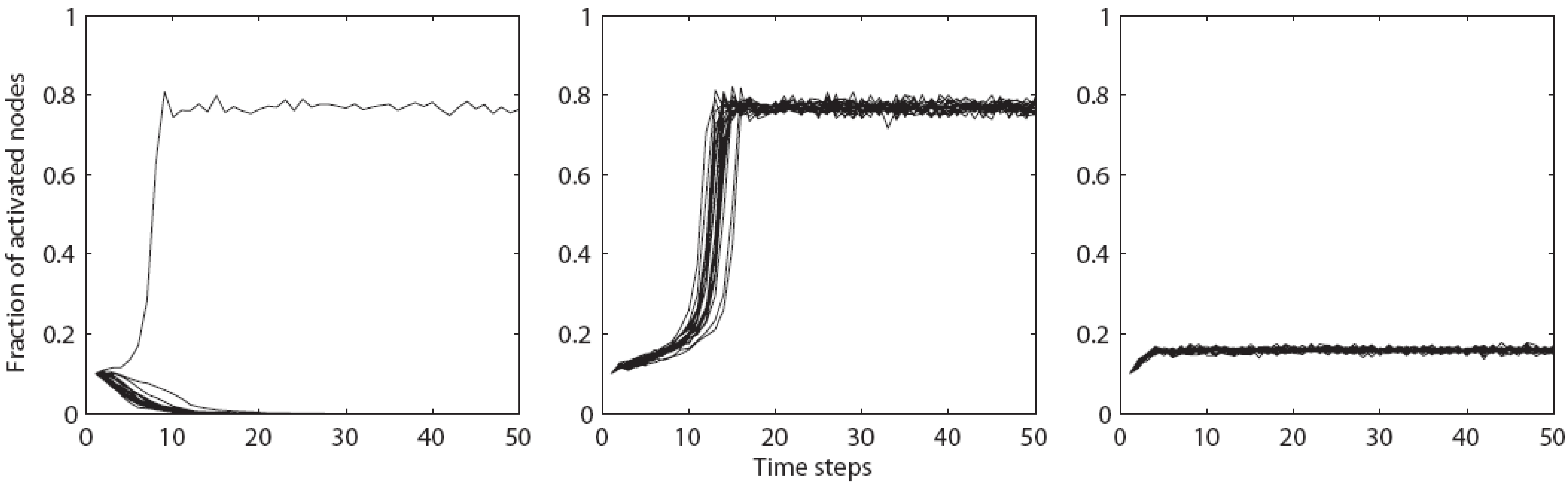
random



small-world

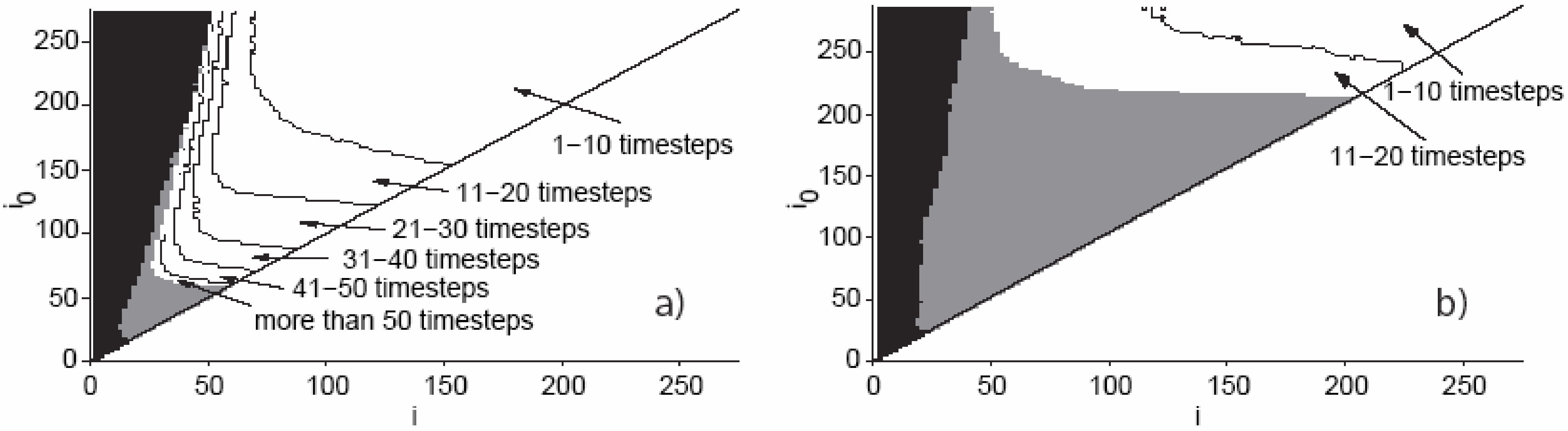
Example activation behaviour

- 30 runs
- 100 (10%) randomly activated initial nodes



random small-world hierarchical cluster

Robustness for starting parameters

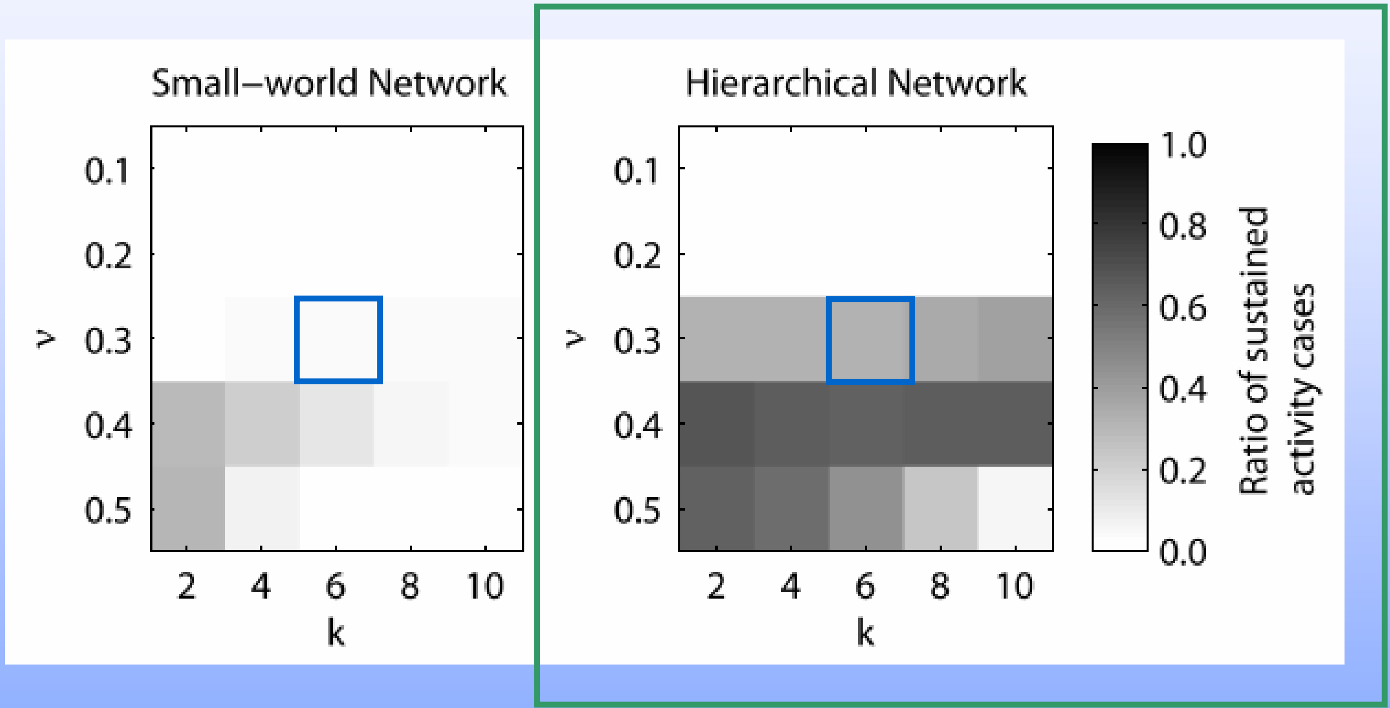


small-world

hierarchical cluster

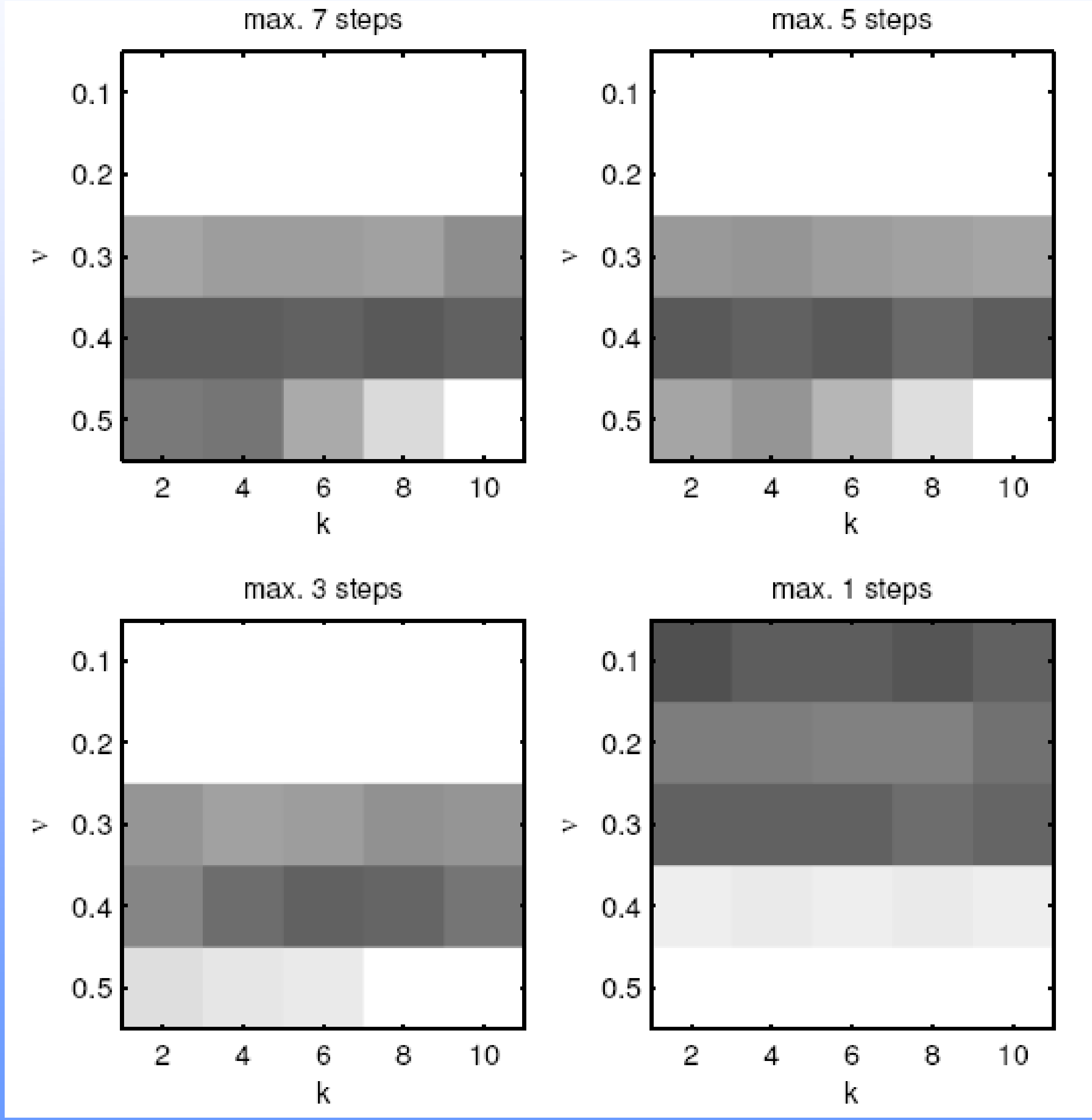
Kaiser, Goerner, Hilgetag (2007) *New Journal of Physics*, 9:110

Robustness for spreading parameters

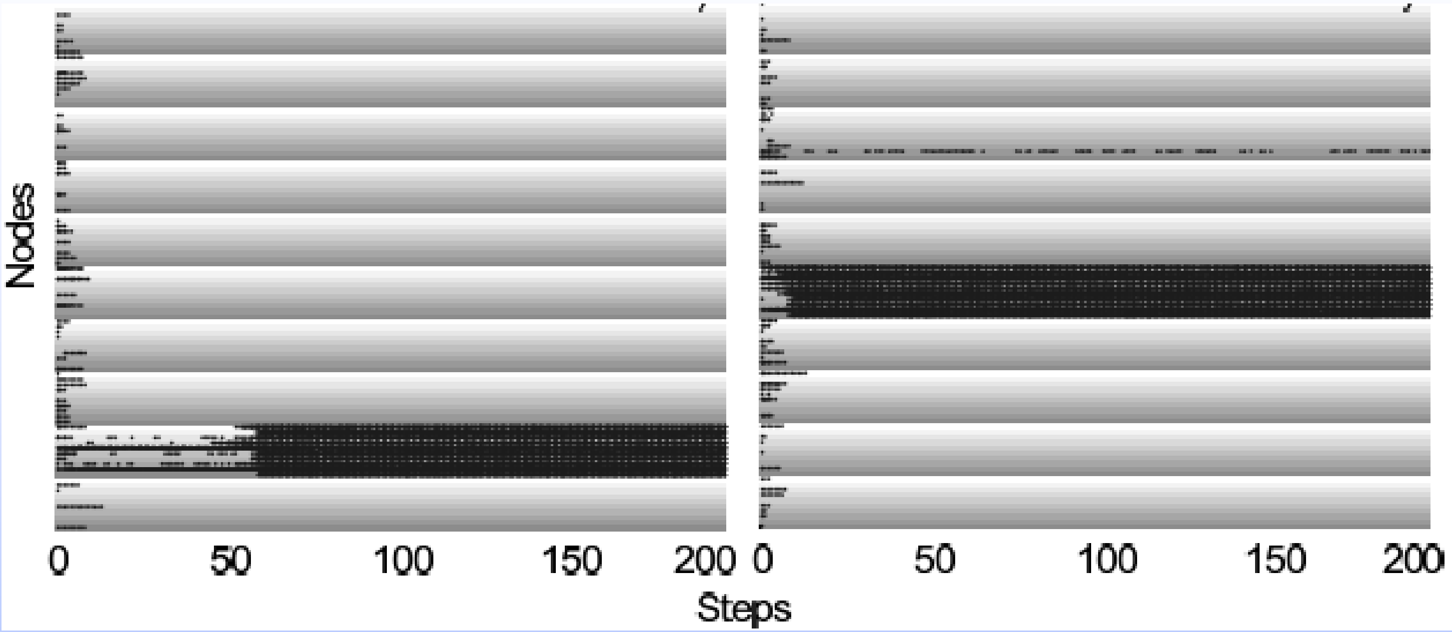


k: activation threshold
v: deactivation probability

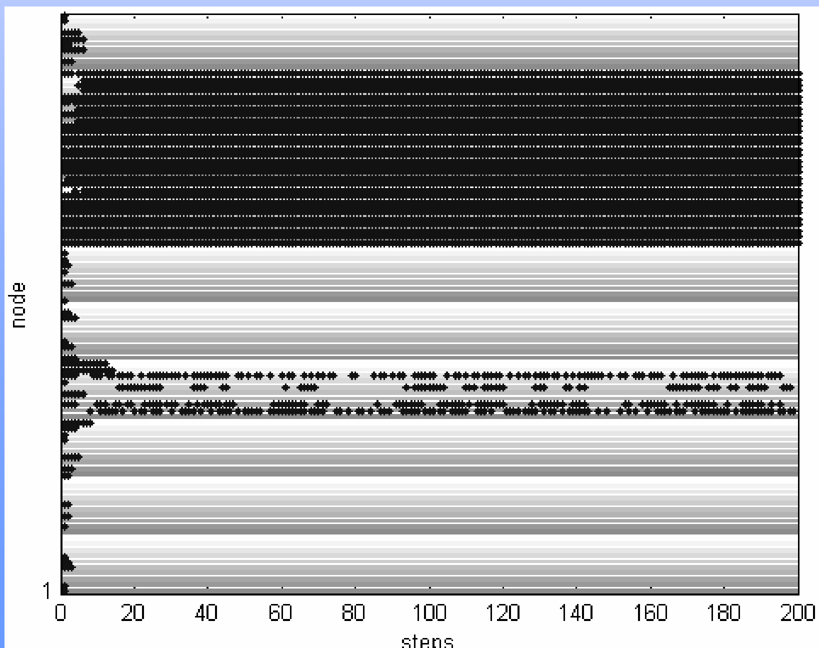
Robustness for node exhaustion



Dependence on inter-cluster connectivity



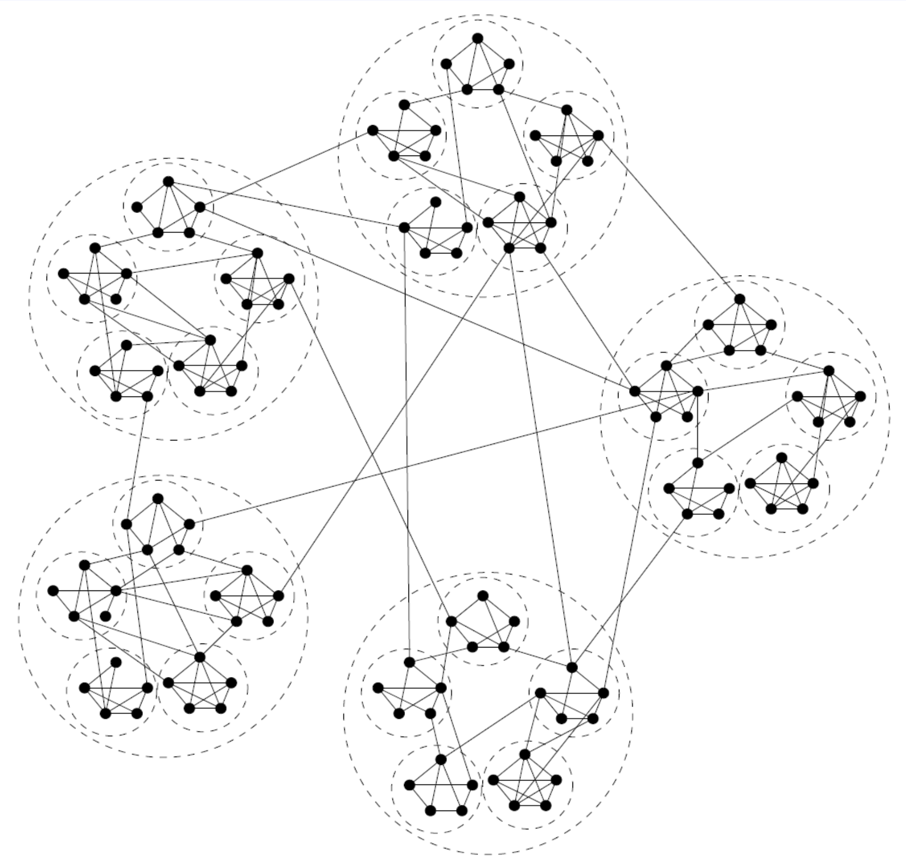
Sustained activity in one cluster



Sustained activity in three clusters for *reduced* inter-cluster connectivity

Do epilepsy patients have larger inter-cluster connections?

Outlook: Hierarchies and activity spreading



subsubcluster activation

→ spatially near nodes

→ rapid feedback

→ rapid oscillation

⬇

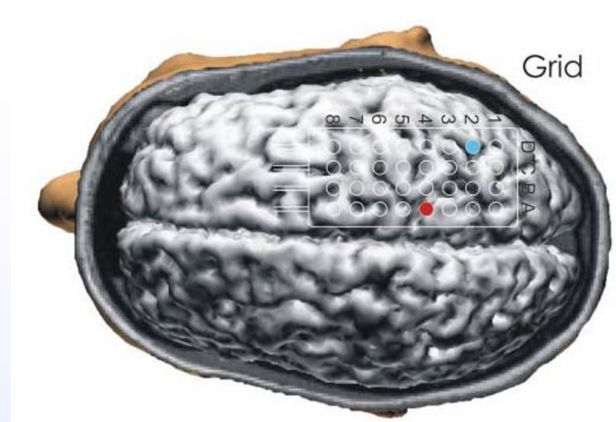
cluster activation

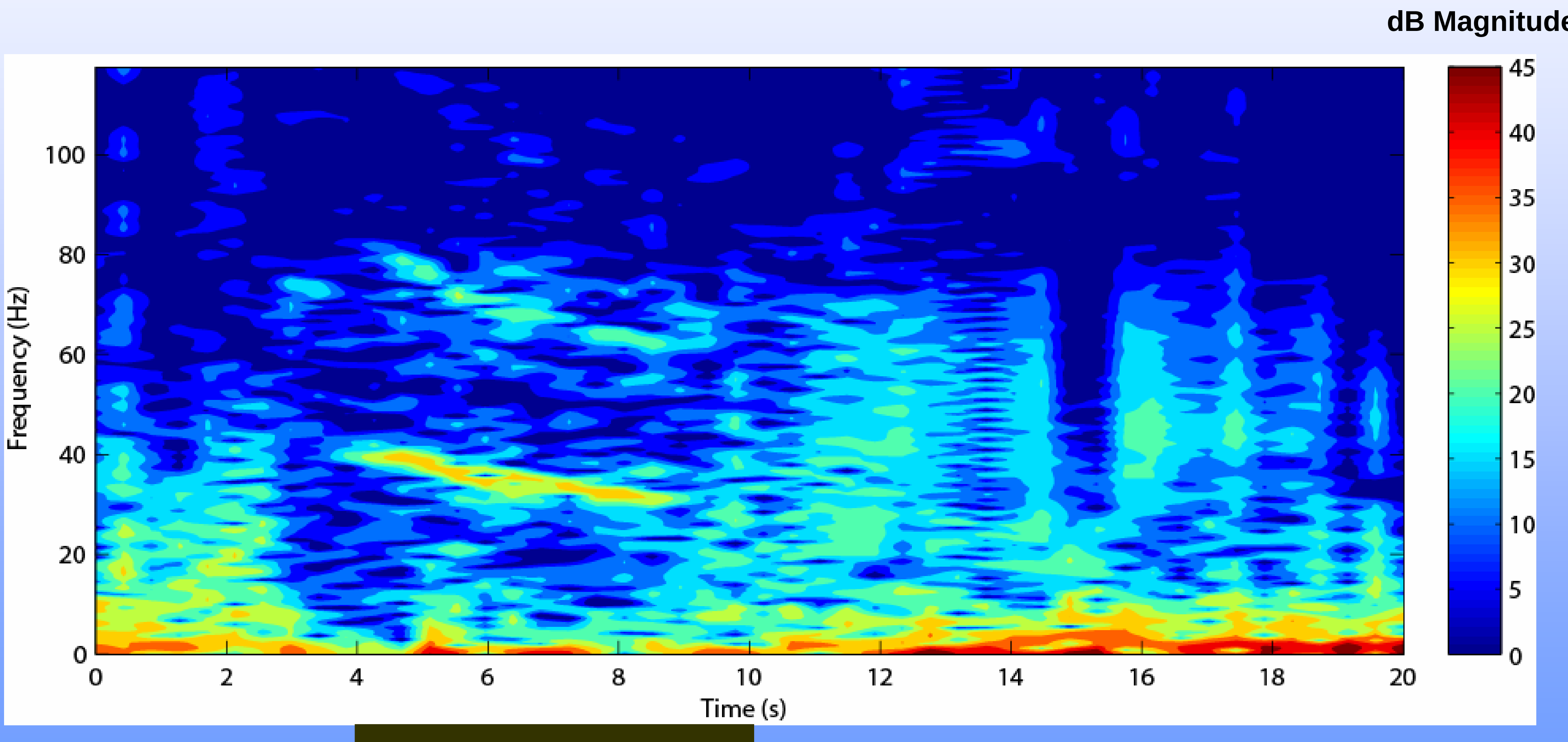
→ spatially near and distant nodes

→ slower feedback

→ slower oscillation

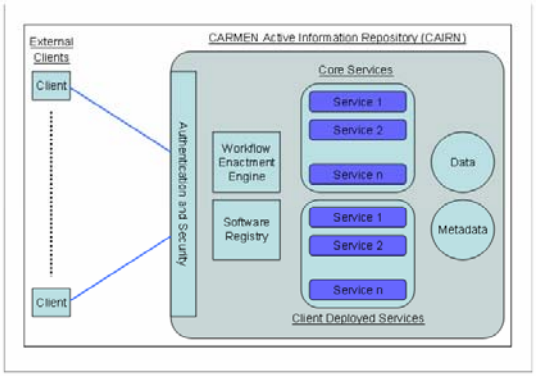
Partial seizure





Xiang and Kaiser, unpublished

www.carmen.org.uk



EPSRC **£4.5M e-science project started in Oct 2006**

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wellcome trust **4-year PhD Programme:**
'Systems Neuroscience: From Networks to Behaviour'
starting October 2008

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Prof. Paul Watson,
Dr Stuart Baker,
Dr Marcus Kaiser,
Dr Phil Lord,
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Prof. Jim Austin
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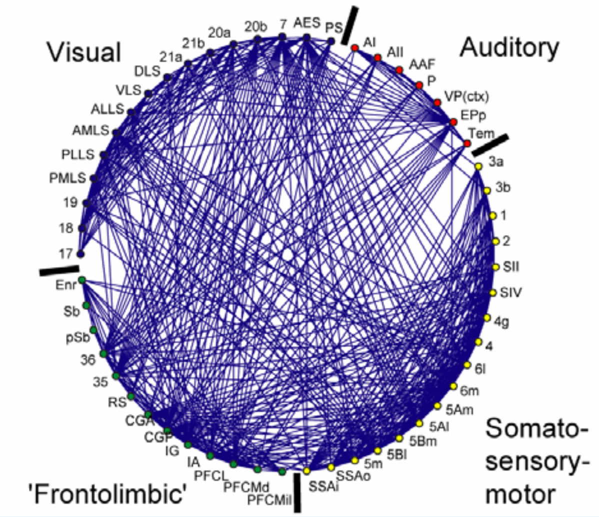
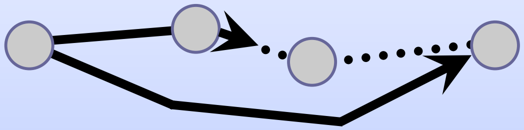
Prof. Roman Borisyuk
Warwick :
Prof. Jianfeng Feng
Imperial College :
Dr Simon Schultz

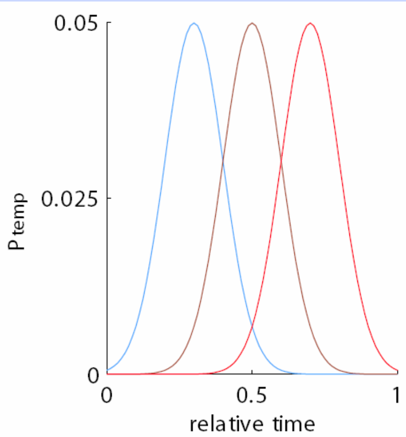


Summary

- **Cortical networks show properties of small-world and scale-free networks and have a modular organization (clusters)**

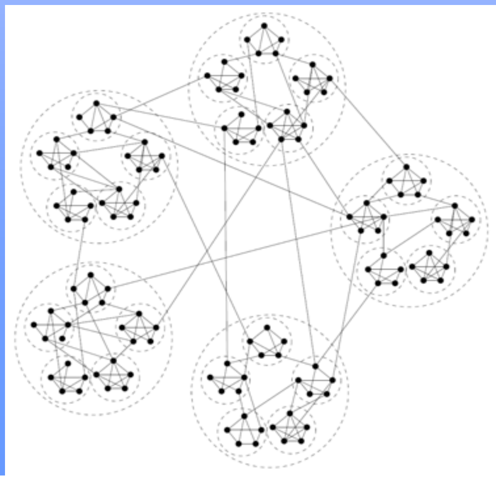
- **Neural systems are optimized for fast processing rather than for saving energy**





- **Spatial growth with time windows generates modular small-world networks**

- **Hierarchical modules enable robust sustained activity without inhibition or external inputs**



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More information at http://www.biological-networks.org/