Large scale network models of brain function

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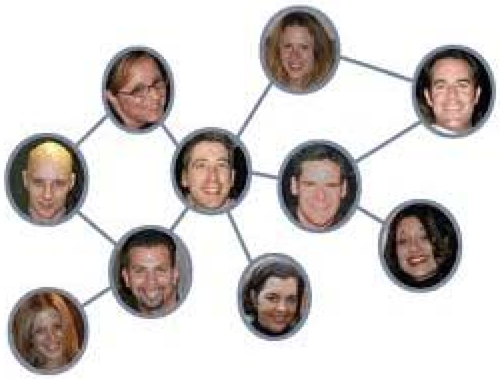
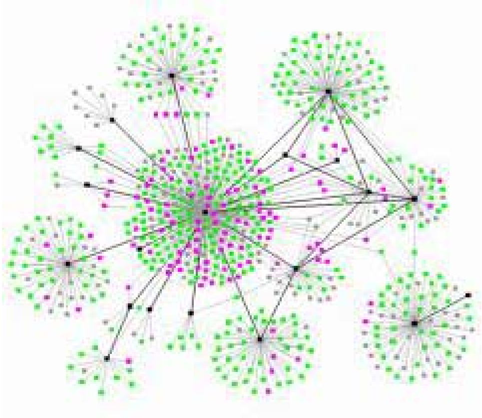
Network science: networks as models of complex systems

Airline route map

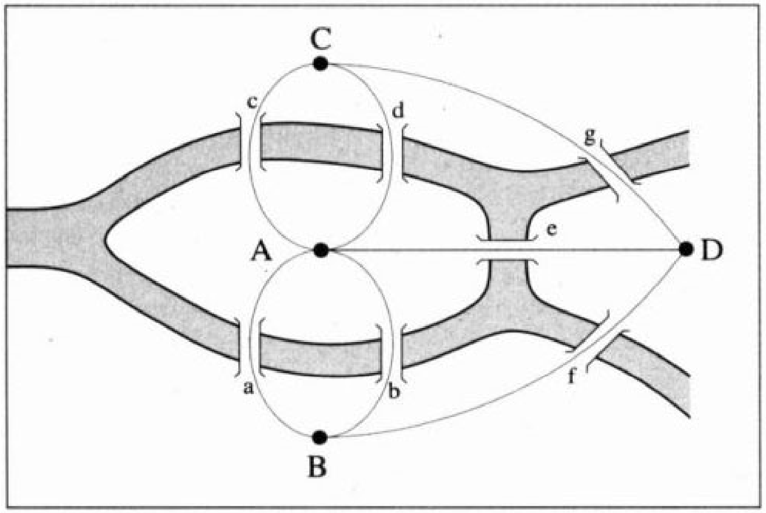
Social networks





Origin of network science: graph theory

Leonhard Euler's 1736 publication on the bridges of Königsberg (Kaliningrad) is the origin of graph theory.



Shortest path

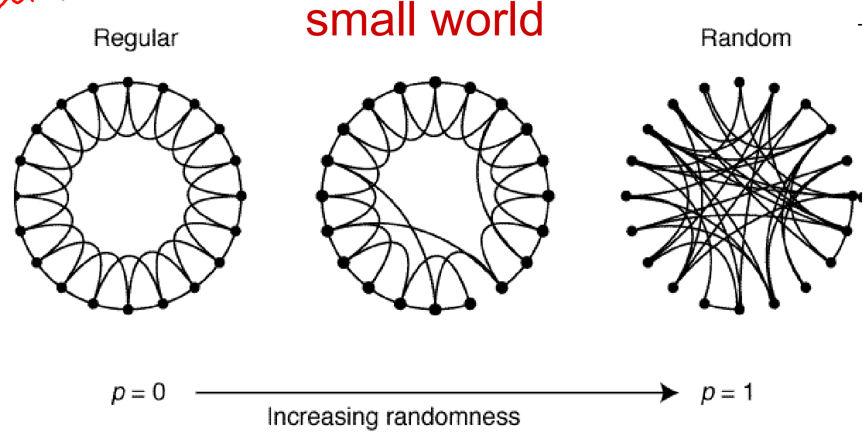
Euler L (1736) *Commentarii Academiae Scientiarum Imperialis Petropolitanae* 8, 128-140.
Sporns (2009) SFN.

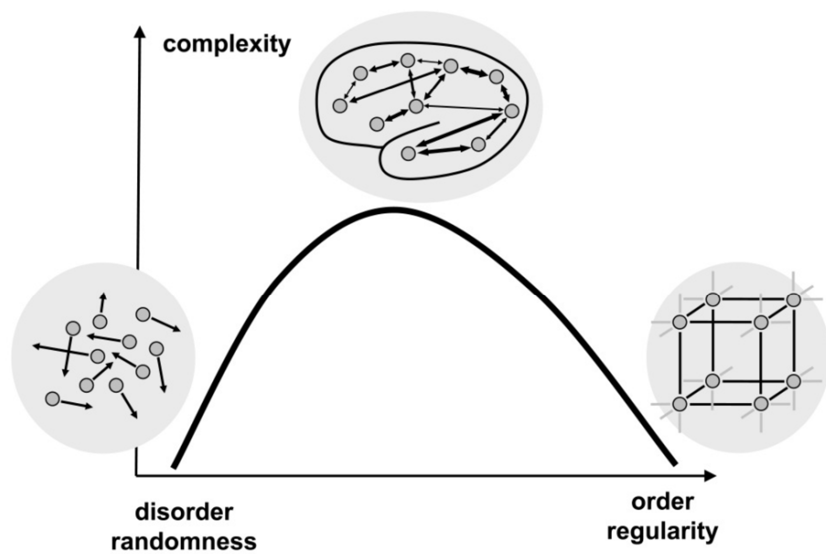
Modern network science

Measures

Research in statistical physics and complex systems has focused on identifying universal principles of network organization, and on common patterns shared among very different networks – e.g. "small world."

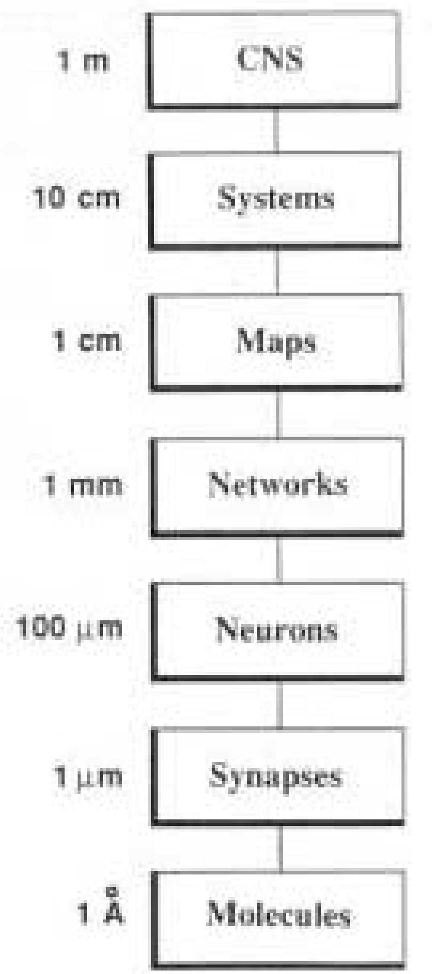
Lattice





Watts & Strogatz (1998) *Nature* 393, 440;   Sporns (2009) SFN.

Spatial / functional unit scale in the CNS

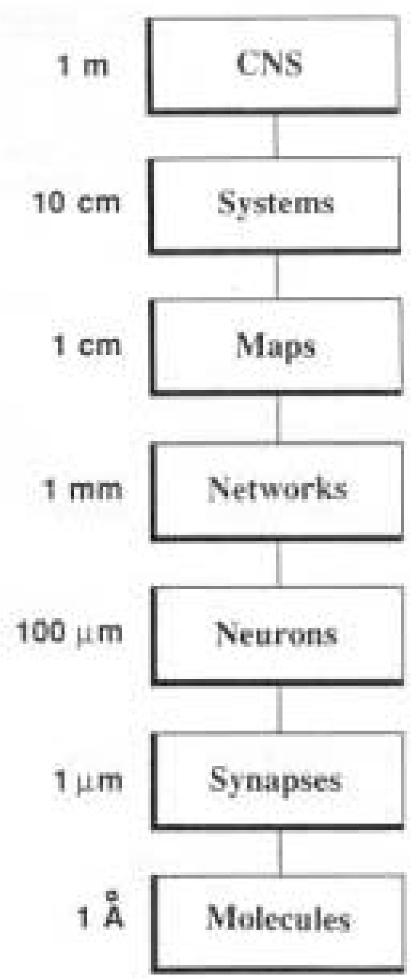


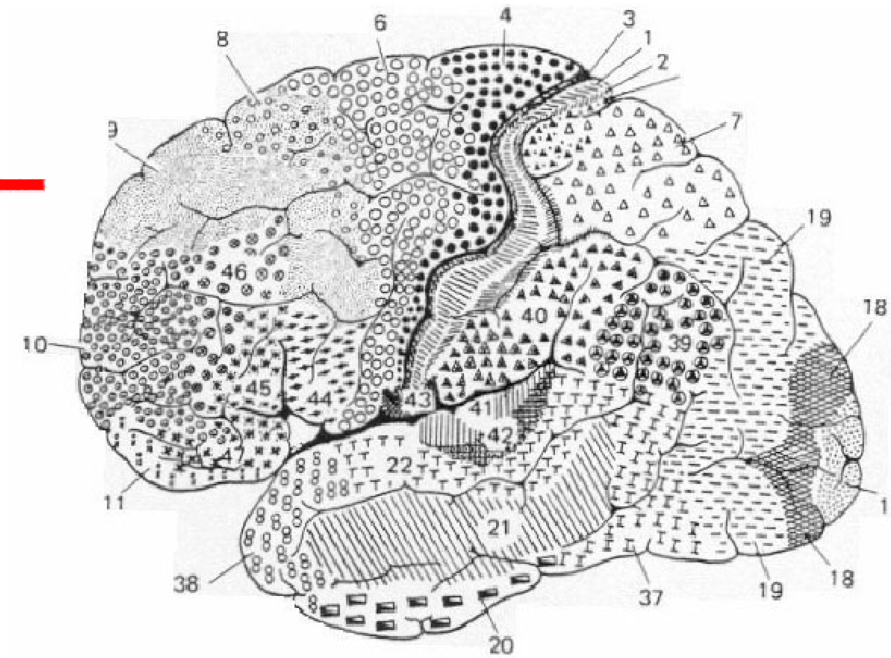
Macroscopic: Anatomically segregated brain regions and inter-regional pathways. Entire Brain

Mesoscopic: Connections within and between microcolumns (minicolumns) or other types of local cell assemblies.

Microscopic: Single neurons and their synaptic connections.

Spatial / functional unit scale

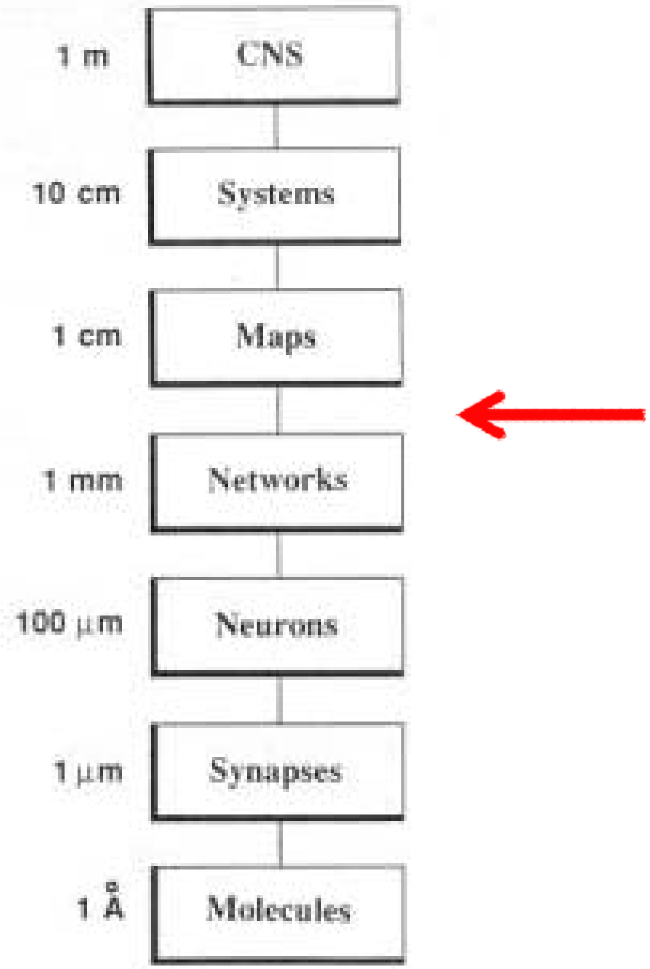


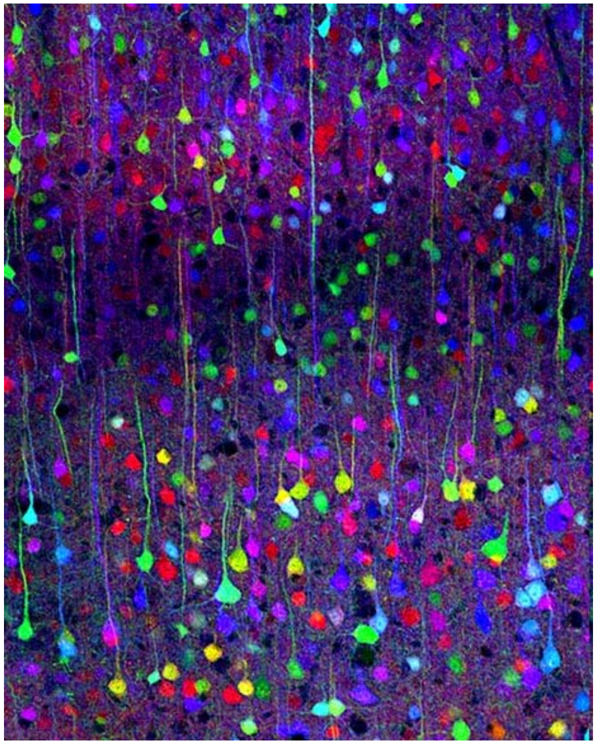


BRODMANN'S AREAS

Macroscopic: Anatomically segregated brain regions and inter-regional pathways.

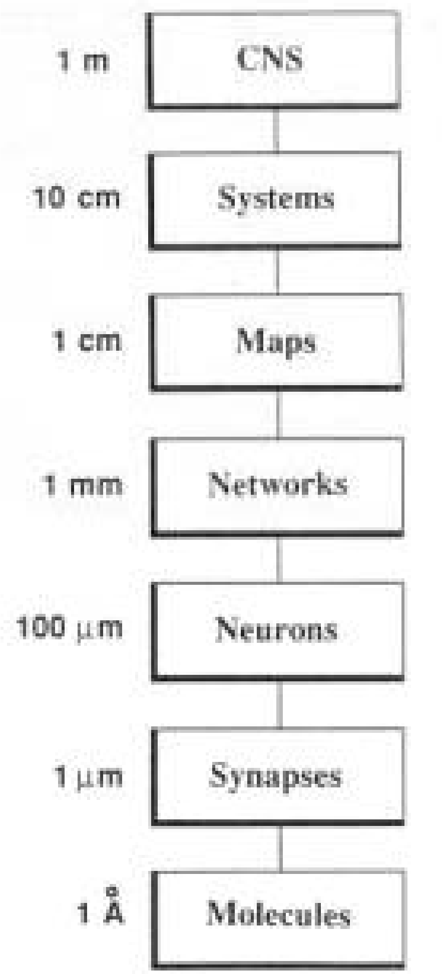
Spatial / functional unit scale

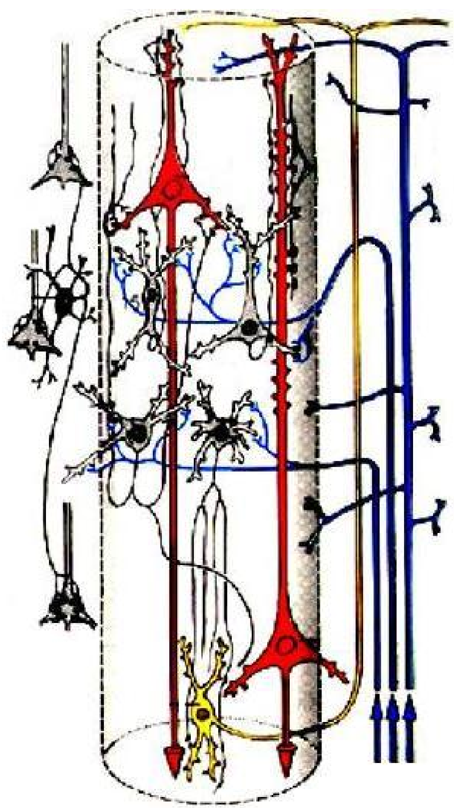




Mesoscopic:
Connections between local cell assemblies.

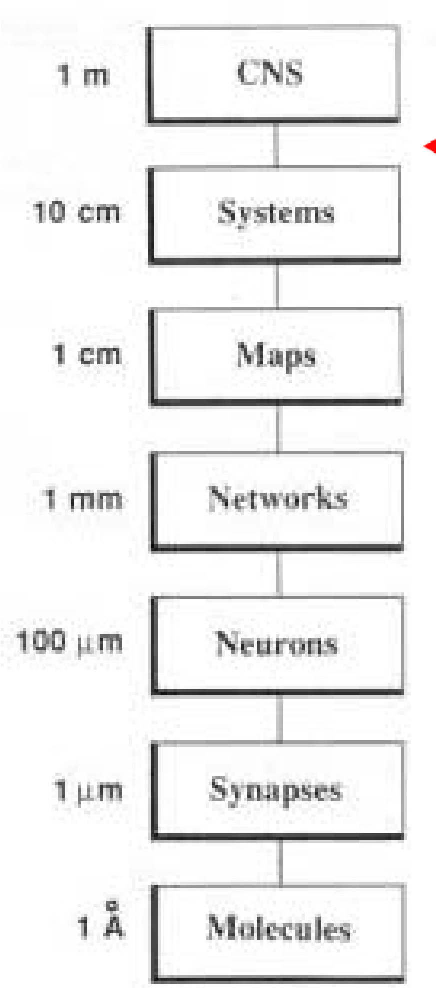
Spatial / functional unit scale

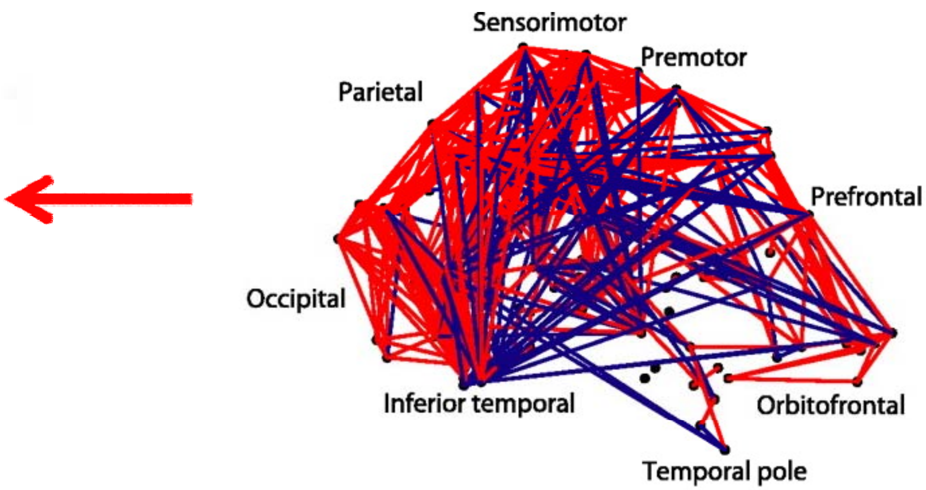




Microscopic: Single neurons and their synaptic connections.

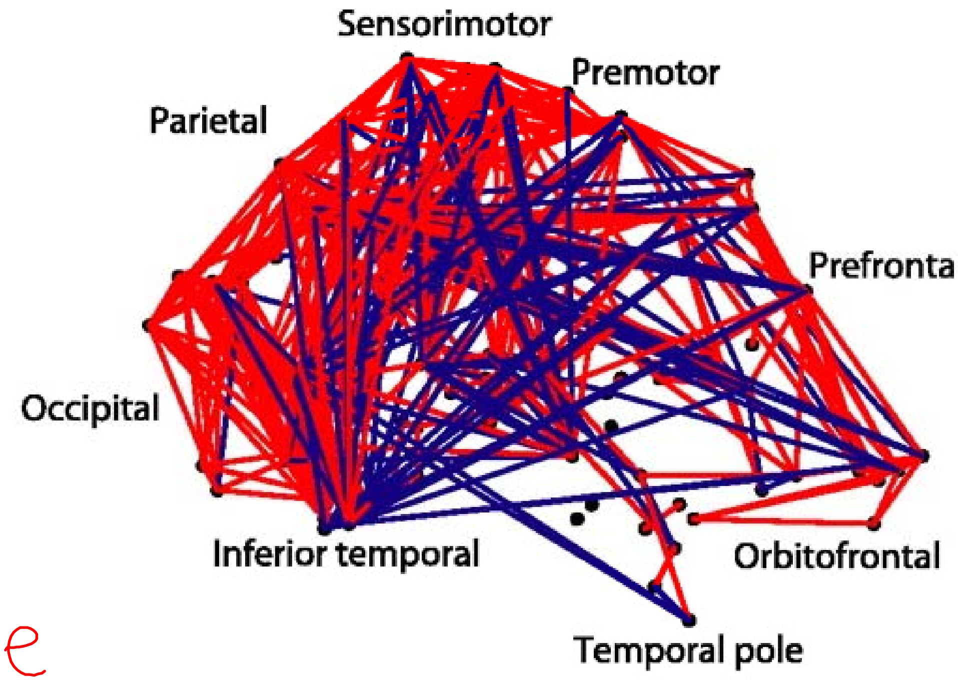
We'll focus on the macroscopic scale





Macroscopic: Anatomically segregated brain regions and inter-regional pathways.

Anatomical and functional Connectivity

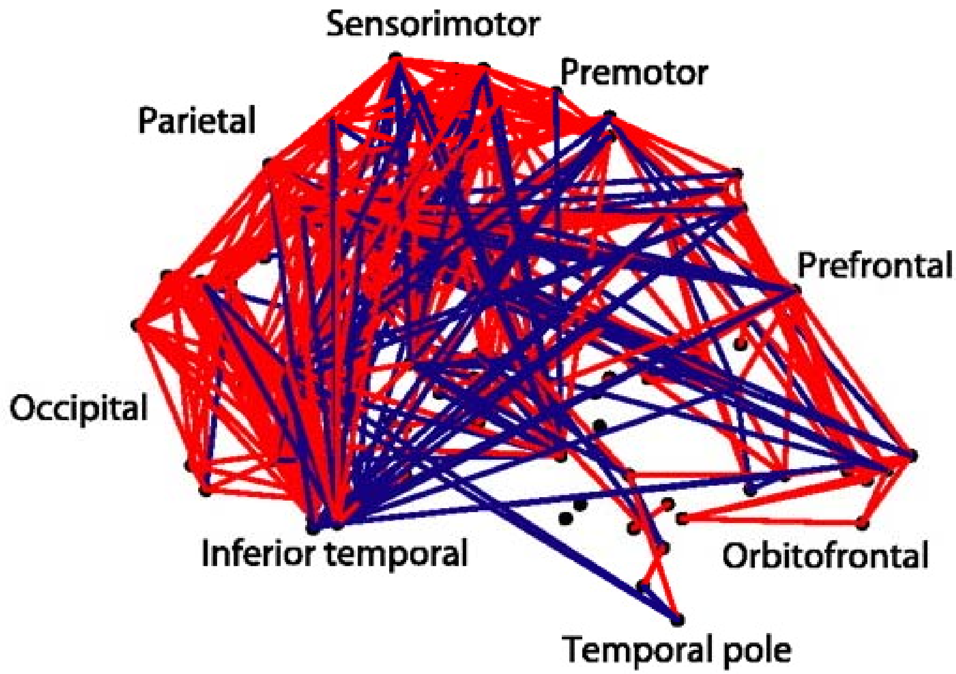


Dependence

Anatomical (Structural) Connectivity: Pattern of structural connections between neurons, neuronal populations, or brain regions.

Functional Connectivity: Pattern of statistical dependencies (e.g. temporal correlations) between distinct neuronal elements.

We'll focus on anatomical connectivity

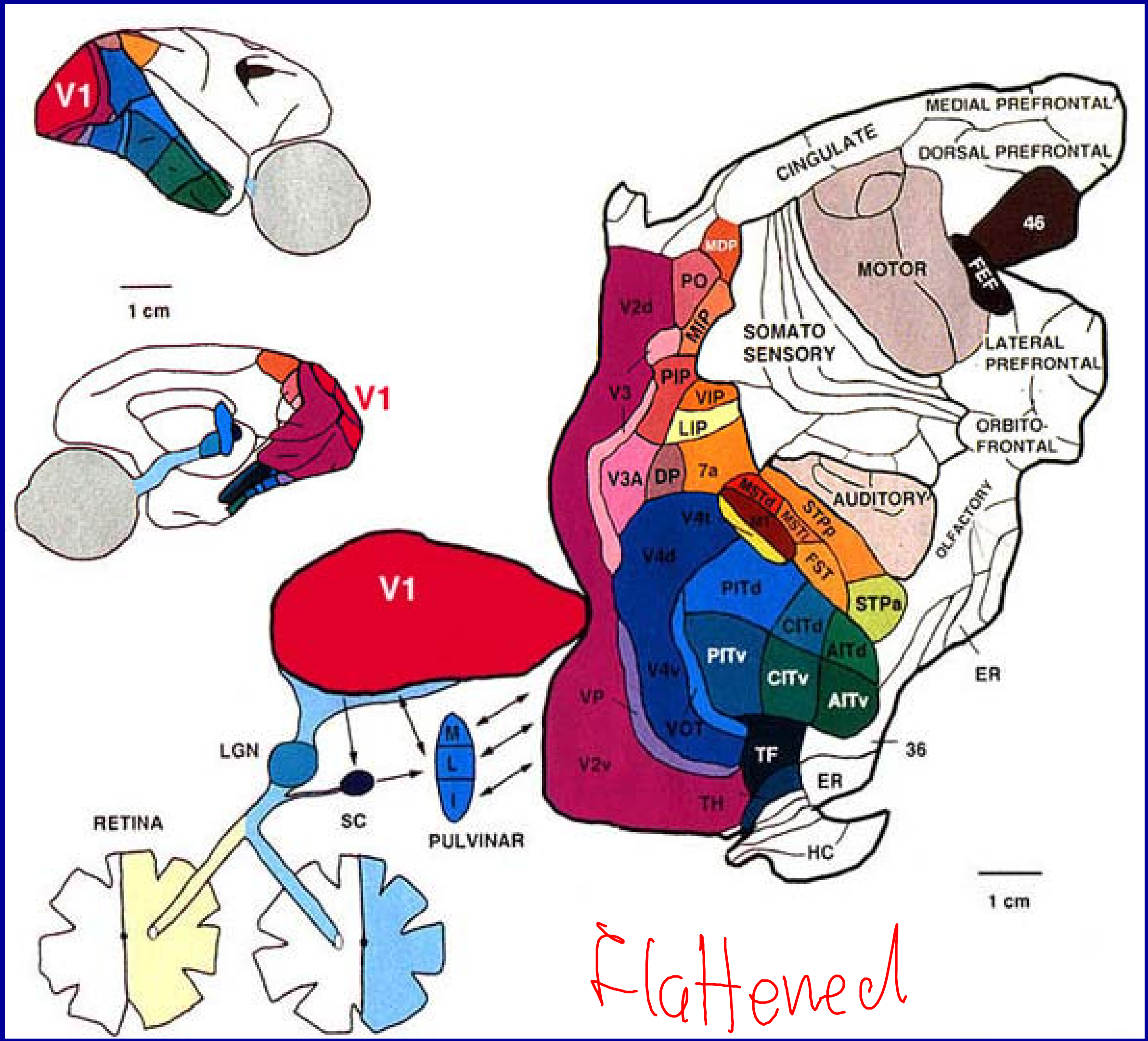


Anatomical (Structural) Connectivity: Pattern of structural connections between neurons, neuronal populations, or brain regions.

Functional Connectivity: Pattern of statistical dependencies (e.g. temporal correlations) between distinct neuronal elements.

Felleman and van Essen's delineation

Macaque

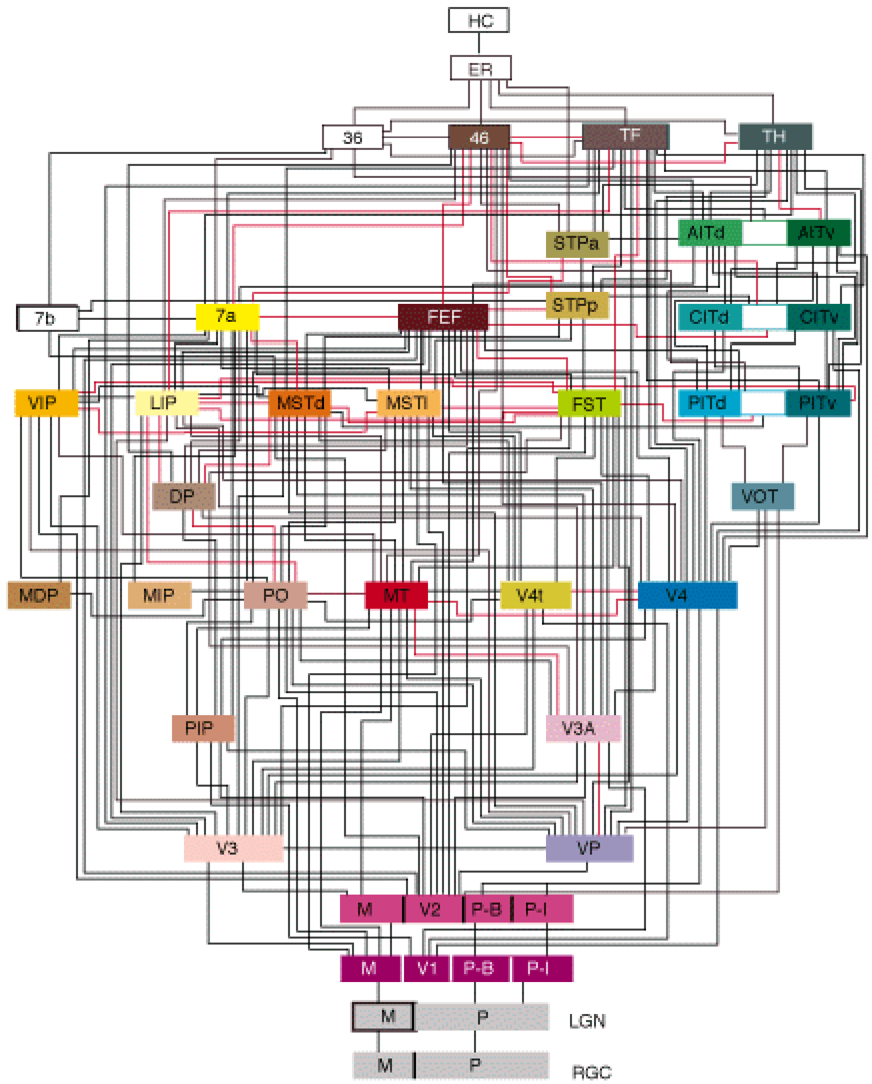


Flattened

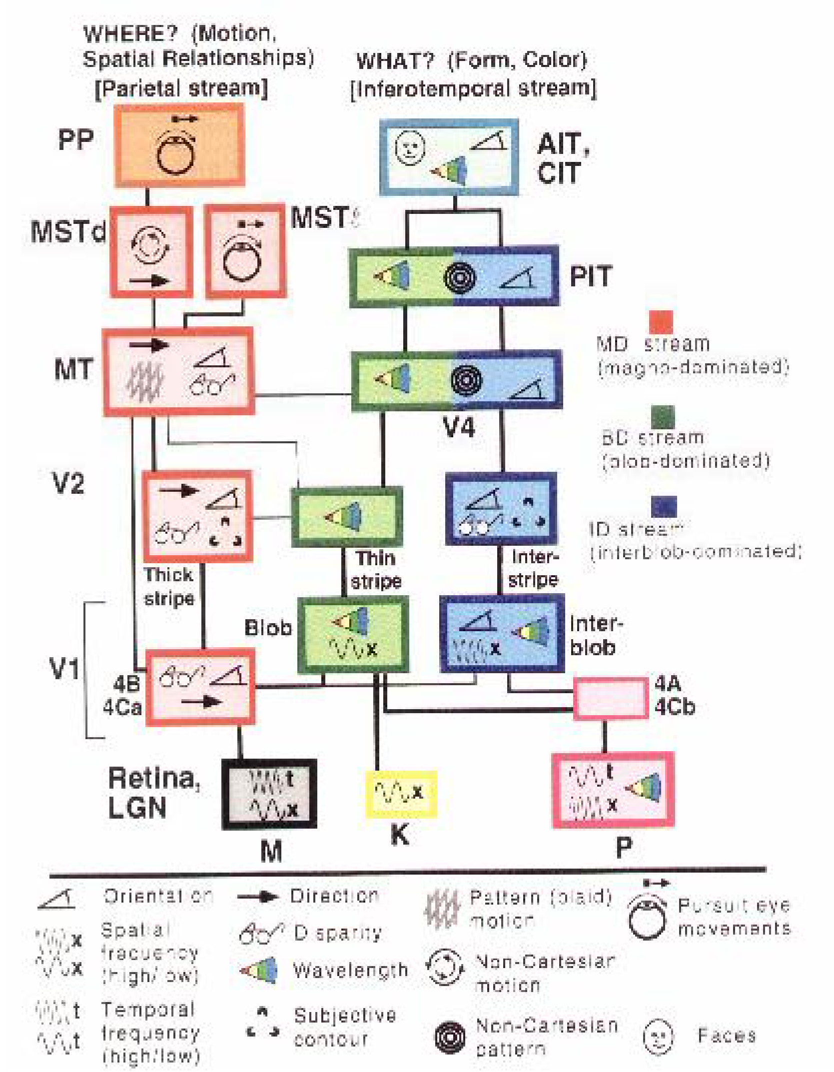
Cortico-cortical connections

Connections

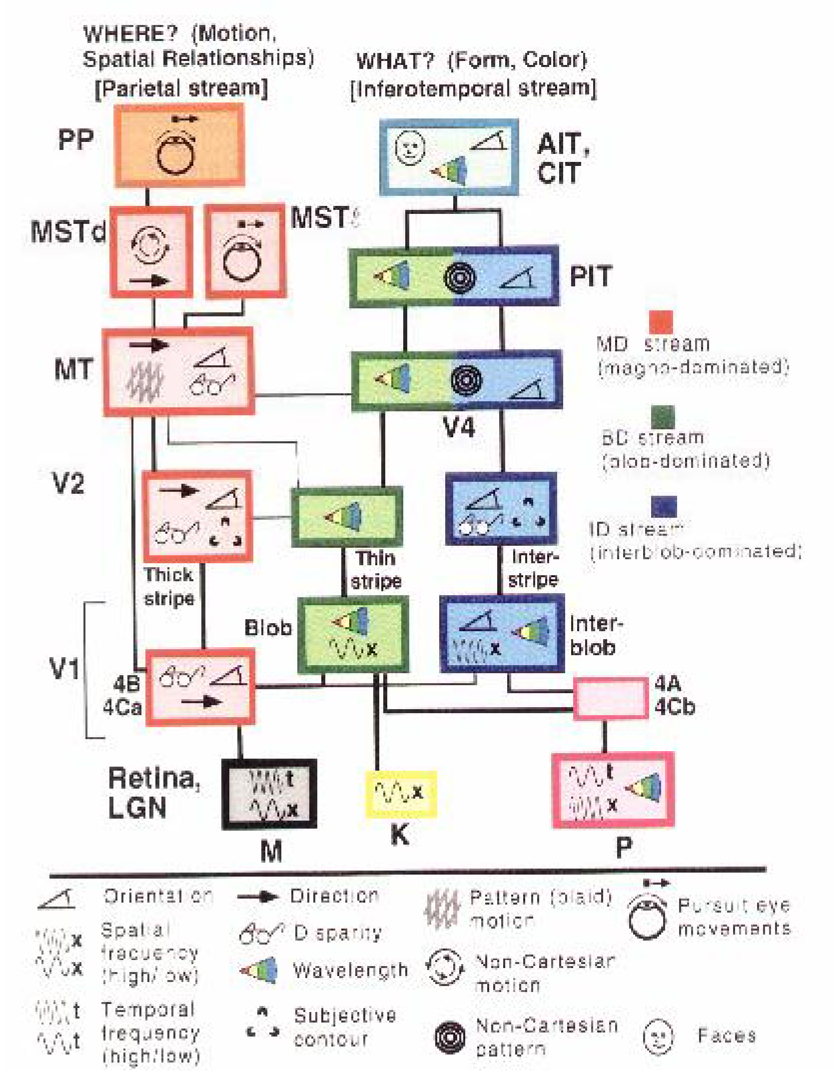
Macaque



Assignment of function: visual areas



Assignment of function: visual areas



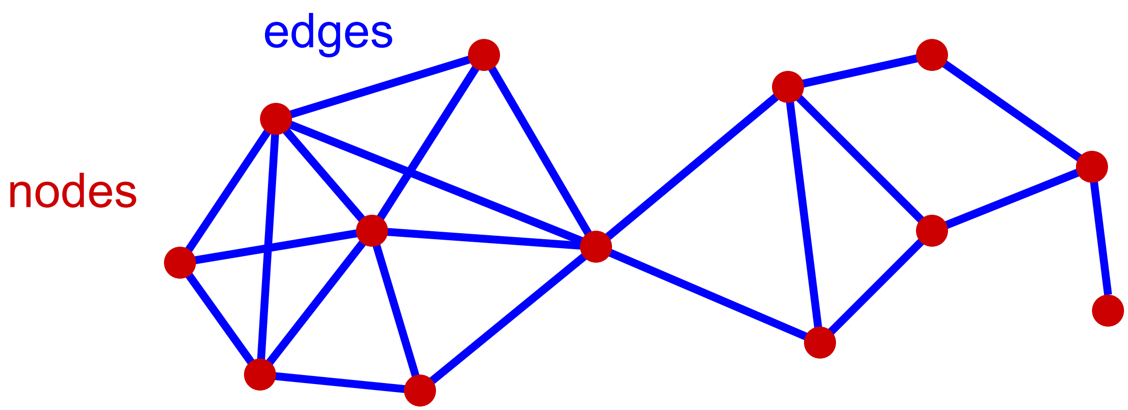
Network measures describe topology. The functional role can be used for interpretation, but is not part of the network analysis.

Features of networks:
Segregation and Integration.
In terms of functional interpretation, segregation is related to specialization.

The architecture of the cerebral cortex is an instance of a small world network

Sporns and Zwi, Neuroinformatics 2004

Graphs basic definitions: nodes and edges



Graphs (networks) consist of nodes and edges, and can be directed or undirected, weighted or binary.

Nodes are discrete network elements and edges describe their mutual relationships.
In the context of the brain, areas and anatomical connections between them can take the roles of nodes and edges, respectively.

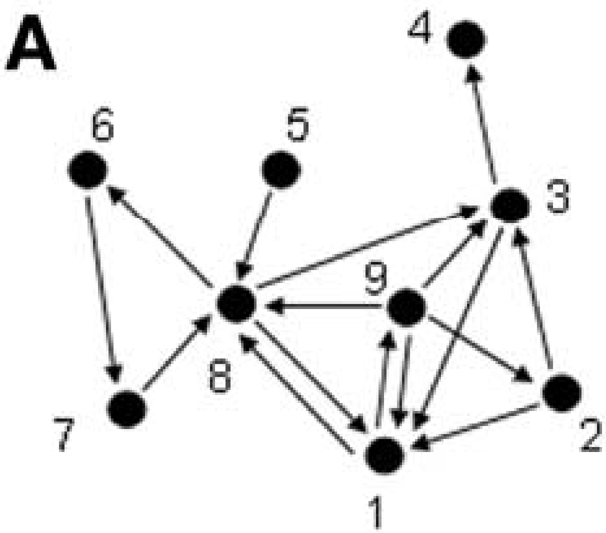
Sporns and Zwi, Neuroinformatics 2004.

Graphs basic definitions: nodes and edges

- The graph consist of N brain areas (vertices) linked by K connection pathways (directed edges).

Digraph composed of N = 9 vertices
and K = 16 directed edges.

Directions



Nodes and Edges from Large-Scale Connectivity Data Sets

- Binary connection matrices obtained from published reviews. Noise level large

- The graph consists of N brain areas (vertices) linked by K connection pathways (directed edges).

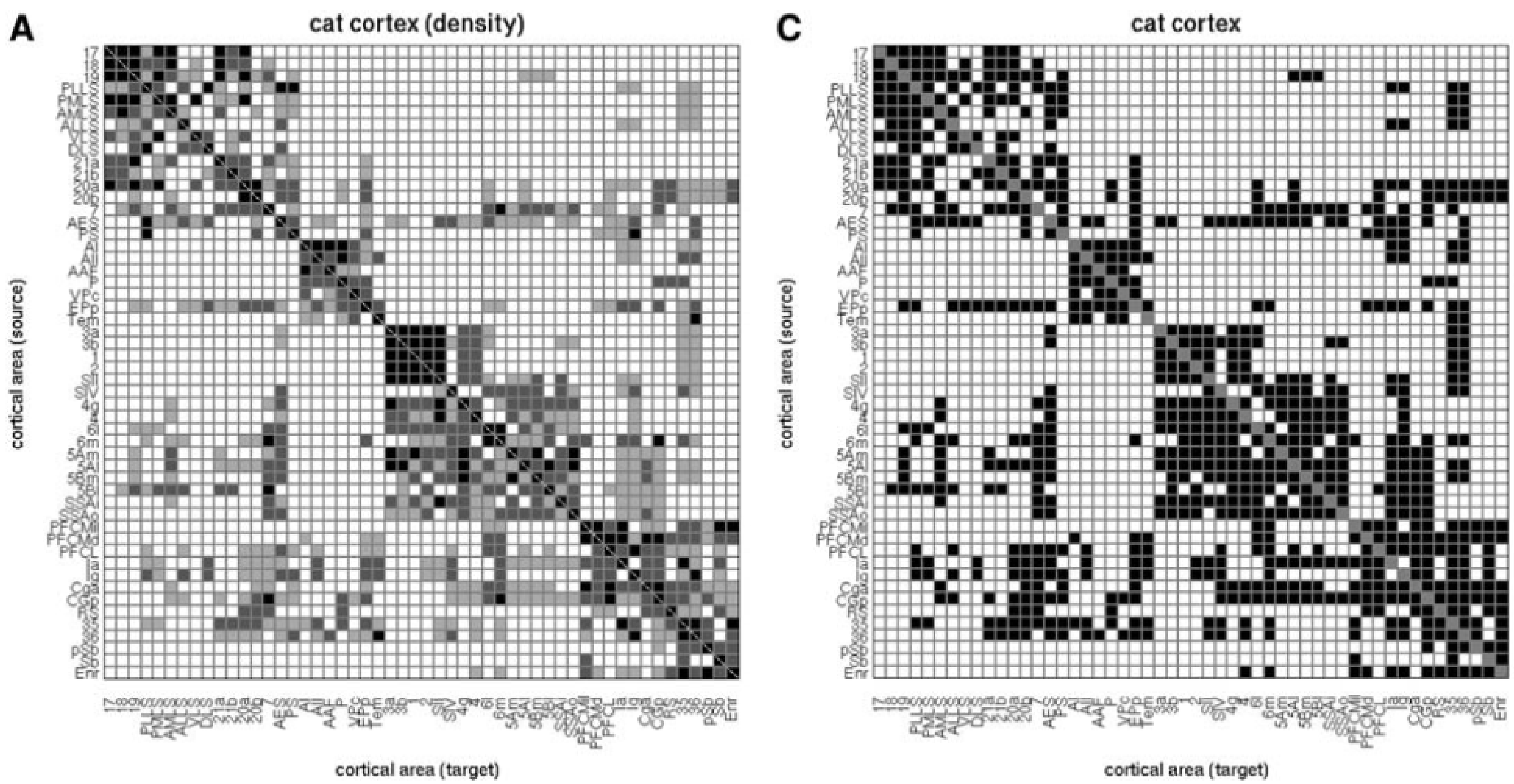
- An entry $c_{ij} = 1$ represents the presence of a pathway.

- An entry $c_{ij} = 0$ represents a connection which is reported absent or unknown.

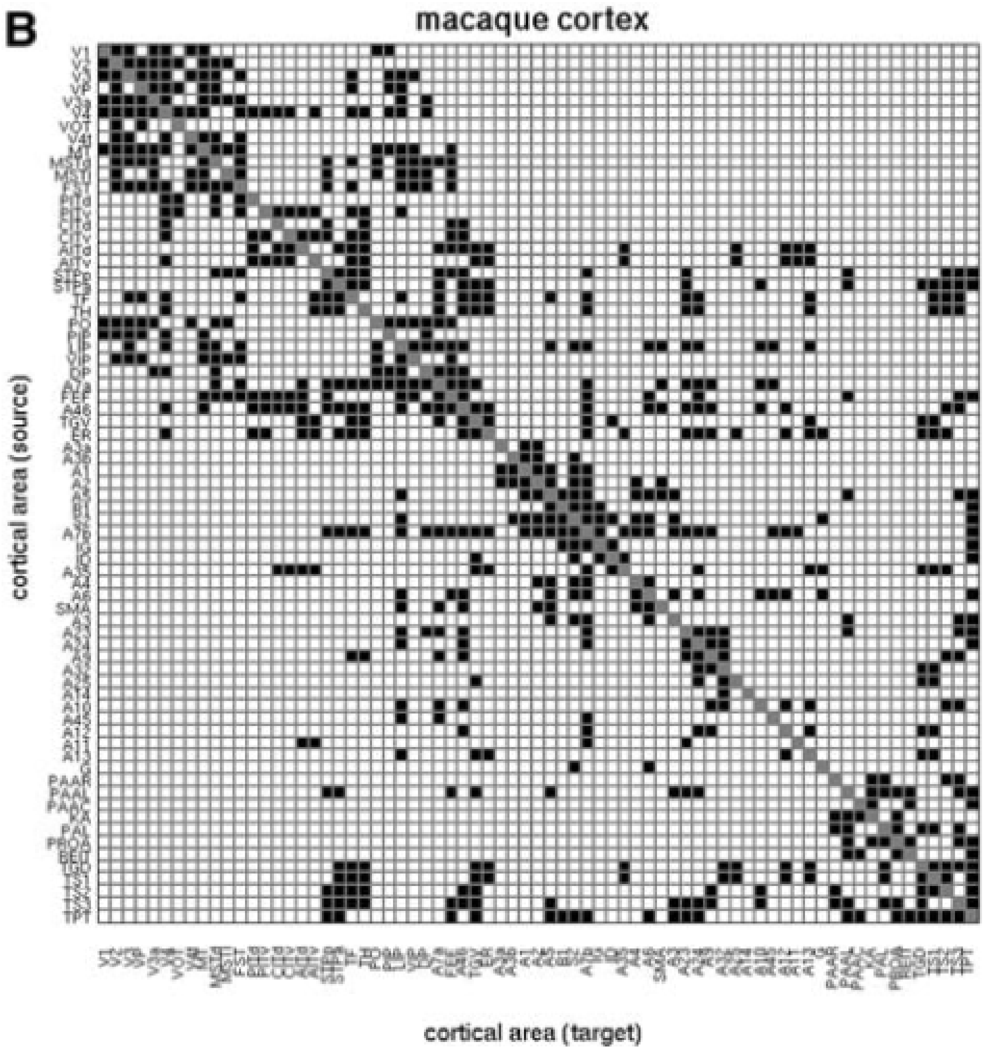
Density-based / binary networks

N = 52
K = 820

Scannel et al. (1999)

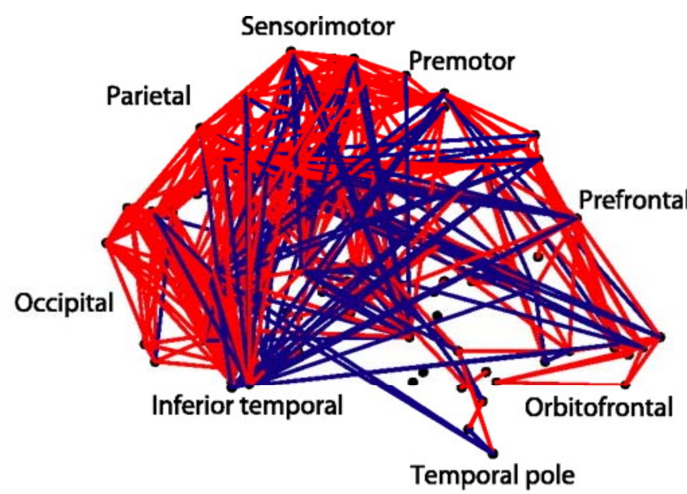


Connectivity of the macaque cortex

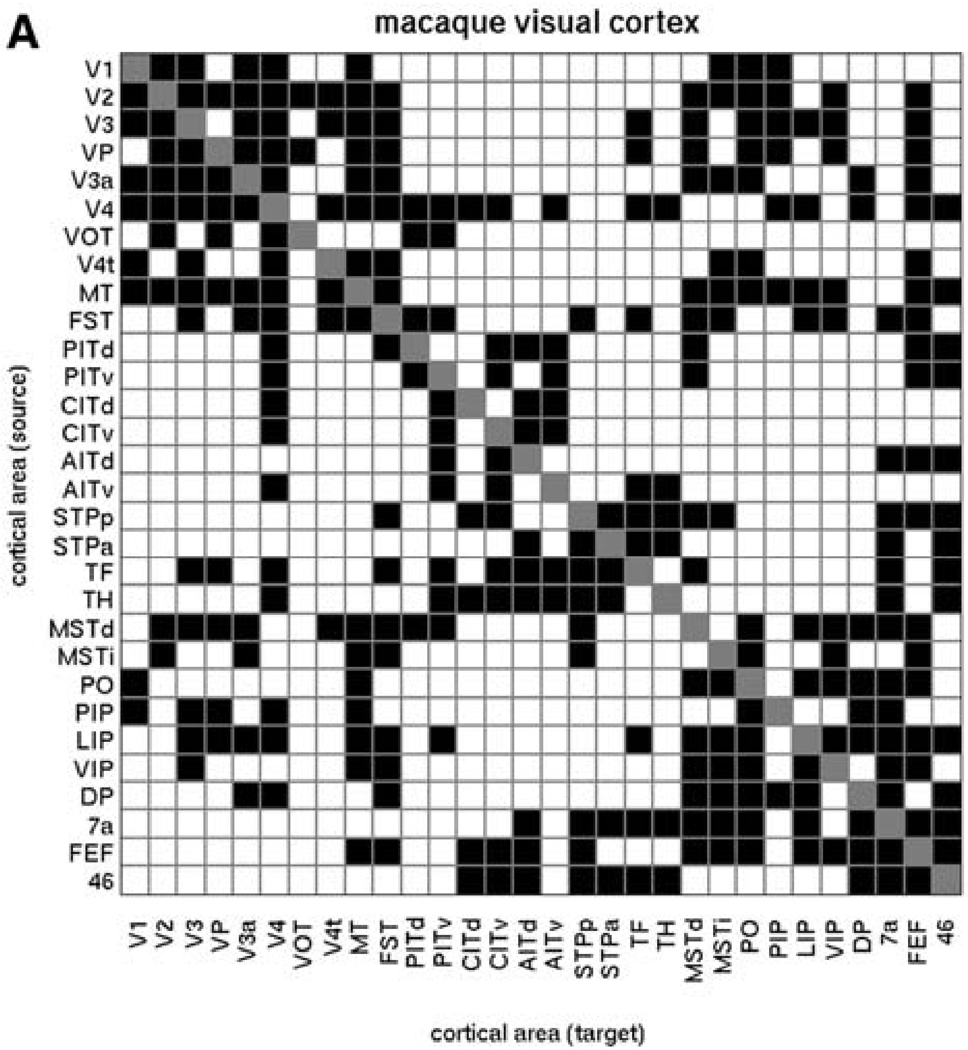


N = 71
K = 746

Young (1993)



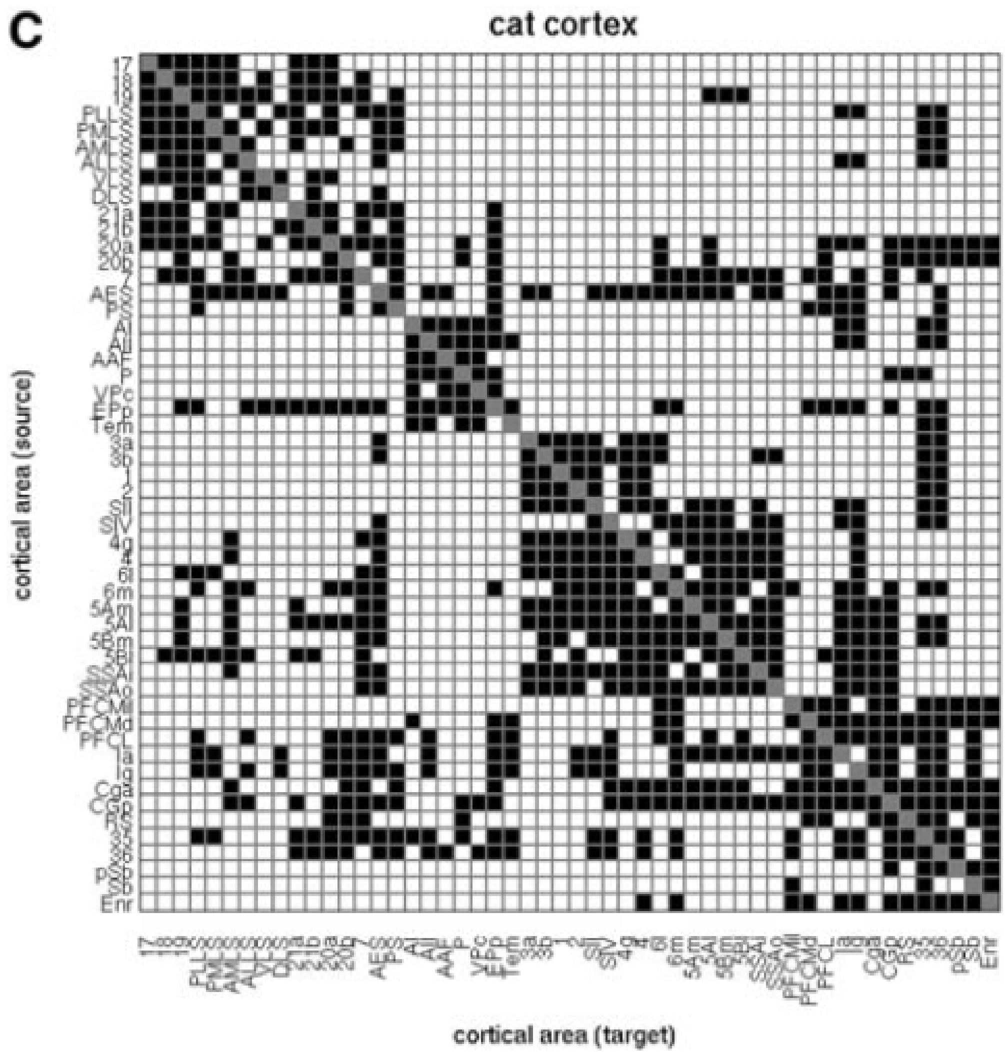
Connectivity of the macaque visual cortex



N = 30
K = 311

Felleman and
van Essen (1991)

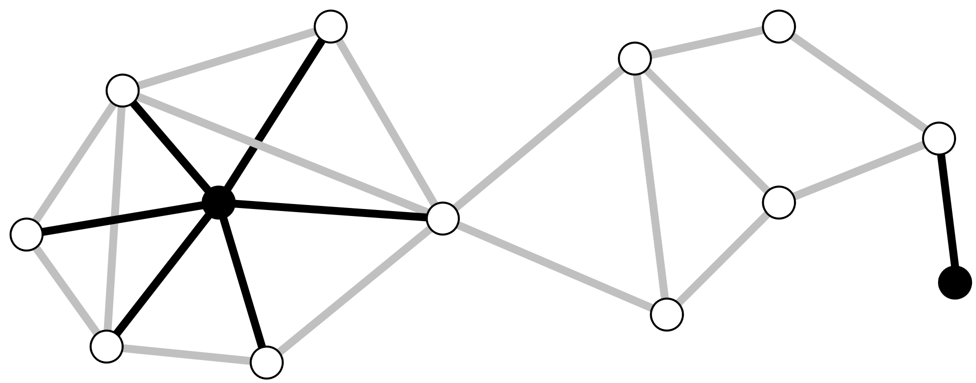
Connectivity of the cat cortex



N = 52
K = 820

Scannel et al. (1999)

Graphs basic definitions: degree



The degree is the total number of edges attached to a node.

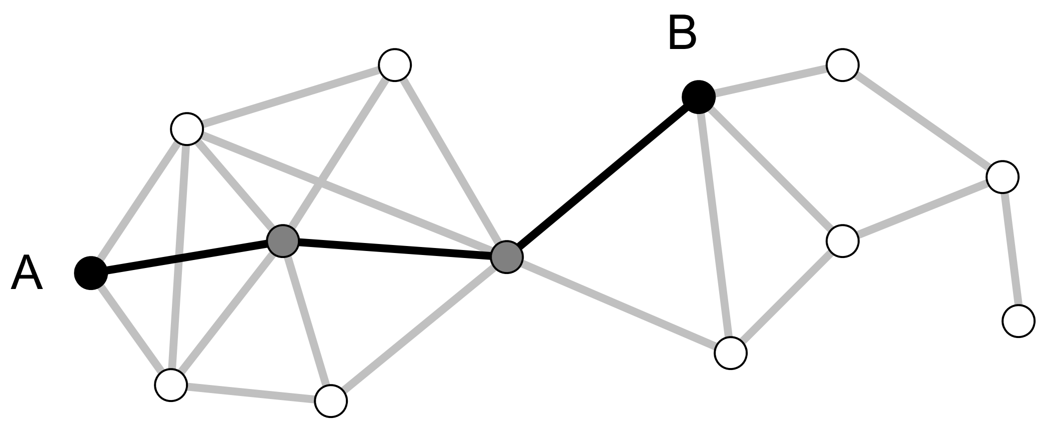
In real-world networks, different nodes have different degree – some are more highly interactive than others.

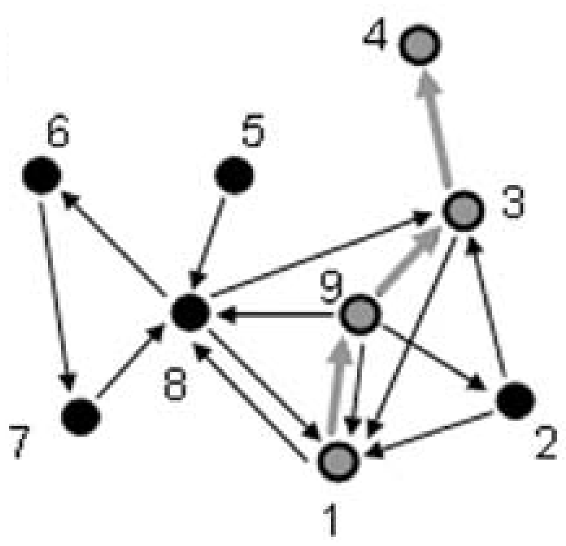
Sporns and Zwi, Neuroinformatics 2004.

Basic graph definitions: path and path length

- Paths are sequences of distinct edges and nodes, linking a source node j to a target node i.

- The length of a path is defined as the number of distinct (directed) edges.





Path from vertex 1 to vertex 4 of length 3, denoted {1,9,3,4}, containing the directed edges (1,9), (9,3), and (3,4).

Path length and distance

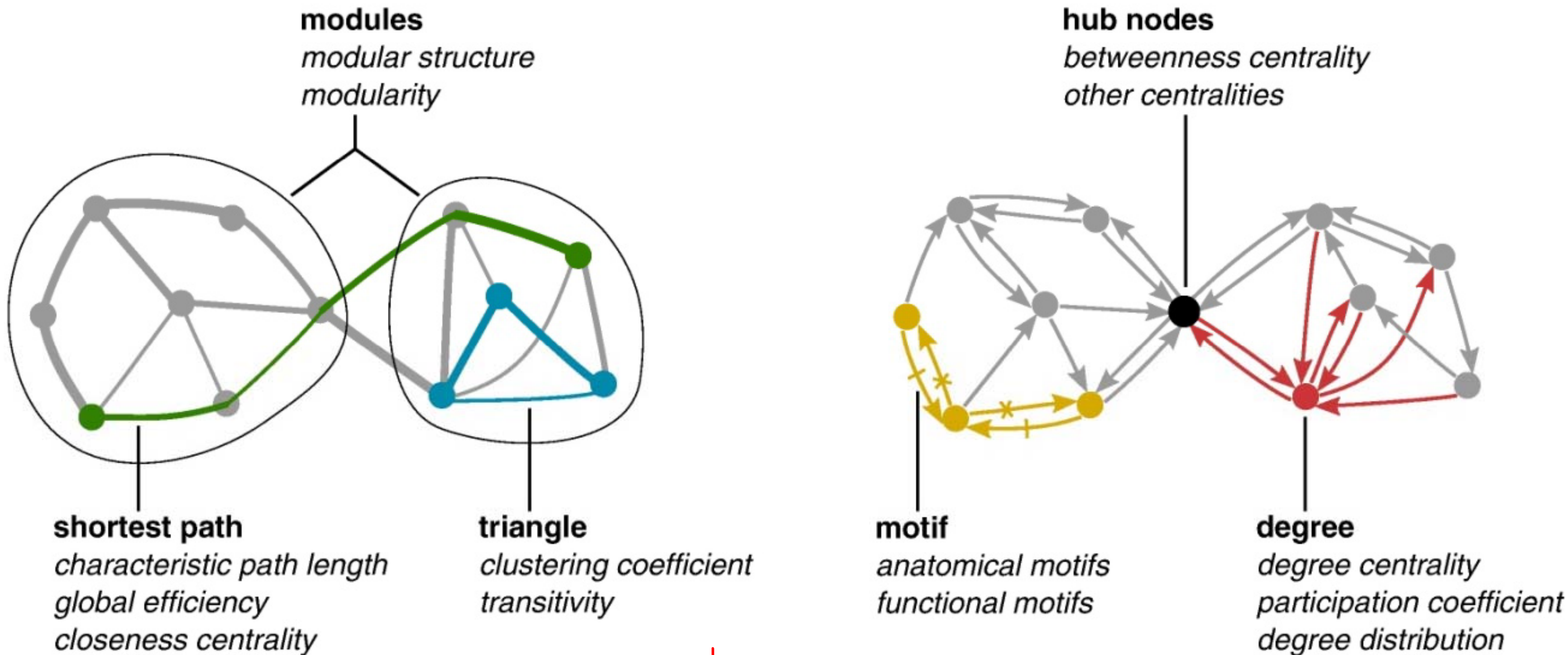
- The characteristic path length λ of a graph is the average length of the shortest possible paths linking any pair of its vertices.

- The length of the shortest path from vertex j to i is also called the distance dij. All distances dij compose the
distance matrix D of the graph. Thus, λ is equal to the average of all entries dij of the distance matrix D.

- The path length of a vertex λ(v) is defined as the average distance between this vertex and all other vertices of the graph (excluding dii).

Paths and distances describe how closely network nodes can interact.
In brain-like terms: functional integration.

Cluster index: triangles



$$\frac{\text{Count number of possible triangles}}{\text{Nodes}}$$

Cluster index

- The cluster index (or “clustering coefficient”) of a vertex v indicates how many connections are maintained between this vertex’s b_v neighbors.

- The vertex’s cluster index $\gamma(v)$ is defined as the ratio of actually existing connections among the b_v neighbors and the maximal number of such connections possible ($b_v^2 – b_v$).

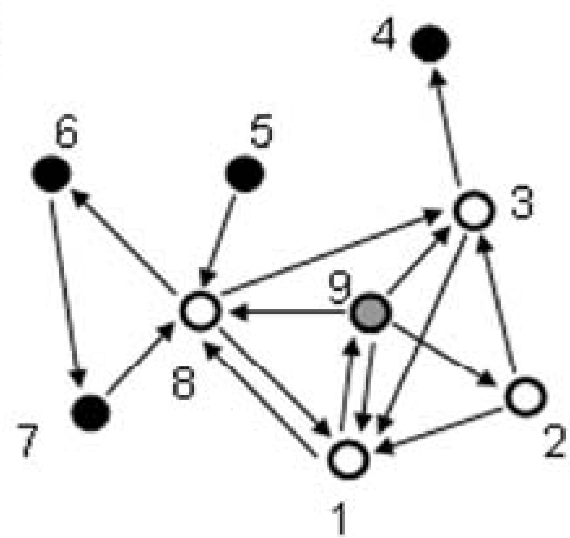
Substract to itsels

- $0 \le \gamma_v(v) \le 1$.

$\frac{6}{4^2-4}$

Cluster index of vertex 9.This vertex’s neighbors are 1, 2, 3, and 8, which maintain 6 connections among them out of 12 possible ($4^2–4$).This results in a cluster index of 6/12 = 0.5.

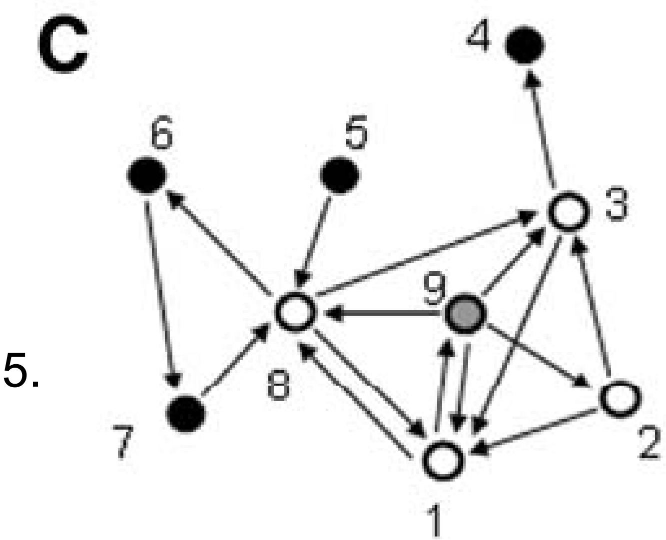
C



Cluster index

- The average of the cluster indices for each vertex is the cluster index γ of the graph.

Cluster index of vertex 9.This vertex's neighbors are 1, 2, 3, and 8, which maintain 6 connections among them out of 12 possible (4^2–4).This results in a cluster index of 6/12 = 0.5.

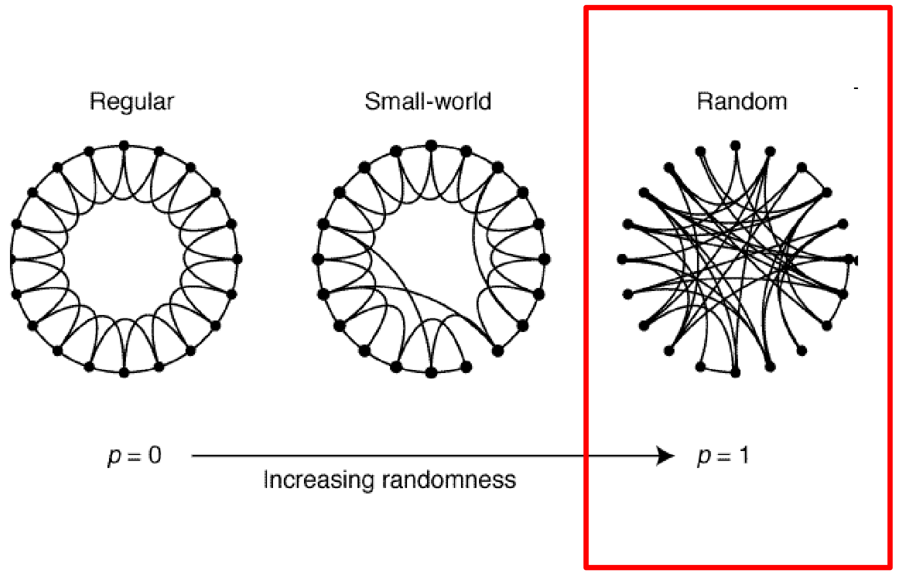


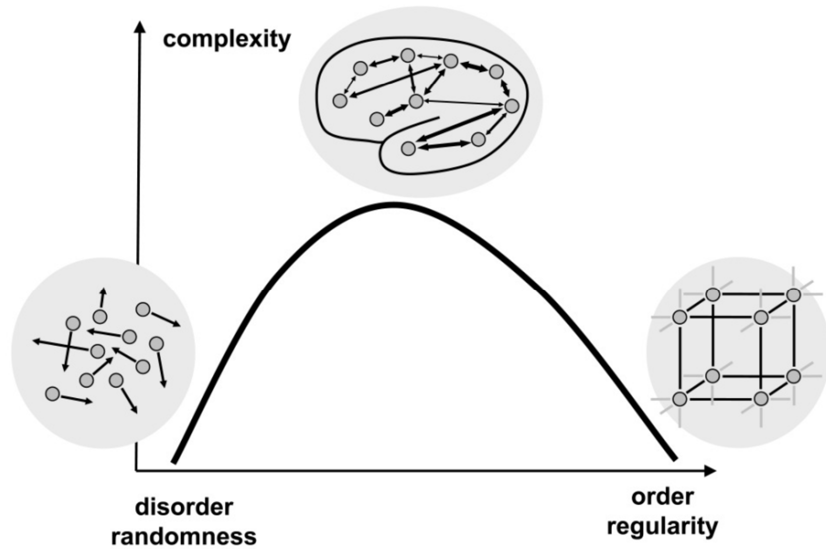
Cluster index describes the degree of 'local' connectivity or segregation to clusters.

Reference networks *('benchmarks'):*
Random and Lattice Matrices

Random connection matrices: assigning connections with uniform probability $K/(N^2\text{–}N)$, while omitting self connections.

Connections



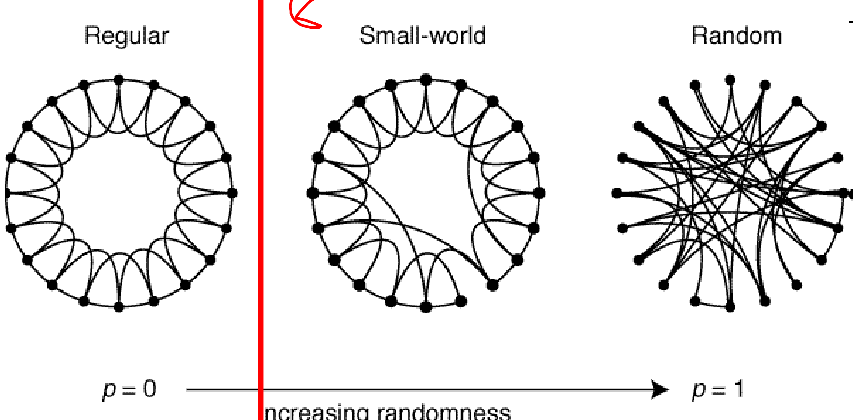


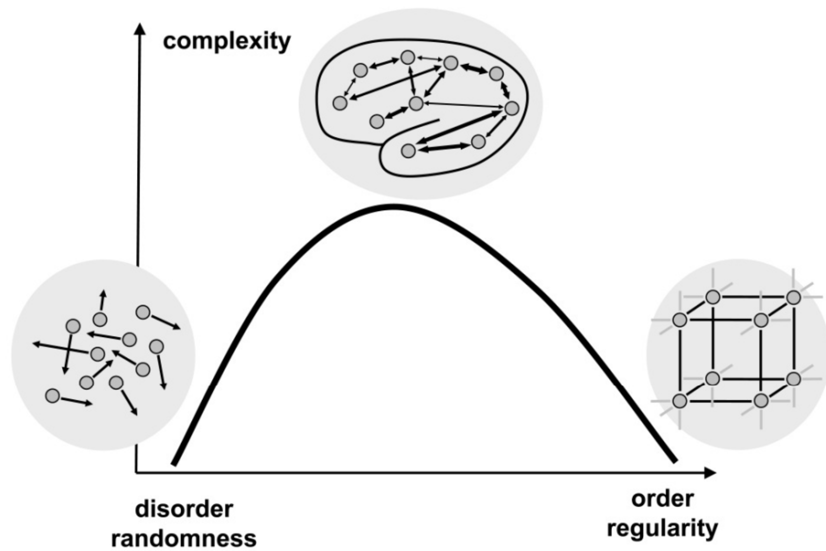
Topology

Reference networks ('benchmarks'): Random and Lattice Matrices

Lattice matrices: filling all entries of the connection matrices directly adjacent to the main diagonal until the limit of K connections is reached.

For example, if K = 2N, this procedure would result in nearest neighbor connectivity (ring topology).





Connected to 2 of its neighbours

Scaling of λ and γ

- Random and lattice networks represent topologies that lie at the extreme ends of a continuous spectrum ranging from totally disordered (random) to totally regular (lattice).

Path length Cluster

- Comparing λ and γ of a network to these extreme topologies provides information about randomness or regularity.

- Generally, for equivalent and sufficiently large N and K, $\lambda_{random} \ll \lambda_{lattice}$ and $\gamma_{random} \ll \gamma_{lattice}$. Cluster around

- Scaled values for λ and γ for a network of unknown topology are calculated as:

$$\lambda_{scl} = (\lambda_{network} - \lambda_{random})/(\lambda_{lattice} - \lambda_{random})$$
$$\gamma_{scl} = (\gamma_{network} - \gamma_{random})/(\gamma_{lattice} - \gamma_{random})$$

0 — 1
Extremes

- Generally, for networks with topologies that are intermediate between random and lattice structures, λ_{scl} and γ_{scl} will be between 0 and 1. λ ↓ is better γ ↑ is better

Path Length (λ, λscl) & Cluster Index (γ, γscl)

Scaled

Topology	λ	γ	λscl	γscl
NHP-VC	*1.73*	*0.53*	*0.22*	*0.56*
R30,311	1.67*	0.36*	(Random)	
L30,311	1.93*	0.66*	(Lattice)	
Rio30,311	1.69*	0.43*	(R; in, out degrees preserved)	
Lio30,311	1.82	0.62	(L; in, out degrees preserved)	
NHP-C	2.37	0.46	0.19	0.62
R71,746	2.03*	0.15*		
L71,746	3.82*	0.66*		
Rio71,746	2.12*	0.24*		
Lio71,746	2.89*	0.90*		

(* stands for $p < 0.001$)

Good Communication

Segregation for Functionality

Comparison to random & lattice graphs

For all three large-scale connection matrices:
λscl are closer to those for random networks;
γscl are closer to those of lattice networks.

$\longrightarrow$

The connection matrices are characterized by very short average distances while maintaining a high degree of clustering.

A comparison to matrices with distributions of in-degrees and out-degrees that are identical yields ~ the same result.

$\longrightarrow$

The low λ and high γ for large scale matrices cannot be explained by their degree distributions (local vertex statistics), but depend on the global arrangement of the connection pattern.

Small Worlds and Cortical Function

- Cortex shows robust small world properties in every cortical network examined.

- The small world topology is characterized by two main features.

- First, the neighborhood surrounding most neuronal elements shares many more interconnections than would be expected by chance (high γscl). Within area

- Second, pairs of neuronal elements are linked by short paths, despite large network size and sparse connectivity (low λscl).

Between areas

Tracer Injections

Small Worlds and Cortical Function

- The analysis compared cortical connection matrices to reference cases that are generated under statistical assumptions.
- This approach allows the identification and comparison of structural features that distinguish neurobiological patterns from random or lattice topologies.
- This comparison is essential as absolute values for path lengths and cluster indices often are not, by themselves, indicative of the presence of small-world connectivity patterns.

Benchmarks

Small Worlds and Cortical Function

- The pervasiveness of small world attributes in cortical networks points to their central functional role. High clustering promotes functional overlap of densely connected neuronal elements, which are functionally segregated from one another and constitute topological modules of the cortical architecture.

- Short paths promote effective interactions between neuronal elements within and across cortical regions, which are essential for functional integration.

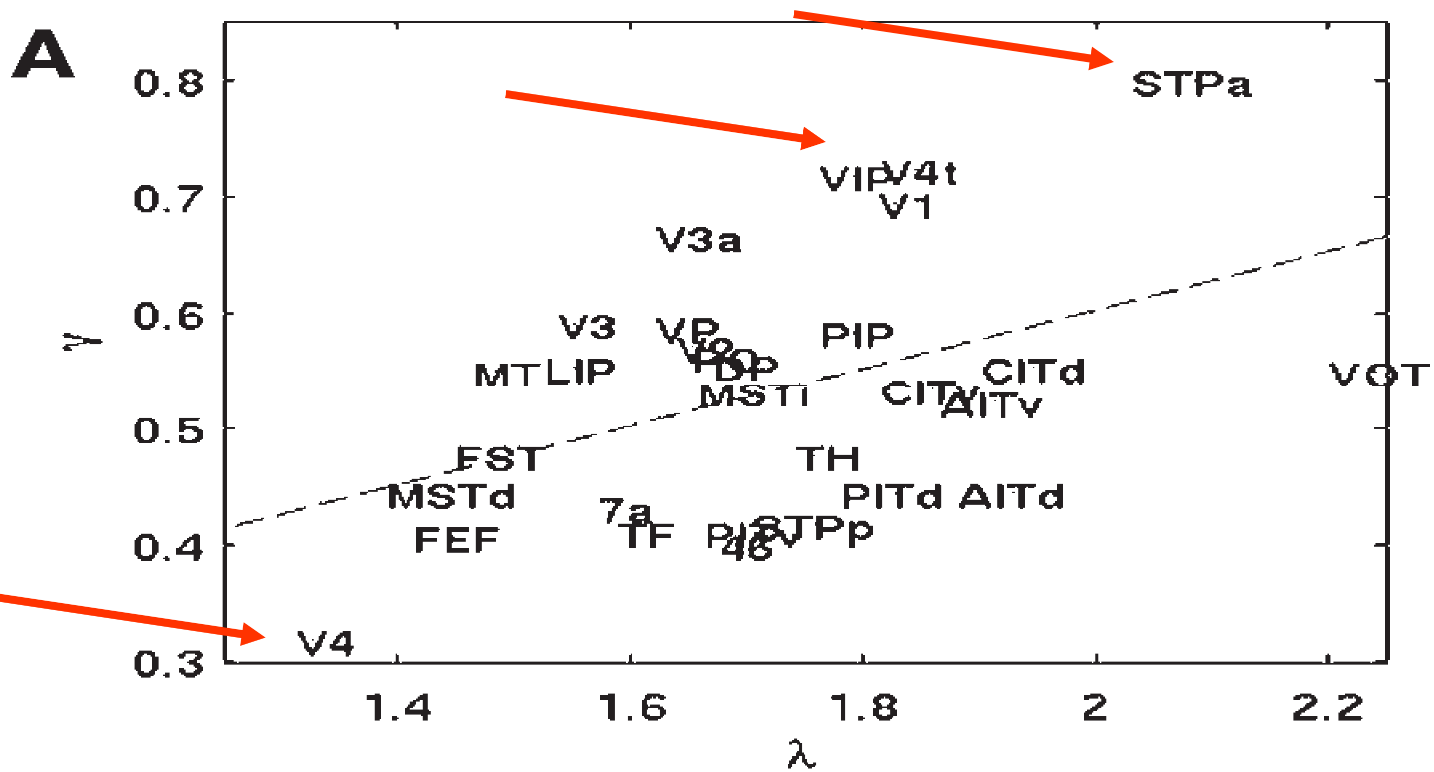
- These features assure the effective integration of multiple segregated sources of information.

- In computer simulations, small world topologies emerge when networks are optimized for complexity, a measure of how well a network combines functional segregation and integration (Tononi et al., 1998; Sporns and Tononi, 2002).

Path length and clustering index of individual nodes

Values for λ and γ represent averages over all brain areas. Individual brain areas show significant variations.

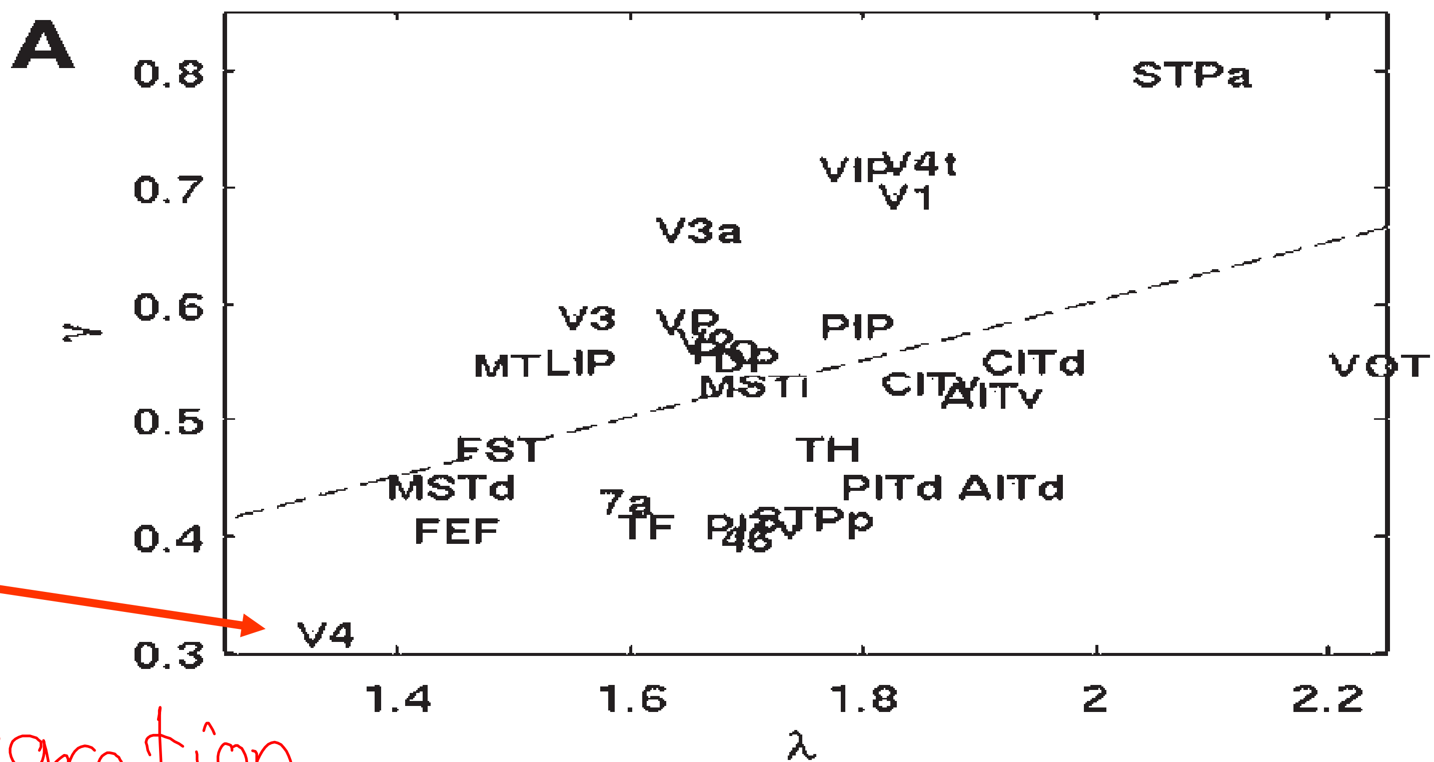
Correlation between the path length λ and the cluster index γ in macaque visual cortex



Tendency of brain areas with a large number of neighbors to have a relatively low γ

Area V4 maintains 21 incoming and outgoing connections, with a γ(V4) = 0.32. Its connectivity is highly diverse, including areas in dorsal and ventral streams, constituting a broad set of neighbors that do not form a single “clique”.

Correlation between λ (path length) and γ in macaque visual cortex



Integration

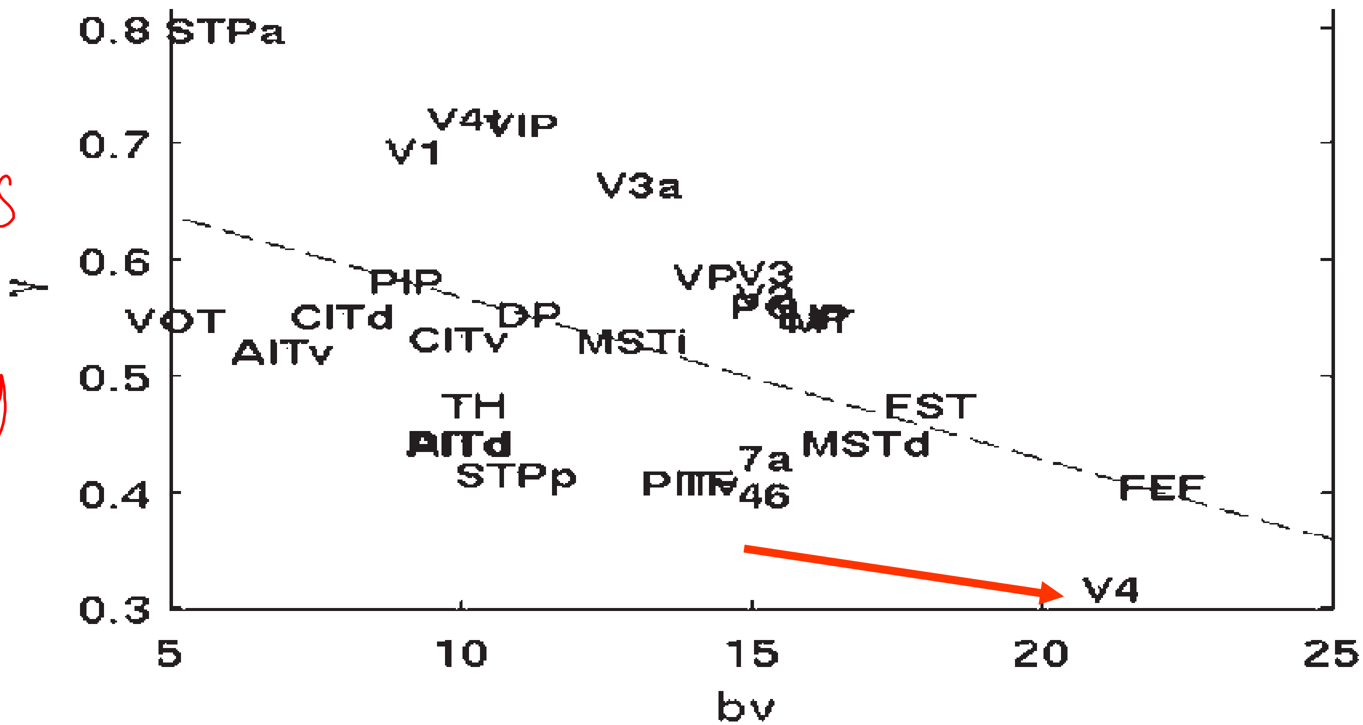
Tendency of brain areas with a large number of neighbors to have a relatively low γ

Area V4 maintains 21 incoming and outgoing connections, with a γ(V4) = 0.32. Its connectivity is highly diverse, including areas in dorsal and ventral streams, constituting a broad set of neighbors that do not form a single “clique”.

Correlation between γ (clustering index) and bv (number of neighbors) in macaque visual cortex

↑ Neighbors

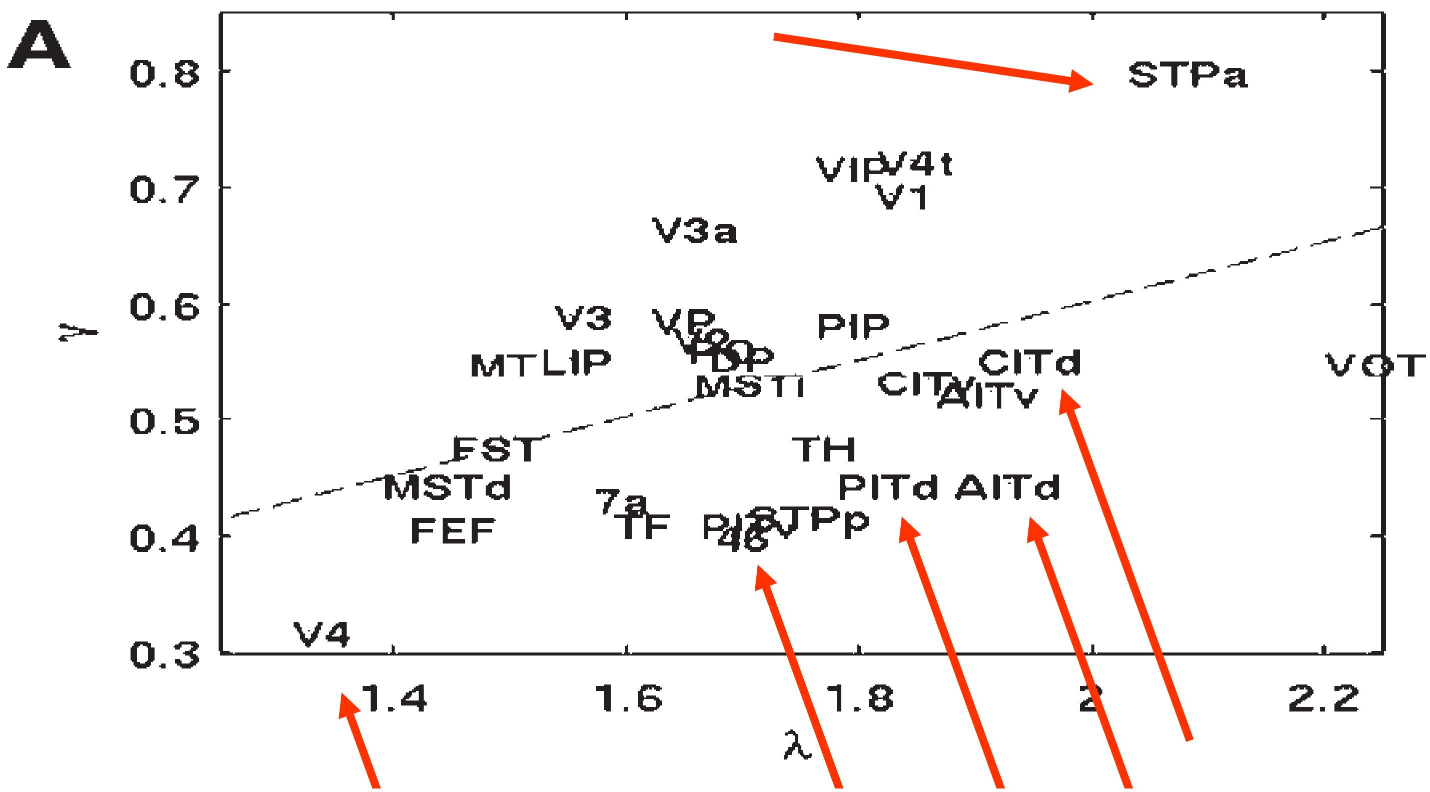
↓ Clustering



Path length and clustering in the ventral stream

All areas generally considered to be members of the ventral stream of primate visual cortex are below the regression line.

Correlation between the path length λ and the cluster index γ in macaque visual cortex



Comparison to random & lattice graphs

- The observed correlations between λ, γ and the size of the neighborhood are absent in random networks.
- Lattice networks do not show much variation in λ and γ across vertices, owing to their mode of construction.

Specialized and Integrative areas

- Strong correlation between $\lambda(v)$ and $\gamma(v)$ for all large-scale cortical connection matrices. Areas with low $\lambda(v)$ and low $\gamma(v)$ tend to maintain larger numbers of pathways with a greater diversity of other brain areas.

- Parietal area A7b in macaque cortex has $\lambda(A7b) = 1.77$ and $\gamma(A7b) = 0.25$ and connects to 28 other areas. Its functional neuronal properties are highly complex and multimodal (Graziano et al., 1999).

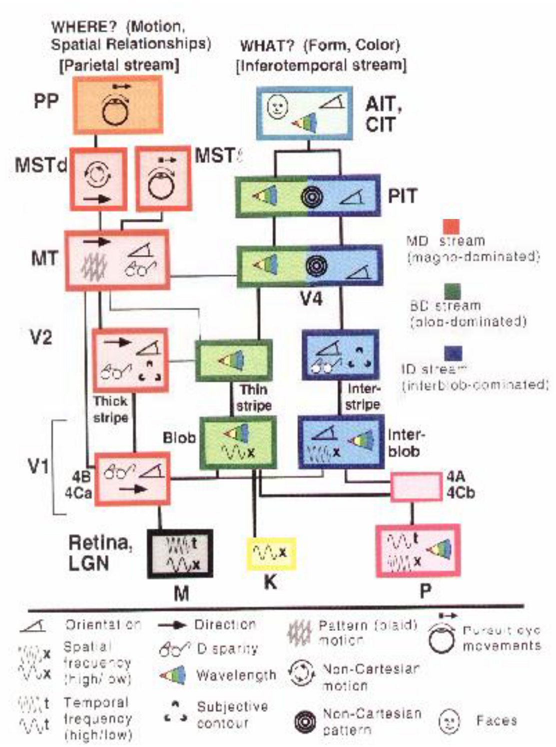
- Areas with high $\lambda(v)$ and high $\gamma(v)$ tended to maintain smaller numbers of pathways, mostly to brain areas that are strongly functionally related. Area A3a of the somato-sensory cortex has $\lambda(A3a) = 3.47$ and $\gamma(A3a) = 1.00$ and connects to only two areas (somato-sensory areas A1 and A2).

- Distinction of more specialized and more integrative cortical areas according to the statistics of their connectional relationship with the rest of the network.

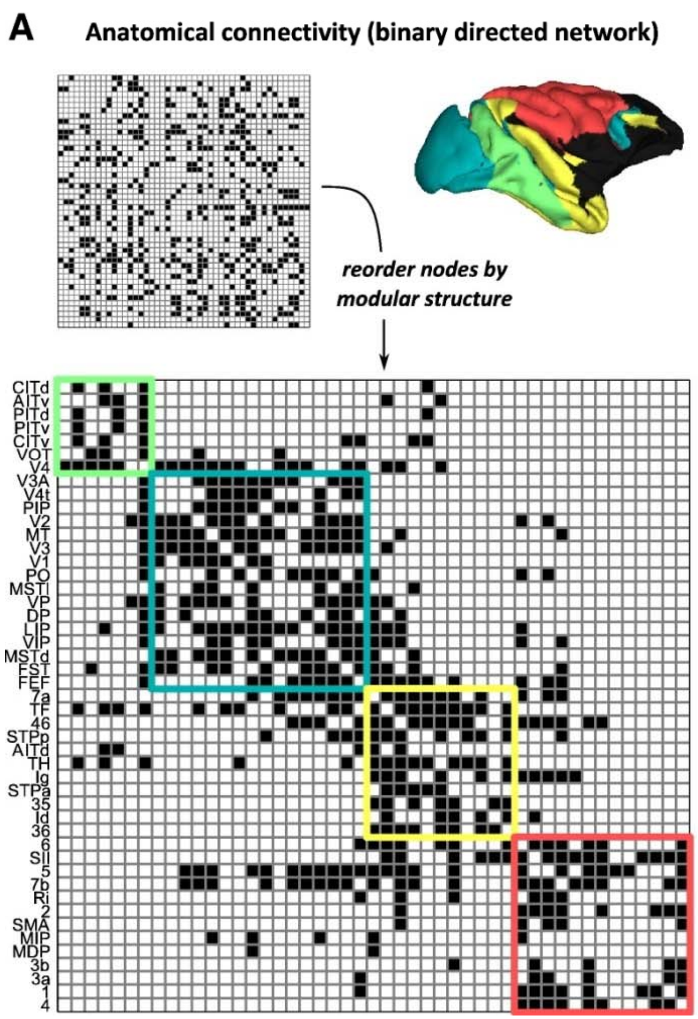
Distance Between Areas

- Metric and topological distances: physical separation (in mm or cm) between areas, compared to “directness” of causal interaction through synaptic linkages.

- In the cortex, metric and topological distances are related.



Distance between areas



In the cortex, metric and topological distances are related.

- Hypothesis: minimizing wiring length.

- In network analysis, it is the topological distance that matters. Absence of any path between two areas precludes causal effects, even if the metric distance is small.

- The effectiveness of a path is also a function of the strengths of the synaptic links, as well as the excitability and responsiveness of its constituent neurons, all factors that are outside the scope of classical graph theory.

Conclusion

- Studies in natural, social and technological systems have shown that small world networks give rise to interesting functional and dynamic properties, including:
- generating complex dynamics (Sporns, 2004);
- An increased propensity for synchronization (Barahona and Pecora, 2002);
- efficient information exchange (Latora and Marchiori, 2001);
- efficient navigability of information (Kleinberg, 2000).

Hypothesis: the small world topology plays a central role in cortical information processing. This role will become more evident as structural analyses of networks are related to the dynamical patterns and states they generate and sustain.