



Brain Network Analysis

Foundation Themes for Advanced EEG/MEG Source
Analysis: Theory and Demonstrations via Hands-on
Examples

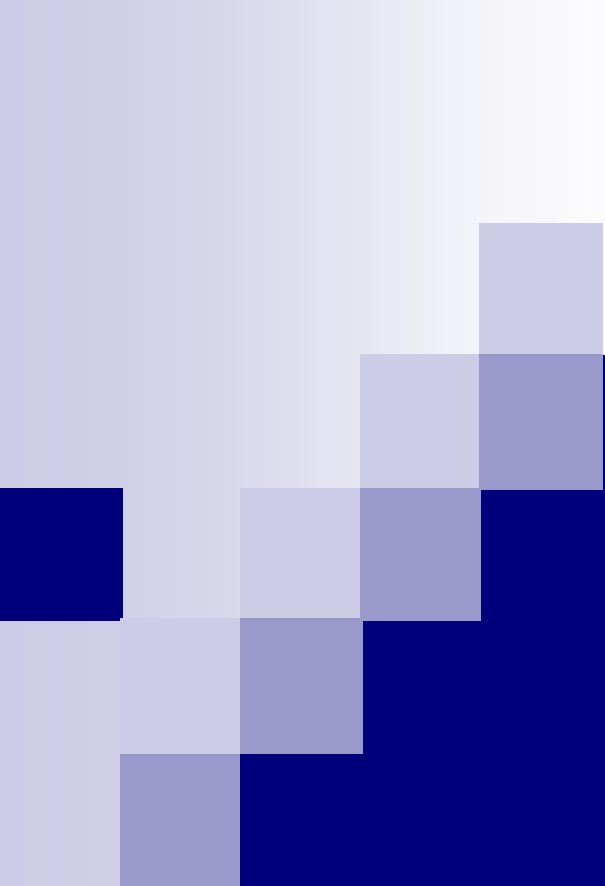
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Seminar organization

1. Network basics
2. Brain functional networks

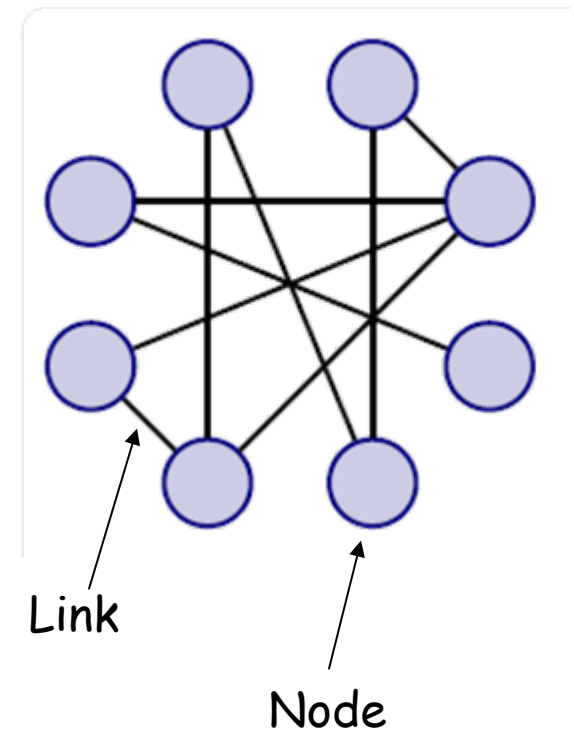


Network basics

Part I

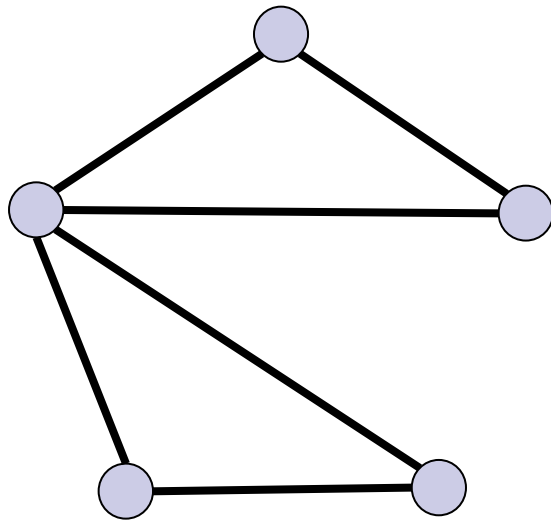
What a network is?

- A network is a set of single elements, systems or entities that are interconnected
- The network concept is formalized through a mathematical model that is called “graph”
- In a graph, the vertices (or nodes) are the single entities while the edges (or links) are the possible connections between them

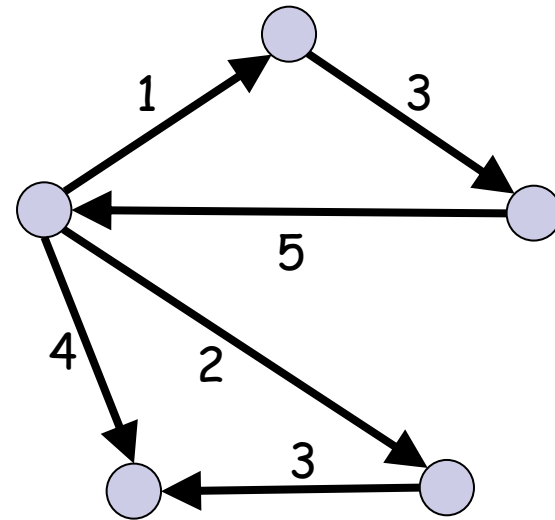


Network characteristics

- Network cardinality that is the number of nodes composing the network, ranges from 0 to ∞
- Network edges can be directed (di-graph) or undirected (graph), weighted or unweighted



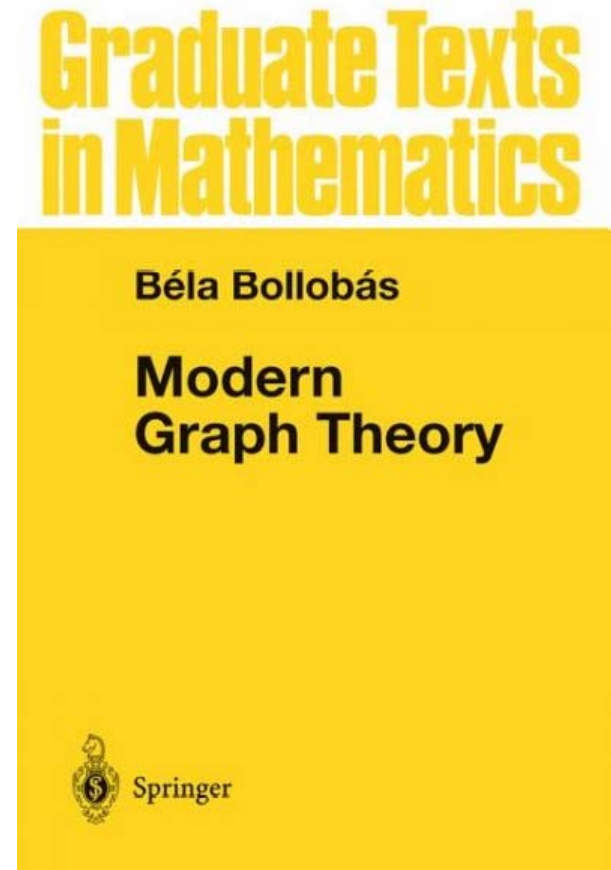
Unweighted undirected graph



Weighted directed graph

Study of Networks

- The analysis of the topological network properties must be addressed by the use of objective mathematical methods
- Graph theory is the appropriate tool for the extraction of characteristic information from any network



(published in 1998)

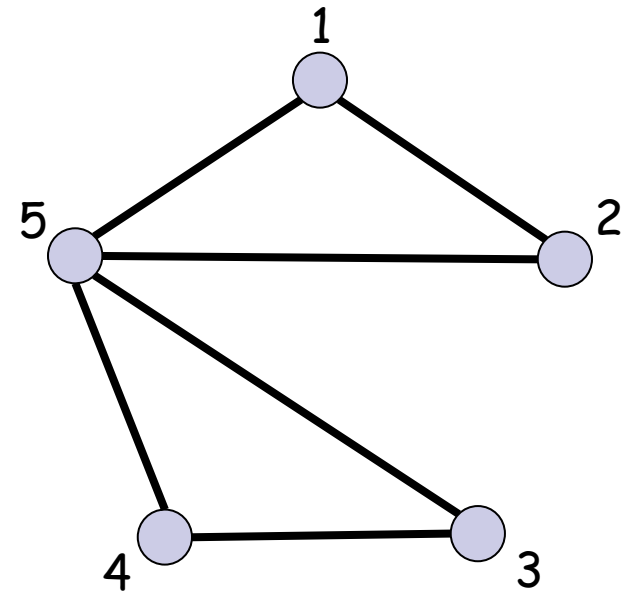
Graph definition

- Given a non empty set $\mathbf{V}$ and a family $\mathbf{E}$ of subsets of $\mathbf{V}$ such that, for each $e \in \mathbf{E}$, $1 \leq |e| \leq 2$, the couple $\mathbf{G} = (\mathbf{V}, \mathbf{E})$ is called a *graph*

$\mathbf{G} = (\mathbf{V}, \mathbf{E}) :$

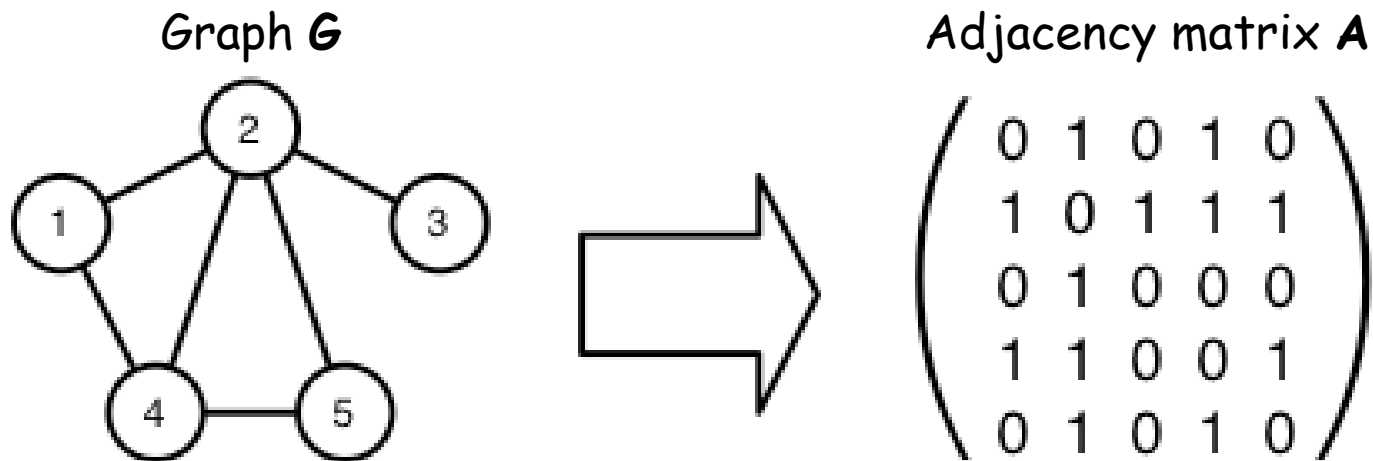
$\mathbf{V} = \{1, 2, 3, 4, 5\}$

$\mathbf{E} = \{(1,2), (1,5), (2,5), (3,4), (3,5), (4,5)\}$



Graph representation

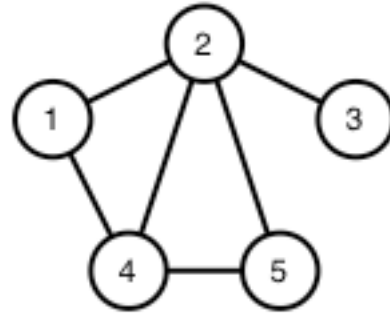
- The easiest way to represent a graph is the *adjacency matrix* **A**



- The link between the node i and j is represented in the adjacency matrix by putting to "1" the element at the row i and at the column j

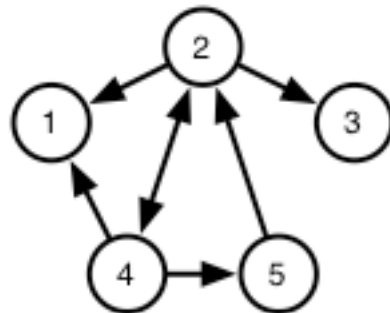
Graph and Digraph adjacency matrices

- Undirected graphs have always symmetric adjacency matrices



$$\begin{pmatrix} 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 \end{pmatrix}$$

- Directed graphs have generally asymmetric adjacency matrices

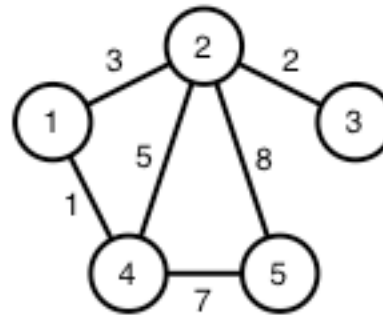


$$\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 \end{pmatrix}$$

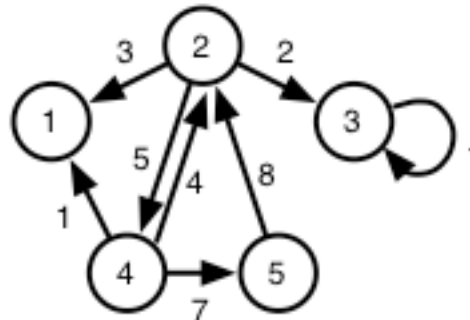
When using adjacency matrices it is mandatory to know if the original graph was directed or undirected

Weighted graph adjacency matrices

- Weighted graphs have a real number (higher or lower than 1) associated to each link. Thus, the adjacency matrix consists of real numbers, indicating the strength of the links



$$\begin{pmatrix} 0 & 3 & 0 & 1 & 0 \\ 3 & 0 & 2 & 5 & 8 \\ 0 & 2 & 0 & 0 & 0 \\ 1 & 5 & 0 & 0 & 7 \\ 0 & 8 & 0 & 7 & 0 \end{pmatrix}$$



$$\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 3 & 0 & 2 & 5 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 1 & 4 & 0 & 0 & 7 \\ 0 & 8 & 0 & 0 & 0 \end{pmatrix}$$

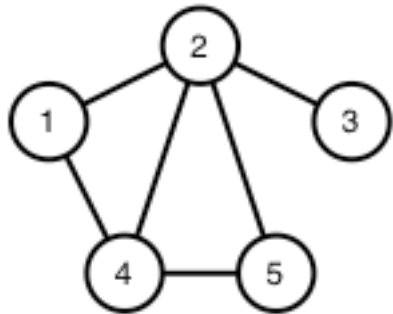


Measures for unweighted graphs

- Density
- Node degree
- Node degree distribution
- Distance between nodes
- Global efficiency
- Local efficiency

Density

- The graph density K is the ratio between the number of existing links L and the number of all the possible links L_{tot}
- In a graph of N nodes the maximum number of links is $N*(N-1)/2$.
Then, $K = L/L_{tot} = 2*L / N(N-1)$



$$\begin{pmatrix} 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 \end{pmatrix}$$

$$N = 5$$

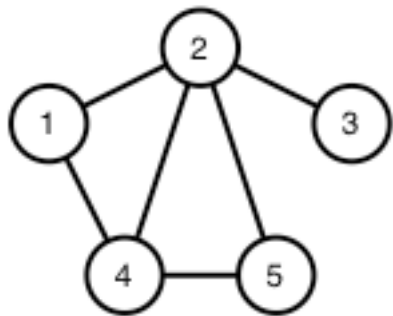
$$L = 6$$

$$K = (2*6) / (5*4) = 0,6$$

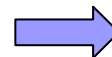
- The network density measures the level of general connectivity of the system. When $K=0$, the network has no connections; when $K=1$ the network is fully connected

Node degree

- The degree of a node g is the number of links connected to that node
- In a graph of N vertices the maximum number of links for a single node is $N-1$



$$\begin{pmatrix} 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 \end{pmatrix}$$

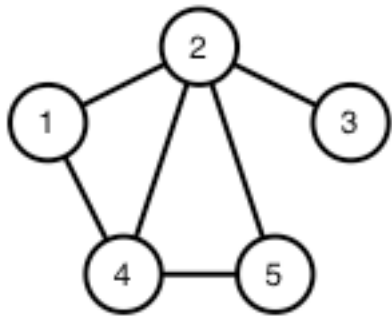


$$\begin{aligned} g(1) &= 2 \\ g(2) &= 4 \\ g(3) &= 1 \\ g(4) &= 3 \\ g(5) &= 2 \end{aligned}$$

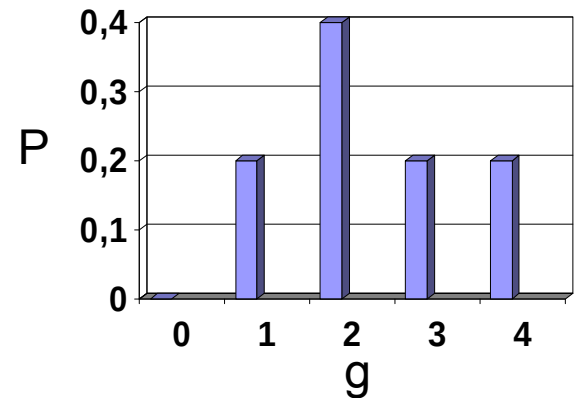
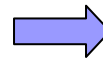
- The *node degree* measures the centrality of a node within the network. The higher is the node degree, the more important is its for the whole system

Degree distribution

- The degree distribution $P(g)$ is the ratio between the number of nodes with degree g and the total number of vertices
- $P(g)$ is the probability that a vertex randomly chosen has exactly g connections.



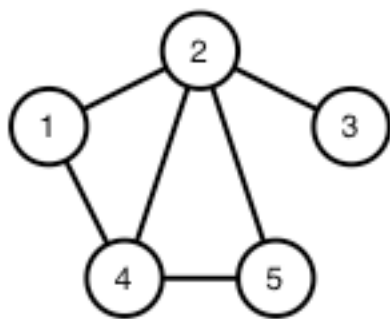
$$\begin{pmatrix} 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 \end{pmatrix}$$



- The *degree distribution* indicates how the links arrange among the nodes within a network

Distance between nodes

- The distance $d(i,j)$ between two nodes i and j in a graph is given by the shortest path that connect them
- A path is a sequence of links connecting two nodes in a graph. In general, nodes could not be linked at all, i.e. $d = \infty$



$$\begin{pmatrix} 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 1 & 1 & 1 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 \end{pmatrix}$$



Distance matrix

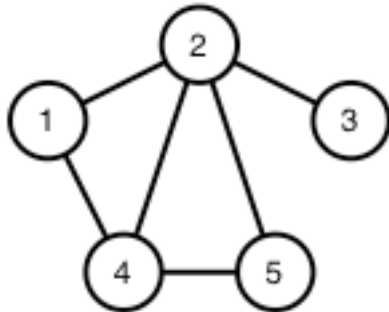
$$D = \begin{pmatrix} x & 1 & 2 & 1 & 2 \\ 1 & x & 1 & 1 & 1 \\ 2 & 1 & x & 2 & 2 \\ 1 & 1 & 2 & x & 1 \\ 2 & 1 & 2 & 1 & x \end{pmatrix}$$

- The *distance* measures the level of interaction between two elements in a network. The higher is the distance, the lower is the interaction

Global efficiency

- The global efficiency E_g of a graph is the arithmetical mean of the inverse of the distance between each pair of nodes (Latora e Marchiori, 2001):

$$E_g = \frac{2}{N(N-1)} \sum_{i \neq j} \frac{1}{d(i,j)}$$



$$D = \begin{pmatrix} x & 1 & 2 & 1 & 2 \\ 1 & x & 1 & 1 & 1 \\ 2 & 1 & x & 2 & 2 \\ 1 & 1 & 2 & x & 1 \\ 2 & 1 & 2 & 1 & x \end{pmatrix}$$



$$N = 5$$

$$E_g = 0,1 * (1 + 0,5 + 1 + 0,5 + 1 + .. + 1 + 1 + 0,5 + 0,5 + 1) = 0,8$$

- Global efficiency measures the “efficiency” in the communication within the network

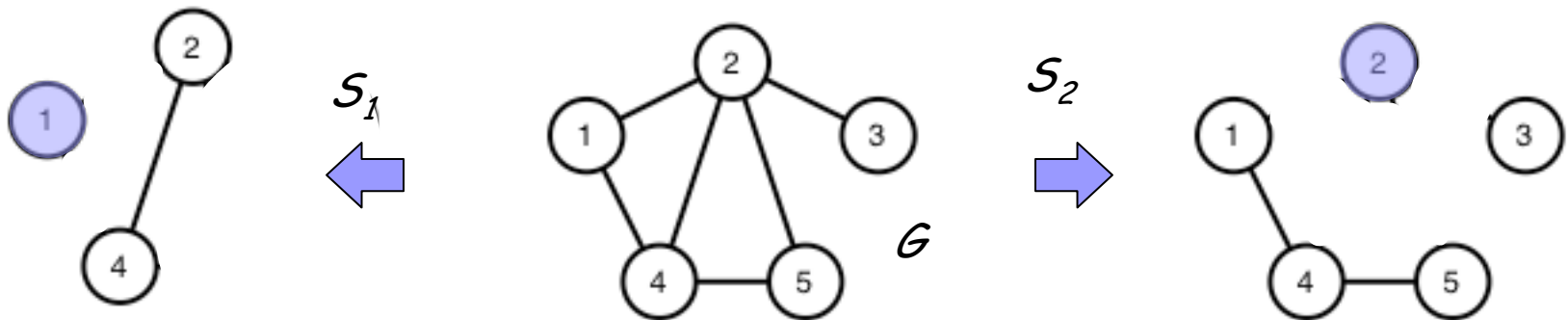
$E_g = 1$, in a fully connected graph; $E_g = 0$, in an empty graph

Local efficiency

- The local efficiency E_l of a graph is the mean of the global efficiencies of each subgraph S of G

$$E_l = \frac{1}{N} \sum_{i=1}^N E_g(S_i)$$

- A graph with N nodes has N subgraphs. Each subgraph is obtained by removing a node and by considering the remaining graph consisting of the nodes that were connected to the removed one.



- *Local efficiency* measures the tendency of the network to form clusters of elements strongly connected

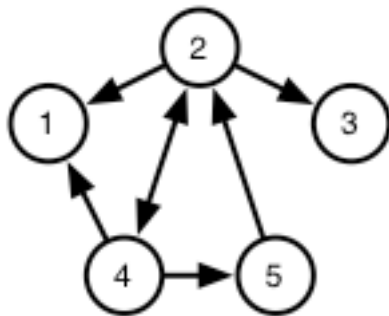


Measures for unweighted di-graphs

- Density
- Node degrees
- Degree distributions
- Distance between nodes
- Global efficiency
- Local efficiency

Density (di-graph)

- The density K of a di-graph is the ration between the number of existing links L and the number of all the possible links L_{tot}
- In a di-graph N nodes the maximum number of edges is $N*(N-1)$. Then, $K = L/L_{tot} = L / N*(N-1)$



$$\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 \end{pmatrix}$$

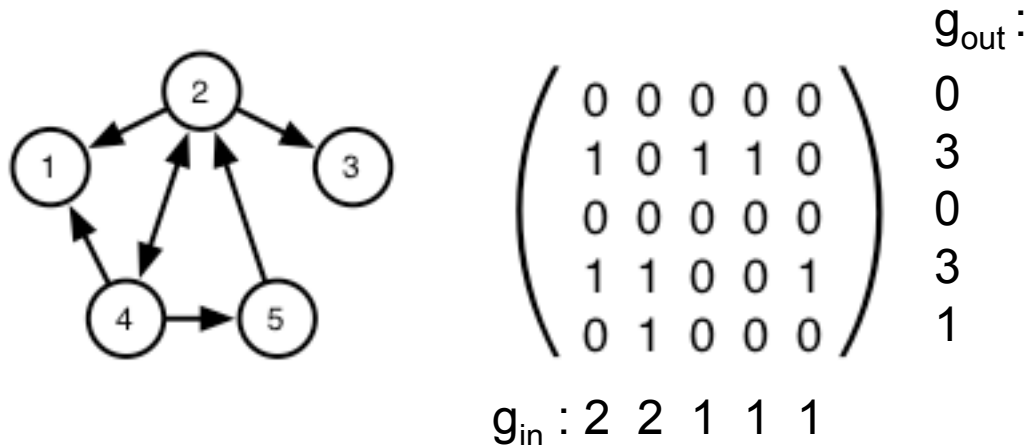
$$N = 5$$

$$L = 7$$

$$K = 7/(5*4) = 0,35$$

Node degrees (di-graph)

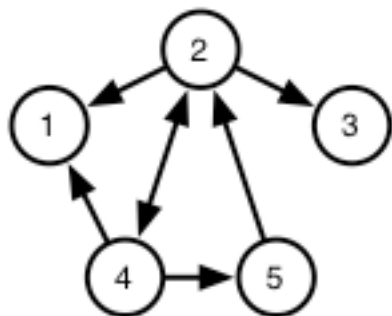
- In a di-graph the in-degree g_{in} indicates the number of links incoming into a node; the out-degree g_{out} is the number of connections outgoing from a vertex



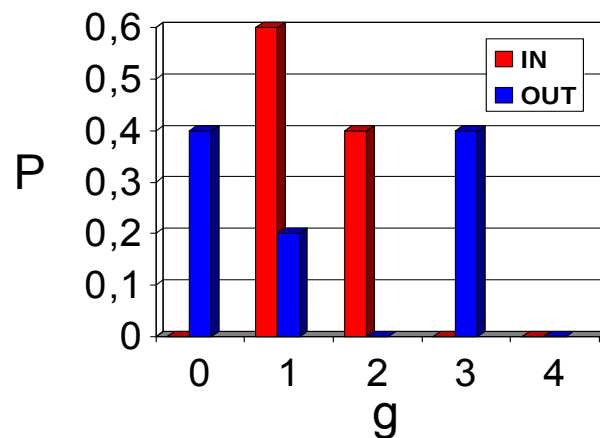
- A high *in-degree* means that an element is influenced by many other units in the system.
- A high *out-degree* indicates a high number of potential targets

Degree distributions (di-graph)

- In a di-graph, the in-degree distribution $P(g_{in})$ is the ratio between the number of nodes with degree g_{in} and the total number of vertices
- Equivalently, the in-degree distribution $P(g_{out})$ is the ratio between the number of nodes with degree g_{out} and the total number of vertices

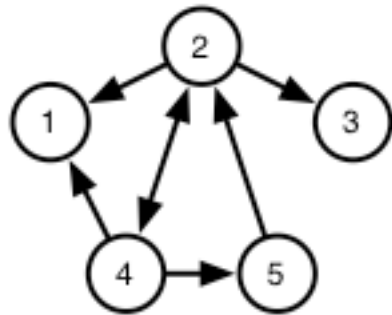


$$\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 \end{pmatrix}$$



Distance between nodes (di-graph)

- The distance $d(i,j)$ between two nodes i and j in a di-graph is given by the shortest path that connect them
- In general, if a directed path exists from the node i to the node j , the contrary is not assured



$$\begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 \end{pmatrix}$$



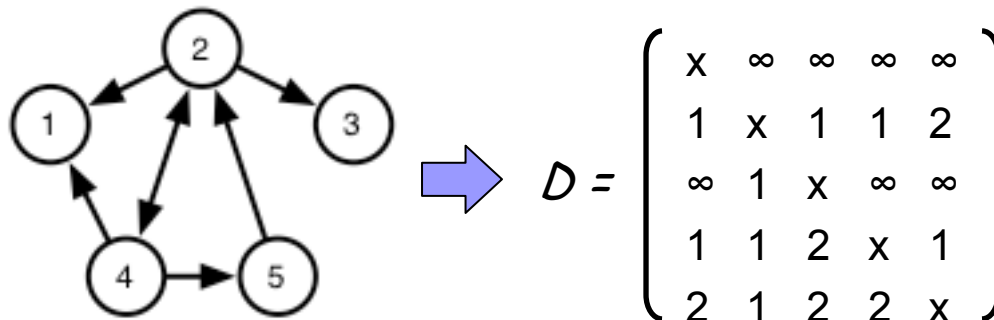
Distance matrix

$$D = \begin{pmatrix} x & \infty & \infty & \infty & \infty \\ 1 & x & 1 & 1 & 2 \\ \infty & 1 & x & \infty & \infty \\ 1 & 1 & 2 & x & 1 \\ 2 & 1 & 2 & 2 & x \end{pmatrix}$$

Global efficiency (di-graph)

- The global efficiency E_g of a graph is the arithmetical mean of the inverse of the distance between each pair of nodes

$$E_g = \frac{1}{N(N-1)} \sum_{i \neq j} \frac{1}{d(i,j)}$$



$$N = 5$$

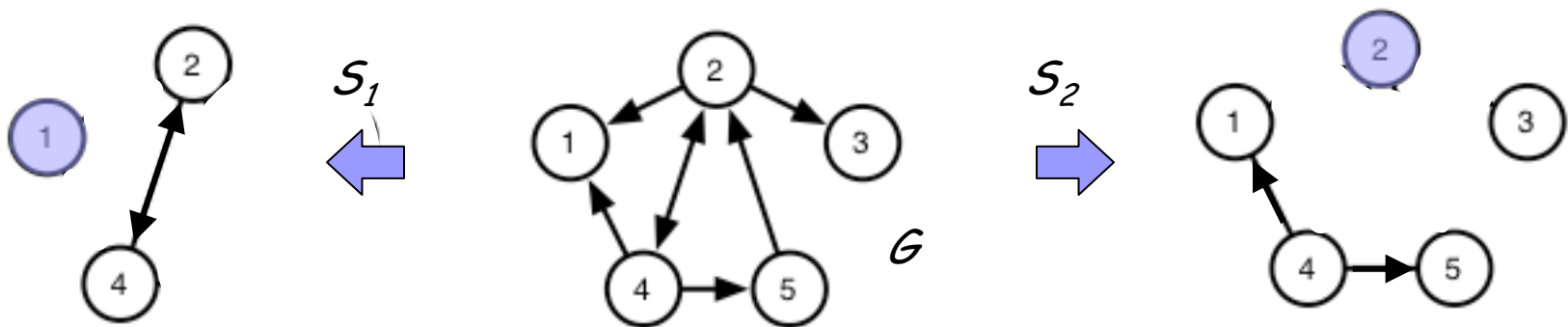
$$E_g = 0,05 * (1+1+1+0,5+1+1+1+0,5+1+0,5+1+0,5+0,5) = 0,525$$

Local efficiency (di-graph)

- The local efficiency E_l of a di-graph is the mean of the global efficiencies of each directed subgraph S of G

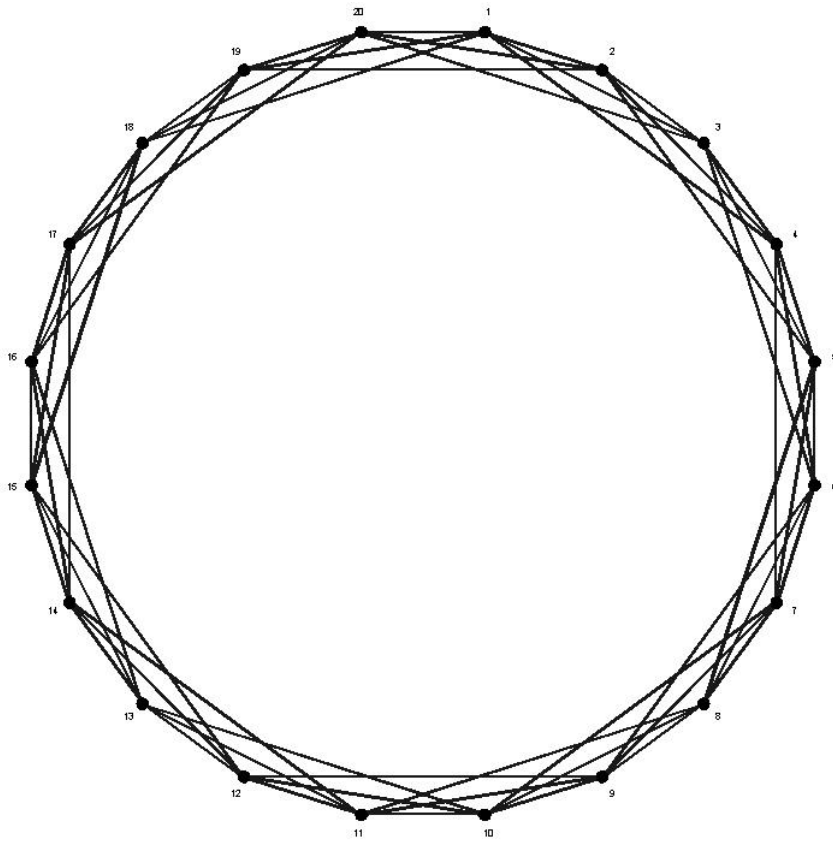
$$E_l = \frac{1}{N} \sum_{i=1}^N E_g(S_i)$$

- A di-graph with N nodes has N subgraphs. Each subgraph is obtained by removing a node and by considering the remaining di-graph consisting of the nodes that were connected (either in or out) to the removed one.

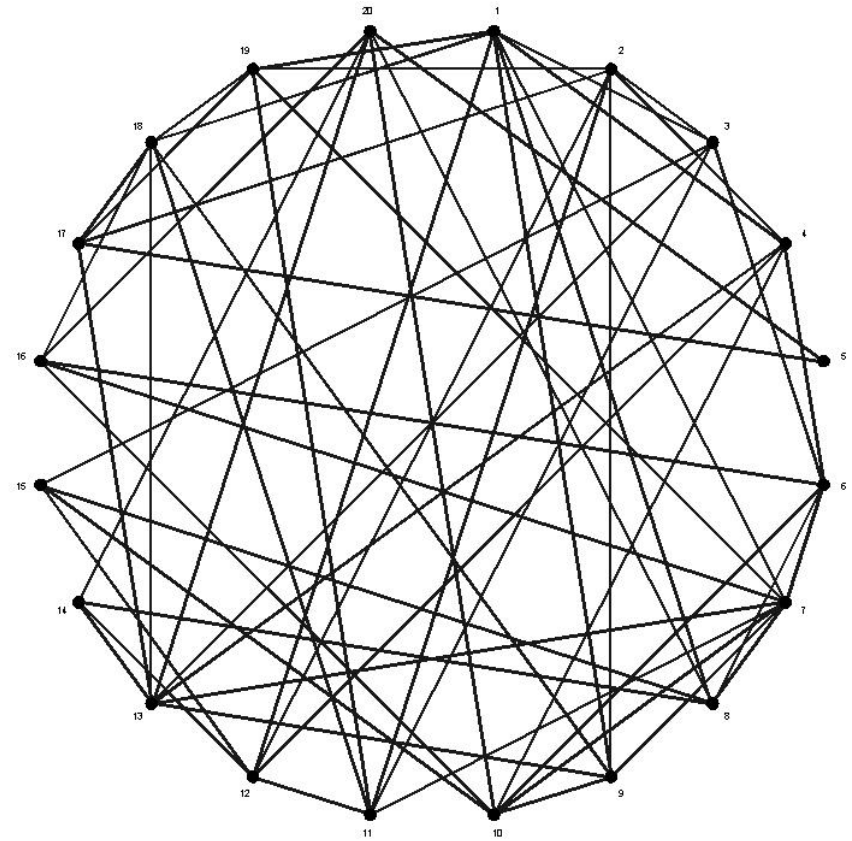


Network reference models

■ Regular graph

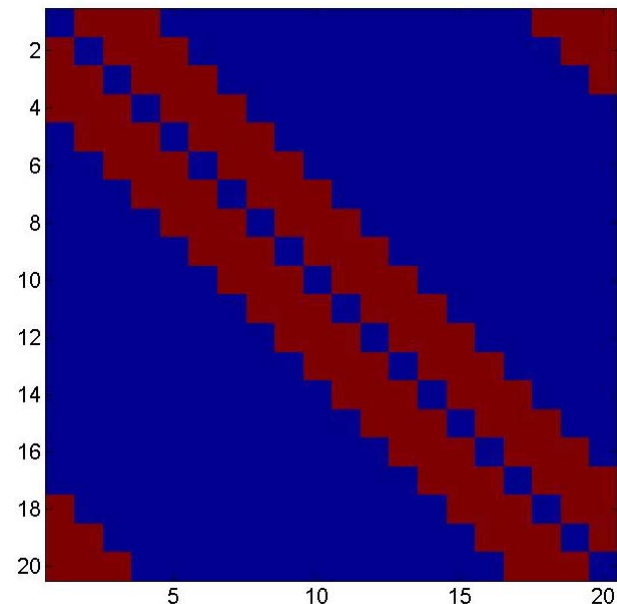
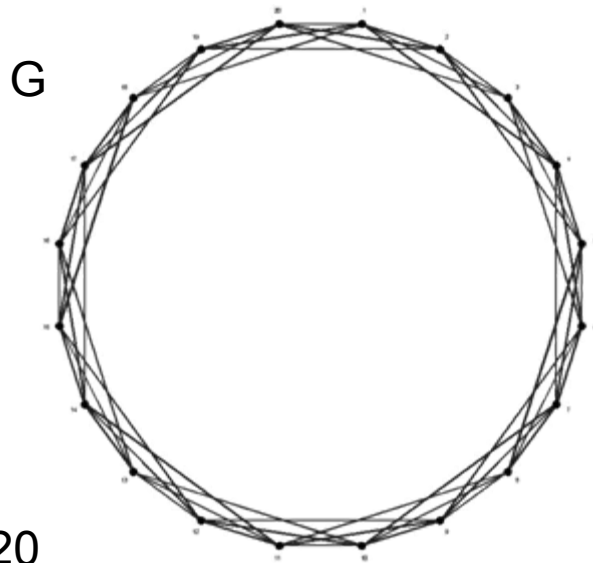


■ Random graph



Regular graph

- The regular graph is the simplest way to conceive a graph
- In the regular graph each node is connected to its M neighbors, leading to a lattice structure



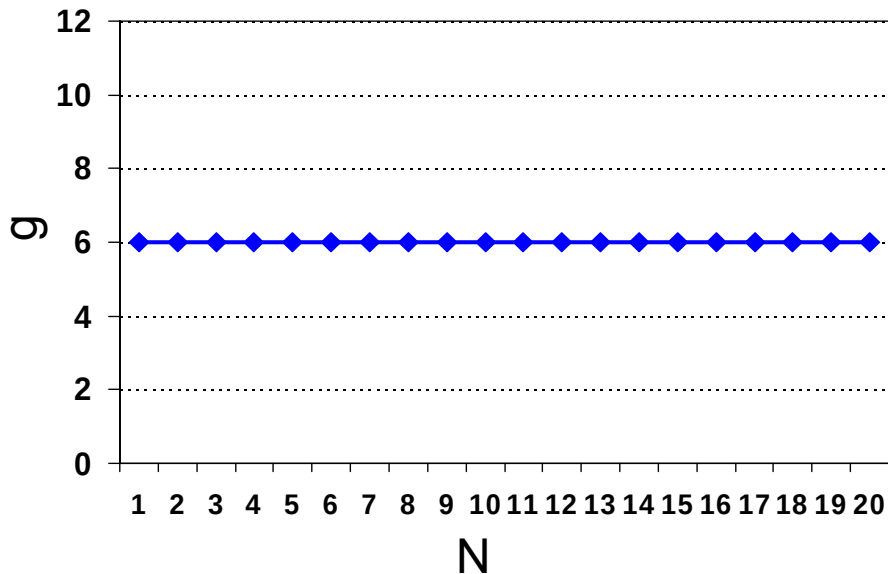
$$N = 20$$

$$M = 6 \rightarrow L = 60$$

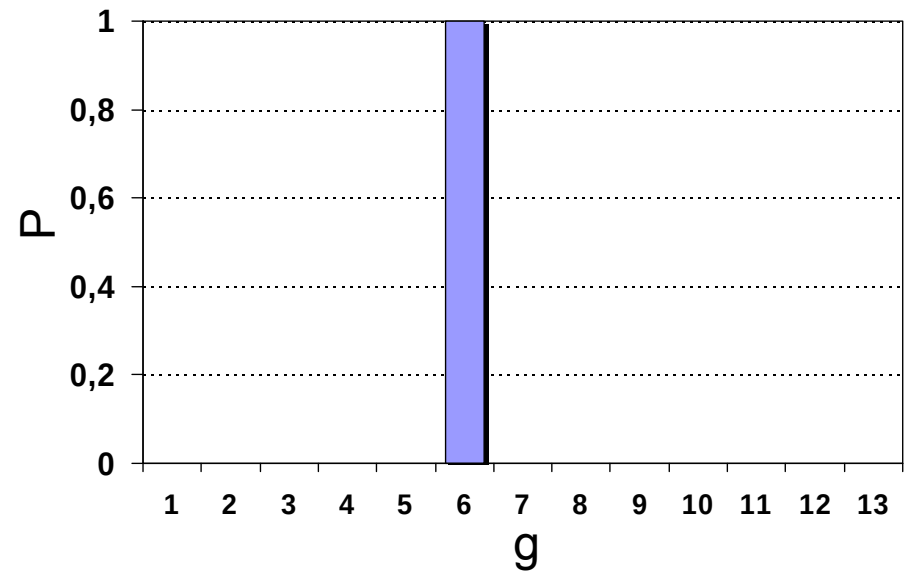
$$K = 2 \cdot 60 / 20 \cdot 19 = 0,316$$

Regular graph features

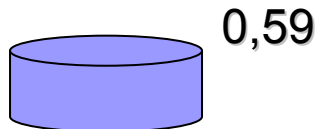
■ Degree



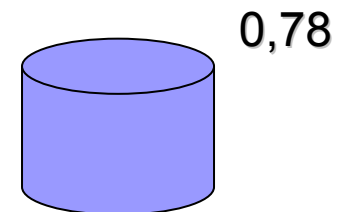
■ Degree distribution



■ Global efficiency

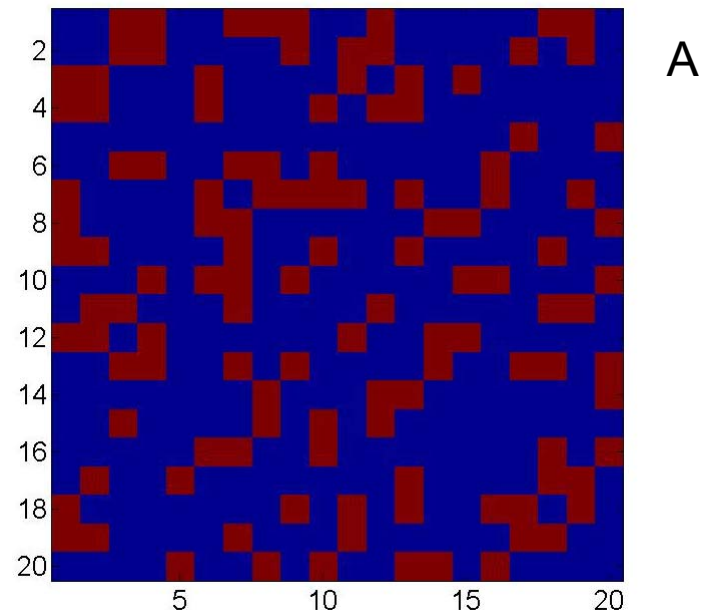
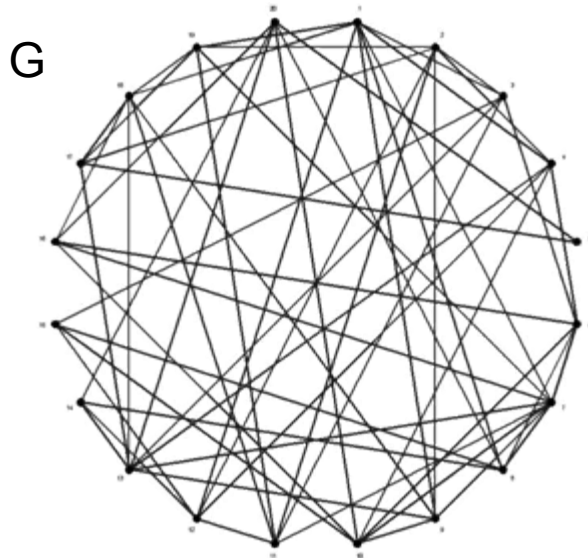


■ Local efficiency



Random graph

- The random graph was proposed firstly by Erdős e R nyi (1959), as an alternative model to the regular graph
- In the random graph, two nodes are connected with a fixed probability p

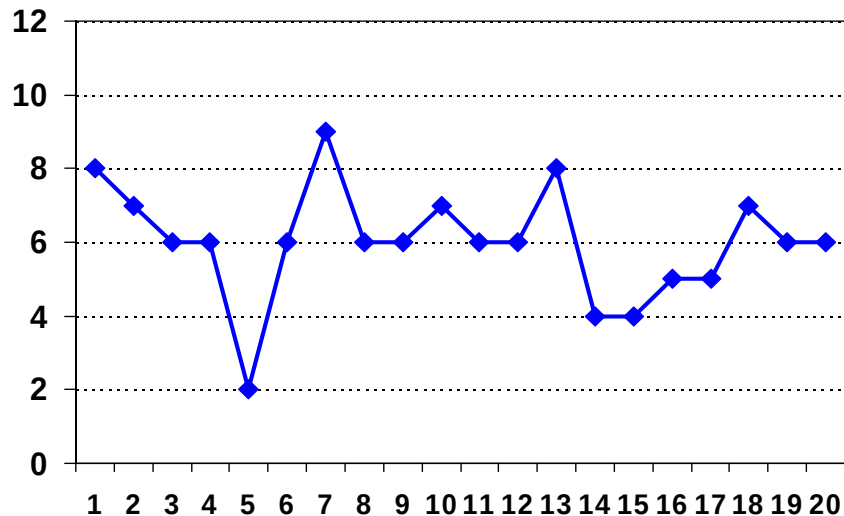


$N = 20$

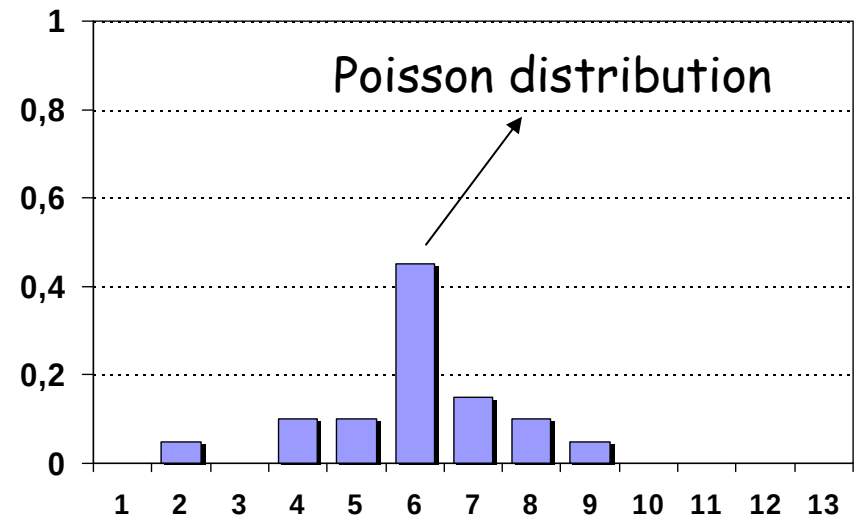
$p = K = 0,316$

Random graph features

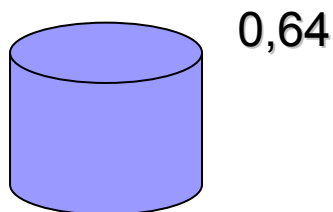
■ Degree



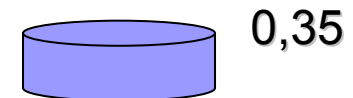
■ Degree distribution



■ Global efficiency

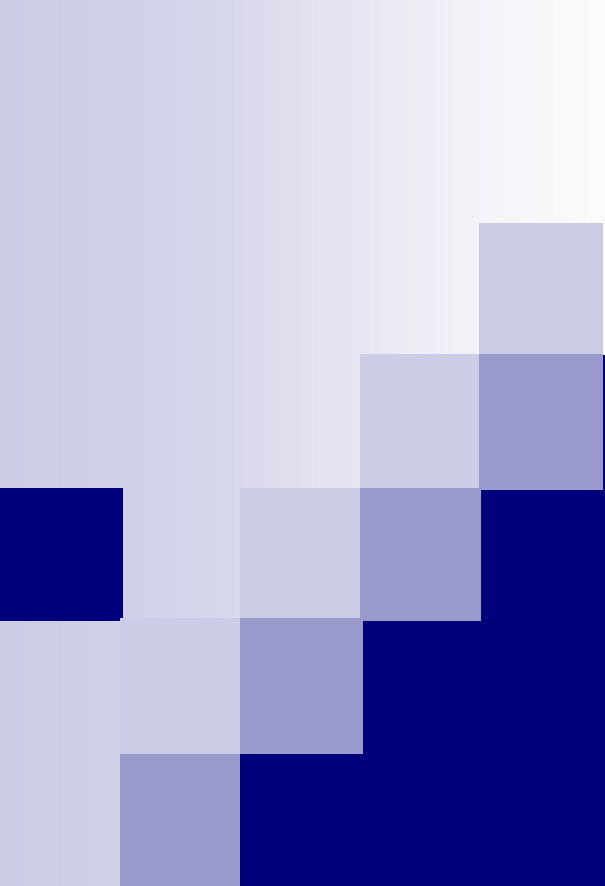


■ Local efficiency



Conclusions (Part I)

- In the regular graph all the nodes have the same degree, while in the random graph the degree distribution tends to follow a “poissonian” law ($N \rightarrow \infty$)
- In the regular graph the nodes tend to form “distant” clusters (high local efficiency), while in the random graphs all the nodes are indifferently “close” (high global efficiency)
- Regular and random models have opposite features, but they do not arrive to point out the brain networks properties, which in general exhibit more complex characteristics

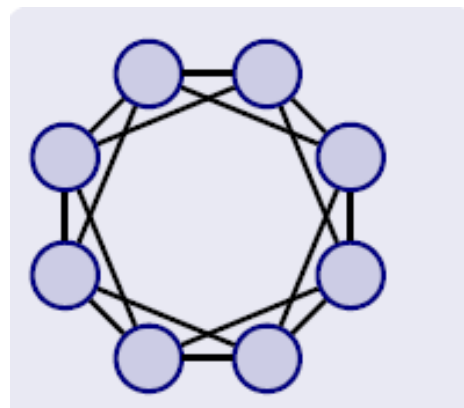


Complex brain networks

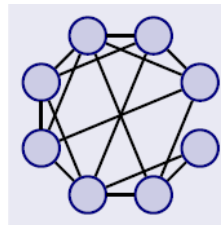
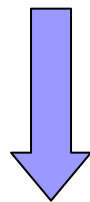
Part II

What a complex network is?

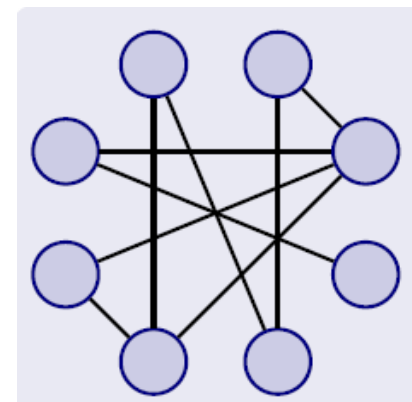
- A complex network is a network with a non trivial topological structure (i.e. their features differ either from regular and random graphs)
- Natural systems exhibit complex features related to the link organization within the network.



Lattice



- degree dist.
- clustering
- assortativity
- community
- hierarchical struct.



Random

Biological networks

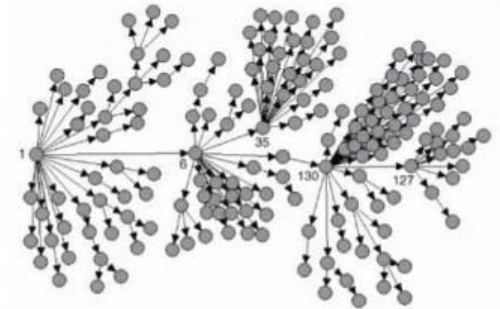
■ Proteomics

- Graph nodes represent proteins
- Links represent the chemical interactions



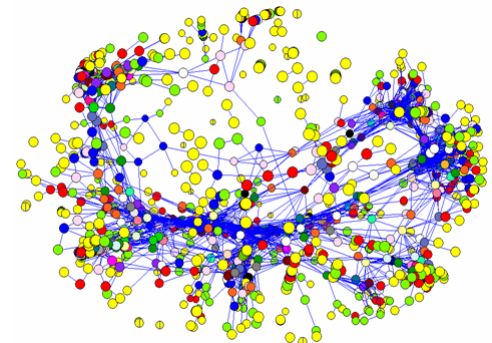
■ Epidemiology

- Graph nodes represent persons
- Links, the contagions



■ Neuroscience

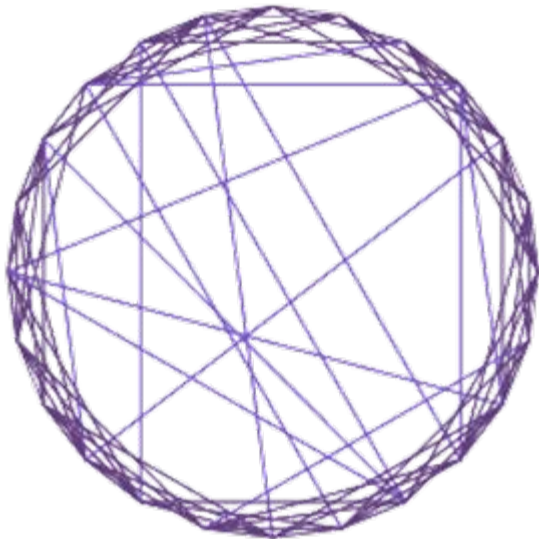
- Graph nodes represent brain regions
- Links, the anatomical or functional connections



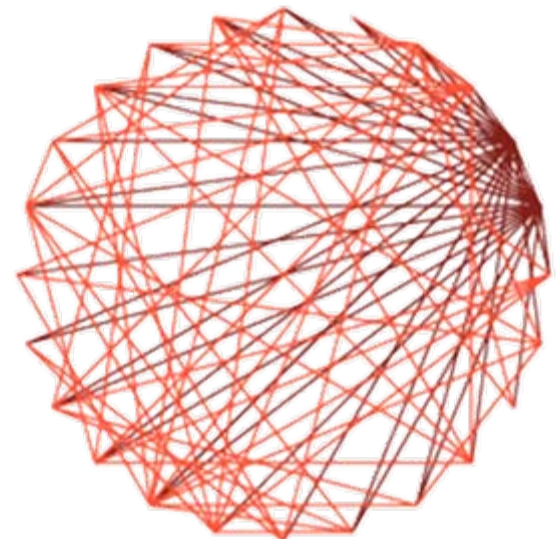
Complex network models

- Those biological real networks have features non completely regular or random
- Do exist other models that can exhibit the same real network topological properties?

"Small-world" graph

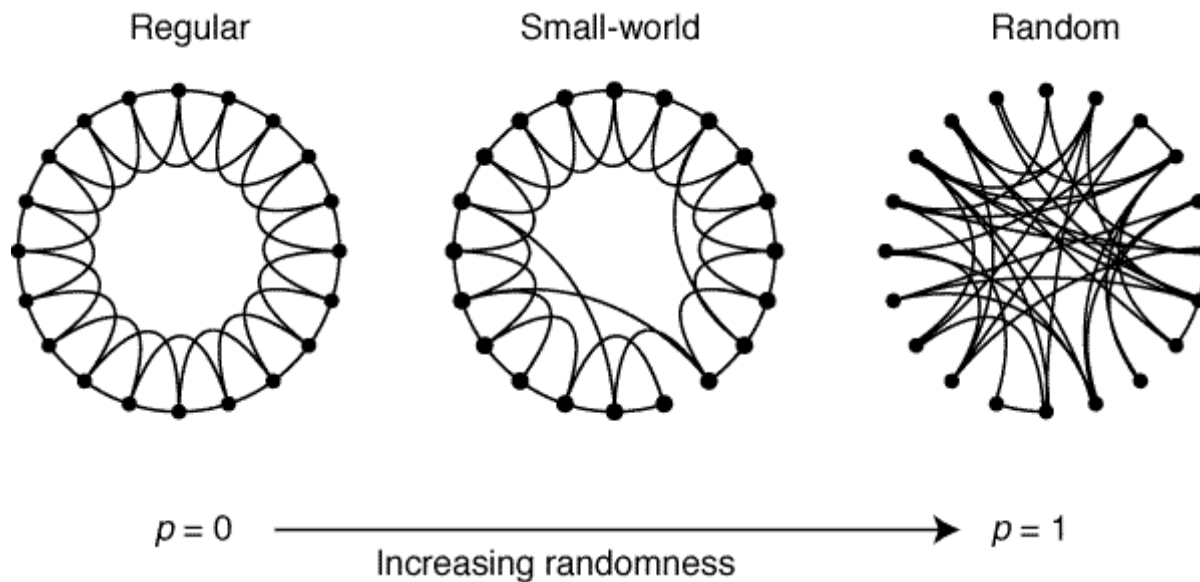


"Scale-free" graph



Small-world graphs

- 1998, first work published on Nature
 - Collective dynamics of 'small-world' networks, Watts e Strogatz



The probability p to reconnect the links randomly leads to an intermediate model between a completely regular graph ($p=0$) and a completely random graph ($p=1$)

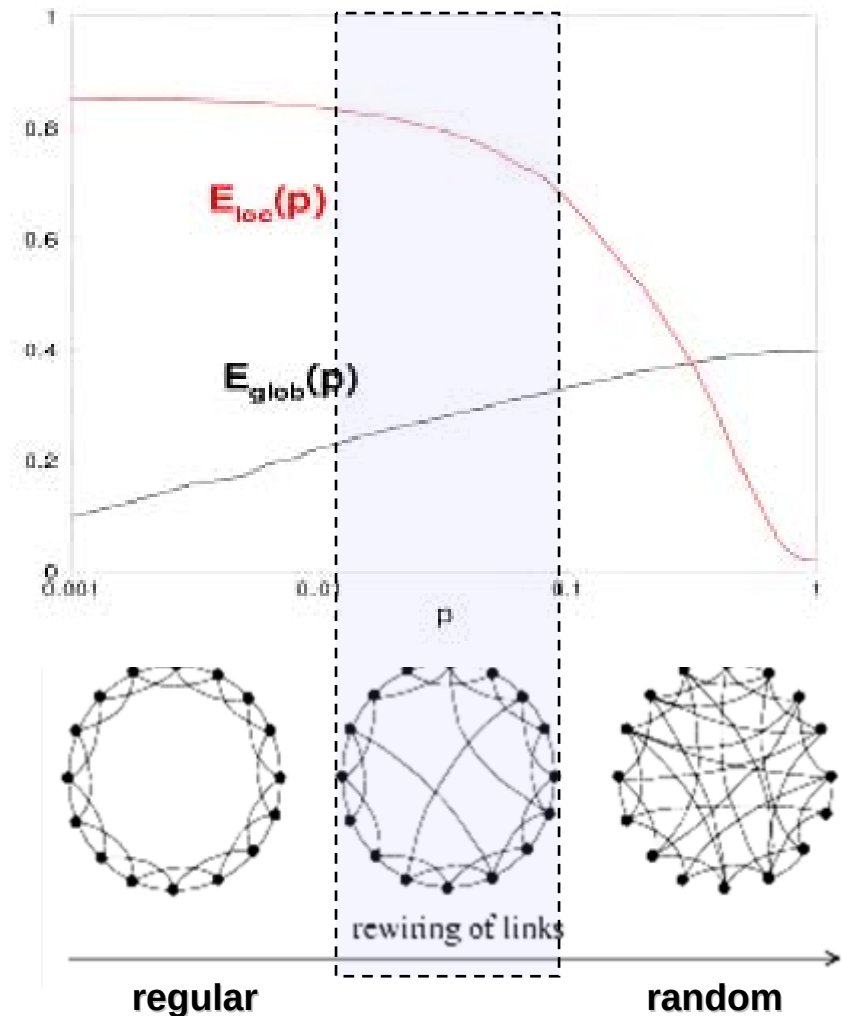
Small-world graphs

- The random reconnection of a little number of links reduces drastically ($\sim 50\%$) the average distance between the nodes within the graph

The global and local efficiency indexes can capture this effect:

$$E_g \text{ regular} < \mathbf{E_g} < E_g \text{ random}$$

$$E_l \text{ regular} > \mathbf{E_l} \gg E_l \text{ random}$$



Small-world networks

- Many real complex networks present small-world features
- The main function of this property is to facilitate the information propagation within the network (i.e. high efficiency)

<i>Unweighted:</i>	E_{glob}	E_{glob}^{random}	E_{loc}	E_{loc}^{random}
Macaque	0.52	0.57	0.70	0.35
Cat	0.69	0.69	0.83	0.67
<i>C. elegans</i>	0.46	0.48	0.47	0.12
Movie Actors	0.37	0.41	0.67	0.00026
WWW	0.28	0.28	0.36	0.000001
Internet	0.29	0.30	0.26	0.0005

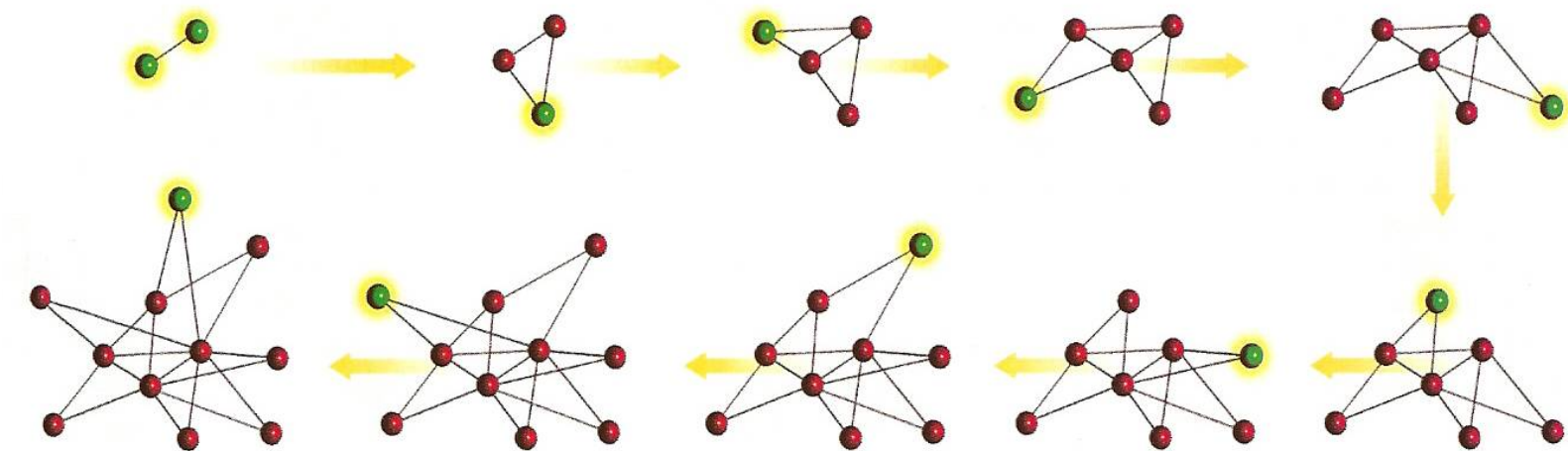
The name of such model derives from the idea that, if a person is one step away from each person they know and two steps away from each person who is known by one of the people they know, then everyone is at most six steps away from any other person on Earth (*6 degree of separation*)

Milgram, *Psych Today* 2, 60 (1967)



Scale-free graphs

- 1999, first work published on Science:
 - Emergence of scaling in random networks, Barabasi e Albert

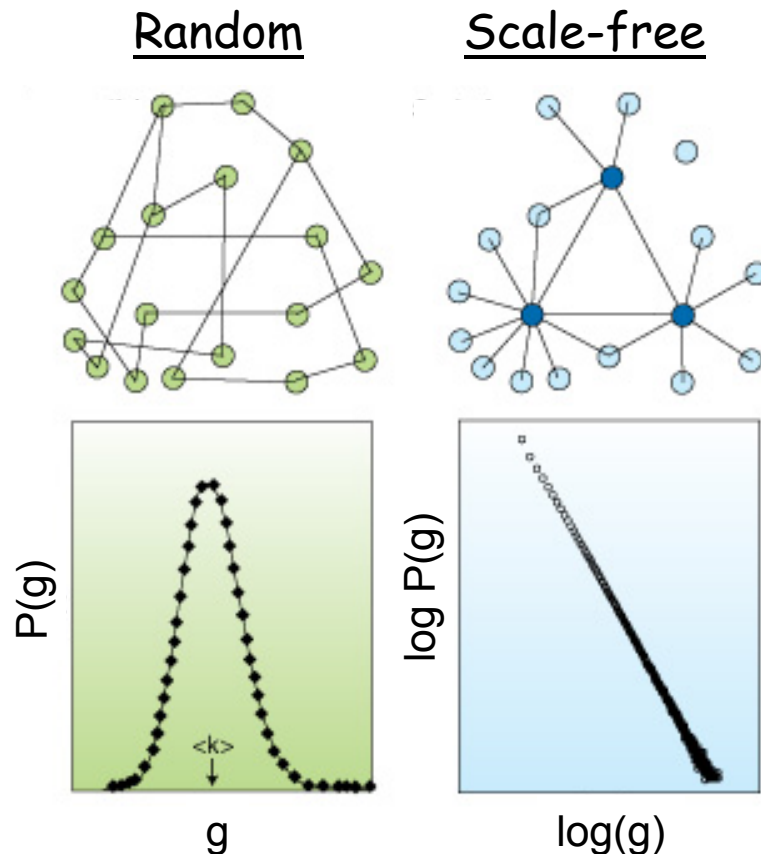


- The scale-free model considers a growing factor of the network itself
- For each added node, the probability that it could be connected to the vertex i is proportional to the degree of i :

$$p_i = g_i / \sum_j g_j$$

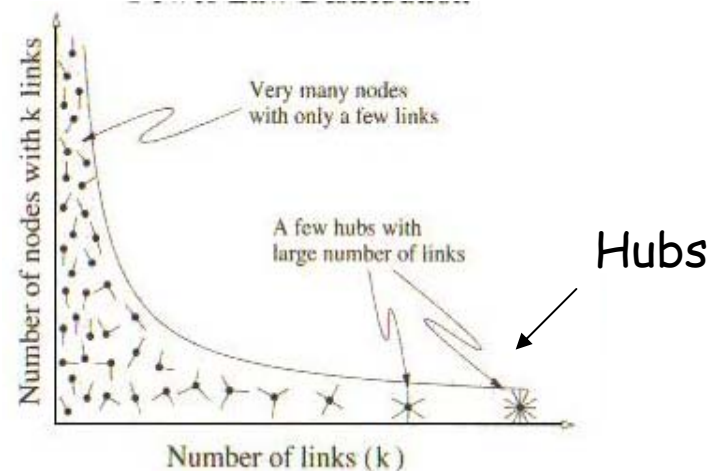
Scale-free graphs

- In scale-free networks there are a lot of nodes with few links and very few vertices with a lot of connections



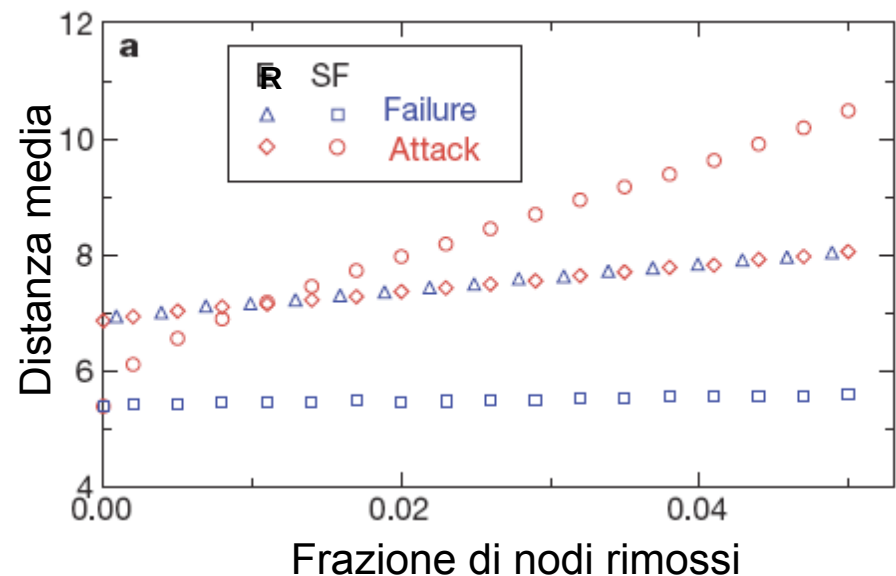
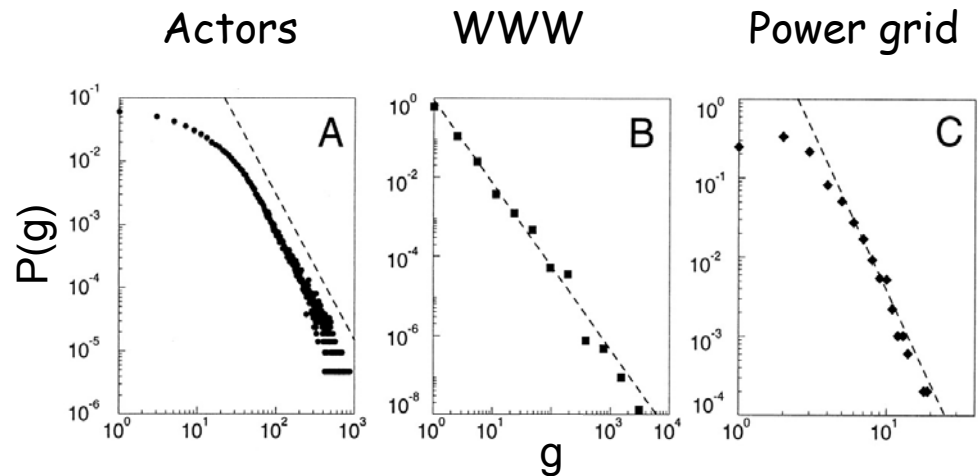
The degree-distribution can detect this structural property. For these networks the distribution follows a power law

$$P(g) = g^{-\gamma}, \quad 2 < \gamma < 3$$



Scale-free networks

- Beside small-world features, real complex networks can also show scale-free attributes
- Scale-free networks (SF) are very resistant to random node damage (failures), but very vulnerable to intentional attacks (attacks).
- Random networks present a medium homogeneous defense against both the type of damages.

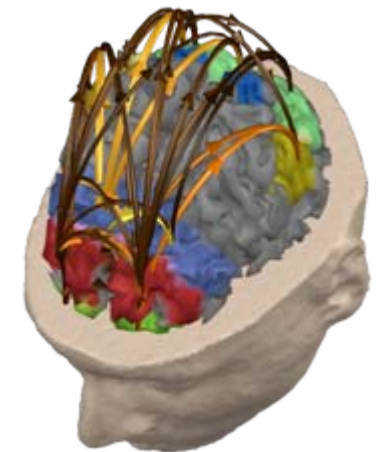


Considerations on complex networks

- Scale-free (SF) and small-world (SW) models reflect properly the attributes of the real complex networks, independently of the nature of the connectivity system
- The theoretical graph measures (degree, distribution, efficiency) can classify and recognize opportunely such models
- These measure are adequate candidates to describe in a concise way the topological organization within a complex network

Brain networks

- Anatomical connectivity (static network): physical connections between neurons or cerebral regions
 - i.e. synaptic junctions, axons, etc,...
- Functional connectivity (changing network): relationships between biological activities of neuronal population or cerebral areas
 - i.e. electrical signals, metabolic signals, etc...



Cross-correlation



undirected graph

Phase difference



oriented graph

Autoregressive models

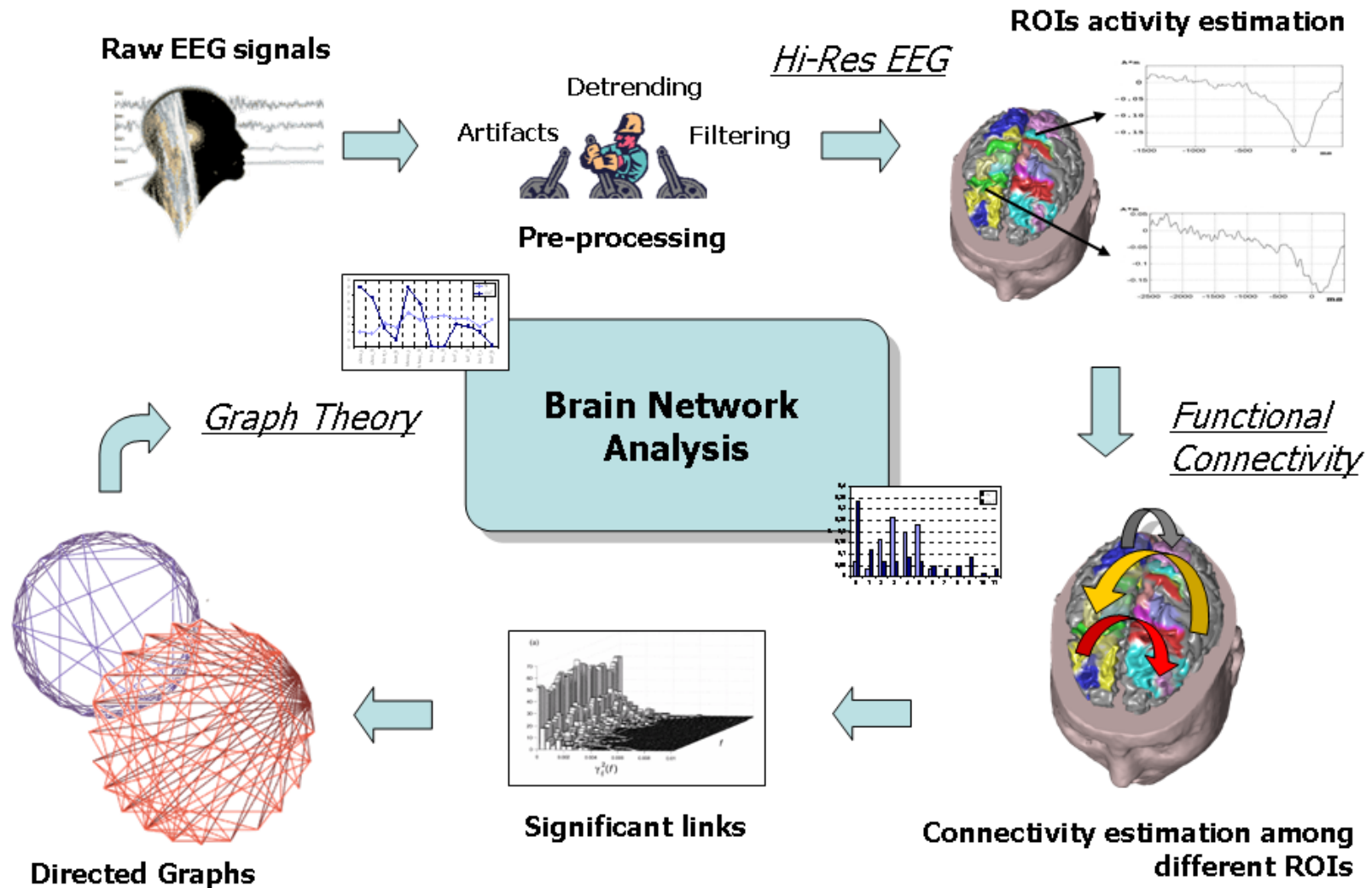


directed graph

Processes in brain networks

- The structure (i.e. the links arrangement in a graph) of a brain network is crucial in the comprehension of its dynamical processes
- A small-world configuration facilitates the information propagation in the network
 - Neuroscience → neuronal communication
- A scale-free configuration allows the identification of the central elements (i.e. hubs) of the network
 - Neuroscience → removal of epileptic source

Brain functional networks



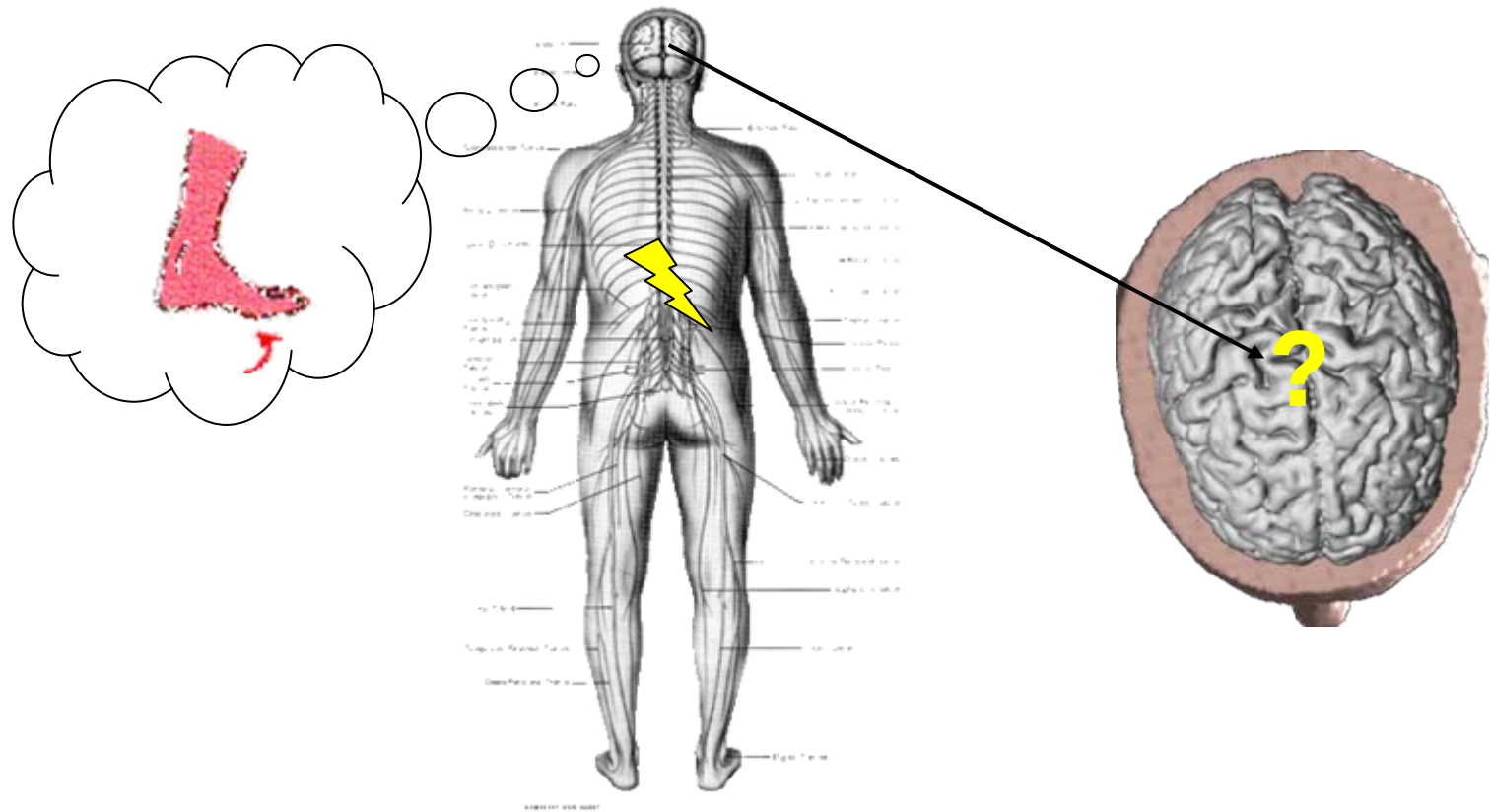


Brain network analysis

1. Cortical plasticity in tetraplegic patients
2. Memory processes evaluation
3. Cortical dynamics during motor acts

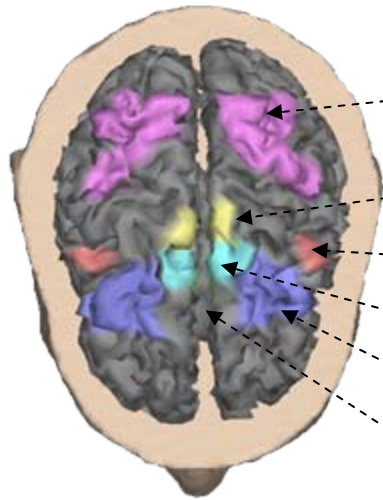
Cortical Plasticity in Tetraplegics

Does spinal cord injury alter the brain behaviour cortex during the attempt of a simple motor task?



Results – Functional Connectivity

SCI



BA7

MIF

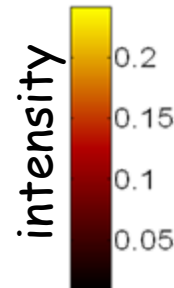
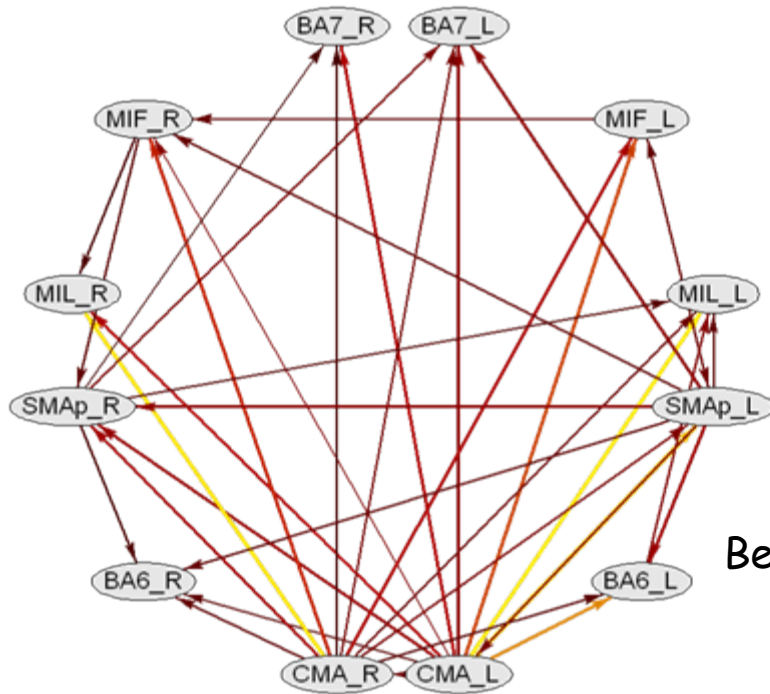
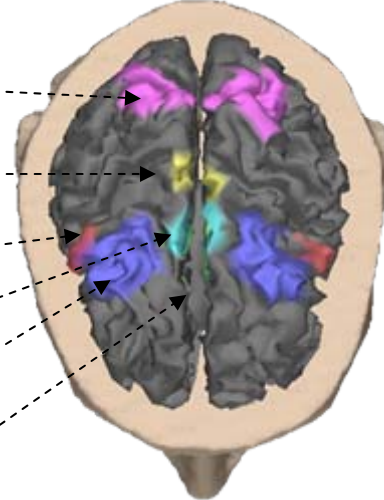
MIL

SMAp

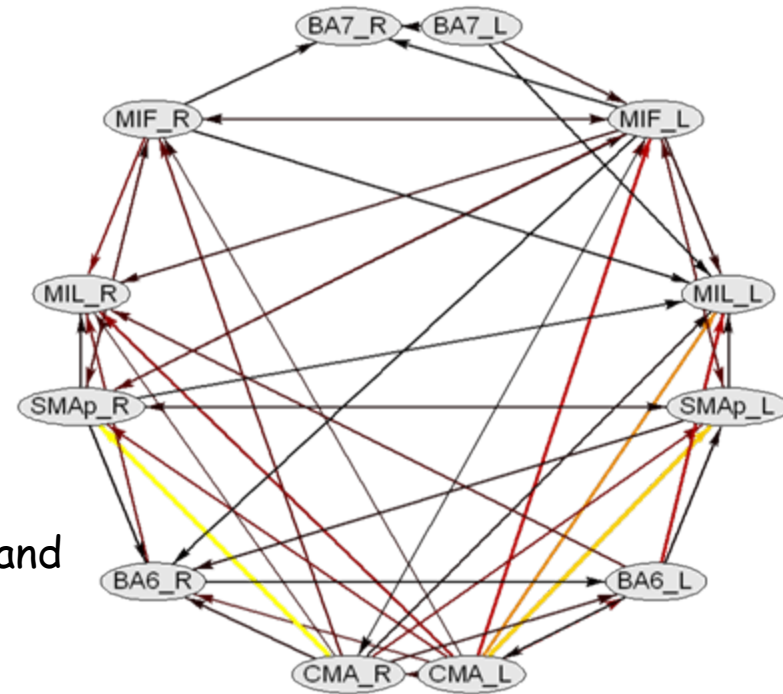
BA6

CMA

Control

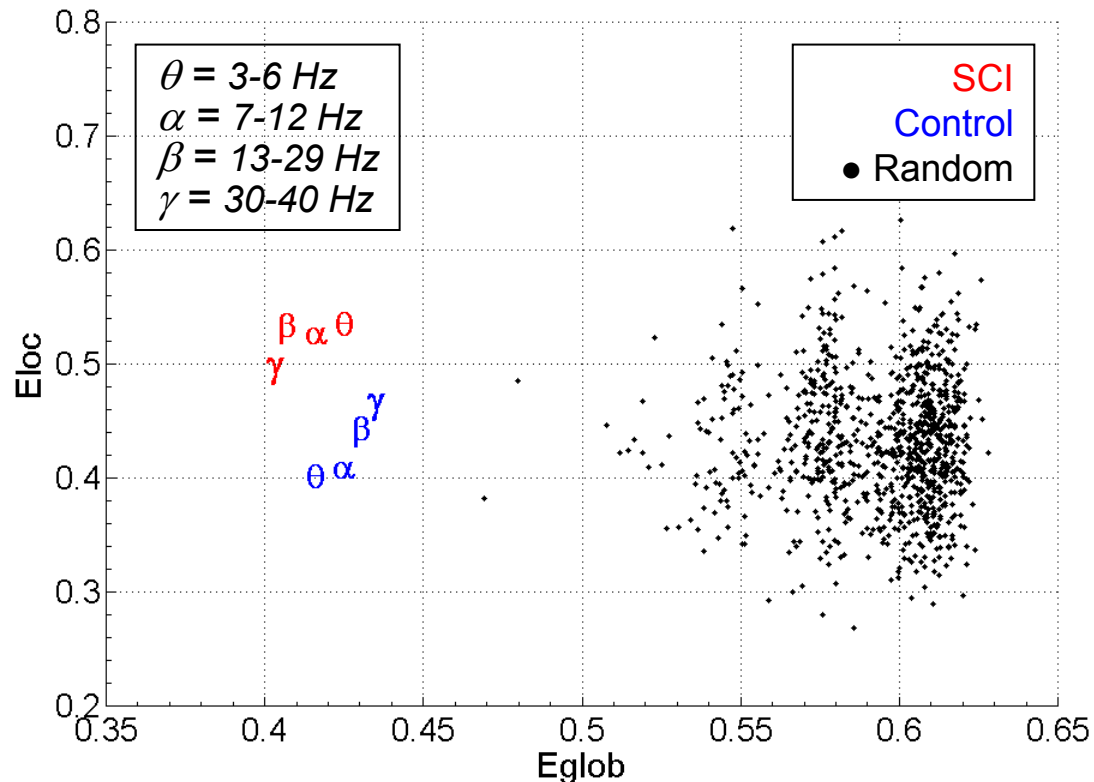


Beta frequency band
(13-29 Hz)



Results – Network Architecture

Scatter plot of global and local efficiency



Average values are grouped by SCI patients (red symbols) and control subjects (blue symbols).

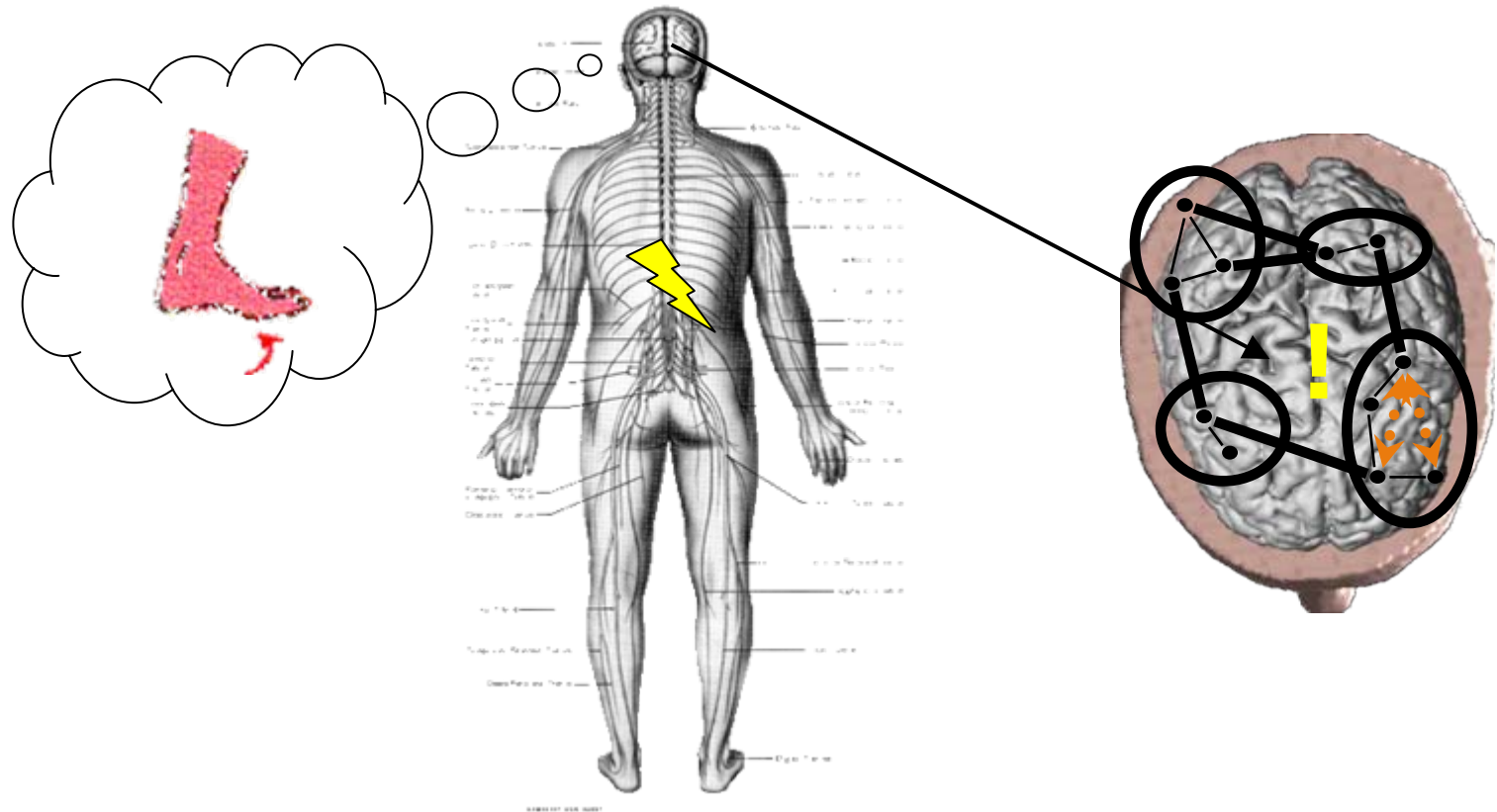
Black dots represent the distribution of 1000 random graphs

Separate z-tests showed that values obtained in the cortical networks are significantly ($p < 0.05$) different from those obtained in random graphs

The higher local efficiency observed in the spinal cord injured population entails a larger level of internal organization and fault tolerance.

Cortical Plasticity in Tetraplegics

The obtained results indicate that the brain network during the attempted movement changes its functional organization by increasing its modularity



This structural improvement suggests a sort of compensative mechanism as a response to the local alteration in the brain after the spinal injury

Memory processes in Neuromarketing

The events we experience in the course of our lives fall into general categories:

- Those we remember



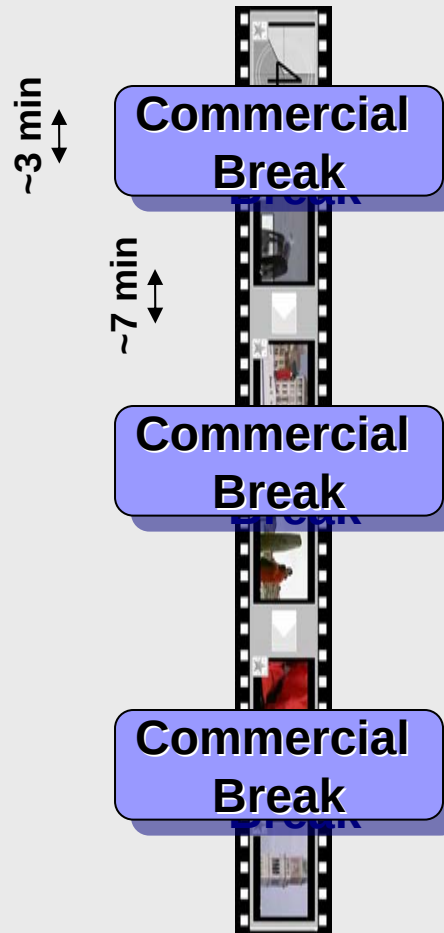
- Those we do not



Can we predict those events that are likely to initiate the later formation of a memory trace?

Methods - Experimental Design

A lifelike experiment !

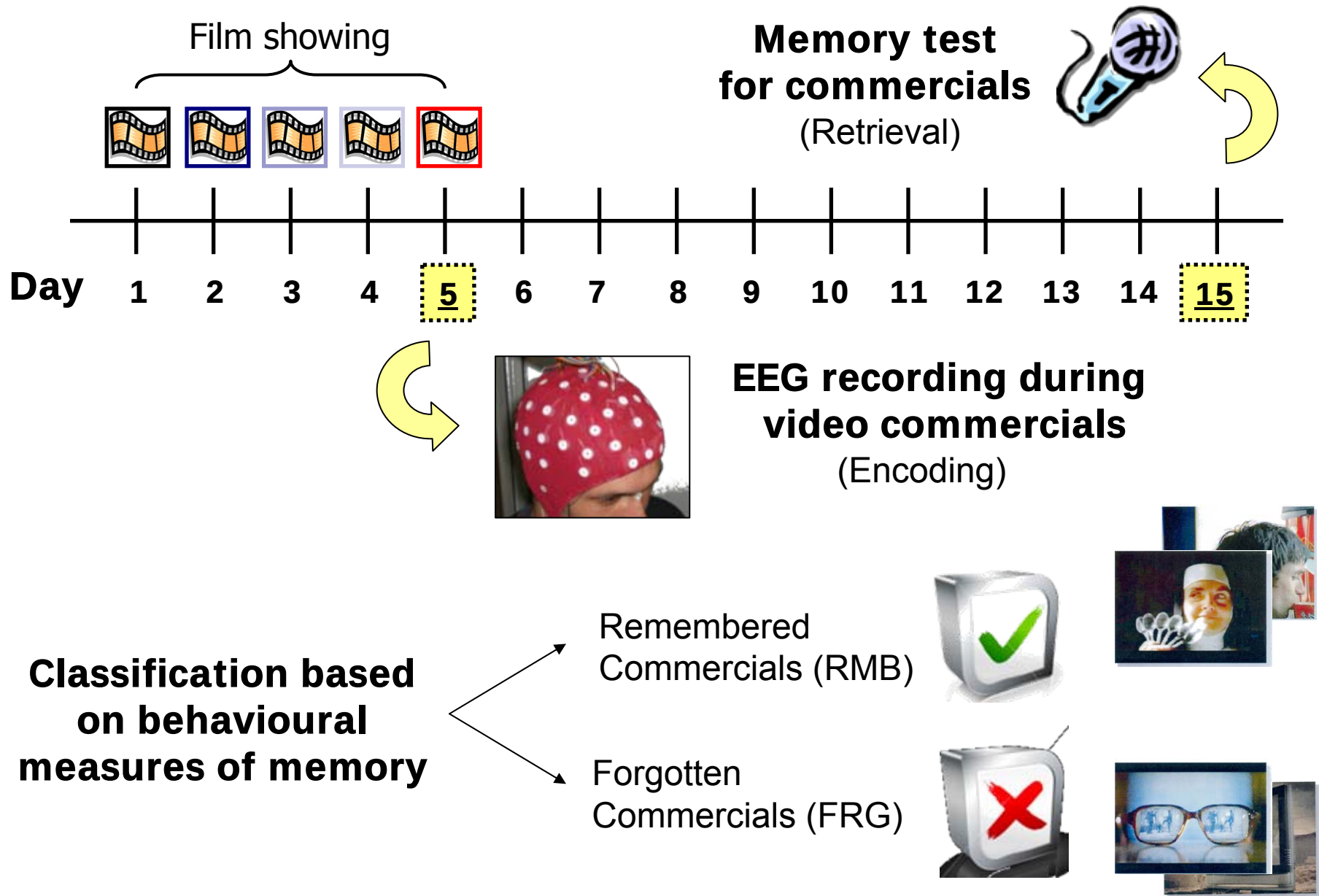


Neutral
Documentary
(~40 min)



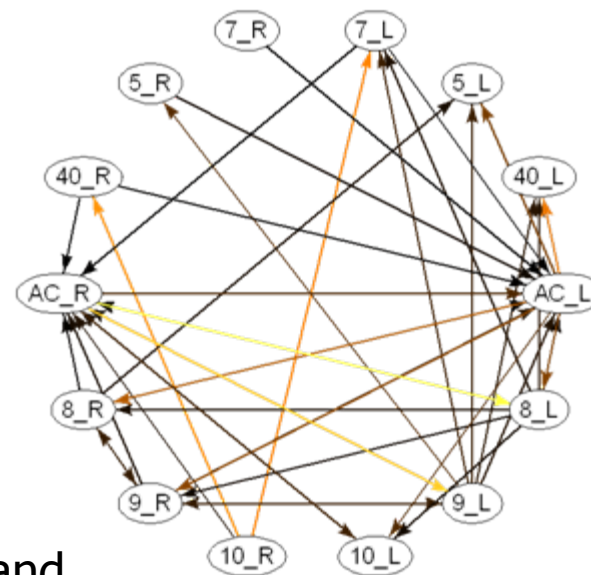
Each commercial break
consists of six different spots

Methods – Spot Classification



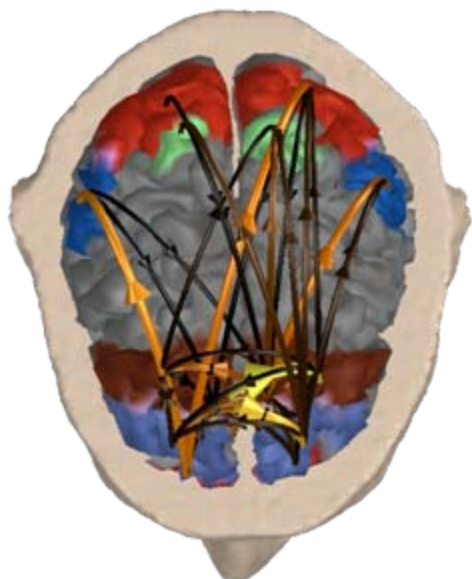
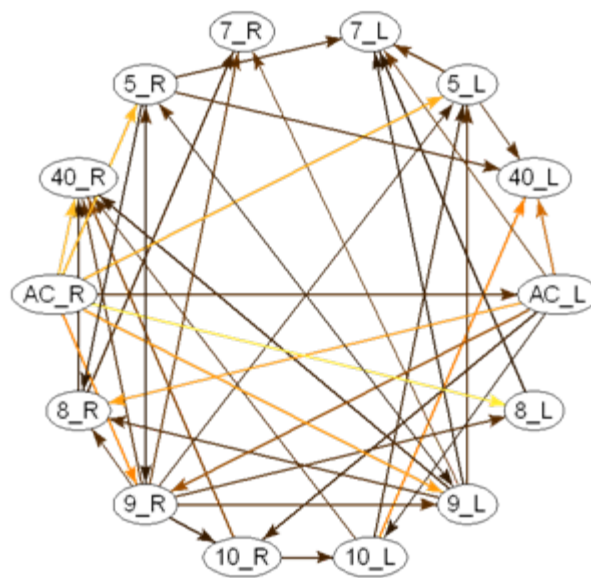
Results – Functional Connectivity

FRG



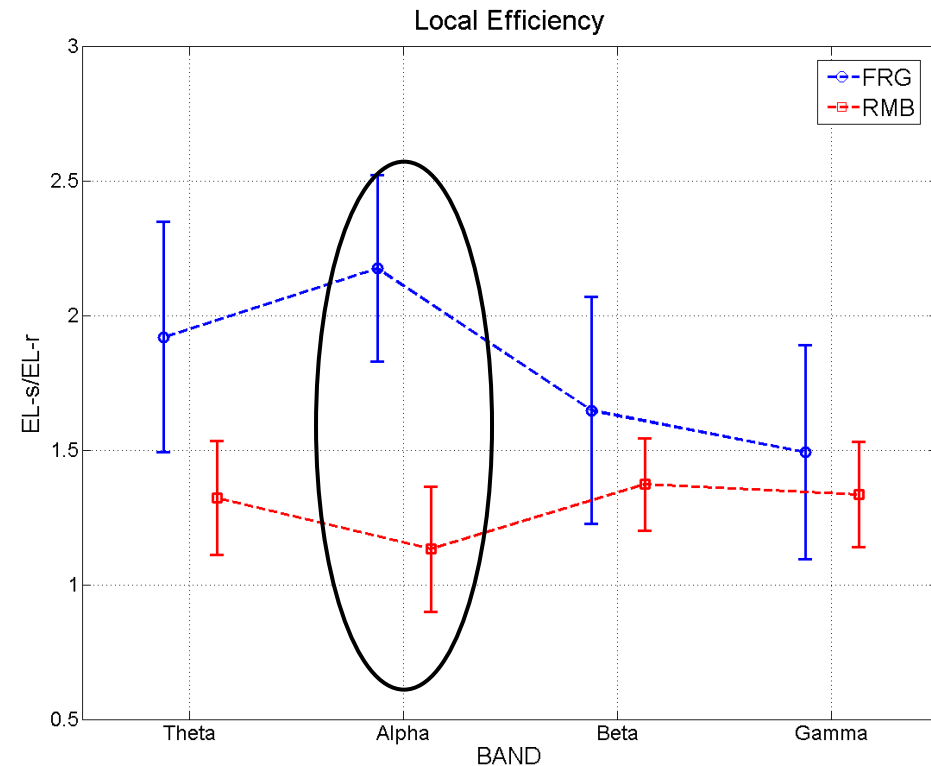
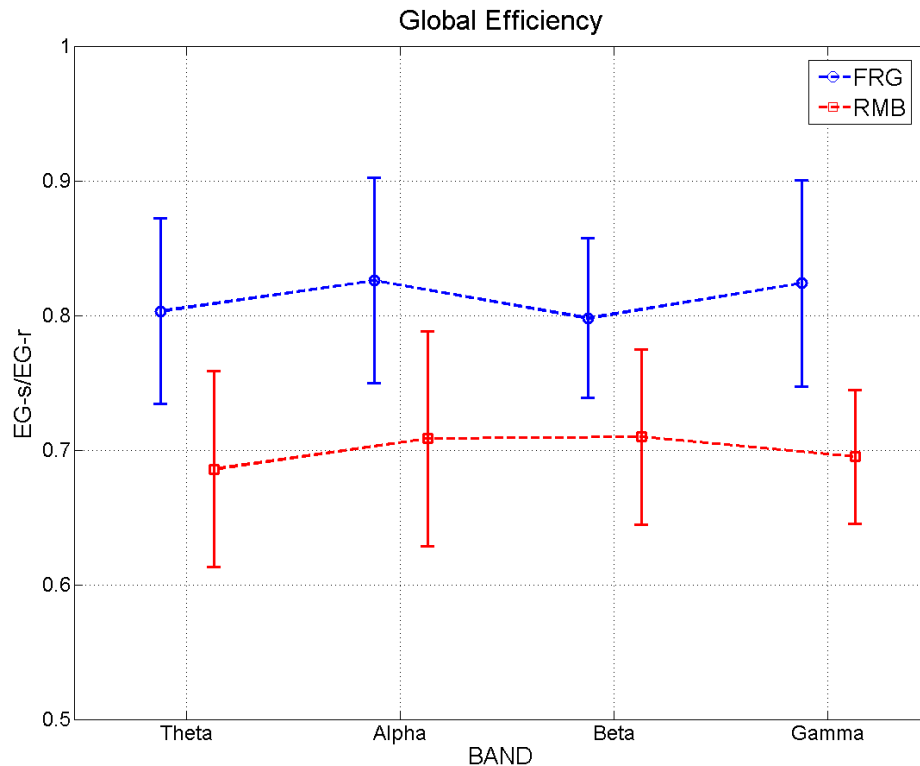
Alpha frequency band
(EEG oscillations between 8 and 12 Hz)

RMB



Results – Network Architecture

- Distance was inversely proportional to the link weight : $d_{ij}=1/w_{ij}$
- Efficiency indexes were scaled by the mean value from 100 random graphs
- ANOVA statistics was performed with a test-level equals to 0.05

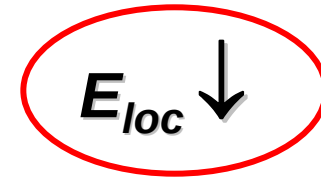
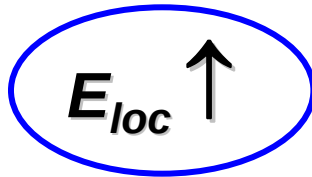


In the Alpha band, the local efficiency (segregation) decreases significantly during the watching of the commercials that will be remembered later.

Memory processes in Neuromarketing

In the Alpha band, the significant decrease of local clustering connections during encoding activity probably reflects the presence of attentional and semantic processes.

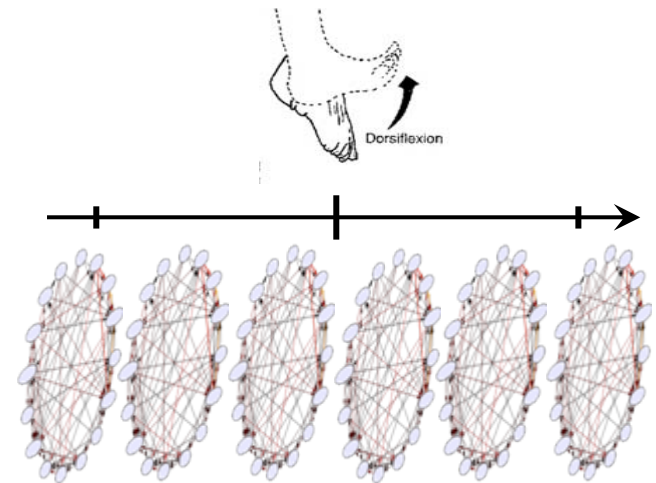
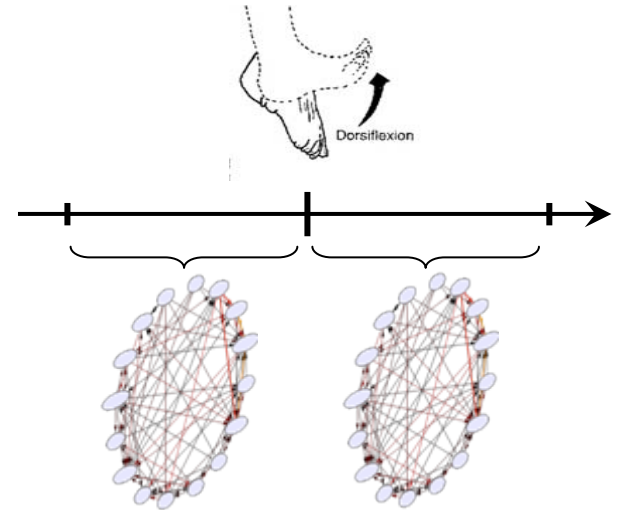
These processes are known to decrease the synchronicity of the Alpha oscillations of the EEG signals



The level of segregation in the brain network can be a predictive index for the successful memory encoding processes

Cortical Dynamics During Foot Movements

- Conventional connectivity methods (Correlation, Coherence, MVAR,...) only give a steady functional network for a certain time interval
- Typically they can give a connectivity pattern every 1-2 consecutive seconds
- However, many cerebral dynamics can occur at a time scale of milliseconds and so particular transient relationships can remain hidden
- Recently, some adaptive methods have been proposed to capture the transient pathways of information (Hesse et al., 2003) giving a functional network in every time sample



Cortical Dynamics During Foot Movements

Subjects

- 5 Healthy subjects



Task

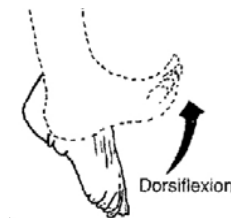
- Foot Movement

Leg EMG triggered
the foot movement



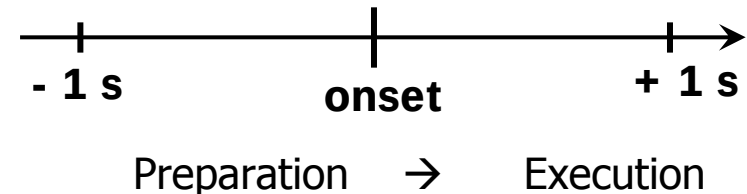
61 EEG channels
cap

200 self-paced trials
every 8 seconds

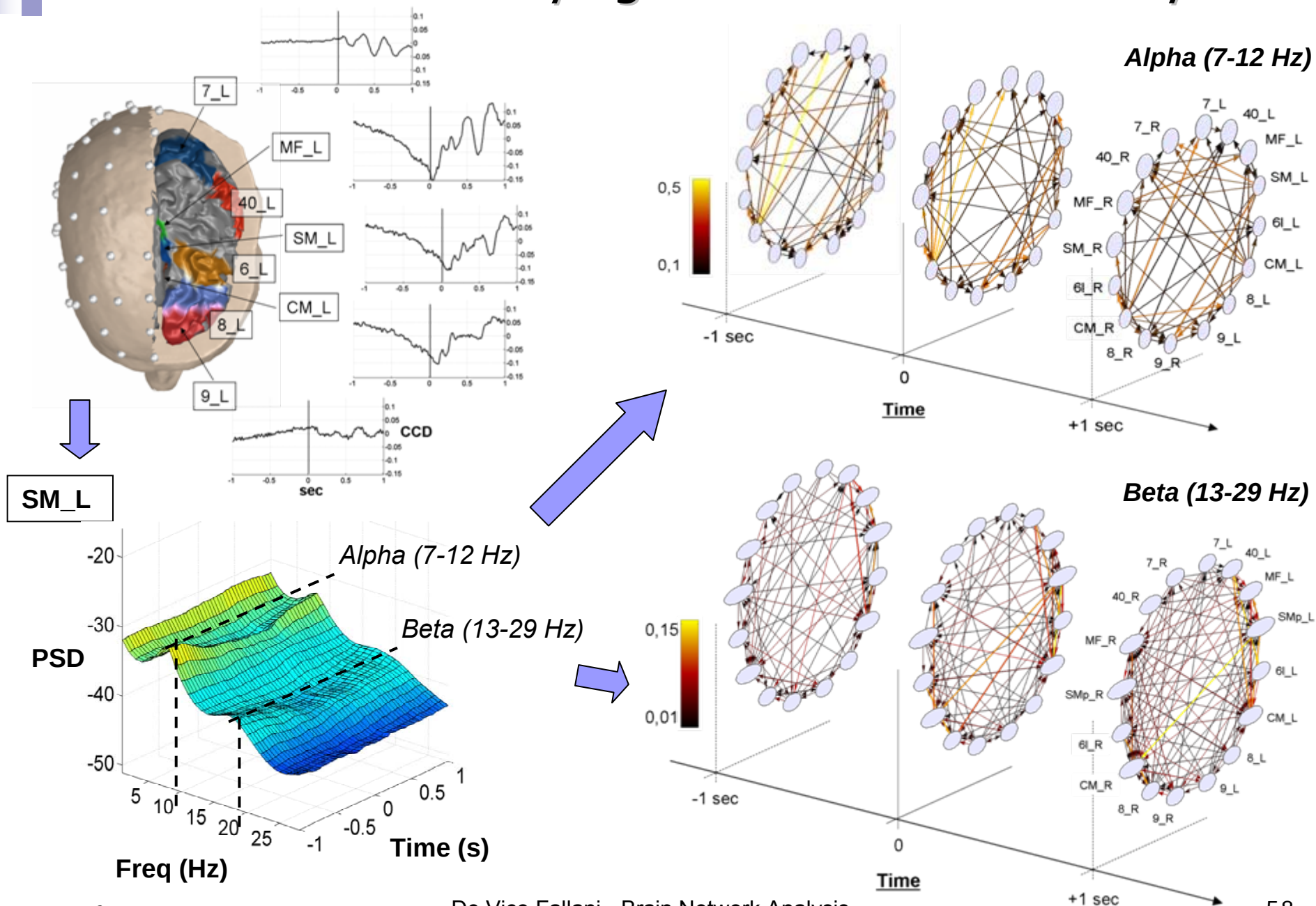


Period of Interest

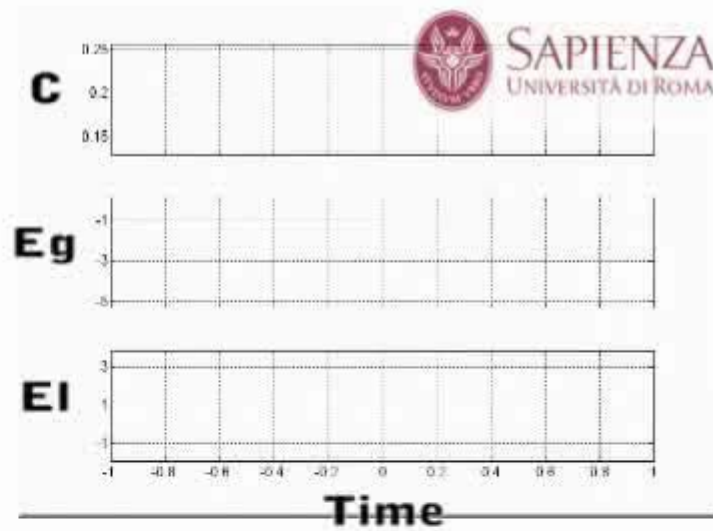
- Preparation and Execution



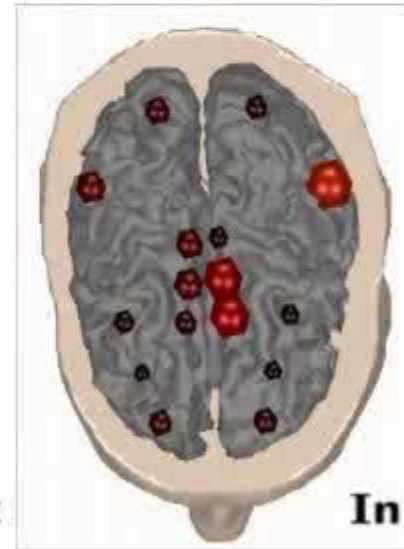
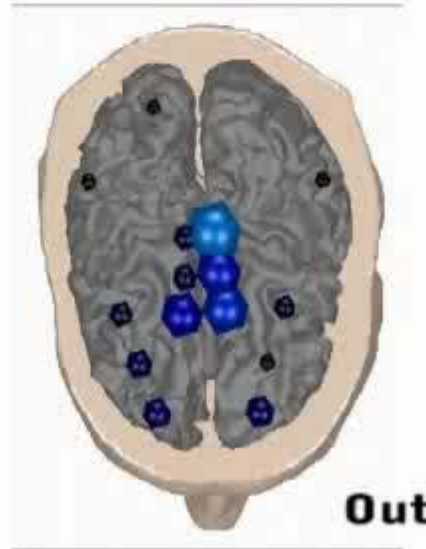
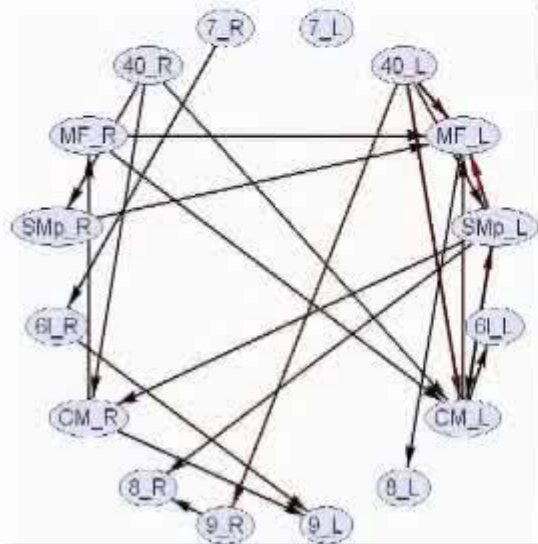
Results – Time-Varying Functional Connectivity



Results – Time-Varying Network Architecture



Cortical network



Degree

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