Master Mathématiques Vision Apprentissage

Functional neuroimaging & Brain-Computer Interfaces

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Outline

- Magnetoencephalography and electroencephalography (M.-C. Corsi) – 18/01 → 08/02

  - **M/EEG data: where it all begins!** - 18/01 – 9:30-12:30AM
  - **Estimating the sources of M/EEG activity** – w/ Théo Papadopoulo (Inria, Sophia-Antipolis) - 25/01 – 9:30-12:30AM
  - **How to further explore M/EEG data to answer scientific questions?** – 01/02 – 9:30-12:30AM
  - **How to use real-time M/EEG data for clinical purpose?** – 08/02 – 9:30-12:30AM **@ Paris Brain Institute!** (+visit of the neuroimaging platform)

Exam

- Format: Practical work in python & open questions
- Estimated time to complete it: 2 hours
- Probably sent after the third lesson (Feb 1st)
- Deadline: **February 22nd** to avoid overlapping with the exam associated to fMRI & the internship

Information & contacts

- Webpage dedicated to the module (updated w/slides): https://project.inria.fr/mvabrainfunctionalimaging/

- For any question related to the module
  - mva-meeg@inria.fr (mailing-list gathering the registered students and the co-lead)

- Co-lead contact info for specific questions
  - fMRI – Bertrand Thirion (Saclay) – bertrand.thirion@inria.fr
  - M/EEG – Marie-Constance Corsi (Paris) – marie-constance.corsi@inria.fr

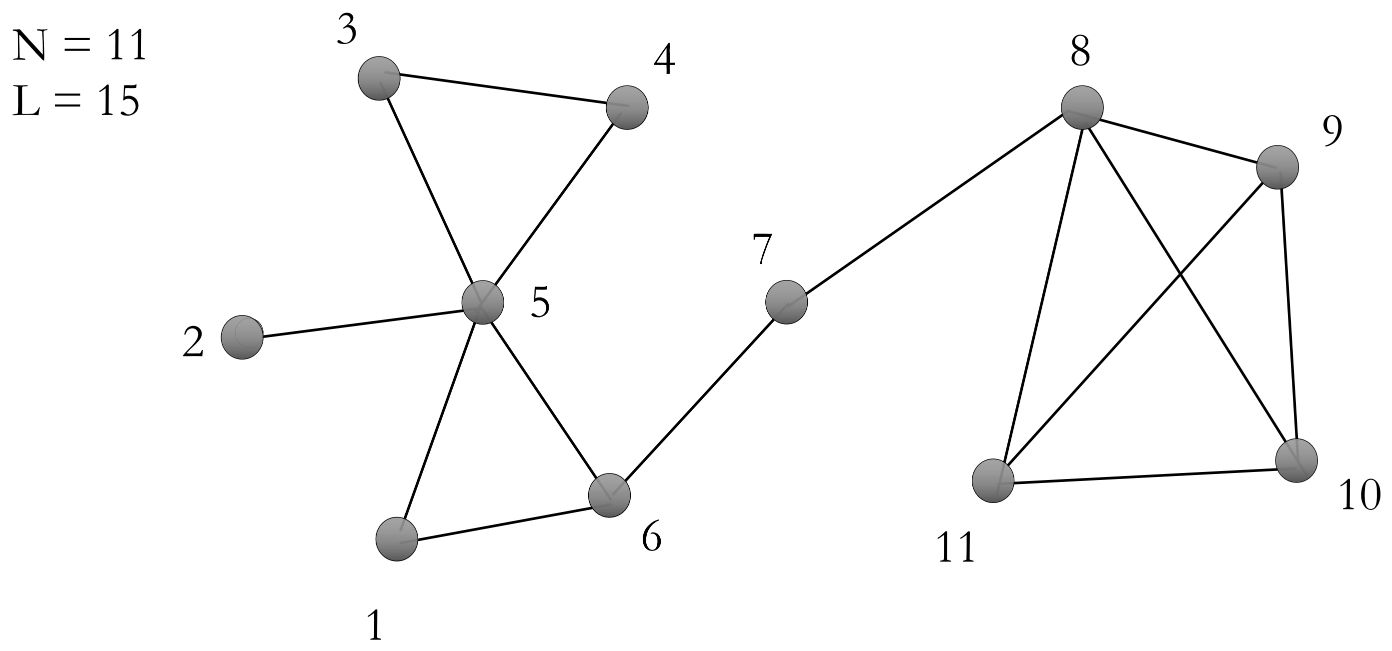
LESSON 3 – ADVANCED M/EEG DATA ANALYSIS

Outline

- The interconnected nature of brain functioning – brain network
    - What is it?
    - How to obtain it?
    - How to use them in the research?

What is a network?

- A Network is a set of elements with connections between them



A network (graph) G = (N, L) consists of a set of $N = \{n_1, \ldots\, n_N\}$ nodes and a set of $L = \{l_1, \ldots l_M\}$ links

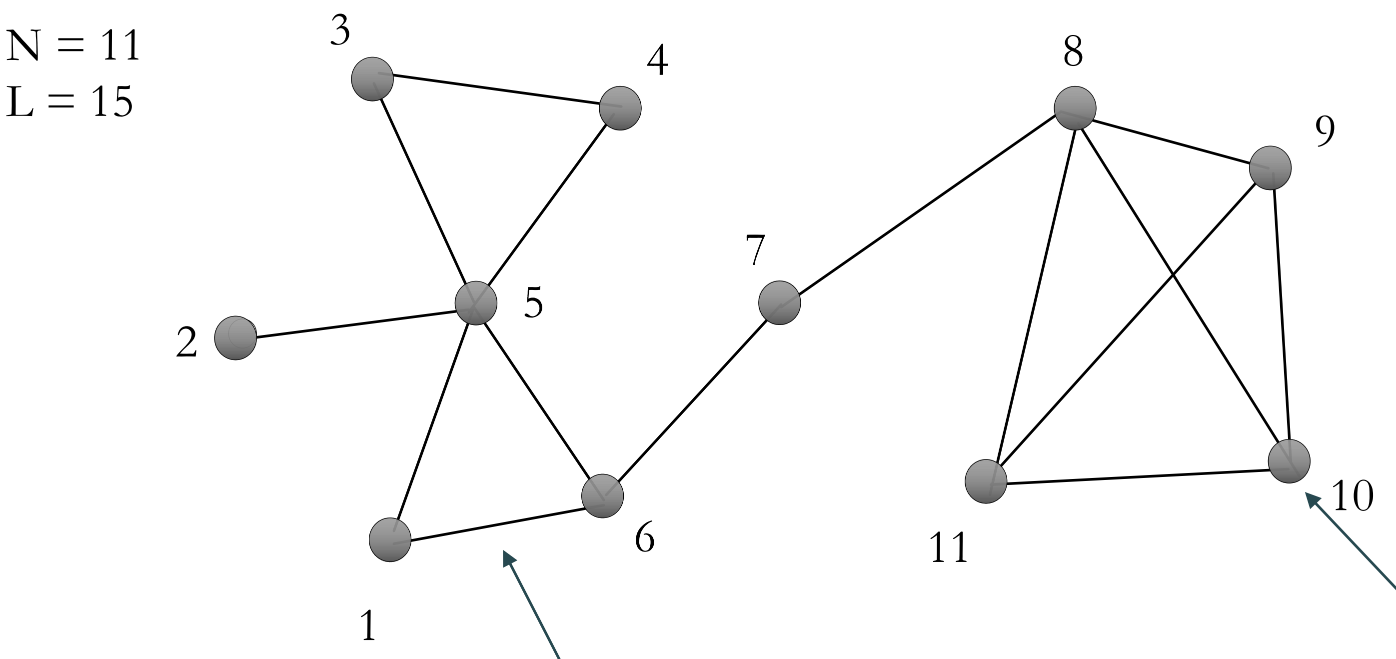
BRAIN NETWORKS - HOW TO GET THEM?

FROM FUNCTIONAL NEUROIMAGING DATA TO BRAIN NETWORKS

Questions addressed in this section

- How to estimate the interactions between ROIs/channels?
- How to choose the most suited estimator? Why?
- What are the pros/cons when dealing with the estimators

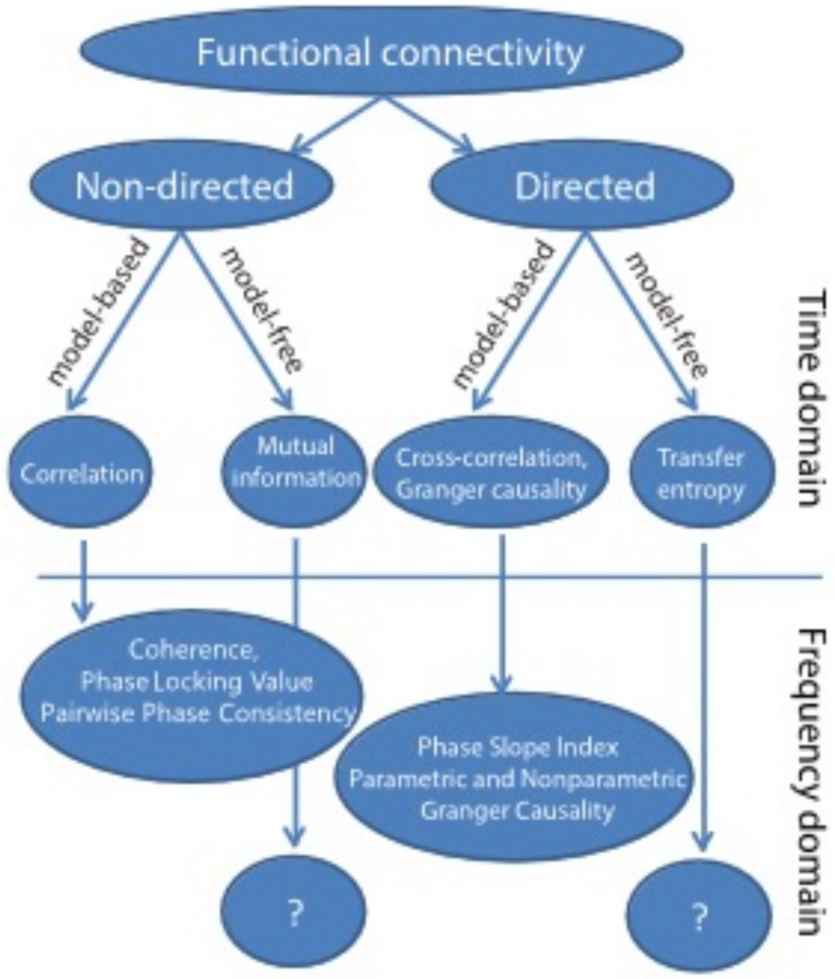
What are the nodes/edges?



Region of interest (ROI) or E/MEG sensor

Edges inferred using statistical approaches from E/MEG signals: **Functional connectivity (FC)** – plethora of estimators

What FC estimators?



Adapted from (Bastos & Schoffelen, Frontiers in Systems Neuroscience, 2016)

Measure of synchronization -> Mostly in frequency domain

What FC estimators? – Measures of synchronization – coherence coefficient

- The coherence coefficient
  - Amount of variance in one of the signals that can be explained by the other signal (or vice-versa)
  - Normalized quantity bounded by 0 and 1
  - Computation

$$coh_{xy}(\omega) = \frac{\left|\frac{1}{n}\sum_{k=1}^{n} A_x(\omega,k)A_y(\omega,k)\, e^{i(\varphi_x(\omega,k)-\varphi_y(\omega,k))}\right|}{\sqrt{\left(\frac{1}{n}\sum_{k=1}^{n} A_x^2(\omega,k)\right)\left(\frac{1}{n}\sum_{k=1}^{n} A_y^2(\omega,k)\right)}}$$

Length of the vector average of the individual trial cross-spectral densities between signal x and y at frequency ω

Square root of the product of the average of the individual trial power estimates of signals x and y at frequency ω

What FC estimators? – Measures of synchronization – coherence coefficient

- The coherence coefficient – frequency equivalent to the time domain cross-correlation function
  - Amount of variance in one of the signals that can be explained by the other signal (or vice-versa)
  - Normalized quantity bounded by 0 and 1
  - Computation

$$S(\omega) = \begin{pmatrix} S_{xx}(\omega) & S_{xy}(\omega) \\ S_{yx}(\omega) & S_{yy}(\omega) \end{pmatrix}$$

Averaged cross-spectral density terms

Power estimates of signals x and y

$$coh_{xy}(\omega) = \frac{\left|S_{xy}(\omega)\right|}{\sqrt{S_{xx}(\omega)S_{yy}(\omega)}}$$

Without | | → coherency

What FC estimators? – Measures of synchronization – a guided tour

- Phase Slope Index, PSI

- Imaginary Part of coherency

- Phase Locking Value

- Other measures to quantify Consistent Phase Differences
  - PLI & derivates
  - PPC
  - PLM

What FC estimators? – Measures of synchronization – a guided tour – PSI

- **Phase Slope Index, PSI**
  - **What?**
    - Phase difference spectrum: assumes time-lagged and linear interactions
    - A more generic quantity to infer dominant unidirectional interactions (Nolte et al, 2008)
  - **How?**
    - Computed from the complex-valued coherency
    - Given a pre-specific frequency bandwidth parameter, computes for each frequency bin the change in the phase difference between neighboring frequency bins, weighted with the coherence
  - **Interpretation?**
    - The sign of the PSI informs about which signal is temporally leading the other one.
  - **Caution**
    - Under situations where interactions are bi-directional, the phase difference spectrum may fail at correctly describing the directionality

- **Imaginary Part of coherency**
  - **What for?**
    - Removing instantaneous interactions that are potentially spurious due to the field spread (cf later)
  - **How?**
    - Projection of the complex-valued coherency onto the imaginary axis (ie y-axis) (Nolte et al, 2004)

- **Phase Locking Value, PLV**
  - **What?**
    - Application of the formula of the computation coherence to amplitude normalized Fourier transformed signals (Lachaux et al, 1999)
  - **How?**

$$PLV_{xy}(\omega) = \frac{\left|\frac{1}{n}\sum_{k=1}^{n} 1_x(\omega,k) 1_y(\omega,k)\ e^{i(\varphi_x(\omega,k)-\varphi_y(\omega,k))}\right|}{\sqrt{\left(\frac{1}{n}\sum_{k=1}^{n} 1_x^2(\omega,k)\right)\left(\frac{1}{n}\sum_{k=1}^{n} 1_y^2(\omega,k)\right)}} = \left|\frac{1}{n}\sum_{k=1}^{N} e^{i(\varphi_x(\omega,k)-\varphi_y(\omega,k))}\right|$$

  - **Interpretation?**
    - Reflects more strictly phase synchronization than coherence because coherence confounds the consistency of phase difference with amplitude correlation

What FC estimators? – Measures of synchronization – a guided tour – others

- **Other measures to quantify consistent Phase Differences**
  - **PLI & derivates** (Stam et al, 2007)
    - **What/How?** evaluates the distribution of phase differences across observations;(averaging the sign)
    - **Why?** Non-zero phase differences cannot be caused by field spread
    - Derivatives more robust against field spread, noise and sample-size bias
  - **PPC - pairwise phase consistency** (Vinck et al, 2010)
    - **What/How?** Quantifies the distribution of phase differences across observation – computed from the distribution of all pairwise differences of the relative phases
    - **Why?** Not biased by the sample size (ie not changing depending on the trial number)
  - PLM – phase linearity measurement (Baselice et al, 2019)

What FC estimators? – Directed FC, a toy example with Granger causality

- **Time domain formulation**
  - Granger causality, result of a model comparison
  - Rooted in the autoregressive (AR) modelling framework
  - Quality of an AR-model quantified by the variance of the model's residuals
    - **1 model reflects a univariate AR-model**, where values of time series x are predicted as a weighted combination of past values of time series x
    - **1 model is a bivariate AR-model**, where the values of time series x are predicted not only based on past values of x, but also based on past values of another time series y

What FC estimators? – Directed FC, a toy example with Granger causality

- **Time domain formulation**
- **Frequency domain formulation**
  - Concept of GC used in the frequency domain (Geweke, 1982)
  - Requires the estimation of 2 quantities
    - The spectral transfer matrix, H(ω) – frequency dependent
    - The covariance of the AR-model's residuals, Σ

    $H(\omega)\Sigma H(\omega)^* = S(\omega)$, with S(ω) being the cross-spectral density matrix for signal pair x, y at frequency ω
  - Computation

$$GC_{x\to y}(\omega) = \ln\left(\frac{S_{yy}(\omega)}{S_{yy}(\omega) - \left(\Sigma_{xx} - \frac{\Sigma_{yx}^2}{\Sigma_{yy}}\right)\left|H_{yx}(\omega)\right|^2}\right)$$

What FC estimators? – Directed FC, a toy example with Granger causality

- Time domain formulation
- Frequency domain formulation

$$GC_{x\rightarrow y}(\omega) = \ln\left(\frac{S_{yy}(\omega)}{S_{yy}(\omega) - \left(\Sigma_{xx} - \frac{\Sigma_{yx}^2}{\Sigma_{yy}}\right)\left|H_{yx}(\omega)\right|^2}\right)$$

- Relationship between frequency domain Granger causality and Coherence

$$GC_{x,y}(\omega) = -\ln\left(1 - \frac{\left|S_{xy}(\omega)\right|^2}{S_{xx}(\omega)S_{yy}(\omega)}\right)$$

$$coh_{xy}(\omega) = \frac{\left|S_{xy}(\omega)\right|}{\sqrt{S_{xx}(\omega)S_{yy}(\omega)}}$$

$$GC_{x,y}(\omega) = GC_{x\rightarrow y}(\omega) + GC_{y\rightarrow x}(\omega) + GC_{x.y}(\omega)$$

Instantaneous causality

What FC estimators? – Directed FC, a toy example with Granger causality

- **Time domain formulation**
- **Frequency domain formulation**
- **Relationship between frequency domain Granger causality and Coherence**
- **Non-parametric vs parametric computation for Granger causality**
  - Parametric computation: with AR models

    ✓ cross-spectral density matrix for a given frequency

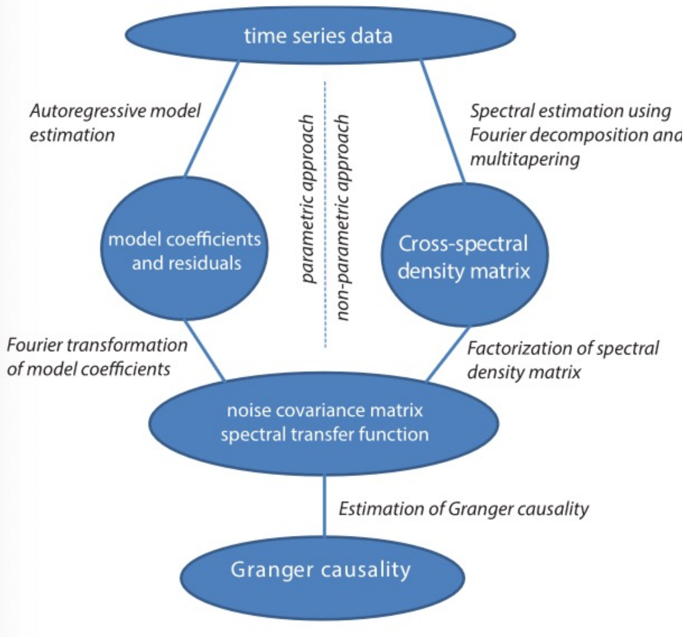
    ✗ particular choice of the appropriate model order can be problematic

    ✗ more sensitive for single-trial estimates – (Brovelli et al, 2012)

  - Non-parametric computation: with Fourier or wavelet-based methods

    ✓ does not require the determination of the model order for the AR

    ✗ requires more data & a smooth shape of the cross-spectral density to converge to a stable result



Adapted from (Bastos & Schoffelen, Frontiers in Systems Neuroscience, 2016)

FC estimators – critical aspects to be considered – spurious connectivity

- **Theory**: use of FC methods to quantify *true* signal interactions between different brain areas

- **Reality**: some conditions may affect the correct estimation and introduce spurious contributions

- **Why?**
  - Because of the volume conduction effect
  - Third-party influences when multiple signals are available

- **How to circumvent it?**
  - Volume conduction
    - Working in the source domain (cf previous lesson)
    - Using FC estimators that remove lag-zero contributions from the estimates
  - Third-party influences
    - Isolating the contribution & remove it from the estimate
    - Using specific estimators

FC estimators – critical aspects to be considered – non-linear interactions

- **What?**
  - Brain functioning – quite controversial
  - Statistical interdependence between different brain signals

  ⇒ The use of linear FC can fail to provide a complete description of the temporal properties of the signal interactions

- **Reality** – most of the studies rely on the linear-based FC for simplicity and intuitive interpretation
  - Coherence and its related estimators (partial coherence, imaginary coherence….)

- **How?**
  - Undirected FC: mutual information, phase-locking value, synchronization likelihood
  - Directed FC: transfer entropy, kernel Granger-causality…

FC estimators – critical aspects to be considered – time-varying dynamics

- **What?**
  - FC typically applied to extract connectivity patterns characterizing relatively long time periods
  - Recent interest in shorter time scales studied with dynamical FC – dFC
- **Why?**
  - To determine how FC fluctuates during specific tasks – cf BCI applications
- **How?**
  - Simplest approach: reducing the length of the time window
  - Standard method:
    - Concatenating the temporal windows associated with multiple repetitions of the same experimental task
    - Averaging the FC estimators over the repetitions
  - Other methods
    - Multi-window spectrum estimation
    - Designed to deal with non-stationary signals
    - …

Functional connectivity estimators – a tour at a glance

	Functional connectivity estimators	Properties		
		Non-linearity	*Time-varying*	*Multivariate*
Undirected	Spectral coherence [42]	-	-	-
	Imaginary coherence [34]	-	-	-
	Phase-Locking Value [43]	✓	-	-
	Weighted phase lag index [44]	✓	-	-
	Partial coherence [39]	-	-	✓
	Synchronization likelihood [45]	✓	-	-
	Mutual information [46]	✓	-	-
	Wavelet coherence [47]	✓	✓	
Directed	Granger causality [48]	-	-	-
	Kernel Granger causality [49]	✓	-	-
	Partial Granger causality [50]	-	-	✓
	Partial directed coherence [41]	-	-	✓
	Transfer Entropy [46]	✓	-	✓
	Directed Transfer Function [51]	✓	-	✓
	Adaptive partial directed coherence [52]	-	✓	✓

Adapted from (Gonzalez-Astudillo et al, JNE, 2021)

From functional connectivity to networks - Thresholding

- **What?**
  - Obtaining sparse networks with a relatively low connection density

- **Why?**
  - To mitigate the uncertainty of the estimated weakest edges
  - To reduce the false positives
  - To facilitate the interpretation of the inferred network topology

- **How?**
  - Simplest way: fix a threshold on the number of stronger links

  - Theoretically-grounded non-parametric methods, based on different criteria:
    - Statistical contrasts with data surrogates
    - Topological optimization
    - Population-based consensus

BRAIN NETWORKS

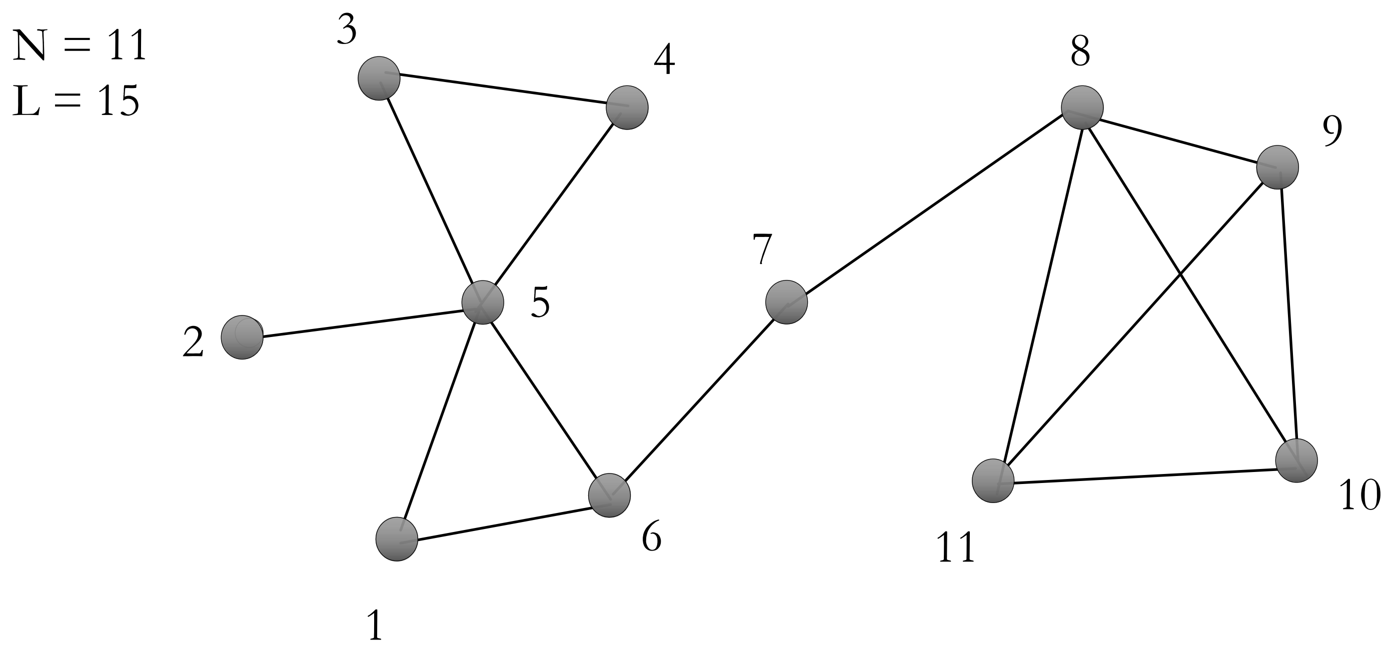
HOW TO CHARACTERIZE THEM?

Questions addressed in this section

- What is a network?
- How to classify/define it?
- How to characterize it?

What is a network?

- A Network is a set of elements with connections between them



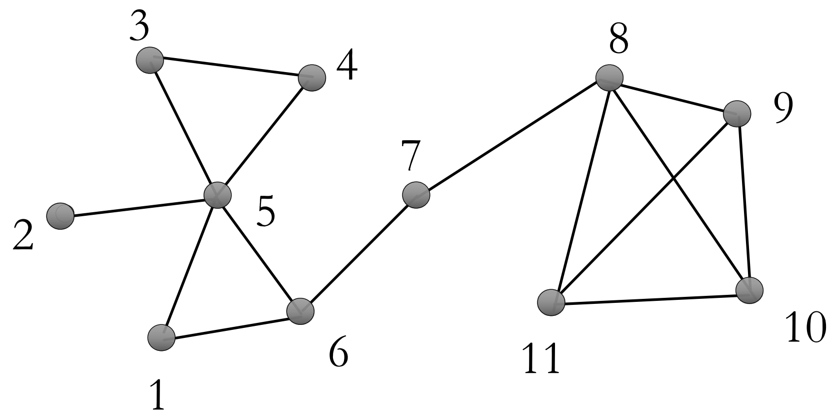
A network (graph) $G = (N, L)$ consists of a set of $N = \{n_1, \ldots n_N\}$ nodes and a set of $L = \{l_1, \ldots l_M\}$ links

Types of networks

- Different classifications of networks, according to the:
  - direction of the links
  - kind of interaction: weighted or unweighted
  - differences between nodes: bipartite or not
  - evolution of their topology: static or evolving
  - dynamics of the nodes: with/without dynamics
  - …

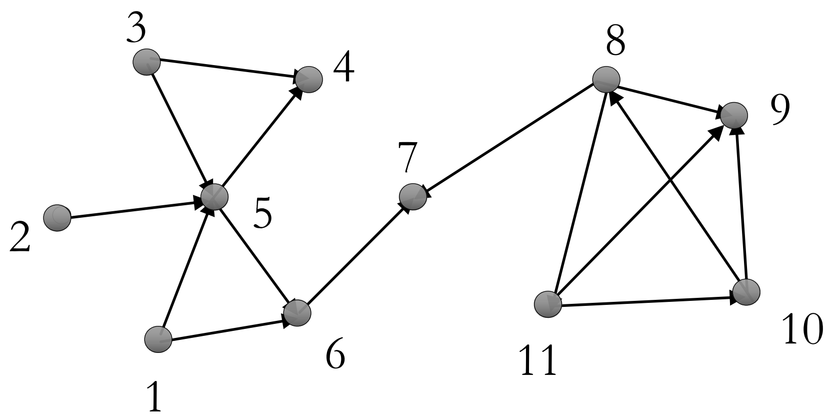
Types of networks – Directed and undirected networks

Undirected network



Router network, power grids, etc…

Directed network

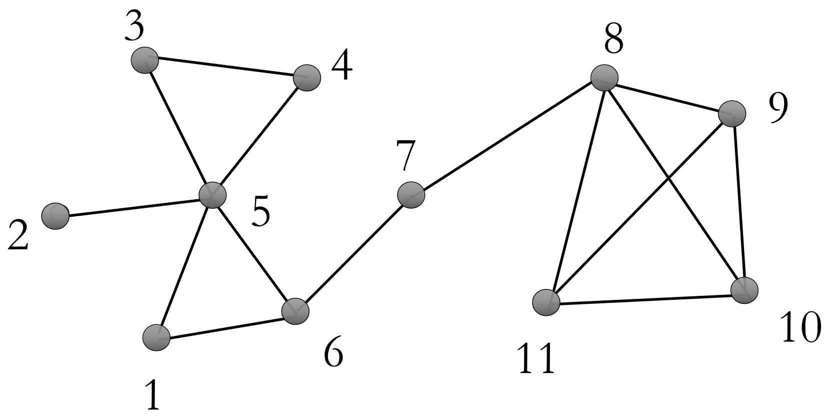


Telephone networks, etc…

=> The direction of the links is crucial in dynamical processes occurring in the network

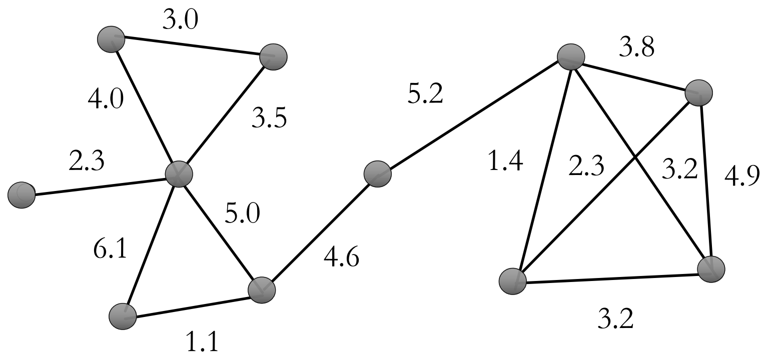
Types of networks – Weighted and unweighted networks

Unweighted network



Citation network, Internet, etc…

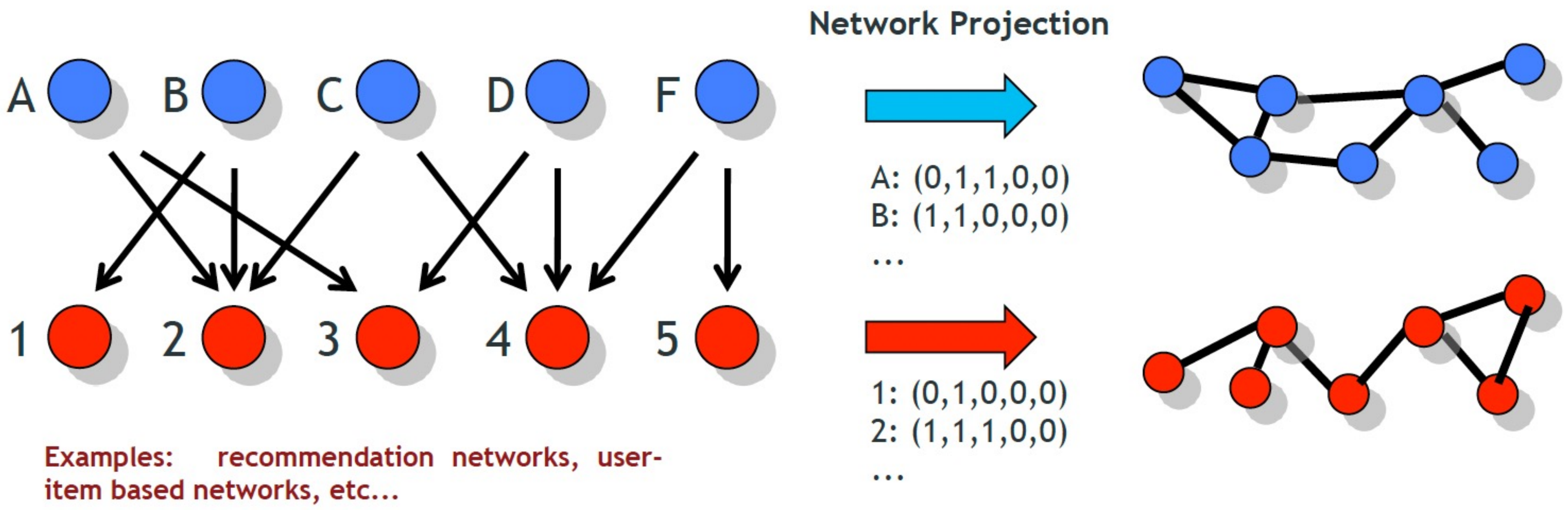
Weighted network



Email networks, collaboration networks, etc…

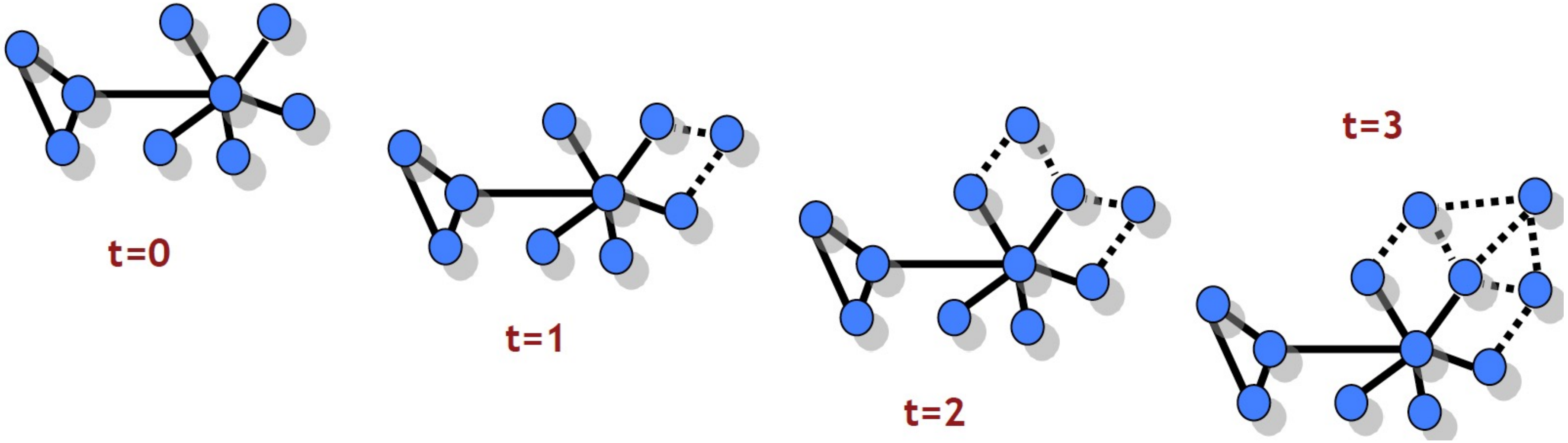
=> The weight of the links is crucial in dynamical processes occurring in the network

Types of networks – Bipartite networks



Adapted from (Buldu, 2013)

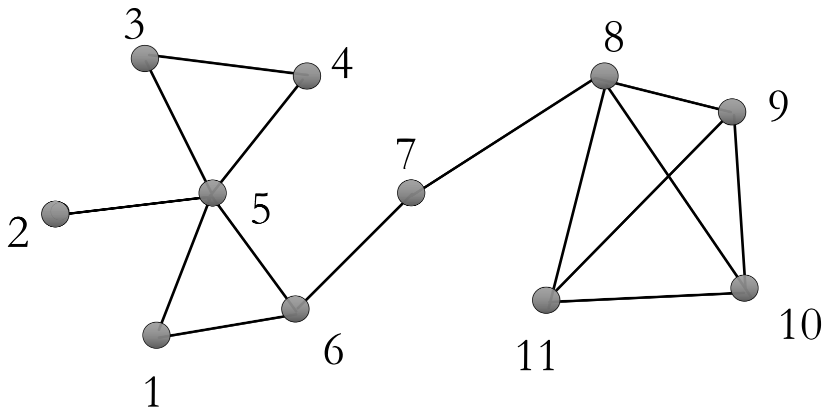
Types of networks – Static or evolving networks



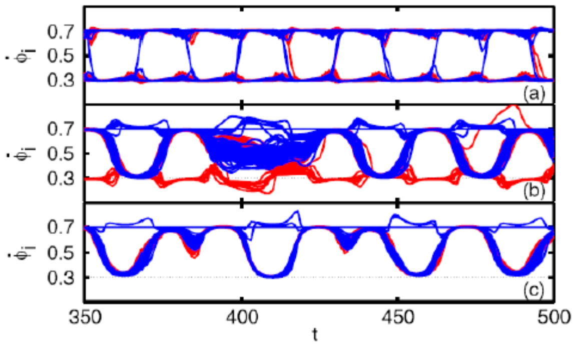
Adapted from (Buldu, 2013)

- Two important questions are addressed when working with evolving networks
  - What are the rules governing the evolution?
  - What consequences have the rules on the final topology?

Types of networks – Networks of dynamical systems



$$\dot{\phi}_i = \begin{cases} \omega_i + \frac{d}{(k_i+k_{p_i})} \sum_{j=1}^{N} a_{ij} \sin(\phi_j - \phi_i) \\ + \frac{d_p k_{p_i}}{(k_i+k_{p_i})} \sin(\phi_{p_i} - \phi_i), \end{cases}$$



Adapted from (Buldu, 2013)

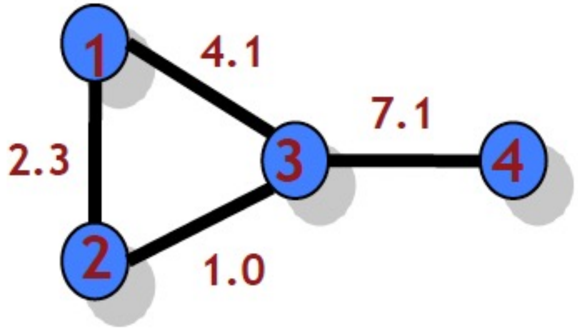
- Influence of the topology in the dynamical processes occurring in the network and vice-versa

Key-concepts when working with networks

- Matrices
- Paths
- Local-scale properties
- Meso-scale properties
- Global-scale properties

Key-concepts w/ networks – Adjacency, Weights & Laplacian matrices

Given a set of N nodes with M connections between them:



Weights Matrix (W):

Entries of the matrix are the weights w_{ij} ($i,j=1, \ldots, N$) of the connections

$$\begin{pmatrix} 0.0 & 2.3 & 4.1 & 0.0 \\ 2.3 & 0.0 & 1.0 & 0.0 \\ 4.1 & 1.0 & 0.0 & 7.1 \\ 0.0 & 0.0 & 7.1 & 0.0 \end{pmatrix}$$

Adjacency Matrix (A):

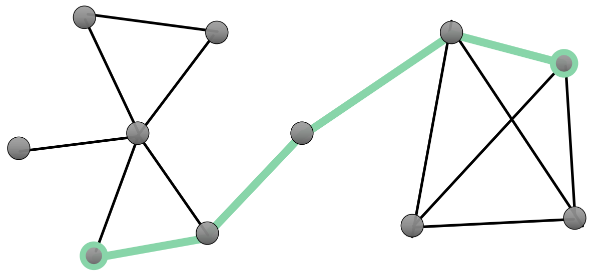
$a_{ij}=1$ if there exists a link between i and j, and $a_{ij}=0$ otherwise

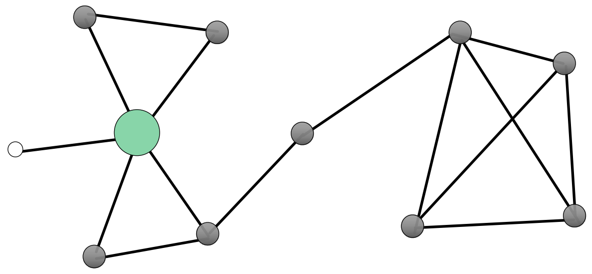
$$\begin{pmatrix} 0 & 1 & 1 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 \end{pmatrix}$$

Adapted from (Buldu, 2013)

- **Shortest path (d_{ij})**

The shortest path d_{ij} between nodes I and j corresponds to the minimal distance (or weight) between all paths that connect i and j





- **Degree or strength**

$$\sum_{j=1, j\neq i}^{N} A_{ij}$$

Objective: identify the most connected nodes in the graph that hold a large part of the overall system's connectivity and therefore represent candidate hubs of the network.

- **Betweenness**

$$C_B(i) = \sum_{h=1, h\neq j}^{N} \sum_{j=1, j\neq i}^{N} \frac{\sigma_{hj}(i)}{\sigma_{hj}}$$

$\sigma_{hj}(\mathrm{i})$ – number of shortest paths between nodes h and j that pass through I

σ_{hj} – number of shortest paths between nodes h and j

Objective: identify nodes which are crucial for the information transfer between topologically distant brain regions

- **Communicability**

$$C_c(i) = \sum_{j=1}^{N} [e^{A}]_{ij}$$

Objective/interpretation: network's capacity for parallel information transfer. Can be particularly suitable for identifying brain areas that are central for the diffusion of information across the network

- **Eigenvector**

$$C_E(i) = \frac{1}{\lambda} \sum_{j=1}^{N} A_{ij} v_j$$

Objective/interpretation: identify brain areas which do not necessarily have a high number of links but that are connected to other central regions

Key-concepts w/ networks – Meso-scale properties

- **Motifs**

Various paradigms for motif detection: counting, sampling, pattern growth methods. After calculating the frequency F (number of occurrences) of a subgraph G the assessment of its significance is given by:

$$Z(G) = \frac{G(G) - \mu(G)}{\sigma(G)}$$

Objective – motifs represent the basic building blocks of a network and may provide a deep insight into the brain network's functional abilities

- **Communities and modularity**.

How? Detection not trivial & plethora of algorithms

Quality of the identified partition can be measured by the so-called modularity index:

$$Q = \frac{1}{2L}\sum_{i=1}^{N}\sum_{j=1}^{N}(A_{ij} - R_{ij})\delta(m_i, m_j)$$

Rij – probability to observe an edge as expected by chance

When Q>0 the network tends to have intramodule connectivity and low intermodule connectivity

When Q <=0 the network lacks a modular structure.

Why? In brain networks, topological modules tend to be spatially localized, and they typically include cortical areas that are known to be specialized for visual, auditory, and motor functions

- **Core-periphery structure**
  - How?
  - Identifying the core of a network can be achieved through methods optimizing a fitness function or via statistical null models
  - Alternative method: separating the nodes in two groups based on the rank, ie node centrality (eg degree). The optimal separating rank position is given by:

$$r^* = argmax(k_r^+) - (k_r^+)$$

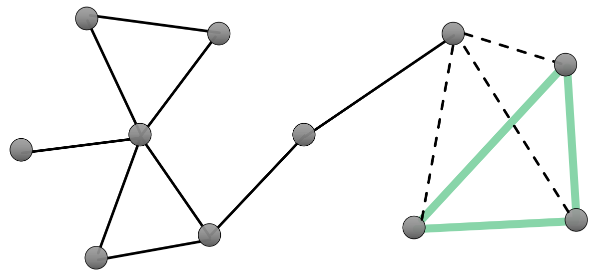
  - Why?
    - Core-periphery organization is thought to emerge as a cost-effective solution for the integration of distributed regions in the periphery

Key-concepts w/ networks – Global-scale properties

- **Characteristic path length & global-efficiency**
  - What?
    - A scalar that measures the global tendency of the nodes in the network to integrate and exchange information.
  - How?
    - Assuming that the information flows through the shortest paths, the characteristic path length is given by

$$P = \frac{1}{N(N-1)} \sum_{i=1, i\neq j}^{N} d_{ij}$$

$$E_{glob} = \frac{1}{N(N-1)} \sum_{i=1, i\neq j}^{N} \frac{1}{d_{i,j}}$$



- Objective/Interpretation
  - An average short distance between the nodes may constitute a biological mechanism to minimize the energetic cost associated with long-range connectivity, and could provide more efficient and less noisy information transfer

Key-concepts w/ networks – Global-scale properties

- **Clustering coefficient**
  - What? Clustering measures the extent to which nodes' neighbors are mutually interconnected.
  - How? Strongly related to the presence of triangles in the network, the clustering coefficient is a normalized scalar given by:

$$C = \frac{1}{N} \sum \frac{2l_i}{k_i(k_i - 1)}$$

- **Local-efficiency**
  - What? Overall tendency of a network to form a clustered group of nodes can be obtained in terms of network global-efficiency.
  - How? The so-called local-efficiency is given by averaging the global-efficiencies of the network's subgraphs:

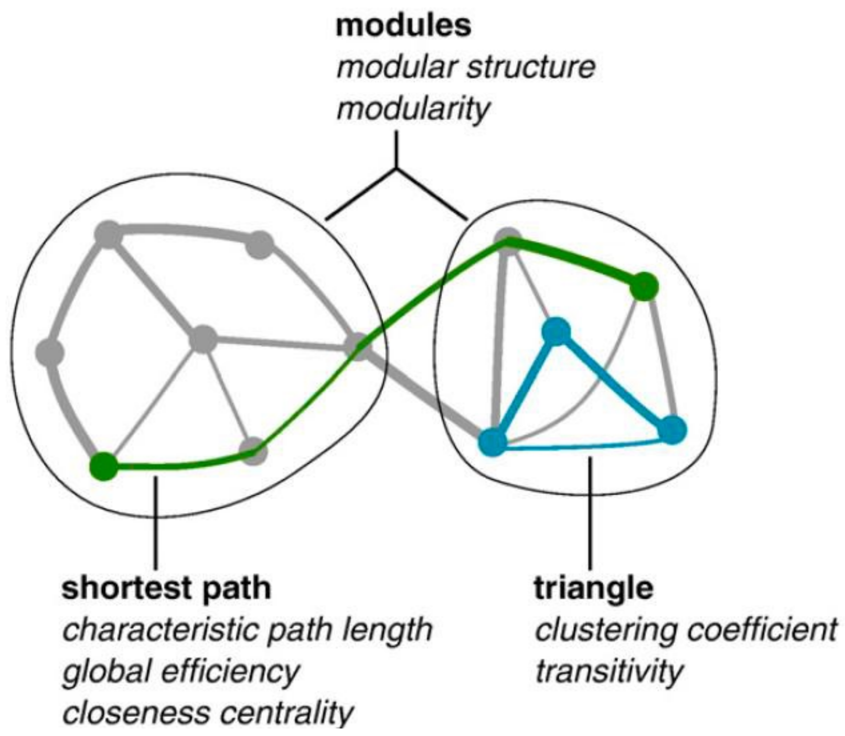
$$E_{loc} = \frac{1}{N} \sum_{i=1}^{N} E_{glob}(G_i)$$

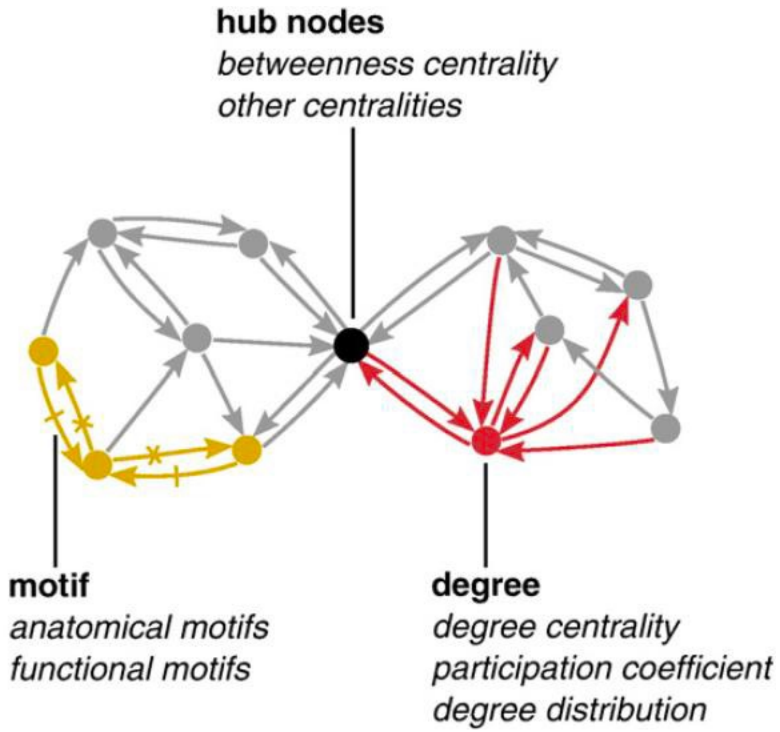
  - Objective/Interpretation: the clustering coefficient and local-efficiency are often interpreted as a measure of functional segregation or specialization

- **Computation of the small-world propensity**
  - How? By normalizing the values of the empirical network with those obtained from network surrogates, such as random graphs

$$\omega = \frac{C}{\mu(C_{rand})} \frac{\mu(P_{rand})}{P}$$

Key-concepts w/ networks – quick sum-up





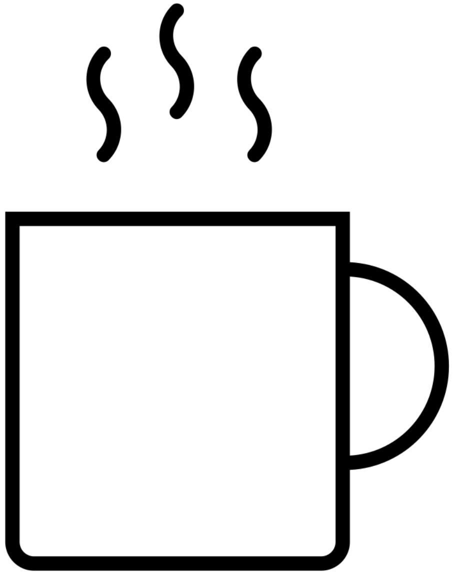
Key-concepts w/ networks – Computational complexity of network metrics

	Network metric	Computational complexity	
		Unweighted	Weighted
Local-scale	Degree	$O(L)$	$O(L)$
	Betweenness	$O(N(N+L))$	$O(N(L+N\log N))$
	Communicability	$O(N^3)$	$O(N^3)$
	Eigenvector	$O(N^2)$	$O(N^2)$
Meso-scale	Motifs	$O(Ng)$	-
	Communities	$O(N\log N)$	$O(N\log N)$
	Modularity	$O(L)$	$O(L)$
	Core-periphery	$O(L+N\log N)$	-
Global-scale	Characteristic path length	$O(N(N+L))$	$O(N(N+L))$
	Global-efficiency	$O(N(N+L))$	$O(N(N+L))$
	Clustering coefficient	$O(L\langle k^2\rangle/\langle k\rangle)$	$O(L\langle k^2\rangle/\langle k\rangle)$
	Local-efficiency	$O(N(\langle k^2\rangle-\langle k\rangle))$	$O(N(\langle k^2\rangle-\langle k\rangle))$

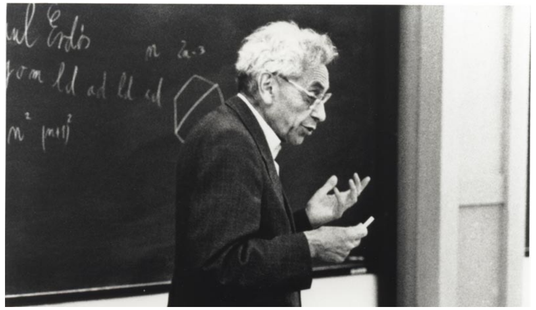
Table 2 - Computational complexity of network metrics. N = number of nodes; L = number of links; g = size of the motif; $\langle k\rangle$ = average node degree; $\langle k^2\rangle$ = node degree variance.

Adapted from (Gonzalez-Astudillo et al, JNE, 2021)

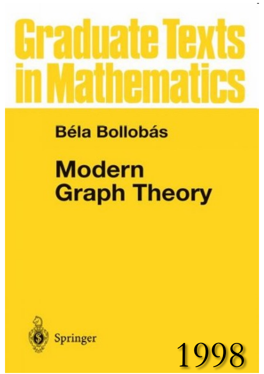
Time for a 15’-break!



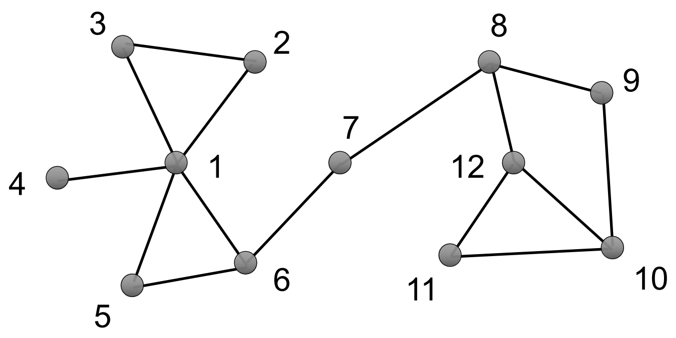
A network theoretic approach



Paul Erdos (1913-1996)

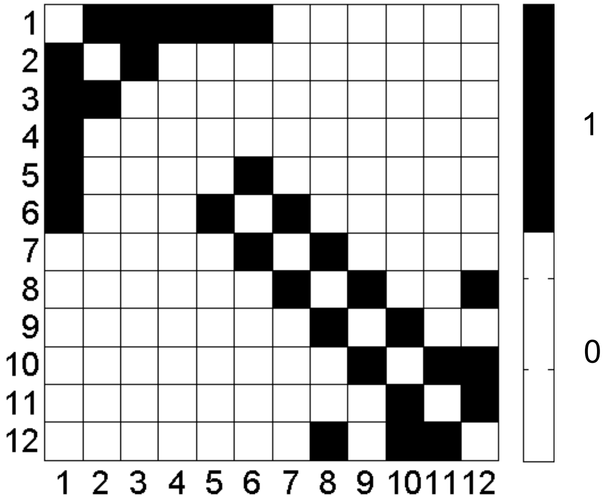


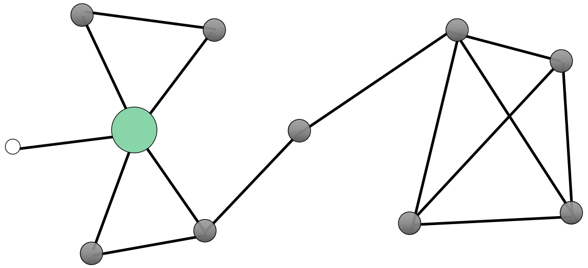
Graph G



N=12

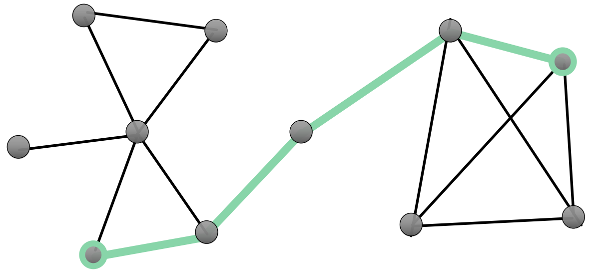
$$\mathbf{A} = \{a_{i,j}\} =$$





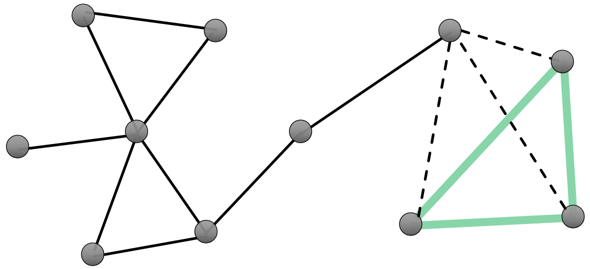
Node degree

$$k(i) = \sum_{j=1}^{N} a_{i,j}$$



Network efficiency

$$E_{glo} = \frac{1}{N(N-1)} \sum_{i,j=1}^{N} \frac{1}{d_{i,j}}$$

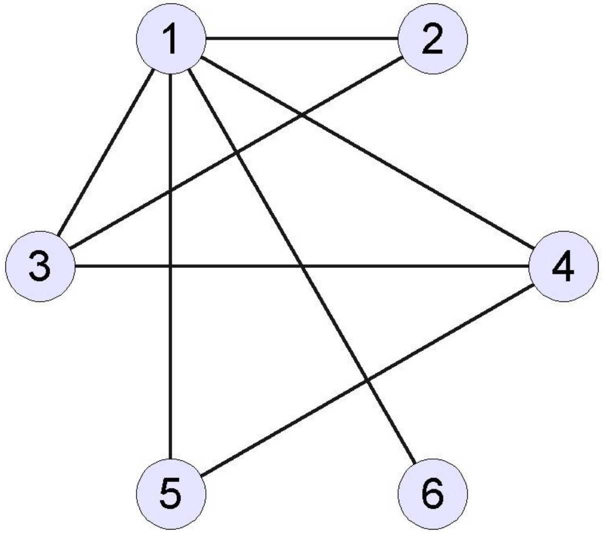


Network clustering

$$E_{loc} = \frac{1}{N} \sum_{i=1}^{N} E_{glob}(i)$$

(Newman, 2003 ; Boccaletti et al, 2006; Da Costa et al, 2011)

1. Draw the graph for the adjacency matrix A:



$$A = \begin{array}{cc} \begin{bmatrix} X & 1 & 1 & 1 & 1 & 1 \\ 1 & X & 1 & 0 & 0 & 0 \\ 1 & 1 & X & 1 & 0 & 0 \\ 1 & 0 & 1 & X & 1 & 0 \\ 1 & 0 & 0 & 1 & X & 0 \\ 1 & 0 & 0 & 0 & 0 & X \end{bmatrix} & \begin{matrix} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \end{matrix} \\ \begin{matrix} 1 & 2 & 3 & 4 & 5 & 6 \end{matrix} & \end{array}$$

2. Compute the degrees k of the nodes of the graph

k(1) = 1 + 1 + 1 + 1 + 1 = 5

k(2) = 1 + 1 = 2

k(3) = 1 + 1 + 1 = 3

k(4) = 1 + 1 + 1 = 3

k(5) = 1 + 1 = 2

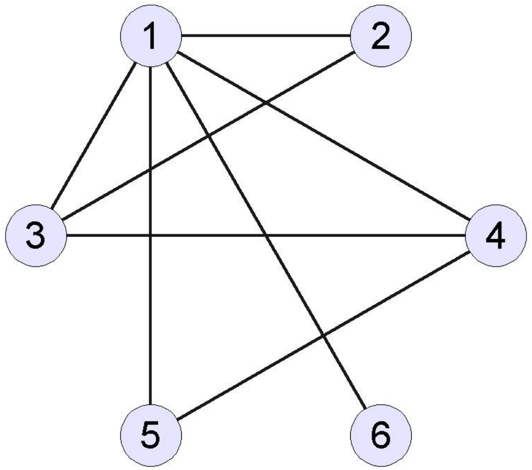
k(6) = 1

$$A = \begin{array}{cc} \left[\begin{array}{cccccc} X & 1 & 1 & 1 & 1 & 1 \\ 1 & X & 1 & 0 & 0 & 0 \\ 1 & 1 & X & 1 & 0 & 0 \\ 1 & 0 & 1 & X & 1 & 0 \\ 1 & 0 & 0 & 1 & X & 0 \\ 1 & 0 & 0 & 0 & 0 & X \end{array}\right] & \begin{array}{c} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \end{array} \\ \begin{array}{cccccc} 1 & 2 & 3 & 4 & 5 & 6 \end{array} & \end{array}$$

Social network properties – time for exercises

https://arxiv.org/ftp/arxiv/papers/2006/2006.13187.pdf
=> Autres métriques

3. Compute the global efficiency E_{glo} of the graph



N = 6

Distance matrix

D =

1	2	3	4	5	6	
X	1	1	1	1	1	1
-	X	1	2	2	2	2
-	-	X	1	2	2	3
-	-	-	X	1	2	4
-	-	-	-	X	2	5
-	-	-	-	-	X	6

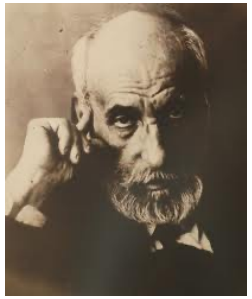
$$E_g = \frac{2}{N(N-1)} \sum_{i \neq j} \frac{1}{d(i,j)}$$

E_{glo} = ((1)*8 + (1/2)*7) * 2/(6*5) = (8 + 7/2) / 15 = (16+7) / (2*15) = 23/30

COMPLEX NETWORKS & THE BRAIN

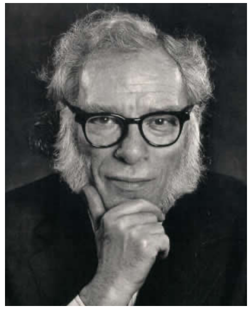
HOW TO USE THEM TO STUDY THE BRAIN?

Brain complexity lies in the network



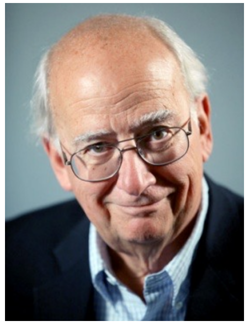
Santiago Ramon y Cajal (Nobel prize in Medicine)

> "As long as our brain is a mystery, the universe, the reflection of the structure of the brain will also be a **mystery**"



Isaac Asimov (from the forewood to *The Three-Pound Universe* by J. Hooper and D. Teresi, 1986)

> "The human brain, then, is the most **complicated** organization of matter that we know"



Danielle S. Bassett & Michael S. Gazzaniga (from *Understanding complexity in the human brain*, 2011)

> "The human mind is a **complex** phenomenon built on the physical scaffolding of the brain, which neuroscientific investigation continues to examine in great detail. However, the nature of the relationship between the mind and the brain is **far from understood**."

Brain complexity

Anatomy/structure

The human brain contains 100 billions (10^{11}) of neurons, 100 trillions (10^{15}) of synapses.
The whole membrane surface is 25.000 m^2, i.e. *the size of four soccer fields*

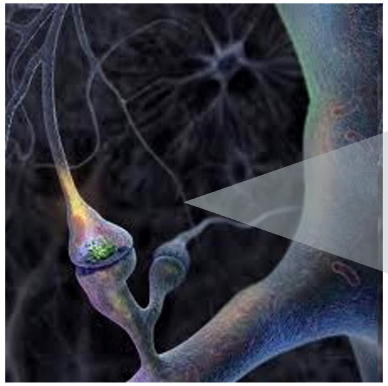
Function

Neurons present a continuous activity. They continually tell the body to keep functioning and do everything necessary to keep ourselves alive.
They never sleep, even when you are sleeping

Several time and spatial scales associated with brain functioning

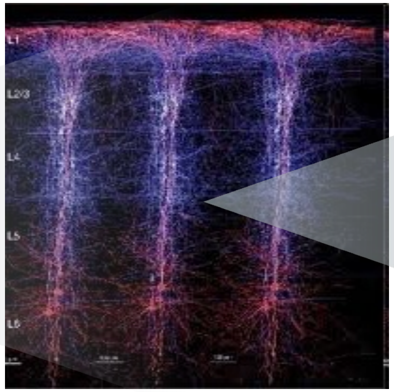
Spatial complexity

Neurons



Micro-scale
(nm, µm)

Columns



Meso-scale
(µm, mm)

Regions

Macro-scale
(mm, cm)

Time complexity

seconds minutes hours days months

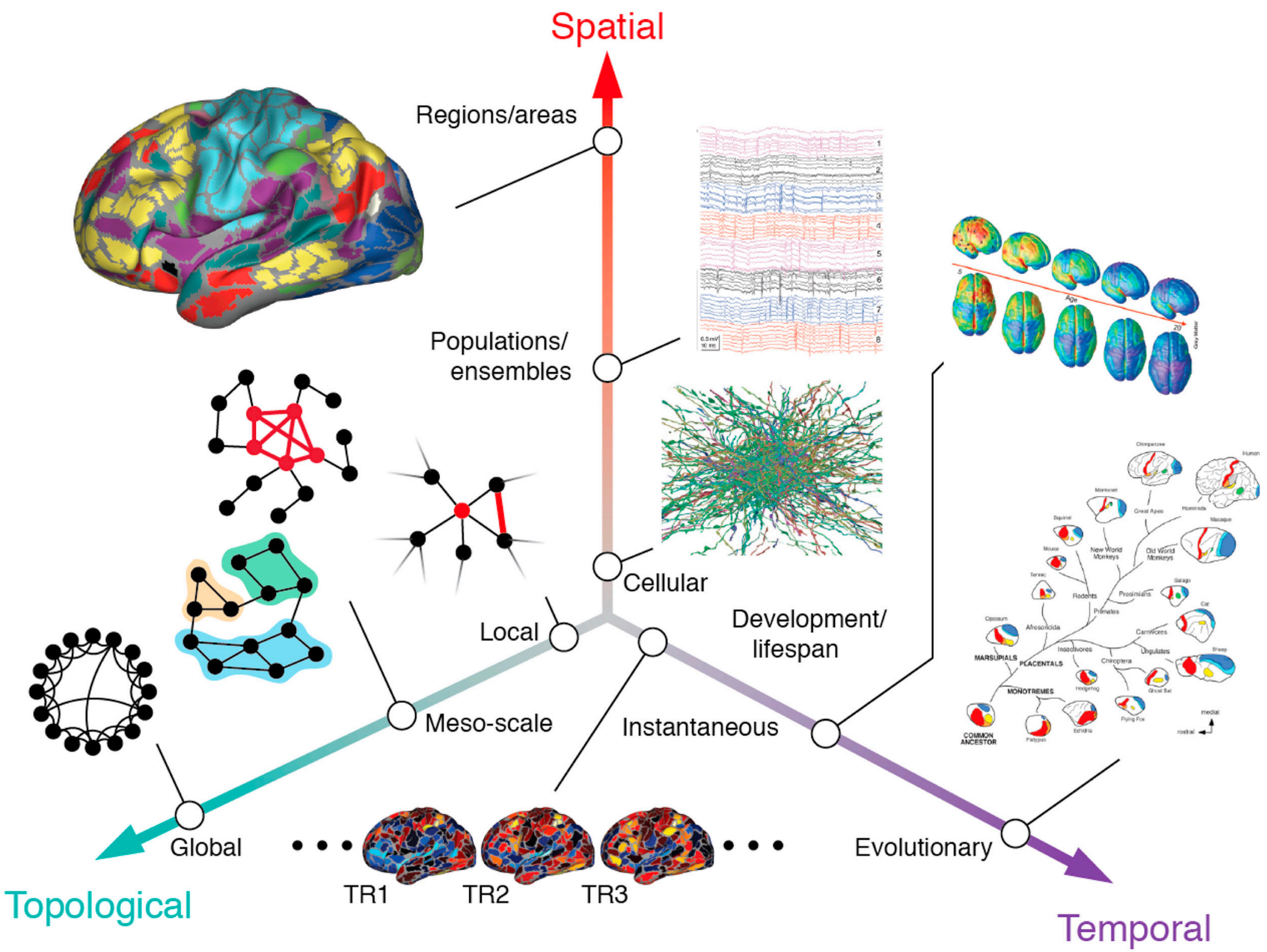
Short-term

eg, Learning / memory

Long-term

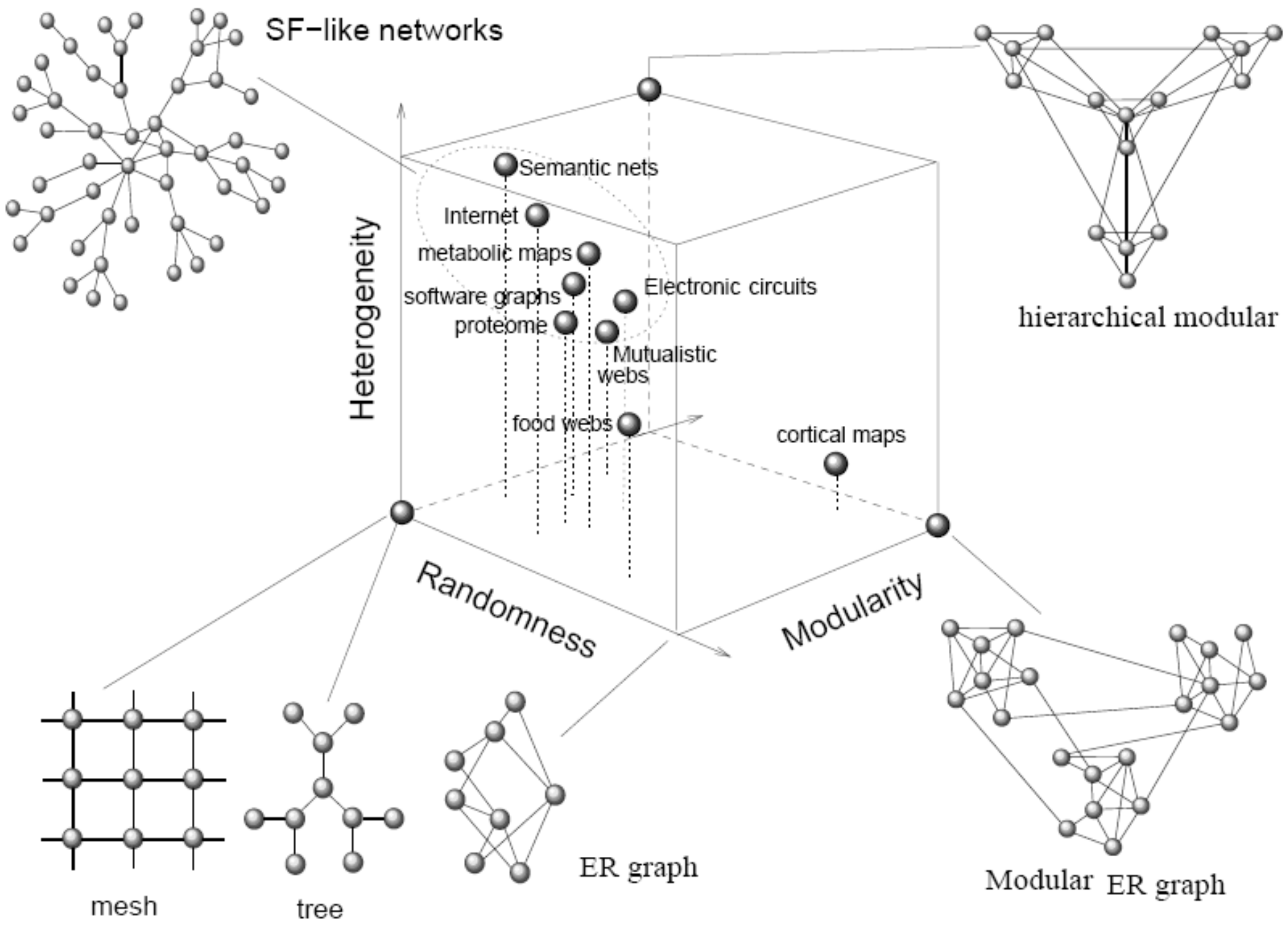
eg, Aging / recovery

Multi-scale brain networks



Adapted from (Betzel & Bassett, NeuroImage, 2017)

What is a complex network?

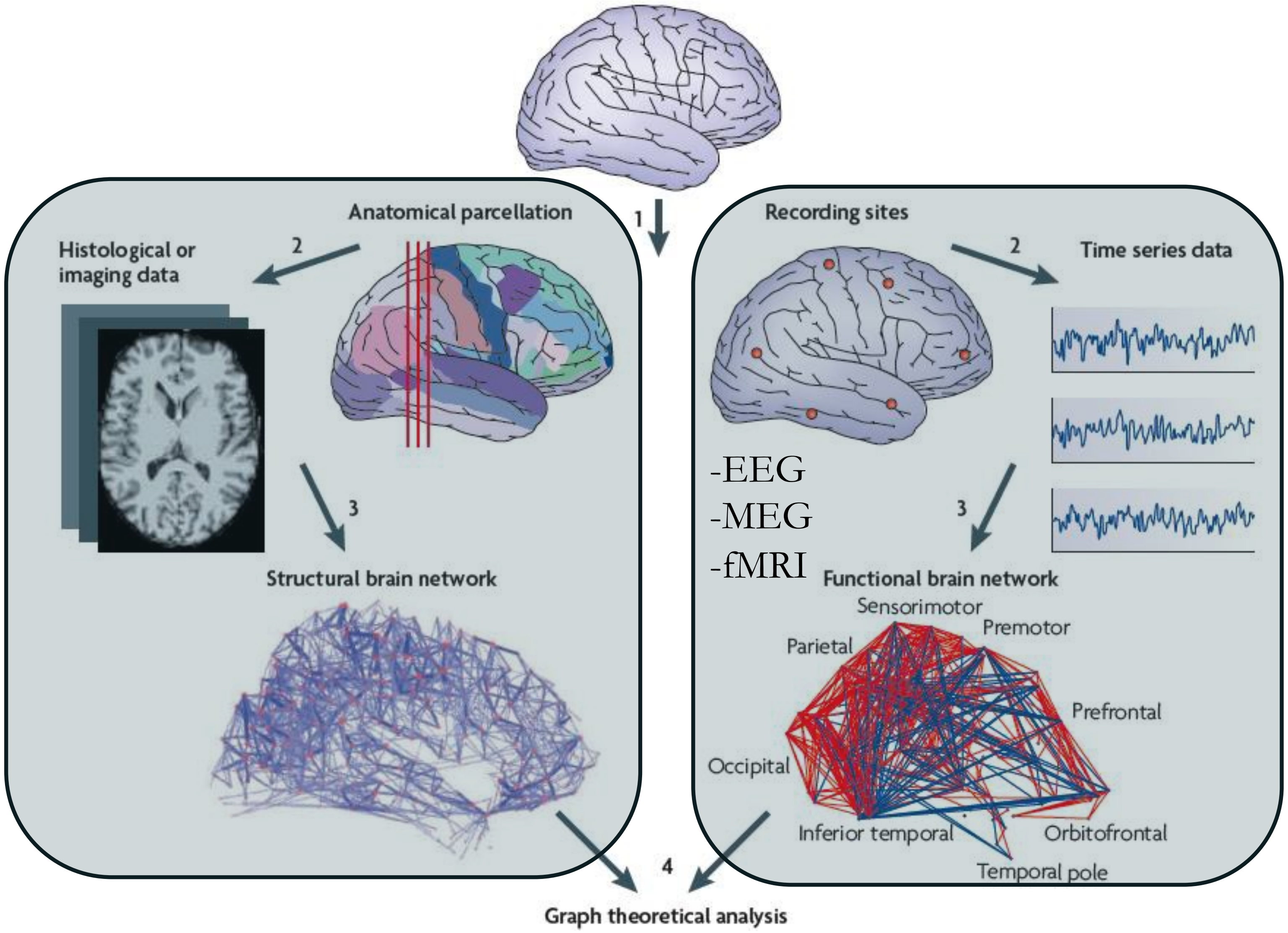


From: R.V. Solé and S. Valverde, Lecture Notes in Physics, 650, 189, 2004

Brain complexity

Anatomical networks

-Histological Analysis
-DTI (MRI)



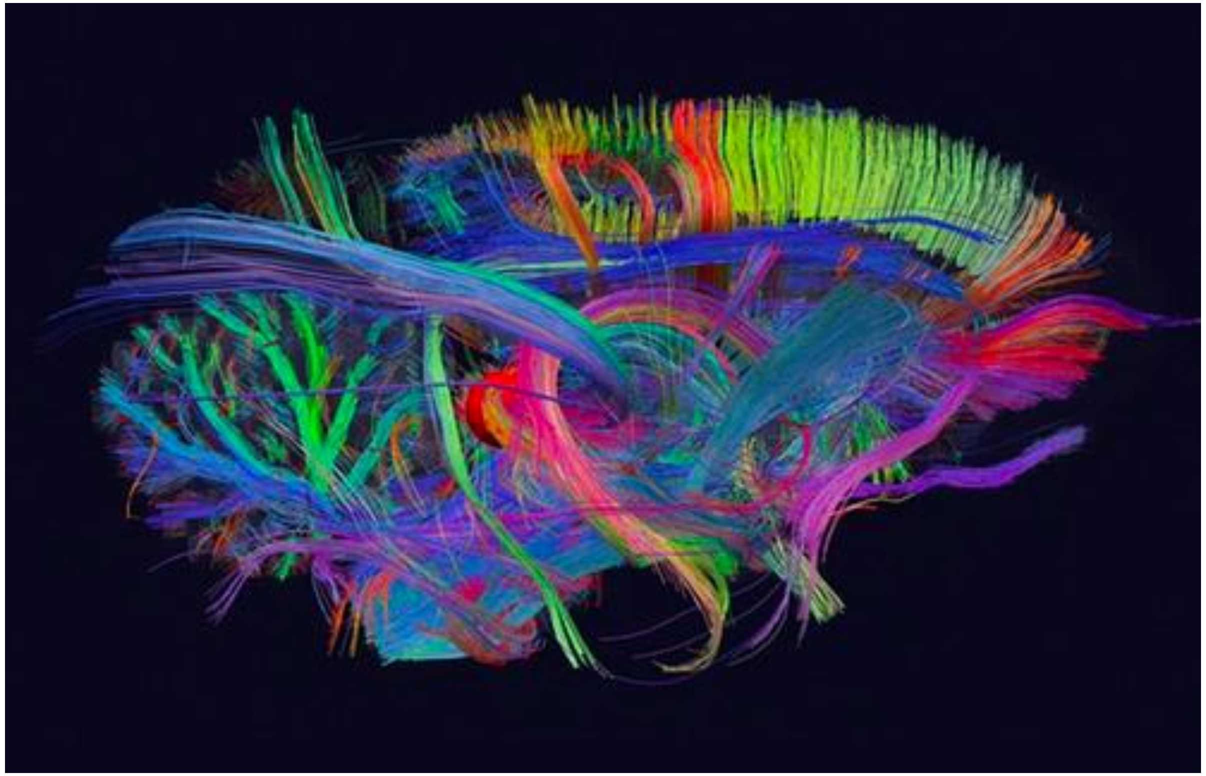
Functional networks

-Cross-correlation
-Wavelet coherence-Sync.
likelihood-Generalized Sync.
-Phase Sync.
-Mutual Info.
-Granger Causality

Adapted from Bullmore & Sporns, Nature Rev. 10, 186 (2009)

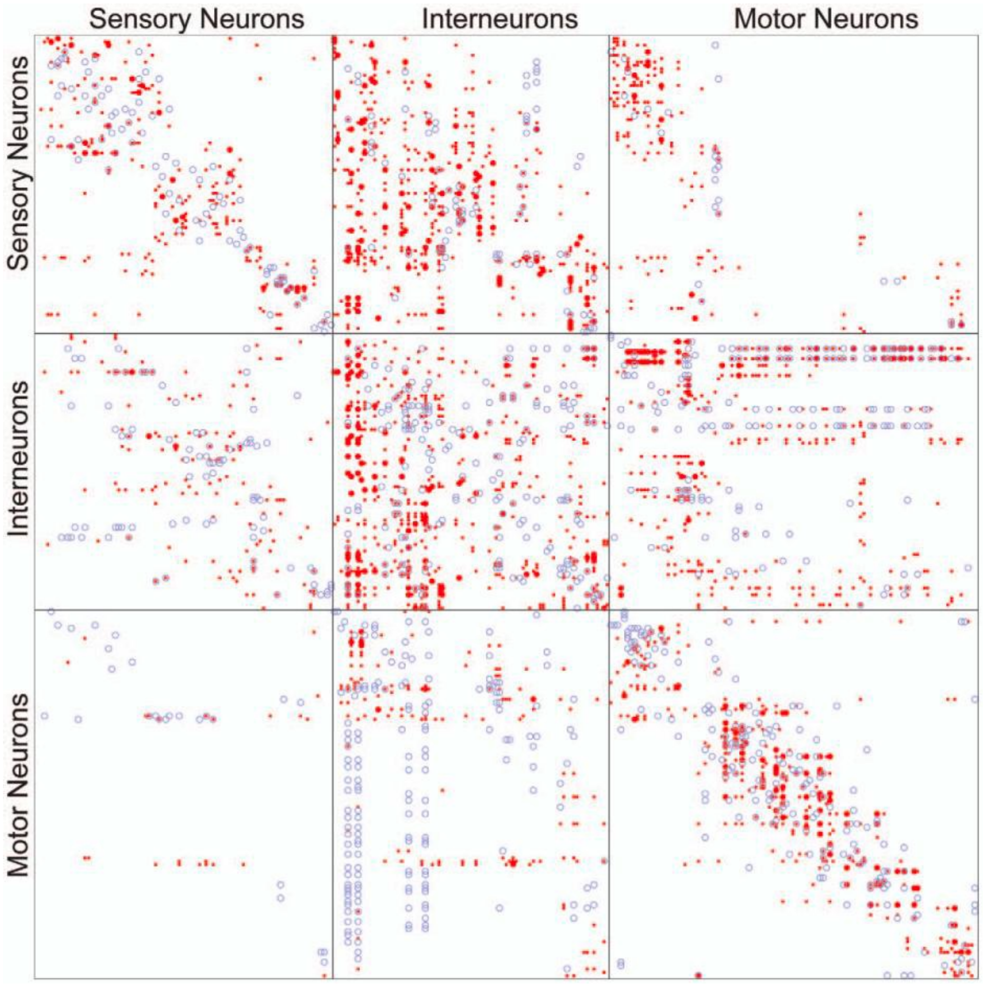
Anatomical networks

A connectome is a comprehensive map of neural connections in the brain.



Sporns et al., PLoS Comp.Biol. (2005)

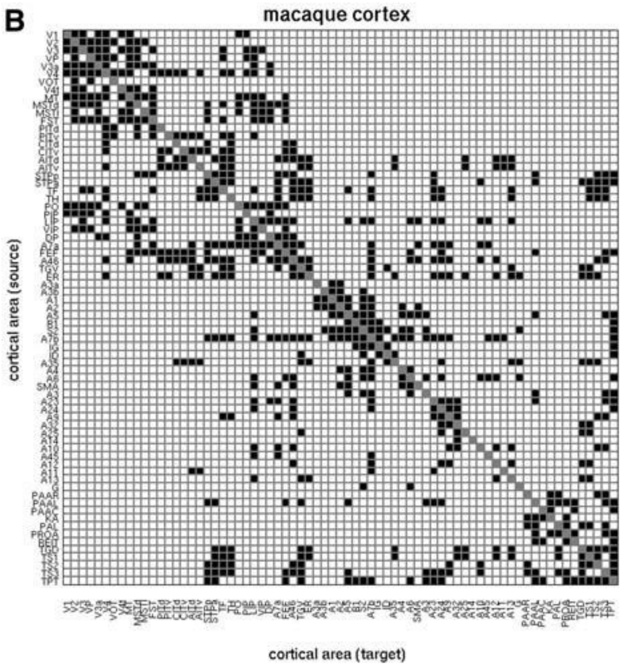
Anatomical networks



Gap juntions connections and chemical synapses of C. Elegans neurons.
From Varshney, PLoSComp. Biol, 7, 1001066 (2011)

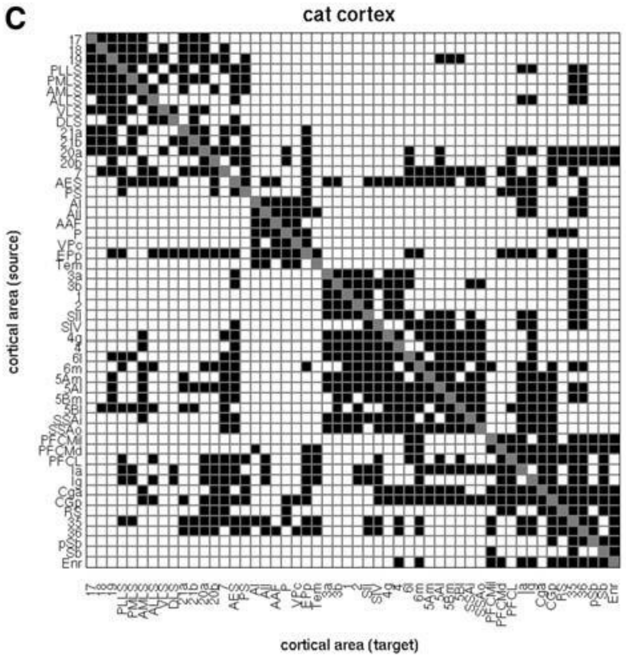
Anatomical networks

Macaque cortex



N=71 Brain Areas and L=746
Small-world
No power-law

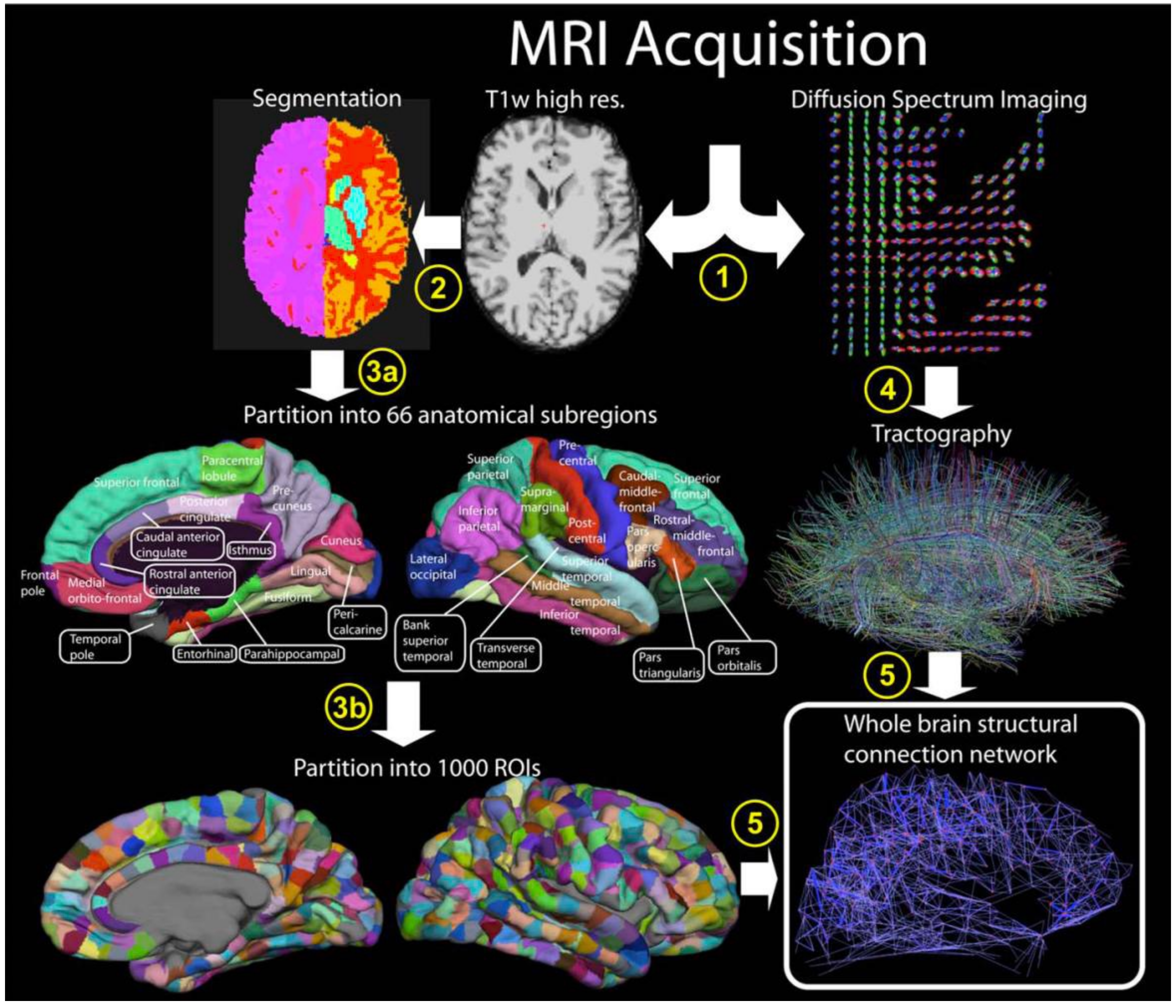
Cat cortex



N= 52 Brain Areas and L=820
Small-world
No power-law

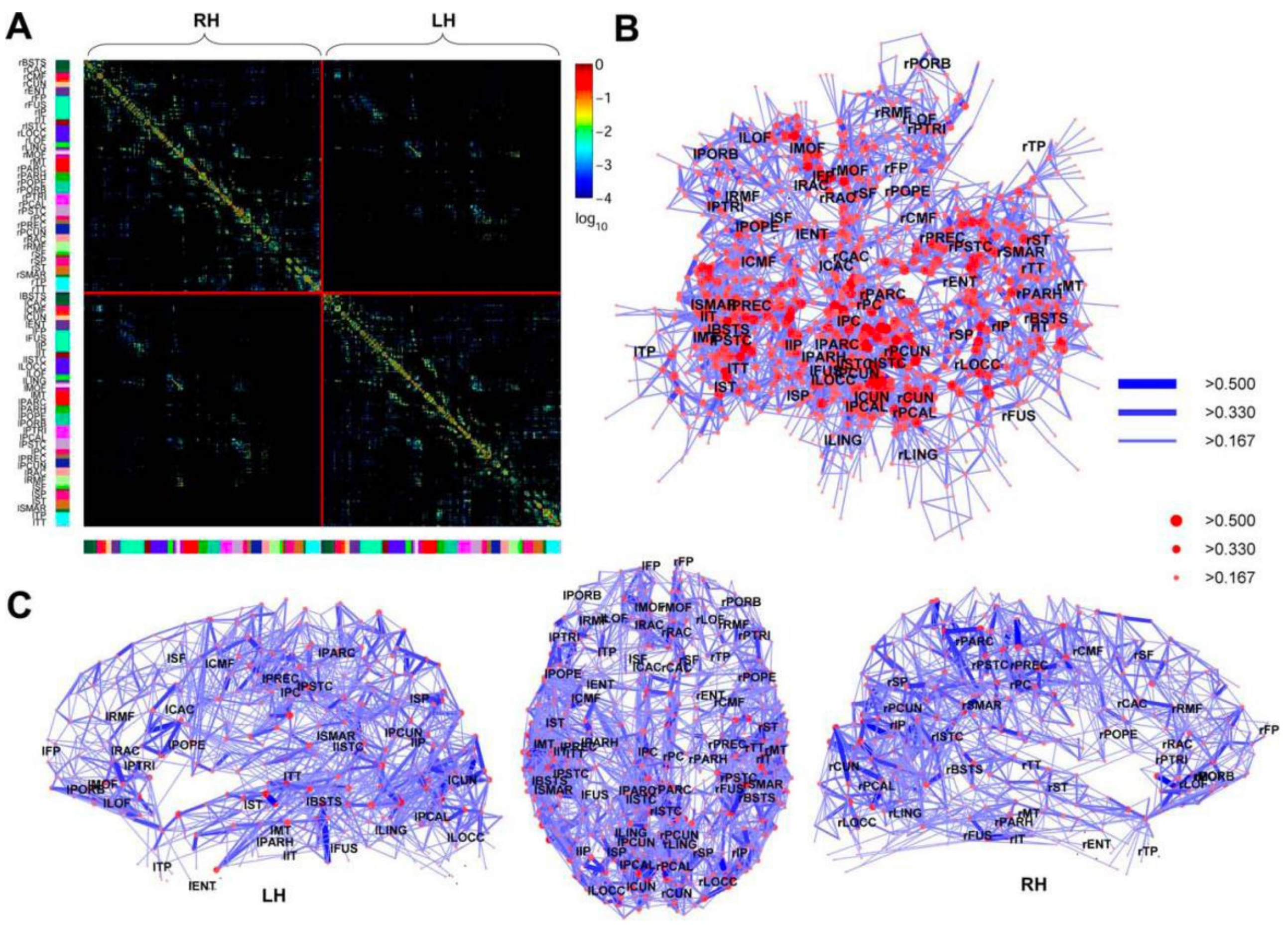
From Sporns et al., Neuroinformatics, 2, 145 (2004)

Anatomical networks



Hagmann et al. (2008) PLoS Biol. 6, e159

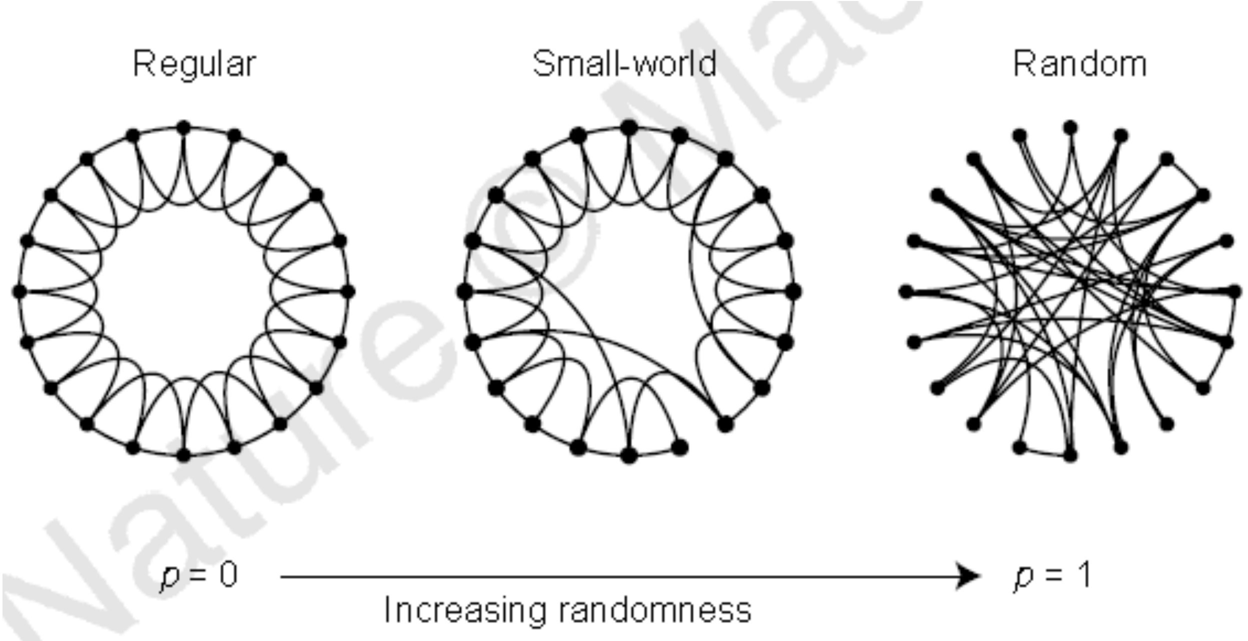
Anatomical networks



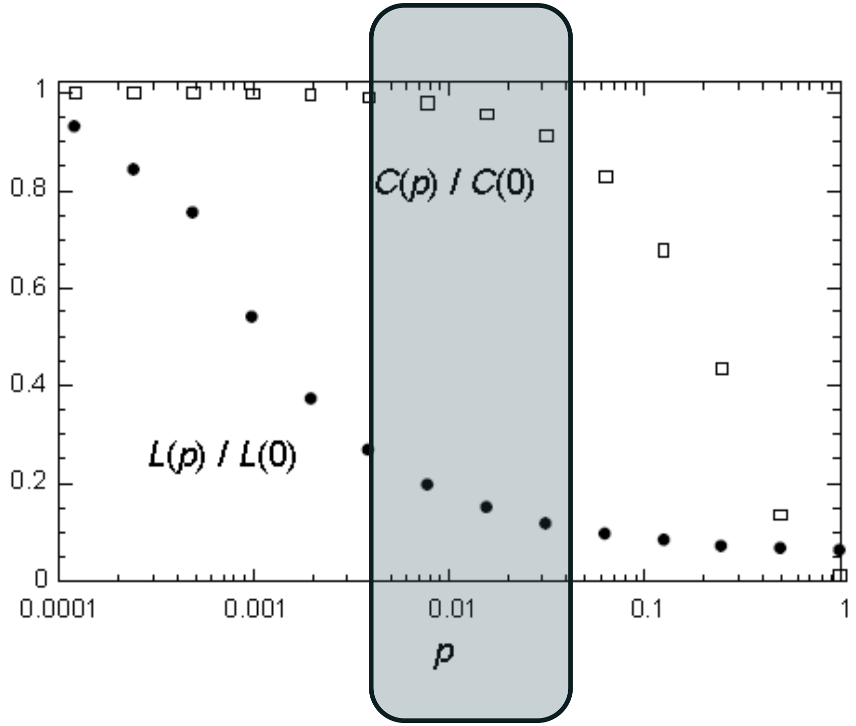
Hagmann et al. (2008) PLoS Biol. 6, e159

Anatomical networks – small-world

The Watts and Strogatz (WS) model



Small-world region



(Watts & Strogatz, Nature, 1998)

Functional brain networks – how to get them?

Limitations:

- Low spatial resolution ($\sim 10^{11}$neurons)
- Overlapping of measurements (not clear parcelation)
- High variability in the results
- Functional networks are not static
- Brain is not an isolated system

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- It is difficult to evaluate causality
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- In EEG and MEG, we only measure cortical activity (missing interactions)

Functional brain networks – how to get them?

Brain activity measurement – cf lesson 1

Limitations:
- Low spatial resolution ($\sim 10^{11}$neurons)
- Overlapping of measurements (not clear parcelation)
- High variability in the results
- Functional networks are not static
- Brain is not an isolated system

Time series analysis

Limitations:
- It is difficult to evaluate causality
- High variability in the results
- Functional networks are not static
- In EEG and MEG, we only measure cortical activity (missing interactions)

Network analysis

Limitations:
- Real networks are weighted and directed
- High variability in the results
- Functional networks are not static

Functional brain networks – why using Complex networks methods?

Complex networks methods give useful information at 3 different levels:

- Characterize the topology of brain functional networks

Functional brain networks – why using Complex networks methods?

Complex networks methods give useful information at 3 different levels:

- Characterize the topology of brain functional networks – the ubiquity of power laws!

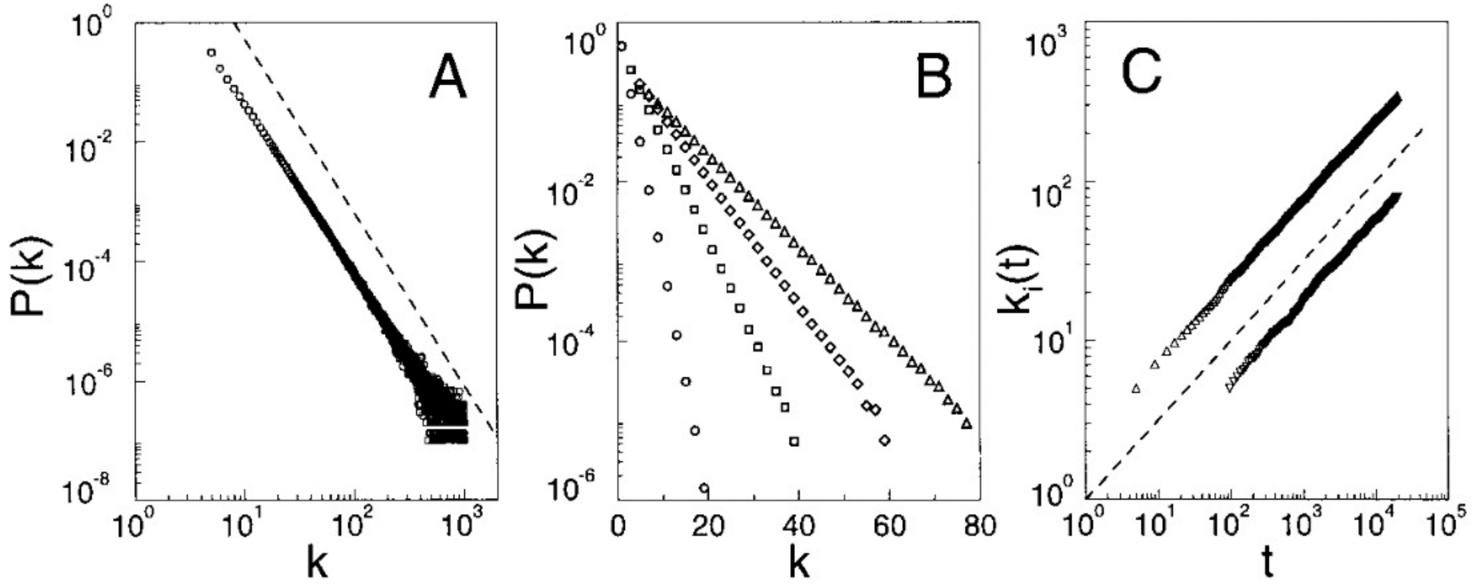

Fig. 2. (**A**) The power-law connectivity distribution at $t = 150{,}000$ (○) and $t = 200{,}000$ (□) as obtained from the model, using $m_0 = m = 5$. The slope of the dashed line is $\gamma = 2.9$. (**B**) The exponential connectivity distribution for model A, in the case of $m_0 = m = 1$ (○), $m_0 = m = 3$ (□), $m_0 = m = 5$ (◇), and $m_0 = m = 7$ (△). (**C**) Time evolution of the connectivity for two vertices added to the system at $t_1 = 5$ and $t_2 = 95$. The dashed line has slope 0.5.

Adapted from (Barabasi & Albert, Science, 1999)

Functional brain networks – why using Complex networks methods?

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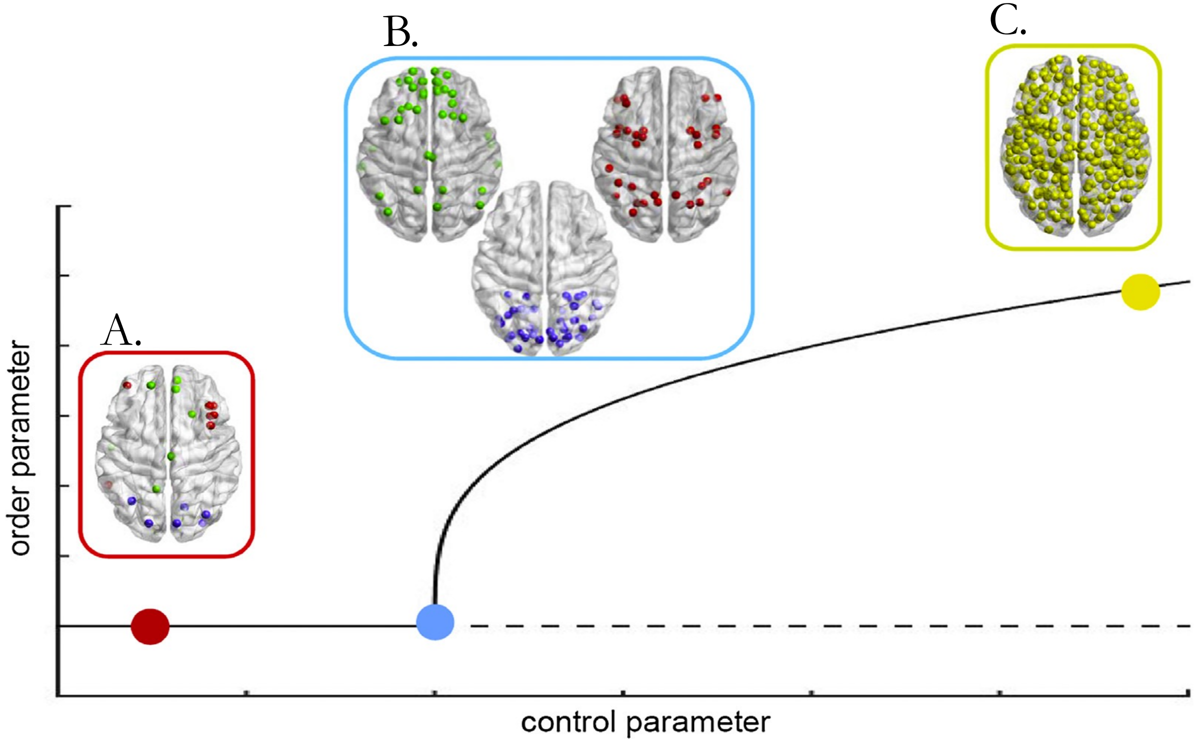
- Characterize the topology of brain functional networks – the ubiquity of power laws!



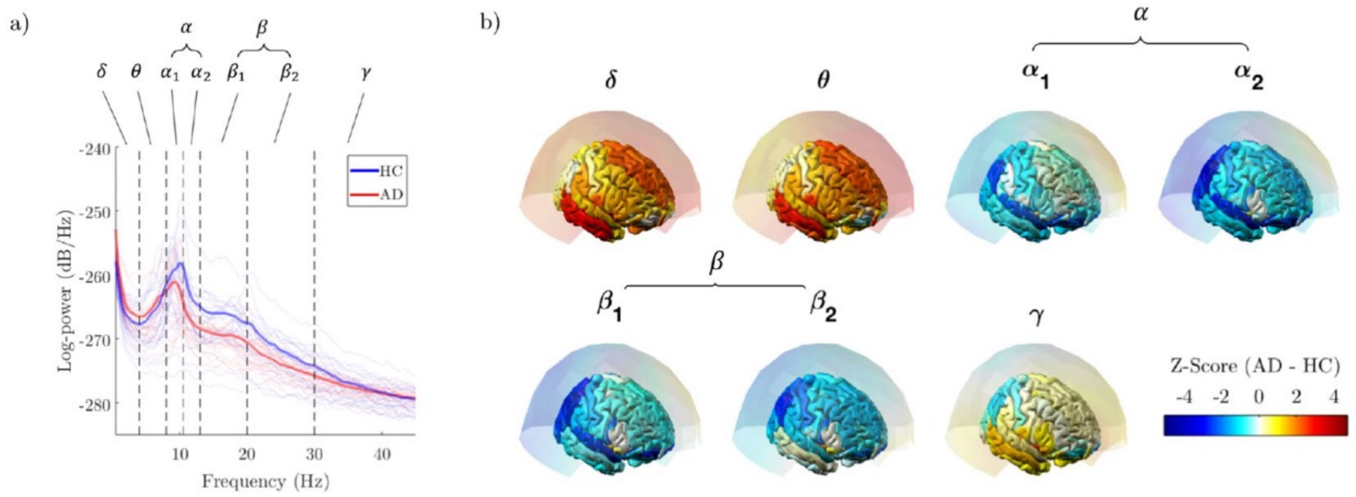
Adapted from (Cocchi et al, 2017)

Functional brain networks – why using Complex networks methods?

Complex networks methods give useful information at 3 different levels:

- Characterize the topology of brain functional networks

- Identify differences between healthy brains and those with a certain pathology



Adapted from (Guillon et al, 2017)

Functional brain networks – why using Complex networks methods?

Complex networks methods give useful information at 3 different levels:

- Characterize the topology of brain functional networks
- Identify differences between healthy brains and those with a certain pathology
- Develop models in order to explain the changes found in impaired functional networks

Functional brain networks – why using Complex networks methods?

Complex networks methods give useful information at 3 different levels:

- Characterize the topology of brain functional networks
- Identify differences between healthy brains and those with a certain pathology
- Develop models in order to explain the changes found in impaired functional networks

Spoiler alert: could be relevant for Brain-Computer Interface…but you will have to wait next week to know more about it!

To go further…

- Tools – with many tutorials
  - Functional connectivity – compute metrics:
    - Python: MNE-Python
    - Matlab: Brainstorm, Fieldtrip

To go further…

- Tools – with many tutorials
  - Functional connectivity – compute metrics:
    - Python: MNE-Python
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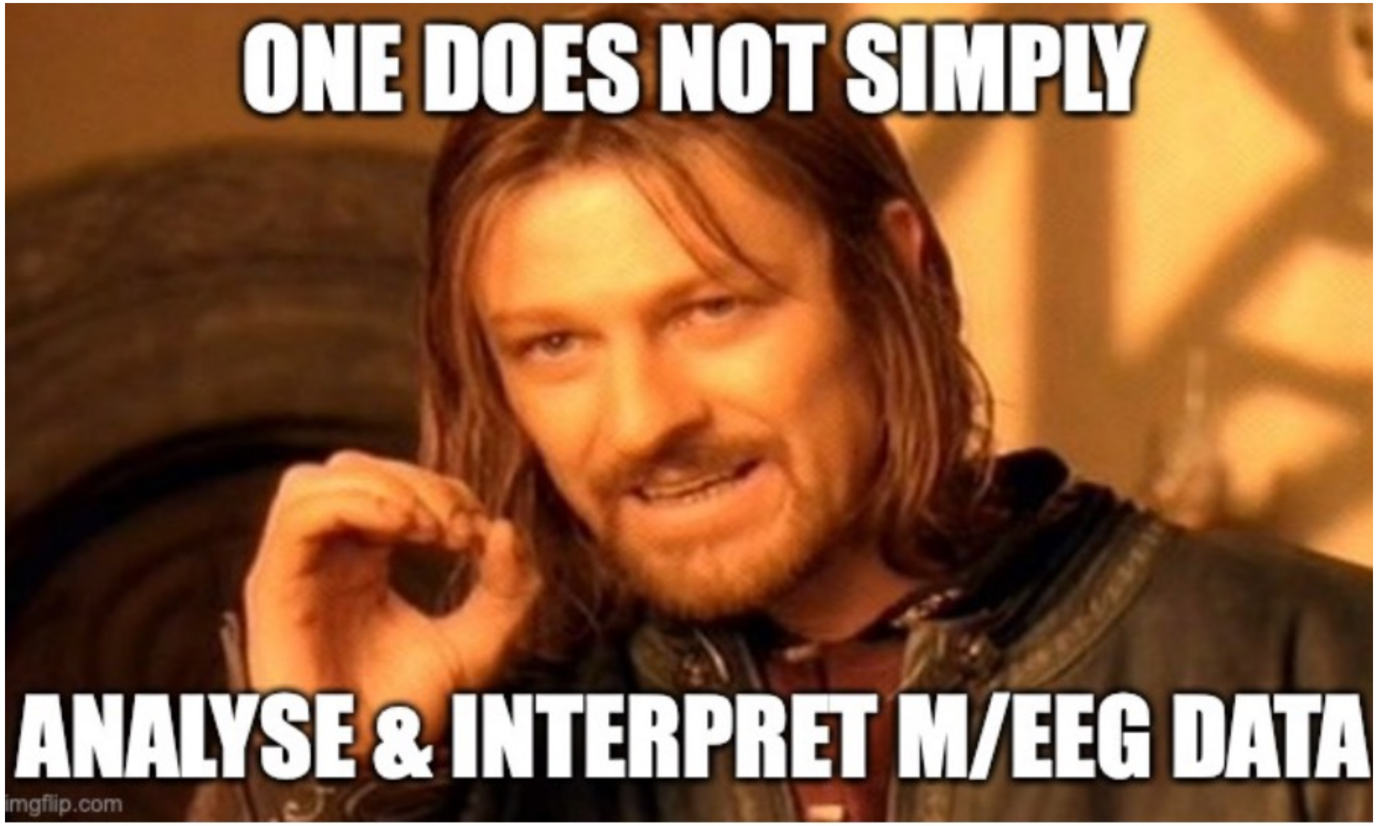
- Papers/books
  - He et al, 2019, IEEE Transactions on Biomedical Engineering - Electrophysiological Brain Connectivity: Theory and Implementation
  - Bastos & Schoffelen, 2016, Frontiers in Systems Neuroscience - A Tutorial Review of Functional Connectivity Analysis Methods and Their Interpretational Pitfalls
  - De Vico Fallani et al, , 2014, Philos Trans R Soc Lond B Biol Sci - Graph analysis of functional brain networks: practical issues in translational neuroscience
  - Fornito & Zalesky, 2017 - Fundamentals of Brain Network Analysis
  - Boccaletti et al, 2006, Physics Reports - Complex networks: Structure and dynamics
  - Rubinov & Sporns, 2010, NeuroImage - Complex network measures of brain connectivity: Uses and interpretations
  - Pernet et al, 2015, Journal of Neuroscience Methods - Cluster-based computational methods for mass univariate analyses of event-related brain potentials/fields: A simulation study



Let's see together an example!

Lesson 3: ✓

Reminder – next week @ Paris Brain Institute!

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