Training school

Graphs in EEG functional connectivity

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Seminar organization

Part I

Brain complexity

Part II

Brain network analysis

Part III

Exercise (paper)

Part IV

Application to brain data

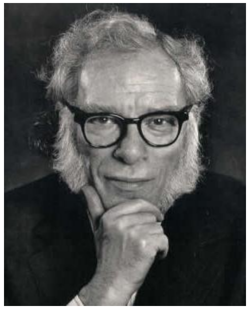
Part V

Exercise (computer)

Brain « quotes »

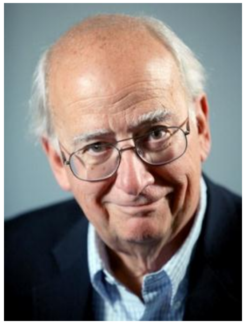
Santiago Ramon y Cajal (Nobel prize in Medicine)

“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* byJ. Hooper and D. Teresi, 1986)

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



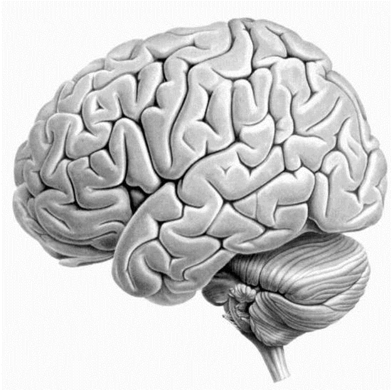
Michael S. Gazzaniga (from *The Mind's Past*, 1998)

“The human brain is generally regarded as a ***complex*** *web of adaptations built into the nervous system, even though no one knows how”*

Two-fold trait of the brain

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*

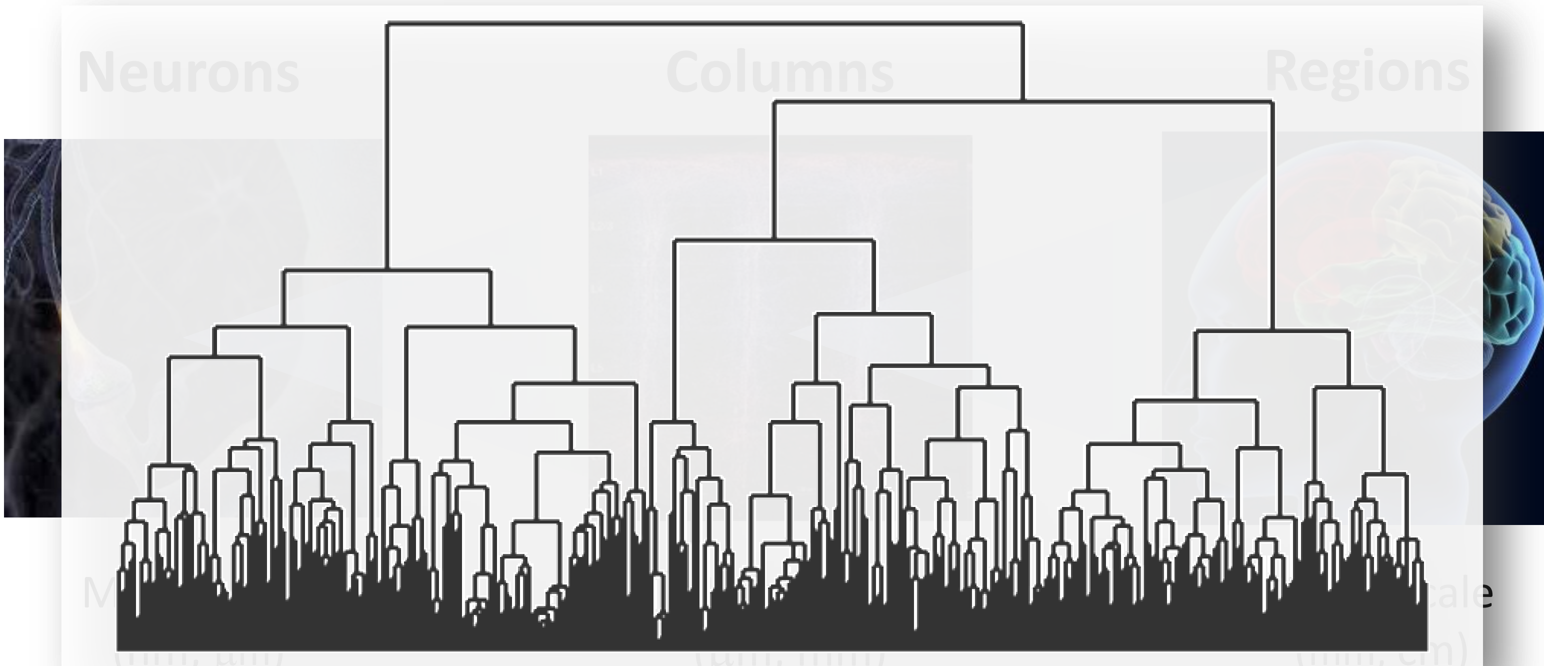


Function

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

Structural spatial scales

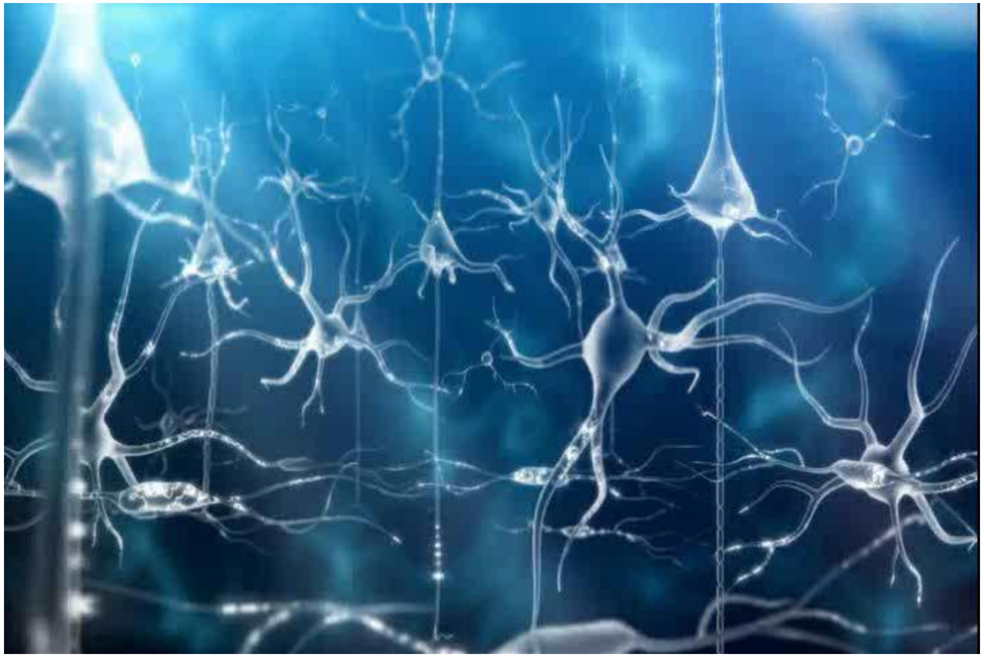
Hierarchical modularity faciliates behavoral adaption (Kirschner and Gerhart, PNAS, 1998)



Each module can change its function without adversely perturbing the remainder of the system

Functional temporal scales

Plasticity occurs over multiple temporal scales



seconds minutes hours days months

→

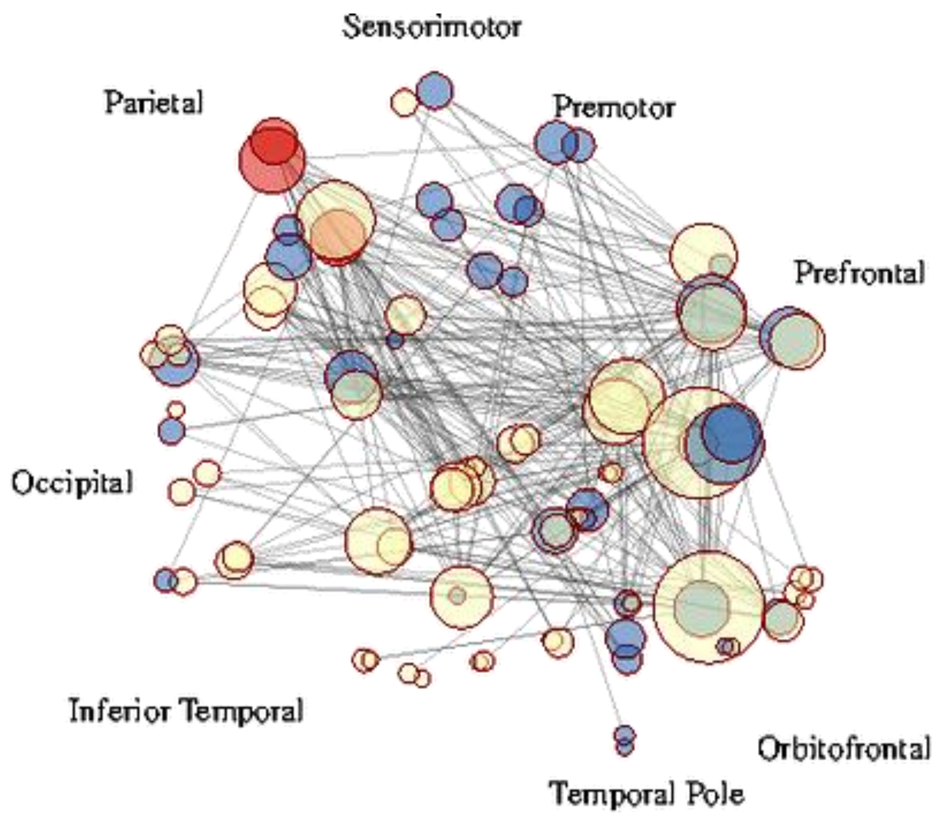
Short-term

eg, Learning / memory

Long-term

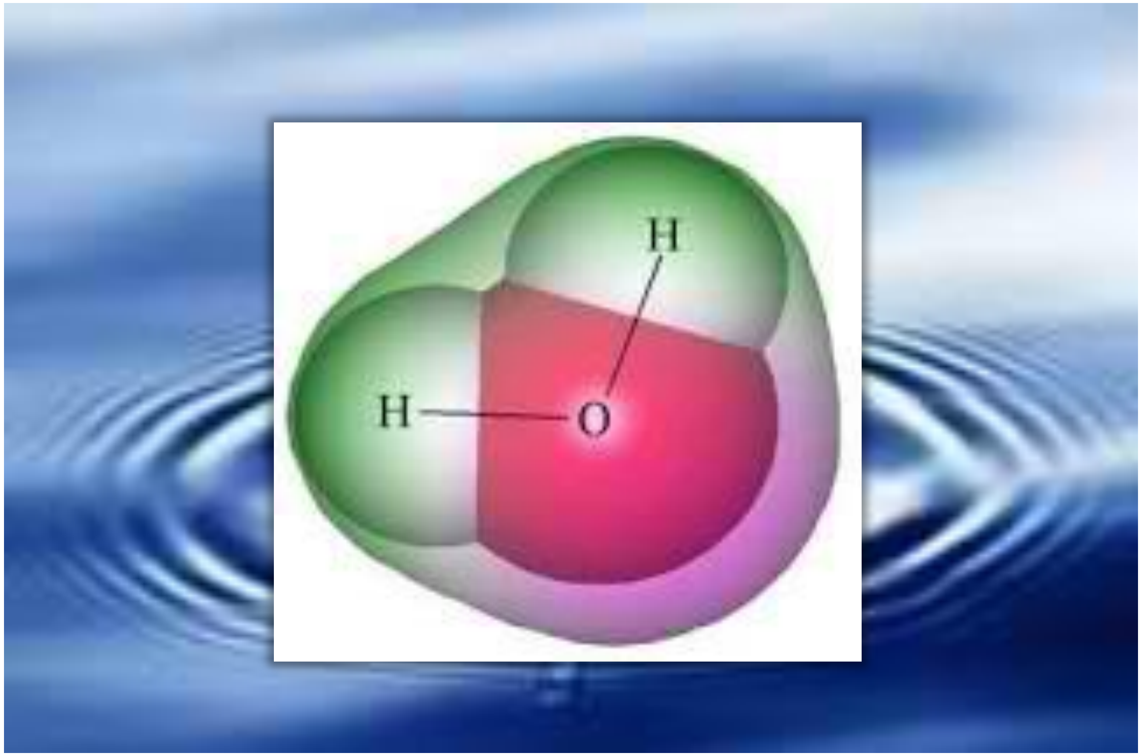
eg, Aging / recovery

The brain: a complex system



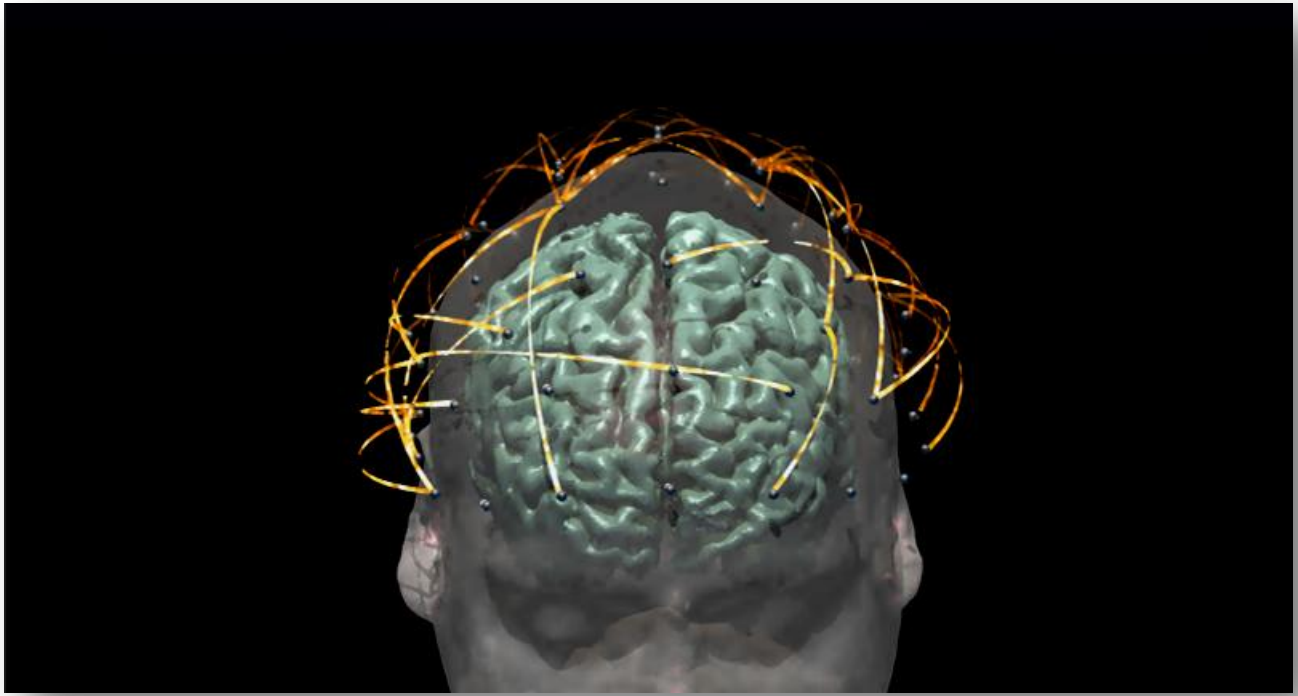
A connected system whose overall behavior can be characterized as ***more than the sum of its parts (i.e. emergence)***

Emergence in ‘small’ system



Emergence is the manner in which complex phenomena arise from a collection of relatively simple interactions between system components

Emergence in the brain



The brain can be studied as a complex system in which mental states **emerge** from the *interaction between multiple physical and/or functional levels*

Part II

Brain network analysis

Neuroimaging

Invasive

+ *Anatomy*

  - Post-mortem dissection

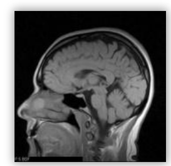
+ *Function*

  - Intracranial electroencephalography (iEEG)

Non-invasive

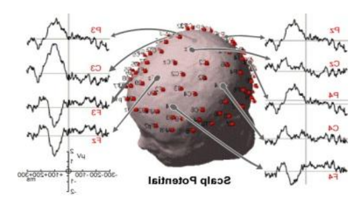
+ *Anatomy*

  - Structural Magnetic Resonance Imaging (sMRI)

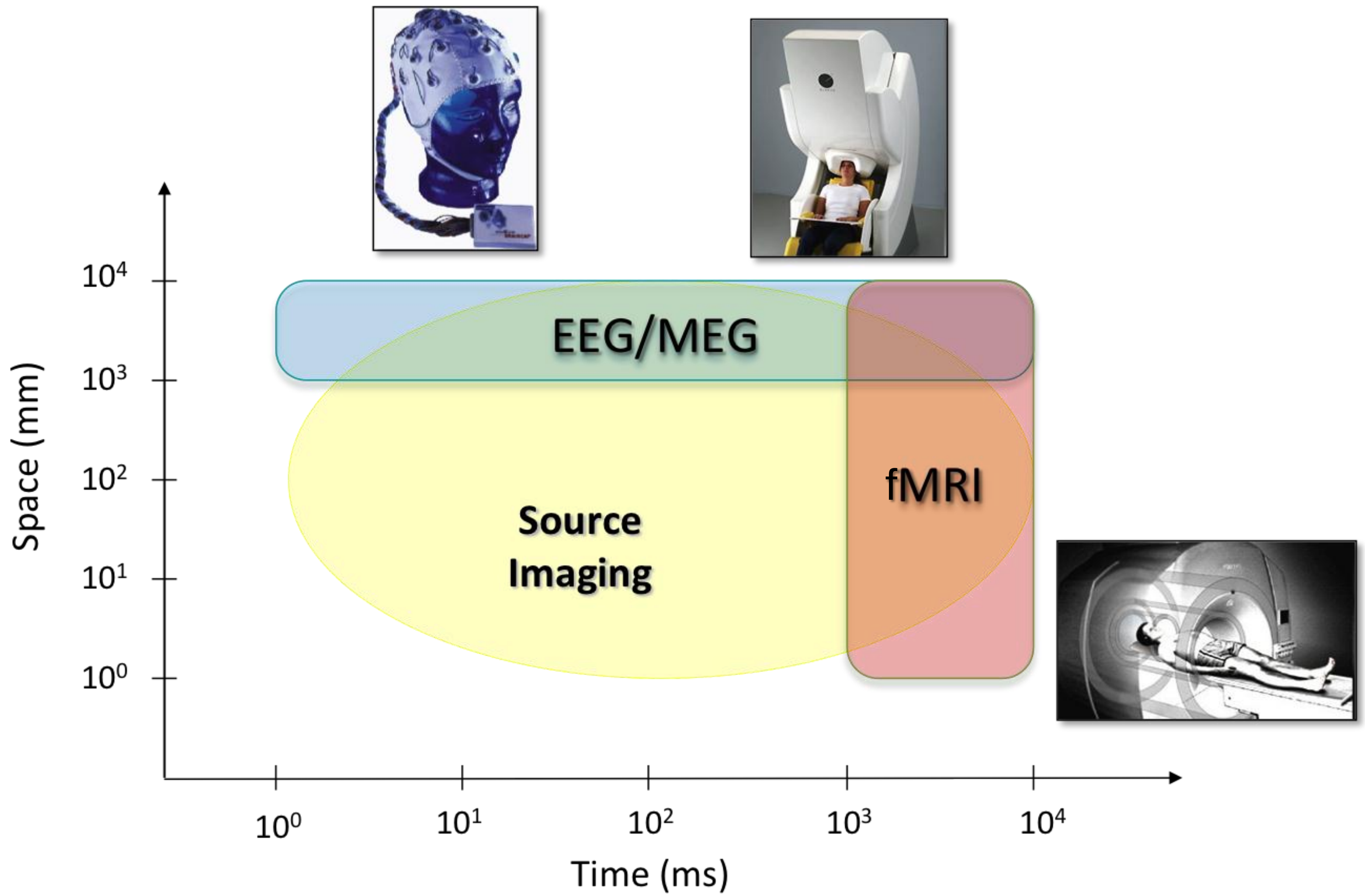


+ *Function*

  - Functional Magnetic Resonance Imagining (fMRI), Electroencephalography (EEG), Magnetoencephalography (MEG)



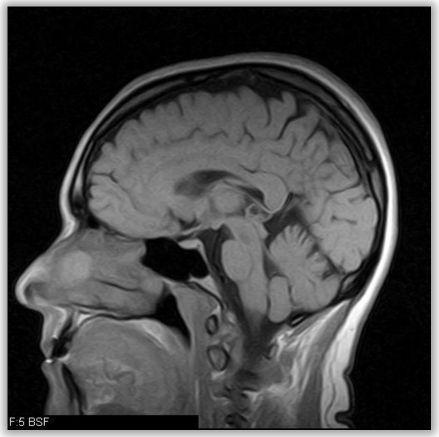
Spatial and temporal resolution



sMRI and fMRI

Structural MRI

MRI makes use of the property of nuclear magnetic resonance (NMR) to image the **3D structure** of the brain.



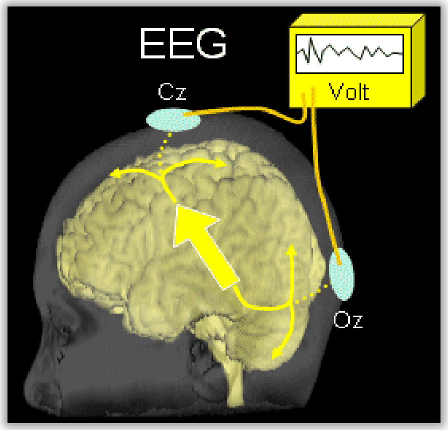
Functional MRI

Functional magnetic resonance imaging is an MRI procedure that measures brain activity by detecting associated changes in **blood flow**.

EEG and MEG

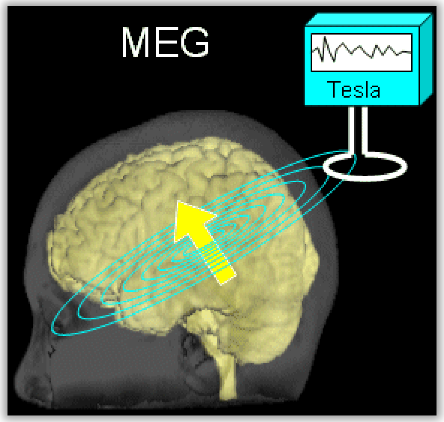
Electroencephalography

EEG is the recording of **electrical activity** along the scalp. EEG measures voltage fluctuations resulting from ionic current flows within the neurons of the brain



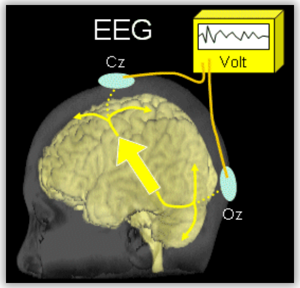
Magnetoencephalography

MEG is a technique for mapping brain activity by recording **magnetic fields** produced by electrical currents occurring naturally in the brain, using very sensitive magnetometers.



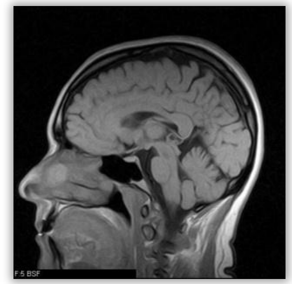
EEG source imaging

Multimodal integration

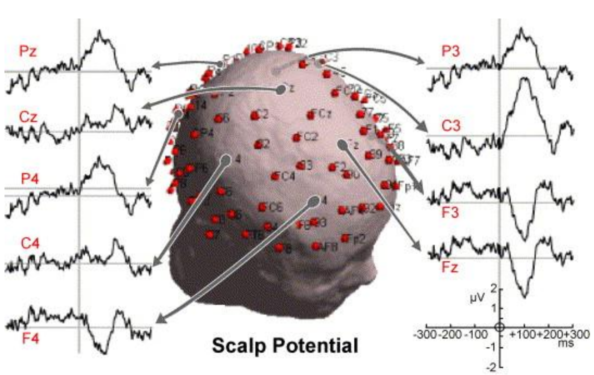


Dynamics

+

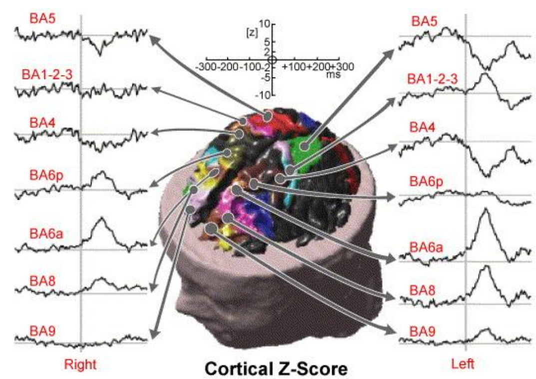


Structure



M scalp electrodes

Linear Inverse

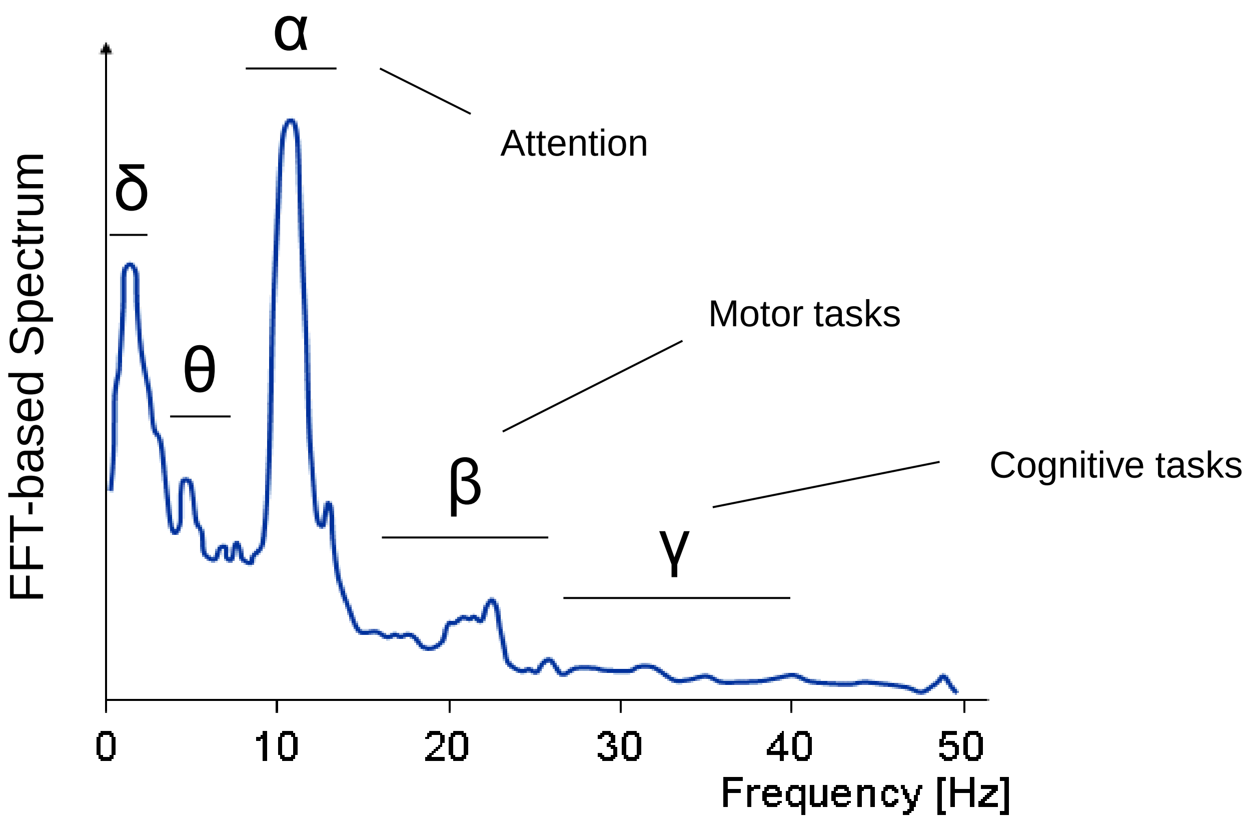


N cortical sources

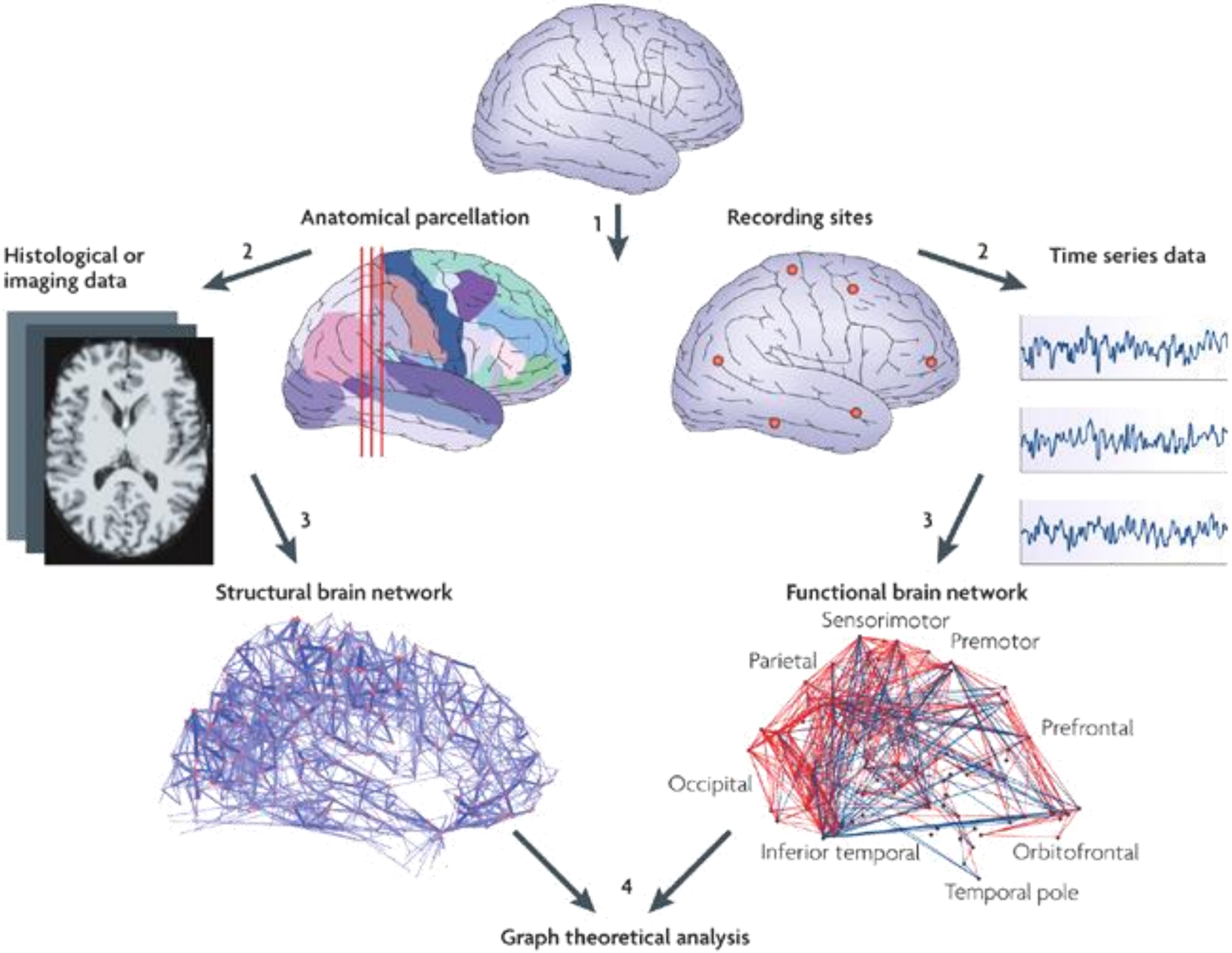
Dale and Sereno, J Cogn Neurosci, 1993

EEG spectral properties

Characteristic oscillatory behavior



Brain network construction

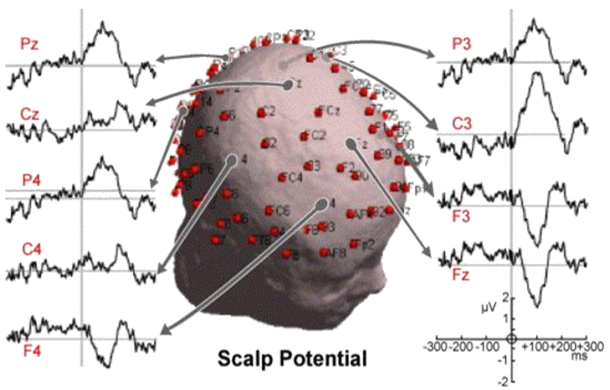


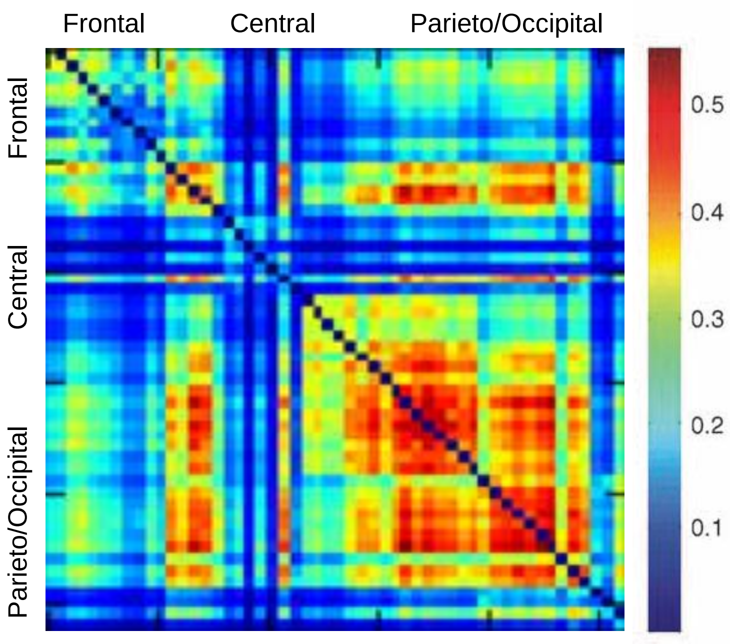
Sporns and Bullmore, Nat Rev Neurosci, 2009

Functional brain networks

Functional connectivity:

statistical dependence between remote temporal signals





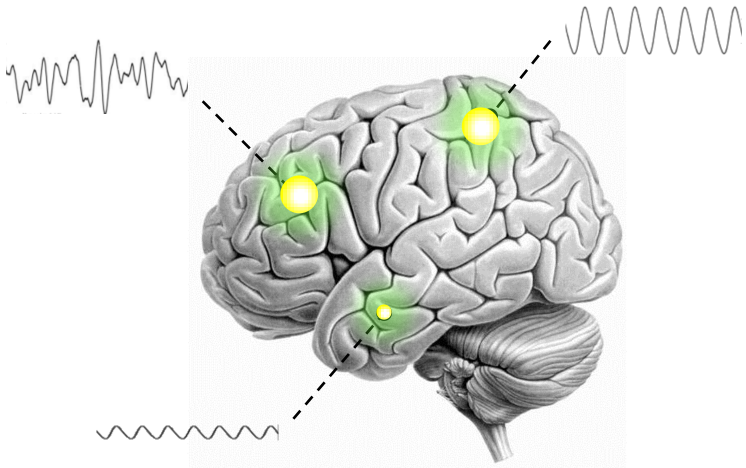
+ Methods

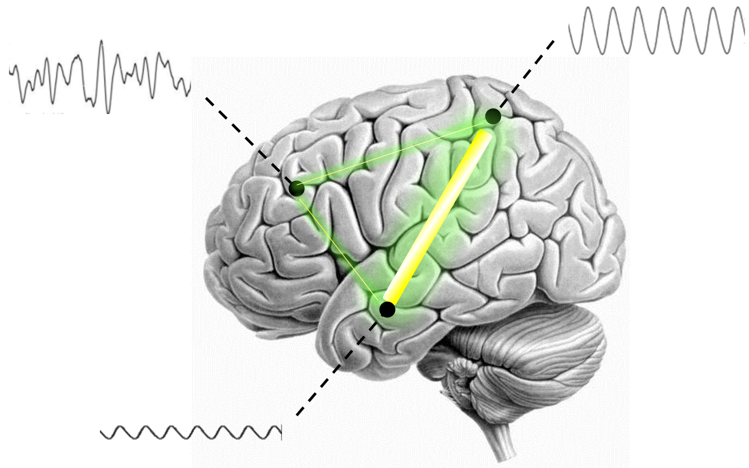
- *Time domain*: Crosscorrelation, Granger-causality
- *Frequency domain*: Spectral coherence, Partial directed coherence

Activity vs functional connectivity

Energy

Correlation coefficient





Activity

univariate analysis of signals

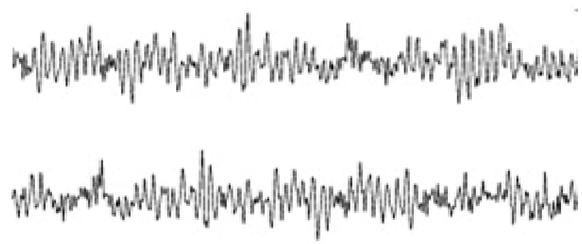
Func. Connectivity

bivariate analysis of signals

Time-domain connectivity

x(t)

y(t)



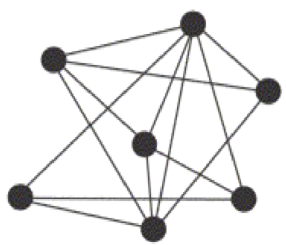
Normalized cross-covariance

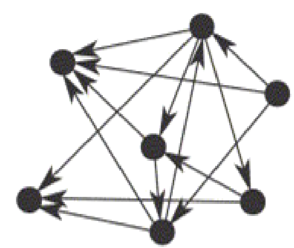
$$C(x,y) = \frac{\sum_{t=1}^{T} (x(t) - \mu_x)(y(t) - \mu_y)}{\sigma_x \sigma_y}$$

Granger causality (AR modeling)

$$G_{x \to y} = \ln\left(\frac{\mathrm{var}(e_y)}{\mathrm{var}(e_{yx})}\right)$$

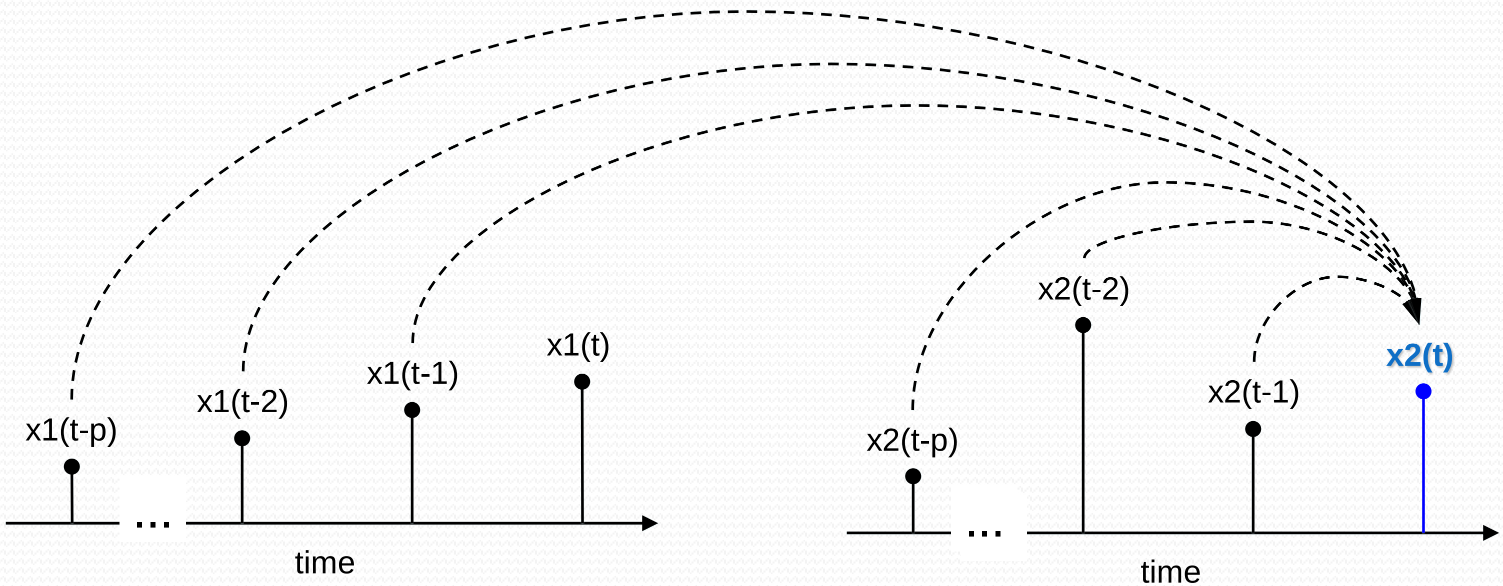
Synchronization
(undirected)





Propagation
(directed)

Granger causality



AR model

Prediction error

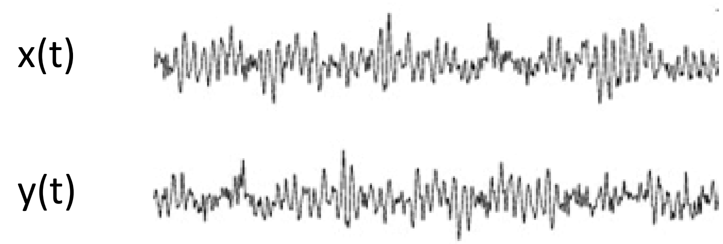
Granger causality

$$x_2'(t) = \sum_{k=1}^{p} a_2(k) x_2(t-k) \xrightarrow{\text{Yule-walker}} e_{x_2} = x_2'(t) - x_2(t)$$

$$x_2''(t) = \sum_{k=1}^{p} a_{2,2}(k) x_2(t-k) + \sum_{k=1}^{p} a_{2,1}(k) x_1(t-k) \xrightarrow{\text{Yule-walker}} e_{x_2 x_1} = x_2''(t) - x_2(t)$$

$$G_{x_2 \leftarrow x_1} = \ln\left(\frac{\mathrm{var}(e_{x_2})}{\mathrm{var}(e_{x_2 x_1})}\right)$$

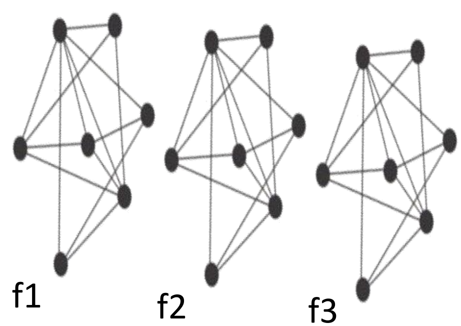
Frequency-domain connectivity



Spectral coherence

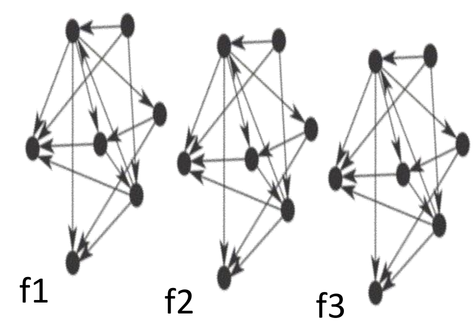
$$SC(x,y,f)=\frac{\left|S_{xy}(f)\right|^2}{S_{xx}(f)S_{yy}(f)}$$

Synchronization
(undirected)



Partial Directed Coherence (AR modeling)

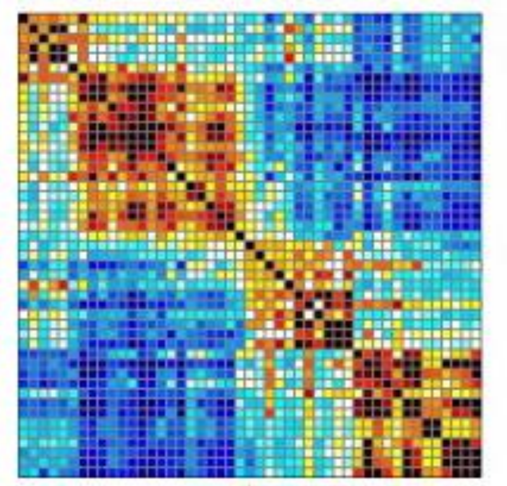
$$PDC(x,y,f)=\frac{\left|A_{xy}(f)\right|}{\sum_i \left|A_{xi}(f)\right|}$$



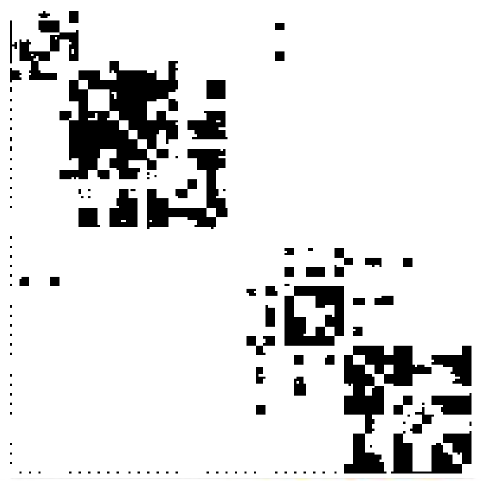
Propagation
(directed)

Connectivity thresholding

Retaining significant links: from fully connected to sparse networks



→ Threshold

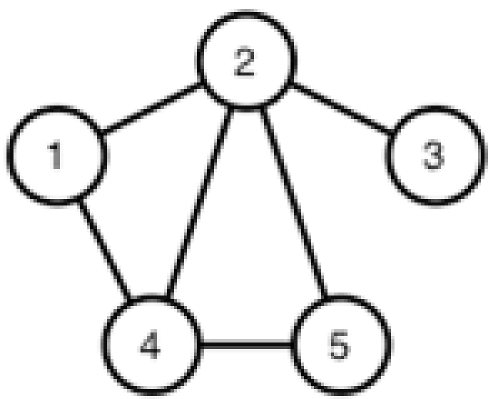


+ **"Optimal" thresholds**
  - range of values, range of percentages, data surrogate, statistical contrasts between group/conditions, minimum spanning tree,…

Toppi et al,Comput Math Meth Med, 2012; Langer et al, PLoS One, 2013

Graph theoretical approach

Brain networks can be usefully represented as graphs



N = 5
L = 6

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

Graph **G**

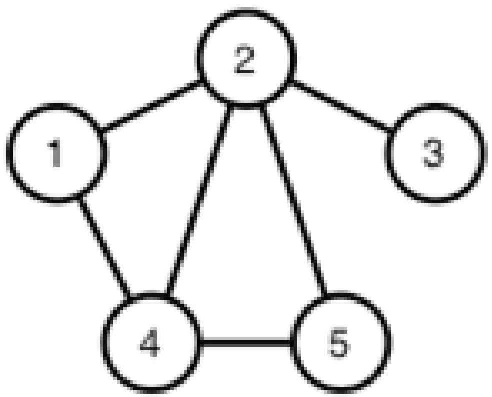
Adjacency matrix **A**

Nodes (N) = brain regions

Links (L) = anatomical or functional connectivity

Basic indexes

Graph indexes are extracted from the adjacency matrix



N = 5
L = 6

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

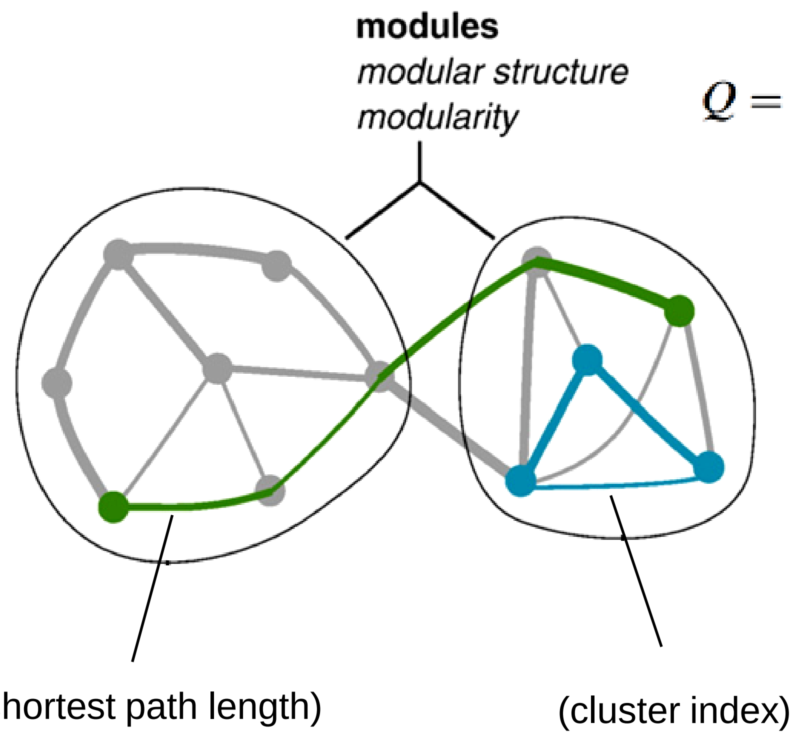
Density (Cost)

$$C = \frac{1}{N(N-1)} \sum_{i>j}^{N} A(i,j)$$

Degree

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

Advanced indexes



$$Q = \sum_{ij} [A_{ij} - P_{ij}] \delta(g_i, g_j)$$

Global efficiency

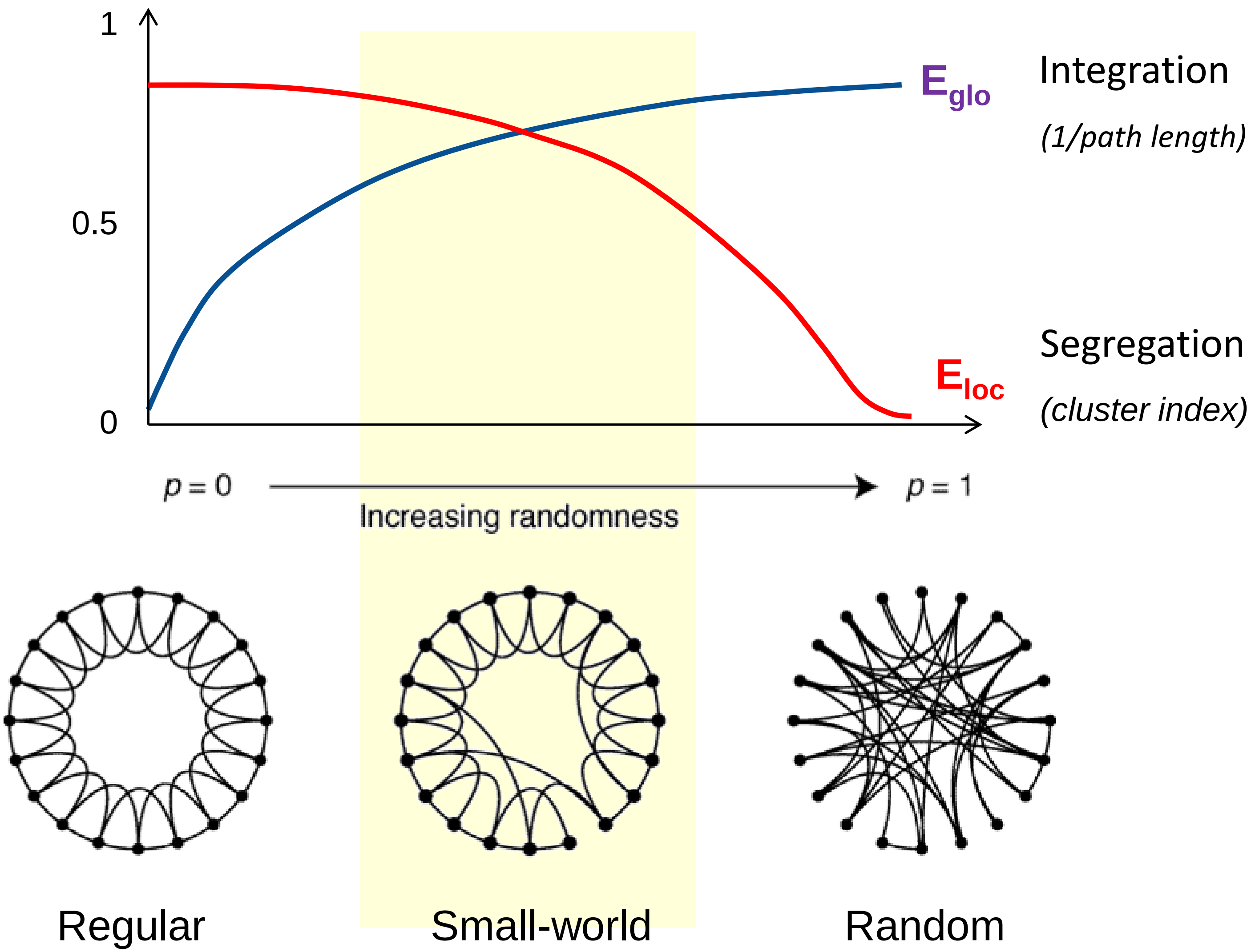
$$Eglo = \frac{1}{N(N-1)} \sum_{i>j}^{N} \frac{1}{d(i,j)}$$

Local efficiency

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

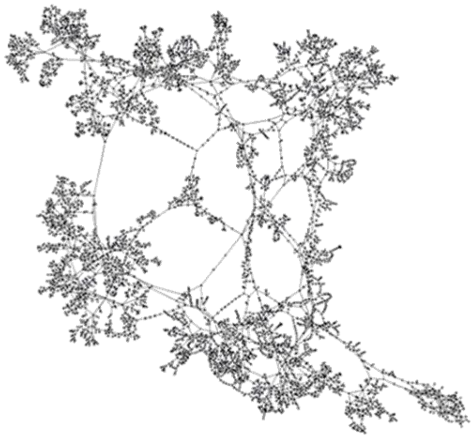
Adapted from Rubinov and Sporns, Neuroimage, 2009

"Small-world" efficient networks

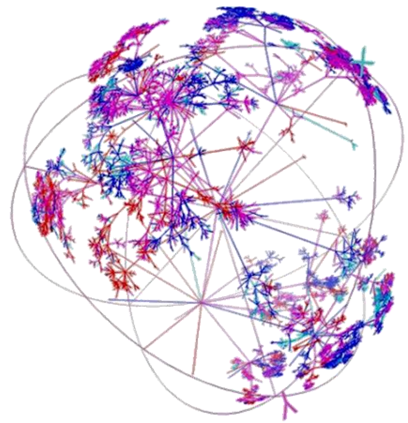


Real small-world networks

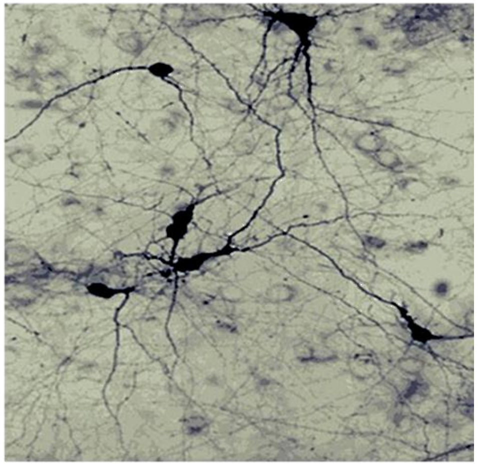
ELECTRICAL POWER GRIDS



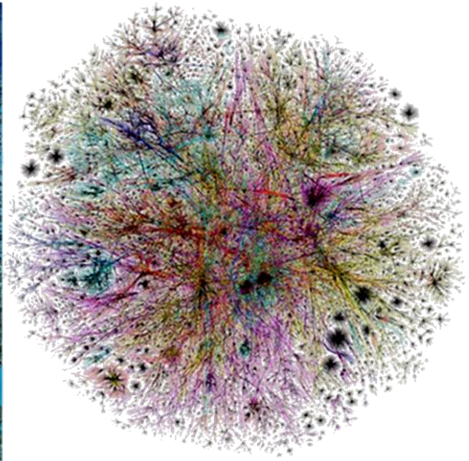
SIX DEGREES OF SEPARATION



NEURAL NETWORK LOGICS



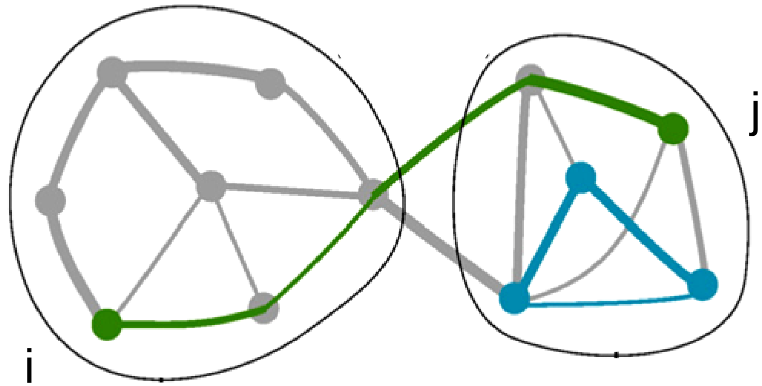
COMPLEX ECOSYSTEMS



STRUCTURE OF THE WEB

TRANSPORT INFRASTRUCTURE

Longer pathways: redundancy



Matrix redundancy $$R_m(i,j) = \sum_{l=1}^{L} P(i,j,l)$$

Vector redundancy $$R_v(l) = \sum_{i=1}^{N}\sum_{j=1}^{N} P(i,j,l)$$

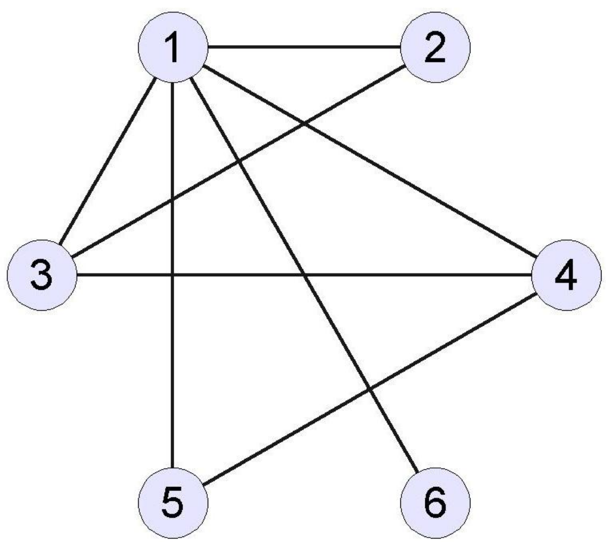
Scalar redundancy $$R_s = \sum_{l=1}^{L}\sum_{i=1}^{N}\sum_{j=1}^{N} P(i,j,l)$$

Part III

Excercise

Excercise

1.1 Draw the graph for the adjacency matrix A:



A =

X	1	1	1	1	1	1
1	X	1	0	0	0	2
1	1	X	1	0	0	3
1	0	1	X	1	0	4
1	0	0	1	X	0	5
1	0	0	0	0	X	6
1	2	3	4	5	6	

Excercise

1.2 Compute the connection density C of the graph

N = 6;
L = 8;

k = L / (N*(N-1))

C = 16 / 6*5 = 16 / 30 = 0,533

k = 2*L' / (N*(N-1))

C = 2*8 / 6*5 = 16 / 30 = 0,533

A =

	1	2	3	4	5	6
1	X	1	1	1	1	1
2	1	X	1	0	0	0
3	1	1	X	1	0	0
4	1	0	1	X	1	0
5	1	0	0	1	X	0
6	1	0	0	0	0	X

Excercise

1.3 Compute the degrees k of the nodes of the graph

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

$k(2) = 1 + 1 = 2$

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

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

$k(5) = 1 + 1 = 2$

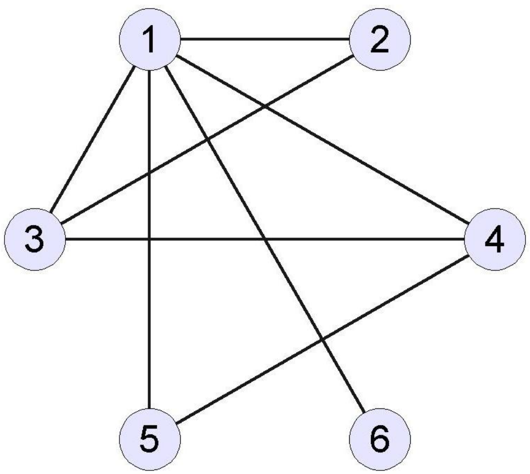
$k(6) = 1$

A =

	1	2	3	4	5	6
1	X	1	1	1	1	1
2	1	X	1	0	0	0
3	1	1	X	1	0	0
4	1	0	1	X	1	0
5	1	0	0	1	X	0
6	1	0	0	0	0	X

Excercise

1.4 Compute the global efficiency Eglo of the graph



N = 6

Distance matrix

D =

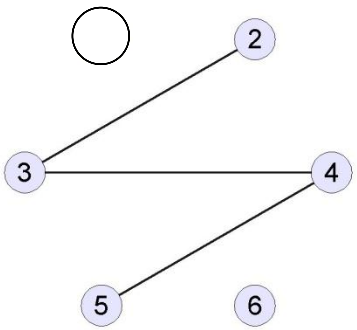
	1	2	3	4	5	6
1	X	1	1	1	1	1
2	-	X	1	2	2	2
3	-	-	X	1	2	2
4	-	-	-	X	1	2
5	-	-	-	-	X	2
6	-	-	-	-	-	X

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

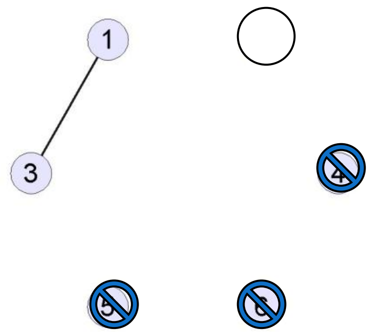
E_{glo} = ((1)*8 + (1/2)*7) * 2/(6*5) = (8 + 7/2) / 15 = (16+7) / (2*15) = 23/30

Excercise

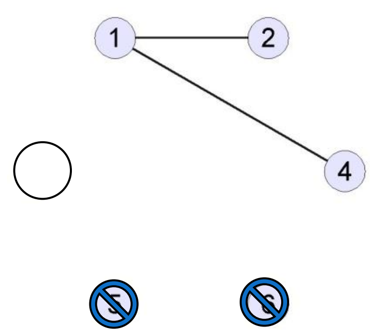
1.5 Compute the local efficiency Eloc of the graph



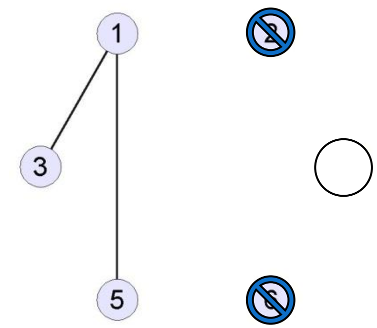
$E_g(S_1) = 0{,}433$



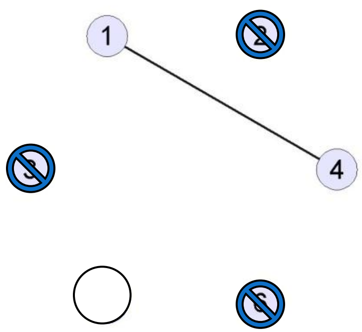
$E_g(S_2) = 1$



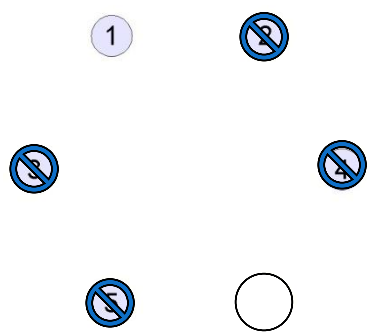
$E_g(S_3) = 0{,}833$



$E_g(S_4) = 0{,}833$



$E_g(S_5) = 1$



$E_g(S_6) = 0$

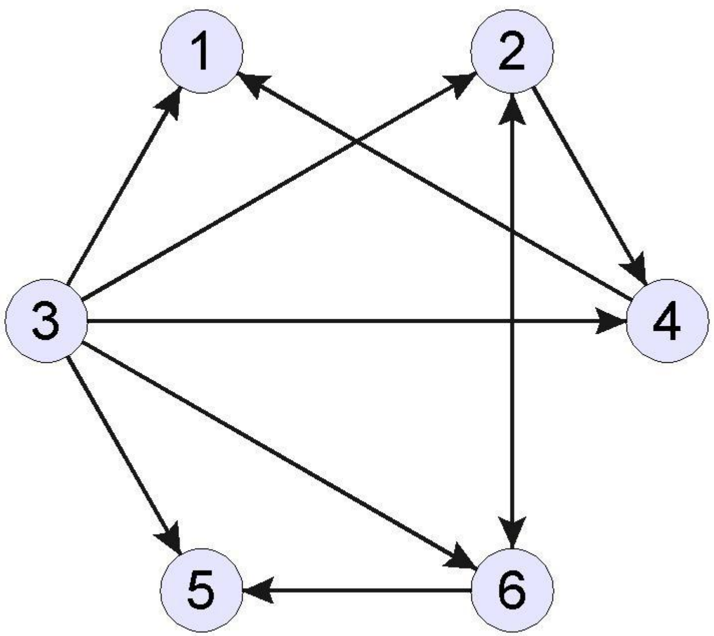
$$E_l = \frac{1}{N} \sum_{i=1}^{N} E_g(S_i)$$

N = 6

$E_{loc} = (0{,}433 + 1*2 + 0{,}833*2) / 6 = 0{,}683$

Excercise 2

2.1 Draw the graph for the adjacency matrix A:



A =

X	0	0	0	0	0	1
0	X	0	1	0	1	2
1	1	X	1	1	1	3
1	0	0	X	0	0	4
0	0	0	0	X	0	5
0	1	0	0	1	X	6
1	2	3	4	5	6	

Excercise 2

2.2 Compute the connection density C of the graph

N = 6;
L = 10;

k = L / (N*(N-1))

k(G) = 10 / 6*5 = 10 / 30 = 0,333

A =

X	0	0	0	0	0	1
0	X	0	1	0	1	2
1	1	X	1	1	1	3
1	0	0	X	0	0	4
0	0	0	0	X	0	5
0	1	0	0	1	X	6
1	2	3	4	5	6	

Excercise 2

2.3 Compute the in- and out-degrees k of the nodes of the graph

$g_{in}(1) = 1 + 1 = 2$ $g_{out}(1) = 0$

$g_{in}(2) = 1 + 1 = 2$ $g_{out}(2) = 1 + 1 = 2$

$g_{in}(3) = 0$ $g_{out}(3) = 1+1+1+1+1 = 5$

$g_{in}(4) = 1 + 1 = 2$ $g_{out}(4) = 1$

$g_{in}(5) = 1 + 1 = 2$ $g_{out}(5) = 0$

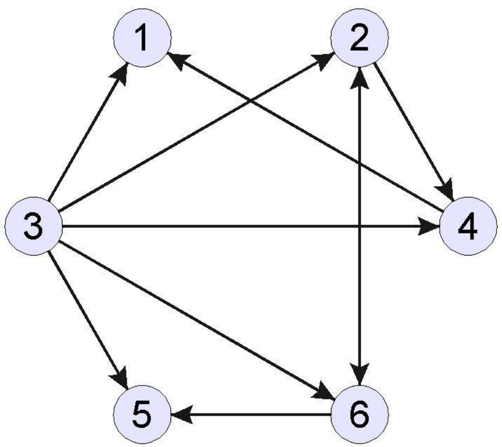
$g_{in}(6) = 2$ $g_{out}(6) = 1 + 1 = 2$

A =

	1	2	3	4	5	6
1	X	0	0	0	0	0
2	0	X	0	1	0	1
3	1	1	X	1	1	1
4	1	0	0	X	0	0
5	0	0	0	0	X	0
6	0	1	0	0	1	X

Excercise 2

2.4 Compute the global efficiency Eglo of the graph



N = 6

Distance matrix

D =

	1	2	3	4	5	6
1	X	∞	∞	∞	∞	∞
2	2	X	∞	1	2	1
3	1	1	X	1	1	1
4	1	∞	∞	X	∞	∞
5	∞	∞	∞	∞	X	∞
6	3	1	∞	2	1	X

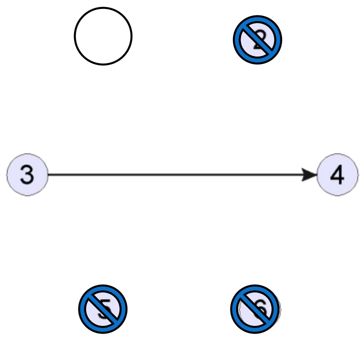
$$E_g = \frac{1}{N(N-1)} \sum_{i \neq j} \frac{1}{d(i,j)}$$

$E_g(G)$ = ((1)*10 + (1/2)*3 + (1/3)*1) / (6*5) = (10 + 3/2 + 1/3) / 30 =

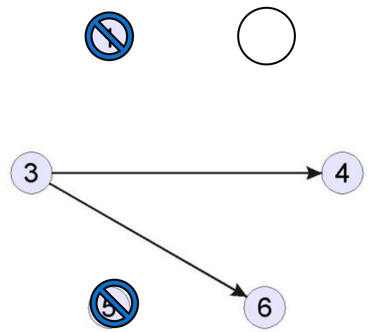
= (60 + 9 + 2) / (6*30) = 71/180 = 0,394

Excercise 2

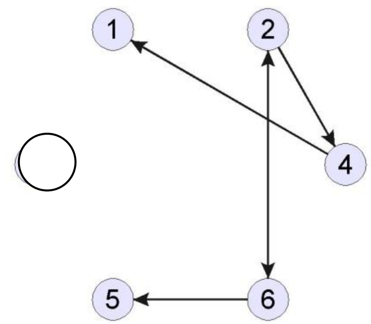
2.5 Compute the local efficiency Eloc of the graph



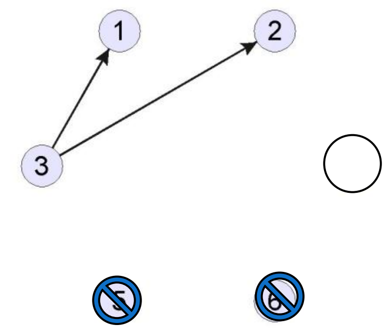
$E_g(S_1) = 0,5$



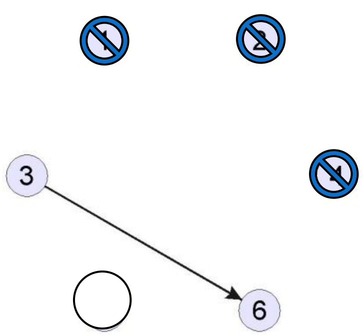
$E_g(S_2) = 0,333$



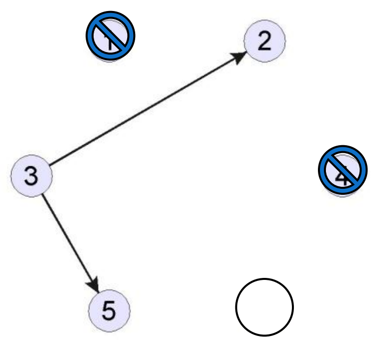
$E_g(S_3) = 0,342$



$E_g(S_4) = 0,333$



$E_g(S_5) = 0,5$



$E_g(S_6) = 0,333$

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

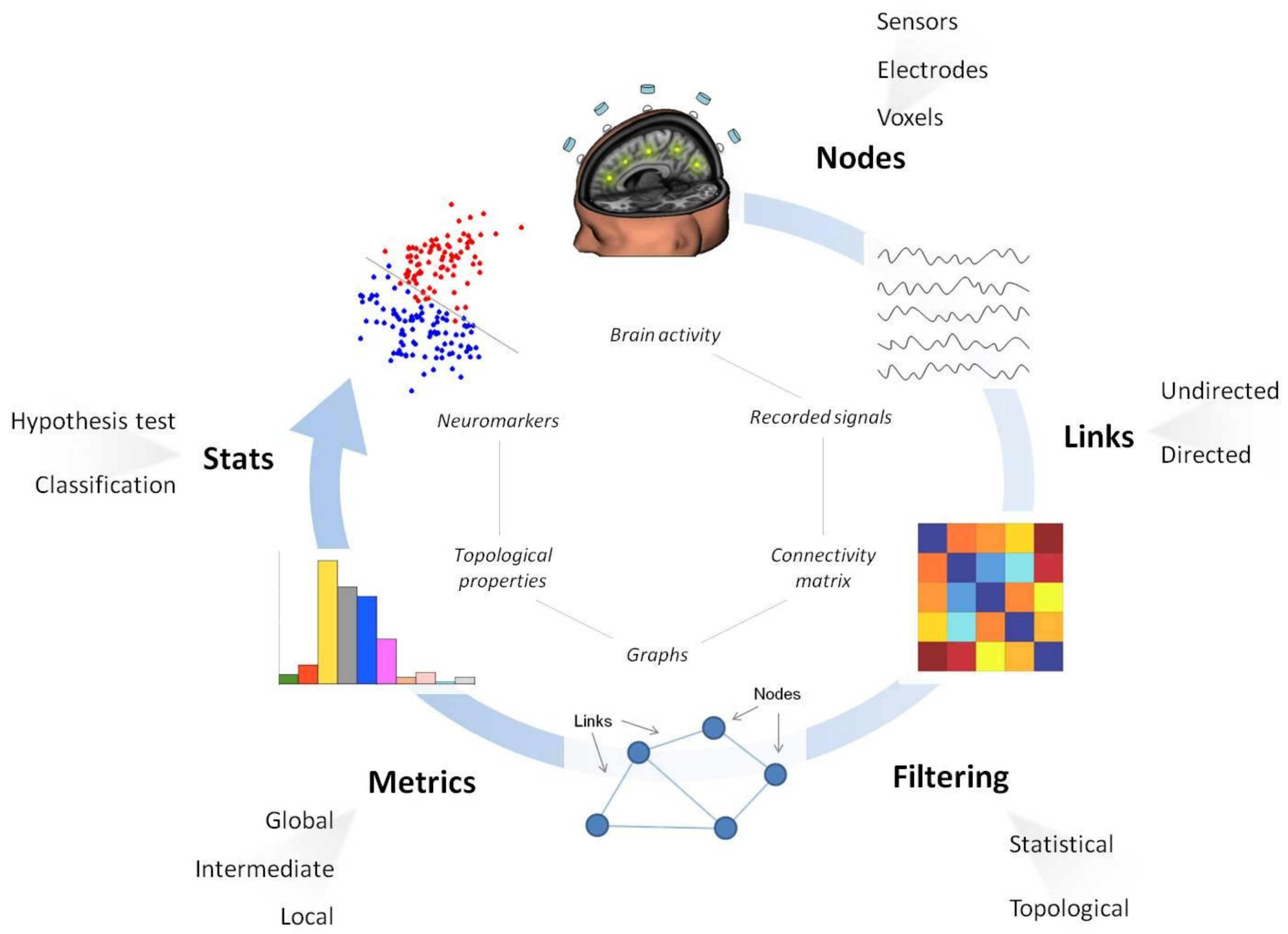
N = 6

$E_l(G) = (0,342 + 0,5*2 + 0,333*3) / 6 = 0,39$

Part IV

Application to brain data

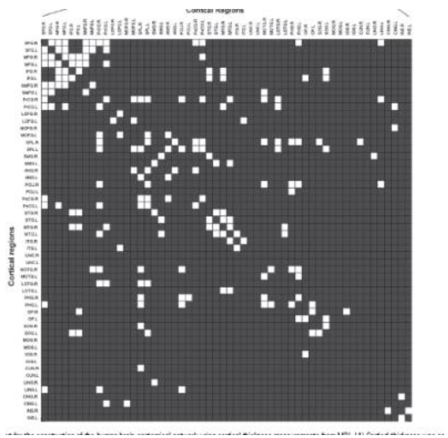
General framework

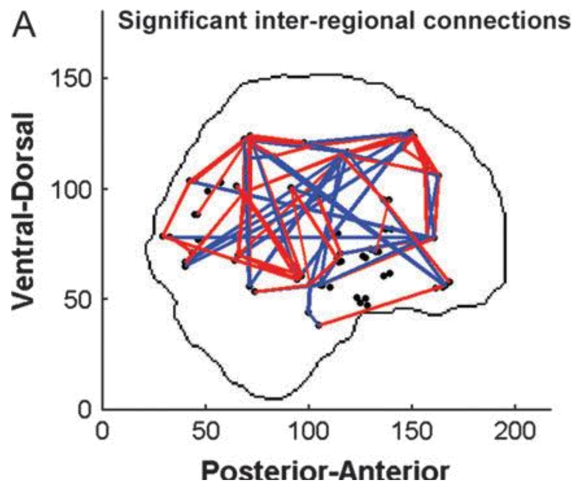


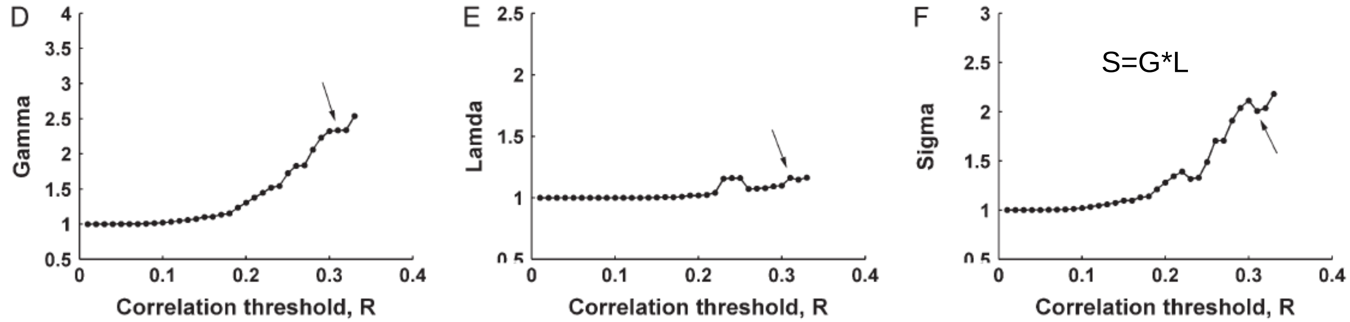
De Vico Fallani et al, Phi Tran Royal Soc B, submitted

Small-world structure

Data=MRI; Nodes=54; Task=Rest; Subj=Healthy.



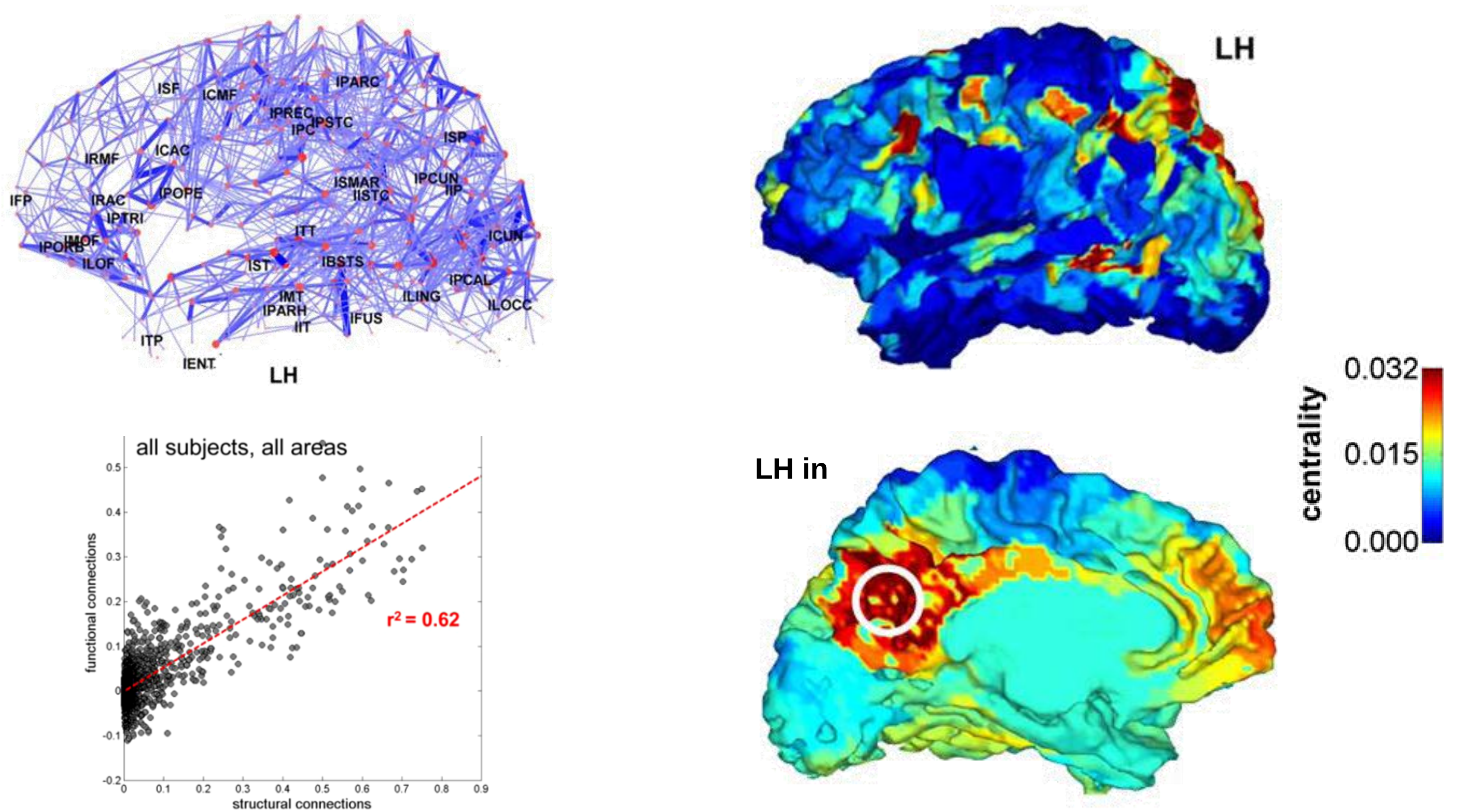




Adapted from He et al, Cerebr Cortex, 2007

Structure vs function

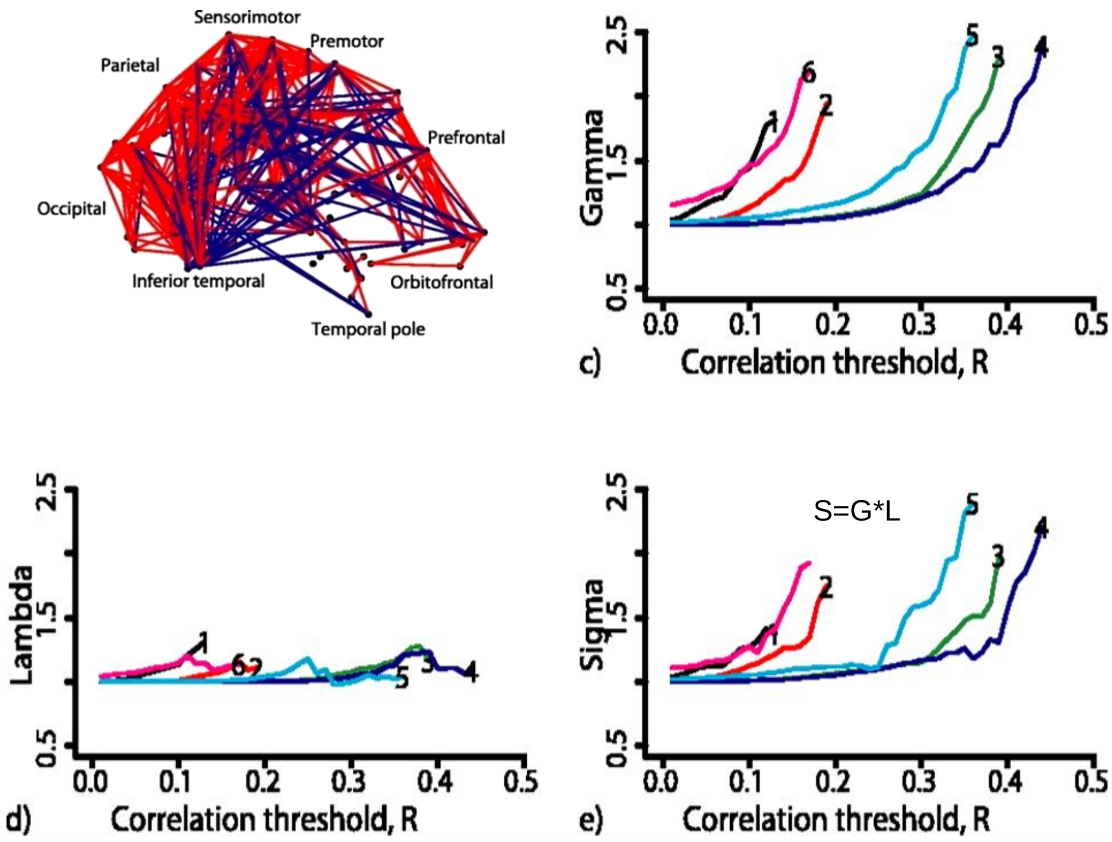
Data=DTI,fMRI; Nodes=998; Task=Rest; Subj=Healthy.



Adapted from Haghmann et al, PLOS Biol, 2008

Small-world function

Data=fMRI; Nodes=90; Task=Rest; Subj=Healthy.

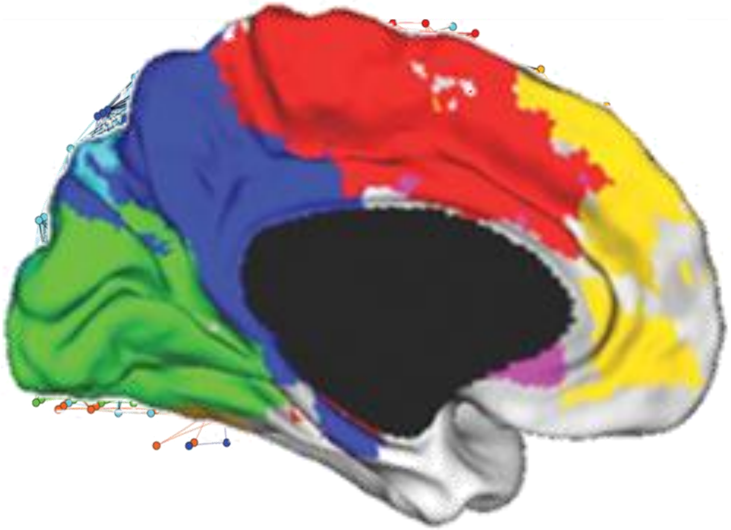


Adapted from Achard et al, J Neurosci, 2006

Modularity function

Data=fMRI; Nodes=1808; Task=Rest; Subj=Healthy.

$$Q = \sum_{ij} [A_{ij} - P_{ij}] \delta(g_i, g_j)$$

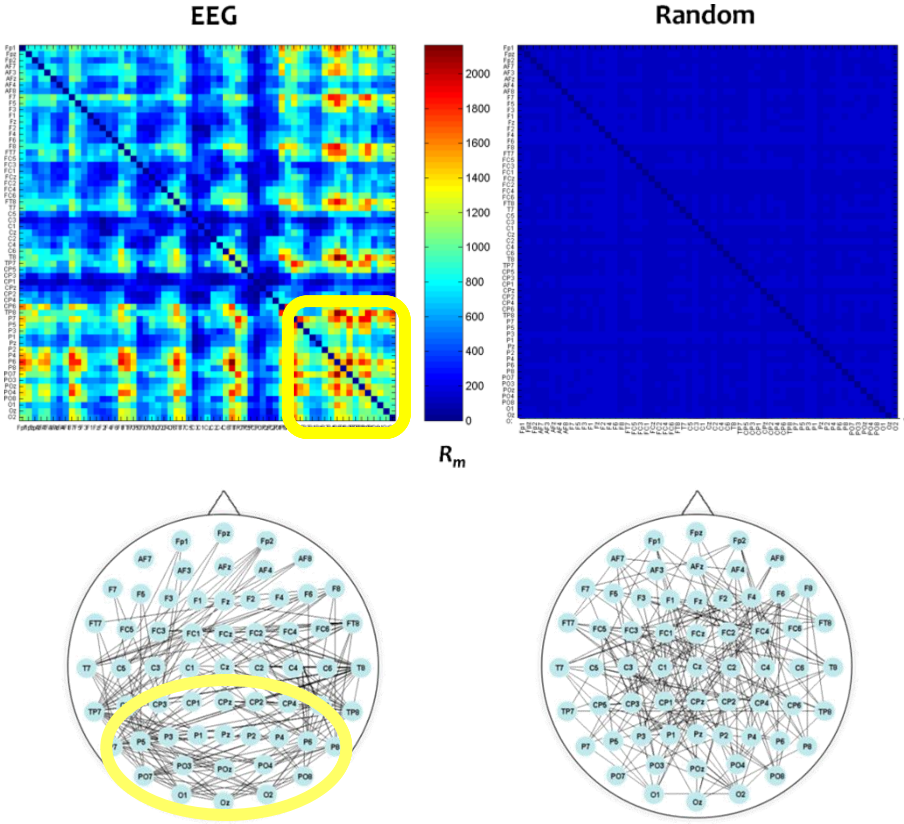


Ventral view

Adapted from Meunier et al, Front Neuroinf, 2009

Redundancy function

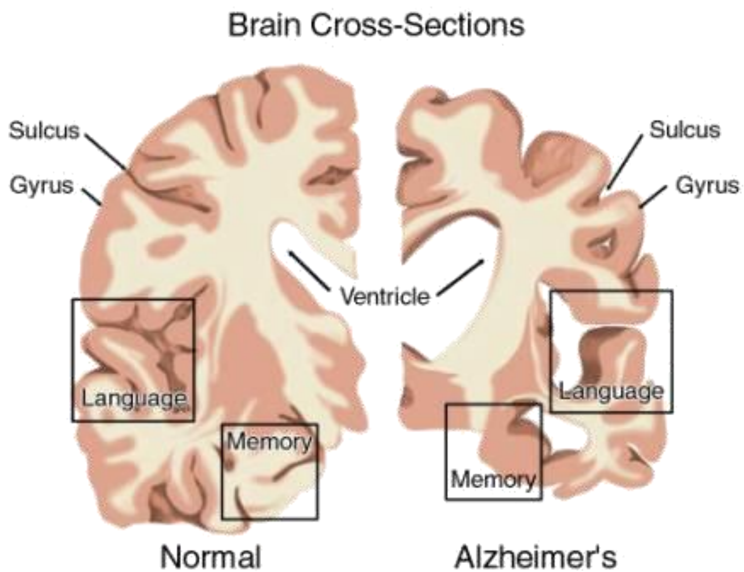
Data=EEG; Nodes=61; Task=Rest; Subj=Healthy.



De Vico Fallani et al, Int J Bifurc and Chaos, 2012

Neurodegeneration: Alzheimer’s

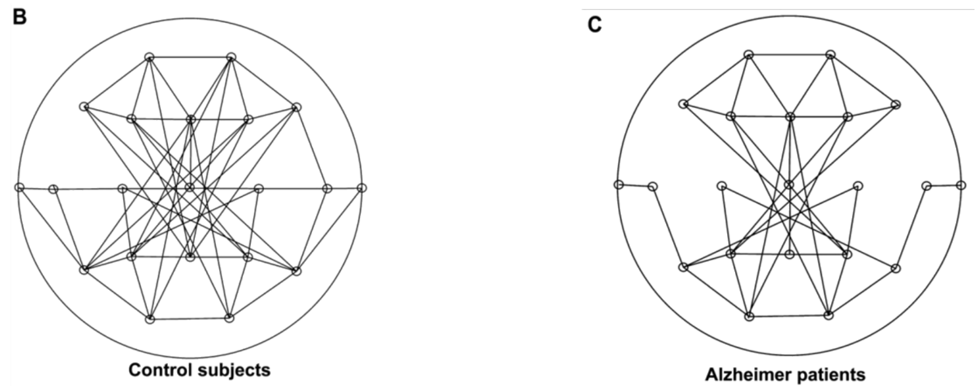
Alzheimer disease, is the most common form of dementia

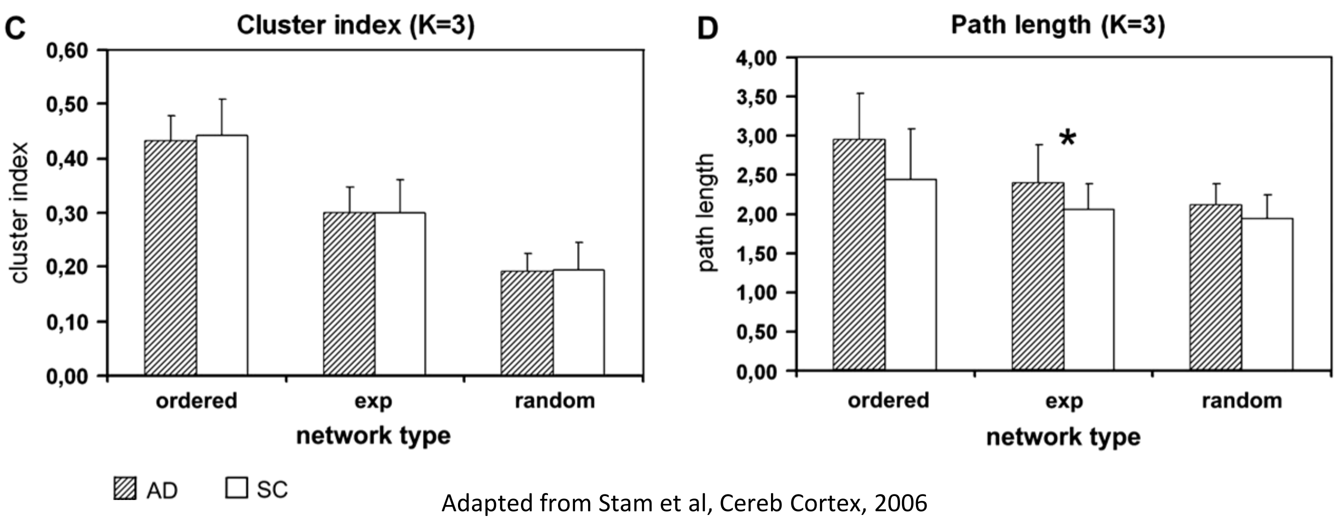


Symptoms can include confusion, irritability, aggression, mood swings, trouble with language, and long-term memory loss

Neurodegeneration: Alzheimer's

Data=EEG; Nodes=18; Task=Rest; Subj=Healthy Vs Disease





Adapted from Stam et al, Cereb Cortex, 2006

Neural disorder: Epilepsy

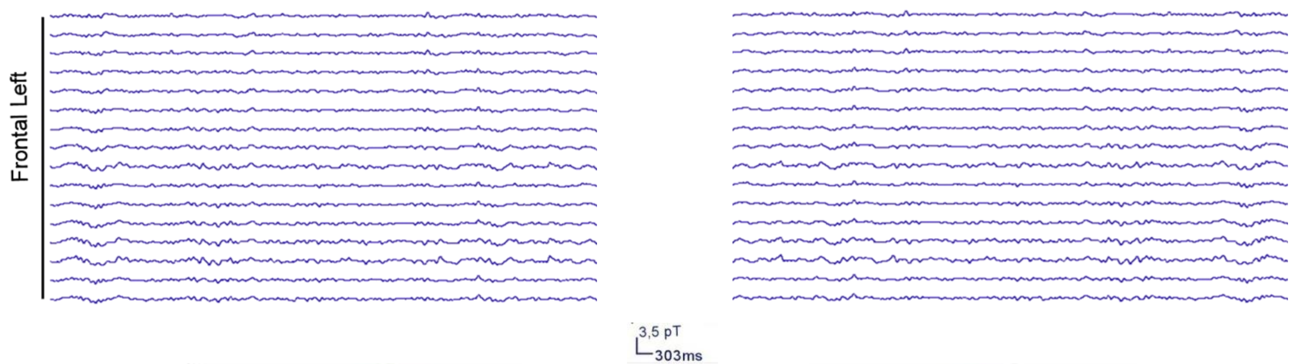
Absence seizures are brief generalized epileptic seizures of sudden onset and termination.

The hallmark of the absence seizures is abrupt and sudden onset impairment of consciousness, interruption of ongoing activities, a blank stare, possibly a brief upward rotation of the eyes

Neural disorder: Epilepsy

Data=MEG; Nodes=151; Task=Rest; Subj=Healthy Vs Disease

Healthy **Patient**

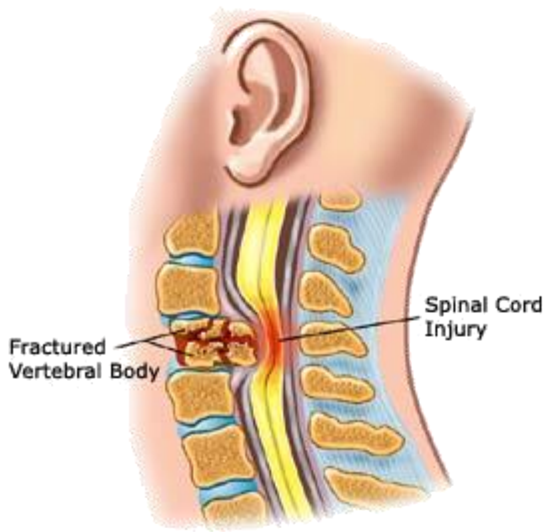


Healthy Epileptic

Adapted from Chavez et al, Phys Rev Lett, 2010

Brain plasticity: spinal cord injury

An injury to the spinal cord that is caused by trauma instead of disease

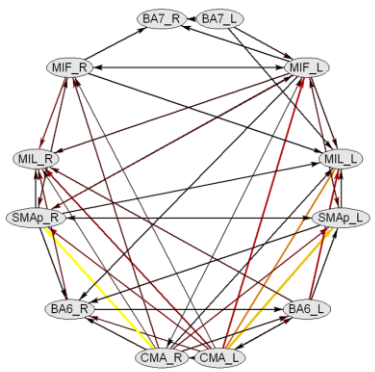


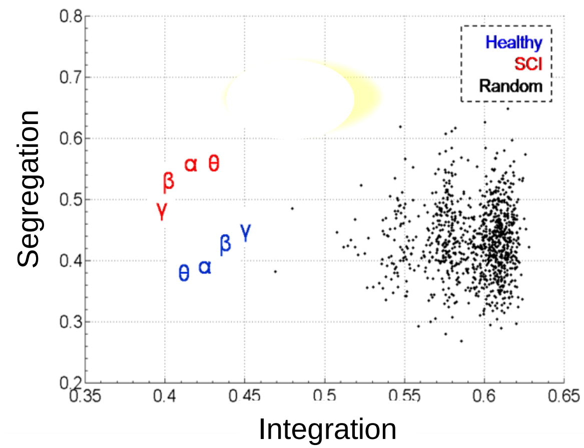
Depending on where the spinal cord and nerve roots are damaged, the symptoms can vary widely, from pain to paralysis to incontinence

Brain plasticity : spinal cord injury

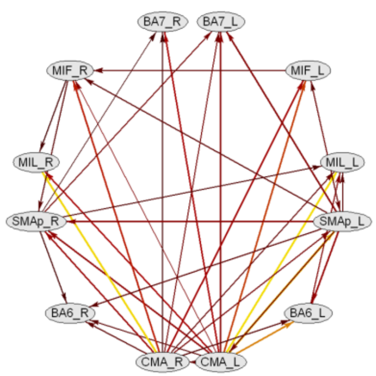
Data=EEG sources; Nodes=12; Task=motor; Subj=Healthy Vs Disease

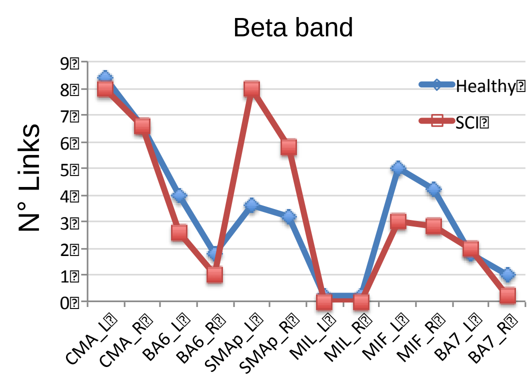
Healthy





SCI

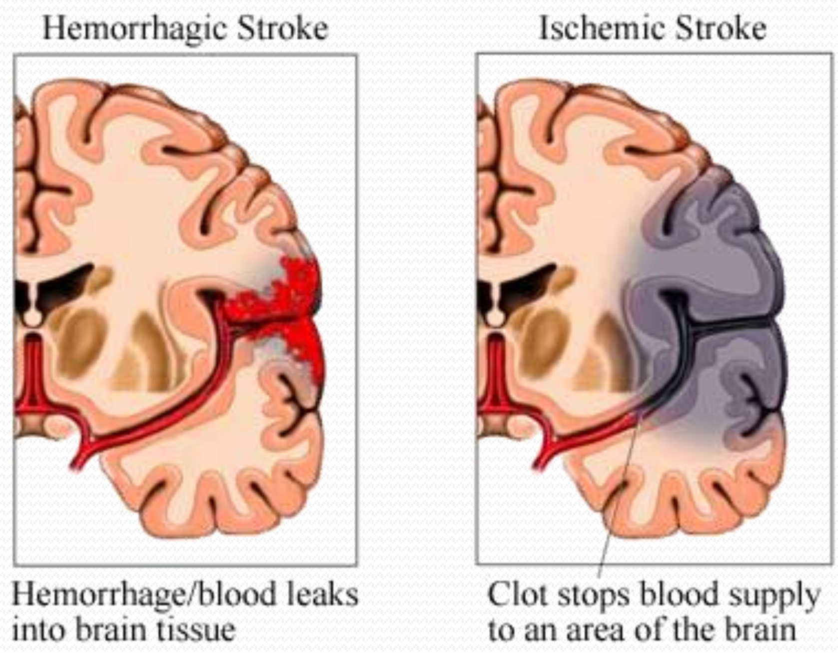




De Vico Fallani et al, Hum Brain Mapp, 2007

Brain plasticity: Stroke

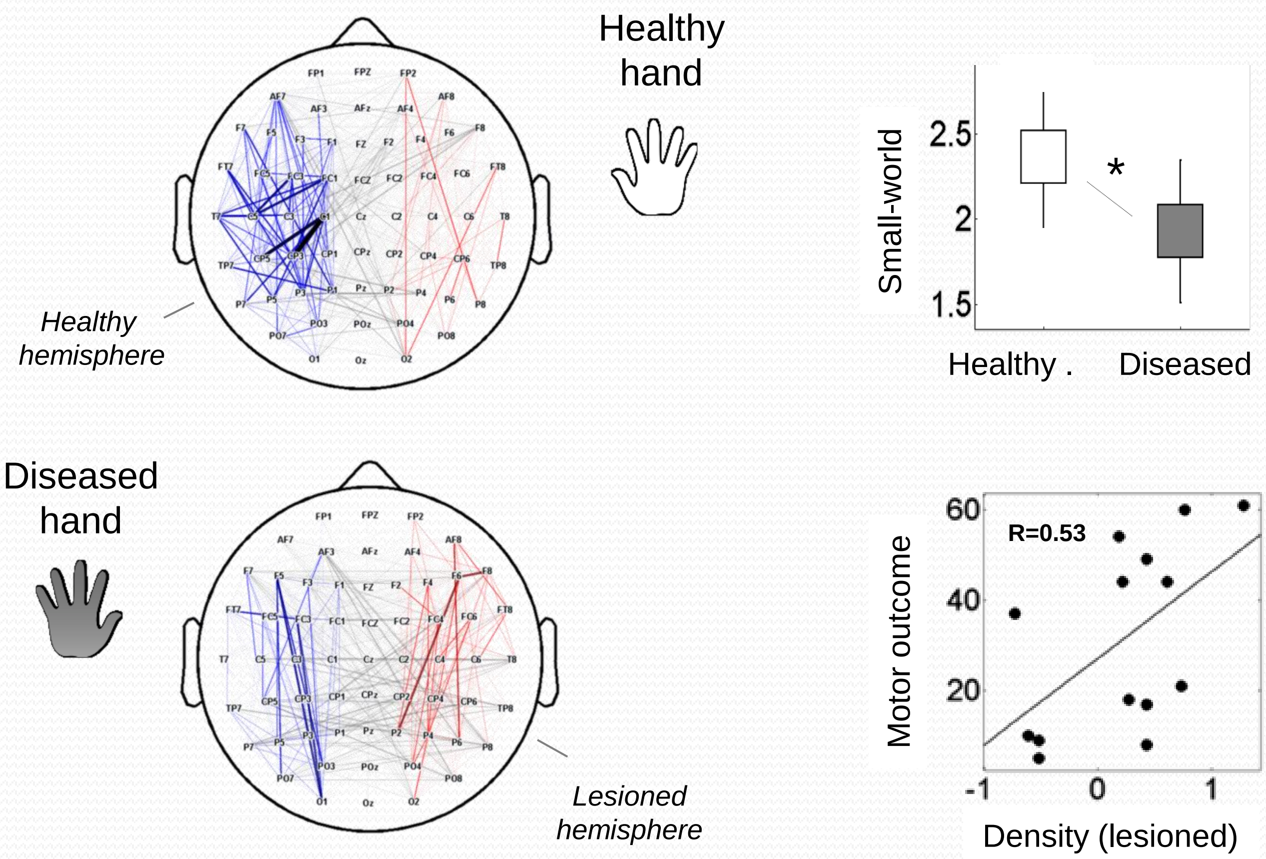
*A **stroke** is a rapid loss of brain function(s) due to disturbance in the blood supply to the brain.*



As a result, the affected area of the brain cannot function, which might result in an inability to move one or more limbs on <u>one side</u> of the body

Brain plasticity: Stroke

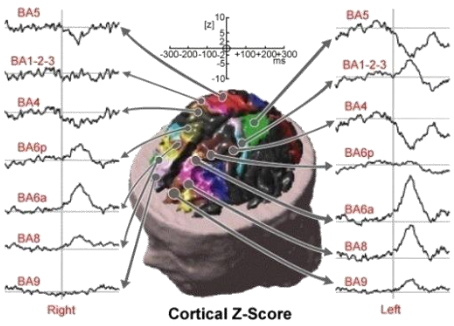
Data=EEG; Nodes=61; Tasks=motor; Subj=Diseased



De Vico Fallani et al, Neuroimage, 2013

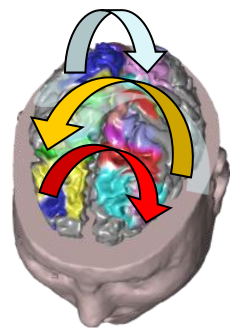
Concluding remarks

Univariate



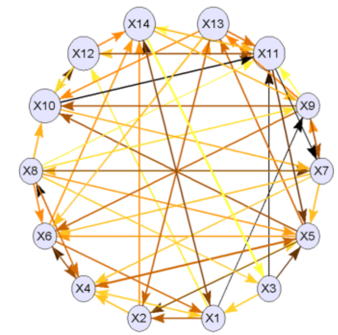
Activity analysis

Bivariate



Connectivity analysis

Multivariate



Graph analysis

1) Appropriate methods for specific questions.

2) Verify operational methodological constraints.

3) Network thresholding.

French brain networks

https://sites.google.com/site/fr2eborn/

FreeBorN

French Brain Networks

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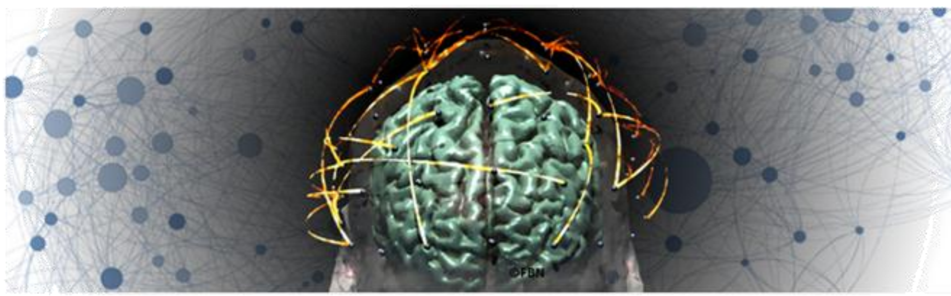

Welcome!

The FreeBorN (FBN) consortium is a free association of scientists working on the French territory. The consortium aims at promoting the interaction and visibility of the research teams studying brain connectivity and network theory.

What's a brain network?

The brain can be conceived as a networked system composed of nodes coincident with different brain sites and links which in the current view can either represent anatomical tracts between brain regions or measures of statistical dependencies between their electrical activity. Recent evidences unveiled that the way brain regions are connected is typically neither regular nor random. Instead brain networks, like other real networked systems, tend to exhibit a complex structure theoretically consistent with the capability of processing information within regional clusters and avoiding excessive connections between clusters. An important goal in these research endeavors is to identify how brain network organization can inform our understanding of the brain's intuitive need to balance the two competing principles of integration and segregation and how alterations in brain structure and dynamics can lead to alterations in human behavior and cognitive function.

Teams
The list of the French teams constituting the FreeBorN (FBN) consortium. Specific information about each team can be found here.

Gallery
A selection of the best pictures from the scientific artciles published by the teams of FBN.

Events
Upcoming national and international events (e.g. conferences, shoots, etc.) concerning topics related to brain networks.

References

Suggested review article

1. Bullmore E, Sporns O. *Complex brain networks: graph theoretical analysis of structural and functional systems*. **Nat Rev Neurosci.** 2009 Mar;10(3):186-98.

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