Redes Funcionales Cerebrales: Estructura y Deterioro

Javier M. Buldú

http://www.complex.etsit.urjc.es/jmbuldu

Complex Systems Group

Universidad Rey Juan Carlos (Fuenlabrada, Madrid, Spain)

&

Center for Biomedical Technology (Boadilla, Madrid, Spain)

Functional Brain Networks: structure and impairment

Javier M. Buldú

http://www.complex.etsit.urjc.es/jmbuldu

Complex Systems Group

Universidad Rey Juan Carlos (Fuenlabrada, Madrid, Spain)

&
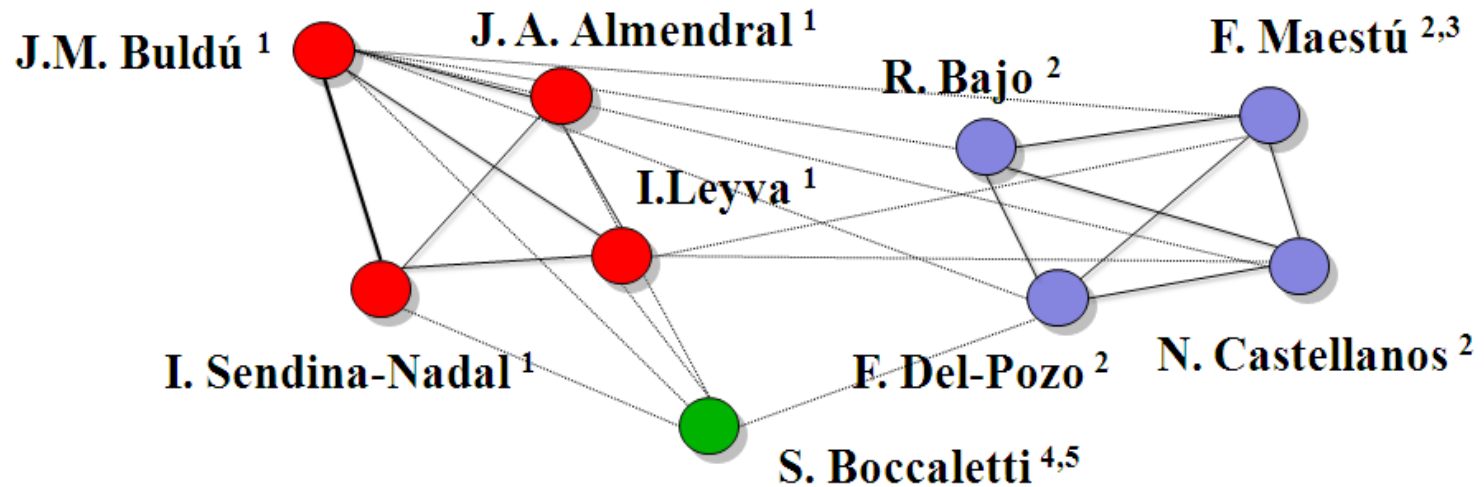
Center for Biomedical Technology (Boadilla, Madrid, Spain)

Collaborators

1.- **Complex Systems Group**, (URJC) and **Laboratory of Biological Networks** (CTB), Madrid, Spain
2.- Laboratory of Cognitive and Computational Neuroscience, CTB , Madrid, Spain
3.- Centro MEG, Complutense University, Madrid, Spain
4.- CNR-Institute for Complex Systems, Florence, Italy
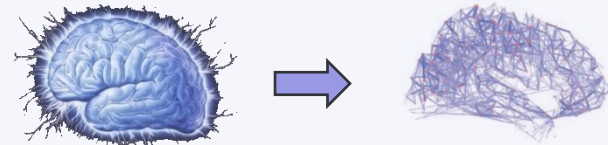**5.-** Computational Systems Biology, Centre for Biomedical Technology, Madrid, Spain

Outline of the Seminar

❑ *Complex networks and the brain*
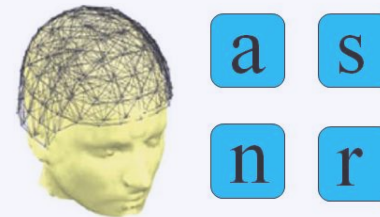
❑ *Anatomical Networks*

❑ *Functional Networks*

❑ *From Healthy to Impaired Networks*

❑ *Applications*

❑ *Mild Cognitive Impairment*

❑ *Evaluation of Trauma Therapy*

❑ *Evolutionary Network Models*

❑ *Mild Cognitive Impairment*

❑ *Evaluation of Trauma Therapy*

❑ *Conclusions*

Outline of the Seminar

❑ **Complex networks and the brain**

    ❑ *Anatomical Networks*

    ❑ *Functional Networks*

    ❑ *From Healthy to Impaired Networks*

❑ *Applications*

    ❑ *Mild Cognitive Impairment*

    ❑ *Evaluation of Trauma Therapy*

❑ *Evolutionary Network Models*

    ❑ *Mild Cognitive Impairment*
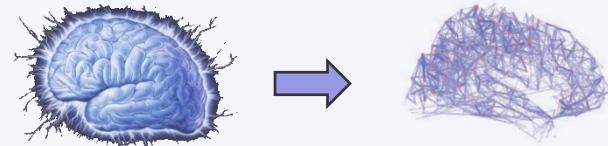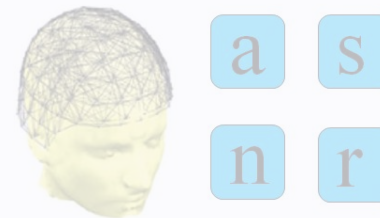
    ❑ *Evaluation of Trauma Therapy*

❑ *Conclusions*

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Read more at: *Boccaletti et al., Phys. Rep., (2006)*
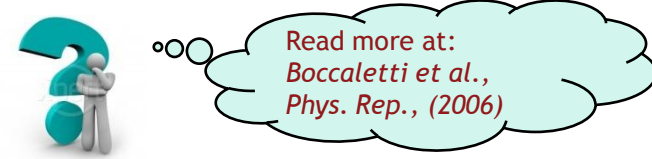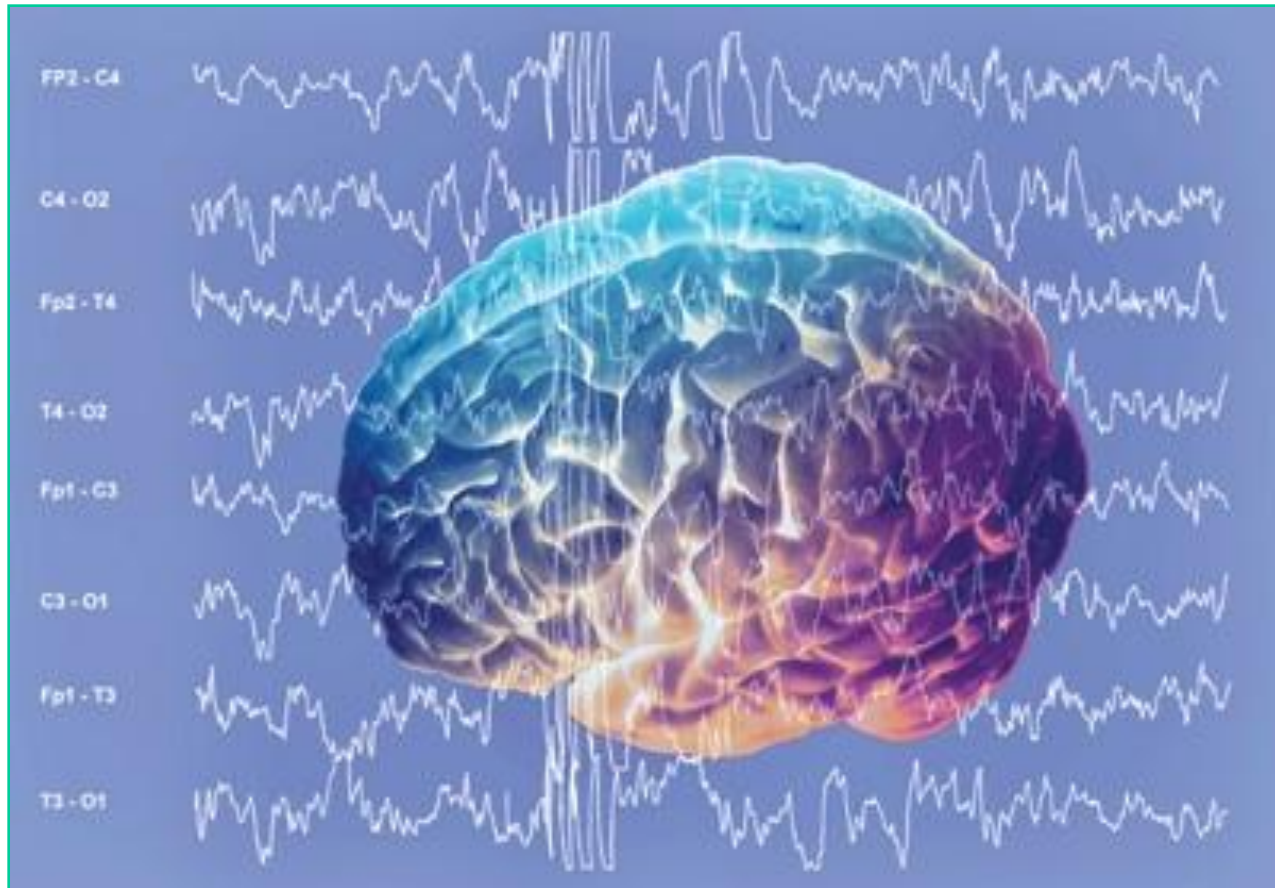
❑ **Complex Networks Analysis has been SUCCESSFULLY applied to many kinds of different COMPLEX SYSTEMS:**
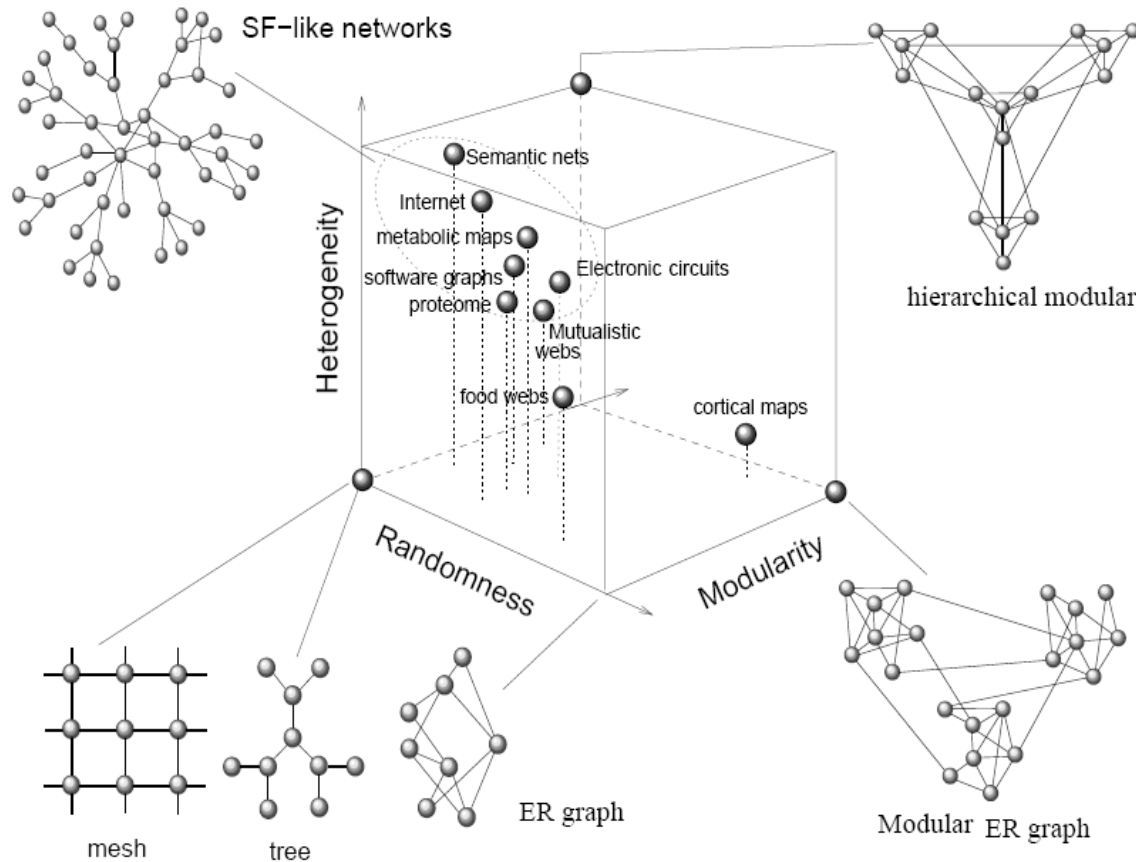
From: R.V. Solé and S. Valverde, Lecture Notes in Physics, **650**, 189, 2004

Complex Networks and the Brain

❑ **The brain is the most challenging complex systems that we are coping with:**

Complex Networks and the Brain

Anatomical Networks

Functional Networks

- **Histological Analysis**
- **DTI (MRI)**

- **EEG**
- **MEG**
- **fMRI**

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

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

Anatomical Networks

Anatomical Networks
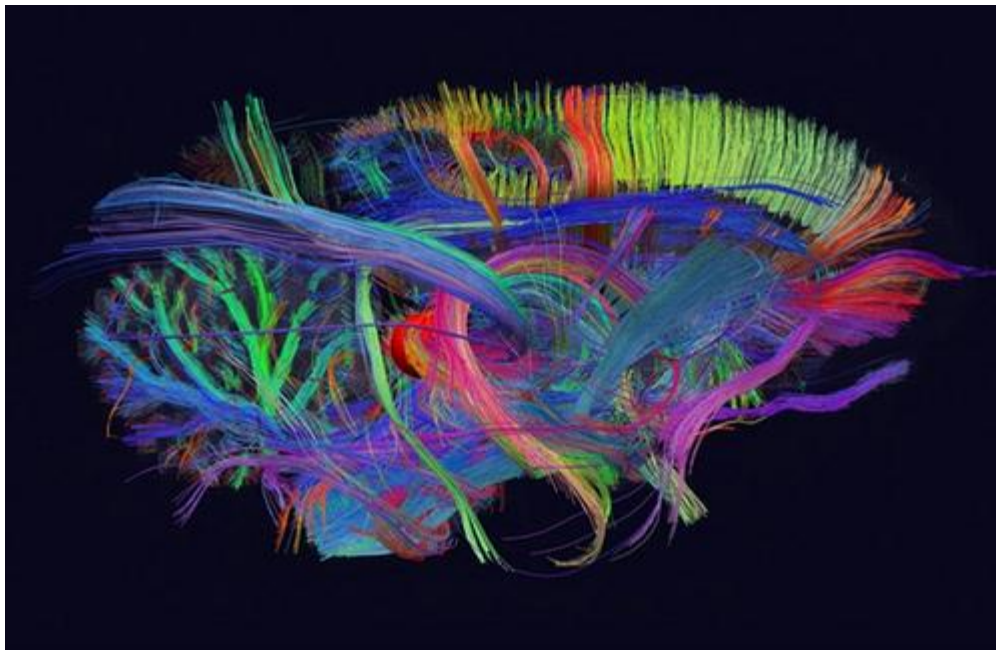
❑ **Anatomical Networks:** The connectome

    ❑ A connectome is a comprehensive map of neural connections in the brain. The production and study of connectomes, known as connectomics, may range in scale from a detailed map of the full set of neurons and synapses of an organism to a macro scale description of the structural connectivity between all cortical areas and subcortical structures.

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos
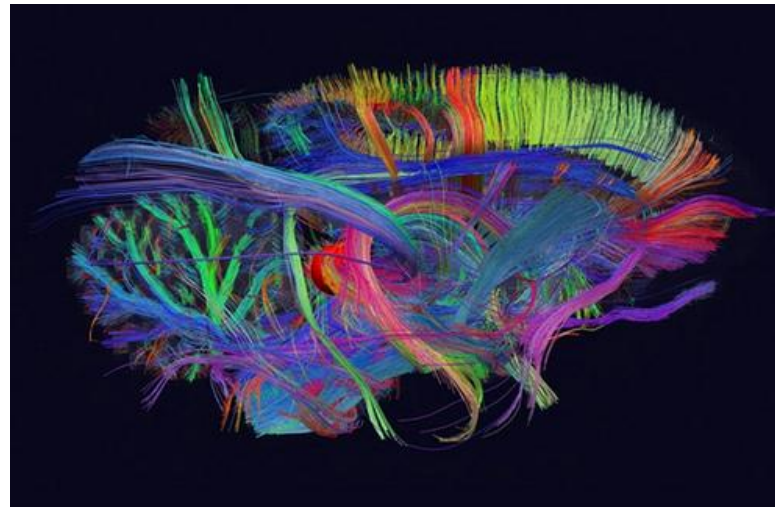
Anatomical Networks

❑ **Anatomical Networks:**

C. Elegans: It is the only living system that has been fully mapped. It has 302 neurons and average degree <k>≈29.

It has low shortest path and high clustering: it is a small-world network.

Existence of network motifs.

The tail of the distribution of degrees p(k) is power-law.
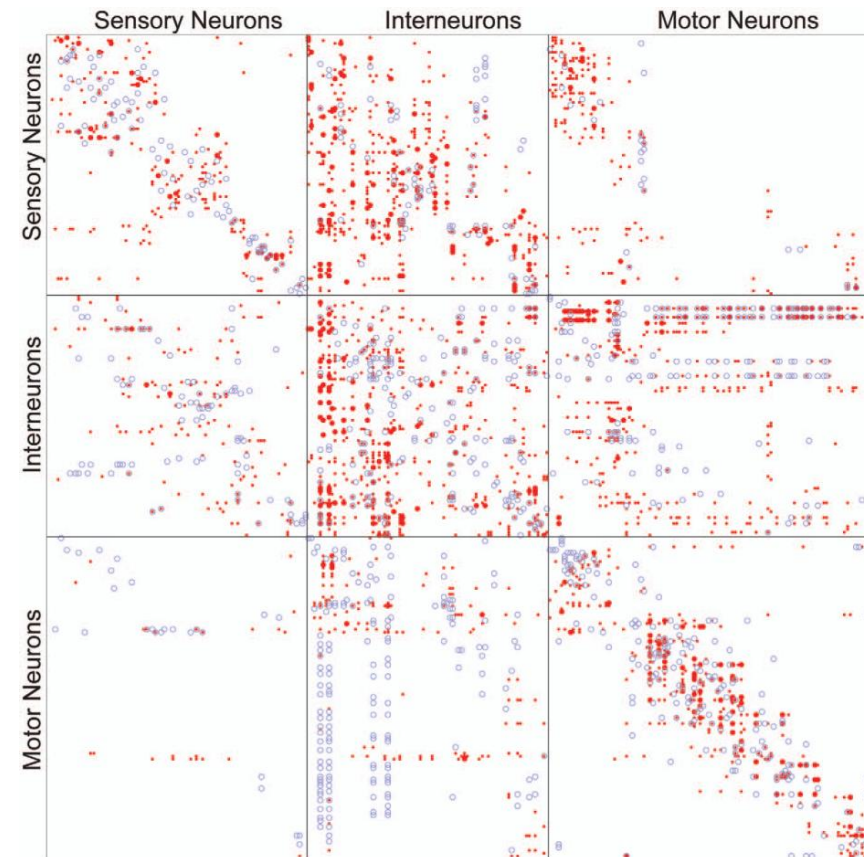
Gap juntions connections and chemical synapses of C. Elegans neurons. From Varshney, PLoS Comp. Biol, 7, 1001066 (2011)

Anatomical Networks

❑ **Other anatomical networks:**

❑ **Macaque cortex:**
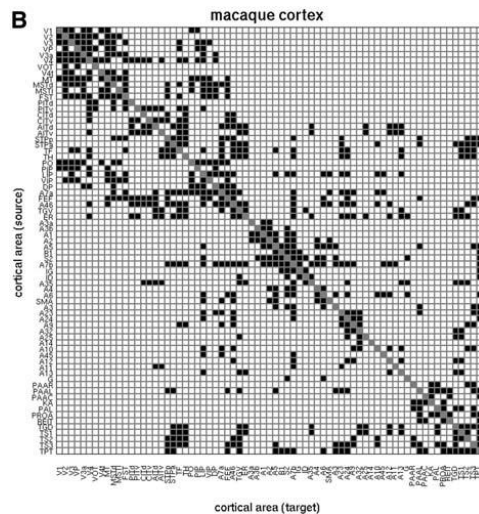
N=71 Brain Areas and L=746
Small-world
No power-law

❑ **Cat cortex:**
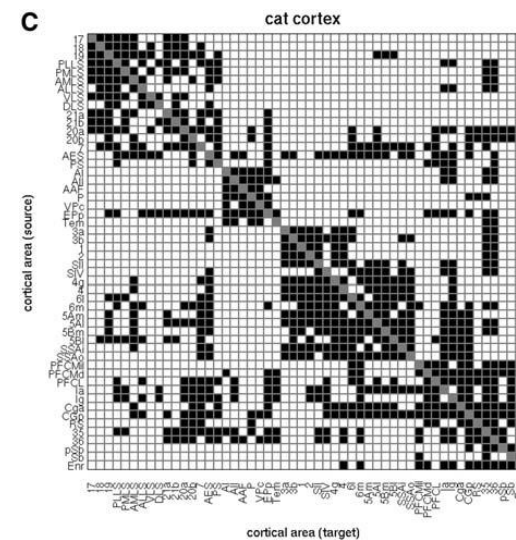
N= 52 Brain Areas and L=820
Small-world
No power-law

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

Anatomical Networks

- **The anatomical structure of Human Brain:**
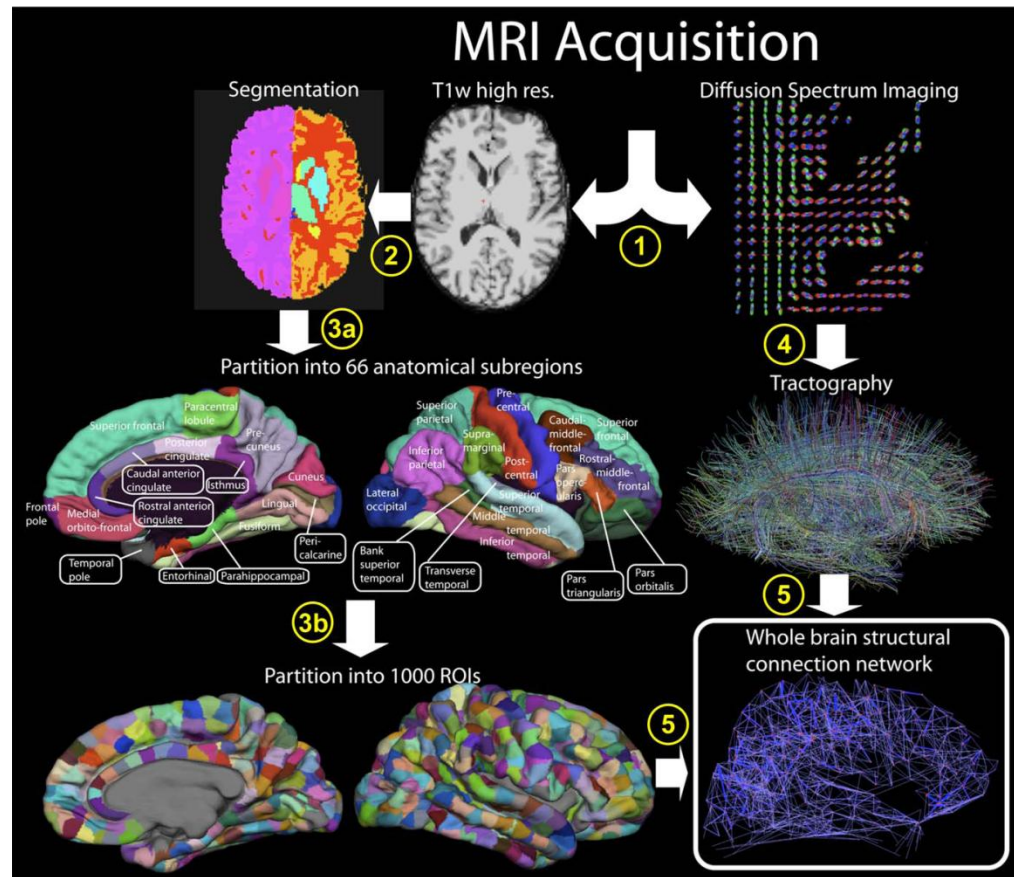
- **Main results are obtained from magnetic resonance imaging**

- **Difussion Tensor Imaging (DTI) and Difussion Spectrum Imaging (DSI) allow reconstruction of region connectivity (white matter) by mesuring the difussion of water molecules.**

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

Anatomical Networks

❑ **The anatomical structure of Human Brain:**

❑ **Exponential** (not scale-free) degree distribution (note that there are 66 subregions and 998 ROIs).

❑ **Small-world** attributes.

❑ **Multiple modules** interlinked by hub regions.

❑ **Positive assortativity**.

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

Anatomical Networks

❑ **Small-world every where!**

Small-World Brain Networks

DANIELLE SMITH BA

Many complex ne
of connections bet
the existence of re
anatomical and fu
and distributed/int
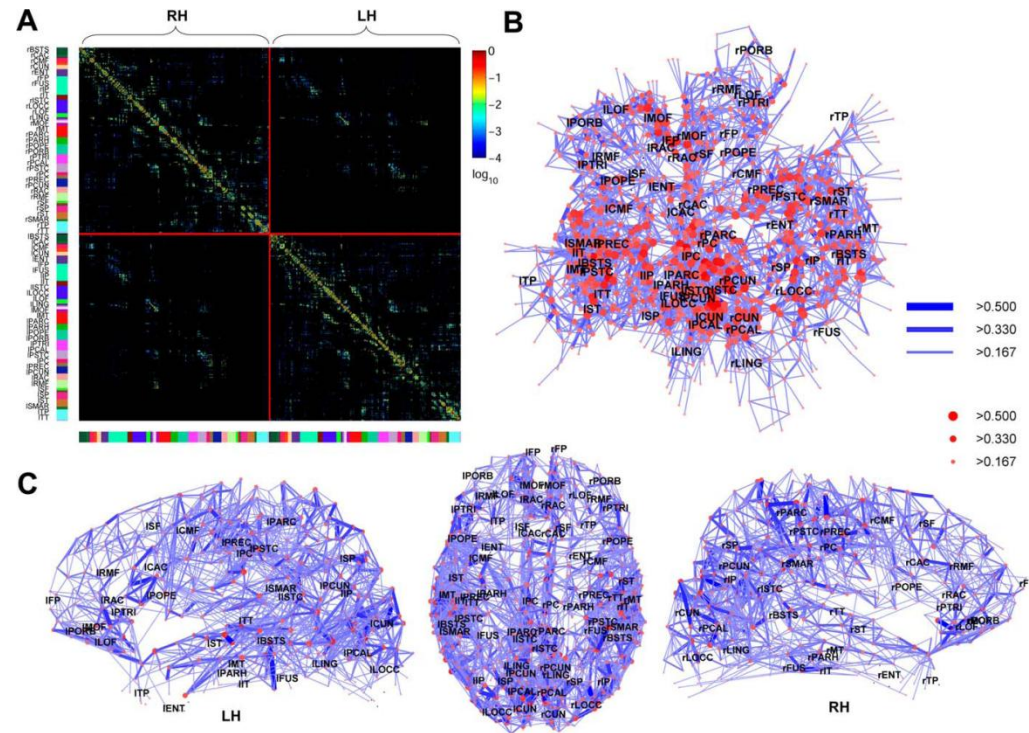minimize wiring co
mathematical con
been applied to qu
in the macaque m
tion pressure to de
niques and concep
from electroencep
the relevance of sn
of brain systems t
models provide a
systems. NEUROS

Behavioral/Systems/Co

A Resilient,

Human Bra

Highly Con

Sophie Achard,[1] Ray
Bullmore[1,3]

[1]Brain Mapping Unit a
Departments of Psyc
Cambridge CB2 2QQ,
Sant Boi de Llobregat
GlaxoSmithKline, Ca

Copyright © 2006 b

Neuroscience
From the Cover

Adaptive rec
functional n

Danielle S. Bas
Thomas Duke,[‡]

*Brain Mapping Unit,
Cambridge CB2 2Q(
[†]Unit for Systems Ne
Institute of Mental He
[‡]Biological and Soft
Cambridge, Cambri
[§]To whom correspon
etb23@cam.ac.uk
Edited by Marcus E.
October 23, 2006

MENTAL HEALTH & EMOTIONAL WELL-BEING

Save & Share   Printer Friendly 🖨
Font Size ᴛT ⊟ ⊞

It's a small world in your brain after all

Abnormal brain organization in Alzheimer's disease patients may
lead to easier diagnoses
by Jane Liaw

Your brain is a complex structure, a vast network of neurons responsible for
thought, feeling, impulse. Michael Greicius, assistant professor of neurology, has
long been fascinated with the mysterious workings of the brain, calling it "the organ
that talks back to you." Now Greicius and his co-workers have discovered
differences in the brain networks between people with Alzheimer's disease (AD)
and healthy controls—differences that may soon lead to easier diagnosis of the
disease.

Networks of all kinds work best when they include many hubs, such that data,
people or other elements can zip between them. This networking structure is called
"small-world" and occurs in many areas of life, including our own brains.

The hubs in small-world networks aren't necessarily close to one another, but they
can be reached from other hubs through just a few steps, making flow more
efficient. Take, for example, the path of news from a small town in the Bay Area,
such as Vallejo. A story from Vallejo might be reported by the media hub in San
Francisco, and perhaps picked up and reprinted by media hubs in New York or
internationally. The news doesn't travel from that Bay Area town to New York
through every small town media outlet in between.
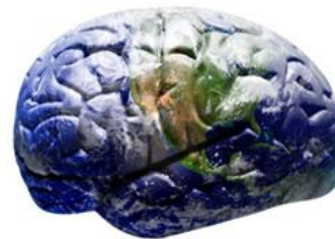
Anatomical Networks

❑ **Small-world every where!... so what?**

One of the first contributions of the Complex Network Theory to biological systems is the seminal paper of Watts and Strogatz

	L_{actual}	L_{random}	C_{actual}	C_{random}
Film actors	3.65	2.99	0.79	0.00027
Power grid	18.7	12.4	0.080	0.005
C. elegans	2.65	2.25	0.28	0.05

The small-world of *C. Elegans* neural network , with an edge joining two neurons if they are connected by either a synapse or a gap junction (n= 282, <k>= 14.). Table from Watts et al., 393, 440 (1998)

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Anatomical Networks

❏ **The Watts and Strogatz (WS) model:**
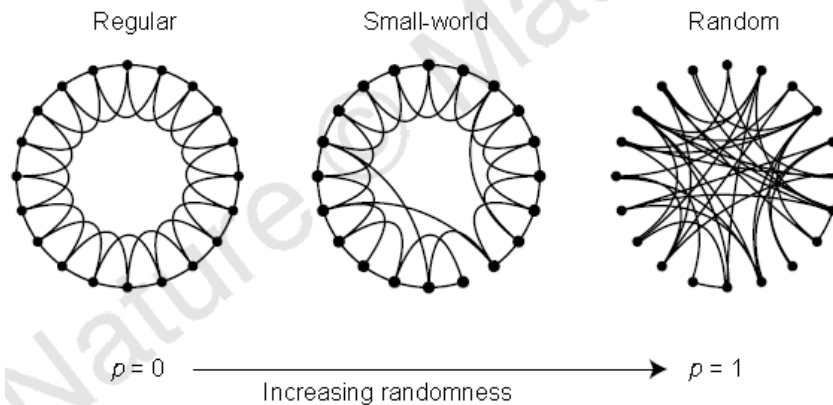
Small-world region
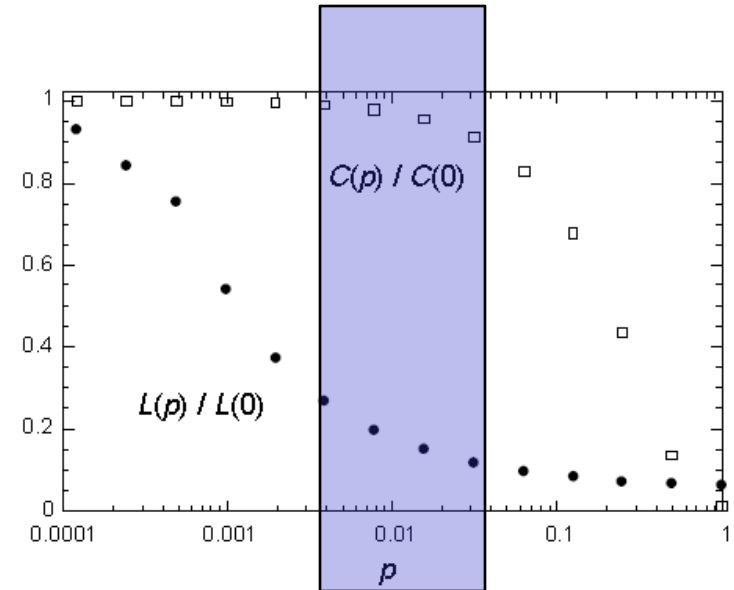
❏ **Nevertheless, the WS model does not take into account many features of the brain networks such as: modularity, assortativity, existence of hubs...**

Anatomical Networks

❑ **... in addition almost any network is small-world!**

The larger the network, the higher probability to be small-world.
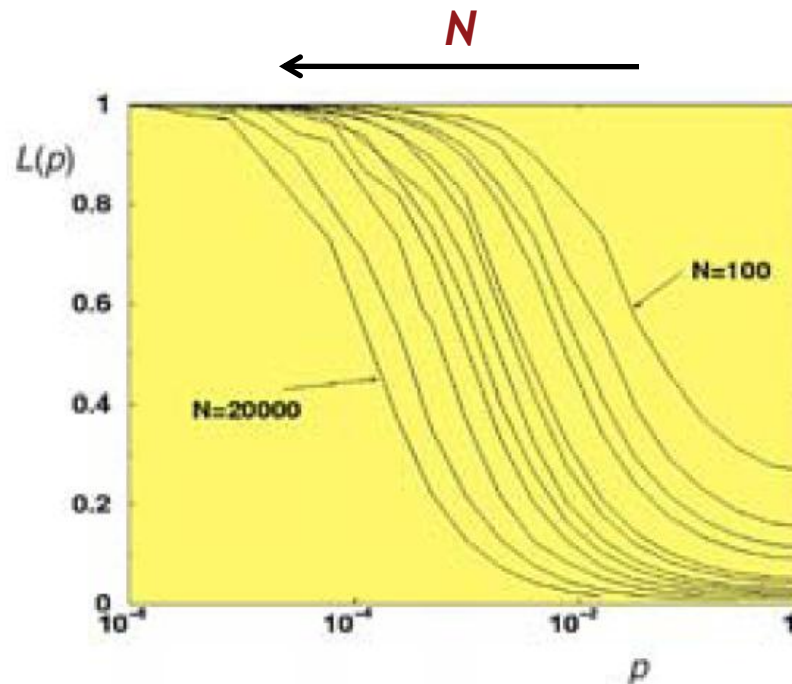
The rewiring of the links in order to entre the small world-region goes with:

$$p \sim 1/N$$

Figure from Barthelemy, PRL, 82,3180 (1999)

❑ Are anatomical networks efficient in transmitting information?

Nonoptimal Component Placement, but Short Processing Paths, due to Long-Distance Projections in Neural Systems

Marcus Kaiser[1,2,3*], Claus C. Hilgetag[3,4]

1 School of Computing Science, University of Newcastle, Newcastle upon Tyne, United Kingdom, 2 Institute of Neuroscience, University of Newcastle, Newcastle upon Tyne, United Kingdom, 3 International University Bremen, School of Engineering and Science, Bremen, Germany, 4 Boston University, Sargent College, Department of Health Sciences, Boston, Massachusetts, United States of America

It has been suggested that neural systems across several scales of organization show optimal component placement, in which any spatial rearrangement of the components would lead to an increase of total wiring. Using extensive connectivity datasets for diverse neural networks combined with spatial coordinates for network nodes, we applied an optimization algorithm to the network layouts, in order to search for wire-saving component rearrangements. We found that optimized component rearrangements could substantially reduce total wiring length in all tested neural networks. Specifically, total wiring among 95 primate (Macaque) cortical areas could be decreased by 32%, and wiring of neuronal networks in the nematode Caenorhabditis elegans could be reduced by 48% on the global level, and by 49% for neurons within frontal ganglia. Wiring length reductions were possible due to the existence of long-distance projections in neural networks. We explored the role of these projections by comparing the original networks with minimally rewired networks of the same size, which possessed only the shortest possible connections. In the minimally rewired networks, the number of processing steps along the shortest paths between components was significantly increased compared to the original networks. Additional benchmark comparisons also indicated that neural networks are more similar to network layouts that minimize the length of processing paths, rather than wiring length. These findings suggest that neural systems are not exclusively optimized for minimal global wiring, but for a variety of factors including the minimization of processing steps.
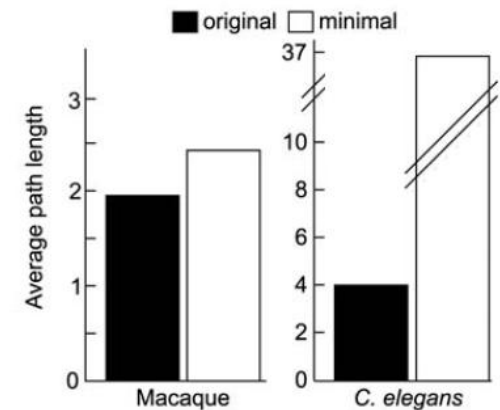
Anatomical Networks

❑ Are anatomical networks efficient in transmitting information?

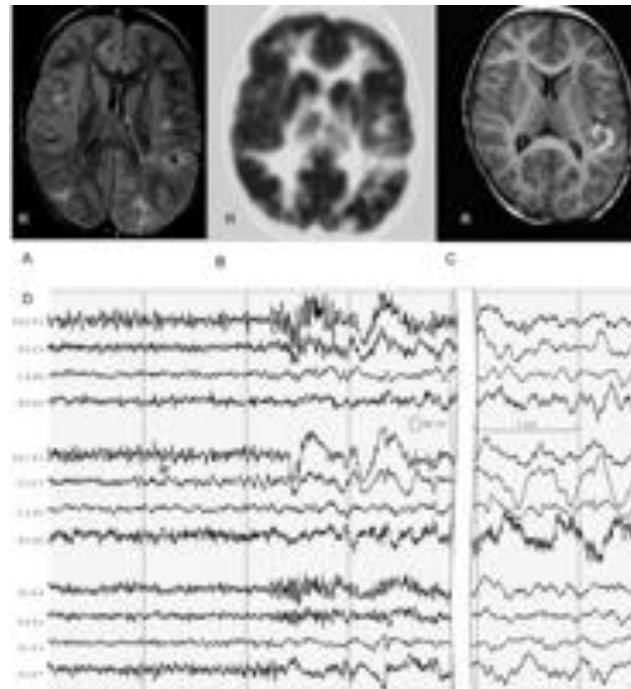**Macaque cortex:**

real

optimized
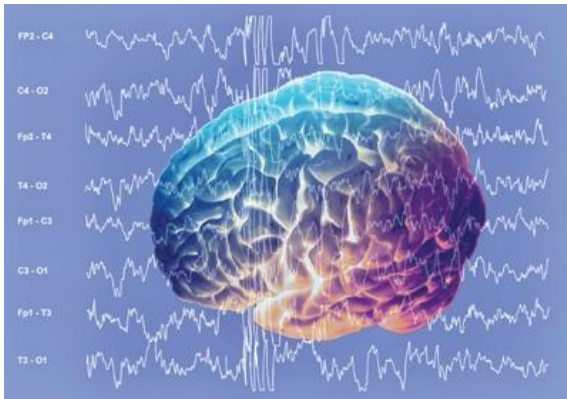
C. Elegans:

real

optimized
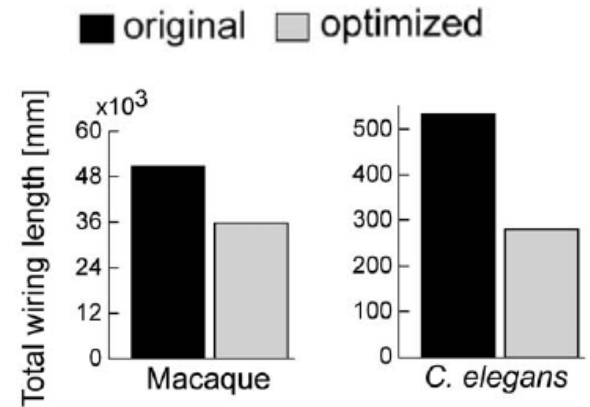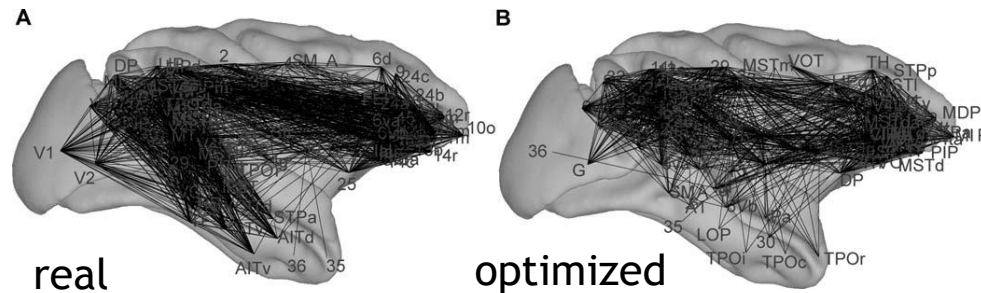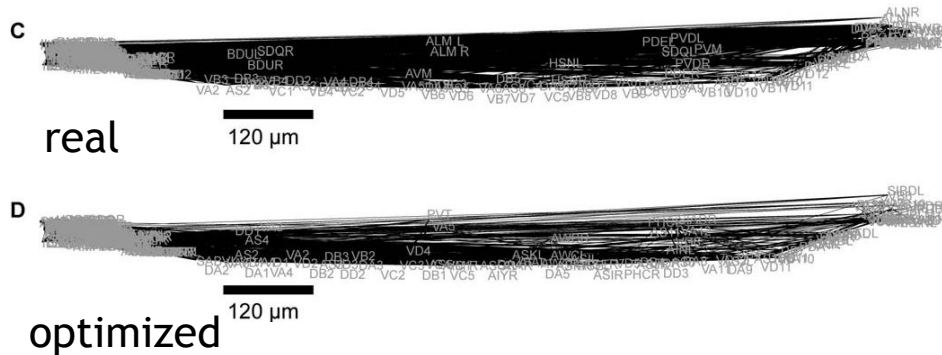
Functional Brain Networks

Functional brain networks

☐ How to obtain a functional network:

STEP 1

Measurement of brain activity

STEP 2
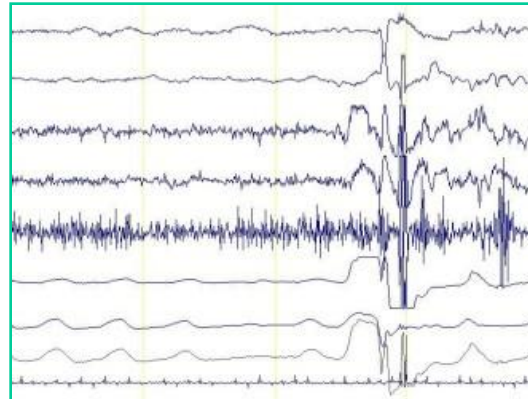
Time series analysis

STEP 3
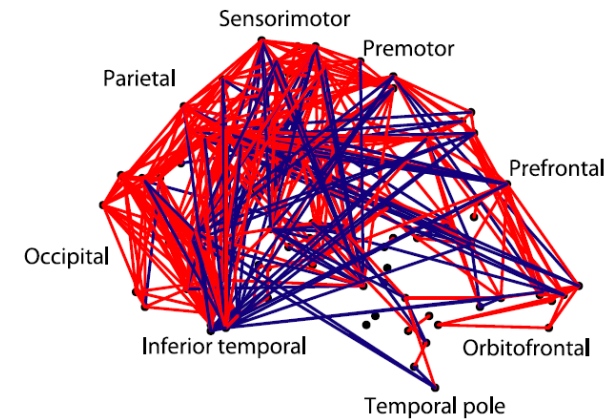
Network Analysis

Functional brain networks

❑ **STEP 1: How to measure the brain activity**

❑ **Functional MRI (fMRI).** The detection of changes in regional brain activity through their effects on blood flow and blood oxygenation (which, in turn, affect magnetic susceptibility and tissue contrast in magnetic resonance images). High spatial resolution (~mm^3) but low temporal resolution (~ seconds).

❑ **Electroencephalography (EEG).** A technique used to measure neural activity by monitoring electrical signals from the brain, usually through scalp electrodes. EEG has good temporal resolution but relatively poor spatial resolution.

❑ **Magnetoencephalography (MEG).** A method of measuring brain activity by detecting perturbations in the extracranial magnetic field that are generated by the electrical activity of neuronal populations. Like EEG, it has good temporal resolution but relatively poor spatial resolution. It has better resolution than EEG.

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Functional brain networks
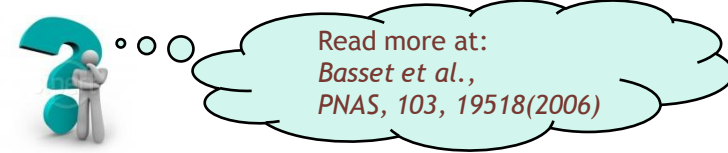
❑ **How to measure the brain activity**

MEG and EEG allow the band decomposition of the signal into frequency bands

Wavelet decomposition level	Frequency range, Hz	Corr	τ	k	L	C	σ	ζ	$S\ (\times10^{-3})$
Resting									
1	37.5–75	0.18 ± 0.02	0.50 ± 0.05	16.3 ± 5.1	4.5 ± 0.5	0.23 ± 0.02	1.9±0.2	61 ± 14	9.7 ± 1.9
2	18.8–37.5	0.26 ± 0.02	0.74 ± 0.04	12.6 ± 3.1	5.2 ± 0.5	0.21 ± 0.02	1.9±0.1	70 ± 41	8.2 ± 2.3
3	9.4–18.8	0.30 ± 0.03	0.81 ± 0.03	12.4 ± 1.8	5.4 ± 0.4	0.20 ± 0.01	1.9±0.2	100 ± 72	6.3 ± 2.7
4	4.7–9.4	0.30 ± 0.03	0.82 ± 0.03	12.3 ± 2.0	5.4 ± 0.4	0.21 ± 0.01	1.9±0.2	106 ± 75	6.4 ± 3.3
5	2.3–4.7	0.30 ± 0.02	0.81 ± 0.02	12.5 ± 2.0	5.2 ± 0.4	0.21 ± 0.01	2.0±0.1	118 ± 71	7.6 ± 2.9
6	1.1–2.3	0.33 ± 0.05	0.83 ± 0.02	13.7 ± 3.3	5.1 ± 0.4	0.23 ± 0.02	1.9±0.1	137 ± 62	6.0 ± 2.4
Tapping									
1	37.5–75	0.18 ± 0.03	0.49 ± 0.09	16.9 ± 5.1	4.4 ± 0.6	0.23 ± 0.02	1.8±0.2	132 ± 21	10.2 ± 3.5
2	18.8–37.5	0.23 ± 0.02	0.69 ± 0.04	13.0 ± 2.6	5.0 ± 0.4	0.21 ± 0.01	2.0±0.1	105 ± 9	9.8 ± 2.7
3	9.4–18.8	0.27 ± 0.02	0.77 ± 0.03	12.2 ± 1.7	5.2 ± 0.4	0.21 ± 0.01	2.0±0.1	118 ± 27	8.4 ± 2.8
4	4.7–9.4	0.28 ± 0.03	0.79 ± 0.02	12.7 ± 2.1	5.2 ± 0.5	0.21 ± 0.01	1.9±0.2	116 ± 35	8.2 ± 2.9
5	2.3–4.7	0.30 ± 0.05	0.81 ± 0.01	13.8 ± 4.9	5.1 ± 0.5	0.21 ± 0.01	1.9±0.2	137 ± 47	7.2 ± 2.6
6	1.1–2.3	0.34 ± 0.06	0.82 ± 0.01	16.7 ± 8.3	4.9 ± 0.8	0.22 ± 0.02	1.7±0.2	144 ± 55	5.2 ± 1.6

Corr: average correlation of the whole brain network before thresholding; τ: threshold applied to wavelet correlation matrices; k: average degree of the network; L: average path length; C: average clustering; σ: small-world scalar value; ζ, characteristic length scale in millimeters; S, synchronizability. *(N=275)*

Functional brain networks

❑ **STEP 1: How to measure the brain activity**

    ❑ **LIMITATIONS:**

        ❑ **Low spatial resolution (we have ~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**

Functional brain networks

❑ **STEP 2: Time series analysis**

   ❑ **We have to extract correlations between nodes/regions**

❑ **Several linear and nonlinear techniques:**

- Cross-correlation
- Wavelet coherence
- Synchronization Likelihood
- Generalized Synchronization
- Phase Synchronization
- Mutual Information
- Granger Causality

For a review read:

Pereda et al, Prog. Neurobiol, 77 (2005)

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos
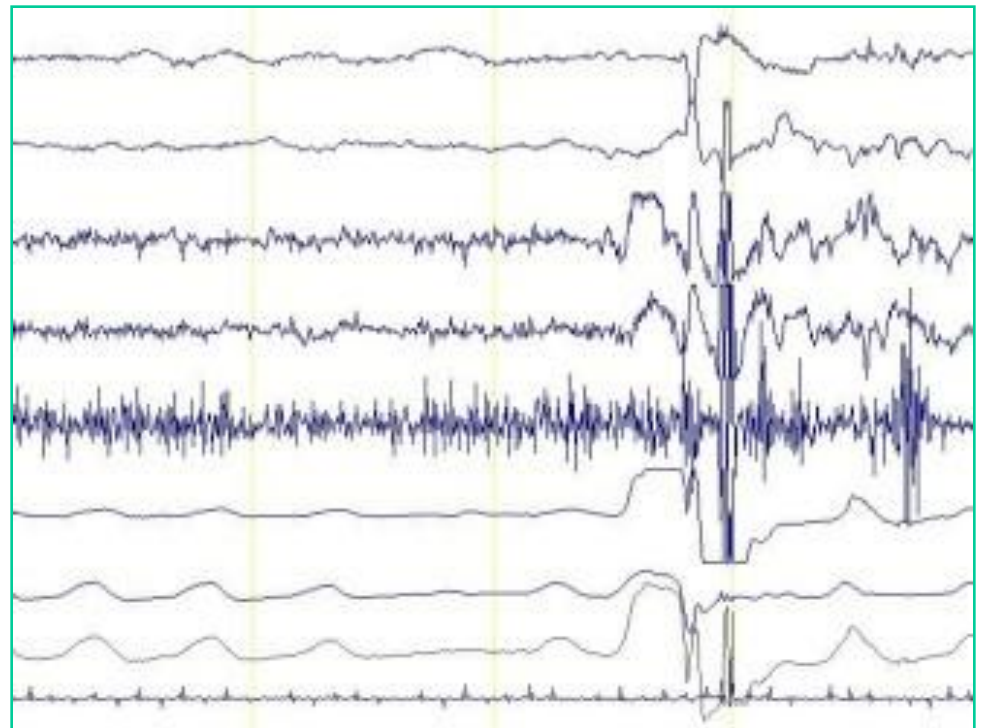
Functional brain networks

❑ **STEP 2: Time series analysis**

    ❑ **LIMITATIONS:**

        ❑ **It is difficult to evaluate causality**

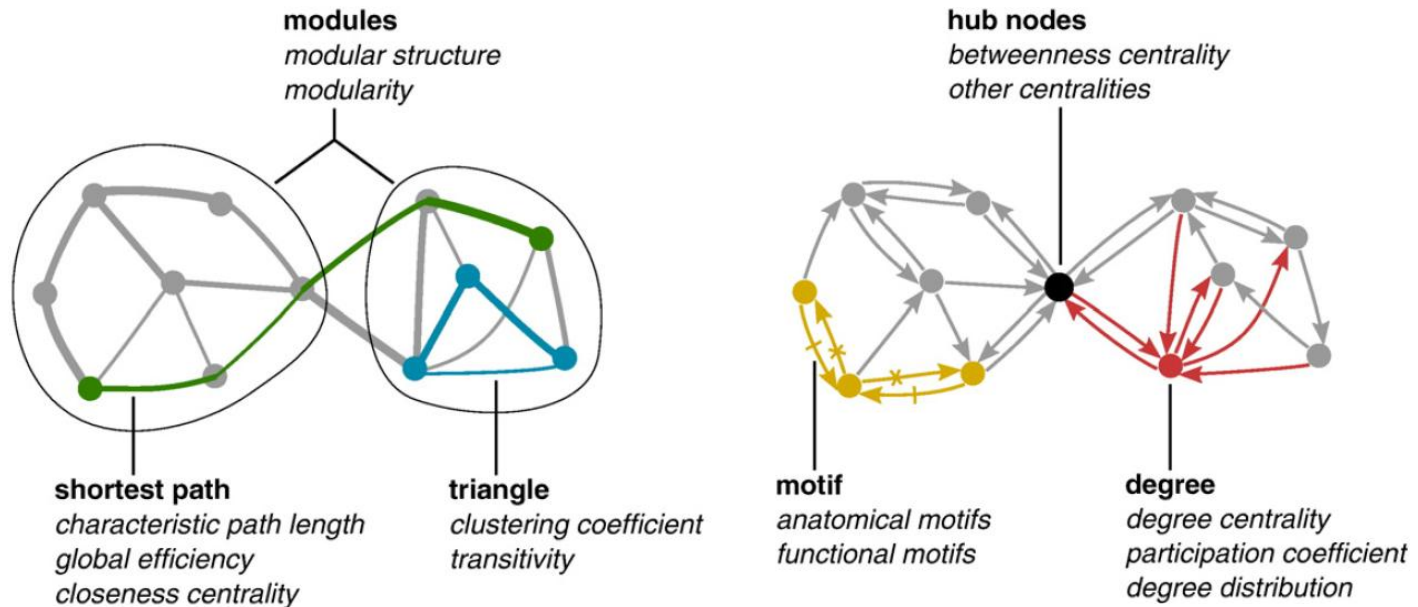   ❑ **High variability in the results**

        ❑ **Functional networks are not static**

        ❑ **In EEG and MEG, we only measure cortical activity (missing interactions)**

Functional brain networks

❑ **STEP 3: Complex Networks Analysis**

❑ **We analyze the network structure and its influence in the processes occurring in it:**

For a review read:
Rubinov et al., Neuroimage, 52, 1059 (2010)

Functional brain networks

- ❑ **STEP 3: Complex Networks Analysis**

  - ❑ **LIMITATIONS:**

    - ❑ **Real networks are weighted and directed**

    - ❑ **High variability in the results**

    - ❑ **Functional networks are not static**

    - ❑ **In EEG and MEG, we only measure cortical activity**

weighted undirected networks
structural datasets: diffusion MRI, structural MRI
functional datasets: functional MRI, MEG
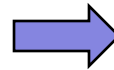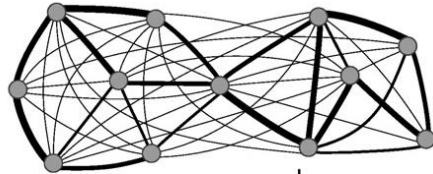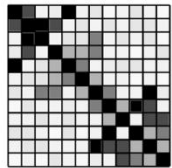
binary undirected networks

Functional brain networks

❑ Complex networks methods give useful information at 3 different levels:

✓ **Characterize the topology of brain functional networks and its influence in the processes occurring in them:**
  ❑ Small-world topology -> High efficiency in information transmission.
  ❑ High clustering -> Good local resilience.
  ❑ Modularity -> Segregation & integration of information.

➢ **Identify differences between healthy brains and those with a certain pathology:**
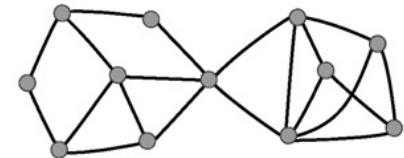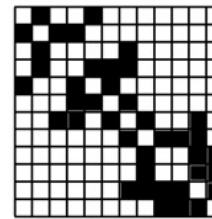 ❑ Quantify evolution towards random topologies.
  ❑ Evaluate the loss of modularity in the networks.
  ❑ Quantify the increase of energy expenses.

➢ **Develop models in order to explain the changes found in impaired functional networks:**
  ❑ Identify what are the rules that determine the network distortion.

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Functional brain networks

❑ What are the main characteristics of brain functional networks:

❑ **Small-world topology** -> High efficiency in information transmission.

❑ **High clustering** -> Good local resilience.

❑ For a low number of nodes: **power-law distribution** with exponential decay

❑ For high number of nodes: **scale-free** behavior

❑ **Modular** networks, related with the anatomical parcelation

❑ **Assortative** networks: hubs are linked together

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Functional brain networks

❑ **Let's se some fingerprints of the functional brain networks:**

PHYSICAL REVIEW LETTERS

Scale-Free Brain Functional Networks

Victor M. Eguíluz,[1] Dante R. Chialvo,[2] Guillermo A. Cecchi,[3] Marwan Baliki,[2] and A. Vania Apkarian[2]

[1]*Instituto Mediterráneo de Estudios Avanzados, IMEDEA (CSIC-UIB), E07122 Palma de Mallorca, Spain*
[2]*Department of Physiology, Northwestern University, Chicago, Illinois, 60611, USA*
[3]*IBM T.J. Watson Research Center, 1101 Kitchawan Rd., Yorktown Heights, New York 10598, USA*
(Received 13 January 2004; published 6 January 2005)

Functional magnetic resonance imaging is used to extract *functional networks* connecting correlated human brain sites. Analysis of the resulting networks in different tasks shows that (a) the distribution of functional connections, and the probability of finding a link versus distance are both scale-free, (b) the characteristic path length is small and comparable with those of equivalent random networks, and (c) the clustering coefficient is orders of magnitude larger than those of equivalent random networks. All these properties, typical of scale-free small-world networks, reflect important functional information about brain states.

Functional brain networks

❑ **Scale-free brain functional networks**

    ❑ Two activities: finger tapping and listening to music

    ❑ ~ 400 events every 2.5 seconds (fMRI)

    ❑ 36 x 64 x 64 brain sites (147456 voxels)

    ❑ The linear cross-correlation is measured

$$r(x_1, x_2) = \frac{\langle V(x_1, t)V(x_2, t)\rangle - \langle V(x_1, t)\rangle\langle V(x_2, t)\rangle}{\sigma(V(x_1))\sigma(V(x_2))}$$

    ❑ Several thresholds are considered in order to obtain the adjacency matrix.
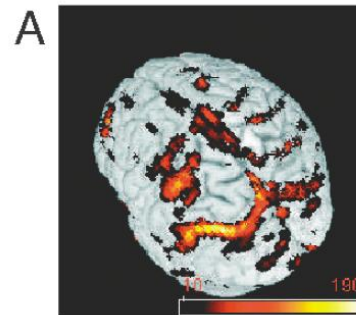
Music   **Finger tapping**
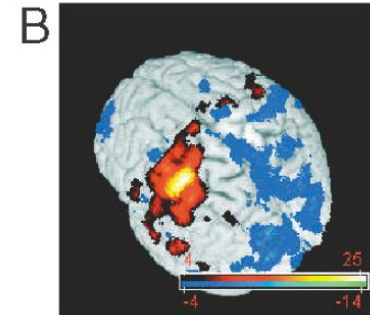
Functional brain networks

☐ **Scale-free brain functional networks**

Scale-free distribution

Finger tapping
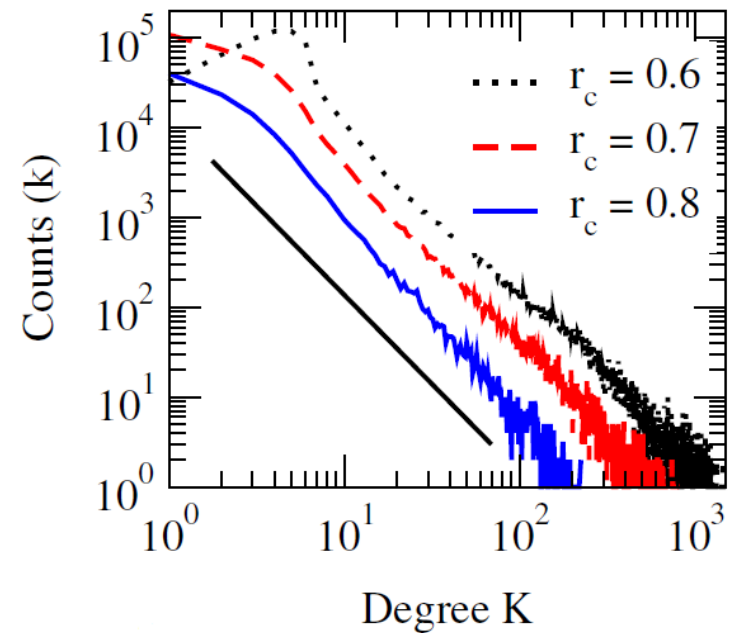
Functional brain networks
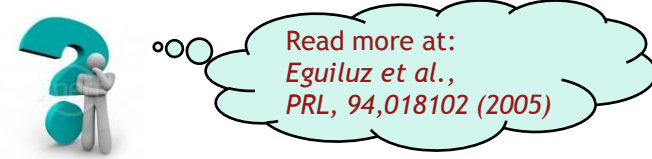
❑ **Scale-free brain functional networks**

fMRI functional networks are small-world, scale-free and assortative
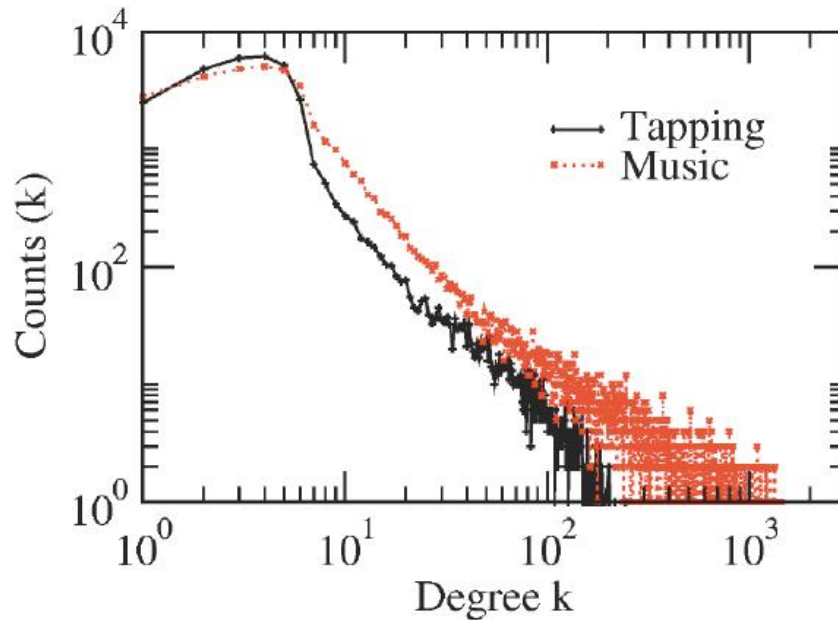
$L \sim L_{random}$

r_c	N	C	L	$\langle k \rangle$	γ	C_{rand}	L_{rand}
0.6	31 503	0.14	11.4	13.41	2.0	4.3×10^{-4}	3.9
0.7	17 174	0.13	12.9	6.29	2.1	3.7×10^{-4}	5.3
0.8	4891	0.15	6.0	4.12	2.2	8.9×10^{-4}	6.0

$C >> C_{random}$
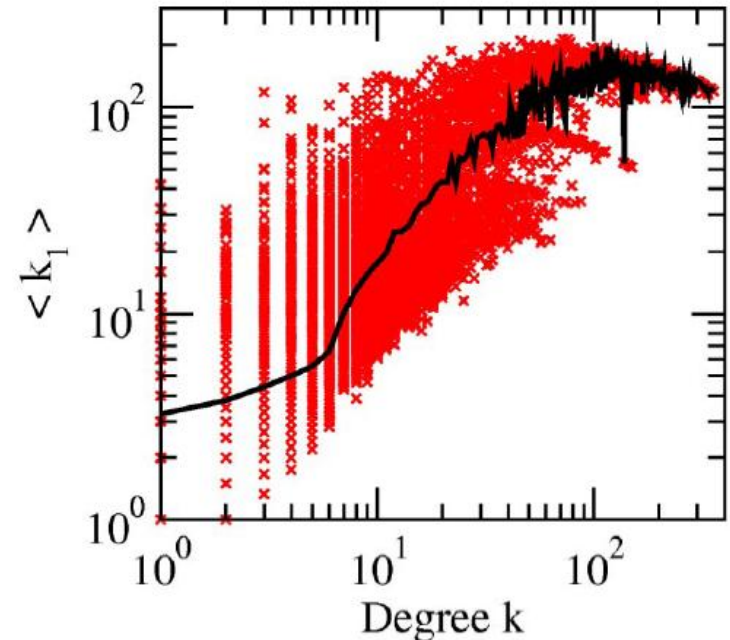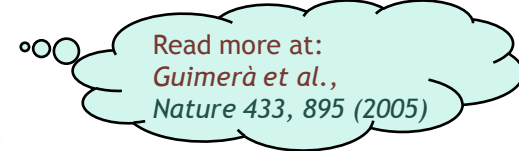
❑ **Defining the role of nodes with regard to the community structure**

Guimerà et al., investigated the role of the nodes inside the community
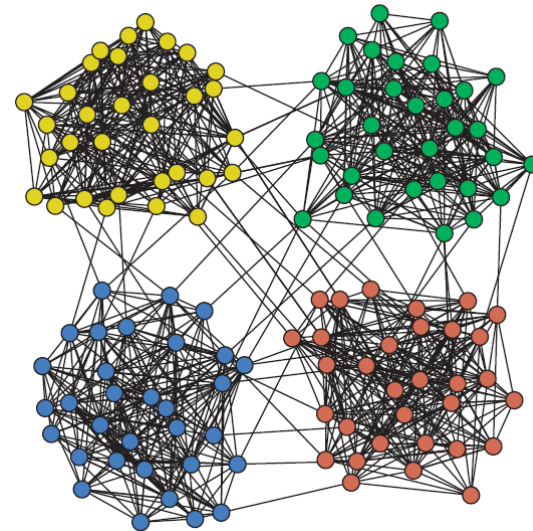
Functional brain networks

❑ **Defining the role of nodes with regard to the community structure**

It is possible to evaluate the functionality of t he nodes from the topological properties:

Within-module connectivity:

$$z_i = \frac{\kappa_i - \bar{\kappa}_{s_i}}{\sigma_{\kappa_{s_i}}}$$

Participation coefficient:

$$P_i = 1 - \sum_{s=1}^{N_M} \left(\frac{\kappa_{is}}{k_i}\right)^2$$
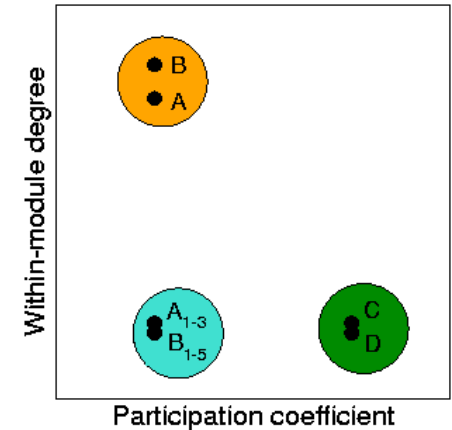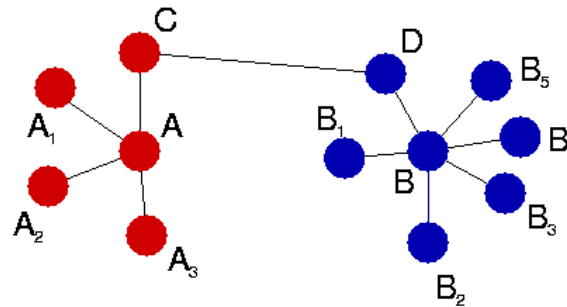
(Figures from R. Guimerà et al., Nature 433, 895 2005)

Functional brain networks

❑ **Community analysis gives information about the network characteristics and the role played by nodes (specially hubs).**

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg
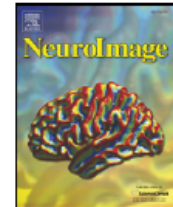
Age-related changes in modular organization of human brain functional networks

David Meunier [a,b], Sophie Achard [a,b,c], Alexa Morcom [d], Ed Bullmore [a,b,*]

[a] Brain Mapping Unit, University of Cambridge, Cambridge, UK
[b] Behavioural and Clinical Neurosciences Institute, University of Cambridge, Cambridge, UK
[c] Grenoble Image Parole Signal Automatique, Centre National de la Recherche Scientifique, Grenoble, France
[d] Centre for Cognitive and Neural Systems, University of Edinburgh, Edinburgh, UK

Functional brain networks

☐ **Community analysis gives information about the network characteristics and the role played by nodes (specially hubs).**
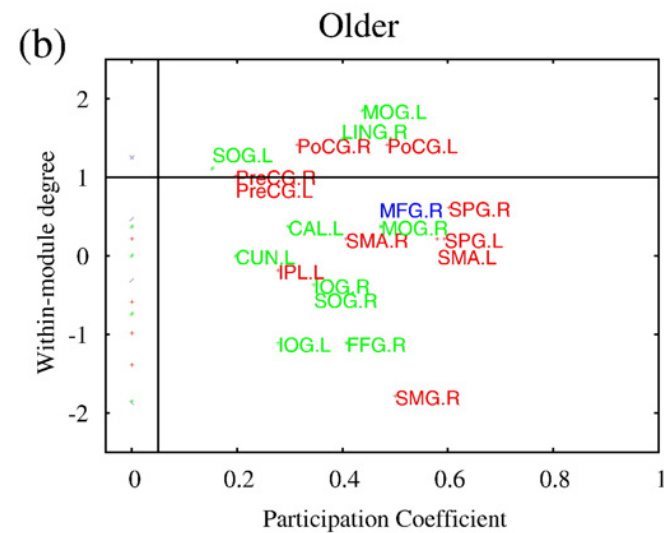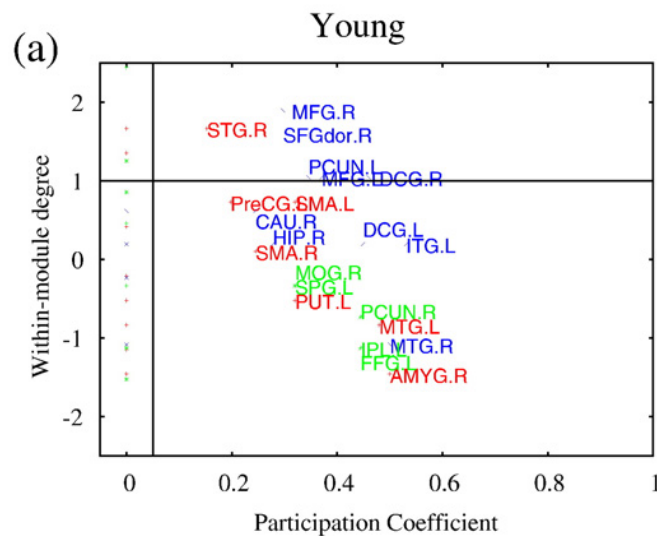
Functional brain networks

❏ **Community analysis gives information about the network characteristics and the role played by nodes (specially hubs).**
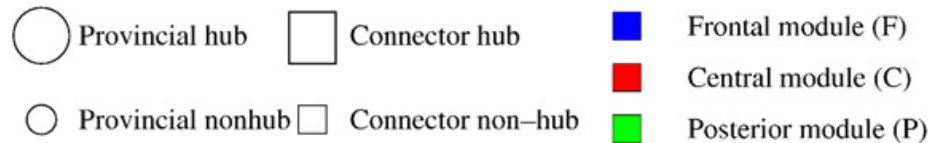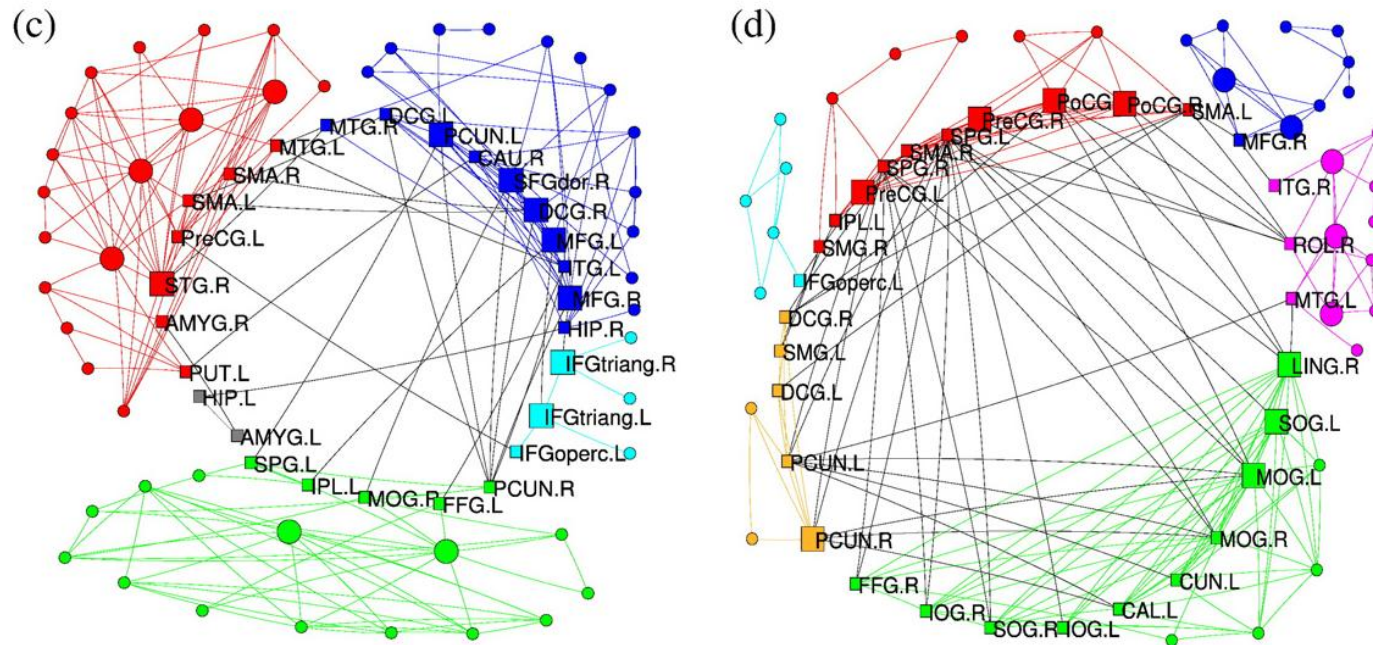
From Healthy to Impaired Networks

From healthy to impaired networks

❑ Complex networks methods give useful information at 3 different levels:

✓ **Characterize the topology of brain functional networks and its influence in the processes occurring in them:**
❑ Small-world topology -> High efficiency in information transmission.
❑ High clustering -> Good local resilience.
❑ Modularity -> Segregation & integration of information.

➢ **Identify differences between healthy brains and those with a certain pathology:**
❑ Quantify evolution towards random topologies.
❑ Evaluate the loss of modularity in the networks.
❑ Quantify the increase of energy expenses.

➢ **Develop models in order to explain the changes found in impaired functional networks:**
❑ Identify what are the rules that determine the network distortion.

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

From healthy to impaired networks

❑ **Complex Network analyses of brain diseases**

    ❑ **Alzheimer.**

        ❑ The overall synchronization of the network is decreased.

        ❑ The average path length increases (probably as a consequence of the reduction of the synchronization).

        ❑ The clustering coefficient is significantly reduced (the network evolves to random topologies).

    ❑ **Mild Cognitive Impairment.**

        ❑ The average synchronization increases.

        ❑ Network outreach increases as a consequence of an unbalanced increase of the synchronization in the long-range connections.

        ❑ The network becomes more random.

❑ **Complex Network analyses of brain diseases**

    ❑ **Schizophrenia.**

        ❑ The small-world properties of the network are impaired (specially at low-frequency bands).

        ❑ Clustering and average path length are shifted to random configurations.

        ❑ The hierarchical configuration of the network is also affected.

    ❑ **Epilepsia.**

        ❑ Synchronization increases during the epileptic episodes.

        ❑ As a consequence, clustering coefficient increases and average path length decreases.

        ❑ Changes are more significant at delta, theta and alpha bands.

Applications

Mild Cognitive Impairment and Traumatic Brain Injury
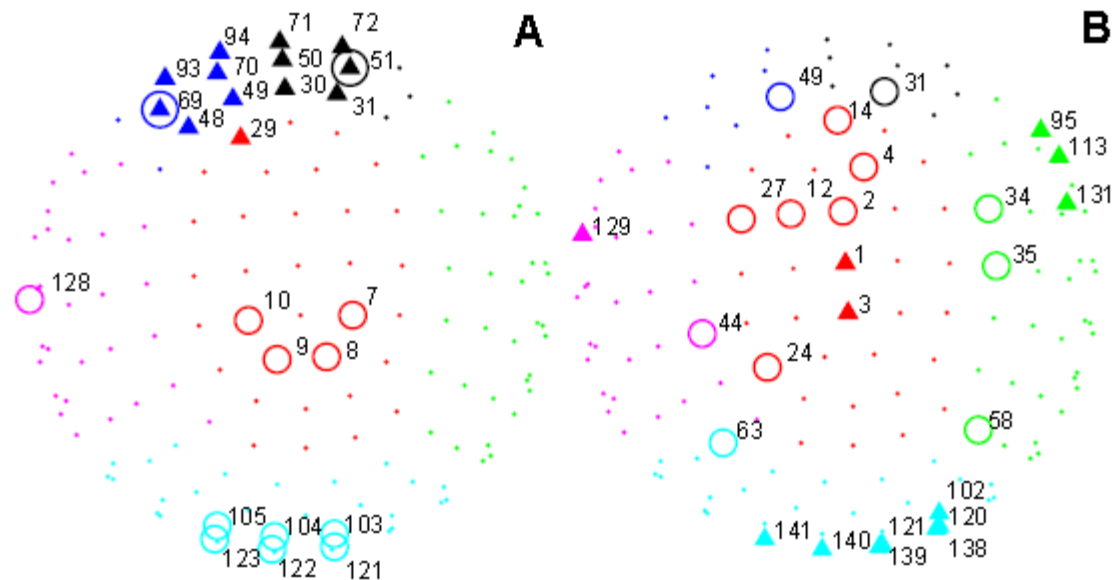
Applications: Mild Cognitive Impairment

Advantages

❏ We have information of the brain as a whole and not only of its isolated components.

❏ We can relate the information contained in the topology with the dynamical processes occurring in it.

❏ We can try to identify differences between healthy and impaired brains in order to understand and prevent different brain diseases.

Drawbacks

❏ We are projecting the activity of billions of neurons into a few nodes.

❏ The activity at each position is strongly influenced by its neighbors.

❏ Experiments are expensive and it is difficult to find volunteers.

❏ There exists a great variability of the recorded activity between individuals (and even in the same individual).

❏ Anatomical and, specially, functional networks are not static.

GOOD NEWS
Possibility of clinical applications

CAUTION! High risk of GIGO
(Garbage In, Garbage Out)

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Applications: Mild Cognitive Impairment

❑ **What is Mild Cognitive Impairment (MCI)?**

A brain disorder in which thinking abilities are mildly impaired. Individuals with MCI are able to function in everyday activities but have difficulty with memory, trouble remembering the names of people they met recently, the flow of a conversation, and a tendency to misplace things. Every year, around 10% of MCI patients develop Alzheimer.

❑ **The experiment**

We performed magnetoencephalograms (MEG) to a group of 19 MCI's patients and 19 control subjects during a memory task. By means of the synchronization likelihood (SL) we quantified the interaction between the 148 channels of the MEG system and we obtained a weighted connectivity matrix between cortical areas.

Memory task experiment → MEG → Time series → Synchronization Likelihood → Weighted Network → Normalization → Complex Networks Analysis
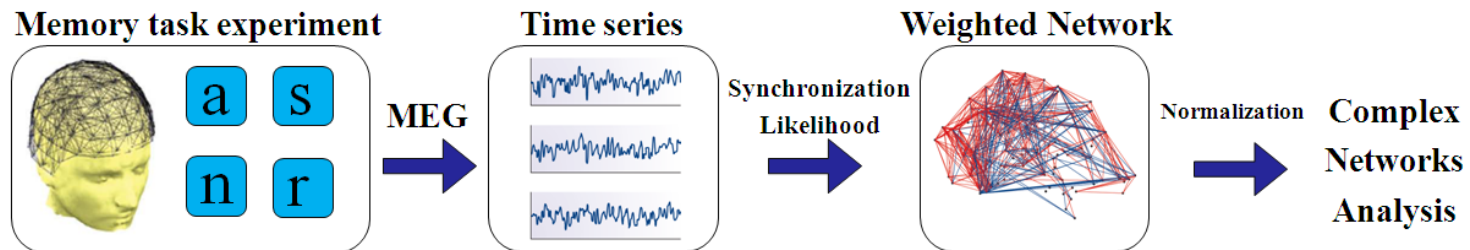
Applications: Mild Cognitive Impairment

❑ **Network normalization allows analysis of the weighted matrices:**

$$M : \mathbb{R} \to [0,1] \implies P\{p_{ij}\} \implies p_{ij} = \frac{\omega_{ij} - min[\omega_{ij}]}{max[\omega_{ij}] - min[\omega_{ij}]}$$
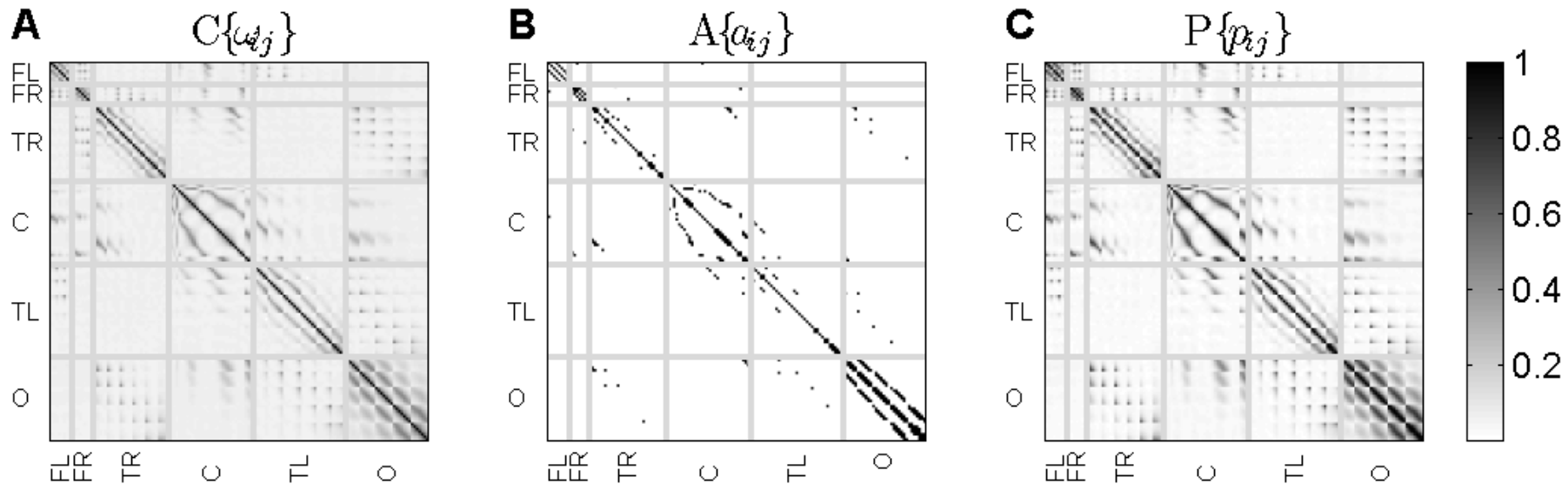
Applications: Mild Cognitive Impairment

❑ **Topological anaylisis of the functional networks of both groups (Control and MCI):**

Matrix normalization (P)

We map the weights of the synchronization matrix ω_{ij} into a continuous bijective map $M{:}R \to [0,1]$. The obtained matrix $P \{p_{ij}\}$ can be interpreted as a matrix of probabilities that tell us how probable the existence of a link between node i and j is.

$$p_{ij} = \frac{\omega_{ij} - \min(\omega_{ij})}{\max(\omega_{ij}) - \min(\omega_{ij})}$$

Mean Shortest path (L)

It measures the shortest topological (not Euclidean) distance l_{ij} between any pair of nodes in the network.

Mean Clustering (C)

It measures the probability that two neighbors of a certain node are also connected with each other.

$$c_i = \frac{\sum\limits_{j,k} P_{ij} P_{jk} P_{ik}}{\sum\limits_{j,k} P_{ij} P_{ik}}$$

Network modularity (Q)

Takes into account the number of links between the nodes of the same community and measures the statistical deviation from a random assignment of nodes between the existing communities

$$Q = \frac{1}{p_{net}} \sum_{i,j} [p_{ij} - \frac{p_i p_j}{p_{net}}]\delta(c_i, c_j)$$

Network outreach (O)

The outreach O_i balances the distance of the connections of a node i with their probability

$$O_i = \sum_{j \in V(i)} p_{ij} d_{ij}$$

Weighted neighbor degree (Knn)

Average number of neighbors of i's neighbors over the average number of i's neighbors.

$$k_i^{NN} = \frac{\sum\limits_{j,k} P_{ij} P_{jk}}{\sum\limits_{j} P_{ij}}$$

Parameter Normalization

We generate a set of 100 network surrogates by random permutation of the matrix coefficients. Next we normalize each network parameter X with the average $\hat{X} = X/X_{ran}$

Applications: Mild Cognitive Impairment

❑ **Differences between the MCI and Control groups:**
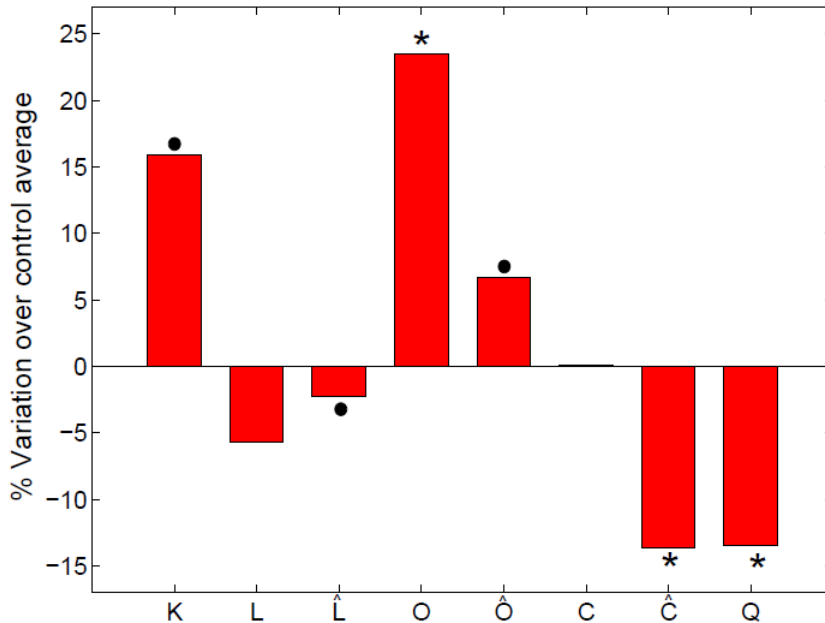
Fig. 4. Percentage of variation and statistical significance. Percentage of variation of the average degree K, average shortest path L and its normalized value $\hat{L} = \frac{L}{L_{ran}}$, network outreach O and normalized outreach $\hat{O} = \frac{O}{O_{ran}}$, clustering C and normalized clustering $\hat{C} = \frac{C}{C_{ran}}$ and network modularity. Circles correspond to $p < 0.03$ and stars to $p < 0.001$, specifically: O ($p = 0.007$), $\hat{C}$ ($p = 0.002$), Q ($p = 0.0033$), K,($p = 0.018$), L_z ($p = 0.025$) and $\hat{O}$ ($p = 0.027$).

❑ **Global Parameters:**

  ❑ The network strength K increases (+15.9%)

  ❑ Network outreach increases (+23.4%) (and more than the increase in K)

  ❑ The network modularity decreases (-13.5%)

❑ **Normalized Parameters:**

  ❑ Normalized clustering decreases (-13.6%):

$$\hat{C}^{\text{CONTROL}} = 1.76 \rightarrow \hat{C}^{\text{MCI}} = 1.52$$
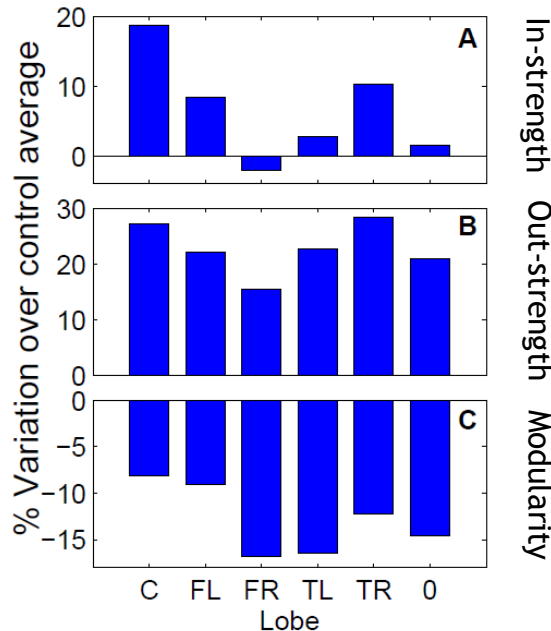
  ❑ Normalized outreach increases (+6.7%):

$$\hat{O}^{\text{CONTROL}} = 0.63 \rightarrow \hat{O}^{\text{MCI}} = 0.67$$

CAUTION! The functional network is becoming random

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Applications: Mild Cognitive Impairment

❑ **Differences between the MCI and Control groups at the INTER-LOBE connections:**

Fig. 5. **Mesoscale analysis**. Percentages of variation in the MCI group with respect to the control one, of the strength inside each lobe (A), the strength of the links going out from each lobe (B), and the lobe modularity (C). In (D), percentages of variation of the lobe-to-lobe strength. Lobe code: 1=central, 2=frontal left, 3=frontal right, 4=temporal left, 5=temporal right and 6=occipital.

❑ **Intra-lobe synchronization:**

   ❑ The intra-lobe synchronization increases

   ❑ The inter-lobe synchronization increases (more than the intra-lobe sync.)

   ❑ Modularity decreases
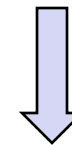
CAUTION! The segregated operation of the brain is decreasing

Applications: Mild Cognitive Impairment

❑ **Degree, clustering, outreach and *knn* distributions:**

    ❑ MCI networks have nodes with higher connectivity.

    ❑ The clustering increases with the degree (in both Control and MCI).

    ❑ For the same degree, outreach is higher at the MCI group.
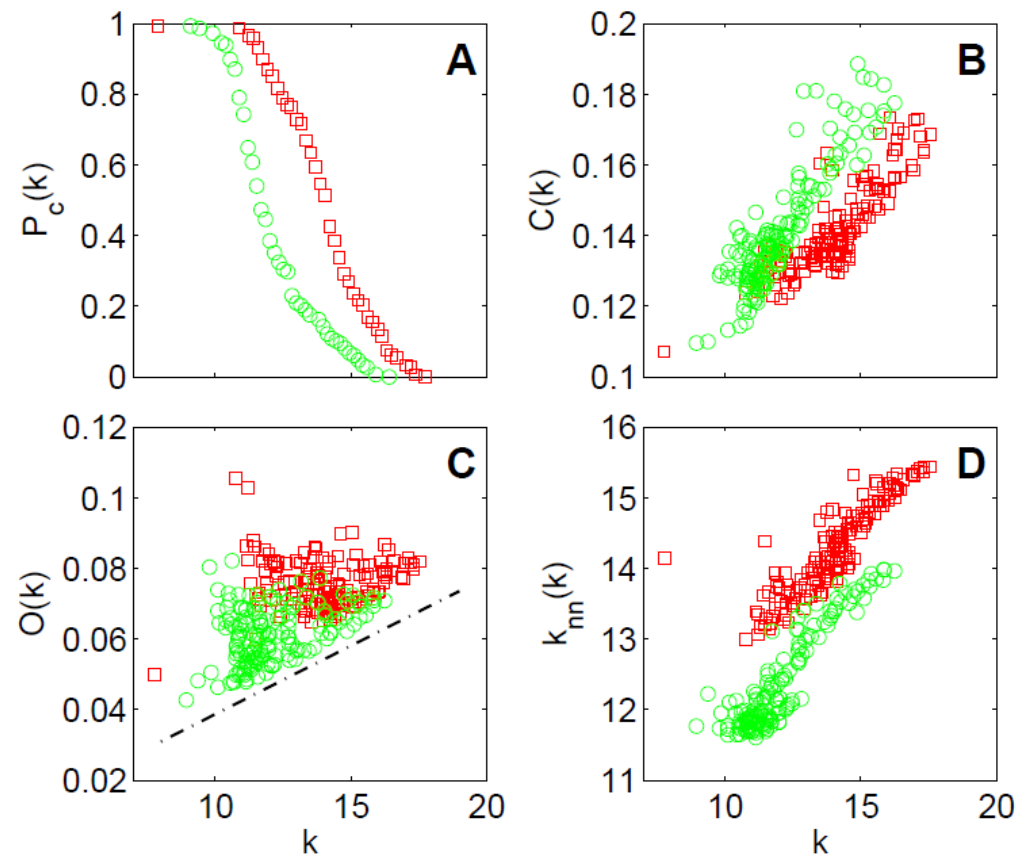
    ❑ Networks are assortative

Fig. 3. **Several network parameter distributions for the control (green circles) and MCI (red squares) groups**. (A) Probability distribution of finding a node with a degree higher than k, (B) clustering coefficient $C(k)$, (C) outreach $O(k)$ and (D) average nearest neighbors degree $k_{nn}(k)$.

Applications: Mild Cognitive Impairment

❑ **From macroscopic (network) to microscopic (node) analysis:**

❑ Within module degree:

$$z_i = \frac{k_i - \bar{k}_{c_i}}{\sigma_{k_{c_i}}}$$

❑ Participation coefficient:

$$p_i = 1 - \sum_{c=i}^{N_c} \left(\frac{k_{c_i}}{k_i} \right)^2$$
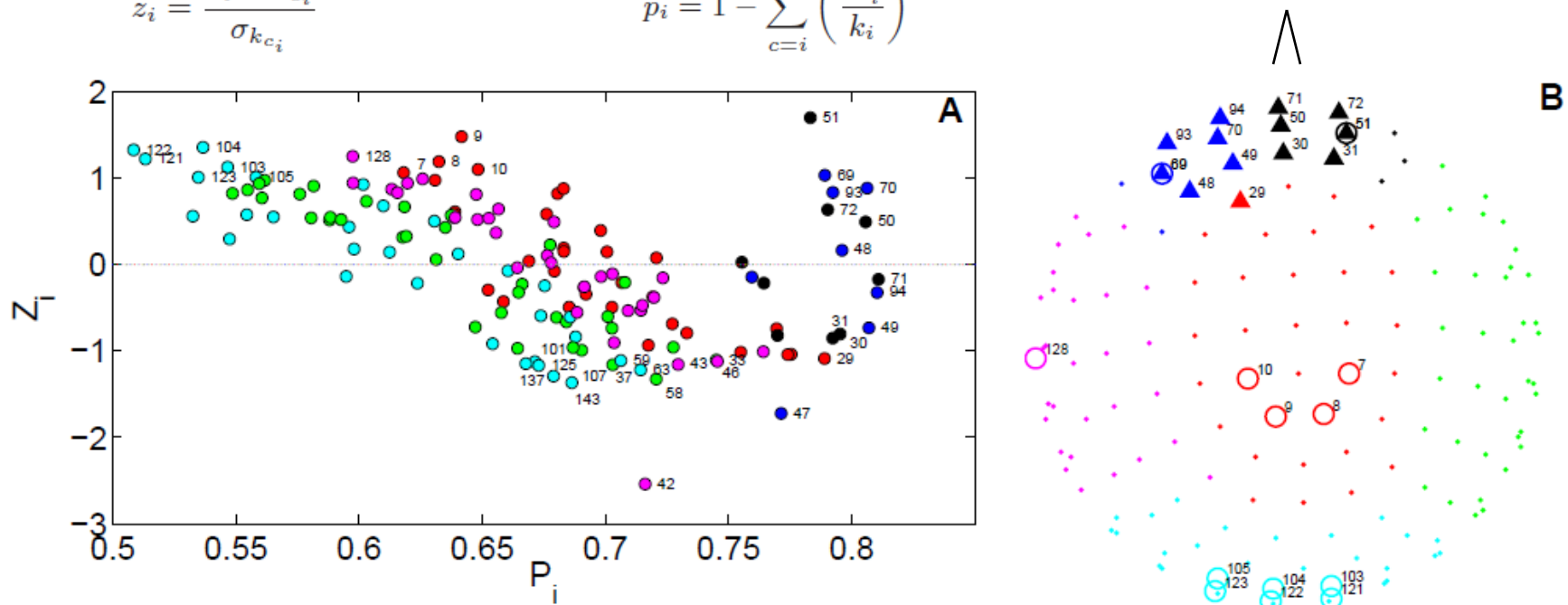
Fig. 6. **Community structure and roles**. (A) Within-module degree z_i for each node in the network of the control group as a function of its corresponding participation coefficient p_i. Only the first 13 nodes with the highest z_i and p_i are labelled. Their positions within the corresponding lobe are marked in (B) with circles for those with the highest z_i and with triangles for those with the highest p_i.

Applications: Mild Cognitive Impairment

❏ **From macroscopic (network) to microscopic (node) analysis:**
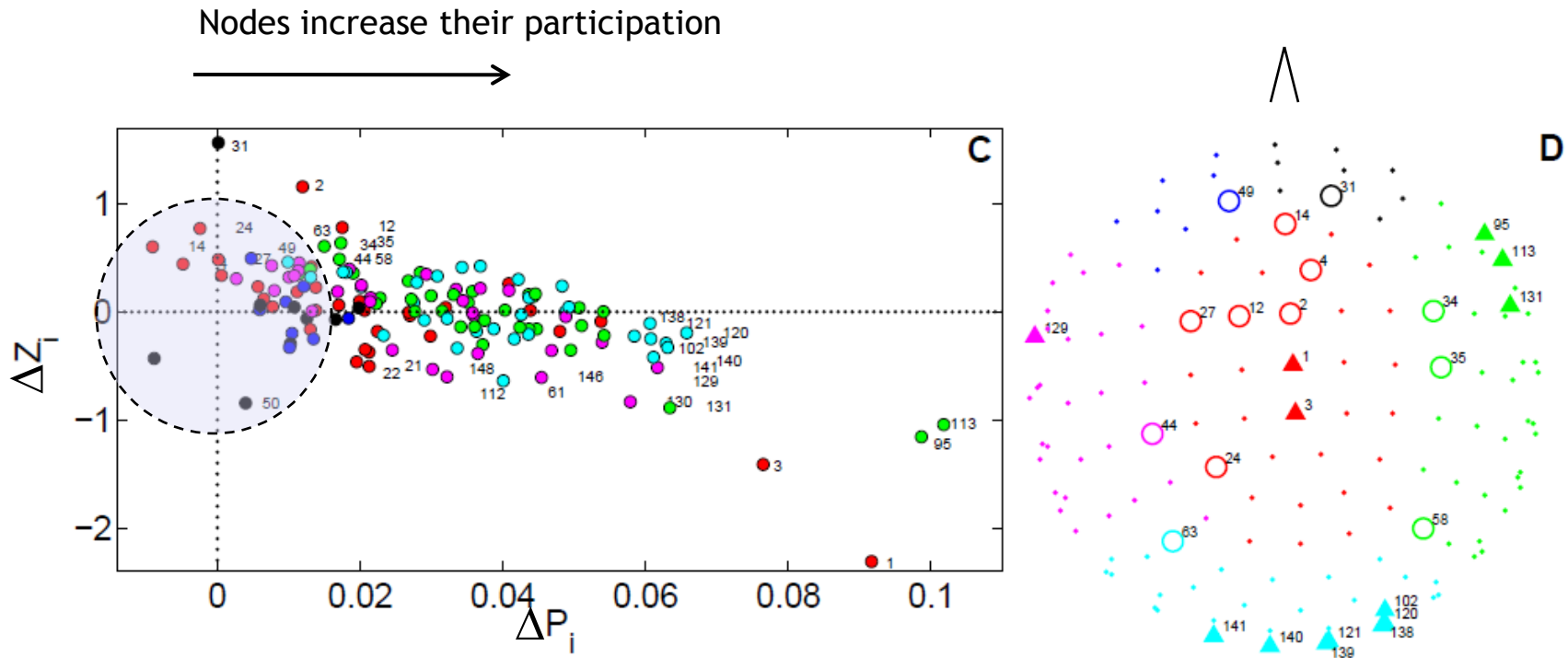
Fig. 6. Community structure and roles. (C) Within-module degree differences between MCI and control group as a function of the participation coefficient differences for each node. Again, only the first 13 nodes with the highest differences are labelled and accordingly marked within their lobe. (D) Position of nodes with higher increase of the z_i (circles) and p_i (triangles). Lobe color scheme: red-central, blue-frontal left, black-frontal right, magenta=temporal left, green=temporal right, and cyan=occipital.

Applications: Mild Cognitive Impairment

❑ **Caution, GIGO is around...**

I'm Swedish!

"Lies, damned lies and statistics"

	1950-55	1956-60	1961-65	1966-70	1971-75	1976-80
Denmark	180.3	179.7	181.0	181.7	181.3	183.7
Sweden	179.6	179.4	180.9	180.5	180.4	181.2
Austria	176.3	177.0	179.2	178.5	178.7	179.6
Belgium	176.2	177.3	177.2	179.4	179.2	179.5
Finland	177.8	179.0	179.6	177.9	178.0	178.7
Greece	174.7	175.4	176.6	177.0	178.4	178.6
Ireland	174.9	176.3	176.1	176.9	177.0	177.4
Italy	172.5	174.3	174.9	174.7	175.4	177.1
Spain	171.3	171.7	173.3	174.7	175.7	176.1
Portugal	168.8	170.0	170.0	169.8	172.1	172.9

From :
The Evolution of Adult Height in Europe: A Brief Note*
Jaume Garcia and Climent Quintana-Domeque

Table 1. Average heights by year of birth, men, centimeters

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos
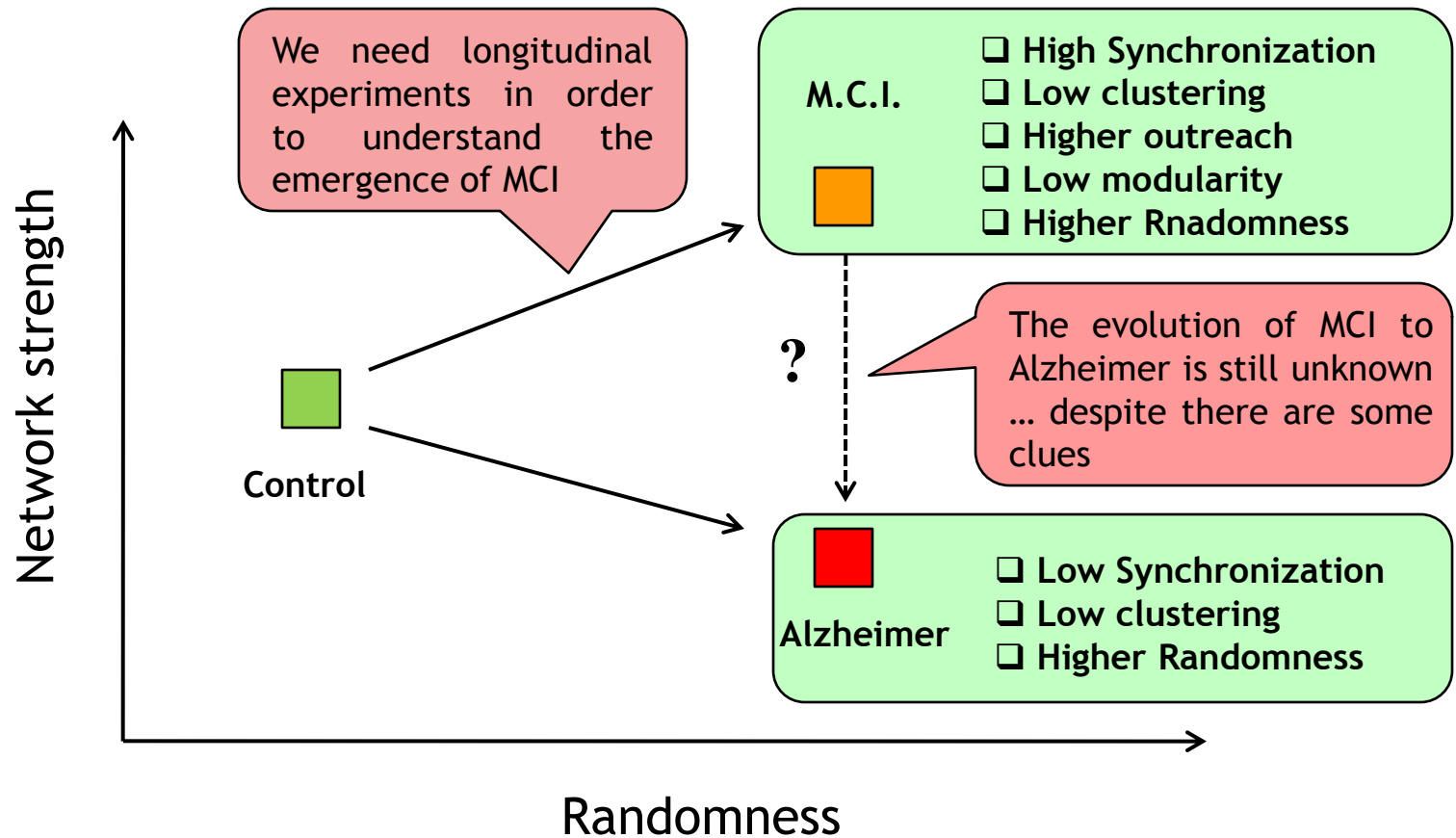
Applications: Mild Cognitive Impairment

❑ **Caution, GIGO is around...**
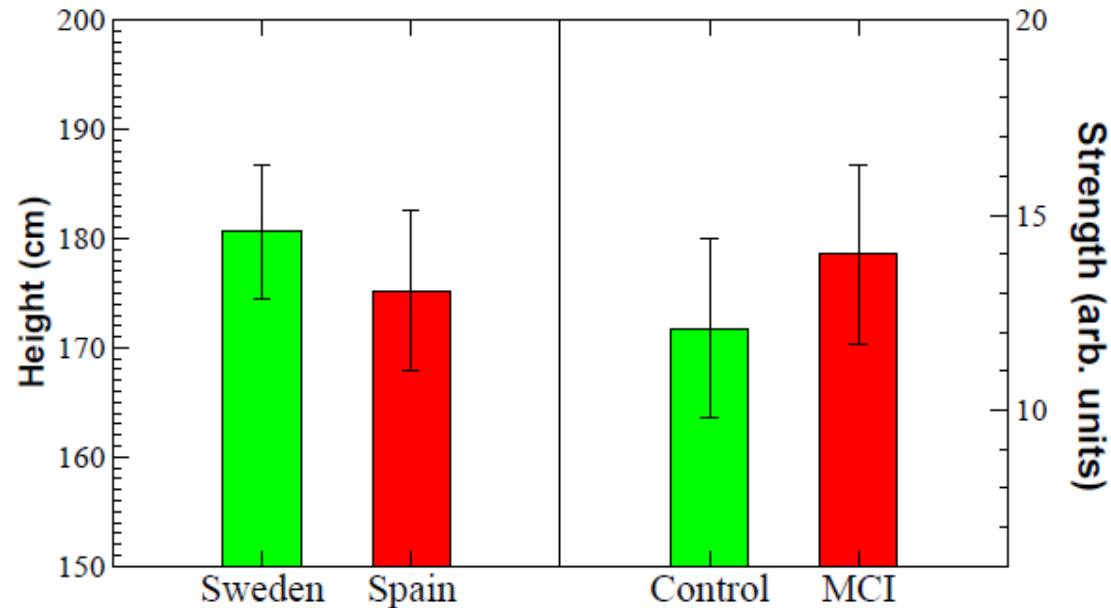
MCI diagnostic must be done by analysing longitudinal recordings

Applications: Mild Cognitive Impairment

❑ **Some conclusions**

Applications: Traumatic Brain Injury (TBI)
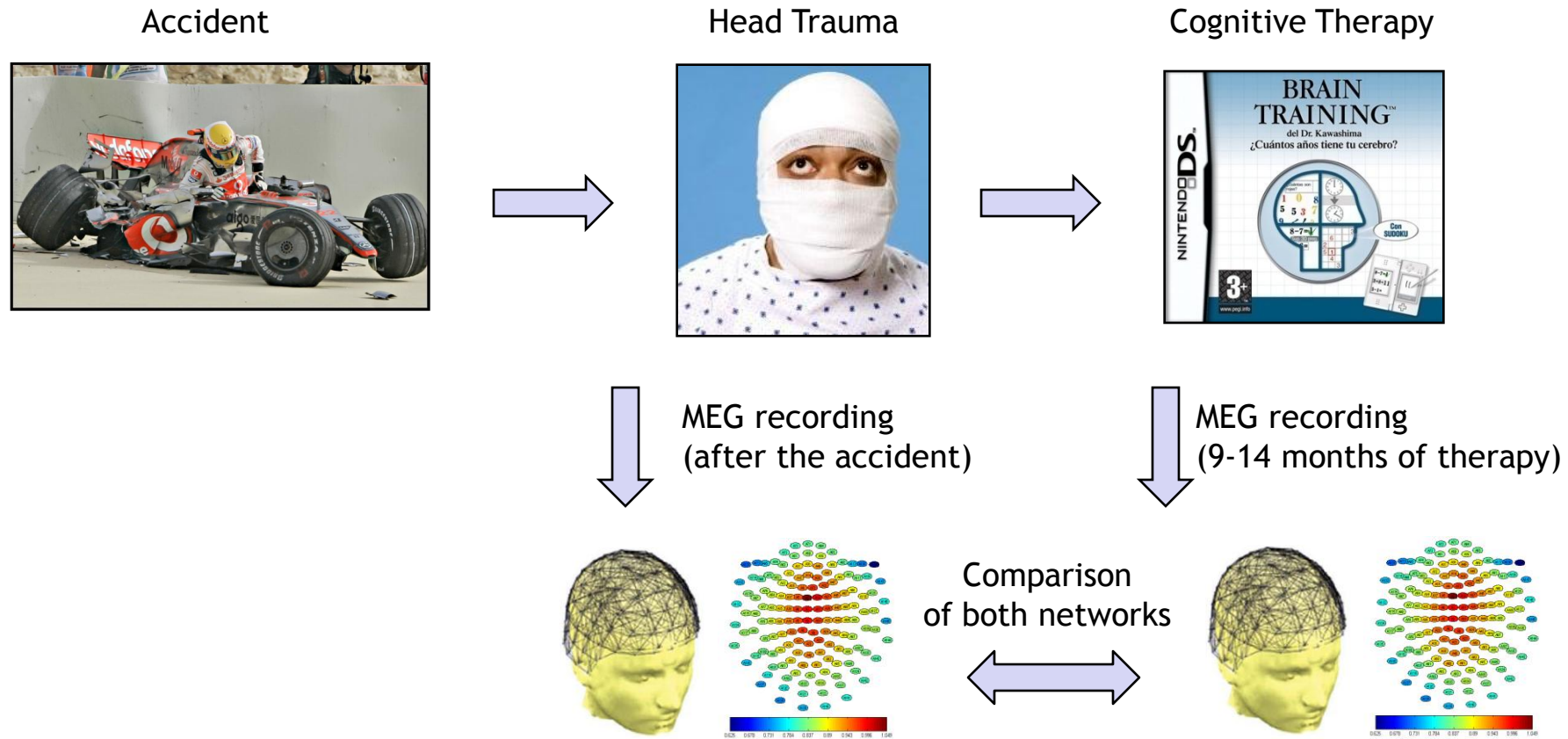
❑ **A good candidate: Trauma recovering therapy**

Accident   Head Trauma   Cognitive Therapy

MEG recording
(after the accident)

MEG recording
(9-14 months of therapy)

Comparison
of both networks

Applications: Traumatic Brain Injury (TBI)

❑ A good candidate: Trauma recovering therapy
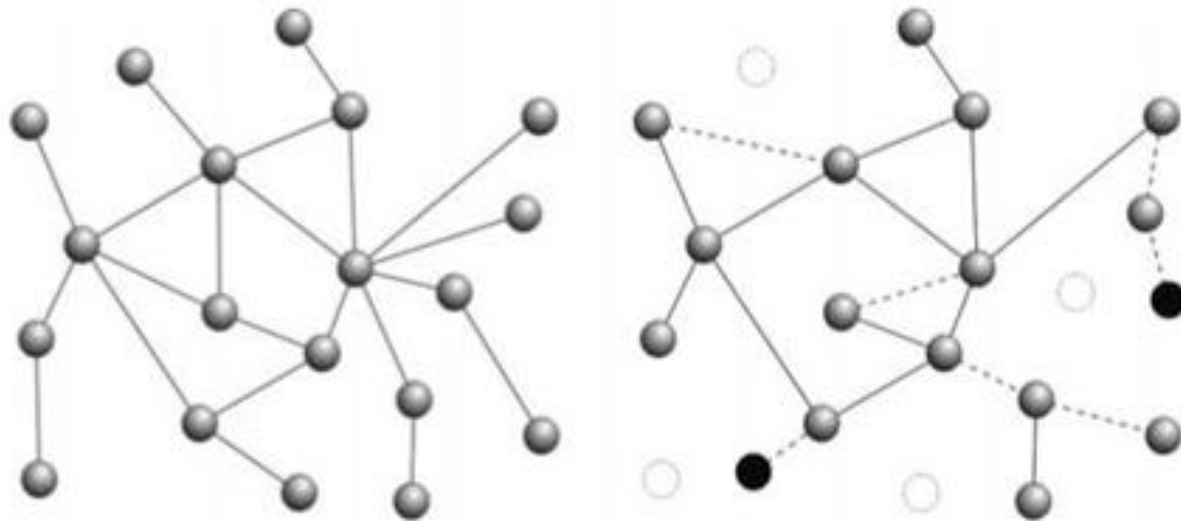
Band δ [1-4 Hz]

Band α [8-13 Hz]
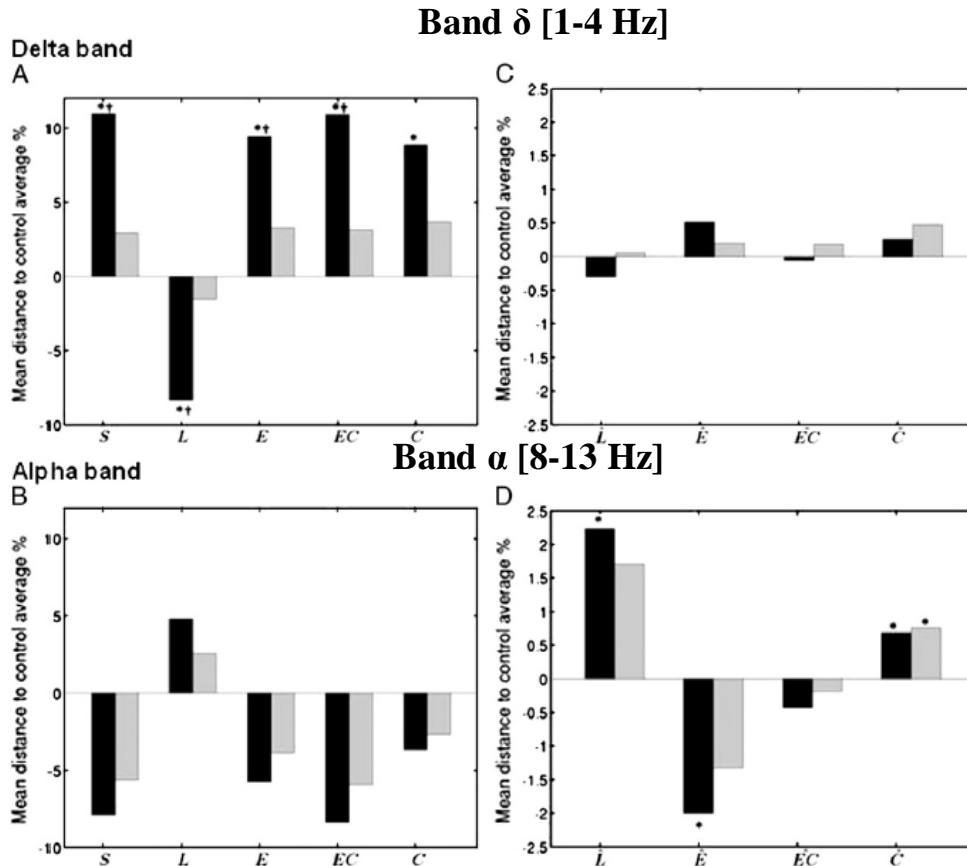
❑ Network changes:

> ❑ The alfa band is overconnected
>
> ❑ The delta band is underconnected
>
> ❑ The cognitive therapy shifts network parameters towards control values
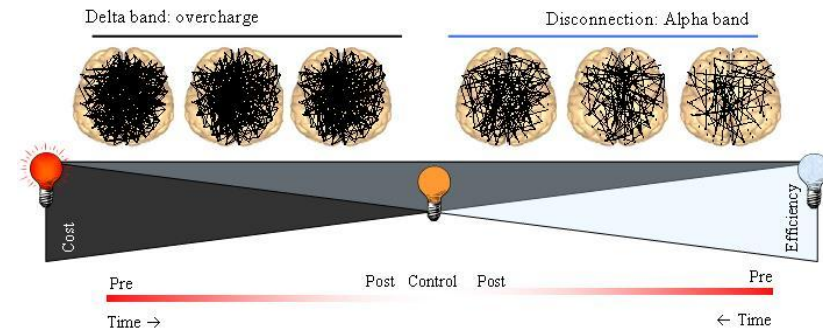
Evolutionary Network Models

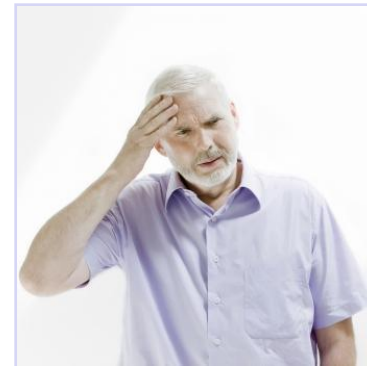## Mild Cognitive Impairment and Traumatic Brain Injury

Evolutionary network models

❑ Complex networks methods give useful information at 3 different levels:

   ✓ **Characterize the topology of brain functional networks and its influence in the processes occurring in them:**
       ❑ Small-world topology -> High efficiency in information transmission.
       ❑ High clustering -> Good local resilience.
       ❑ Modularity -> Segregation & integration of information.

   ✓ **Identify differences between healthy brains and those with a certain pathology:**
       ❑ Quantify evolution towards random topologies.
       ❑ Evaluate the loss of modularity in the networks.
       ❑ Quantify the increase of energy expenses.

   ➢ **Develop models in order to explain the changes found in impaired functional networks:**
       ❑ Identify what are the rules that determine the network distortion.

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Evolutionary network models

❑ **Two specific applications of network modeling:**

    ❑ **Mild Cognitive Impairment**
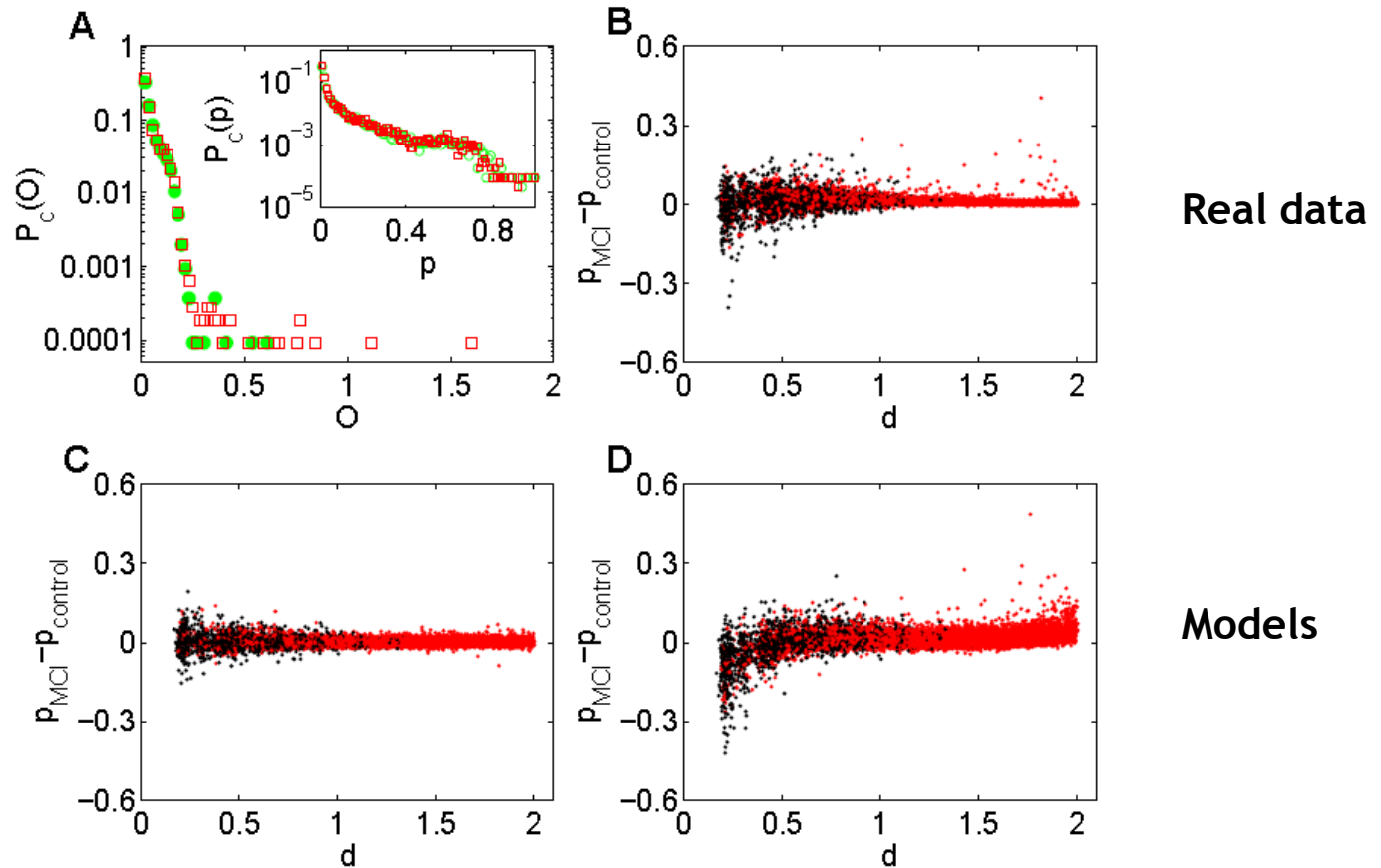

    ❑ **Traumatic Brain Injury**

Evolutionary network models

❑ **Mild Cognitive Impairment: Real data versus evolutionary models**

Real data

Models

Evolutionary network models

❑ **Develop models in order to explain the changes found in impaired functional networks:**

1) We select a link randomly.

2) We change the weight of the link according to a certain function:

$$w'_{ij}=w_{ij}\,[1+\lambda+\eta]\,\xi(d_{ij})$$

3) We normalize and recalculate the network parameters.

4) We go back to step 1.

w'_{ij}= *modified link weight*
w_{ij} = *previous link weight*
λ=*degradation rate ($\lambda >0$)*
η= *noise term*
$\xi(d_{ij})$= *length dependence function*
d_{ij}= *link length*

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Evolutionary network models

❑ **Develop models in order to explain the changes found in impaired functional networks:**

Healthy brain

Impaired brain

○ Length independent
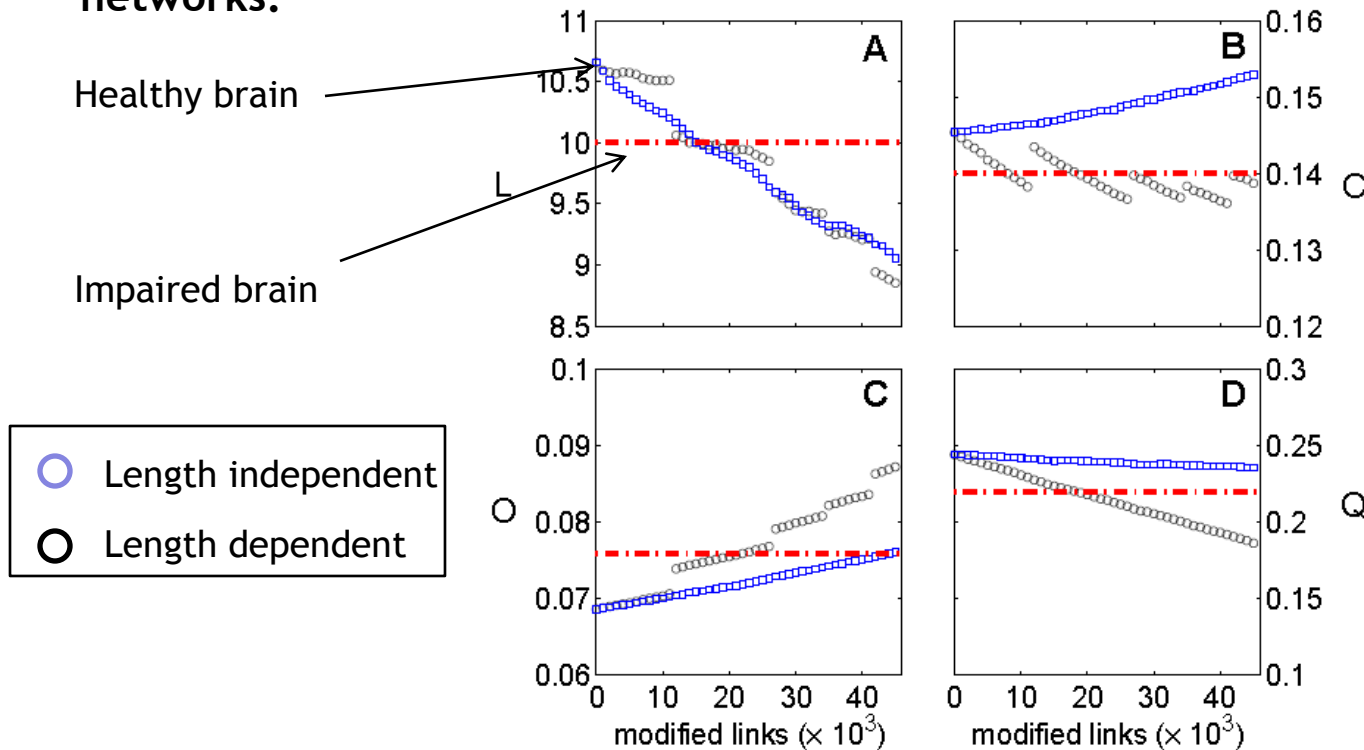
○ Length dependent

Figure 6. Modeling the disease. Evolution of network parameters [shortest path (A), clustering (B), outreach (C) and modularity (D)] as the number of impaired links increases. Red dashed lines are the mean values of the MCI group. Blue squares correspond to $\xi(d_{ij}) = 1$ and black circles to $\xi(d_{ij}) = \beta_d(\gamma \bar{d} - d_{ij})^3$. Parameters used in the simulations are given in Fig. 5 caption.

CSG · CTB centro de tecnología biomédica · Universidad Rey Juan Carlos

Evolutionary network models

❑ **Modeling network recovery in Traumatic Brain Injury (TBI):**

$$A_t^i = T^i A_{t-1}^i \qquad \Longrightarrow \qquad T^i = m \left[\frac{A_0^i}{\max(A_0^i)} \right] + b$$

Contrasting model (T+):

The goal of this model is enhancing those links with higher initial weights. This leads to an increase of the relative difference between higher and lower weights along the evolution.

$$m_i = \frac{1-k}{1-\min(A_0^i)}$$

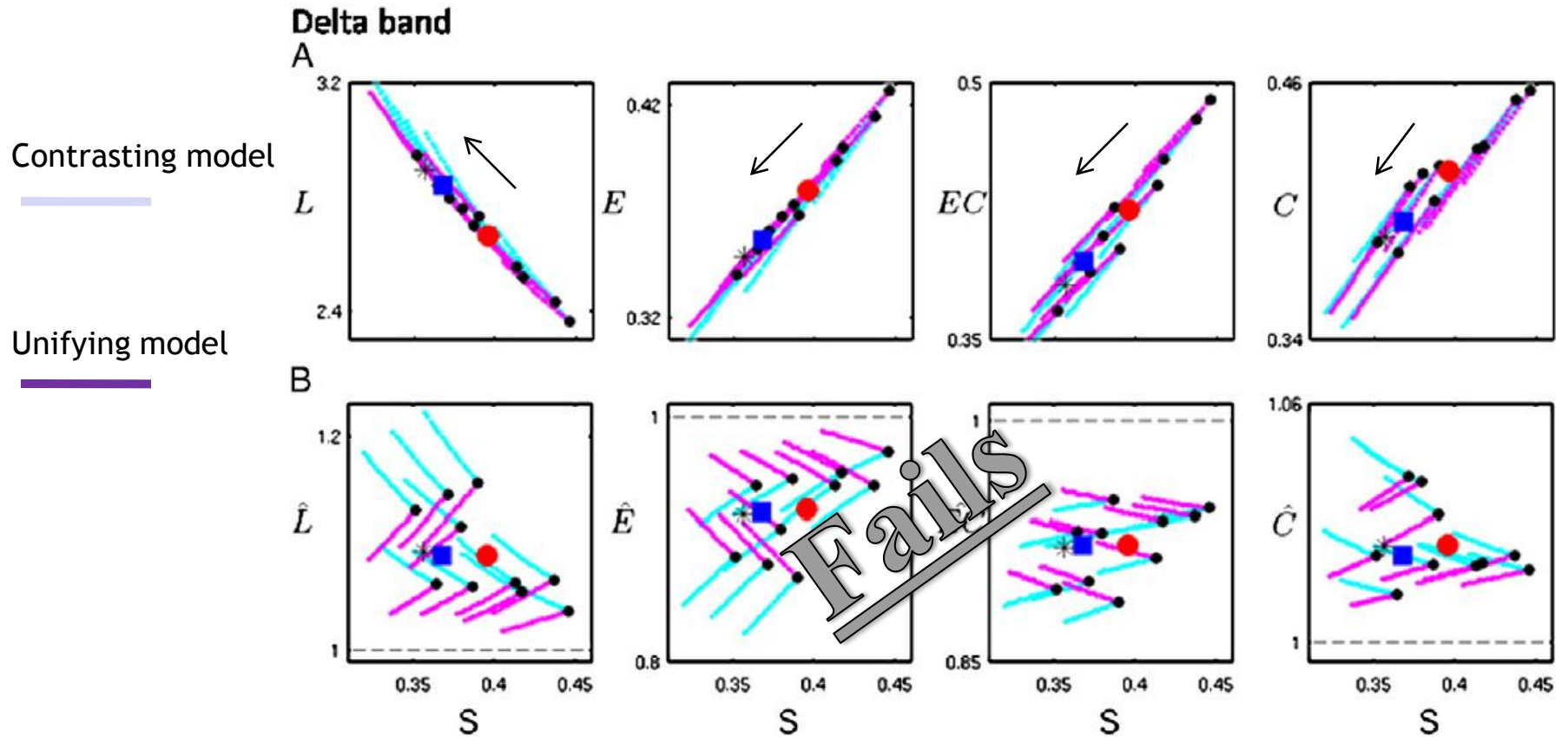$$b = \frac{k-\min(A_0^i)}{1-\min(A_0^i)}$$

Unifiying model (T-):

the global average strength of the matrix decreases and, in addition, the relative differences between link weights are reduced at each time step.

$$m_i = \frac{k-1}{1-\min(A_0^i)}$$
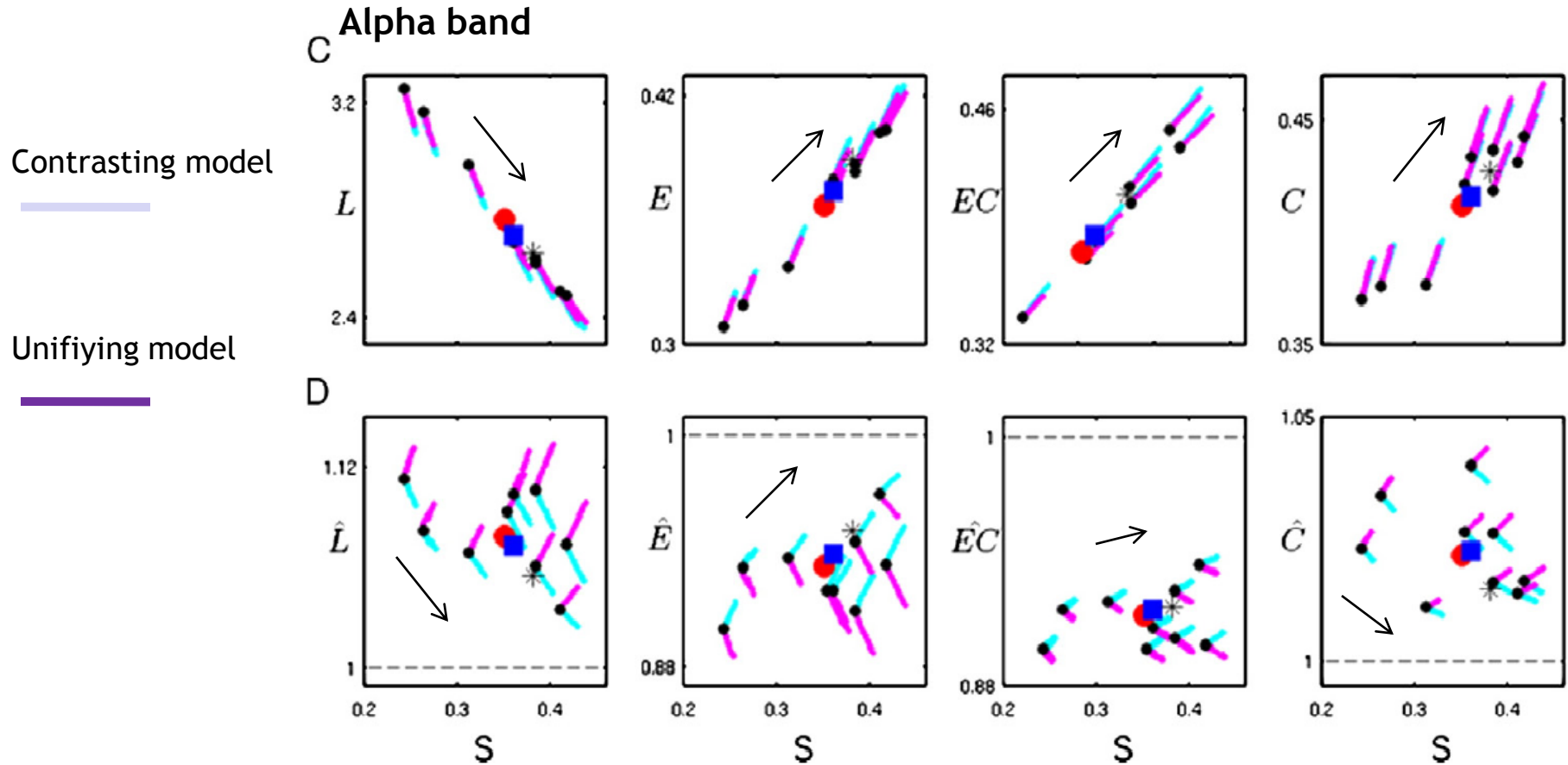
$$b = \frac{1-k\cdot\min(A_0^i)}{1-\min(A_0^i)}$$

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos

Evolutionary network models

Evolutionary network models

Complex Systems Group (URJC & CTB)
Seminar at U.P.M., March 2011

Conclusions

❑ Complex networks methods give useful information (from another perspective) about how functional brain networks behave.

❑ Network parameters give hints about how brain functional connectivity is affected by different diseases. They can be use in order to distinguish between healthy and damaged brains.

❑ We can develop evolutionary network models that mimic the evolution/recovery of different diseases.

❑ We have to be cautious since there is a high variability in the results.

❑ Its application to the early detection of brain diseases is still missing. Longitudinal experiments would help in order to understand the evolution of brain impairments and its early detection.

Thanks for your attention!

More information at:

http://complex.etsit.urjc.es

or

javier.buldu@urjc.es

CSG

CTB centro de tecnología biomédica

Universidad Rey Juan Carlos