Aalto University
School of Science

# Human Brain Networks

## Aivoaakkoset BECS-C3001

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# Why?

## 1. Why brain networks?

# Why do we want to study brain networks?

- **The brain is a network with** ~10^10 neurons and ~10^4 connections per neuron
- As for **genomics** in the $20^{th}$ century, many authors are now praising the ***connectomics*** as the current revolution in neuroscience
- Multi-million projects like the **Human *Connectome* Project, the BRAIN initiative**
- **Charting the *connectome*** presents challenges

# What?

## 2. What is a connectome?

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# The connectome

The connectome is the complete description of the structural connectivity (the physical wiring) of an organism's nervous system.

***Olaf Sporns (2010), Scholarpedia, 5(2):5584.***

# Human genome vs Human connectome

- The human genome contains over **3 billion base pairs** organized into 22 paired chromosomes
- The human connectome contains **~10^14 connections**

# What?

## 3. What is a network?



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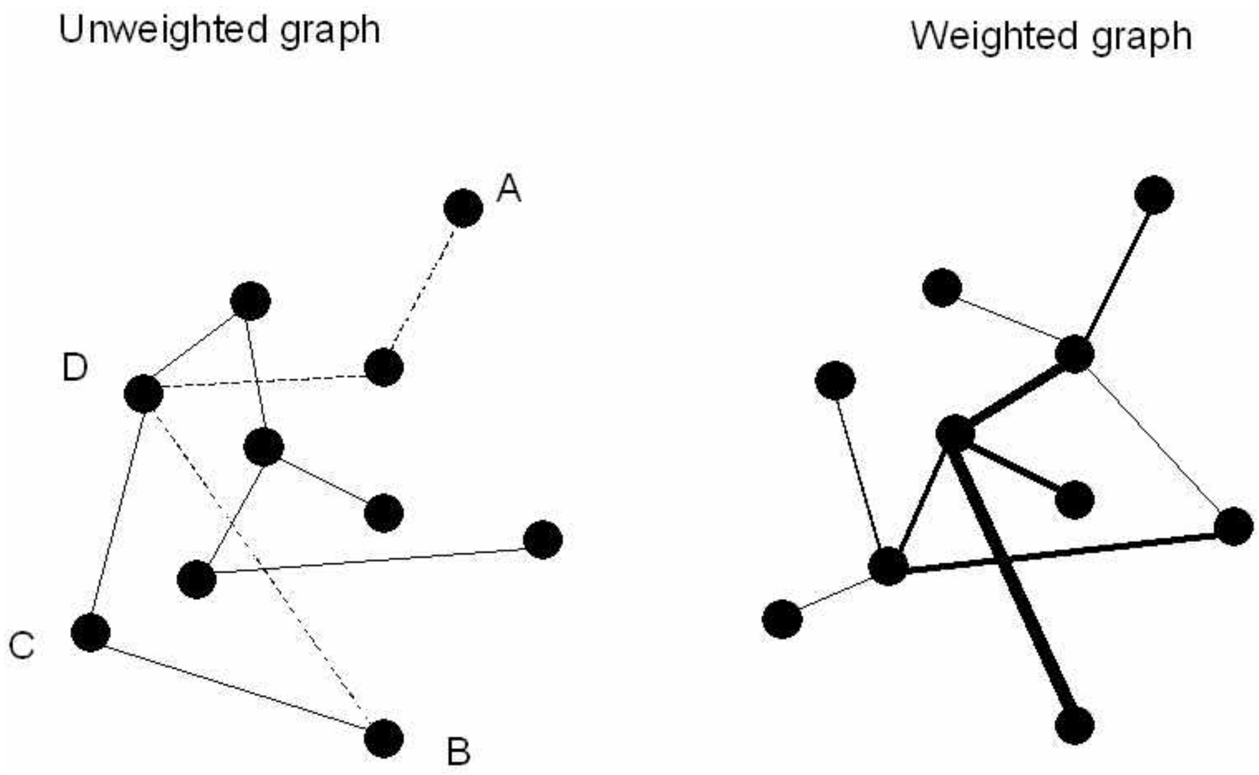
# A (complex) network, a graph




Newman, M. E. J., **Networks: An introduction**. Oxford University Press, Oxford, March 2010.

# Many types of networks

- **Physical networks**
  - ***Power grid network***
  - ***Physical layer of the internet***
  - ***Water distribution network***
  - ***Transportation networks (roads, rails)***
- **Non-physical networks**
  - ***Social networks (Facebook, Twitter, etc.)***
  - ***Stock Market***
  - ***IP layer of the internet***
  - ***Citations in science***

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# Complex network

From Wikipedia, the free encyclopedia

In the context of network theory, a **complex network** is a graph (network) with non-trivial topological features—features that do not occur in simple networks such as lattices or random graphs but often occur in real graphs. The study of complex networks is a young and active area of scientific research inspired largely by the empirical study of real-world networks such as computer networks and social networks.

**Network science**

Theory · History

Graph · **Complex network** · Contagion
Small-world · Scale-free ·
Community structure · Percolation ·
Evolution · Controllability · Topology ·
Graph drawing · Social capital ·
Link analysis · Optimization
Reciprocity · Closure · Homophily
Transitivity · Preferential attachment
Balance · Network effect · Influence

**Types of Networks**

Information · Telecommunication
Social · Biological · Neural
Interdependent · Semantic
Random · Dependency · Flow

**Contents** [hide]



## Definition [ edit source | edit beta ]

Most social, biological, and technological networks display substantial non-trivial topological features, with patterns of connection between their elements that are neither purely regular nor purely random. Such features

# What?

## 4. What is brain connectivity?

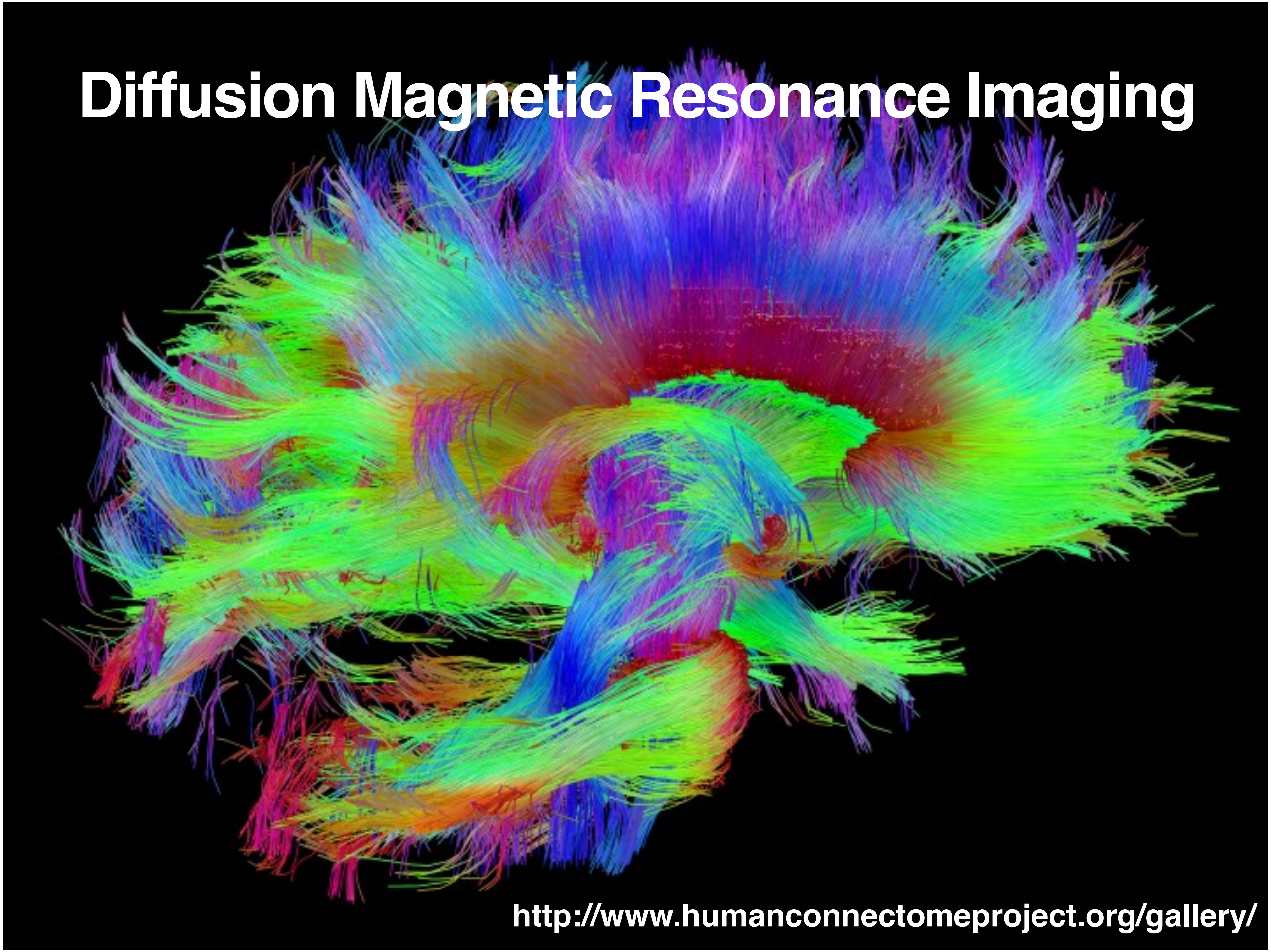
# Connectivity in neuroscience

- **Structural connectivity (estimating actual connections)**
  - ***Invasive*** *(tract tracing methods, 2 photon calcium imaging)*
  - ***Non invasive*** *(Diffusion Tensor and Diffusion Spectral Imaging)*
- **Functional connectivity (based on temporal "co-variance")**
  - ***Invasive*** *(intracranial recordings)*
  - ***Non invasive*** *(fMRI, M/EEG, simulated data)*

**Craddock, et al. (2013). Imaging human connectomes at the macroscale. Nature Methods, 10(6), 524–539. (*)**

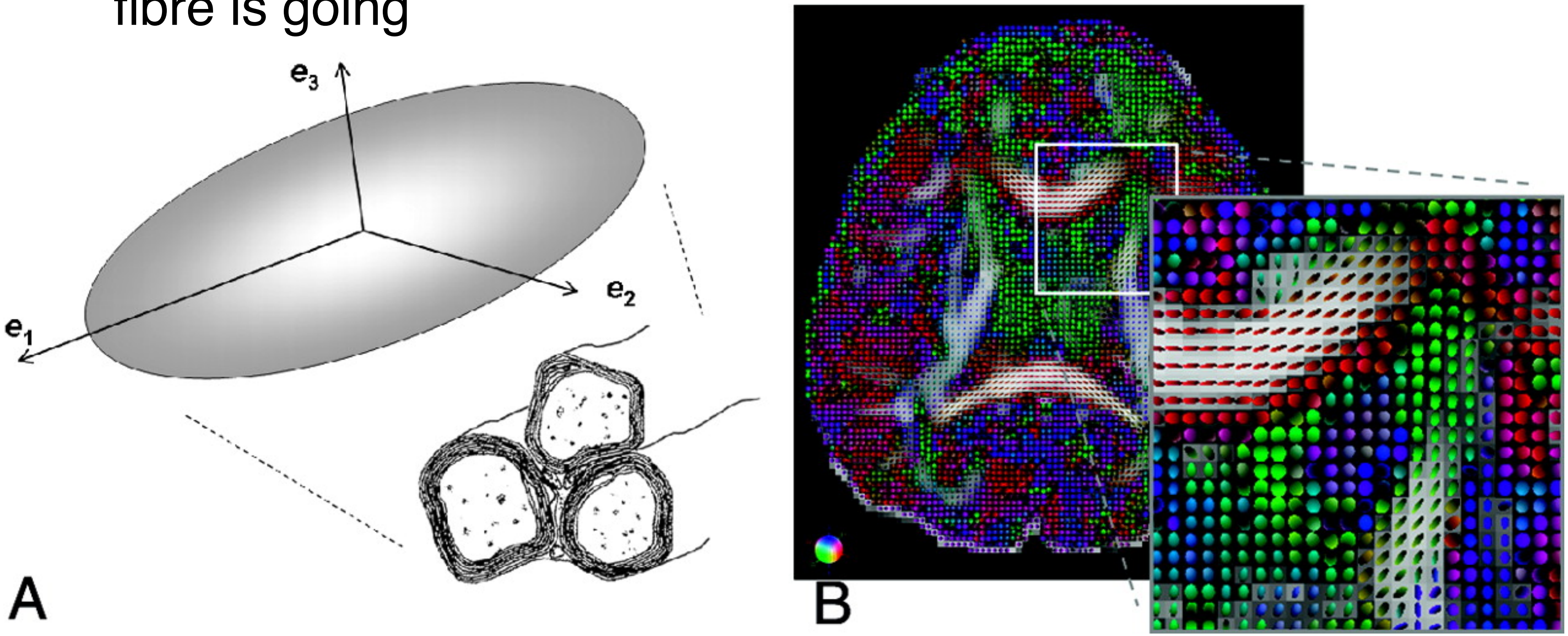
# How?

## 5. How do we estimate structural brain networks non invasively?


Diffusion Magnetic Resonance Imaging
http://www.humanconnectomeproject.org/gallery/

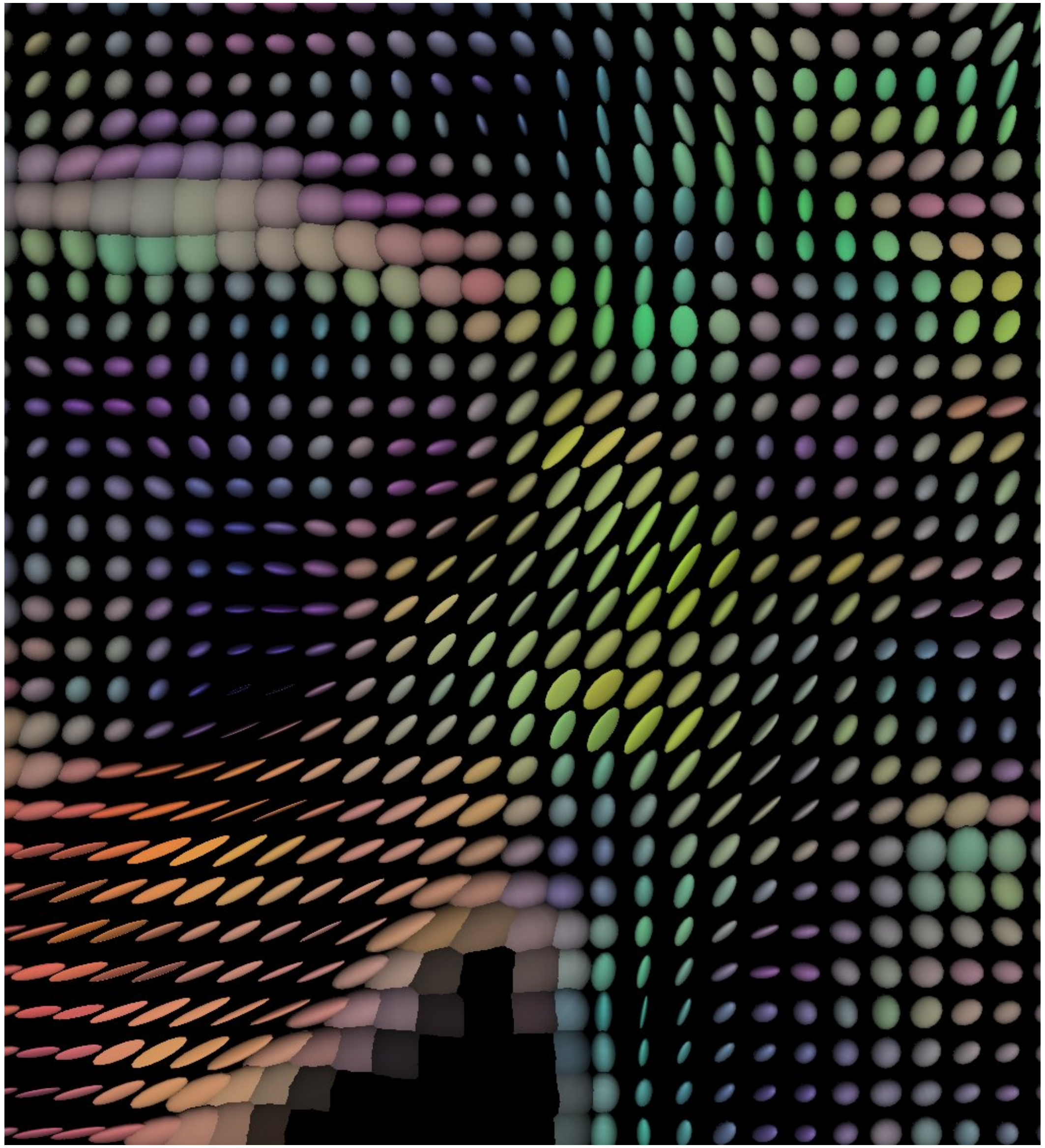
# Diffusion MRI

- For every voxel we measure the **diffusion of water**
- We can determine the main direction(s) along which the fibre is going



# Diffusion MRI

- By following the directions of diffusion **we can reconstruct the tracts**



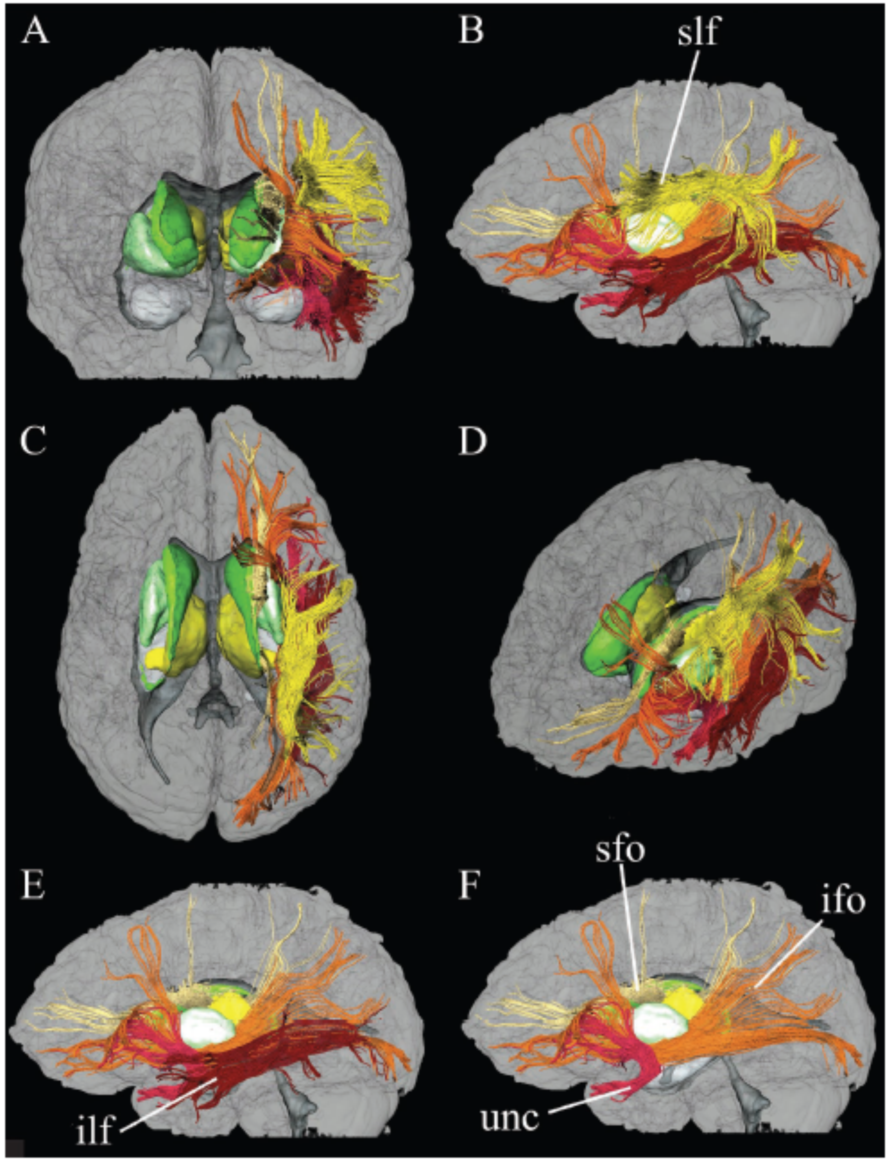



**Figure 4.** Four viewing angles of 3D depictions of association fibers. *A,* Anterior view; *B,* left lateral view; *C,* superior view; *D,* oblique view from right anterior angle. Reconstructed fibers are superior longitudinal fasciculus (*slf,* yellow), inferior longitudinal fasciculus (*ilf,* brown), superior fronto-occipital fasciculus (*sfo,* beige), inferior fronto-occipital fasciculus (*ifo,* orange), and uncinate fasciculus (*unc,* red). *E, F,* Left lateral views without superior longitudinal fasciculus *(E)* and inferior longitudinal fasciculus *(F).*

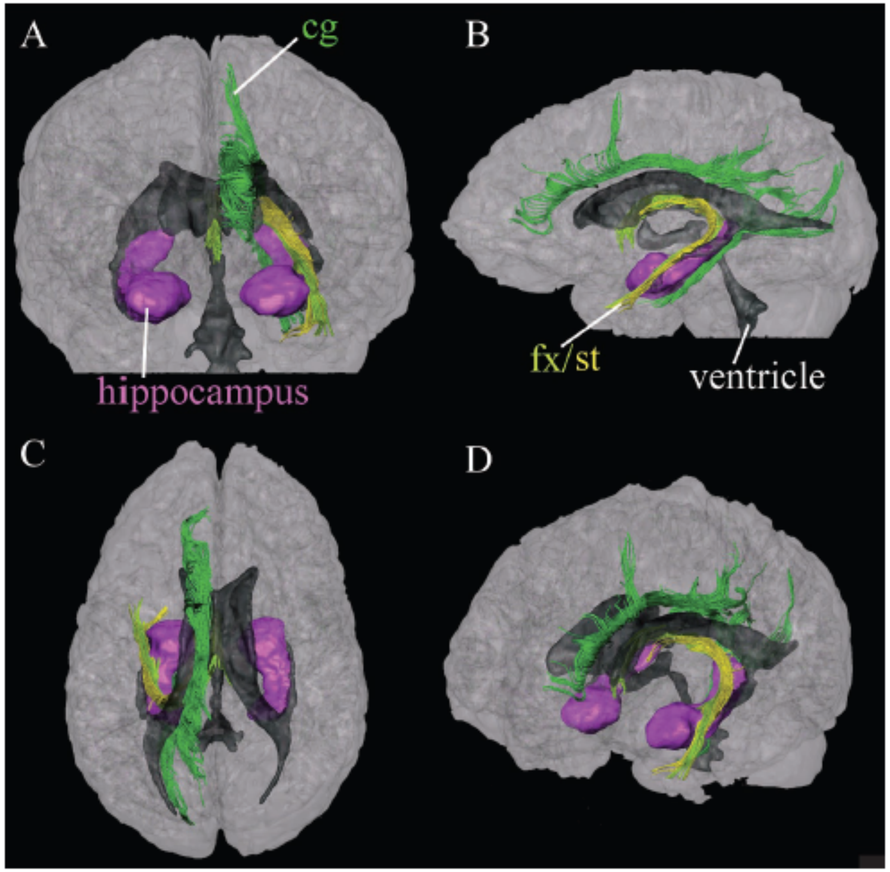


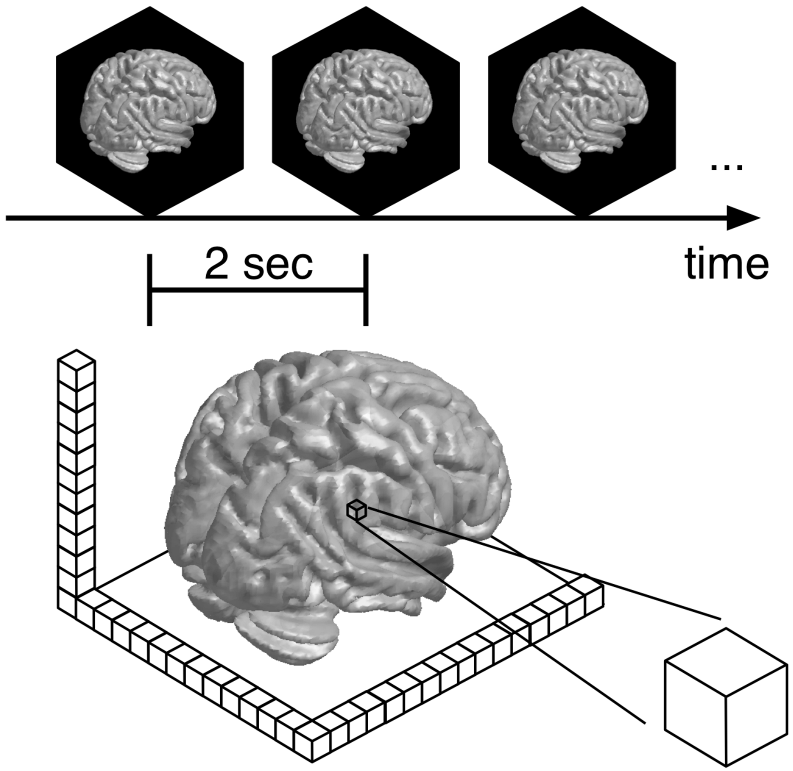

**Figure 5.** Four viewing angles of 3D depictions of limbic system fibers. *A,* Anterior view; *B,* left lateral view; *C,* superior view; *D,* oblique view from right anterior angle. Reconstructed fibers are cingulum (*cg,* dark green), fornix (*fx,* light green), and stria terminalis (*st,* yellow). For anatomic guidance, hippocampus and amygdala (purple) and ventricles (gray) are also shown.

Wakana, S., et al. (2004). Fiber tract-based atlas of human white matter anatomy. Radiology, 230(1), 77–87.

# How?

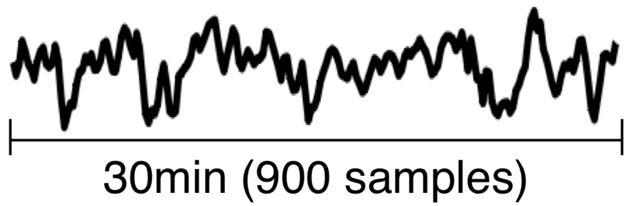
## 6. How do we estimate functional brain networks non invasively?

# Functional magnetic resonance imaging (fMRI)



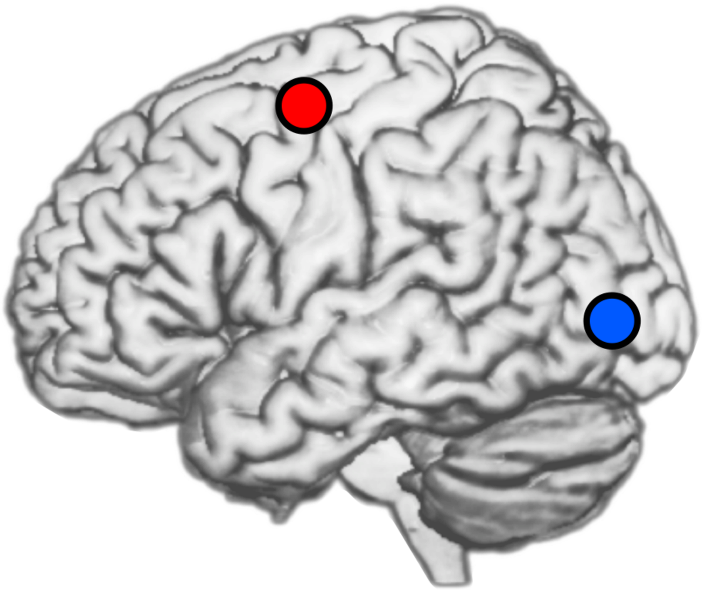

- We measure **multiple time series** at once
- We can consider them **independently** (e.g. GLM) or we can look at **mutual relationships**

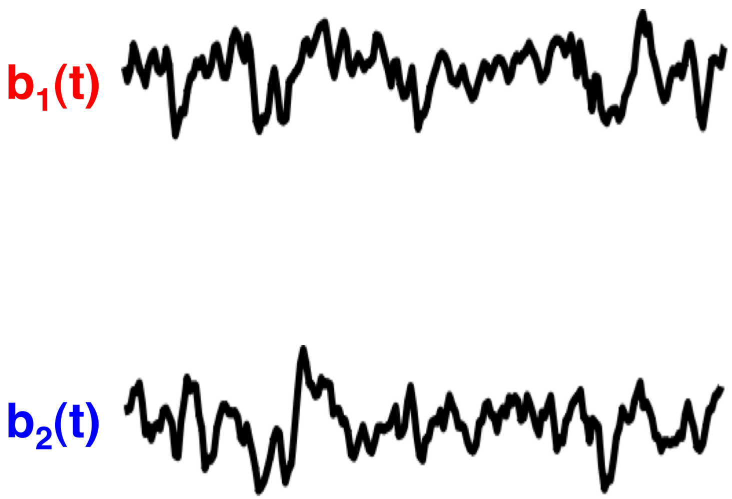
**Blood Oxygen Level signal**



# Building a functional network

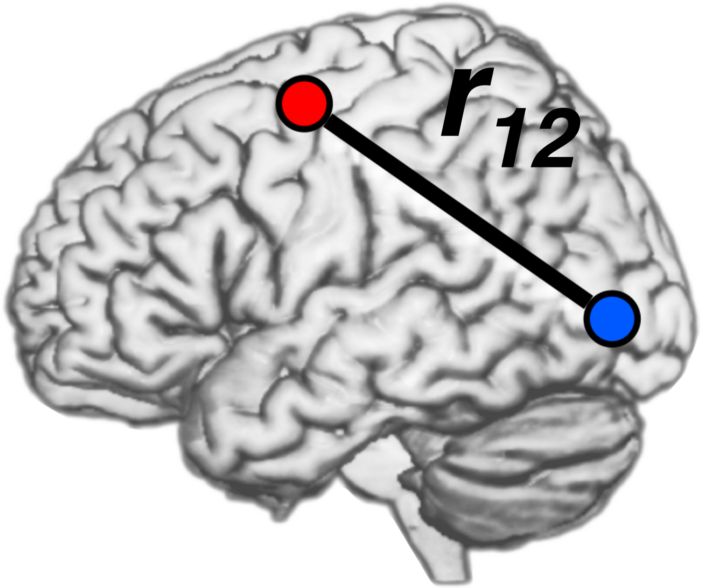
At each **node** we measure a **time series**
We compute their **similarity**

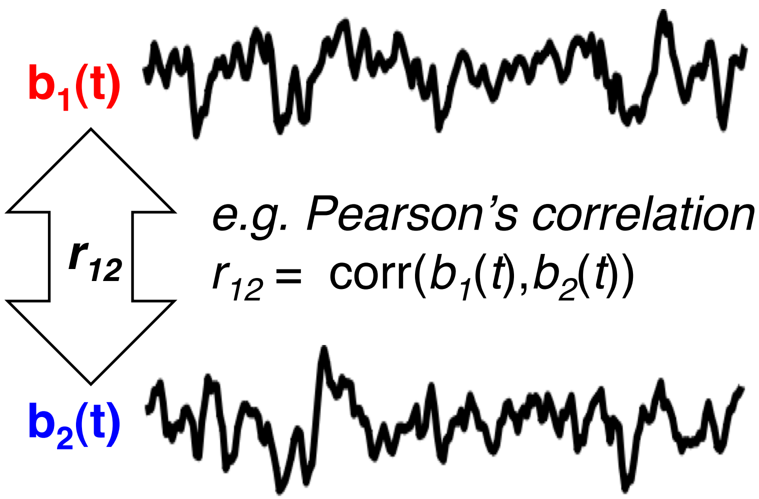




# Building a functional network

Similarity value used as **weight of the edge** between the two nodes. Repeat for each pair of nodes.



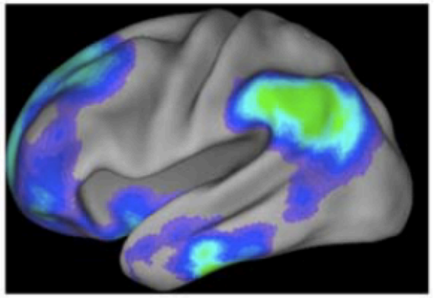



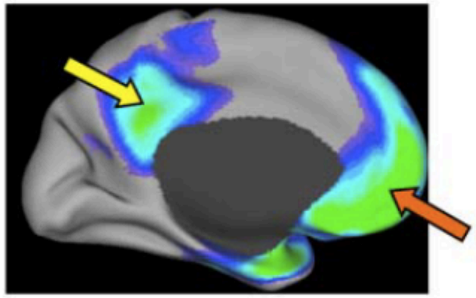

*e.g. Pearson's correlation:*

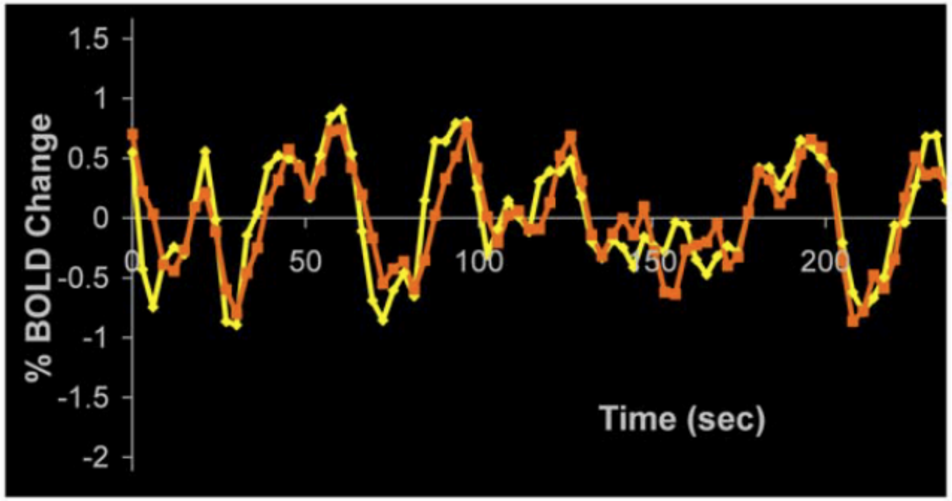
$r_{12} = \text{corr}(b_1(t), b_2(t))$

# The activity of the brain at rest is ideal for estimating the connectome

By looking at regions that change together in time we can **estimate their connectivity**








Raichle, M. E. (2010). Two views of brain function. Trends in Cognitive Sciences, 14(4)

# Network topology

## Network level features

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# What?

## 7. What is a small world network?



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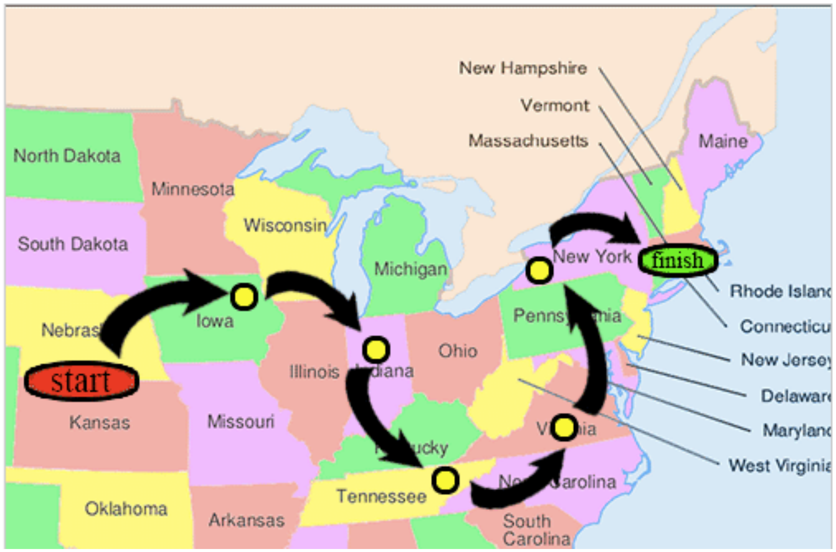
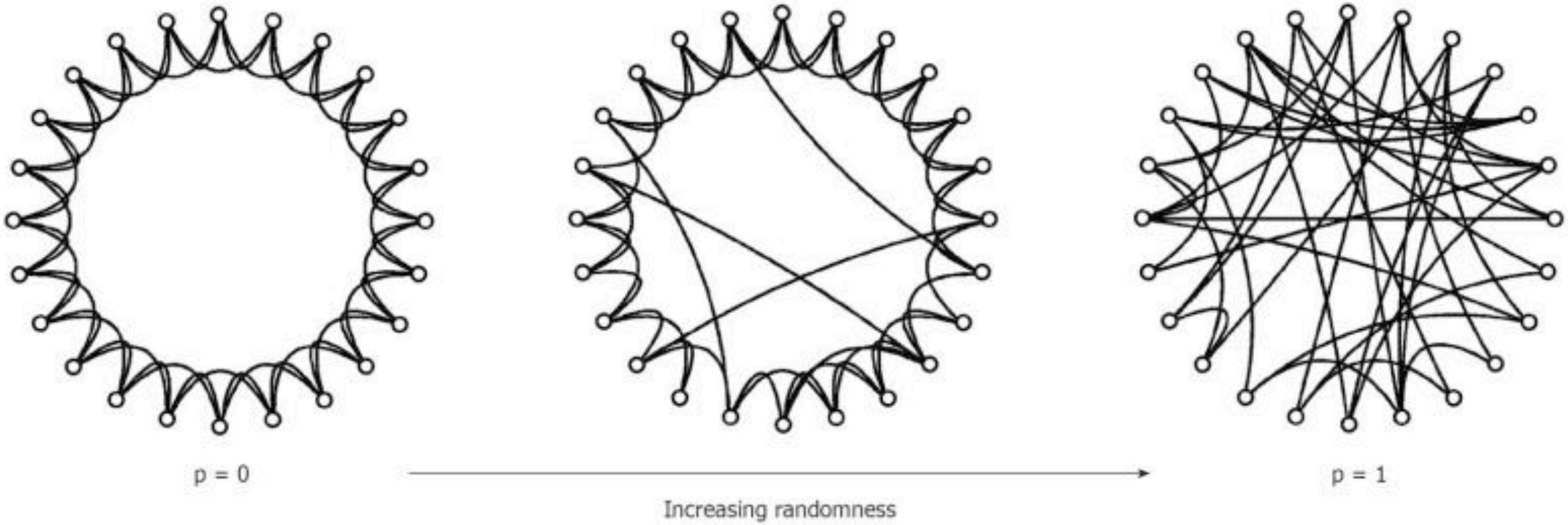
# The small world experiment
# Stanley Milgram (1969)

- Try to send a letter to Boston through a **chain of people** by only forward it to a friend who might know the final recipient
- **Six degrees of separation** i.e. an *average path* of 6 links in the network



# Small world networks




Watts, D. J., & Strogatz, S. H. (1998). Collective dynamics of “small-world” networks. Nature, 393(6684), 440–2. doi:10.1038/30918

# Small world networks

Small world networks are present in biological system as an efficient way to keep the average path low and limit connection cost.

**The brain is a small world network.**

# Why?

## 8. Why is the brain a small world network?



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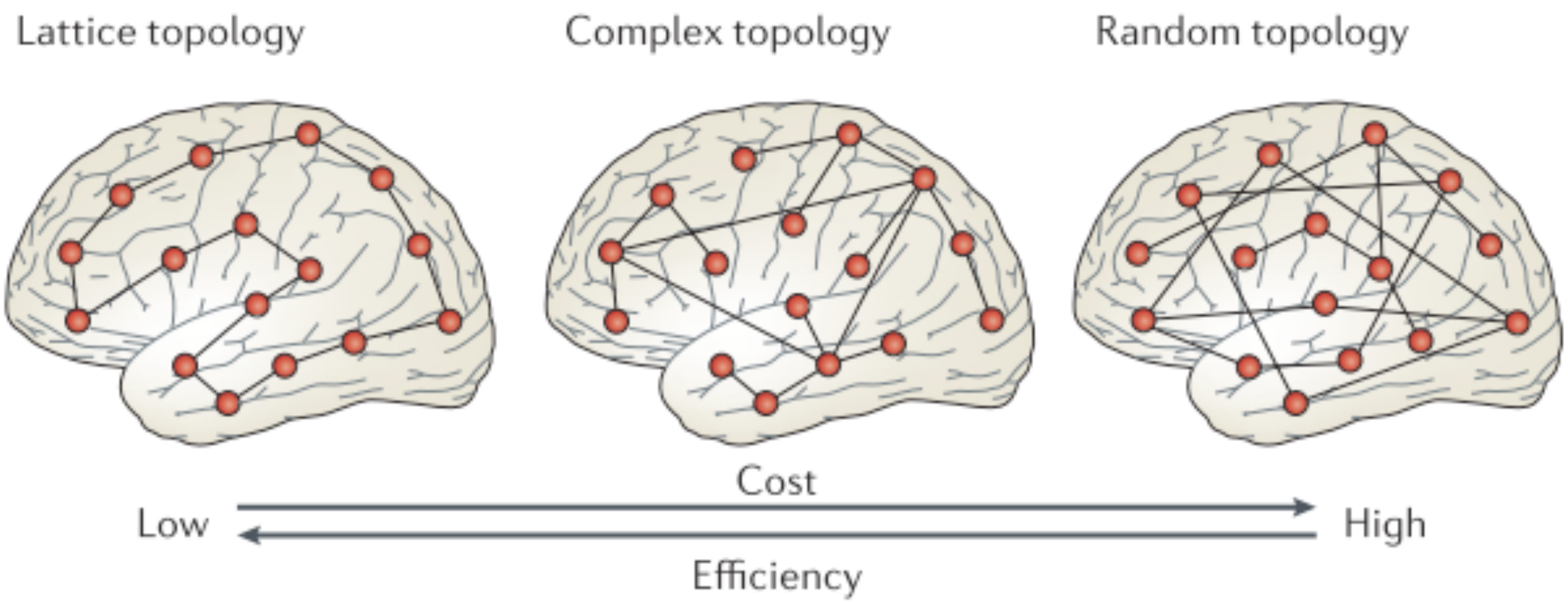
# The small-world configuration is the optimal to optimize communication cost and efficiency




**Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. Nature reviews. Neuroscience, 13(5), 336–49.(*)**

# Network topology

## NODE LEVEL FEATURES

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# What?

## 9. What is a hub?



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# What is a hub?

A hub is the effective center of an activity, region, or network…

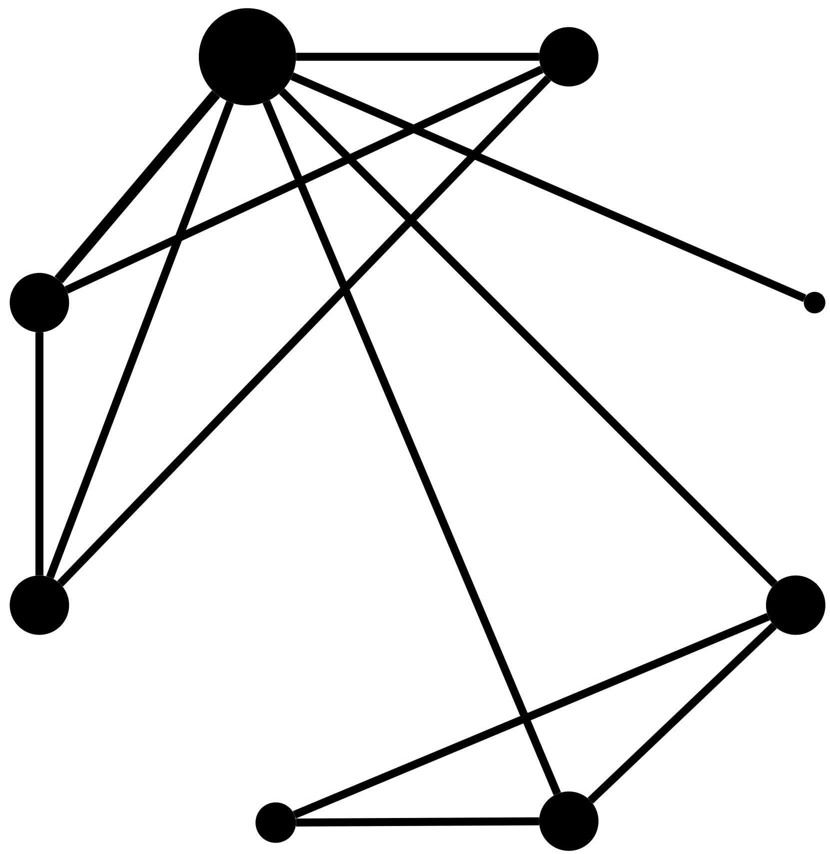
i.e. **an important node in the network**

# How?

## 10. How can we quantify a hub?

# Microscopic (node level) measures

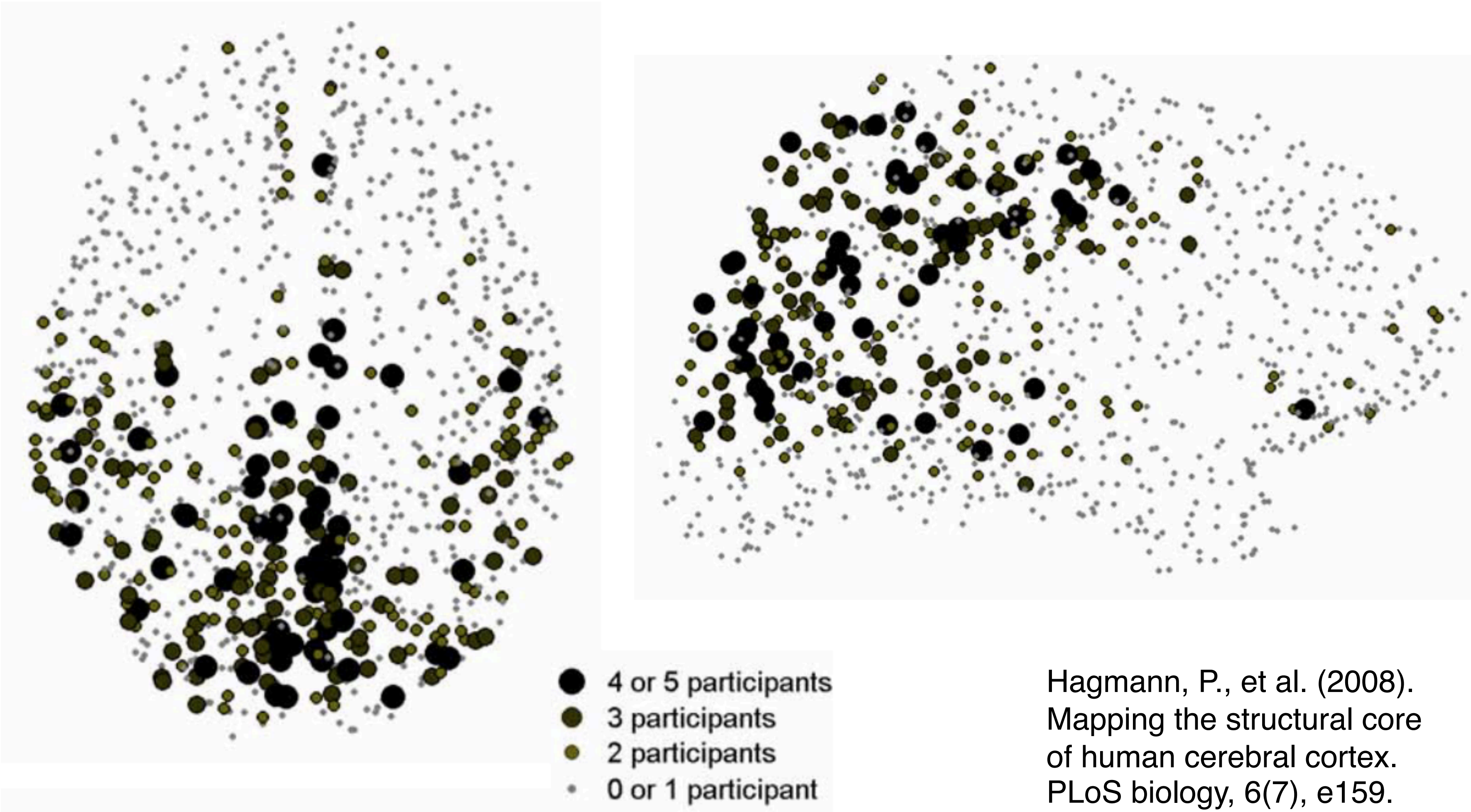
- **Node degree/strength**
  How strong is a node?
- **Clustering**
  How close is the node with the neighbours?
- **Closeness centrality**
  How distant is the node?
- **Betweenness centrality**
  How many shortest paths through the node?



# What?

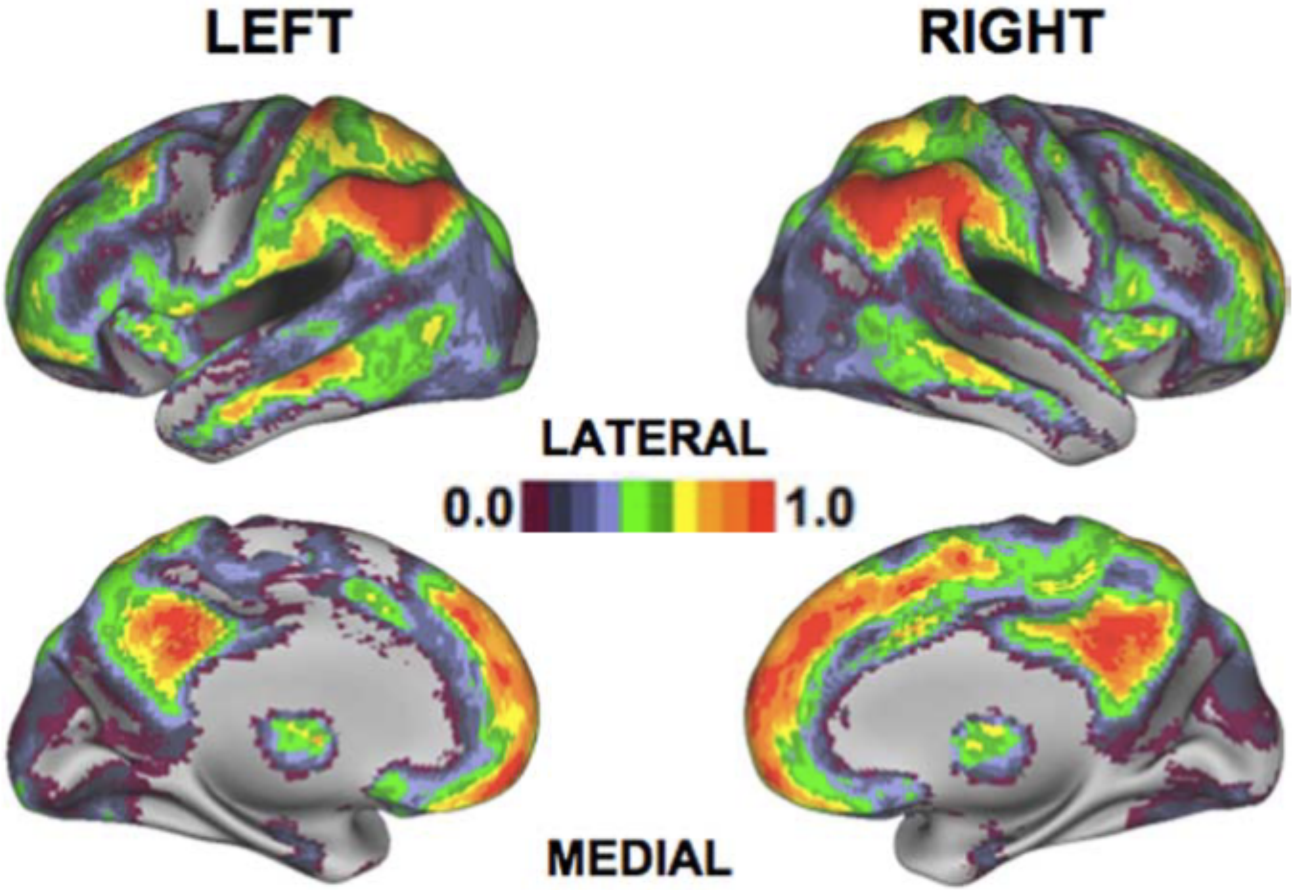
## 11. What are the hubs in the brain?

# Cortical hubs in the human brain



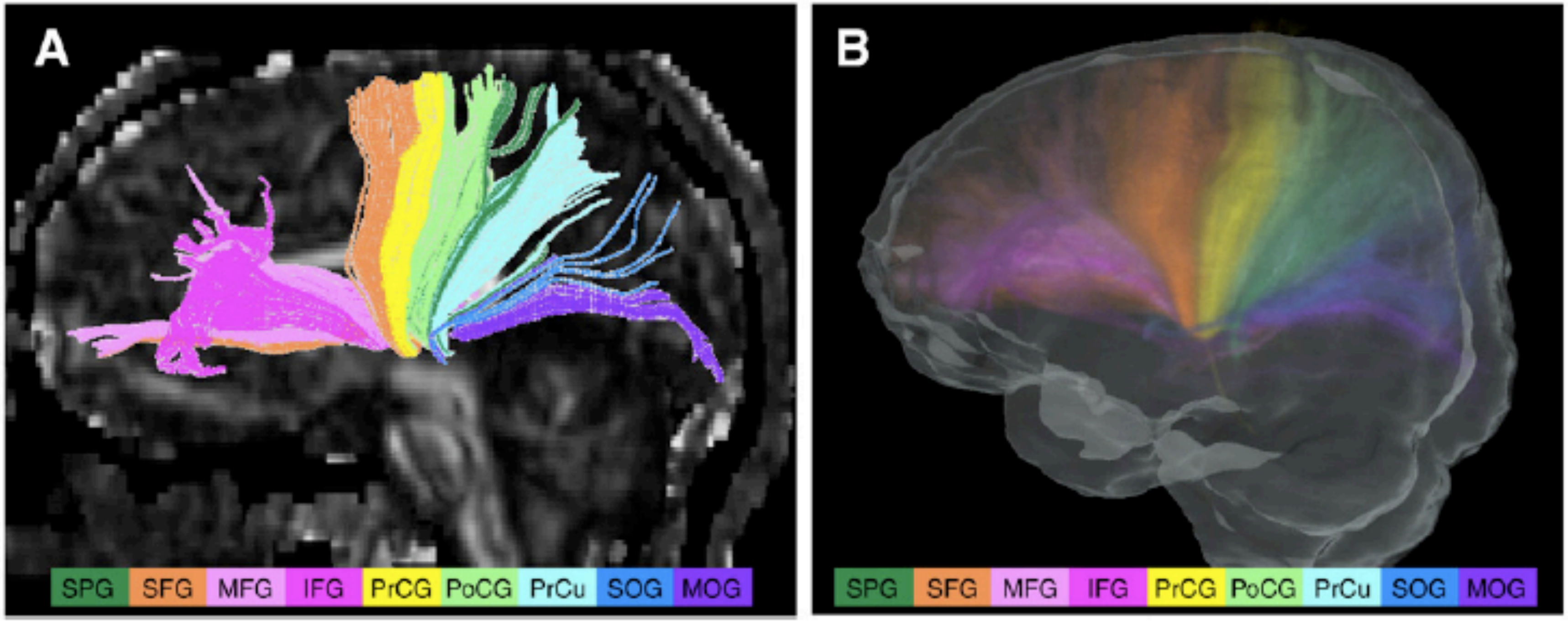

Hagmann, P., et al. (2008). Mapping the structural core of human cerebral cortex. PLoS biology, 6(7), e159.

# Cortical hubs in the human brain




Buckner, R. L., et al. (2009). Cortical hubs revealed by intrinsic functional connectivity. The Journal of neuroscience 29(6), 1860–73.

# Sub-cortical hubs in the human brain: the thalamus




Zhang et al. (2010) Atlas-guided tract reconstruction for automated and comprehensive examination of the white matter anatomy. Neuroimage. 2010 Oct 1;52(4):1289-301.

# Why?

## 12. Why are there hubs in the brain?



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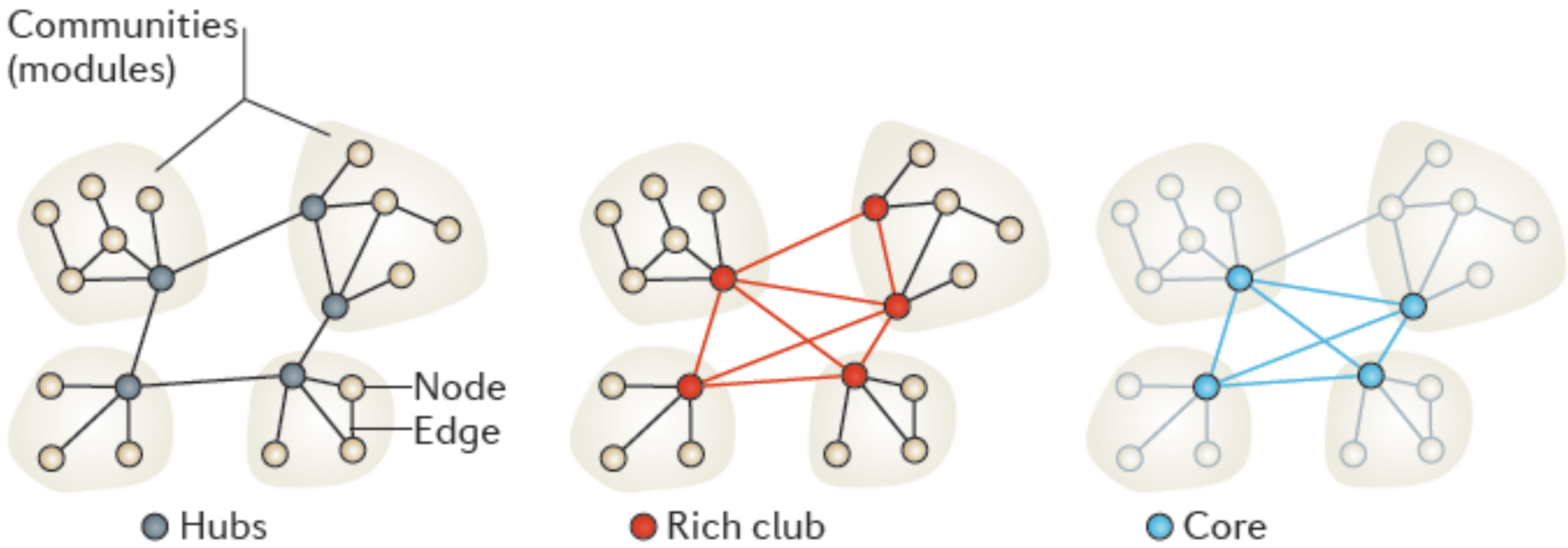
# Small world topology implies **segregation and integration**

- **Small world topology implies high clustering:** within a region we have more connections, regions are specialized (e.g. visual cortex, auditory cortex)
- **Small world topology implies short path:** densely connected regions are joined together by long-range links
- **Clustering -> Segregation**
- **Short path -> Integration**

**Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. Nature reviews. Neuroscience, 13(5), 336–49.(*)**

# A *rich club* of strong hubs is at the core of the human brain

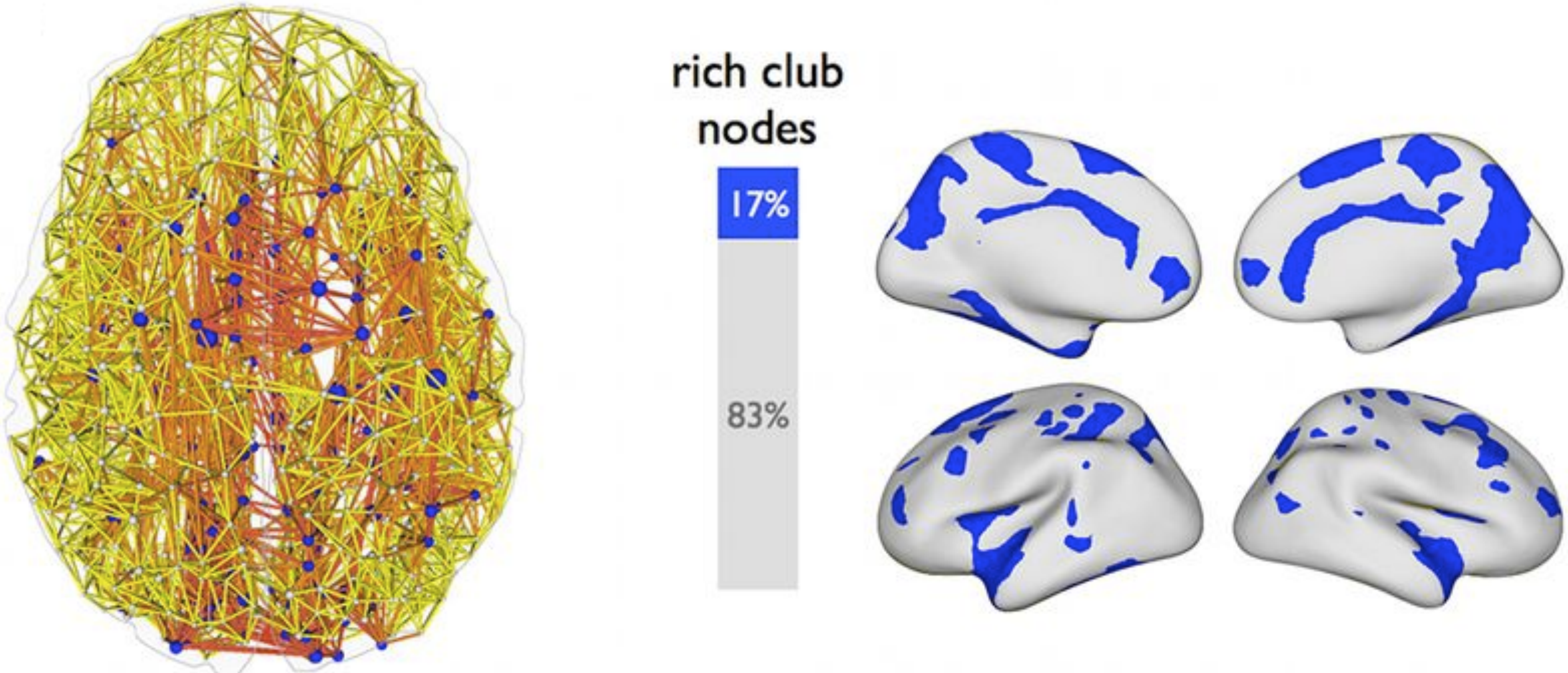



**Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. Nature reviews. Neuroscience, 13(5), 336–49.(*)**

# Where?

## 13. Where are the rich club nodes in the brain?

# Location of the rich club




Van den Heuvel, M. P., & Sporns, O. (2013). An Anatomical Substrate for Integration among Functional Networks in Human Cortex. The Journal of neuroscience, 33(36), 14489–500.

# What?

## 14. What is a module?

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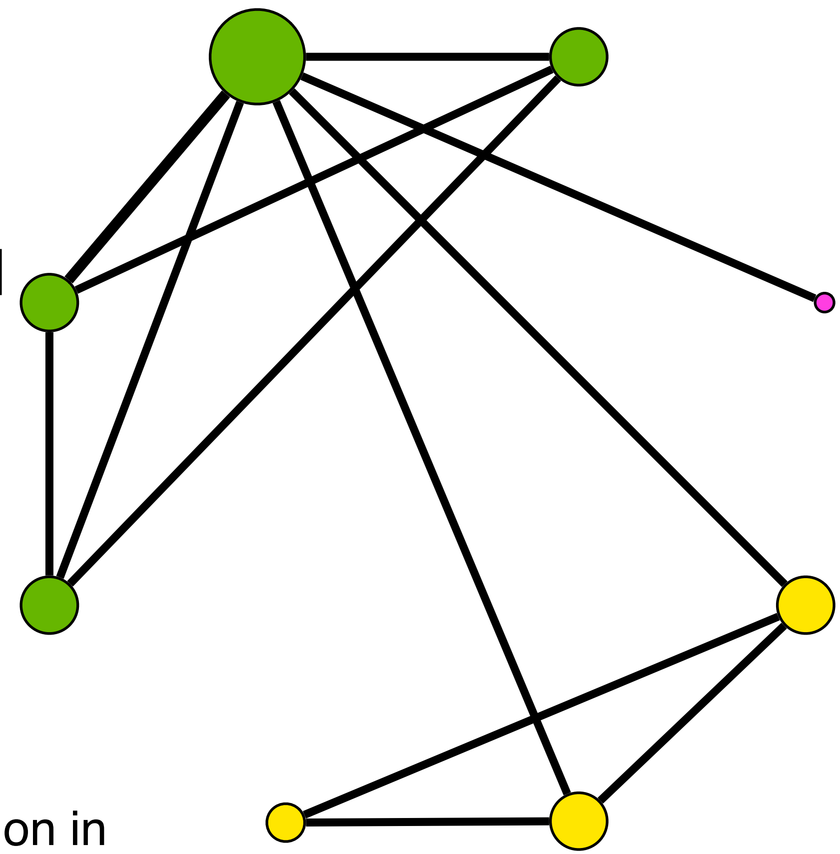
# Quantifying modules in networks

## Communities/clusters

Finding subsets of nodes that are forming a module, i.e. they are more connected with each other than with other parts of the network



Fortunato, S. (2010). Community detection in graphs. Physics Reports, 486(3-5), 75–174

# What?

## 15. What are the modules in the brain?

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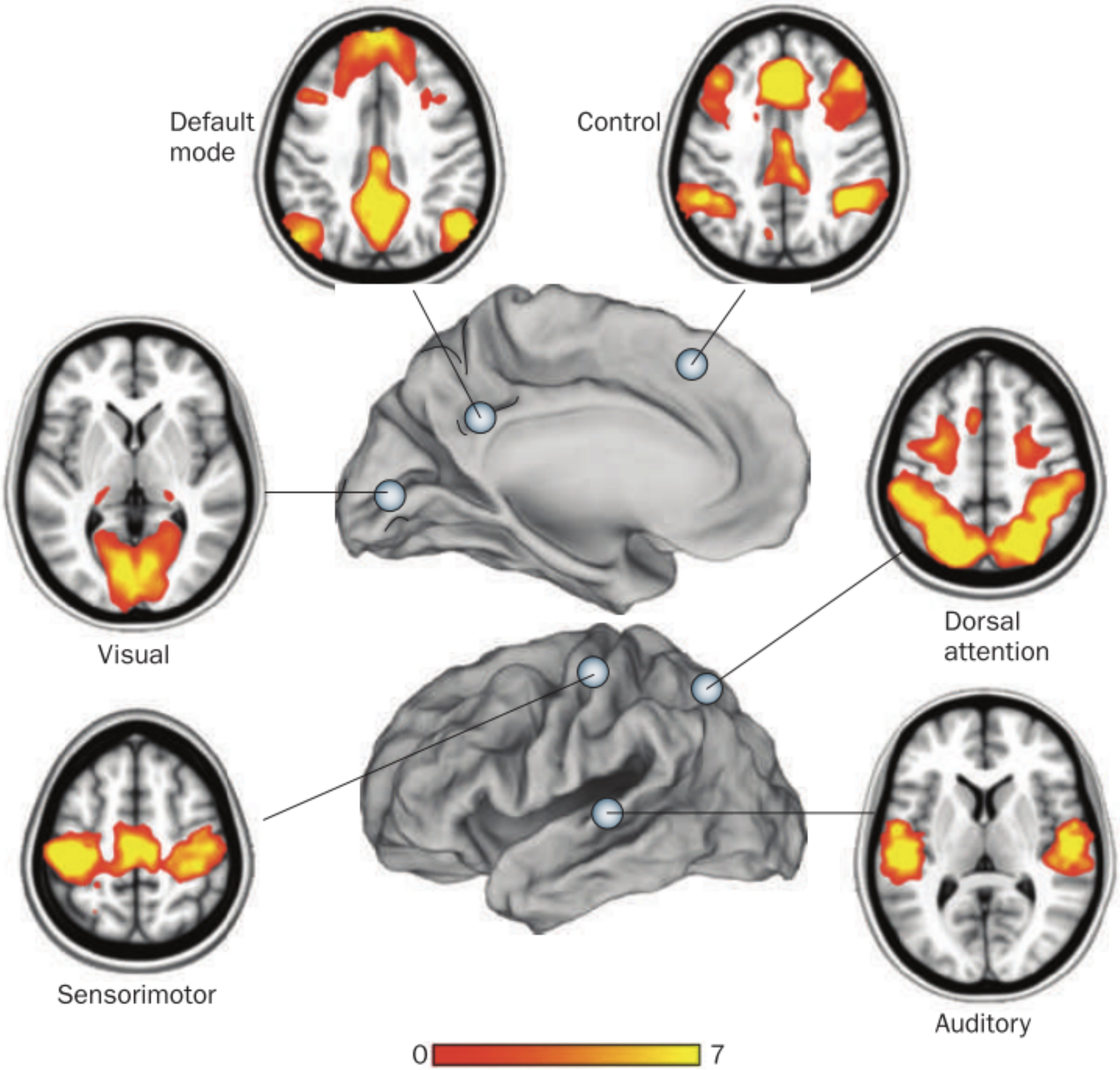
# The networks of the human brain

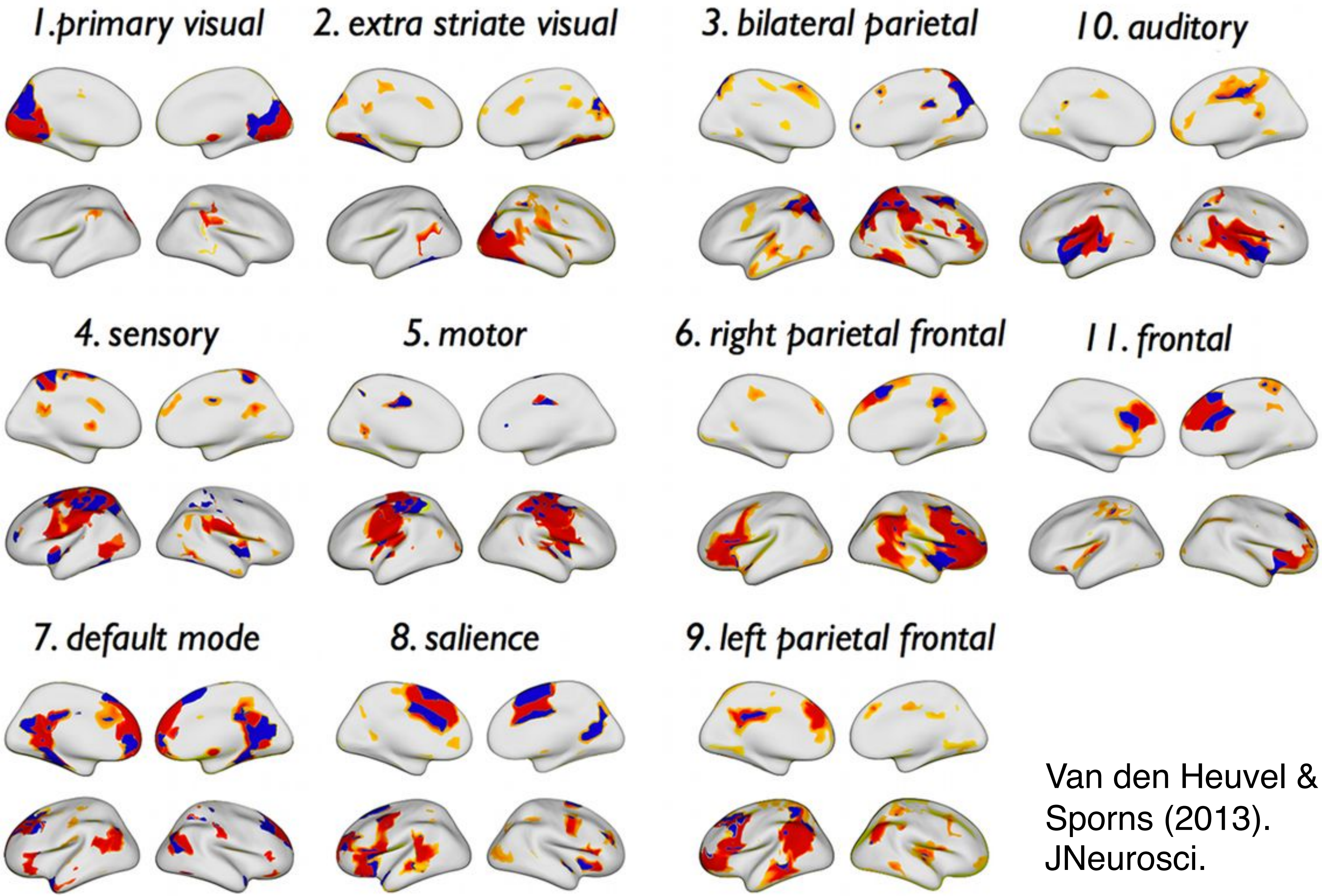
- We look at **which regions are more connected with each other (clustering)**
- We identify **~6 main modules** in the human cortex that corresponds to important cognitive functions
- They are often called "**networks**" although they are technically sub-networks




Zhang, D., & Raichle, M. E. (2010). Disease and the brain's dark energy. Nature reviews. Neurology, 6(1), 15–28.

# What?

## 15. What is the overlap between modules and rich hubs?

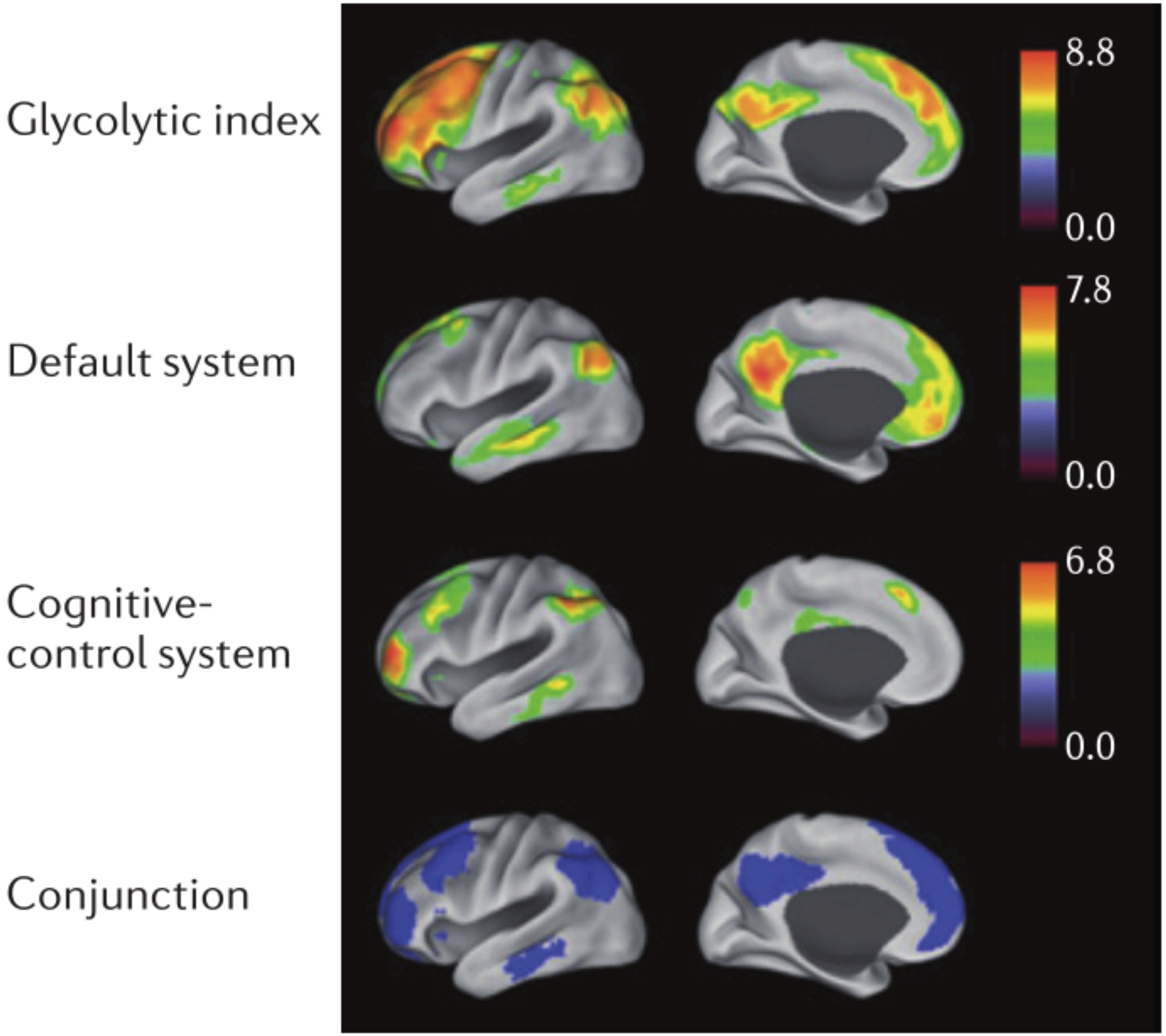



Van den Heuvel & Sporns (2013). JNeurosci.

# What?

## 16. What is the relationship between hubs and brain energy consumption?

# Energy consumption in the brain




**The most important (central) hubs are those with higher glycolytic index, i.e. higher metabolic cost.**

Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. Nature reviews. Neuroscience, 13(5), 336–49.(*)

# What?

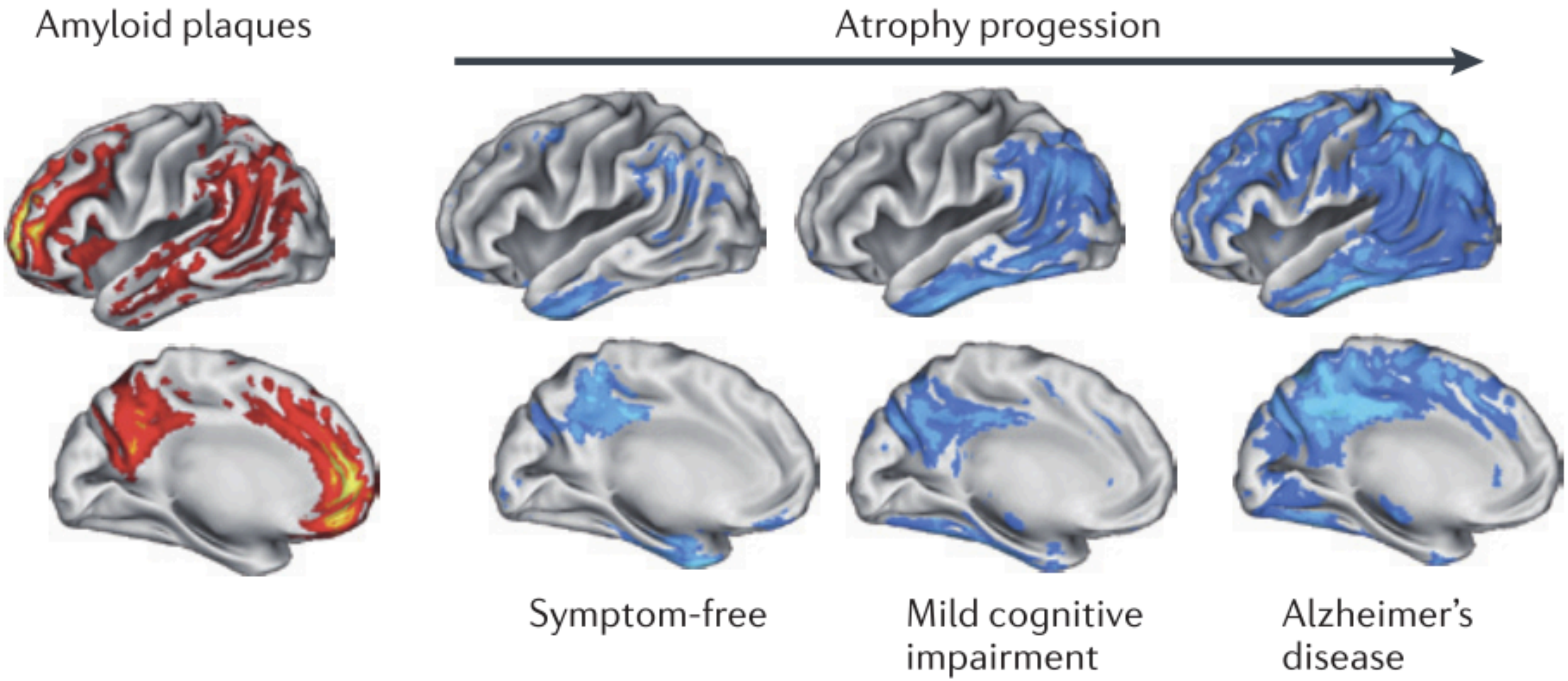
## 17. What is the impact of this research on society?

# Mapping the connectome and clinical applications

- The **connectome** will provide **novel insights on the functioning of the brain**
- There are multiple **mental diseases that are caused by dysfunctions of brain networks**, for example:
  - Alzheimer's disease
  - Schizophrenia
  - Autism

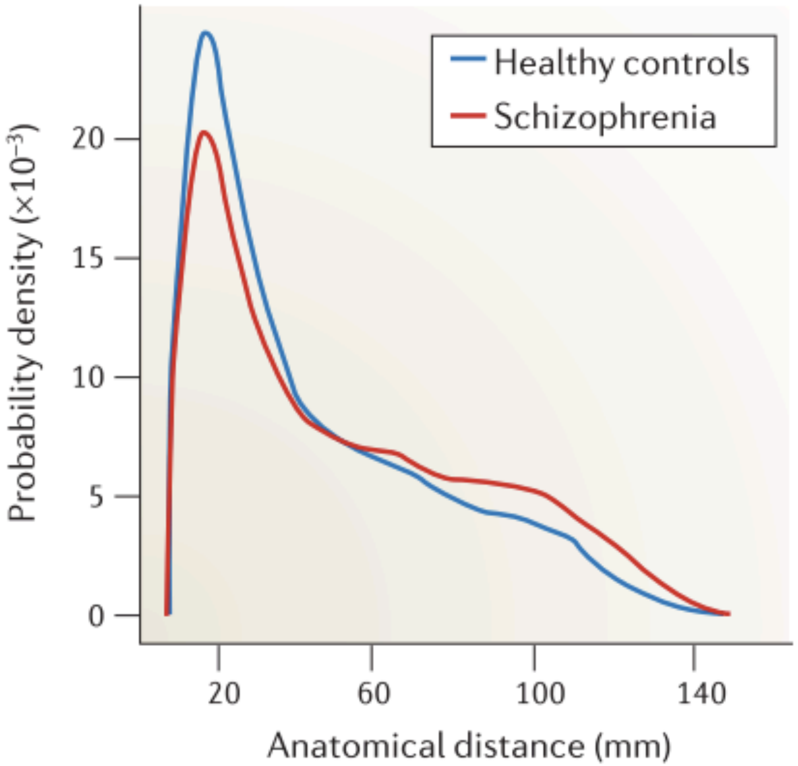
# Alzheimer’s disease

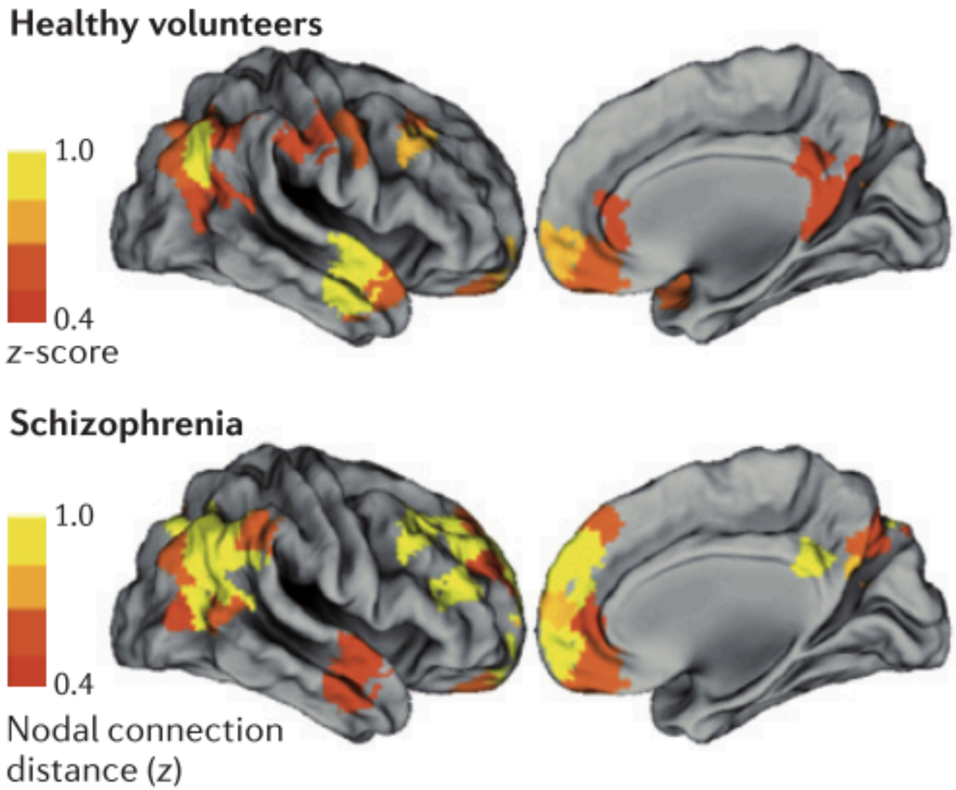
- **The most expensive hubs are attacked by the disease**



# Schizophrenia

- **Unbalanced small-worldness**

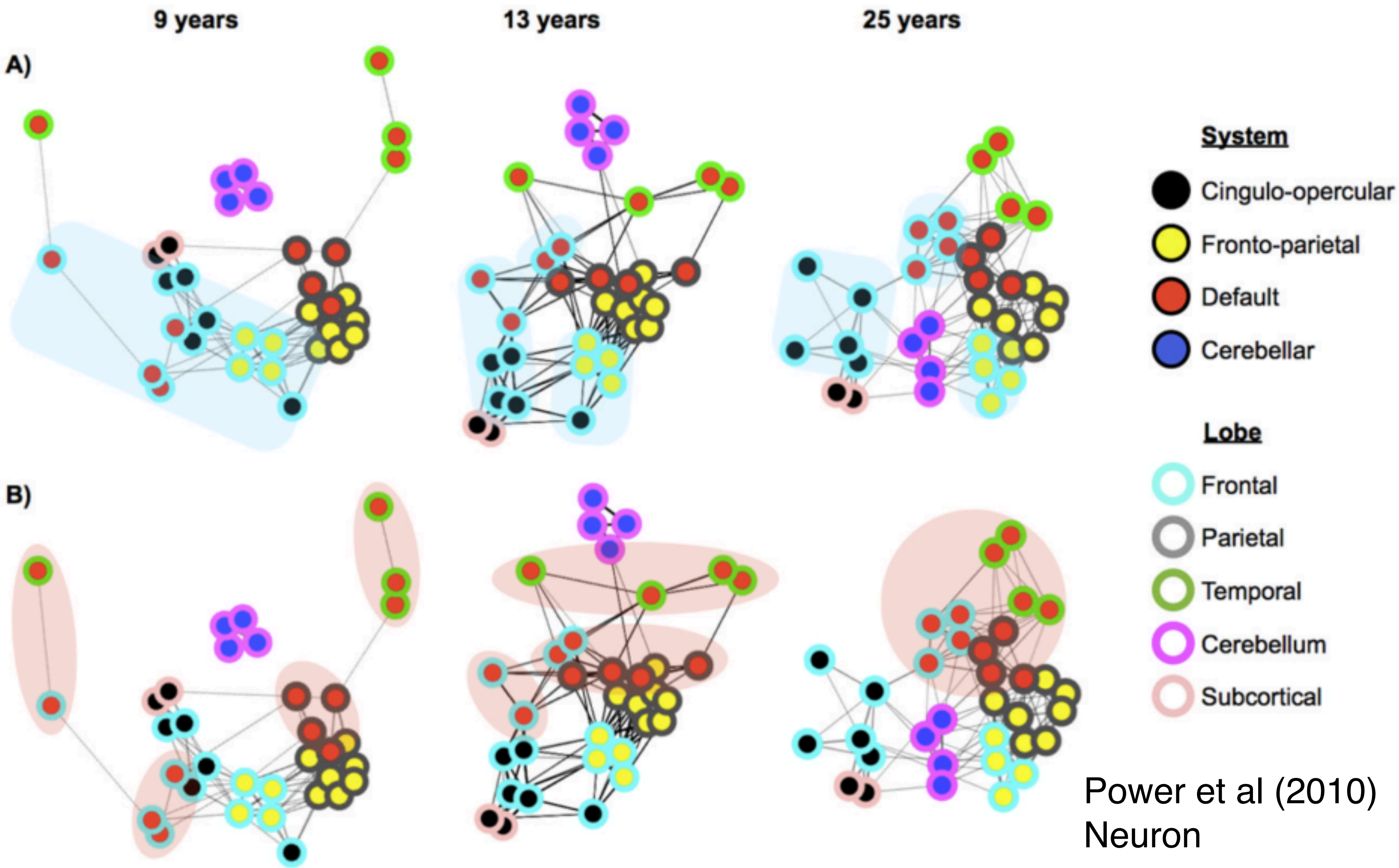


# The future?

## 18. What are the future challenges?

# Evolution of brain networks in time




Power et al (2010)
Neuron

# Evolution of brain networks in time

- We know that brain networks evolve in time (e.g. during development)
- How can we quantify faster changes due to stimuli?
- How can we quantify and predict the impact of brain diseases in time?

# Two important references and a book

**Bullmore, E., & Sporns, O. (2012). The economy of brain network organization.**
Nature reviews. Neuroscience, 13(5), 336–49.

**Craddock, et al. (2013). Imaging human connectomes at the macroscale.** Nature Methods, 10(6), 524–539.

**Networks of the Brain**
Sporns, O; 2010, MIT Press.