Mapping the human brain

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January 7th, 2019

Why?

Many brain pathologies are related to changes in the neural network

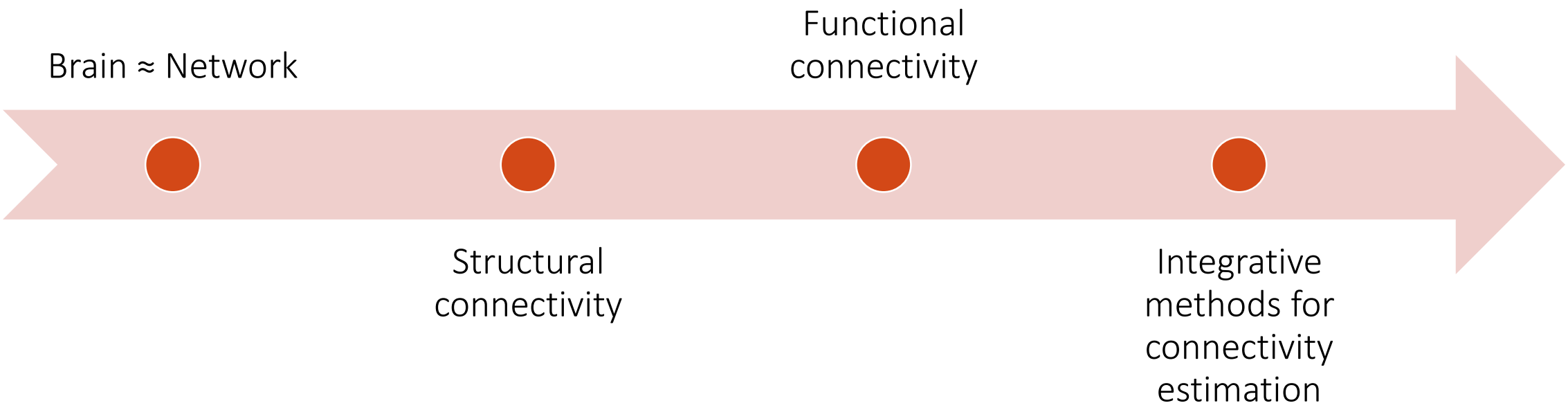
Main difficulties

The Human Brain is a complex multiscale biomechanism.

Very high dimensionality (10^{11} neurons in a single human brain).

Relatively poor quantitative tools are available for measuring the brain.

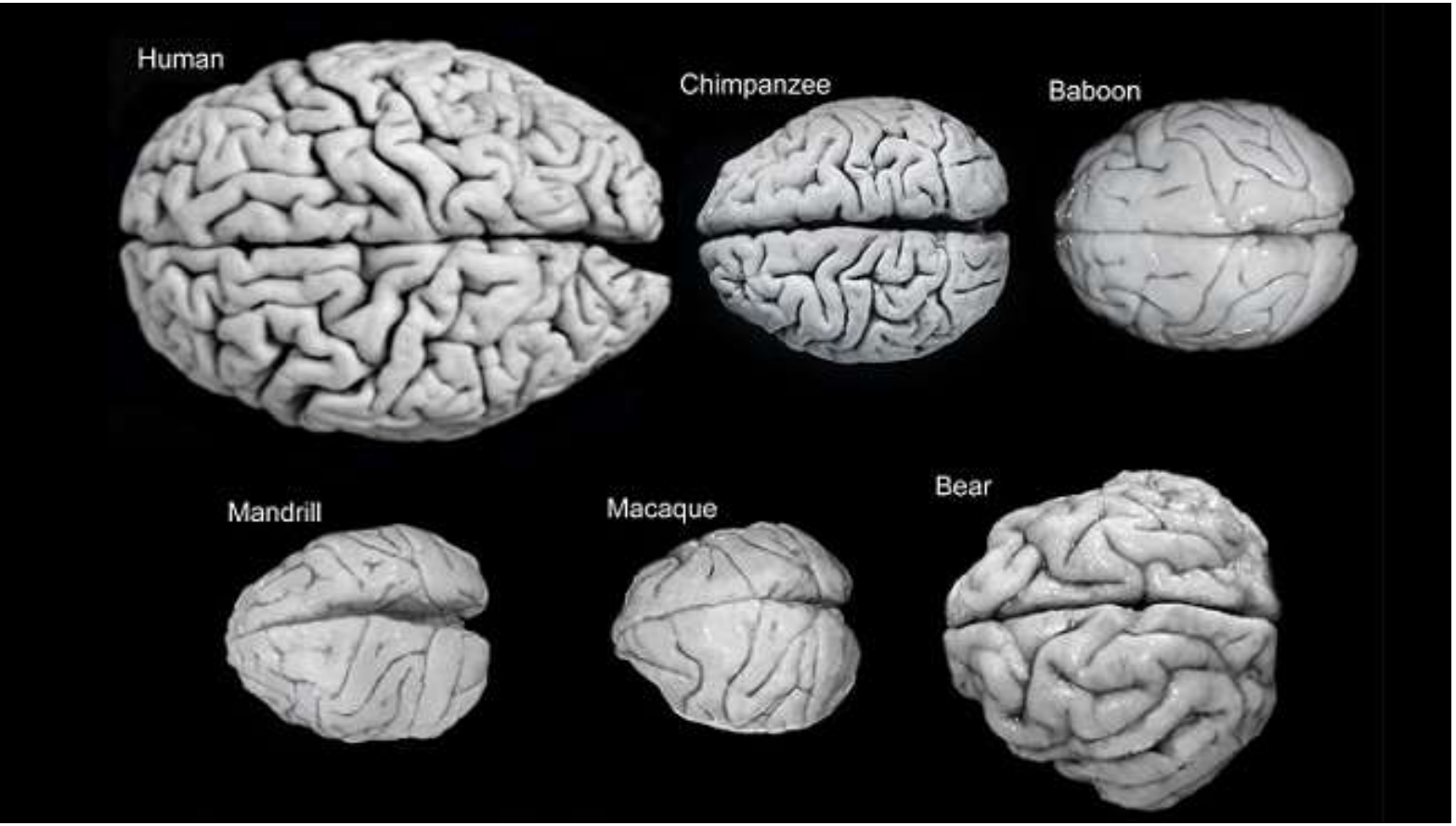
Mapping the human brain

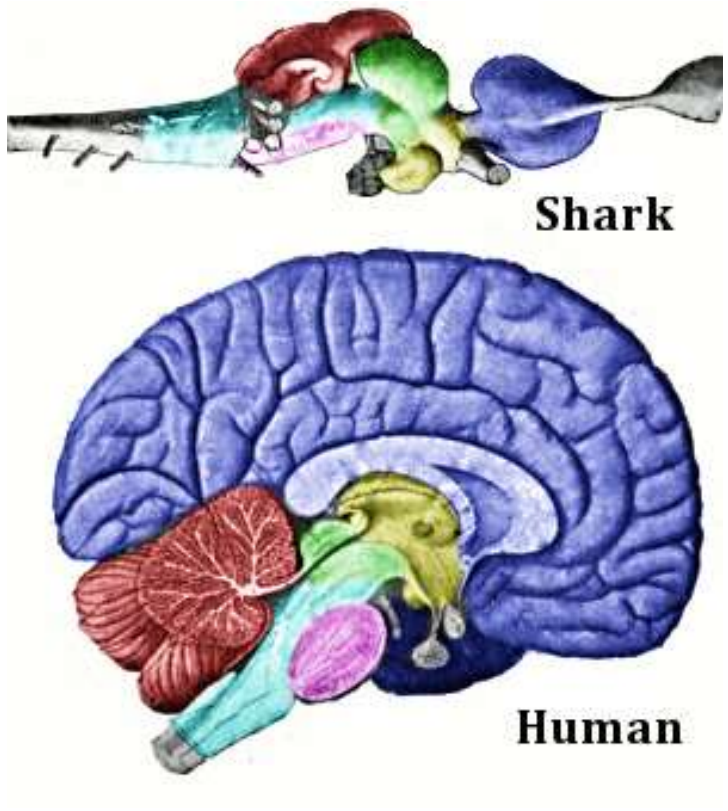


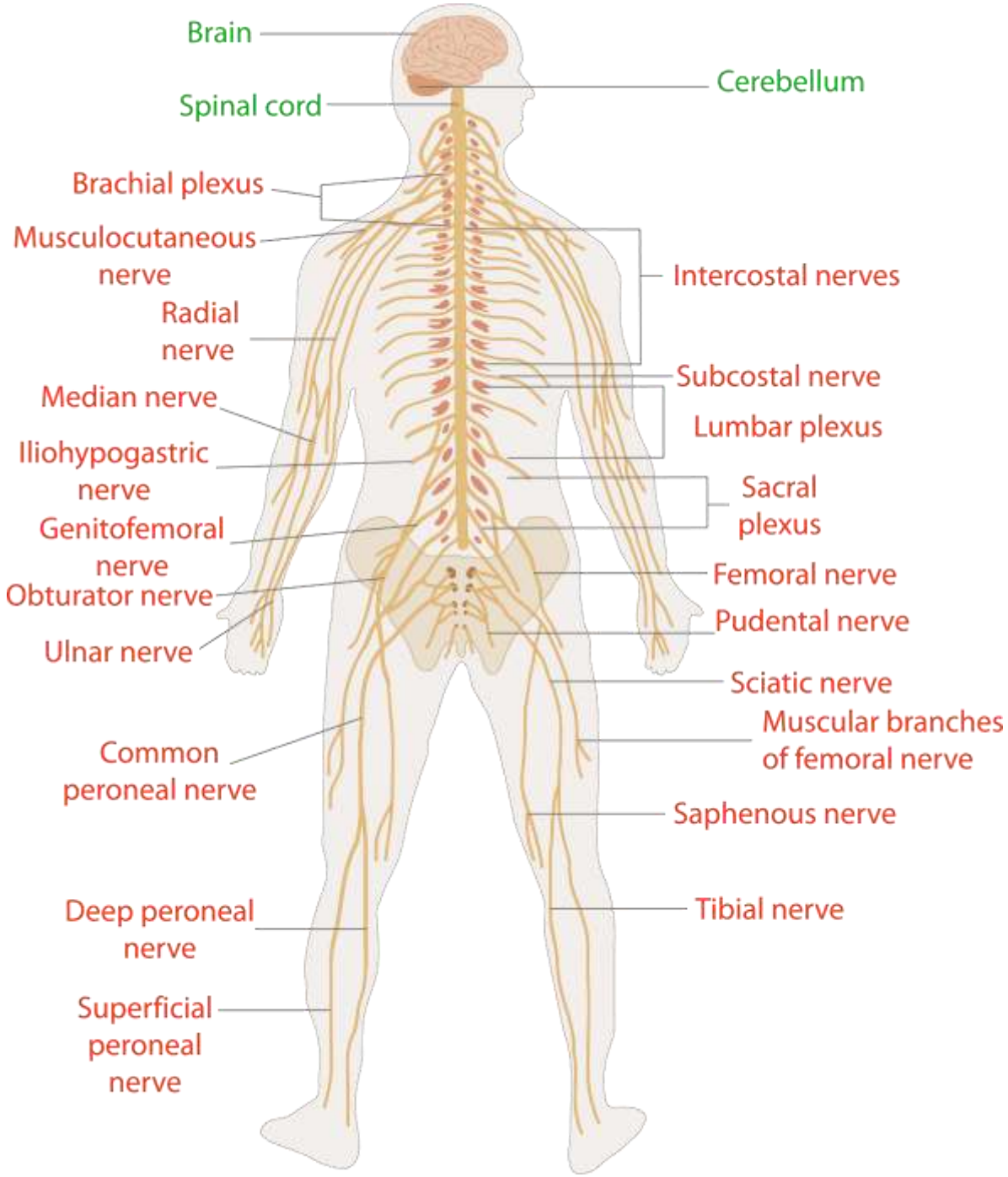
Chapter 1

The Human Brain is a Network

The Human Brain



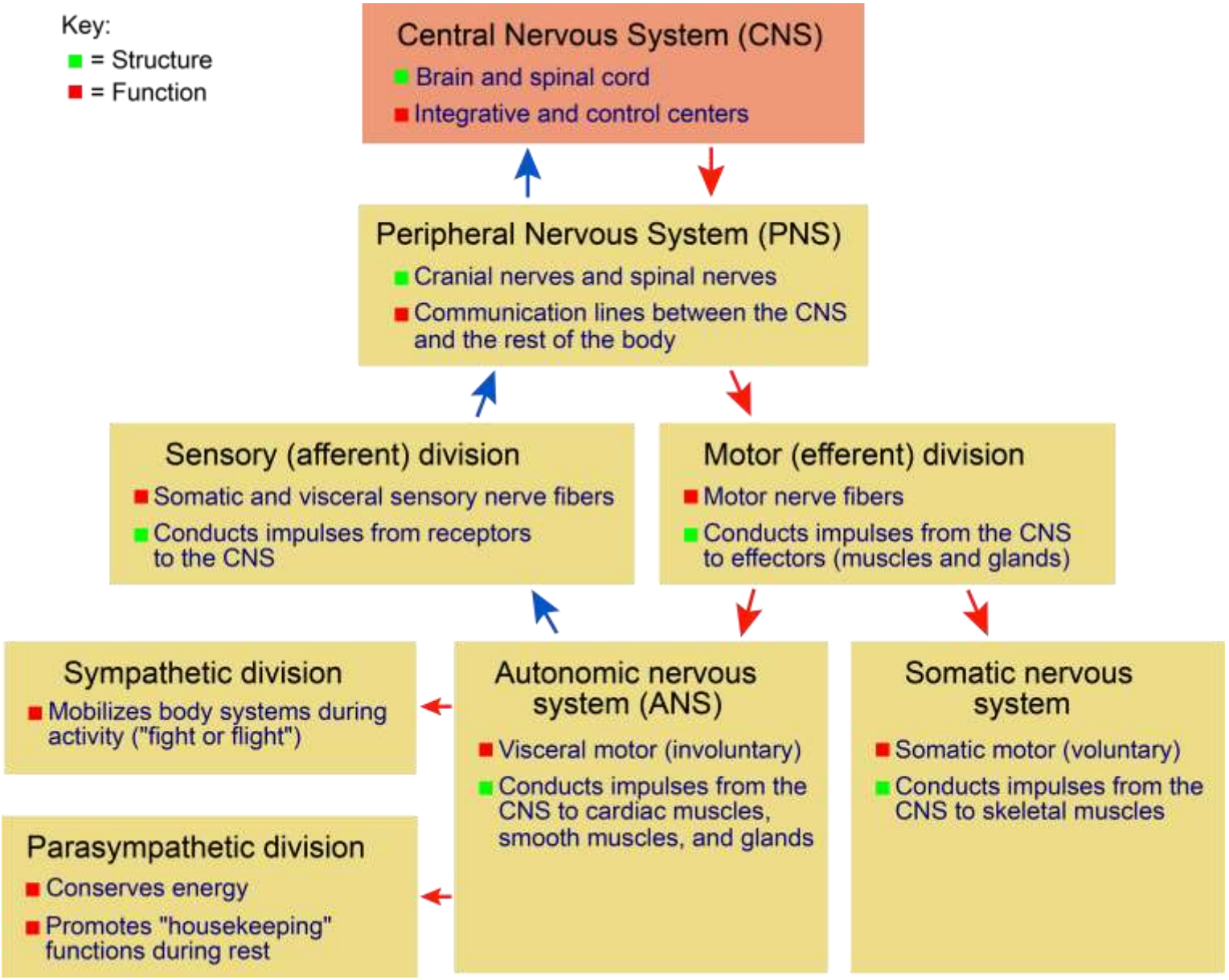




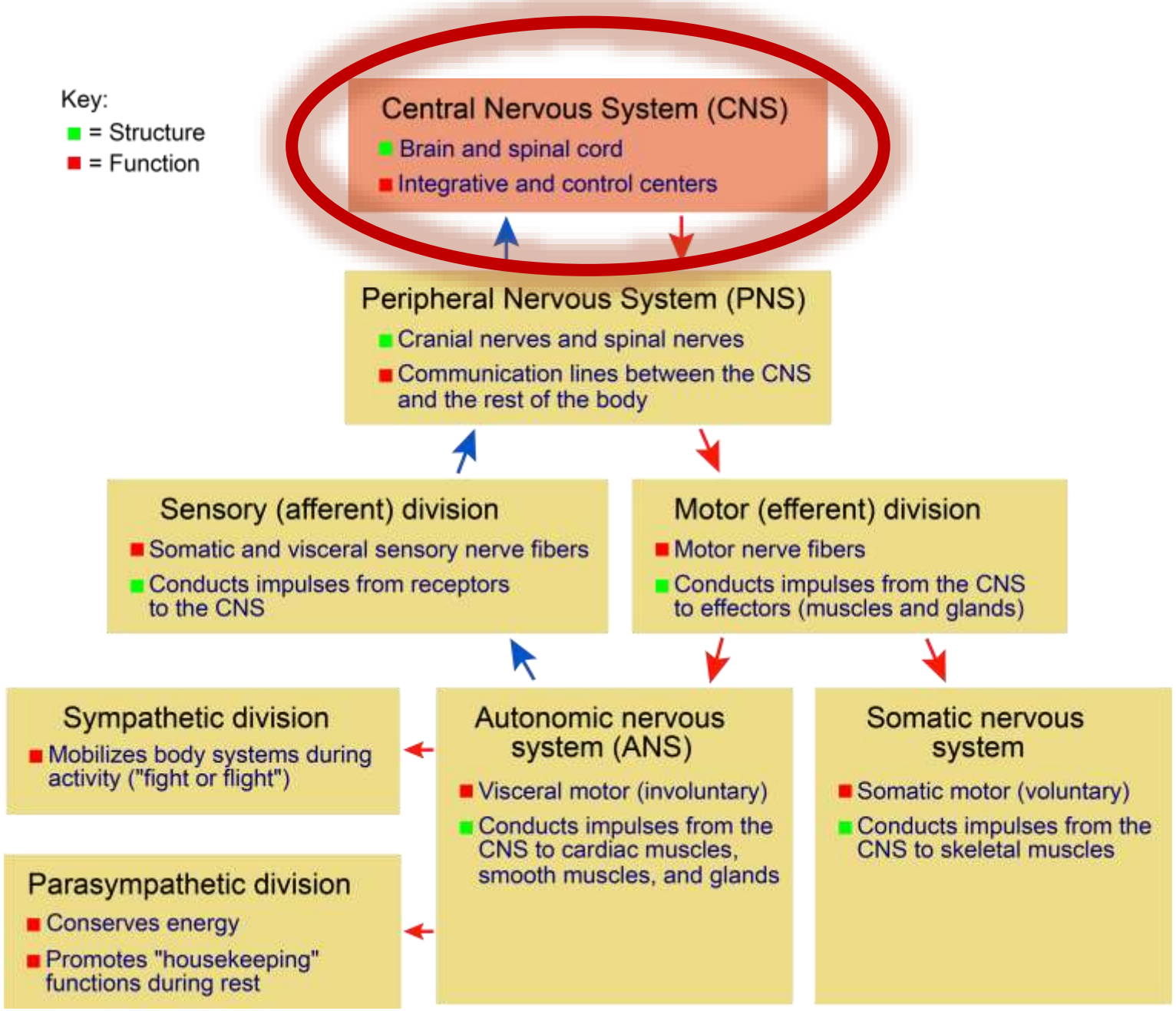
Nervous System

- Central
- Periphereal

Nervous System

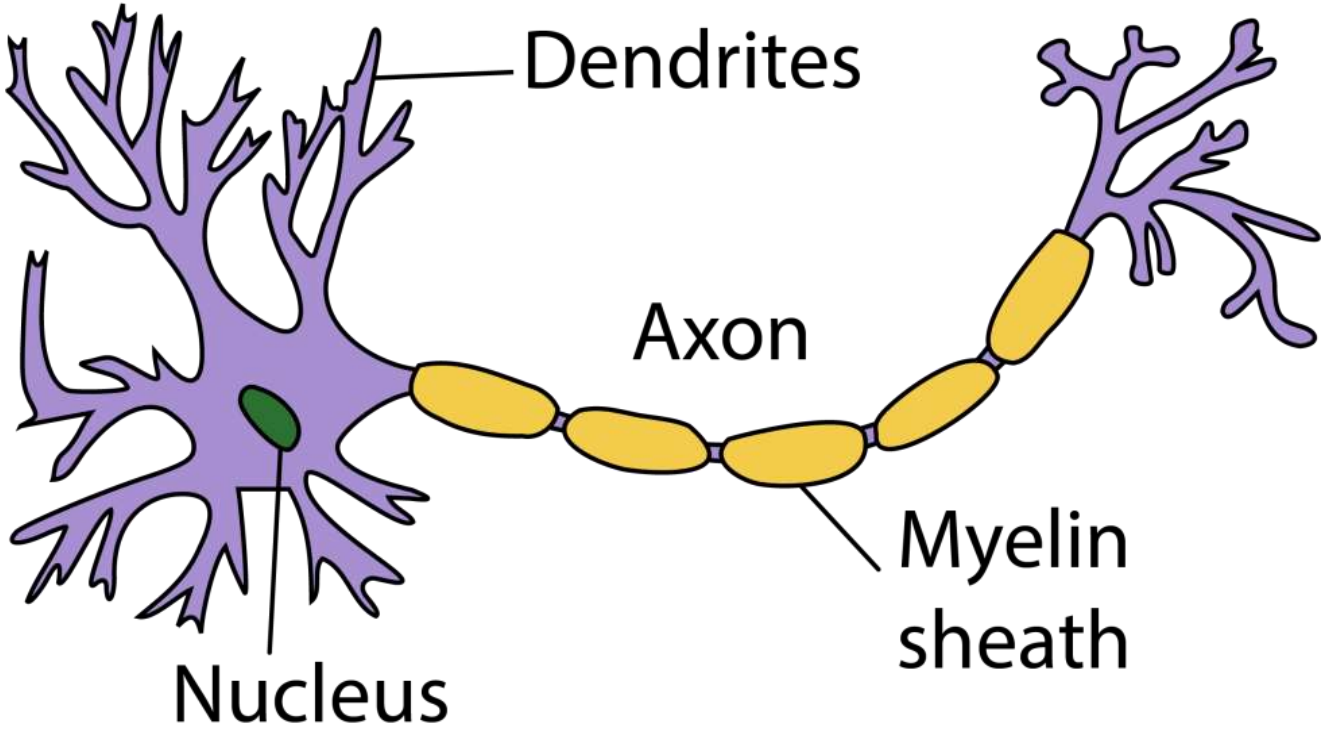


Nervous System

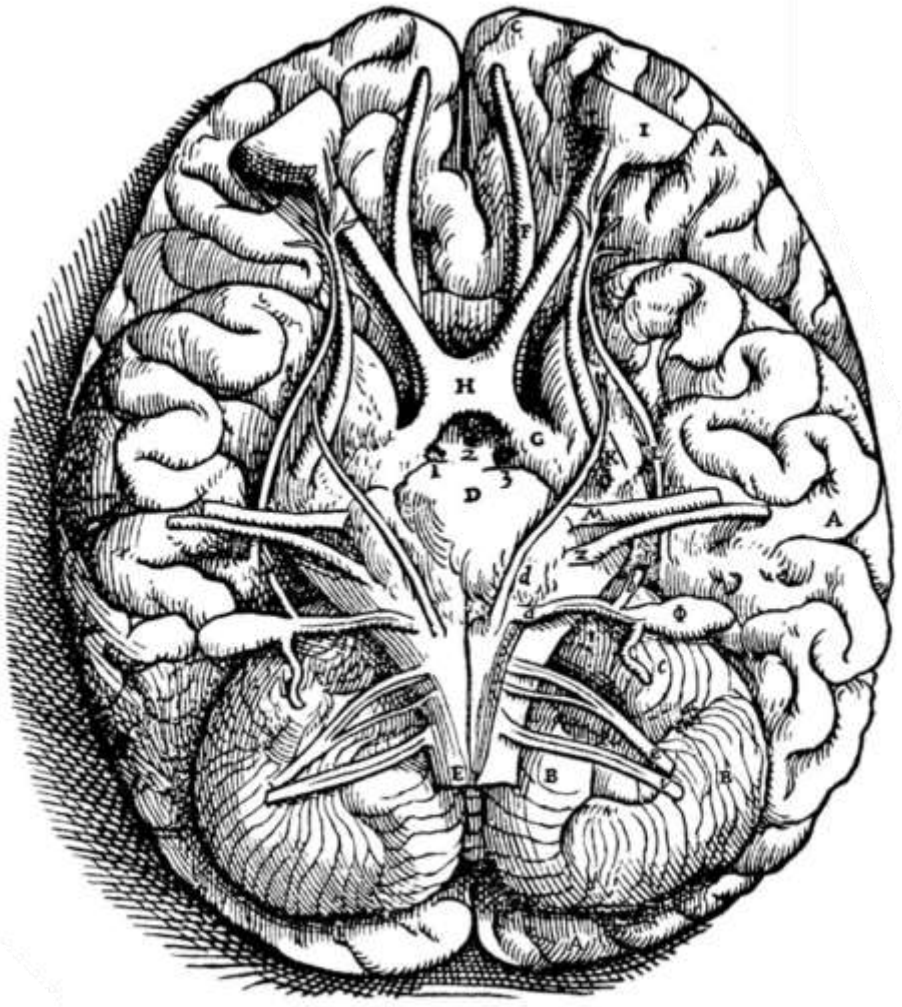


The Neuron

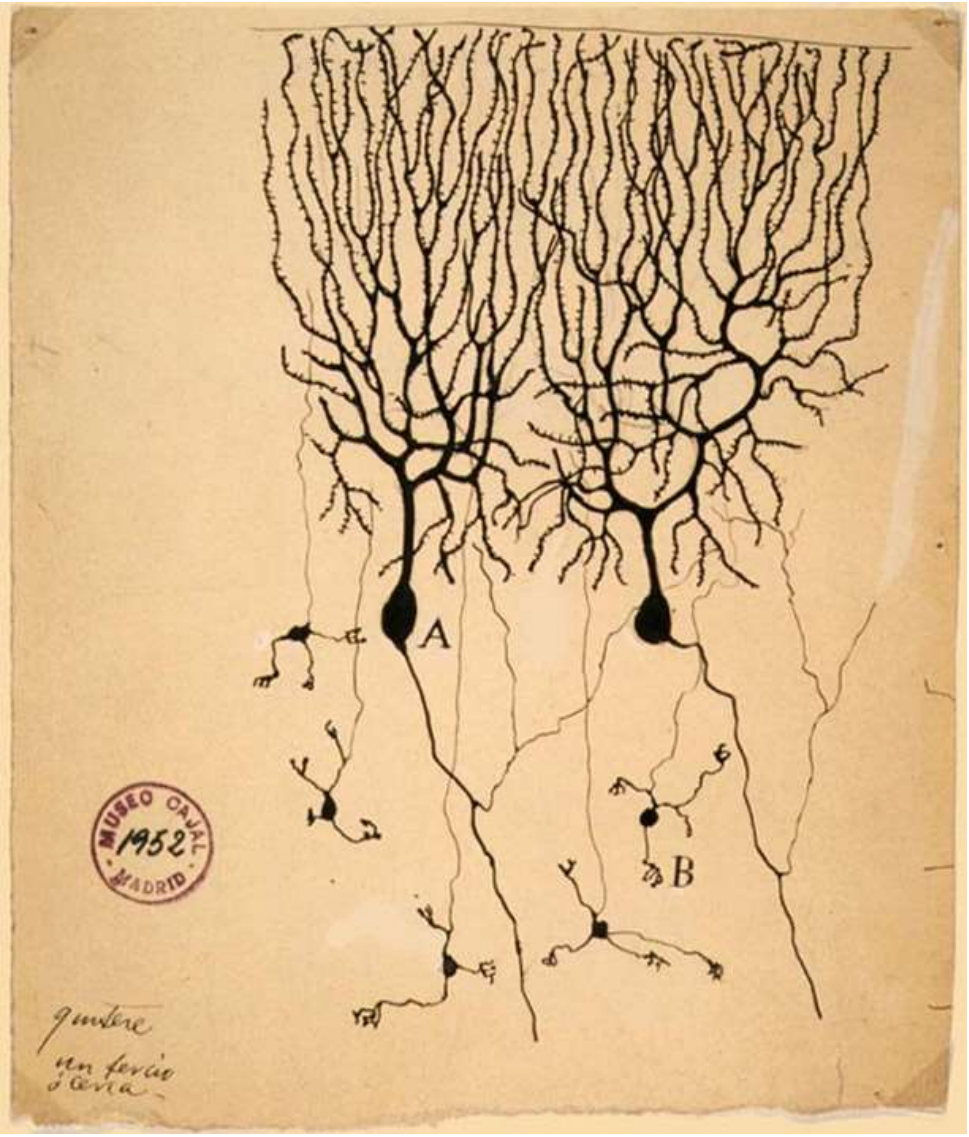
40 neuroscientists have been awarded **17 Nobel prizes** from 1906 to 2014.



Before computers

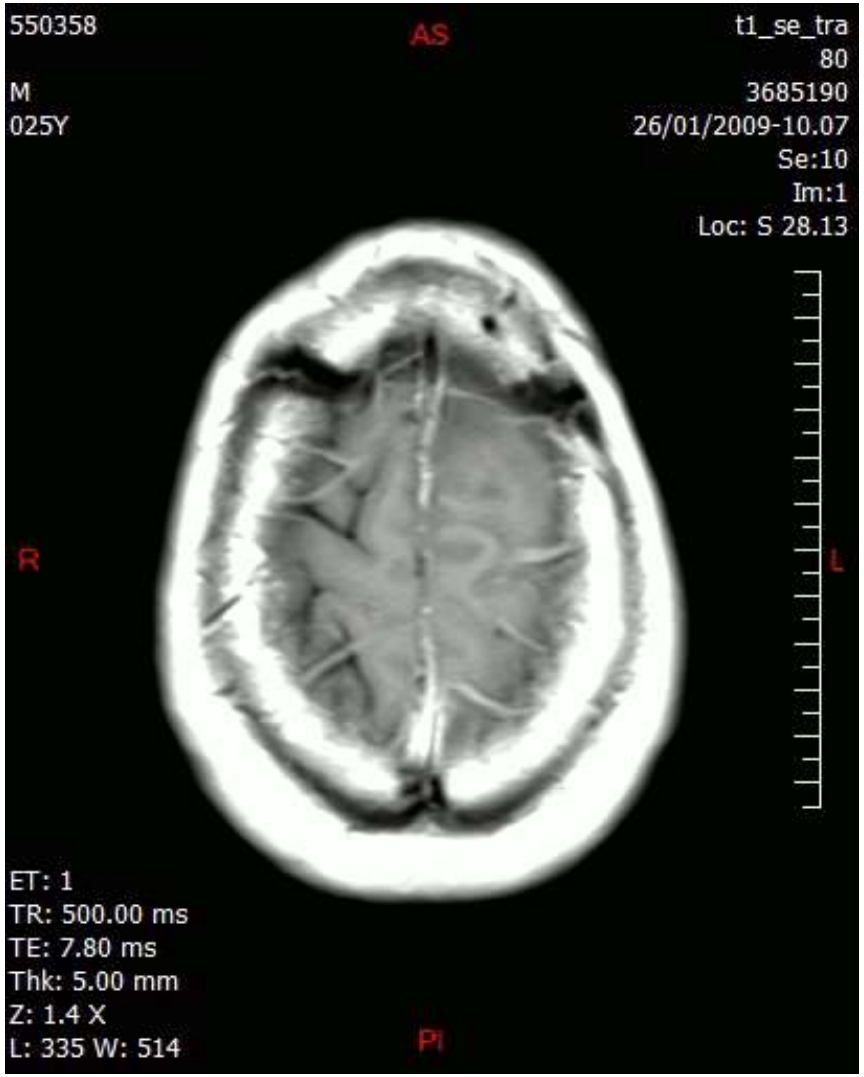


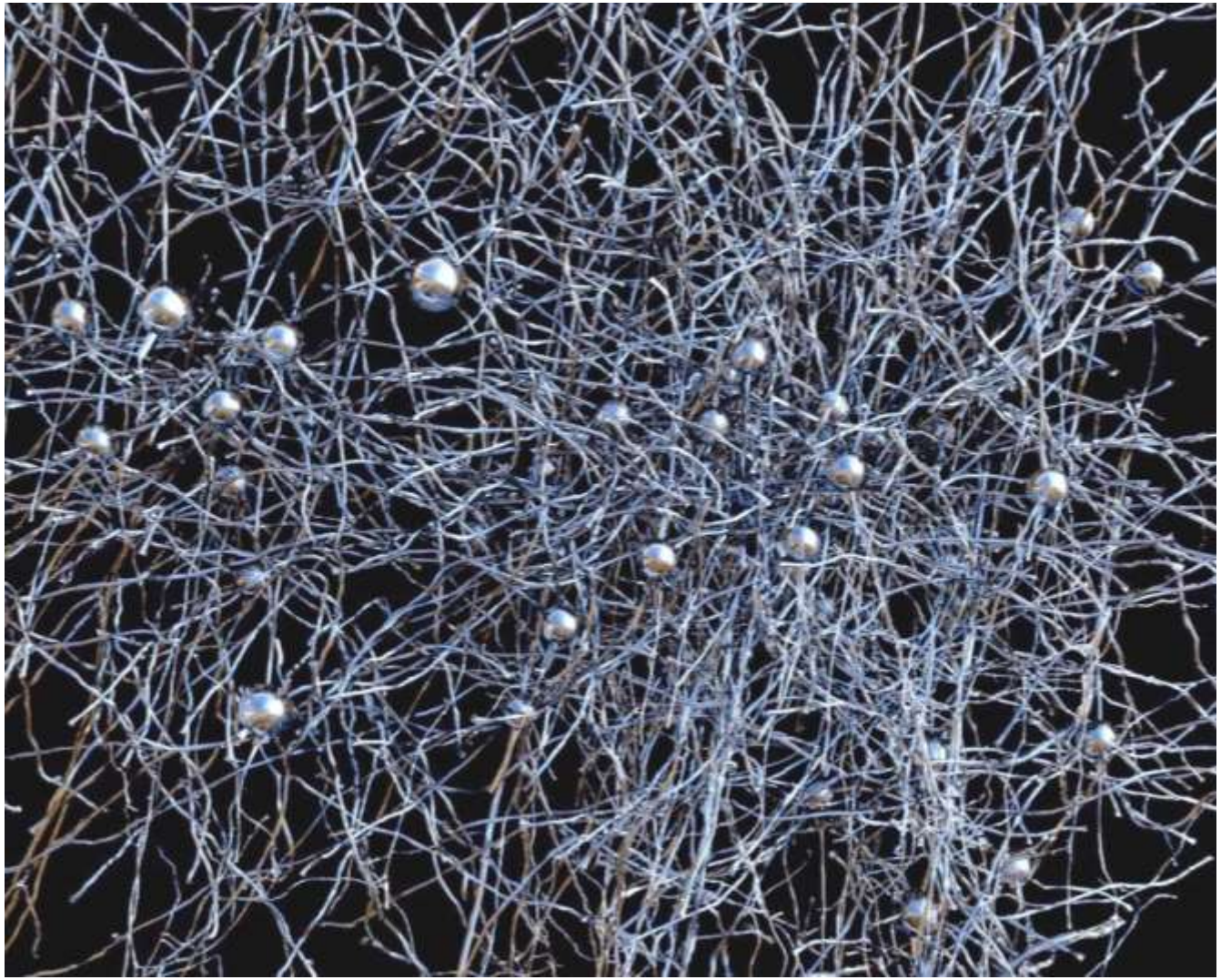
De humani corporis fabrica, Andreas Vesalius, 1543



Santiago Ramón y Cajal, 1890 ca.

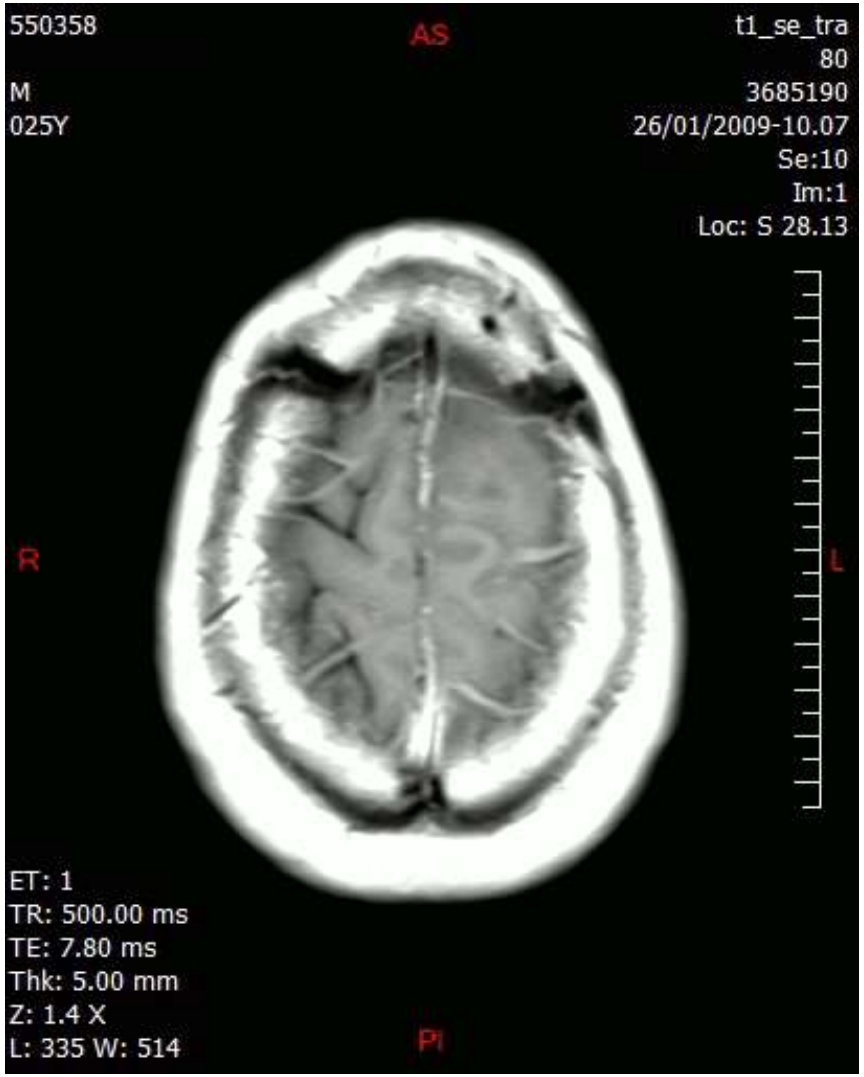
In the digital era

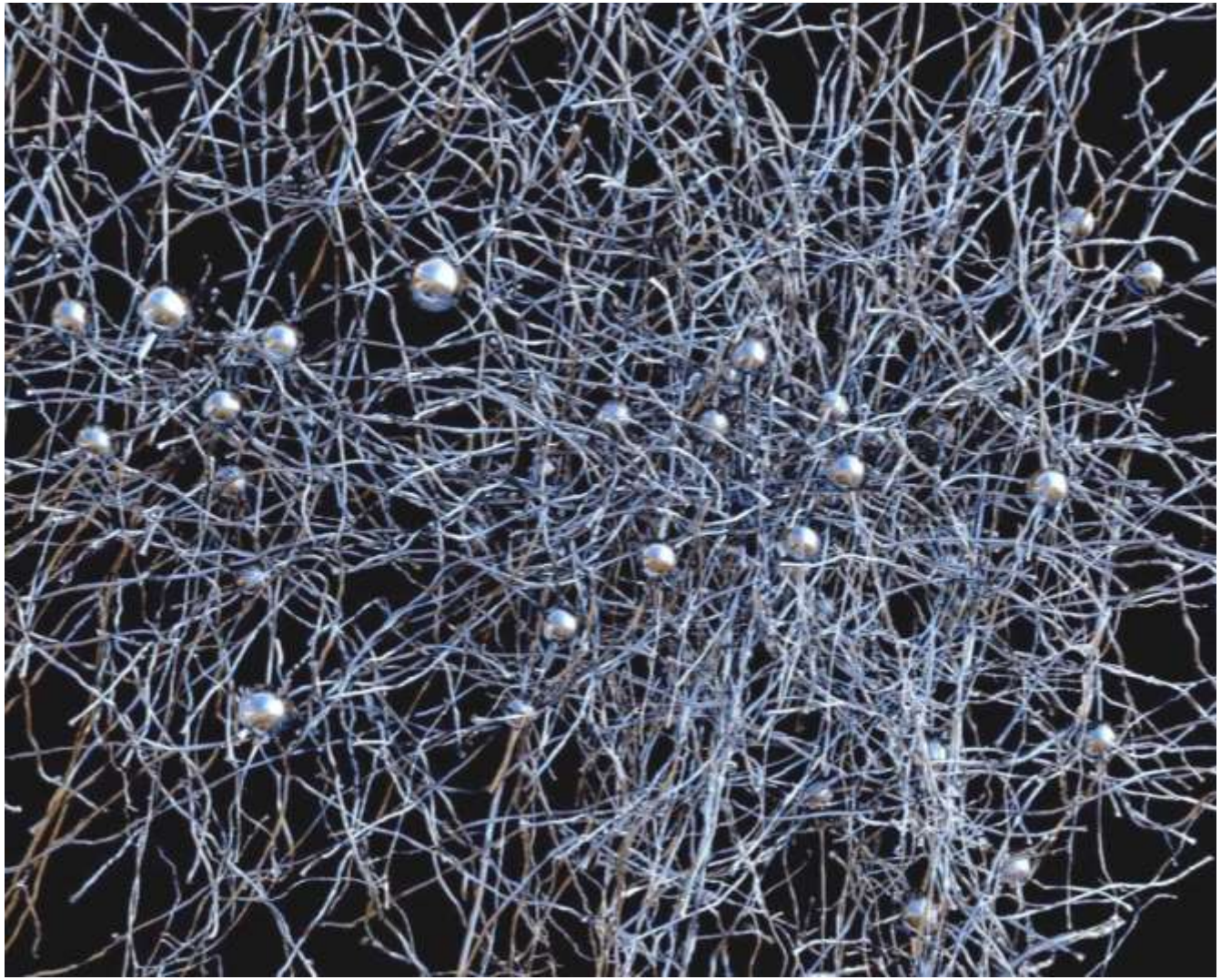


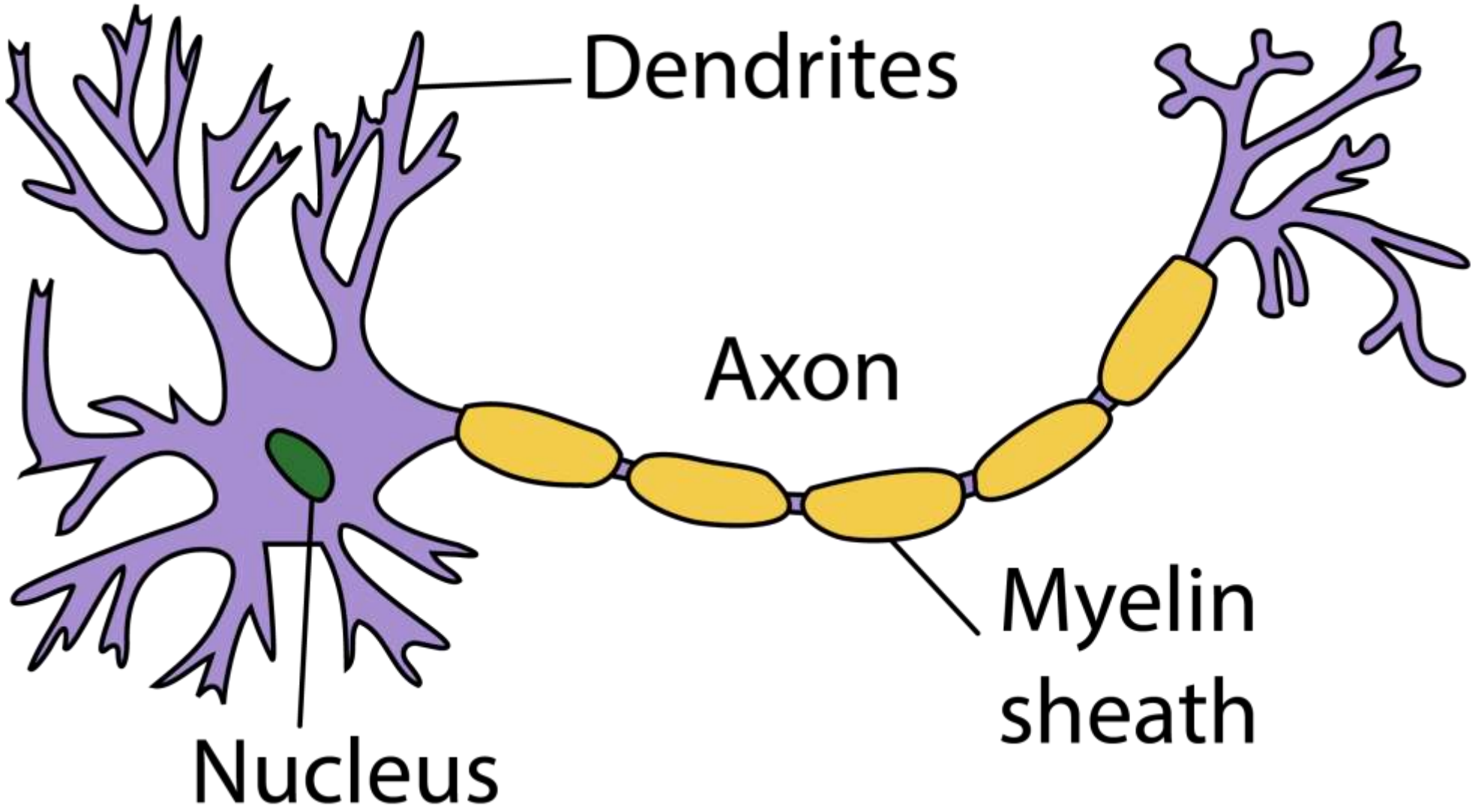


In the digital era

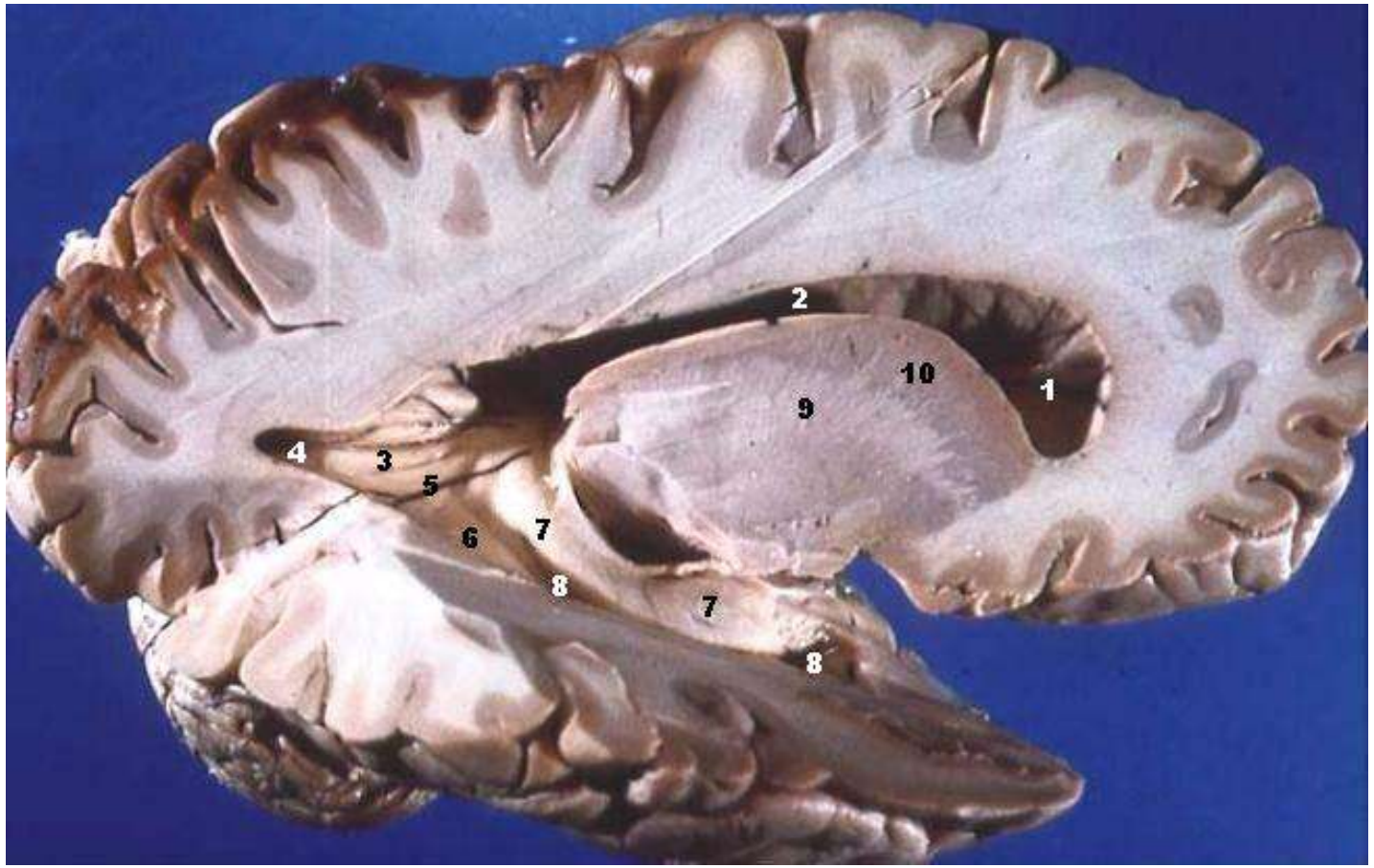
- Signal Processing
- Computer Vision
- Computational Geometry

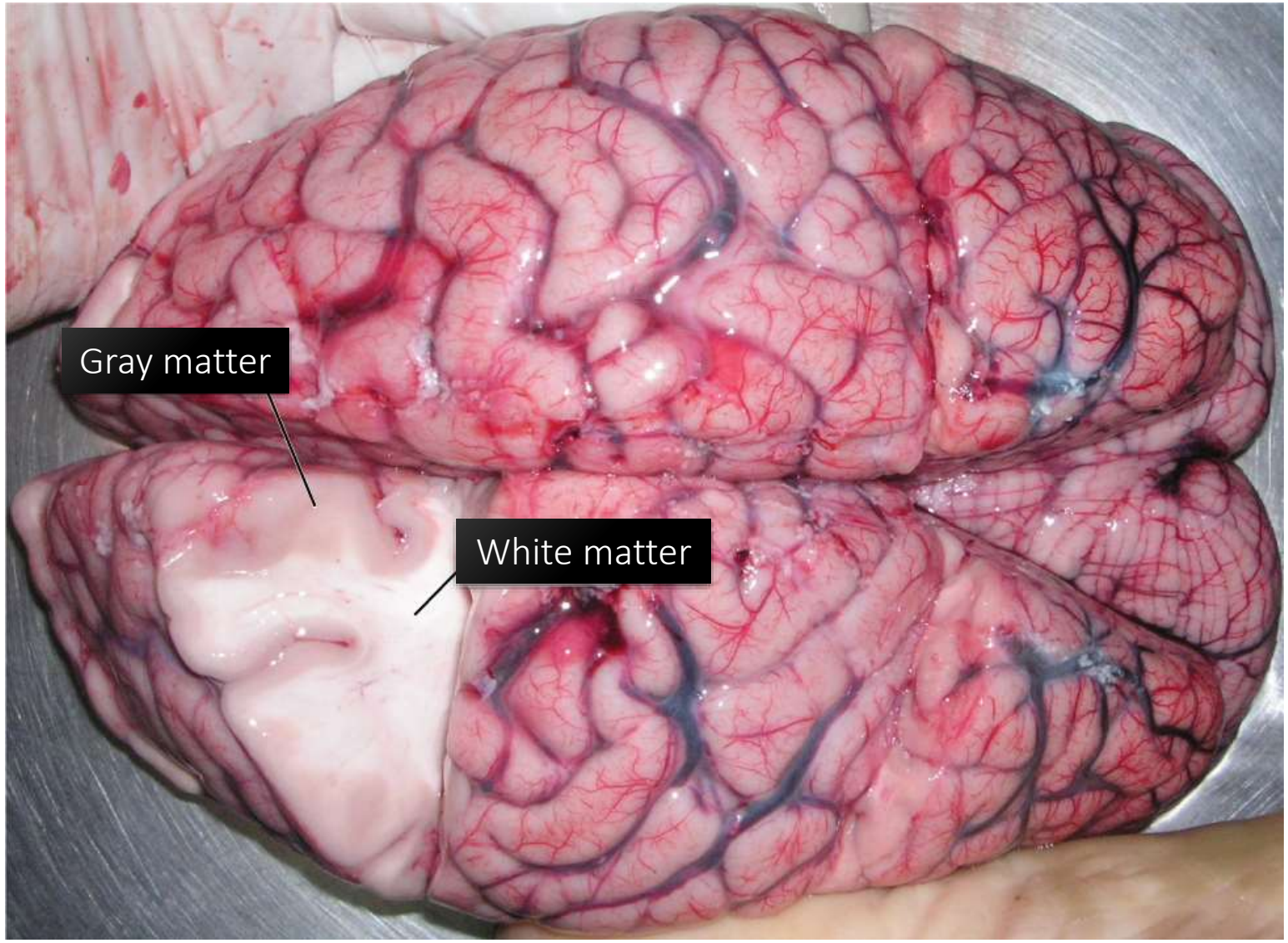





Dendrites
Axon
Myelin sheath
Nucleus

Axonal Termination and Axonal Pathways





GM: axonal terminations

WM: axonal pathways

Terminations + Pathways = GRAPH

Terminations → Nodes

Pathways → Edges

Terminations + Pathways = GRAPH

Terminations → Nodes

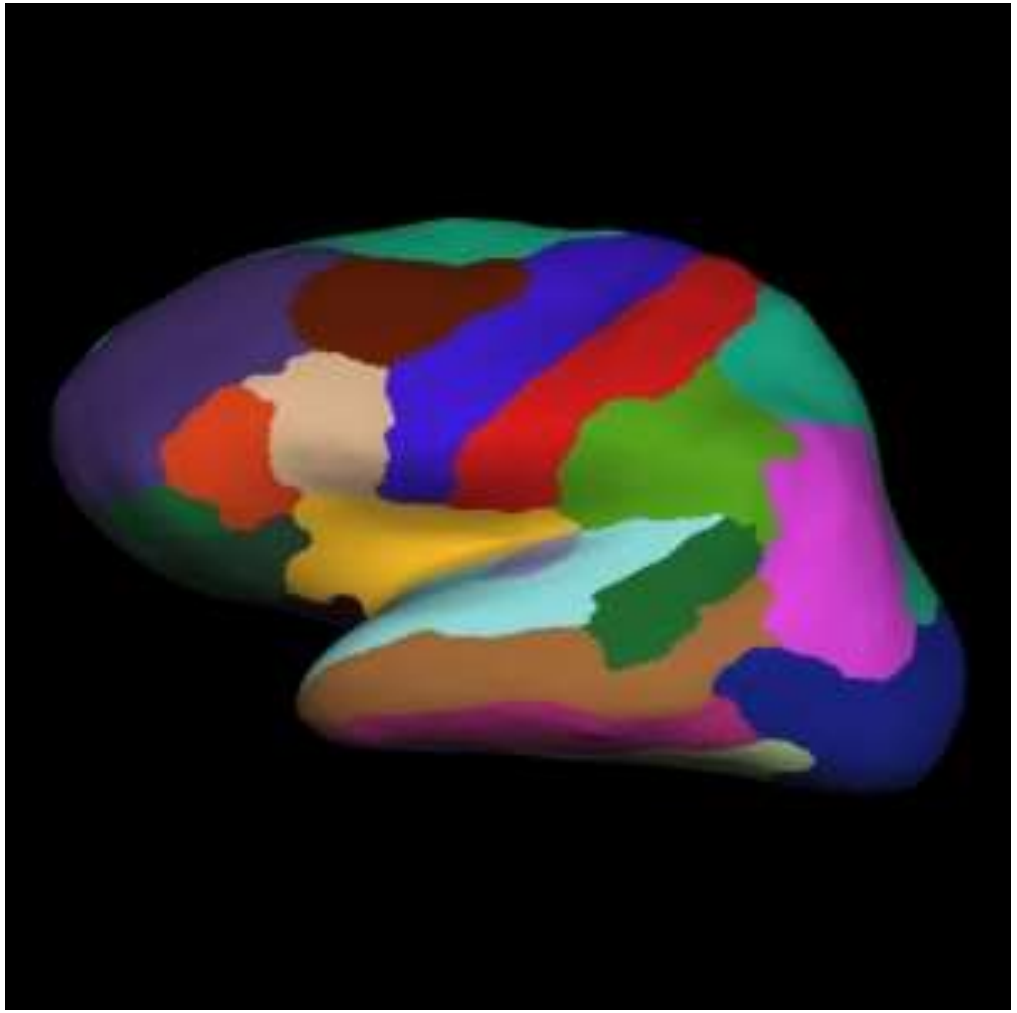
Pathways → Edges

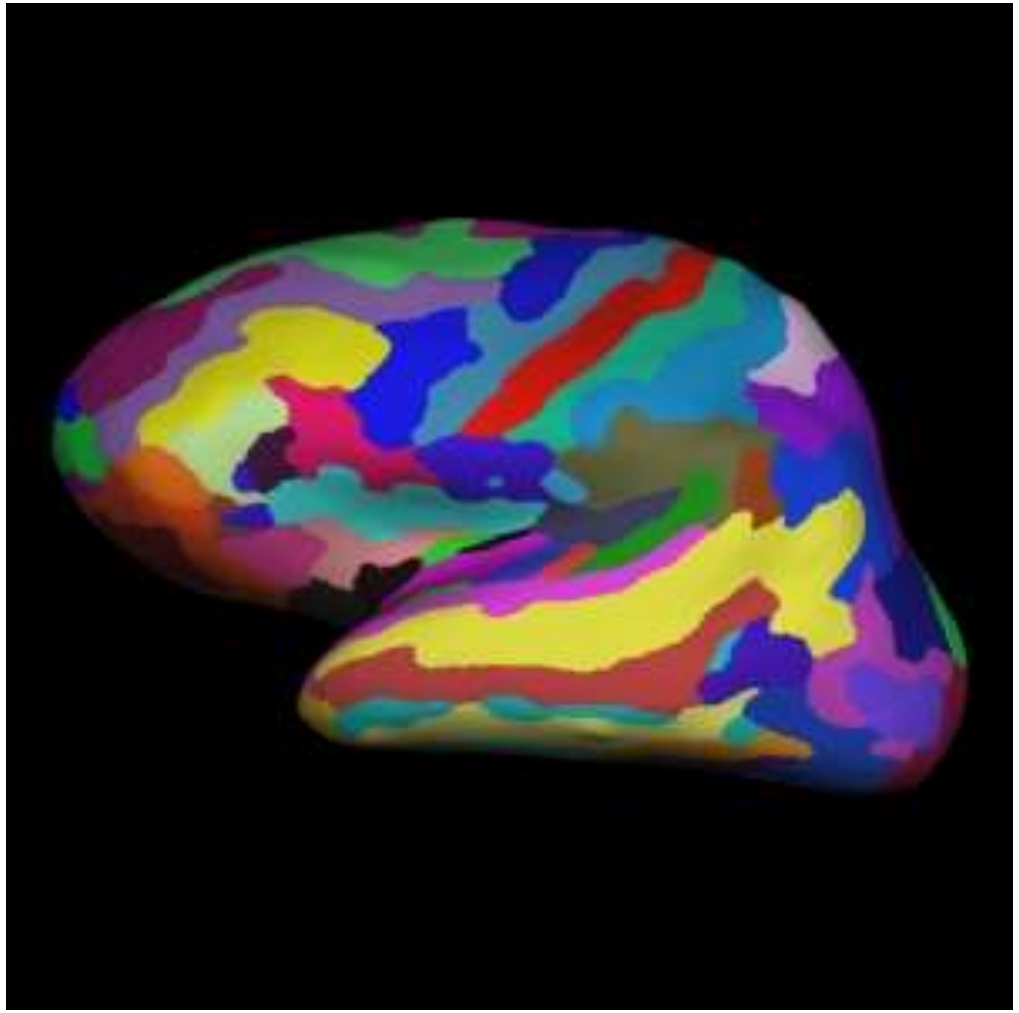
connectome

Problem

A single human brain contains around **100 billion neurons**

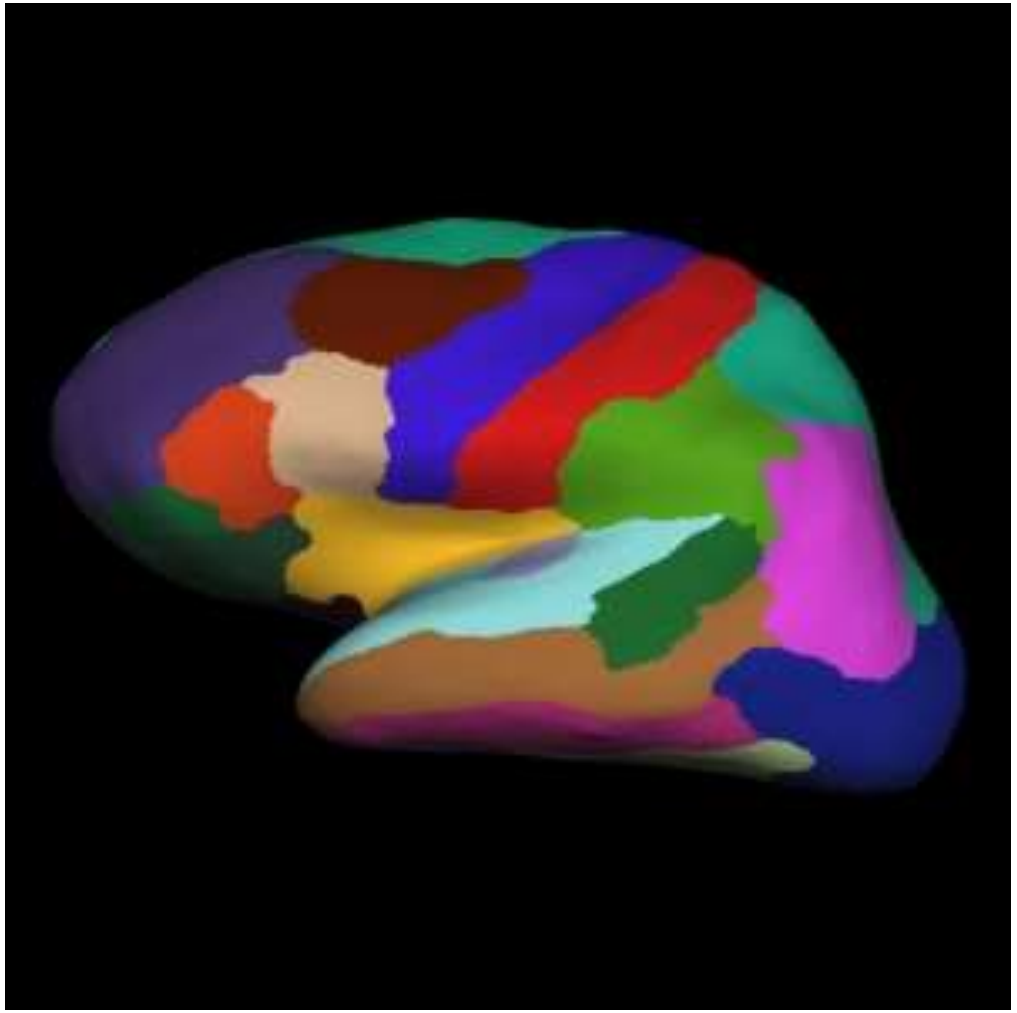
Parcellation

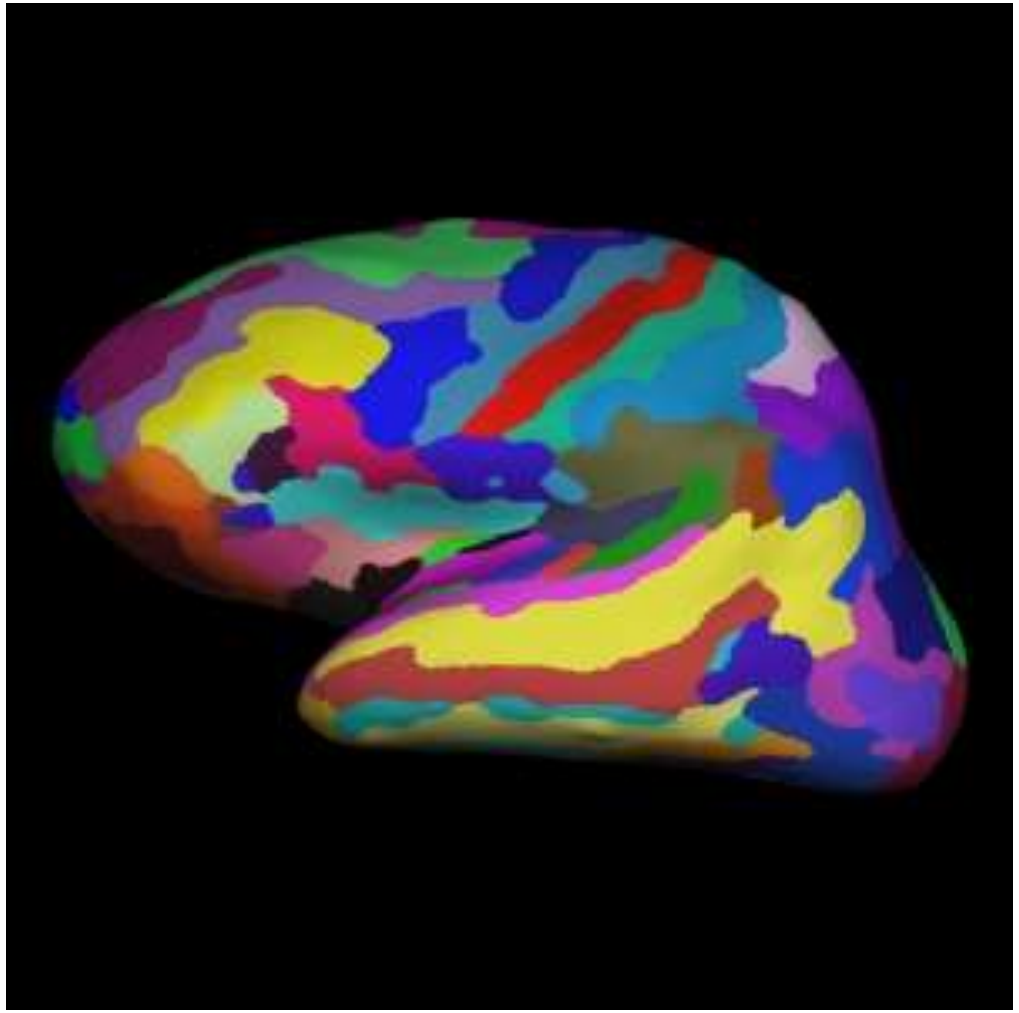




Parcellation

- Clustering
- Pattern Recognition
- Big Data



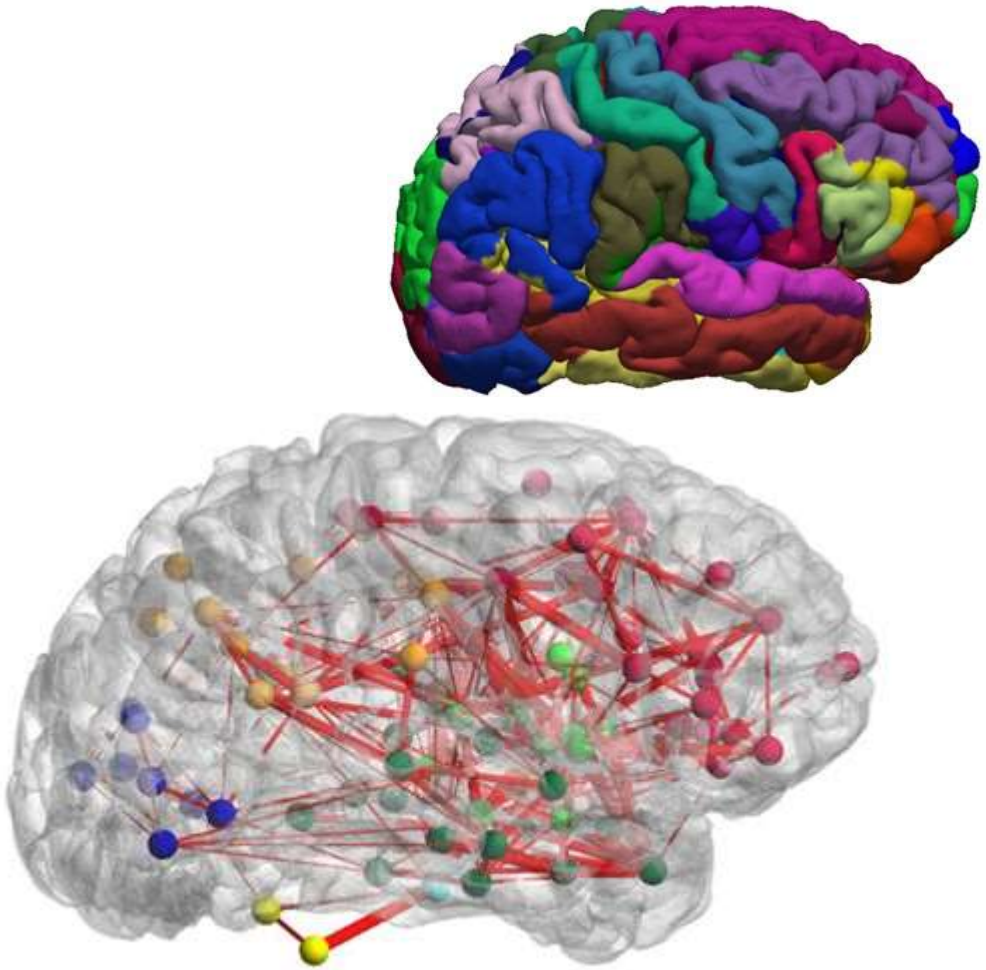


How to build a connectome

Consider two distinct cortical regions (parcels)

Estimate the strength of the connectivity

- Structural
- Functional



Structural Connectome

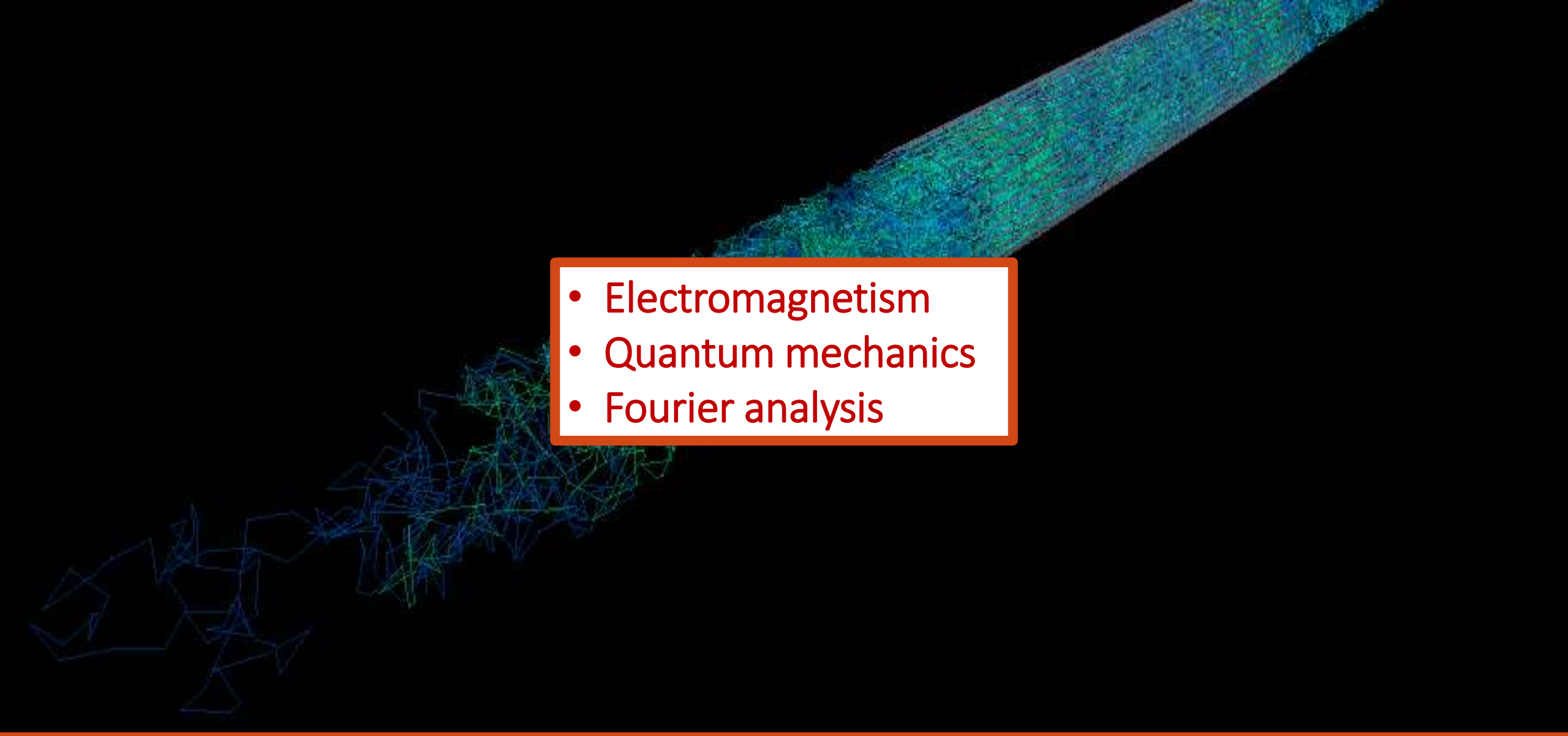
Estimate the anatomical connections between cortical regions.

Functional Connectome

Describe patterns of statistical dependence among cortical regions.

Chapter 2

Structural Connectivity Estimation



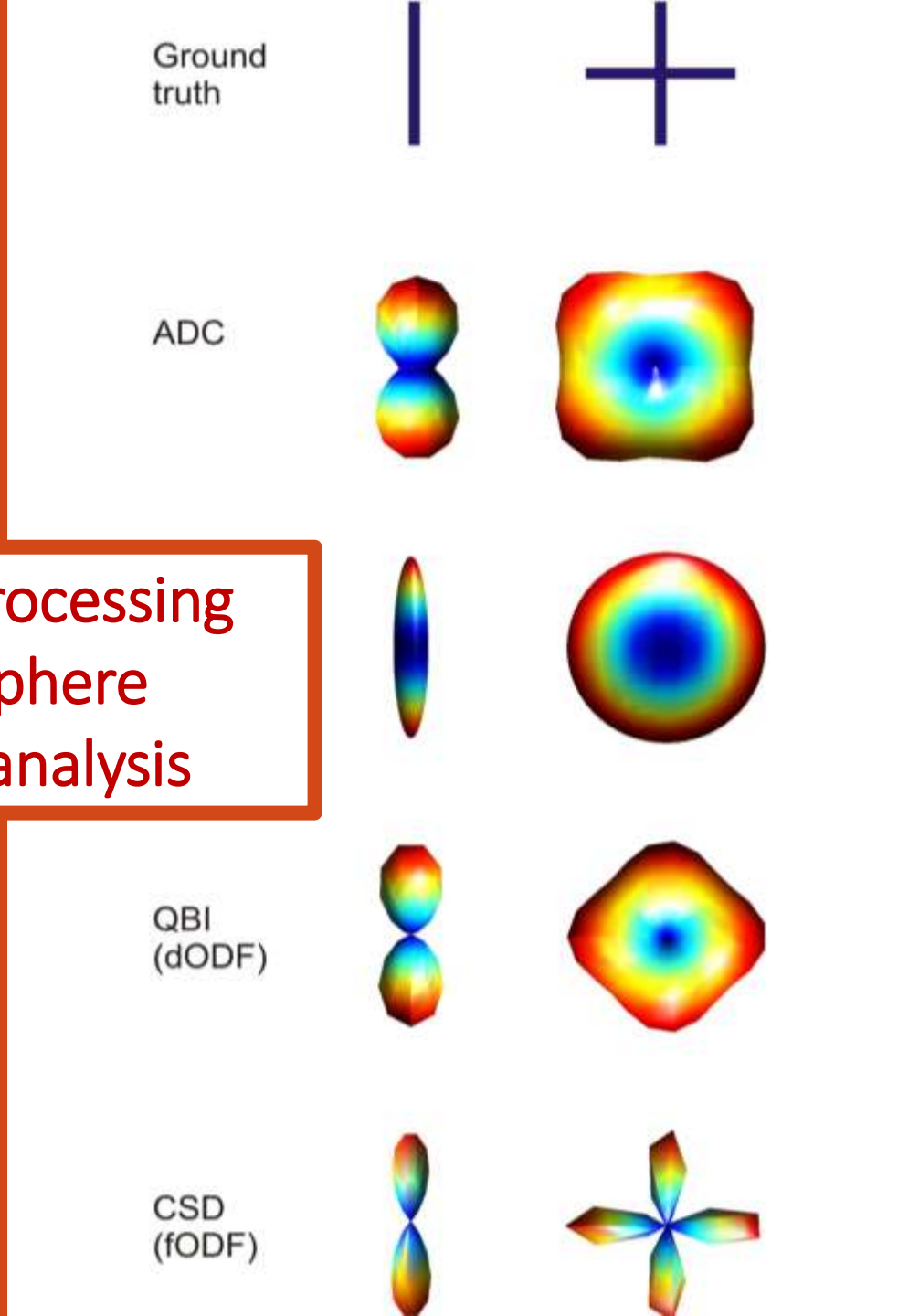
- Electromagnetism
- Quantum mechanics
- Fourier analysis

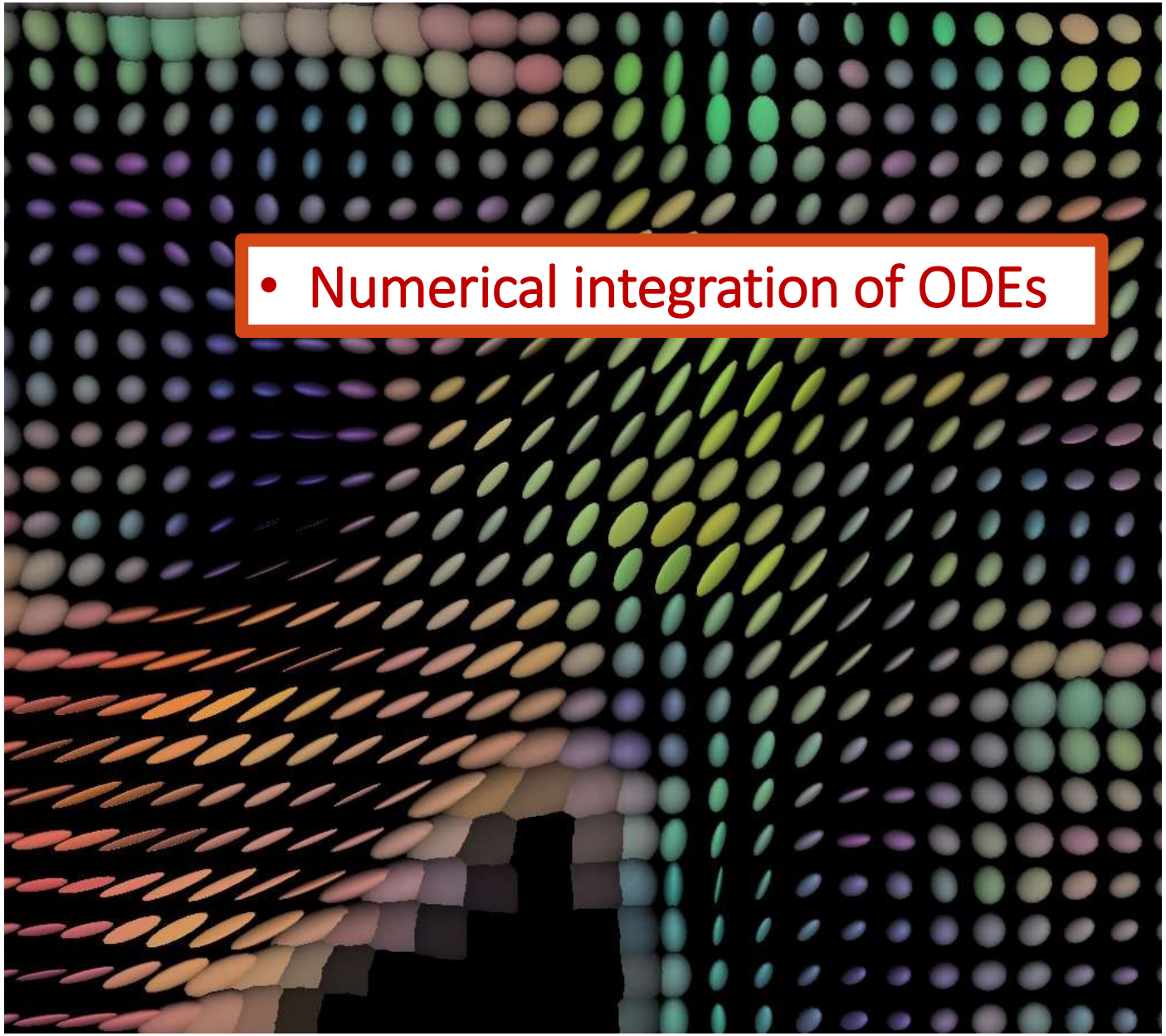
Diffusion Magnetic Resonance Imaging

estimates the random Brownian motion of water molecules within a voxel of tissue.

Local Reconstruction of Diffusivity

- Signal processing on the sphere
- Fourier analysis



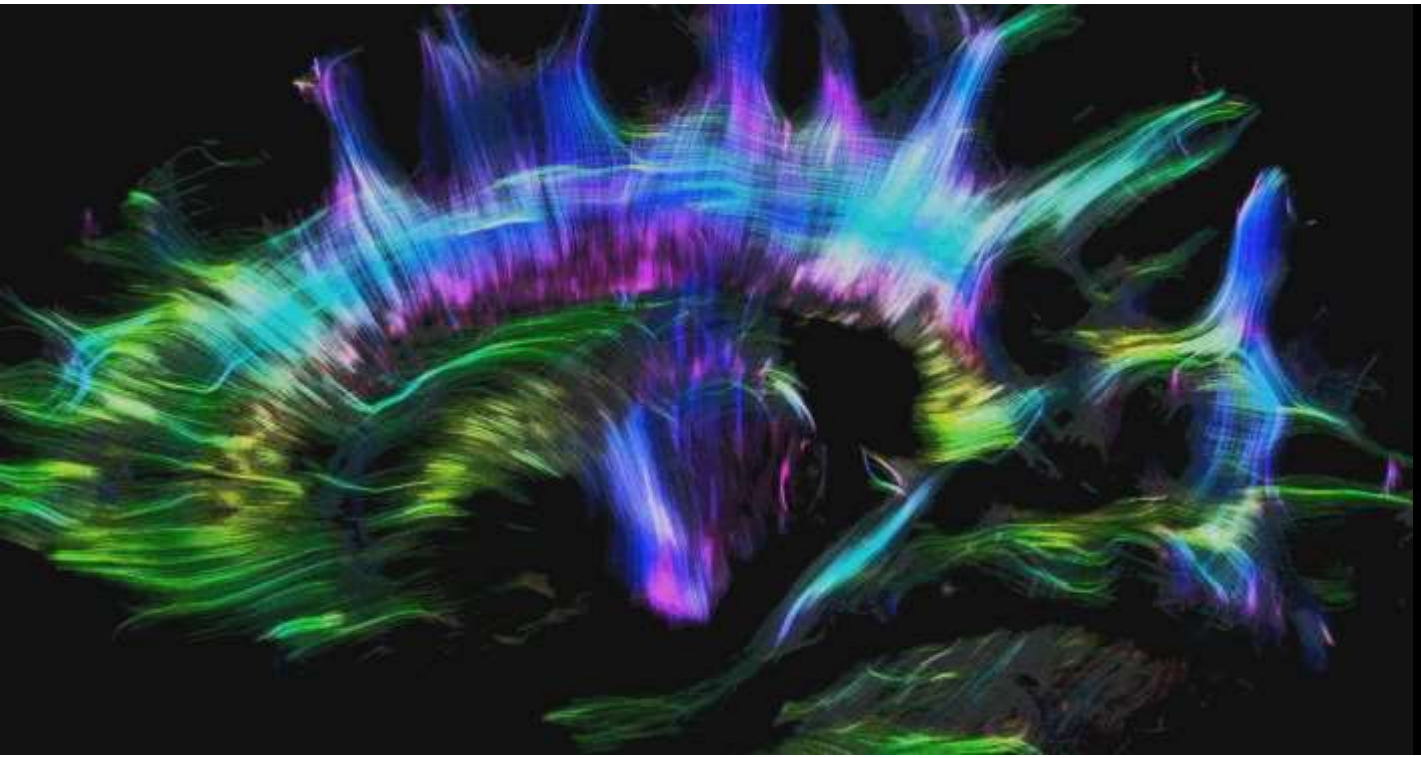


- Numerical integration of ODEs

Get streamlines by integrating along the local direction.

Probabilistic approaches admit the possibility of not following the principal eigenvector.

Tractography a.k.a. fiber pathways estimation



Structural Connectivity Estimation

Streamline Count

- Count the streamlines connecting two regions

Weighted connectome

- Assign a weight to each streamline and sum the weights of the streamlines connecting two regions

Problems of tractography

Streamlines are **not quantitative**

- Missing volume information
- Duplicates

It generates **false positive connections**

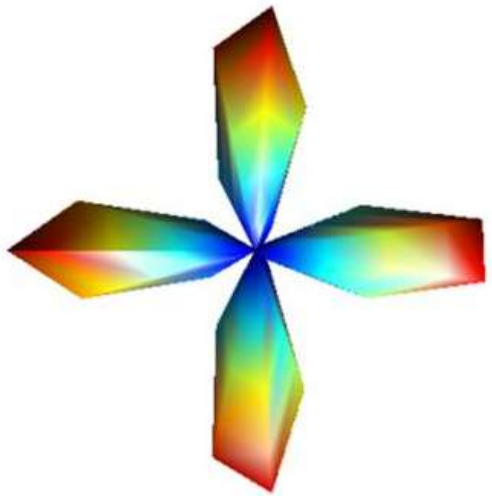
- High sensitivity
- Low specificity

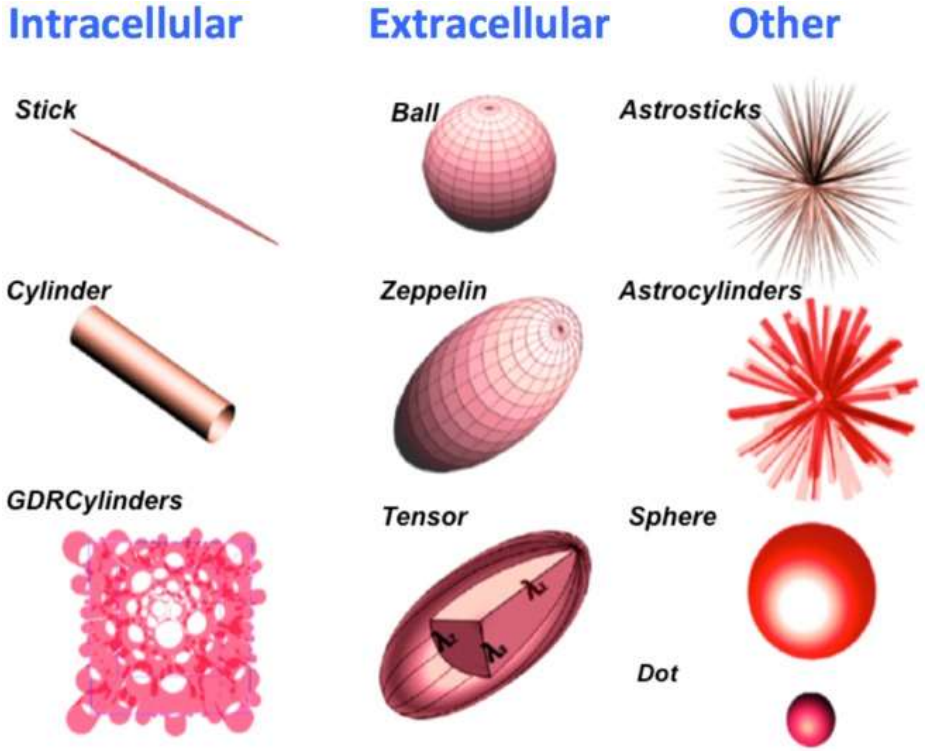
Weighted Connectome

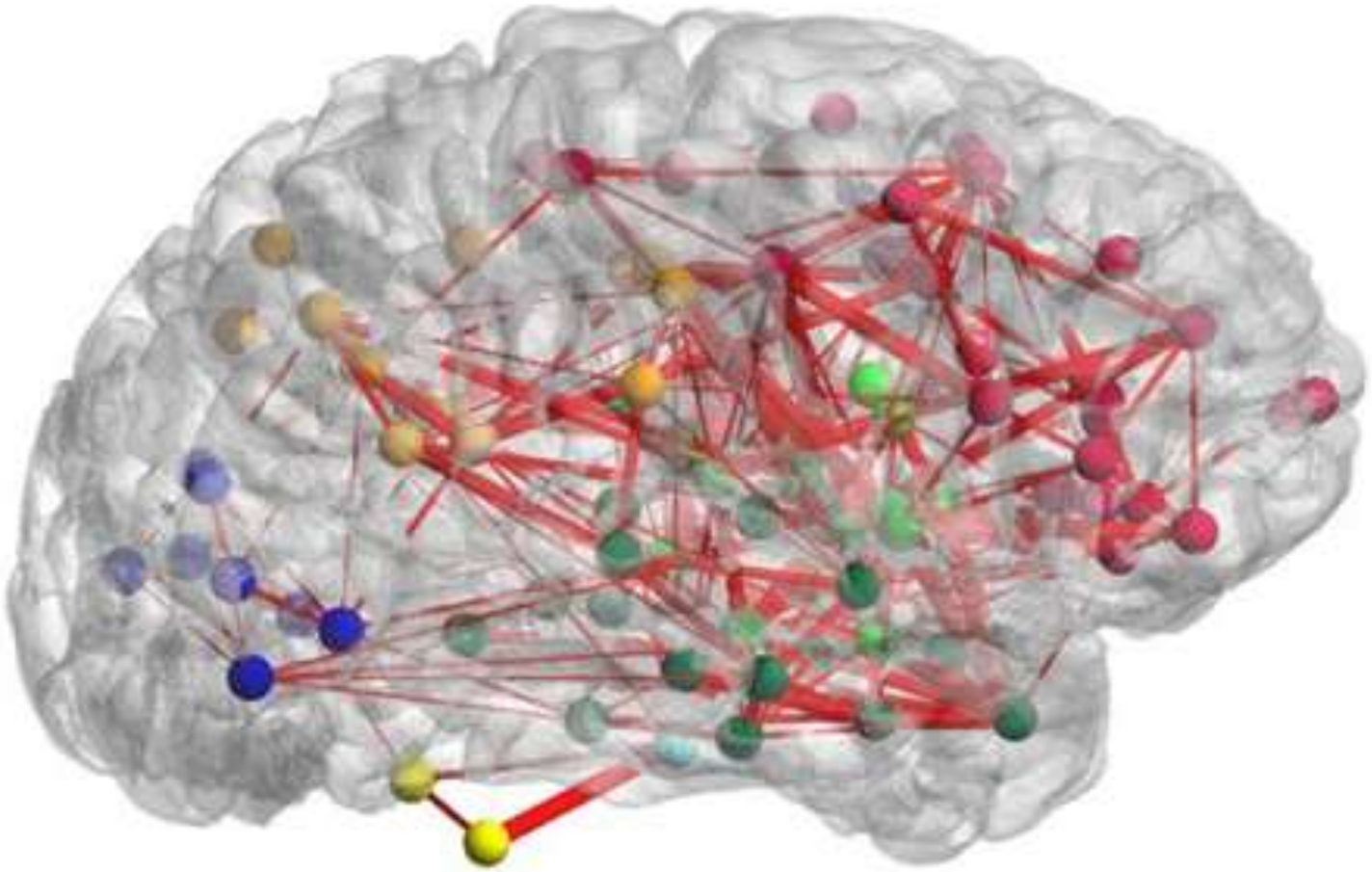
Spherical Deconvolution Informed Filtering of Tractograms (SIFT)

Convex Optimization Modelling for Microstructure Informed Tractography (COMMIT)

Linear Fascicle Evaluation (LiFE)

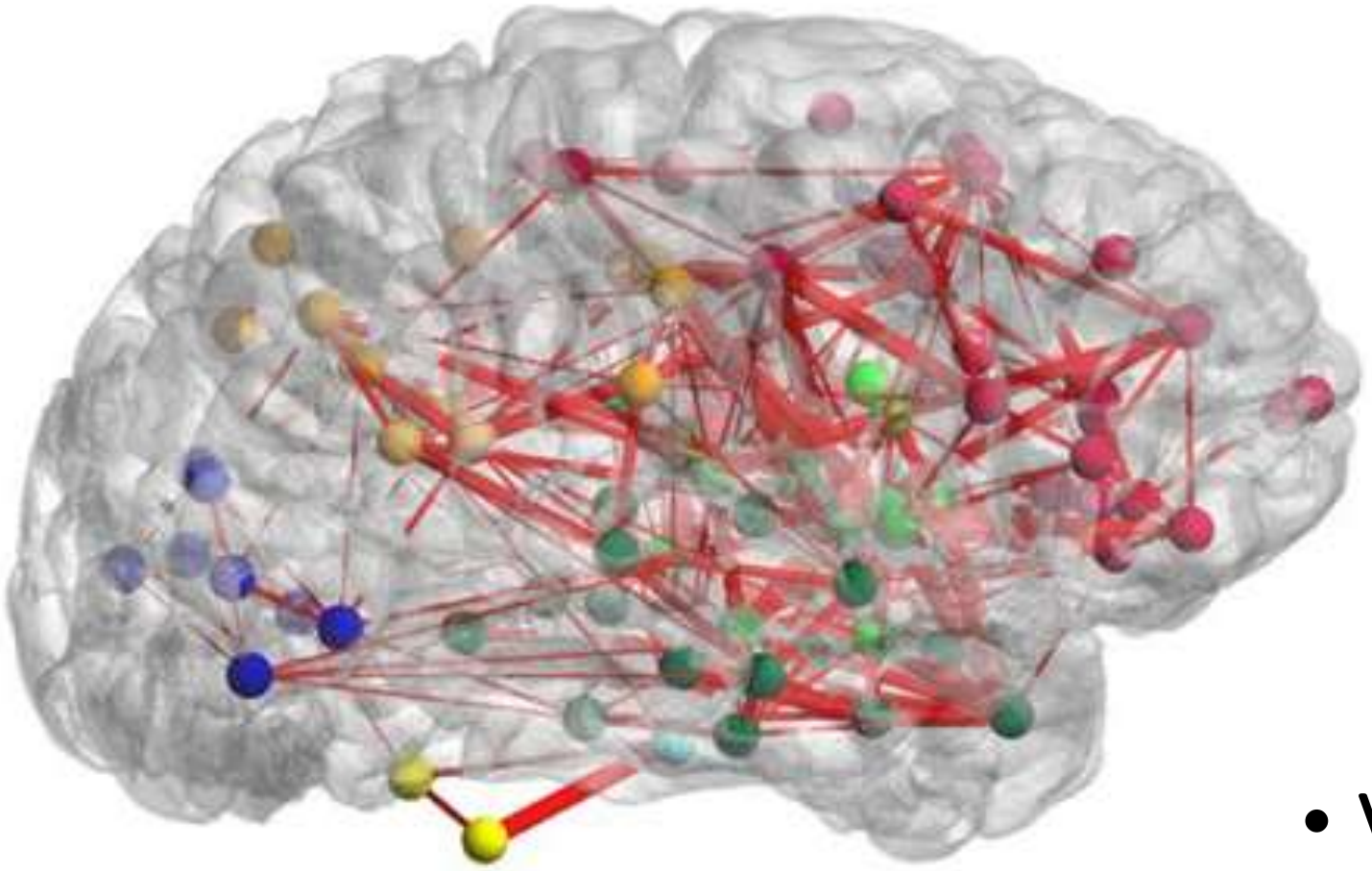






Structural Connectivity

Edge thickness represents the number of streamlines connecting the two regions or the sum of the weights associated to the streamlines.



Structural Connectome

Edge thickness represents the number of streamlines connecting the two regions or the sum of the weights associated to the streamlines.

- Very Sparse
- Temporally stable

Chapter 3

Functional Connectivity Estimation

Functional information

Functional MRI (fMRI)

- Blood Oxygen Level Dependent imaging (BOLD)

Electro/Magneto encephalography (EEG/MEG)

- Measure the electric/magnetic field generated by the electrical activity of the brain

Functional information

- Signal Processing
- Linear/Non-Linear Inverse problems
- Time series analysis

Functional MRI (fMRI)

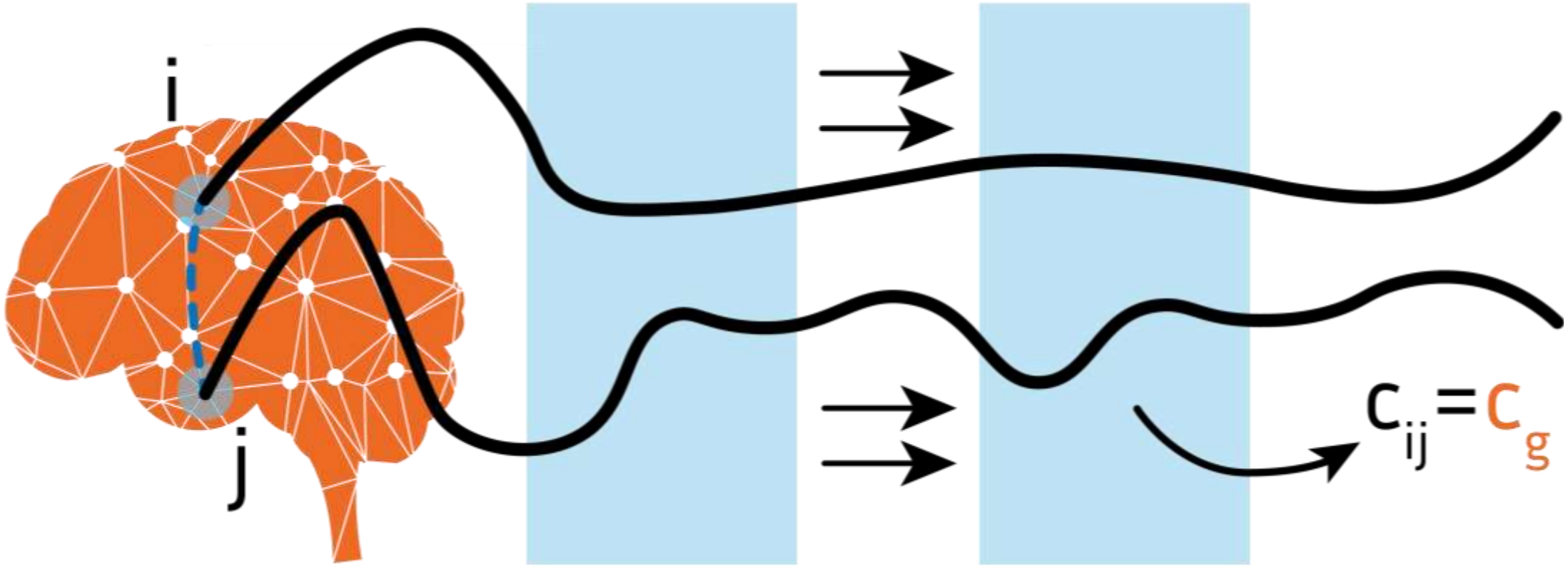
- Blood Oxygen Level Dependent imaging (BOLD)

Electro/Magneto encephalography (EEG/MEG)

- Measure the electric/magnetic field generated by the electrical activity of the brain

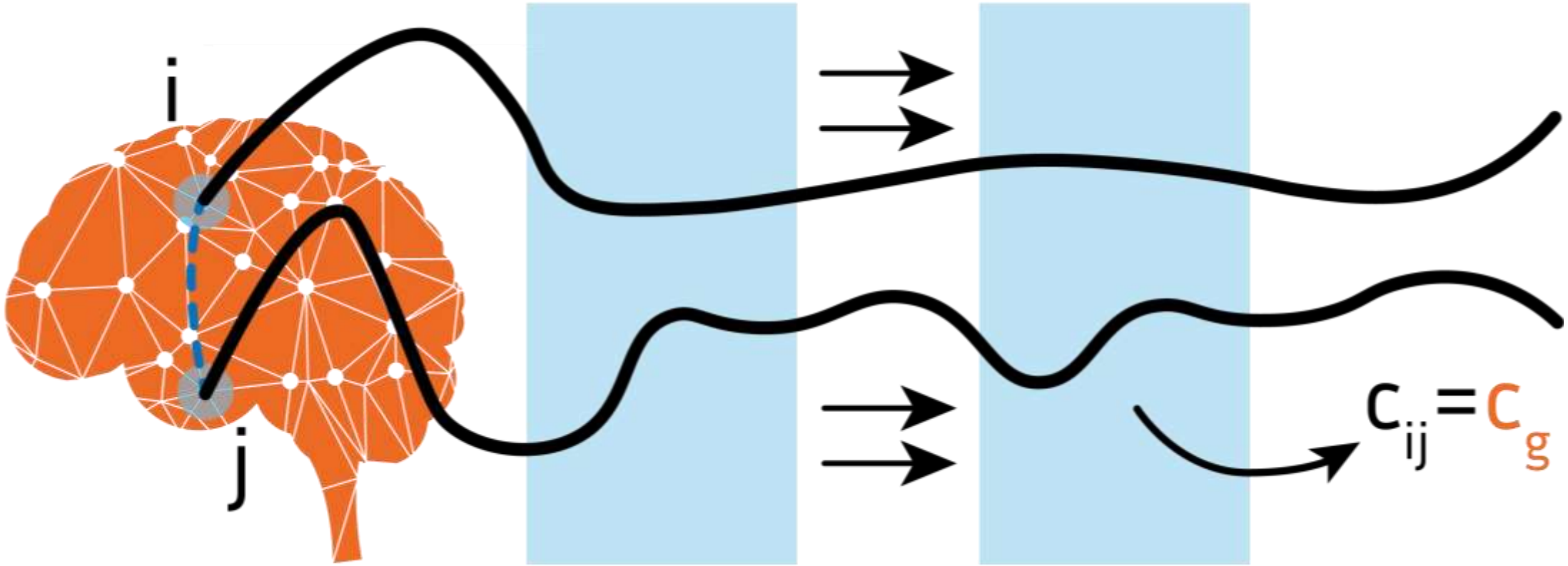
ONE **TIME SERIES** IN EACH REGION

Functional Connectivity



Correlation between the activity in two regions

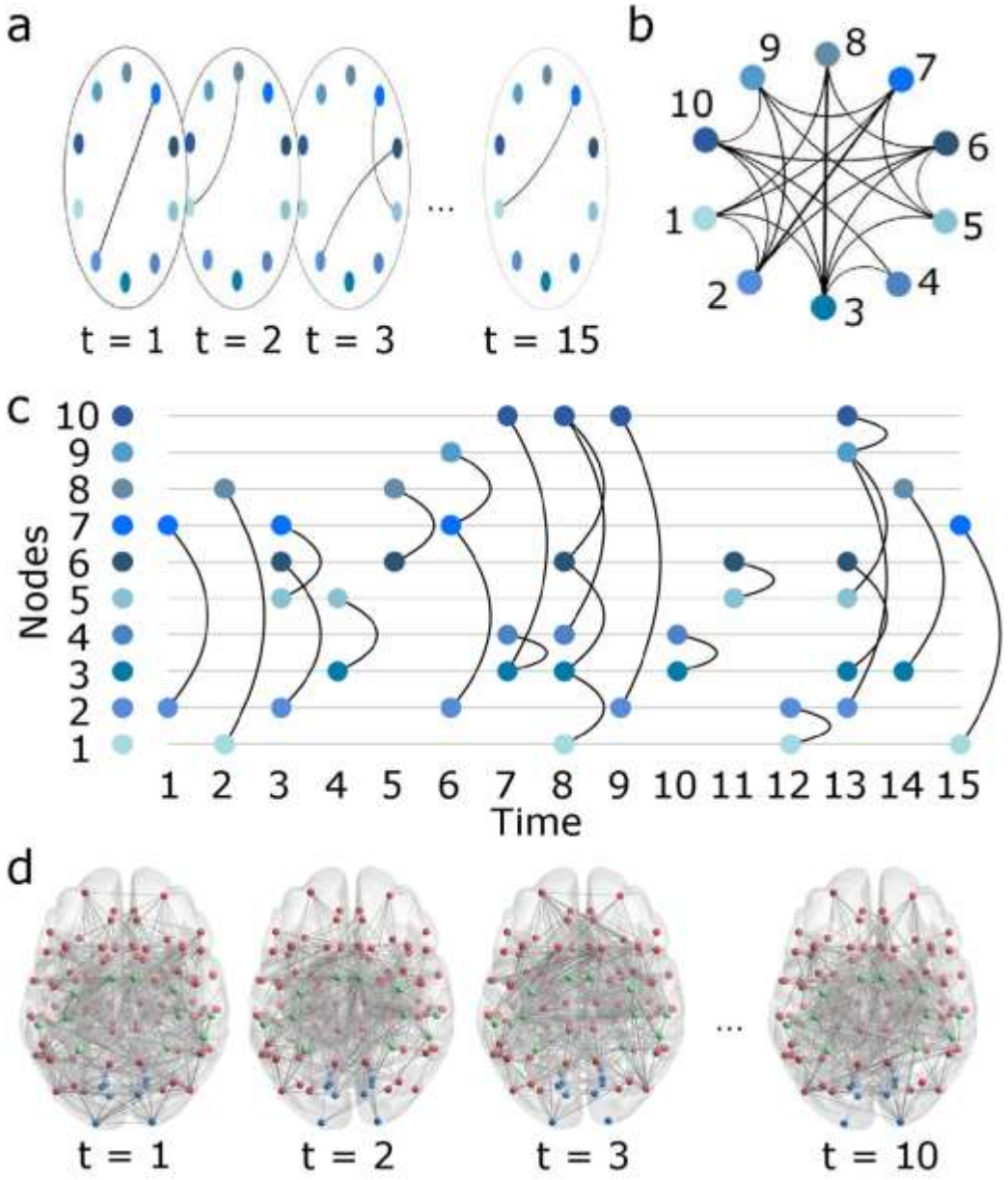
Functional Connectome



- Not Sparse
- Strongly changes over time

Dynamic Functional Connectivity

- Graph theory
- Network analysis



Chapter 4

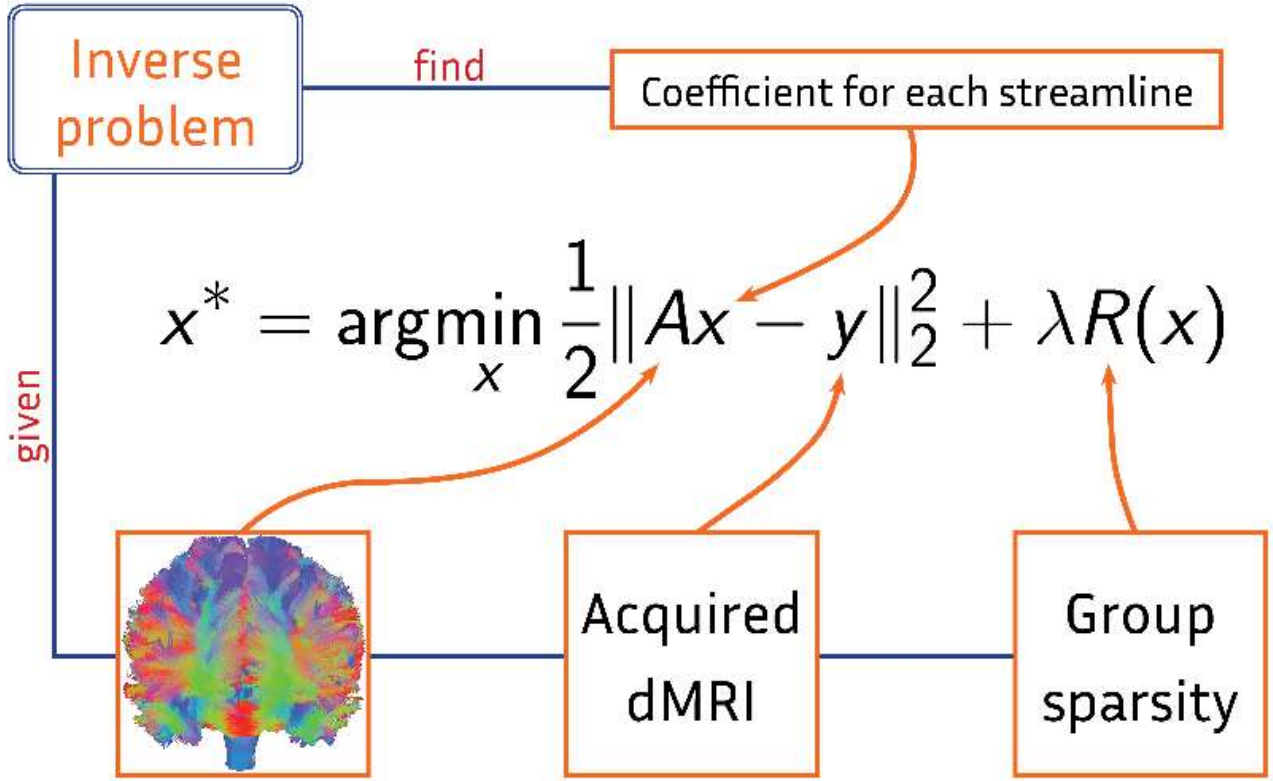
Integrative methods for connectivity estimation

Objective

Use **functional information** as a prior while estimating **structural connectivity**.

COMMIT

Convex Optimization Modelling for Microstructure Informed Tractography



- Convex analysis
- Numerical Optimization

- Describe the dMRI signal by means of a tractogram.
- Forward model from tractography to dMRI signal.
- Find the minimal subset of streamlines explaining the signal.

Regularization Term

- Promote sparsity group-wise
- **Preserve fiber groups that show high functional correlation**

$$R(x) = \sum_{g \in \mathcal{G}} \frac{1}{w_g} \|x_g\|_2$$

Non Functionally informed

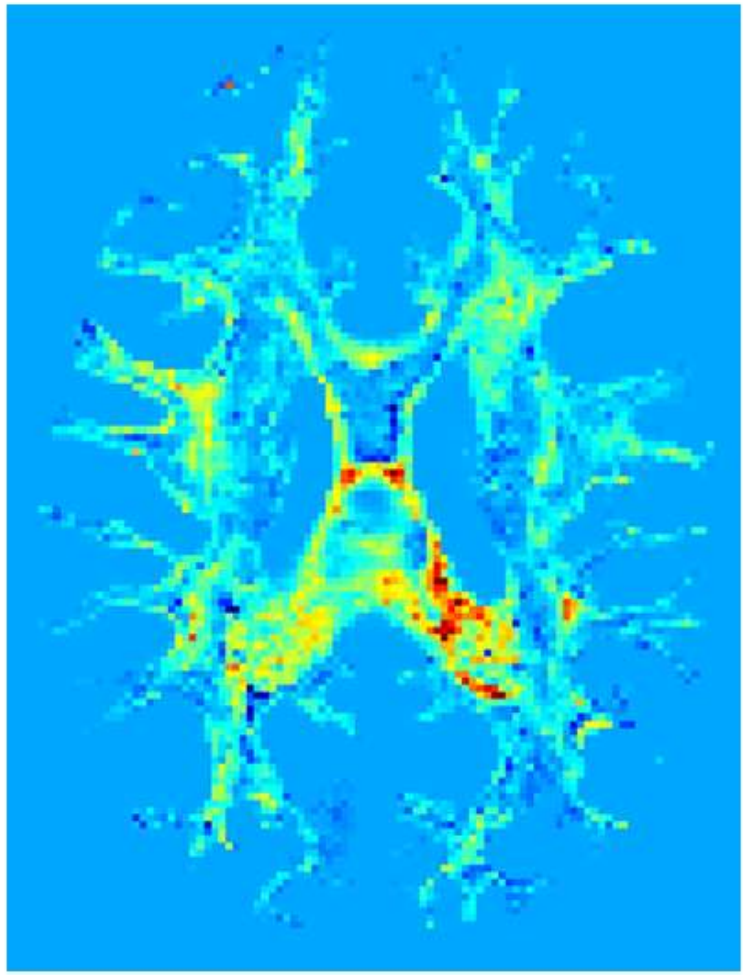
$$w_g = \sqrt{N}$$

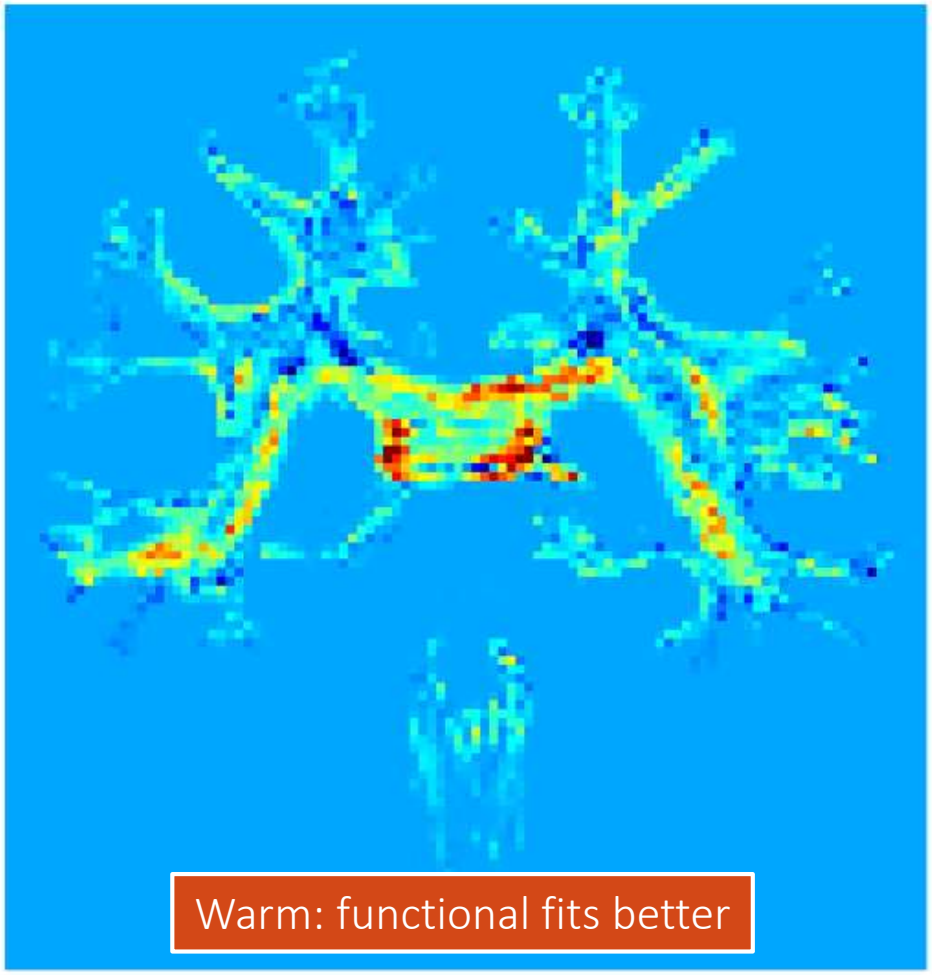
Functionally informed

$$w_g = \sqrt{N}(1 + c_g)$$

Preliminary Results

	without functional		with functional	
	% removed	residual	% removed	residual
Subject 1	12.26	958.47	16.01	931.07
Subject 2	18.85	828.58	24.19	808.27
Subject 3	13.55	847.07	16.35	828.95





Warm: functional fits better

Connectivity analysis of the new method

Connectivity analysis of the new method

Work in progress

No available ground truth

Connectivity analysis of the new method

- Integration
- Segregation
- Persistent homology

Topological

Data

Analysis

- Algebraic Topology
- Graph Theory

HOT TOPICS

- How to get rid of the **false positive connections** in tractography
- Design of **realistic phantoms** for the human brain
  Diffusion MRI / Functional MRI / EEG / MEG
- Development of **validation techniques** for connectivity estimation
- Characterization of pathology by means of **topological features of the connectome**

Take Home Message

The human brain is a network

Can be studied as a graph

Structural connectomes describe the anatomical connections betweek cortical regions

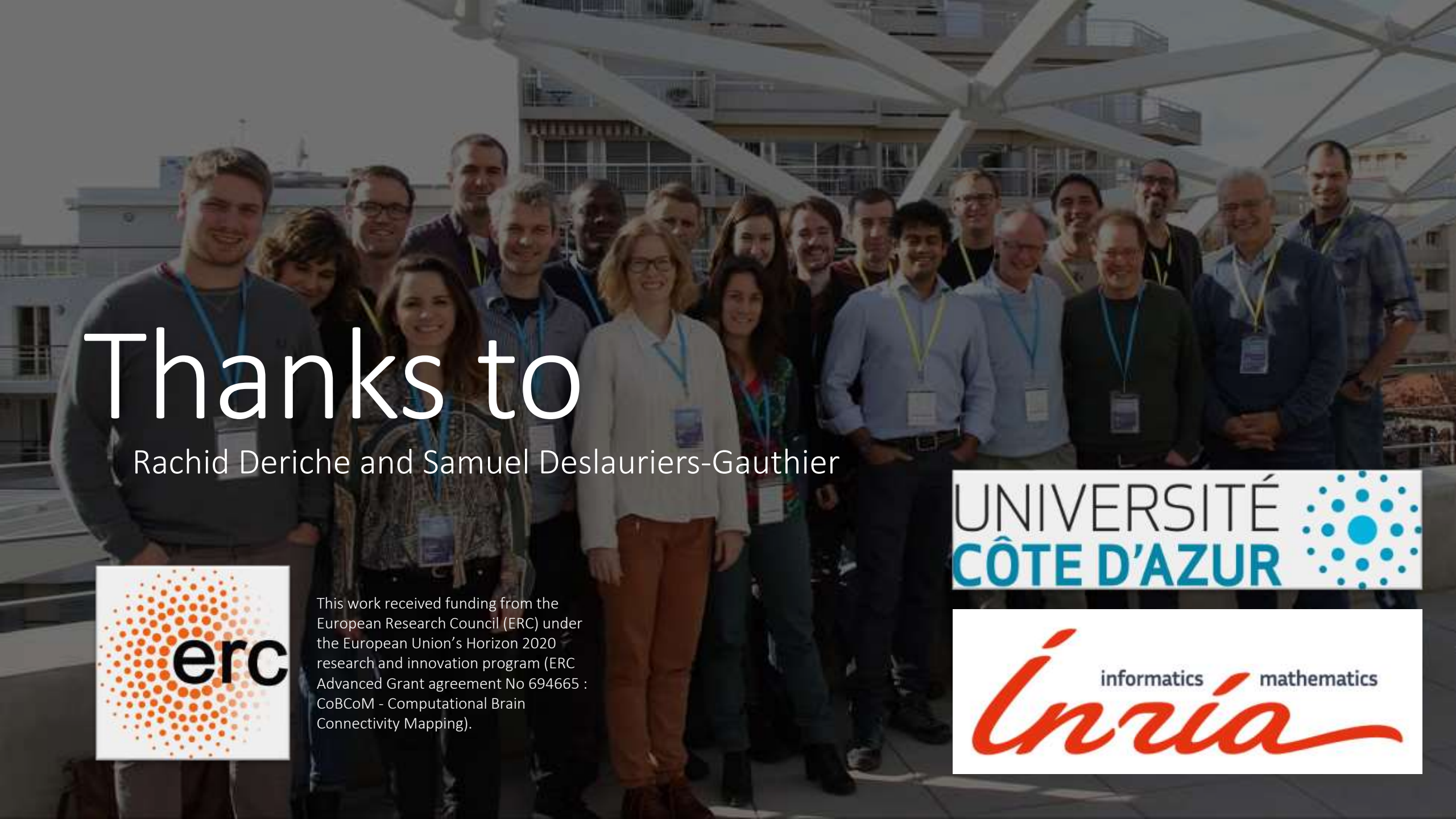
Are subject to low specificity problems

Functional connectomes describe the correlation between the activations in cortical regions

Strongly depend on the task

Validation of connectivity estimation is difficult

No ground truth, no null models



Thanks to

Rachid Deriche and Samuel Deslauriers-Gauthier

This work received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (ERC Advanced Grant agreement No 694665 : CoBCoM - Computational Brain Connectivity Mapping).