Diffusion MRI imaging for brain connectivity analysis

principles and challenges

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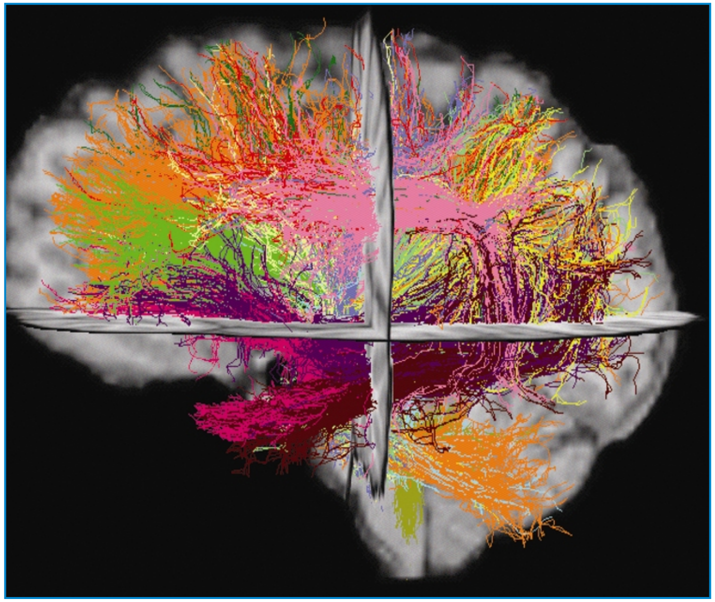
From Brownian motion to Diffusion MRI - Motivation

- MR imaging is now established as the most important modality in neuro-imaging

- Recent advances allow to obtain *in vivo* information on the architecture of the (brain) tissues
  - New MR sequences
  - New algorithmic developments

- This opens new perspectives in fundamental neurosciences as well as in clinical practice



Outline

- Basics of diffusion
- Imaging the diffusion by MRI
  - Diffusion-Tensor MRI & beyond
- From Diffusion MRI to Brain connectivity analysis
- Applications and challenges

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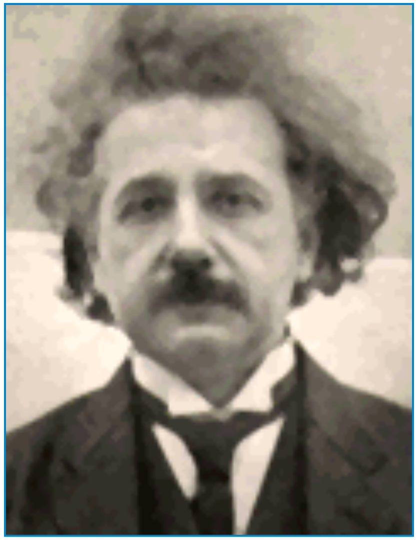
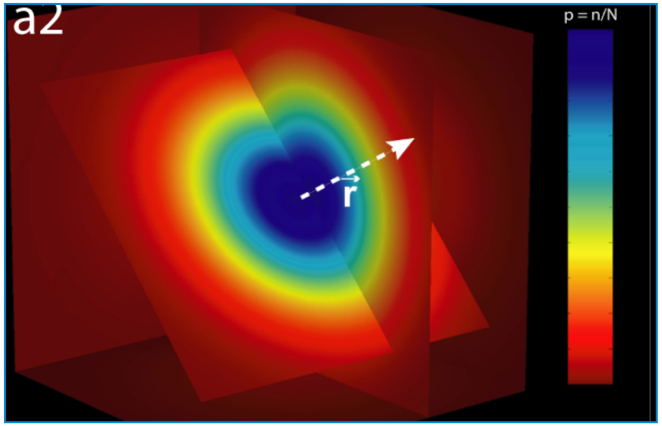
Basics of diffusion

- Molecular diffusion – Brownian motion
  - First formally described in 1905 by A. Einstein
  - We will consider water molecule diffusion
    - *Example: in a glass of water, molecules diffuse randomly and freely, only constrained by the boundaries of the container*

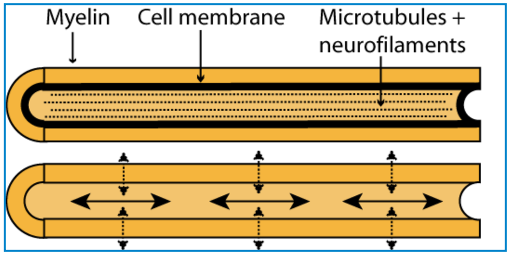


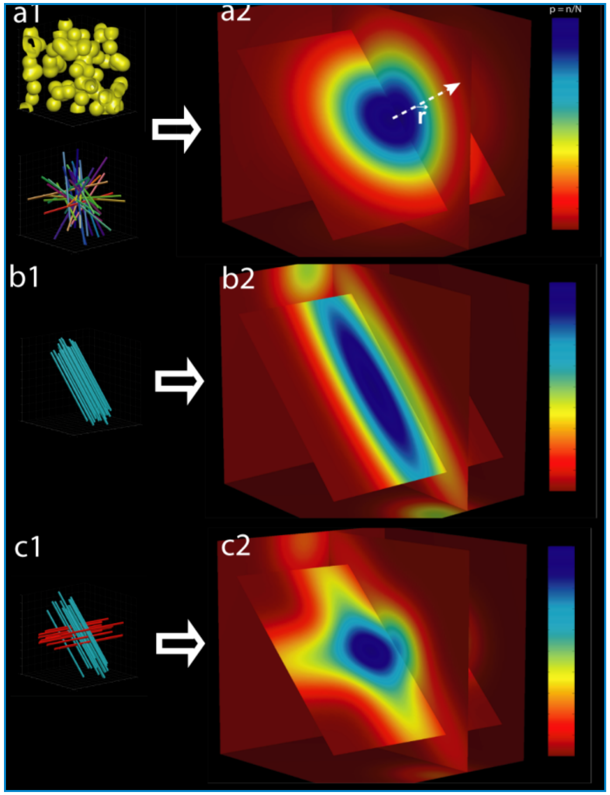
- For homogeneous media, this diffusion *pdf* is an isotropic Gaussian
  - With $\sigma^2=2D\Delta$
  - D is the diffusion coefficient
    - *Function of medium viscosity, t°, …*
- For a 3D volume, we use here the color-coding of the pdf



Diffusion in complex media

- neuronal tissues : fibrillar structure
  - *Tightly packed, coherently aligned axons*
  - *Diffusion more restricted in direction perpendicular to the axonal orientation than along its parallel direction*
  - *This is anisotropic diffusion, as opposed to isotropic diffusion*
- fiber crossings
  - *Certainly not a Gaussian pdf then.*





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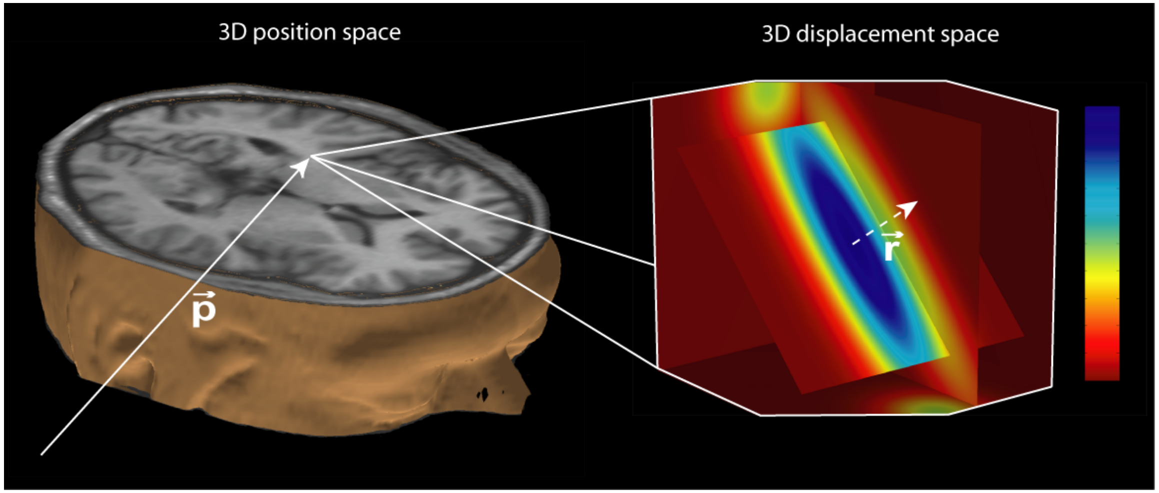
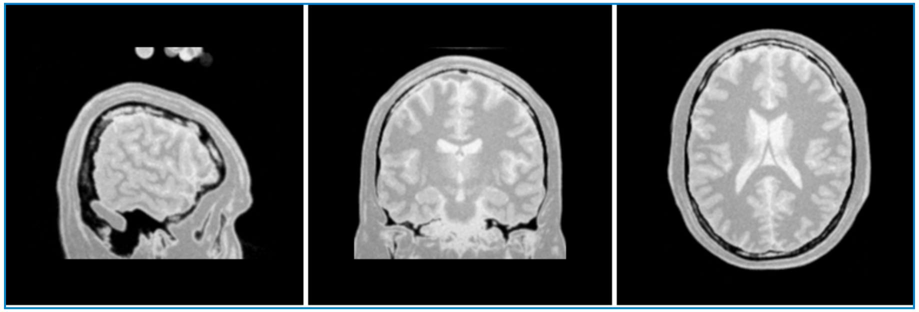
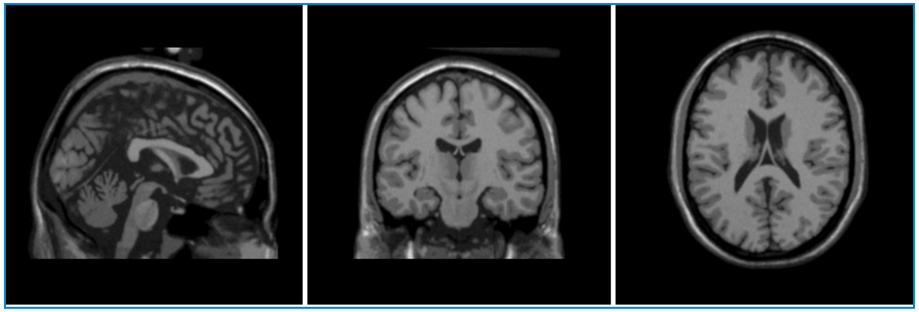
- Imaging the diffusion of the 3D volume would ideally give a 6D data set



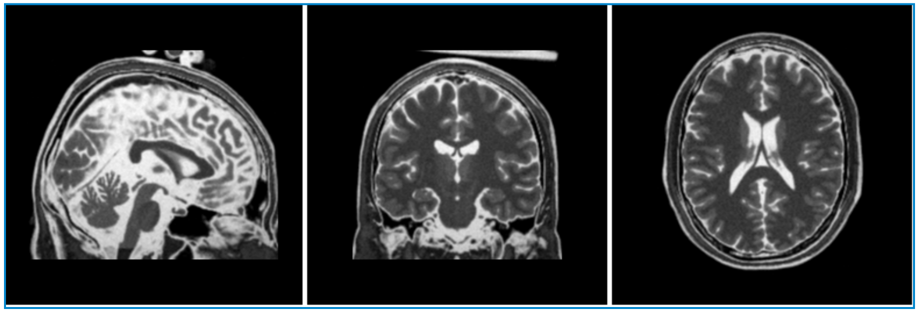
MR imaging



PD-weighted MRI



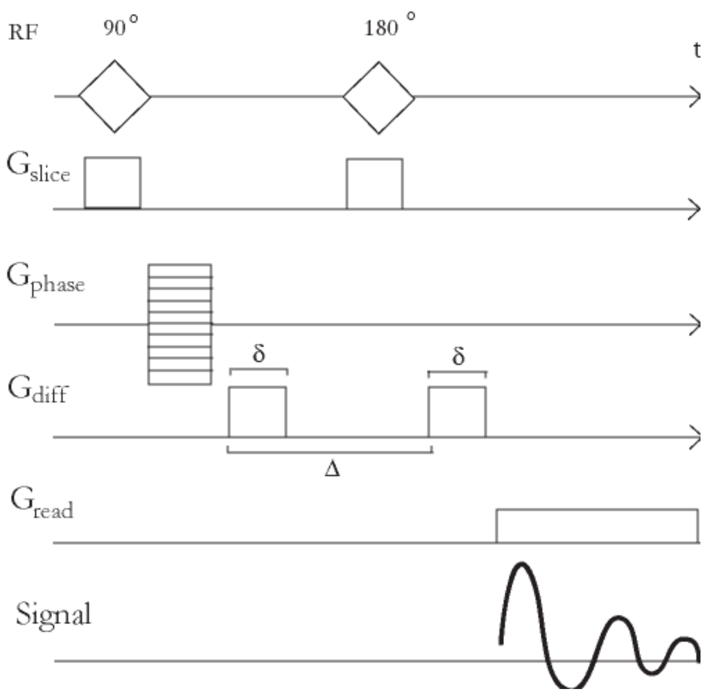
T1-weighted MRI



T2-weighted MRI

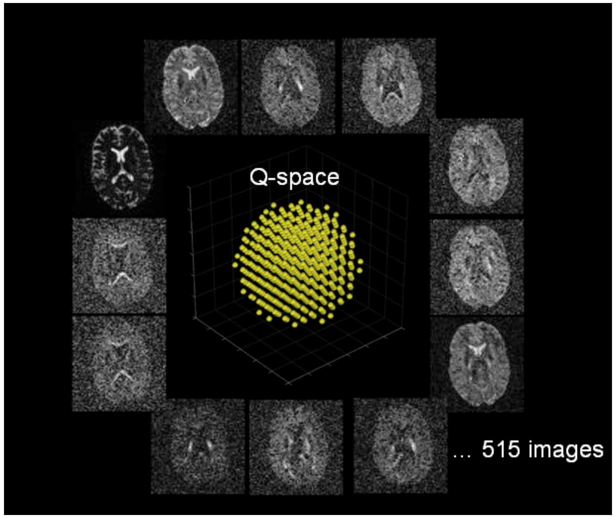
Diffusion weighted MRI

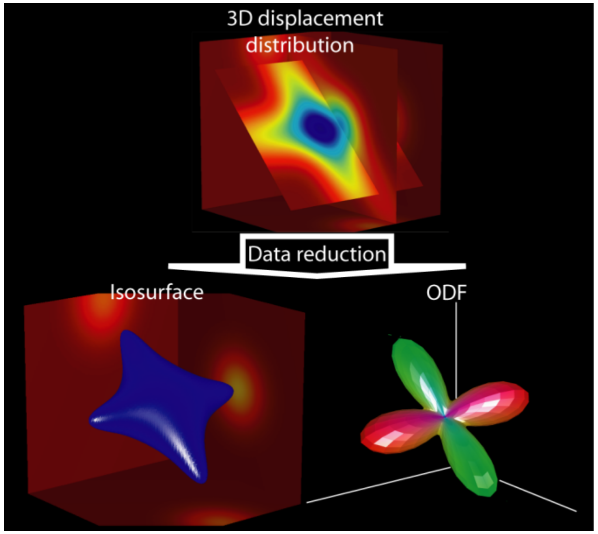
- It is possible to construct MR sequences that will be sensitive to diffusion in one given direction:
  - In addition to classical MR image sequences, diffusion MRI adds two gradients and a 180° RF pulse
  - Result: an image with low intensity in regions where the diffusion is high along the applied diffusion gradient direction



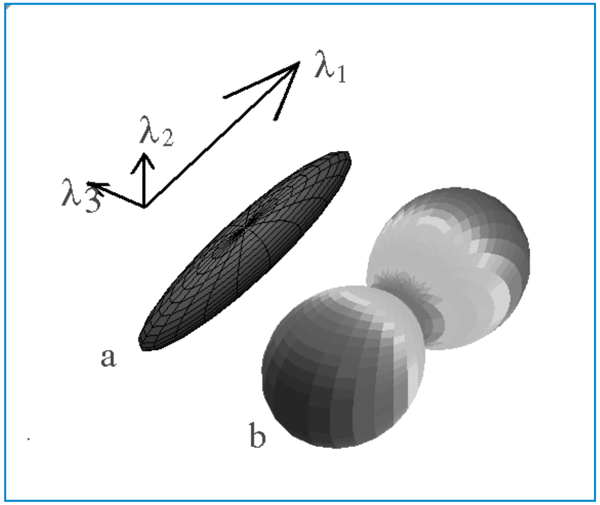
Diffusion spectrum imaging: DSI

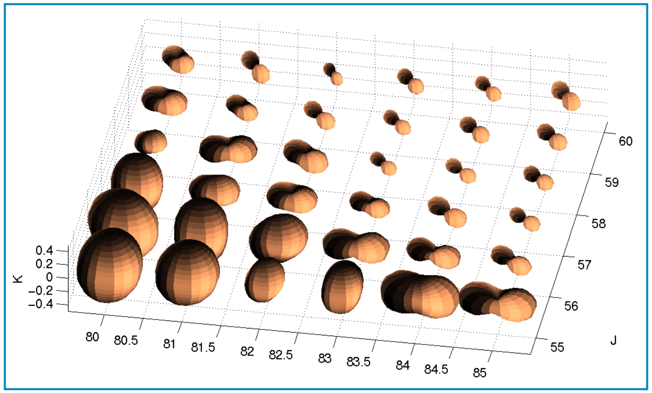
- If we want to reconstruct the whole diffusion *pdf* at every point of a brain, we need to acquire images
  - with a large number of diffusion gradient directions
  - with many diffusion gradient intensities
  - Some 515 images are classically used
  - By Fourier Transform, we can reconstruct the *pdf* at every voxel => This is DSI
  - Very heavy but very rich information !
  - Most of the time, reduced to an ODF



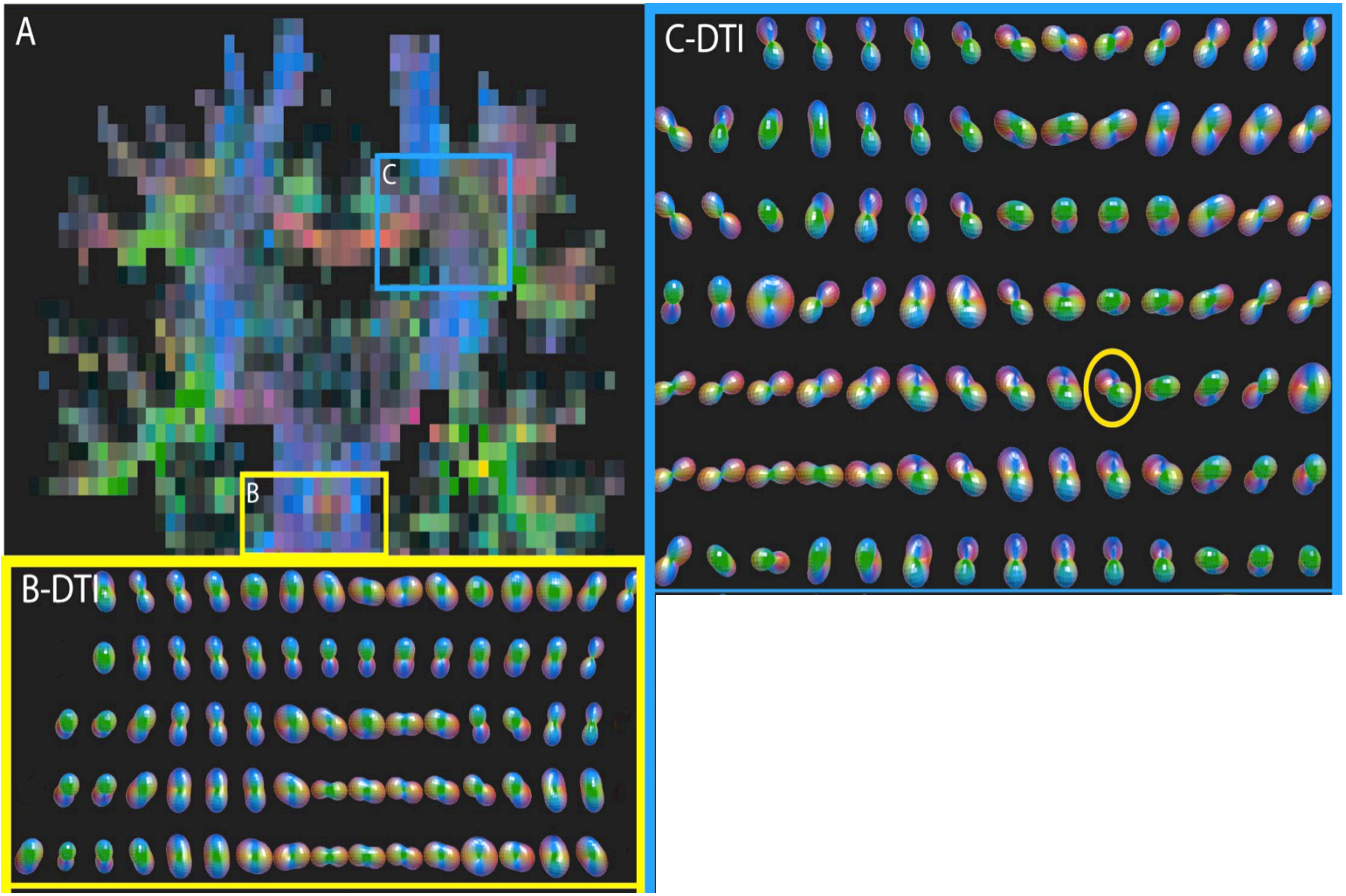


- Diffusion Tensor Imaging (DTI)
  - Let us assume that the diffusion *pdf* is Gaussian, but anisotropic (influenced by the tissue architecture)
    - *A 3D anisotropic Gaussian has 6 degrees of freedom*
    - *It is fully characterized by its covariance matrix, a 3x3 symmetric matrix called the Diffusion Tensor*
    - *Can thus be obtained the acquisition of diffusion images in 6 different directions of the diffusion gradient*

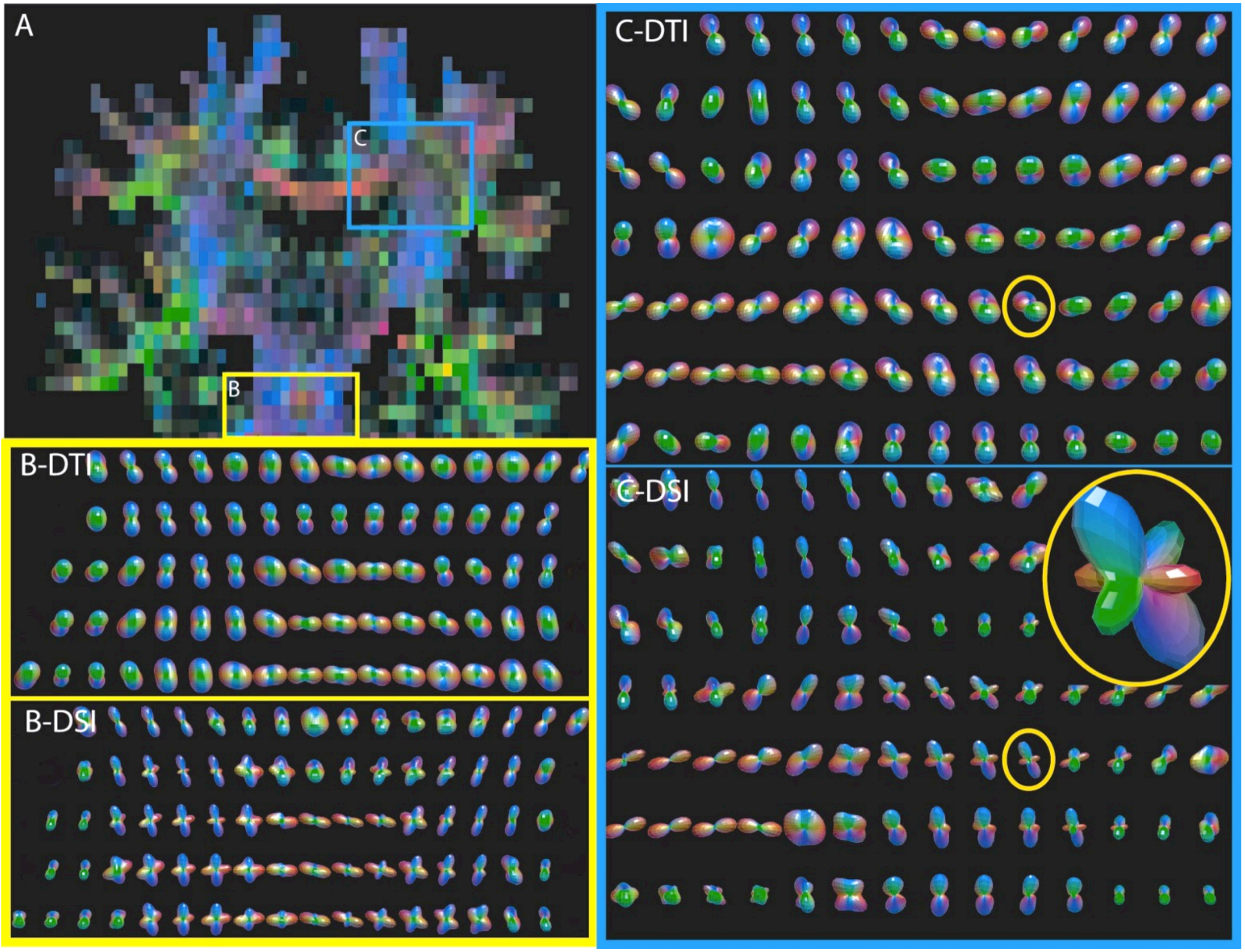




DTI



DSI vs. DTI



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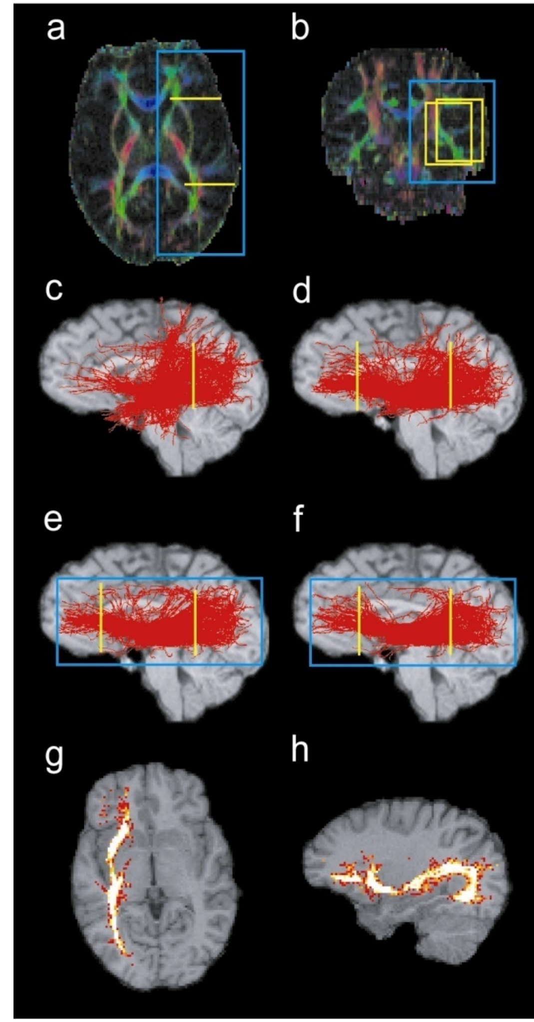
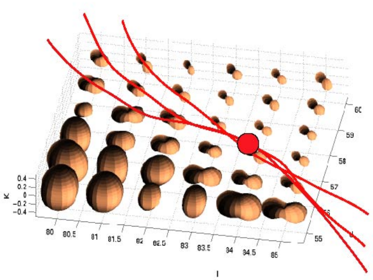
DT-MRI tractography

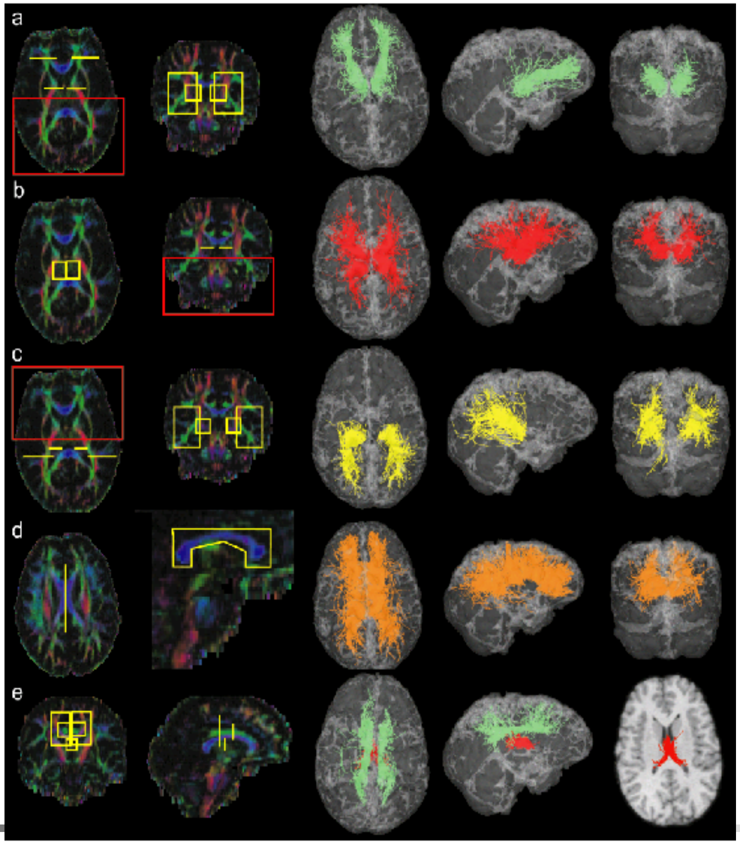
- Diffusion-MRI of the brain
  - Tensor field or field of ODF's
- Fibre tracking
  - Infer from a diffusion field axonal trajectories i.e. brain connectivity
  - Computation of trajectories following principal directions of diffusion in the tensor field
- Whole brain simulation
  - Trajectories are initiated all over the brain's WM
  - Result is an estimate of the whole brain connectivity (millions of lines)
- Tract selection, virtual dissection
  - Fibre selection using ROIs

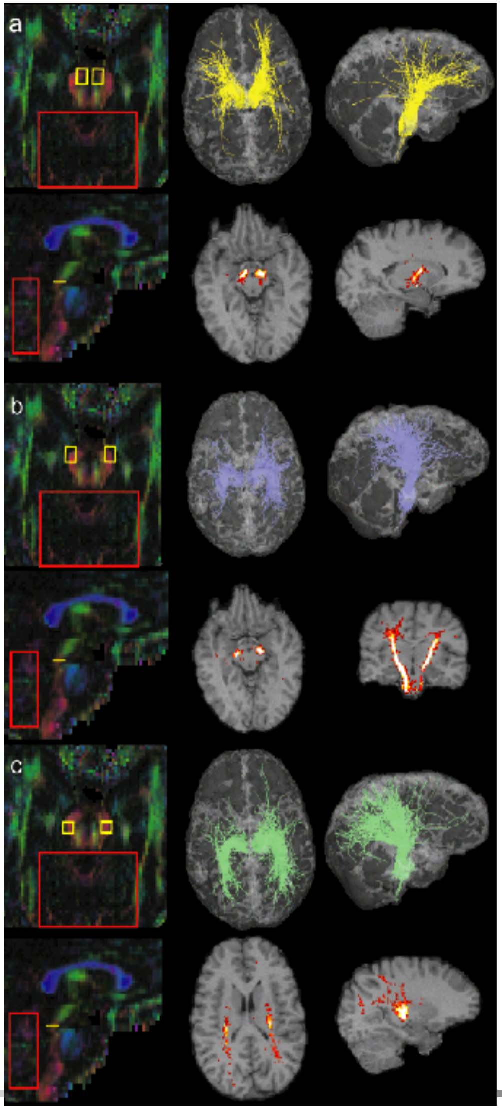




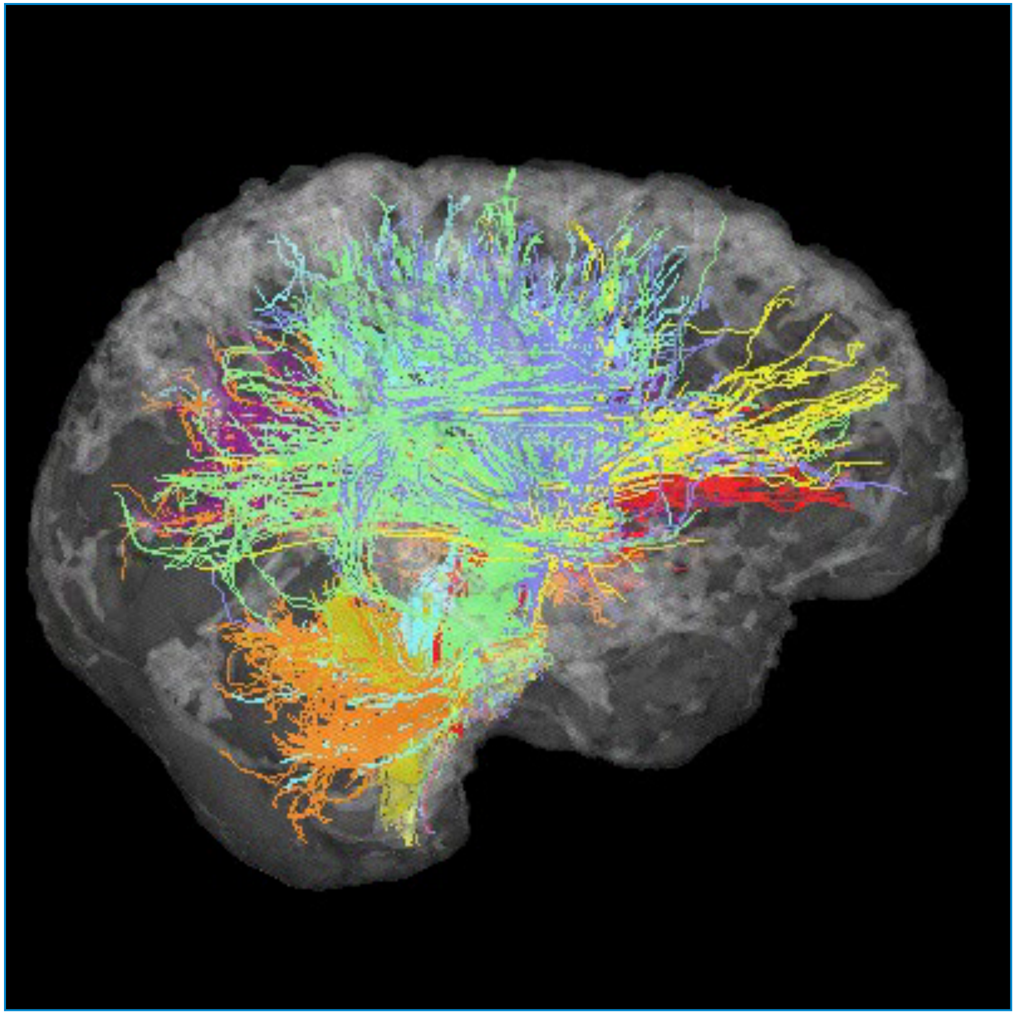
Fibre-tracking, results

- Thalamic projections
- Cortico-spinal and cortico-bulbar tracts

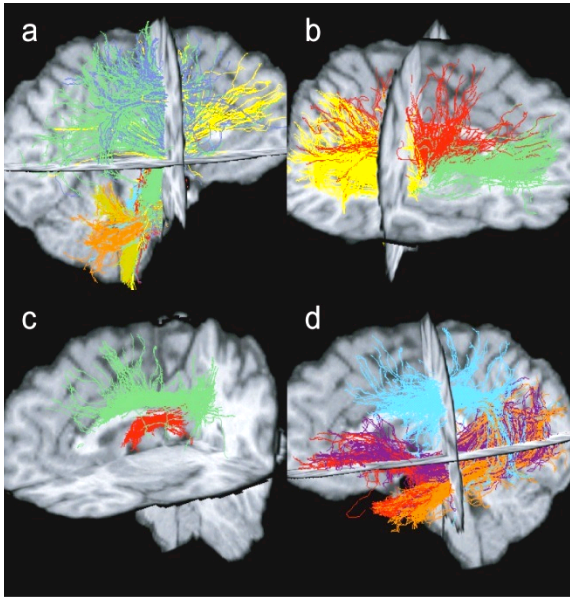


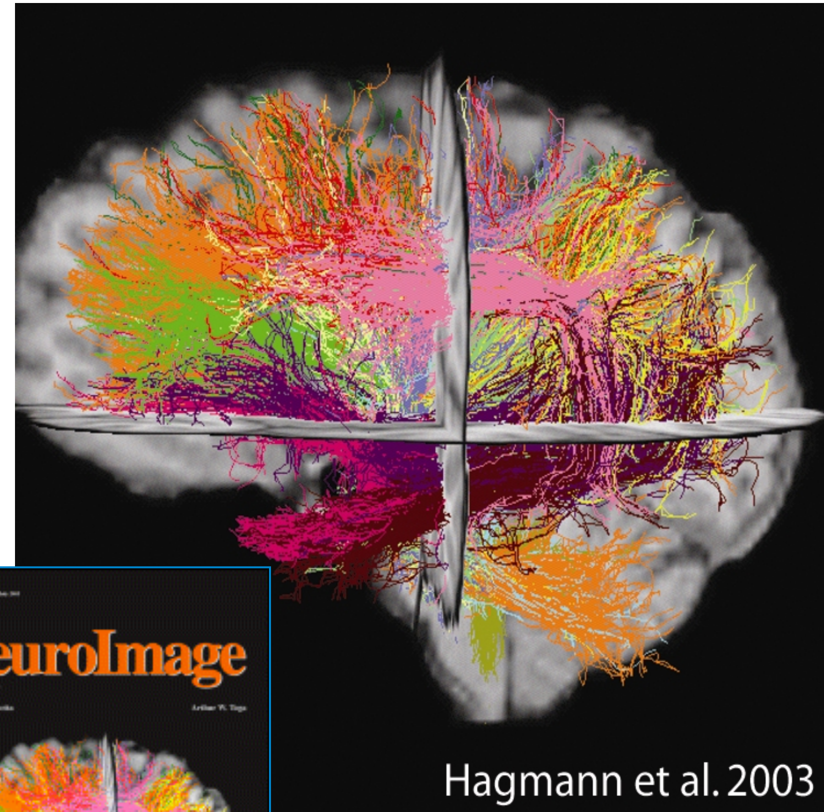


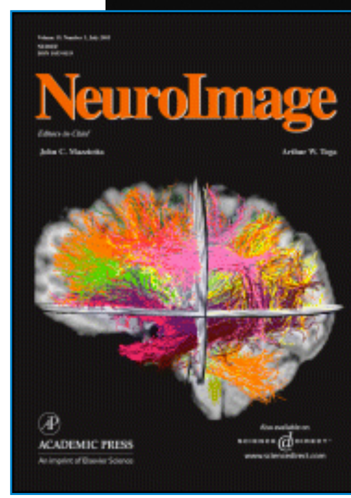
Fibre-tracking, results



References







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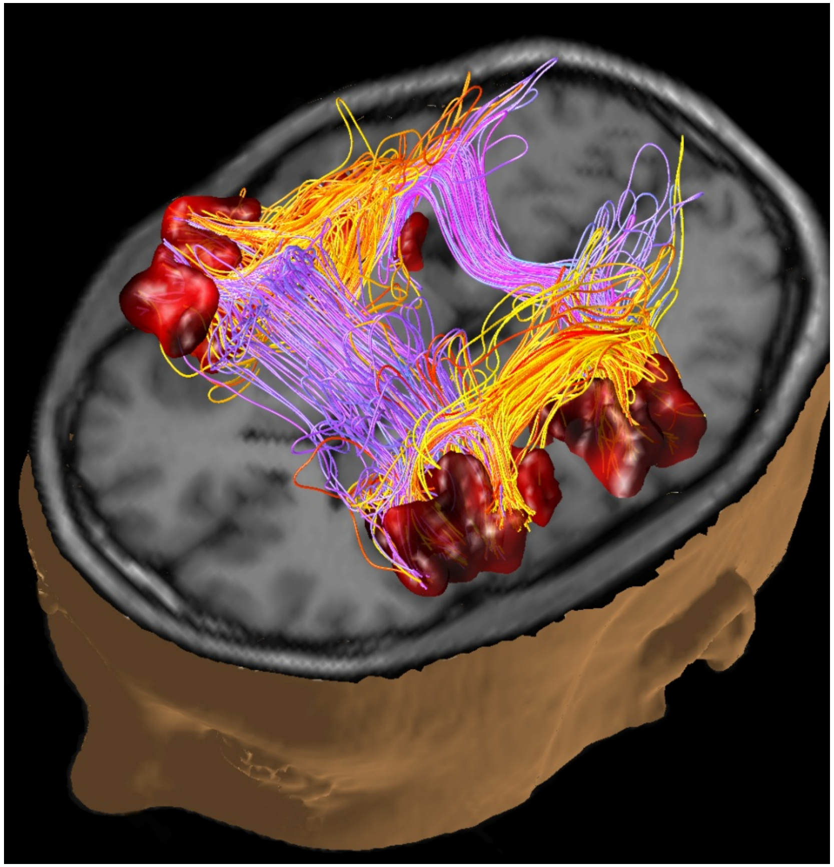
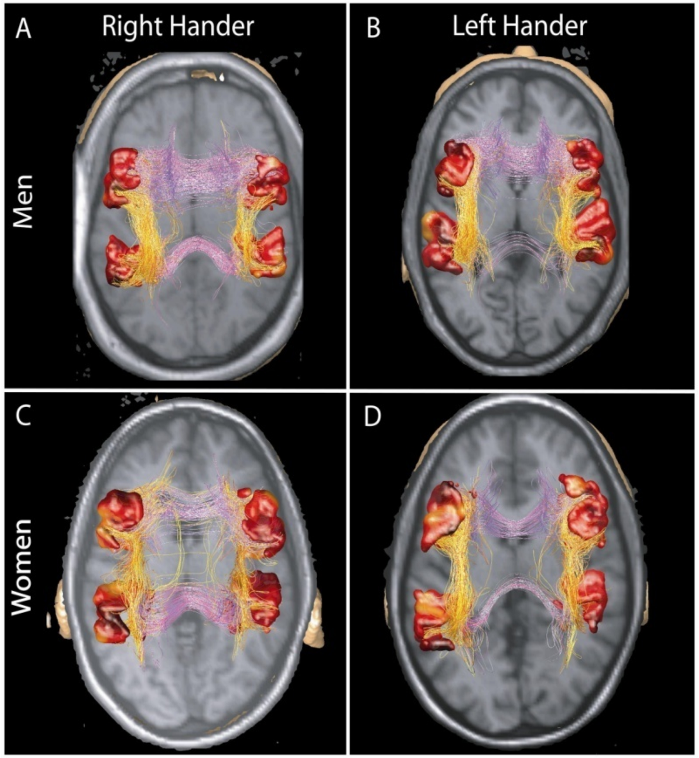
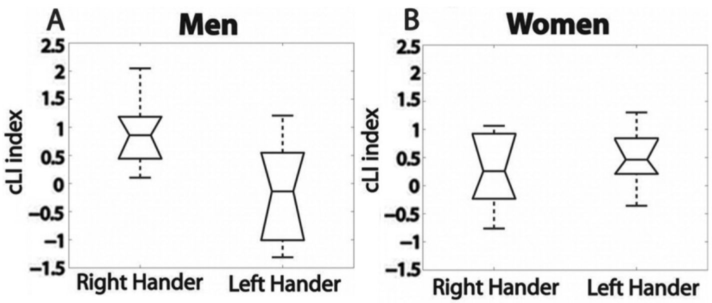
Application: study of language networks







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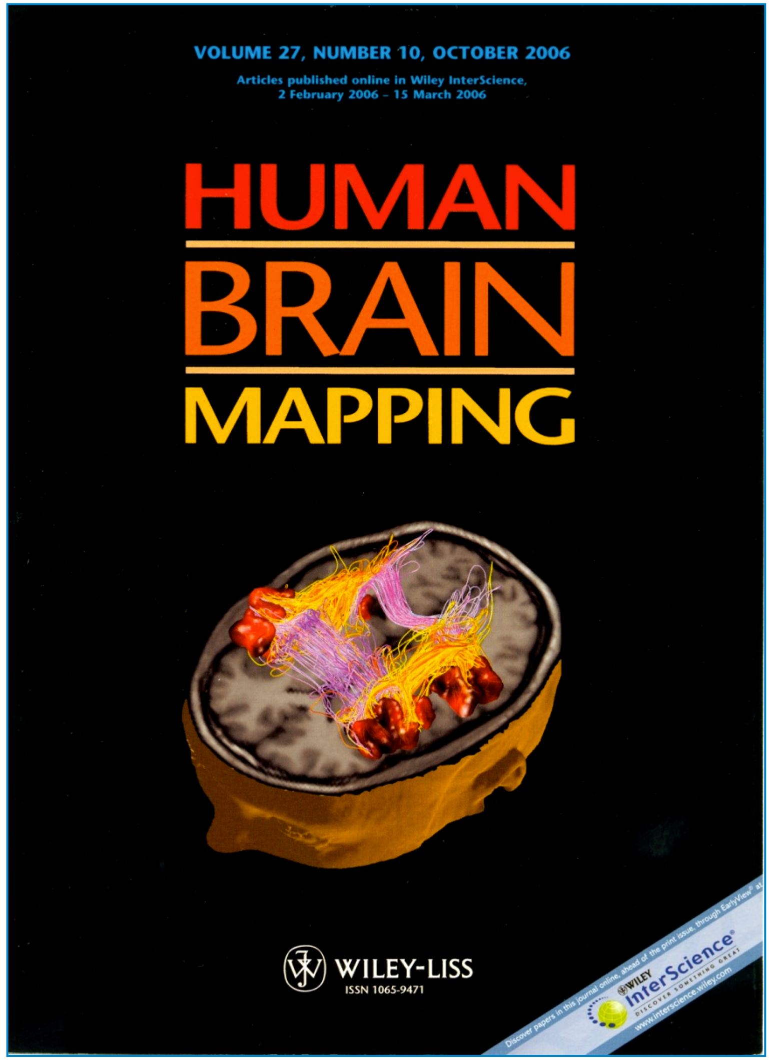
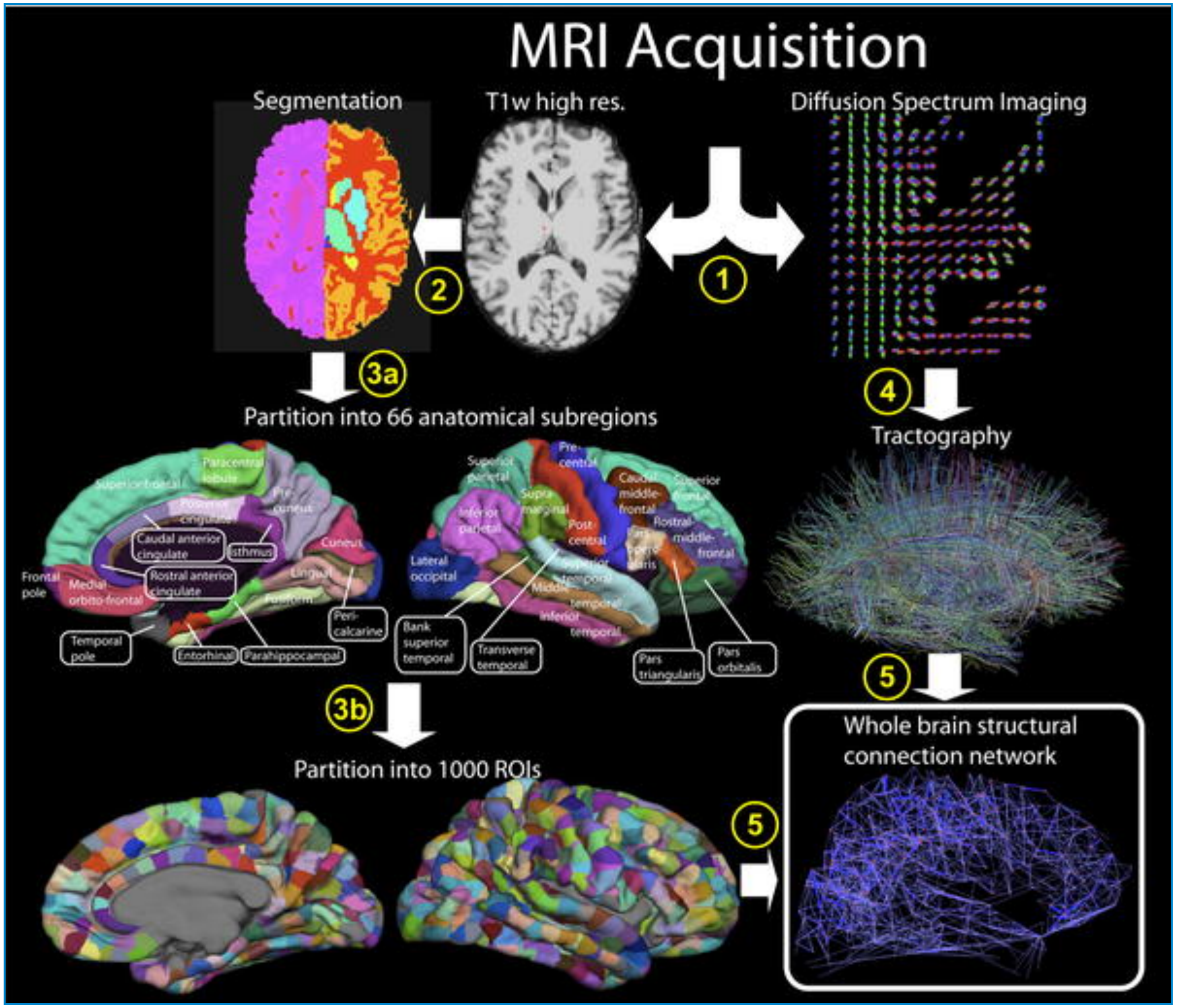
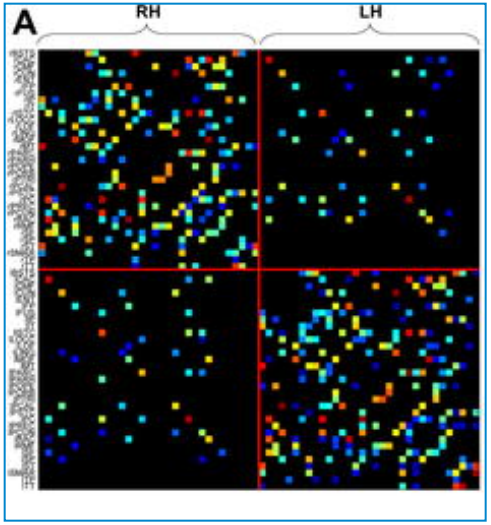


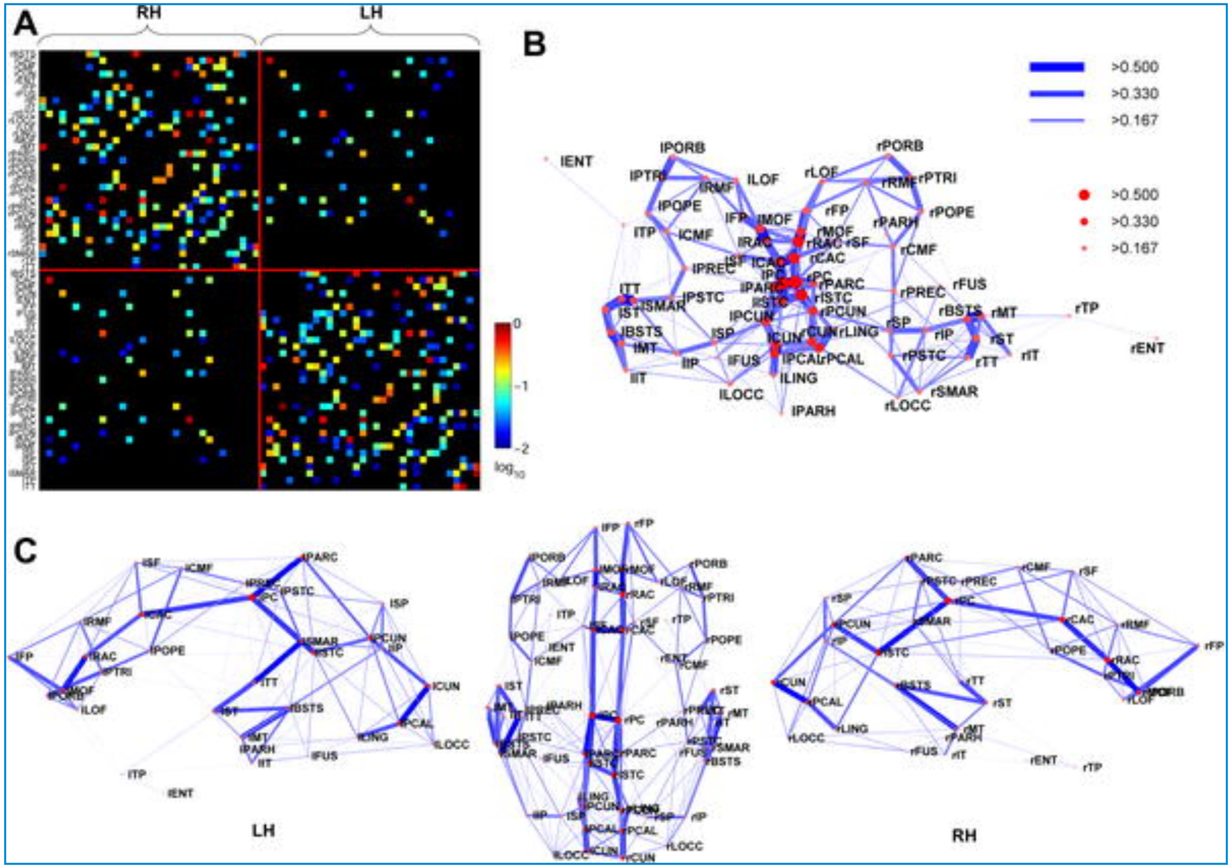
Towards brain connectivity analysis





Towards brain connectivity analysis

Connection matrix & network connectivity backbone



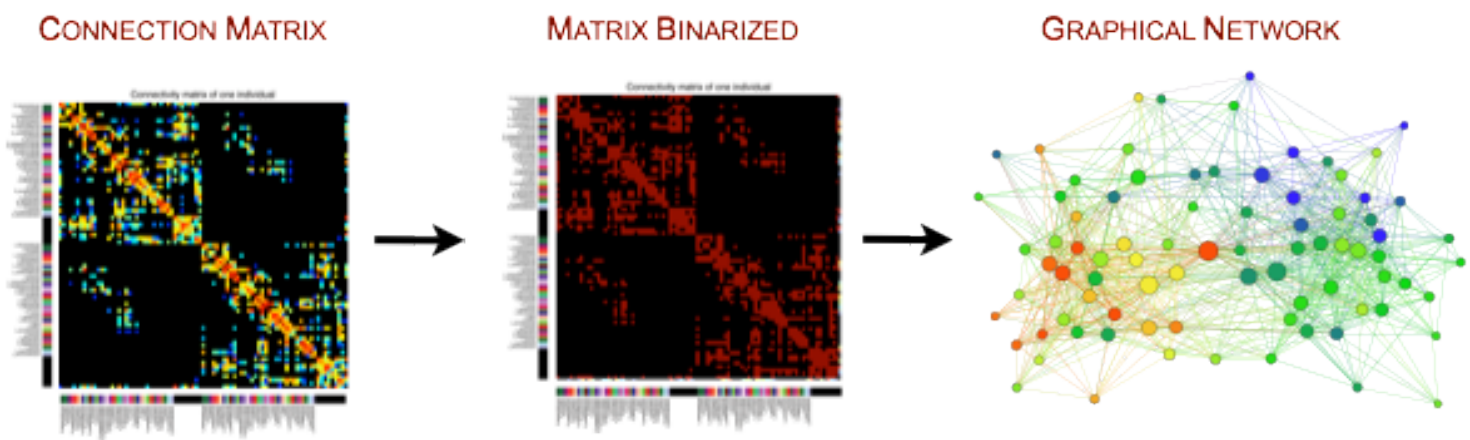
PLoS Biology, 2008, PNAS, 2009, J. Neurosc. Meth. 2010

- Brain connectivity analysis by diffusion MR imaging
  - Epilepsy
  - Schizophrenia
  - Normal and pathological brain developments
    - *Normal : Hagmann et al, PNAS 2011*
    - *Pathological : IUGR : HBM2010, ISMRM 2010, HBM2011*
  - Strokes & brain plasticity

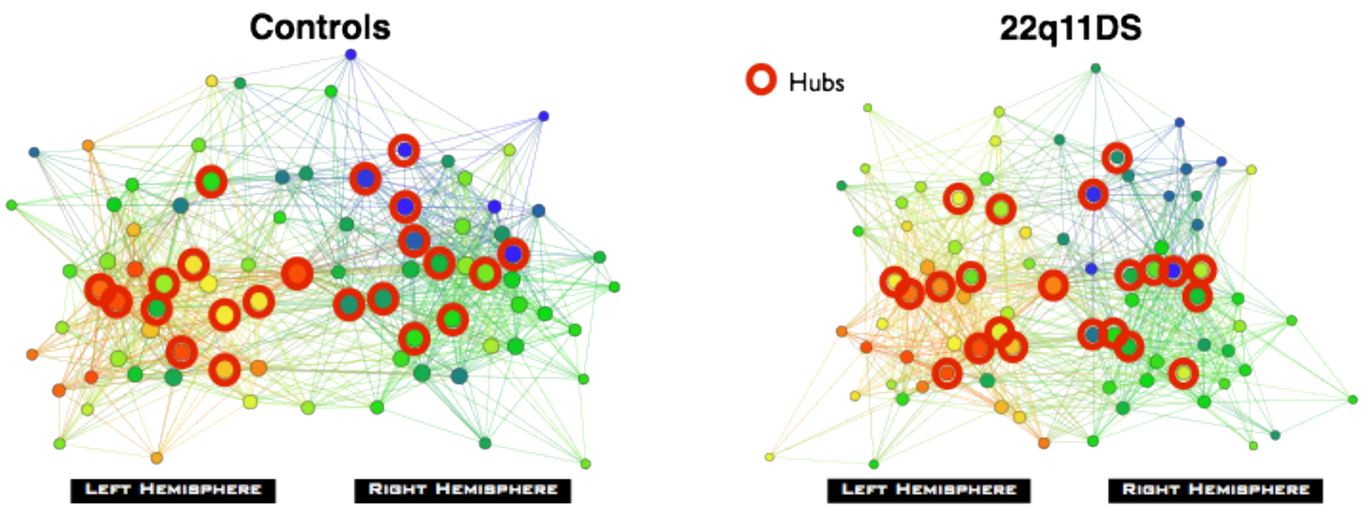
Network analysis of 22q11DS Patients

Marie-Christine Ottet, Marie Schear, Stephan Eliez, Univ. Geneva

- Syndrome: 22q11DS:
  - Microdeletion on chromosome 22, 30% risk for developing schizophrenia
- Representation of the brain as a graphical network
  - Nodes: cortical regions
  - Edges: fiber bundle linking two nodes
  - Hubs: nodes specialized in linking distinct sub-network together



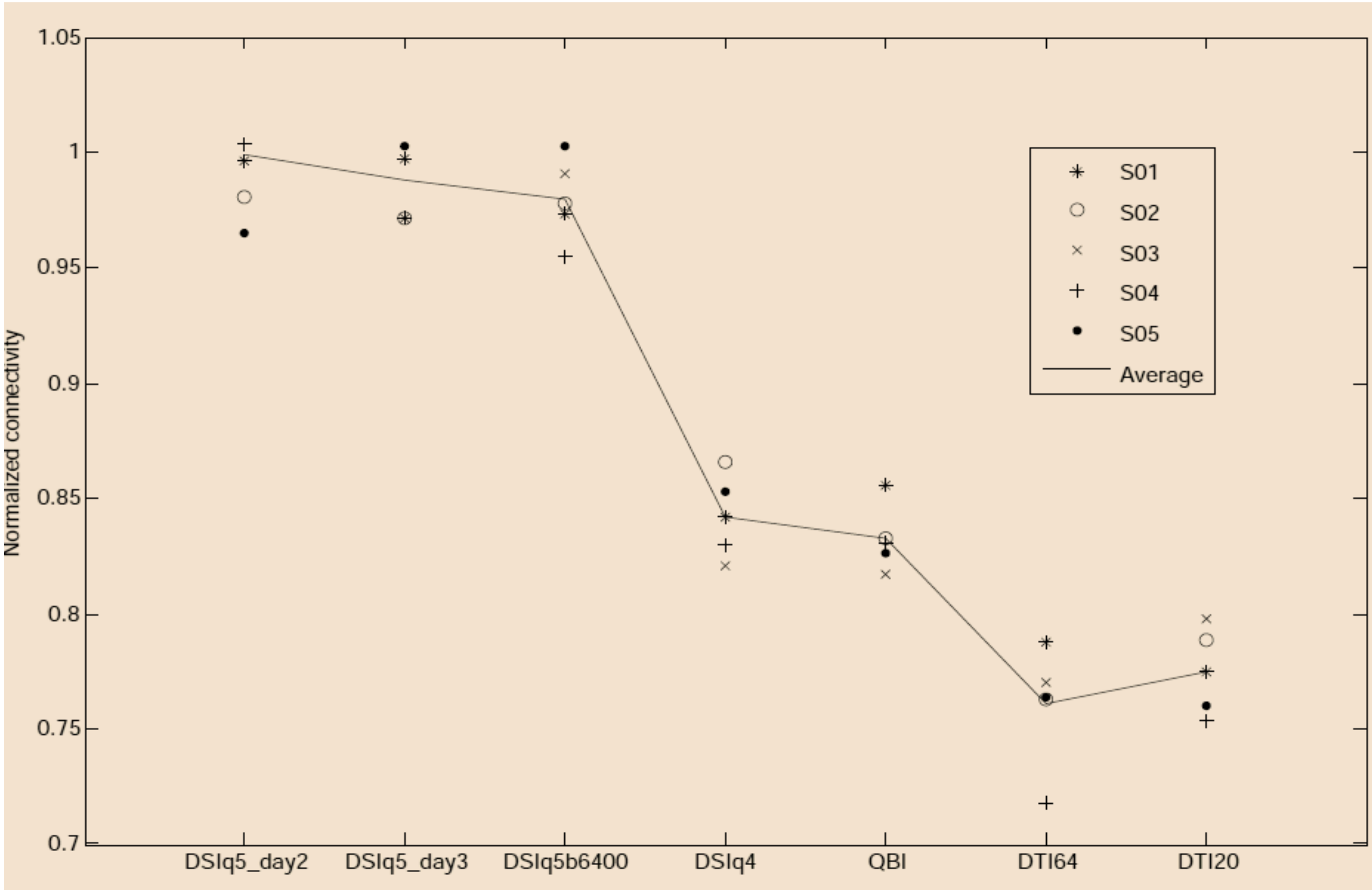
Network analysis of 22q11DS Patients



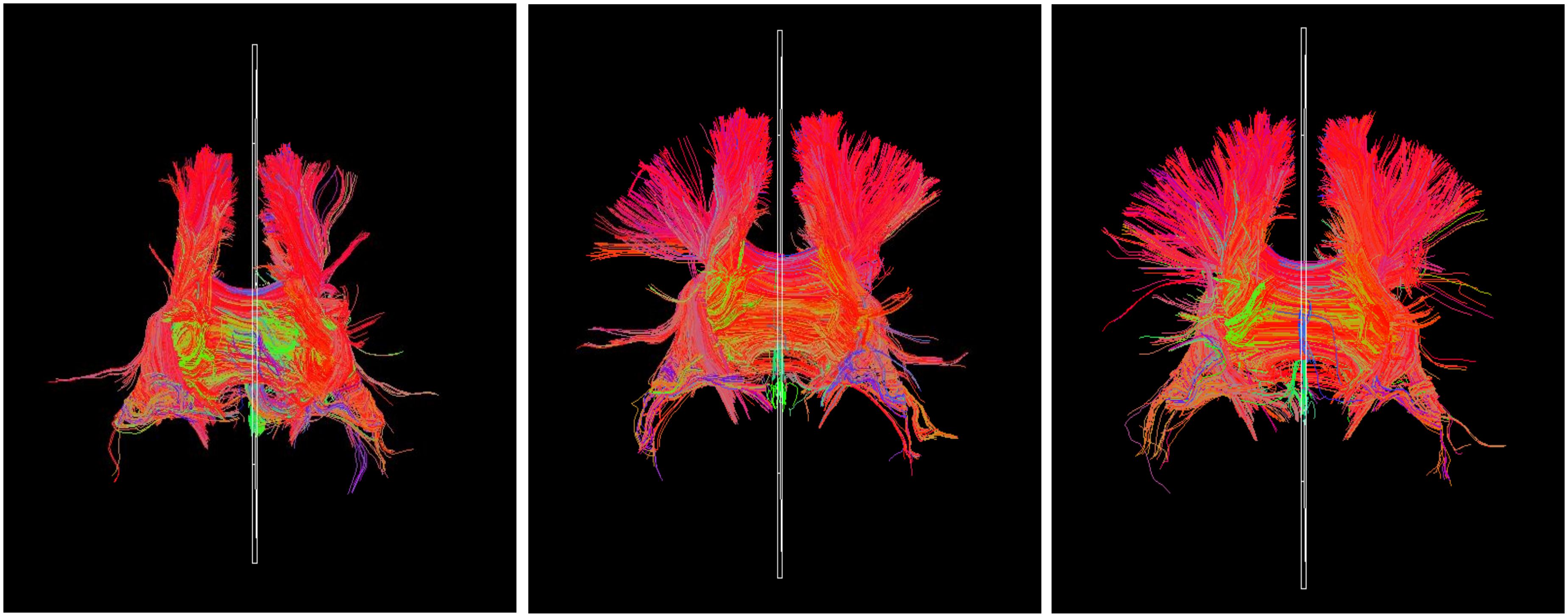
- Results between 30 patients and 30 controls:
  - Degree loss => loss of connectivity
  - Efficiency loss => loss of the capacity to process information locally
  - Path length gain => more difficult to transfer information
  - Altered hubs distribution (red circles) => Alteration of the core organization of the network
- Conclusion :
  - The microdeletion 22q11 disorganizes the structural brain network. This network alteration may explain psychiatric outcome in these patients.

- Methodological aspects of diffusion MR imaging:
  - DSI acquisition & Reconstruction
  - Tractography
  - Cortical parcellation
  - Statistical analysis

Comparison of different diffusion schemes

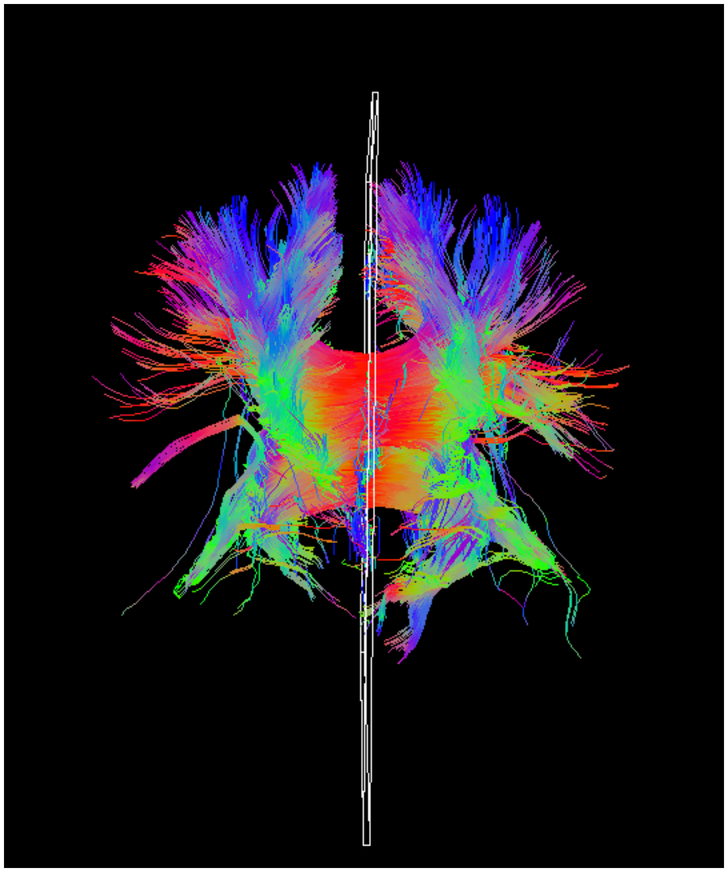


Comparison of different diffusion schemes



DTI q-ball DSI

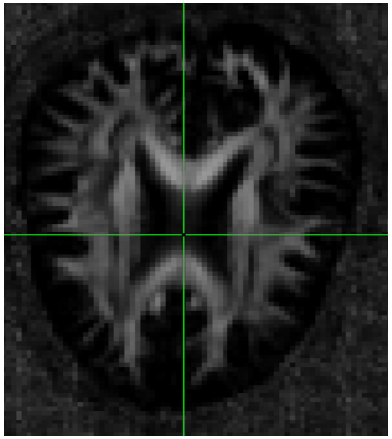
- Global tractography



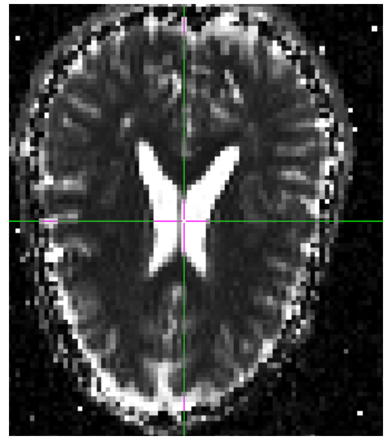
Advanced scalar maps

Alessandra Griffa (EPFL), Philipp Baumann & Patric Hagmann (CHUV)

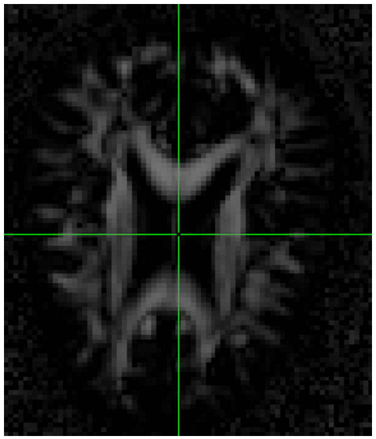
GFA

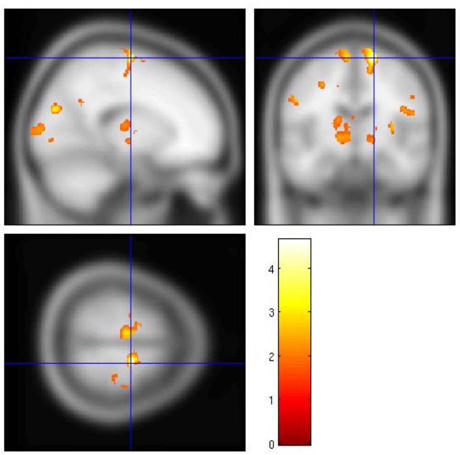


ADC

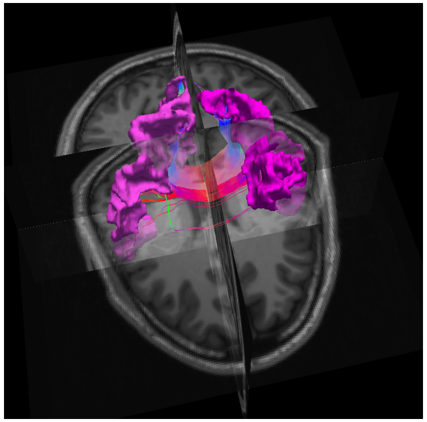


skewness





VBQ – voxel-based quantification

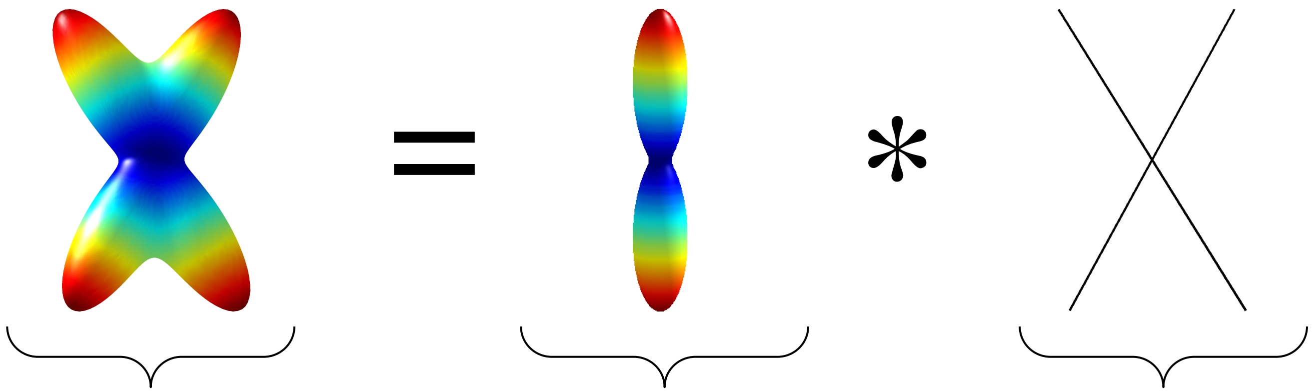


Investigate connectivity between left and right motor cotices

Sparsity in diffusion MRI

Alessandro Daducci (EPFL) & Yves Wiaux (EPFL-Univ. Geneva)

- ODF can be expressed as a **convolution** over the unit sphere:



ODF: directional information about diffusion process recovered with the data

KERNEL: axisymmetric template estimated from the data by tensor fitting

fODF: directional information about underlying fiber directions

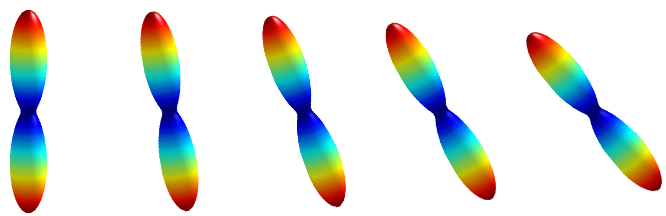
- The **fODF** (fiber ODF) is what we are interested in
- KEY POINT: it is a <u>very sparse</u> function on the unit sphere!
- We can exploit this sparsity to reduce the acquisition time

Inverse problem formulation

$$\text{minimize } ||Ax - y||_2 \text{ subject to } ||x||_1 \leq \tau$$

where:

- y is the acquired **data**
- A is the **overcomplete dictionary** of kernels estimated from the data (rotated along each possible direction):

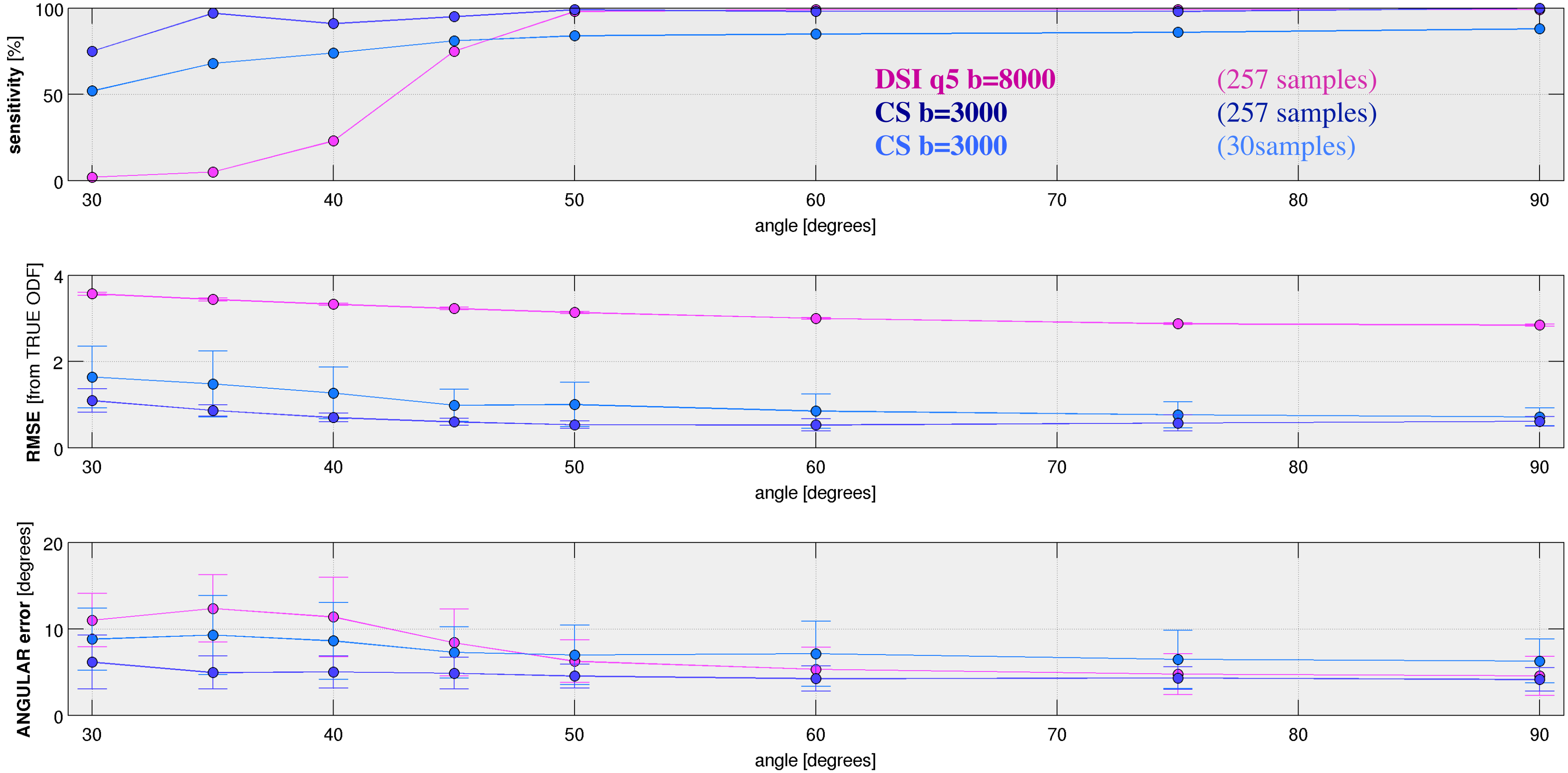


- x is the **fODF** we want to recover (contributions, i.e. volume fractions, of each atom to the final ODF)

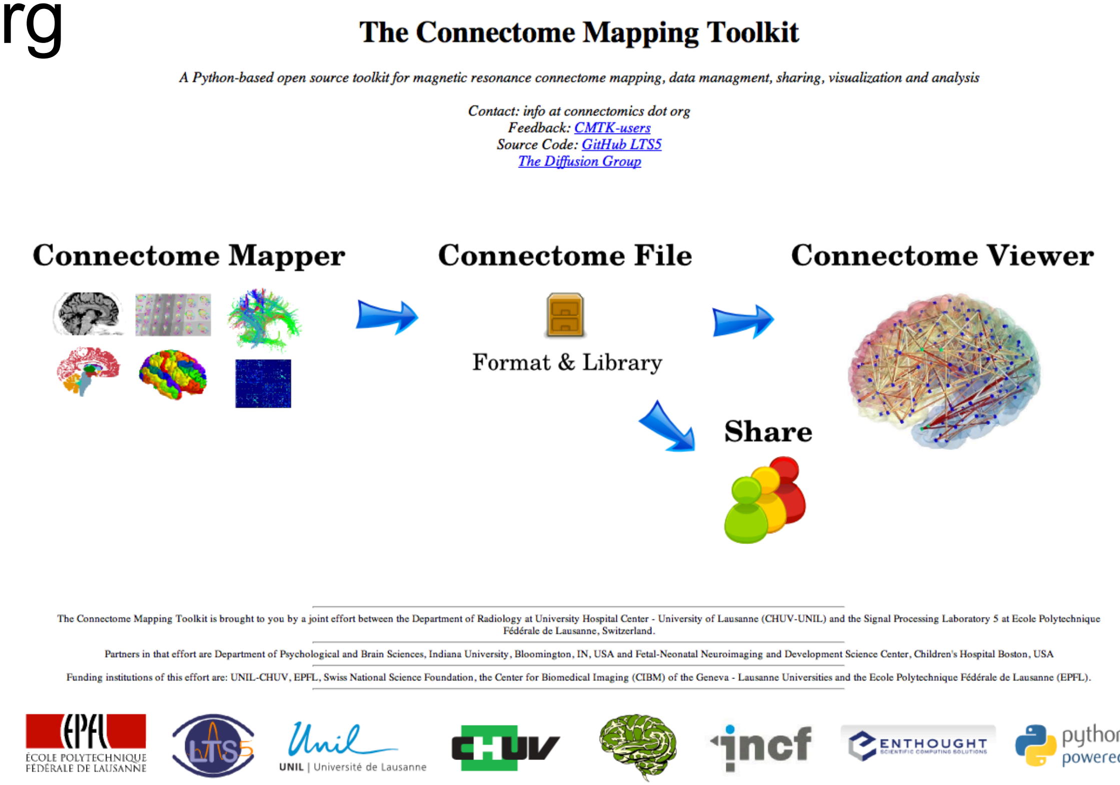
NB: the *volume fractions* sum up to 1 => upper bound τ is easily set
=> **LASSO formulation** is more convenient

Preliminary results

- Simulated data: 2 fibers crossing at different angles, variable diffusivities (ranges normally found in human brain), Rician noise (SNR=30)



- Tools: CMTK: the Connectome Mapping Toolkit
  - www.cmtk.org



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  - Miss Alessandra Griffa
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  - Dr Cristina Granziera
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Thank you for your attention!