Diffusion MRI:
Principles and Applications

Outline

- Basics of diffusion
  - What is “diffusion” and why it is important
  - Diffusion MRI in a nutshell
- Main applications
  - Characterization of *tissue properties*
  - Estimation of *tissue structure*
  - Reconstruction of *neuronal fiber tracts*
  - Estimation of *structural brain connectivity*
- Intro to local reconstruction techniques
  - Diffusion Spectrum Imaging (DSI)
  - Diffusion Tensor Imaging (DTI)
  - Q-BALL Imaging (QBI)
  - Constrained Spherical Deconvolution (CSD)

What is diffusion?

- **Random movement of molecules** due to thermal agitation from regions of high to regions of low concentration
  - *EXAMPLE*: in a glass of water, molecules diffuse randomly and freely, only constrained by the boundaries of the container

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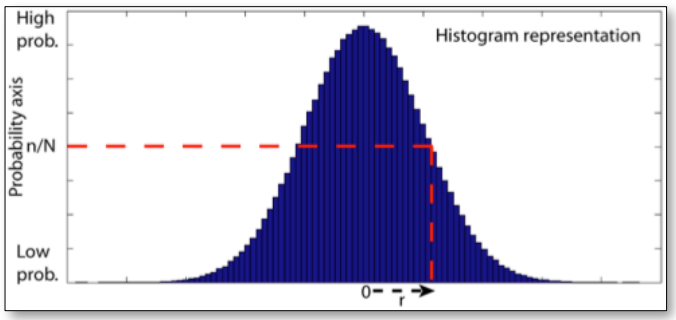
  - *EXAMPLE*: in a glass of water, molecules diffuse randomly and freely, only constrained by the boundaries of the container
- First noted by **Robert Brown** in 1828
  - *"…random motion without any apparent cause..."*
- Formally described by **Albert Einstein** in 1905

mean displacement of molecules

$$\langle r^2 \rangle \propto t\ \mathrm{D}$$

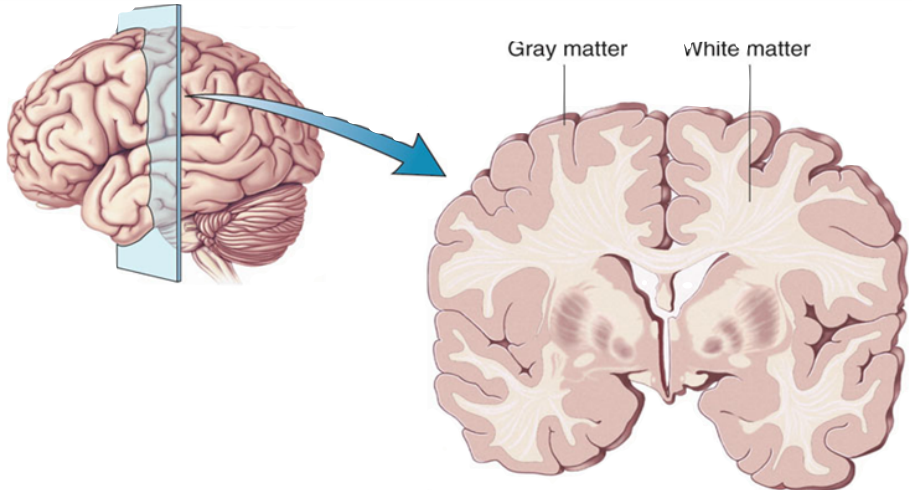
coefficient of diffusion of the medium

observation time

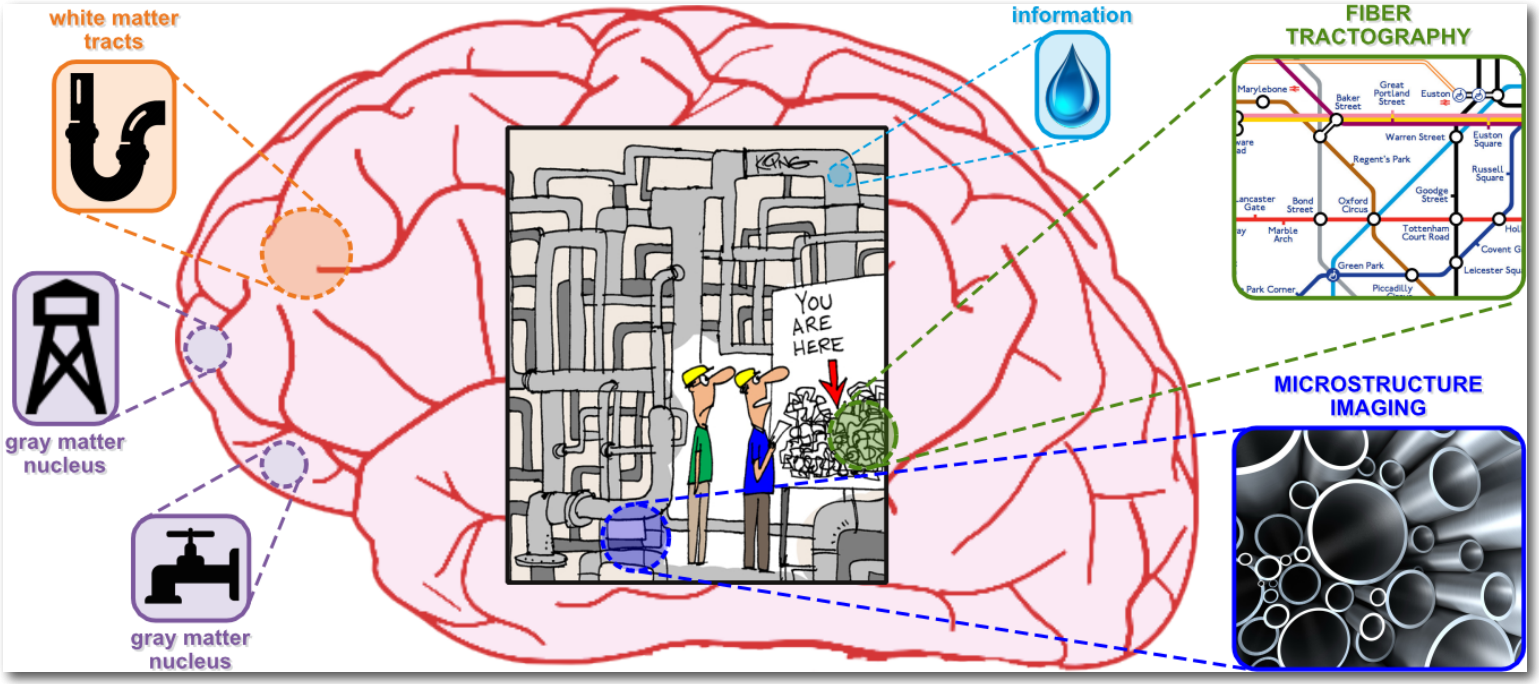


What happens in the brain? (1/2)

- Rough **brain anatomy**:
  - *gray-matter* : neuronal cell bodies
  - *white-matter* : mainly myelinated tracts
  - *Cerebrospinal fluid* (CSF)

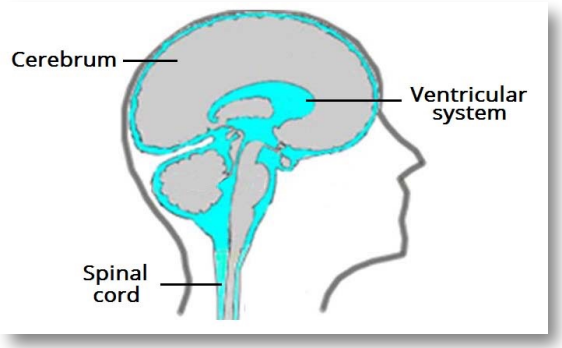


- **Metaphor:** "connectivity" as "water supply network"

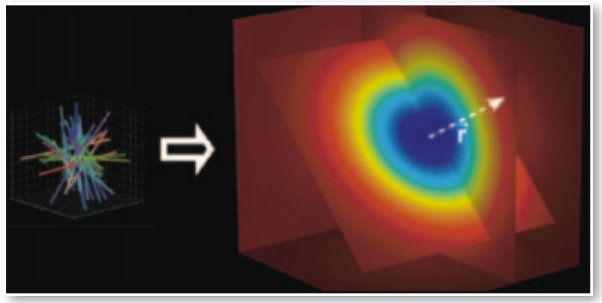


What happens in the brain? (2/2)

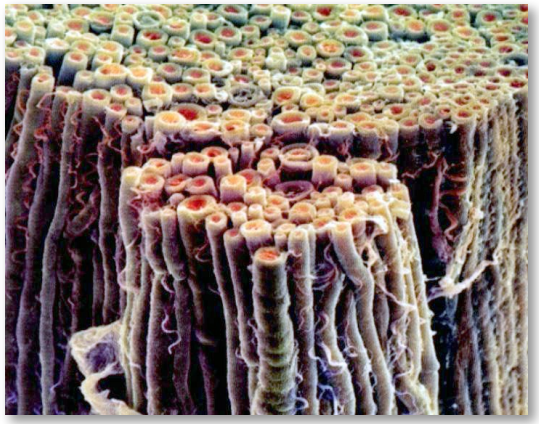
Cerebrospinal Fluid (CSF)

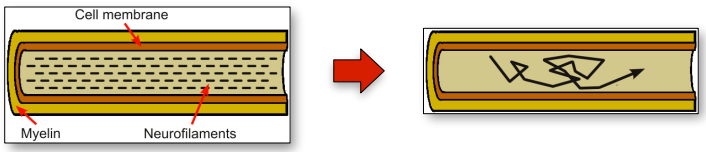


- Displacements are *isotropic*
- *Variance* depends on the fluid's properties

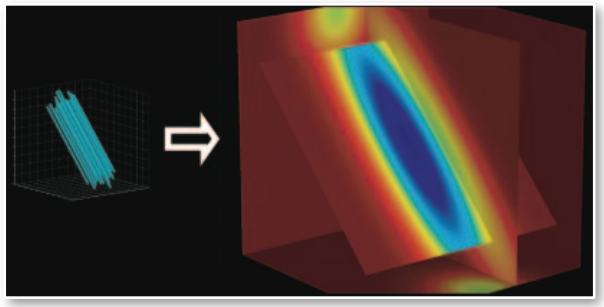


Neuronal tracts (white-matter)



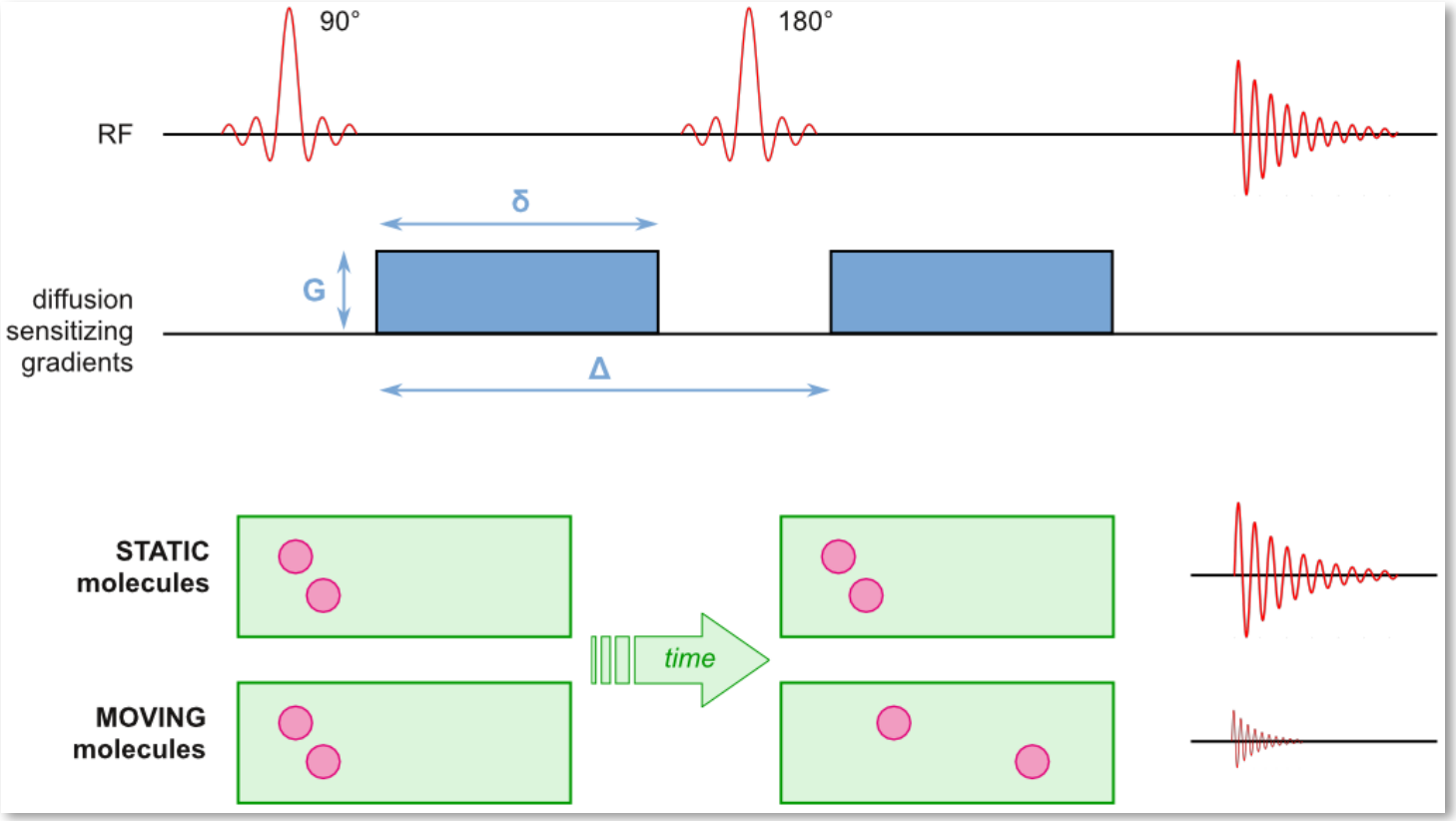


- Diffusion more *restricted* perpendicular to the tracts
- *Degree of restriction* depends on tissue properties



Diffusion MRI in a nutshell

- MRI sequences are **sensitive to diffusion** by inserting two additional *magnetic field gradient pulses*
  - The goal is to **change phase** of moving molecules
  - Movement ➡ phase differences ➡ **signal cancels out**/drops



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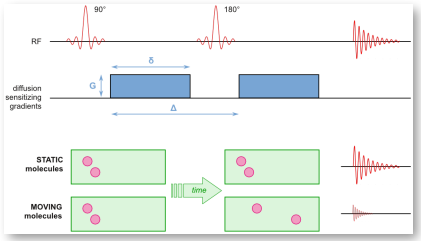
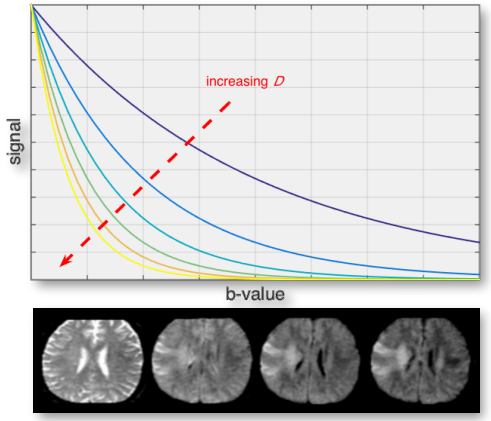
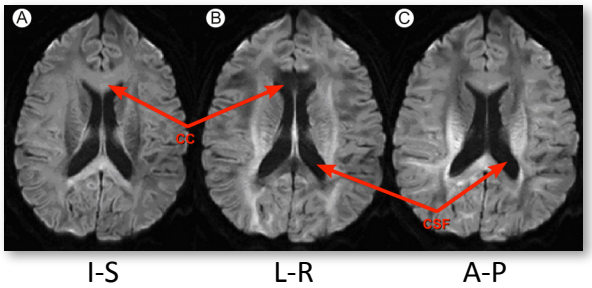
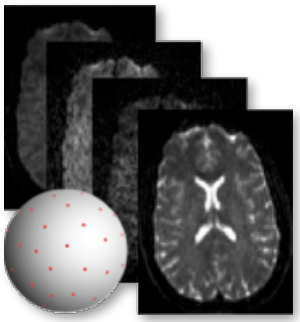


- Signal **decays** as: $\text{signal} \propto e^{-b\,D}$
  - *D* : *diffusion coefficient* of the tissue
  - *b* : *diffusion weighting*/contrast of the images (δ, Δ, |**G**|)



- **NOTE**: signal strongly depends on
  - the *b-value* (*b*)
  - the *diffusion coefficient* (*D*)
  - the *gradient direction* (**G**)

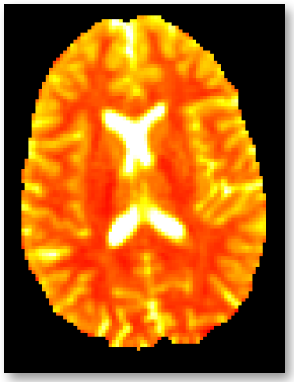


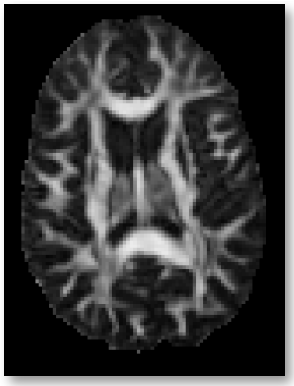


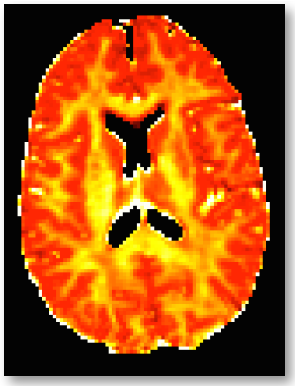
Main applications (1/3)

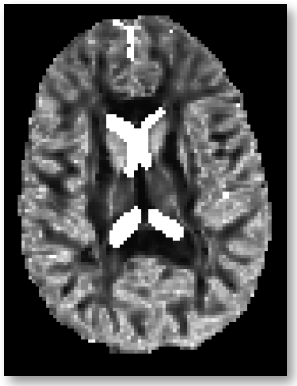
Scalar maps

- Estimate *local features* of the tissue


diffusion coefficient

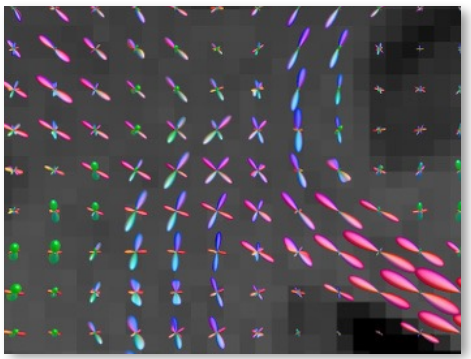

diffusion anisotropy

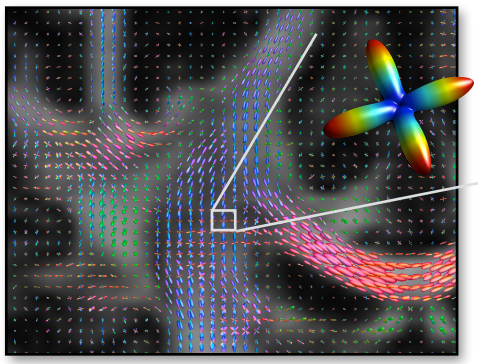

axonal density

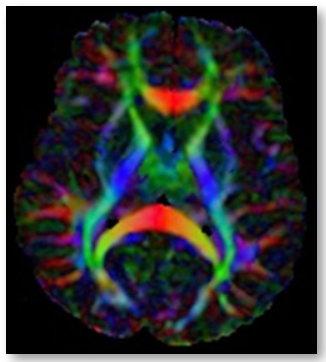

axonal dispersion

Intra-voxel fiber structure

- Estimate the *number and orientation of fiber populations* in each voxel



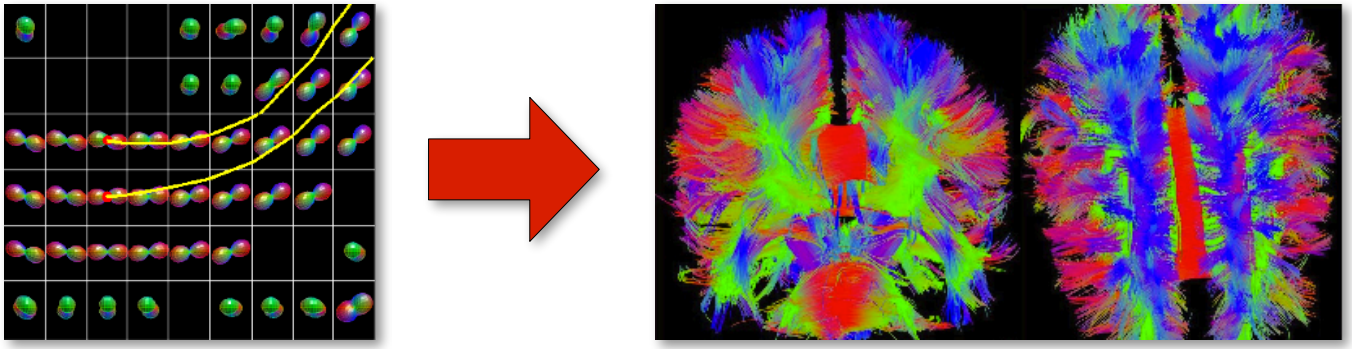




Main applications (2/3)

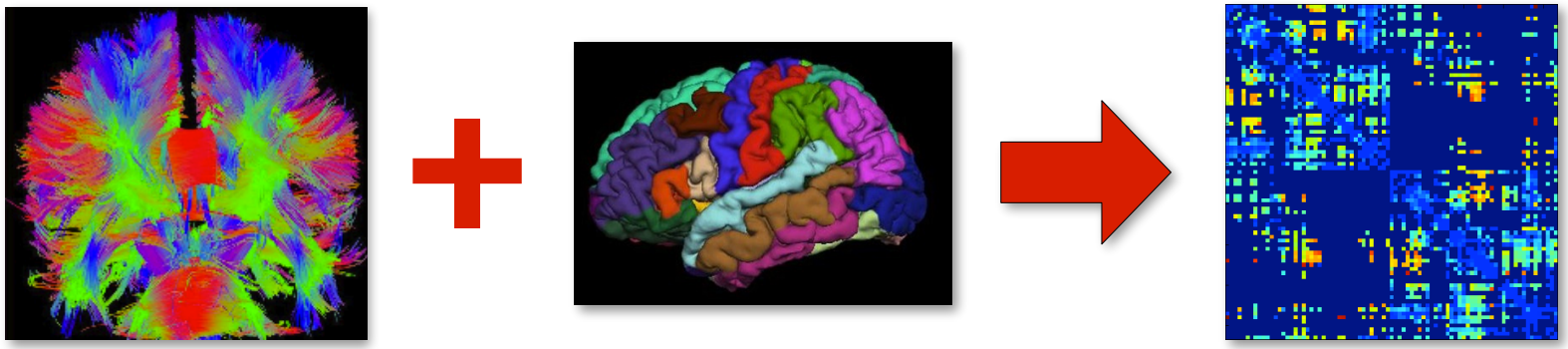
Fiber-tracking

- Infer *axonal trajectories* by exploiting the diffusion information in each voxel



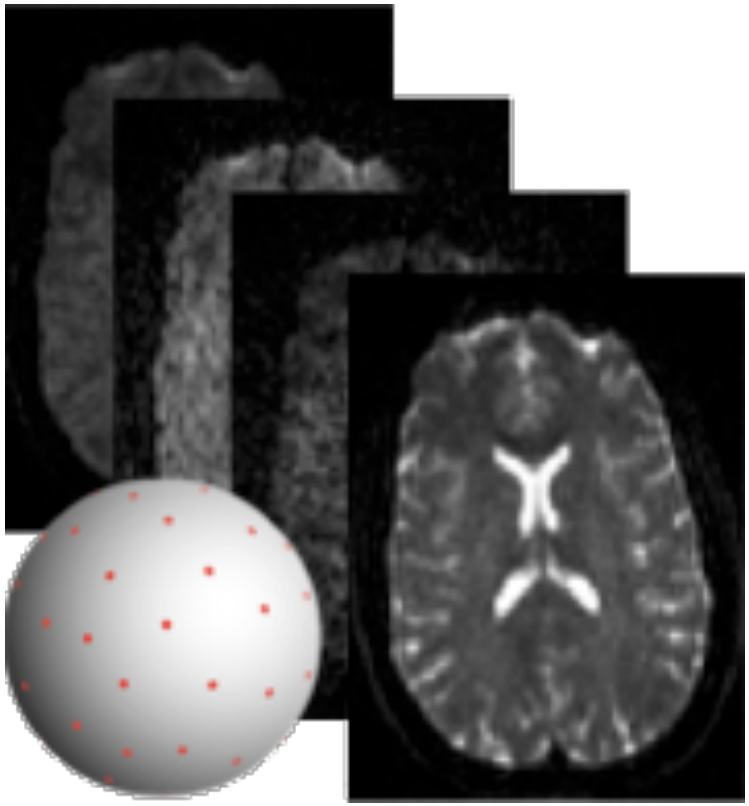
Connectivity analysis

- *In-vivo* and *non-invasive* assessment of structural wiring of the brain



fiber-tracking | cortical segmentation | connectivity matrix

Main applications (3/3)



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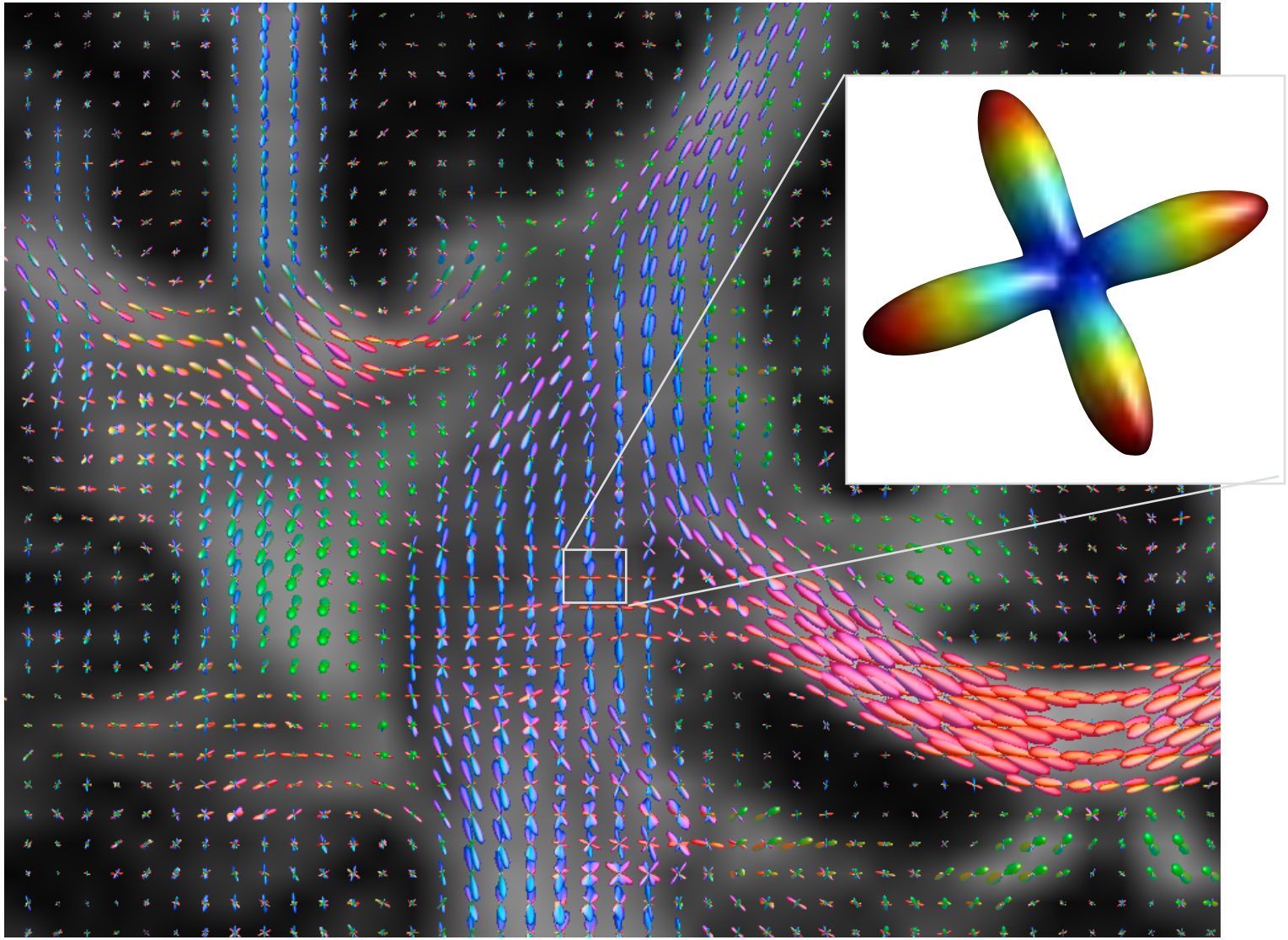

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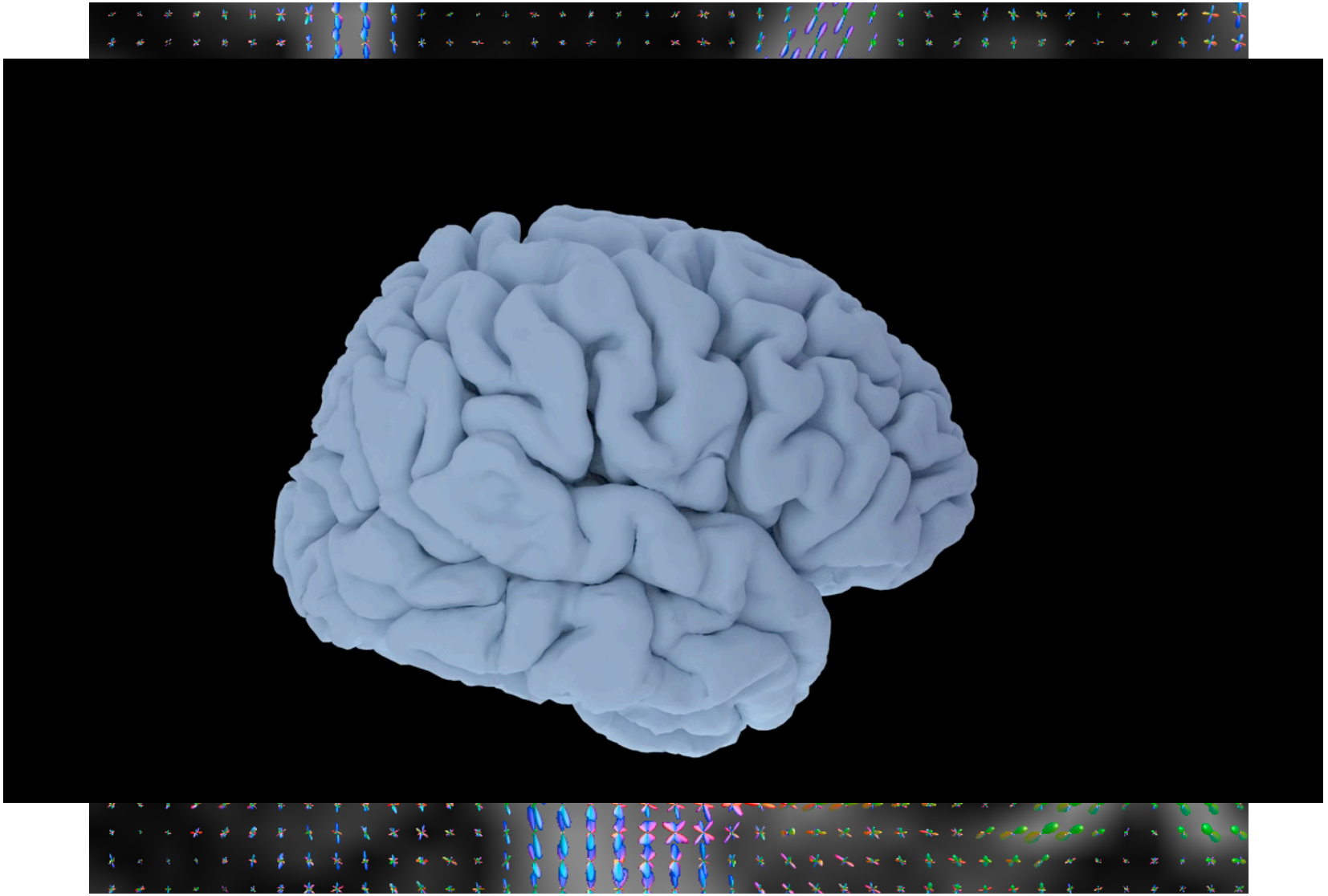

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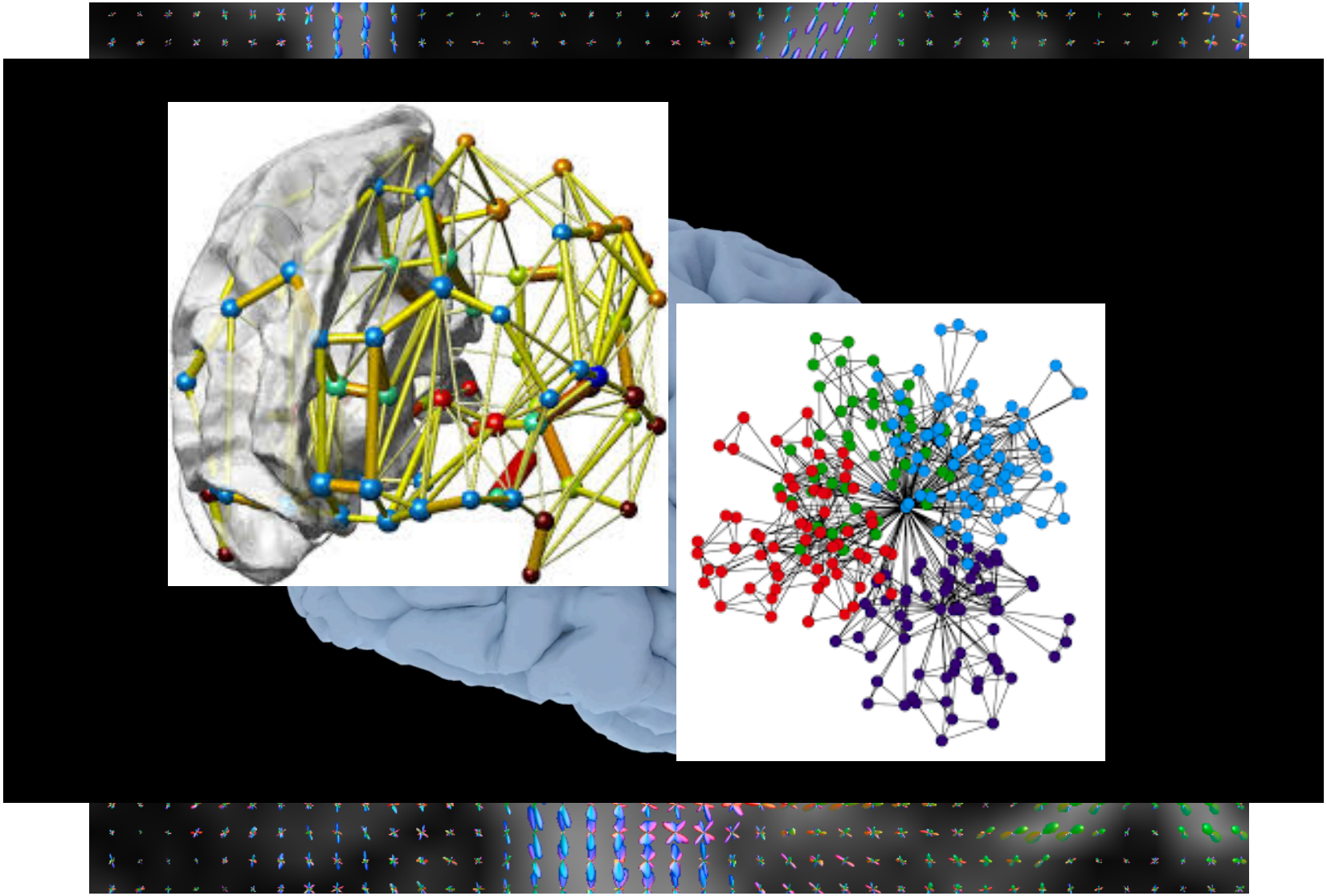


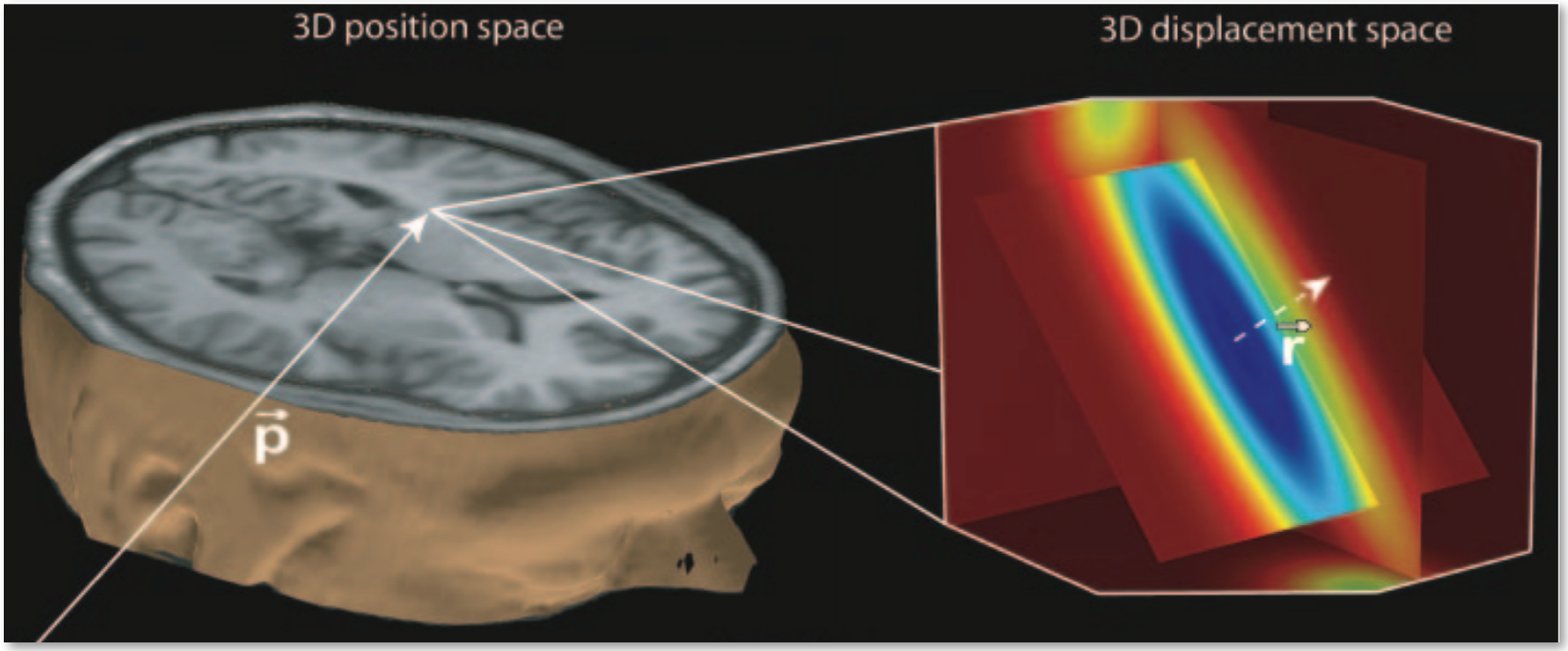
EAP, ODF and fODF

EAP *(Ensemble Average Propagator)*

- In each voxel, 3D PDF giving the *probability of water displacements* ➡ diffusion MRI is a **6D modality**
- Related to the *signal attenuation* by a **3D FFT**:

$$\mathrm{P}(\vec{r}) = \int_{\mathbb{R}^3} E(\vec{q})\, e^{-2\pi i \vec{q}\cdot\vec{r}}\, d\vec{q}$$

q-space



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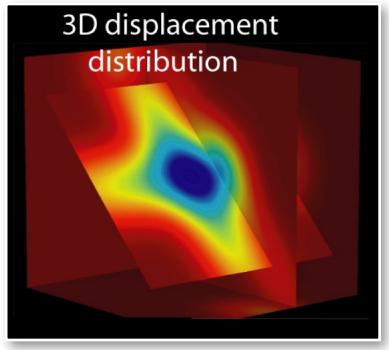
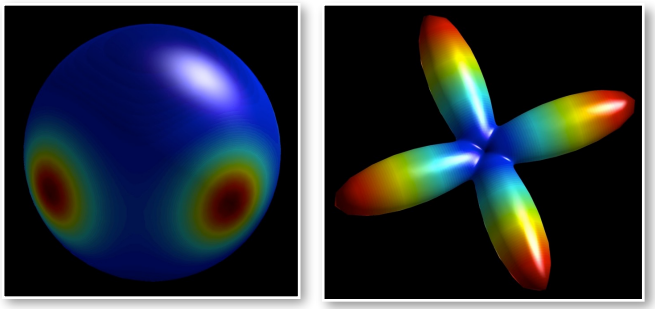


ODF or dODF *(Orientation Distribution Function)*

- Probability of diffusion *along a given direction*:

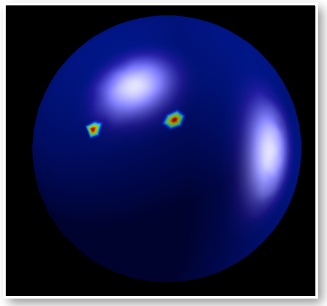
$$\mathrm{ODF}(\hat{r}) = \int_{\mathbb{R}_+} P(r, \hat{r})\, r^2\, dr$$

- Function on the sphere



FOD or fODF *(fiber ODF)*

- Probability of having a fiber population *along a given direction*
- Function on the sphere



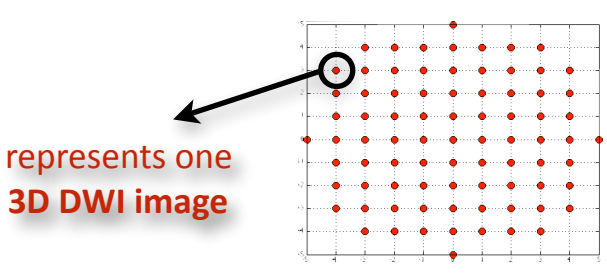
Diffusion SPECTRUM Imaging (DSI) (1/2)

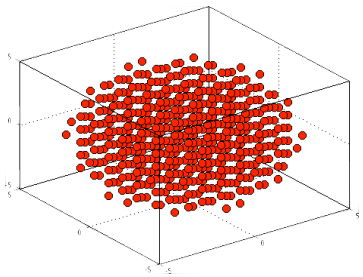
- Exploits the **3D Fourier Transform relationship** between the *MR signal* and the *displacement distribution* (EAP)

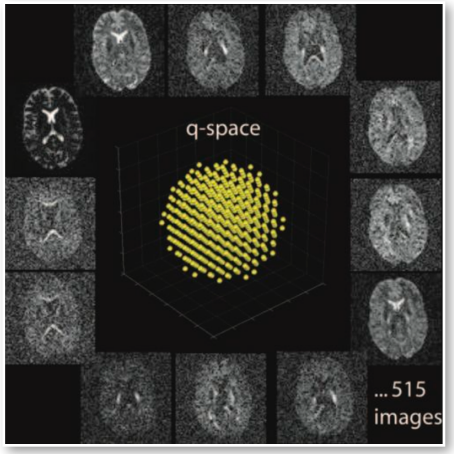
$$\mathrm{P}(\vec{r}) = \int_{\mathbb{R}^3} E(\vec{q})\, e^{-2\pi i \vec{q}\cdot\vec{r}}\, d\vec{q}$$

SIGNAL *E(q)* ⟷ **FFT** ⟷ **EAP** *P(r)*

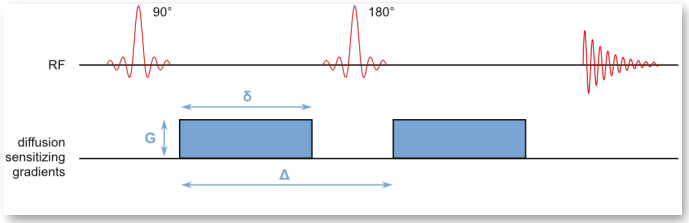
- The q-space must be **properly sampled**
  - Data must be sampled in a *dense 3D cartesian grid*
  - Usual protocol: 515 samples with $b_{max} \simeq 8000$ s/mm^2







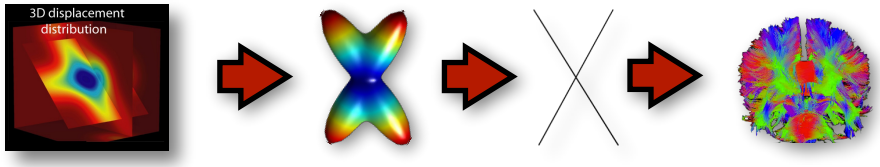
- Measures *directly* water displacements making **"almost" no assumptions**
  - "almost" ➡ *short pulse condition* is required



Diffusion SPECTRUM Imaging (DSI) (2/2)

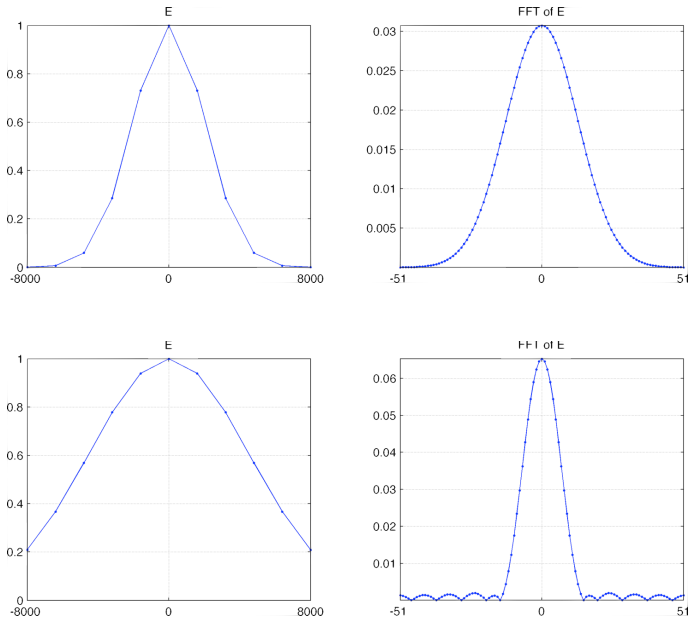
Advantages:

- Model free
- Complex fiber configurations recovered
- Recovers the EAP
  (even though radial information is usually ignored!!!)



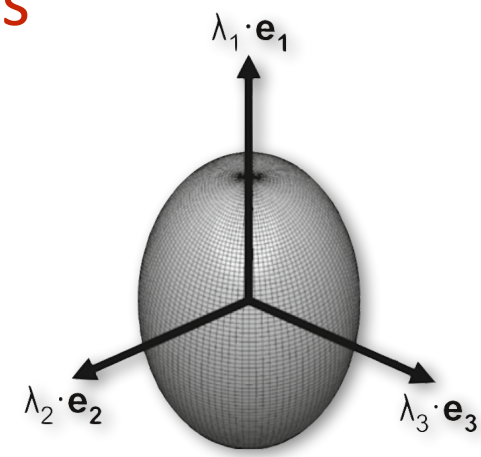
Limitations:

- Long acquisitions (≈ 30-40 min)
- Motion sensitive
- High b-values + long TE ➡ low SNR
- Short pulses never met ➡ smooth EAP
- No useful maps from the EAP
- Severe truncation artifacts
  - Inherent to FFT and “relatively low” b-values
  - Hanning filter mitigates but introduces blurring

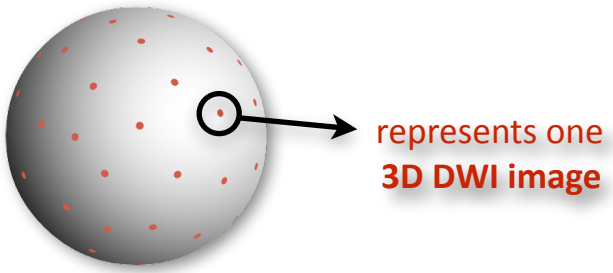


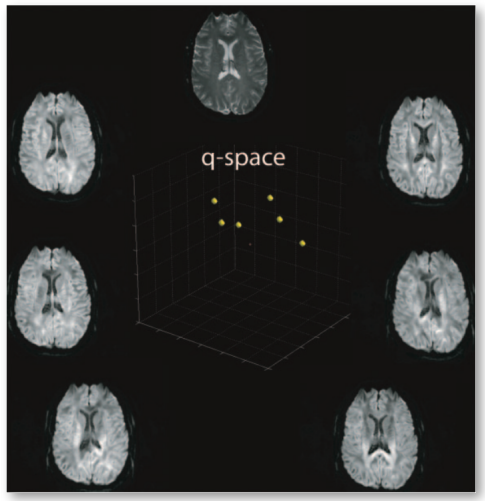
Diffusion TENSOR Imaging (1/2)

- **Assumption**: displacements of water molecules follow a *multivariate gaussian distribution*
  - Process fully characterized by its **covariance matrix** (3x3 symmetric positive semi-definite matrix)
  - Usually represented as an ellipsoid
  - 6 degrees of freedom (3 rotations + 3 variances)



- This matrix, i.e. **diffusion tensor**, can be estimated acquiring *6+1 DWI images* (at least)





  - Usual protocol: 6-32 directions with b ≃ 1000 s/mm^2

Diffusion TENSOR Imaging (2/2)

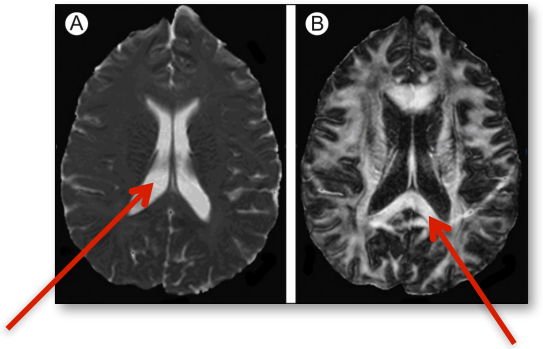
Advantages:

- *Fast* acquisitions (≈ 4-5 min) ➡ clinically feasible
- Does not require special hardware
- Useful *scalar maps*, e.g.
  - Mean Diffusivity (**MD**) :

$$\bar{\lambda} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

  - Fractional Anisotropy (**FA**) :

$$\mathrm{FA} = \sqrt{\frac{3}{2}} \sqrt{\frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

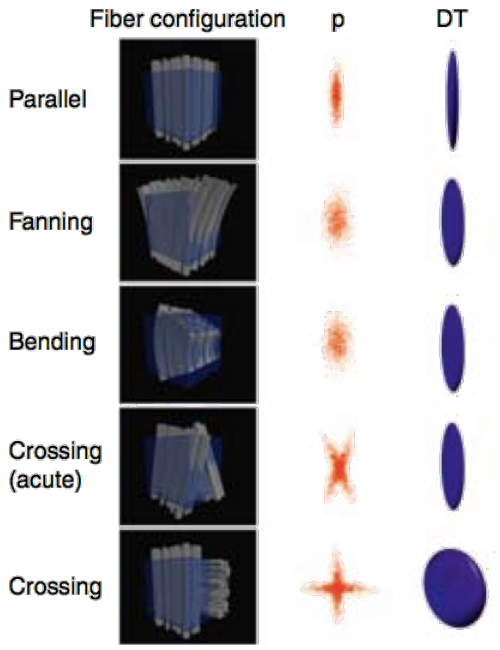


Mean Diffusivity:
high values = fast diffusion

Fractional Anisotropy:
high values = fiber bundles

Limitation(s):

- Complex fiber configurations *cannot be modeled*
  - majority of voxels in the brain
  - Enough for characterization of major bundles, but inadequate for whole brain connectivity analyses
  - NB: acquiring more data does overcome this limitation!

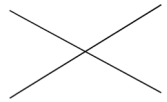


HARDI: overview (1/3)

High angular resolution diffusion imaging (HARDI):

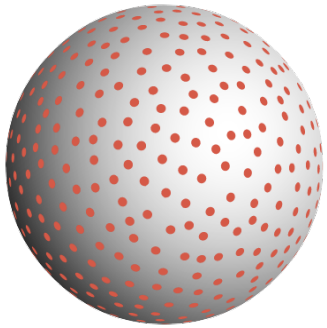
- Focus on *angular information*:
  - The radial component is discarded/averaged
  - No access to tissue micro-structural features, e.g. axonal diameter and density

dODF

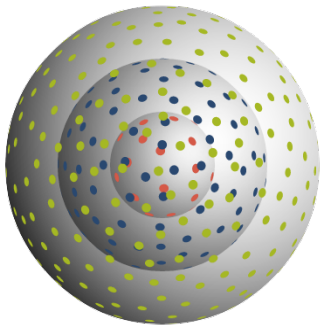


fODF

- Usually based on *spherical sampling*
  (at least 60 samples in q-space)



1-shell



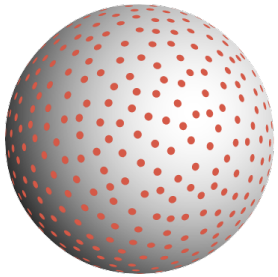
multi-shell

Vast literature of methods:

- Multi-Tensor fitting (Tuch et al, 2002)
- Q-BALL (QBI) (Tuch, 2004)
- Q-BALL in Constant Solid Angle (QBI_{CSA}) (Aganj et al, 2010)
- Constrained Spherical Deconvolution (CSD) (Tournier et al, 2004)
- Diffusion Orientation Transform (DOT) (Ozarslan et al, 2006)
- ...

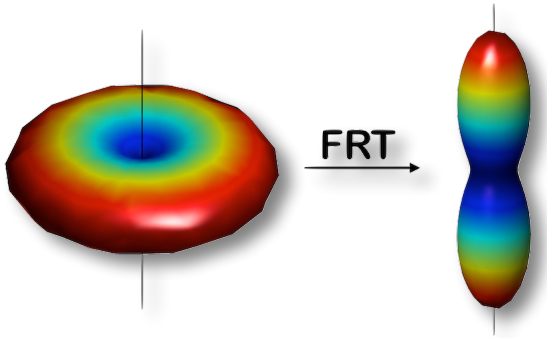
HARDI: Q-BALL imaging (2/3)

- **IDEA**: data is acquired on a *single shell* and the ODF is approximated by means of *Funk-Radon Transform (FRT)*



Samples distributed on a single-shell

Same idea behind CT, but on the sphere

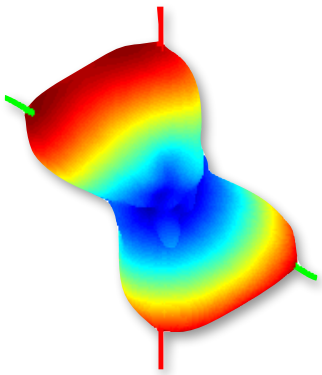


measured signal ODF

- **Notes**:
  - Model free
  - FRT induces blurring
  - ODF is only approximated (missing r^2 term in the integral)

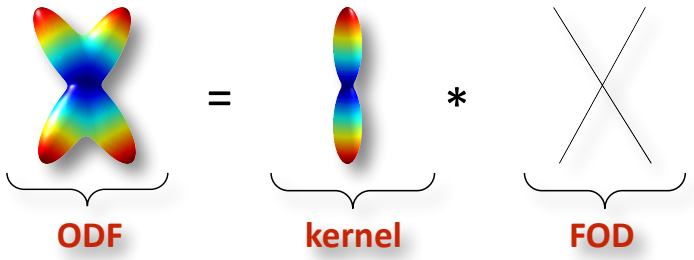
} ODF are smooth

  - Usual protocol: >=60 directions with b ≃ 3000 s/mm^2

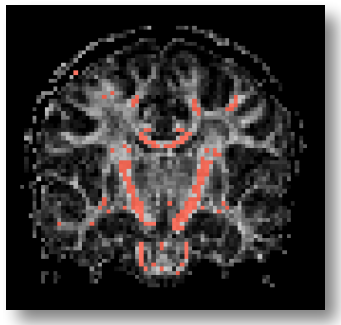


HARDI: constrained spherical deconvolution (3/3)

- **Assumption**: ODF can be seen as a convolution on the sphere



- The **kernel** characterizes the diffusion response-function of a single fiber; can be estimated from the data:
  - Identify known areas with only one fiber population
  - Fit a tensor in each voxel and average



- **Notes**:
  - Model based
  - High angular accuracy (i.e. sharper profiles), but sensitive to noise
  - Assumes the *same diffusion properties* across the whole brain
  - Usual protocol: <=60 directions with b ≃ 3000 s/mm^2