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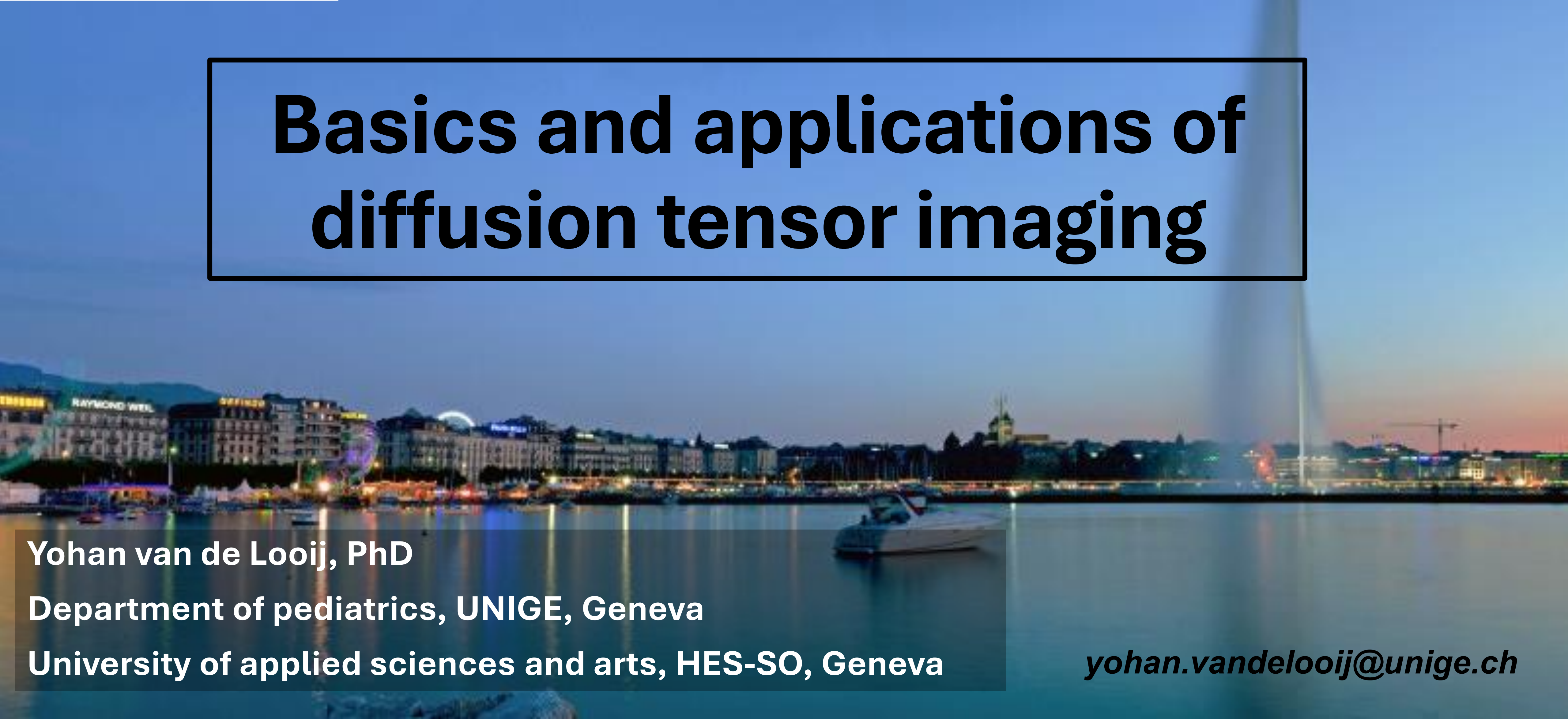

Basics and applications of diffusion tensor imaging

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Overview

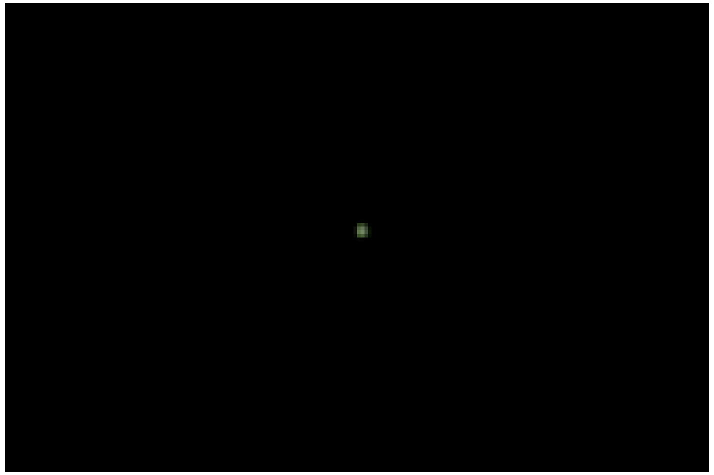
1. What is diffusion?
2. Diffusion coefficient
3. Stejskal-Tanner sequence
4. In the brain : anisotropic diffusion
5. How measure the diffusion tensor
6. Parameters derived from the diffusion tensor
7. Fiber tracking
8. Important parameters of DTI experiments
9. Pitfalls in DTI
10. Applications

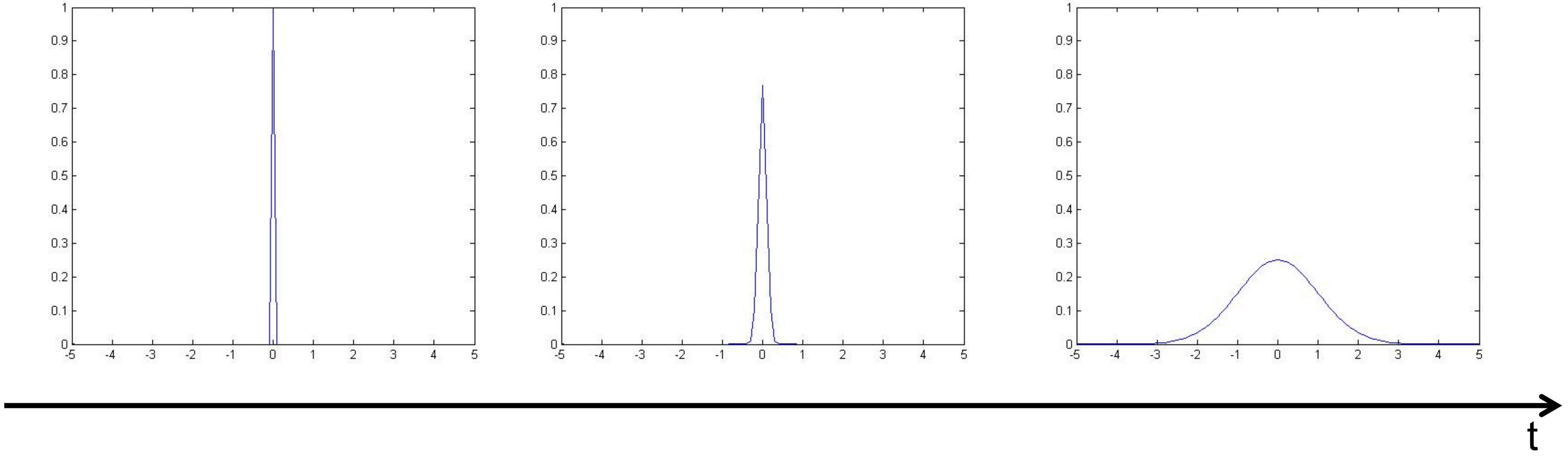
Overview

1. What is diffusion?

Diffusion or Brownian motion

Diffusion: random motion (bump) of particles suspended in a fluid due to thermal agitation





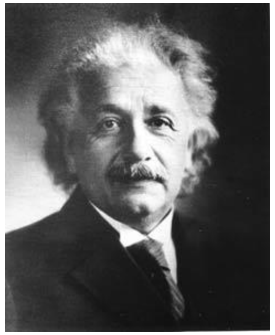
Movie: ©J-F Colonna, http://www.lactamme.polytechnique.fr

History of the Brownian motion

First observed (by chance) by Robert Brown in 1827 [1]

> *[…] **This plant was Clarckia pulchella, of which the grains of pollen** […] **were filled with particles or granules of unusually large size.** […] **While examining the form of these particles immersed in water, I observed many of them very evidently in motion**[…]*

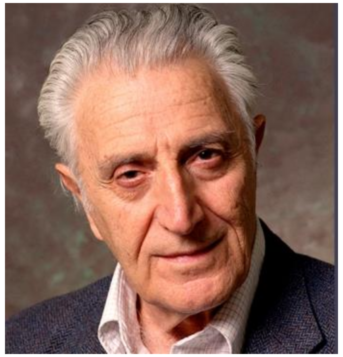
Then described theoretically by Albert Einstein during his PhD in 1905 [2]



[1] R. Brown, Philos Mag (1828) *[2] A. Einstein, Thèse (1905)*

Diffusion and NMR signal

1949, Erwin L. Hahn (1921-2016): NMR signal sensitive to diffusion [3] ➔ Attenuation of the spin echo under static magnetic field inhomogeneities.



1965, Edward O. Stejskal and John E. Tanner: NMR sequence, based on the application of pulsed gradient magnetic fields ➔ measurement of diffusion coefficient [4].

1994, Peter J. Basser and Denis Le Bihan: first publication about DIFFUSION TENSOR IMAGING (DTI) [5].

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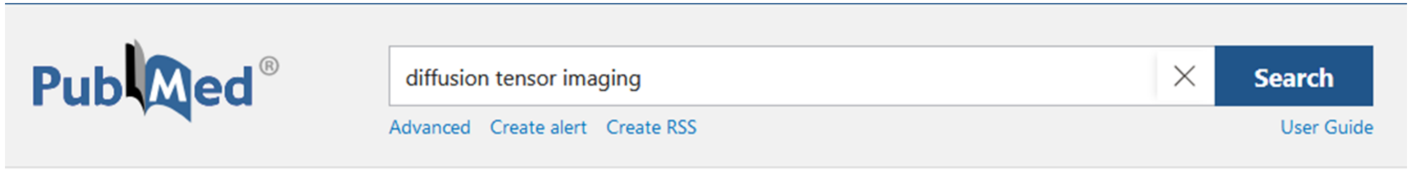
[3] EL. Hahn, Phys Rev (1950)

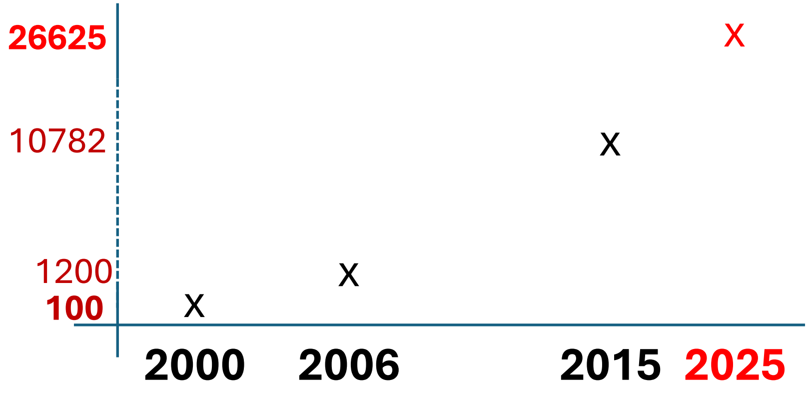
[4] Stejskal - Tanner, J Chem Phys (1965)

[5] PJ. Basser, Biophys J (1994).

DTI, recent but so wide…



diffusion tensor imaging



- DTI has been recently discovered (30 years…)
- Non-invasive tool to probe brain microstructure
- A lot of medical and biologic applications/characterizations
- *fiber tracking* is the only non-invasive method to image fibers of the white matter in the brain
- More recently, multi compartments models…

Powerful tool in neuroimaging to characterize tissue microstructures

Overview

2. Diffusion coefficient

The diffusion coefficient

The **diffusion coefficient is a physicochemical property of a substance depicting** ease of mobility of this substance inside another **by the diffusion phenomena**

Einstein relation

temperature

$$D = \mu_p k_B T$$

mobility

Boltzmann's constant

Stokes law

$$\mu_p = \frac{1}{6\pi\eta r}$$

Particle radius

viscosity

Einstein-Stokes relation

$$D = \frac{k_B T}{6\pi\eta r}$$

Spherical particles diffusing in a solution

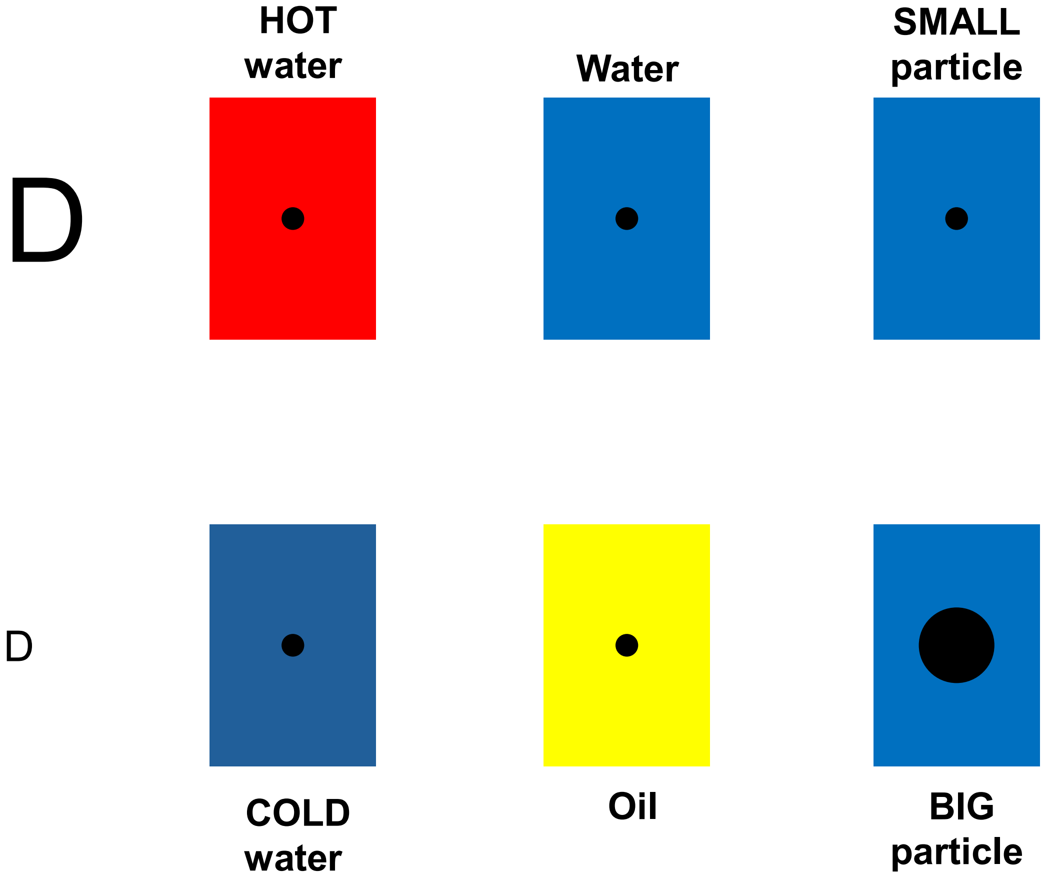
Boltzmann's constant: physical constant relating energy at the individual particle level with temperature

Einstein-Stokes relation says…

Einstein-Stokes relation

$$D = \frac{k_B T}{6\pi\eta r}$$

Spherical particles diffusing in a solution

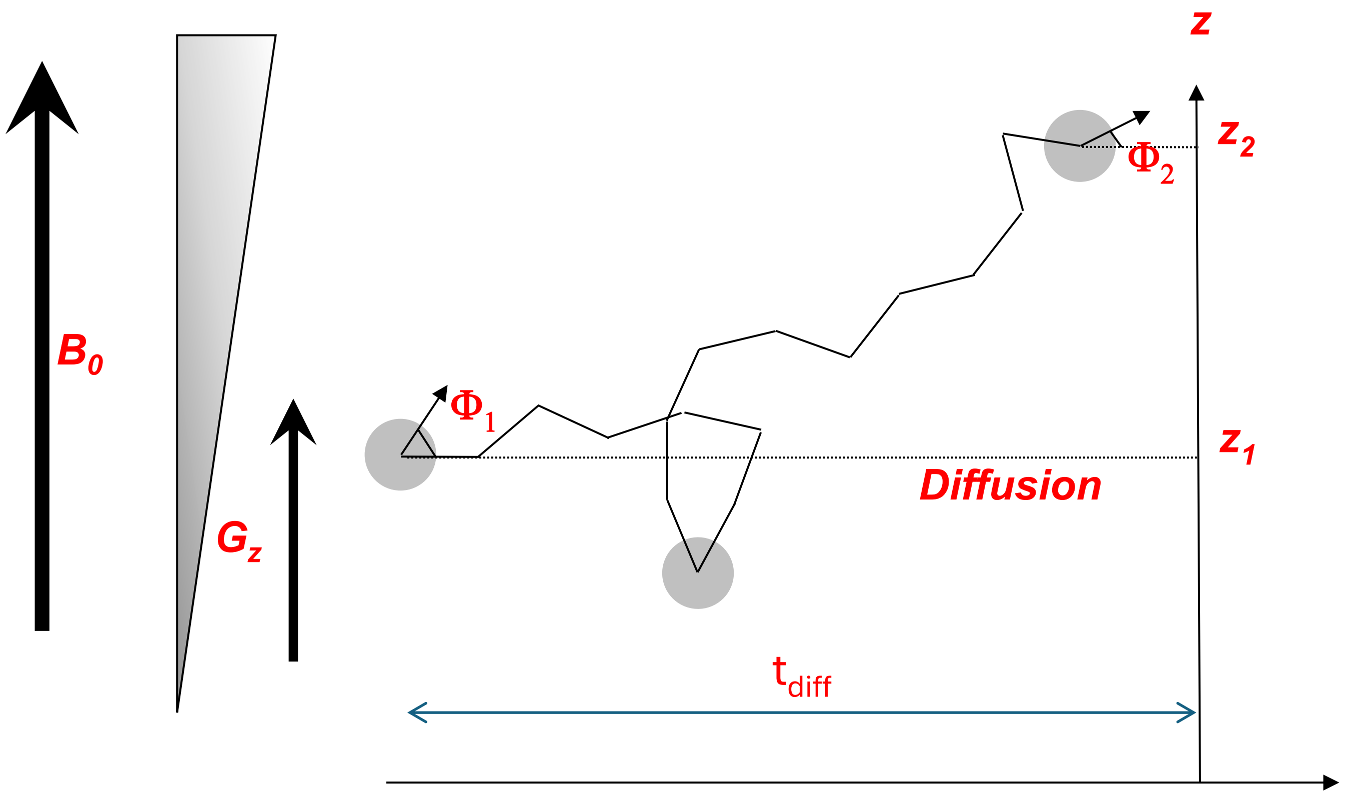


Brownian Motion

↑ ↑

Diffusion and magnetic field

Freely diffusing molecule, under static magnetic field B_0 and a magnetic field gradient G_z, along Z direction:



Accumulated phase during displacement?

$$\omega = \gamma B = \gamma(B_0 + G_z z)$$

Diffusion and magnetic field gradient

Dephasing: $$\frac{d\varphi}{dt} = \omega = \gamma B = \gamma(B_0 + G_z z)$$

Accumulated phase: $$\varphi = \int \omega dt = \gamma \int B_0 dt \boxed{+ \gamma \int G_z z dt}$$

phase is position dependent

From z_1 to z_2, dephasing: $$\Delta\varphi = \gamma(z_2 - z_1) \int (G_z dt)$$

Phase term, affects the signal: $$S = S_0 \exp(\, i\Delta\varphi)$$

with: $$\langle Z^2(t_{diff}) \rangle = 2Dt_{diff}$$

diffusion

No diffusion

Magnitude of the attenuation: $$\left| {}^{S}/{}_{S_0} \right| = \sqrt{e^{i^2(z_2-z_1)^2\gamma^2\left(\int Gdt\right)^2}} = \sqrt{e^{-\boxed{(2Dt_{diff})\gamma^2 \int G^2 dt}}}$$

b-value

A molecule diffusing freely under a magnetic field gradient acquires a position-dependent phase

Root mean square displacement and diffusion

$D_{\text{free-water}} \approx 3.0 \times 10^{-3}\ \text{mm}^2.\text{s}^{-1}$ at T=37°C
Diffusion time (measurement in MRI)≈ 20 ms

} Mean distance = 12 μm

In the tissues/brain:
The «real» diffusion coefficient $D_{\text{water-brain}} = D_{\text{water-water}} = D_{\text{free-water}}$

BUT, diffusing particle in the brain meets obstacles/interactions (Organelles, cell membranes, myelin, macromolecules…)

Measure the «real» diffusion coefficient is impossible in the brain:
- MRI resolution 1mm (population of molecules)
- obstacles

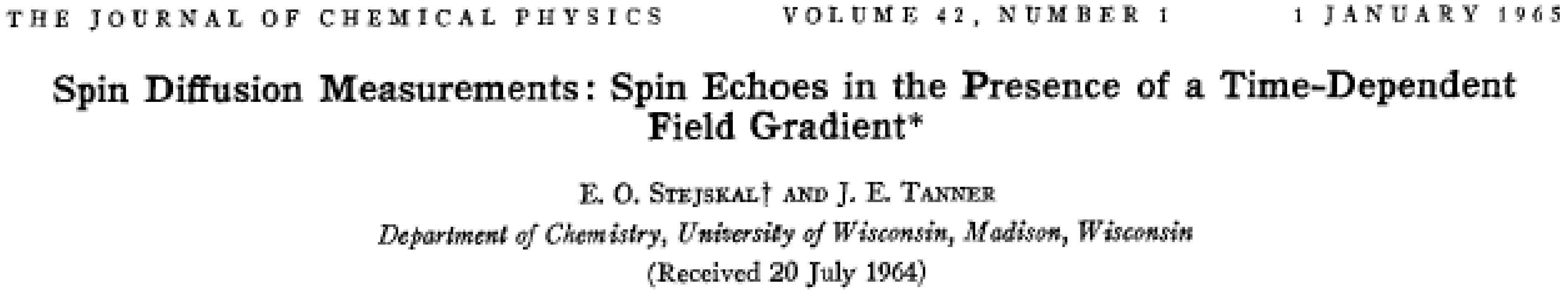
Measure the «real» diffusion coefficient would take a diffusion time (measurement time) enough short to measure the diffusion of the particle before it meets obstacles or has interaction…

➔ **Apparent Diffusion Coefficient** (ADC) $\approx 0.7 \times 10^{-3}\ \text{mm}^2.\text{s}^{-1}$

Overview

3. Stejskal-Tanner sequence

Sequence Stejskal-Tanner and *b*-value



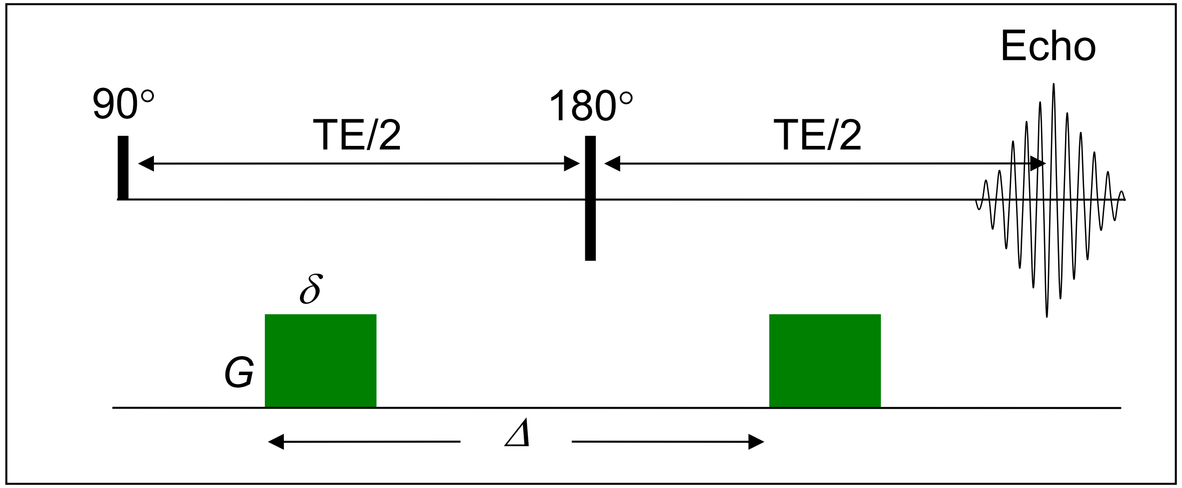
THE JOURNAL OF CHEMICAL PHYSICS VOLUME 42, NUMBER 1 1 JANUARY 1965

Spin Diffusion Measurements: Spin Echoes in the Presence of a Time-Dependent Field Gradient*

E. O. Stejskal† and J. E. Tanner

Department of Chemistry, University of Wisconsin, Madison, Wisconsin

(Received 20 July 1964)

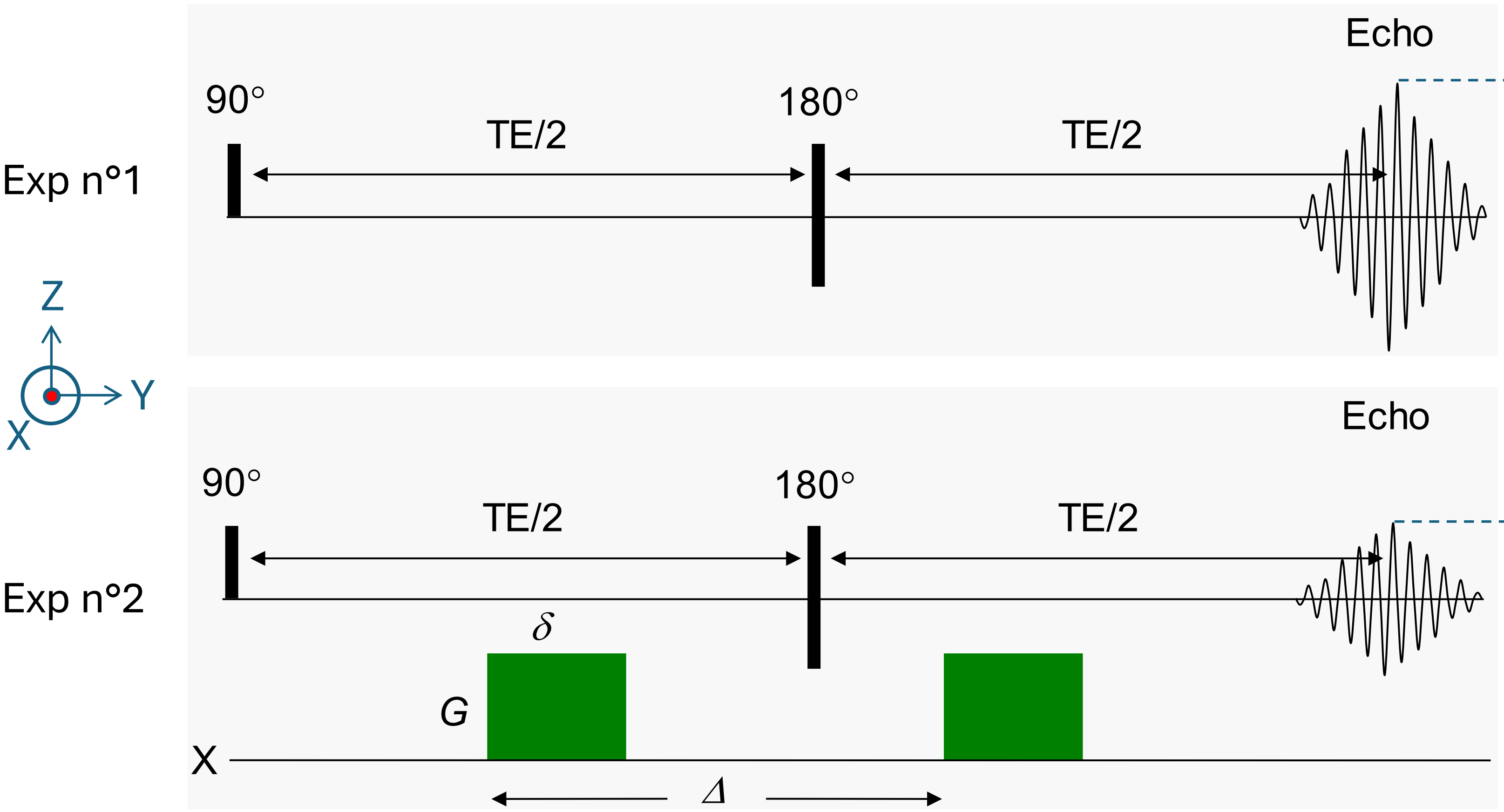


$$b = \gamma^2 \int_0^{TE} \left(\int_0^{t} G(t')dt' \right)^2 dt$$

$$b = \gamma^2 G^2 \delta^2 \boxed{\left(\Delta - \frac{\delta}{3}\right)}$$

Effective diffusion time

Sequence Stejskal-Tanner: principle



$b=\gamma^2 G^2 \delta^2 (\Delta - \delta/3)$

$S_{dw}=S_0 exp^{-bD}$

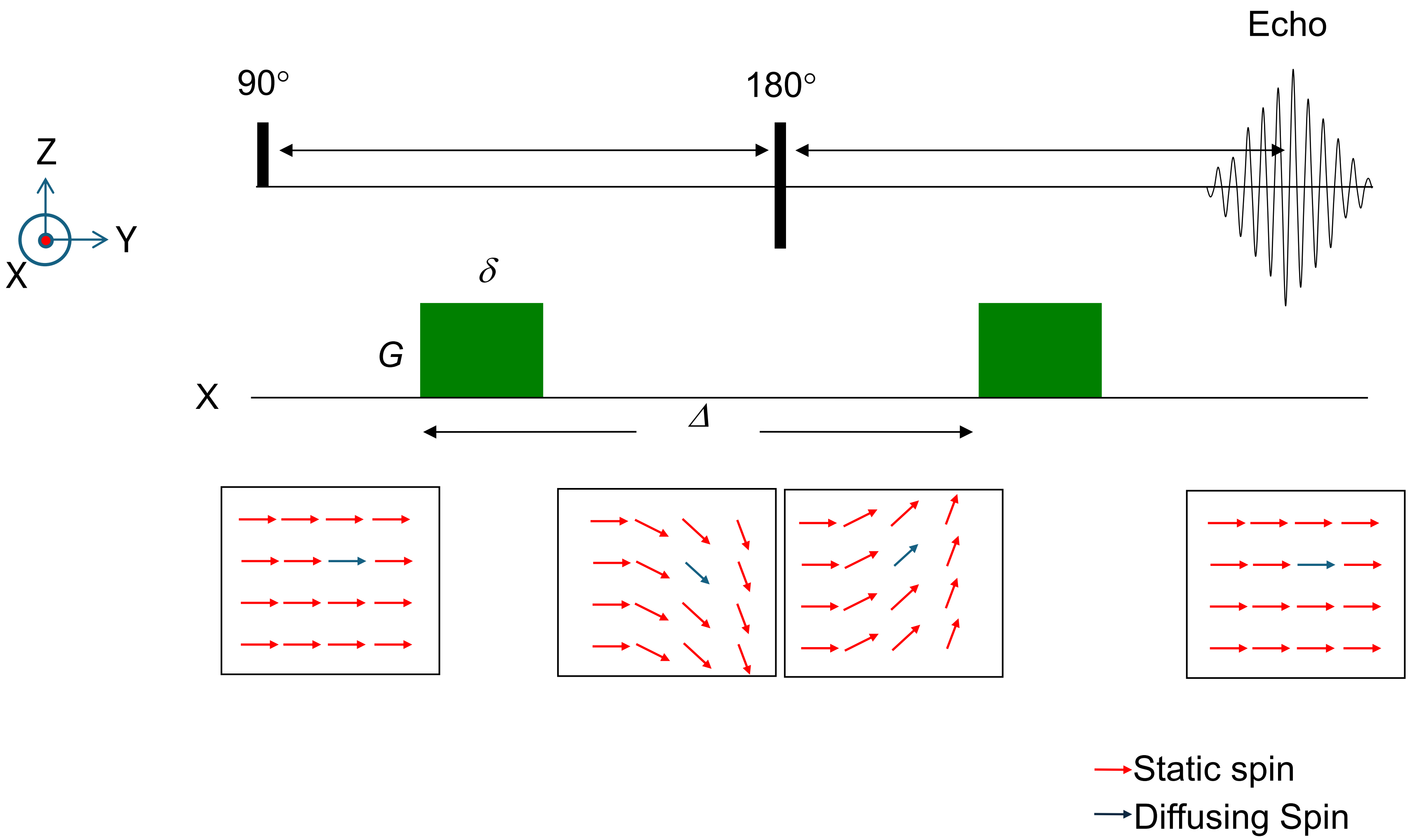
→

$D=\ln(S_0/S_{dw})/b$

Why S_{dw} attenuated?

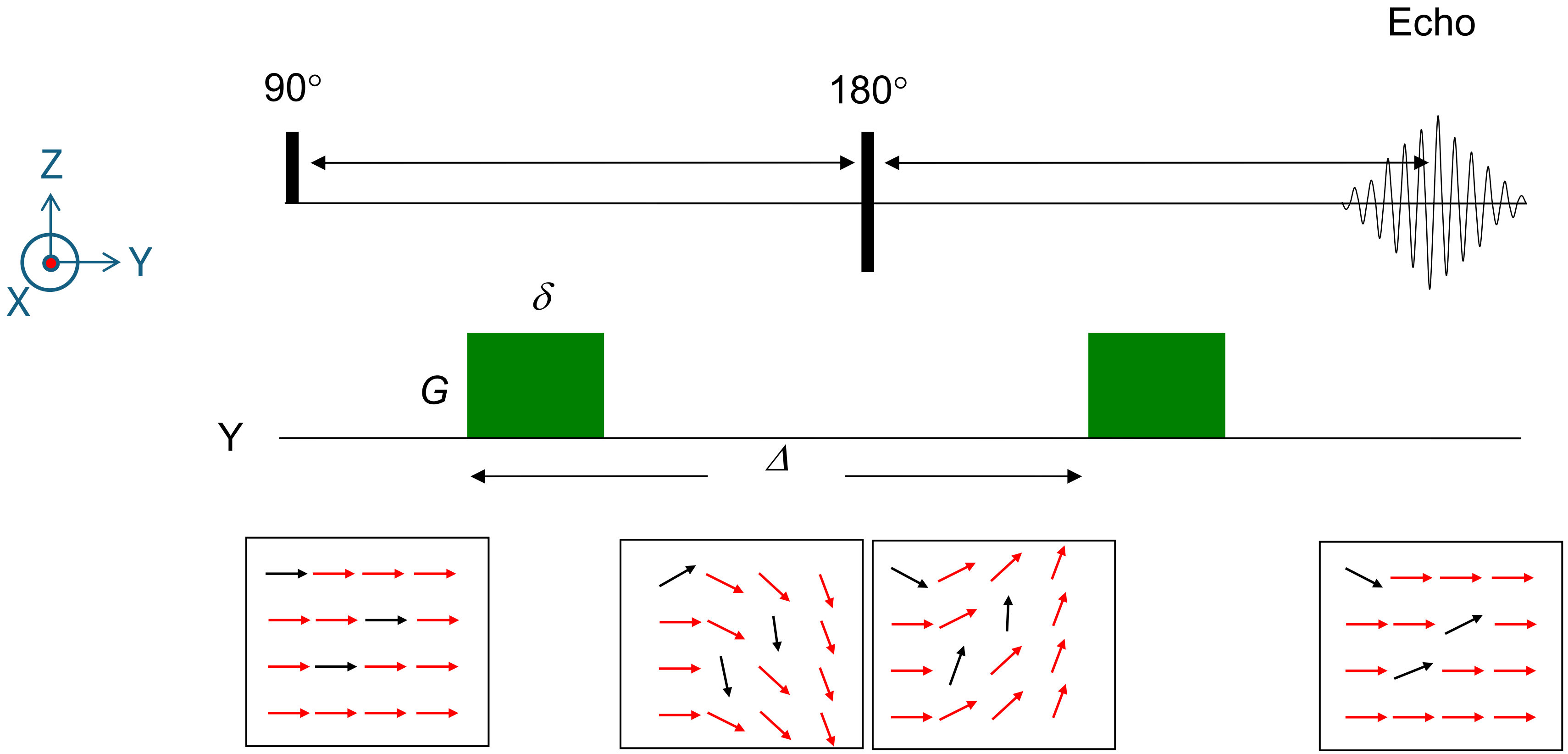
Sequence Stejskal-Tanner: signal attenuation

Excitation	*Encoding*	*Inversion*	*Decoding*	*Acquisition*



Sequence Stejskal-Tanner: signal attenuation

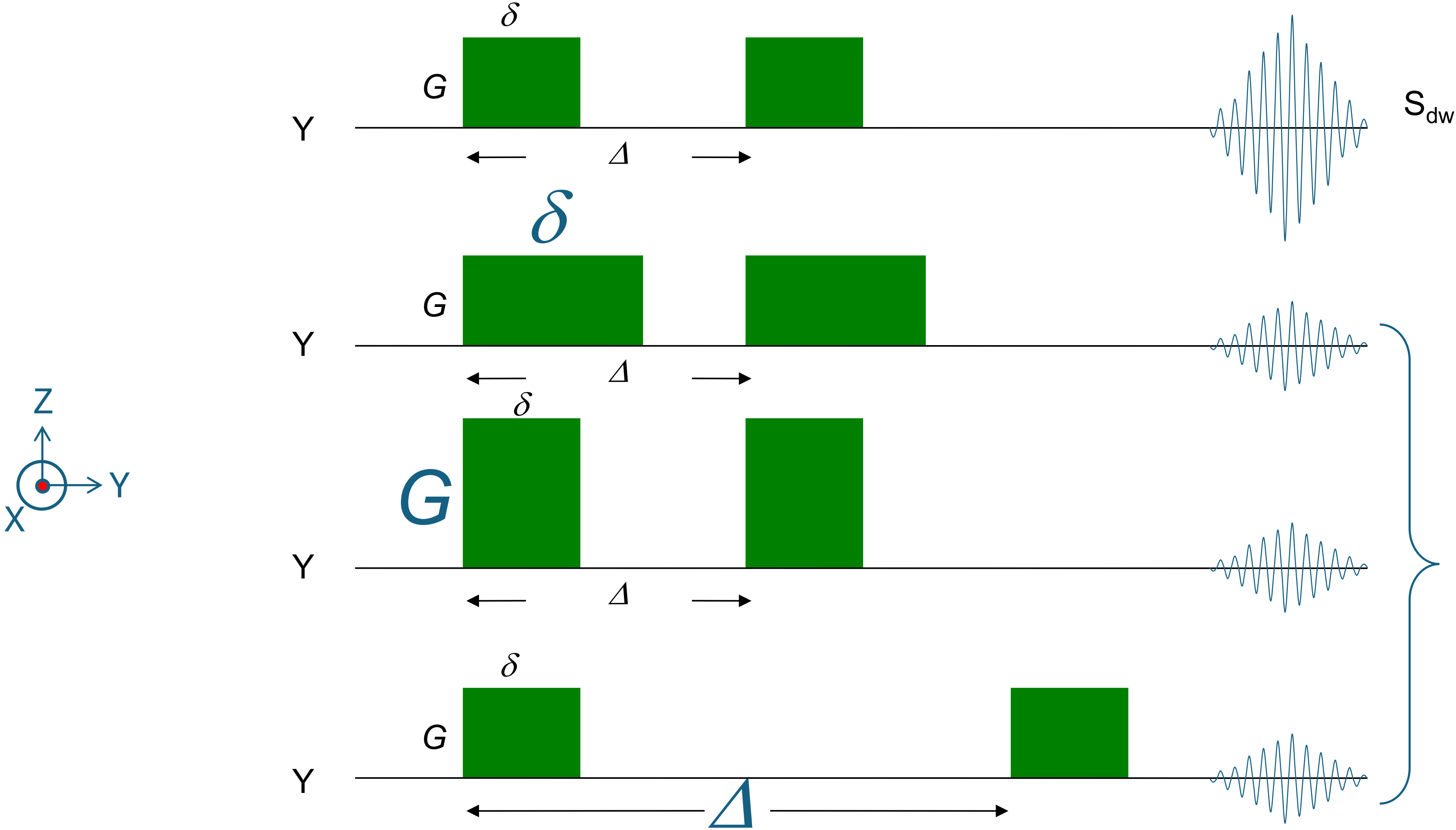
Excitation	*Encoding*	*Inversion*	*Decoding*	*Acquisition*



$$S = S_0 e^{-bD}$$

→Static spin
→Diffusing Spin

Stejskal-Tanner: measure

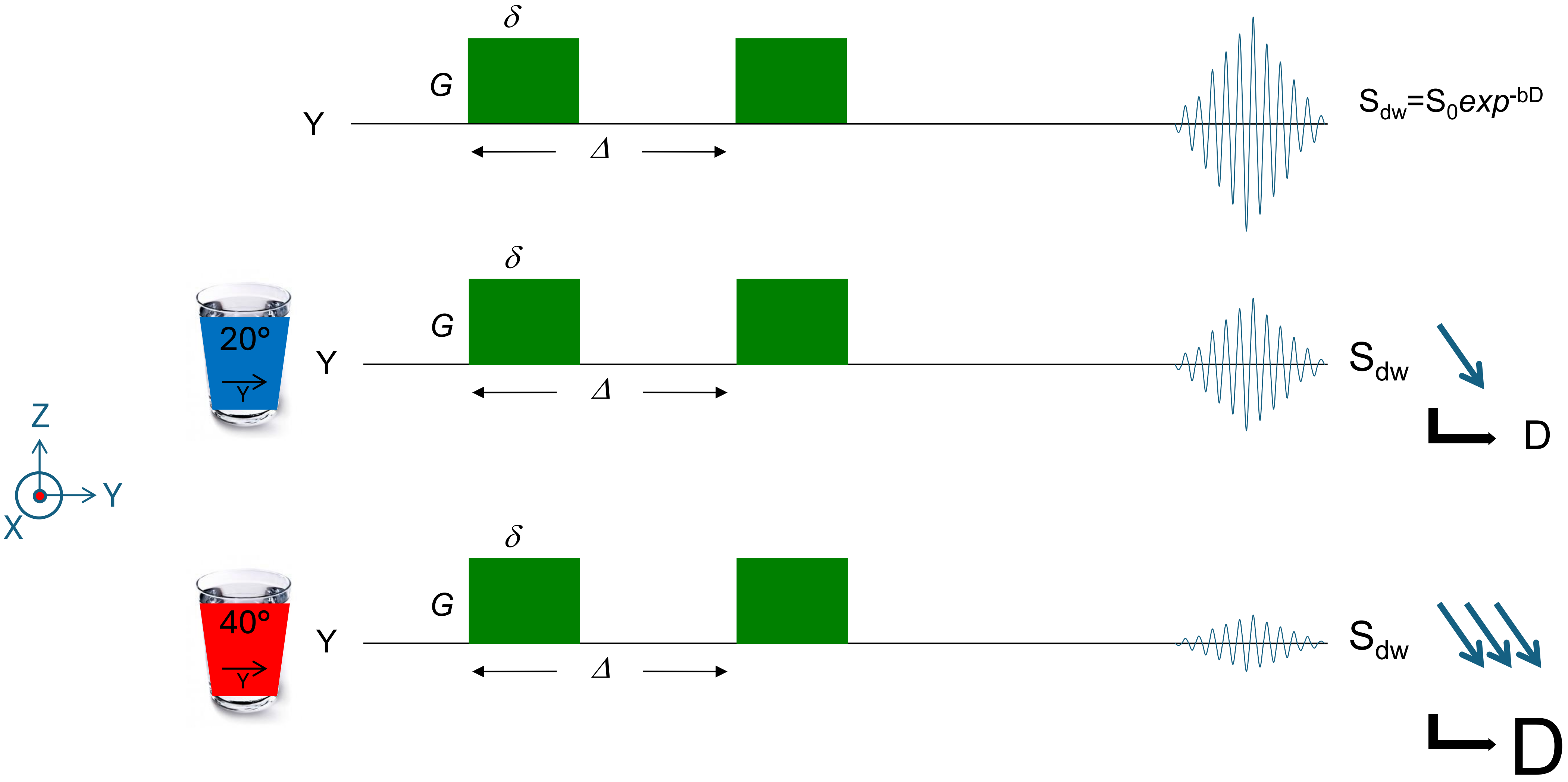


$S_{dw}=S_0 exp^{-bD}$

b ↗

S_{dw} ↘

Stejskal-Tanner: coefficient D



$S_{dw}=S_0 exp^{-bD}$

S_{dw} ↘ → D

S_{dw} ↘↘↘ → D

Diffusion without equations

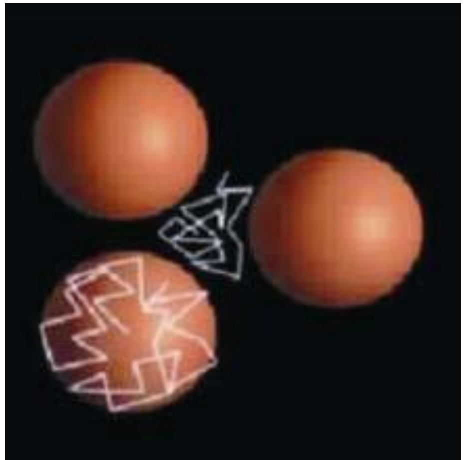
- http://blog.ismrm.org/2017/06/06/dwe-part-2/

D scalar *i.e.* measurement in only one direction : Y

Overview

4. Diffusion in the brain

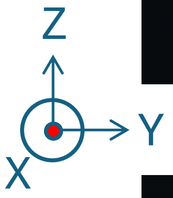
Diffusion in the brain

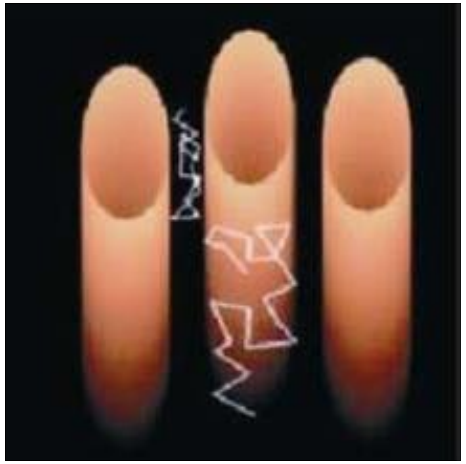


➔ **Free diffusion**

➔ Isotropic media: D is the same in all the directions

➔ Glass of water





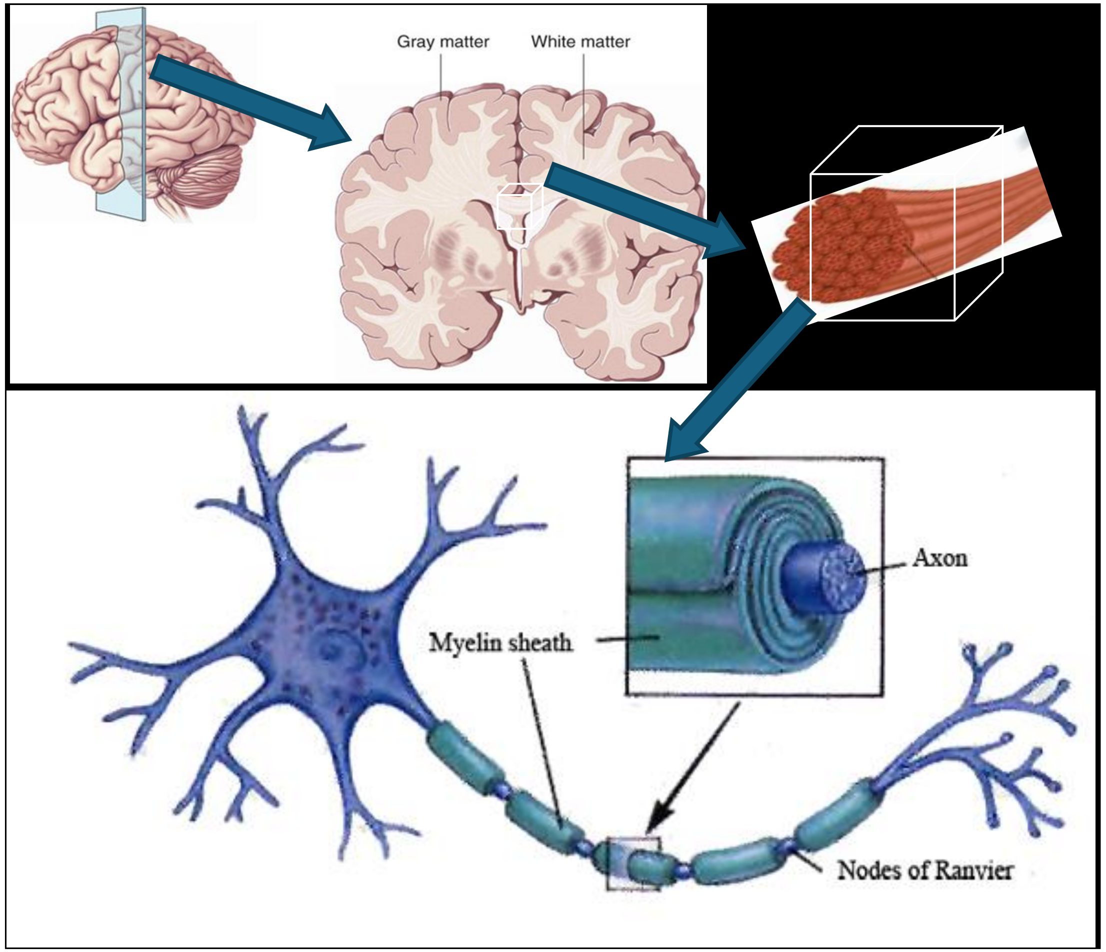
➔ **Restricted diffusion**

➔ Anisotropic media: D changes as a function of the direction

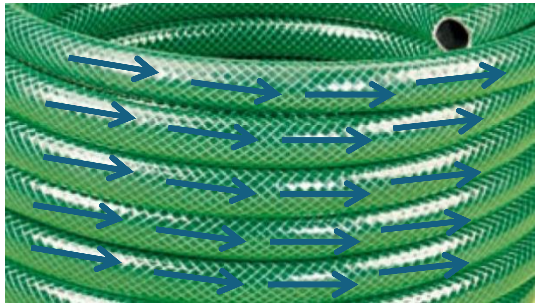
➔ Hosepipe

Anisotropy in the white matter

White matter ←→ *Bundles of myelinated fibers*



Myelin is a fatty substance that surrounds the axons, with very low permeability to the water.



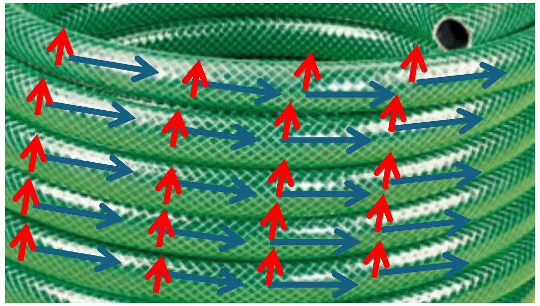
Myelinated Fibers

⬇

Restricted diffusion

Anisotropy in the white matter

Isotropic media: $D_{//} \approx D_{\perp}$



Anisotropic media: $D_{//} >> D_{\perp}$

Pitfall: during cerebral development, already anisotropy in white matter before myelinization… oriented structures

Overview

5. Diffusion tensor

3D measurement: the diffusion tensor

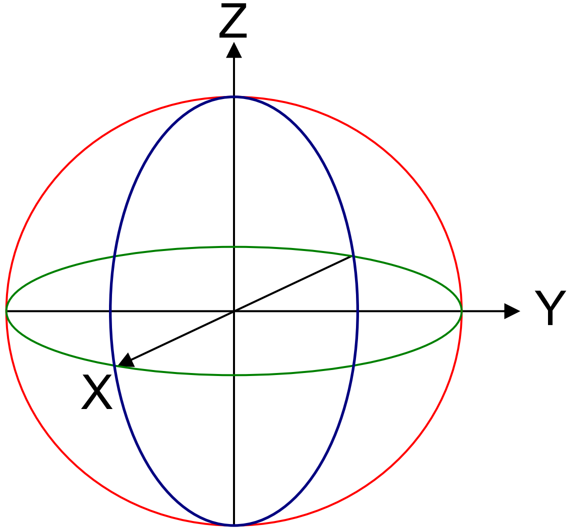
Diffusion coefficient is direction dependent

Scalar is not sufficient in a heterogeneous media (*i.e.* brain)

➔ 3D measurement

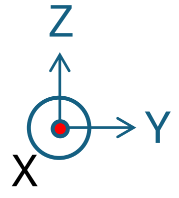
➔ The diffusion tensor

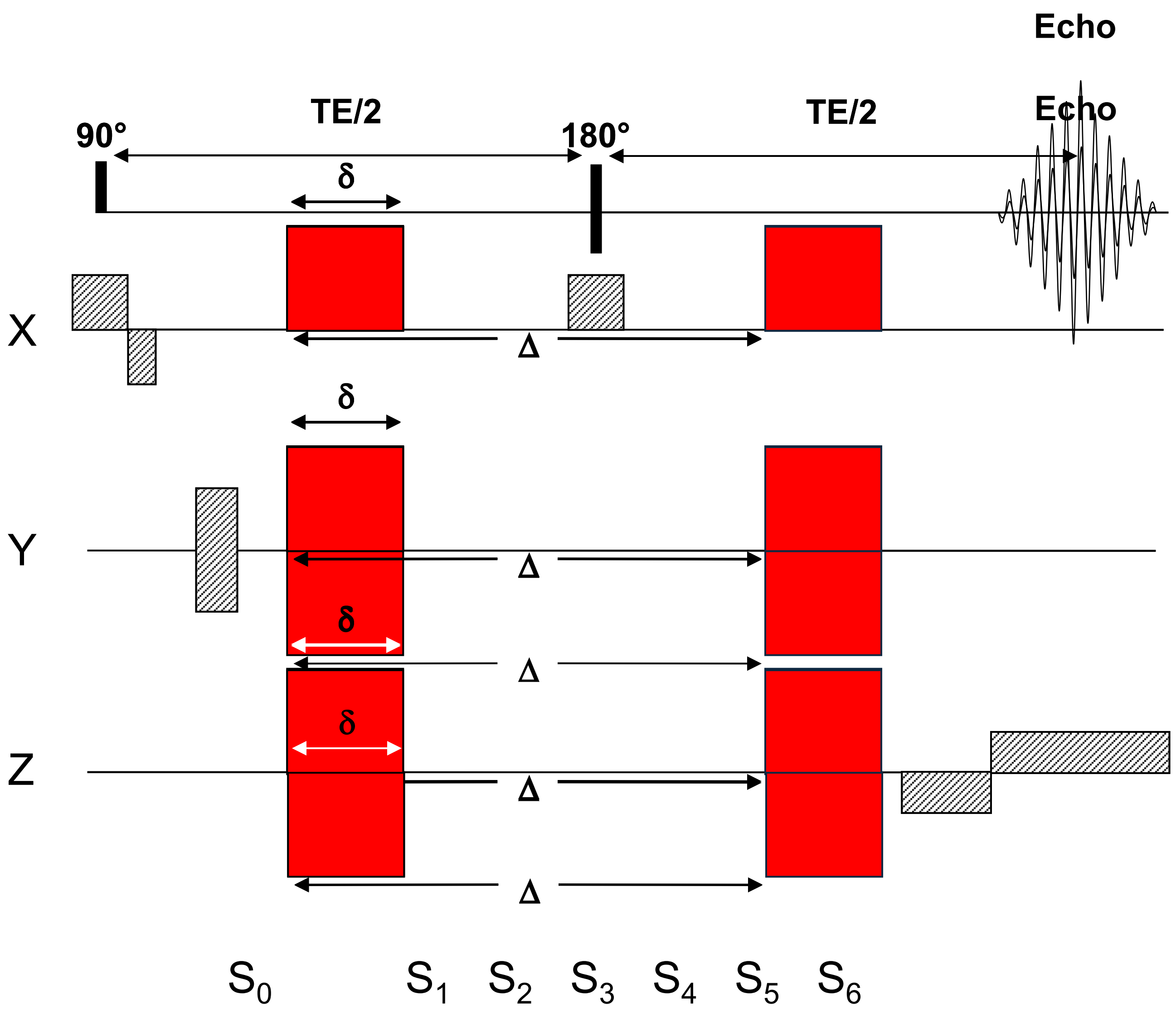
$$[D] = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$

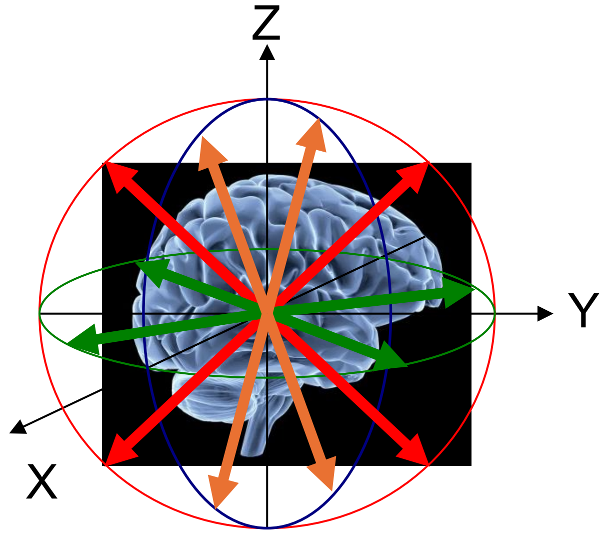


➔ Matrix 3×3 defined:
- Symmetric: $D_{ij} = D_{ji}$ (6 terms = 6 unknowns)
- Positive: mm^2/s

Diffusion tensor acquisition







Diffusion tensor acquisition

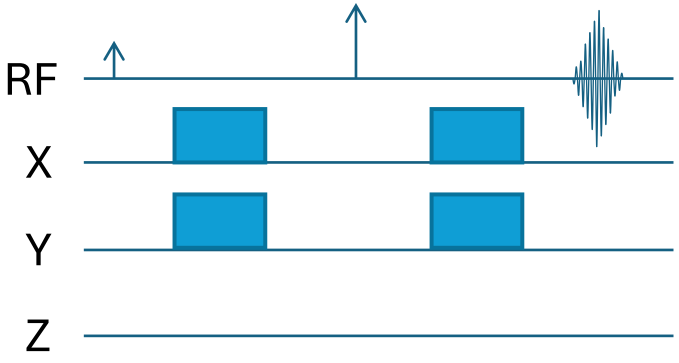
For each of the 6 experiments, signal attenuation:

$$\frac{S_k}{S_0} = \exp\left[-\left(b^k_{xx}D_{xx} + b^k_{yy}D_{yy} + b^k_{zz}D_{zz} + 2b^k_{xy}D_{xy} + 2b^k_{xz}D_{xz} + 2b^k_{yz}D_{yz}\right)\right]$$

$$[b^k] = \begin{bmatrix} b_{xx} & b_{xy} & b_{xz} \\ b_{xy} & b_{yy} & b_{yz} \\ b_{xz} & b_{yz} & b_{zz} \end{bmatrix}$$

Contribution to the signal attenuation of all the gradients applied in the sequence

Example with experiment 1, attenuation $S_1/S_0=\exp(-[b_1].[D])$

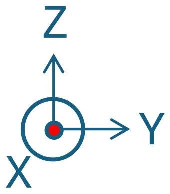


$$[b^1] = \begin{bmatrix} b_{xx} & b_{xy} & 0 \\ b_{xy} & b_{yy} & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

Diffusion tensor acquisition

Solving the system gives the diffusion tensor:

$$[D] = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$

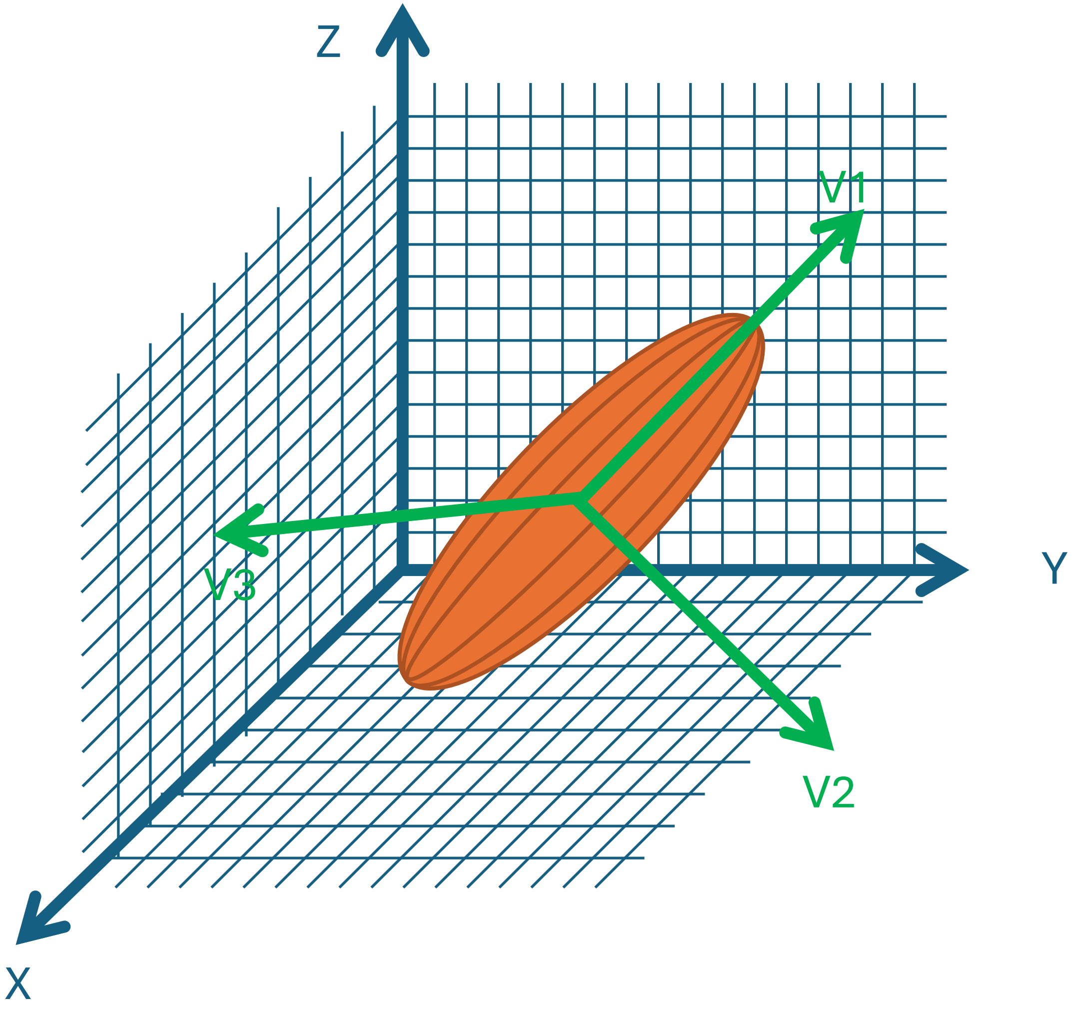


➔ Diagonalization of the tensor: **Diagonalization** is the process of finding a corresponding new basis (eigenvectors) in which the tensor is diagonal (eigenvalues)

Diagonalization

In the basis (X,Y,Z)

$$[D] = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$



In the basis (V1,V2,V3)

$$[D] = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

Let’s play with the DT

Diagonalization of the tensor:

$$\begin{bmatrix} \vec{V}_1 & \vec{V}_2 & \vec{V}_3 \end{bmatrix} . \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix} . \begin{bmatrix} \vec{V}_1 \\ \vec{V}_2 \\ \vec{V}_3 \end{bmatrix} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

eigenvectors

eigenvalues or diffusivities

➔ Diagonalization of the tensor : write the tensor in a new basis (eigenvectors) in which this tensor is diagonal (eigenvalues)

To each eigenvalue	λ_1	λ_2	λ_3
➔ 1 eigenvector	$\vec{V}_1$	$\vec{V}_2$	$\vec{V}_3$

The eigenvector associated with the maximal eigenvalue gives the principal diffusion direction for each pixel of an image.

Overview

6. Parameters derived from the tensor

Parameters derived from the tensor

Mean diffusivity

⬇

<eigenvalues>:

$$MD = \frac{1}{3}(D_{\mathrm{max}} + D_{\mathrm{med}} + D_{\mathrm{min}})$$

⬇

MOBILITY

Fractional anisotropy

⬇

Std of eigenvalues normalized [0,1]:

$$FA = \sqrt{\frac{(D_{\min} - D_{med})^2 + (D_{med} - D_{\max})^2 + (D_{\max} - D_{\min})^2}{2(D_{\min}^2 + D_{med}^2 + D_{\max}^2)}}$$

⬇

ANISOTROPY

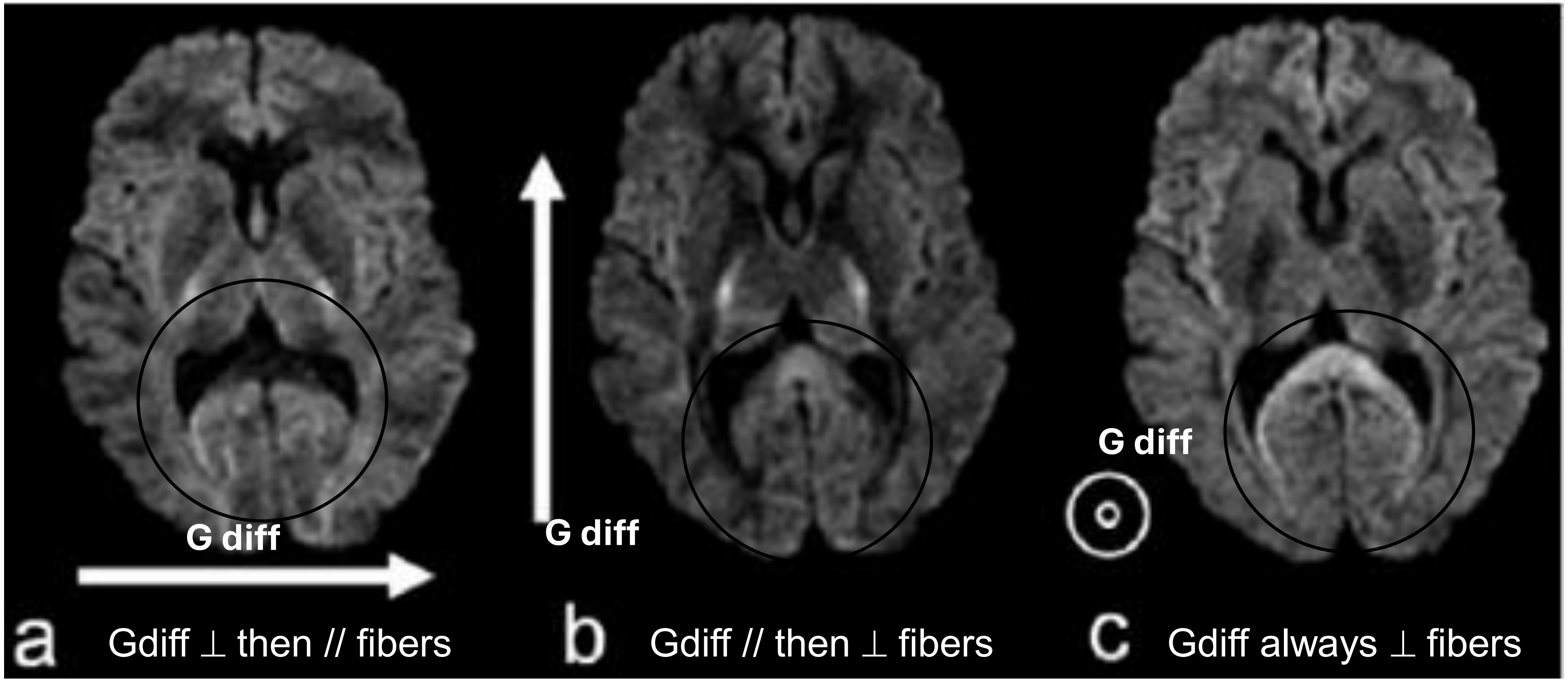
Parallel (Axial) diffusivity

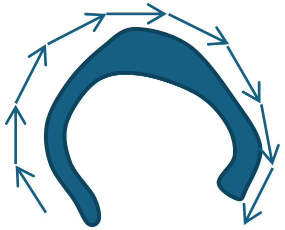
$$Dax = (D_{\mathrm{max}}\ \ )$$

Orthogonal (Radial) diffusivity

$$Dorth = \frac{1}{2}(D_{\mathrm{med}} + D_{\mathrm{min}})$$

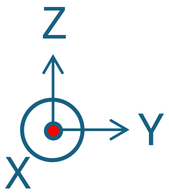
DTI in images, corpus callosum

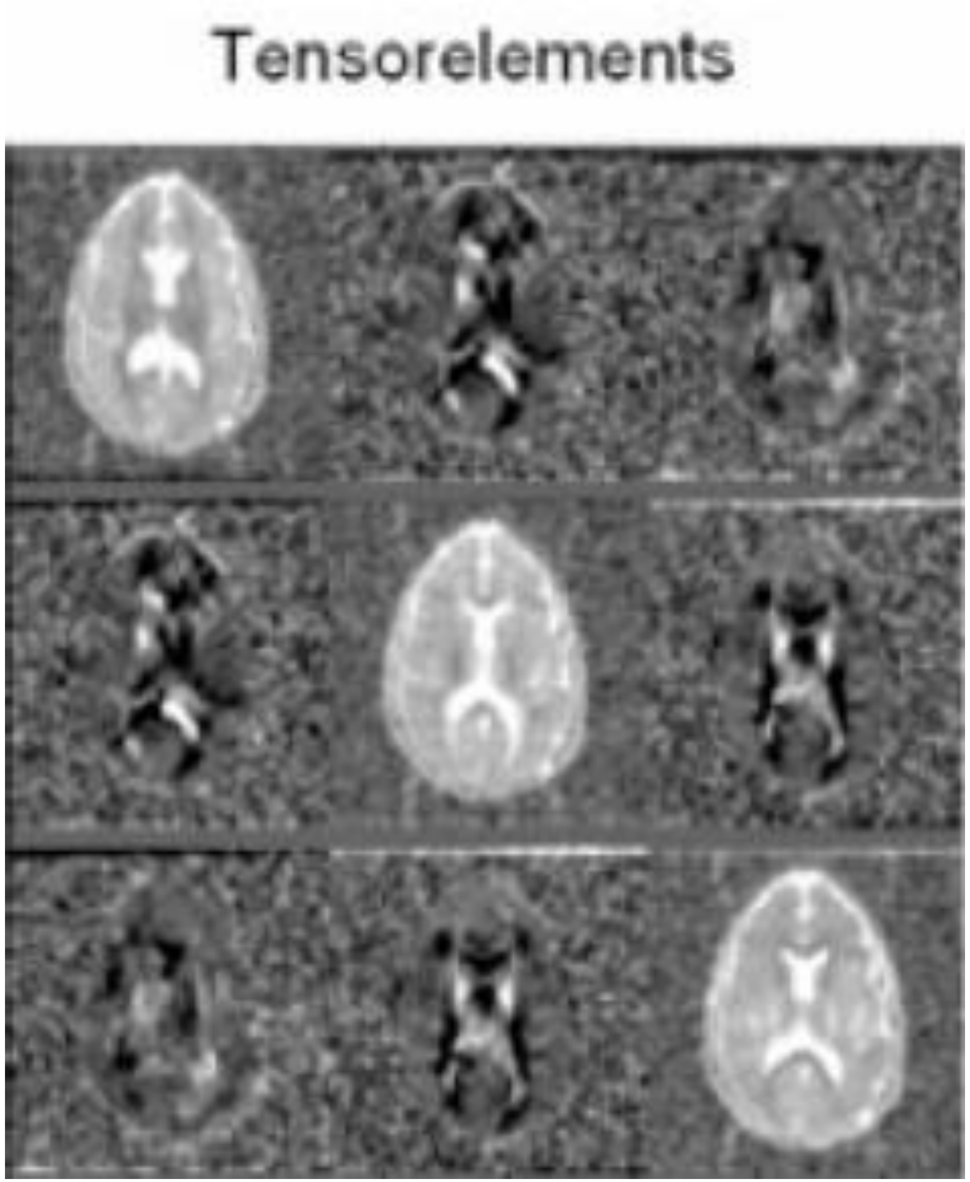




Tensor elements…

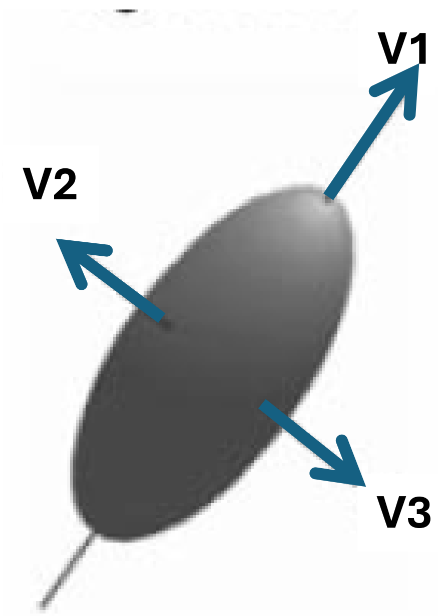
$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$





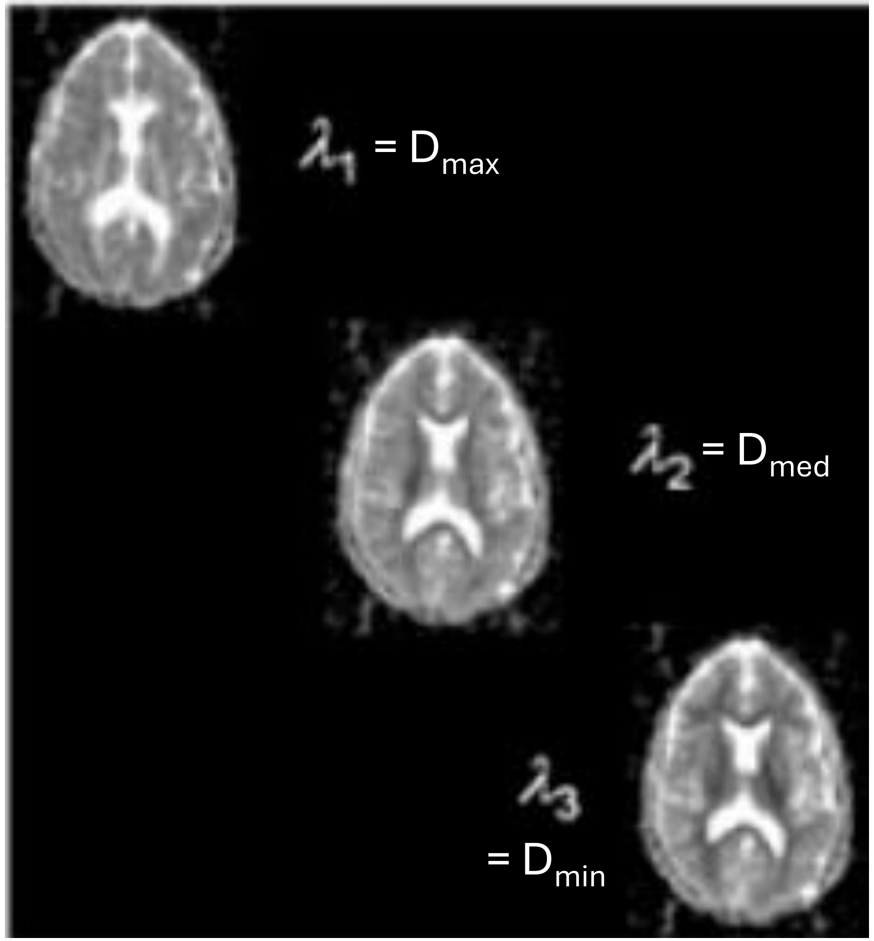
Diagonalization…

Eigenvectors



$$\begin{bmatrix}\vec{V}_1\\ \vec{V}_2\\ \vec{V}_3\end{bmatrix}$$

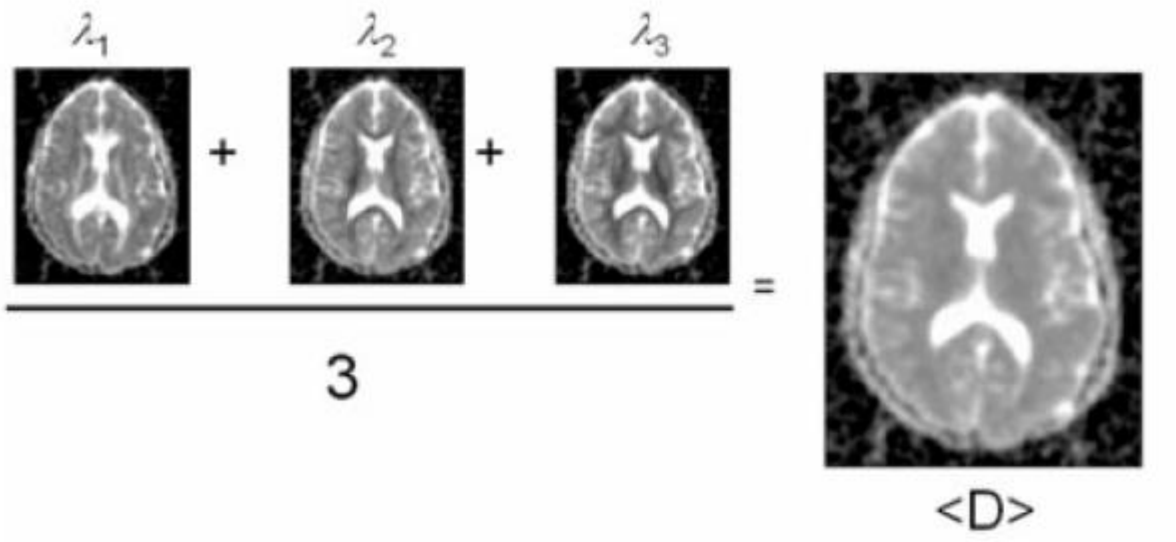
Eigenvalues



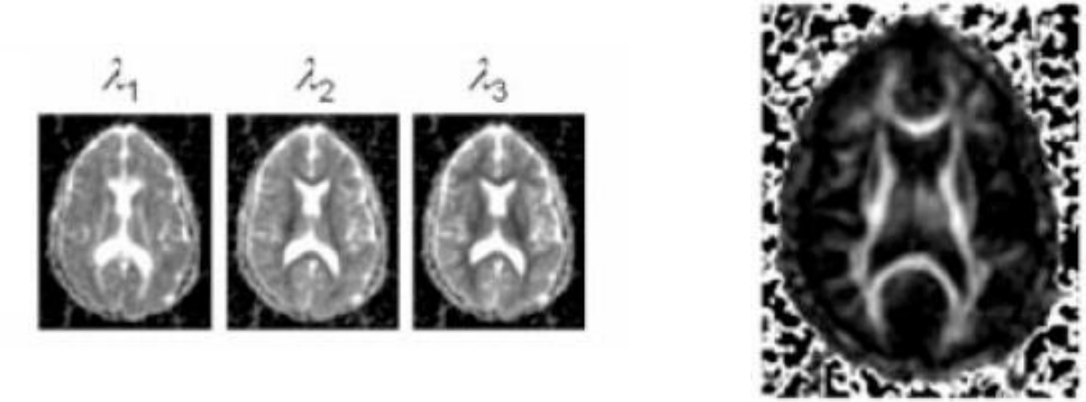
$$\begin{bmatrix} D_{\mathrm{min}} & 0 & 0 \\ 0 & D_{med} & 0 \\ 0 & 0 & D_{\mathrm{max}} \end{bmatrix}$$

Parameters derived from the tensor

$$\langle D \rangle = \frac{1}{3}(\lambda_1 + \lambda_2 + \lambda_3)$$

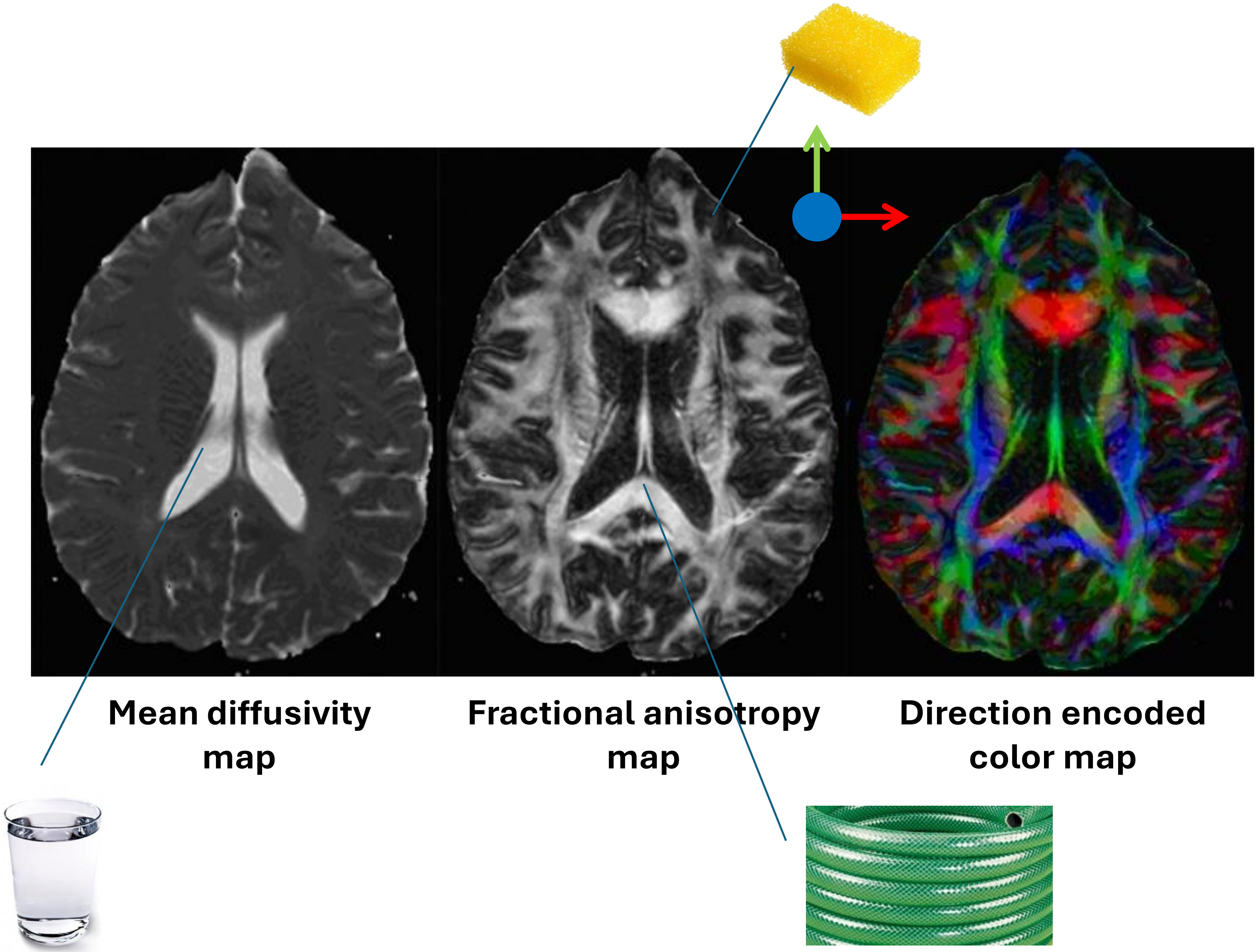


$$FA = \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_3 - \lambda_1)^2}{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$



FA

Parameters derived from the tensor: maps

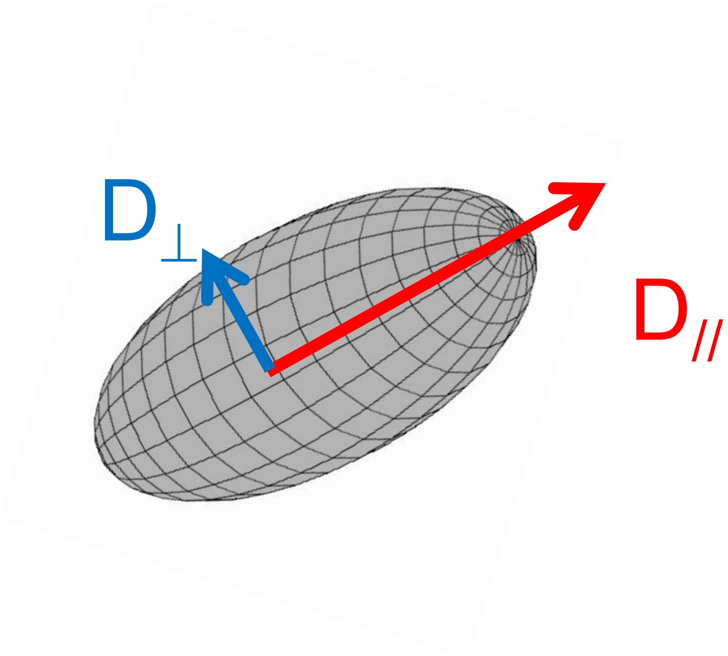


Mean diffusivity map

Fractional anisotropy map

Direction encoded color map

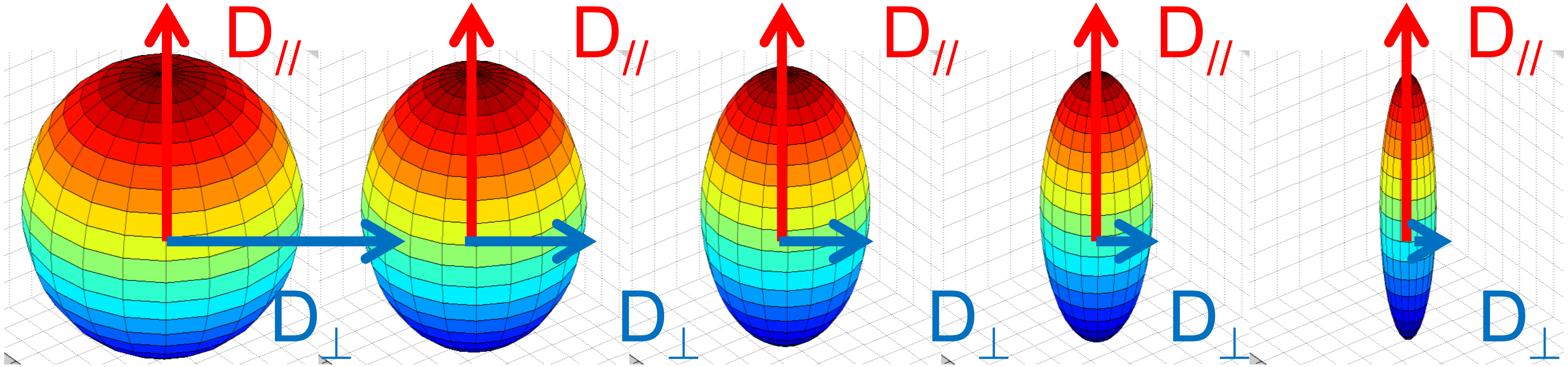
Graphic representation of the tensor



Diffusion ellipsoids

- Major axis weighted by axial diffusivity
- Minor axis weighted by radial diffusivity

Graphic representation of the tensor

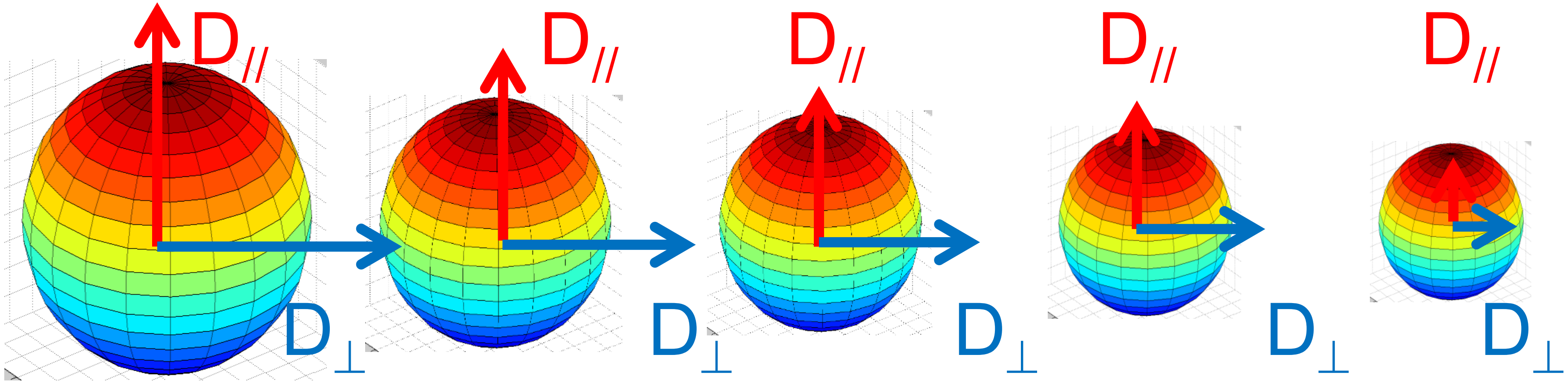


Isotropic

FA → 0

Anisotropic

FA → 1



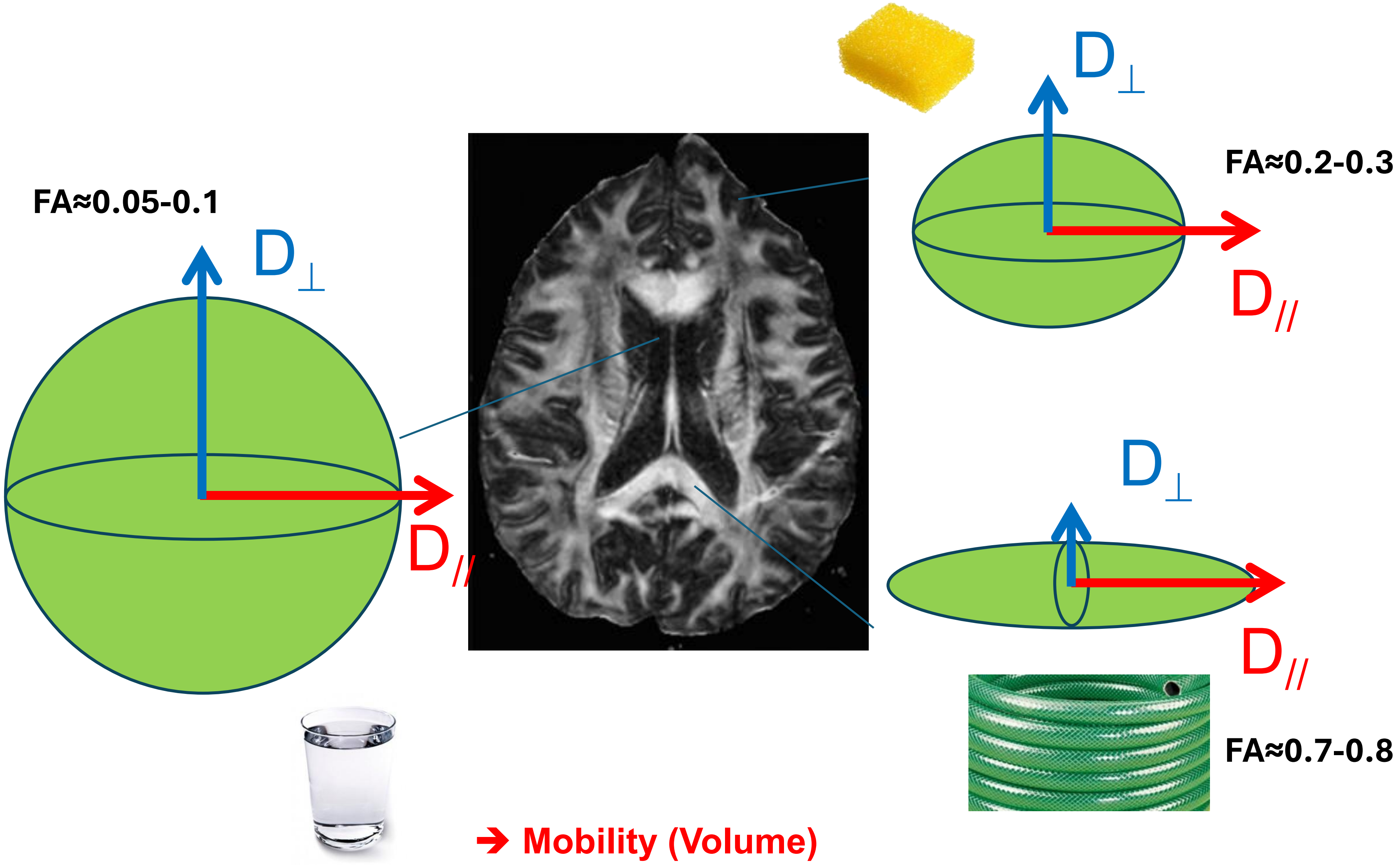
Mobility+++

MD+++

Mobility ---

MD ----

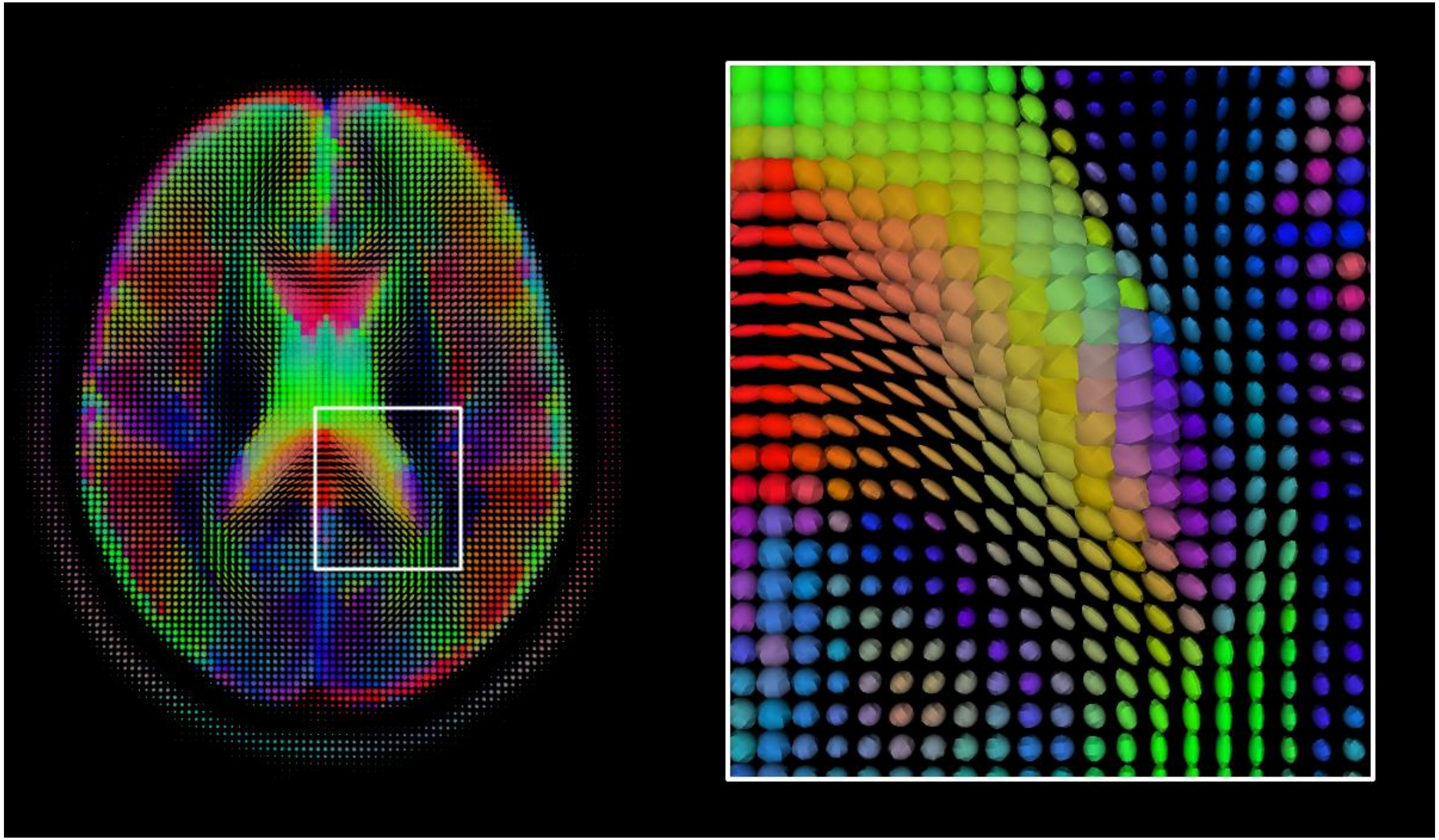
Graphic representation of the tensor



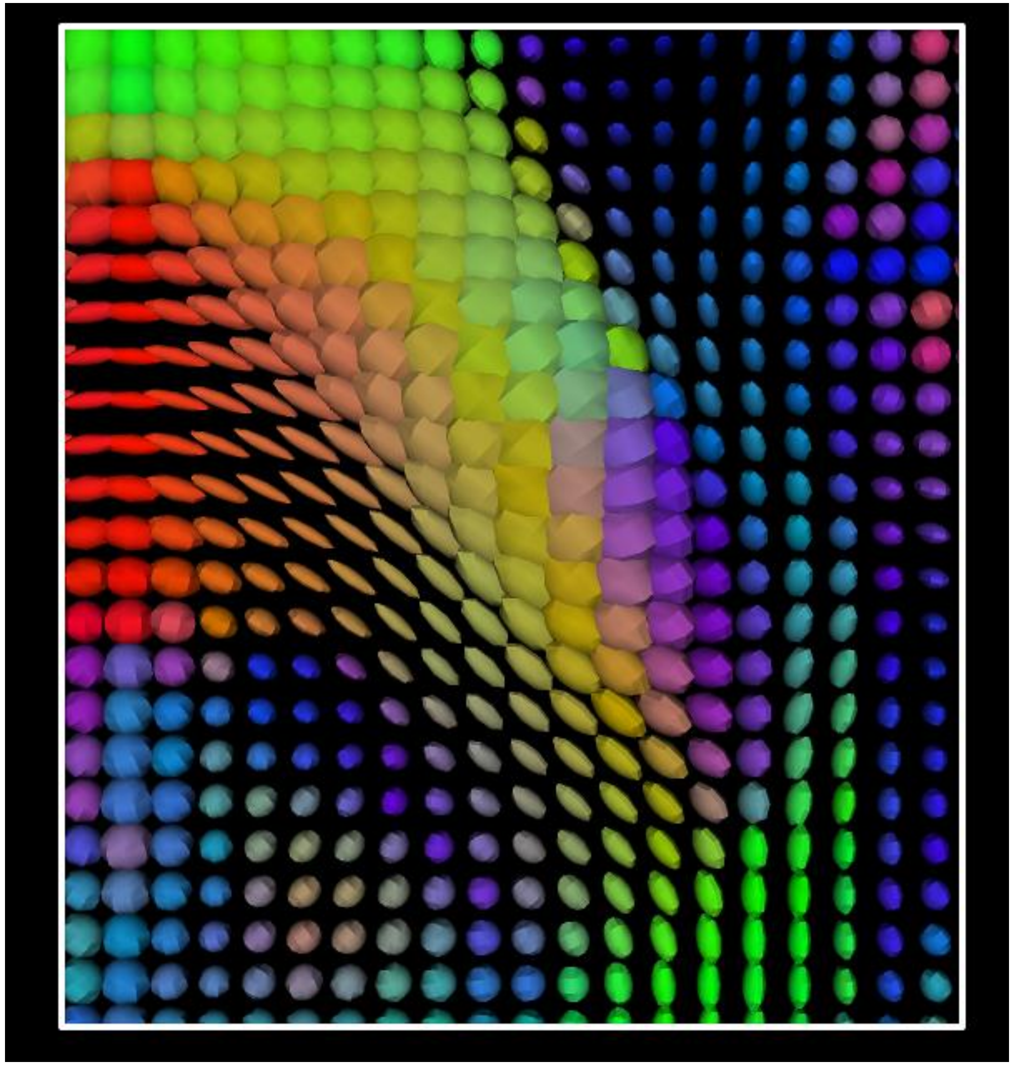
➔ **Mobility (Volume)**

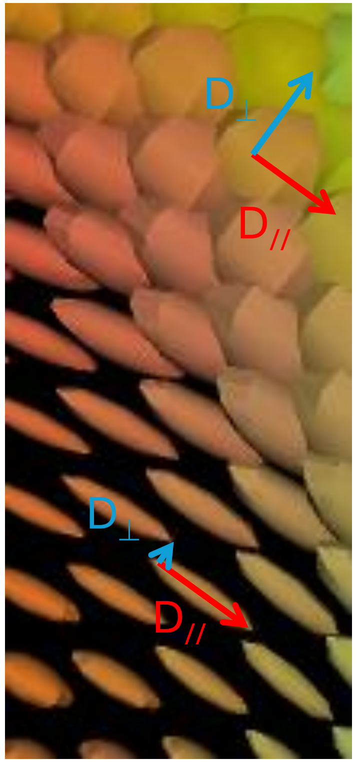
➔ **Anisotropy (Shape)**

Graphic representation of the tensor



Graphic representation of the tensor



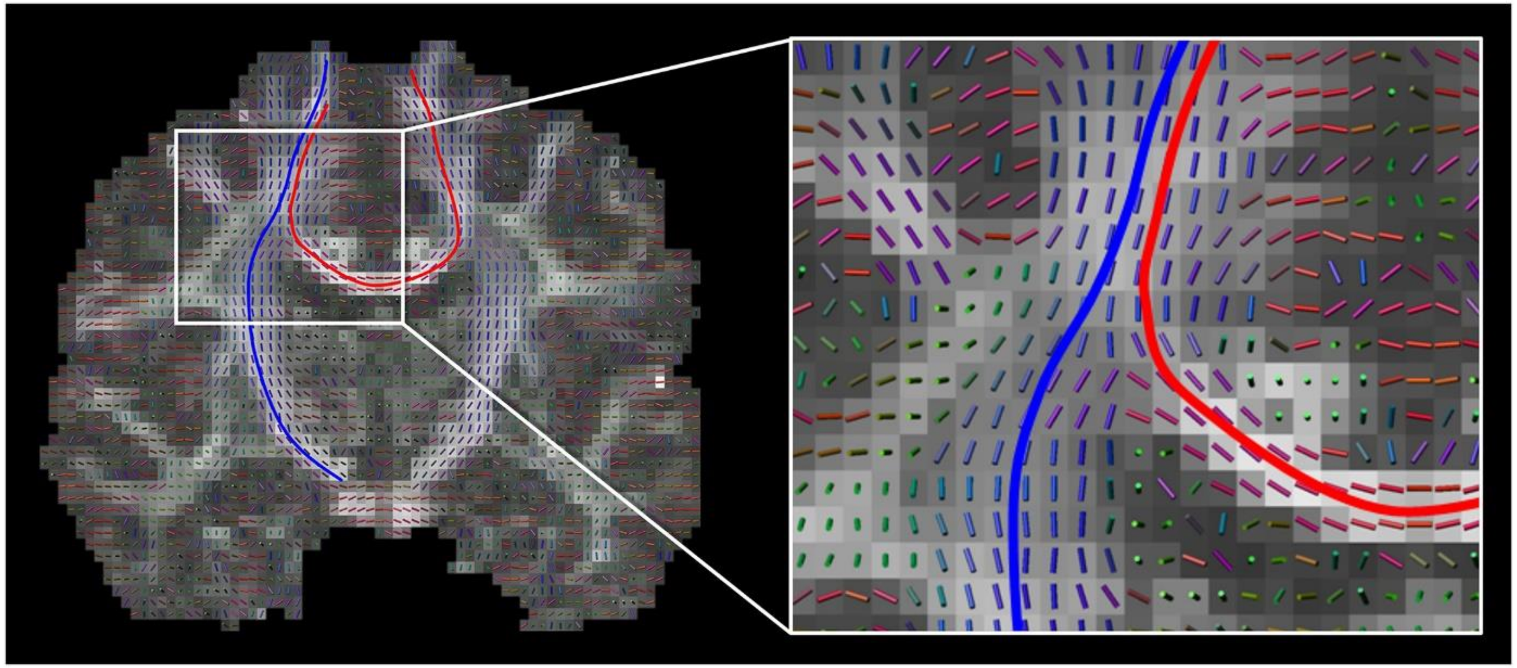


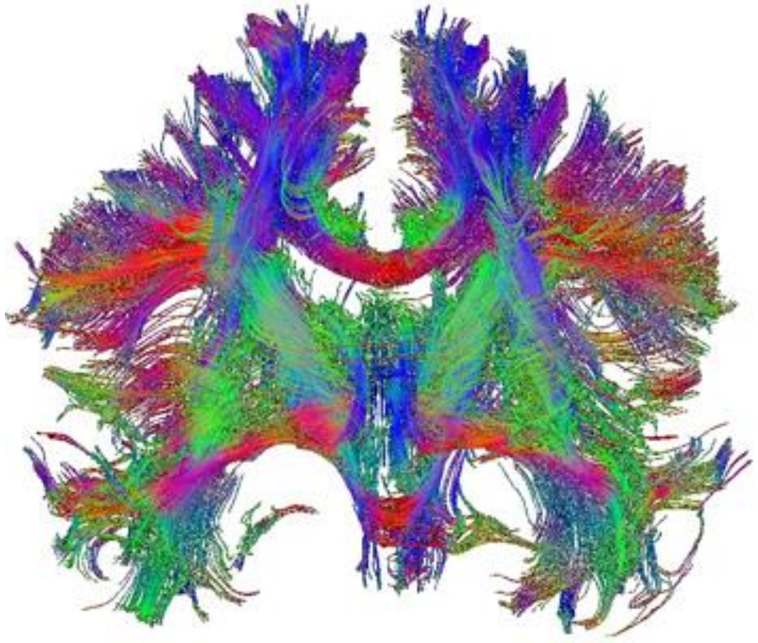
Overview

7. Fiber tracking

Tractography or fiber tracking

Reconstruction of the white matter fibers, principle : link eigenvectors





©ETHZ Institute for Biomedical Engineering

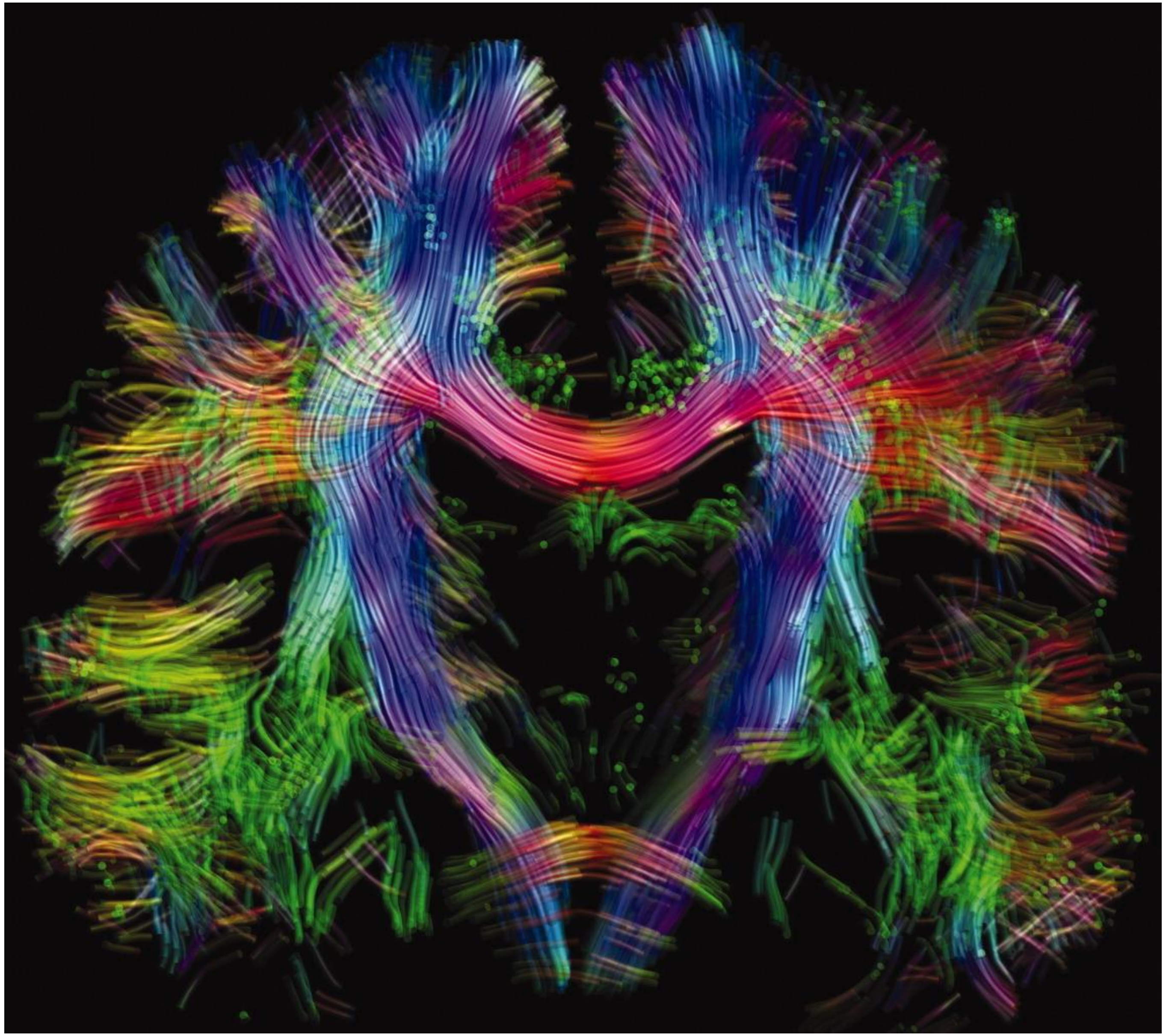
Stop criteria:

- ➔ FA threshold
- ➔ Limit angle

- **Deterministic methods**
- **Probabilistic methods**

Jeurissen B et al. NMR in Biomed 2017

Tractography or fiber tracking



Tournier JD et al. MRM 2011

Keep in mind

Parameters derived form the diffusion tensor:

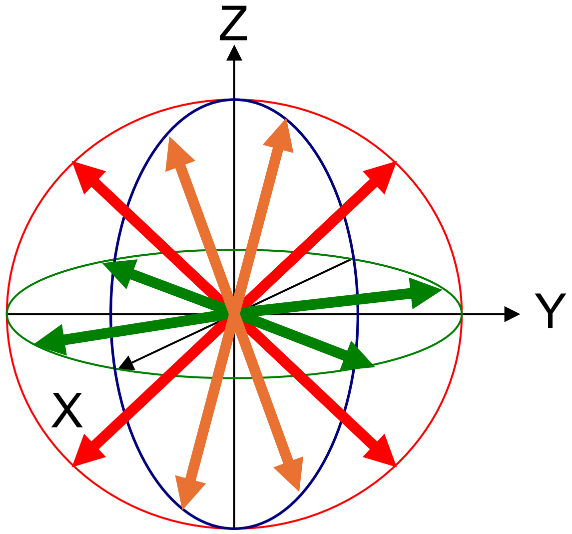
- **Mean diffusivity or apparent diffusion coefficient: MD or ADC**
- **Axial or parallel diffusivity along the principal diffusion direction (*i.e.* along fibers in WM) :** $D_{//}$
- **Radial or orthogonal diffusivity perpendicular to the principal diffusion direction (*i.e.* orthogonal to the fibers in WM) :** $D_{\perp}$
- **Fractional anisotropy, close to 0 in ventricles (isotropic – glass of water) and to 1 in white matter (anisotropic - hosepipe) : FA**

Overview

8. Important parameters of DTI experiments

Diffusion gradient sampling scheme

Diffusion gradient sampling scheme: → Number, Orientations } diffusion gradients



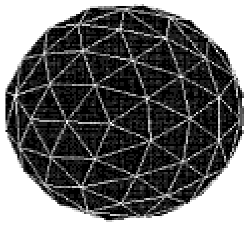
At least 6 non collinear directions: x = y +1 and 2x = 2y + 2

Spatial repartition

The orientations must be the most uniform as possible on the diffusion sphere

Electromagnetic repulsion of charges on a sphere (maximization of the distance between charges)

Geometrical polyhedral figure

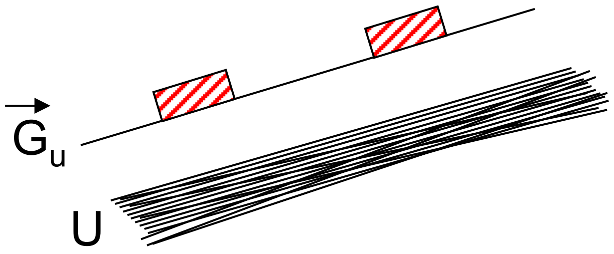


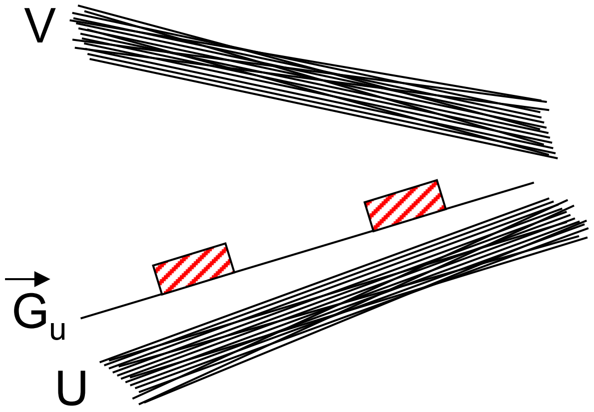
➔ **Clinical scanner 30 directions routinely used (solving the system by linear regression, N equations, M unknowns with N>M)**

➔ **Preclinical scanners, less directions, rodent brains less heterogeneous**

BUT, As much direction as possible or only six carefully chosen?

Diffusion gradient sampling scheme





Uniform gradient sampling scheme on the diffusion sphere

⬇

One gradient direction « collinear » to the fibers

⬇

Good directional information

Low gradient sampling scheme

⬇

One direction under sampled

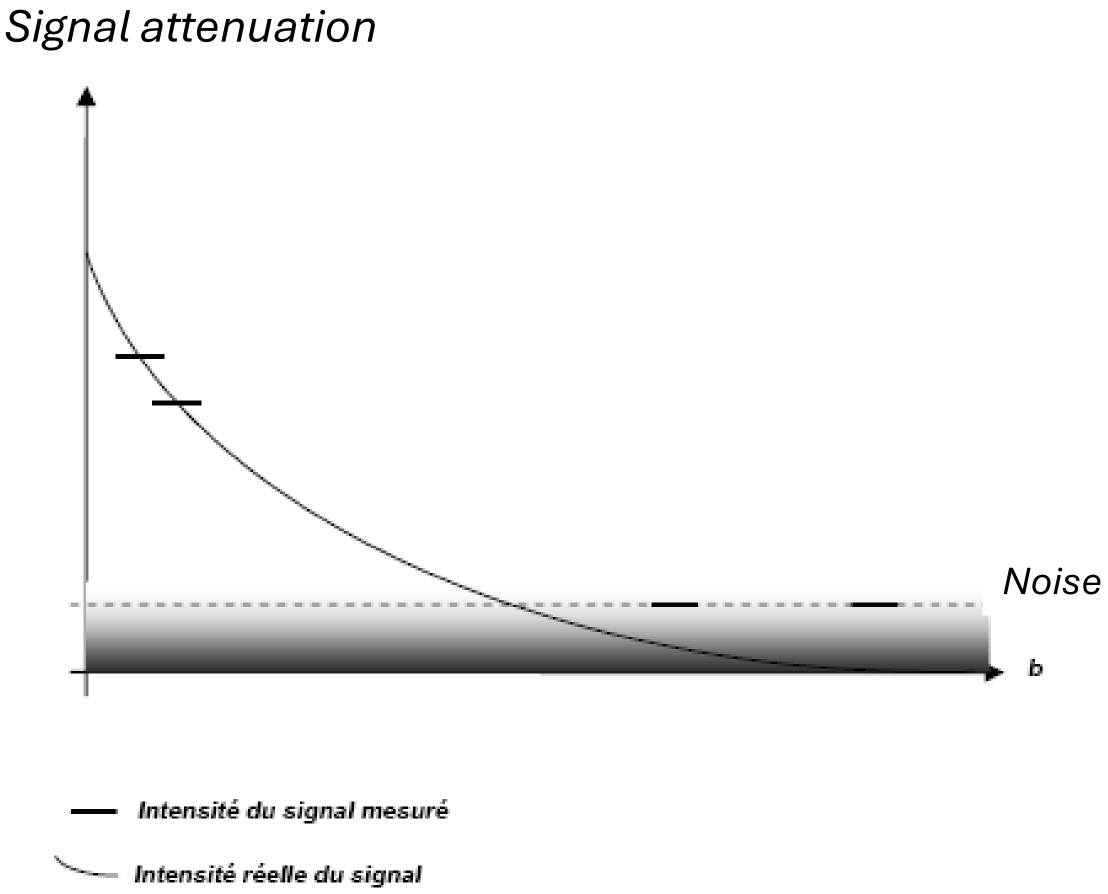
⬇

Information biased in one direction

➔ The orientations must be the most uniform as possible on the diffusion sphere, especially when the fibers disposition is a priori unknown

➔ It is more beneficial to use many gradient orientations when the sample is complex and heterogeneous (>20 for accurate determination of FA in human brain (DK Jones MRM2003))

b-value : diffusion sensitivity



_b_-value: diffusion sensitivity of the sequence ➔ $S=S_0e^{-bD}$

b too low:
➔ DW attenuation in the order of Noise level

b too high:
➔ DW Signal under the noise level

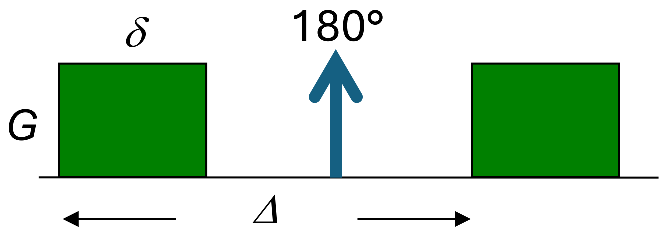
Optimal *b*-value:
bD = 1 ➔ $e^{-bD} = 0.4$

No optimal *b*-value in an anisotropic media… in the brain b = 1000 s/mm2, mean value between white (700) and gray matter (1300) optimal b-value

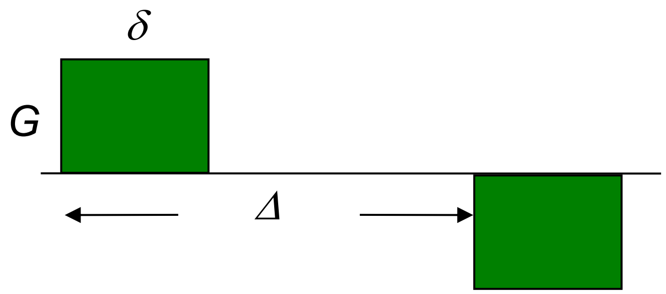
LeBihan D et al. Neuroimage 2012

b-matrix

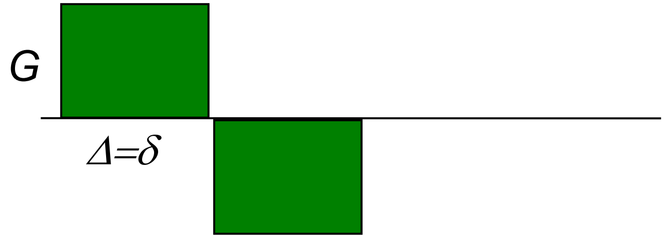
Each gradient refocused before TE contributes to the b-value



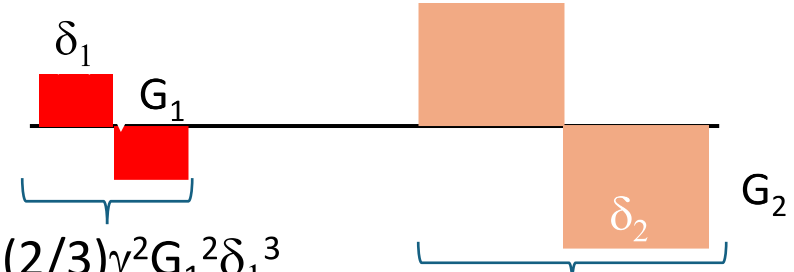
$b=\gamma^2G^2\delta^2(\Delta-\delta/3)$



$b=\gamma^2G^2\delta^2(\Delta-\delta/3)$



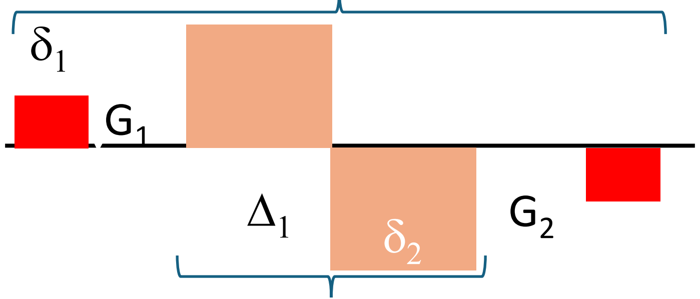
$b=(2/3)\gamma^2G^2\delta^3$



$b_1=(2/3)\gamma^2G_1^2\delta_1^3$

$b_2=(2/3)\gamma^2G_2^2\delta_2^3$

$b_1=\gamma^2G_1^2\delta_1^2(\Delta_1-\delta_1/3)$



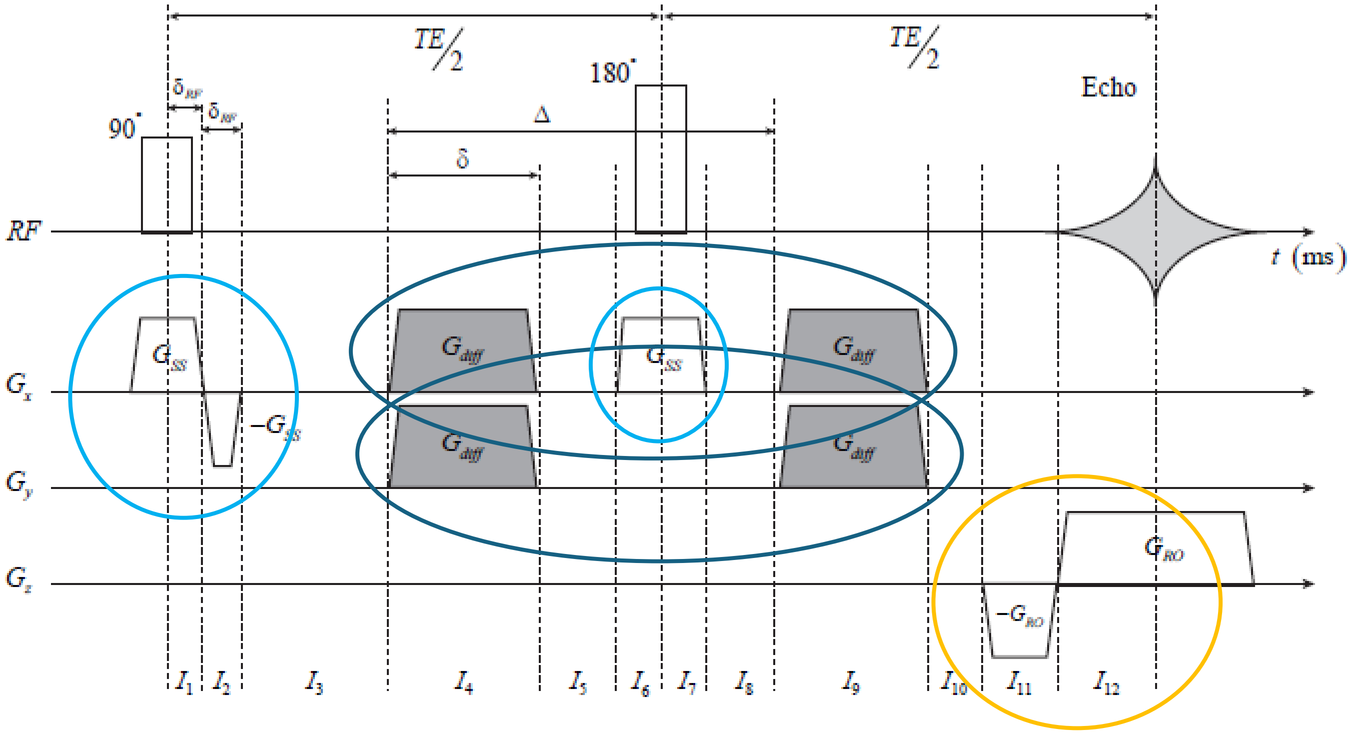
$b_2=(2/3)\gamma^2G_2^2\delta_2^2$

cross term:

$\mathbf{b_{1x2}=2\gamma^2G_1G_2\delta_1\delta_2^2}$

$$b=\gamma^2\int_0^{TE}\left(\int_0^{t}G(t')dt'\right)^2dt$$

b-matrix in the SE sequence



cross term:

$b_{diffXslice}=2\gamma^2 G_{diff} G_{SS} \delta \delta_{RF}^2$

$b_{diffXdiff}=2\gamma^2 G^2_{diff} \delta^3$

$b_{diff\text{-}x}=\gamma^2 G_{diff}^2 \delta^2 (\Delta-\delta/3)$

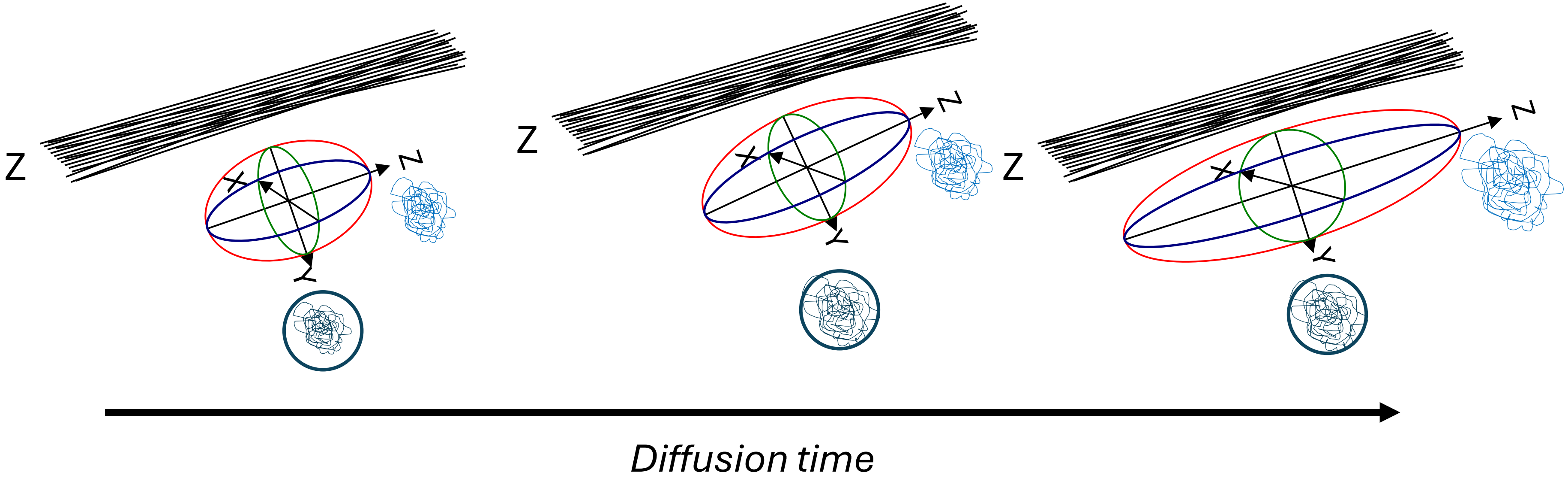
$b_{diff\text{-}y}=\gamma^2 G_{diff}^2 \delta^2 (\Delta-\delta/3)$

$b_{sl}=2x(2/3)\gamma^2 G_{ss}^2 \delta_{RF}^3$

$b_{ro}=(2/3)\gamma^2 G_{RO}^2 I_{11}^3$

$$[b]=\begin{bmatrix} b_{sl}+b_{diff}+b_{slXdiff} & b_{slXdiff}+b_{diffXdiff} & 0 \\ b_{slXdiff}+b_{diffXdiff} & b_{diff} & 0 \\ 0 & 0 & b_{ro} \end{bmatrix}$$

Diffusion time



Diffusion time

Increase diffusion time

➔ *Saturation of the radial diffusion (i.e. r.m.s displacement reaches a constant, we reach the barriers of the media)*

➔ *Maximization of the axial diffusion (no barriers, r.m.s displacement increases)*

Accuracy in the determination of the principal diffusion direction +++

Jones DK et al. MRM 2002

Overview

9. Pitfalls in DTI

Pitfalls in DTI

DTI sequence uses bipolar pulsed field gradients inserted into a conventional MRI sequence (e.g. spin echo EPI):

1. **Pitfalls related to MR Imaging sequences:**
    - Motion artifacts
    - Geometric distortions/susceptibility artifacts
    - Ghosting

2. **Pitfalls related to diffusion MRI**
    - Eddy currents
    - Lack of specificity: multi-compartment models

LeBihan D et al. JMRI 2006

Gradient induced Eddy currents

Eddy currents appear during rapid switch-on/switch-off of the magnetic field gradients ➡ Spatiotemporal magnetic field perturbations

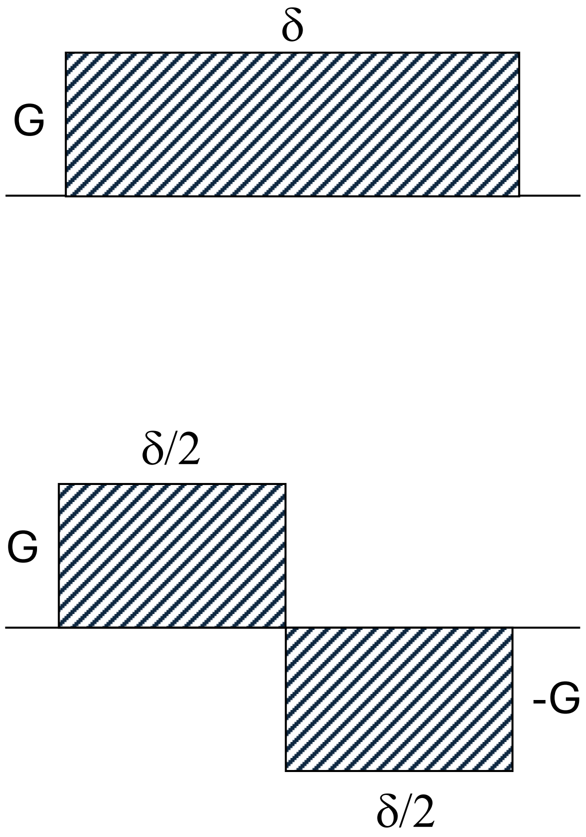
➔ an Eddy current creates a magnetic field that opposes the magnetic field that created it (Lenz’s law)

➔ modeled as a sum of exponentially decaying components, each with independent amplitudes and time-constants

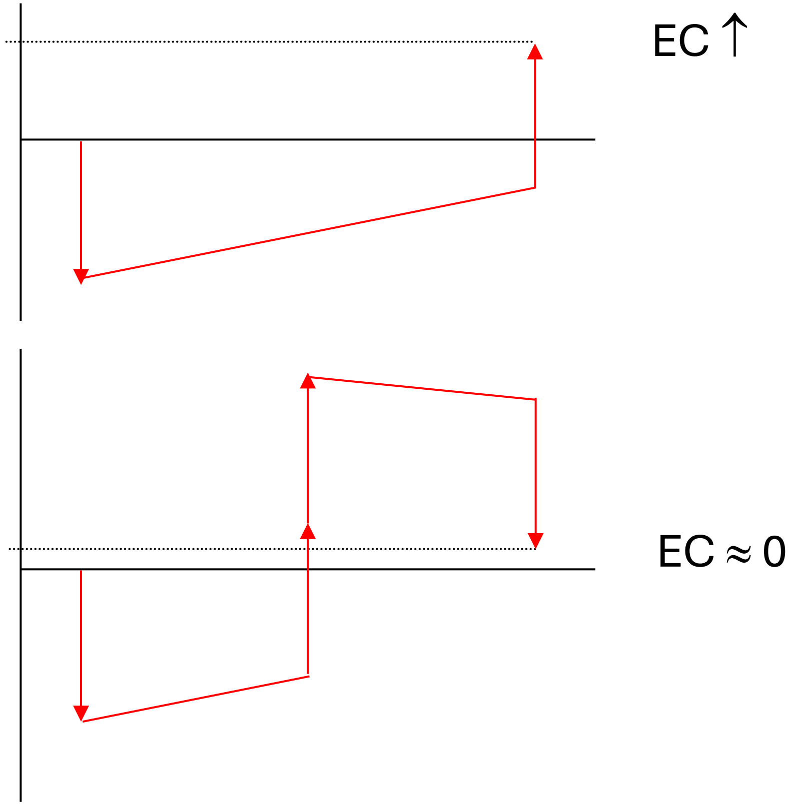
Several magnetic field gradients (diffusion MRI sequence) ➡ EC created by each gradient are summed together

Eddy currents and DTI

Gradients

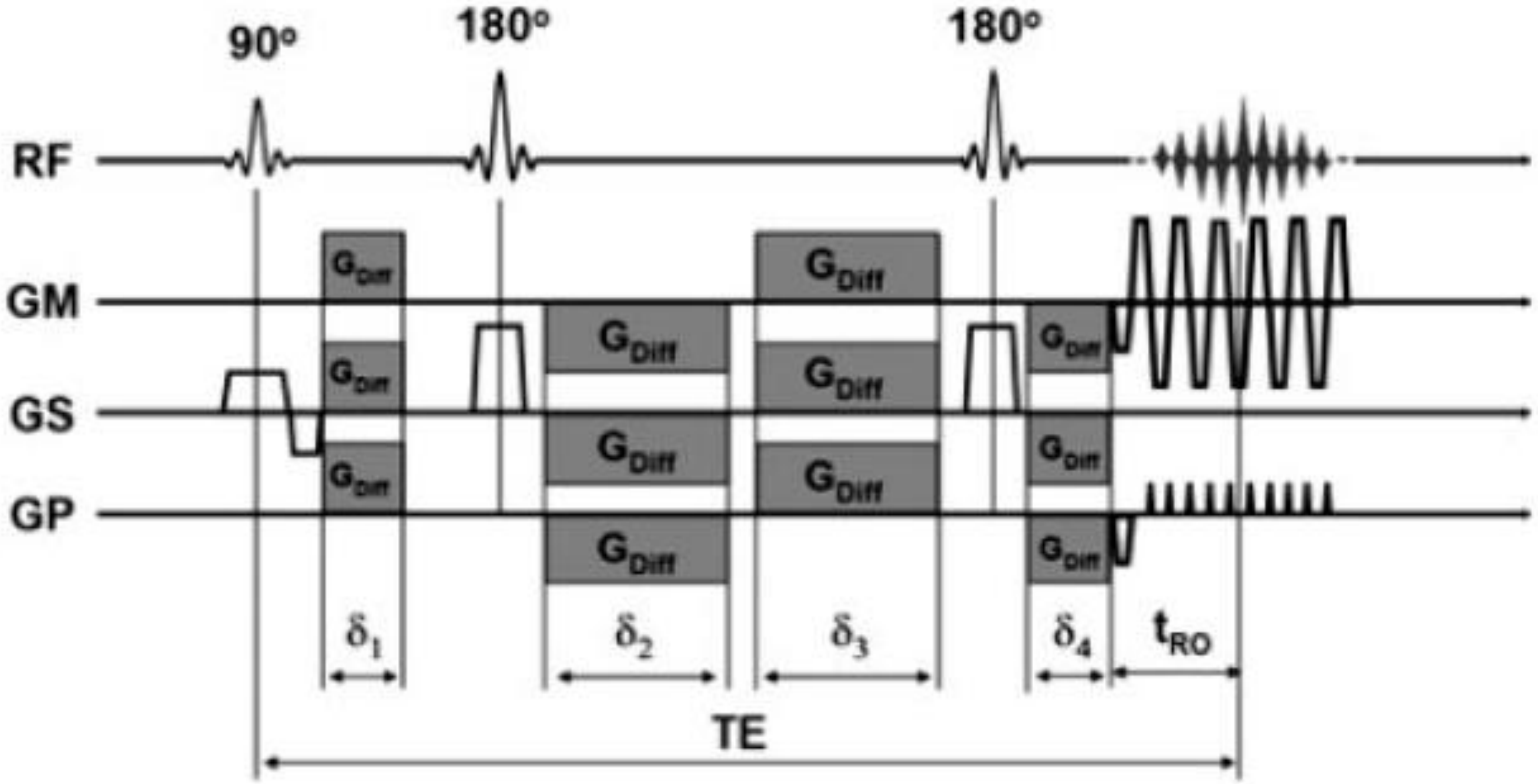


Eddy currents



EC created by the first gradient are compensated by the second one

Twice refocused spin echo sequence



- **By playing with the durations of the diffusion gradients ($\delta_{1,2,3,4}$) once can cancel Eddy currents**
- **TRSE sequence currently the routine DTI sequence in clinic**

[6] Reese TG. MRM2003

Multi-compartment models

Why these models?

1. Classical model of the diffusion tensor based on several assumptions including that diffusion is Gaussian…
    - TRUE isotropic media
    - FALSE anisotropic media

2. DTI derived indices (*e.g.* Diffusivities, FA) are not tissue-specific, for instance FA decrease with:
    - Myelination defect,
    - Axonal diameter increase,
    - Diffuse axonal injuries,
    - Inter-axonal edema

Multi-compartment models

Image resolutions / size of the cellular structures
➔ voxel, different population of molecules
➔ Experiencing different diffusion properties

The diffusion signal corresponds to a mix of these different compartments

Mathematic models : free-hindered-restricted
- Free diffusion (very fast/anisotropy ~ 0) ➔ CSF
- Hindered diffusion (fast/low anisotropy) ➔ extra-axonal
- Restricted diffusion (slow, direct° ⊥/high anisotropy) ➔ intra-axonal

Free

Hindered

Restricted

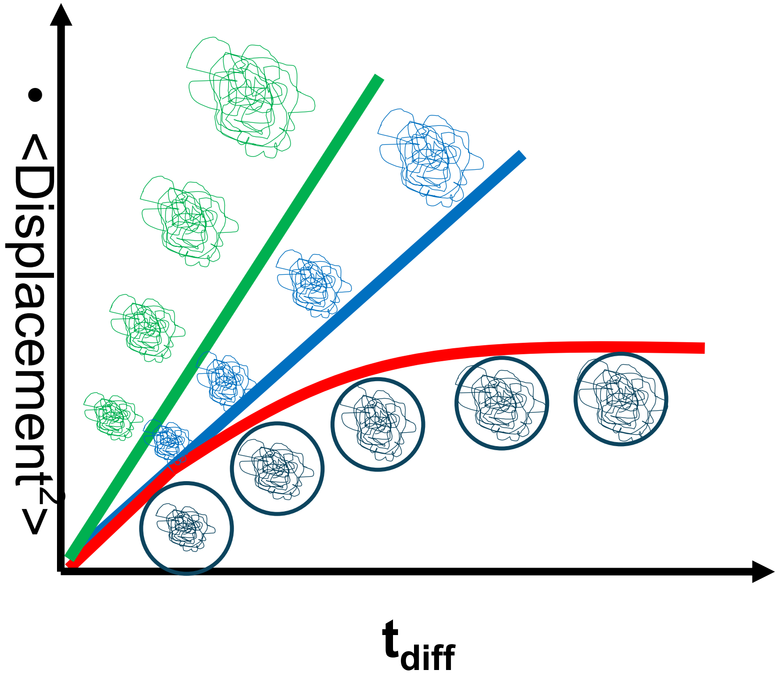
Assaf Y et al. MRM 2004

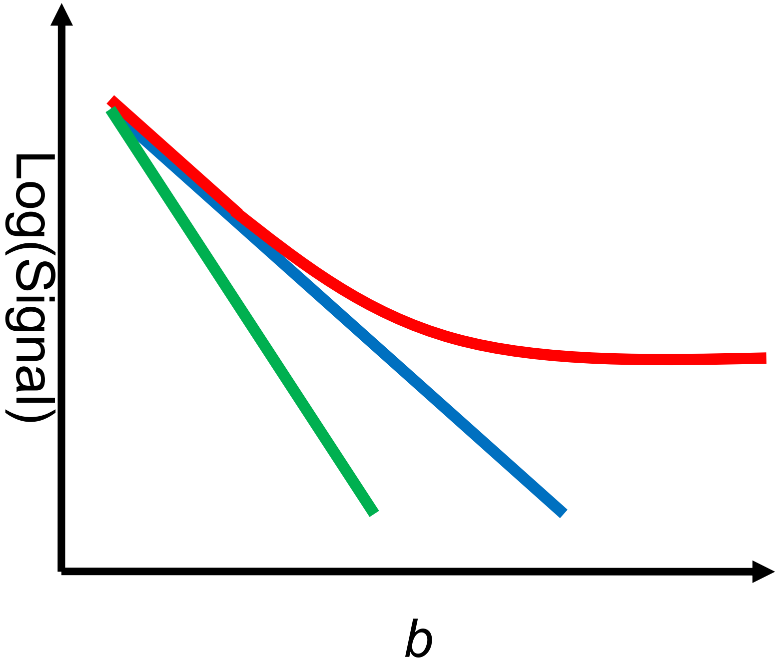
Multi-compartment models

Free

Hindered

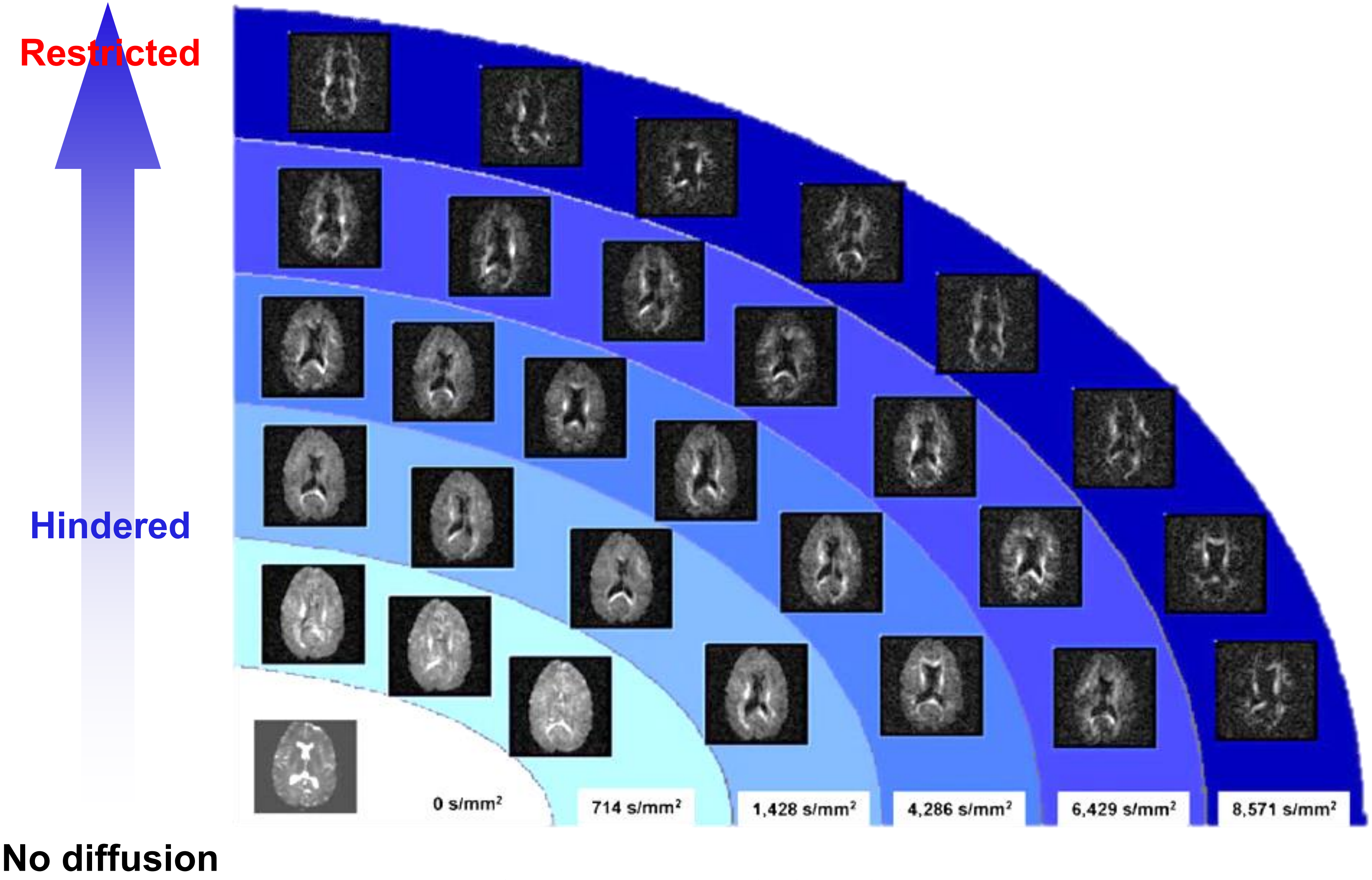
Restricted





Assaf Y et al. MRM 2004

Experimental scheme: CHARMED



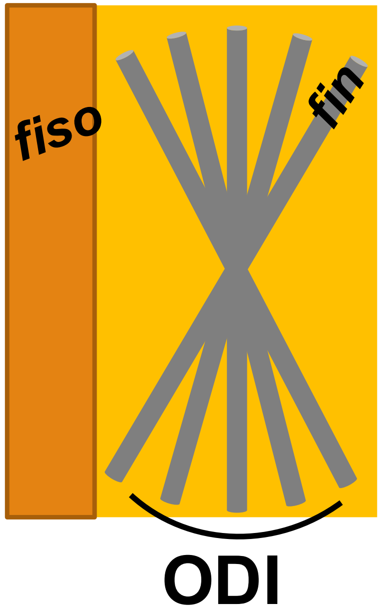
Multi b / 1 t_{diff} / multi direction

Assaf Y et al. MRM 2004

NODDI – SMT – WMTI

Separation of the signal : isotropic = free water (Gaussian diffusion) + Extra-cellular = hindered water (classical tensor) + intra-cellular = restricted (sticks-distribution)

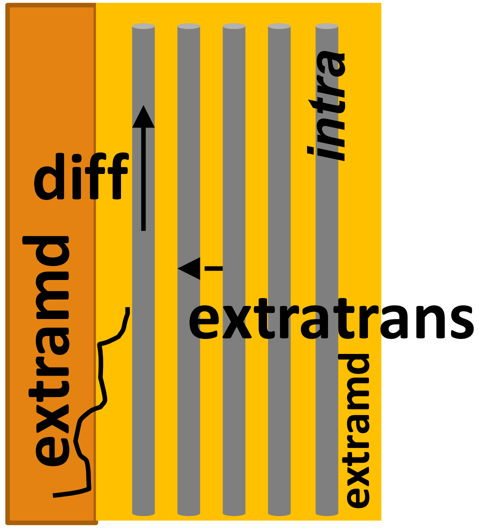
NODDI:



GM and WM

Zhang H Neuroimage 2012

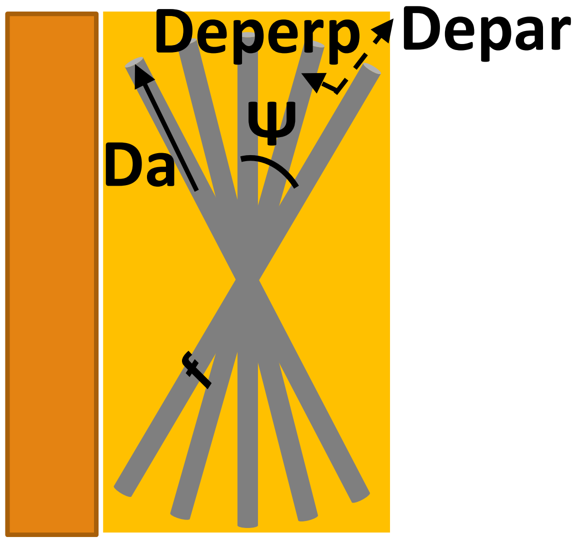
SMT:



GM and WM

Kaden E Neurimage 2016

WMTI:



WM

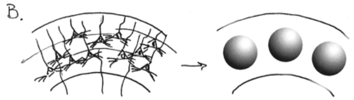
Jespersen SN Neuroimage 2018

NODDI - SMT - WMTI

GM + WM

NODDI

- fin : intraneurite (dendrites or neurons) volume factions, neuron density in the voxel i.e. fraction of restricted water
- ODI : orientation dispersion index, fanning of the fibers
- fiso : isotropic volume fraction (free water i.e. csf)



SMT

- intra : intraneurite (dendrites or neurons) volume factions,
- Intrinsic water diffusivity : diff, intra-axonal diffusivity
- Extraneurite mean diffusivity : extramd, extra-axonal mean diffusivity high in CSF
- Extraneurite transverse diffusivity : extratrans, extra-axonal transverse diffusivity

Similar assumptions…

WM

WMTI

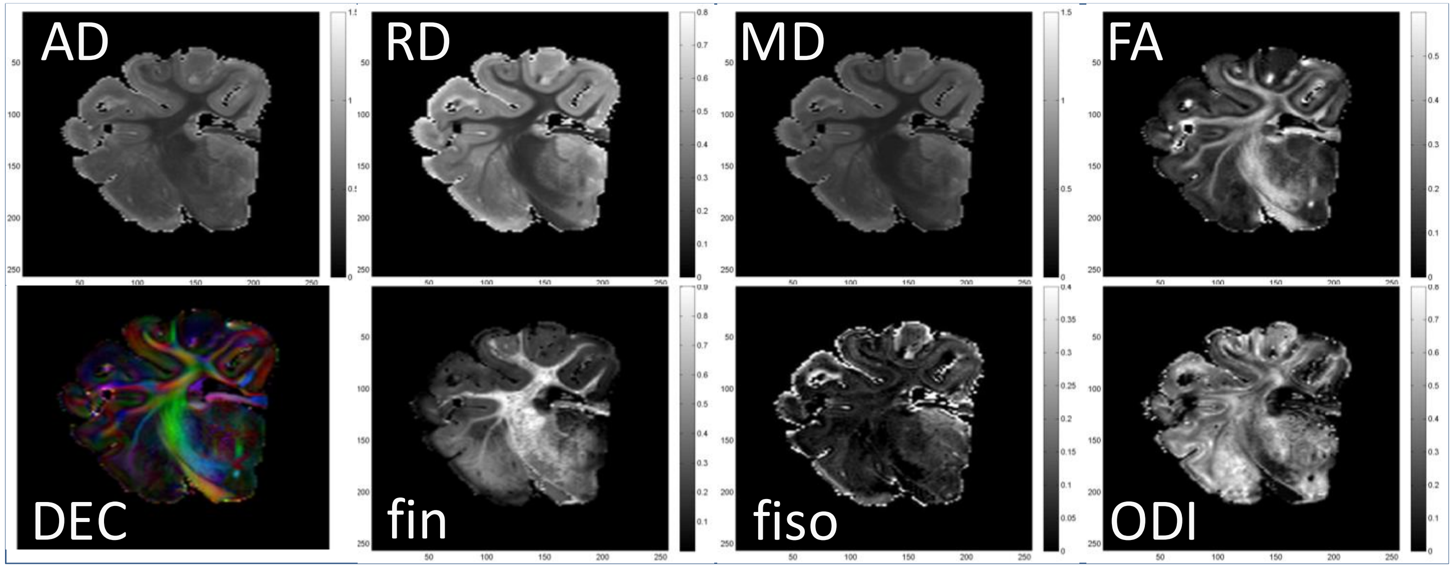
- f : intraneurite (dendrites or neurons) volume factions, neuron density in the voxel i.e. fraction of restricted water
- C2 = $(\cos\Psi)^2$ ←→ close to 1 when $\Psi=0°$, close to 0 when $\Psi=90°$… fanning
- Da : Diffusivity intra-axonal
- Depar : Diffusivity extracellular – parallel
- Deperp : Diffusivity extracellular – perpendicular

Less parameters set before the fit…

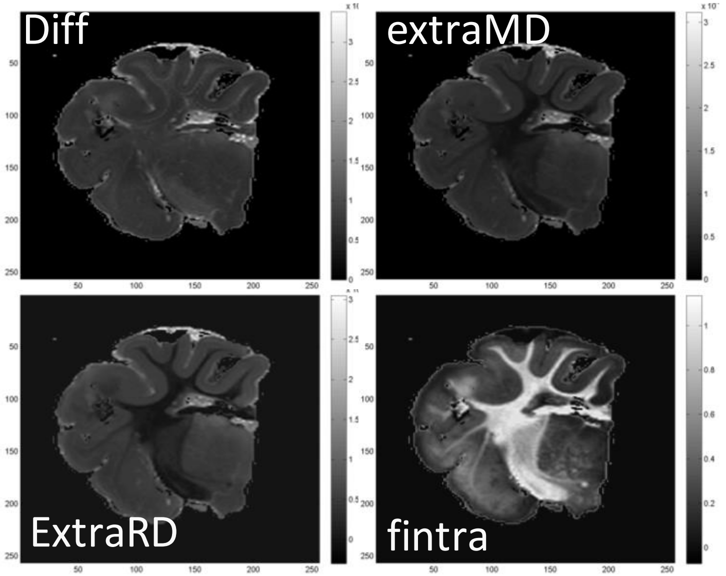
More demanding…

NODDI - SMT - WMTI

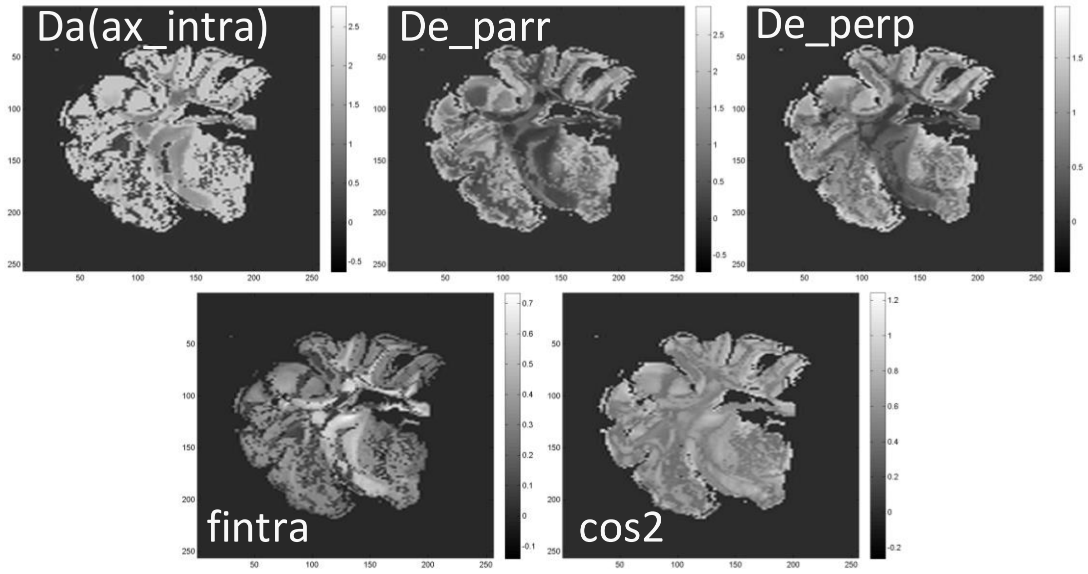
NODDI



SMT



WMTI



Van de Looij Y unpublished results

Overview

10. Applications

Ischemia

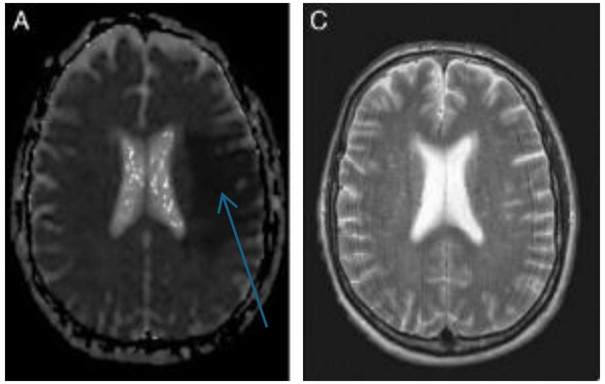
DTI technic more sensitive that conventional MRI (T_1/T_2) to catch microstructure changes:

1990-1991: cat, Moseley et al. ➔ ↓ ADC very early post ischemia (min) whereas hours for conventional MRI

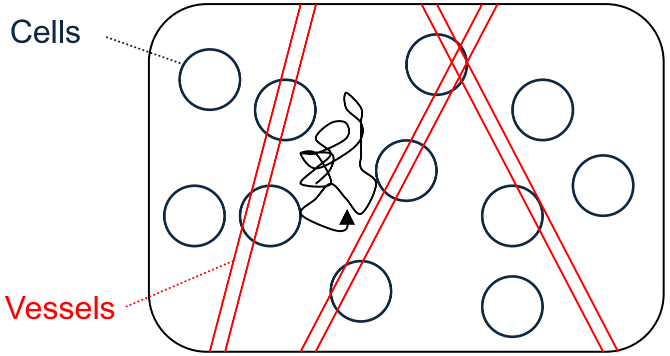
1996: confirmation in humans with rapid ↓ ADC whereas it takes hours to see something on T_2W MRI. (Sorensen G et al.)

Why edema is a so good candidate?
Cerebral edema: Accumulation of excessive fluid (including water) in the substance of the brain intra-cellular (cytotoxic) and/or extra-cellular space (vasogenic)

- **DTI allows early detection of post-ischemia or post-trauma cytotoxic edema.**
- **Not detectable by other non-invasive technics.**



Interpretation of ADC: mobility



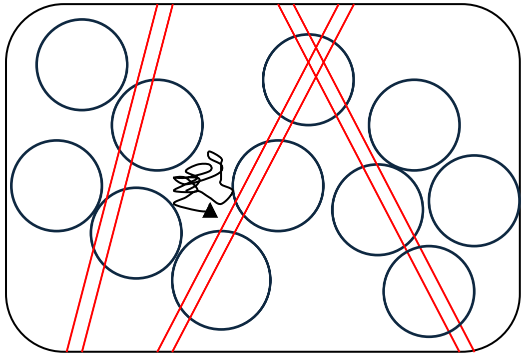
Healthy tissue

↓

Extracellular mobility
« normal »

↓

ADC
« normal »



No BBB breakdown

Cellular swelling

Cellular edema

↓

Extracellular mobility reduced

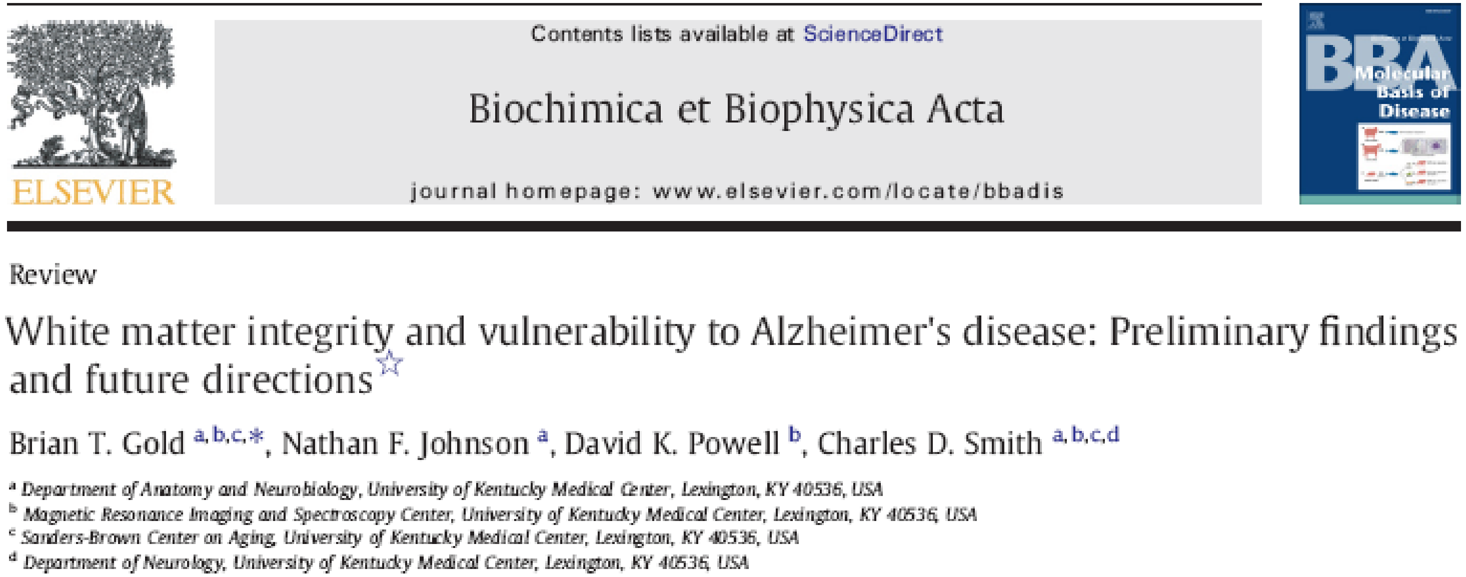
↓

Decrease of ADC

↑ of the tortuosity due to cellular swelling BUT with b=1000, DW Signal mainly intracellular??? Or, layer of water molecules bound (slow D) to the inflating cell membrane surface ↑ with swelling

Jelescu I NMR in Biomed 2014

Alzheimer disease



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journal homepage: www.elsevier.com/locate/bbadis

Review

White matter integrity and vulnerability to Alzheimer's disease: Preliminary findings and future directions ☆

Brian T. Gold [a,b,c,*], Nathan F. Johnson [a], David K. Powell [b], Charles D. Smith [a,b,c,d]

[a] Department of Anatomy and Neurobiology, University of Kentucky Medical Center, Lexington, KY 40536, USA
[b] Magnetic Resonance Imaging and Spectroscopy Center, University of Kentucky Medical Center, Lexington, KY 40536, USA
[c] Sanders-Brown Center on Aging, University of Kentucky Medical Center, Lexington, KY 40536, USA
[d] Department of Neurology, University of Kentucky Medical Center, Lexington, KY 40536, USA

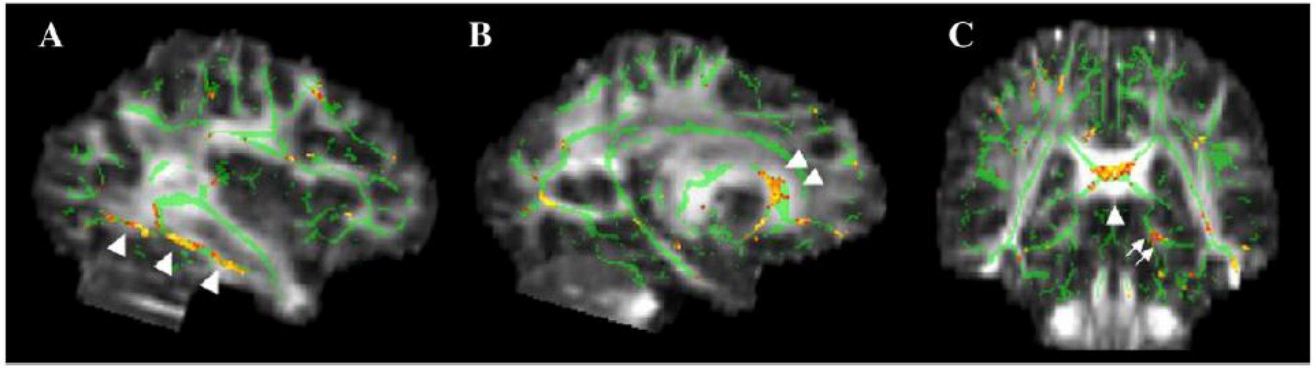
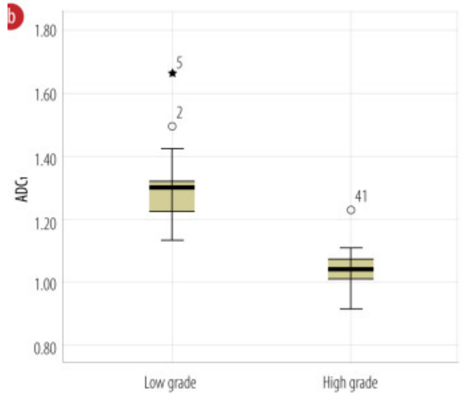


Fig. 3. Regions of decreased fractional anisotropy in normal, high AD-risk subjects. The anatomic underlay used for illustration is the MNI-space registered target fractional anisotropy (FA) image. The registered average FA skeleton is represented in green. Warmer colors on red-orange scale indicate higher t-values of FA decreases for the high AD-risk group compared to low AD-risk group. The patterns of FA decreases indicated by the arrowheads correspond to the inferior fronto-occipital fasciculus (A) and inferior fronto-occipital fasciculus/uncinate fasciculus (B). Decreased FA in the high AD-risk group was also evident in the splenium of the corpus callosum (C; single arrowhead) and the posterior cingulum bundle on the left (C; double arrowheads).
Adapted from Smith et al. (2010) with permission.

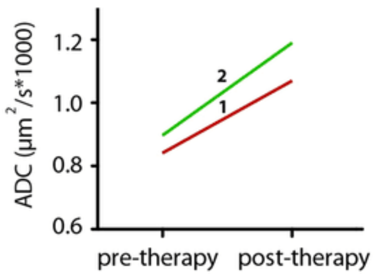
Tumors



Characterization of the tissues low grade / high grade glioma [1]

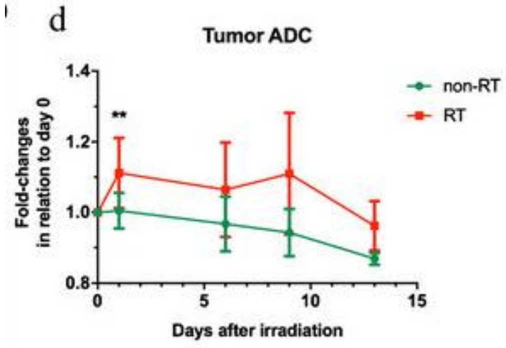
+grade Tumors: ↓ ADC, why?

- High cellularity
- Tissue Disorganization
- Increase of the tortuosity



Treatment monitoring (radio- or chemotherapy) [2]

- Treatment has an effect ➔ ↑ADC
- Differentiation between non perfused but viable tissue and necrotic tissue

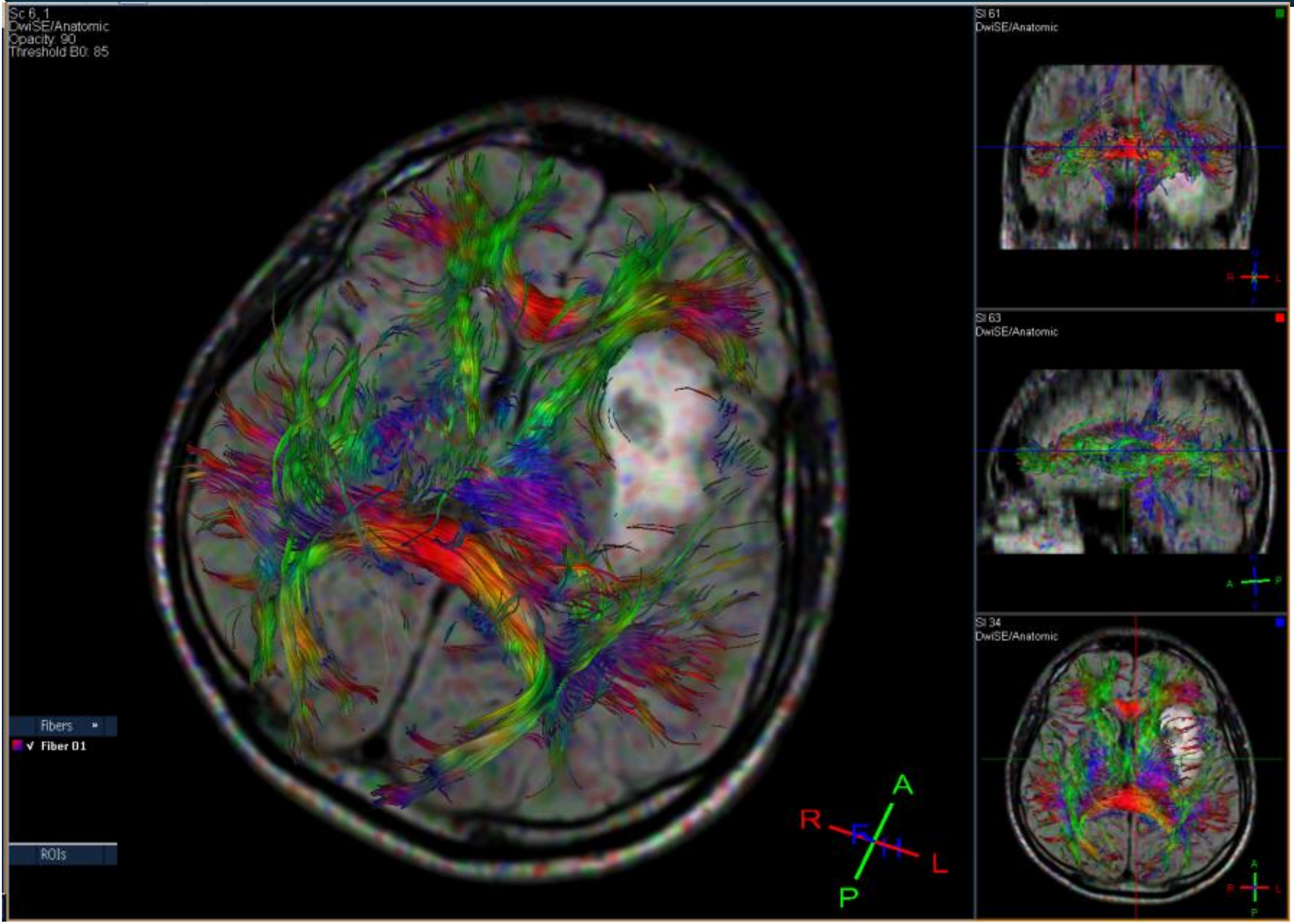


Differentiation of the changes post-therapy and residual

- ↓ ADC in the tumor whereas ↑ADC in the post-treatment induced vasogenic edema [1]

[1] Jakab A Neuroradiology 2010, [2] Awasthi R. J Comput Assist Tomo 2010

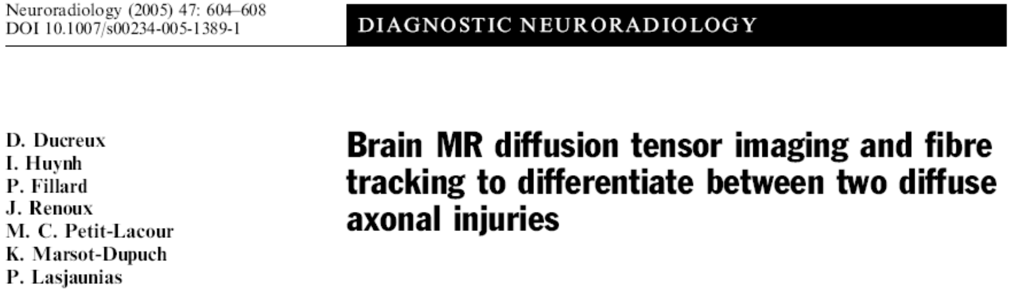
Tumors



Map of the distortions of the white matter due to cerebral tumor
➔ Help for neurosurgery
➔ Regeneration of the fibers after surgery

Bammer R EJR 2003

Clinic: traumatic brain injury



Neuroradiology (2005) 47: 604–608
DOI 10.1007/s00234-005-1389-1

DIAGNOSTIC NEURORADIOLOGY

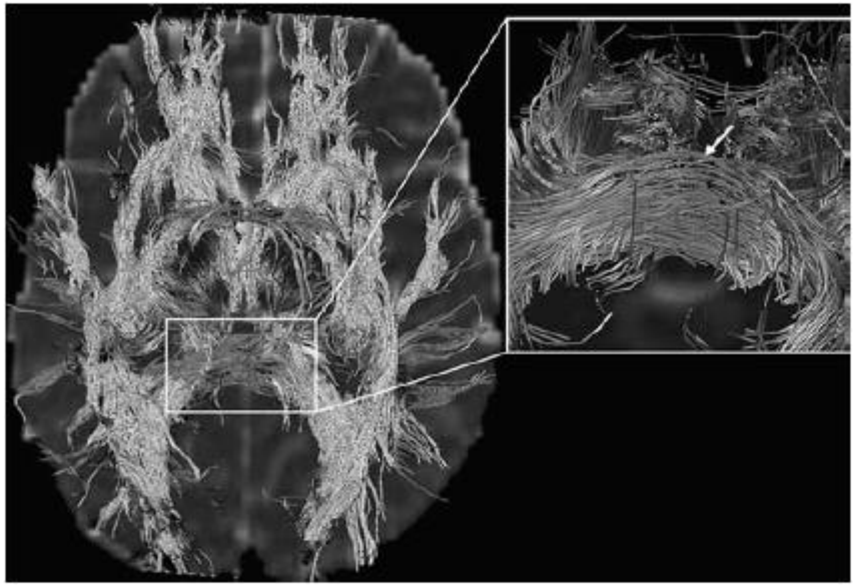
D. Ducreux
I. Huynh
P. Fillard
J. Renoux
M. C. Petit-Lacour
K. Marsot-Dupuch
P. Lasjaunias

Brain MR diffusion tensor imaging and fibre tracking to differentiate between two diffuse axonal injuries

Case reports: 2 men, 19 y, car crash

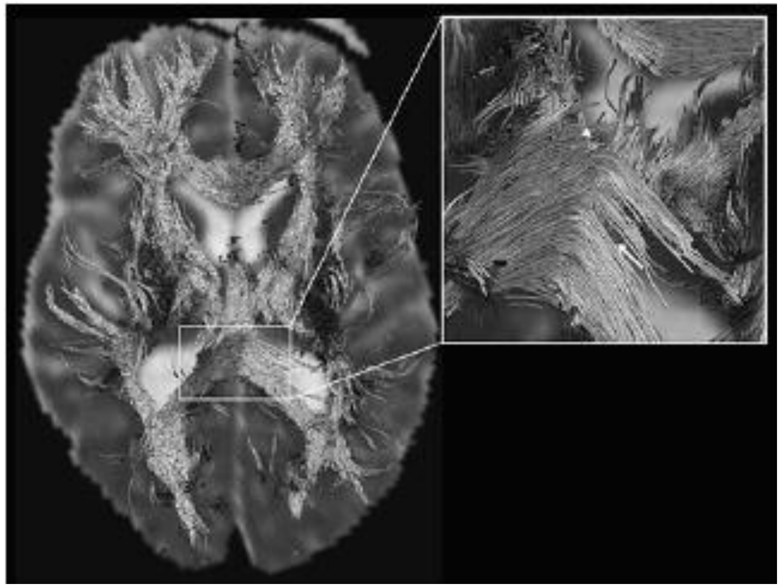
Decrease of FA in the injured WM

GCS = 7, DTI-Tract. 2D post trauma.



FT: no alteration of the CC fibers

GCS = 4, DTI-Tract. 1D post trauma.

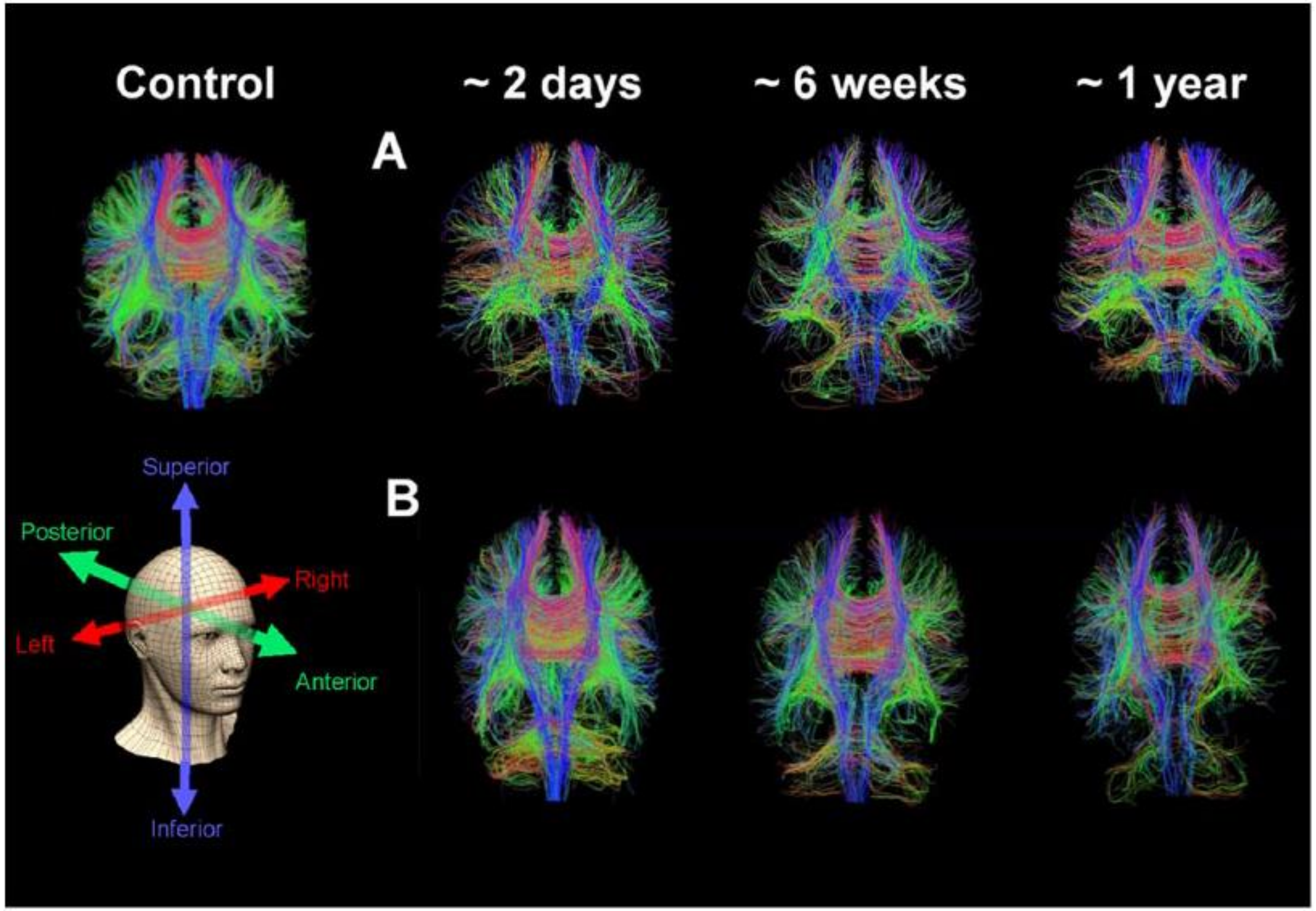


FT: alteration of the CC fibers

Glasgow coma scale ranges from 3 to 15 based on eye, verbal, motor response.

No direct information about the connectivity following TBI <u>BUT</u> predictive tool after severe TBI… not so easy

Clinic: traumatic brain injury



Fiber tracking 2d, 6w and 1y after severe TBI

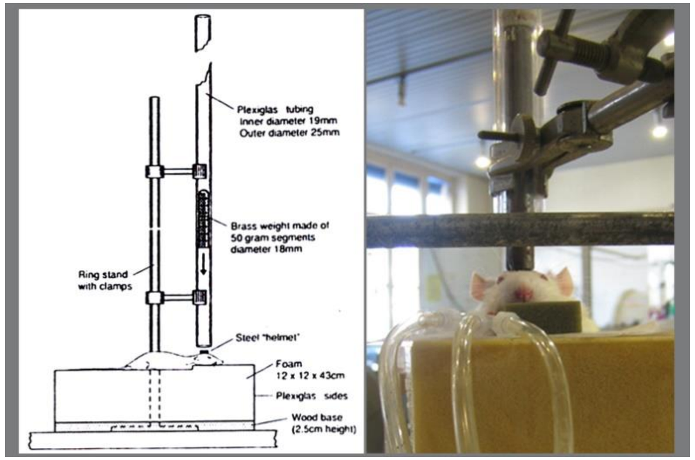
A: WM regeneration

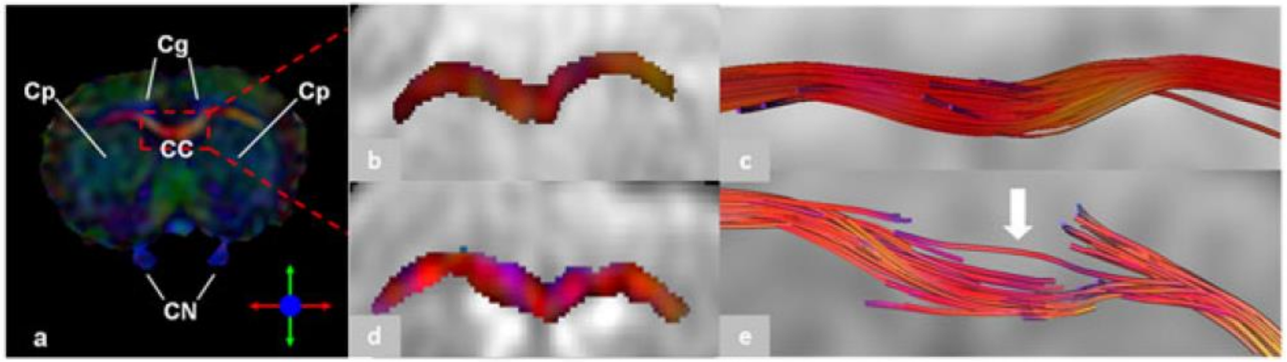
B: WM loss

Newcombe et al. Neurorehabilitation and Neural Repair 2015

Traumatic brain injury

Dropping a 500 g metallic mass from a height of 1.5 m onto a metallic disc positioned on the center of the animal skull (diffuse the injury and avoid skull fracture) ➔ whiplash





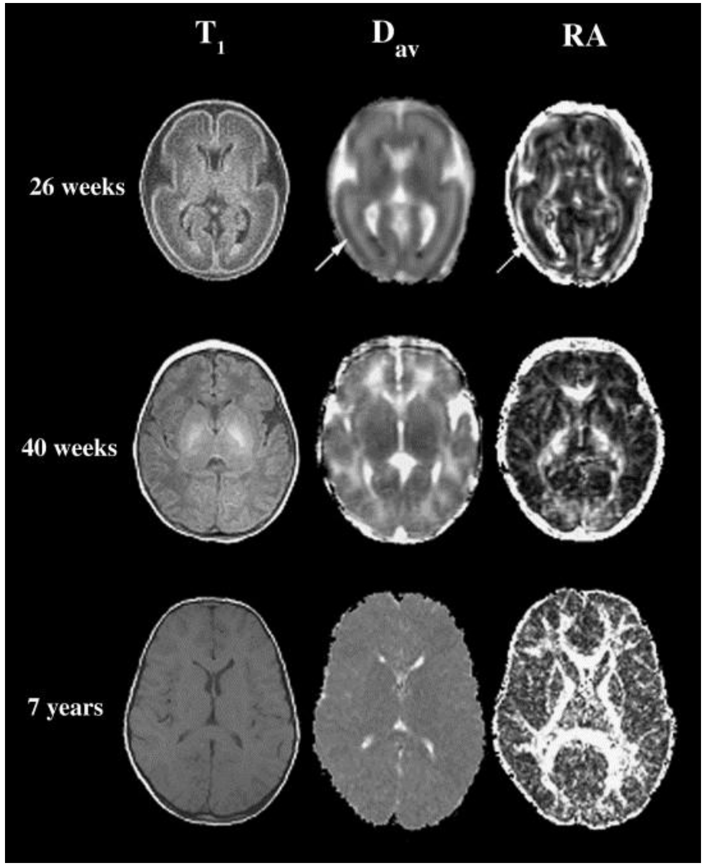
MD/ADC ➔ Early detection and characterization of the brain edema

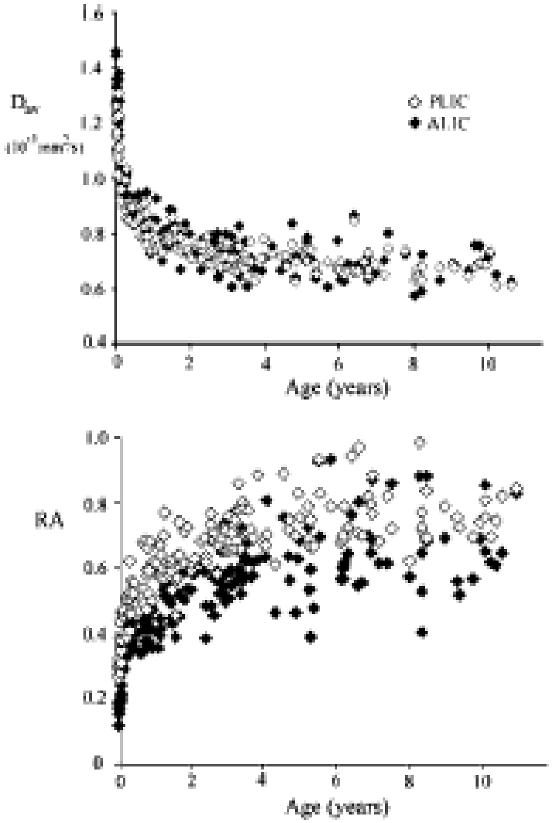
FA ➔ detection of diffuse axonal injuries

Fiber tracking ➔ catch place of the lesions in the WM

Van de Looij et al. NMR in Biomedicine 2011

White Matter development





↓ADC and ↑FA : Myelination/ Decrease cerebral water content

BUT

FA increases before myelination process begins ➔ Other processes influence diffusion

Hüppi PS, Ped Res 1998

Cortical development

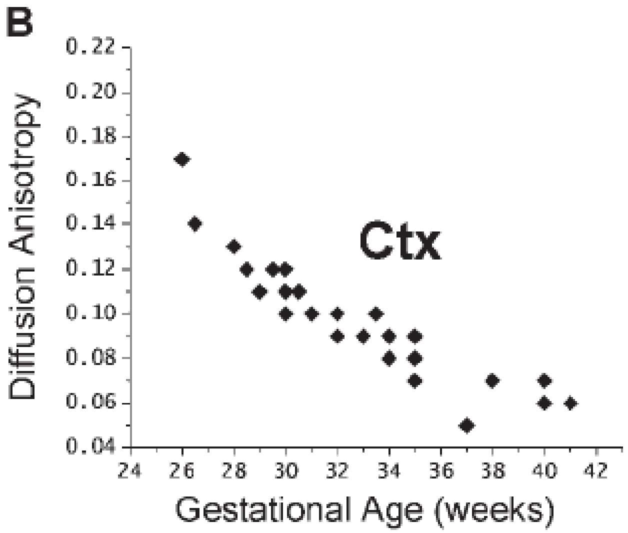
In the cortex :

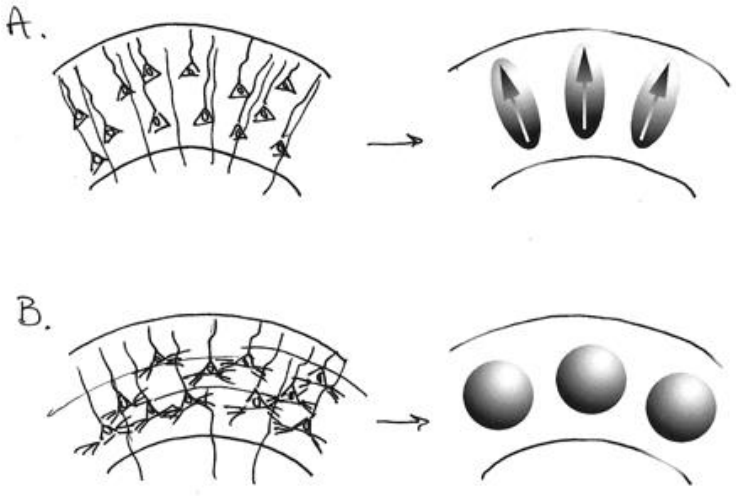
FA ↑ 15 to 27 weeks of gestation

➔ Active neuronal migration along radial glia

FA ↓ 32 weeks of gestation to term

➔ Neocortical maturation with dendritic arborization

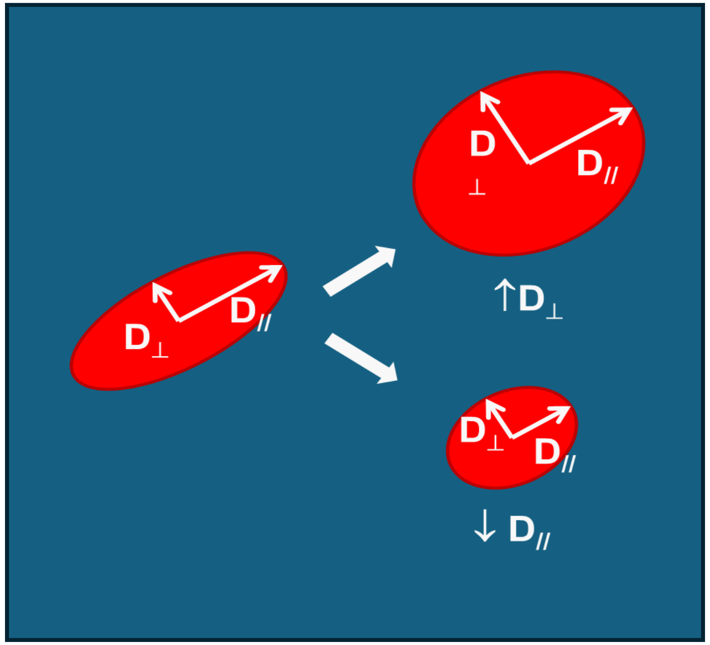




McKinstry RC Cereb Cortex 2002

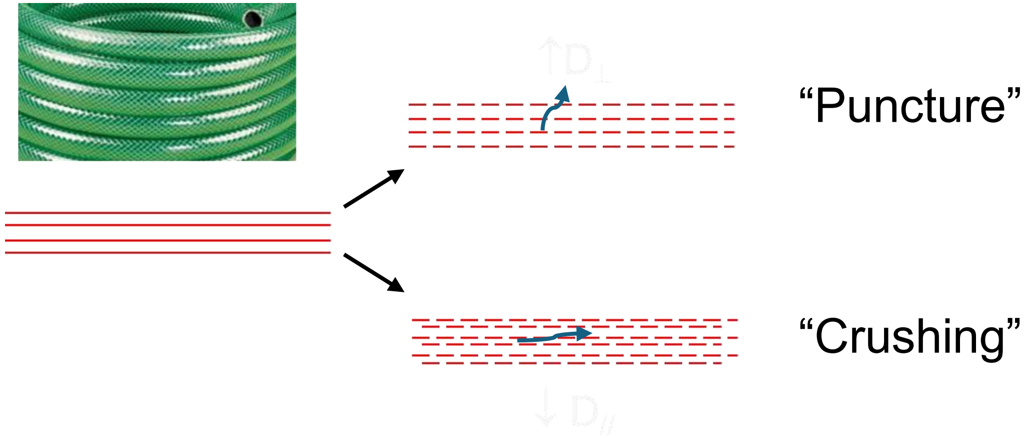
FA changes interpretation

FA change can be due to axial or radial diffusivity change:



Myelination defect

Diffuse axonal injuries



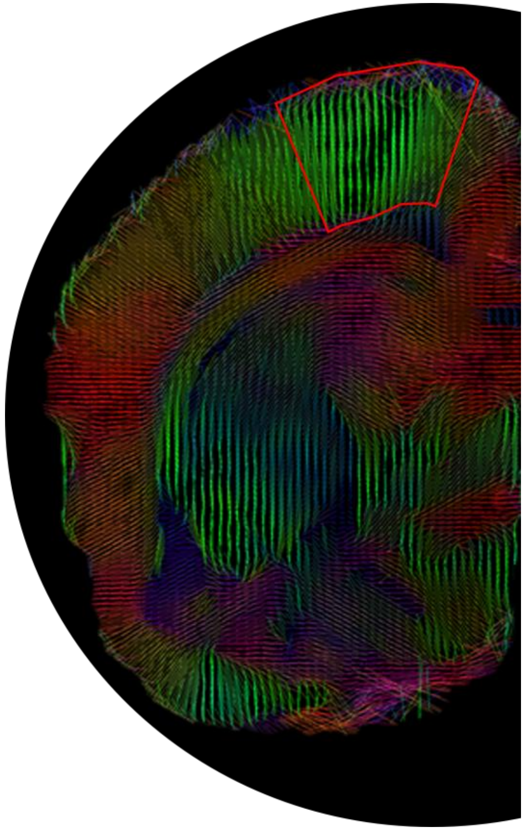
Lack of specificity ➔ Multi-compartment models

What about NODDI specificity?

Examine the associations between NODDI and DTI parameters with histology

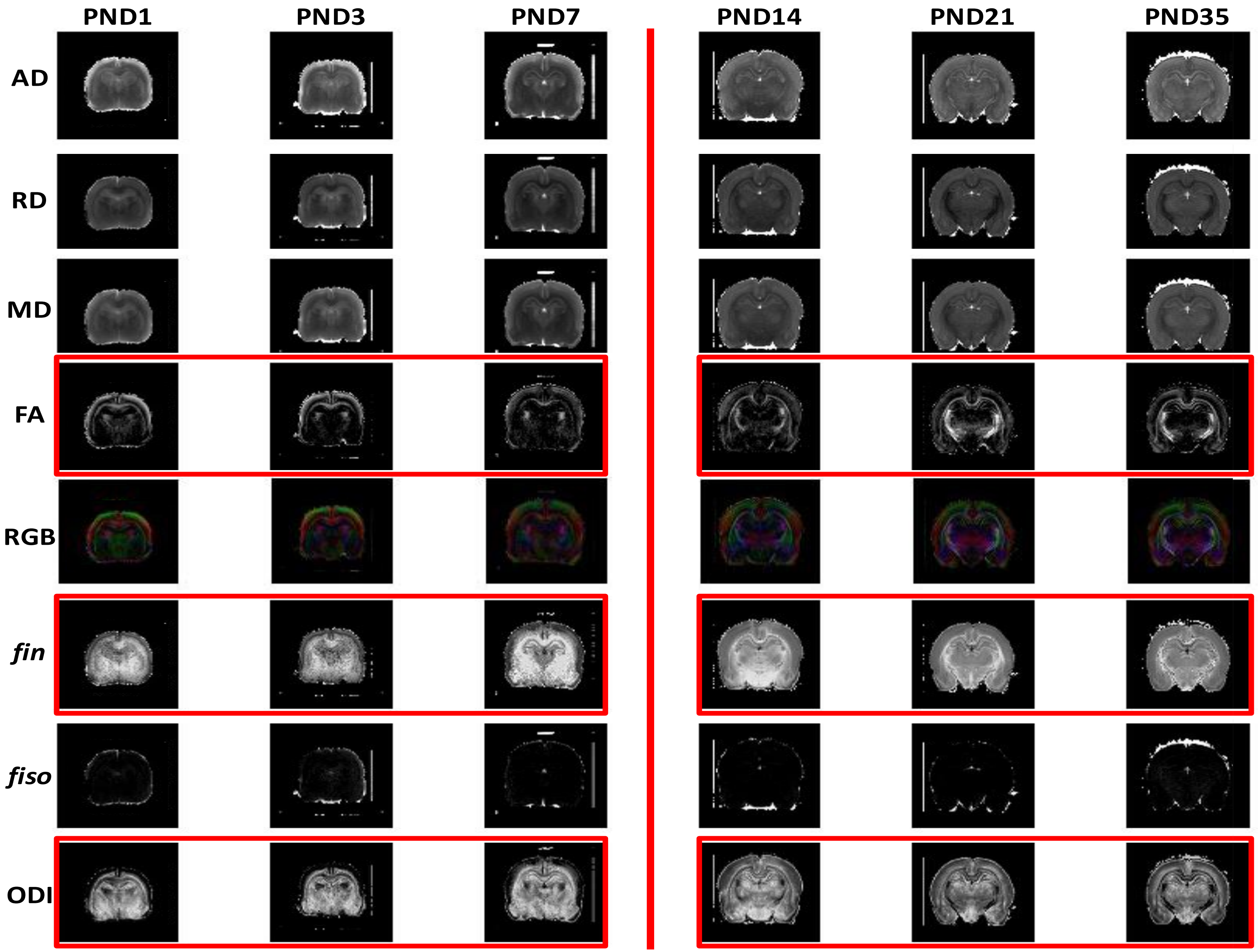
- *Neuronal dendritic complexity WITH Orientation Dispersion Index (ODI)*
- *Cellular process density WITH Neurite Density Index (fin or NDI)*

in the developing cerebral cortex of the neonatal rat



White P., **van de Looij Y.** et al. in preparation

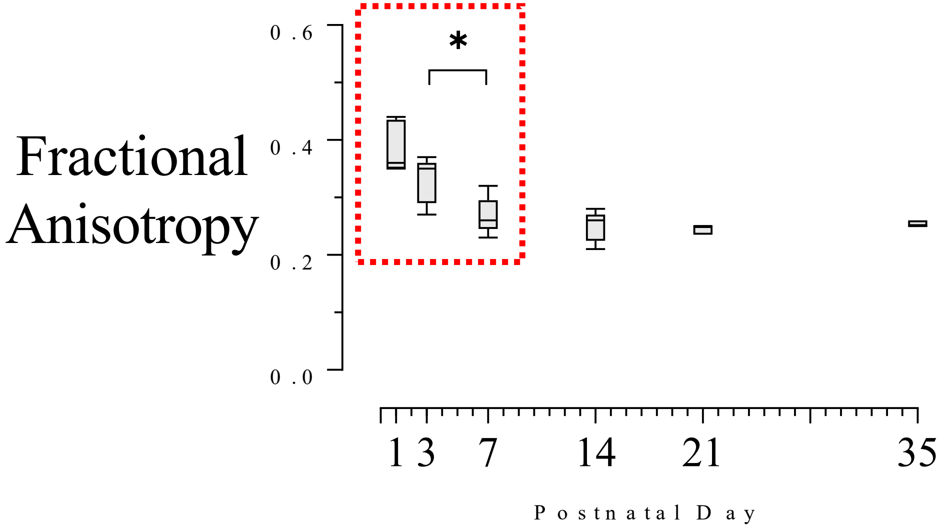
Longitudinal MRI



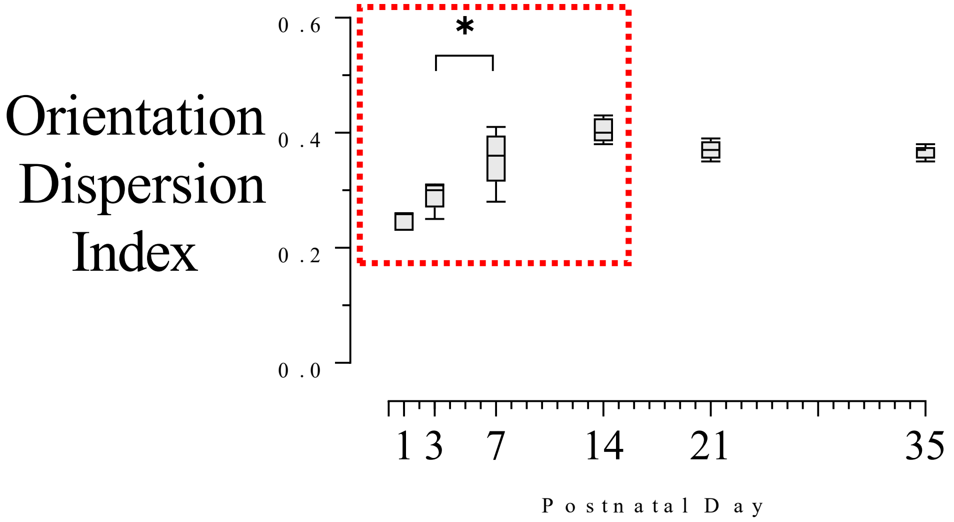
White P., **van de Looij Y.** et al. in preparation

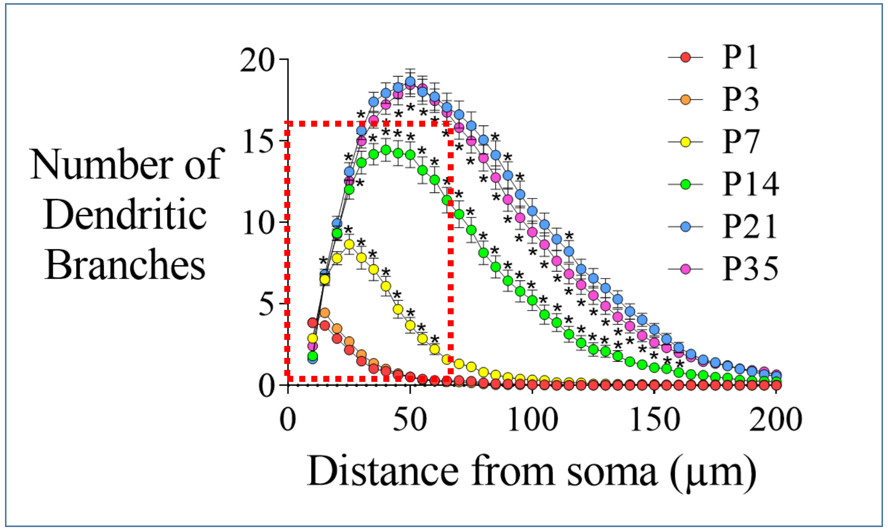
Neuronal Dendritic morphology

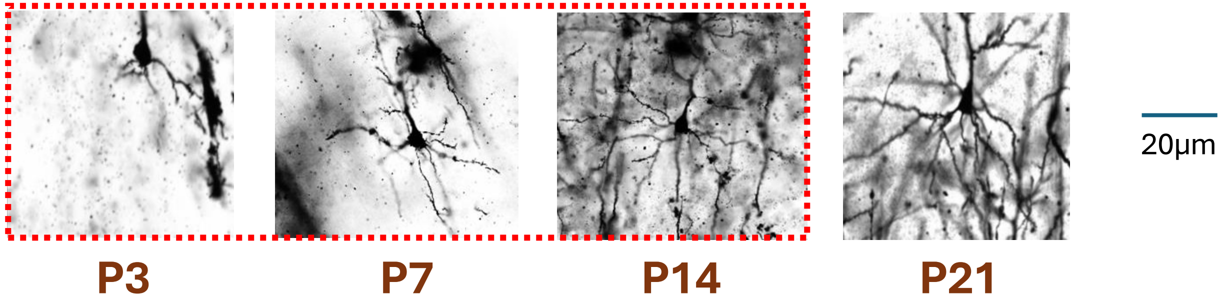
DTI



NODDI







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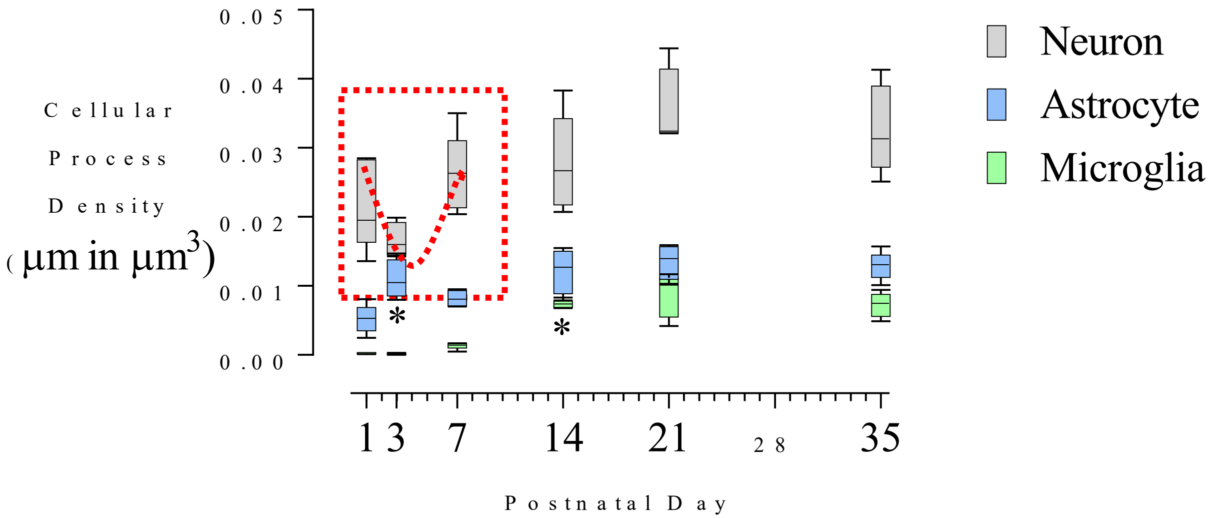
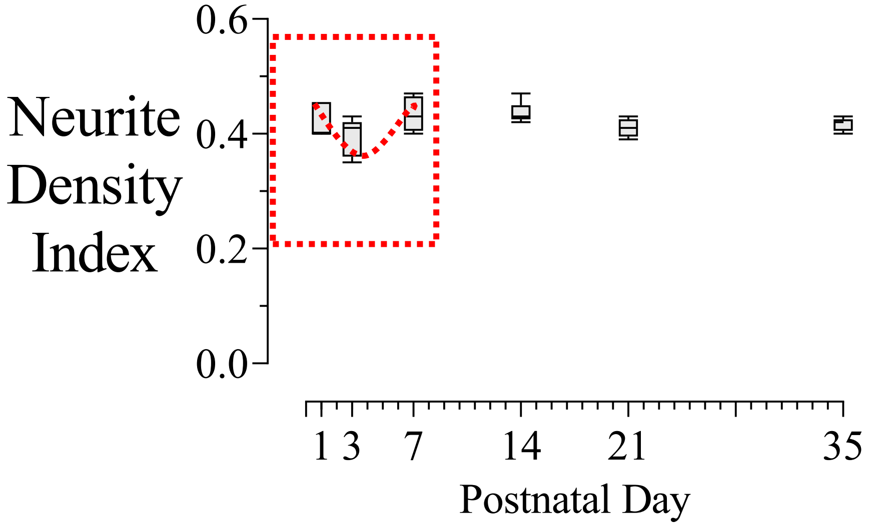
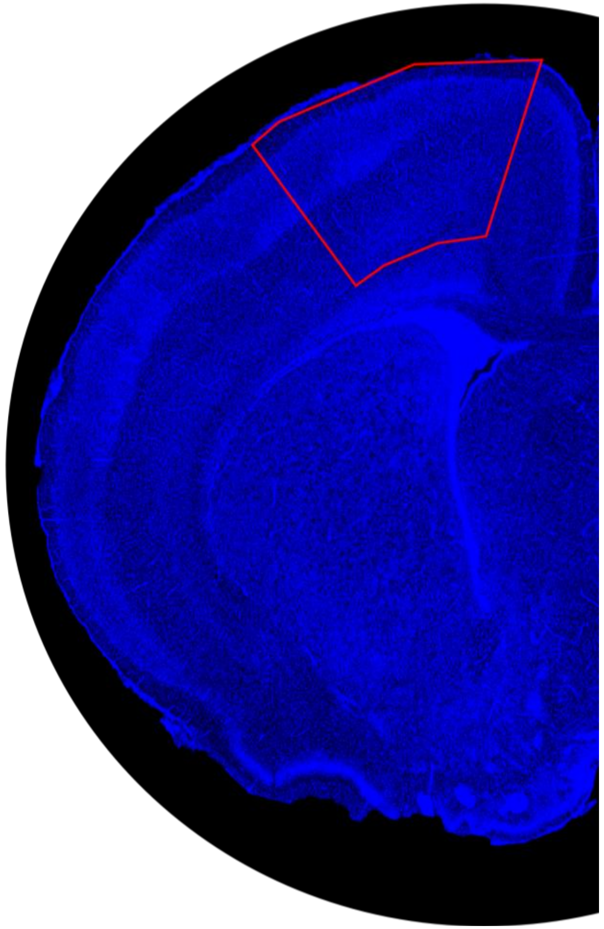
Dendritic density

Neuronal dendritic density



NODDI Neurite density





White P., **van de Looij Y.** et al. in preparation

NODDI specificity

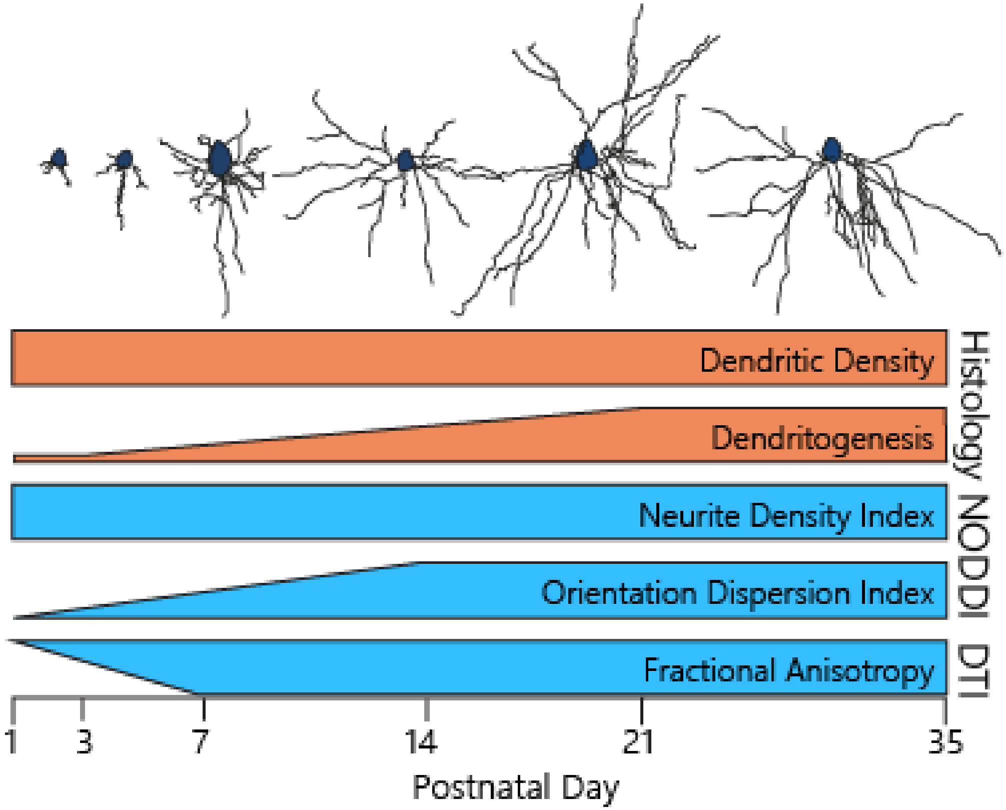
- **NODDI and DTI have similar sensitivity to cellular changes in cortical development.**

  ↳ FA and ODI reflect dendritic growth

- **NODDI is specific to cortical tissue microstructure**

  ↳ ODI reflects neuronal dendritogenesis

  NDI reflects neuronal dendritic density



White P., **van de Looij Y.** et al. in preparation

Conclusion

- DTI is a powerful tool for neuroimaging
- Probe non-invasively brain microstructures
- But not without pitfalls…
  - Exact origin not fully understood (compartmentation…)
  - Modeling not yet ideal
  - Important to choose the right sequences/parameters as a function of the application

Thank you for your attention....

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h e d s

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