

Diffusion in Python

Rafael Neto Henriques

Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, PT

Champalimaud Centre for the Unknown





- Free and open source software project for computational anatomy in Python.
- It focuses on diffusion MRI analysis but also contains algorithms that are generic for medical imaging e.g. denoising, registration.
- DIPY is an international project which brings together scientists across labs and countries ...
- ... to share their **state-of-the-art code** and expertise in the same codebase, accelerating scientific research in medical imaging.





 More than 100 contributors from more than 30 Universities & Institutions

Dipy Installation

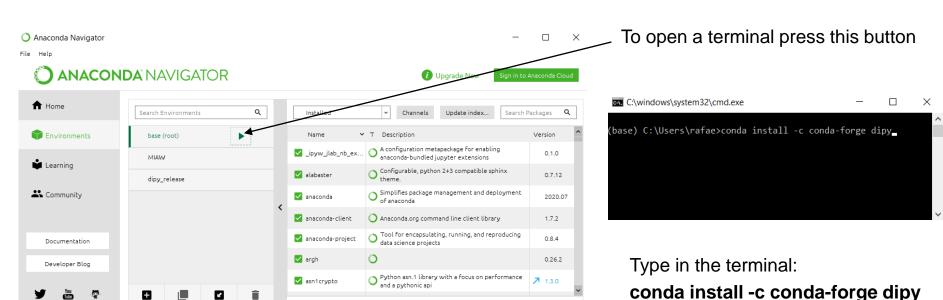


- To install all python dependencies, we recommend to install first anaconda (https://www.anaconda.com/).
- After Anaconda installation, open the Anaconda Navigator App

Remove

Create

325 packages available



Dipy Installation



• Some of the visualization methods require the <u>FURY</u> library and this can be installed separately (for the time being only on Python 3.4+):

pip install fury

 You can also install dipy using pip, for this you need to install first some of dipy dependencies:

> pip install nibabel pip install dipy pip install fury



Why Diffusion MRI?

Rafael Neto Henriques

Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, PT

Motivation – why diffusion MRI?

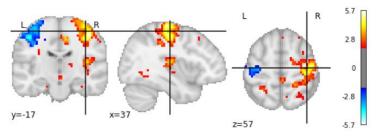
Diffusion MRI

MRI allows the imaging the structure and function of entire tissues non-invasively

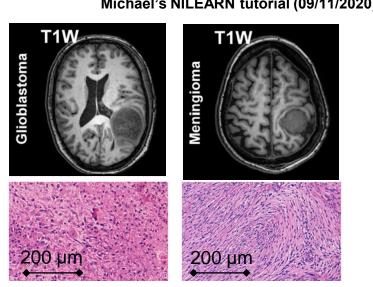
Typical resolution: 1-2 mm

But we may be interested in information related to lower resolutions

- Tissue maturation (myelination and axonal pruning)
- Tissue degeneration (axonal loss and demyelination)
- Characterization of pathologies

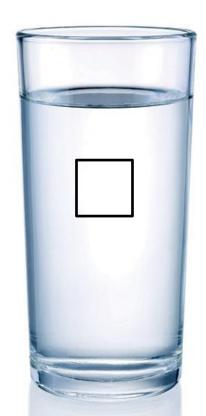


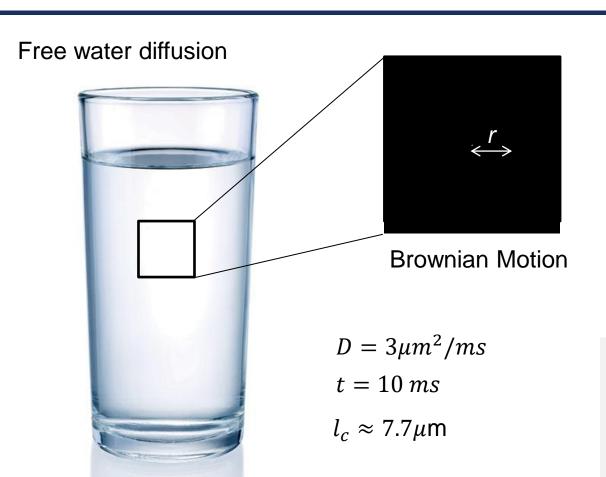
Michael's NILEARN tutorial (09/11/2020)



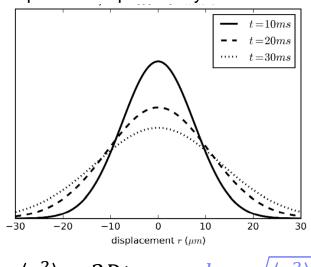
Adapted from Szcepankiewicz et al., Neuroimage 2015

Free water diffusion





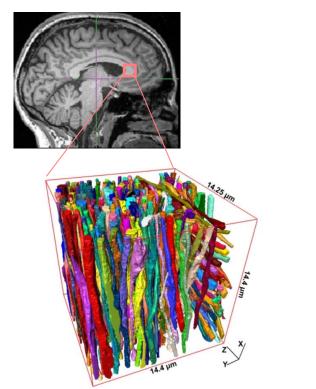
Displacement probability distribution



$$\langle r^2 \rangle = 2Dt$$
 $l_c \equiv \sqrt{\langle r^2 \rangle}$

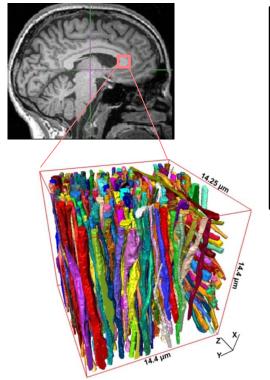
- Isotropic
- Gaussian

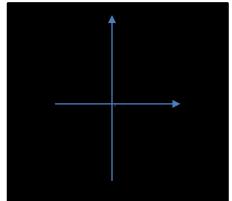
Diffusion in biological tissues



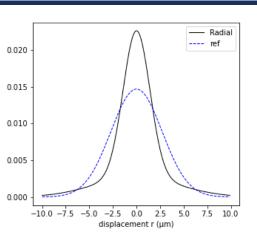
Adapted from Abdollahzadeh et al., Sci Rep 2019

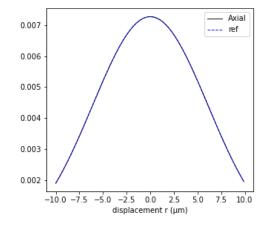
Diffusion in biological tissues





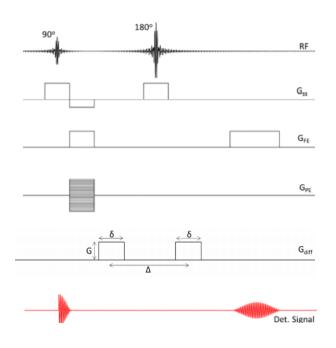
- Anisotropic
- Non-Gaussian





Adapted from Abdollahzadeh et al., Sci Rep 2019

Diffusion-weighted Magnetic Resonance Imaging (dMRI)



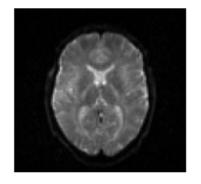


Illustration of a pulse diagram for a standard spin-echo sequence

Diffusion-weighted Magnetic Resonance Imaging (dMRI)

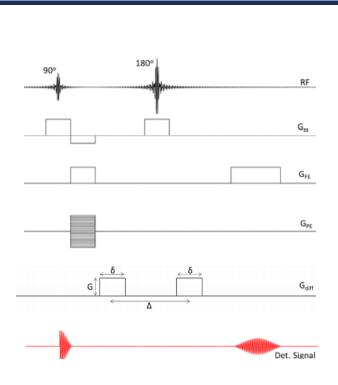
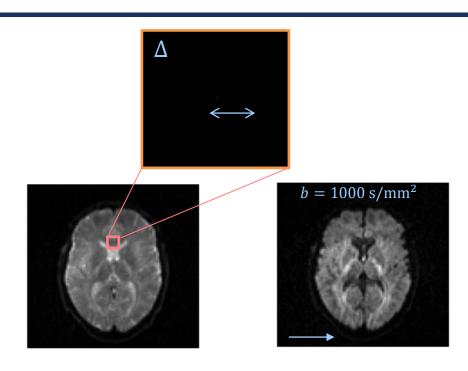


Illustration of a pulse diagram for a standard spin-echo sequence



$$S(b, \mathbf{n}) \approx S_0 \exp(-bD(\mathbf{n}))$$

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



Reconstructing DTI using Dipy

Rafael Neto Henriques

Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, PT

Diffusion Tensor Imaging (DTI)

 Diffusion Tensor Imaging (DTI) models diffusion in each voxel using a 2nd order tensor:

Basser et al. MRM 1994

$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

Diffusion Tensor

For the voxel sample

Axial diffusivity (AD) is the diffusion parallel to "fibres"

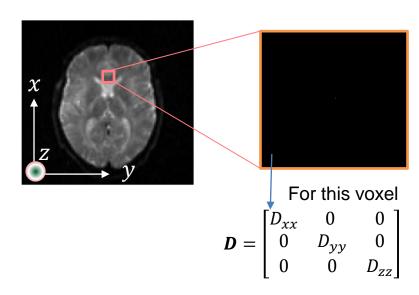
$$AD = D_{xx}$$

Radial diffusivity (RD) is the diffusion perpendicular to "fibres"

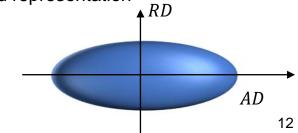
$$RD = (D_{yy} + D_{zz})/2$$

Mean diffusivity (MD) is the diffusivity averages across directions

$$MD = (D_{xx} + D_{yy} + D_{zz})/3$$



Ellipsoid representation



Diffusion Tensor Imaging (DTI)

Diffusion Tensor Imaging (DTI) models diffusion in each voxel using a 2nd order tensor:

Basser et al. MRM 1994

$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

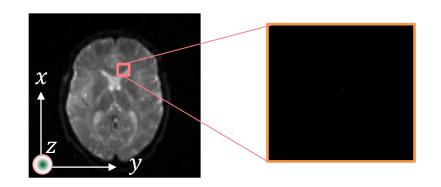


AD, RD and MD can be more generally computed from eigen-value decomposition

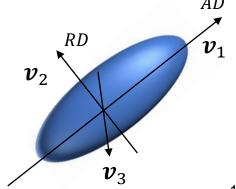
$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix} = \begin{bmatrix} \boldsymbol{v}_1 & \boldsymbol{v}_2 & \boldsymbol{v}_3 \end{bmatrix} \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \begin{bmatrix}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

$$AD = \lambda_1$$
 $RD = (\lambda_2 + \lambda_3)/2$ $MD = (\lambda_1 + \lambda_2 + \lambda_3)/3$

$$MD = (\lambda_1 + \lambda_2 + \lambda_3)/$$



Ellipsoid representation

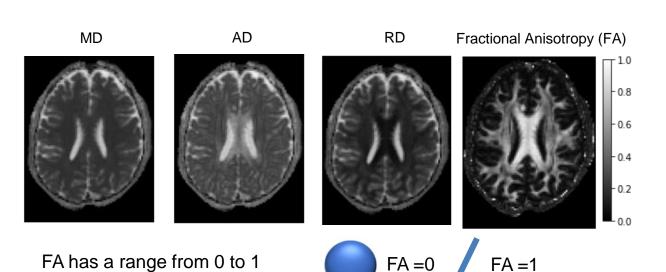


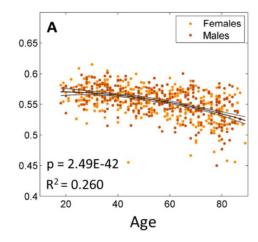
Diffusion Tensor Imaging

 Diffusion Tensor Imaging Model involves the fitting of the model:

$$S(b, \mathbf{n}) = S_0 \exp \left(-b\mathbf{n} \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix} \mathbf{n}^T\right)$$

- In addition to S_0 acquisition, it requires at least the acquisition of six direction for a non-zero b-value





FA is typically used as a marker of tissue maturation or degeneration



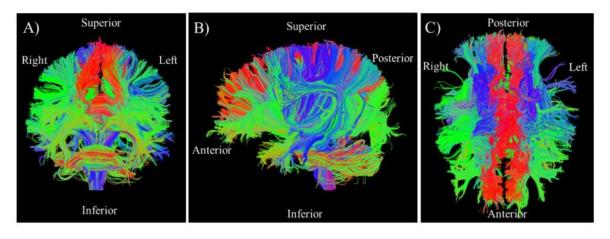
Introduction to DTI tractography

Rafael Neto Henriques

Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, PT

Tractography

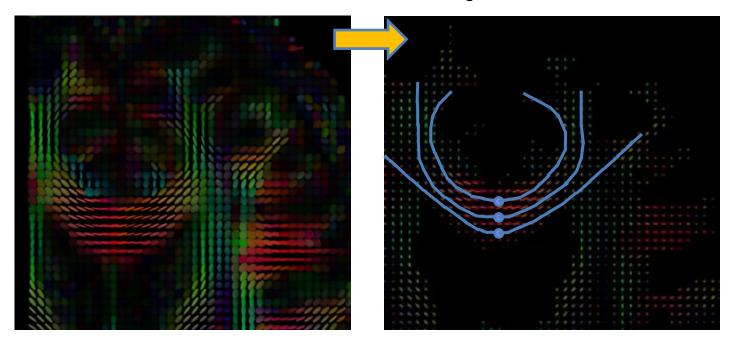
 Tractography is the 3D reconstruction of "white matter" bundles from dMRI data.



- In this workshops, two types of local tracking algorithms will be described:
 - Deterministic Tractography
 - 2. Probabilistic Tractography

Deterministic Tractography

1. Extract directions from a given model



- 2. Define streamline starting points seeds
- 3. Tracking stopping criterium (e.g.):
- Reaching out of brain voxels
- Reaching grey matter
- Reaching voxels with low FA
- Reaching voxels with discrepant directions

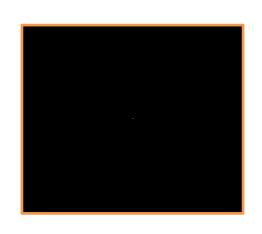
4. Pathways propagation algorithm

Resolved pathways does not correspond to "real" white matter fibres. Pathways are also referred to as **streamlines**.

Probabilistic Tractography

- Probabilistic Tractography directions are sampled from orientation distribution functions (ODF)
 - ODF can be calculated from the displacement probability distribution

$$ODF(\mathbf{n}) \equiv \frac{1}{Z} \int_0^\infty P(s\mathbf{n}, \Delta) s^2 ds$$





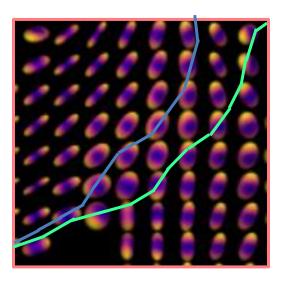
$$ODF(n) = \frac{1}{4\pi |\mathbf{D}|^{1/2}} \left(\frac{1}{n^T \mathbf{D}^{-1} n}\right)^{3/2}$$



Probabilistic Tractography

 Tractography is the 3D reconstruction of "white matter" bundles from dMRI data.







High angular resolution diffusion imaging

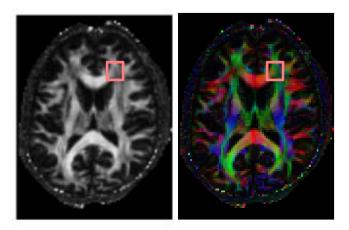
Rafael Neto Henriques

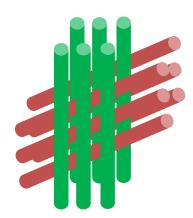
Champalimaud Research, Champalimaud Centre for the Unknown, Lisbon, PT

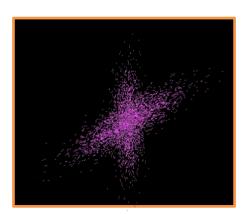
Propagator

- DTI models dMRI signals as an 2nd order tensor which can be used to infer the main direction of well aligned structures.
- DTI fails to represent the directionality of more complex structures

Crossing fibre examples





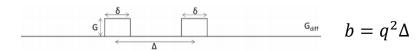


 The displacement probability distribution (Propagator), however, can provide more complete information of the direction of structures

Diffusion Spectrum Imaging

 Diffusion Spectrum Imaging (DSI) is a model free approach to reconstruct the propagator

Narrow pulse assumption ($\delta \ll \Delta$)



$$\frac{S(\boldsymbol{q},\Delta)}{S_0} = \int P(\boldsymbol{r},\Delta) e^{-2\pi i \boldsymbol{q}^T \boldsymbol{r}} d\boldsymbol{r}, \qquad \boldsymbol{q} = q \boldsymbol{n}$$

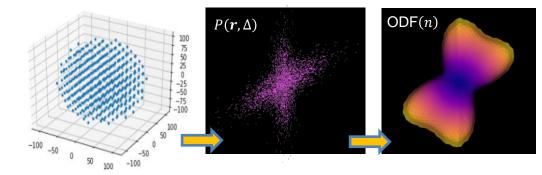


$$P(\mathbf{r}, \Delta) = F\left(\frac{S(\mathbf{q}, \Delta)}{S_0}\right)$$

$$ODF(\mathbf{n}) \equiv \frac{1}{Z} \int_0^\infty P(s\mathbf{n}, \Delta) \, s^2 ds$$

Wedeen et al. MRM 2005

 Propagator and ODF is calculated directly from signals sampled from different q vectors



- Requires a huge set of q vectors (long acquisition times),
- Requires the acquisition of high magnitudes of **q** (b-values not available in current clinical scanners)

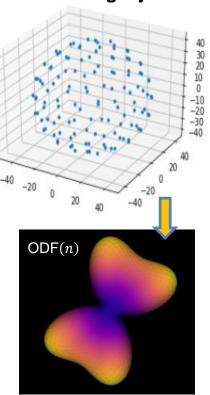
High Angular Resolution Diffusion Imaging (HARDI)

 Q-ball imaging was proposed to reconstruct the ODF from acquisition at single q vector magnitudes (single shell acquisitions)

$$P(\mathbf{r}, \Delta) = F\left(\frac{S(\mathbf{q}, \Delta)}{S_0}\right)$$

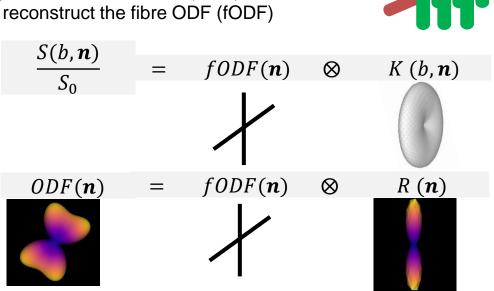
- The information of other q magnitudes is extrapolated based on model assumptions
 - E.g. assuming that along directions diffusion is Gaussian

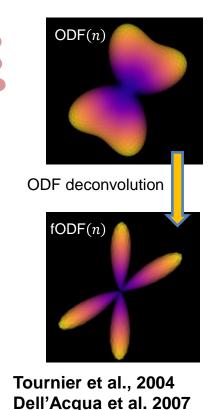
Tuch et al. MRM 2004 Aganj et al. MRM 2010



Constrained Spherical Deconvolution (CSD)

- Diffusion provides indirect inference of tissue properties.
 - ODF provides a smooth probability distribution of the direction of maximum diffusivity
- Constraint spherical deconvolution (CSD) was proposed to reconstruct the fibre ODF (fODF)





Descoteaux et al., 2009



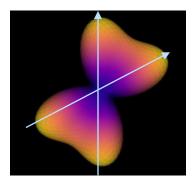
HARDI Tractography

Deterministic and Probabilistic Tractography from HARDI can be performed in a similar way than DTI tractography

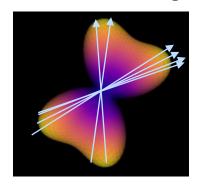
As DTI tractography it involves the following steps:

- Direction generation.
 - For deterministic tracking, directions are extracted from the ODF/fODF peaks
 - For probabilistic tracking, directions are randomly sampled according to the ODF/fODF
- 2. Define streamline seeds
- 3. Tracking stopping criterium
- 4. Pathways propagation algorithm

Deterministic direction generator



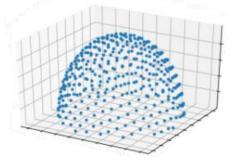
Probabilistic direction generator



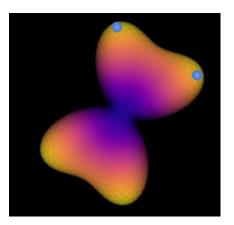
HARDI Tractography

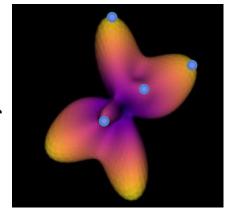
Inputs of the algorithm to detect the maximum direction

Sphere - discrete directions for maximum evaluation.



- Relative_peak_threshold threshold to remove small peaks that may be related to noise
- min_separation_angle the minimum distance between peaks





Noisy ODF



Pre-processing diffusion MRI data

Rafael Neto Henriques

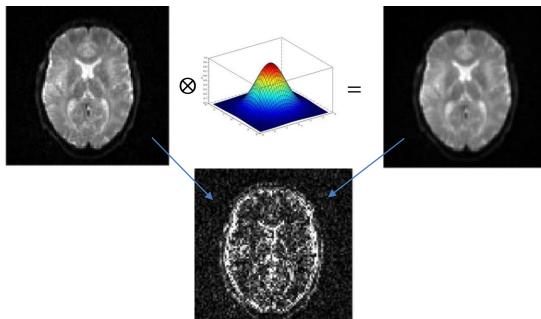
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Pre-processing diffusion MRI data

- 1. Denoising
- 2. Gibbs Artefact correction
- 3. Motion, B0 inhomogeneity, eddy currents

1. Denoising

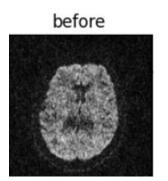
- Diffusion MRI data suffers from low SNR
 - Diffusion gradient attenuation, long echo times
- Strategies to suppress noise artefacts
 - Gaussian Smoothing

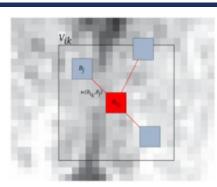


1. Denoising

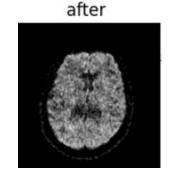
- Diffusion MRI data suffers from low SNR
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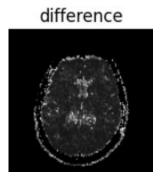
Non-local means





Coupe et al., IEEE Trans Med Imaging 2008 Coupe et al., IEEE Trans Med Imaging 2011



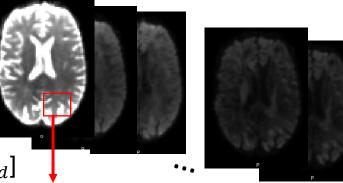


DIPY's example: <u>example-denoise-gibbs</u>

1. Denoising

- Diffusion MRI data suffers from low SNR.
 - Diffusion gradient attenuation, long echo times
- Strategies to suppress noise artefacts
 - Gaussian Smoothing

 $X [N_v \times N_d]$



Non-local means

PCA denoising

Manjón et al., 2013 Veraart et al., 2016

$$\frac{1}{N}X^{T}X = U\Lambda^{2}U^{T}$$
0 100 200 300 400 500

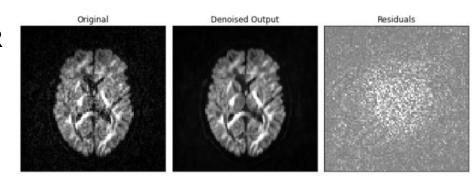
1. Denoising

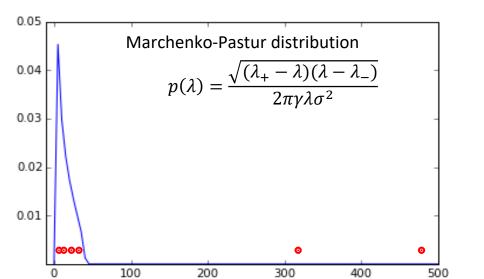
- Diffusion MRI data suffers from low SNR
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Non-local means

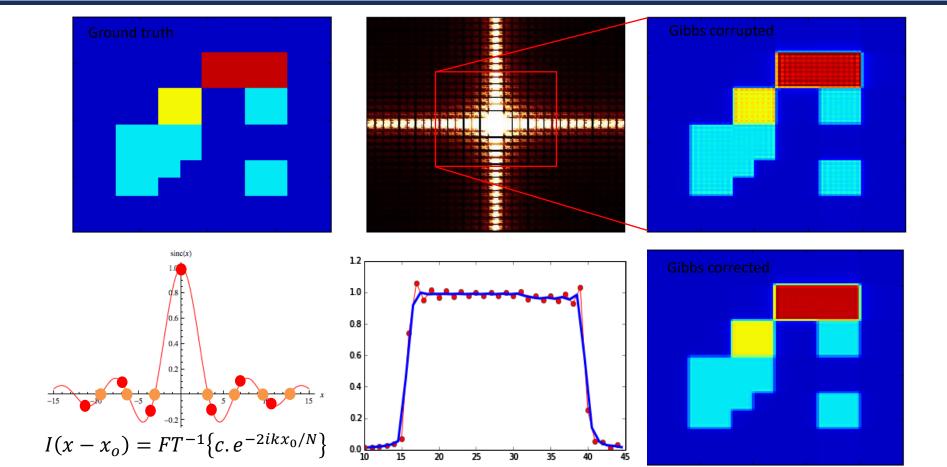
PCA denoising

Manjón et al., 2013 Veraart et al., 2016

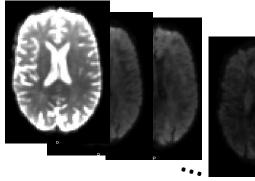


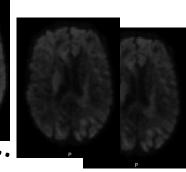


2. Gibbs Artefacts



- Diffusion MRI acquisitions involves the acquisition of several images
 - Motion Misalignments



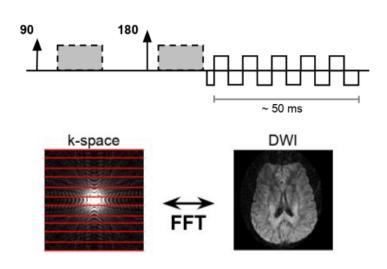


- Image Registration
 - See for example the dipy tutorials:

Affine Registration in 3D

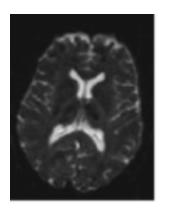
Symmetric Diffeomorphic Registration in 3D

- Diffusion captures information of water displacements in the order of the microns Head motion can happen in the order of the millimetres
- Due to its speed, the most commonly used sequence for dMRI is EPI (Echo Planar Imaging).

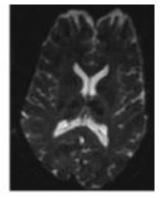


Turner et al., Radiology 1990

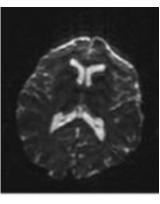
B0 inhomogeneities



Reference

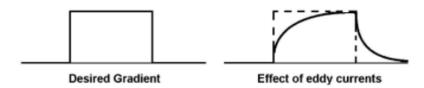


Positive blips

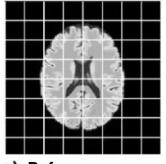


Negative blips

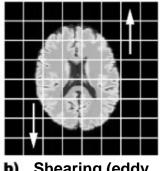
Switching ON/OFF of the strong diffusion gradients induces eddy currents



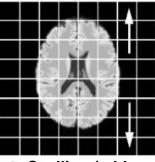
Eddy currents overlap with imaging gradients producing geometric distortions



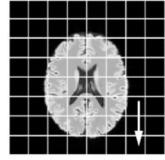
a) Reference



b) Shearing (eddy currents in readount)



 c) Scalling (eddy currents in phase encoding)



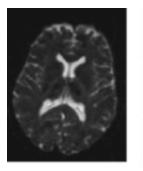
 d) Scalling (eddy currents in sliceselect)

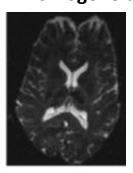


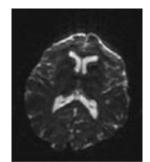
 Advance strategies to simulataneously correct motion, B0 inhomogeneities and eddy currents are available in FSL

 If you are interested in using these tools give a look to FSL documentation before acquiring your data

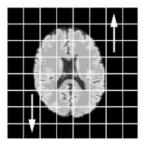
B0 inhomogeneities

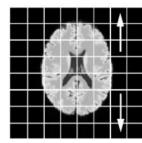


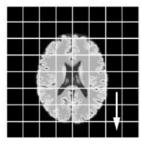




Eddy currents









Quantifying tissue microstructure

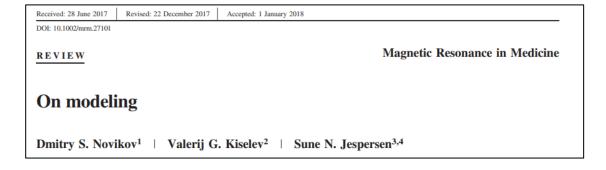
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Diffusion MRI modelling

1. Phenomenological model (Signal Representations)

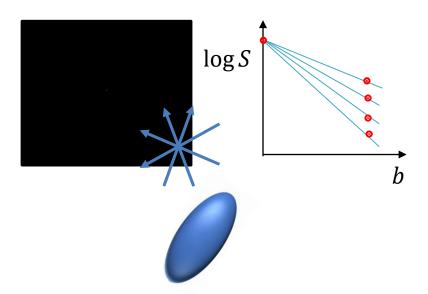
2. Mechanistic Model (Microstructural Models)



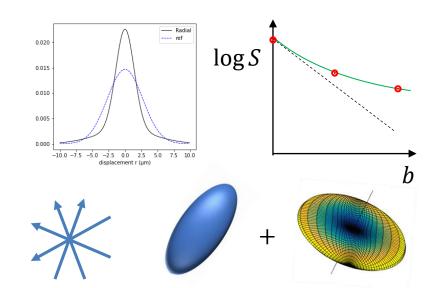
Signal Representations

1. Signal representations quantify diffusion properties without considering its biological underpinnings, e.g.

DTI quantifies diffusion anisotropy from signals for different directions



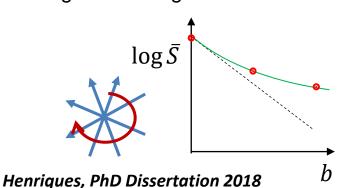
DKI quantifies anisotropy and non-Gaussian diffusion from signals for different directions and b-values

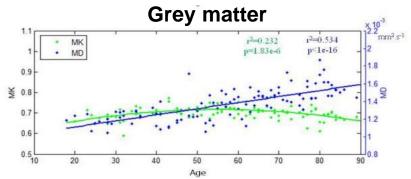


Signal Representations

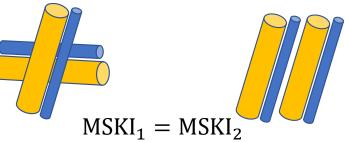
- Advantages of measuring non-Gaussian diffusion
- 1. Non-Gaussian properties can be used to study microstructural alterations even in regions with low anisotropy (e.g. grey matter)

2. Non-Gaussian properties can be extracted even for signals averaged across directions



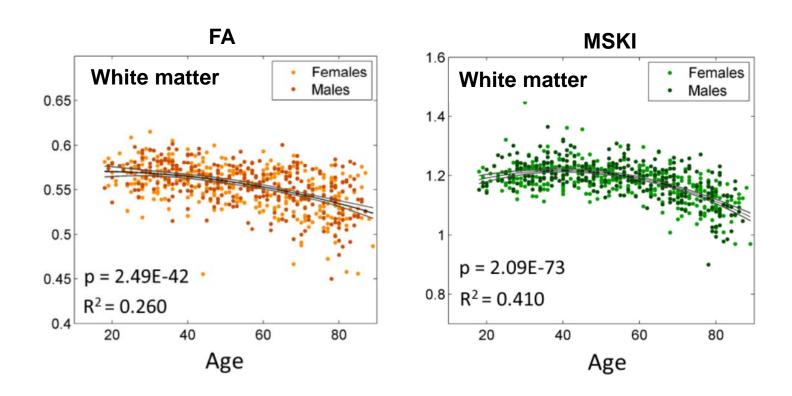


Henriques, Master Dissertation 2012



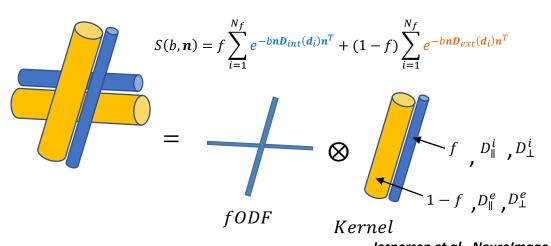
Study microstructural alterations independent to changes on tissue dispersion/crossing

Signal Representations



2. Microstructural models uses biophysical models to directly estimate microstructural properties

- IVIM
- Stanisz's Nerve Model
- Ball & Stick
- CHARMED
- Neurite Density Model
- AxCaliber / Active Ax
- NODDI
- \\/\/\TI
- VERDICT
- LEMONADE
- TEdDI
- SMT
- SMT2
- Fiber-ball imaging
- fw-DTI



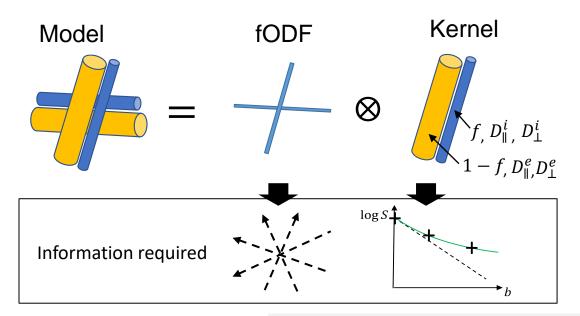
So many models!!!

Jespersen et al., Neurolmage 2007

Most of techniques corresponds to the same models!

Basically they are just a different set of Constraints!

The number of parameter on models is limited to the information provided by dMRI data - **degrees of freedom (DOF)**



To decrease the number of fitted parameters assumptions and constraints are required

Example of Microstructural Models:

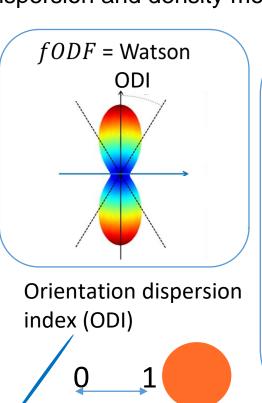
- Neurite orientation dispersion and density model (NODDI)
- 2. Spherical Mean Technique (SMT)
- 3. White Matter integrity Model (WMTI)
- 4. Free water Diffusion Tensor Imaging (fwDTI)

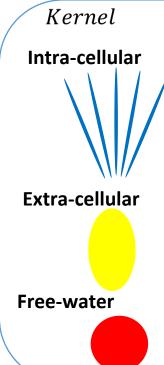
1. Neurite orientation dispersion and density model (NODDI)

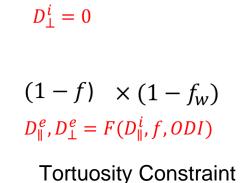
Zhang et. al., NeuroImage. 2012

 $f \times (1 - f_w)$ $D_{\parallel}^i = 1.7 \mu m^2 / ms$

DOF Multiple - directions Multiple -bvalues Log S







 $f = D - 3 \mu m^2 / m s$

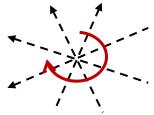
 f_w $D_w = 3 \, \mu m^2 / ms$

2. Spherical Mean Technique (2 compartmental Model)

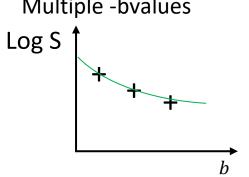
Kaden et. al., Neurolmage. 2016

DOF

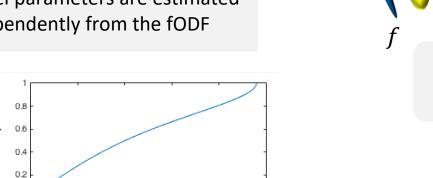
Multiple - directions

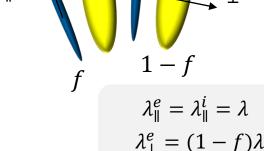


Multiple -bvalues

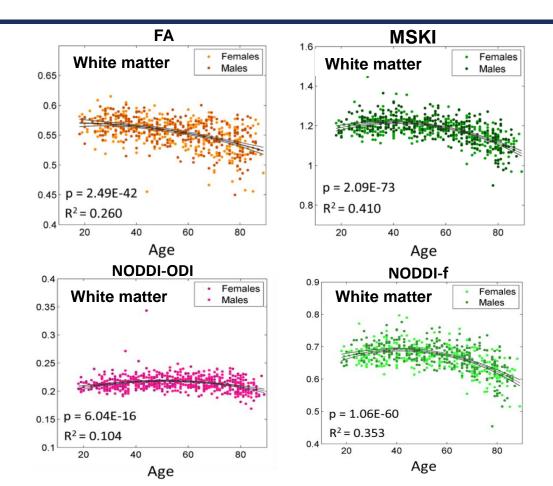


Signals are averaged so that kernel parameters are estimated independently from the fODF



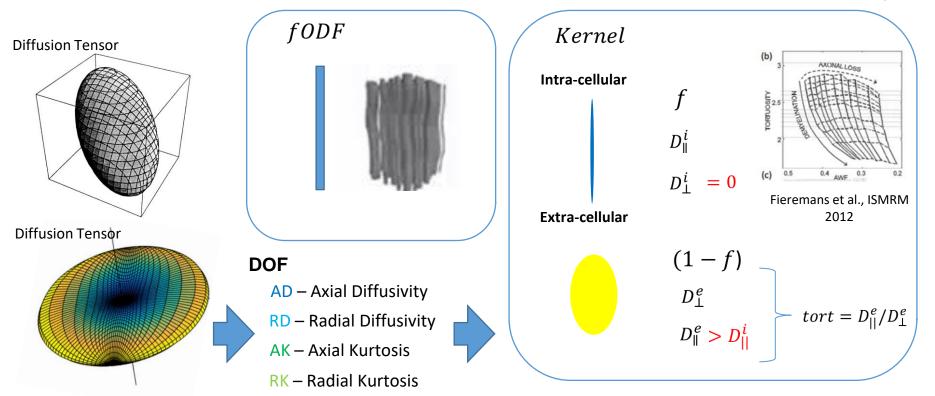


Improper model assumptions might compromise specificity!



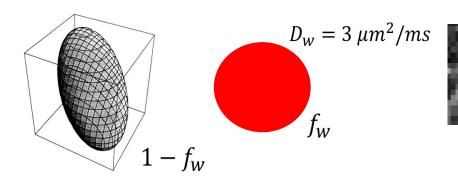
3. White Matter Tract Integrity (WMTI) Model

Fieremans et. al., Neurolmage. 2011



4. Free water DTI

Uses microstructural model components to resolve confounding sources of signal representation models 1) To remove partial volume effects



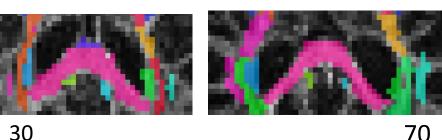
Diffusion Tensor + Free water

AD – Axial Diffusivity

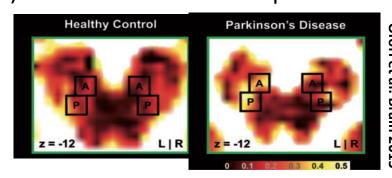
RD – Radial Diffusivity

MD – Mean Diffusivity

FA – Fractional Anisotropy

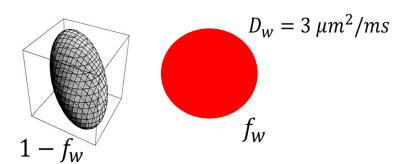


2) Free-water as a more specific measure



Ofori et al. Brain 2015

4. Free water DTI – single shell fitting











Marc Golub

Rita Nunes

Magnetic Resonance in Medicine 62:717-730 (2009)

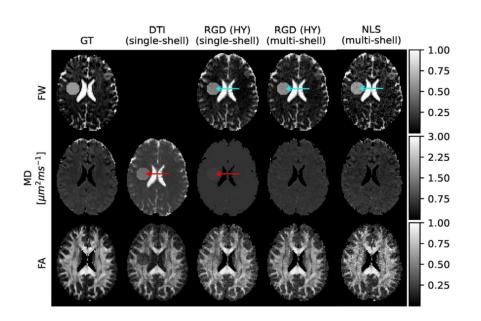
Free Water Elimination and Mapping from Diffusion MRI

Ofer Pasternak,1* Nir Sochen,2 Yaniv Gur,2 Nathan Intrator,1 and Yaniv Assaf3,4

- Spatial regularization
- Initial Solution

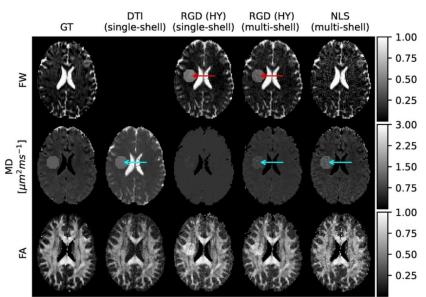
4. Free water DTI – single shell fitting

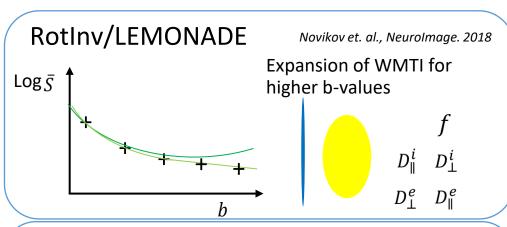
Golub et al. MRM 2020 (accepted)

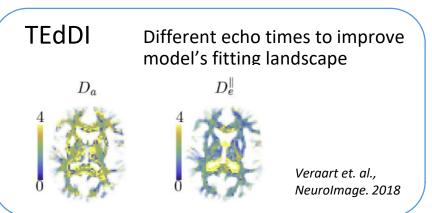


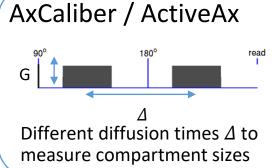
Free water DTI estimates from single bvalue data might seem plausible but must be interpreted with care

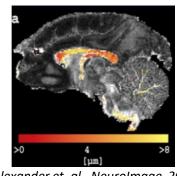
Marc Golub1, Rafael Neto Henriques21, Rita G. Nunes11











Alexander et. al., Neurolmage. 2010

Non-Conventional sequences

 Double diffusion encoding

Mitra Phys Rev B 1995

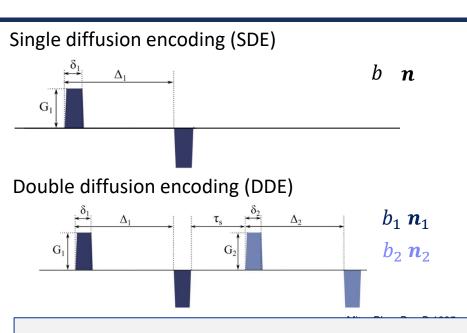
Q-trajectory encoding

Lasič et al. Front. Phys. 2014





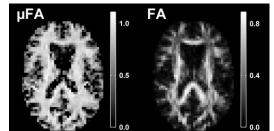
Advanced diffusion sequences



Tensor-valued diffusion MRI in under 3 minutes: an initial survey of microscopic anisotropy and tissue heterogeneity in intracranial tumors

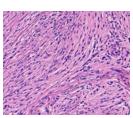
Nilsson et al. MRM 2019

Microscopic Fractional Anisotropy (μ FA)

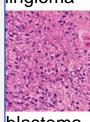


Shemesh & Cory MRM 2011

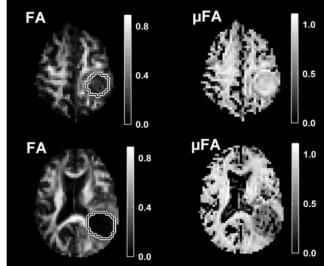
Szczepankiewicz et al.. Neurolmage 2015



hingioma



blastoma



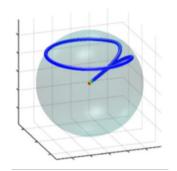
Szczepankiewicz et al., Neurolmage 2016

Advanced diffusion sequences

Single diffusion encoding



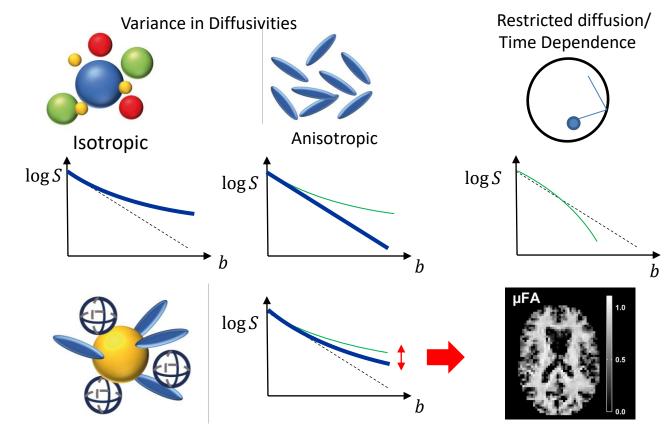
Isotropic diffusion Encoding



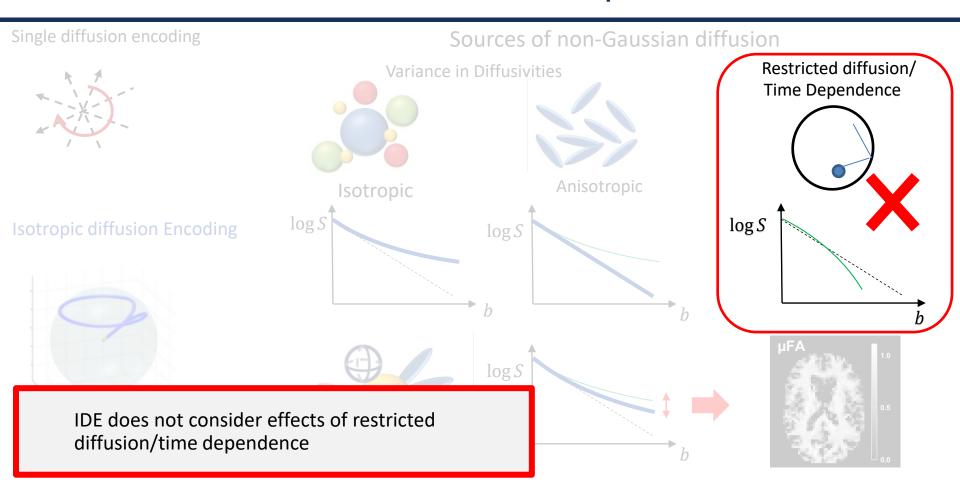
Lasič et al. Front. Phys. 2014

Westin et al., 2016

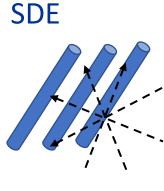
Sources of non-Gaussian diffusion



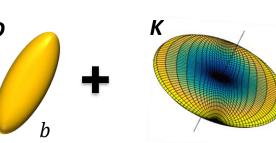
Advanced diffusion sequences



CTI is based on the cumulant expansion of DDE signals



 $\log S = -bD + \frac{1}{6}b^2D^2K$

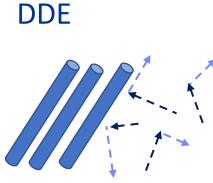


Jensen et al., MRM 2005

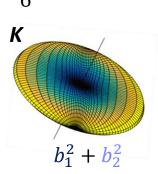
 $\log S = -(b_1 + b_2)D + \frac{1}{6}(b_1^2 + b_2^2)D^2K + b_1b_2D^2Z$

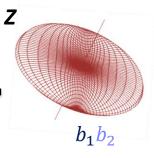
Jespersen, NMR Biomed 2011

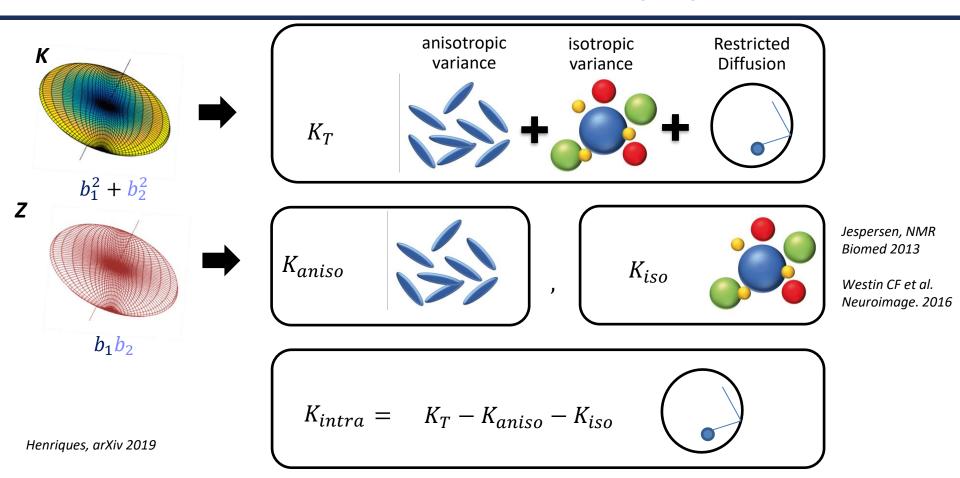
Henriques et al., Neurolmage 2015













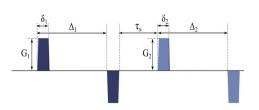
- 16.4T Aeon
- DDE experiments:
 - $-\Delta$ =13ms, t=13ms, δ =1.5ms
 - TR = 2200 ms, TE=52 ms
 - Resolution: 130×130x800 µm³
 - Thickness = 0.8 mm
 - 16 averages

~10h



- 9.4T Biospec
- DDE experiments:
 - $-\Delta$ =12ms, t=12ms, δ =3ms
 - TR = 3000 ms, TE = 48.5 ms
 - Resolution: 200×200x1000 μm³
 - 2 averages

~2h



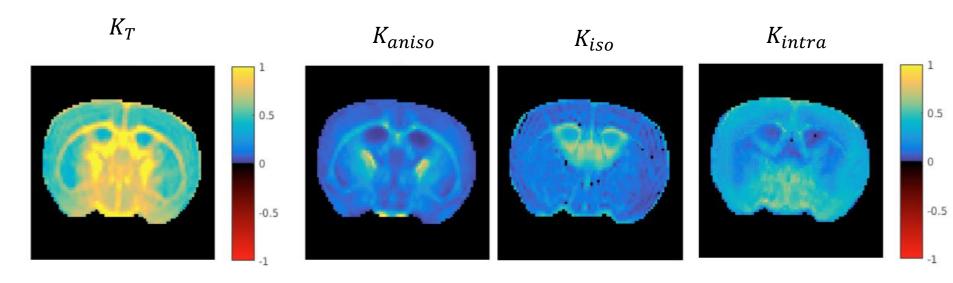


Ex-vivo mouse brain (37°C)



Two In-vivo rat brain

Ex-vivo results Henriques et al. NeuroImage 2020



- K_{aniso} is the main source in white matter
- K_{iso} has larger values in the b
- K_{intra} is non zero

Measures do not depend on a microstructural model

