



FAKULTNÍ NEMOCNICE
OLOMOUC



Sekce pro funkční mapování mozku
Česká společnost pro klinickou neurofyzilogii
České lékařské společnosti Jana Evangelisty Purkyně



Faculty of Medicine
and Dentistry

Palacký University
Olomouc

Diffusion tensor imaging (DTI)

principles and data analysis with FSL

Pavel Hok

Functional magnetic resonance imaging lab

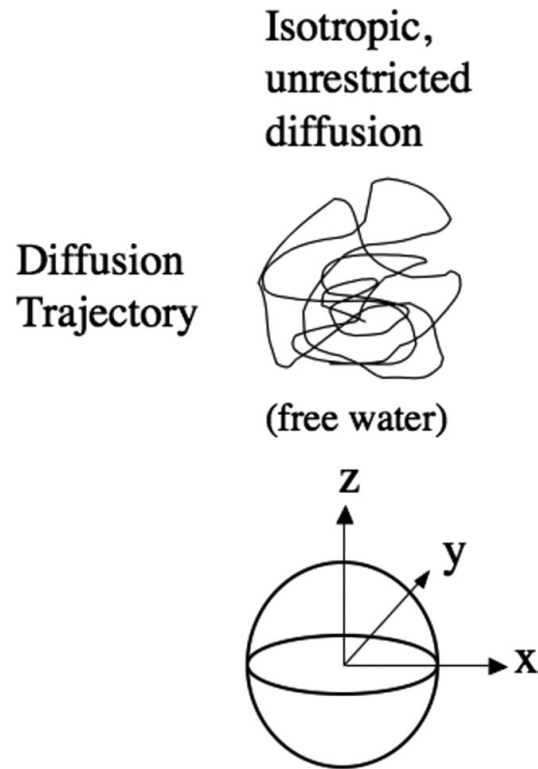
Department of neurology
Faculty of medicine and dentistry
Palacky university and University hospital Olomouc

Educational course: Neuroimaging
CEITEC Brno
15th November 2016

Contents

- Theory
 - Physiology and physics
 - Principles of diffusion-weighted imaging
 - Artefacts
- Workflow
 - Applications
 - Acquisition
 - Analysis

Theory: Diffusion

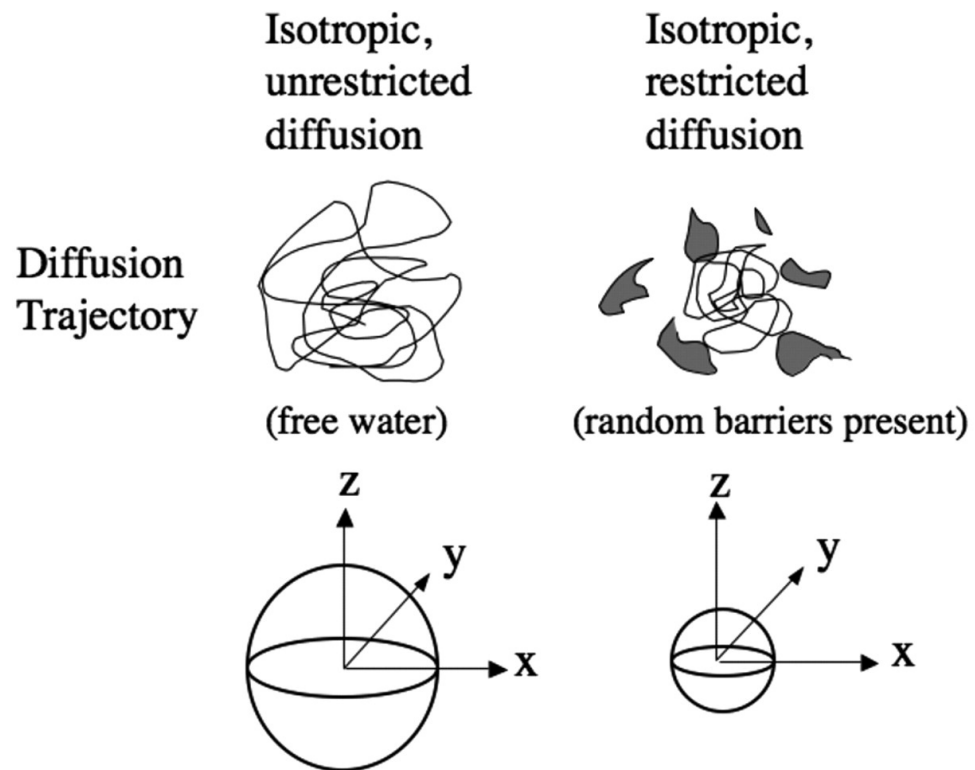


Brownian motion

diffusion
constant (D)

$$r^2 = 6Dt$$

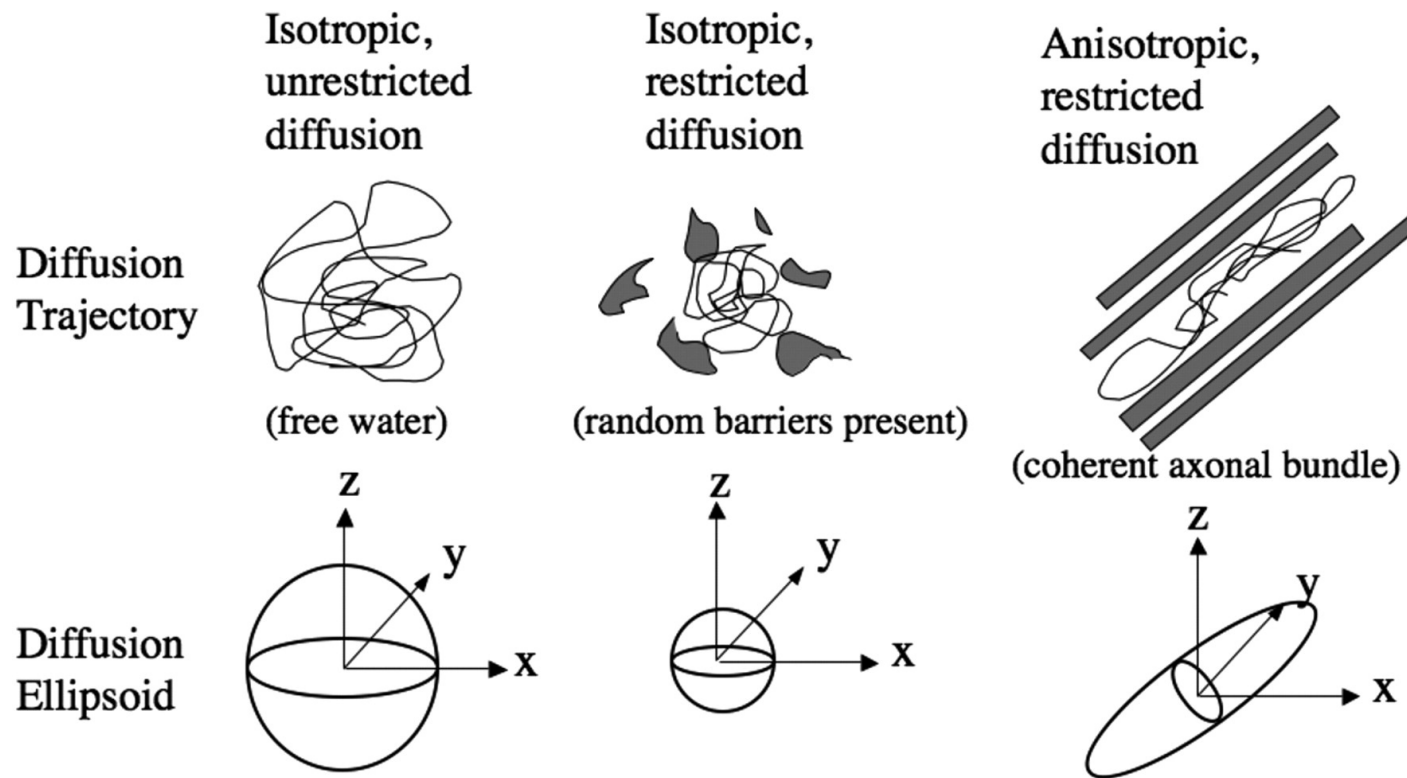
Theory: Diffusion



diffusion
constant (D)

apparent diffusion coefficient (ADC)

Theory: Diffusion



isotropic vs. anisotropic diffusion

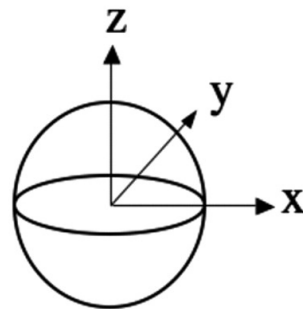
Theory: Diffusion tensor

Diffusion
Trajectory

Isotropic,
unrestricted
diffusion



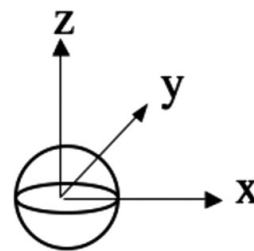
(free water)



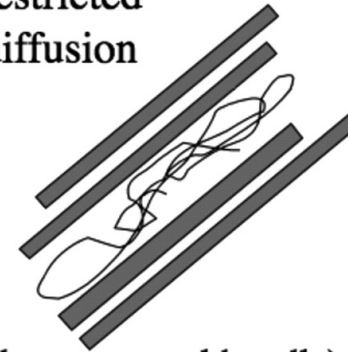
Isotropic,
restricted
diffusion



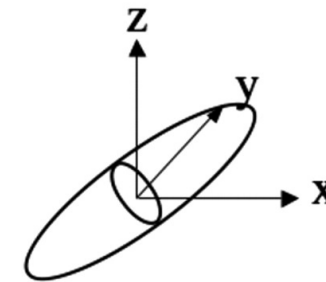
(random barriers present)



Anisotropic,
restricted
diffusion



(coherent axonal bundle)



ellipsoid

diffusion
tensor

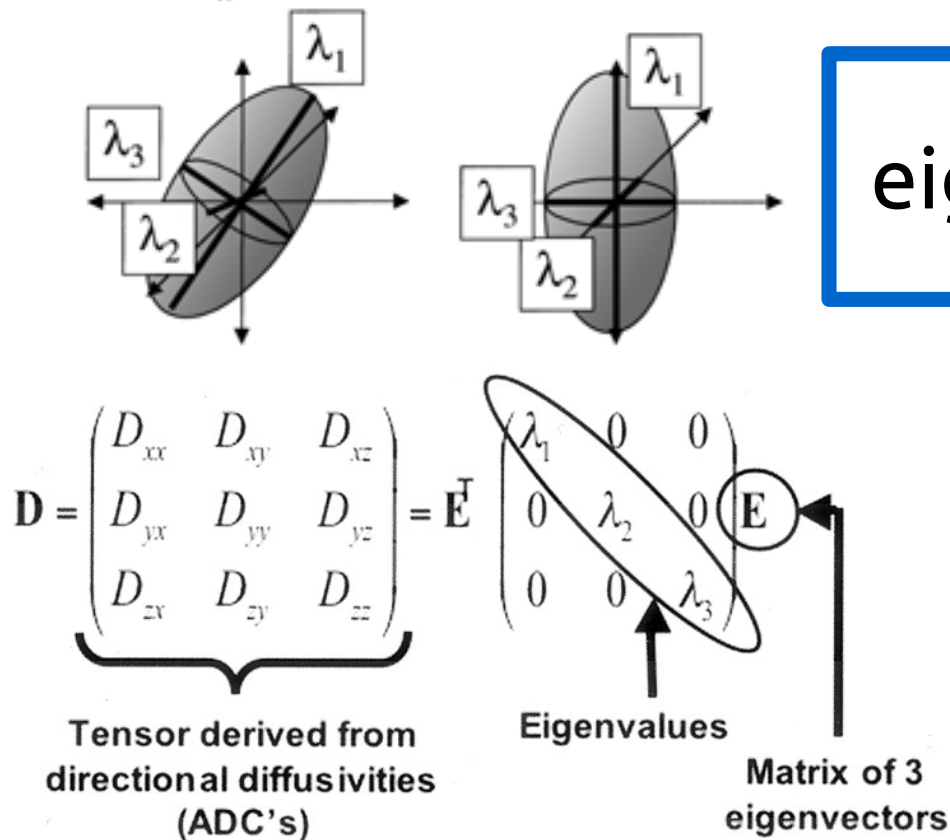
$$\begin{bmatrix} D & 0 & 0 \\ 0 & D & 0 \\ 0 & 0 & D \end{bmatrix}$$

$$\begin{bmatrix} D_{eff} & 0 & 0 \\ 0 & D_{eff} & 0 \\ 0 & 0 & D_{eff} \end{bmatrix}$$

$$D_{eff} < D$$

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

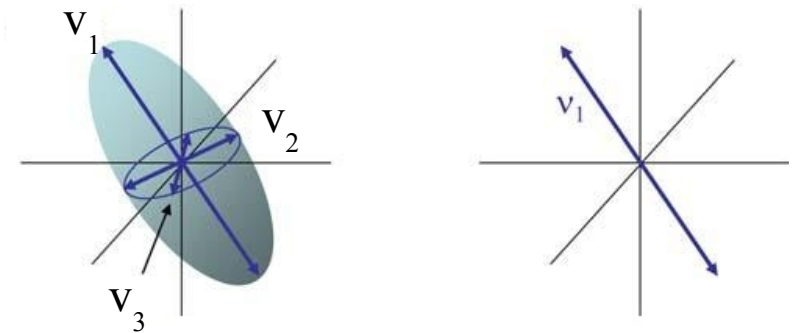
Theory: Diffusion tensor



eigenvectors

principal eigenvector

eigenvalues



$$\mathbf{D}\mathbf{E} = \mathbf{E}\mathbf{\Lambda}$$

$$\begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \begin{pmatrix} v_{1x} & v_{2x} & v_{3x} \\ v_{1y} & v_{2y} & v_{3y} \\ v_{1z} & v_{2z} & v_{3z} \end{pmatrix} = \begin{pmatrix} v_{1x} & v_{2x} & v_{3x} \\ v_{1y} & v_{2y} & v_{3y} \\ v_{1z} & v_{2z} & v_{3z} \end{pmatrix} \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

and

$$\mathbf{D}\mathbf{E}\mathbf{E}^T = \mathbf{D} = \mathbf{E}\mathbf{\Lambda}\mathbf{E}^T$$

$$\mathbf{E}^T\mathbf{E}\mathbf{\Lambda} = \mathbf{\Lambda} = \mathbf{E}^T\mathbf{D}\mathbf{E}$$

Theory: Diffusion tensor

- Scalar measures

- Trace

$$\text{Tr} = \lambda_1 + \lambda_2 + \lambda_3$$

- Mean diffusivity

$$\text{MD} = \text{Tr}/3$$

- Axial (longitudinal) diffusivity

$$D_a = \lambda_1$$

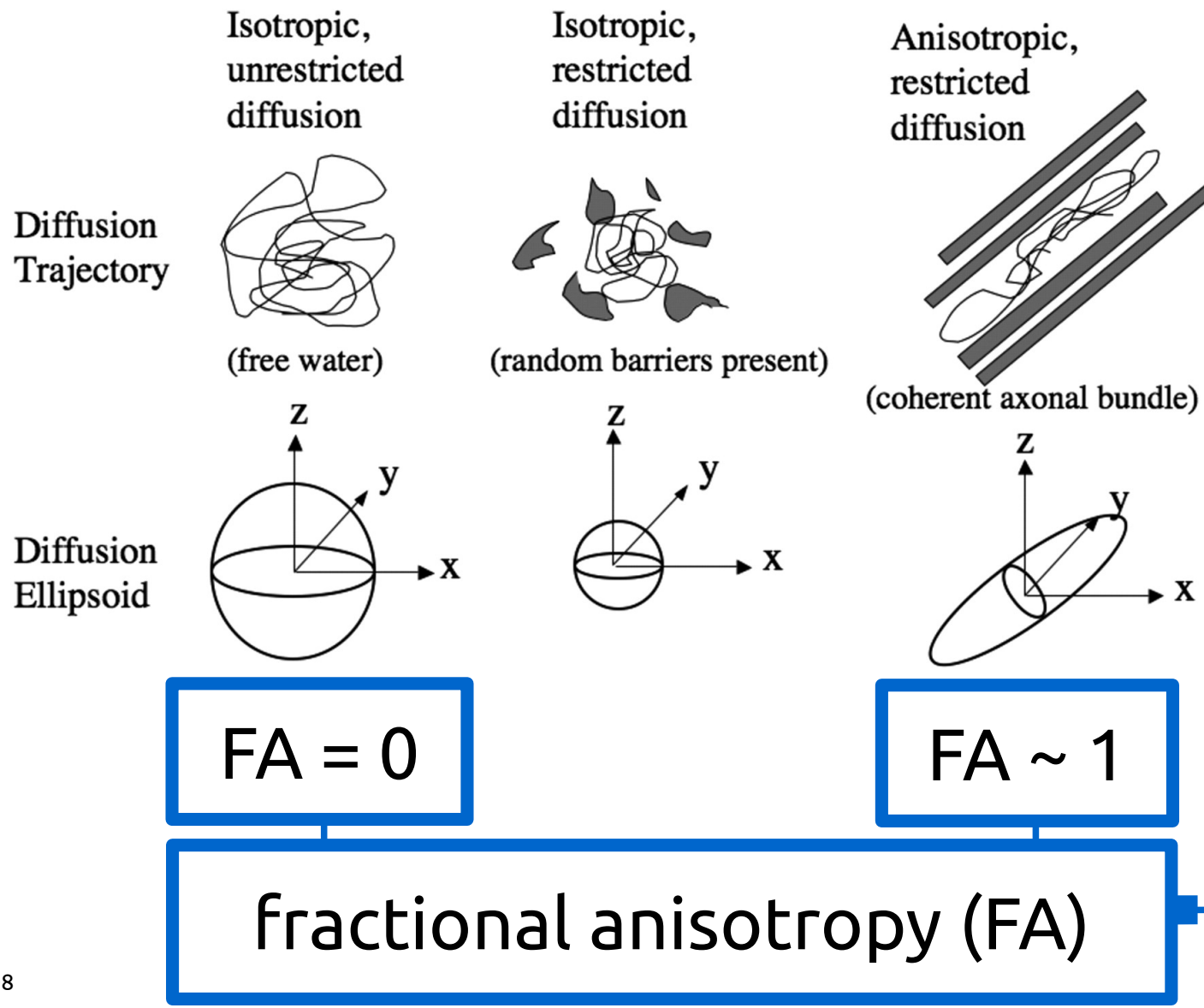
- Radial (perpendicular) diffusivity

$$D_r = (\lambda_2 + \lambda_3)/2$$

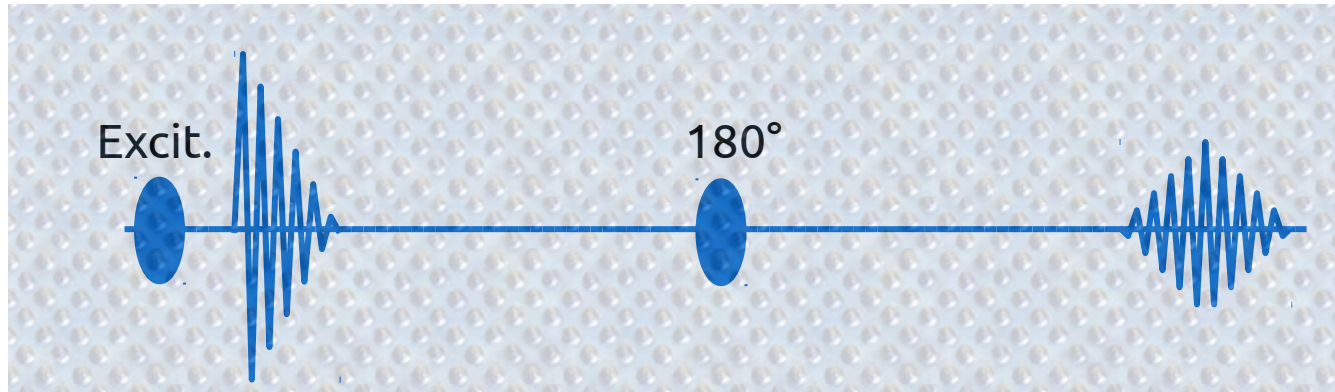
- Fractional anisotropy

$$\text{FA} = \sqrt{\frac{3[(\lambda_1 - D_{\text{av}})^2 + (\lambda_2 - D_{\text{av}})^2 + (\lambda_3 - D_{\text{av}})^2]}{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$

Theory: Diffusion tensor



Theory: Diffusion weighting

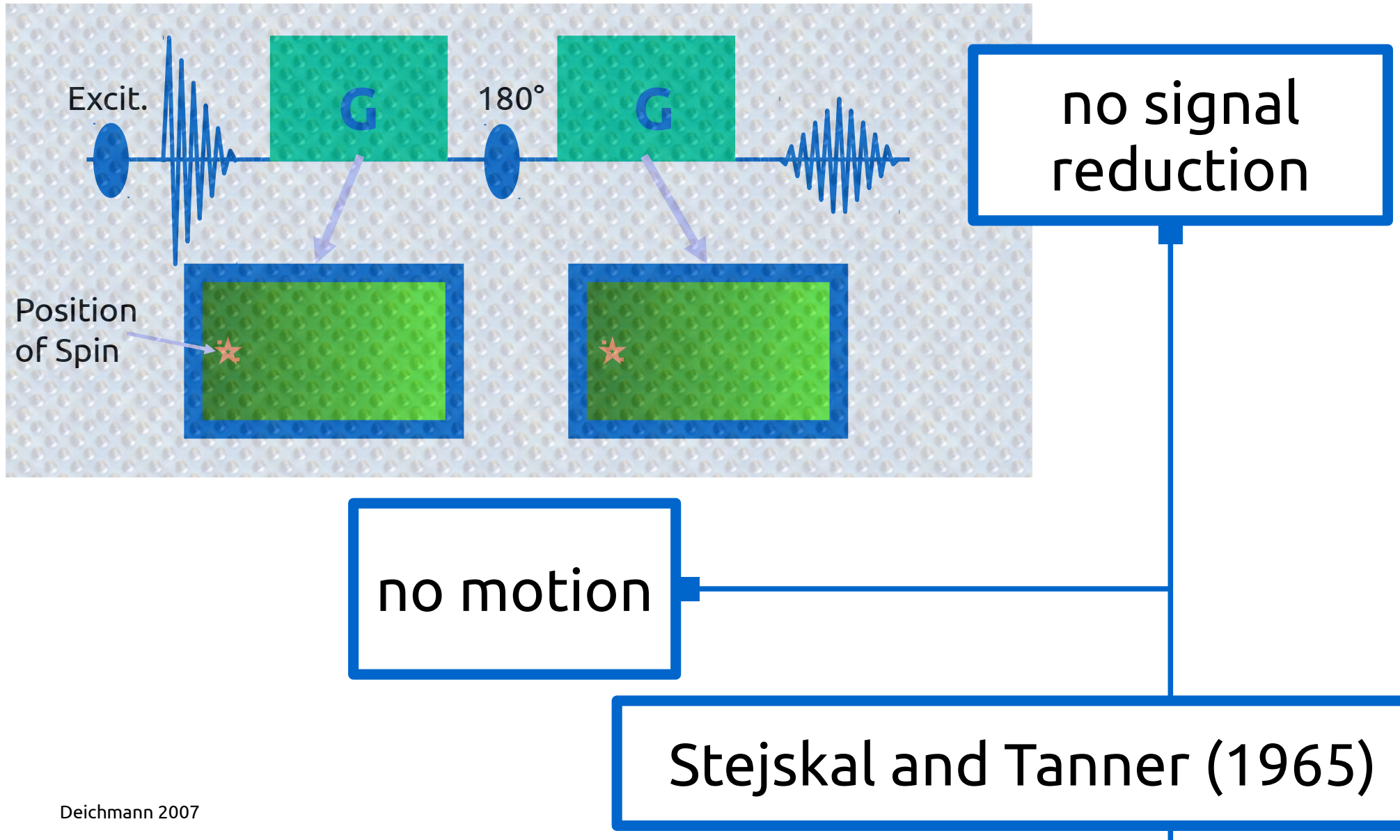


dephasing

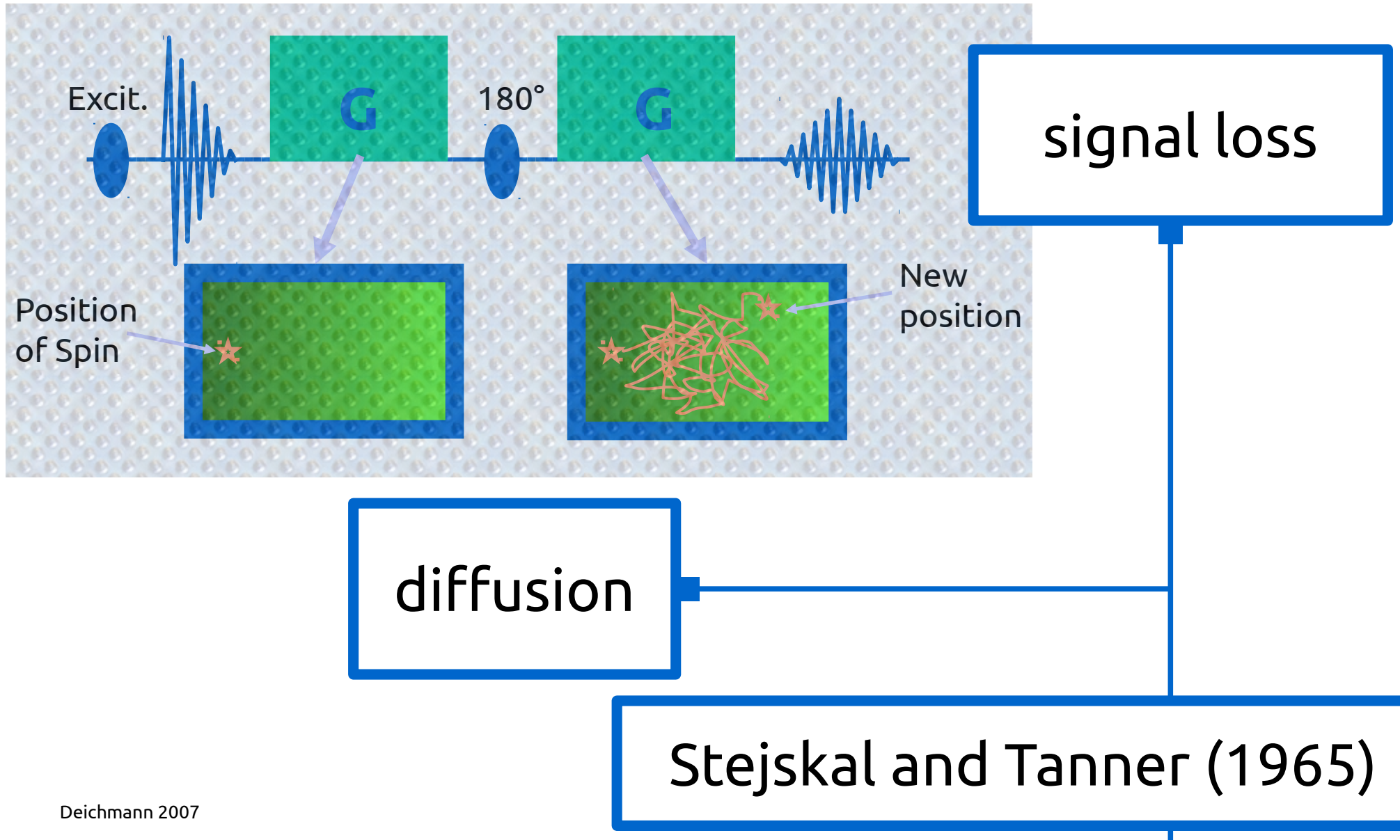
rephasing

spin echo

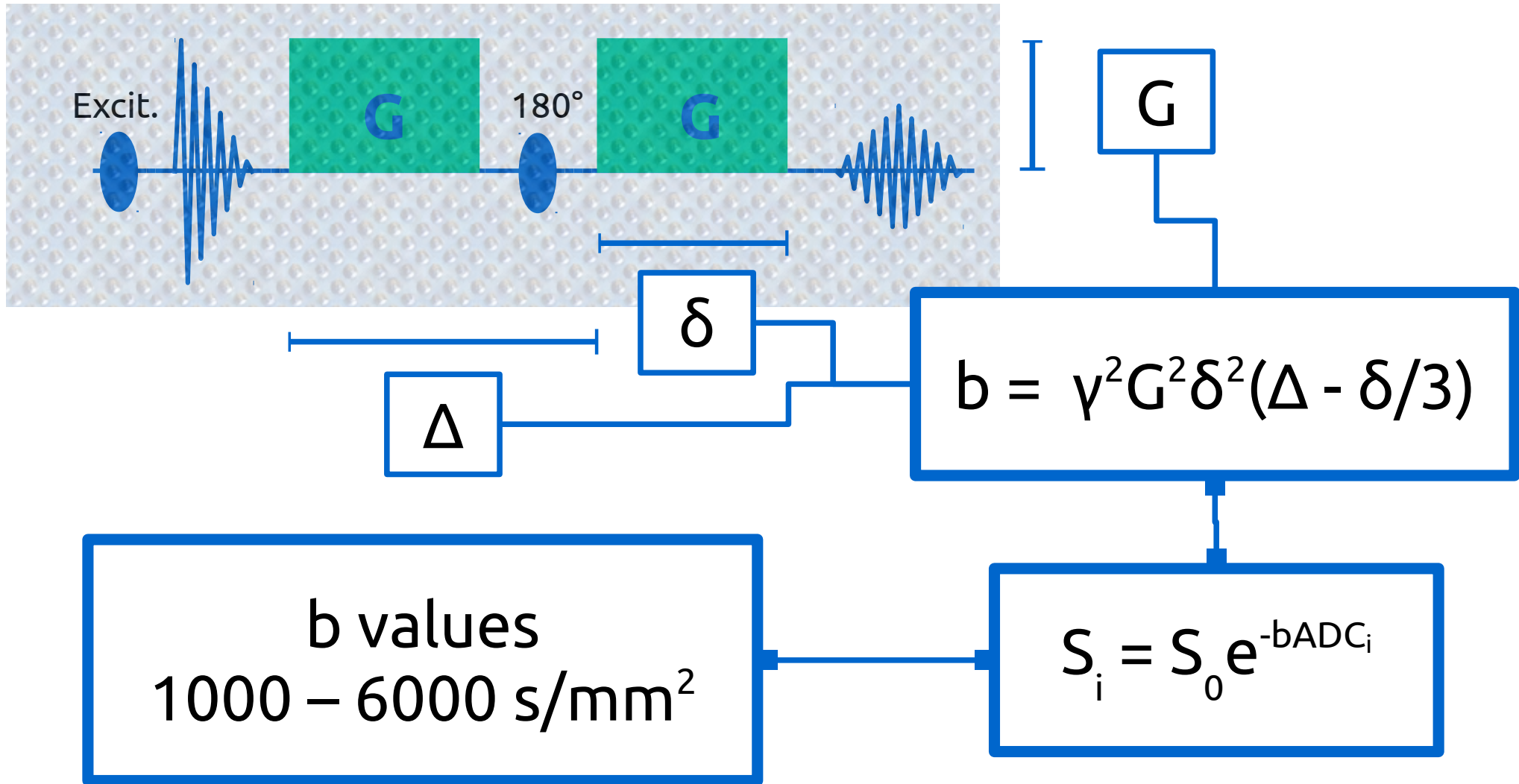
Theory: Diffusion weighting



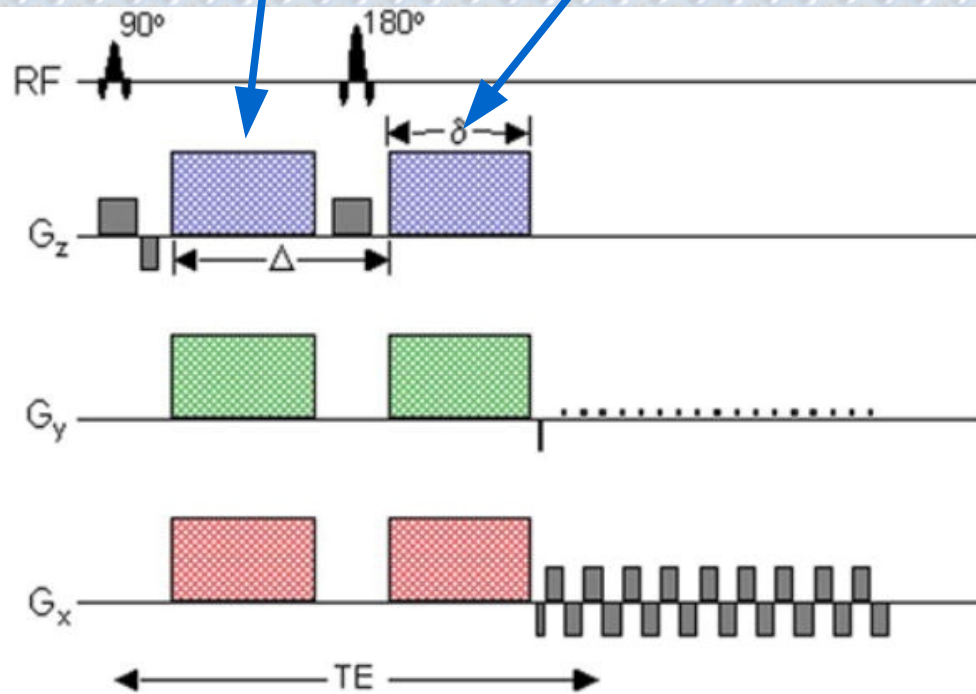
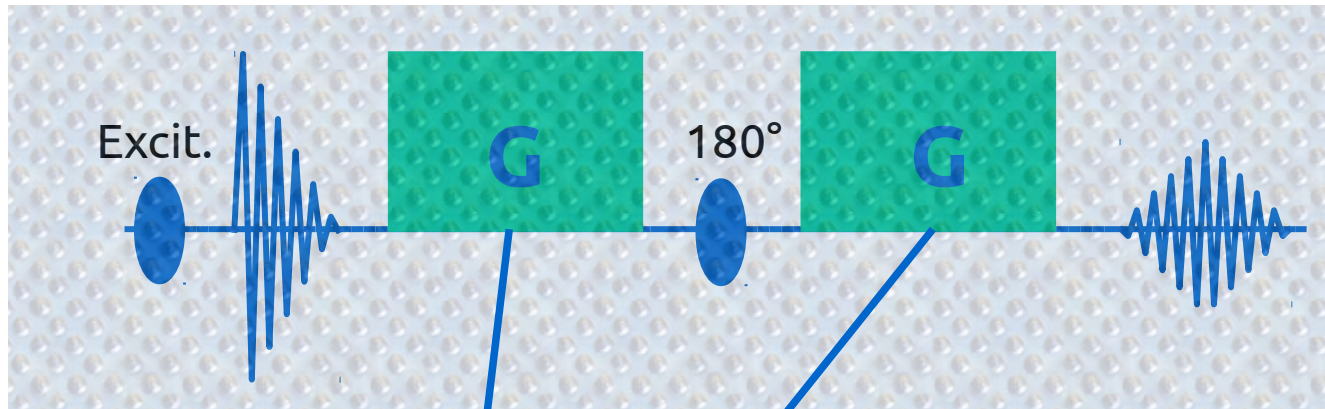
Theory: Diffusion weighting



Theory: Diffusion weighting

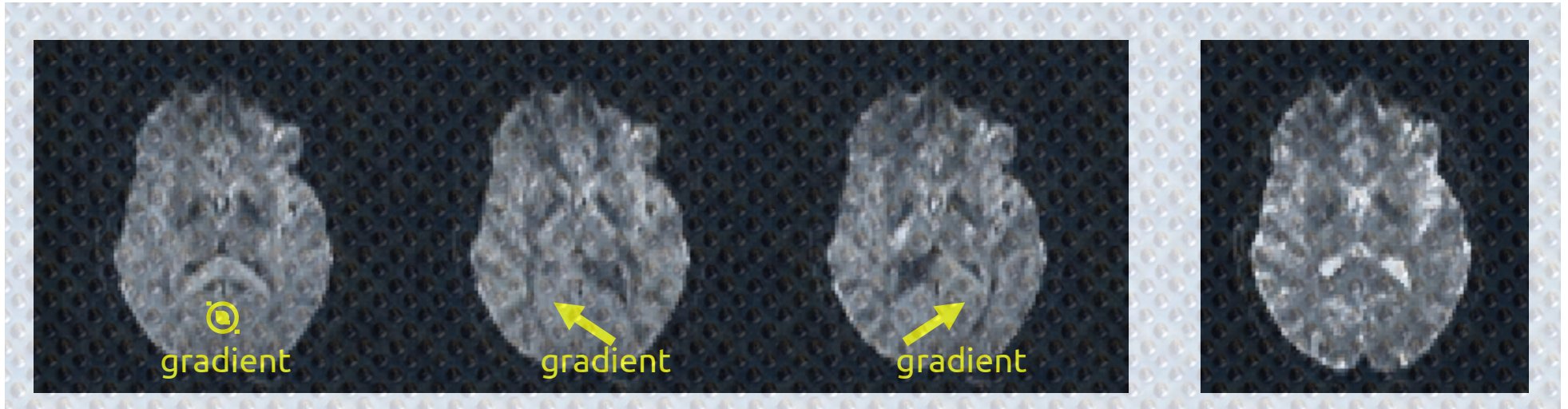


Theory: Diffusion weighting



echo planar
imaging

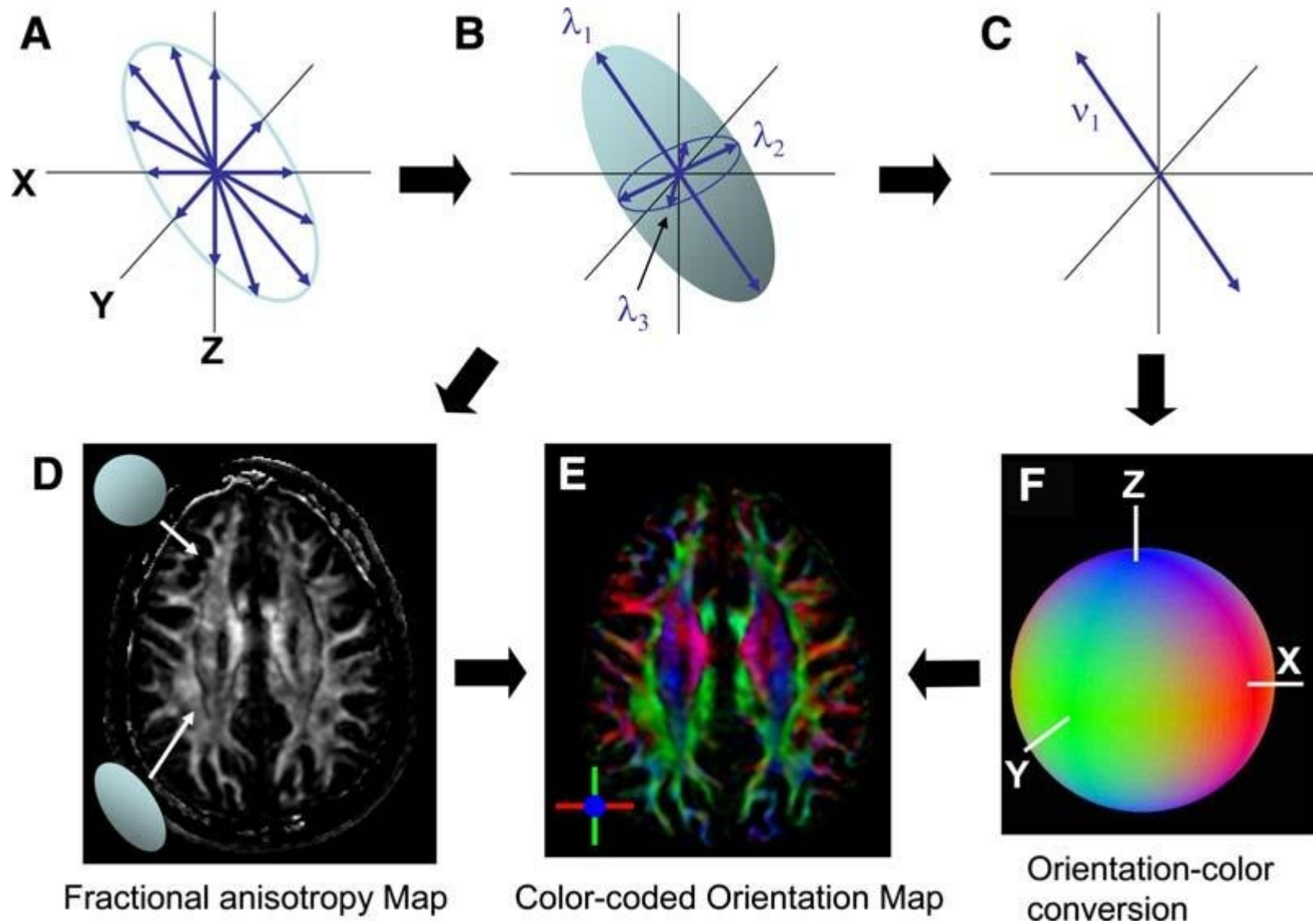
Theory: Diffusion weighting



gradient directions
(b vectors)

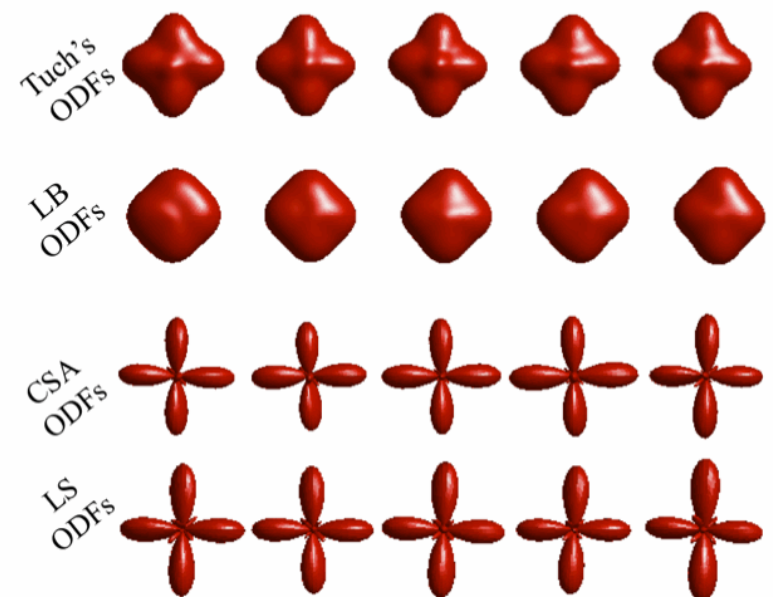
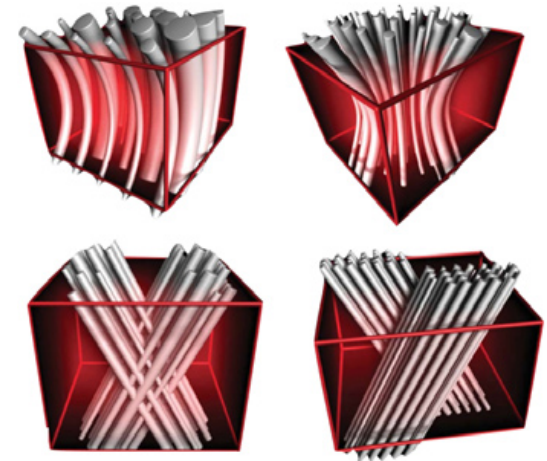
no diffusion
weighting
($b = 0$)

Theory: Diffusion tensor imaging



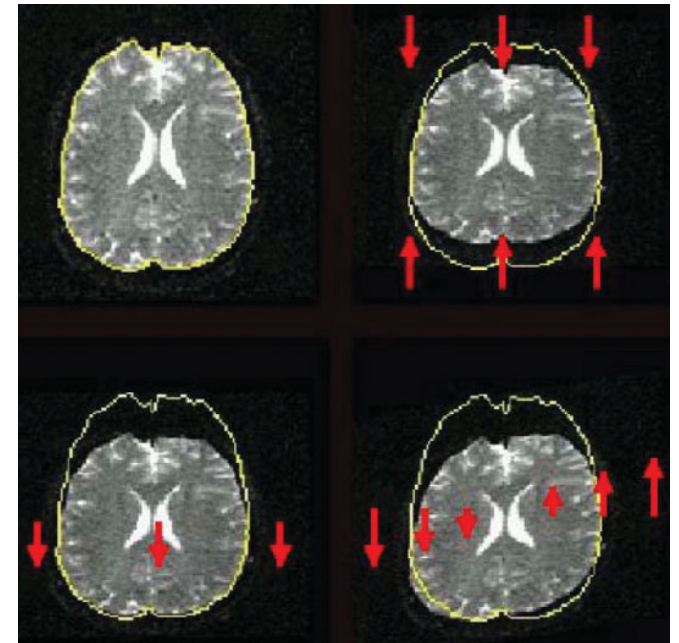
Theory: Crossing fibres

- Problem: DT ignores partial voluming and crossing fibres
- Solution: more complex diffusion models
 - balls and sticks (Behrens et. al 2003)
 - q-ball orientation distribution function (ODF) (Tuch 2004)
 - constant solid angle (CSA) ODF (Aganj et al. 2010)

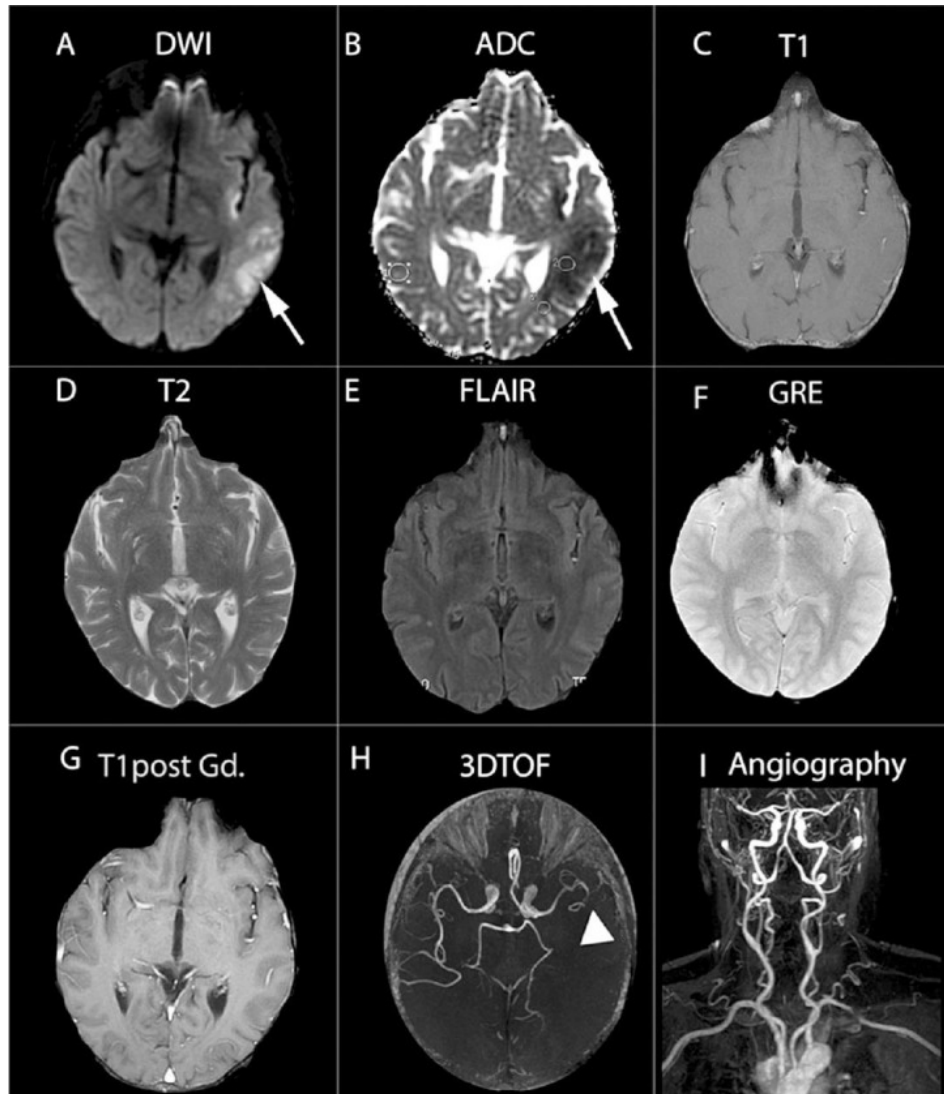


Theory: DTI artefacts

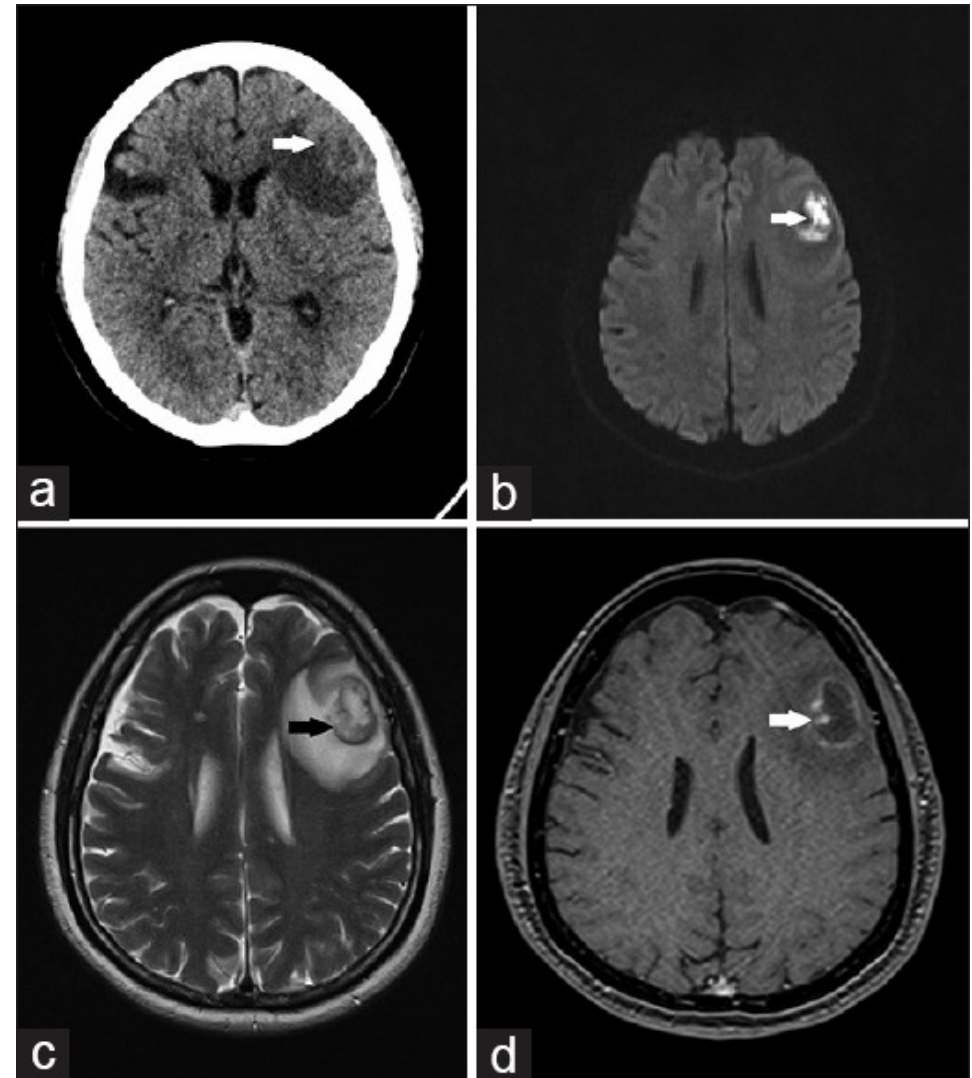
- Motion
 - signal loss → check your data!
- Diffusion gradients
 - eddy currents – geometric distortions (typically skewing and compression) that vary among volumes → preprocessing
- EPI
 - constant geometrical distortions around air/tissue boundaries → acquire fieldmap or image with opposite PE direction!



Applications: Clinical routine



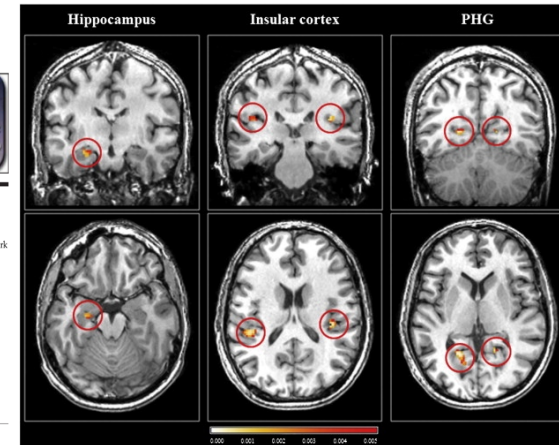
Ernesto Roldan-Valadez and
Mariana Lopez-Mejia 2014



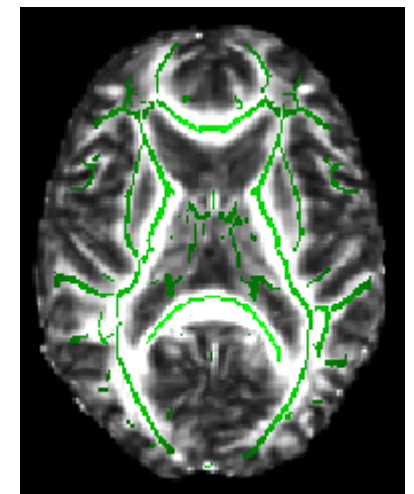
Chokkappan et al. 2016

Applications: DTI group statistics

- Measures
 - FA – integrity of the white matter
 - MD – rapid plasticity
- Methods
 - Voxel-based
 - how to align FA images?
 - Tract-based spatial statistics (TBSS) – FSL
 - projection onto a "mean FA skeleton"

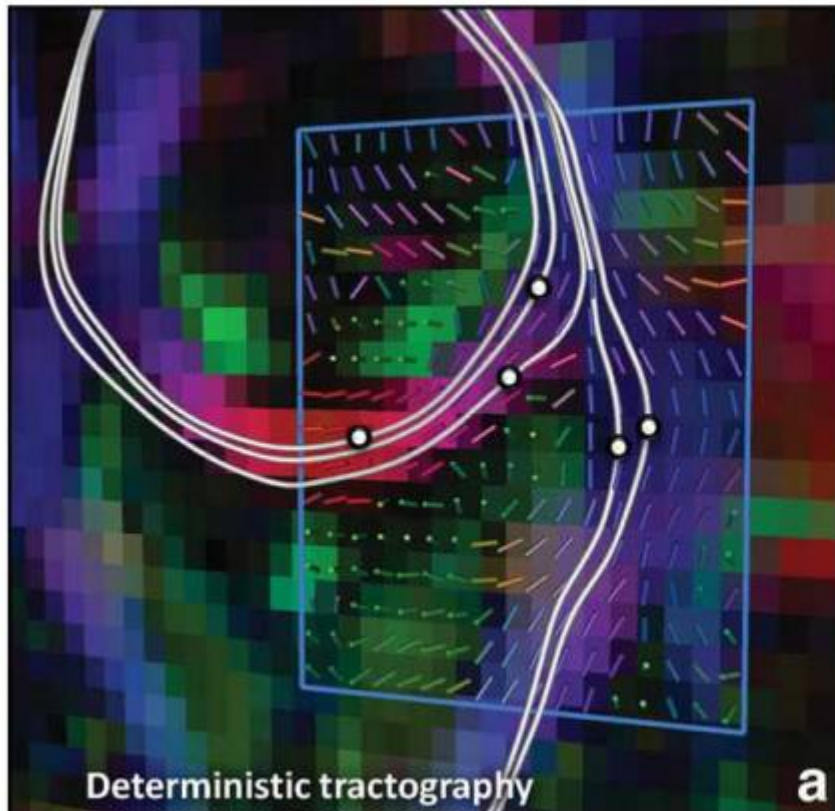


Tavor et al. 2013
Schmidt-Wilcke et al. 2014

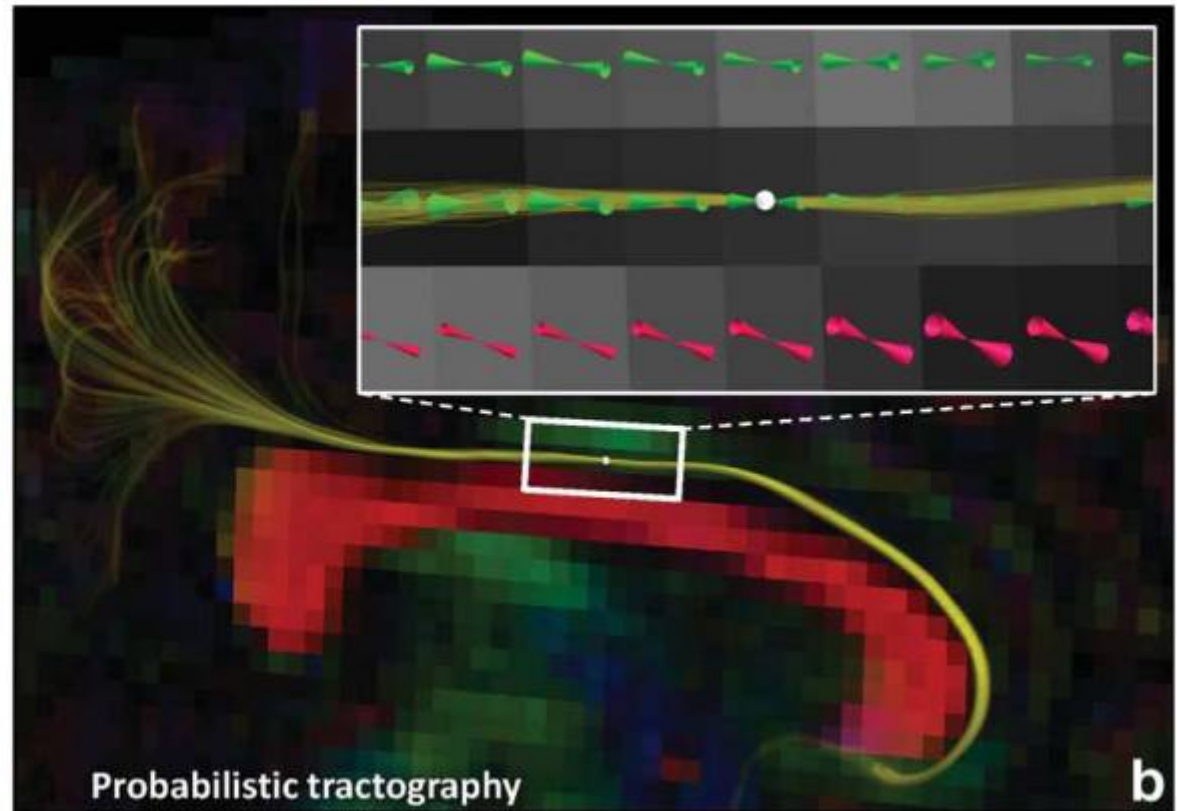


<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TBSS>

Applications: Tractography



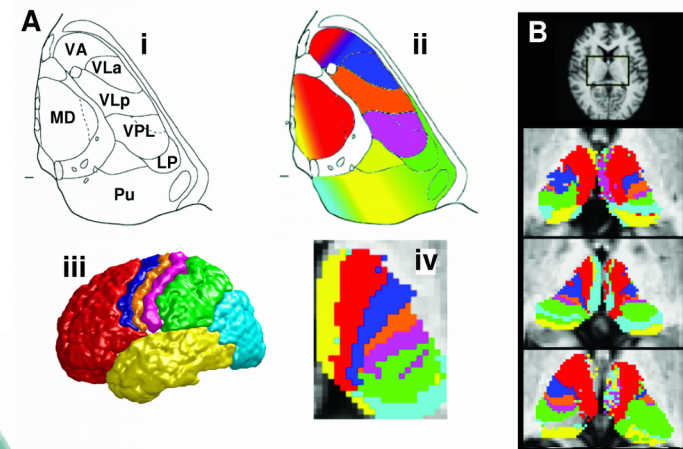
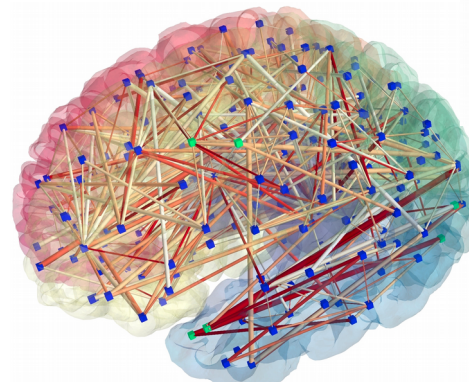
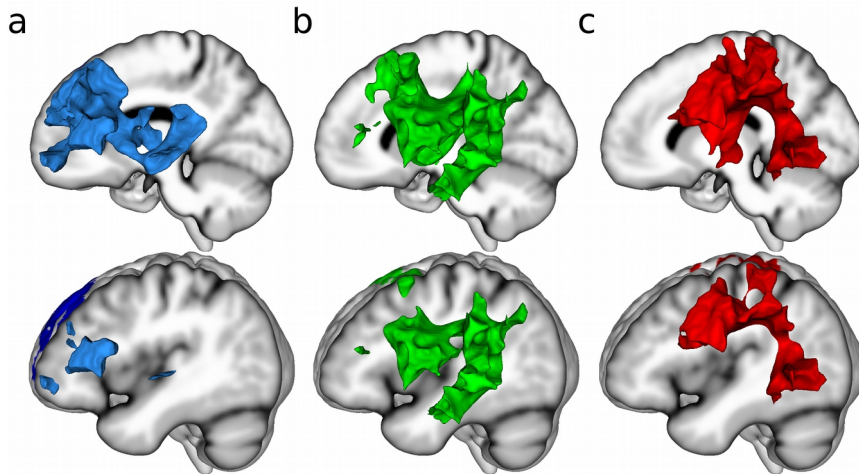
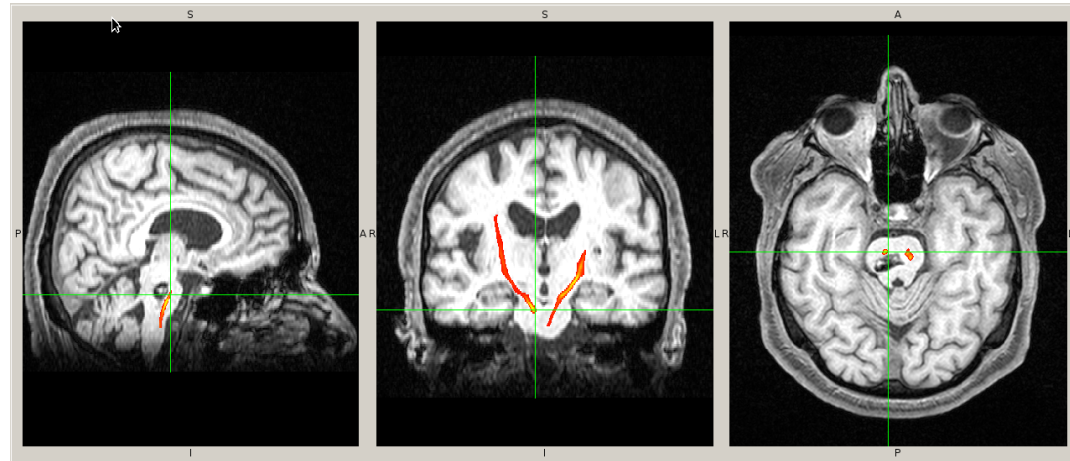
deterministic:
one direction



probabilistic:
distribution of directions

Applications: Tractography

- Clinical
 - Pre-surgical mapping
- Research
 - Structural connectivity
 - Priors for brain connectom
 - Connectivity-based parcellation



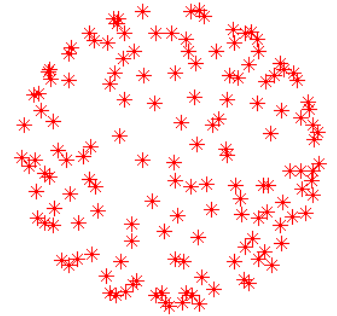
Acquisition parameters

- Different parameters based on application and hardware
- **Example acquisition parameters** (Soares et al. 2013)
 - **Spin Echo (SE) EPI**, but also Fast Spin Echo (FSE), Stimulated Echo Acquisition Mode (STEAM)
 - parallel imaging (GRAPPA) reduces EPI artefacts
 - HCP: multi-band factor 3 for faster imaging
 - resolution 2-2.5 mm isotropic, no gap between slices
 - HCP: 1.25 mm isotropic
 - acquisition matrix 96×96 – 128×128 , FOV 240–256 mm
 - TE 50–70 ms, TR 8.5–12 s
 - HCP: TE 89.5 ms, TR 5520 ms

Acquisition parameters

- **Diffusion gradient directions**

- 3 – clinical routine ADC
- 6 – minimum for tensor estimation
- 20-30 – borderline for tractography
- >60 high-angular-resolution diffusion imaging (HARDI)
- up to ~300 per session in Human Connectome Project
- preferably full-sphere sampling, no co-linear directions
- one b_0 image per 5-10 diffusion directions



- **Multi-shell acquisition**

- several b values (HCP: 1000, 2000, and 3000)
 - more sensitive to crossing fibres

Acquisition: DTI extensions

- **DTI issues:**

- classical DTI assumes Gaussian (normal) displacement distribution of water, but
 - violated in the presence of cellular membranes
 - diffusion becomes non-monoexponential at higher b
 - at least 2 diffusion components

- **Solutions:**

- **Q-space imaging** (Assaf et al. 2002)
 - $b \sim 14,000 \text{ s/mm}^2$
- **diffusion spectrum imaging (DSI)** (Wedeen et al. 2005)
- **diffusion kurtosis imaging (DKI)** (Jensen et al. 2005)
 - b value $\sim 2000 \text{ s/mm}^2$

Analysis: Toolboxes

- **FMRIB Software Library (FSL)**
- MedINRIA
- FreeSurfer
- DTI-TK
- BrainVoyager
- TrackVis
- DTIStudio
- preprocessing: AFNI, SPM
- ...

Analysis: FDT

FMRI's Diffusion Toolbox

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

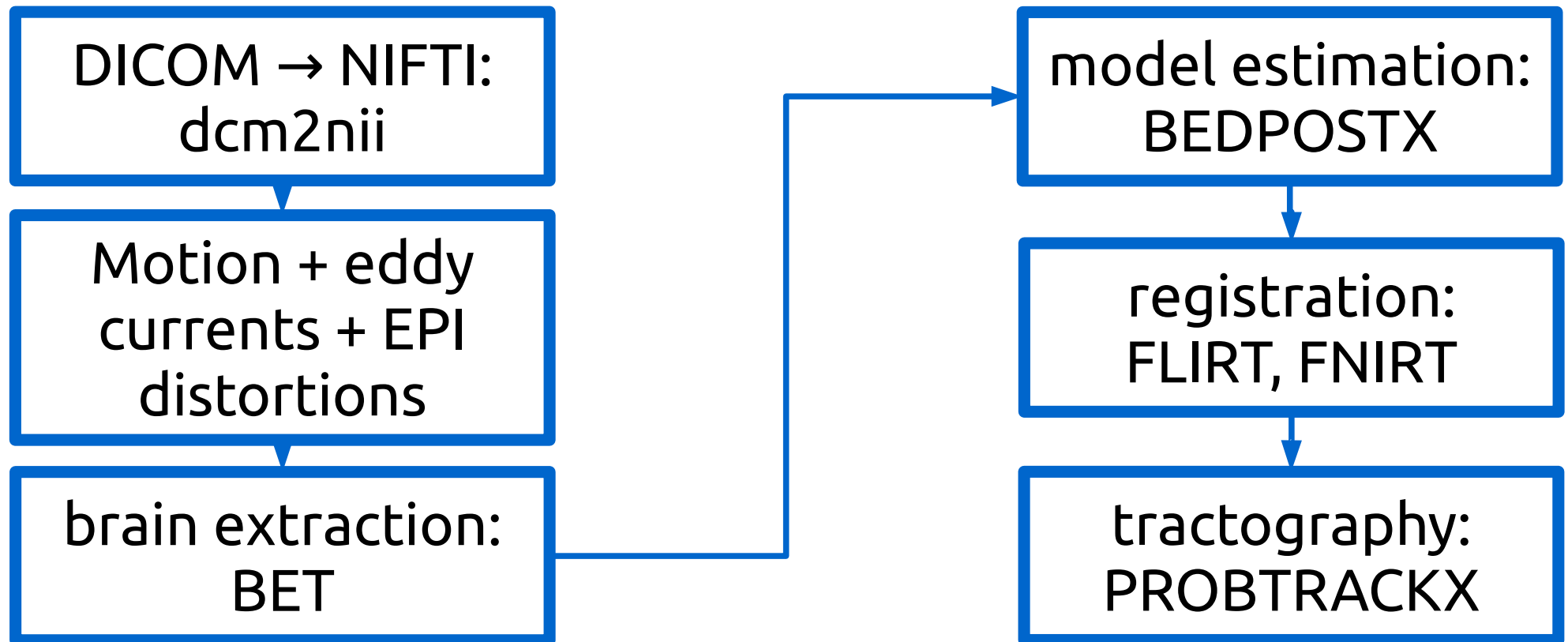
FMRI Software Library



The Oxford Centre for
Functional MRI of the Brain,
Nuffield Department of
Clinical Neurosciences

<http://www.fmrib.ox.ac.uk/>

Analysis: FDT pipeline



<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide>

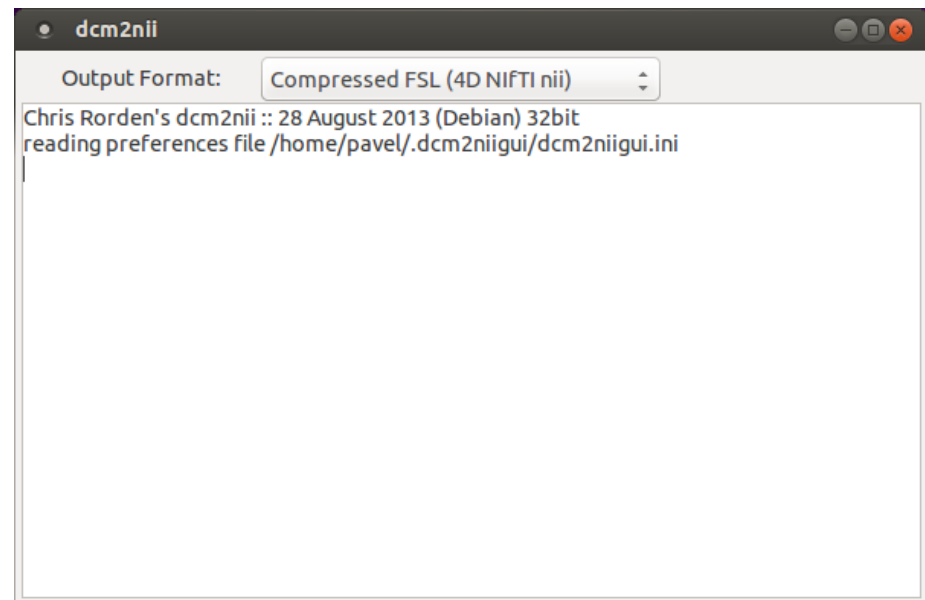
Analysis: FDT pipeline

DICOM → NIFTI:
dcm2nii

Motion + eddy
currents + EPI
distortions

brain extraction:
BET

MRICron: dcm2nii, dcm2niigui



<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide>

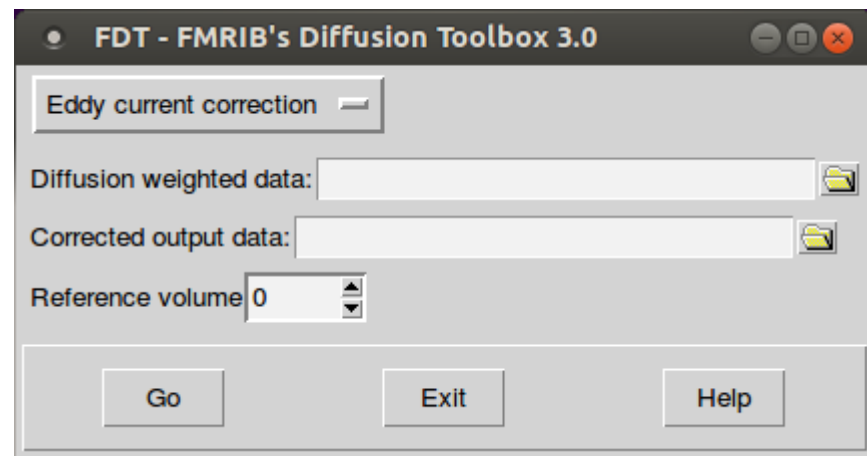
Analysis: FDT pipeline

DICOM → NIFTI:
dcm2nii

Motion + eddy
currents + EPI
distortions

brain extraction:
BET

FMRI's Diffusion Toolbox



motion + eddy currents only

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide>

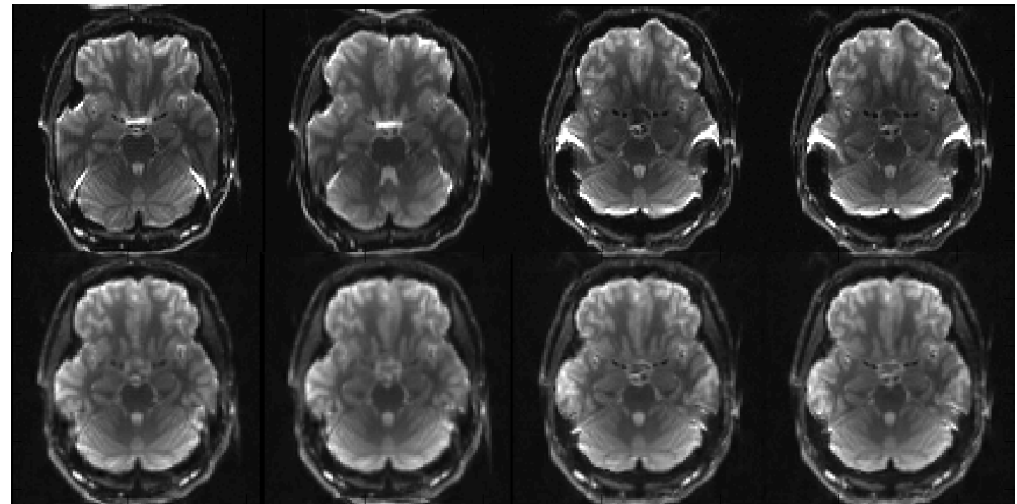
Analysis: FDT pipeline

DICOM → NIFTI:
dcm2nii

Motion + eddy
currents + EPI
distortions

brain extraction:
BET

TOPUP



EPI distortions

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TOPUP>

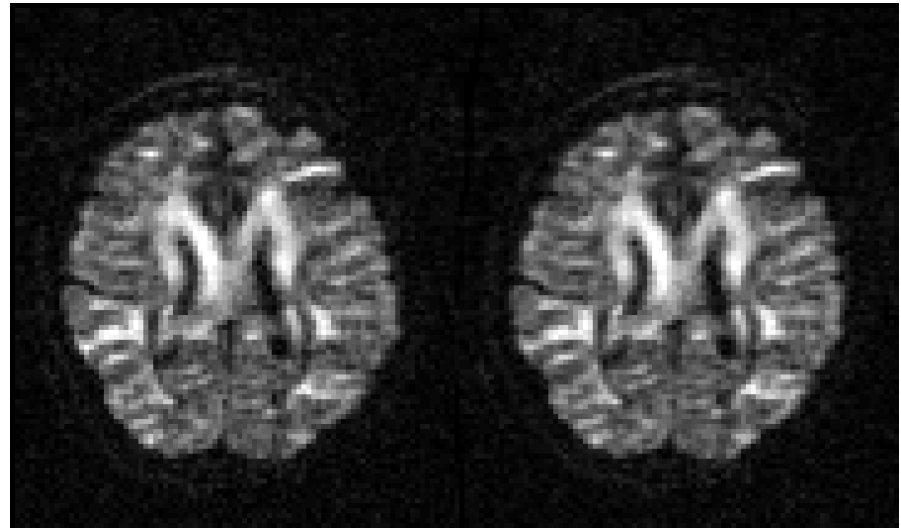
Analysis: FDT pipeline

DICOM → NIFTI:
dcm2nii

Motion + eddy
currents + EPI
distortions

brain extraction:
BET

EDDY



(EPI distortions) + motion + eddy

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/EDDY>

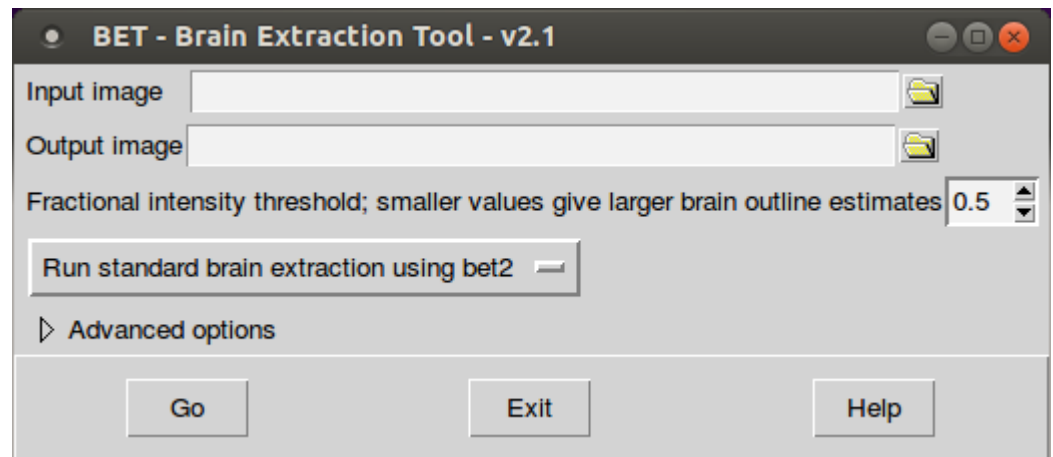
Analysis: FDT pipeline

DICOM → NIFTI:
dcm2nii

Motion + eddy
currents + EPI
distortions

brain extraction:
BET

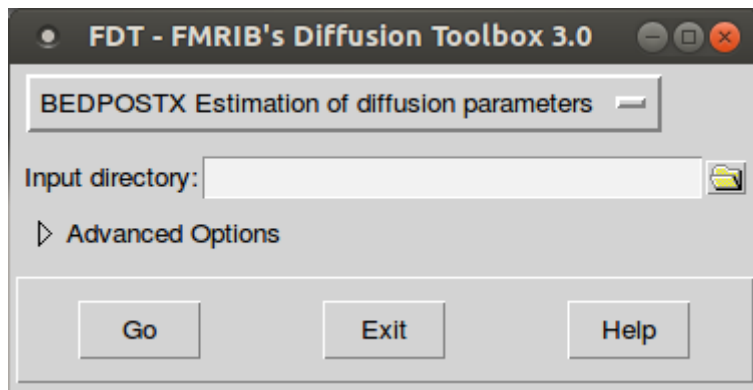
Brain Extraction Tool



<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/BET>

Analysis: FDT pipeline

Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques



model estimation:
BEDPOSTX

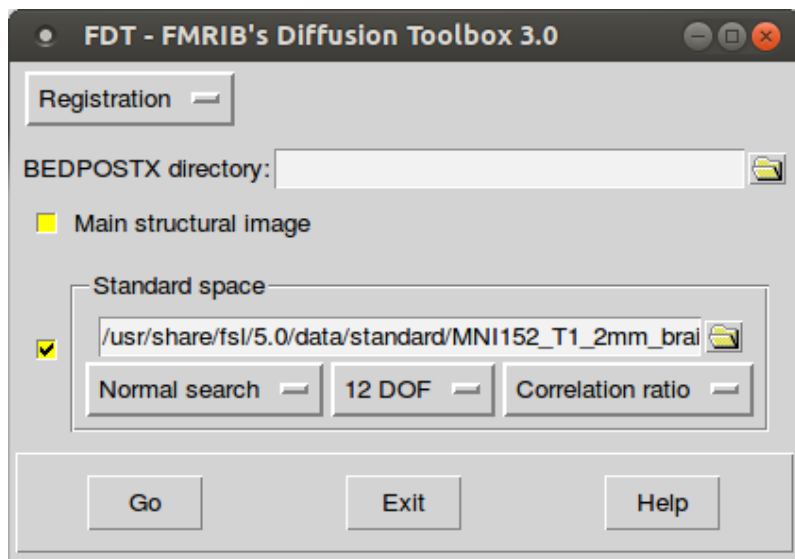
registration:
FLIRT (FNIRT)

tractography:
PROBTRACKX

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide>

Analysis: FDT pipeline

built-in FMRIB's (Non-)Linear Image Registration Tool



model estimation:
BEDPOSTX

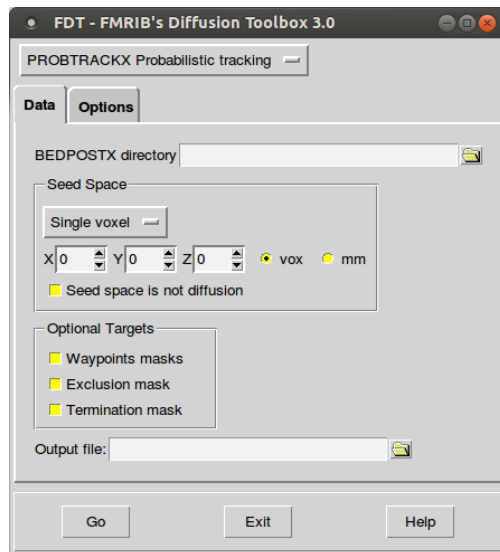
registration:
FLIRT, FNIRT

tractography:
PROBTRACKX

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide>

Analysis: FDT pipeline

Probabilistic Tractography with Crossing Fibres



model estimation:
BEDPOSTX

registration:
FLIRT, FNIRT

tractography:
PROBTRACKX

<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide>

Analysis: PROTRACKX

FDT - FMRIB's Diffusion Toolbox 3.0

PROBTRACKX Probabilistic tracking

Data Options

BEDPOSTX directory: dti.bedpostx

Seed Space

Single mask

Seed Image/Surface: masks/my_seed.nii.gz

☒ Seed space is not diffusion

☒ nonlinear

Select Seed to diff transform: dti.bedpostX/xfms/str2diff_warp.nii.gz

Select diff to Seed transform: dti.bedpostX/xfms/diff2str_warp.nii.gz

☐ surface

Optional Targets

☐ Waypoints masks

☐ Exclusion mask

☒ Termination mask: masks/midline+csf.nii.gz

☐ Classification targets

Output directory: probtrackX/my_seed

Go Exit Help

FDT - FMRIB's Diffusion Toolbox 3.0

PROBTRACKX Probabilistic tracking

Data Options

Basic Options

Number of samples: 5000

Curvature threshold: 0.2

☐ Verbose

☒ Loopcheck

Advanced Options

☒ Use modified Euler streamlining

Maximum number of steps: 2000

Step length (mm): 0.5

☐ Use anisotropy to constrain tracking

☐ Use Distance correction

Subsidiary fibre volume fraction threshold: 0.01

Minimum length threshold (mm): 0.0

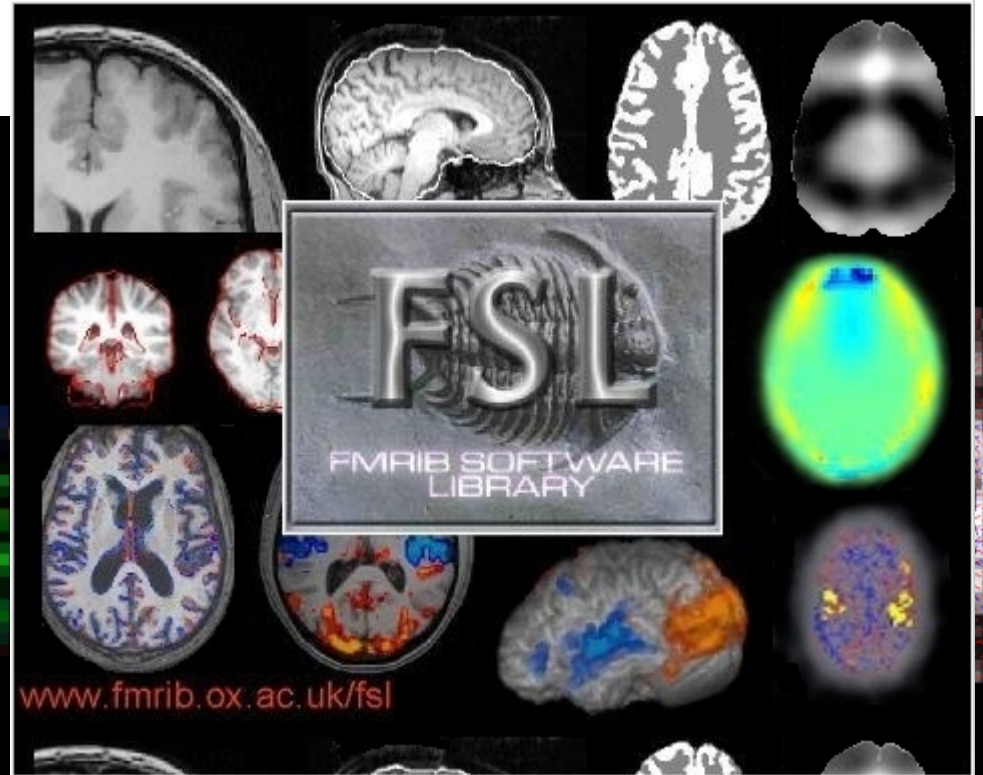
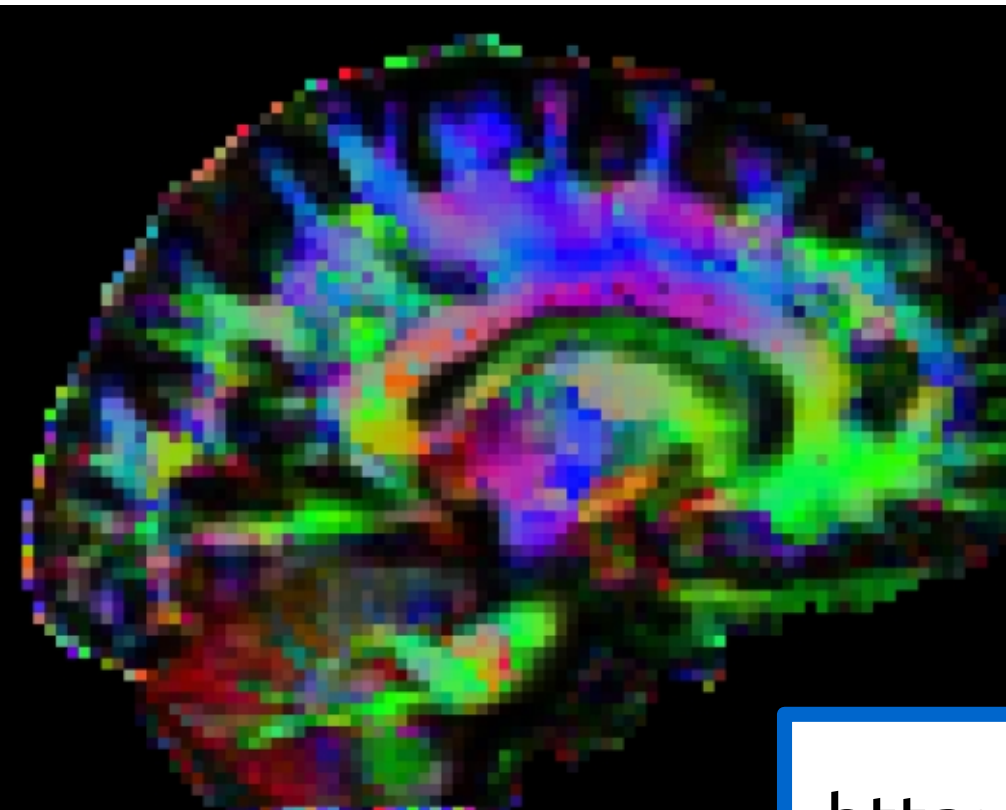
Seed sphere sampling (mm): 0.0

Waypoint Options

Matrix Options

Go Exit Help

Analysis: FSLView

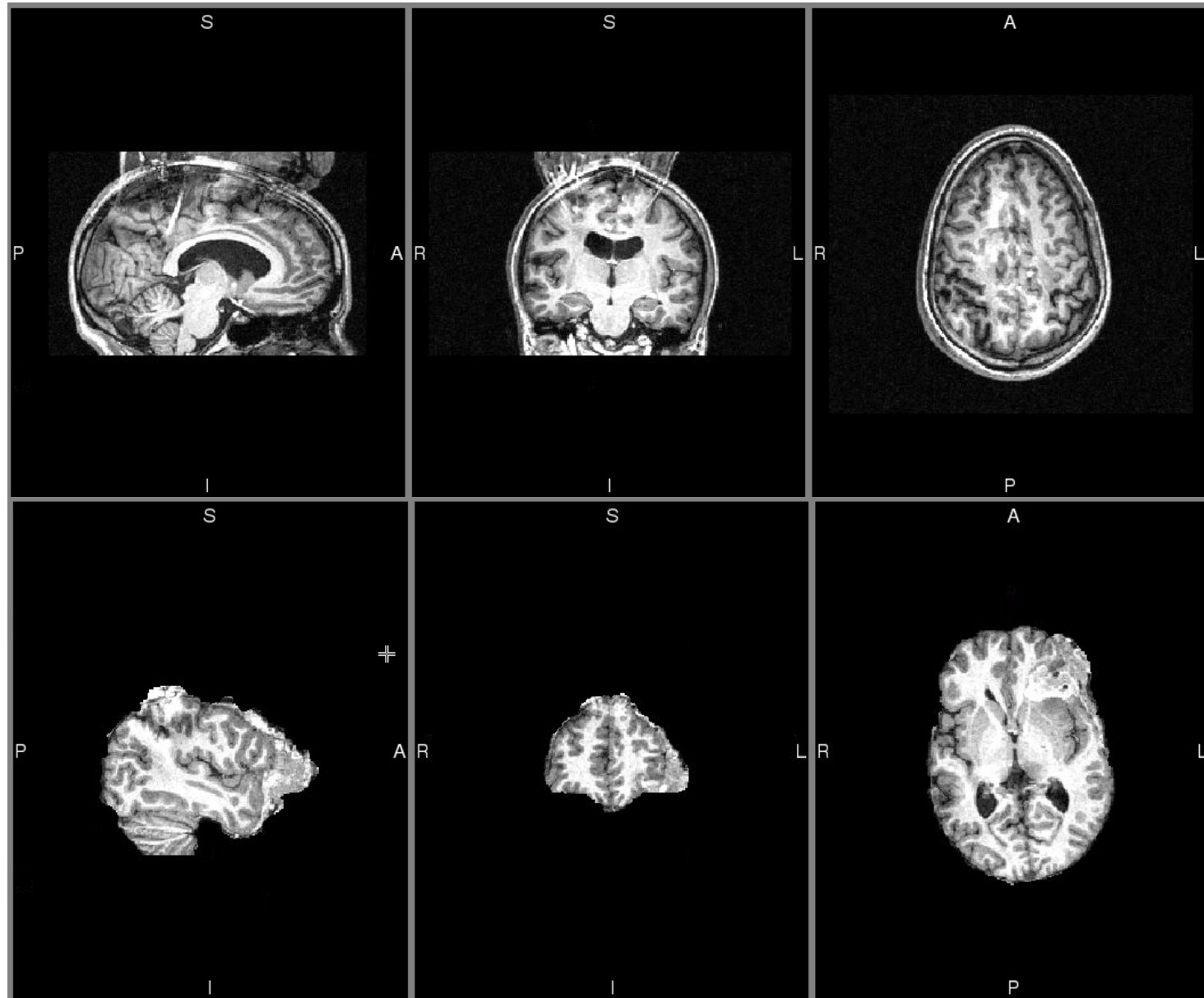


<http://fsl.fmrib.ox.ac.uk/fsl/fslview/>

Pitfalls: T_1 -weighted template

Nyquist

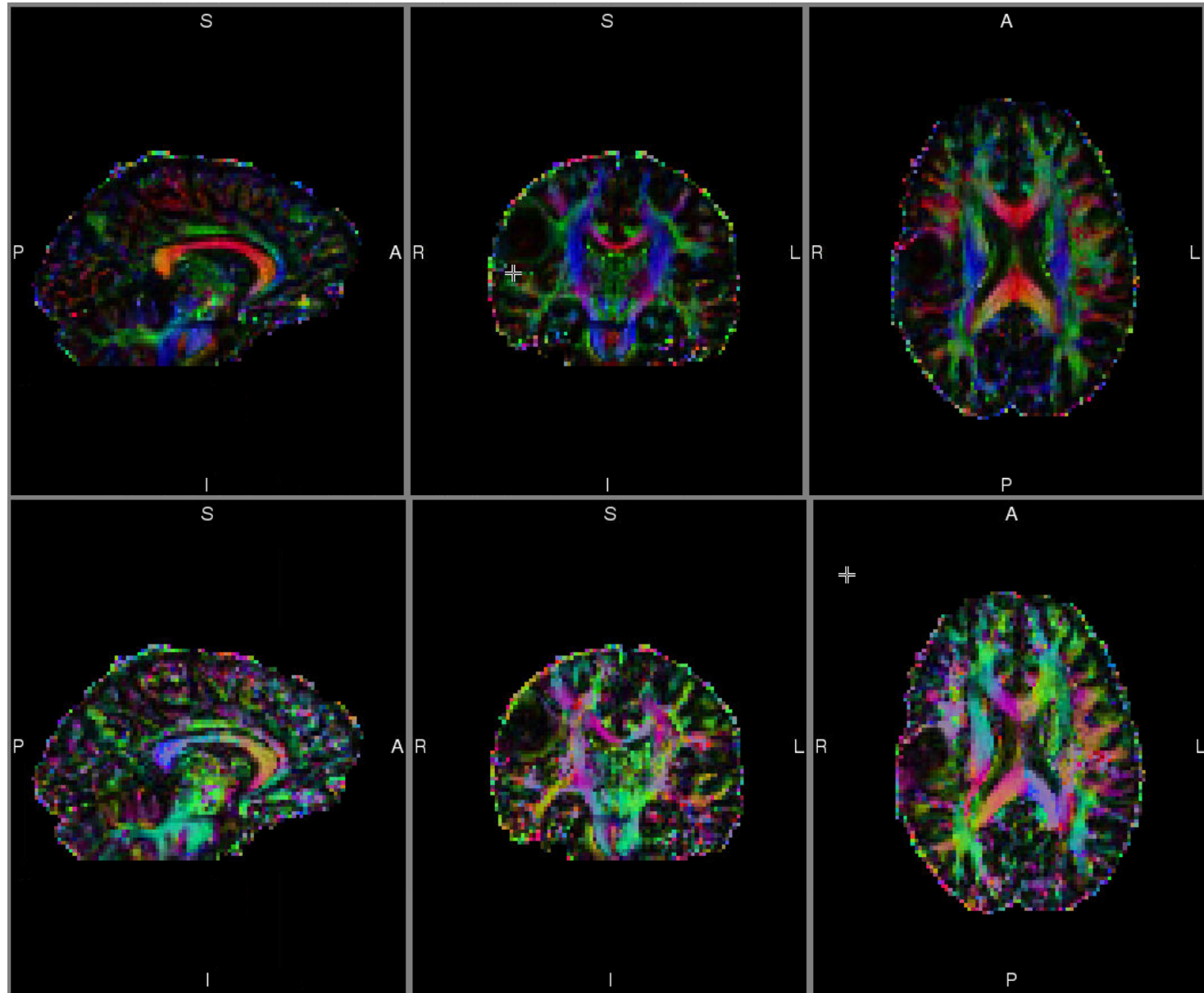
BET fails



Pitfalls: b vectors

bvecs OK

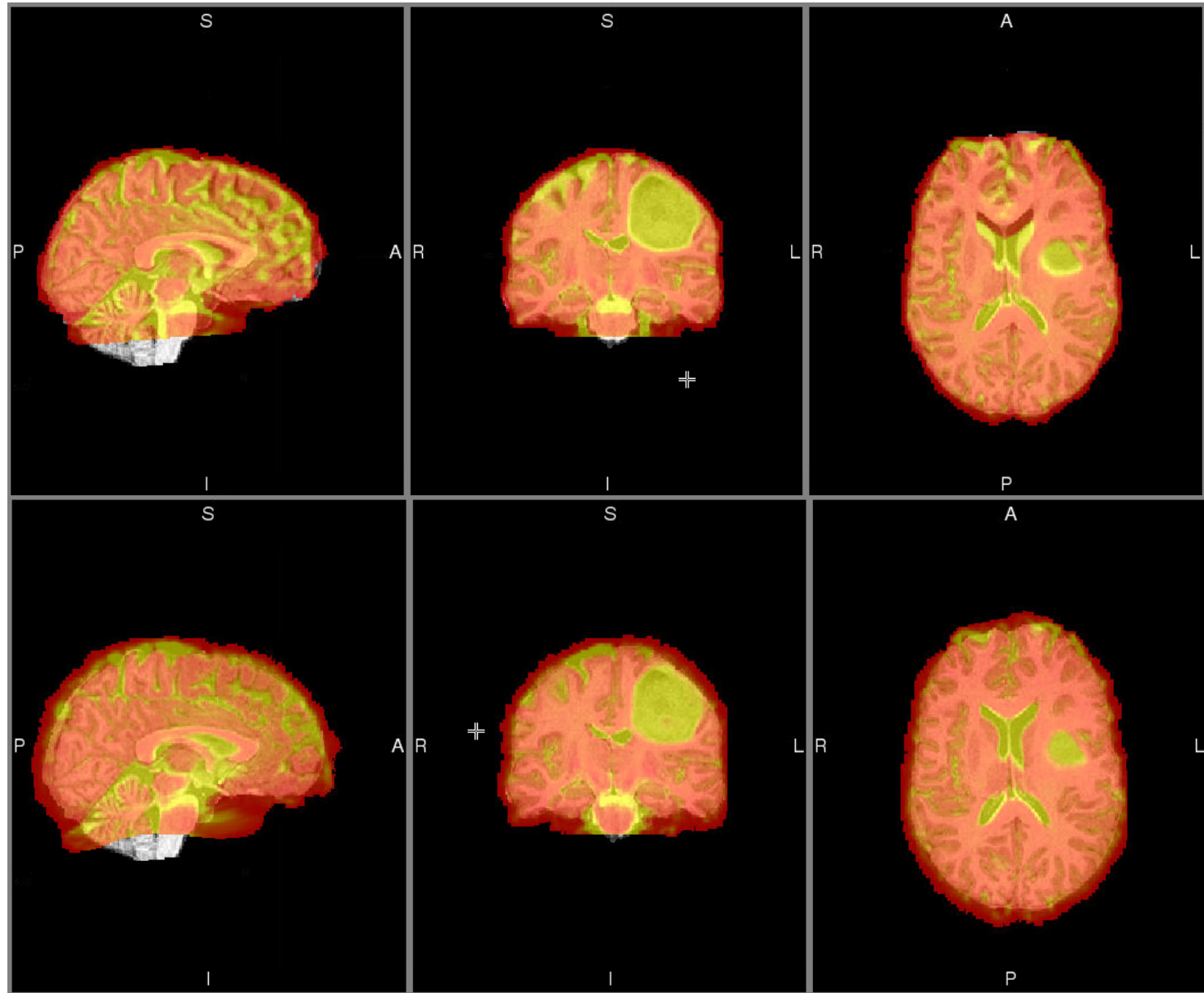
bvecs BAD



Pitfalls: Registration/Unwarping

linear

non-linear



Bottom line

Thank you for your attention!



References

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