MRC Cognition and Brain Sciences Unit

UNIVERSITY OF CAMBRIDGE

Introduction to Diffusion MRI

Marta M. Correia
MRC Cognition and Brain Sciences Unit

Overview

- Basic concepts
- Diffusion weighting and MRI
- Modelling of diffusion MRI signal
  - The diffusion tensor model
  - Scalar metrics

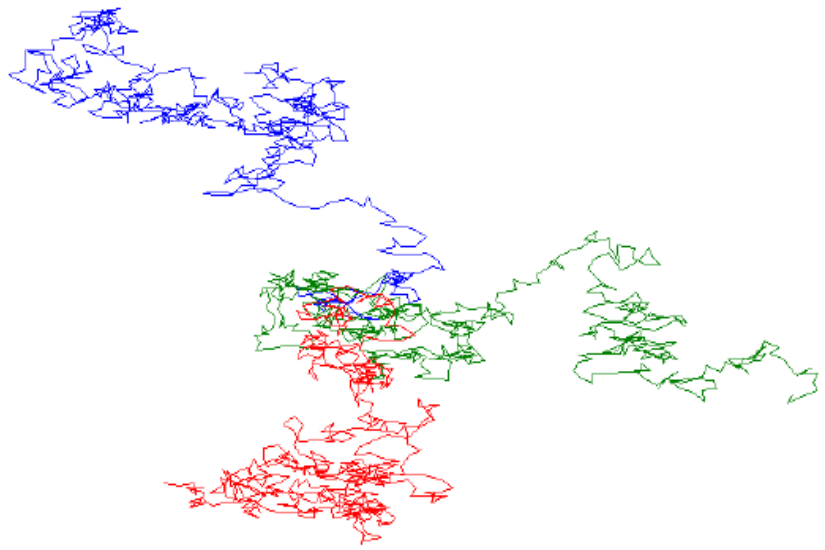
- Common artefacts
- Quality Control

Basic concepts

Concept of Molecular Diffusion

- Molecular diffusion refers to the random translational motion of molecules (also called Brownian motion) that results from the thermal energy carried by these molecules.

- In a free medium, molecular displacements obey a 3D Gaussian distribution.
- Molecules travel randomly in space over a distance that is statistically well described by a diffusion coefficient *D*.
- *D* depends only on the mass of the molecules, the temperature and viscosity of the medium.

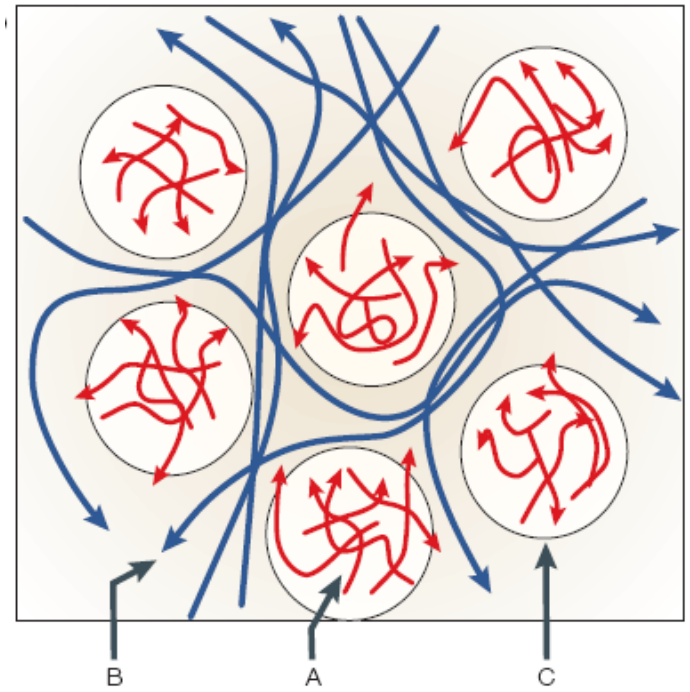


Three random walks originating from a common starting point.

Diffusion in the Brain

- During their diffusion driven displacements, molecules probe tissue structure on a microscopic scale, well beyond the usual image resolution (mm).
- During diffusion, water molecules move in brain tissues bouncing off, crossing or interacting with many tissue components, such as cell membranes, fibres and macromolecules.
- The movement of water is impeded by these obstacles, and the diffusion displacement distribution is no longer Gaussian.

The non-invasive observation of the water diffusion-driven displacement distributions *in vivo* provides unique clues to the fine structural features and geometric organization of neural tissues and also to changes in these features with physiological and pathological states.



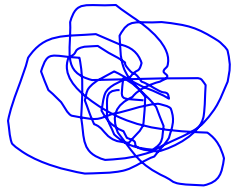
In biological tissues, obstacles modulate the free diffusion process.

Isotropic vs Anisotropic Diffusion

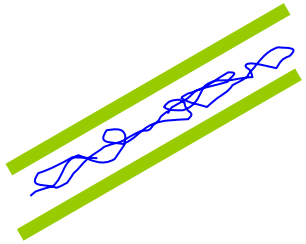
- Free diffusion (no obstacles) occurs equally in all directions. This is called **isotropic diffusion**.
- If the water diffuses in a medium having barriers, the diffusion will be uneven. Barriers can be many things (cell membranes, molecules, axons, etc), but in white matter the principal barrier is the myelin sheath of axons.
- Bundles of axons provide a barrier to perpendicular diffusion and a path for parallel diffusion along the orientation of the fibres. This is termed **anisotropic diffusion**.

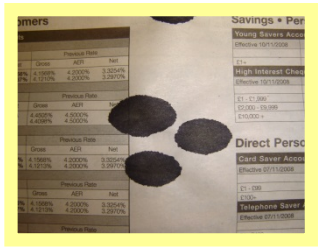
Diffusion trajectory

Isotropic
Diffusion (free water)



Anisotropic Diffusion
(coherent axonal bundle)

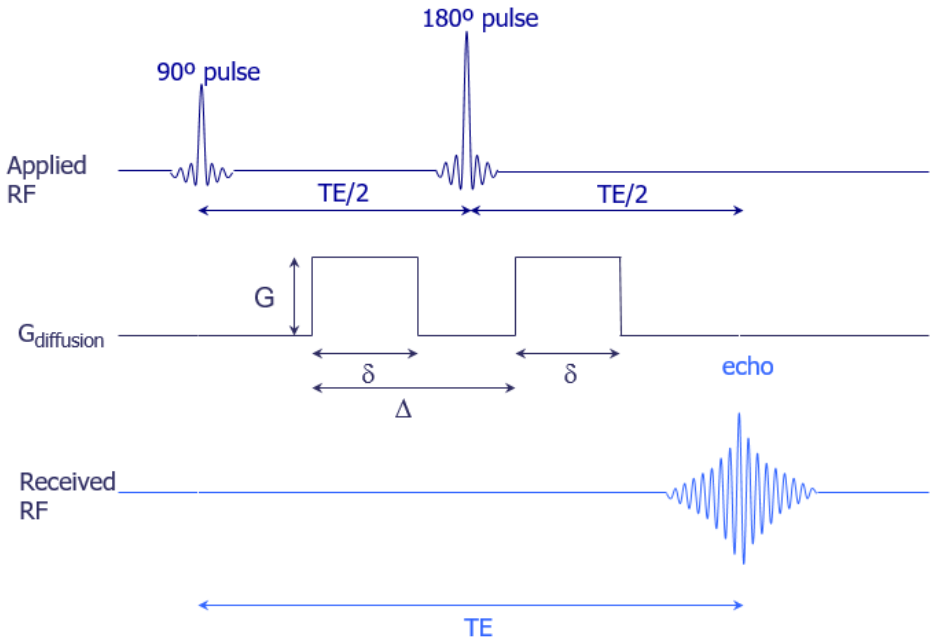




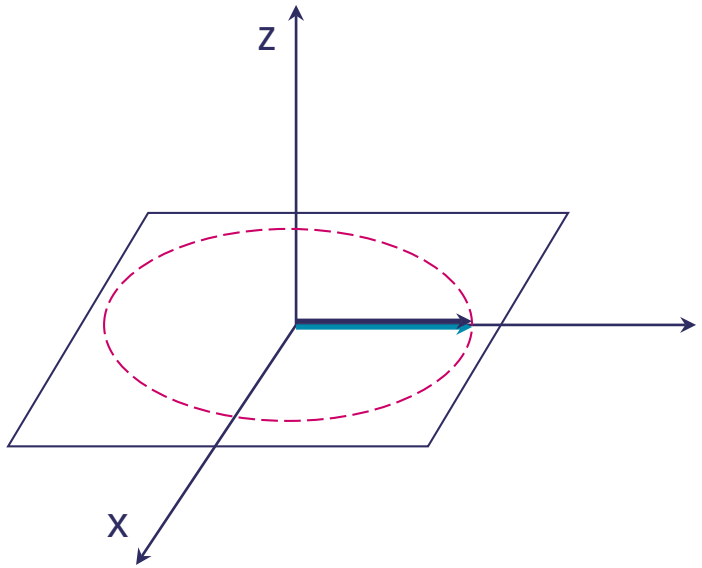
Diffusion weighting and MRI

Diffusion-weighting gradients

- Magnetic field gradients are primarily used for spatial encoding, they can also be used for other purposes.
- Diffusion-weighting gradients can be incorporated in the pulse sequence to sensitise the MRI signal to the motion of water molecules.
- The most commonly used diffusion sequence is a modification of the spin echo sequence called pulsed gradient spin echo (PGSE).
- In this sequence, the motion of spins is reflected in attenuation of the spin echo signal.

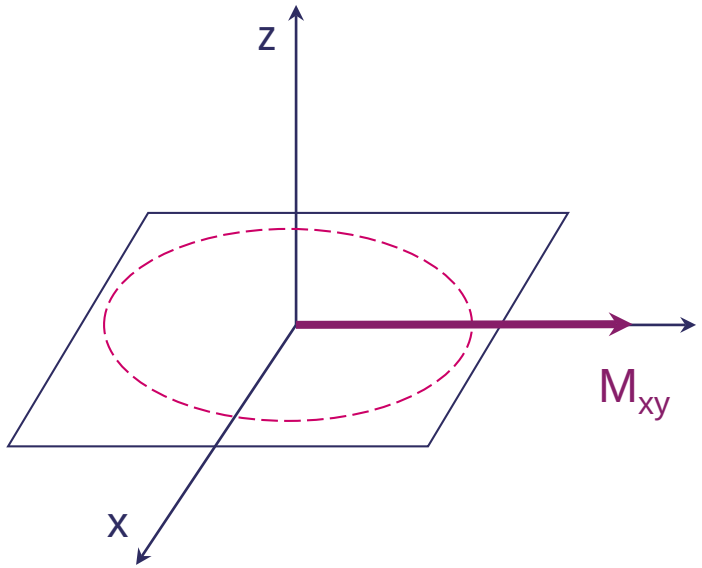


PGSE step-by-step (1)



- The 90º RF pulse tips the net magnetization onto the transverse plane.
- All spins are initially in phase.

PGSE step-by-step (1)



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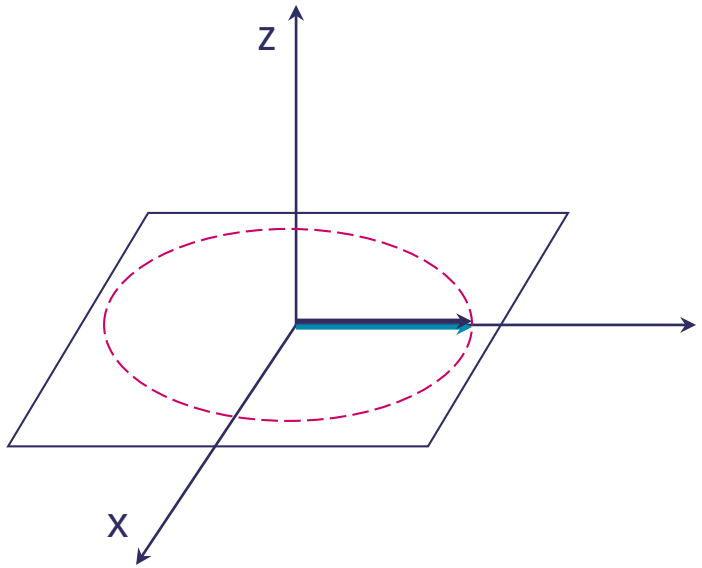
PGSE step-by-step (1)



- The 90º RF pulse tips the net magnetization onto the transverse plane.
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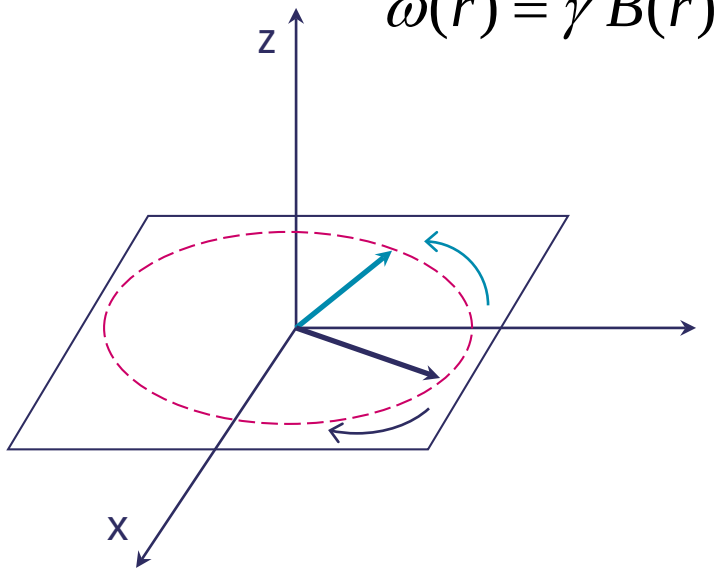
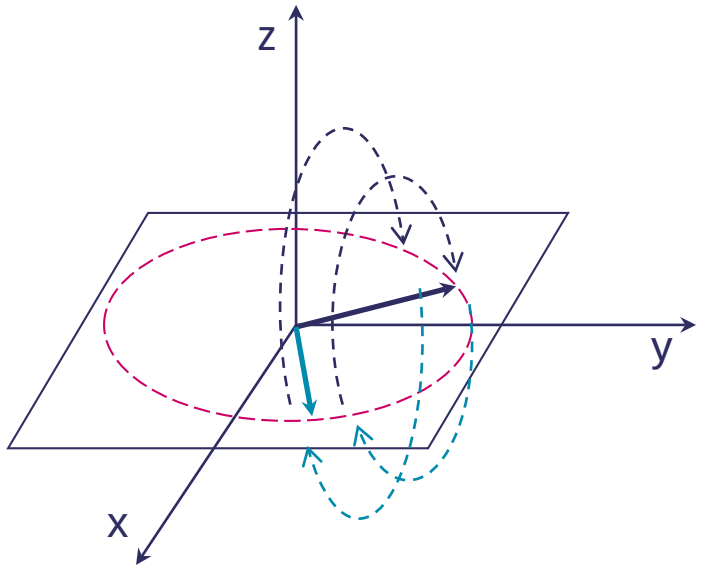
PGSE step-by-step (2)

$$\omega(r) = \gamma B(r)$$



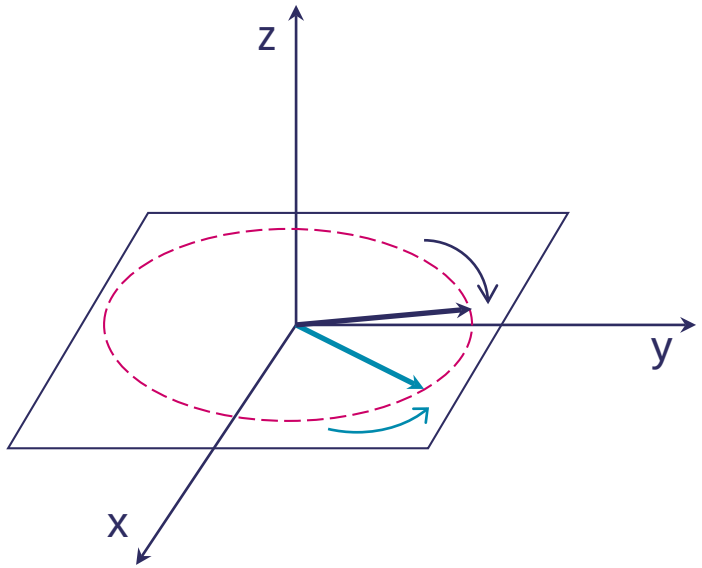


- The spins de-phase naturally and due to the presence of the DW gradient.
- The final phase shift of each spin depends on its spatial location, $d\phi_1 = \gamma G \delta z_1$.

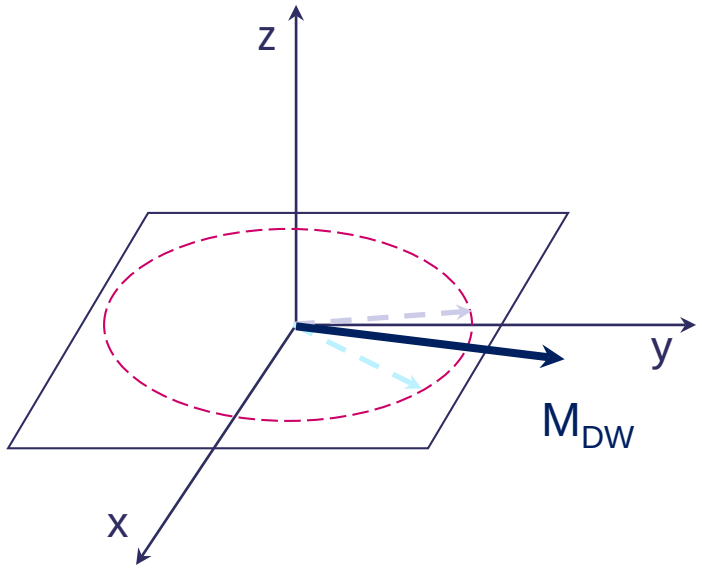
- At time TE/2, the 180º pulse is applied. Immediately after this the phases of the spins are reversed:

$$d\phi_1 \longrightarrow -d\phi_1$$

PGSE step-by-step (3)

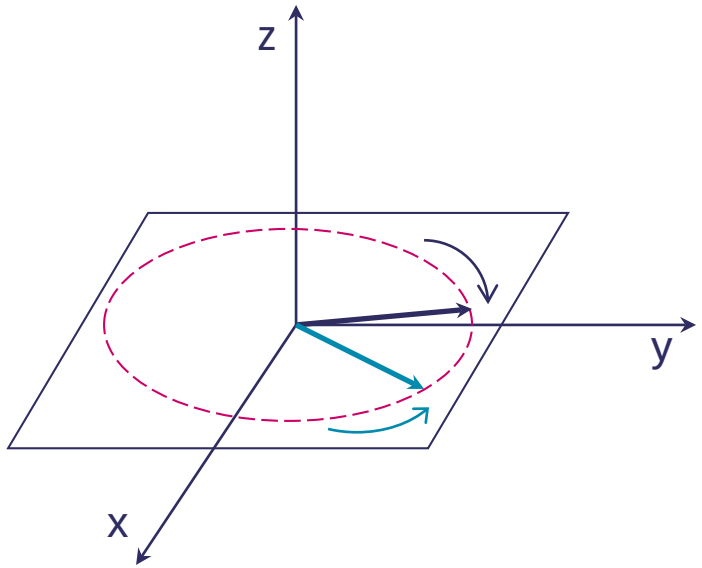


- The second DW gradient causes another phase shift, $d\phi_2 = \gamma G \delta z_2$.
- If the spins have moved between gradients, $z_1 \neq z_2$, and $d\phi_{total} = \gamma G \delta (z_2 - z_1) \neq 0$.



- Due to the combined effect of motion and the DW gradients, not all spins will re-phase perfectly and at time TE the amplitude of the echo will be smaller.

PGSE step-by-step (3)



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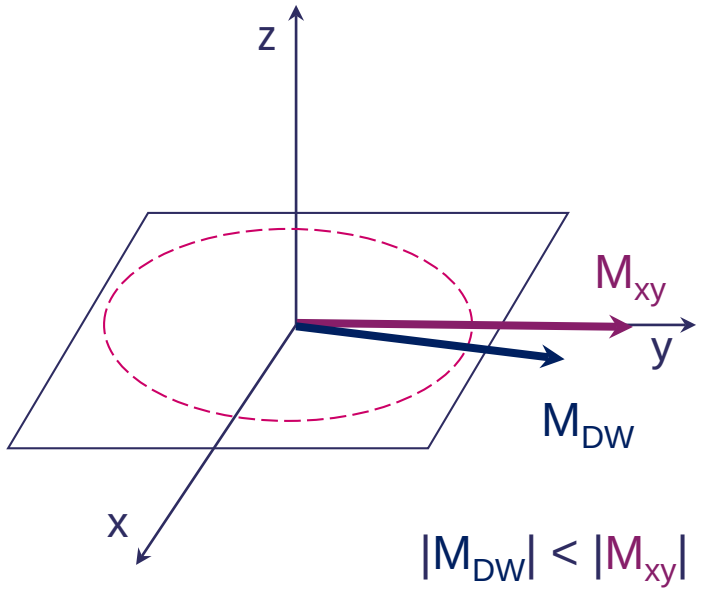


- Due to the combined effect of motion and the DW gradients, not all spins will re-phase perfectly and at time TE the amplitude of the echo will be smaller.

The diffusion MRI signal

- MRI signal profile as a function of the direction (θ,ϕ) of the DW gradients, $S(\theta,\phi)$:
  - isotropic voxel:
  - anisotropic voxel:

- Changing the gradient direction changes the amount of attenuation seen, depending on how much motion there is along that specific direction.

The diffusion weighting parameter (b-value)

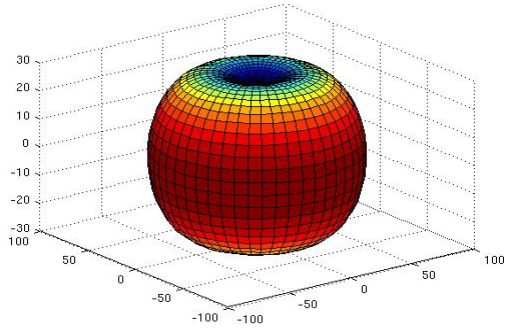
$$b = (\gamma G \delta)^2 (\Delta - \delta/3)$$

DW gradient intensity

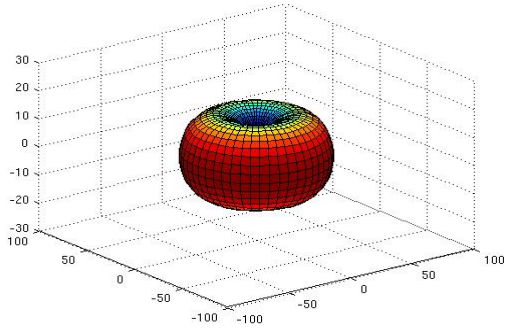
spacing between gradients

gradient duration

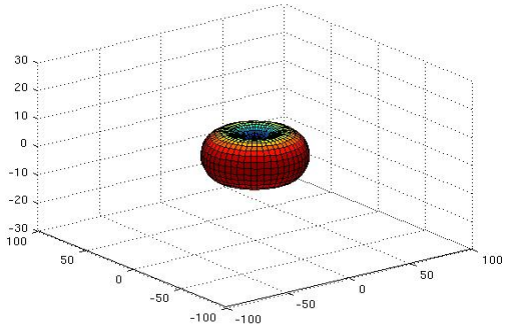
b = 1000 s/mm²



b = 2000 s/mm²

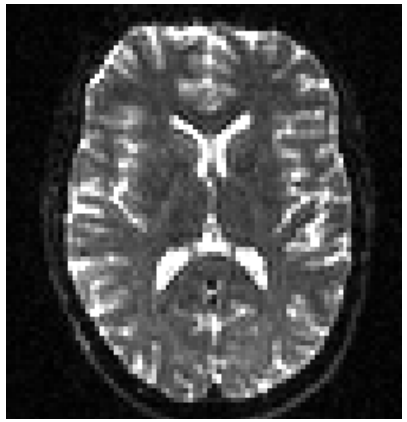


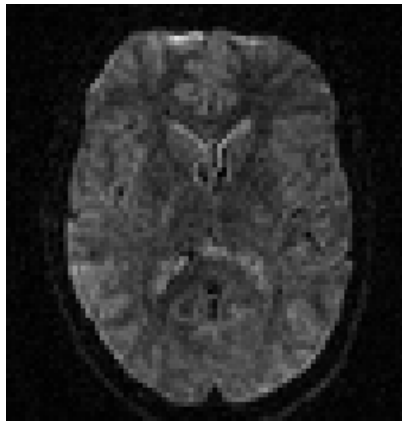
b = 3000 s/mm²



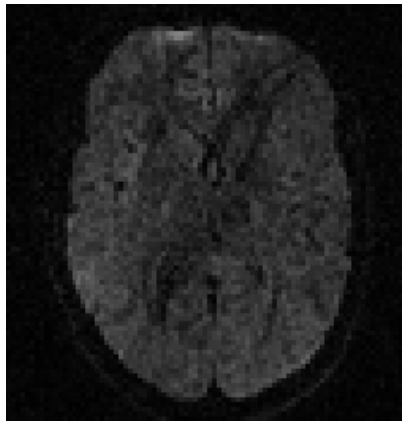
Changing the b-value in the Brain

$b = 0$ s/mm^2

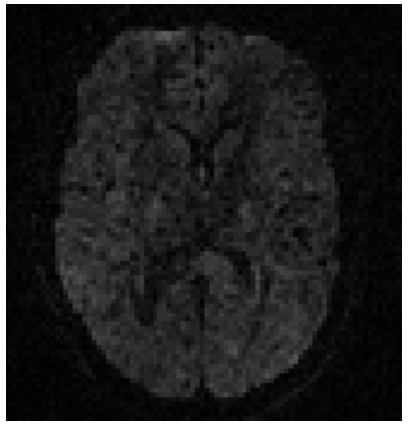




$b = 400$ s/mm^2



$b = 800$ s/mm^2



$b = 1200$ s/mm^2

Gaussian Modeling of the Diffusion Signal

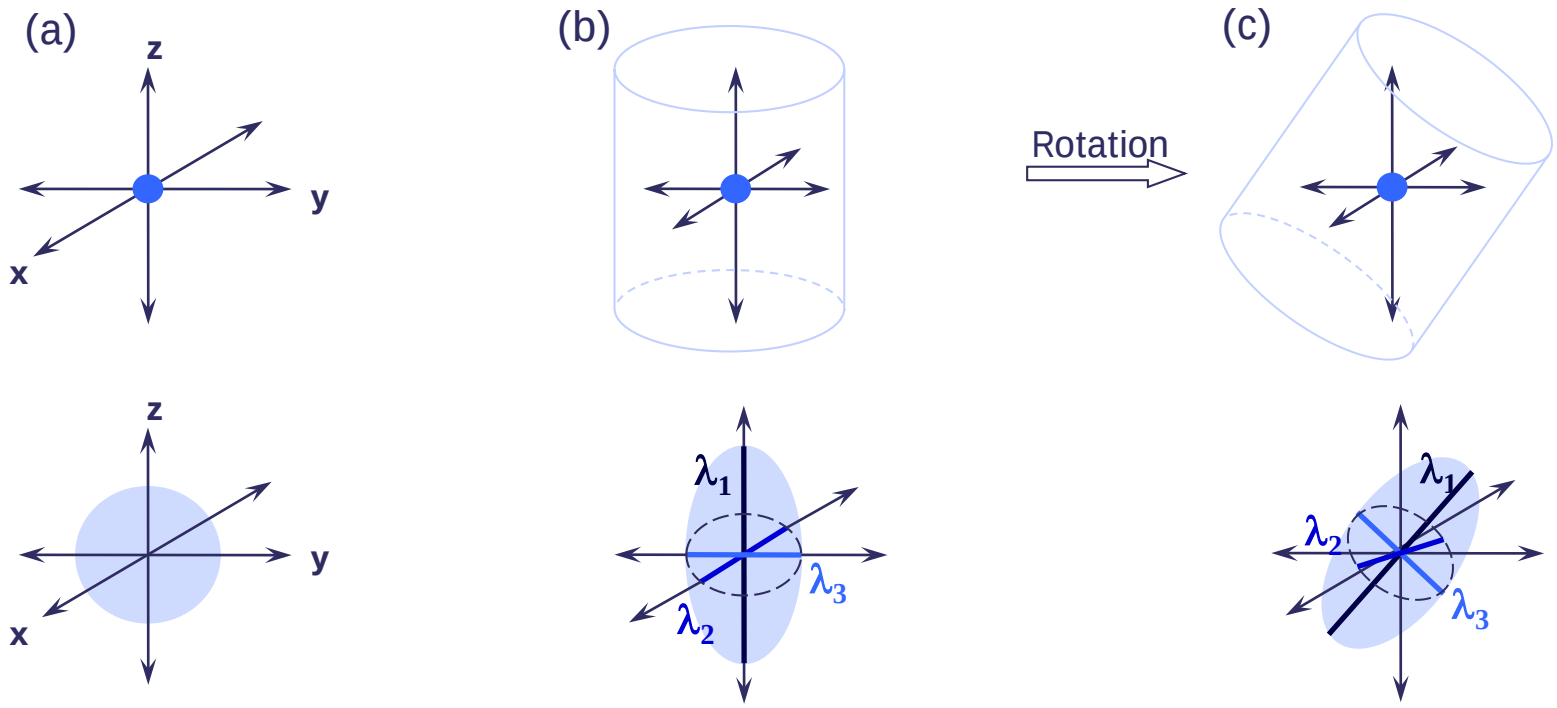
The Diffusion Tensor Model

- Diffusion is a 3D process and water molecules mobility in tissues is not necessarily the same in all directions.
- Organized fibrous tissues, such as muscle and cerebral white matter, demonstrate anisotropic diffusion.
- The simplest model that can characterise Gaussian diffusion in which the displacements pert unit time are not the same along all directions is the **diffusion tensor**.
- This is a 3x3 symmetric matrix:

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

- The diagonal elements correspond to diffusivities along the three orthogonal axes.

The Diffusion Ellipsoid



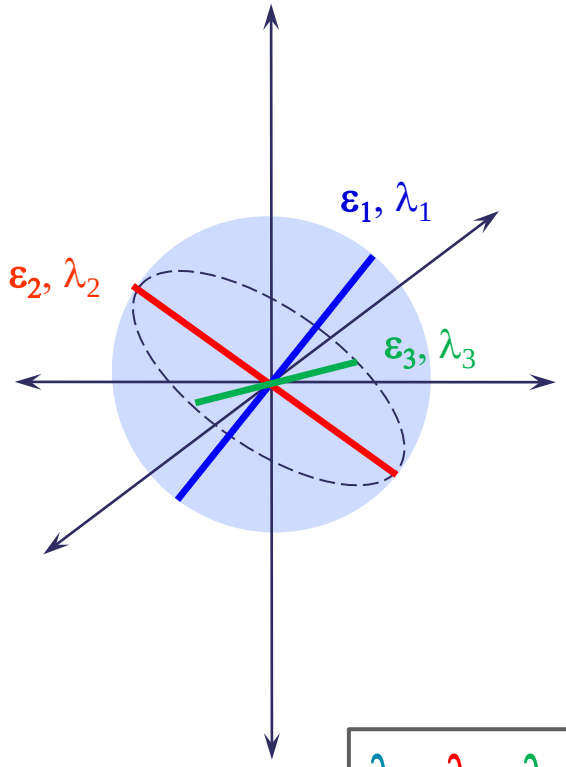
$$\begin{bmatrix} D & 0 & 0 \\ 0 & D & 0 \\ 0 & 0 & D \end{bmatrix}$$

$$\begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

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

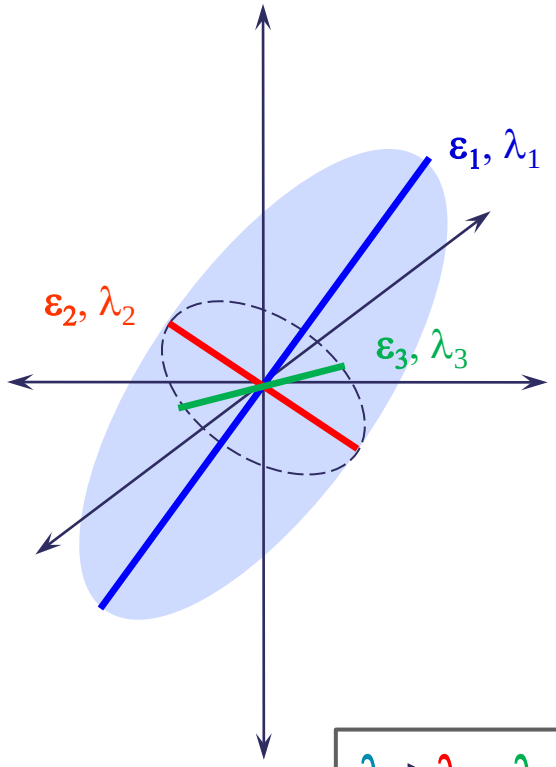
Eigenvalues and eigenvectors

Isotropic Diffusion



$\lambda_1=\lambda_2=\lambda_3$

Anisotropic Diffusion



$\lambda_1>\lambda_2\sim\lambda_3$

How to estimate the diffusion tensor (1)

- When the tensor formalism is incorporated in the Bloch equations, it can be shown that the signal attenuation due to diffusion is given by:

$$S(b,\vec{r}) = S_0\, e^{-b\,\vec{r}^{\,T}\,\underline{D}\,\vec{r}}$$

where *b* is the diffusion weighting parameter, and $\vec{r}$ is the direction of the encoding gradient.

- This equation can be expanded to:

$$S(b,\vec{r}) = S_0 \exp\left\{\begin{array}{c} -br_x^2 D_{xx} - br_y^2 D_{yy} - br_z^2 D_{zz} \\ -2br_x r_y D_{xy} - 2br_x r_z D_{xz} - 2br_y r_z D_{yz} \end{array}\right\}$$

How to estimate the diffusion tensor (2)

- Applying logs to both sides of this equation:

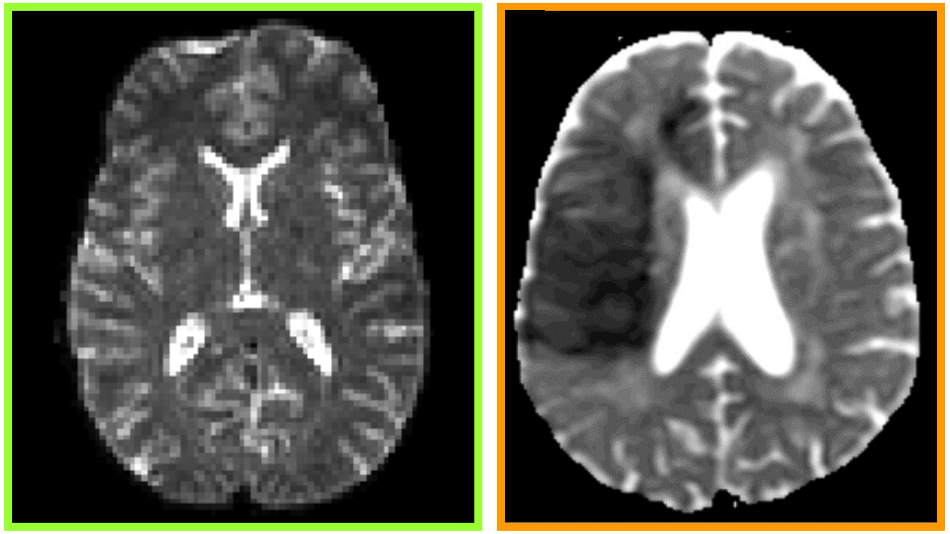
$$\log\left(S(b,\vec{r})\right) = \log\left(S_0\right) - b\left\{\begin{array}{c} r_x^2 D_{xx} + r_y^2 D_{yy} + r_z^2 D_{zz} \\ + 2r_x r_y D_{xy} + 2r_x r_z D_{xz} + 2r_y r_z D_{yz} \end{array}\right\}$$

- As the tensor is symmetric, there are only six unknown elements to determine.
- These are estimated from a series of diffusion-weighted images acquired with gradients applied along non-collinear and non-coplanar directions.

Mean diffusivity (MD)

- Measurements of the DT and its components have been found to have several applications in the human brain.

- **Mean diffusivity map:** MD is the average value of the rate of diffusion on each voxel. MD maps contain very useful information for detecting and evaluating brain ischemia and stroke.



$$MD = \frac{D_{xx} + D_{yy} + D_{zz}}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

MD maps of a healthy brain (left) and a stroke patient (right).

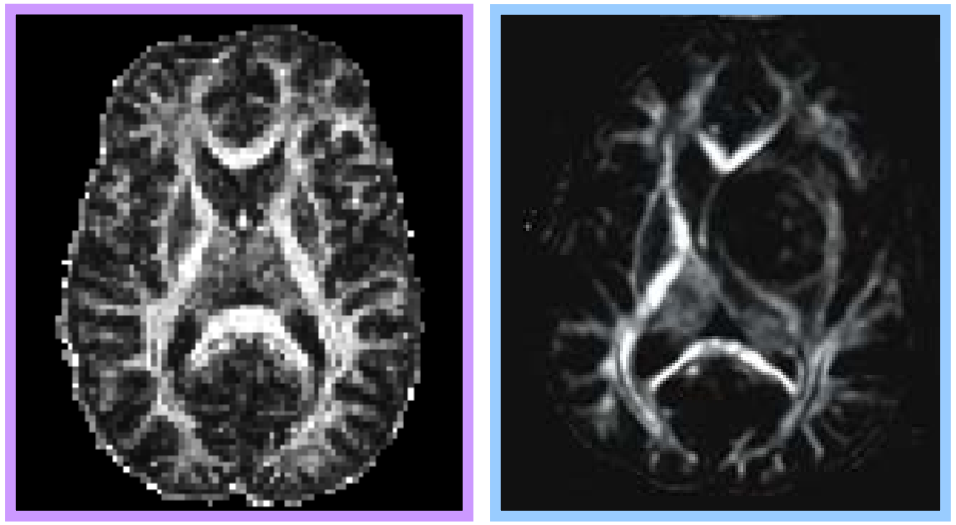
Fractional Anisotropy (FA)

- **Fractional Anisotropy map:** FA is a measure of the degree of diffusion anisotropy, and it is calculated from the diffusivity constants λ_1, λ_2, λ_3.

$$FA = \sqrt{\frac{3((\lambda_1 - <\lambda>)^2 + (\lambda_2 - <\lambda>)^2 + (\lambda_3 - <\lambda>)^2)}{2(\lambda_1^{\,2} + \lambda_2^{\,2} + \lambda_3^{\,2})}}$$

- FA produces high values for white matter (highly anisotropic) and low values for grey matter(isotropic).

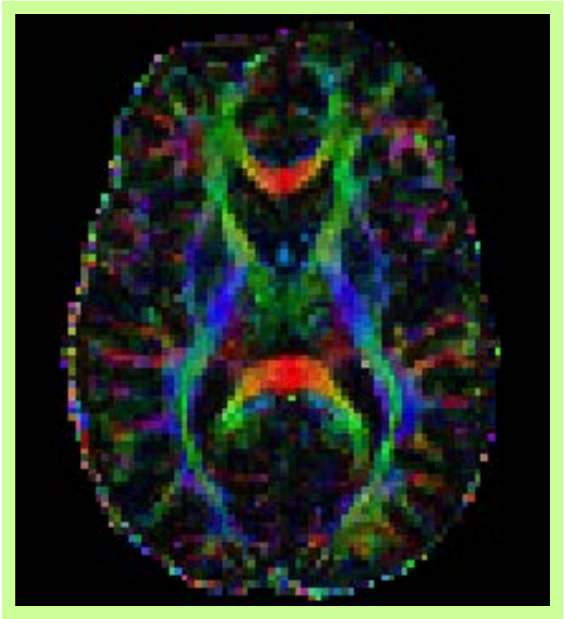
- It has been used to study white matter in terms of morphology, disease and trauma, brain development and neurosurgical planning.



FA maps of a healthy brain (left) and a brain tumour patient (right).

Colour coded FA maps

- Let ε_1 designate the longest axis of the diffusion ellipsoid.
- ε_1 can be identified with the main direction of diffusion.
- This directional information can be added to the FA map using a colour code:



Red indicates directions in the *x* axis: right to left or left to right.

Green indicates directions in the *y* axis: front to back or back to front.

Blue indicates directions in the *z* axis: foot-to-head direction or vice versa.

Colour coded FA map.

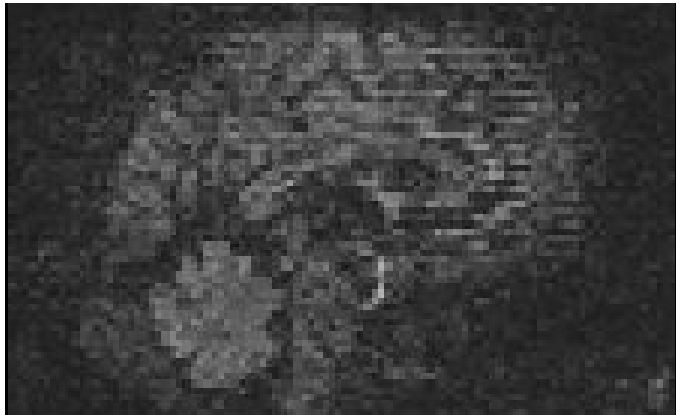
Summary

- MRI can successfully encode the motion of spins due to molecular diffusion.
- In anisotropic tissue, the diffusion MRI measurements are highly dependent on the direction of the applied gradient.
- Reliable inference of the tensor values in all structures requires sufficient sampling of non-collinear gradient directions and appropriate choice of b-values.
- Different diffusion tensor metrics reflect different properties of the underlying tissue structure.

Common Artefacts and Quality Control

Common artefacts

- **Motion artefacts**
  - Stripping and signal voids

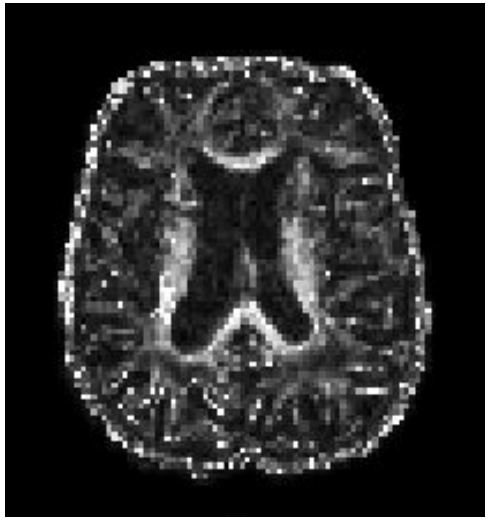


  - Mismatch of voxels across volumes -> poor modelling

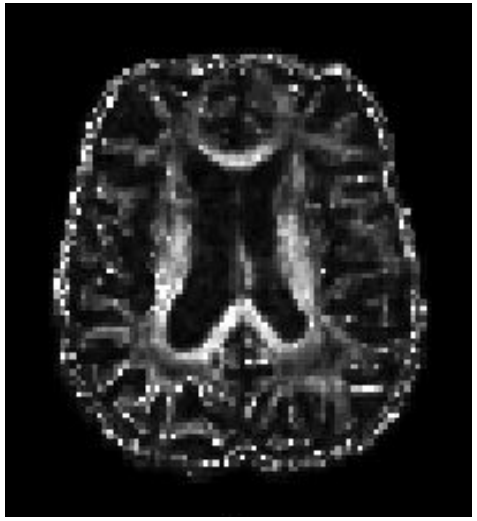
Motion artefacts

- Can this be corrected?

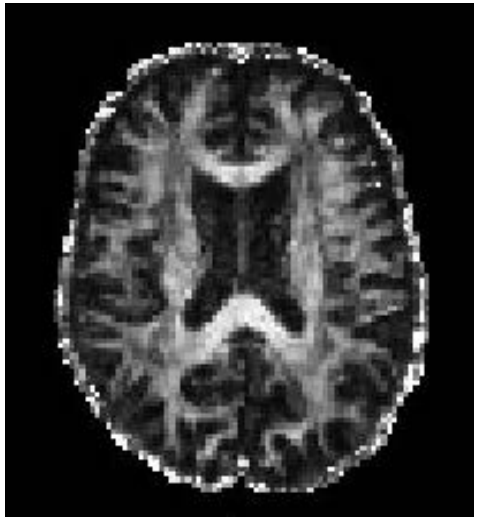
- Effect on FA maps



FA map
before correction



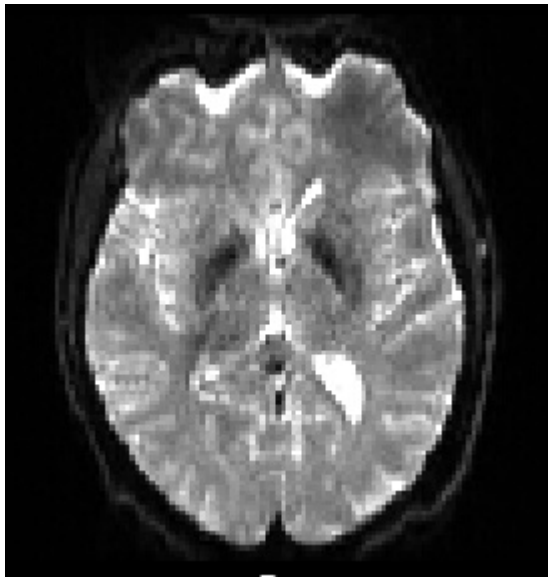
FA map
after correction



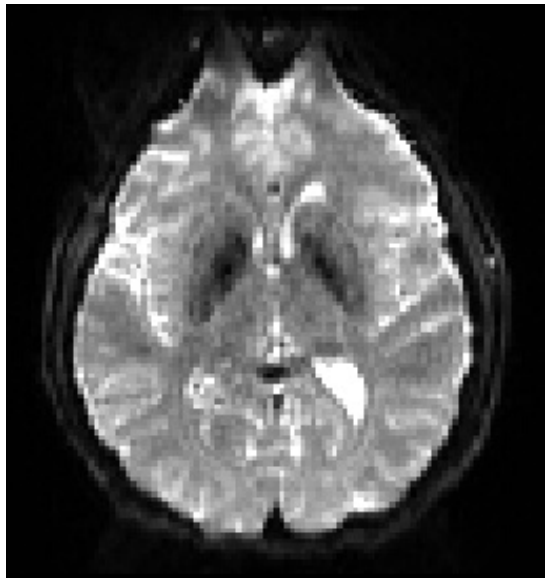
'Good' FA map

Common artefacts

- **EPI distortion**
  - Brain distortion in areas of high susceptibility



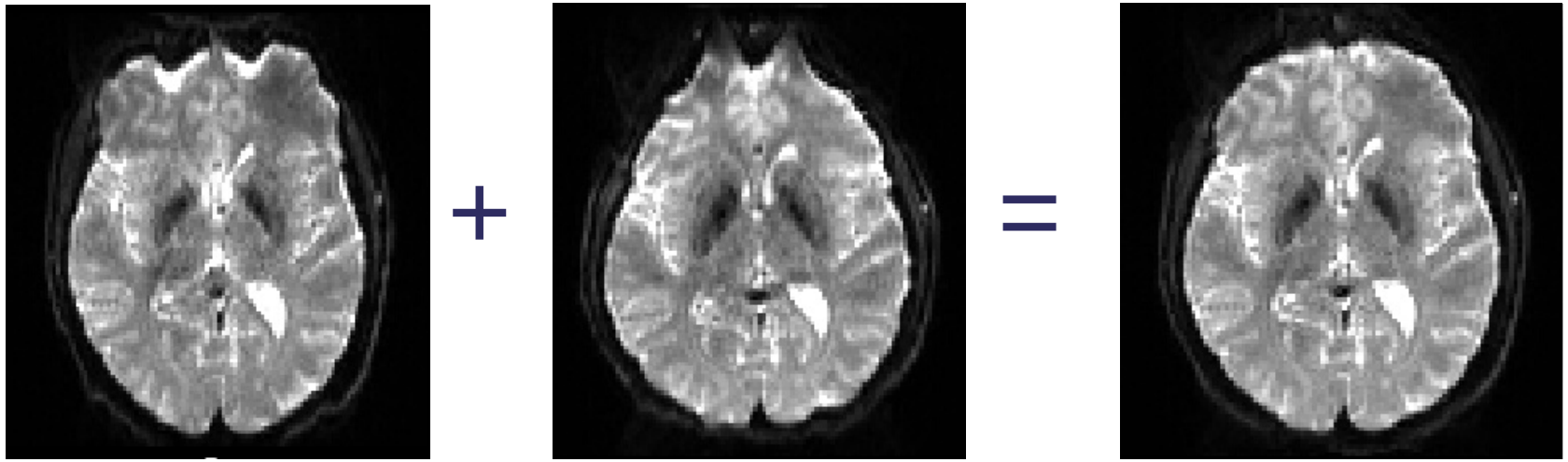
A>>P



P>>A

EPI distortion

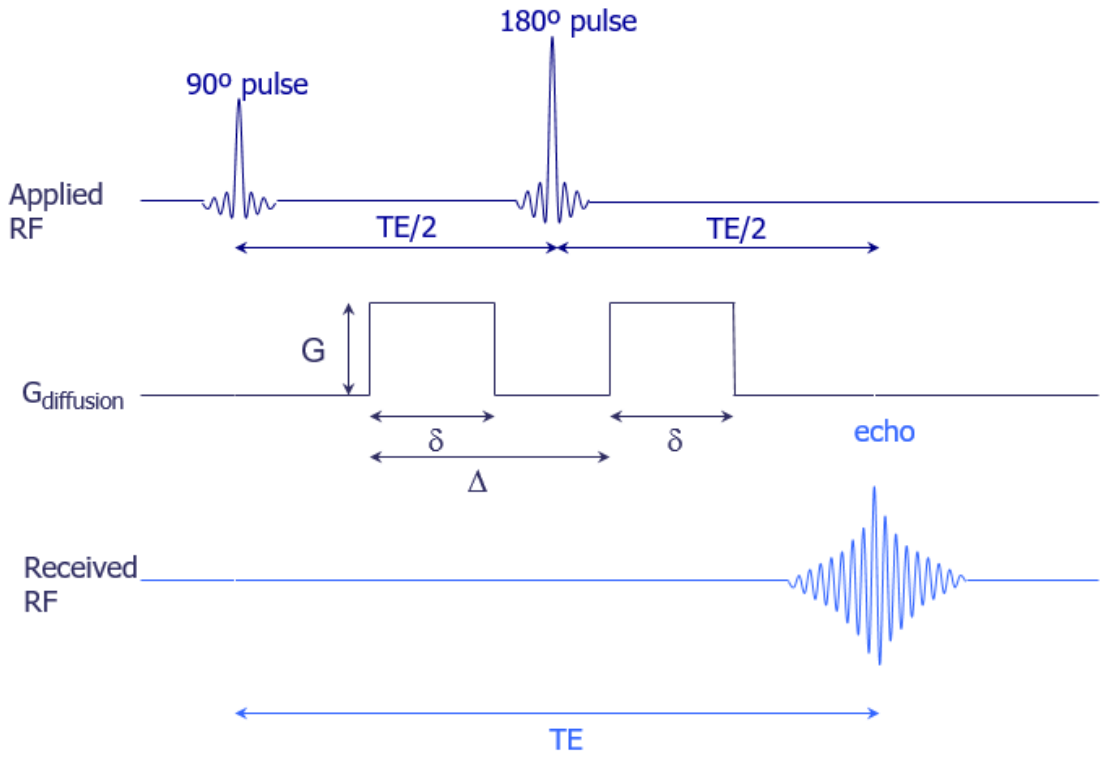
- Can this be corrected?



A>>P P>>A

Common artefacts

- Eddy currents



Eddy currents

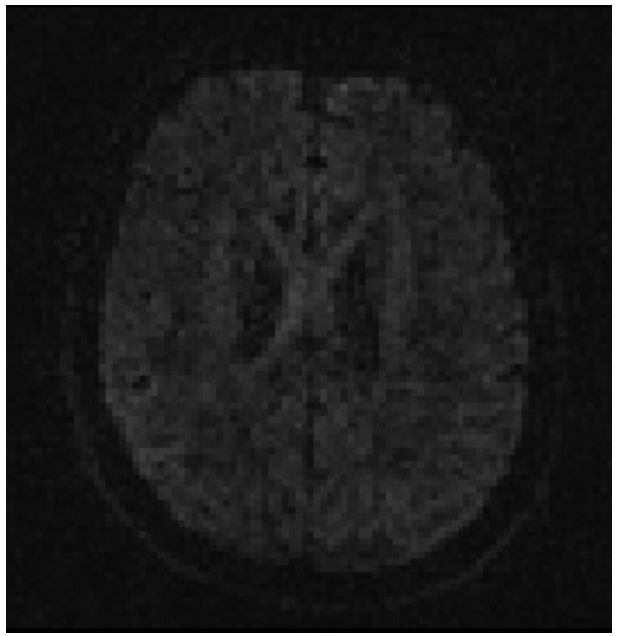
- Can this be corrected?
    - Acquisition: Twice refocused SE sequence

Eddy currents

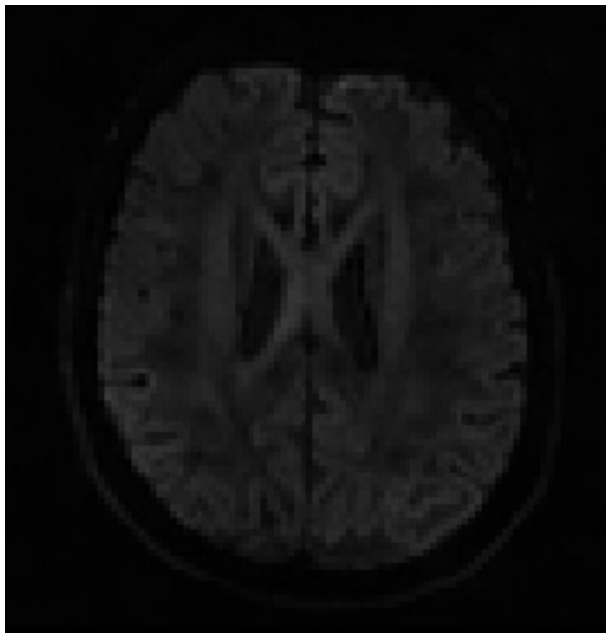
- Can this be corrected?
  - Acquisition + modelling: topup + eddy (fsl)
    - A->P and P->A acquisitions
    - Mapping and correction of distortions
    - Slightly increased scanning time
  - Realignment of volumes using 6/12 parameter registration (eddy_correct, fsl)

Common artefacts

- **Poor SNR**
  - Can this be corrected?

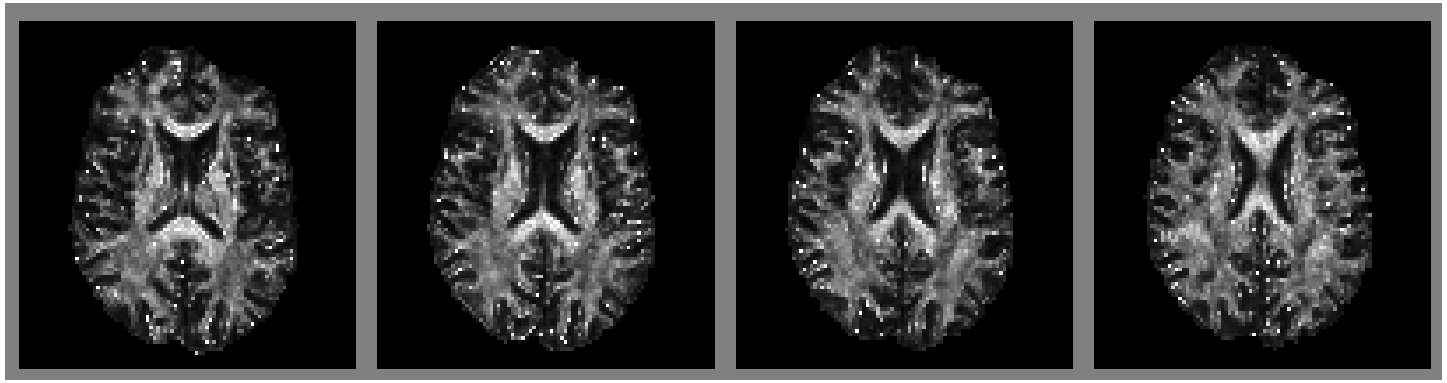


Local-PCA denoising



Common artefacts

- **FA > 1 (or speckled images)**



- Can this be corrected?
  - Apply smoothing or other de-noising methods (e.g. local PCA)
  - Consider acquiring more than one b-value (with corresponding increase in acquisition time)

Quality Control

- Check that you have the expected number of volumes:

$$N_{total} = N_0 + N_b \times N_d$$

- Check your b-values are as expected
- Visually inspect all your data and reject any datasets with extreme artefacts (e.g. stripping)
  - Consider an automatic stripping detection algorithm
- Check motion parameters after motion correction and reject any outliers
- Check the model fit residuals and reject any outliers
- If running a multi-centre study, check also basic imaging parameters, especially TE.

MRC Cognition and Brain Sciences Unit

UNIVERSITY OF CAMBRIDGE

Thank you

Introduction to Diffusion MRI (Marta Correia) - Feedback
https://www.surveymonkey.com/r/J33NDJC