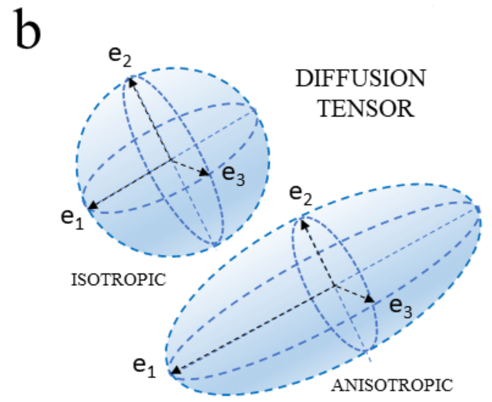
Main diffusion principles for neuroimaging

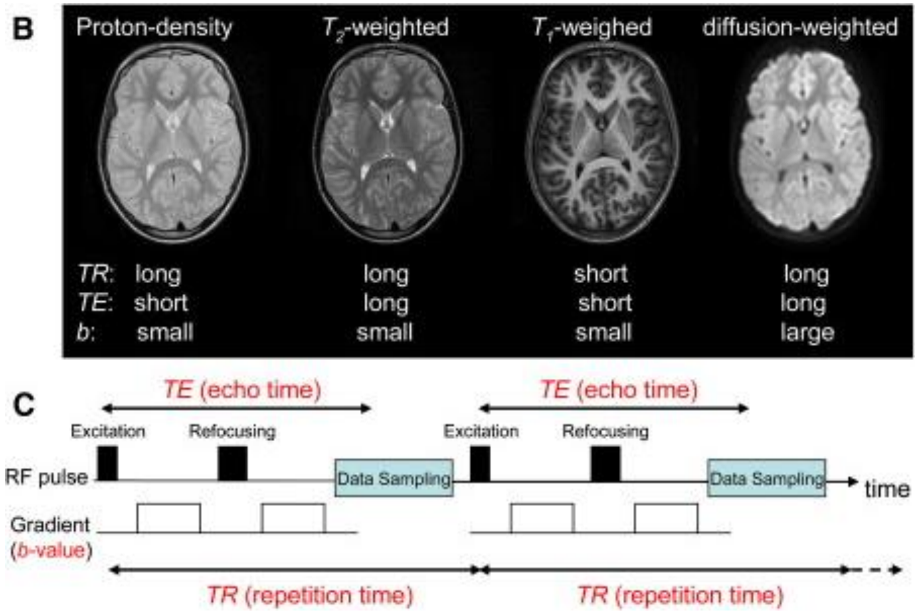
- MRI measures the **diffusion** (random motion) of water molecules within each voxel of biological tissue.
- **Isotropic** diffusion: random, free movement with no directionality
  - Gray matter or cerebrospinal fluid
- **Anisotropic** diffusion: restricted movement, greater diffusion in certain directions over others
  - White matter (nerves), tumours/other lesions or infarcts



MRI: magnetic resonance imaging

MRI contrasts

- T1-weighted (we use FSPGR), T2-weighted (we have FIESTA), DWI (we use single-shell (b = 1000 s/mm^2) +b=0 s/mm^2, 60 directions)



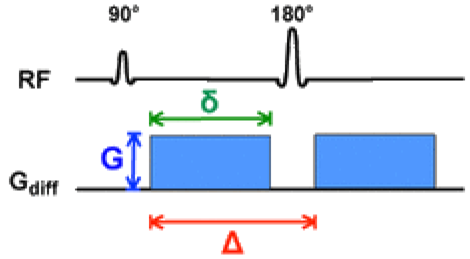
b-value: degree/strength of diffusion weighting

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

G = gradient amplitude

δ = time of applied G

Δ = duration between paired G



FSPGR: fast spoiled gradient-recalled

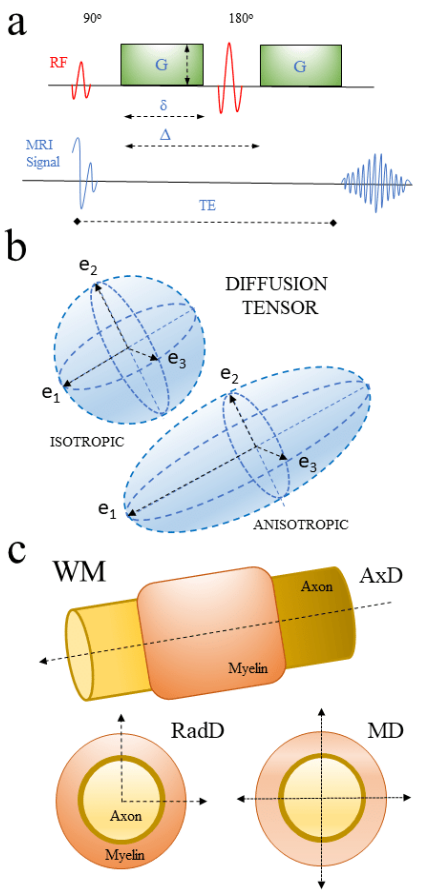
FIESTA: fast imaging employing steady-state acquisition

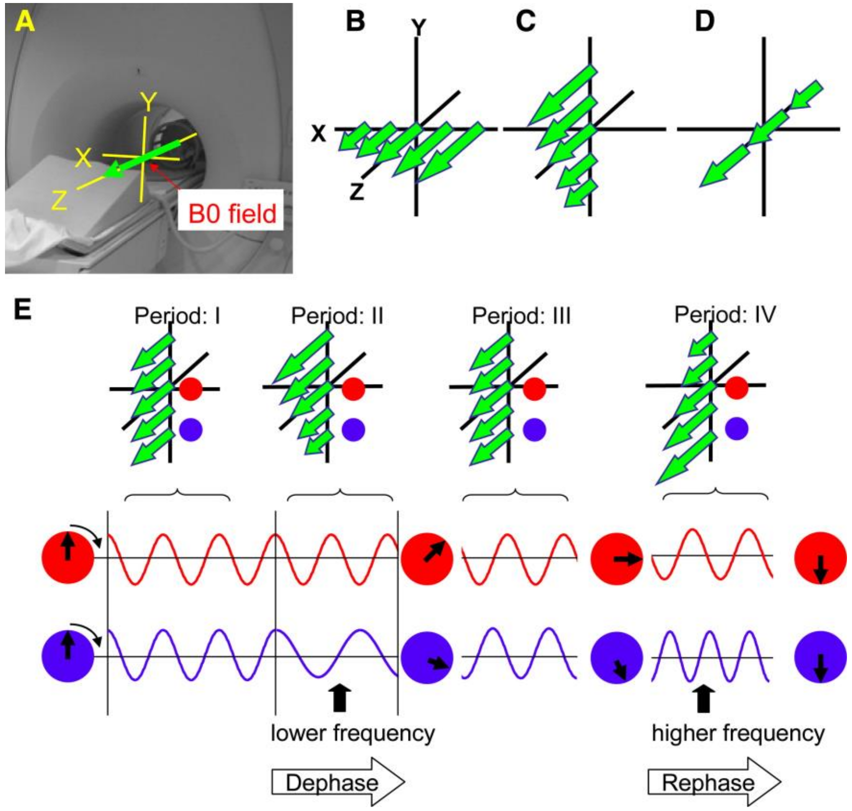
T1: spin-lattice relaxation

T2: spin-spin relaxation

DWI: diffusion-weighted imaging

Diffusion-weighted imaging





- Slight modification of the traditional MR spin echo sequence
- Pt goes in MRI scanner
- 180-degree RF pulse applied
- Symmetric pair of diffusion-sensitizing gradients (fig. a) applied sequentially on either side of the 180-degree RF pulse
  - First pulse dephases the proton spins (reduces their emitted signal)
  - Second pulse rephases spins (increases their emitted signal)
    - If there is proton movement (greater isotropy) in between the application of both pulses, the second pulse cannot fully rephase the spins, and there is resultant signal decay. Signal decay is represented by darker black or grey voxels on an MR image.
    - If there is little to no proton movement (greater anisotropy), the second pulse can more efficiently rephase the spins, and there is greater signal release. Signal release is represented by brighter white voxels on an MR image.
- Very advantageous for clinical studies, because is non-invasive and objective in identifying structural changes.

MRI: magnetic resonance imaging (MR: magnetic resonance)
RF: radiofrequency
WM: white matter

AxD: axial diffusivity
RadD: radial diffusivity
MD: mean diffusivity (apparent diffusion coefficient)

The diffusion tensor model

- Diffusion-weighting of MR images creates ADC maps that can be analyzed using the diffusion-tensor model.

ADC is a single scalar number, but to explain all possible fiber directions we need to use the **3x3 tensor matrix**:

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

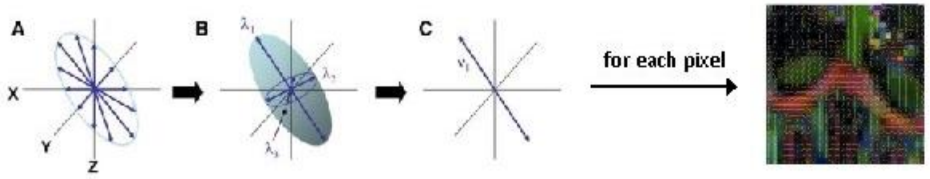
- A 9-element symmetric matrix (or <u>3x3 tensor</u>) describes all possible diffusion directions for a singular nerve fibre population within a singular voxel.
- The root mean squared displacement of water molecules in each direction (x, y, z) within each voxel on a structural image can be modeled as a <u>diffusion ellipsoid</u> (the mathematical representation of a diffusion ellipsoid is called a <u>tensor</u>).
  - The ADC in each direction (x, y, z) is represented by D.
    - For each direction (x_1, y_2, z_3), D is determined by the <u>projection</u> of ε_1, ε_2, ε_3 onto unit vector v.

$$ADC = \begin{bmatrix} D_{xx} & D_{yz} & D_{zx} \\ D_{xy} & D_{yy} & D_{zy} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix} \xrightarrow[\textit{eigendecomposition}]{} v = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} + v^T = [v_1 \ v_2 \ v_3]$$

$$D = \mathbf{v}^T \mathbf{D} \mathbf{v} = \lambda_1(\mathbf{v} \cdot \varepsilon_1)^2 + \lambda_2(\mathbf{v} \cdot \varepsilon_2)^2 + \lambda_3(\mathbf{v} \cdot \varepsilon_3)^2$$

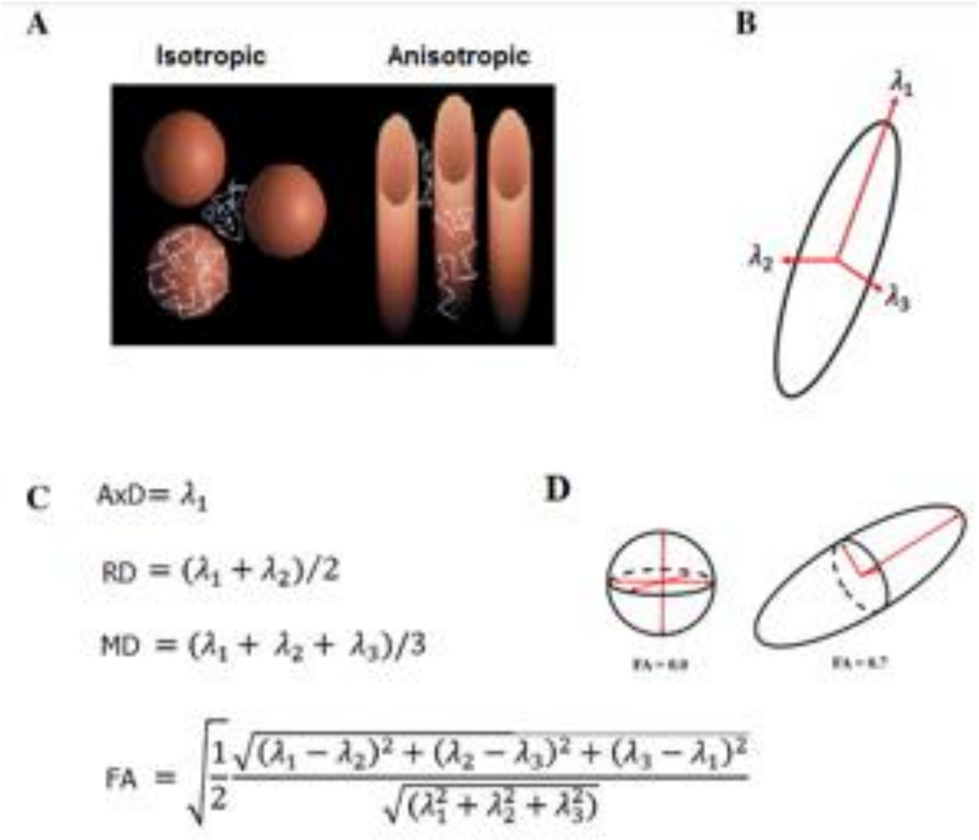
$$ADC = v \Lambda v^T$$

    - v^T is a column vector $(x, y, z)^T$ that is the transpose of row vector v (x, y, z).
  - Each tensor that represents the diffusion within each voxel has three eigenvalues: λ_1, λ_2, λ_3 and three eigenvectors: ε_1, ε_2, ε_3 that can be derived from it and used in various formulas to measure metrics like fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity.



ADC: apparent diffusion coefficient
MR: magnetic resonance imaging

Diffusion-tensor model metrics



- Structural metrics obtained from diffusion-weighted images with the <u>diffusion-tensor model</u>:
  - **FA:** measures WM microstructure coherence (myelin integrity). Decreases when there is WM damage.
  - **MD/ADC:** represents the overall diffusion coefficient. Decreases when there is good WM integrity.
  - **RD:** measures diffusion perpendicular to the direction of a WM bundle. Increases when there is more myelin damage.
  - **AD:** measures WM integrity (along the principal diffusion axis; dominant diffusion direction within a voxel). Decreases when there is WM damage.
- There are other structural metrics that different DWI-processing models can obtain. For instance, WM nerve fibre cross-section could be derived with a fixel-based analysis model. We however will be considering metrics derived with the diffusion-tensor model.

FA: fractional anisotropy
MD/ADC: mean diffusivity/apparent diffusion coefficient
WM: white matter
RD: radial diffusivity
AD: axial diffusivity