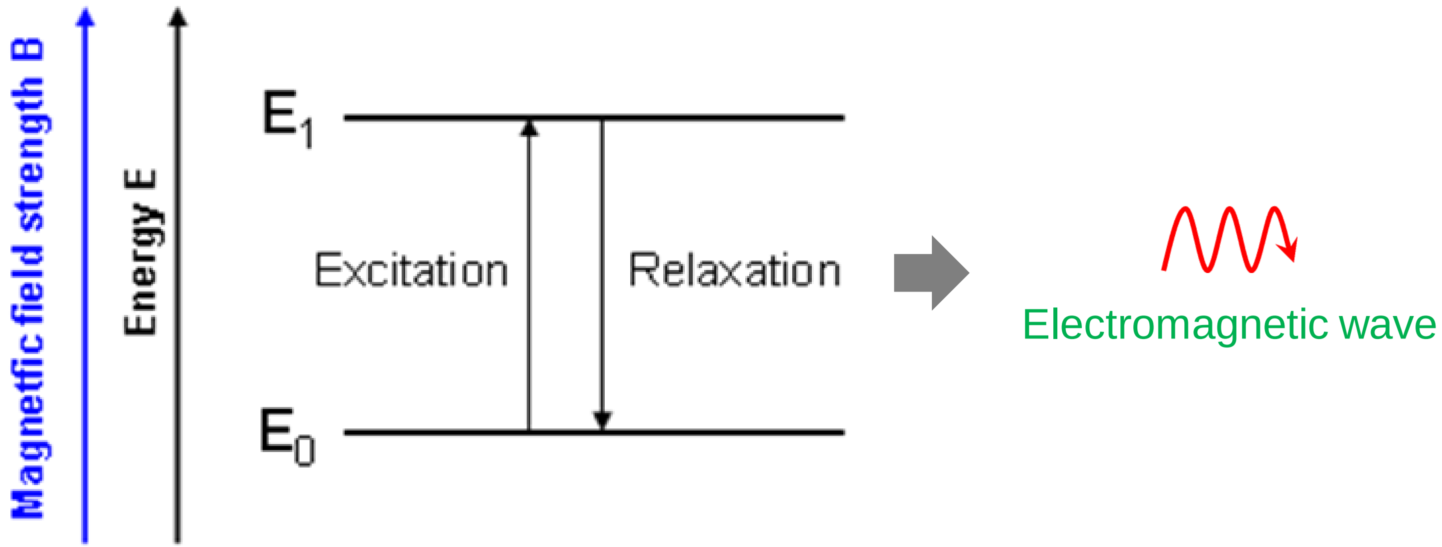
Medical/Bio Research Topics Ⅰ: Week 07 (18.04.2024)

Diffusion-weighted MRI (1): Basic Principles and Introduction

확산가중 자기공명영상 (1): 원리 및 소개

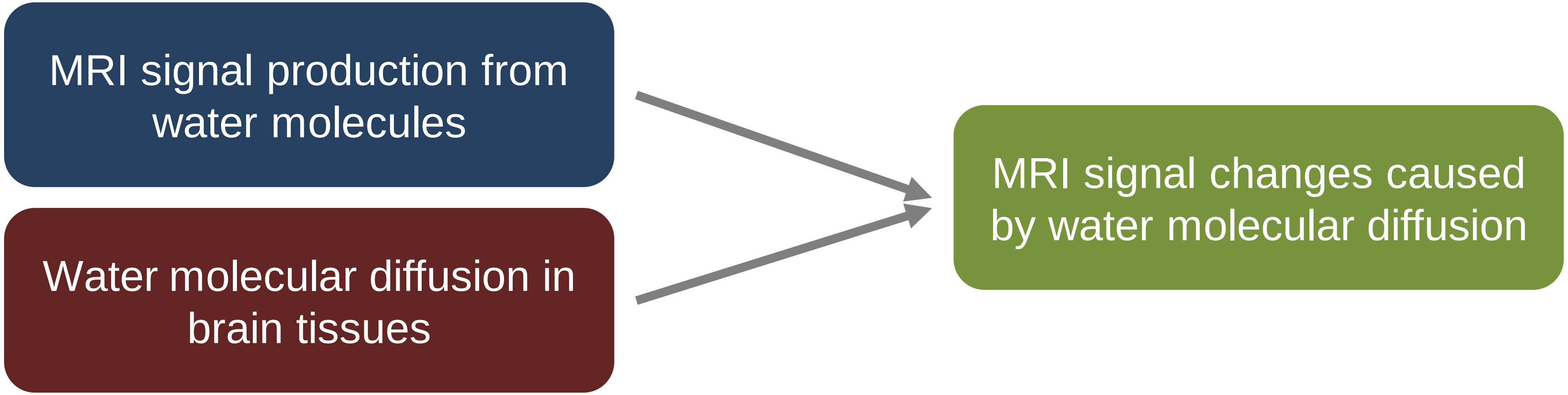
MRI: Principles

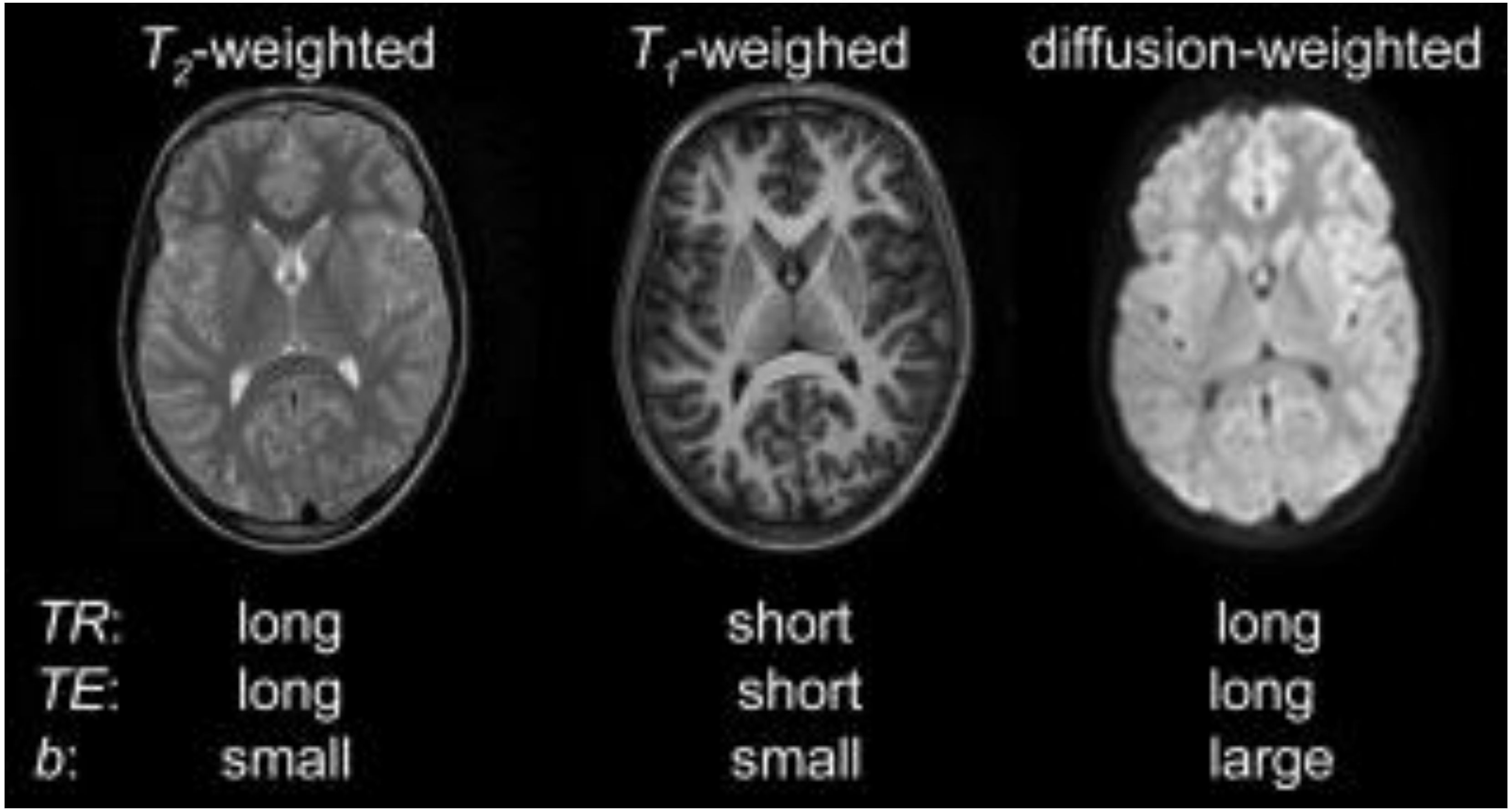
- Excites hydrogen nuclei (protons) into releasing electromagnetic waves (in radio frequency) and then records the locations of the waves with high accuracy



Diffusion-weighted MRI (dMRI)

- MRI technique primarily for examining the local microstructure and anatomy of white matter
- Employs directional characteristics of diffusion



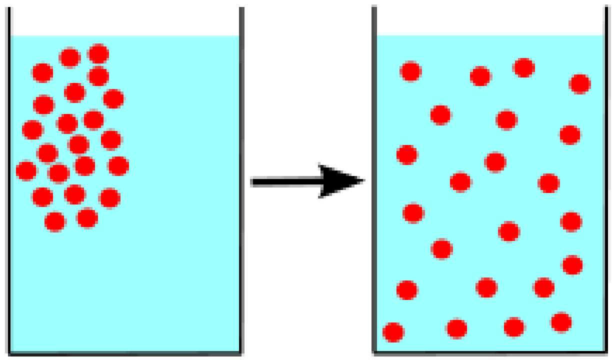


[Mori and Zhang, 2006]

Various types of MRI contrasts

Diffusion

- Physical process in which particles tend to spread steadily from regions of high concentration to regions of lower concentration

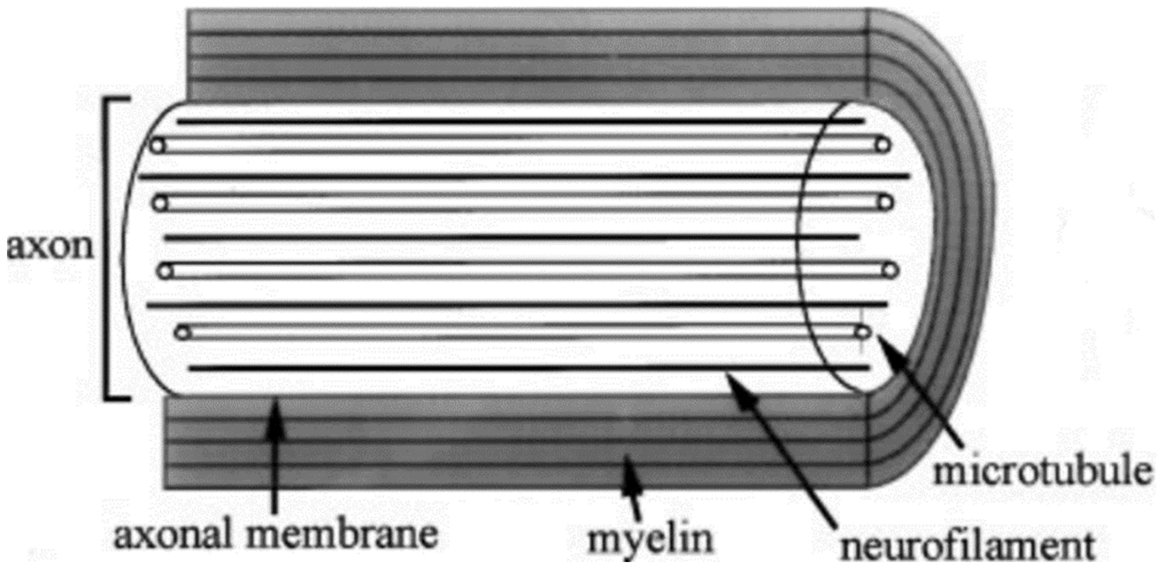


- Considered a macroscopic manifestation of Brownian motion

- Brownian motion on the microscopic scale
  - Random motion of particles in a given medium with no preferred direction, leading to the spread of the particles evenly throughout the medium over a period of time
  - Mean squared displacement in terms of time elapsed and diffusivity: $\left\langle r^2 \right\rangle = 2Dt$
    - r: average distance that a particle moves in a particular direction in a time period t
    - D: diffusion coefficient

- Movement of water molecules in a heat-driven random fashion in brain tissues
  - Unless the movement is constrained by barriers

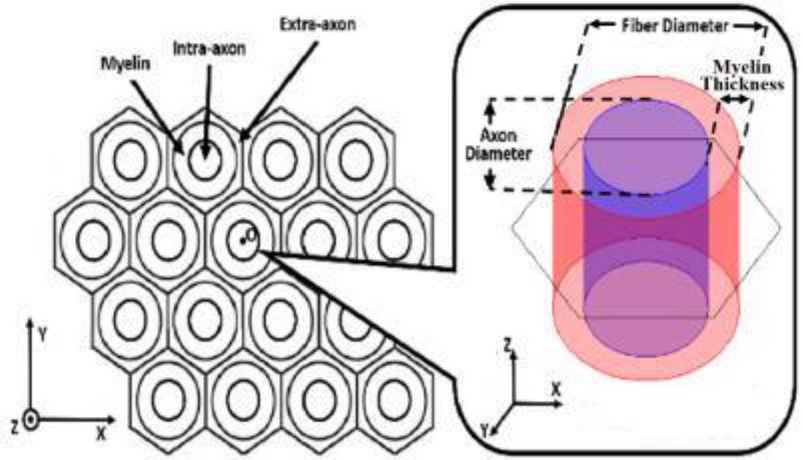
Fibrous structures in white matter

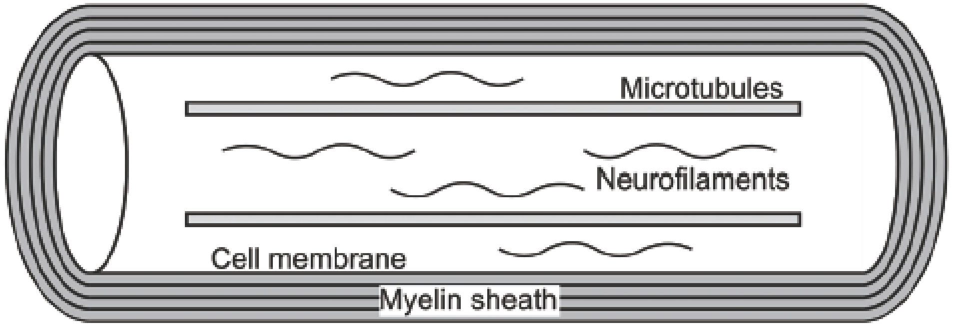


[O'Donnell and Westin, 2011]

- Diffusion anisotropy in white matter
  - Directional effect of diffusion dominantly in white matter primarily due to the presence of arrays of myelinated axons
    - Water diffuses more readily along the length of axon fibres than across them
  - Axon fibre (nerve fibre)
    - Not just a single axon but often refers to a complex structure involving multiple axons (a bundle of axons) that are grouped together, traveling through the brain or spinal cord, also known as a fibre tract
    - Functions as a unit within the nervous system to facilitate rapid communication across different regions

- Nerve vs. nerve fibre
  - A nerve is a bundle of many nerve fibres, often accompanied by connective tissue, blood vessels, and other components that contribute to the nerve's structure and function
  - A nerve fibre is the microscopic component of a nerve
  - Axon $\Rightarrow$ axon fibre (nerve fibre) $\Rightarrow$ nerve

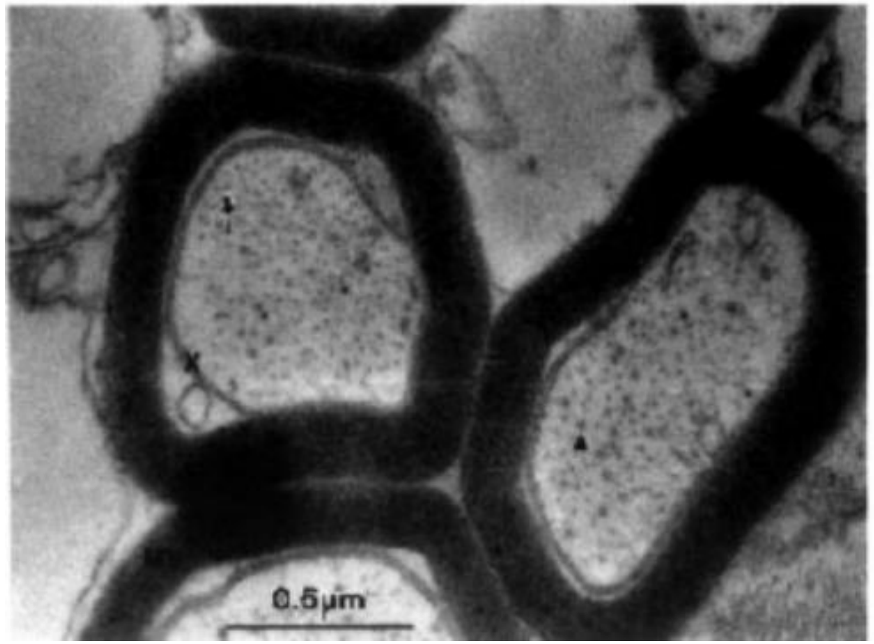


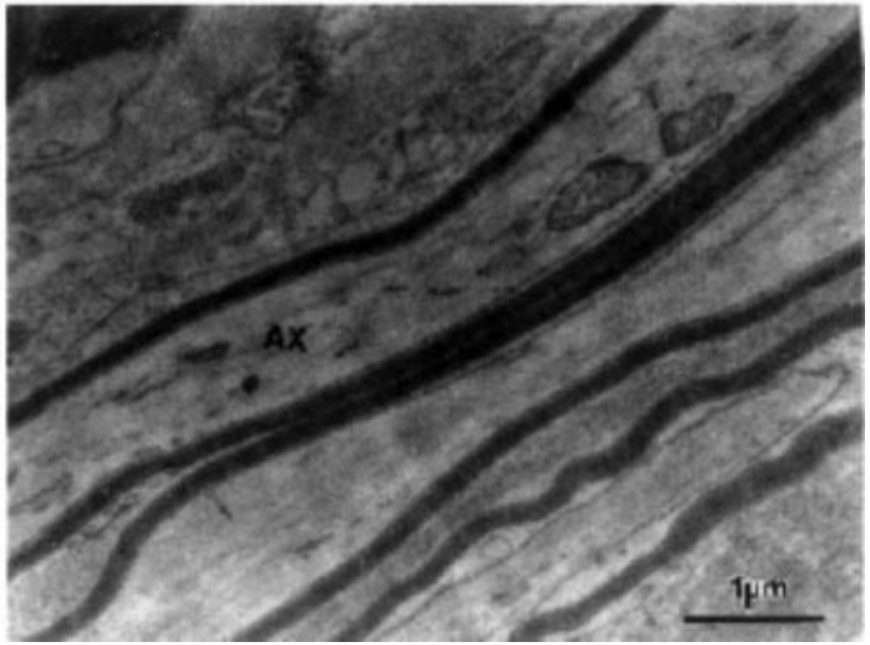


- Cytoskeleton
  - Microtubules (25 nm diameter)
  - Neurofilaments (10 nm diameter)
  - Microfilaments (7 nm diameter)
- Axonal membranes
- Myelin sheath

[Noguerol et al., 2017]

Potential sources of diffusion anisotropy in a myelinated axon



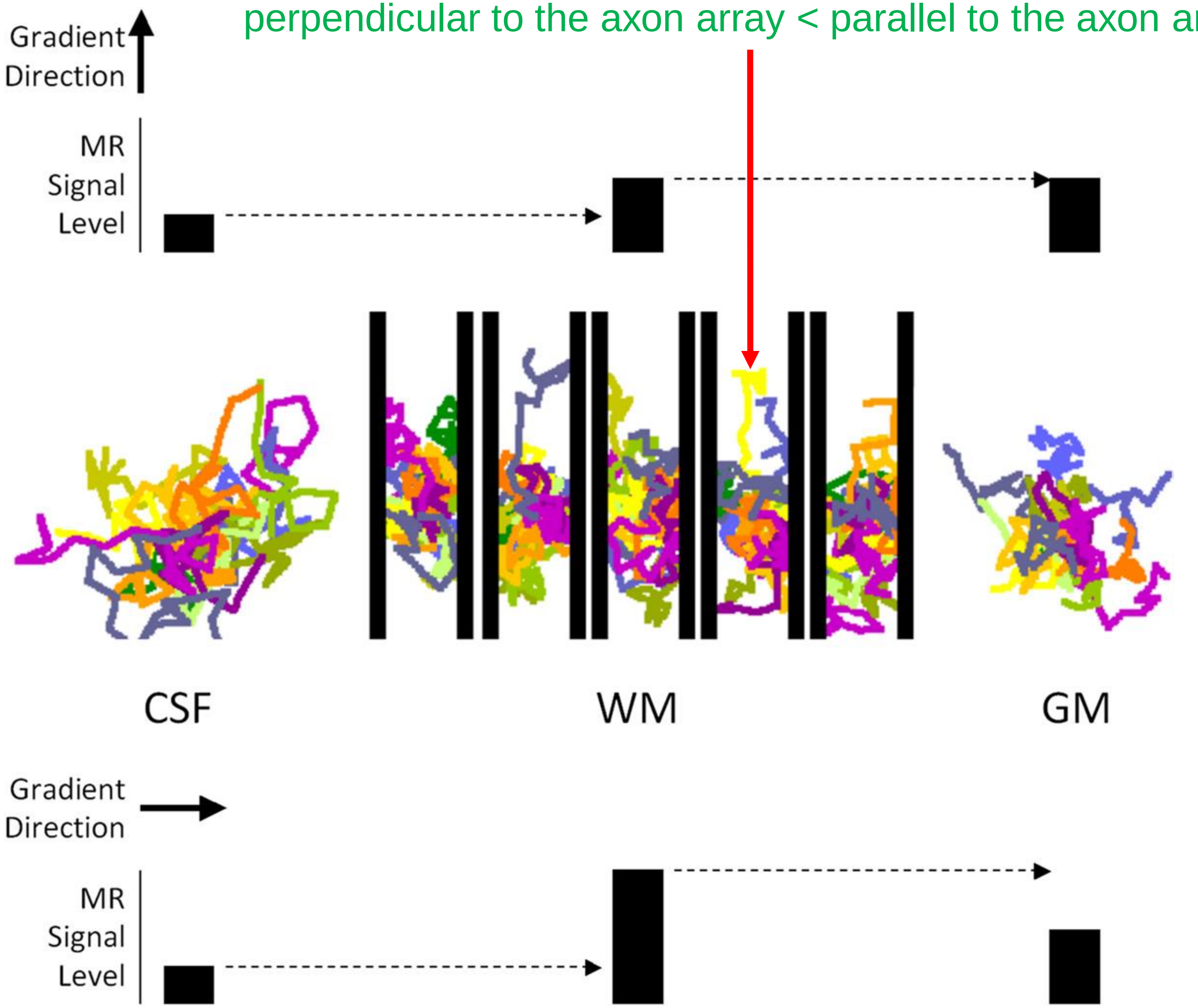


[Beaulieu, 2002]

Transverse and longitudinal sections of myelinated optic nerves of the garfish

- Present-day human brain dMRI
  - "White matter imaging" technique
    - White matter is the current focus of dMRI
    - The directional impact of diffusion is most readily measured for microscopic diffusion barriers in white matter
  - Measures water molecular diffusion on a "microscopic scale"
    - Sensitive to the root mean square water molecule displacement in a particular direction on the order of μm for a diffusion coefficient of ~1,000 $\mu m^2/s$ and a time period of ~0.01 s
    - Pertains to the measurement of the average Brownian diffusion behaviour of the water molecules over a great many cells and axons within a voxel

Directional dependence of diffusion:
perpendicular to the axon array < parallel to the axon array



[Alger, 2012]

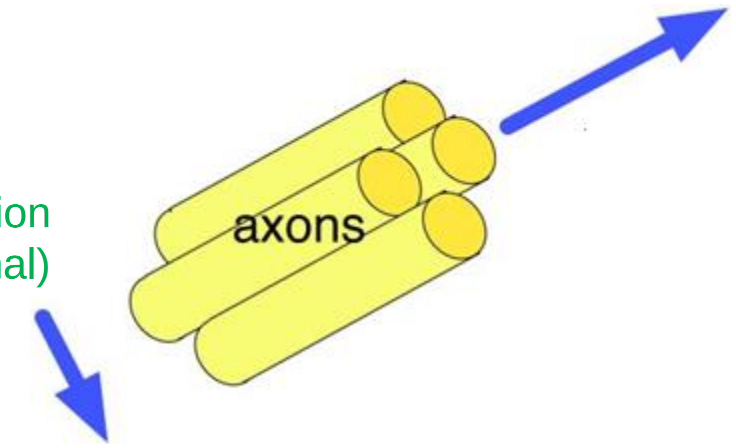
Directional impact of water molecular diffusion on MRI signal changes

Diffusion-weighted Contrast

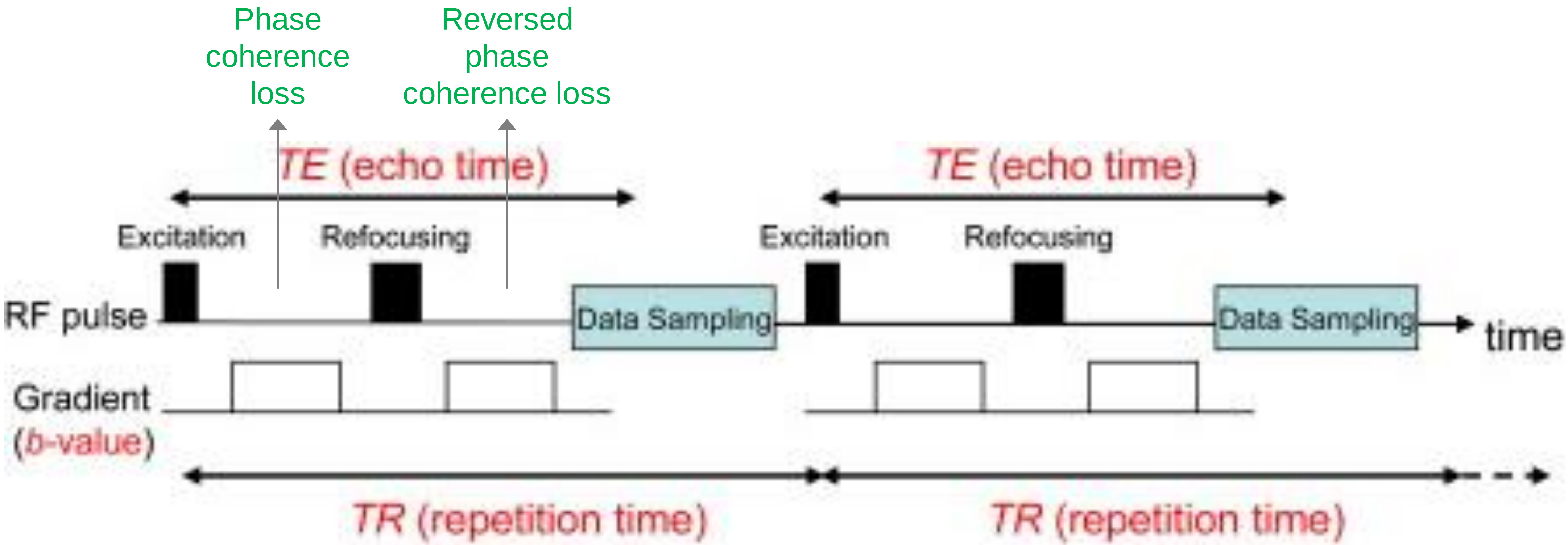
- MRI signal changes caused by diffusion

More diffusion
(More decrease in an MRI signal)

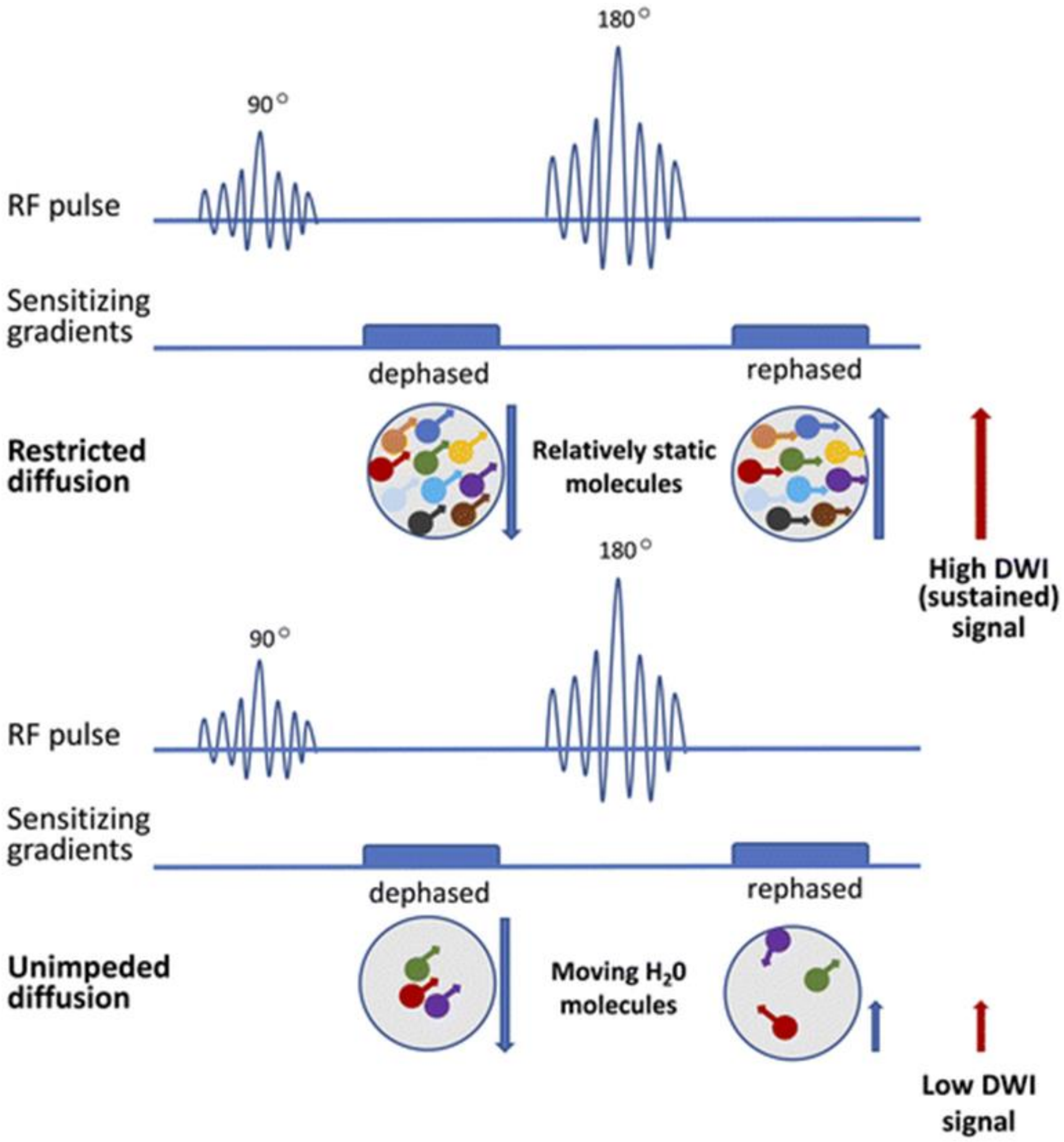
Less diffusion
(Less decrease in an MRI signal)



- Implemented by applying diffusion-sensitizing gradients that encode the amount and direction of hydrogen nuclei movement during the time between the application of them



[Mori and Zhang, 2006]



[Lall et al., 2018]

MRI pulse sequence for the diffusion-weighted contrast

- Directional dependence of diffusion
  - With different diffusion weighting
    - By assuming exponential diffusion-weighted signal attenuation

MRI signal measured with diffusion weighting

Diffusion coefficient

$$\frac{S}{S_0} = e^{-\boxed{\gamma^2 G^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right)} D} = e^{-bD}$$

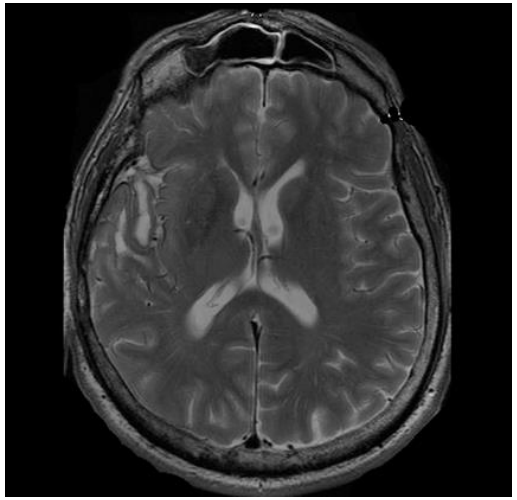
b-value

MRI signal measured without diffusion weighting

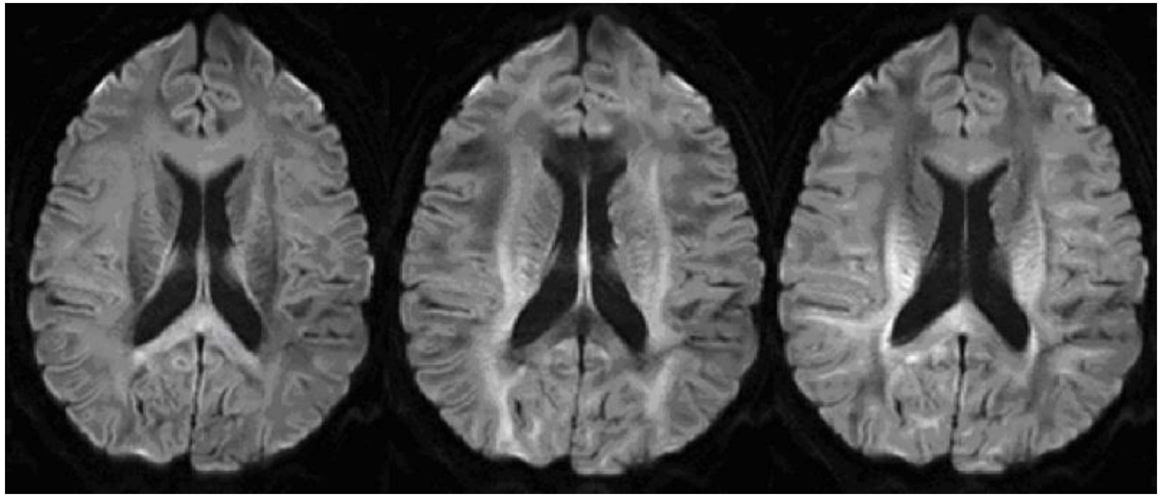
Diffusion coefficient $$D = \frac{1}{b} \log \frac{S_0}{S}$$

More signal decrease → higher diffusion coefficient

Less signal decrease → lower diffusion coefficient



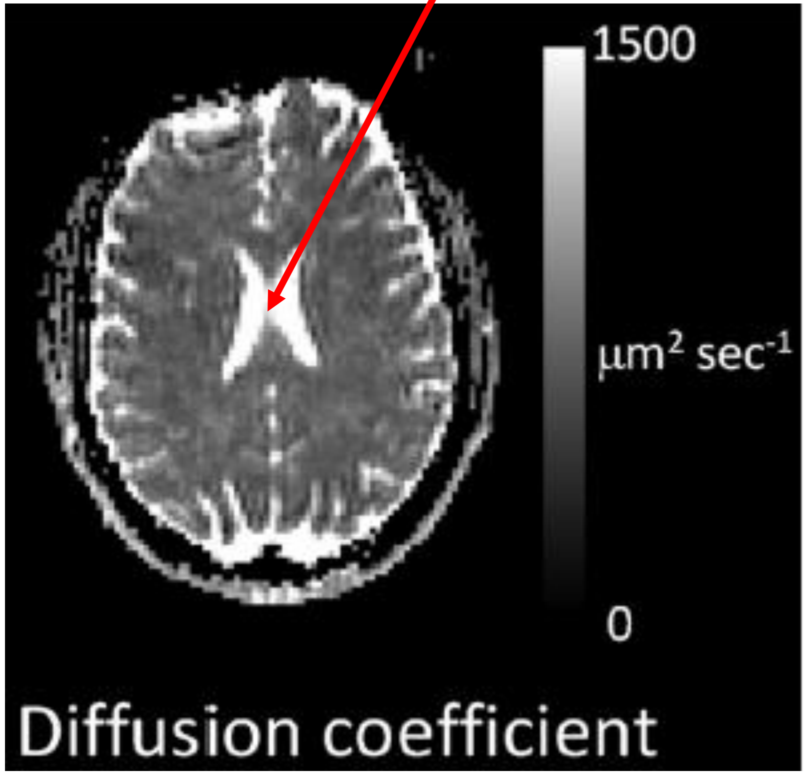
Without the diffusion-sensitizing gradient



With the diffusion-sensitizing gradient in *x*-, *y*-, and *z*-directions

With and without the diffusion-sensitizing gradient

Free diffusion of water in cerebrospinal fluid



[Alger, 2012]

Map of diffusion coefficients

- *b*-value
  - Summarizes the influence of the diffusion-sensitizing gradient on the diffusion weighted image
    - The higher the *b*-value, the stronger the diffusion weighting, but the smaller the diffusion-weighted signal
  - Widespread use of intermediate values of ~ 1000 s/mm^2 in the human brain

– In different diffusion-sensitizing gradient directions

- By following the assumption that water molecule movement (diffusion) can be characterized by a Gaussian distribution

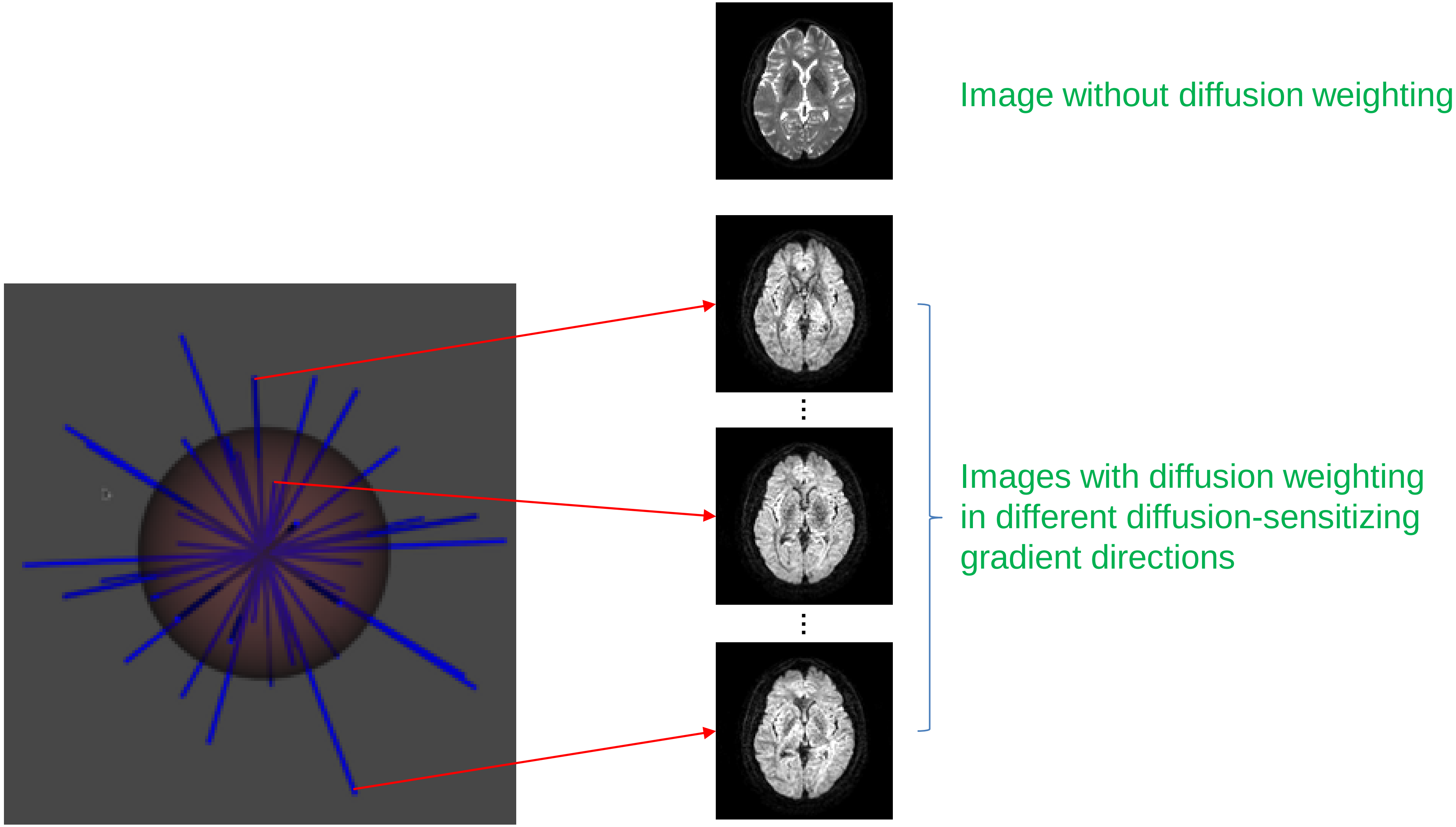
Diffusion tensor

$$\frac{S}{S_0} = e^{-b\vec{g}^T \mathbf{D} \vec{g}}$$

Direction of the diffusion-sensitizing gradient

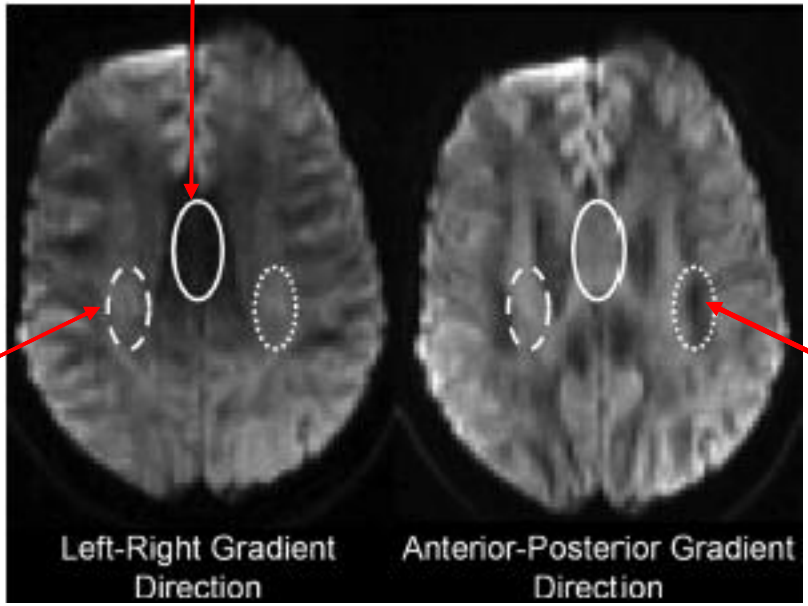
- **D**: diffusion tensor (symmetric positive definite matrix)
  - 3 × 3 symmetric matrix, each component of which describes water molecular diffusion associated with a pair of axes *xx*, *yy*, *zz*, *xy* (or *yx*), *xz* (or *zx*), and *yz* (or *zy*)

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



Diffusion weighting in different diffusion-sensitizing gradient directions

Left–right-oriented
corpus callosum splenium



Superior-inferior-oriented
pyramidal tracts

Anterior–posterior-oriented
temporofrontal pathway

[Alger, 2012]

Impacts of different diffusion-sensitizing gradient directions

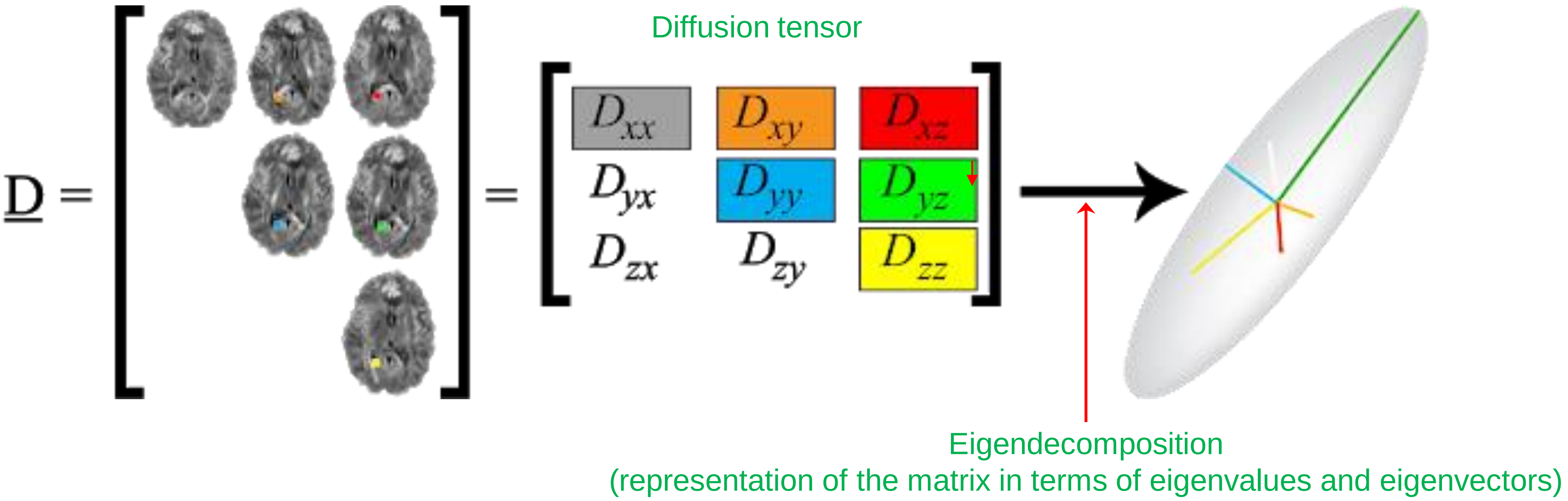
Diffusion Model

- Describes diffusion properties within a voxel
- Diffusion tensor model
  - Based on the assumption that the probability density function describing the random displacement of water molecules due to diffusion is Gaussian
    - Characterized by its mean (assumed to be zero for molecular diffusion) and its variance (represented by the diffusion tensor)
  - Implies that diffusion is isotropic or anisotropic but still smooth and continuous without abrupt changes in diffusion directions

- Preprocessing before diffusion modelling
  - Correction for unwanted variation
    - Head motion
    - Eddy current-induced distortion
      - Eddy currents (Foucault currents)
        - » Loops of electric current induced in nearby conductors by a changing magnetic field
        - » Generated in MRI scanners, particularly during dMRI, because of the rapid switching on and off of the gradient fields used to create the diffusion sensitization
        - » Cause additional magnetic fields that distort the main magnetic field (B0) uniformity
      - Mitigated by aligning images that have been distorted differently due to the eddy currents induced by different diffusion-sensitizing gradient directions
    - Inhomogeneity-induced distortion

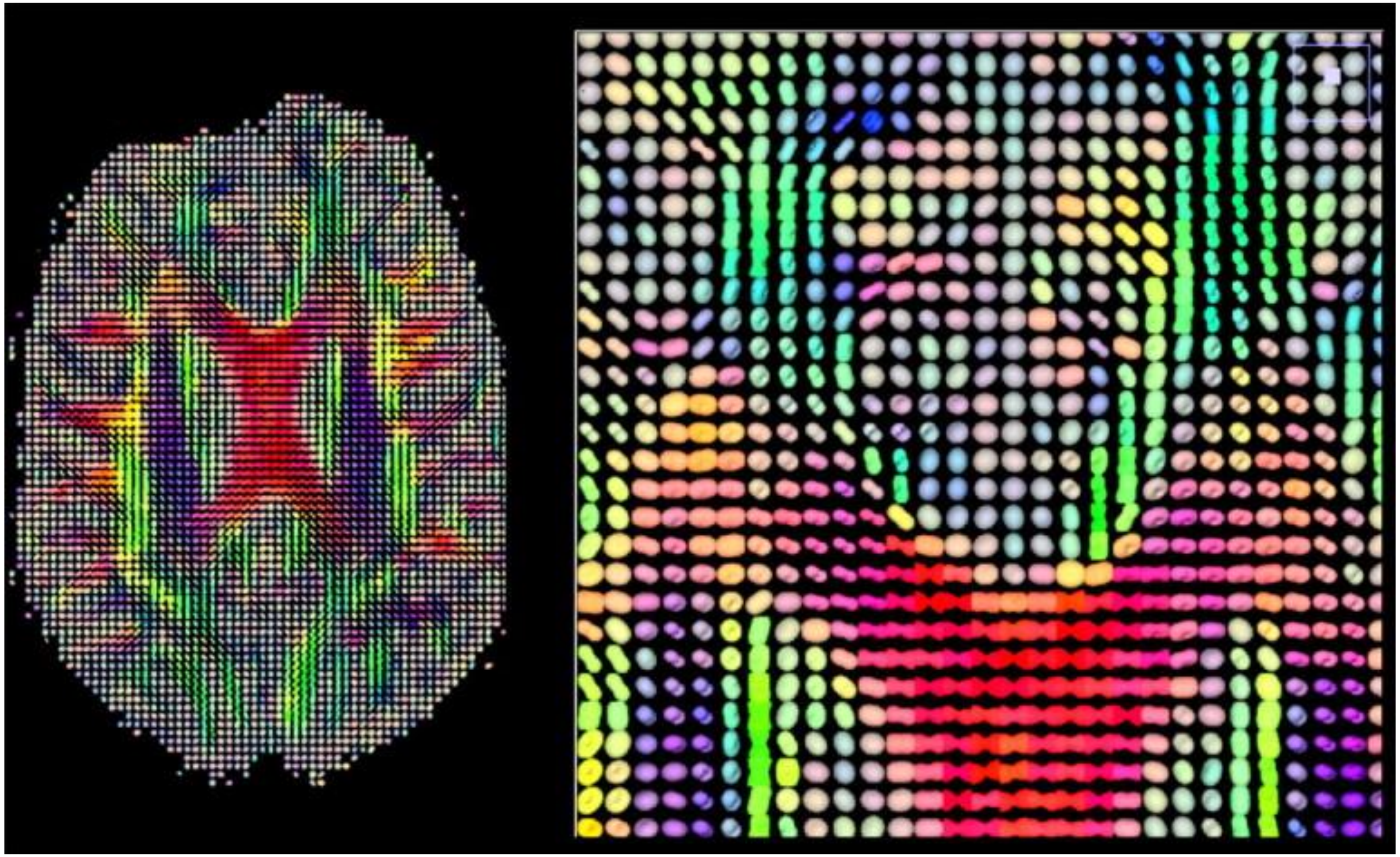
Diffusion Tensor

- Encapsulates the covariance matrix of the Gaussian distribution of water molecule displacements in 3D space, describing how diffusion varies along different spatial axes
- Diagonalizing it by its eigensystem (eigenvectors and eigenvalues) simplifies the model by aligning it with directions in which the diffusion measurements do not linearly interfere with each other, allowing for clearer analysis and visualization of anisotropic diffusion



[https://thewinnower.com/papers/3523-the-diffusion-tensor-and-its-relation-to-fa-md-ad-and-rd]]

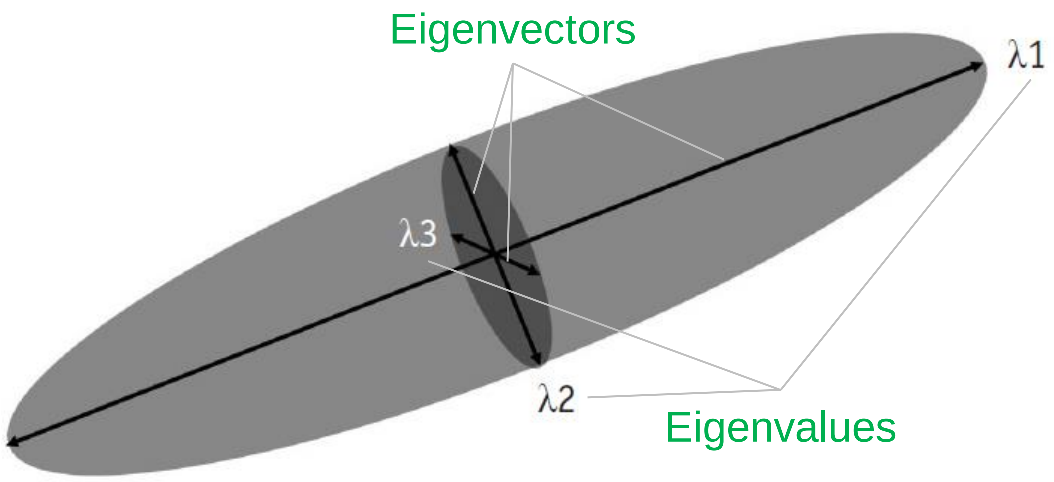
Diffusion tensor and its ellipsoid representation



[Alger, 2012]

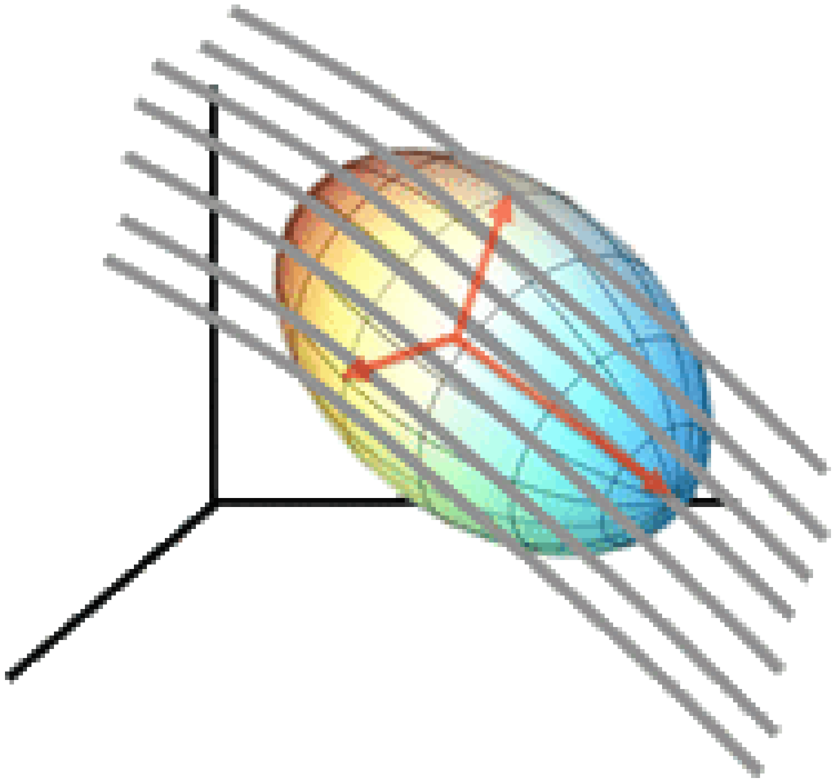
Diffusion ellipsoids derived from the diffusion tensors measured for each voxel

- Represents averaged diffusion properties of many axons within a voxel



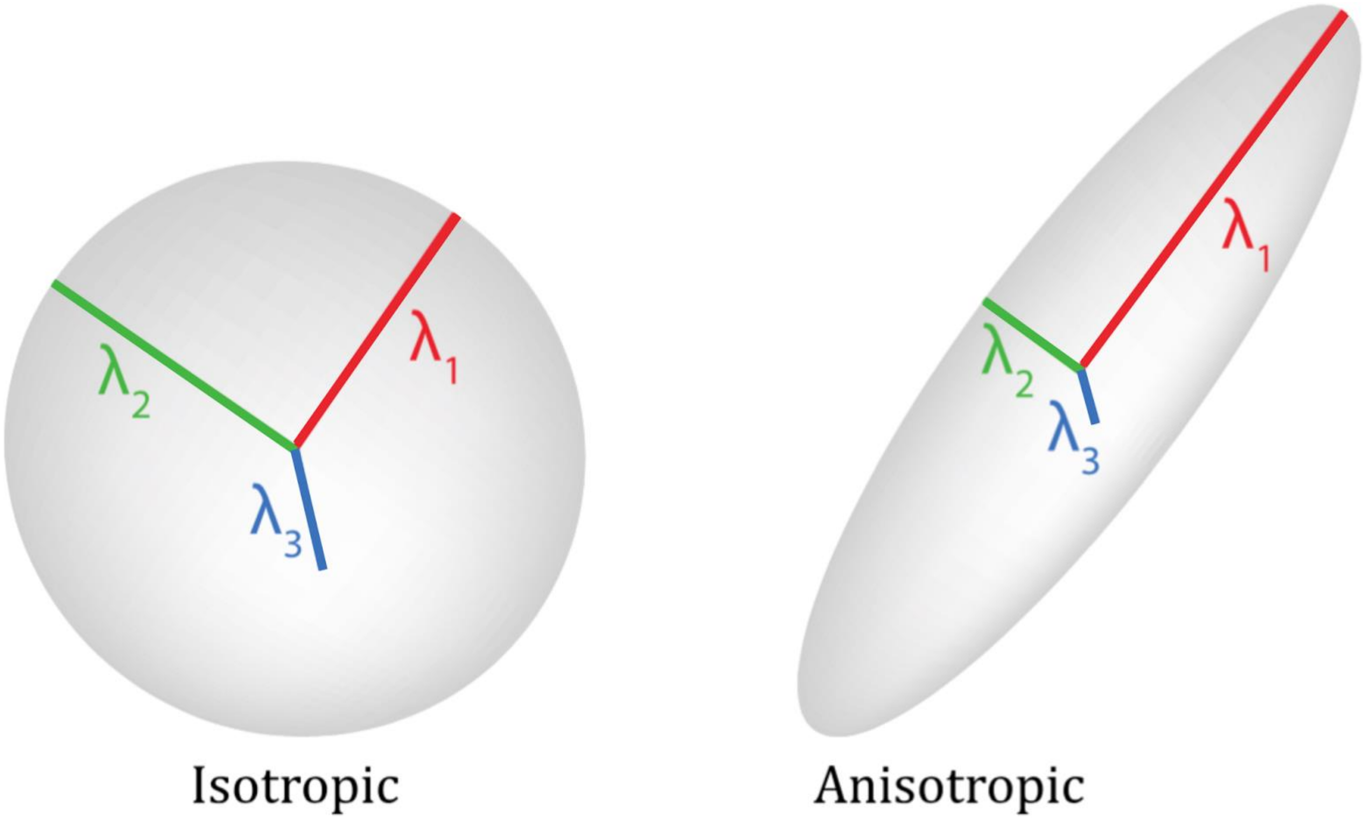
  – Principal direction of diffusion
    - Given by the main axis (principal eigenvector; eigenvector of the largest eigenvalue) of the ellipsoid

- Assumed to be aligned with the dominant fibre orientation within the voxel



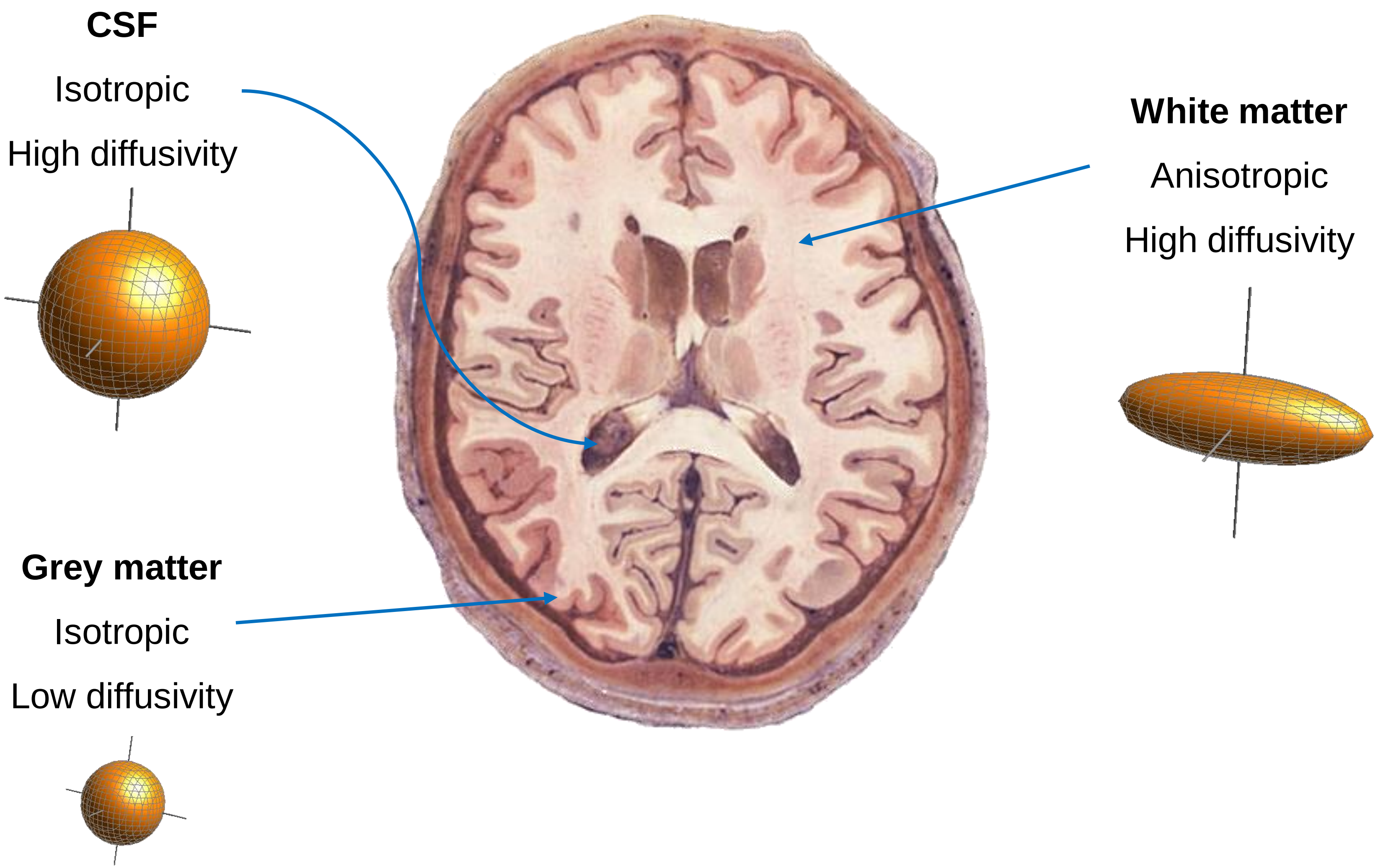
[https://mriquestions.com/diffusion-tensor.html]

- Scalar invariants that are quantities independent of the coordinate system in which the diffusion tensor is expressed
  - Characterize aspects of water molecular diffusion, such as the magnitude and anisotropy (directional dependence), offering insights into tissue structure and organization
  - Fractional anisotropy (FA)
    - Measures the degree of anisotropy (how much the diffusion is directionally dependent) within a voxel
    - Ranges from 0 (completely isotropic diffusion) to 1 (highly anisotropic diffusion), where a high value indicates anisotropic diffusion (when water molecules diffuse more freely along the length of the fibre tracts than across them), whereas a low value suggests isotropic diffusion (when water molecules spread evenly in all directions, typically in areas without structural barriers)



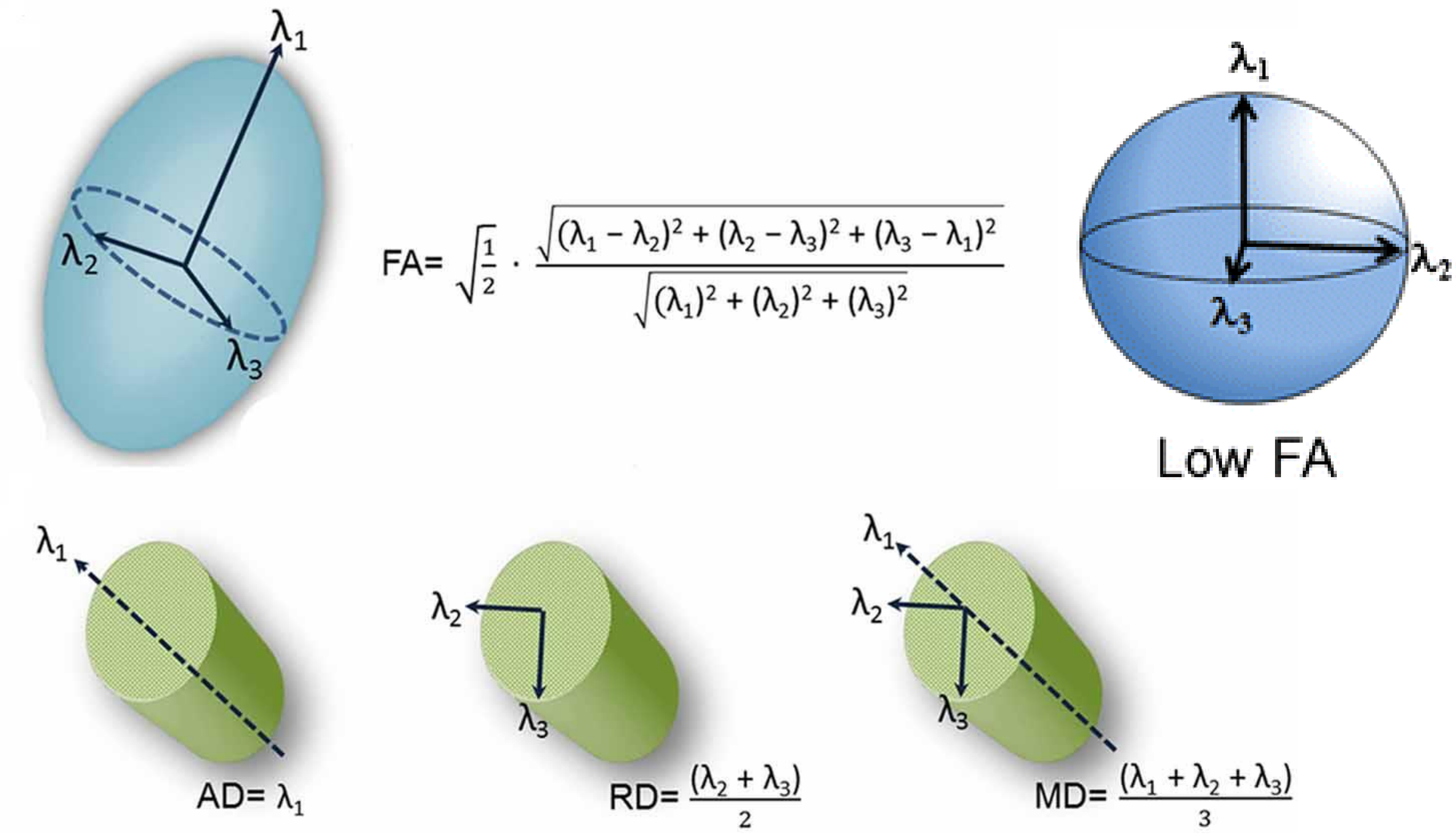
[http://www.diffusion-imaging.com/2015/10/what-is-diffusion-tensor.html]

Isotropic and anisotropic diffusion represented by ellipsoids



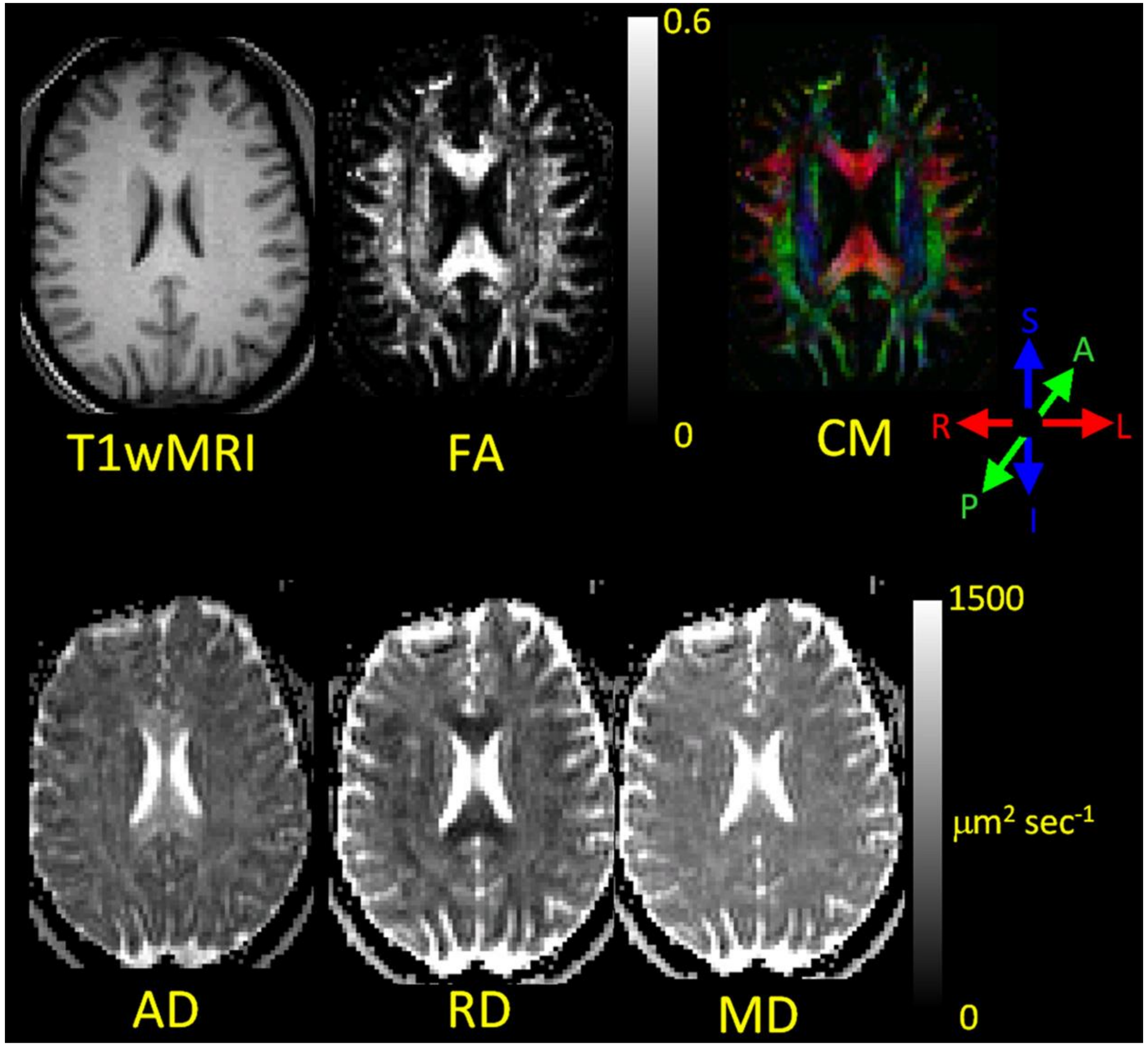
Isotropic and anisotropic diffusion in different brain tissues

- Mean diffusivity (MD)
  - Measures the average rate of diffusion within a voxel, irrespective of direction
- Axial diffusivity (AD)
  - Measures the rate of diffusion along the dominant fibre orientation within a voxel
- Radial diffusivity (RD)
  - Measures the average rate of diffusion perpendicularly to the dominant fibre orientation within a voxel
  - Indicative of reduced myelin integrity (degeneration or reduction of myelin around axons)



[DeSouza et al., 2016; Mabrouk, 2018]

Diffusion tensor-derived measures

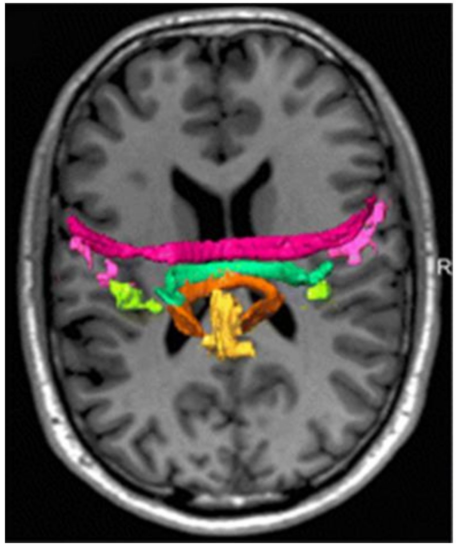


[Alger, 2012]

Maps of diffusion tensor-derived measures

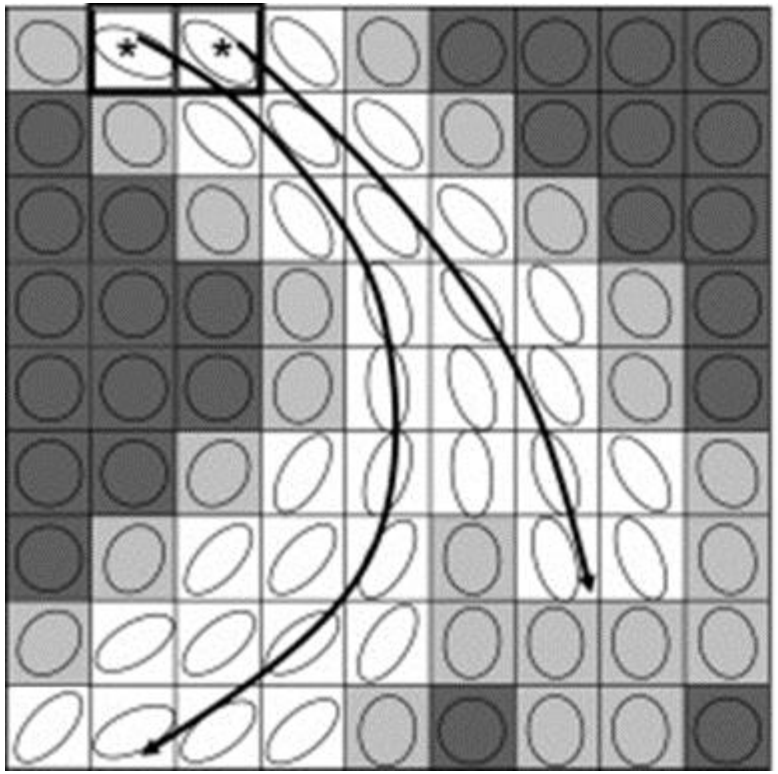
White Matter Tractography

- Reconstructs whiter matter fibre tracts (structures of nerve fibres into which axons are bundled together)



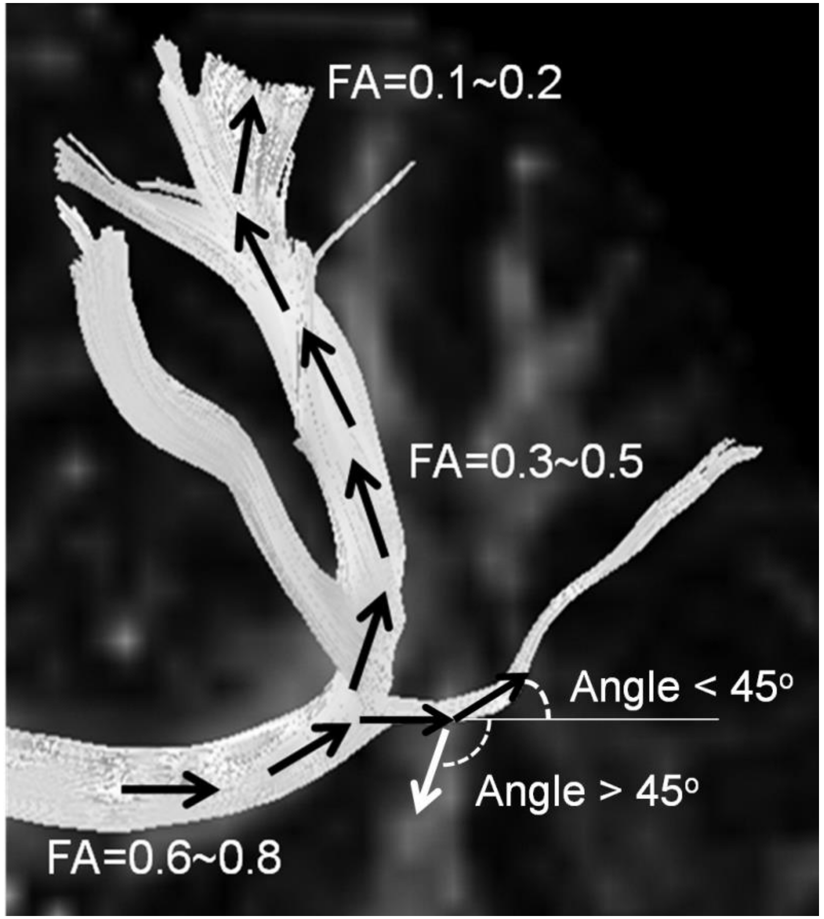
[Wahl et al., 2007]

- Two primary forms
  - In a deterministic way by following the principal eigenvector direction from voxel to voxel
  - In a probabilistic way by estimating a probability distribution of travelling directions at each voxel
    - By considering that there is uncertainty associated with the determination of the principal eigenvector's orientation at each voxel
    - By tracking streamlines a great number of times with the principal eigenvector orientation being chosen at random from the distribution of probable orientations of the principal eigenvector at each voxel

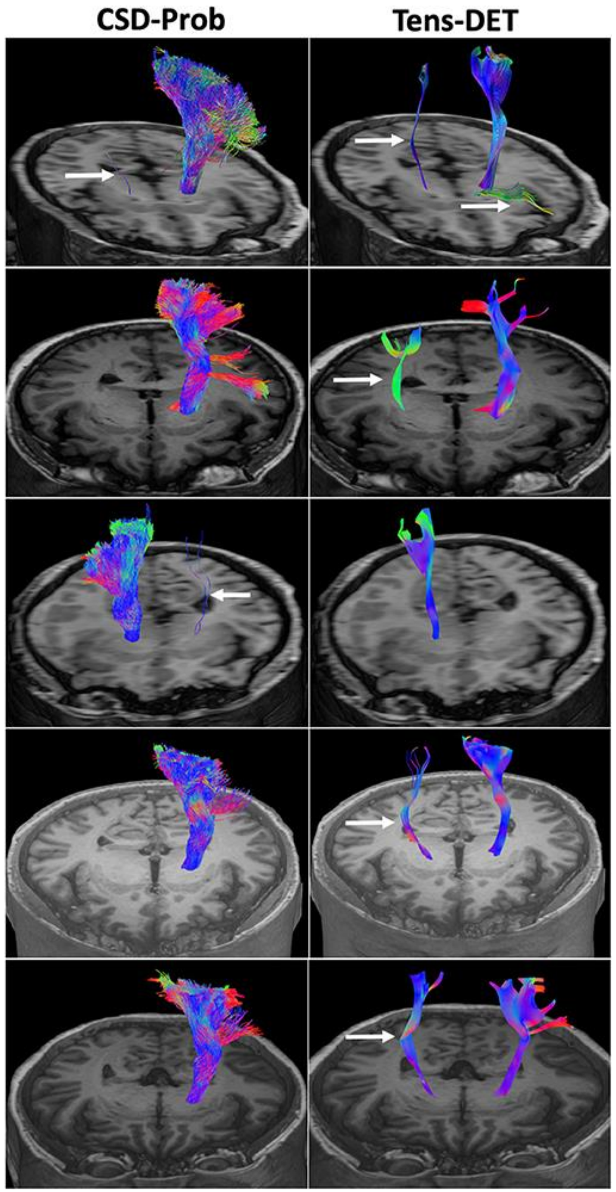


[Mori and Zhang, 2006]

Reconstruction of white matter fibre tracts in a deterministic way

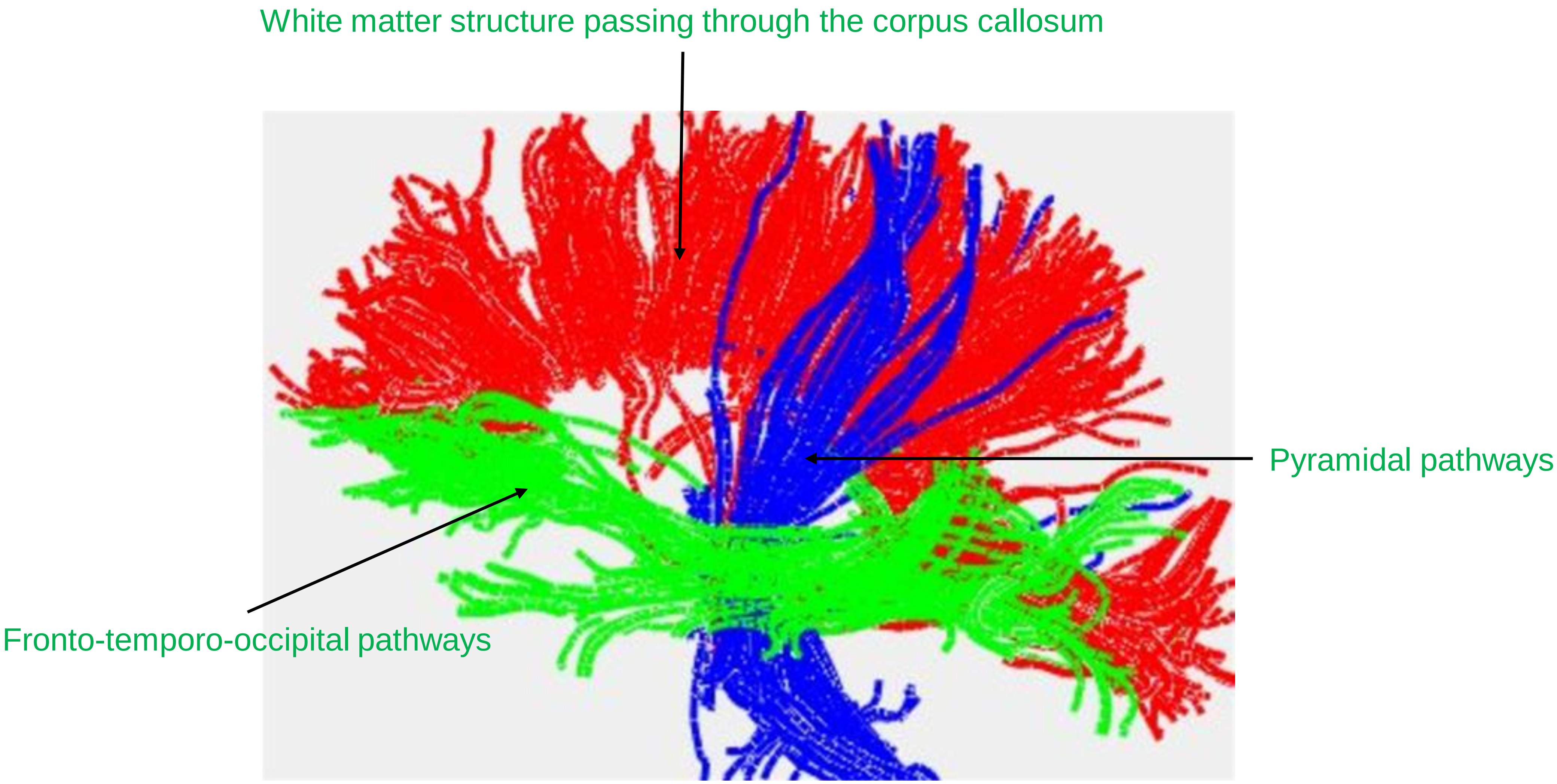


Tracking a streamline by filtering out anatomically unrealistic pathways

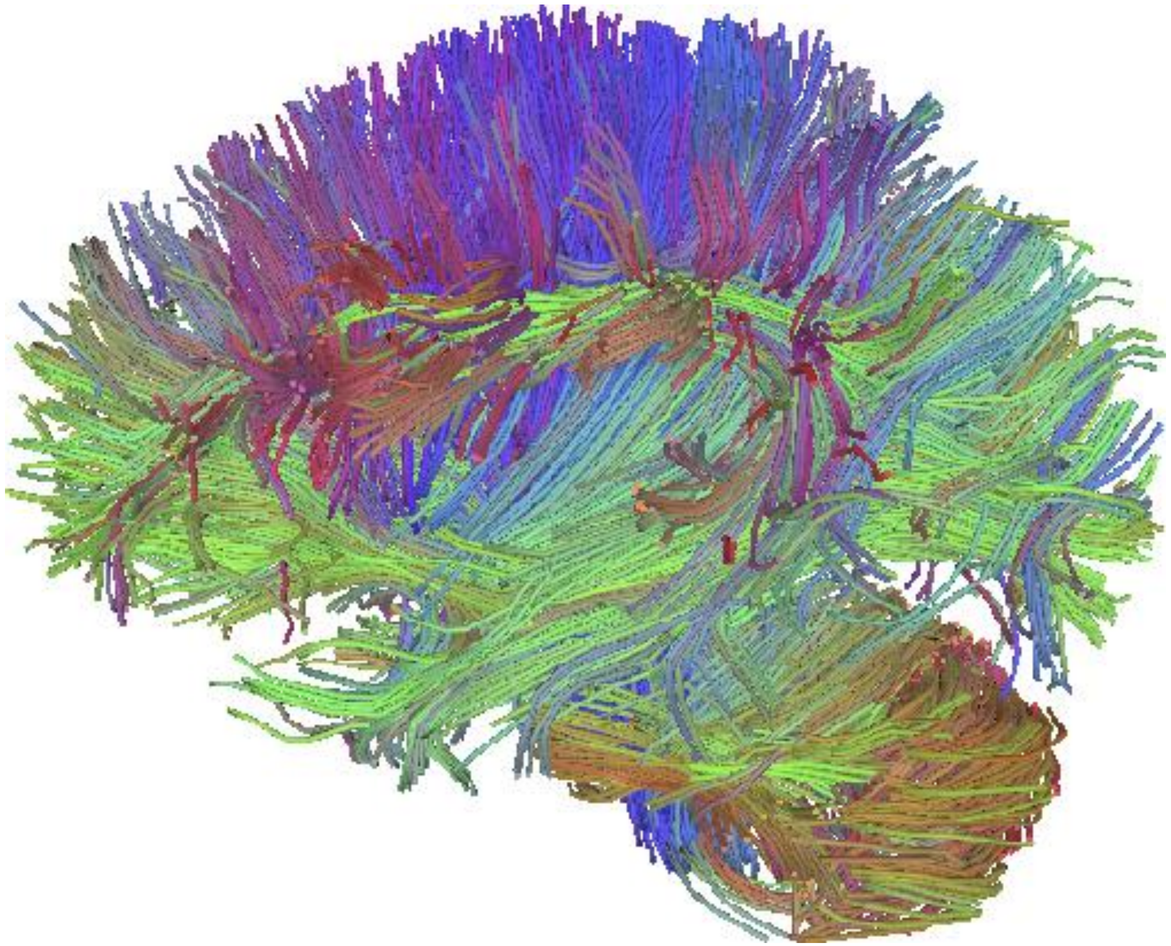


[Sheng et al., 2021]]

Probabilistic and deterministic ways for white matter tractography



Reconstruction of white matter fibre tracts



[https://api.semanticscholar.org/CorpusID:125412525]

Reconstruction of whole brain white matter fibre tracts