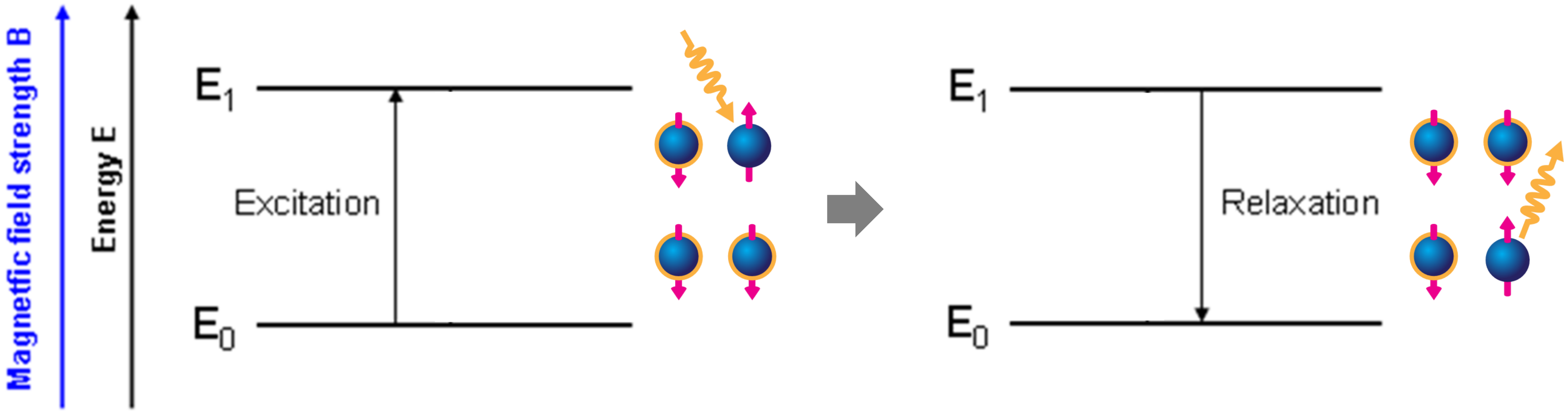
Medical/Bio Research Topics Ⅰ: Week 07 (15 April 2025)

Diffusion-weighted MRI (1): Basic Principles

확산가중 자기공명영상 (1): 기본 원리

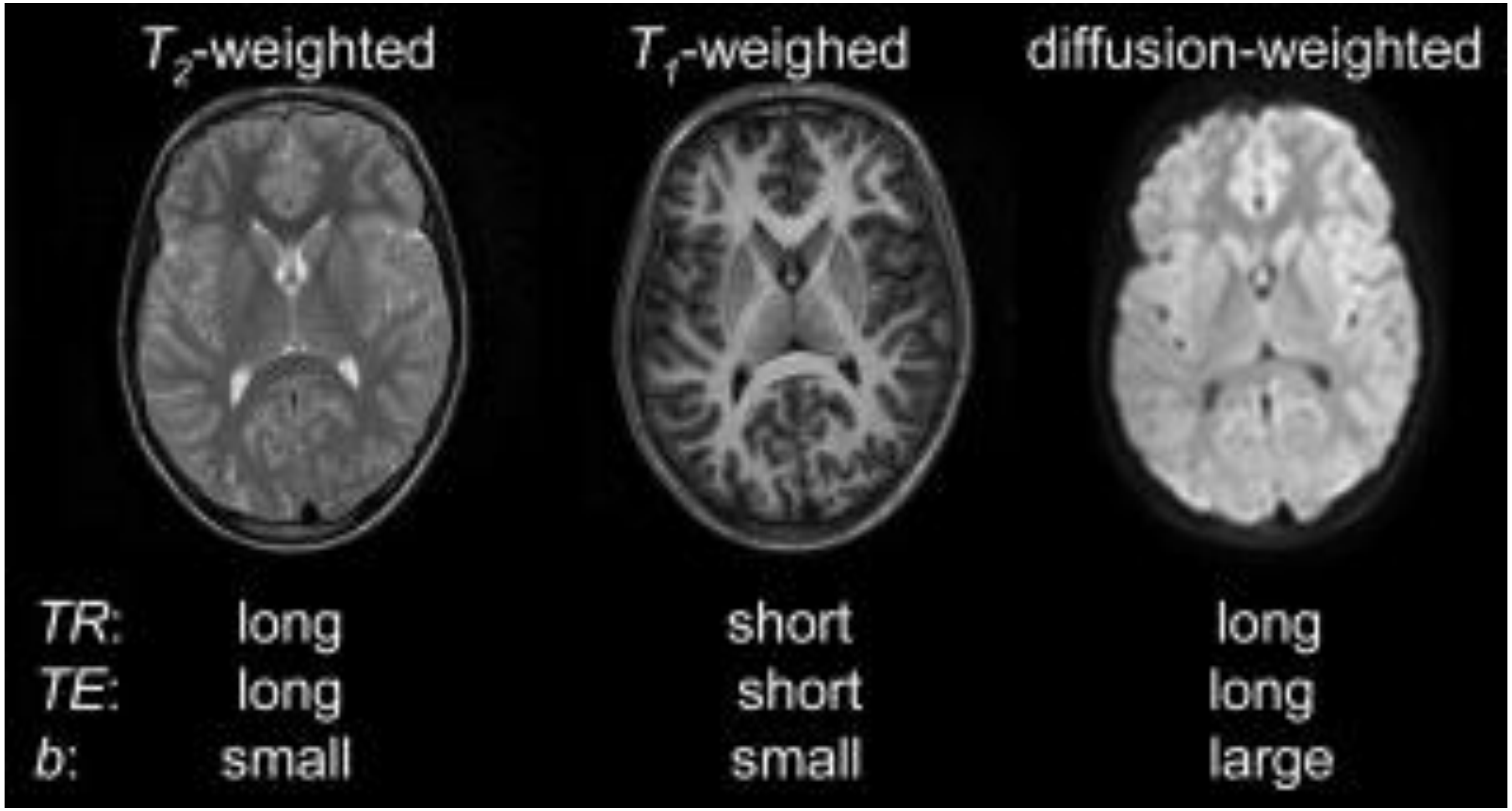
MRI Principles

- Medical application of nuclear magnetic resonance (NMR)
  - Generates different contrasts between tissues based on the relaxation properties of hydrogen nuclei therein



Diffusion-weighted MRI (dMRI)

- MRI technique primarily for examining tissue microstructure through water molecule diffusion patterns
- Applications of dMRI
  - Microstructural analysis
  - White matter tractography

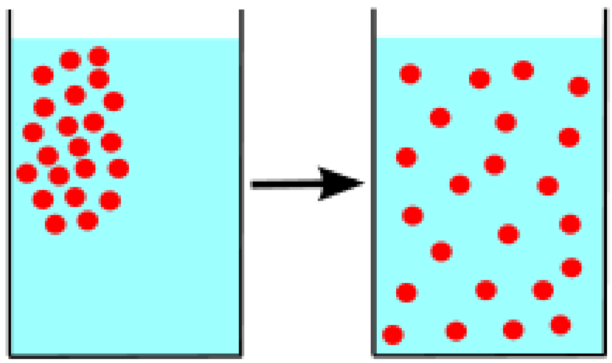


[Mori and Zhang, 2006]

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

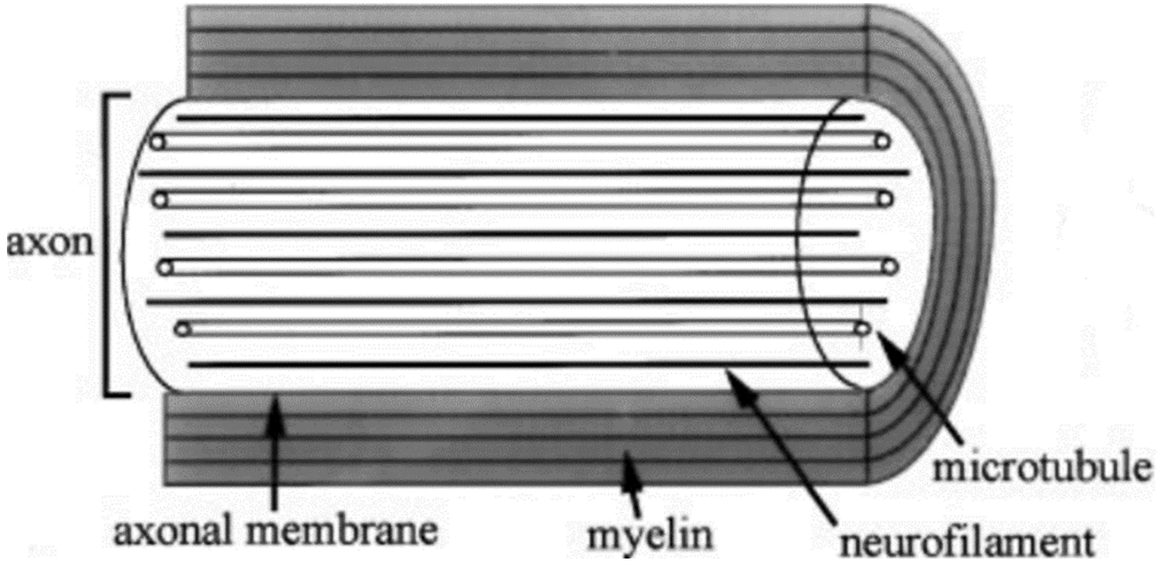


- Considered a macroscopic manifestation of Brownian motion

- 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: $\langle r^2 \rangle = 2Dt$
    - *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

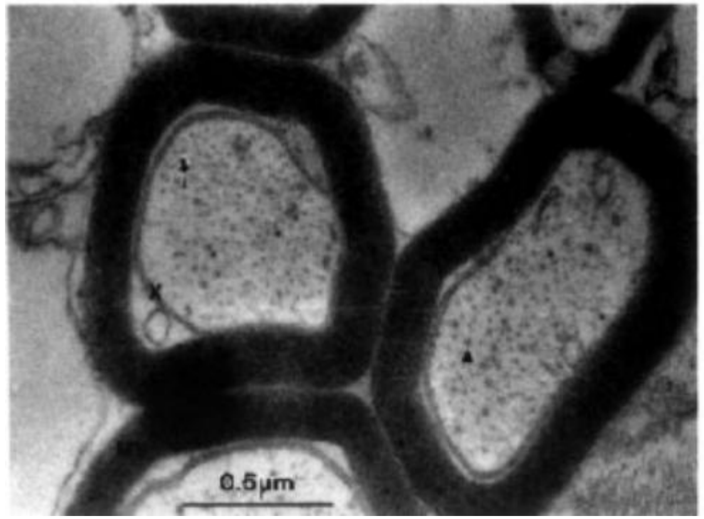
Fibrous structures in white matter



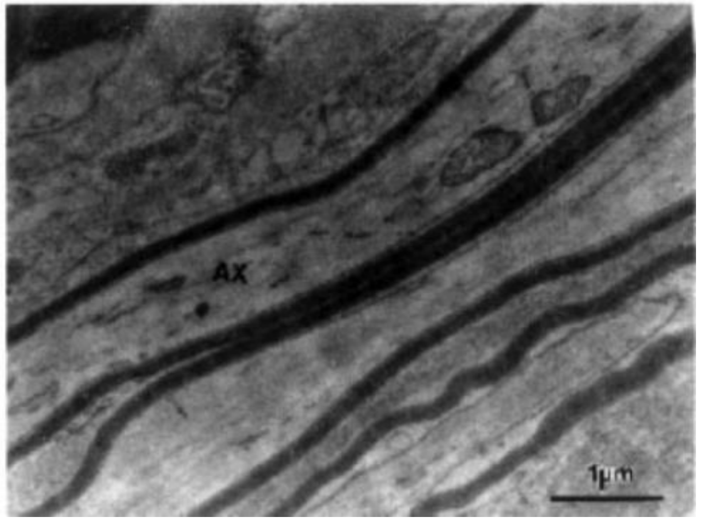
[O'Donnell and Westin, 2011]

- 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 fibers than across them

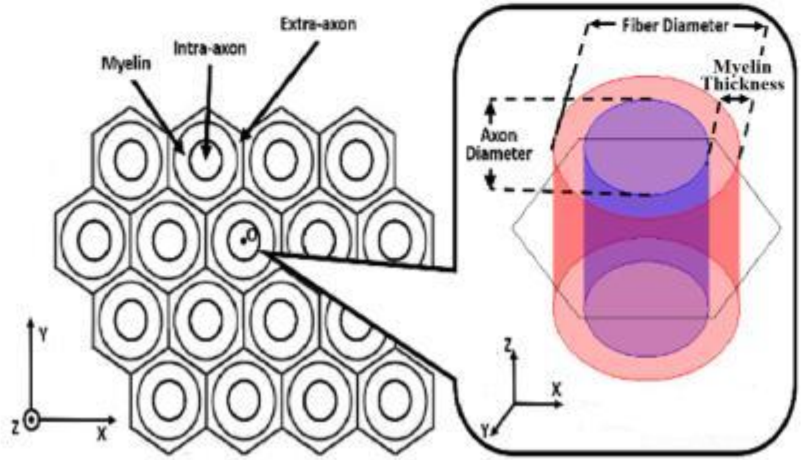
Transverse section

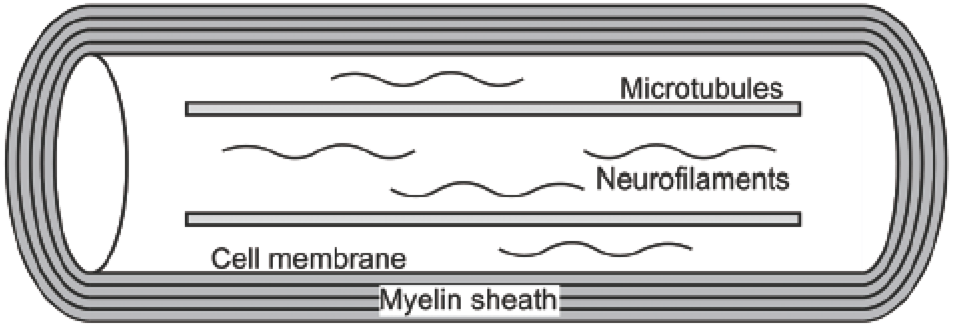


Longitudinal section



[Beaulieu, 2002]





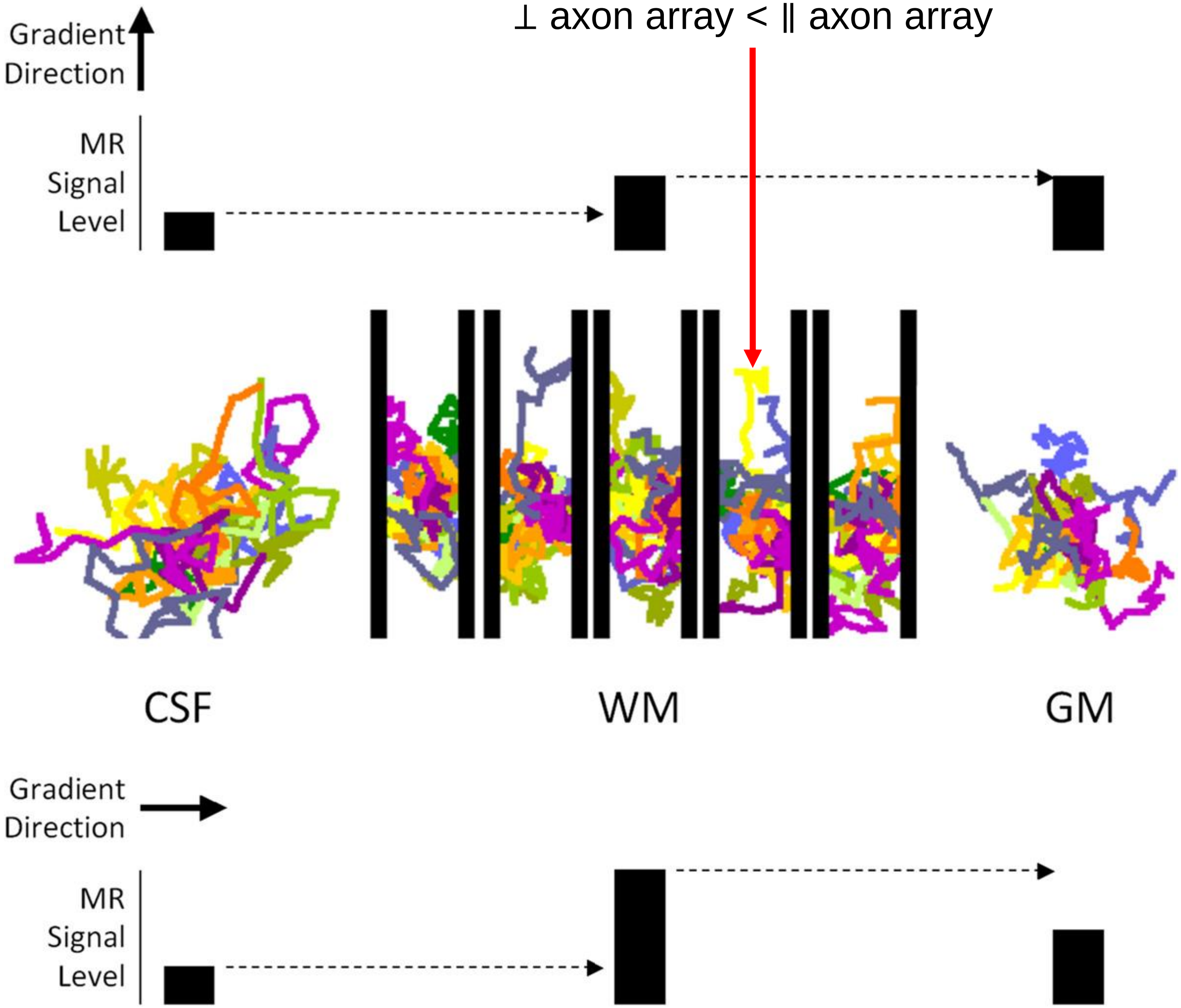
- Cytoskeleton
  - Microtubules (25 nm diameter)
  - Neurofilaments (10 nm diameter)
  - Microfilaments (7 nm diameter)
- Axonal membranes
- Myelin sheath

[Noguerol et al., 2017]

Potential Sources of Diffusion Anisotropy in a Myelinated Axon

- 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 molecule 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 behavior of the water molecules over a great many cells and axons within a voxel

Directional dependence of diffusion:
⊥ axon array < ∥ axon array



[Alger, 2012]

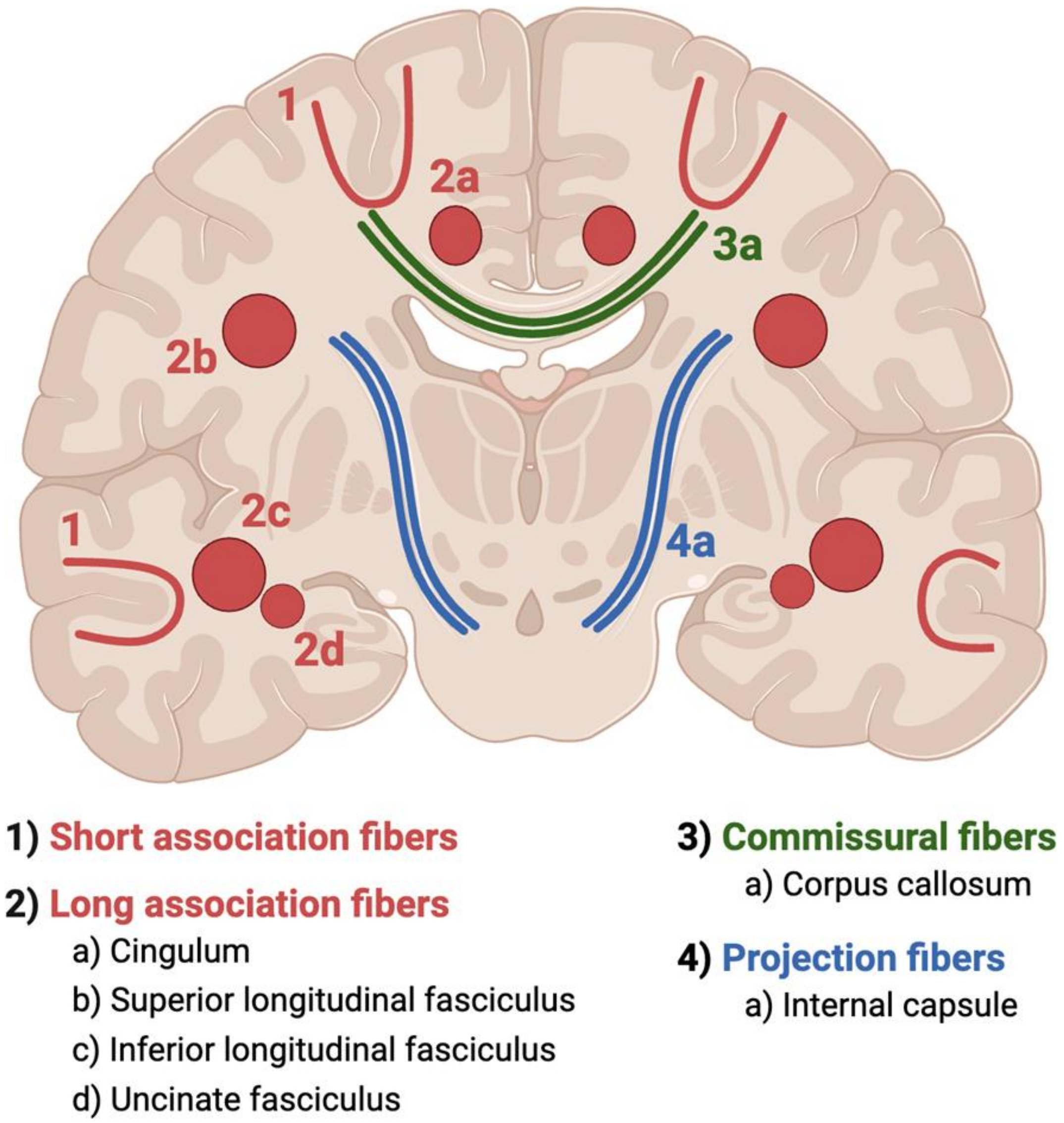
Directional Impact of Water Molecule Diffusion on MRI Signal Change

Central Nervous System Hierarchy

- From individual components to whole structure
  - Axon → axon fiber/nerve fiber → tract → white matter
- Axon
  - Long projection of a single neuron
  - Conducts electrical impulses away from the cell body
  - Single cellular structure

- Axon fiber/nerve fiber
  - Essentially the same as an axon, but often used when discussing axons in their functional context
  - Can be either myelinated or unmyelinated
  - "Nerve fiber" is a slightly broader term that can also include dendrites in some contexts
- Tract
  - Collection of multiple axon fibers with similar functions, origins, and destinations
  - Organized pathways within the central nervous system
  - For example, corticospinal tract, optic tract, spinothalamic tract

- White matter
  - Complete collection of all tracts
  - Contains all organized projection pathways in the central nervous system
  - Surrounds the gray matter in the spinal cord and lies beneath the gray matter in the cerebrum



[https://www.biorender.com/template/white-matter-tracts-coronal-section]

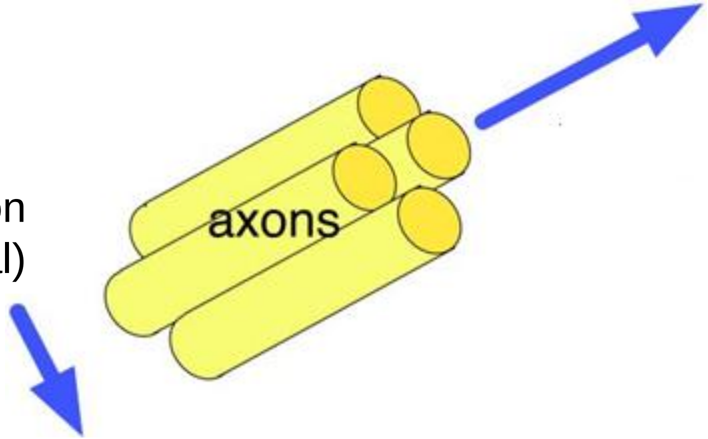
White Matter Tracts

Diffusion-weighted Contrast

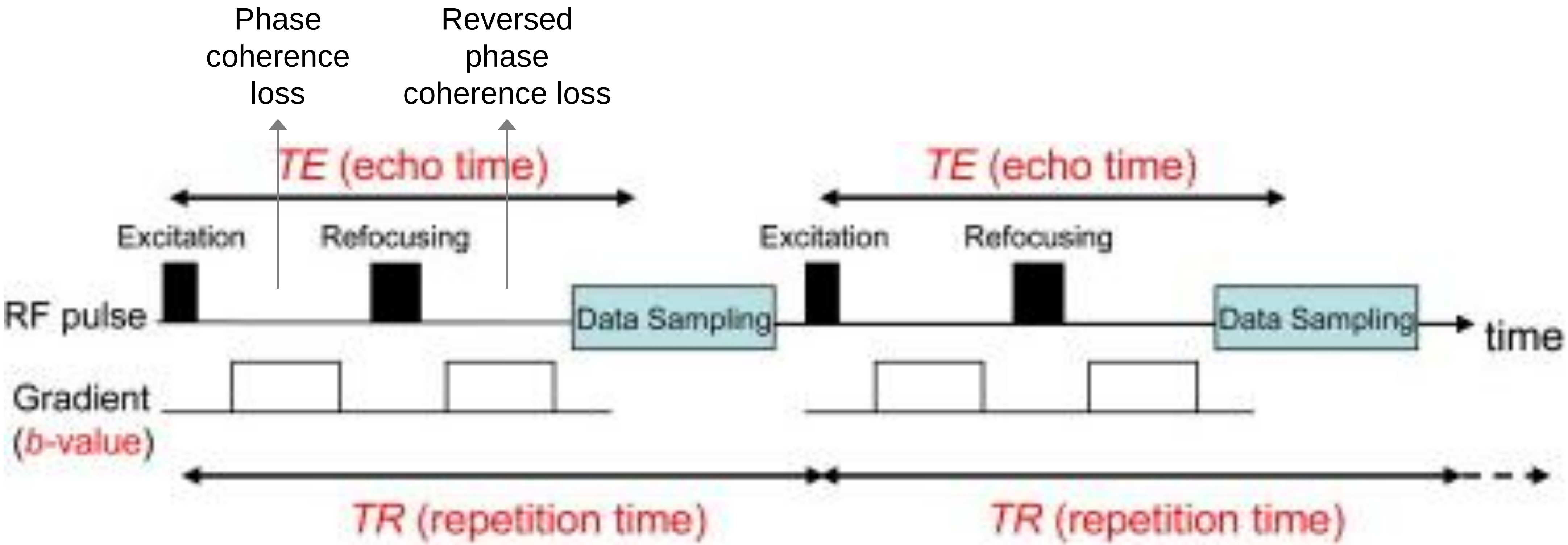
- MRI signal changes caused by diffusion

More diffusion
(More decrease in an MRI signal)

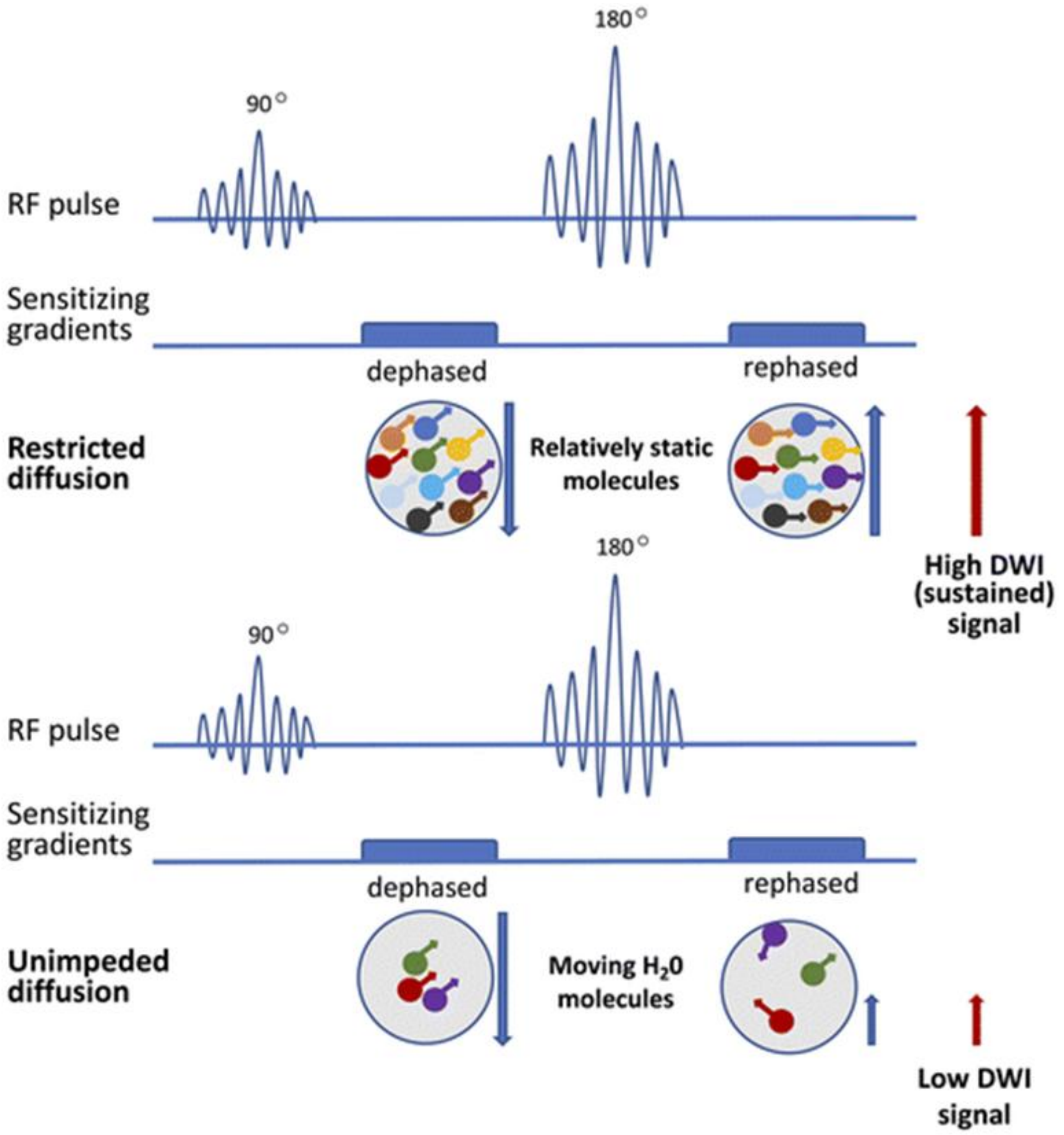
Less diffusion
(Less decrease in an MRI signal)



- 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

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

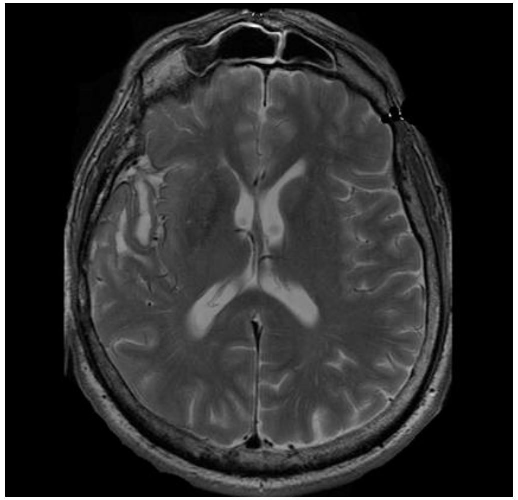
b-value

MRI signal measured without diffusion weighting

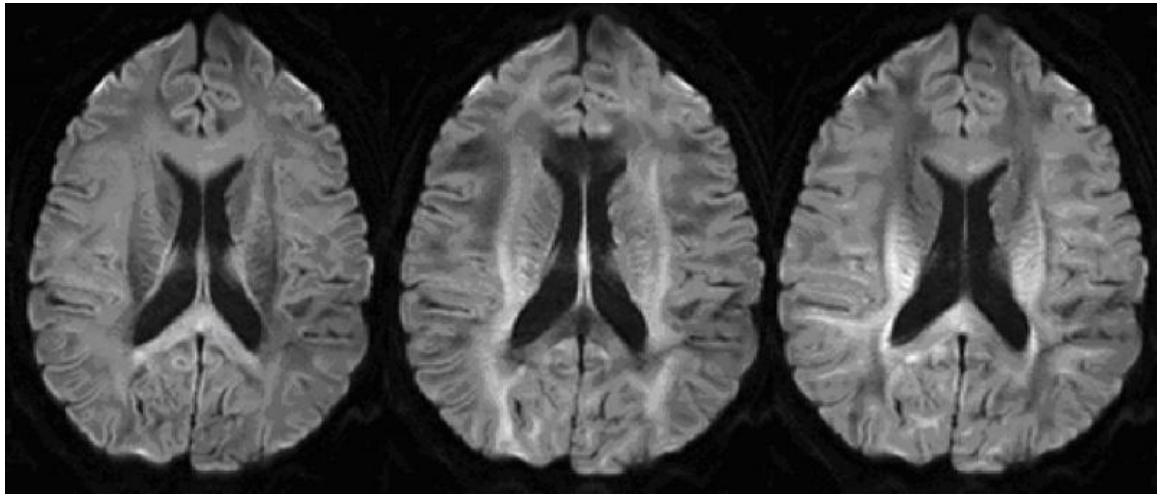
Diffusion coefficient $$D = \frac{1}{b} \log \frac{S_0}{S}$$

More signal decrease
→ higher diffusion coefficient

Less signal decrease
→ lower diffusion coefficient



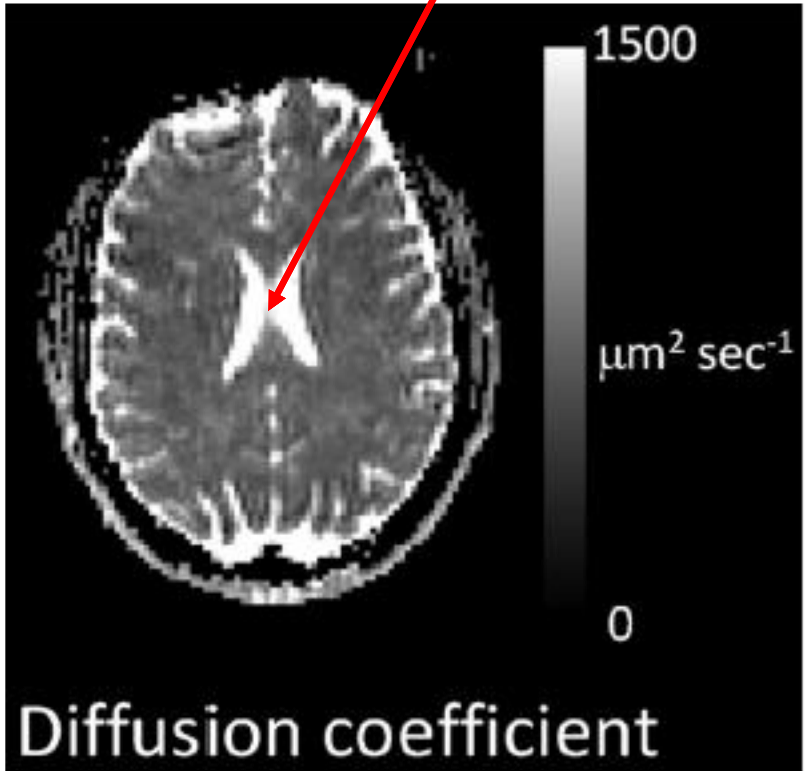
Without the diffusion-sensitizing gradient



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

Images Acquired 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

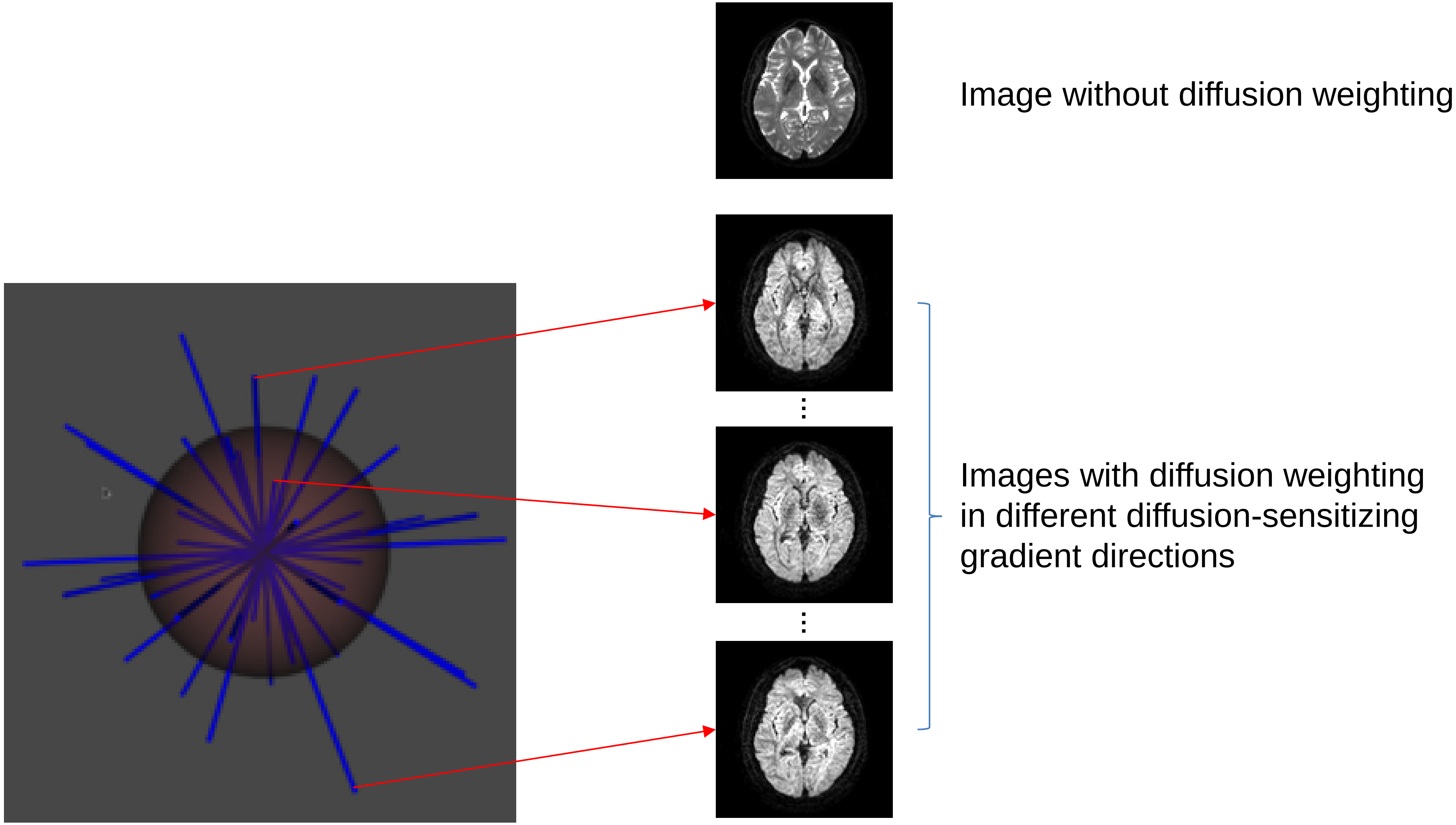
Diffusion tensor

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

Direction of the diffusion-sensitizing gradient

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

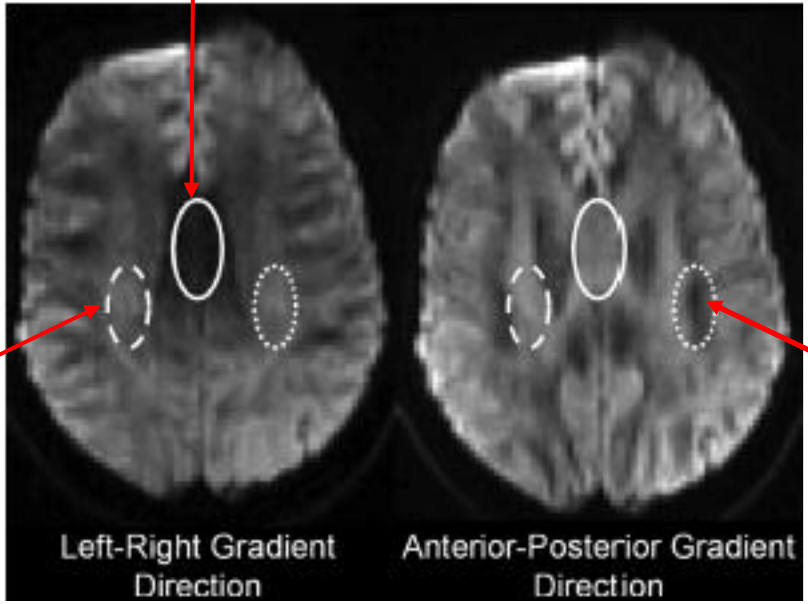
$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$



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]

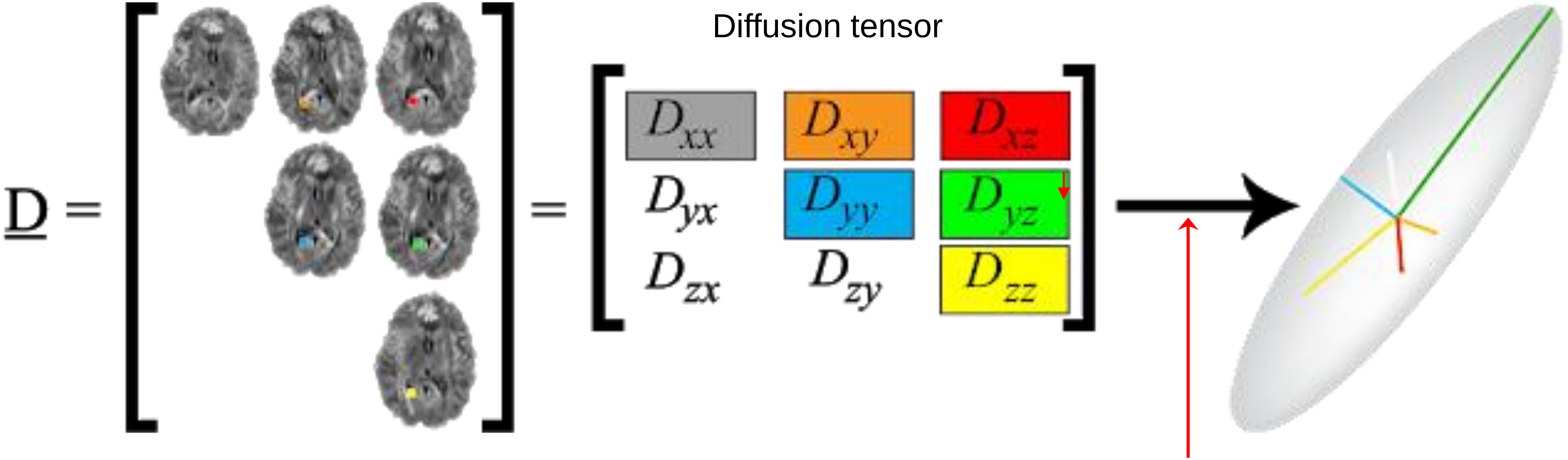
Impacts of Different Diffusion-sensitizing Gradient Directions

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 water molecule 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

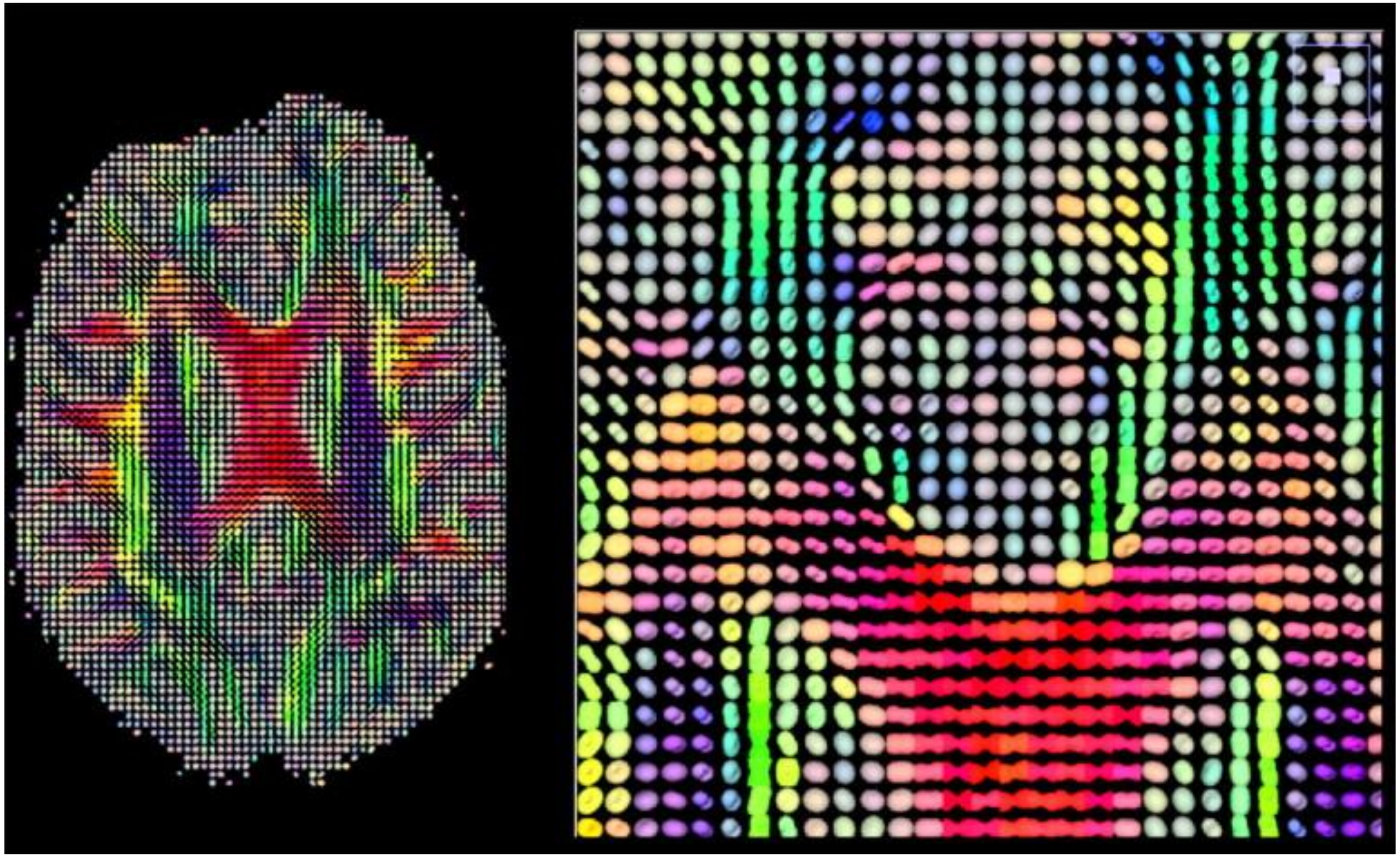
Diffusion Tensor

- 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



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

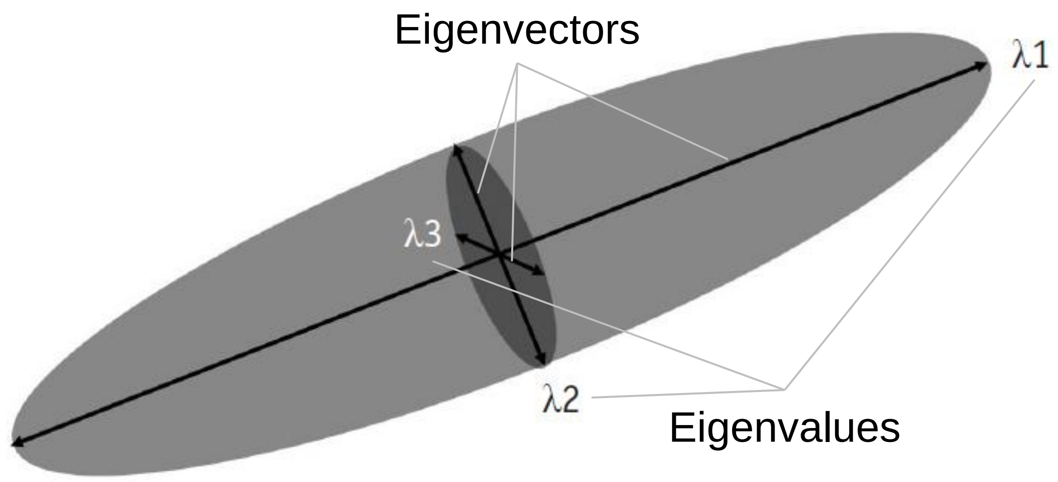
Diffusion Tensor and Its Ellipsoid Representation



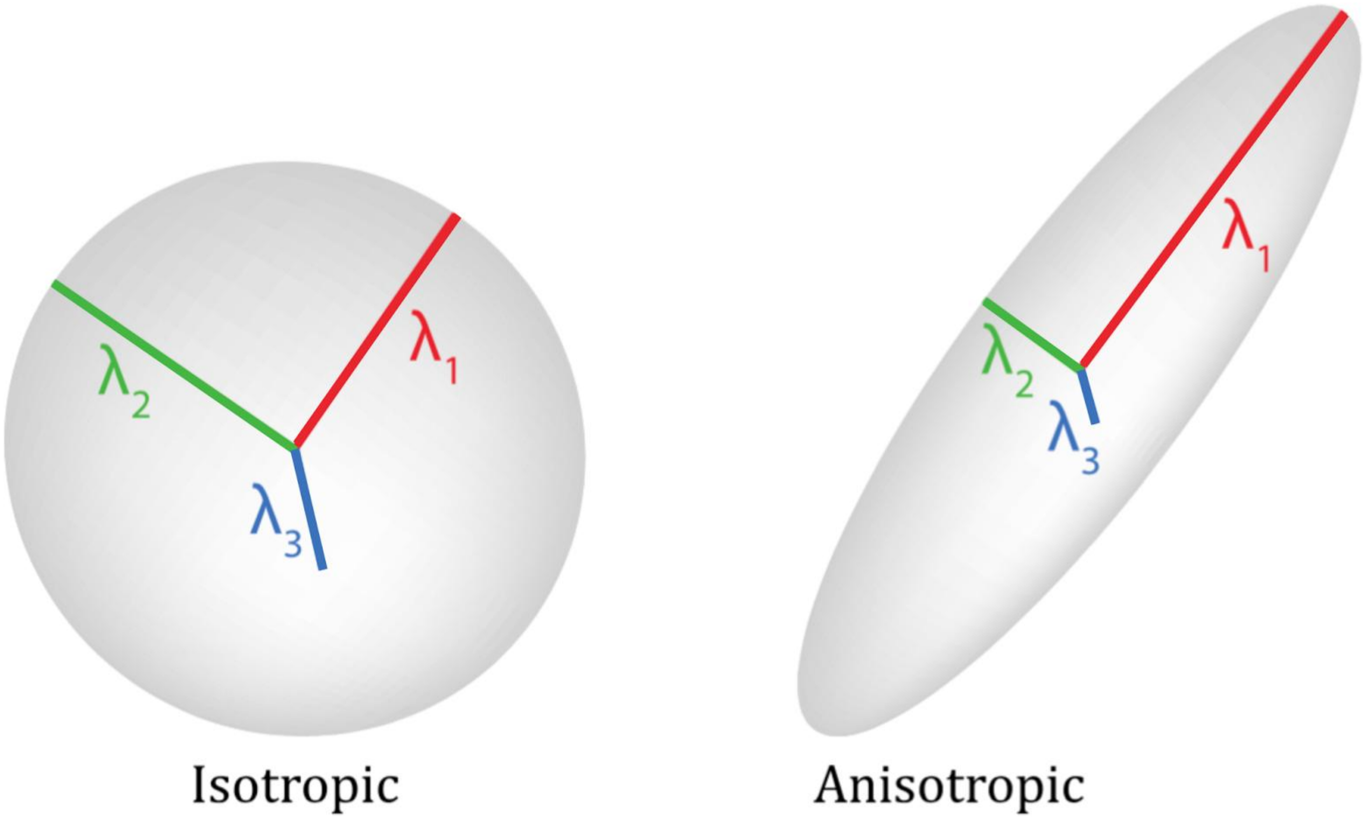
[Alger, 2012]

Diffusion Ellipsoids Derived from the Diffusion Tensors Measured for Each Voxel

- Represents averaged diffusion properties of numerous axons within a single voxel

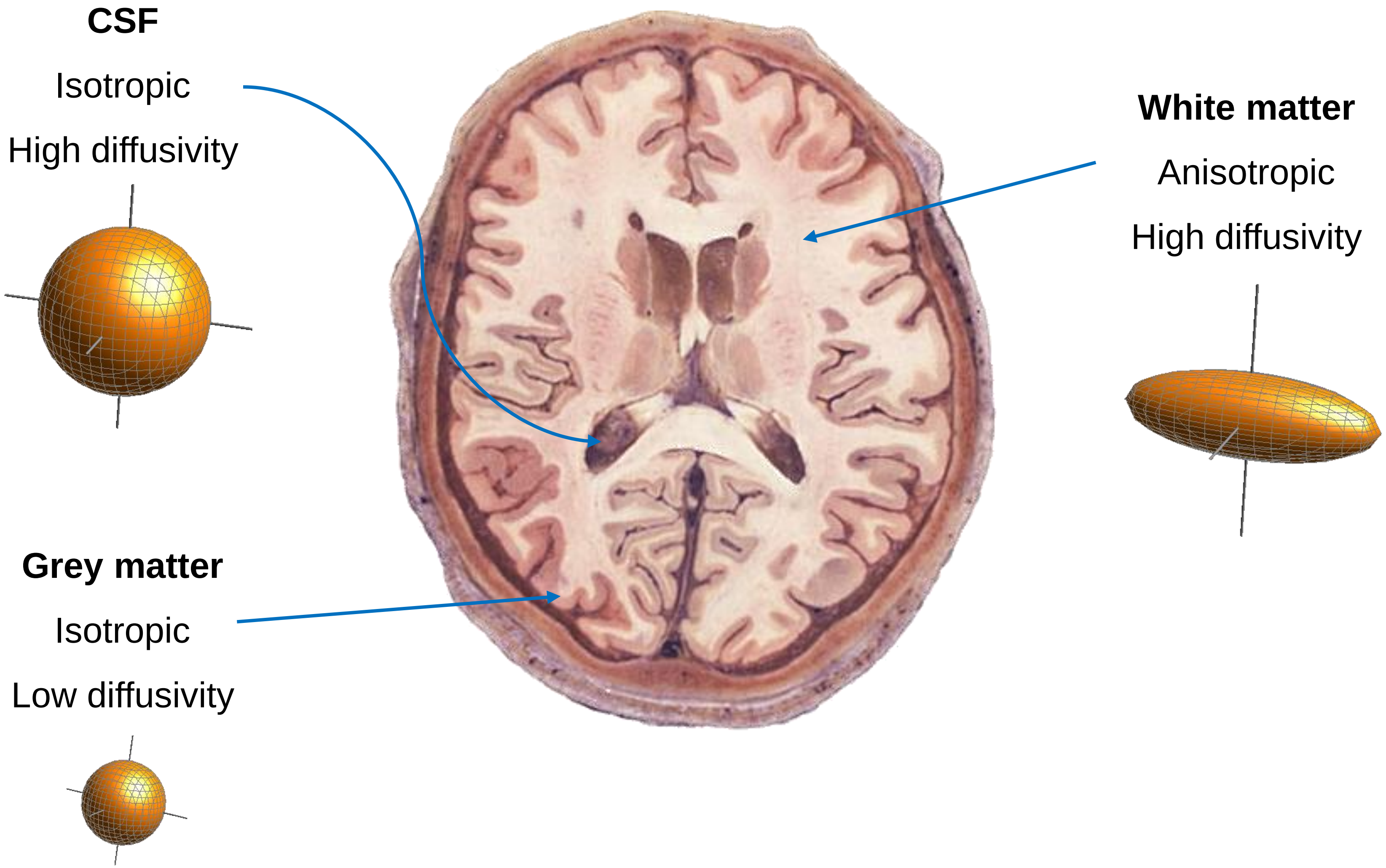


  - Magnitude and anisotropy of diffusion
    - Offer insights into tissue structure and organization



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

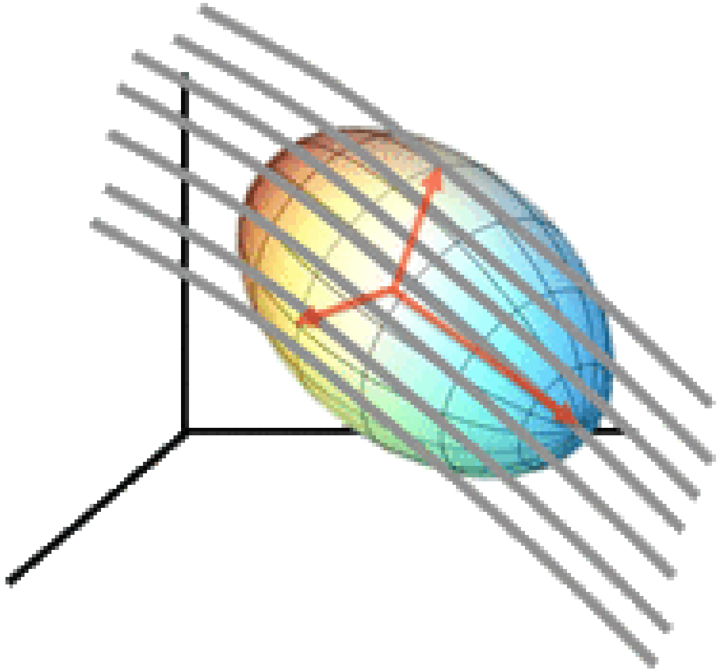
Isotropic and Anisotropic Diffusion Represented by Ellipsoids



Isotropic and Anisotropic Diffusion in Different Brain Tissues

– Principal direction of diffusion

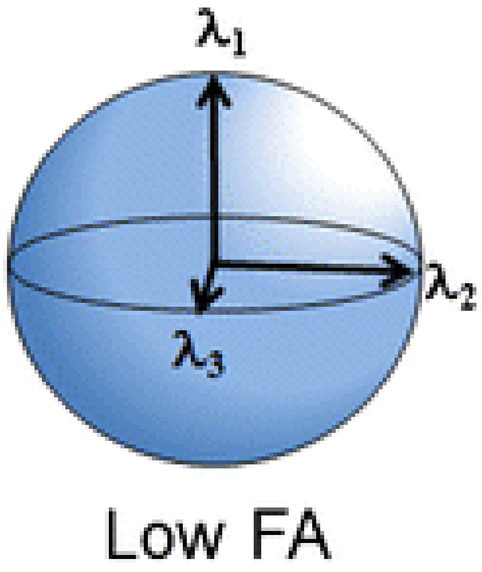
- Given by the main axis (principal eigenvector; eigenvector of the largest eigenvalue) of the ellipsoid
- Assumed to be aligned with the dominant fiber orientation within a voxel



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

Microstructural Analysis with dMRI

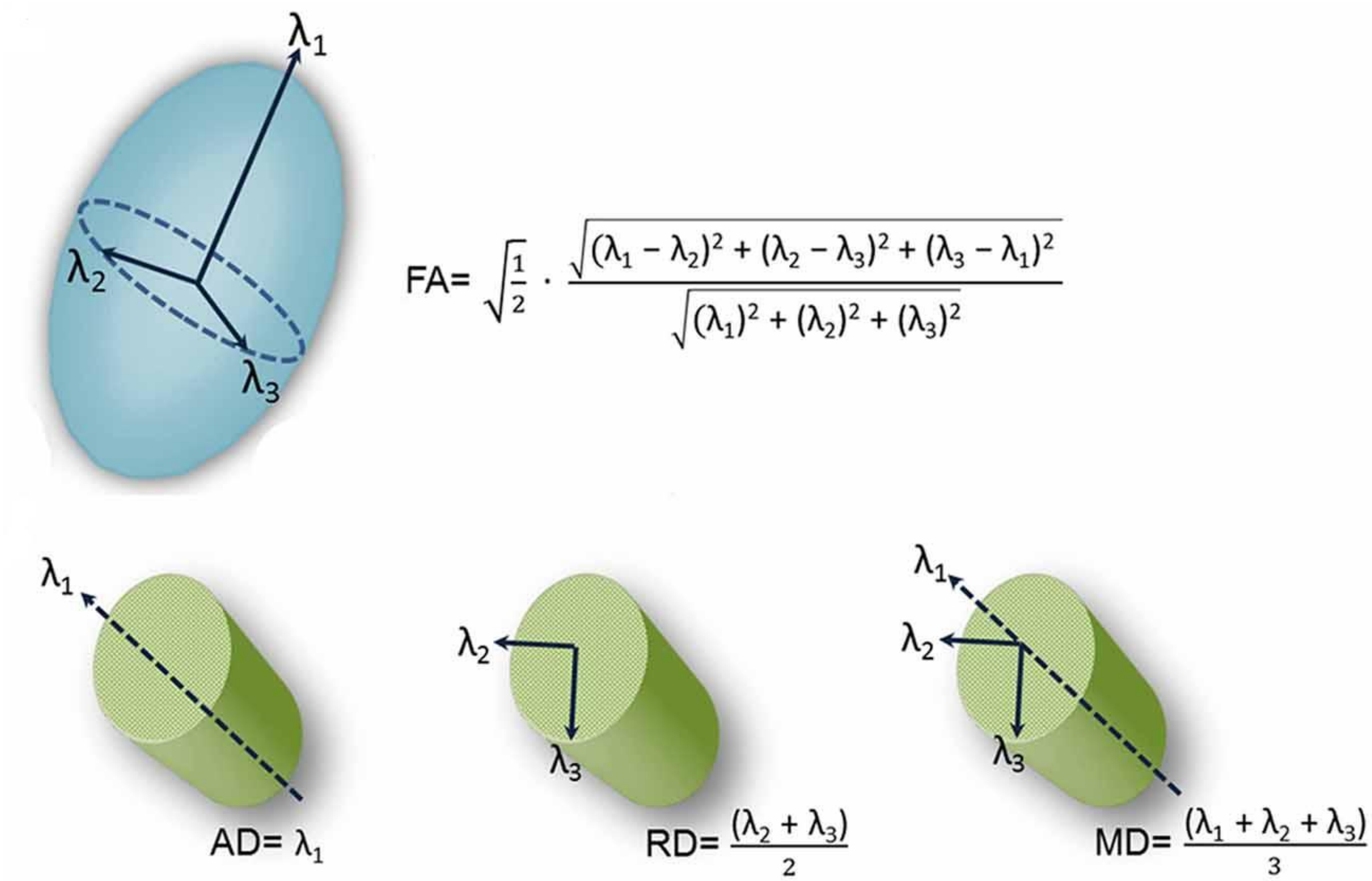
- Diffusion tensor metrics
  - Represent the magnitude and anisotropy (directional dependence) of water molecule diffusion within a voxel
  - Fractional anisotropy (FA)
    - Measures the degree of anisotropy (how much the diffusion is directionally dependent) within a voxel
    - Ranges from 0 (completely isotropic diffusion) to 1 (highly anisotropic diffusion)



[Mabrouk, 2018]

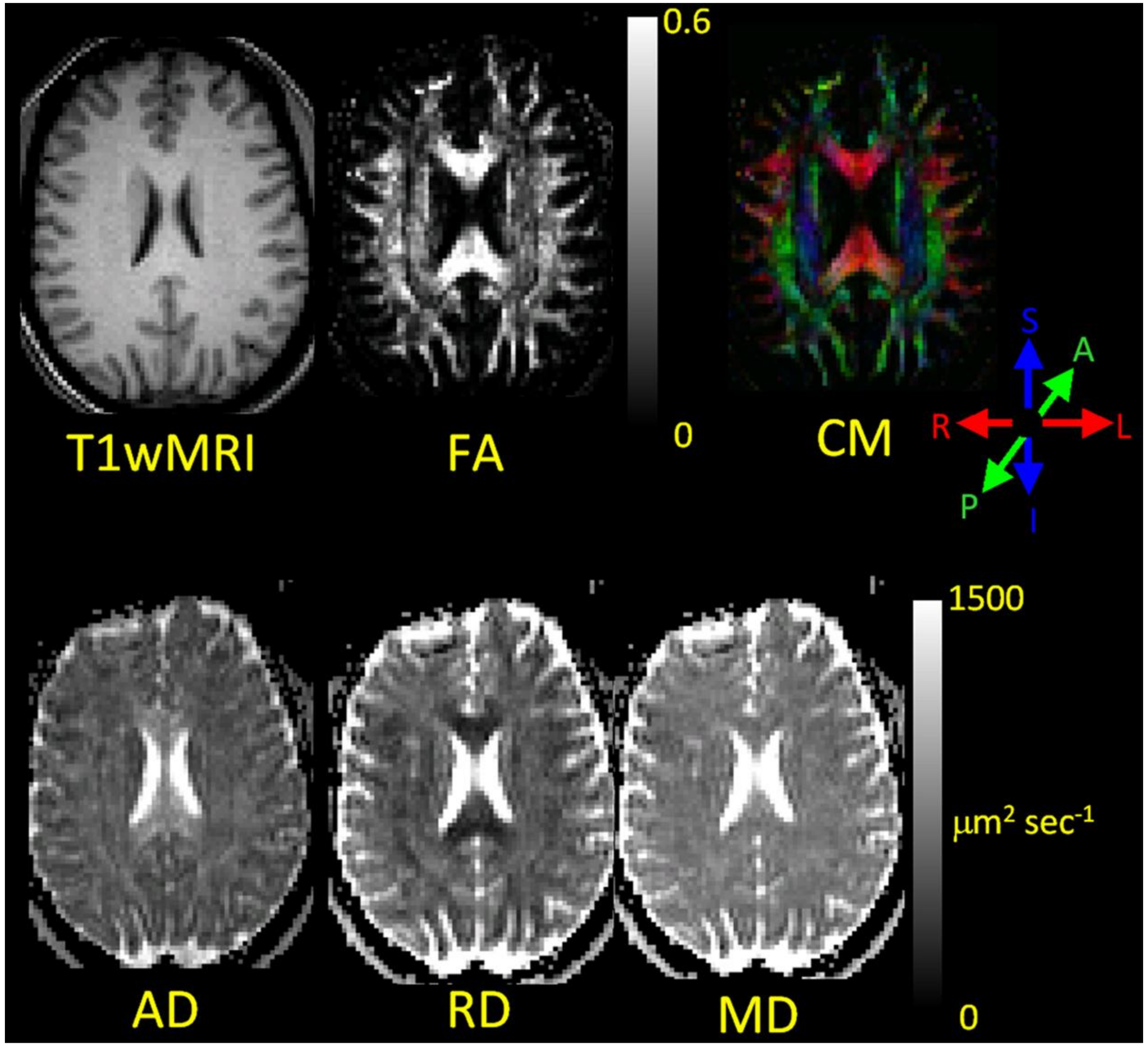
Isotropic and Anisotropic Diffusion Representing Different FA Values

- 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 fiber orientation within a voxel
- Radial diffusivity (RD)
  - Measures the average rate of diffusion perpendicularly to the dominant fiber orientation within a voxel
  - Indicative of reduced myelin integrity (degeneration or reduction of myelin around axons)



[DeSouza et al., 2016]

Diffusion Tensor Metrics

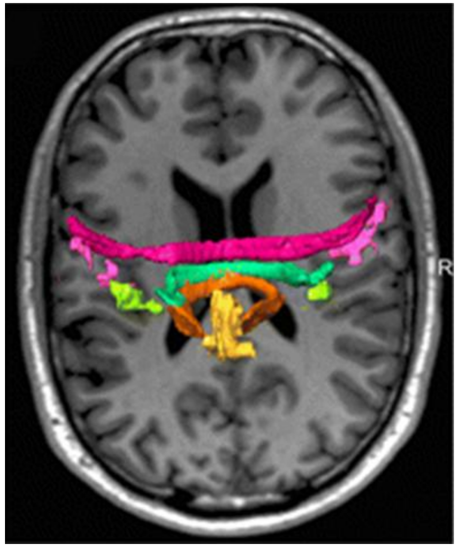


[Alger, 2012]

Maps of diffusion tensor-derived measures

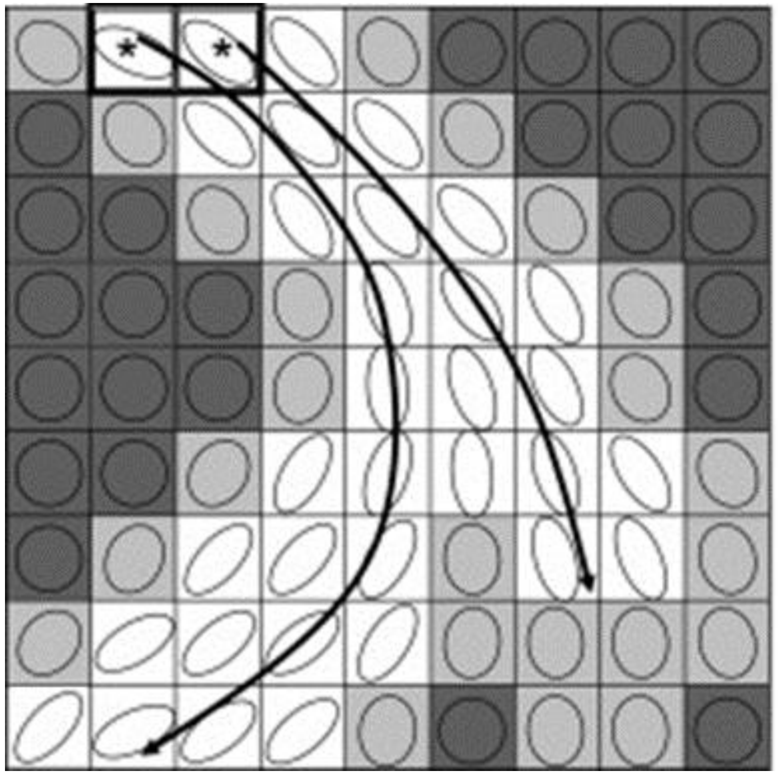
White Matter Tractography with dMRI

- Diffusion anisotropy enables tractography and visualization of major white matter pathways in the brain



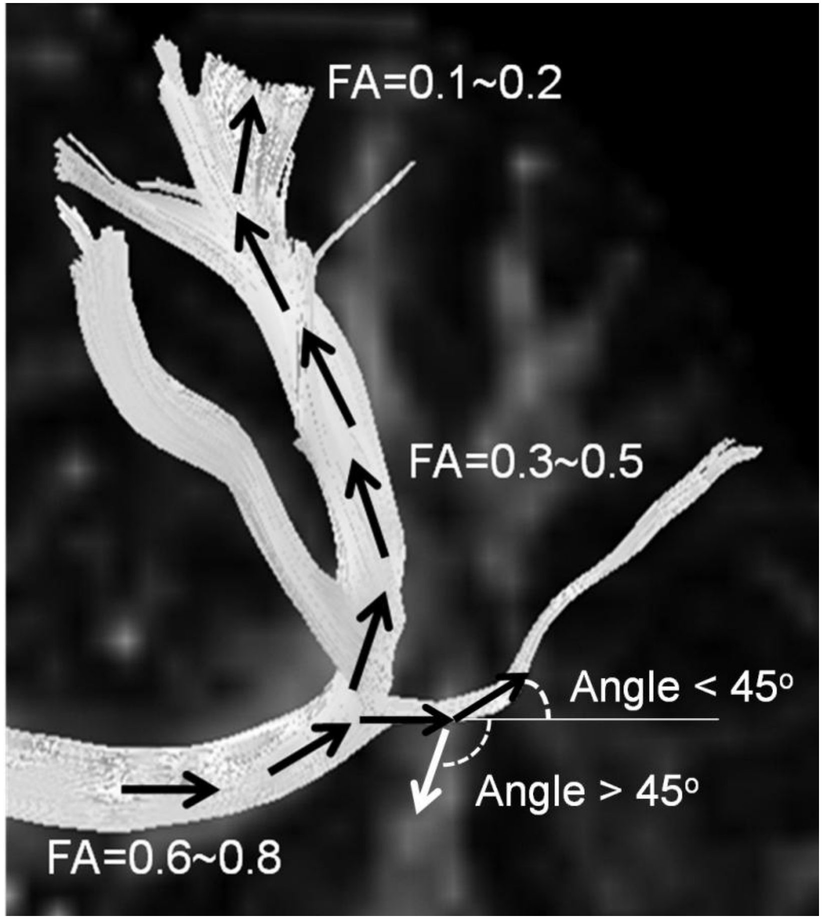
[Wahl et al., 2007]

- 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



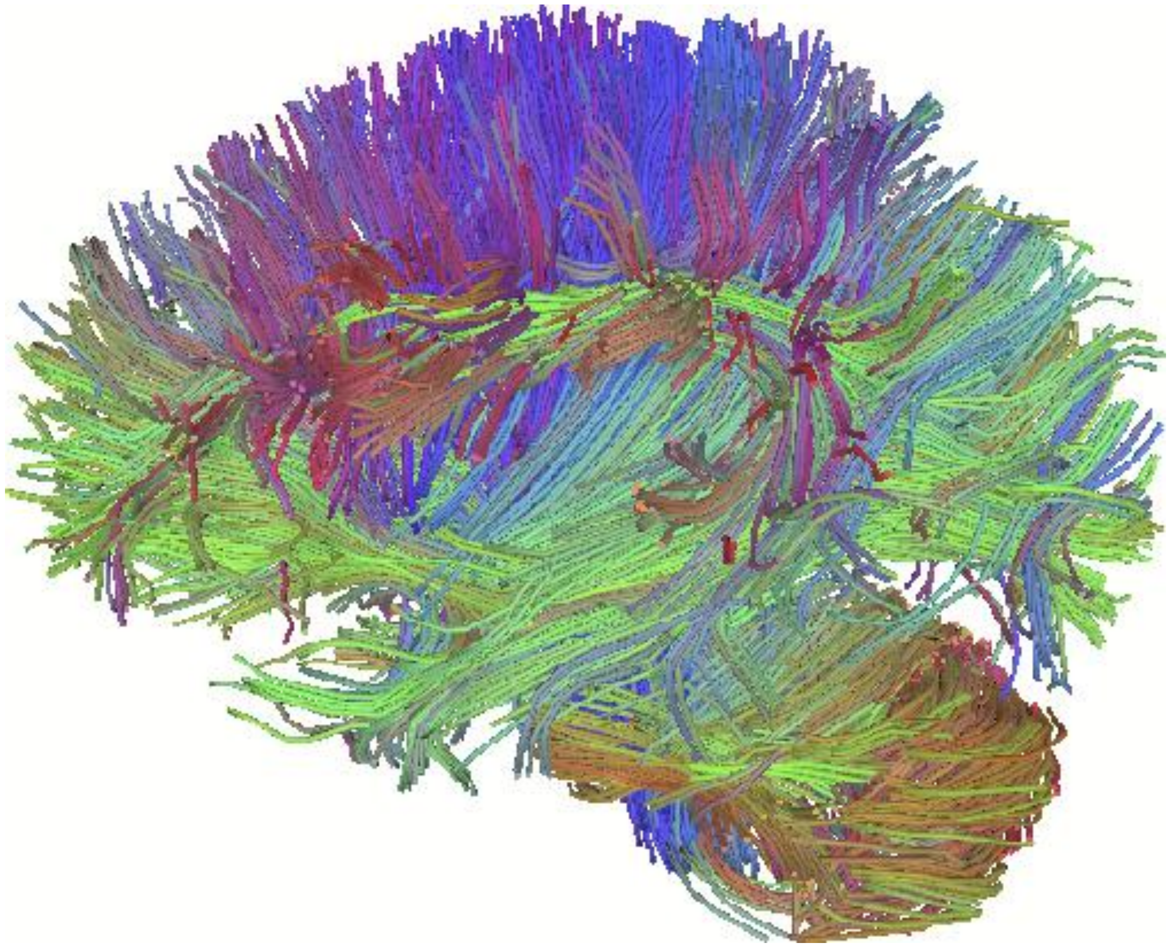
[Mori and Zhang, 2006]

Reconstruction of White Matter Tracts in a Deterministic Way



Tracking a Streamline by Filtering Out Anatomically Unrealistic Pathways

Reconstruction of White Matter Tracts



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

Reconstruction of Whole Brain White Matter Tracts