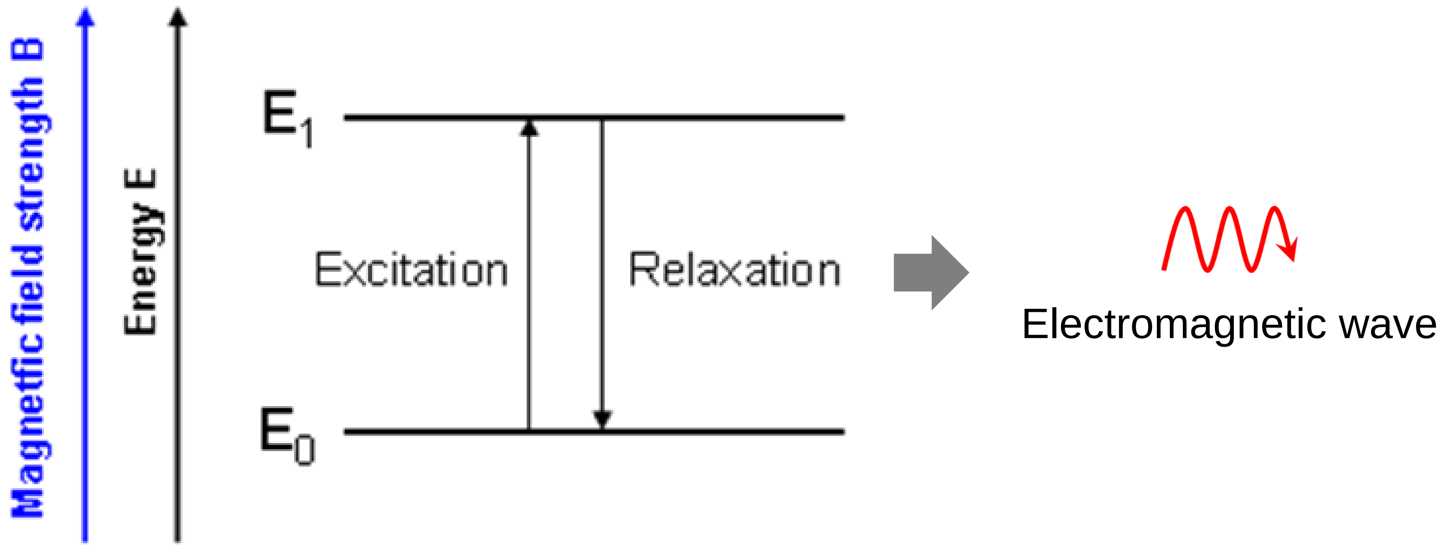
Medical/Bio Research Topics Ⅱ: Week 05 (01.10.2024)

Diffusion-weighted MRI: Fundamental Principles and Data Processing

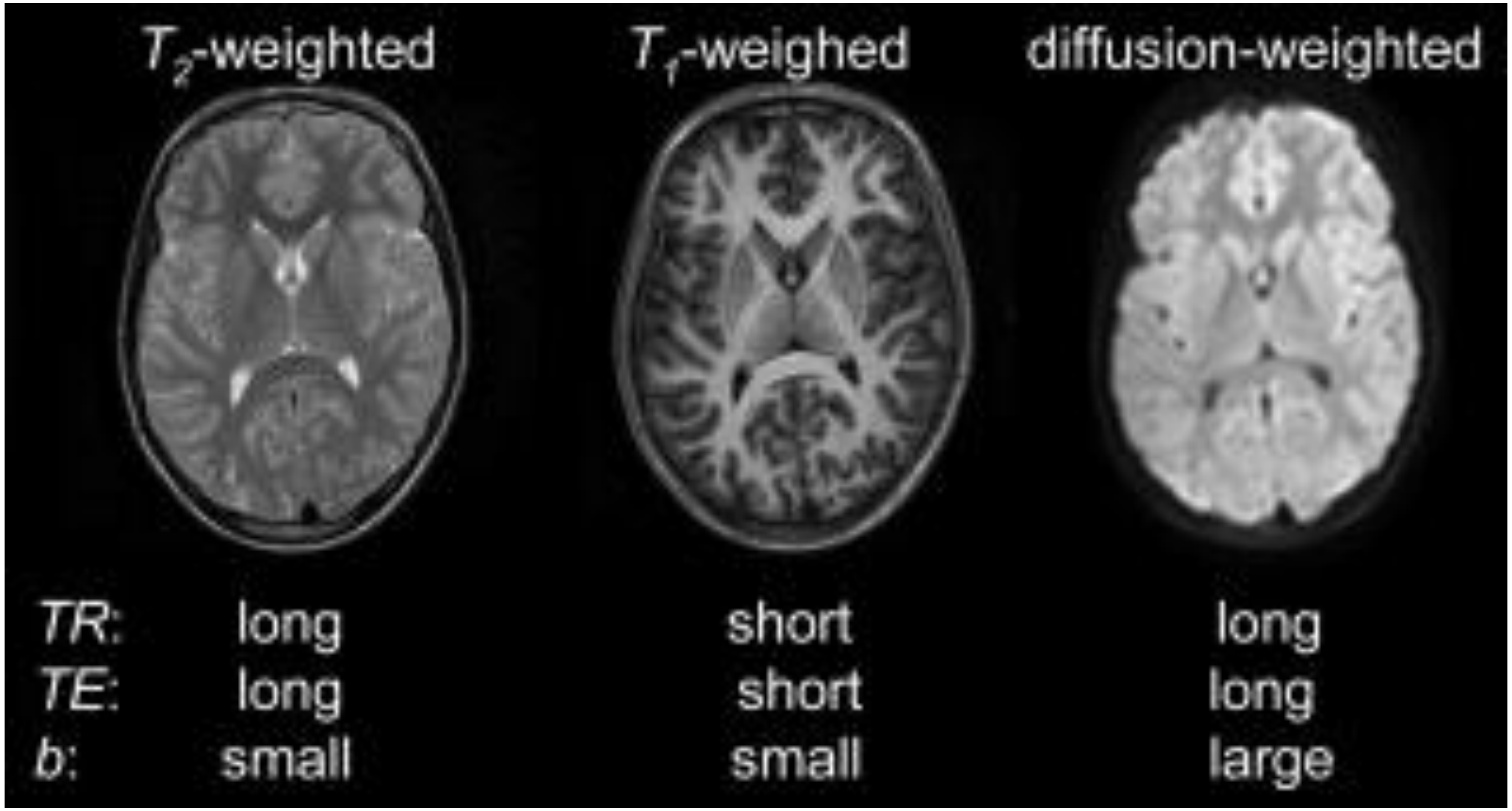
확산가중 자기공명영상: 기본 원리 및 데이터 처리 방법

MRI Principles

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



- MRI contrast mechanisms
  - T1-weighted contrast
    - Primarily uses a spin-echo or a gradient-echo sequence
    - With short Echo Time (TE) and short Repetition Time (TR) to maximize T1 contrast and minimize T2 effects
  - T2-weighted contrast
    - Primarily uses a spin-echo sequence
    - With long TE to allow for T2 decay and long TR to minimize T1 effects
  - Diffusion-weighted contrast: T2 weighting + diffusion weighting
    - Typically uses a gradient-echo echo-planar imaging (EPI) sequence
    - Applies diffusion-sensitizing gradients
    - With even longer TE to accommodate the diffusion gradients and typically longer TR to allow for the additional gradients and to reduce T1 effects

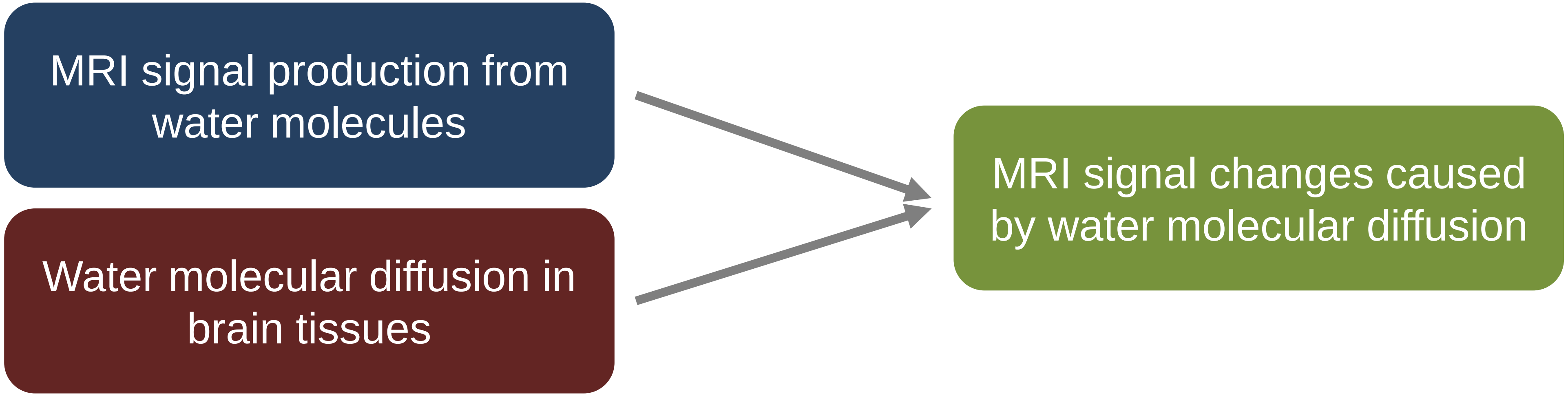


[Mori and Zhang, 2006]

Various types of MRI contrasts

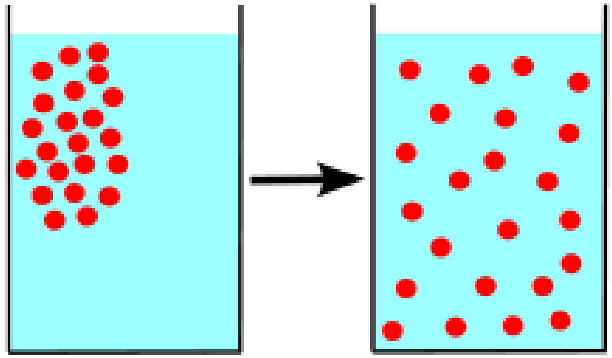
Diffusion-weighted MRI (dMRI)

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



Diffusion

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

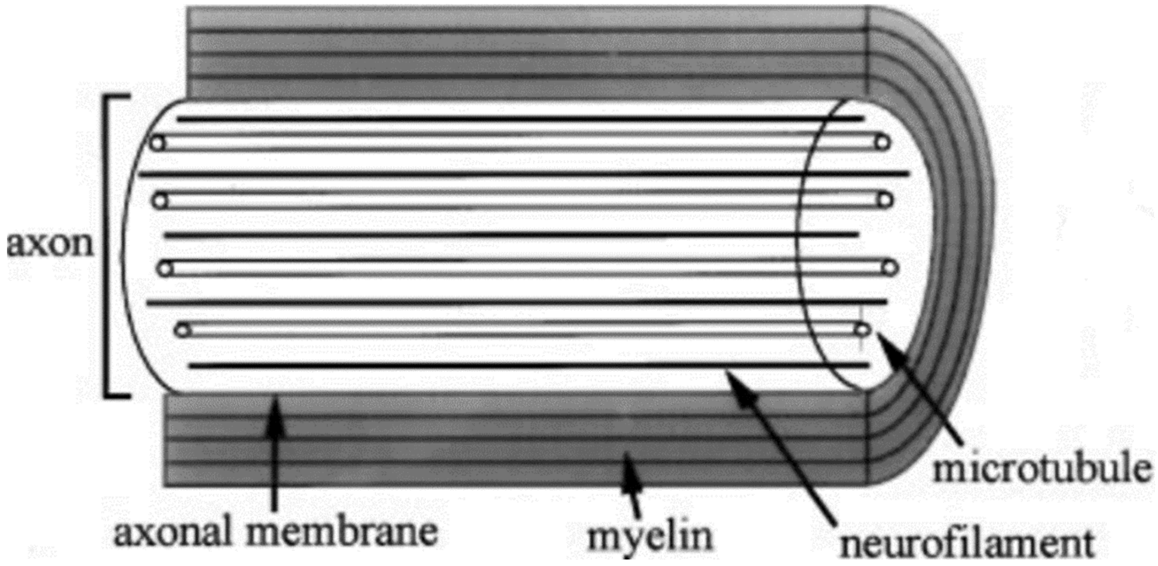


- Considered a macroscopic manifestation of Brownian motion

- 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: $\langle r^2 \rangle = 2nDt$
    - $<r^2>$: mean squared distance that a particle moves in a particular direction in a time period t
    - n: number of dimensions (1 for one dimension, 2 for two dimensions, 3 for three dimensions)
    - D: diffusion coefficient

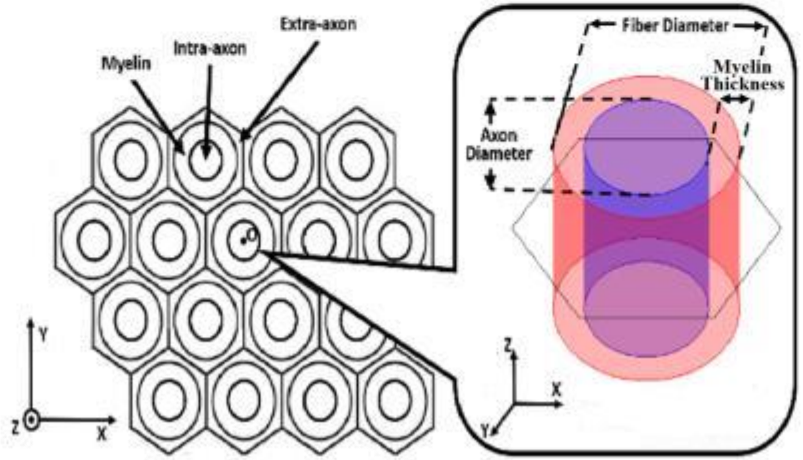
- Movement of water molecules in a heat-driven random fashion in brain tissues
  - Unless the movement is constrained by barriers

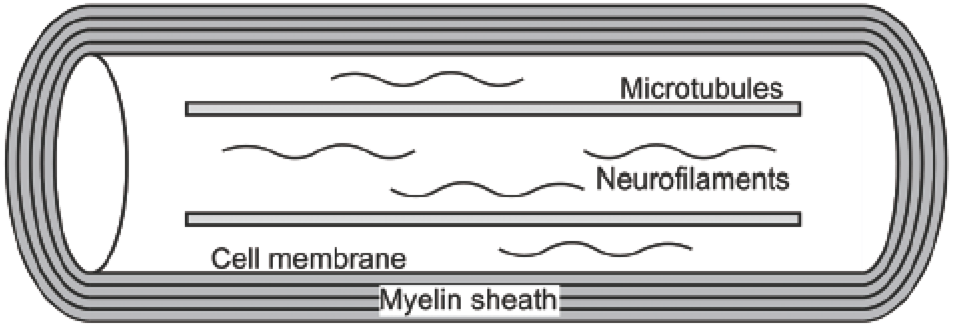
Fibrous structures in white matter



[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
  - Bundle of axons: fibre tract
    - Not just a single axon but often refers to a complex structure involving multiple axons that are grouped together, traveling through the brain or spinal cord
    - Functions as a unit within the nervous system to facilitate rapid communication across different regions
    - Also referred to as fasciculus (especially in the central nervous system), white matter tract, axon pathway, or nerve tract

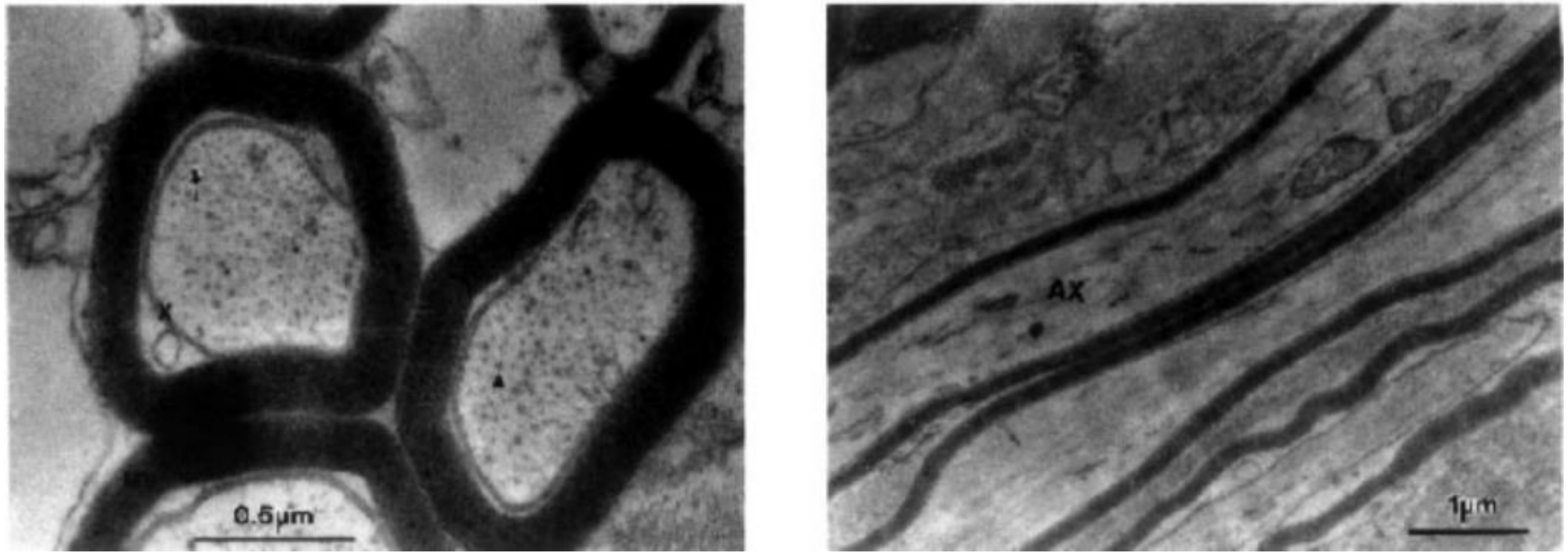




- Cytoskeleton
  - Microtubules (25 nm diameter)
  - Neurofilaments (10 nm diameter)
  - Microfilaments (7 nm diameter)
- Axonal membranes
- Myelin sheath

[Noguerol et al., 2017]

Potential sources of diffusion anisotropy in a myelinated axon

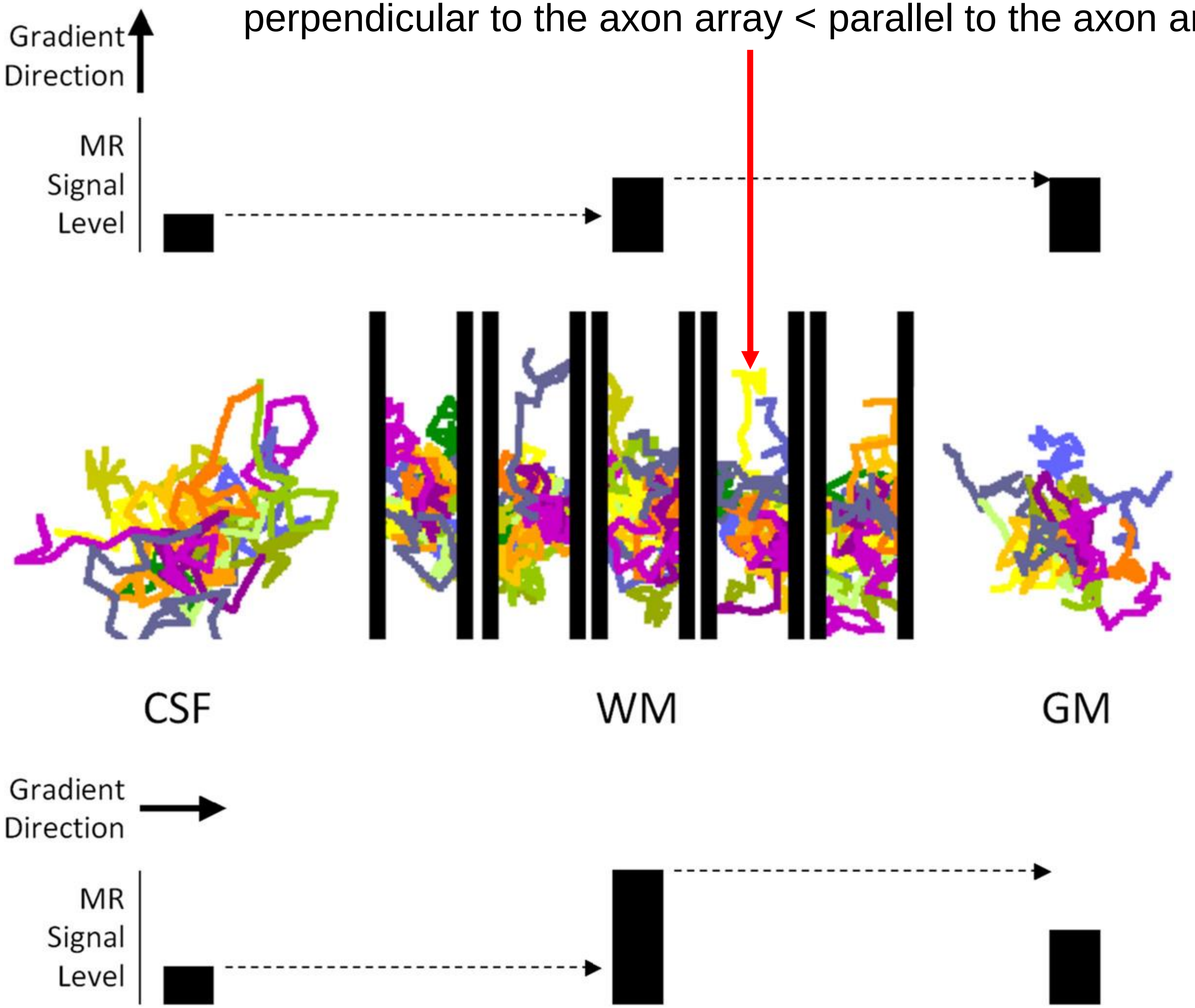


[Beaulieu, 2002]

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 $\mu m^2/s$ (or 0.001 mm^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

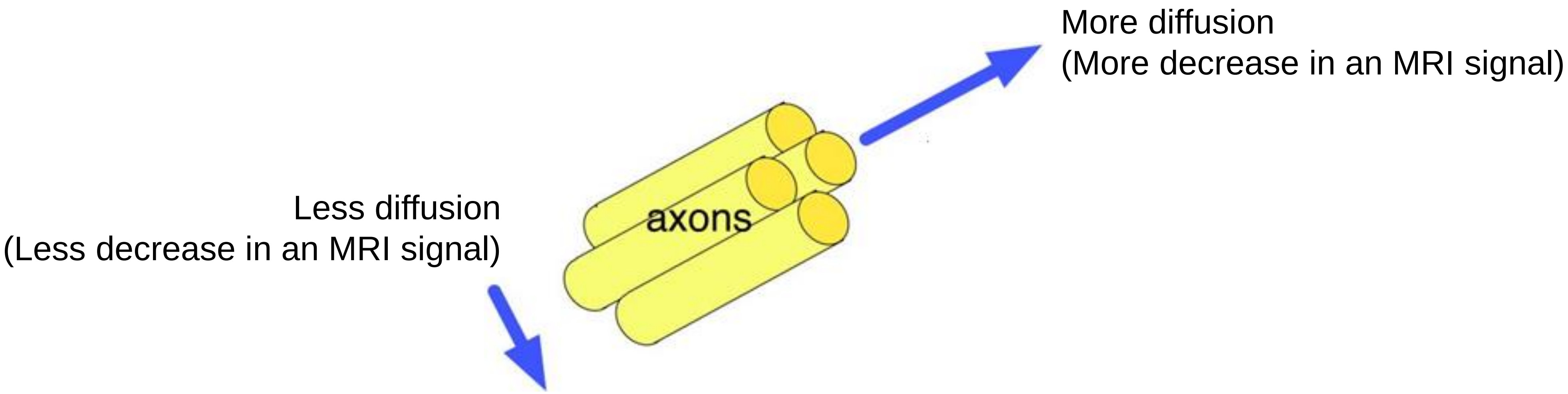


[Alger, 2012]

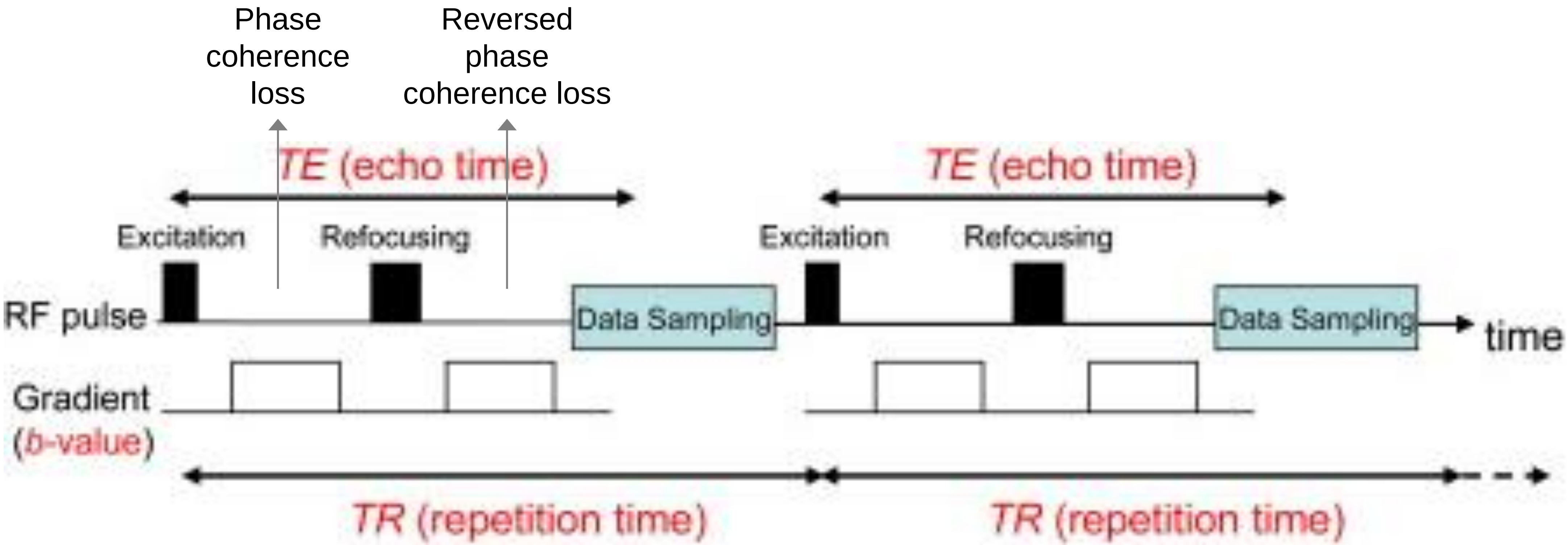
Directional impact of water molecular diffusion on MRI signal changes

Diffusion-weighted Contrast

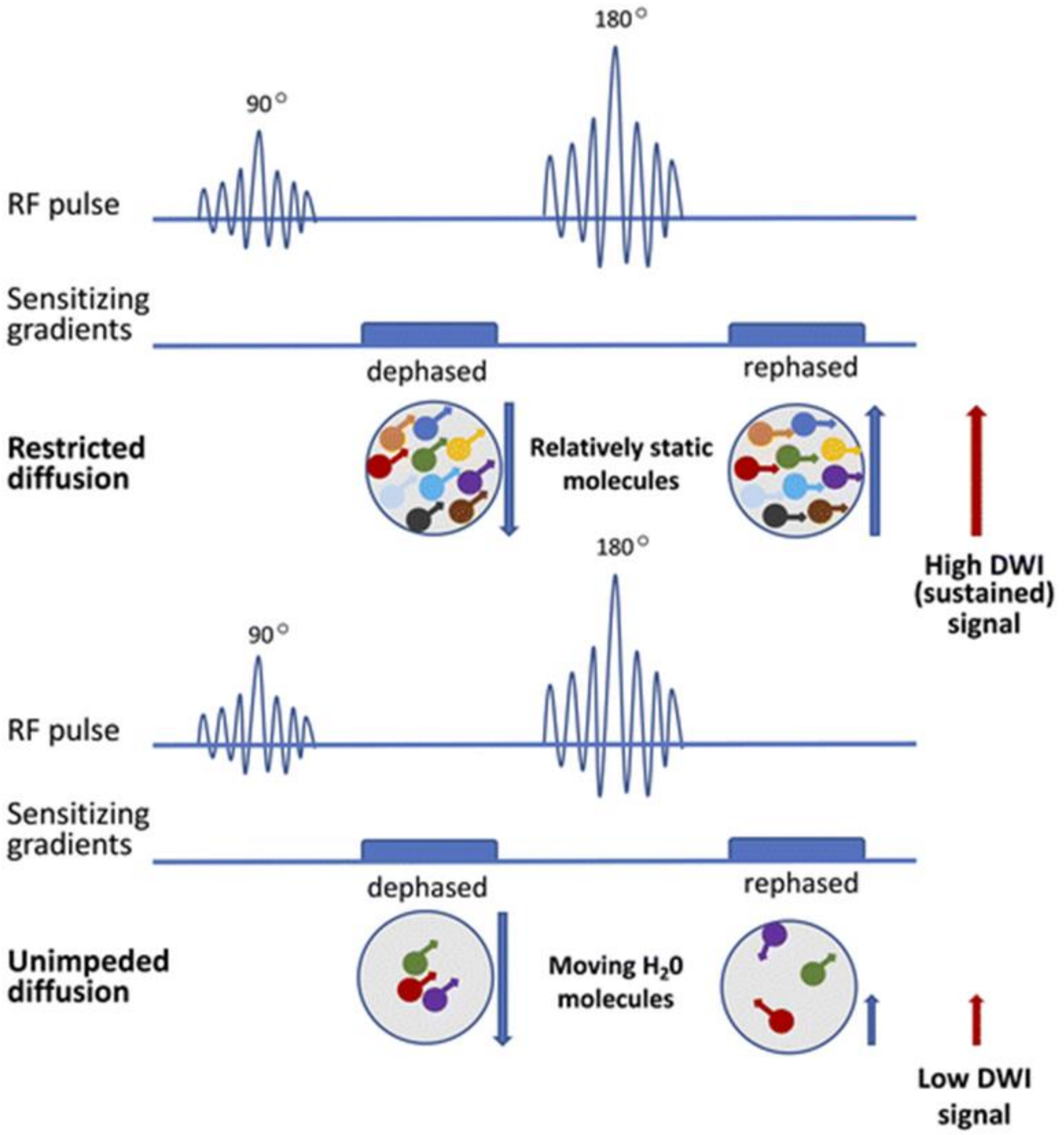
- MRI signal changes caused by diffusion



- 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

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

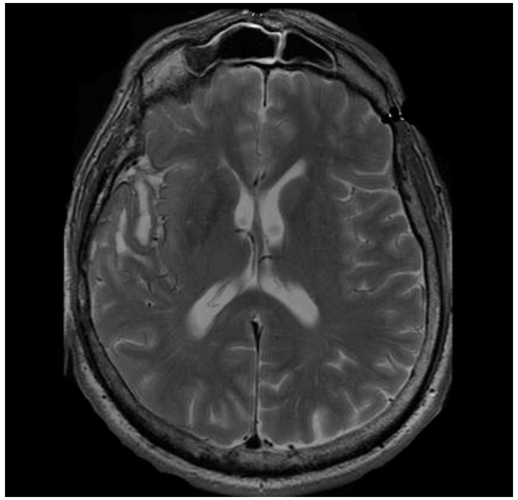
b-value

MRI signal measured without diffusion weighting

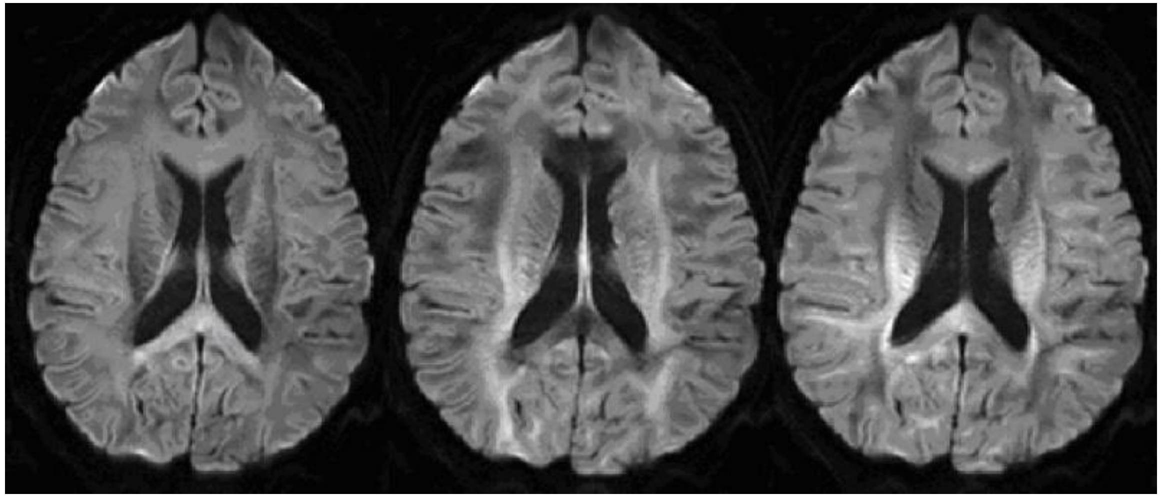
Diffusion coefficient $$D = \frac{1}{b} \log \frac{S_0}{S}$$

More signal decrease
→ higher diffusion coefficient

Less signal decrease
→ lower diffusion coefficient



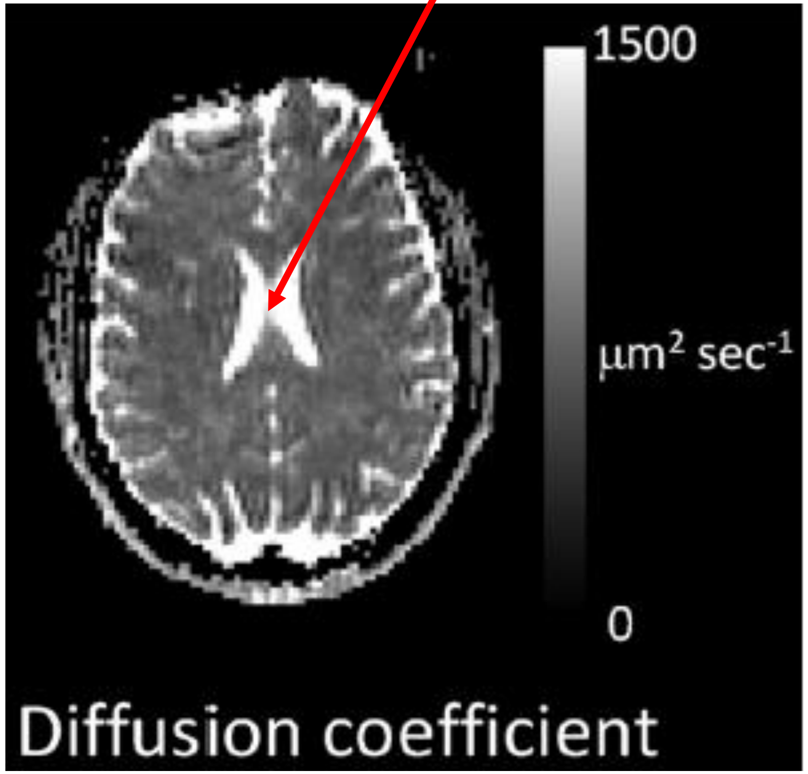
Without the diffusion-sensitizing gradient



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 ~1,000 s/mm^2 in the human brain
    - When *b*-value = 1,000 s/mm^2, the signal attenuation for free water at body temperature (37°C) is $\exp(-1{,}000\ \text{s/mm}^2 \times 0.001\ \text{mm}^2/\text{s}) \approx 0.37$ (63% signal attenuation for free water, but less attenuation for water molecules in tissues), representing a balance between sufficient diffusion weighting and adequate signal-to-noise ratio

– In different diffusion-sensitizing gradient directions

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

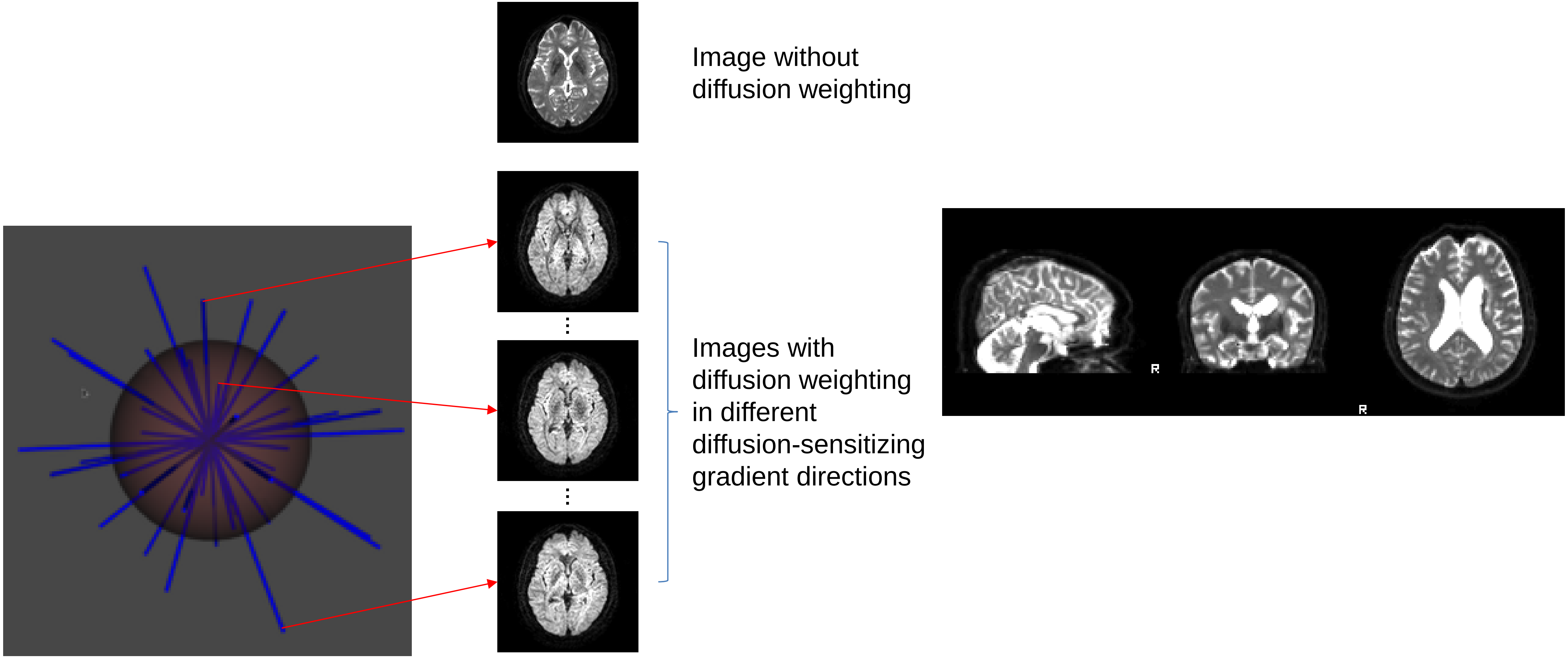
Diffusion tensor

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

Direction of the diffusion-sensitizing gradient

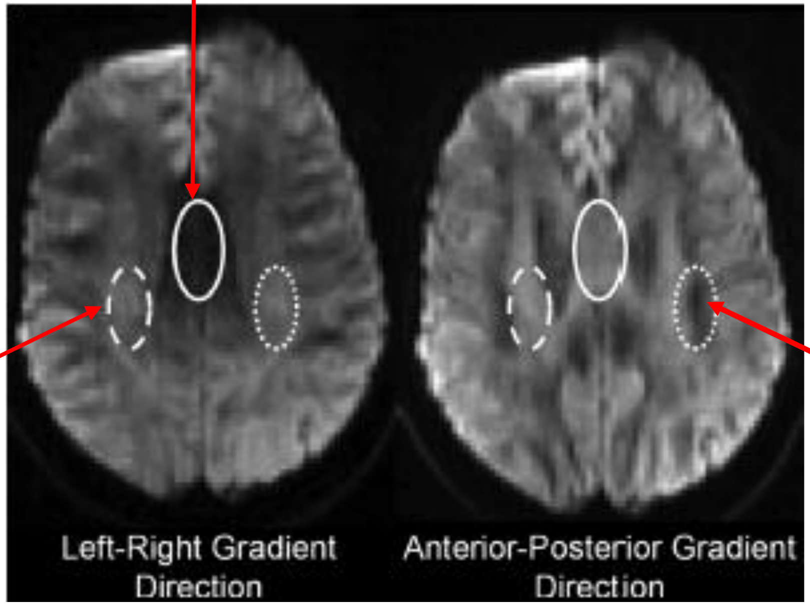
- **D**: diffusion tensor (symmetric positive definite matrix)
  - 3 × 3 symmetric matrix, each component of which describes water molecular diffusion associated with a pair of axes *xx*, *yy*, *zz*, *xy* (or *yx*), *xz* (or *zx*), and *yz* (or *zy*)

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



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 of finding a water molecule at position **r** after time *t* in a diffusion process follows a Gaussian distribution:

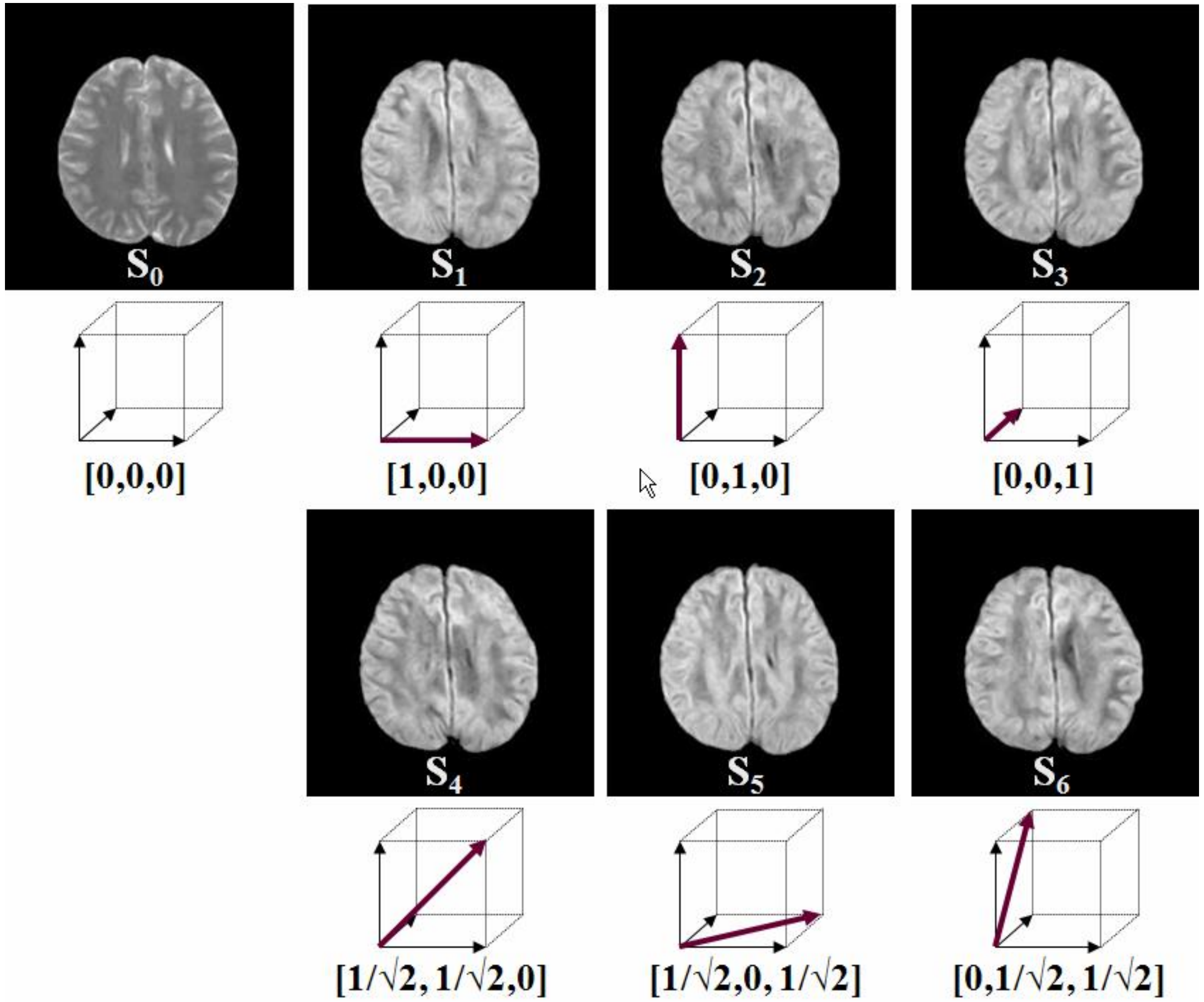
$$P(\mathbf{r},t)=\frac{1}{\sqrt{(4\pi t)^3|\mathbf{D}|}}\exp\left(-\frac{1}{4t}\mathbf{r}^T\mathbf{D}^{-1}\mathbf{r}\right)$$

    - Characterized by its mean (assumed to be zero for molecular diffusion) and variance-covariance (represented by the diffusion tensor **D**)

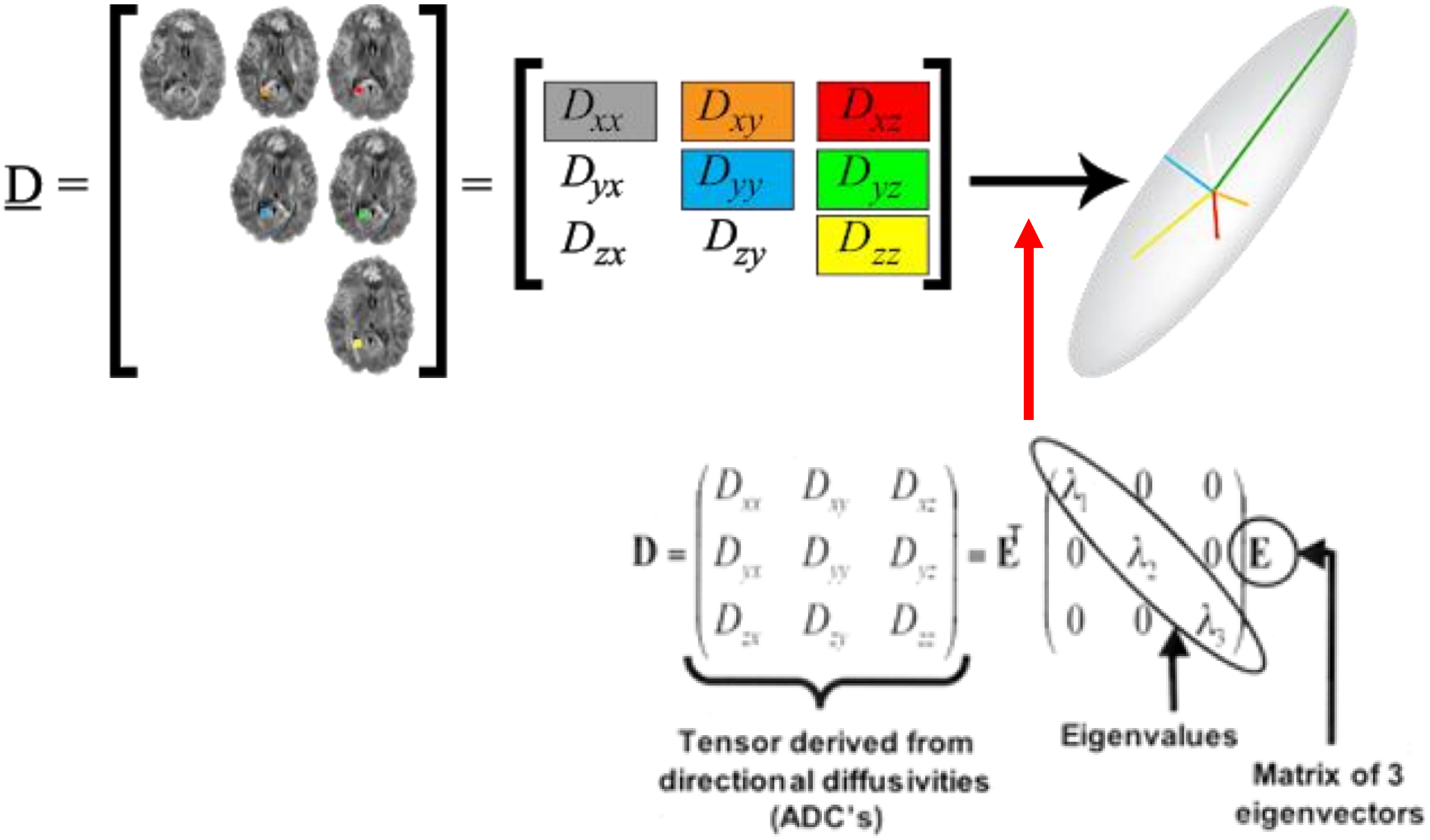
- Preprocessing before diffusion modelling
  - Correction for unwanted variation
    - Head motion
    - Eddy current-induced distortion
      - Eddy currents (Foucault currents)
        - » Loops of electric current induced in nearby conductors by a changing magnetic field
        - » Generated in MRI 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
    - Susceptibility artifact (B0 inhomogeneity-induced distortion)

Diffusion Tensor

- Encapsulates the variance-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

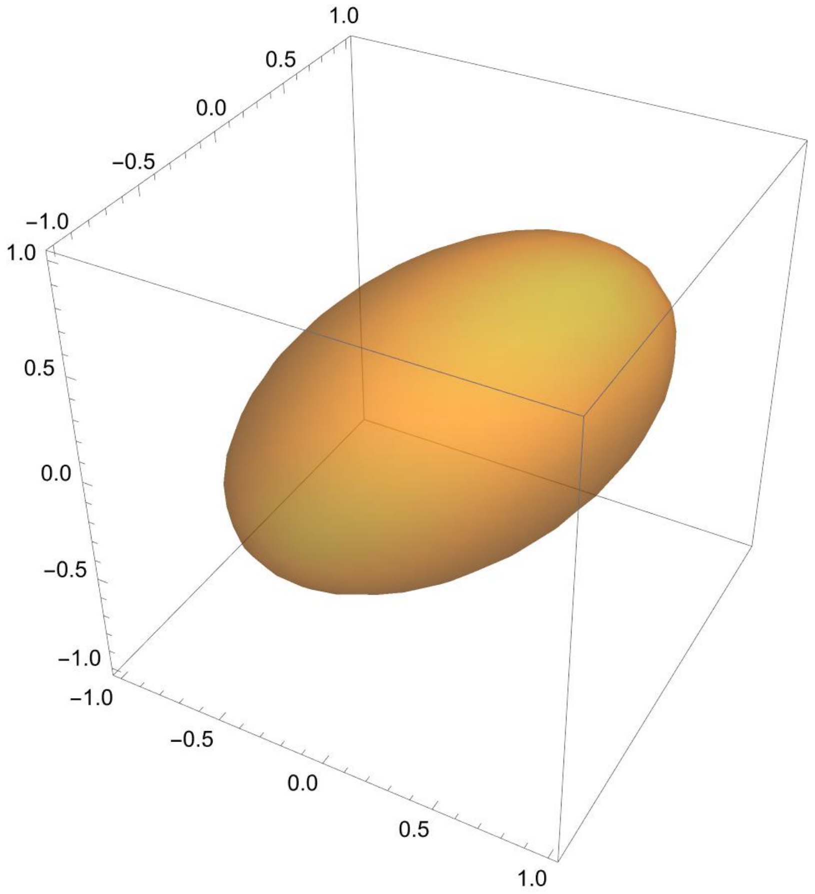


MRI signals measured without and with diffusion weighting

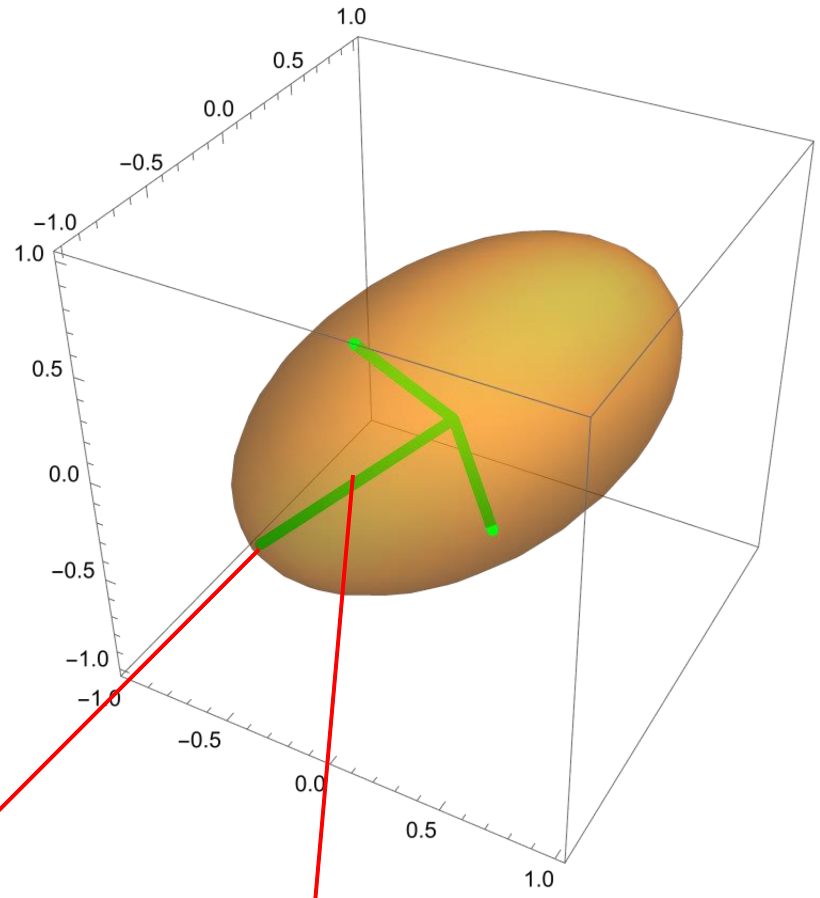


https://www.blog.brainsightai.com/post/from-dti-to-hardi]]

Diffusion tensor and its ellipsoid representation



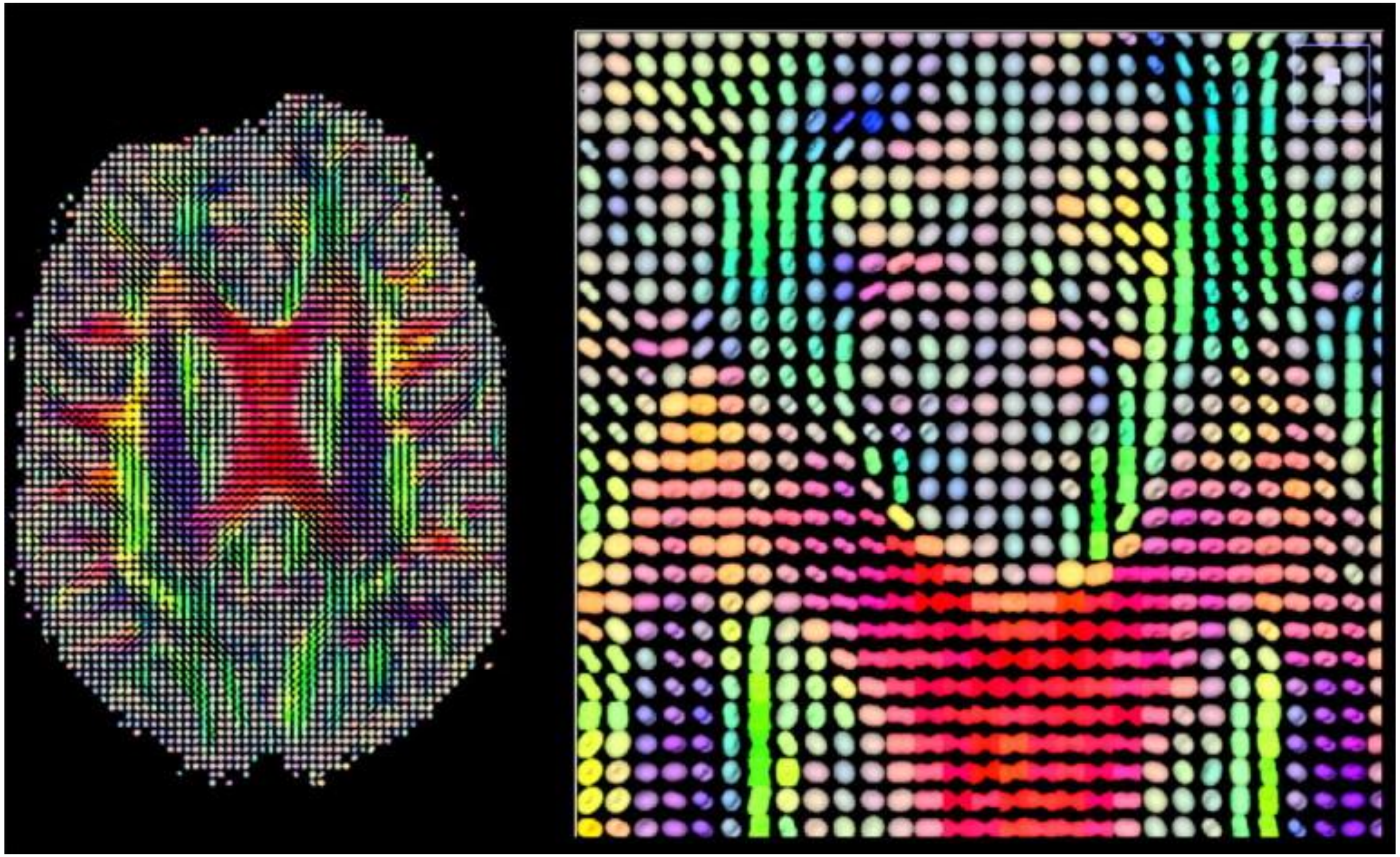
Eigendecomposition



$$\begin{pmatrix} 20 & -8 & -6 \\ -8 & 23 & -1 \\ -6 & -1 & 17 \end{pmatrix}$$

$$\begin{pmatrix} 0.68 & -0.69 & -0.25 \\ -0.30 & -0.57 & 0.76 \\ -0.67 & -0.44 & -0.59 \end{pmatrix}^{T} \begin{pmatrix} 30.4 & 0 & 0 \\ 0 & 20.1 & 0 \\ 0 & 0 & 9{,}5 \end{pmatrix} \begin{pmatrix} 0.68 & -0.69 & -0.25 \\ -0.30 & -0.57 & 0.76 \\ -0.67 & -0.44 & -0.59 \end{pmatrix}$$

Eigenvectors Eigenvalues



[Alger, 2012]

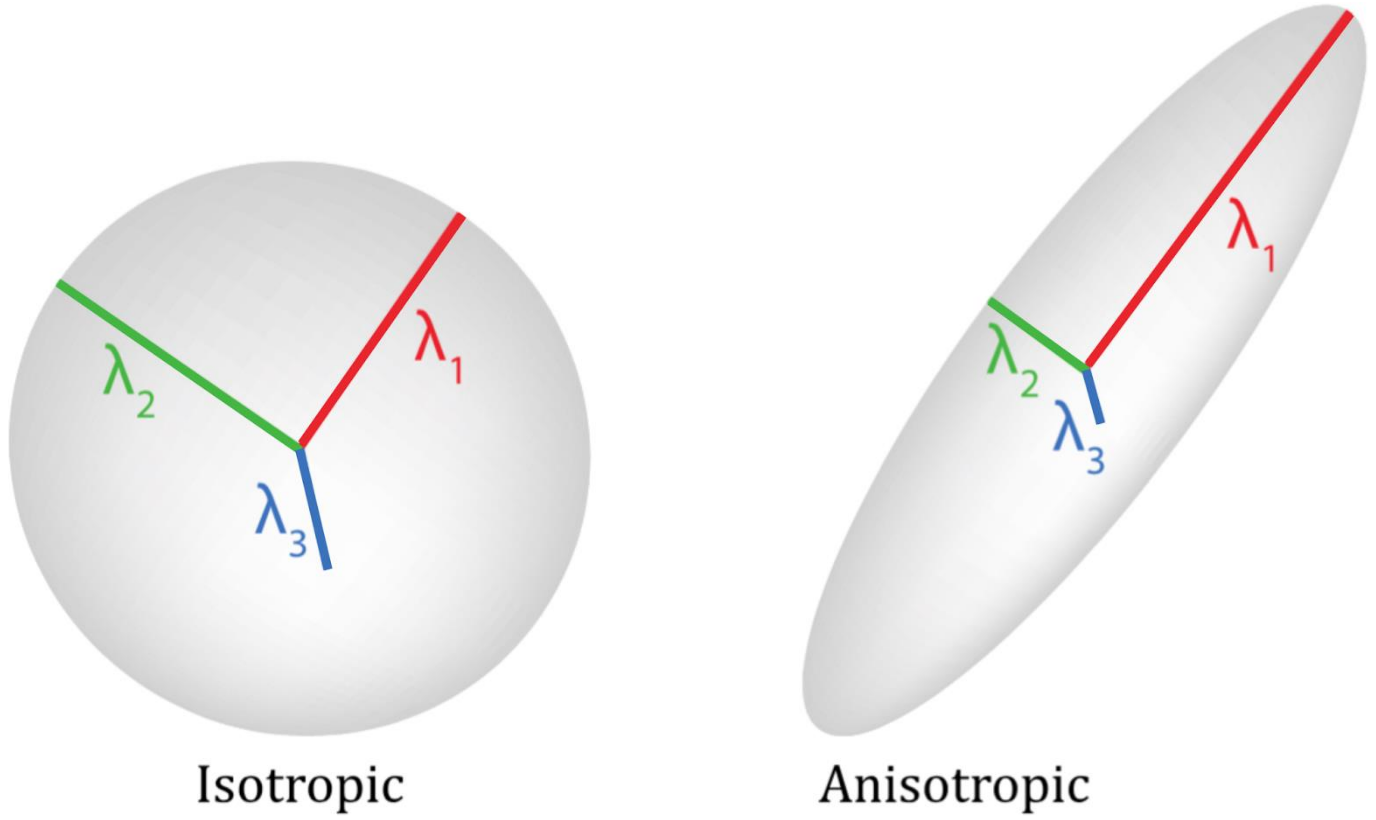
Diffusion ellipsoids derived from the diffusion tensors measured for each voxel

White Matter Microstructure

- Characterized by the averaged diffusion properties of numerous axons within a single voxel
- Diffusion tensor metrics
  – Scalar invariants (remaining invariant under coordinate transformations, thus independent of the orientation of the imaging scan or the subjects' positioning) of the diffusion tensor
  – Characterize aspects of water molecular diffusion, such as the magnitude and anisotropy (directional dependence), offering insights into tissue structure and organization

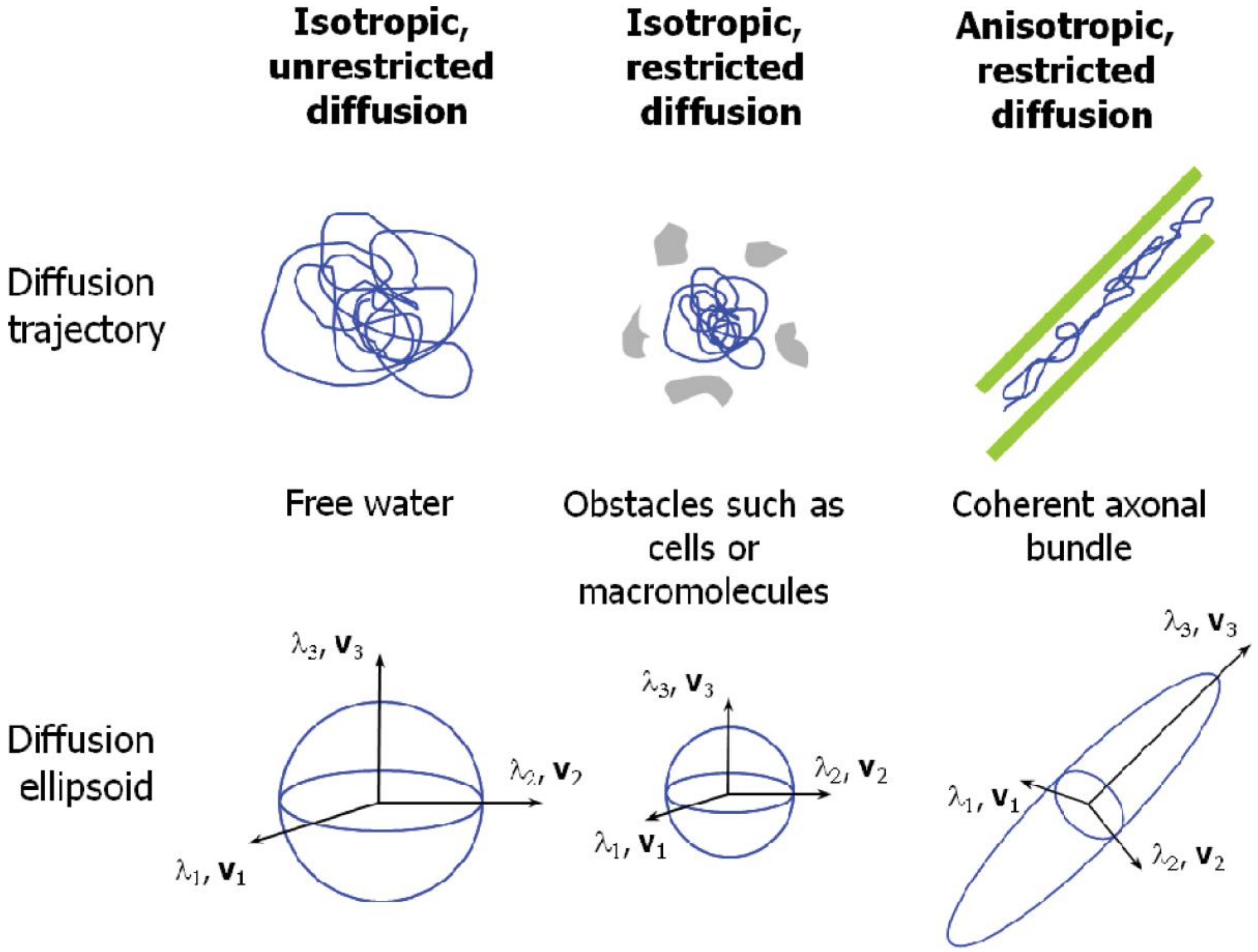
- Fractional anisotropy (FA)
  - Measures the degree of anisotropy (how much the diffusion is directionally dependent) within a voxel
  - Ranges from 0 (completely isotropic diffusion) to 1 (highly anisotropic diffusion), where a high value indicates anisotropic diffusion (when water molecules diffuse 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)

Low FA **High FA**



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

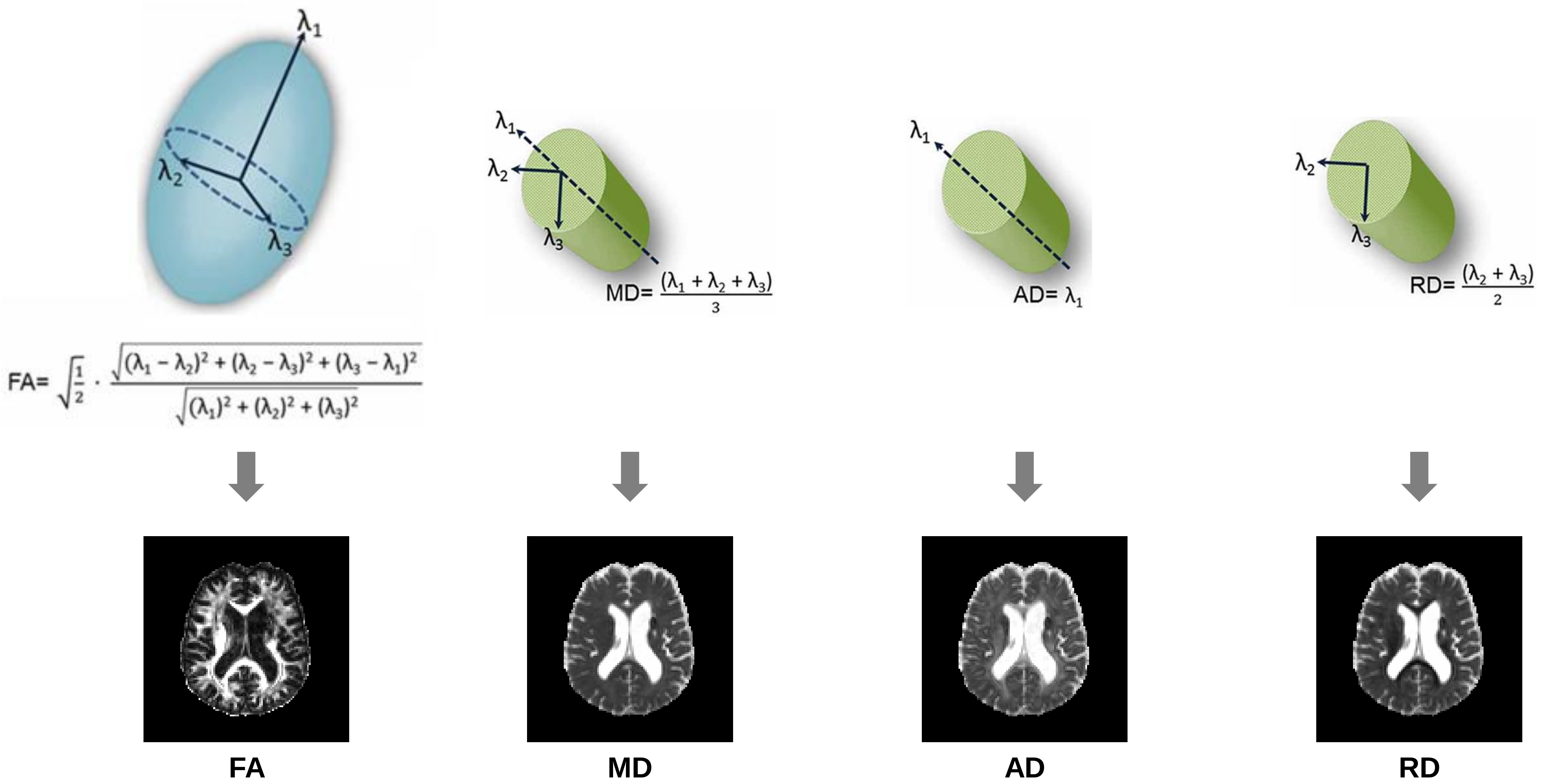
Low and high FA values corresponding to isotropic and anisotropic diffusion



[Geva et al., 2011]

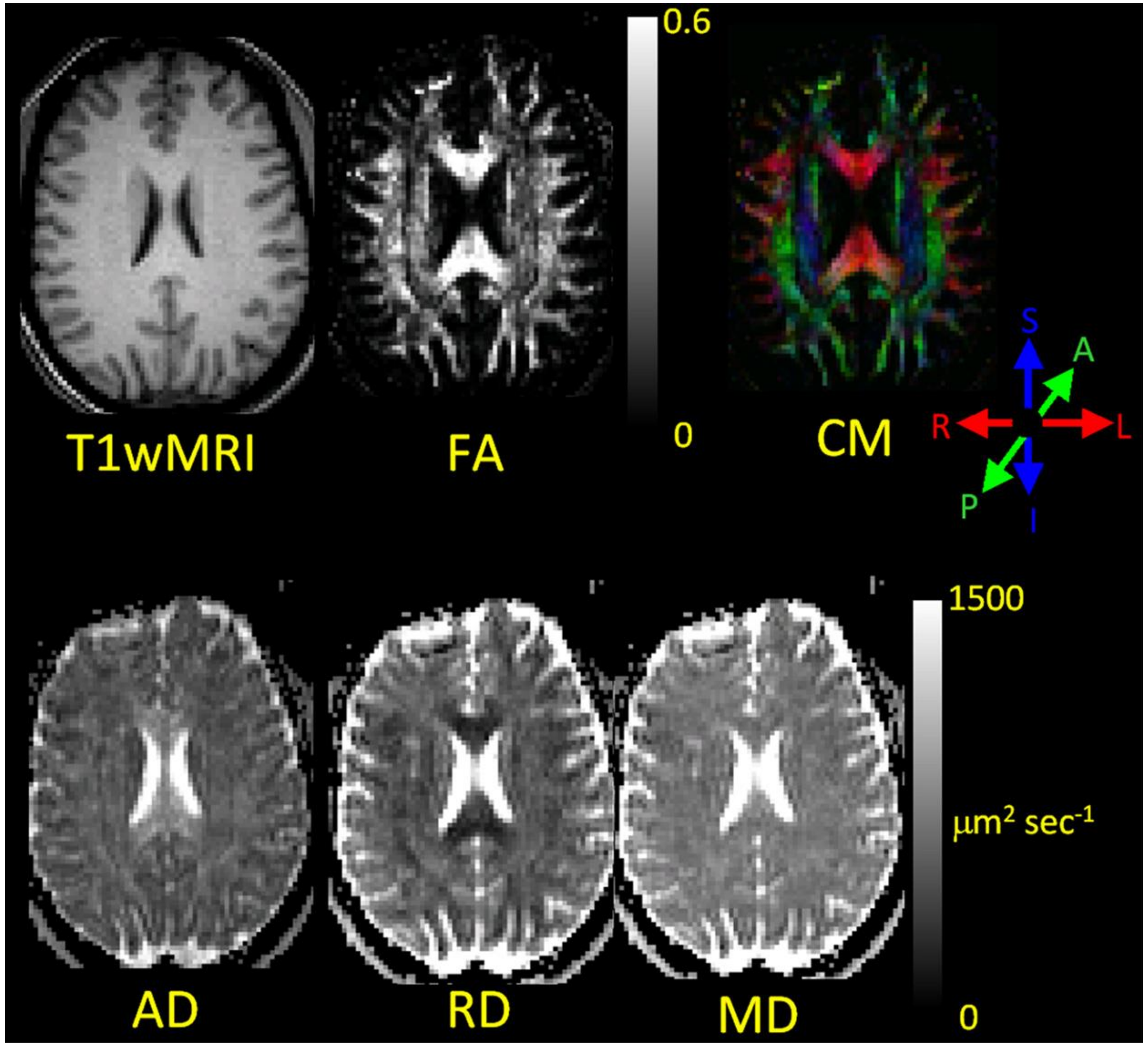
Isotropic and anisotropic diffusion represented by ellipsoids

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



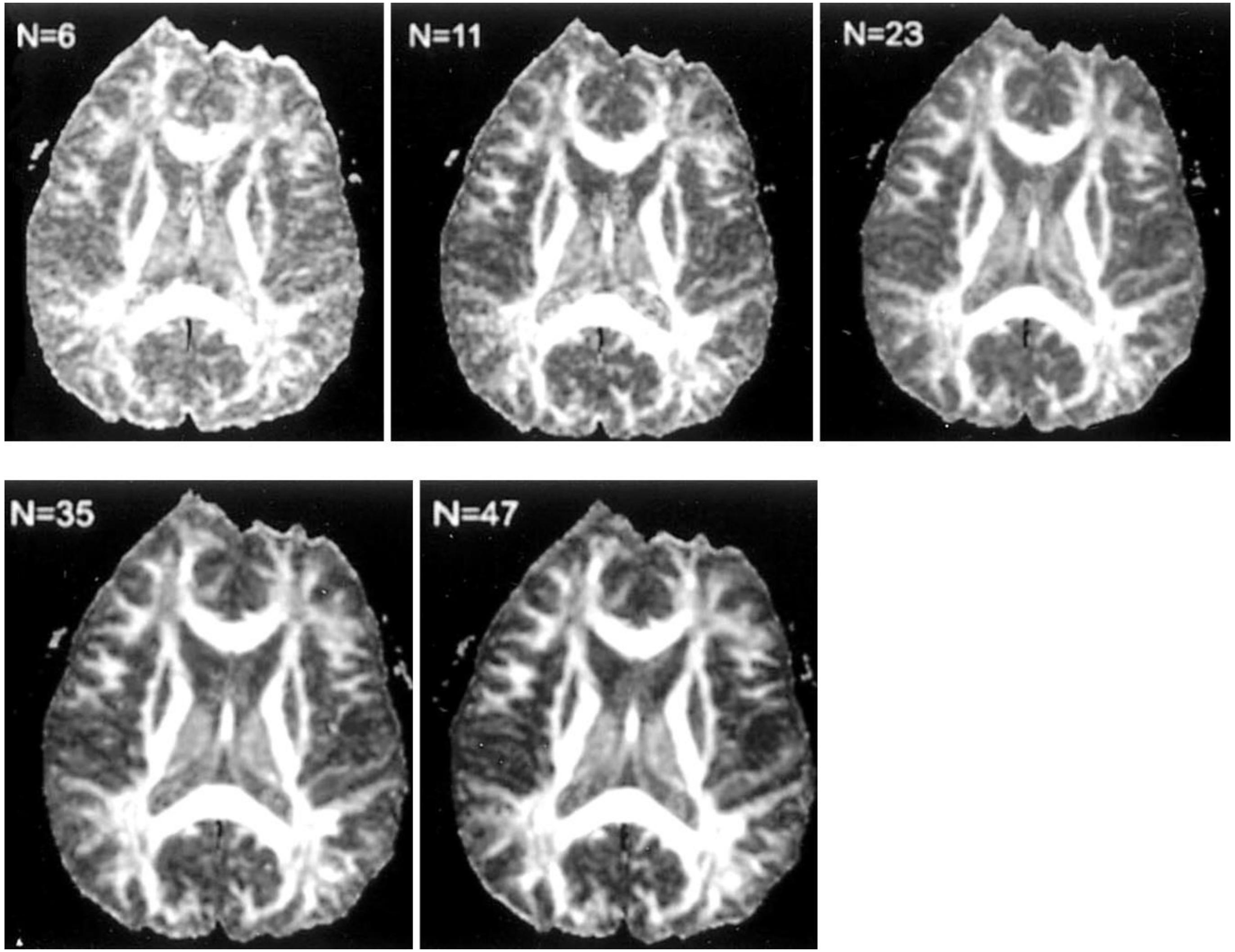
[DeSouza et al., 2016]

Computation of diffusion tensor metrics



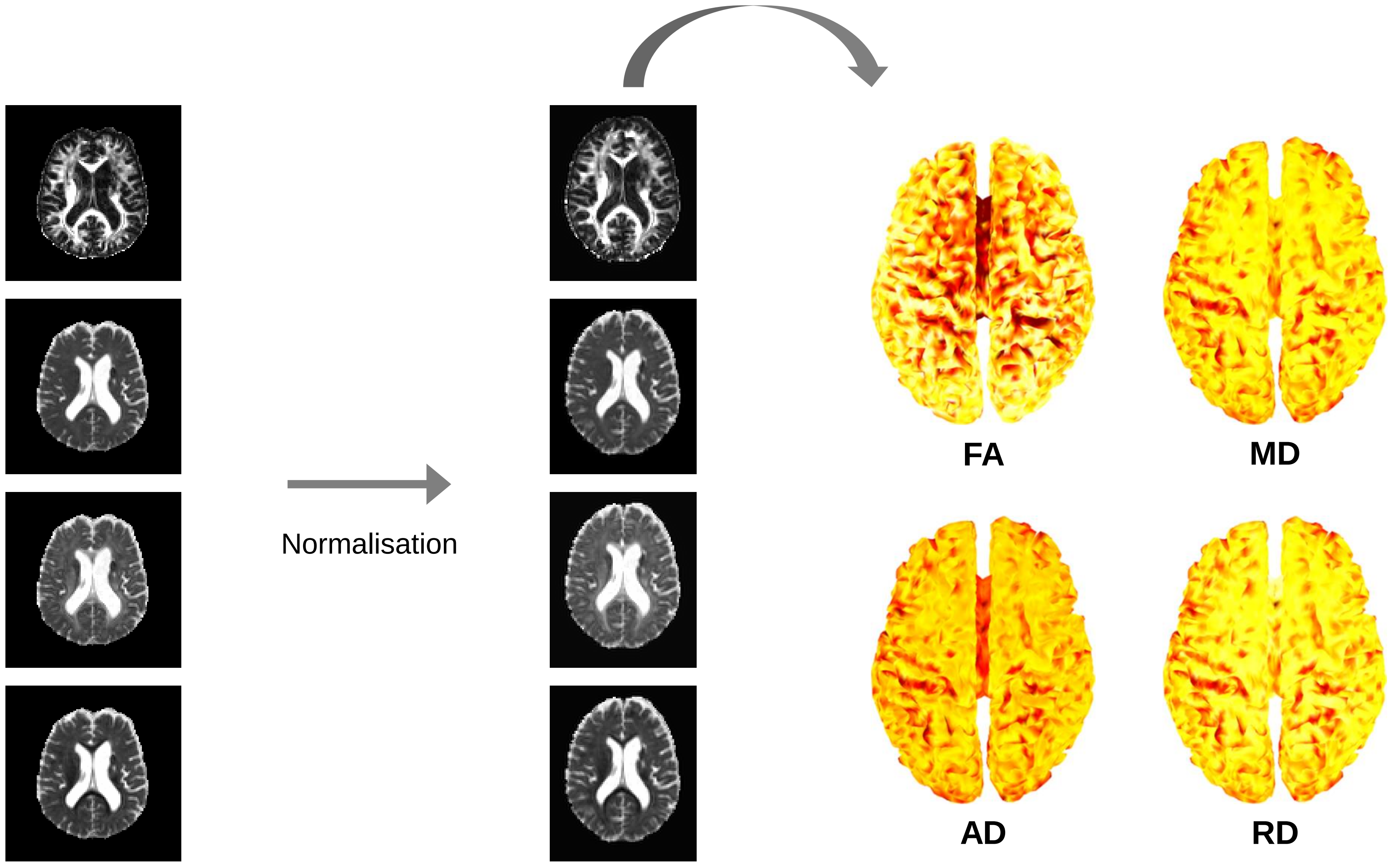
[Alger, 2012]

Maps of diffusion tensor metrics



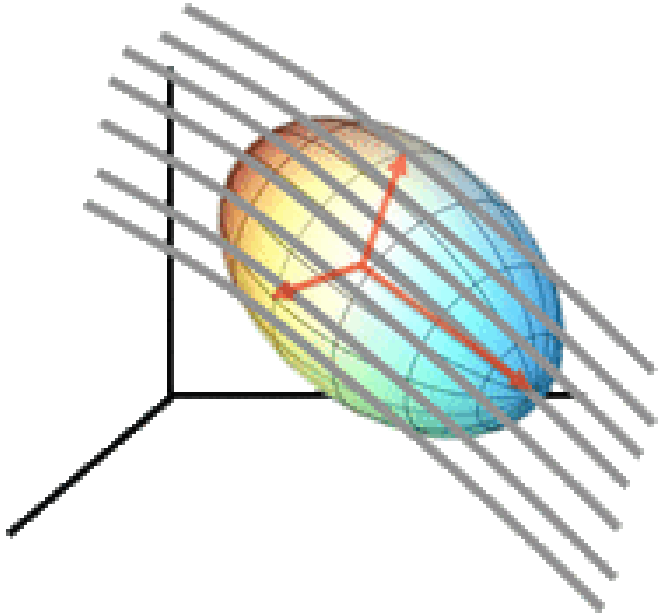
[Chang et al., 2005]

FA maps according to different numbers of diffusion-sensitizing gradient directions



Features of white matter microstructure

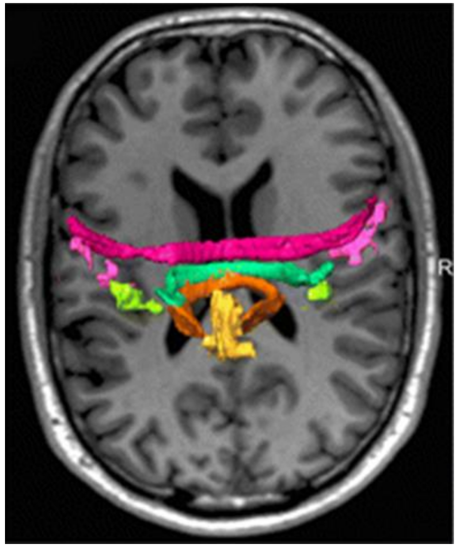
- Principal direction of diffusion
  - Given by the main axis (principal eigenvector; eigenvector of the largest eigenvalue) of the ellipsoid
  - Assumed to be aligned with the dominant fibre tract orientation within the voxel



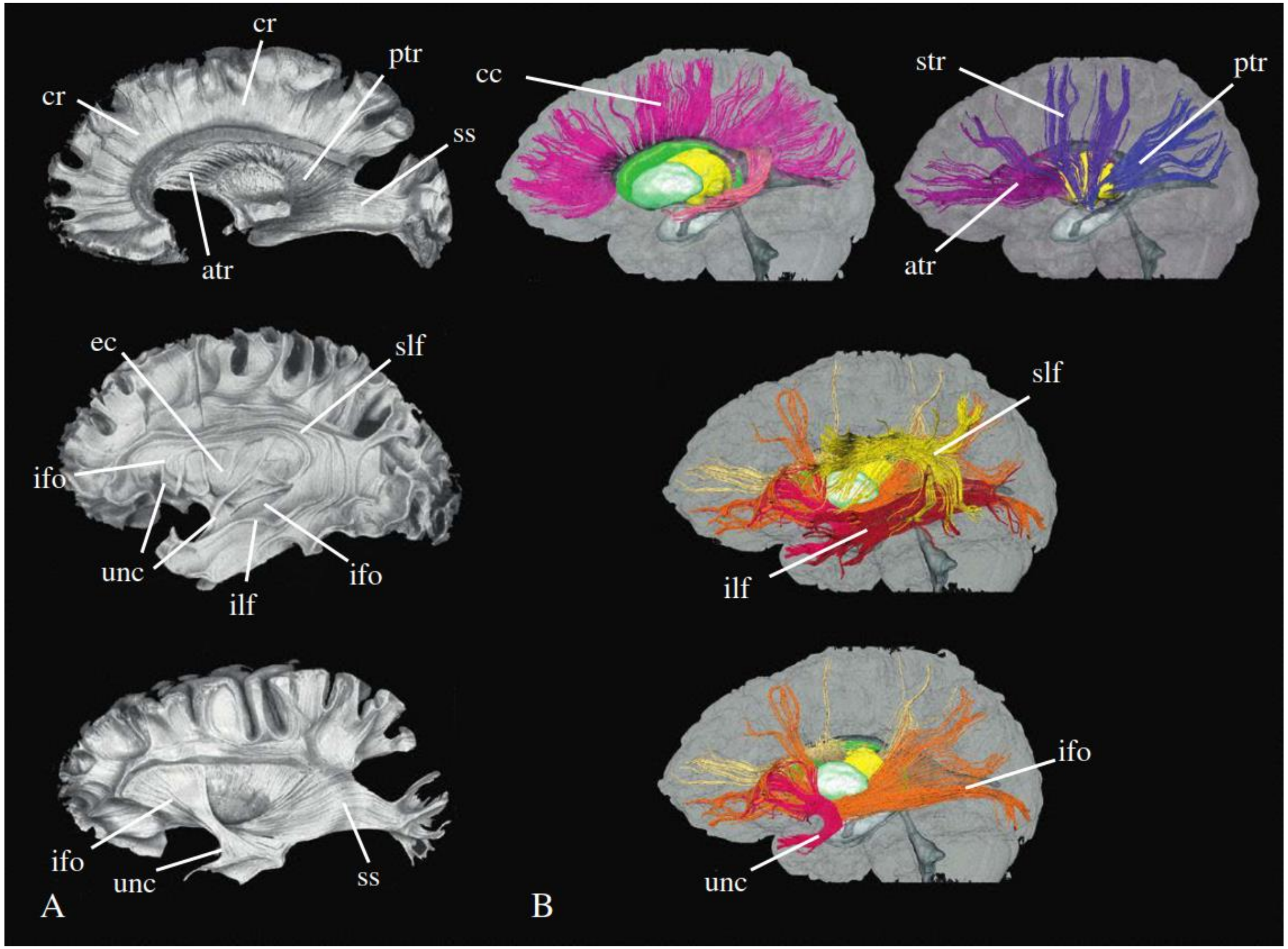
[https://mriquestions.com/diffusion-tensor.html]

White Matter Tractography

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



[Wahl et al., 2007]

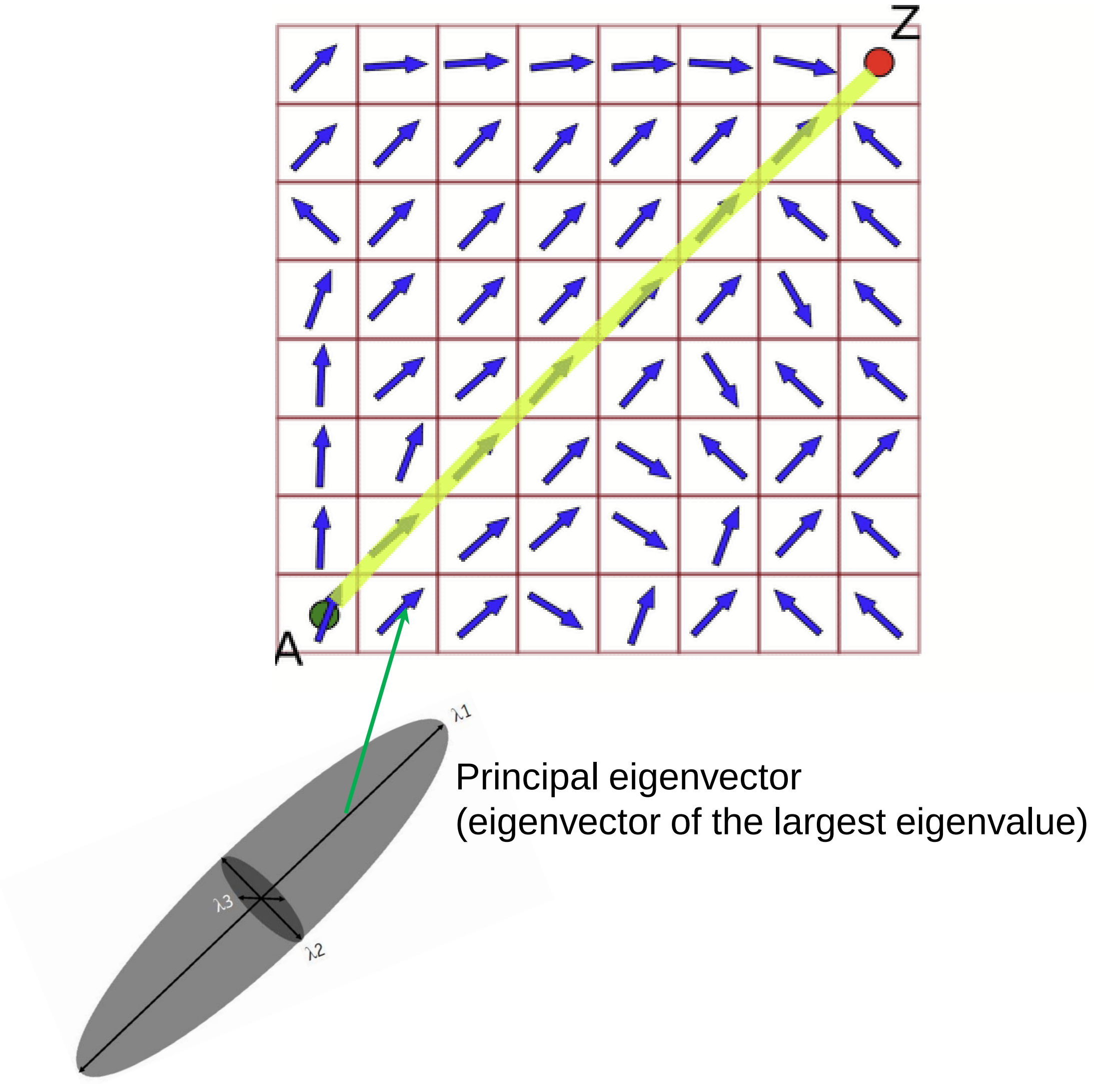


[Oishi et al., 2011]

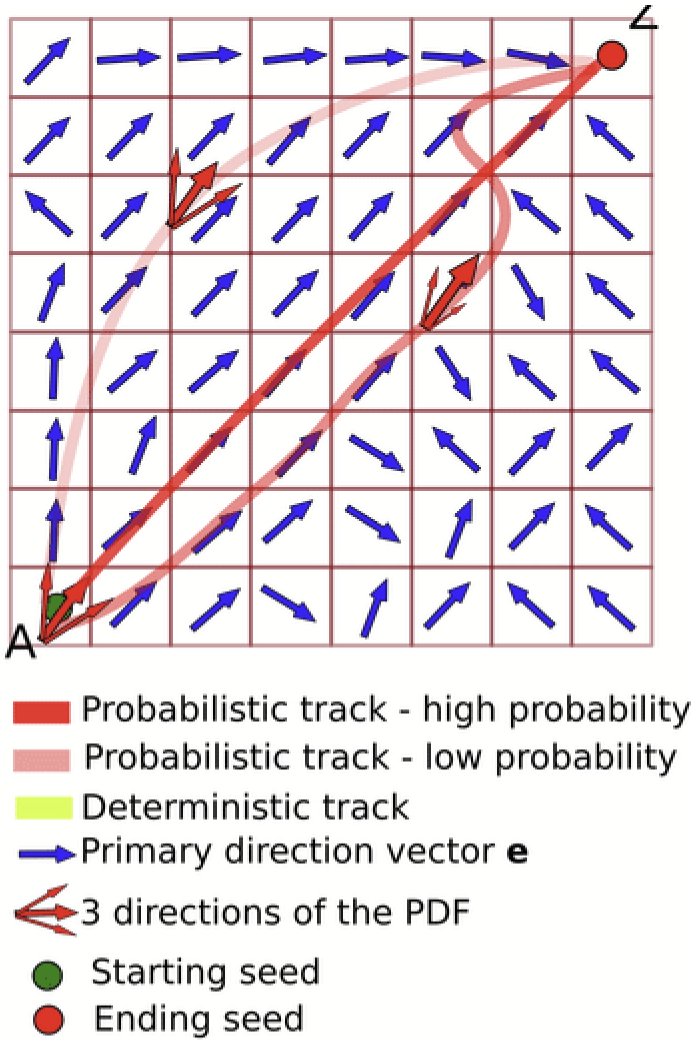
Comparison between postmortem preparation and dMRI-based white matter reconstructions

- 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 direction at each voxel
    - By tracking streamlines a great number of times with the principal eigenvector direction being chosen at random from the distribution of probable orientations at each voxel

Deterministic

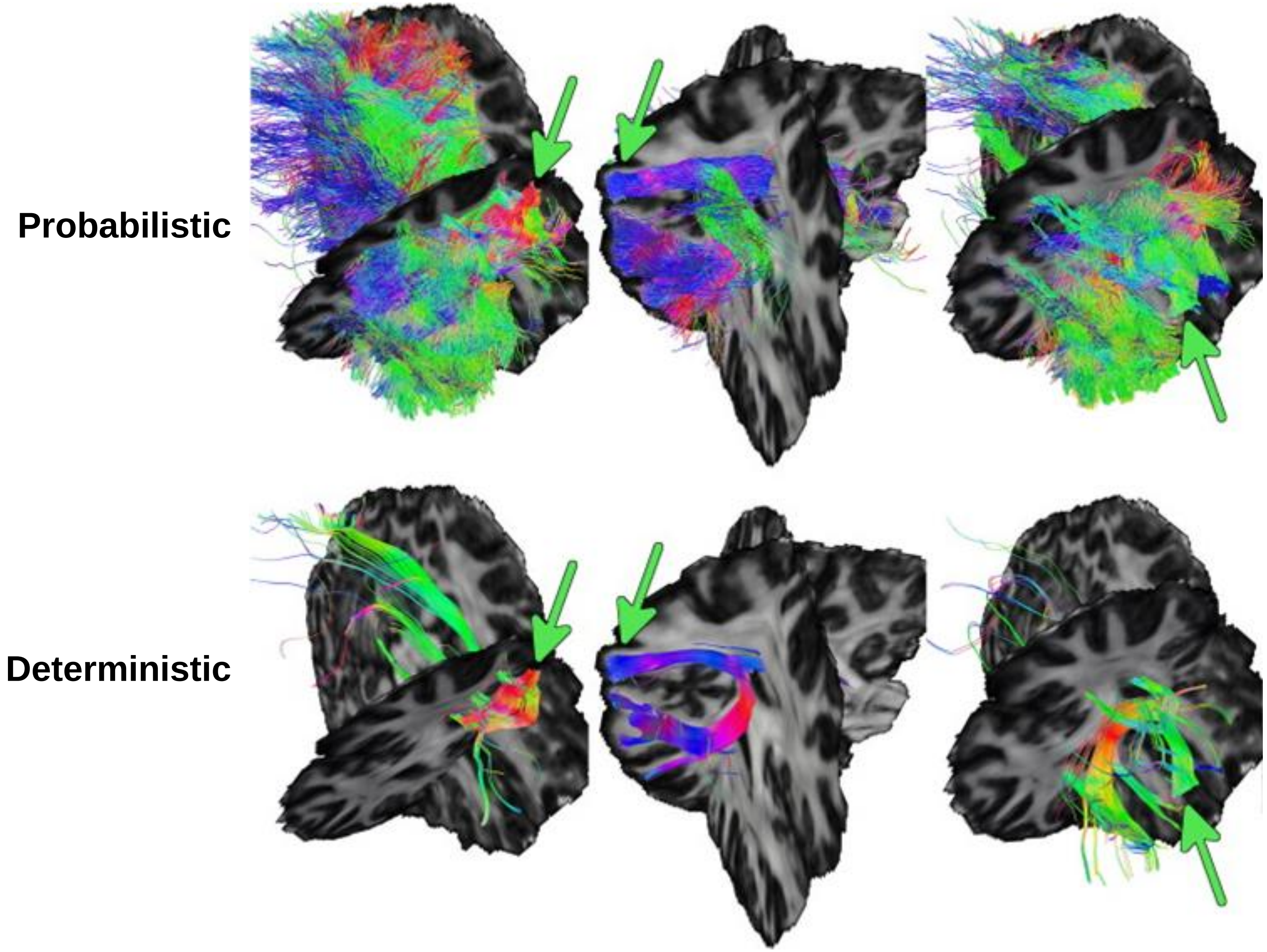


Probabilistic



[Garyfallidis, 2012]

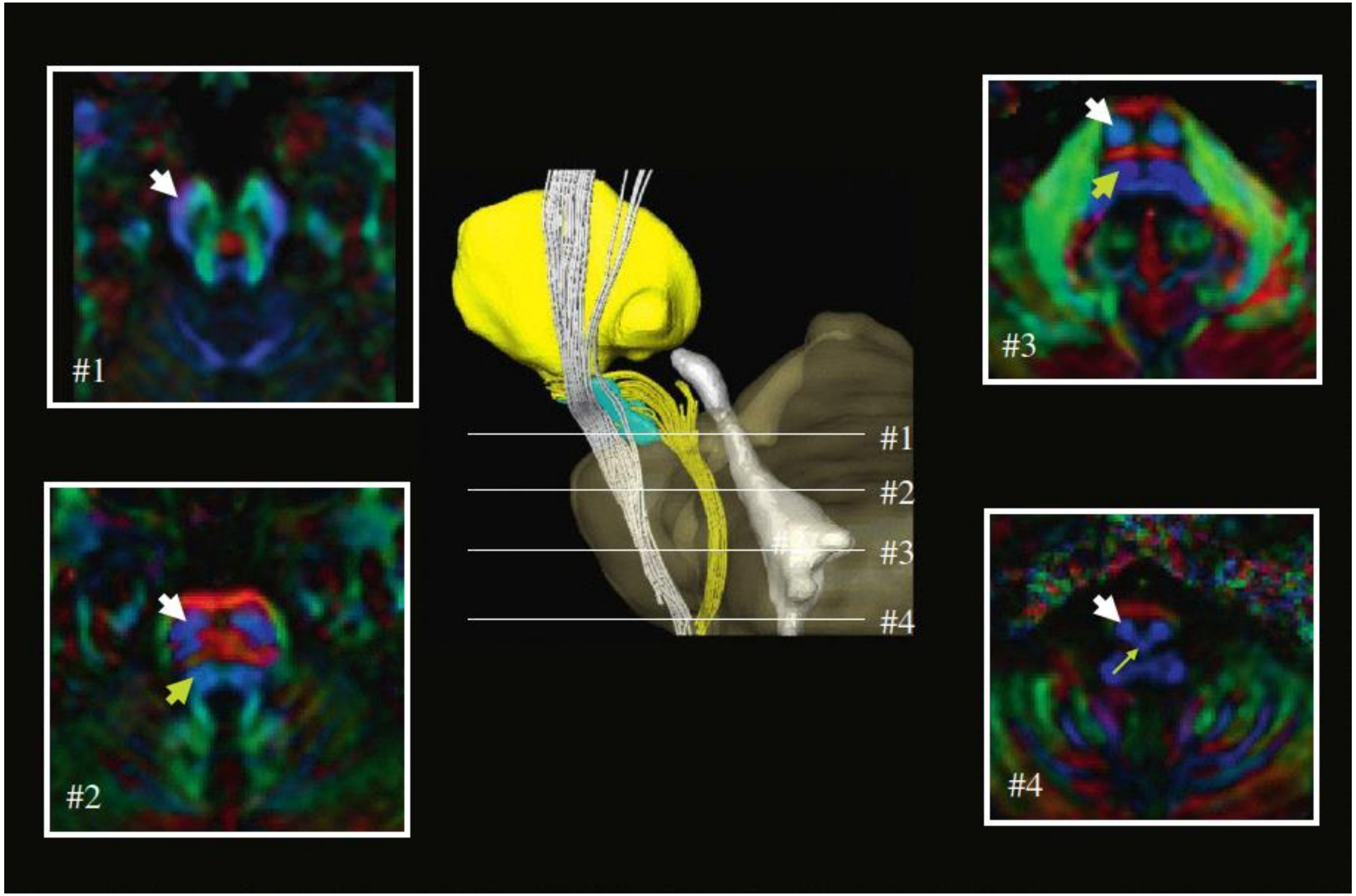
Deterministic and probabilistic ways for white matter tractography



[Schreiber et al., 2014]

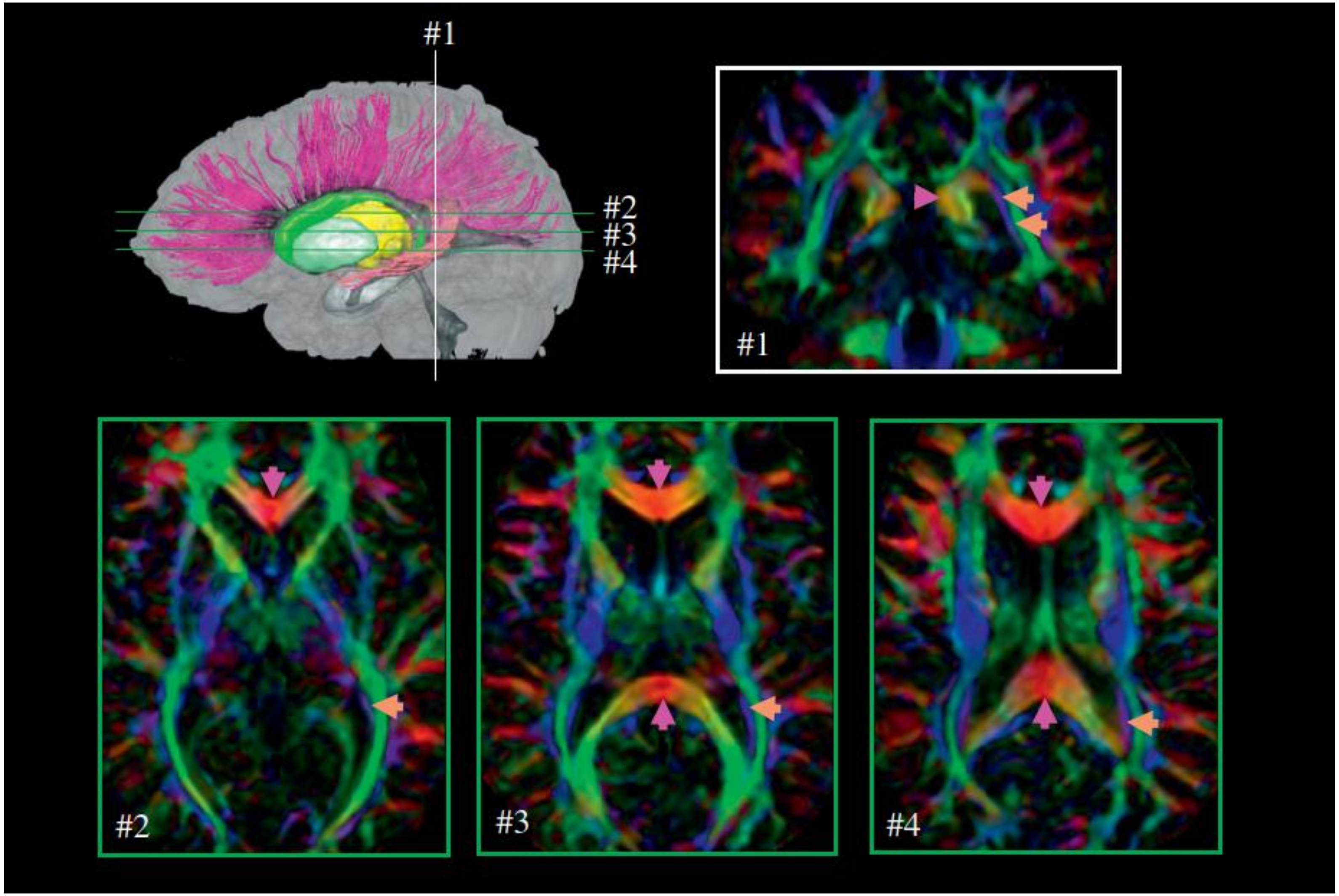
Comparison between probabilistic and deterministic tractography

- White matter fibre tract
  - Segmented white matter
  - Based on information about:
    - Terminations of each white matter fibre tract into the cortex
    - Histologically-derived definitions for each white matter fibre tract



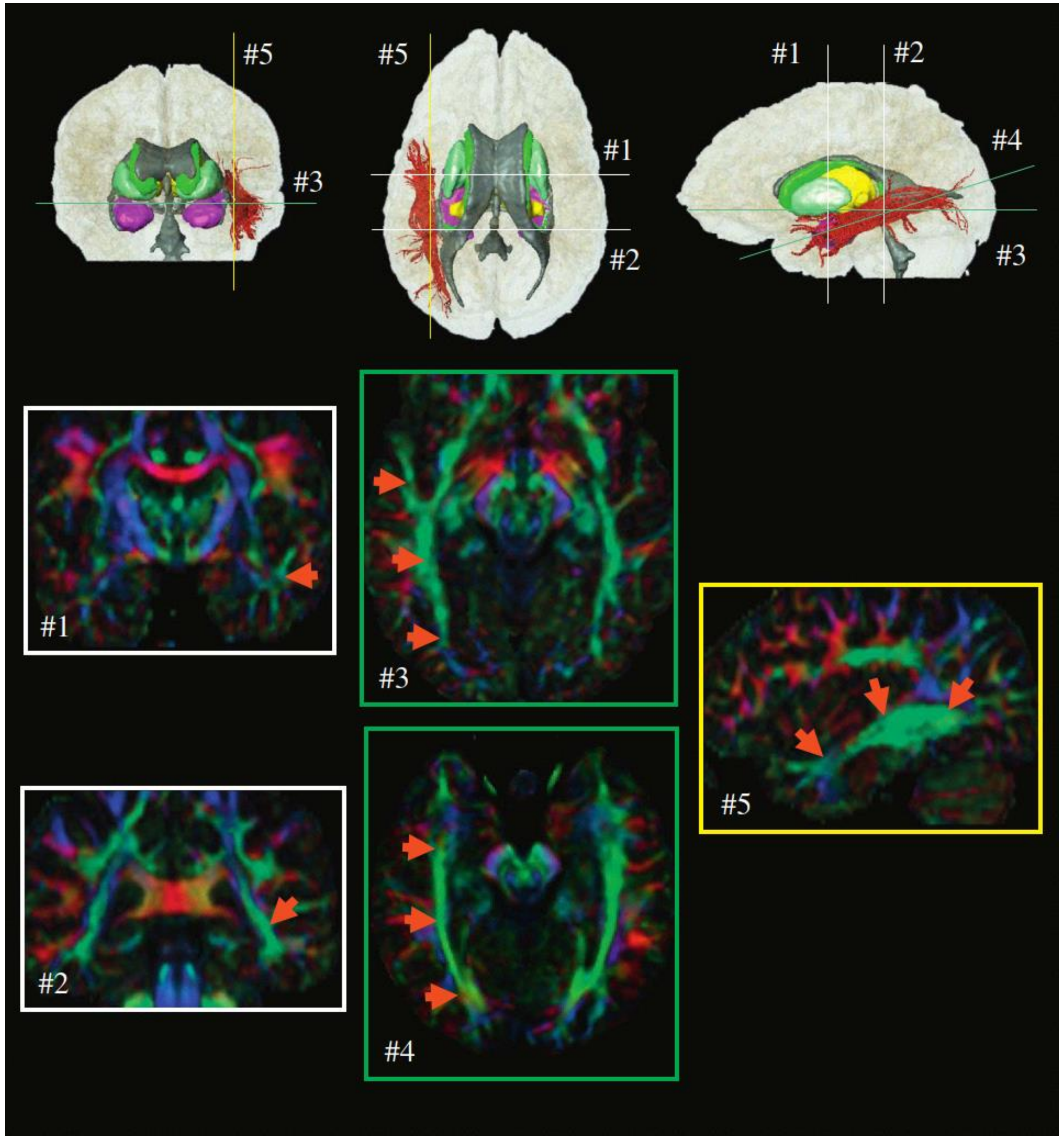
[Oishi et al., 2011]

Trajectory of the corticospinal tract



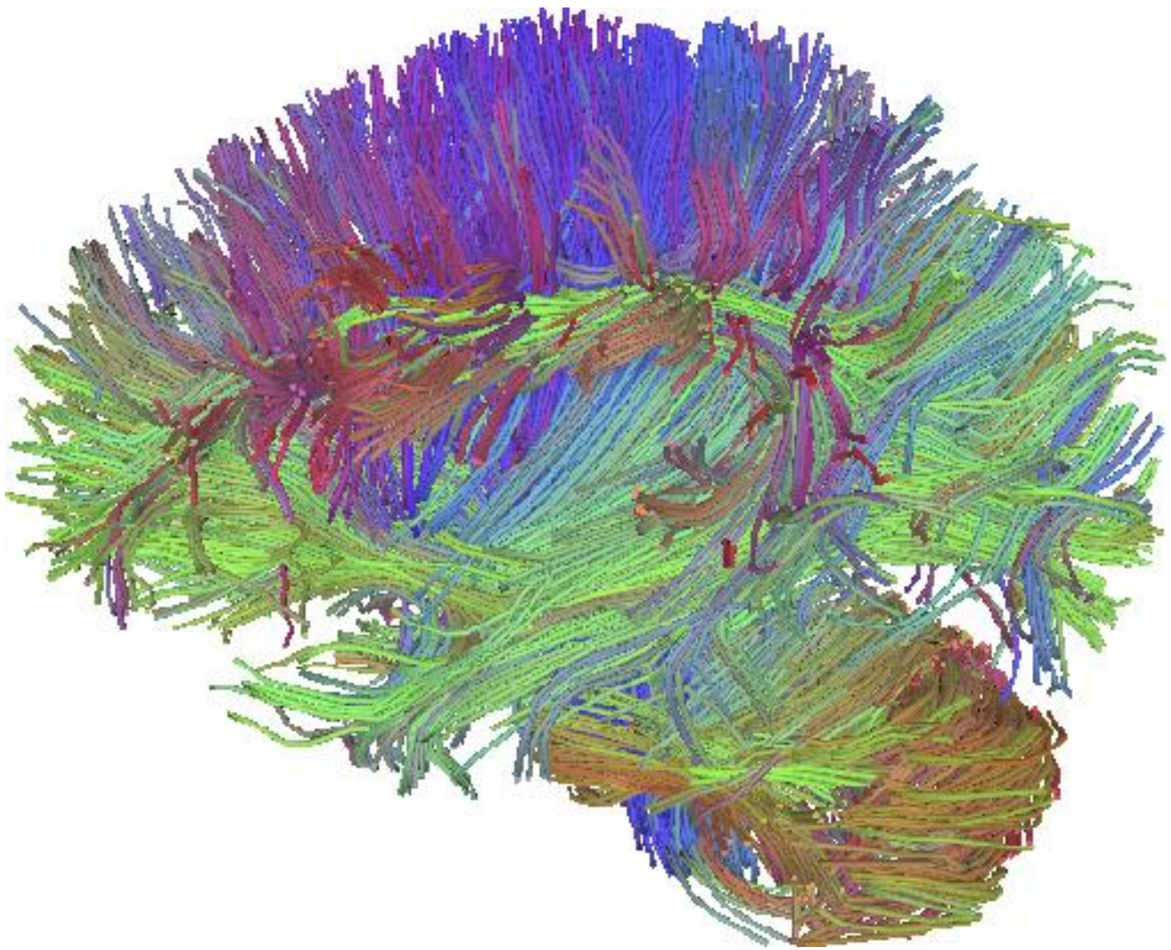
[Oishi et al., 2011]

Trajectory of the corpus callosum



[Oishi et al., 2011]

Trajectory of the inferior longitudinal fasciculus

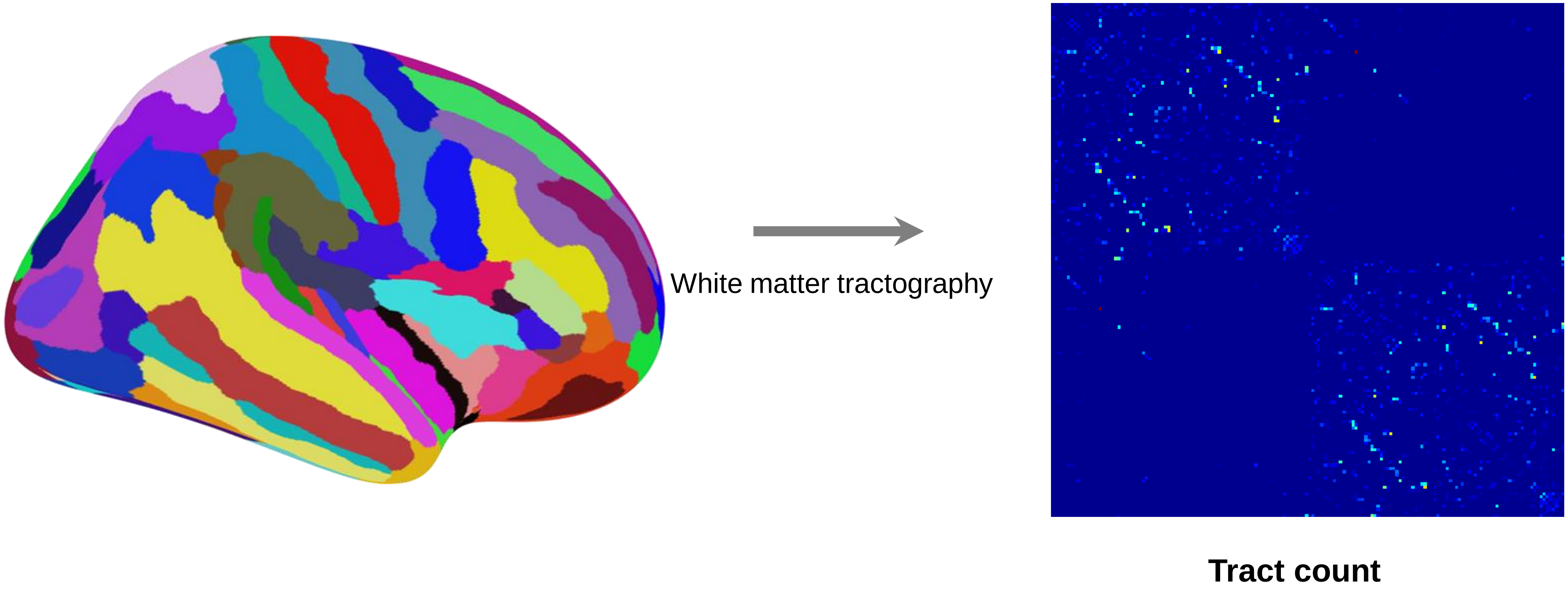


[https://api.semanticscholar.org/CorpusID:125412525]

Reconstruction of whole brain white matter fibre tracts

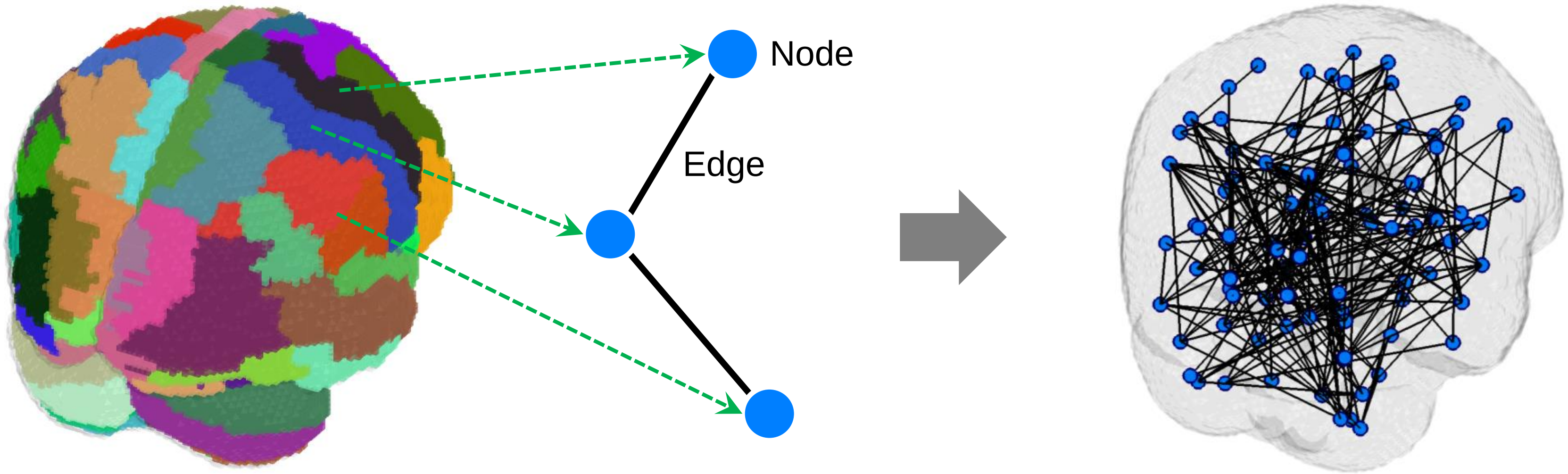
[https://www.mrtrix.org/]]

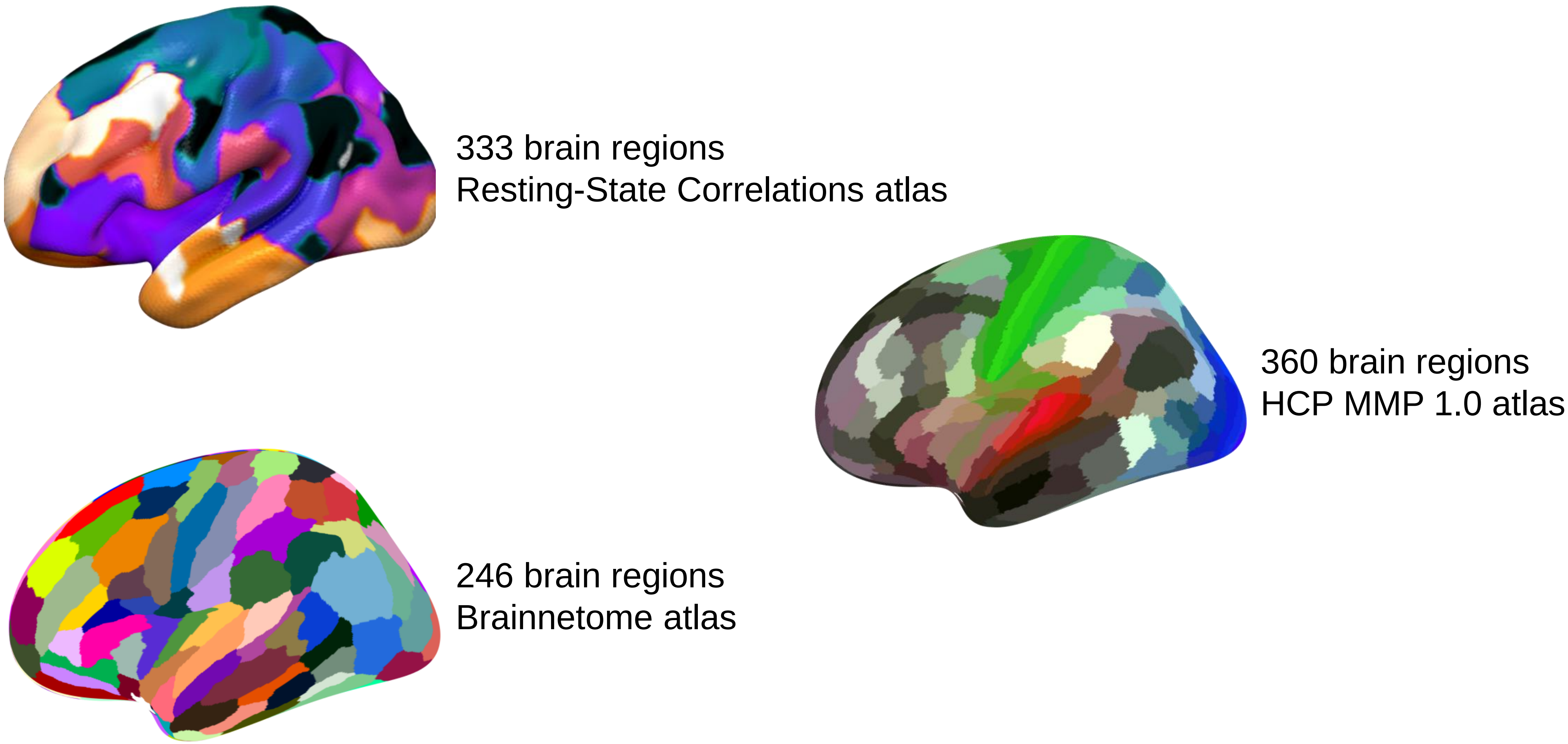
Determination of white matter fibre tracts



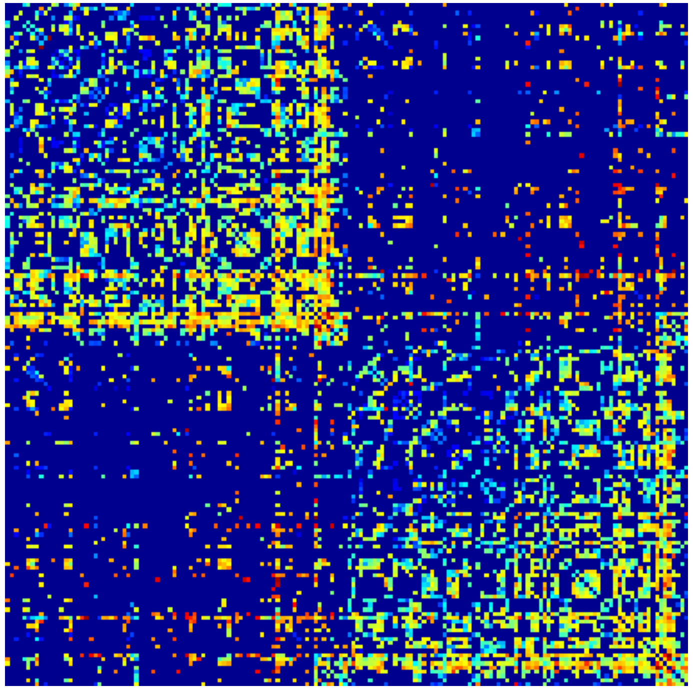
Structural brain network

- Network
  - Set of nodes and edges
  - Structural brain network
    - Nodes: pre-defined brain regions
    - Edges: connectivity (white matter fibre tracts) between brain regions

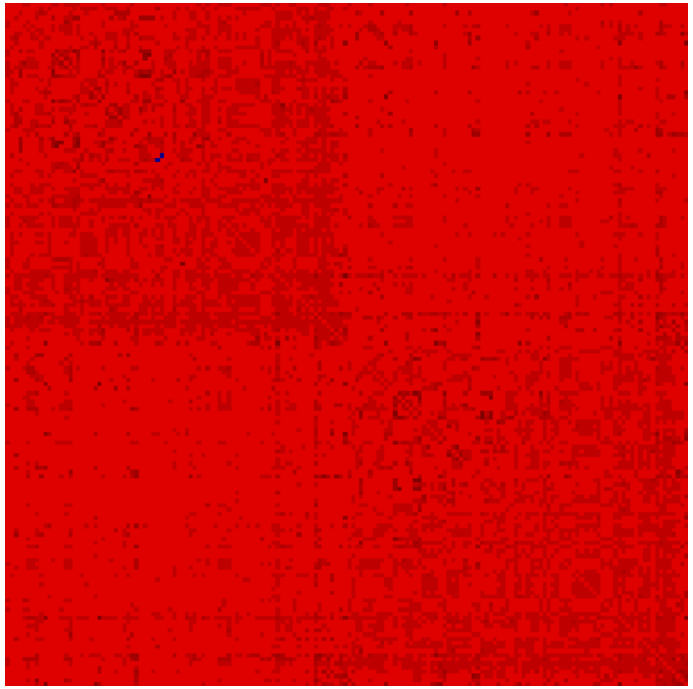




Brain atlases delineating heterogeneous nodes with varying definitions and quantities



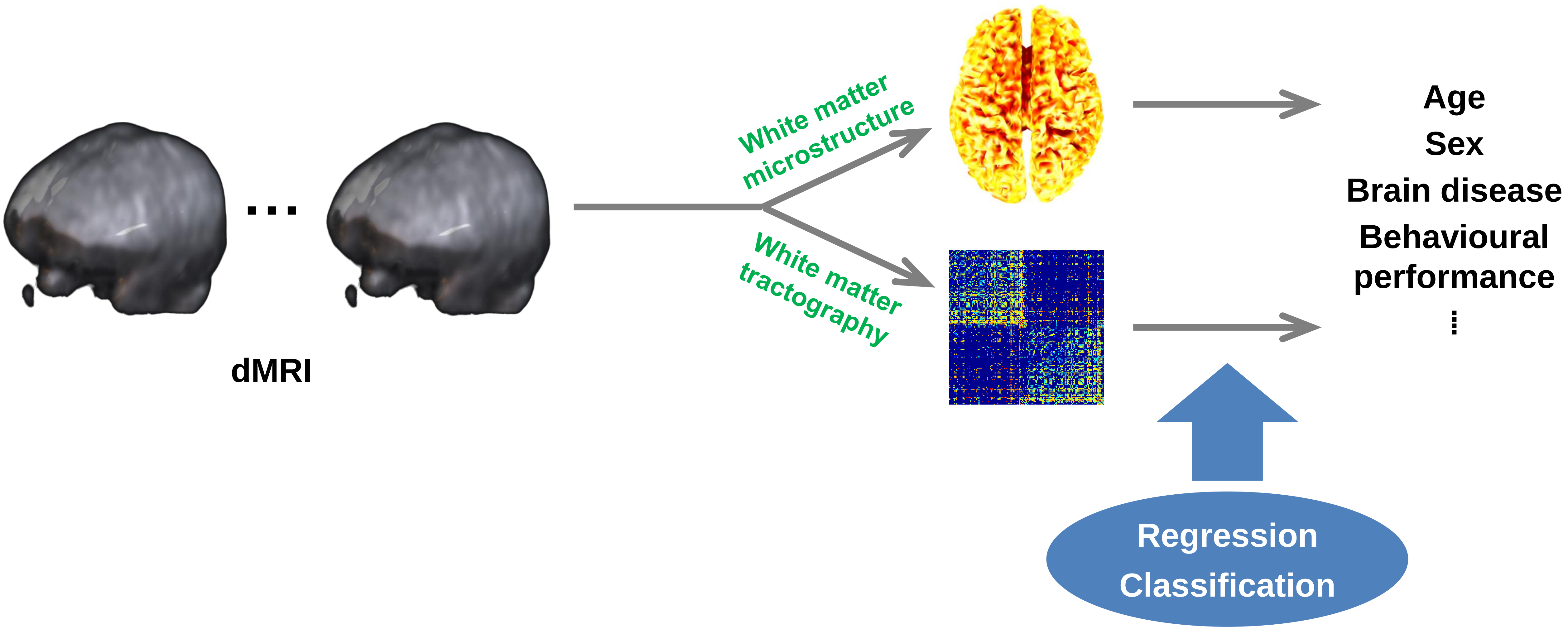
FA



MD

Structural brain networks based on diffusion tensor metrics

- Graph-theoretical analysis
  - Characterize the topological properties of structural brain networks
    - Connection topology of the brain
    - Efficiency of information transfer within the brain
    - Key regions in the brain.
    - Brain's resilience to damage or attack


dMRI
White matter microstructure
White matter tractography
Age
Sex
Brain disease
Behavioural performance
Regression
Classification