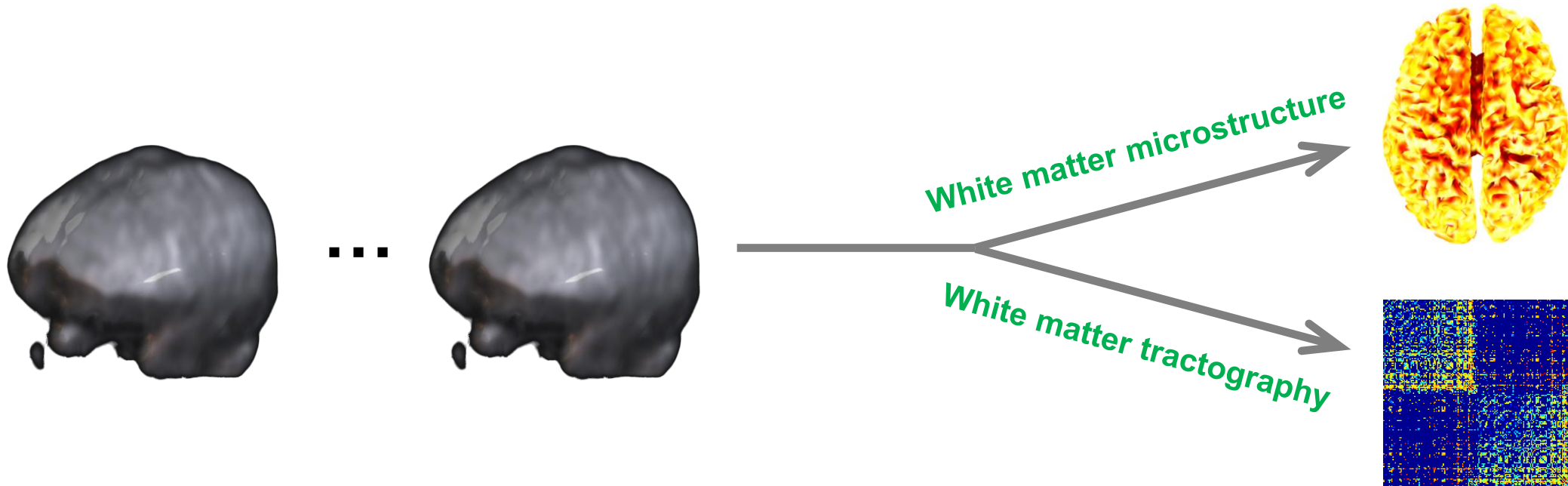


## Diffusion-weighted MRI (2): Data Processing Methods

확산가중 자기공명영상 (2):  
데이터 처리 방법

# Brain Mapping with Diffusion-weighted MRI (dMRI)

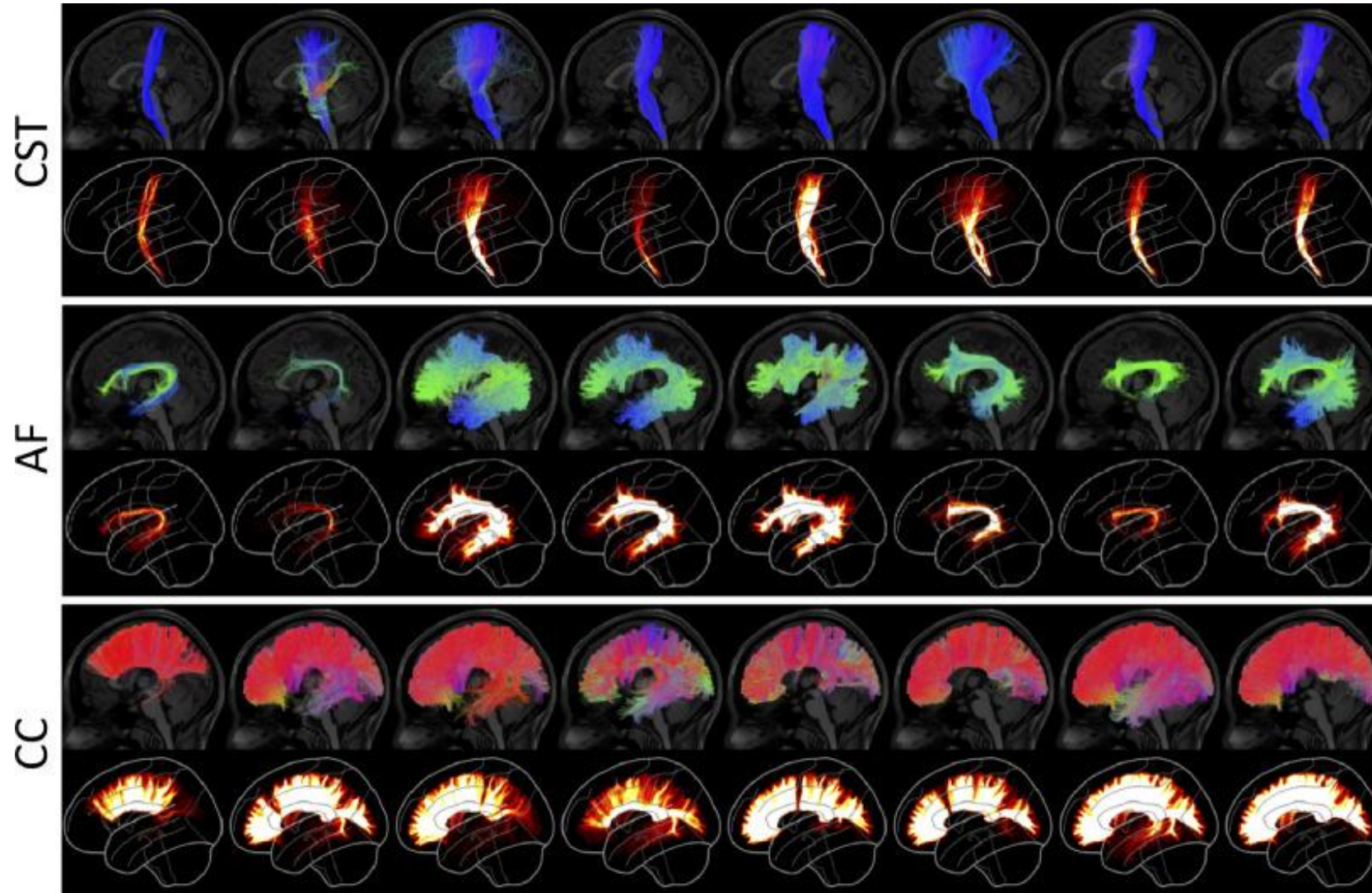
- Diffusion-weighted MRI



# Analytical Variability in dMRI

- Variability of white matter tractography [\[Schilling et al., 2021\]](#)
  - Resulted from different protocols for white matter bundle segmentation

From the same probabilistic streamline set

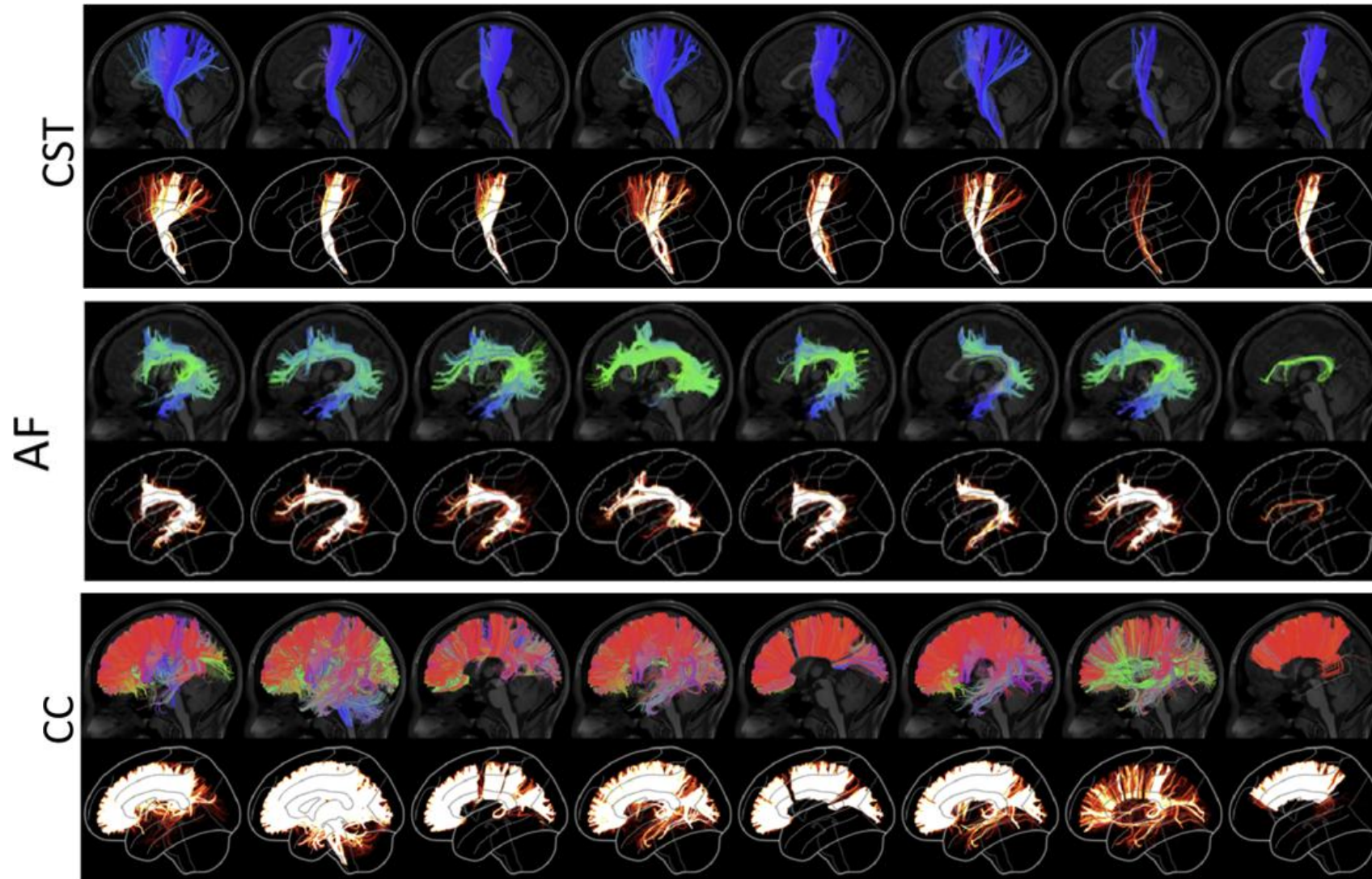


[Schilling et al., 2021]

**Analytical Variability in White Matter Tract Dissection Using Different Protocols**



From the same deterministic streamline set



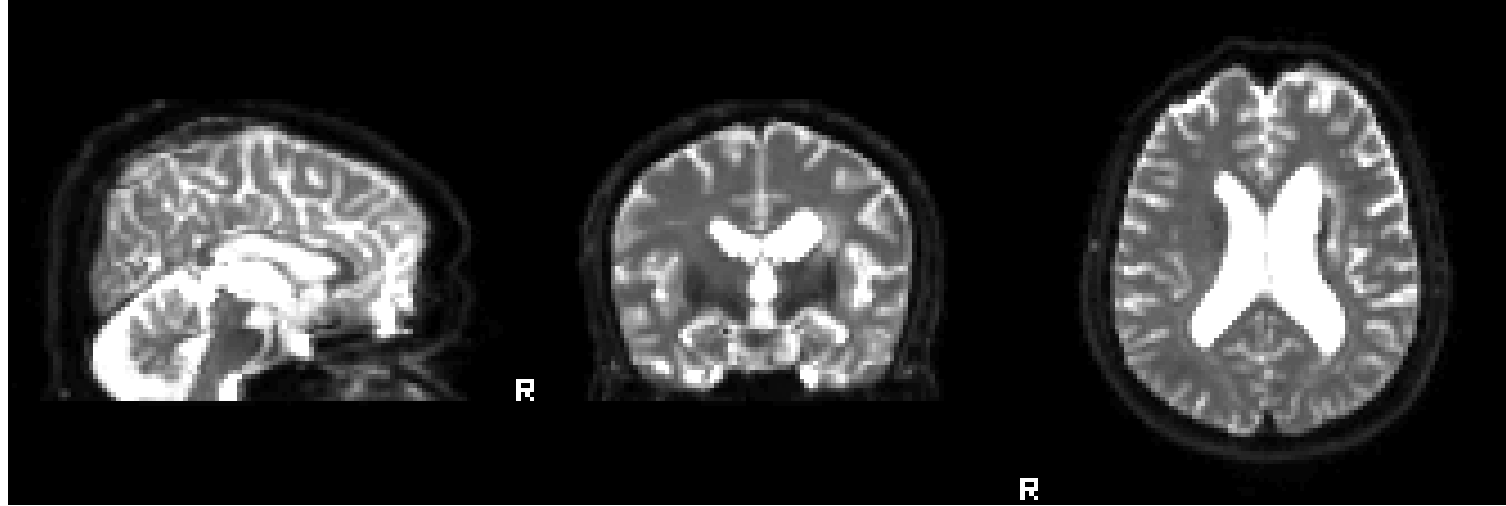
[Schilling et al., 2021]

**Analytical Variability in White Matter Tract Dissection Using Different Protocols**

# Preprocessing

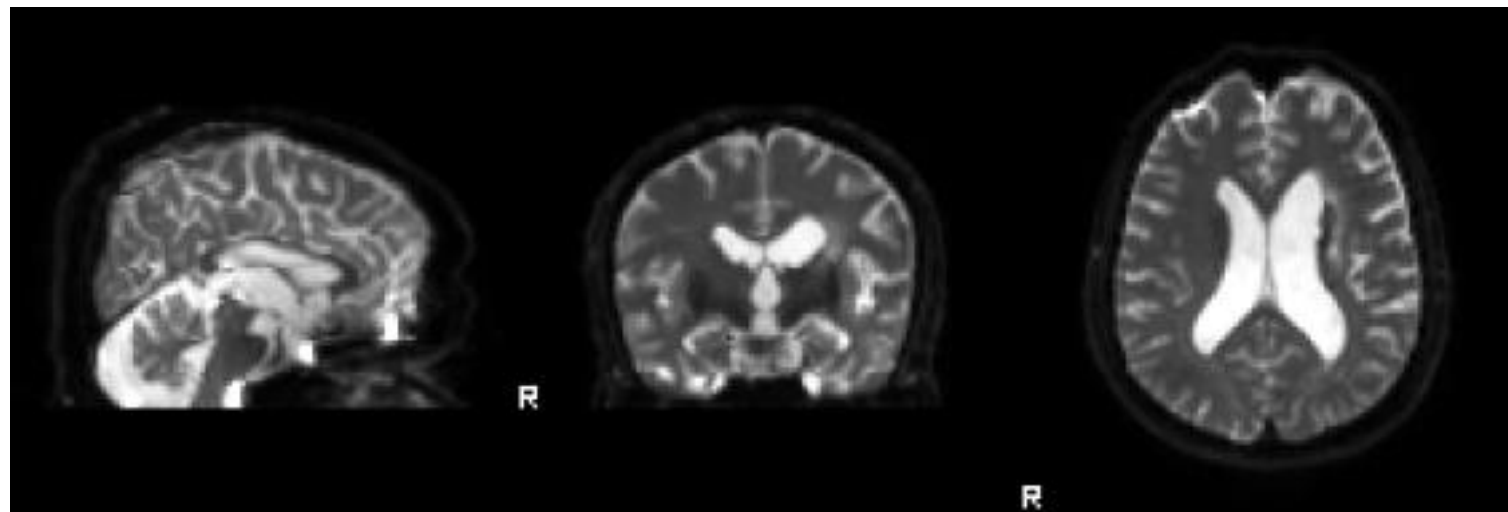
- Numerous steps to clean dMRI data before diffusion modeling
  - Correction for unwanted variation
    - Head motion
    - Eddy current-induced distortion
    - Inhomogeneity-induced distortion

# [dMRI: Preprocessing]

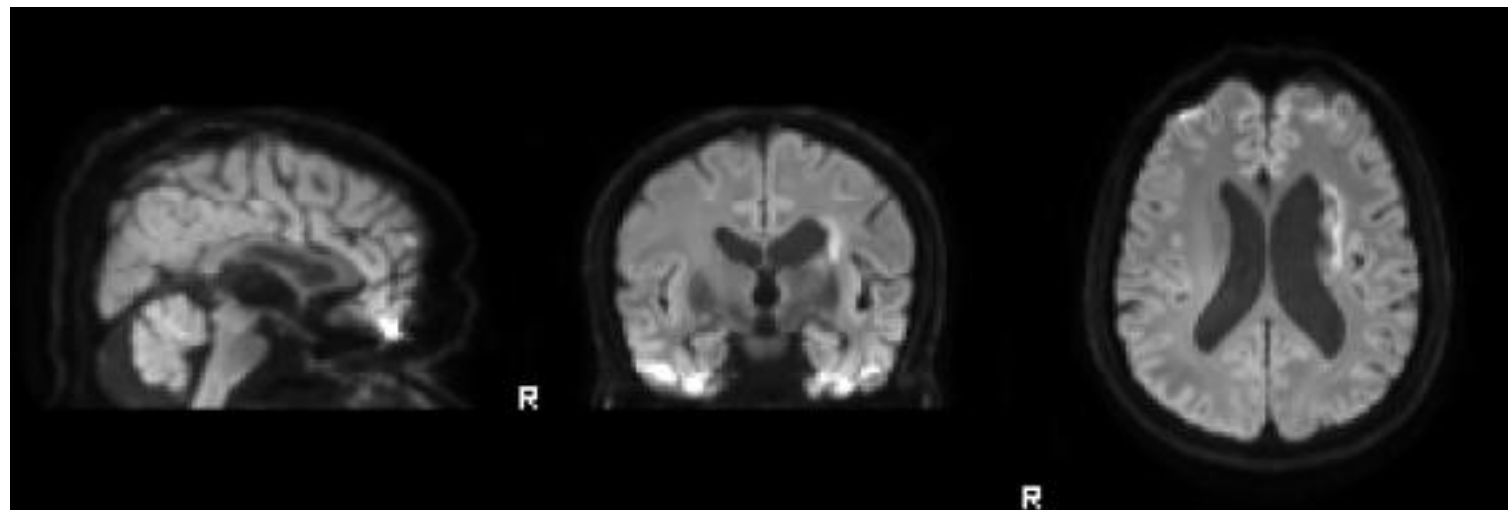


- 46 scans
  - 1 scan without diffusion weighting
  - 45 scans with diffusion weighting at  $b = 1000 \text{ s/mm}^2$

Average image for  $b = 0 \text{ s/mm}^2$



Average image for  $b = 1,000 \text{ s/mm}^2$





–  $b$ -values

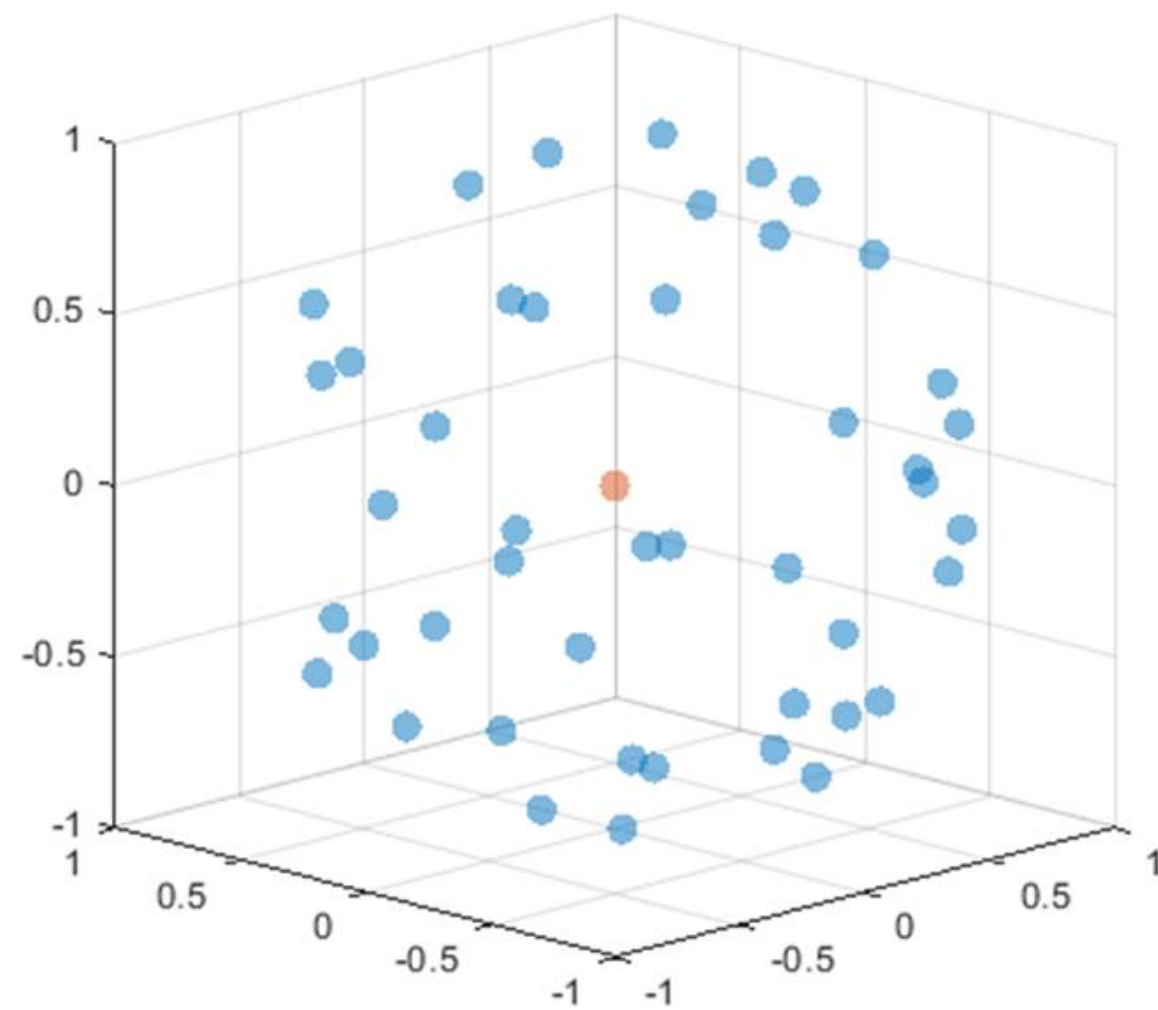
0    1000    1000    1000    1000    1000    1000    ...    1000

46 values

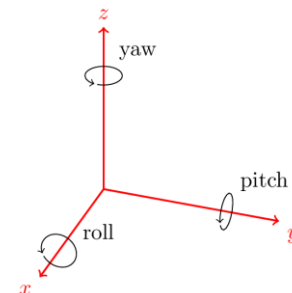
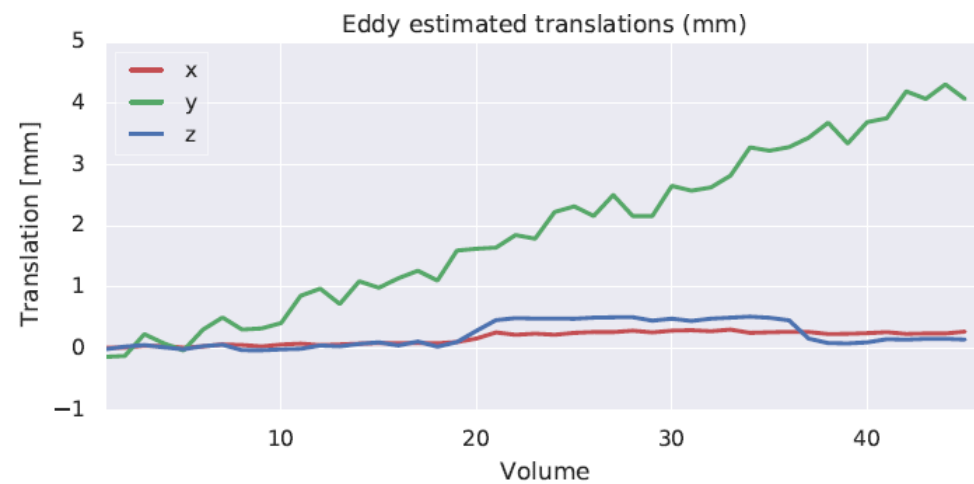
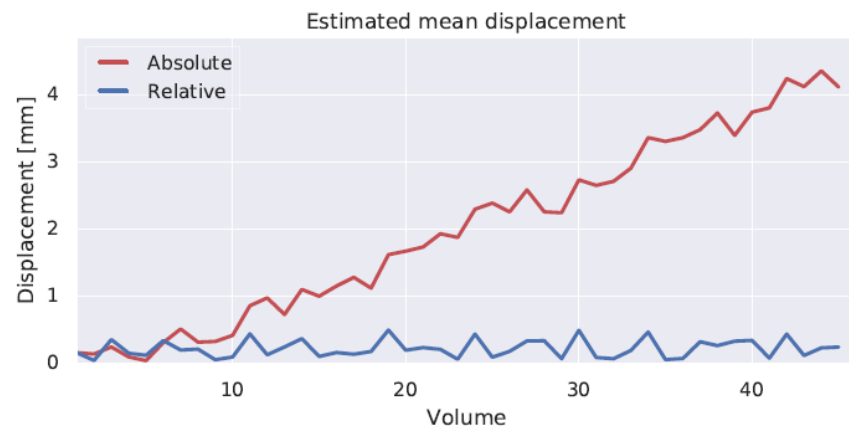
–  $b$ -vectors

0	0.2488	-0.4396	0.6565	-0.3743	0.2818	...	0.4357
0	0.9672	0.7676	-0.0606	-0.5783	0.0936	...	0.8473
0	-0.0588	0.4671	-0.7513	0.7245	0.9545	...	0.3021

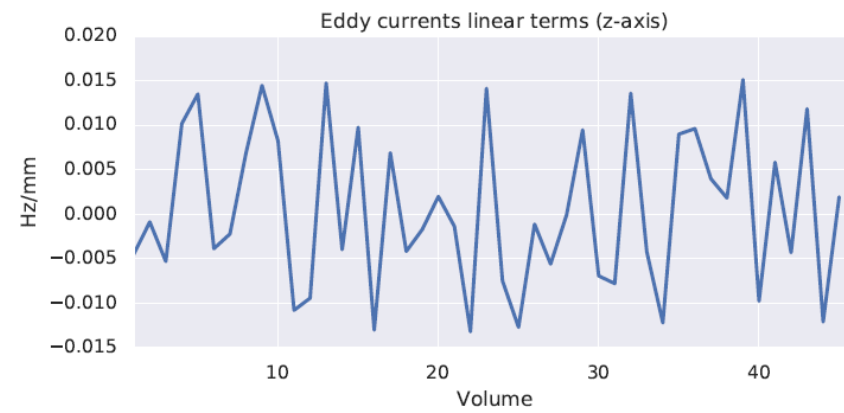
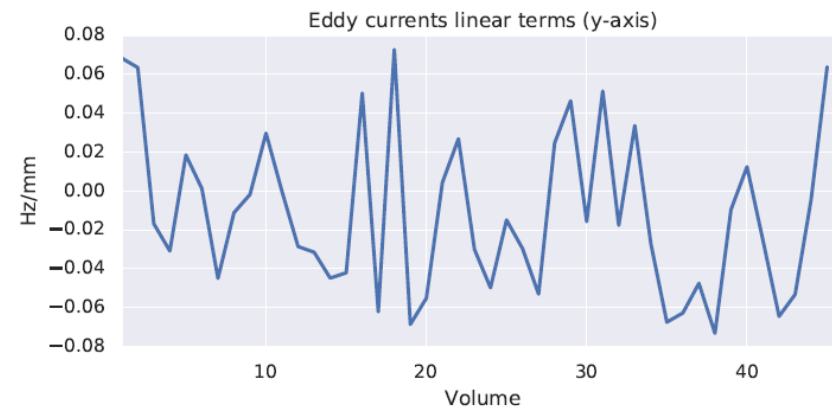
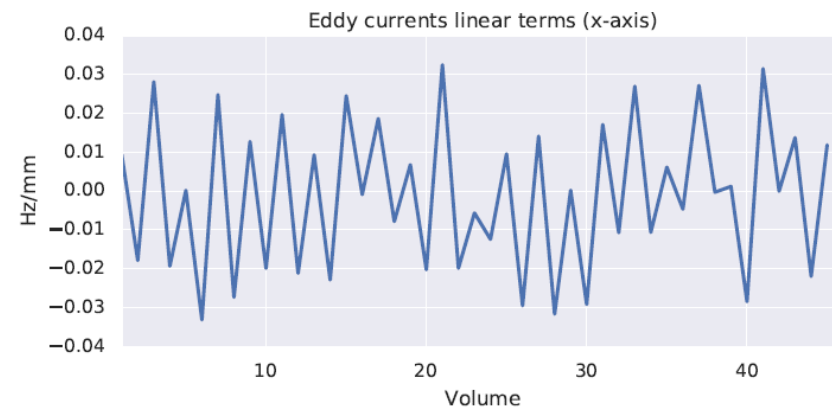
46 vectors



**Diffusion-sensitizing Gradient Directions**



## Estimated Head Motion



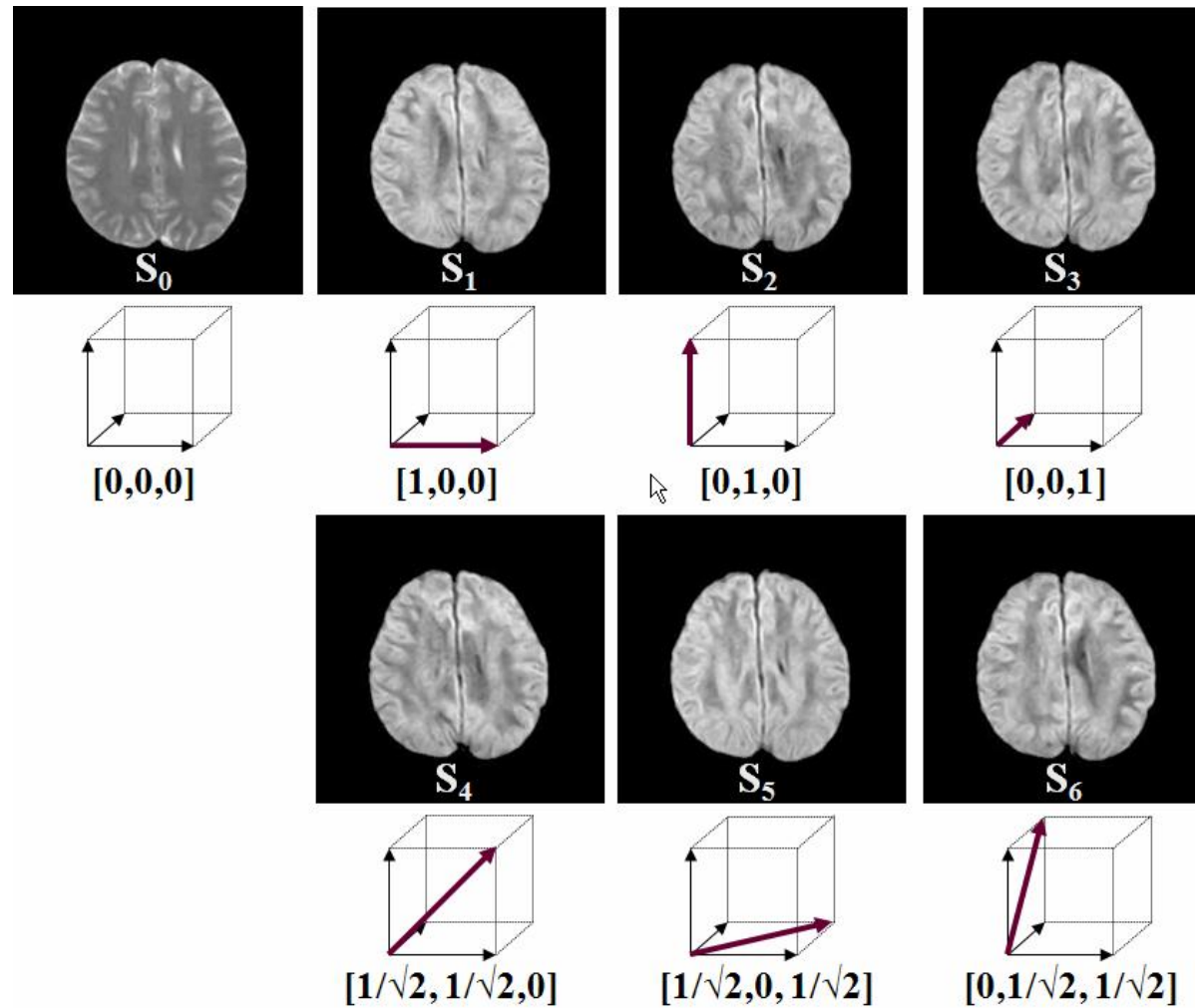
**Estimated Eddy Currents**

# White Matter Microstructure

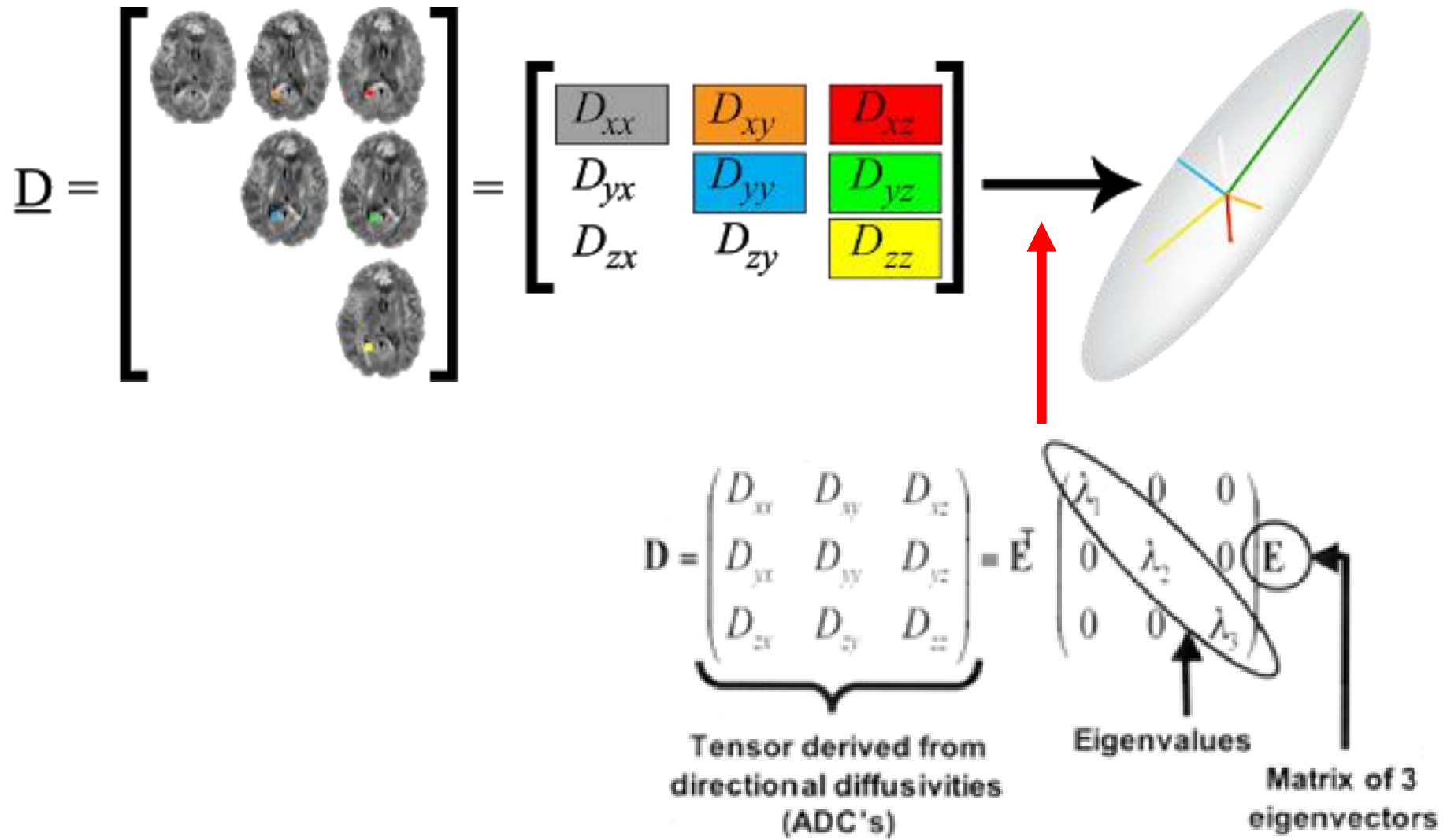
- Given the notion that diffusion measurement is sensitive to water molecule diffusion on a "microscopic scale"
  - Mean squared displacement in terms of time elapsed and diffusivity:  $\langle r^2 \rangle = 2Dt = \sim \mu\text{m}$
  - Through measurement of the average Brownian diffusion behavior of water molecules by aggregating diffusion properties over a great many cells and axons within a voxel

- Diffusion tensor model
  - Represents the directional dependence of diffusion by a diagonalized matrix or an ellipsoid
  - Depicts only a single fiber population at each voxel based on the assumption that the probability density function describing the random displacement of water molecules due to diffusion is Gaussian
    - Not proper to voxels that have multiple fiber populations crossing or highly curving fiber bundles



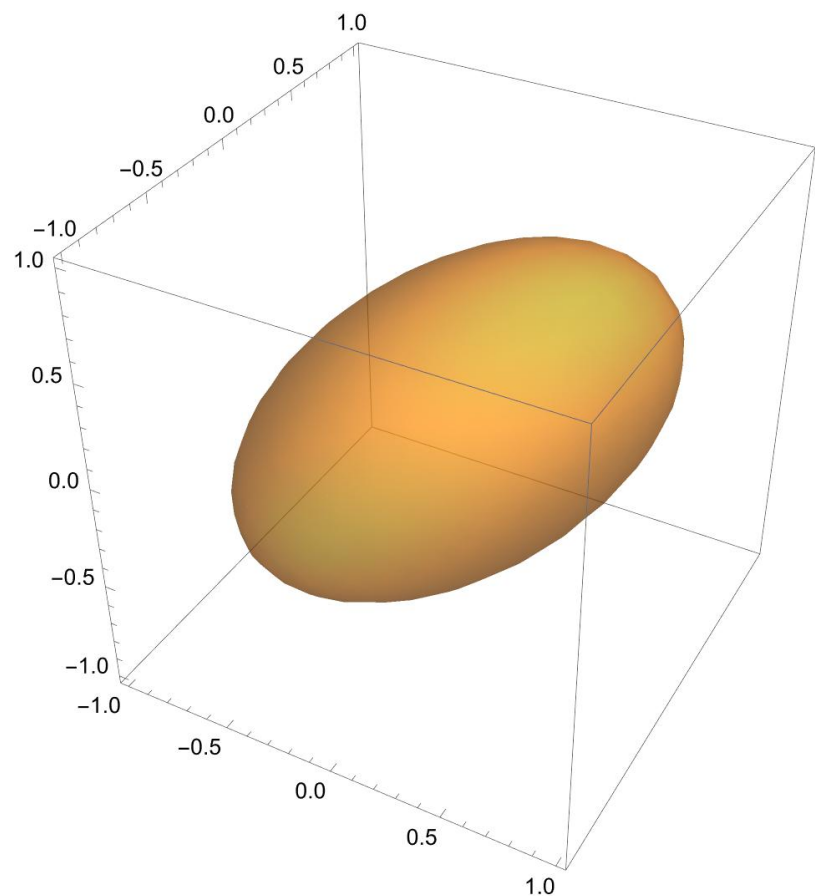


**MRI Signals Measured without and with Diffusion Weighting**

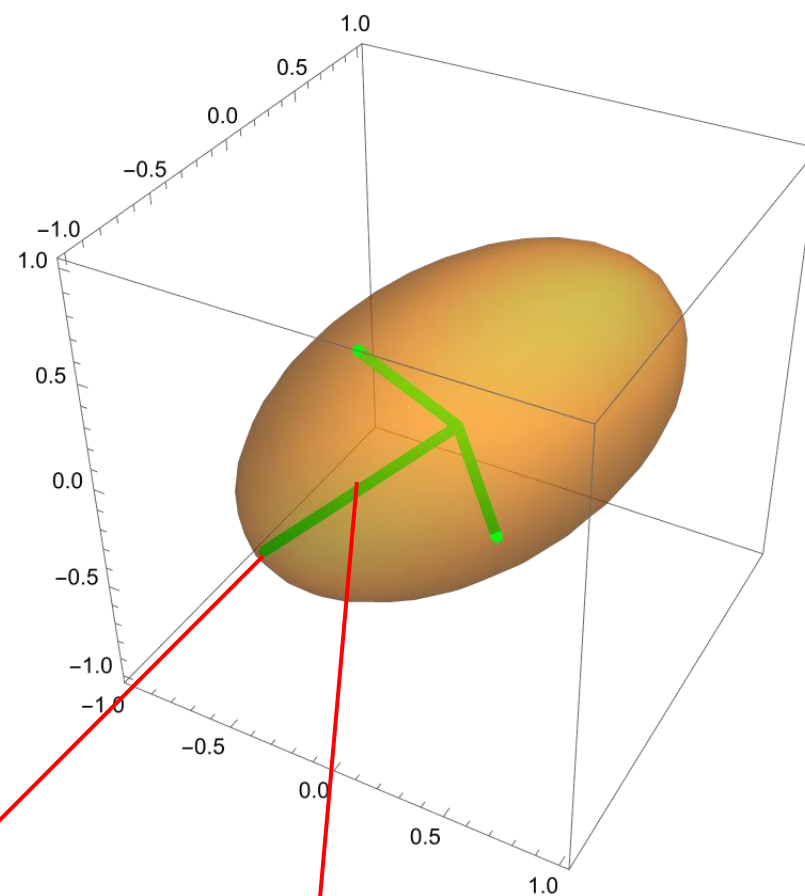


<https://www.blog.brainsightai.com/post/from-dti-to-hardi>]]

## Diffusion Tensor and Its Ellipsoid Representation

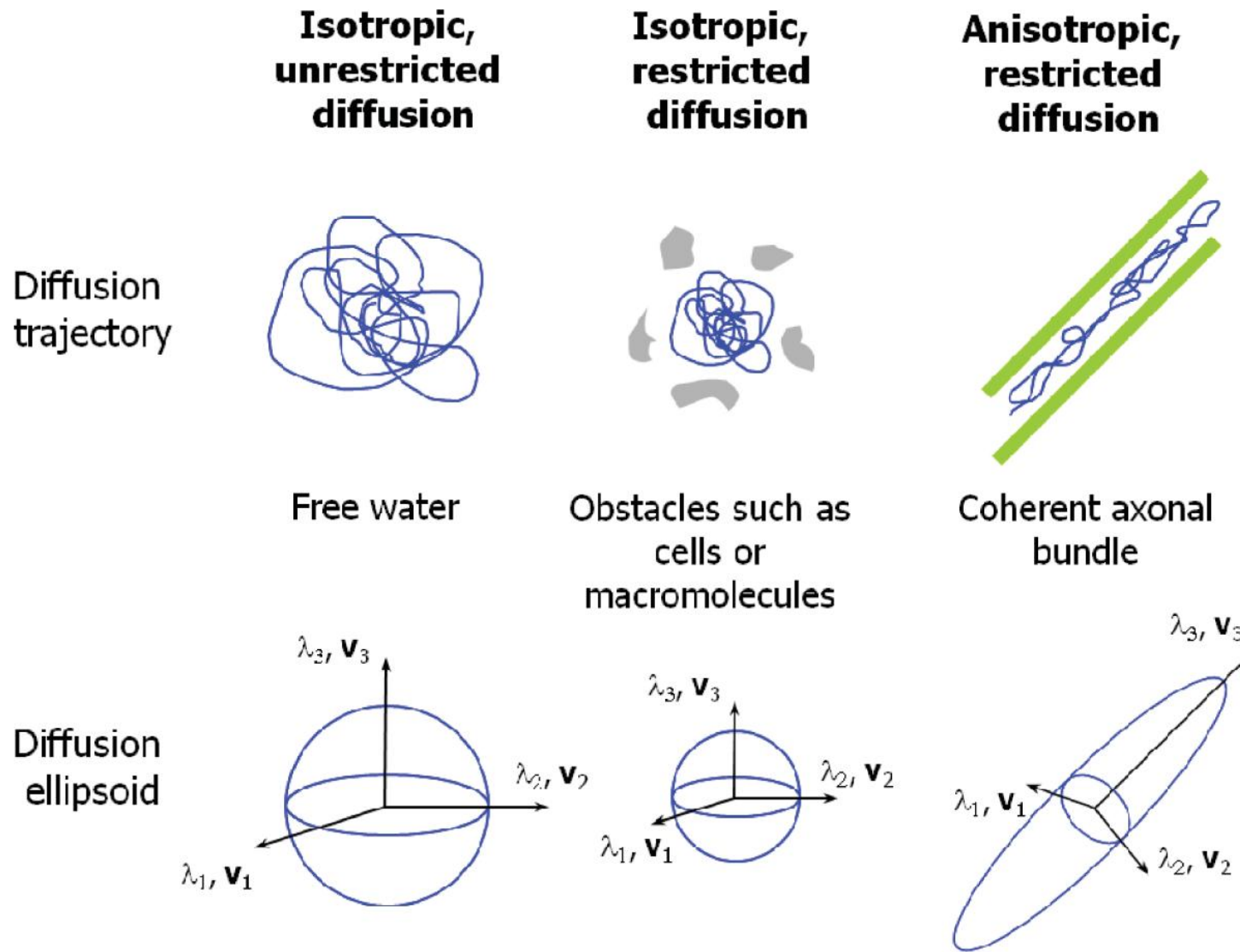


→  
Eigendecomposition



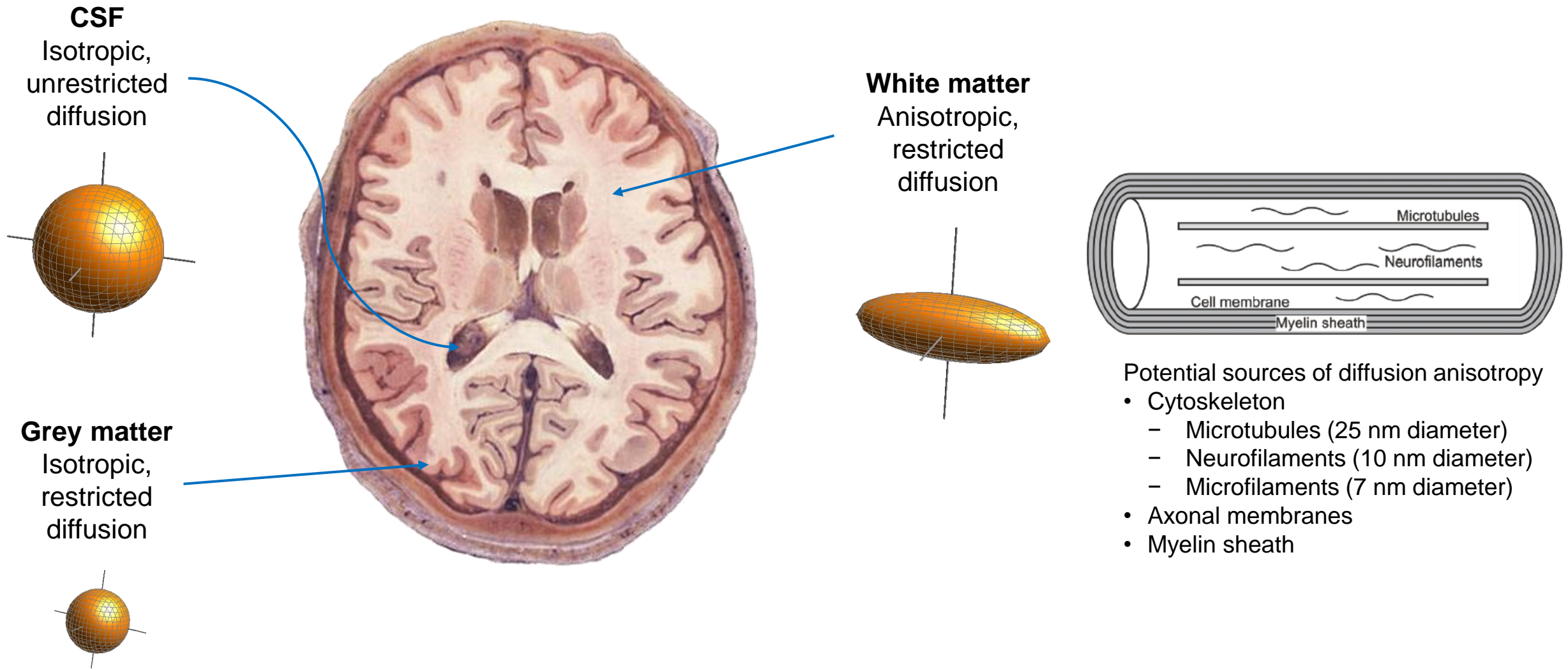
$$\begin{pmatrix} 20 & -8 & -6 \\ -8 & 23 & -1 \\ -6 & -1 & 17 \end{pmatrix}$$

$$\begin{pmatrix} 0.68 & -0.69 & -0.25 \\ -0.30 & -0.57 & 0.76 \\ -0.67 & -0.44 & -0.59 \end{pmatrix}^T \begin{pmatrix} 30.4 & 0 & 0 \\ 0 & 20.1 & 0 \\ 0 & 0 & 9.5 \end{pmatrix} \begin{pmatrix} 0.68 & -0.69 & -0.25 \\ -0.30 & -0.57 & 0.76 \\ -0.67 & -0.44 & -0.59 \end{pmatrix}$$



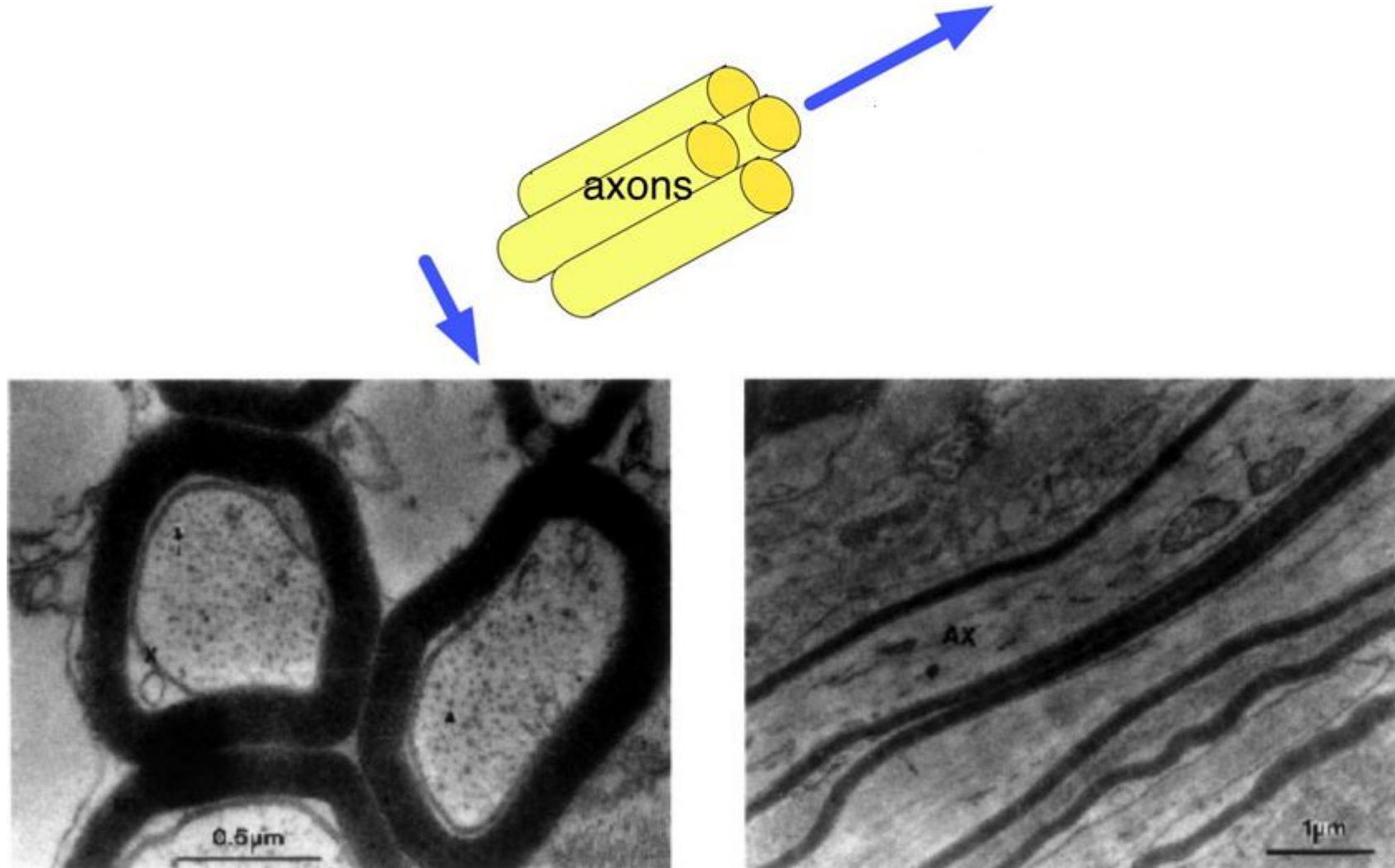
[Geva et al., 2011]

**Isotropic and Anisotropic Diffusion Represented by Ellipsoids**



[Noguerol et al., 2017]]

## Isotropic and Anisotropic Diffusion in Brain Tissues

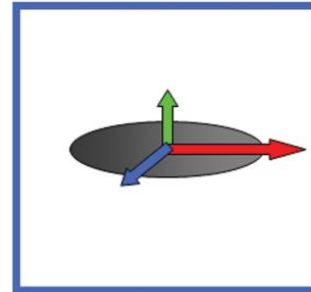
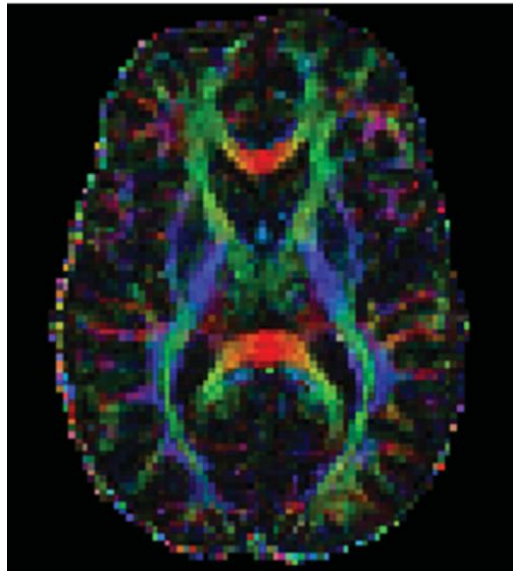
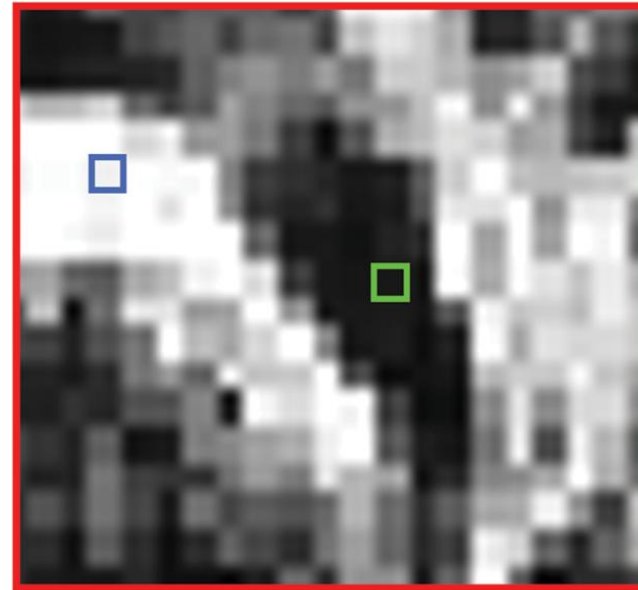
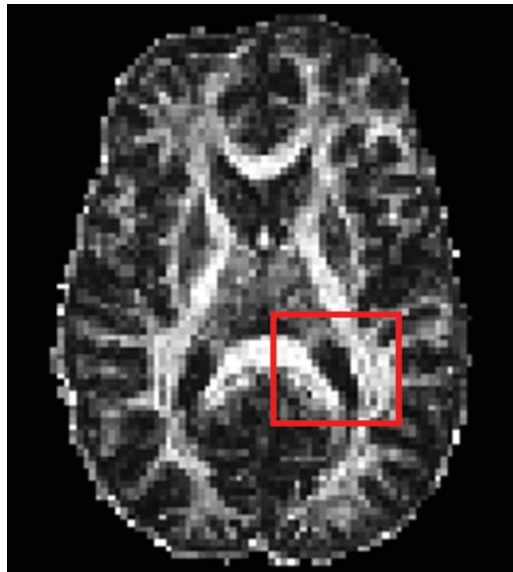


[Beaulieu, 2002]]

## Transverse and Longitudinal Sections of Myelinated Optic Nerves of the Garfish



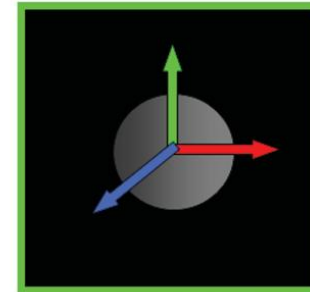
- Diffusion tensor metrics
  - Characterize aspects of water molecule diffusion, such as the magnitude and anisotropy (directional dependence), offering insights into tissue structure and organization
  - Fractional anisotropy (FA)
  - Mean diffusivity (MD)
  - Axial diffusivity (AD)
  - Radial diffusivity (RD)



**Anisotropic  
diffusion**

$$\lambda_1 \gg \lambda_2 = \lambda_3$$

high FA



**Isotropic  
diffusion**

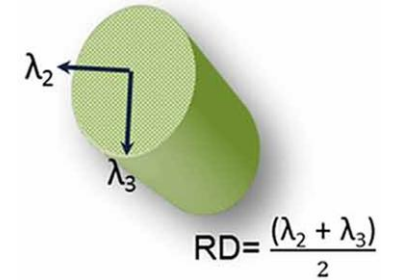
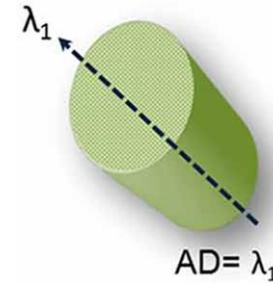
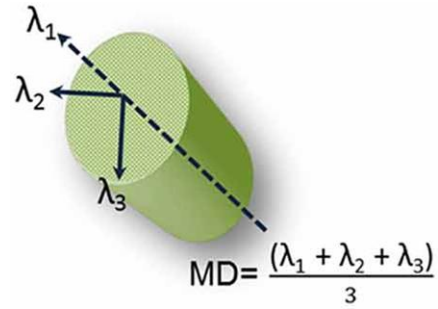
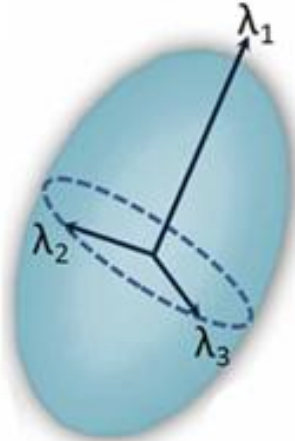
$$\lambda_1 = \lambda_2 = \lambda_3$$

low FA

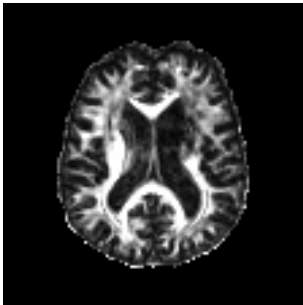
[Geva et al., 2011]

**Directional Information Added to an FA Map**

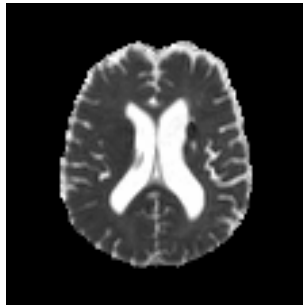
# [dMRI: Diffusion Modeling]



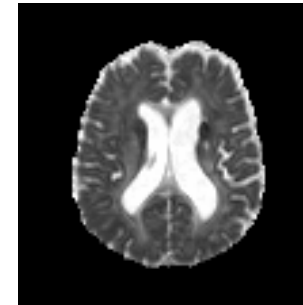
$$FA = \frac{1}{\sqrt{2}} \cdot \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_3 - \lambda_1)^2}}{\sqrt{(\lambda_1)^2 + (\lambda_2)^2 + (\lambda_3)^2}}$$



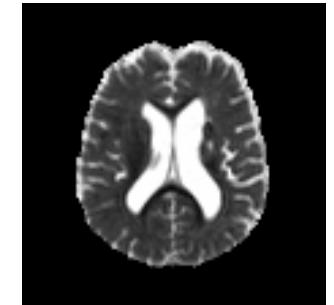
FA



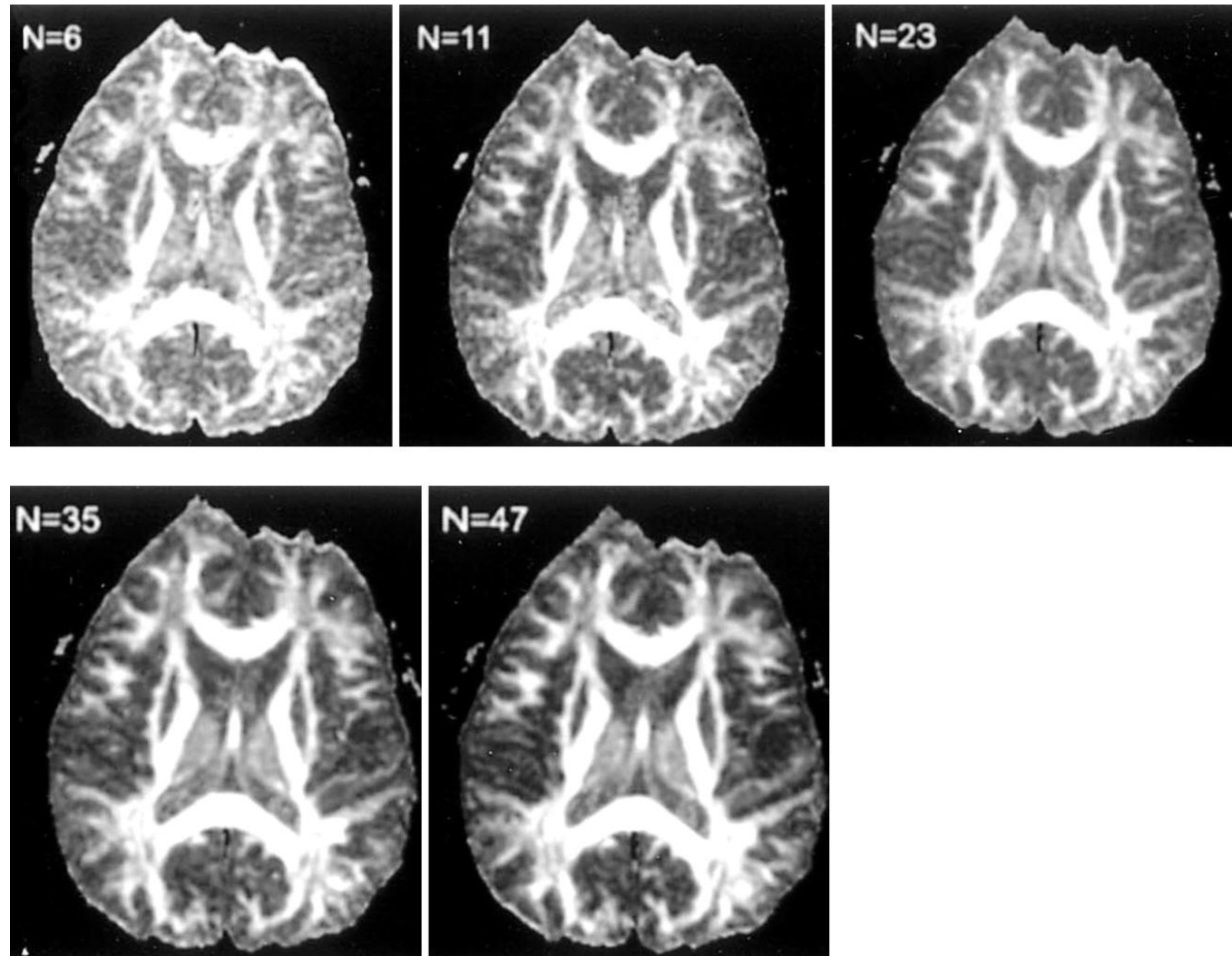
MD



AD

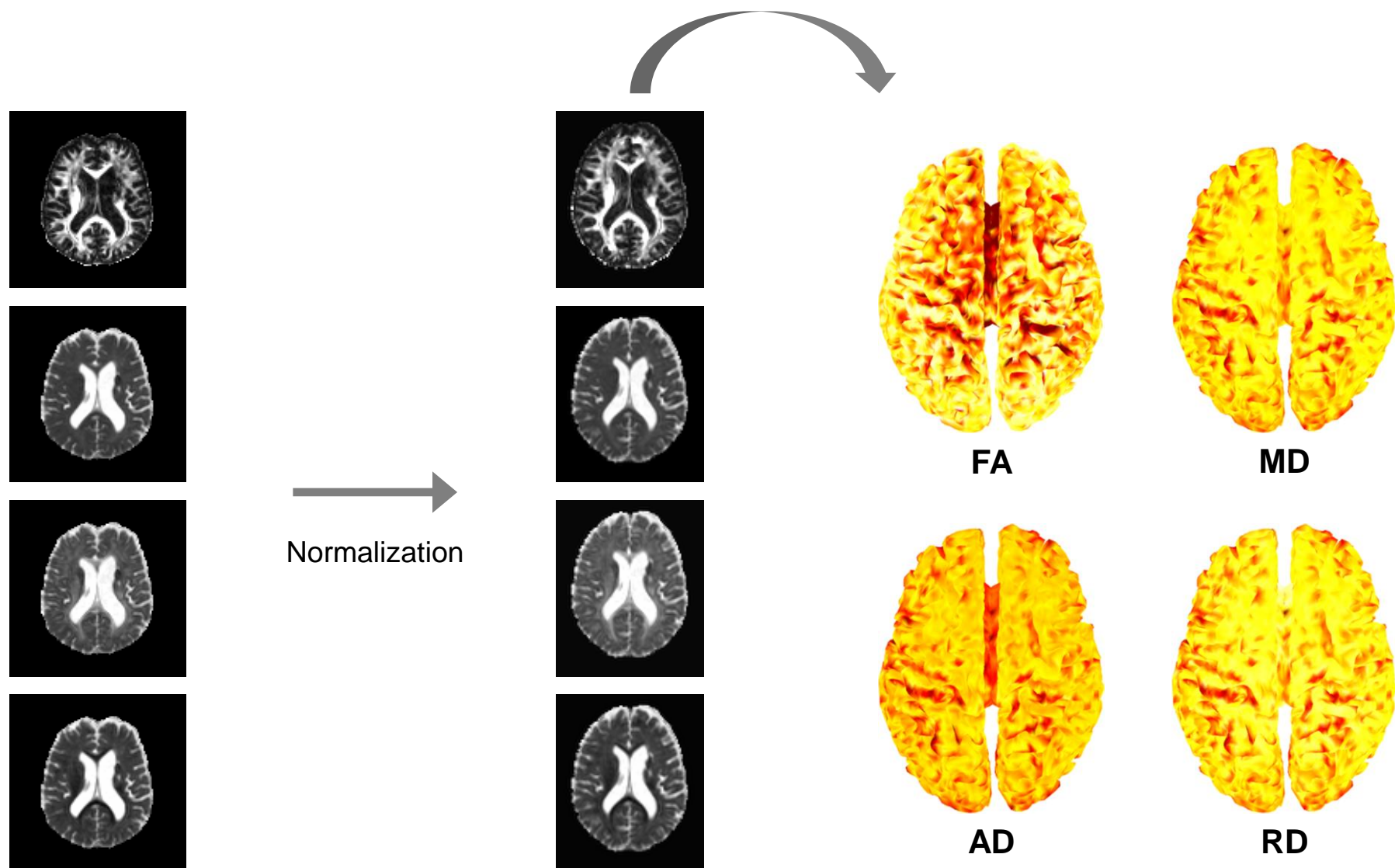


RD



[Chang et al., 2005]

**FA Maps According to Different Numbers of Diffusion-sensitizing Gradient Directions**



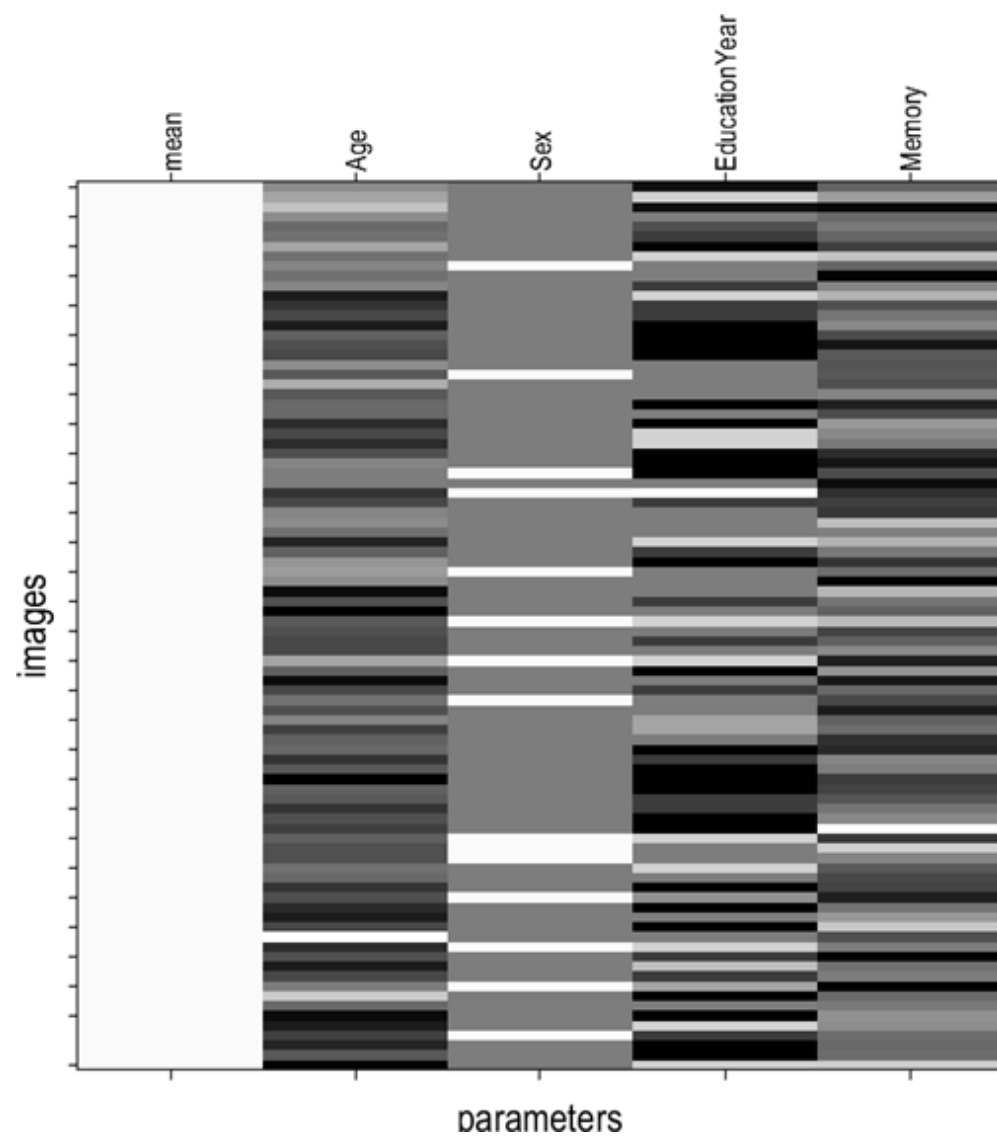
**Information of White Matter Microstructure**

# [Statistical Analysis of dMRI]

- $FA \sim$   
Age +  
Sex +  
Education year +  
Memory performance



# Design matrix



# Output

Regression



Positive correlation



Negative correlation

- MD  $\sim$

Age +

Sex +

Education year +

Memory performance

# Output

## Regression

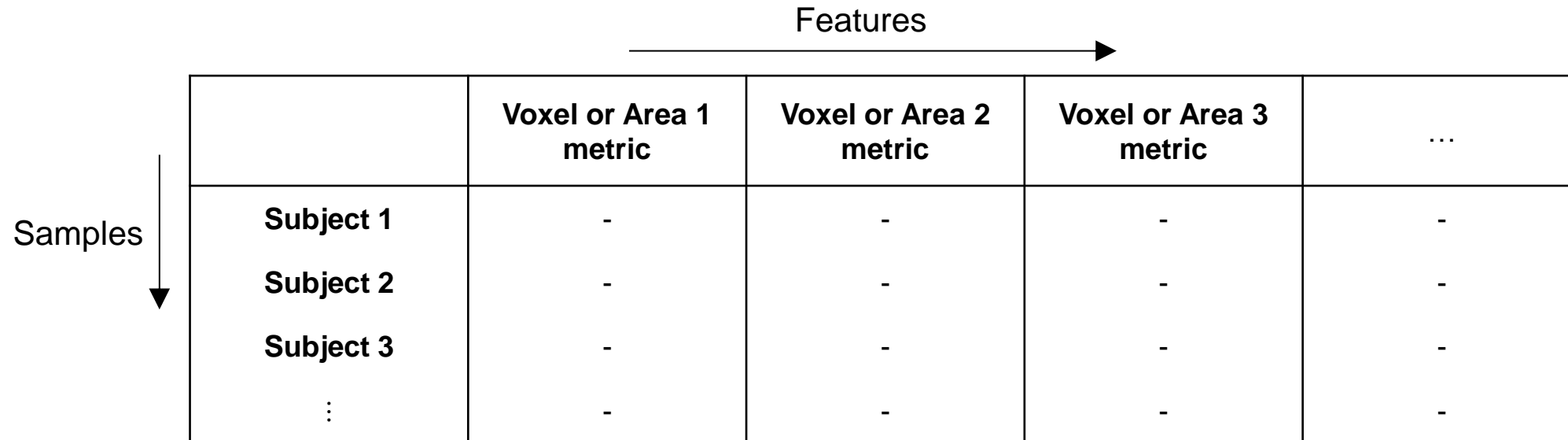


Positive correlation



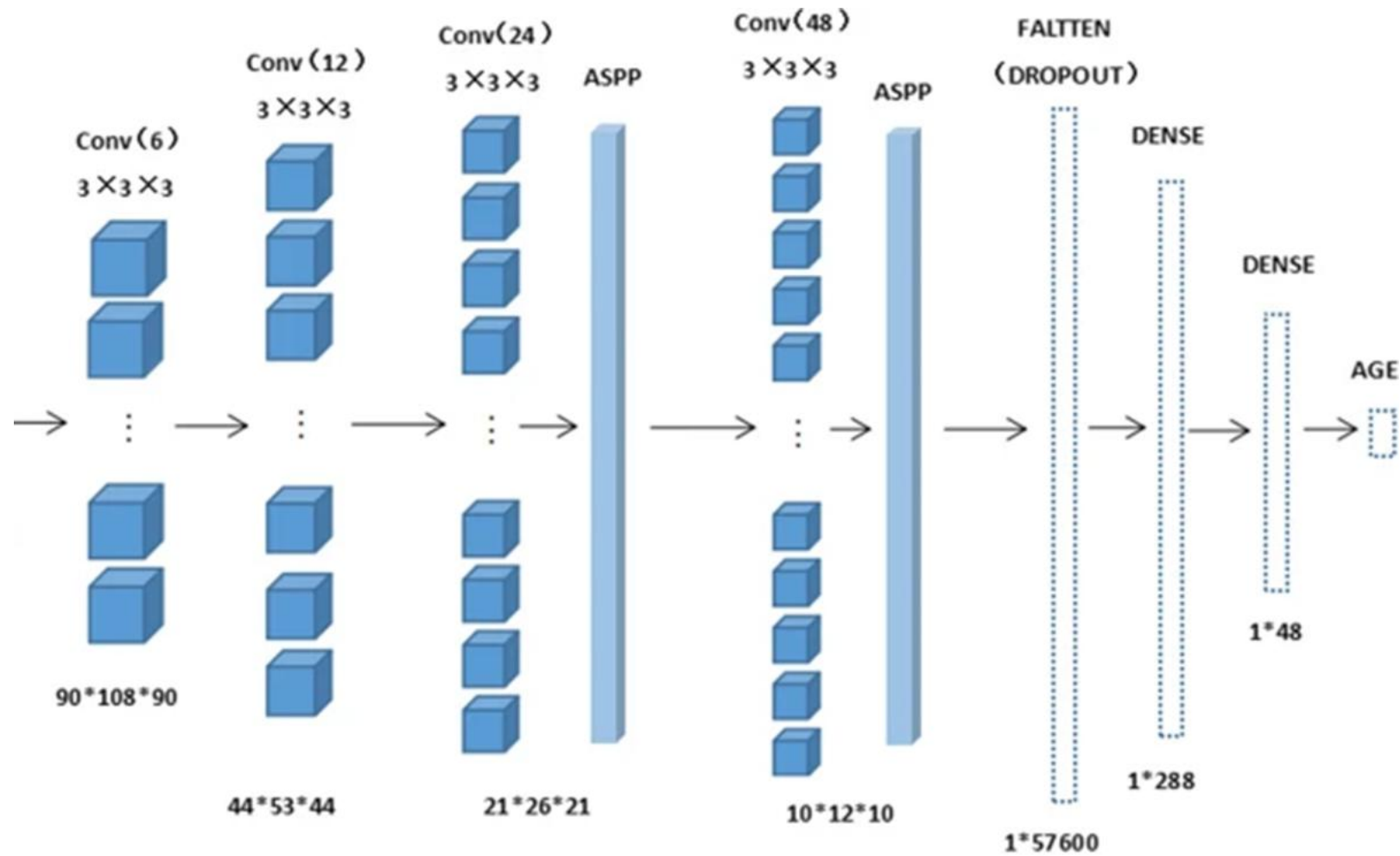
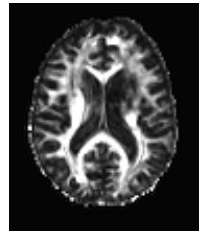
Negative correlation

- Input to machine learning models
  - Table of voxel-wise or area-wise metric values for diffusion tensors



		Features →			
		Voxel or Area 1 metric	Voxel or Area 2 metric	Voxel or Area 3 metric	...
Samples ↓	Subject 1	-	-	-	-
	Subject 2	-	-	-	-
	Subject 3	-	-	-	-
	⋮	-	-	-	-

- Diffusion tensor metric map



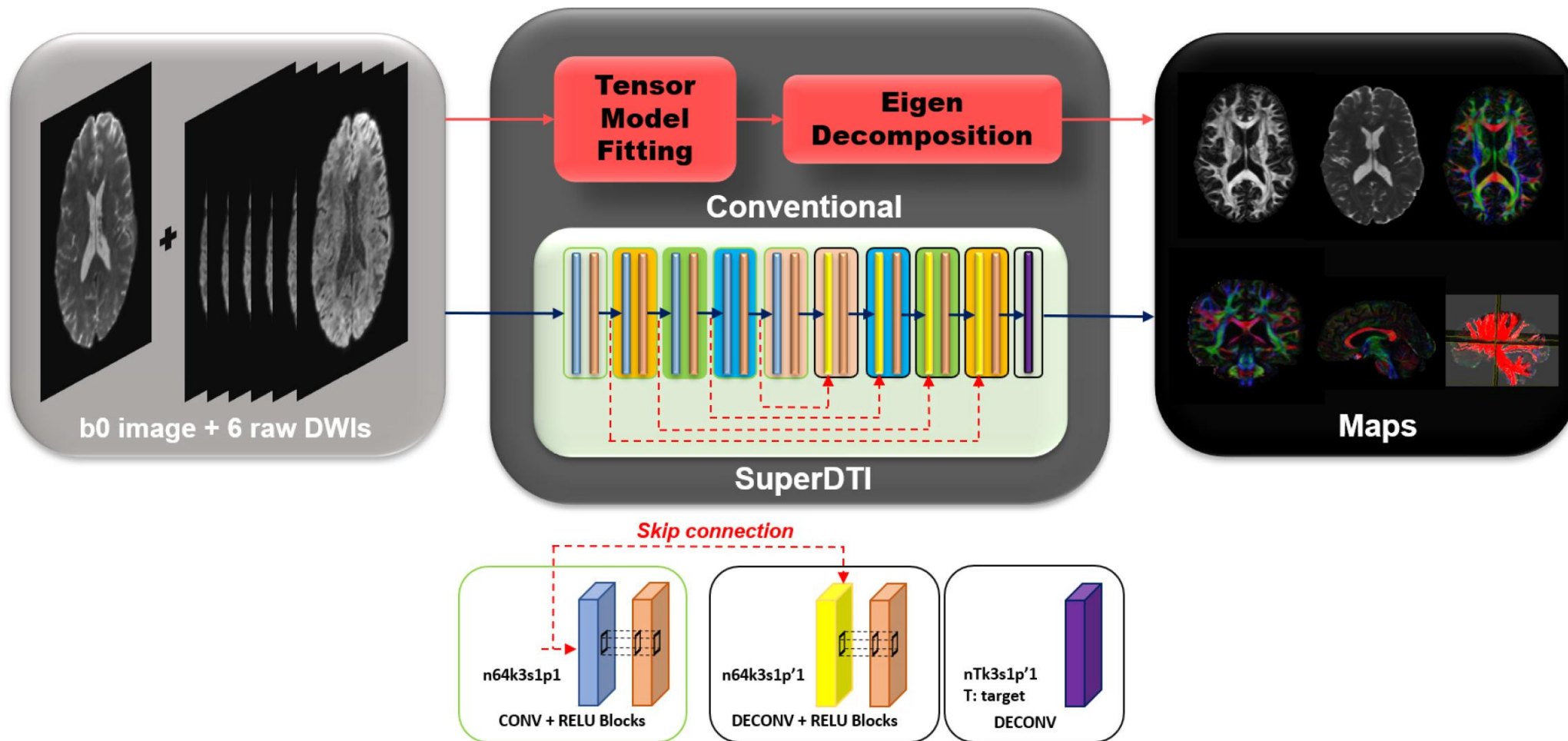
[Adapted from Wang et al., 2023]

## Application of Deep Learning to Diffusion Tensor Metric Maps



# Automated Diffusion Tensor Metrics Computation

- Employs deep learning algorithms to overcome limitations of traditional tensor fitting methods
- Enables to improve computation accuracy and reduce noise sensitivity



[Li et al., 2021]

## SuperDTI: Diffusion Tensor Metrics Estimation

# Computational Representation of White Matter Pathways

- White matter tractography hierarchy
  - Streamline → bundle
- Streamline
  - Fundamental unit of tractography, representing a single reconstructed fiber trajectory from a seed point through the brain
  - Highly dependent on algorithm parameters (seed density, step size, angular threshold, etc.)
    - Number of streamlines does not directly correspond to actual axon counts; rather it represents a computational estimation

- Bundle

- Collection of streamlines that share similar trajectories and anatomical locations
- Represents an anatomical structure believed to serve a common functional role
- Can be defined through automatic or semi-automatic algorithms or expert manual segmentation
- Examples include well-known white matter pathways

- Relationship between biological and tractography hierarchies
  - Scale mismatch
    - A single voxel contains millions of axons, but generates far fewer streamlines
  - Resolution limitations
    - MRI resolution ( $\sim 1\text{-}2\text{ mm}$ ) is insufficient to directly visualize individual axons ( $\sim 1\text{-}10\text{ }\mu\text{m}$ )
  - Indirect measurement
    - Diffusion MRI measures water molecule movement as a proxy for tissue organization

## – Validation challenges

- Direct comparison between tractography results and actual neural pathways in living human brain is nearly impossible

## – Model assumptions

- All tractography algorithms are based on simplified models that cannot fully capture complex biological reality

## – Interpretative caution

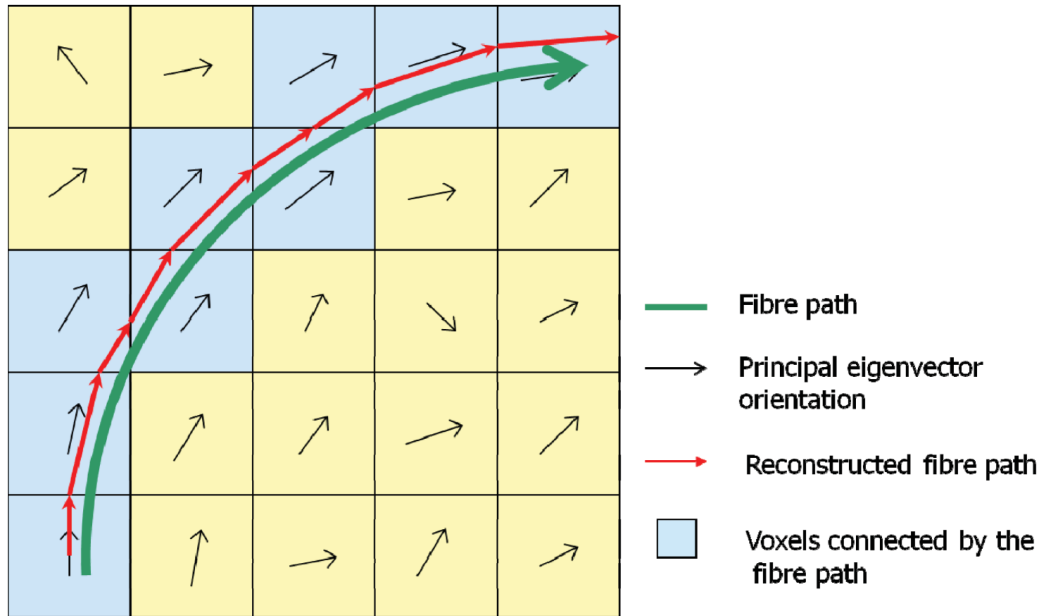
- Streamline-based connectivity metrics should be considered estimations rather than direct representations of anatomical connections

# White Matter Tractography

- Map of connectional anatomy of white matter
  - Bundled streamlines that reflect where organized white matter tracts are likely to be
  - Based on how strongly and in what directions water molecules diffuse given physical constraints in the brain

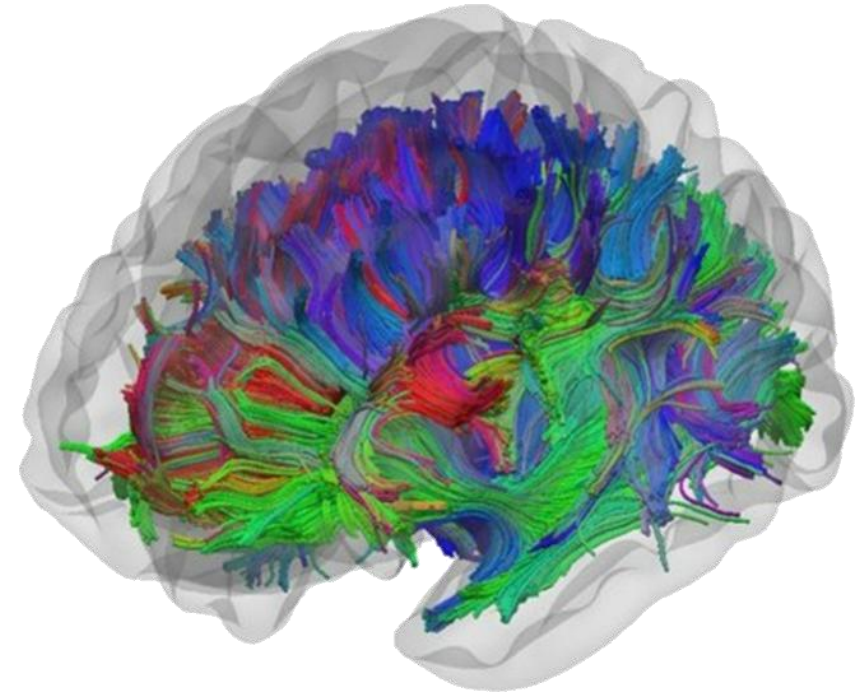
- Tractography vs tracking vs tractogram
  - Tractography
    - Comprehensive technique that uses dMRI data to reconstruct and visualize white matter pathways in 3D
    - Encompasses both the tracking algorithms and visualization methods
  - Tracking
    - Algorithmic process of following the direction of nerve fibers to calculate their paths
  - Tractogram
    - Final output or result of tractography
    - Complete set of reconstructed white matter pathways displayed together





Streamlines based on common  
directions of water molecule diffusion

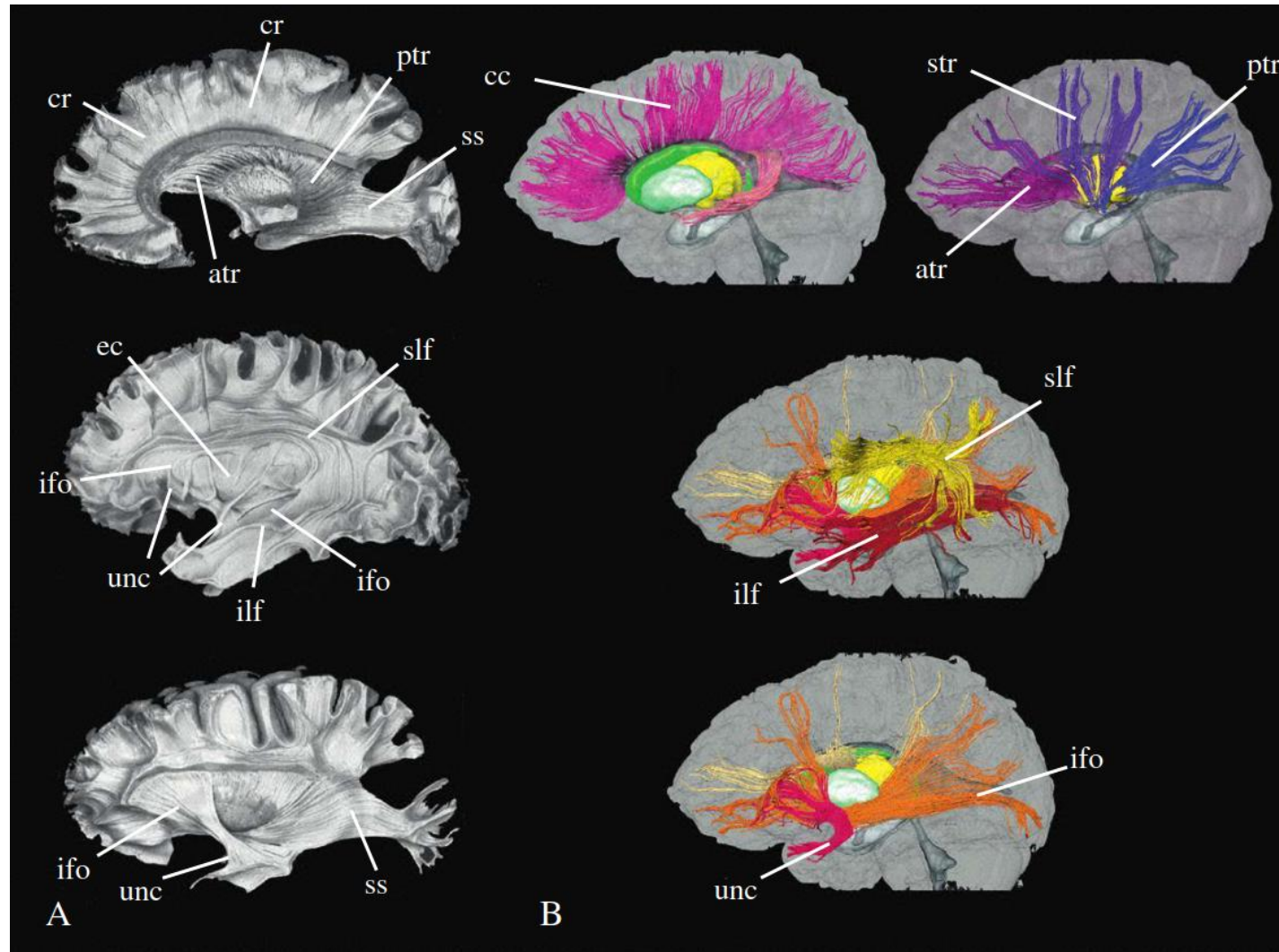
Across the brain



White matter tracts

[Geva et al.,2011]

## White Matter Tractography

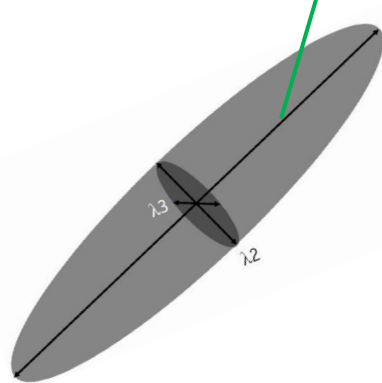
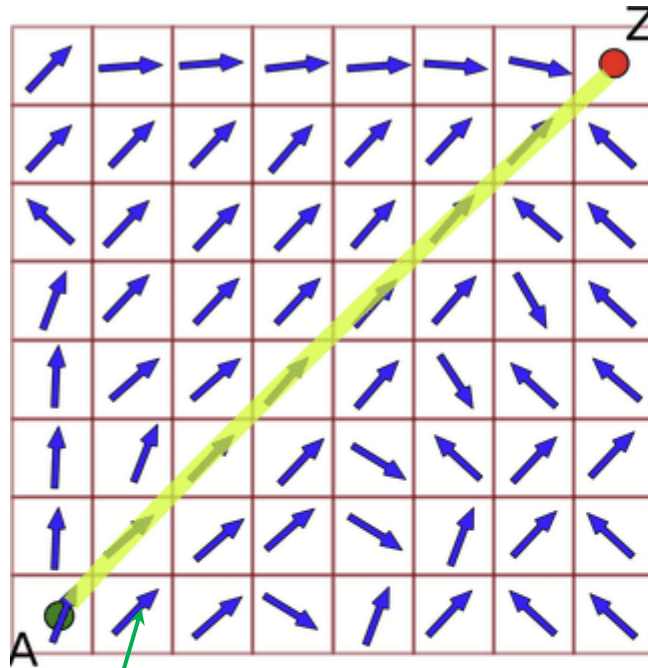


[Oishi et al., 2011]

## Comparison between Postmortem Preparation and dMRI-based White Matter Reconstructions

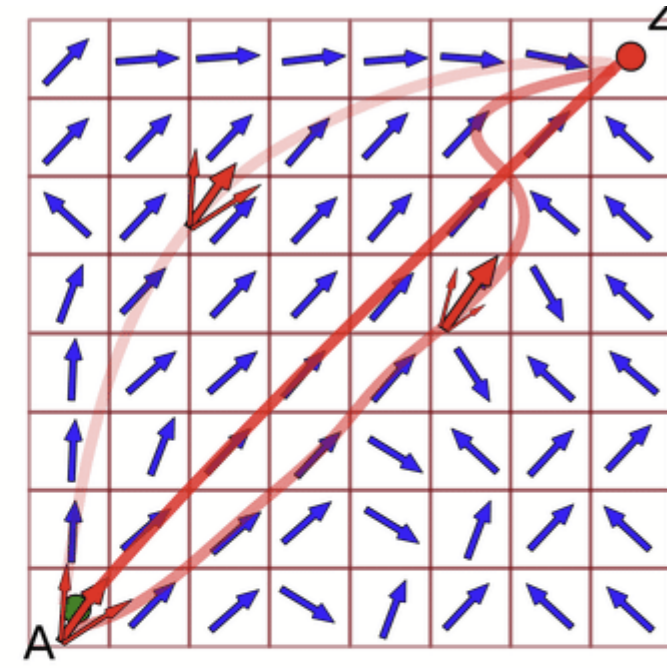
- Deterministic vs probabilistic tractography
  - Deterministic by strictly following the directions of water molecule diffusion
    - Each seed point produces one unique streamline following the dominant diffusion direction at each step
  - Probabilistic by inferring a probability of different directions of water molecule diffusion at any given location
    - Multiple streamlines are generated from each seed point by sampling from a distribution of possible directions, representing uncertainty in fiber orientation

## Deterministic



Principal eigenvector  
(eigenvector of the largest eigenvalue)

## Probabilistic



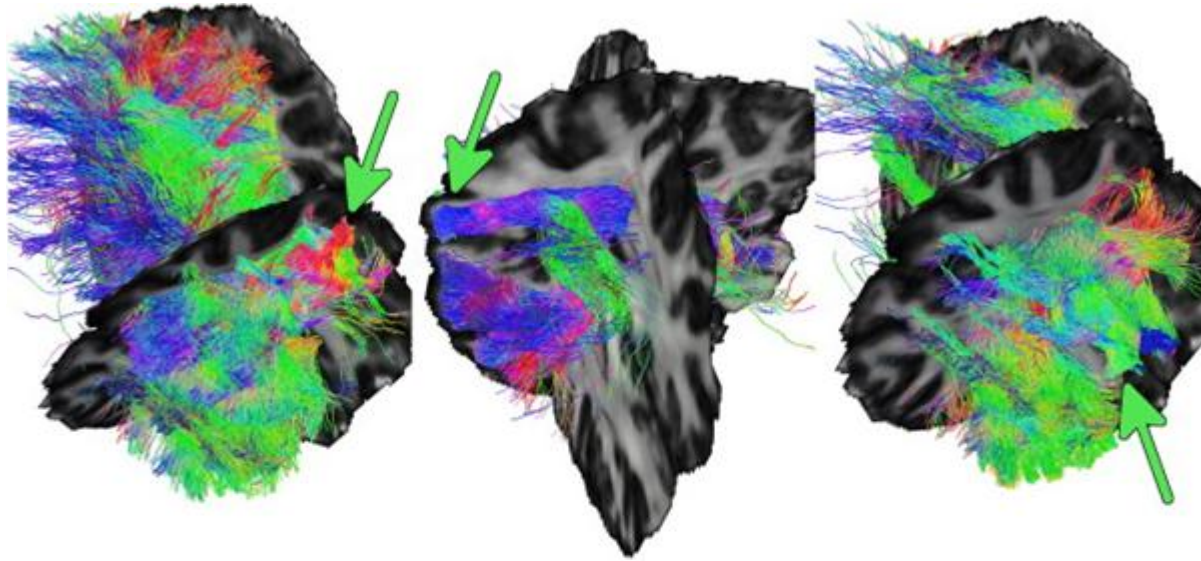
- Probabilistic track - high probability
- Probabilistic track - low probability
- Deterministic track
- Primary direction vector  $\mathbf{e}$
- ↔ 3 directions of the PDF
- Starting seed
- Ending seed

[Garyfallidis, 2012]

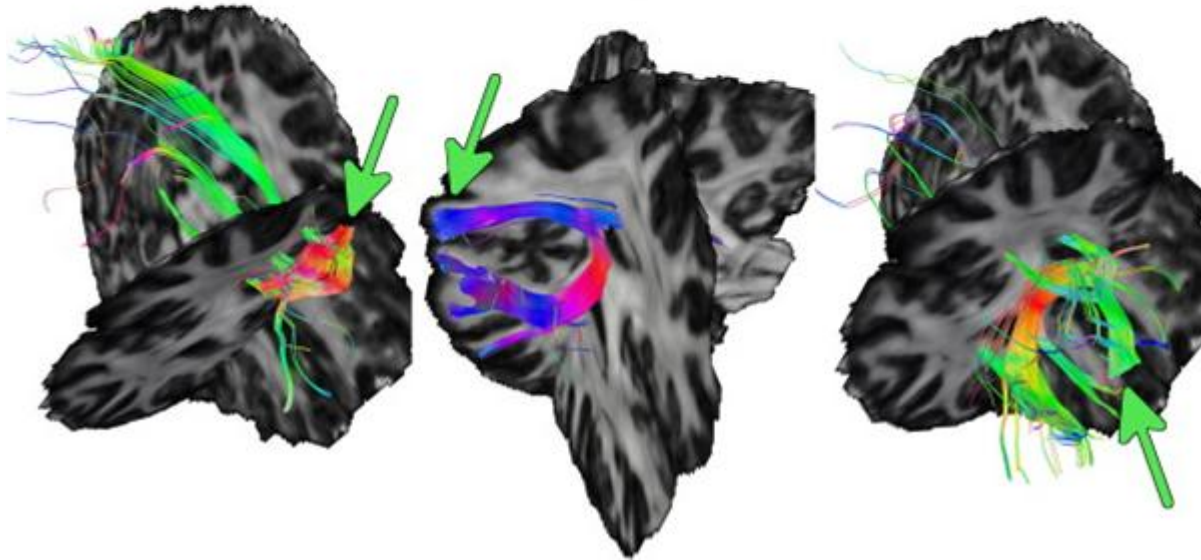
## Deterministic and Probabilistic Ways for White Matter Tractography



**Probabilistic**



**Deterministic**



[Schreiber et al., 2014]

**Comparison between Probabilistic and Deterministic Tractography**

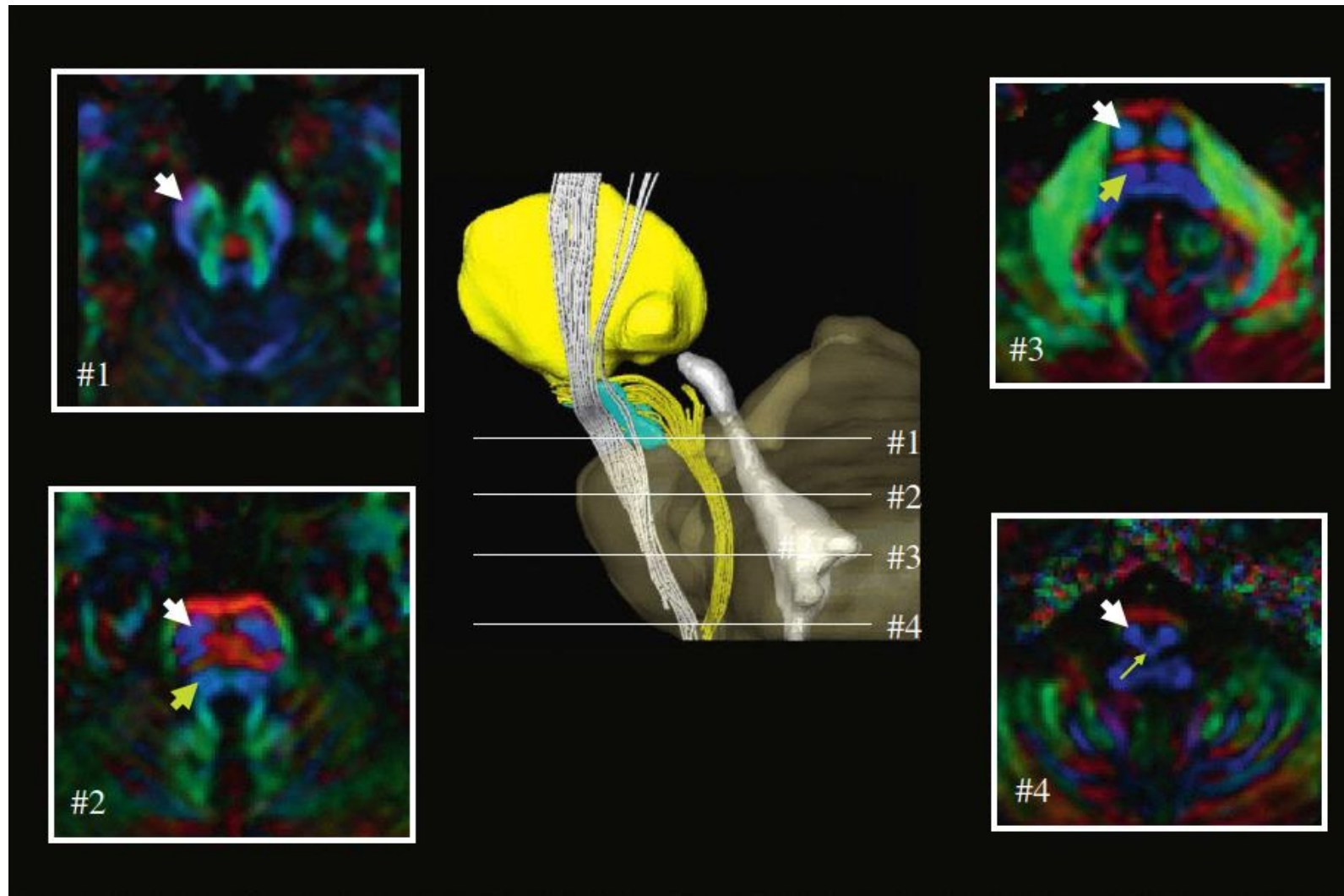
- Bundle as a computational representation of a white matter tract
  - Isolated specific white matter pathway
    - Specificity: Connection between particular areas
    - Isolation: Identifiable pathway with defined trajectories
  - Based on information about:
    - Terminations in specific grey matter structures
    - Histologically-derived definitions
  - Identified by filtering streamlines based on various criteria (length, curvature, anatomical areas they pass through)



[\[https://www.mrtrix.org/\]](https://www.mrtrix.org/)

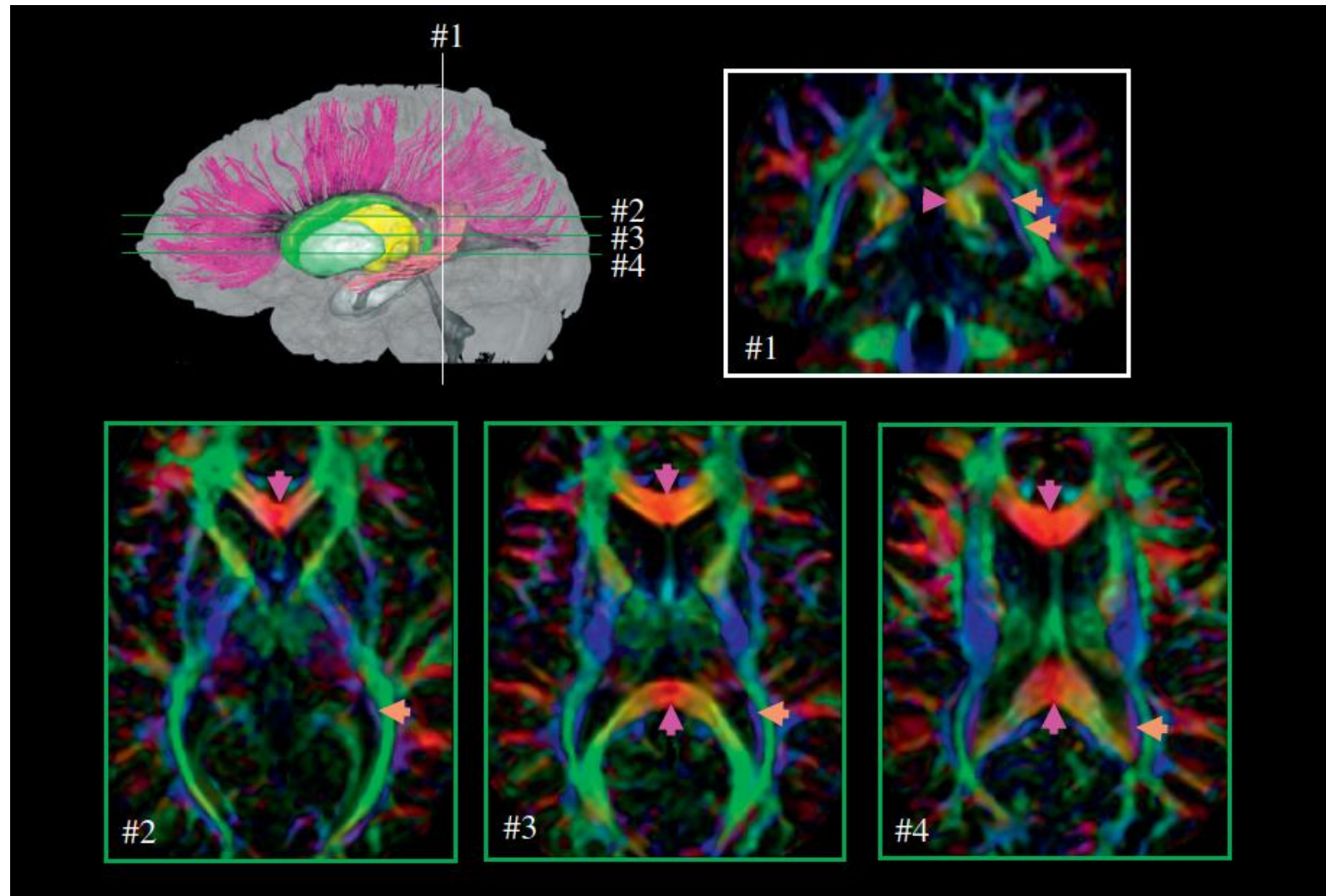
## Determination of White Matter Bundles





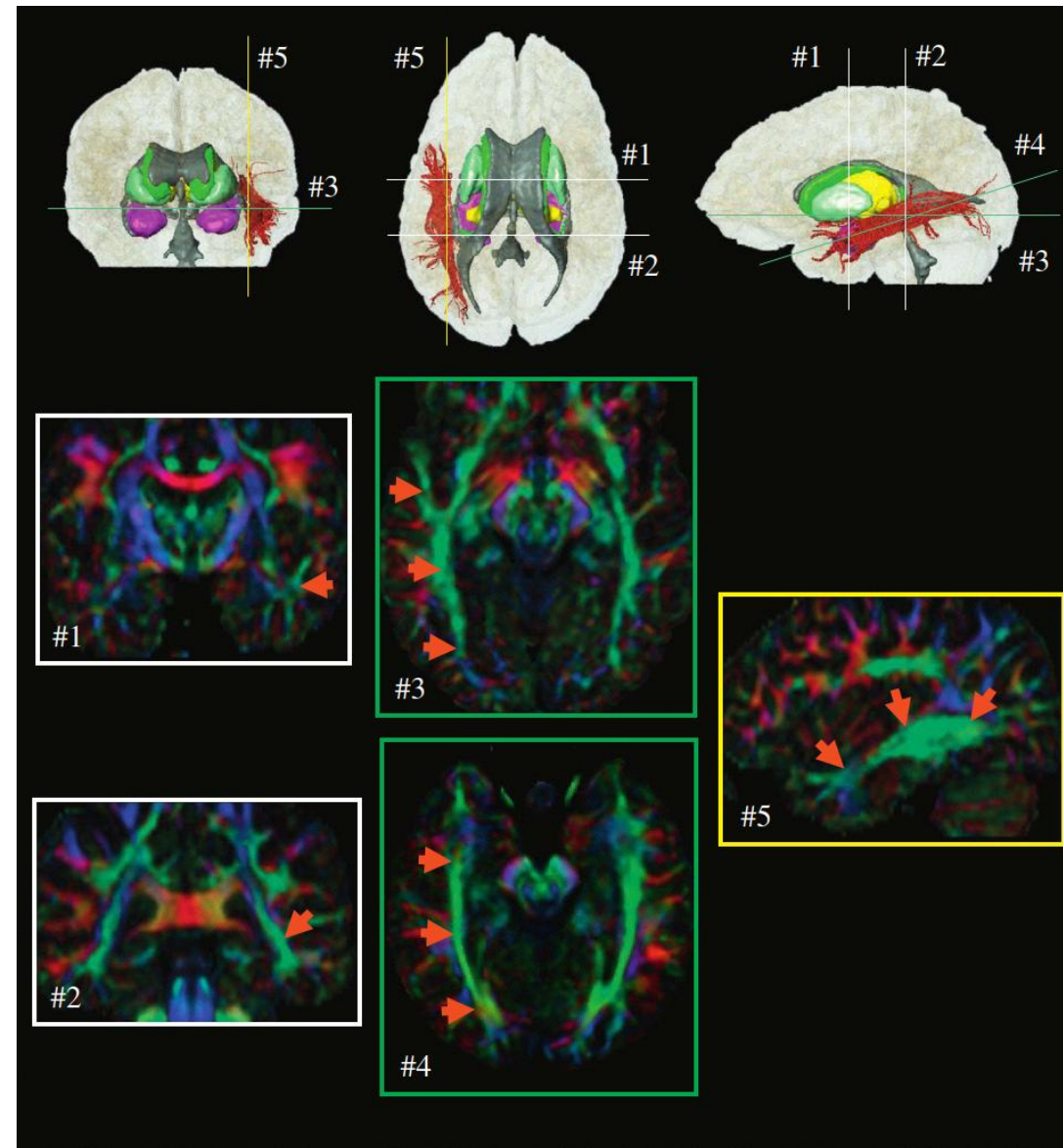
[Oishi et al., 2011]

**Trajectory of the Corticospinal Tract**



[Oishi et al., 2011]

## Trajectory of the Corpus Callosum

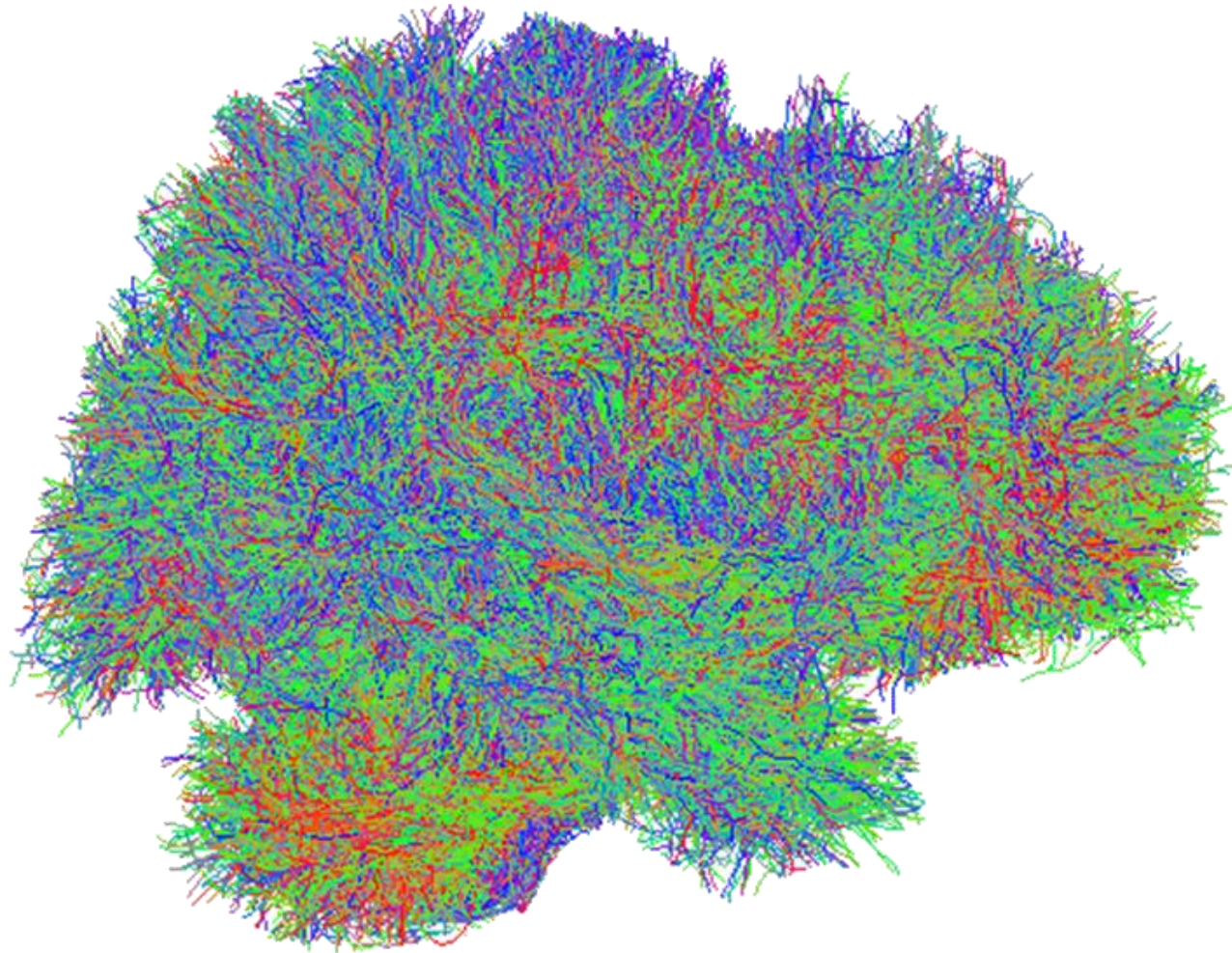


[Oishi et al., 2011]

## Trajectory of the Inferior Longitudinal Fasciculus



# [dMRI: White Matter Tractography]

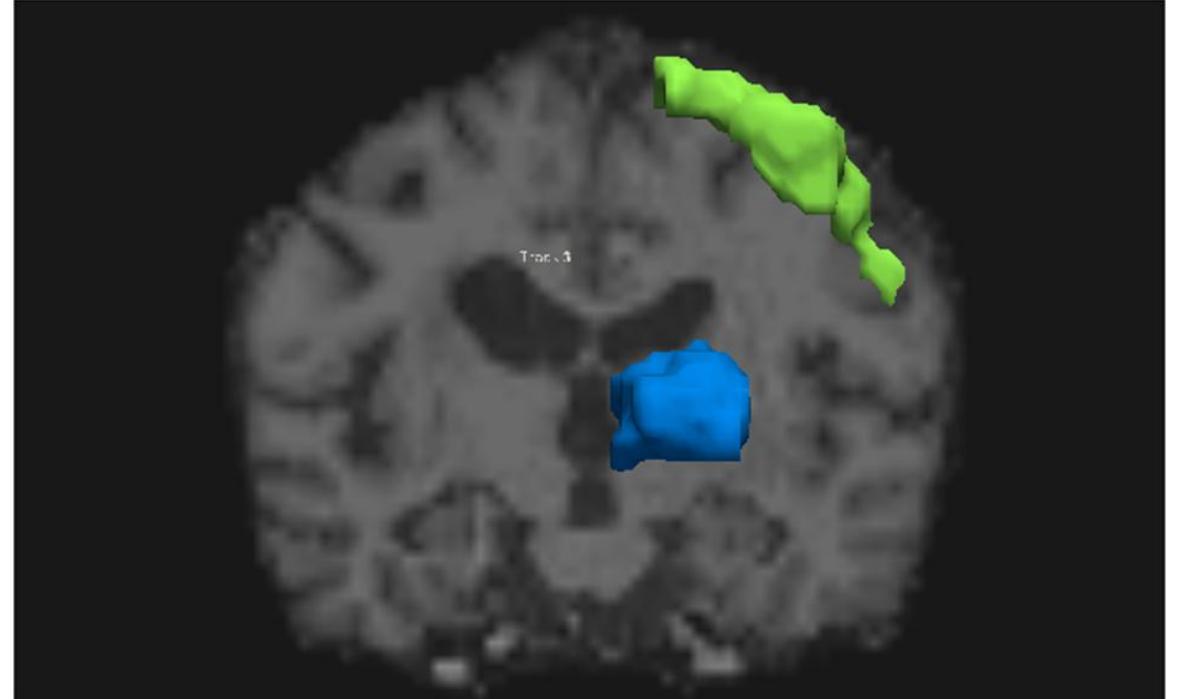
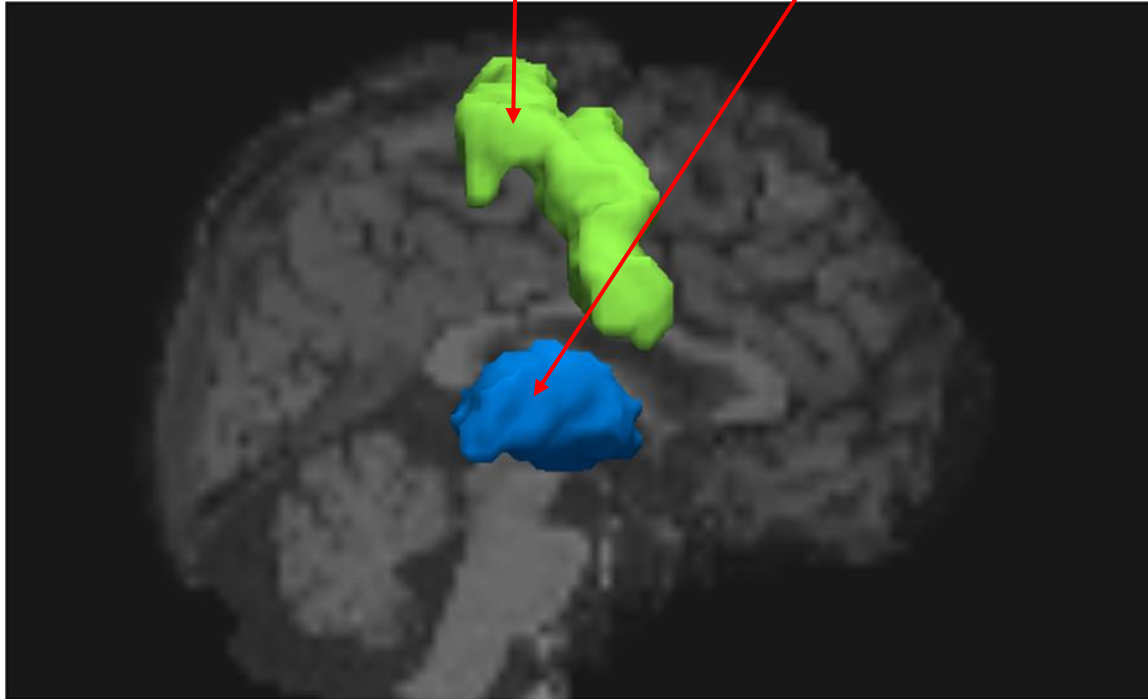


1,500,000 streamlines

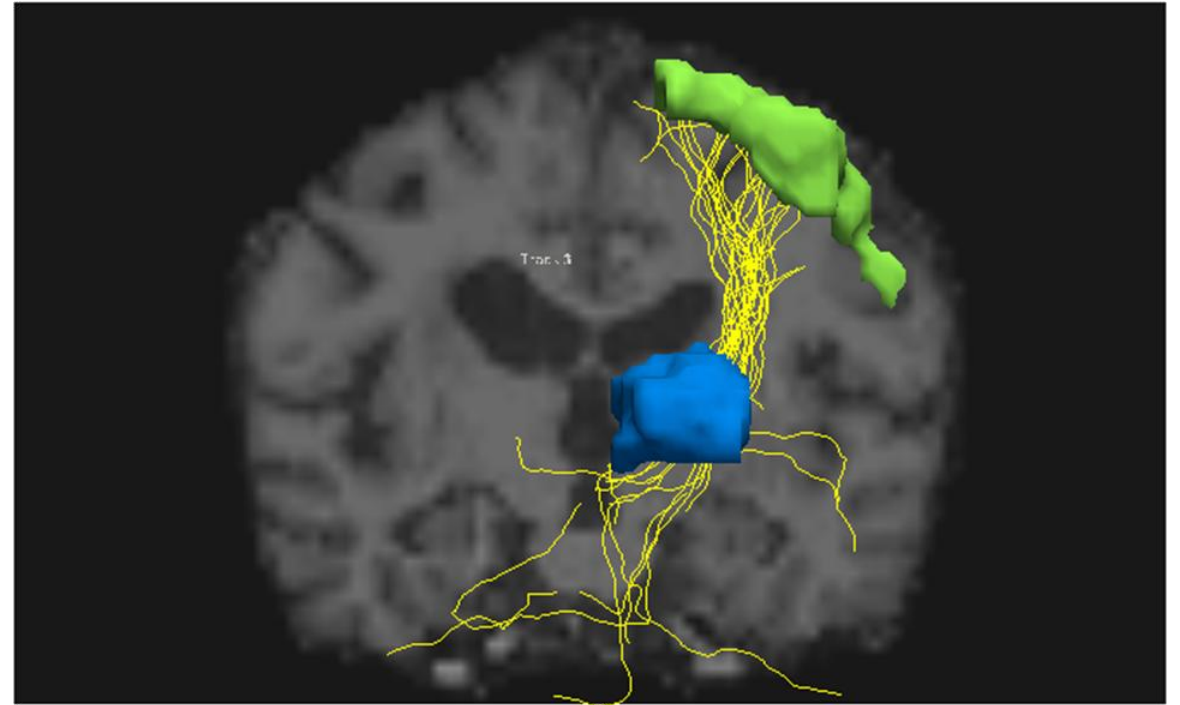
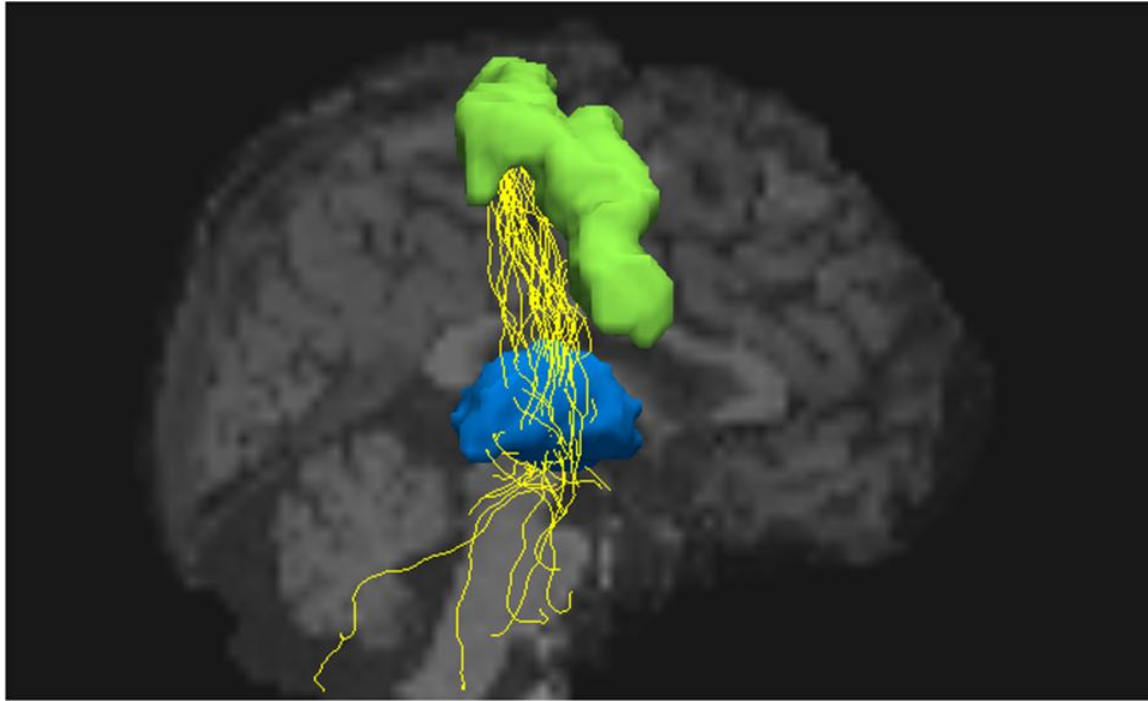
**Whole Brain White Matter Tractography**

Precentral gyrus

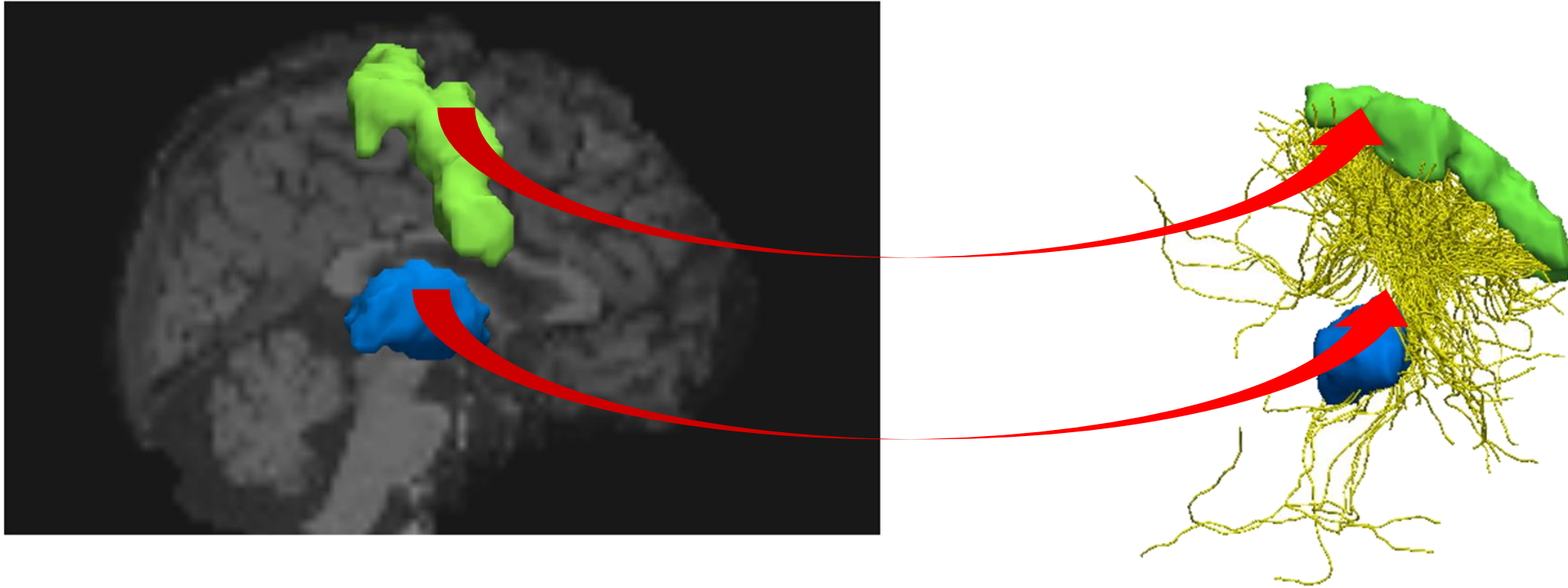
Thalamus



**Terminations of Streamlines**



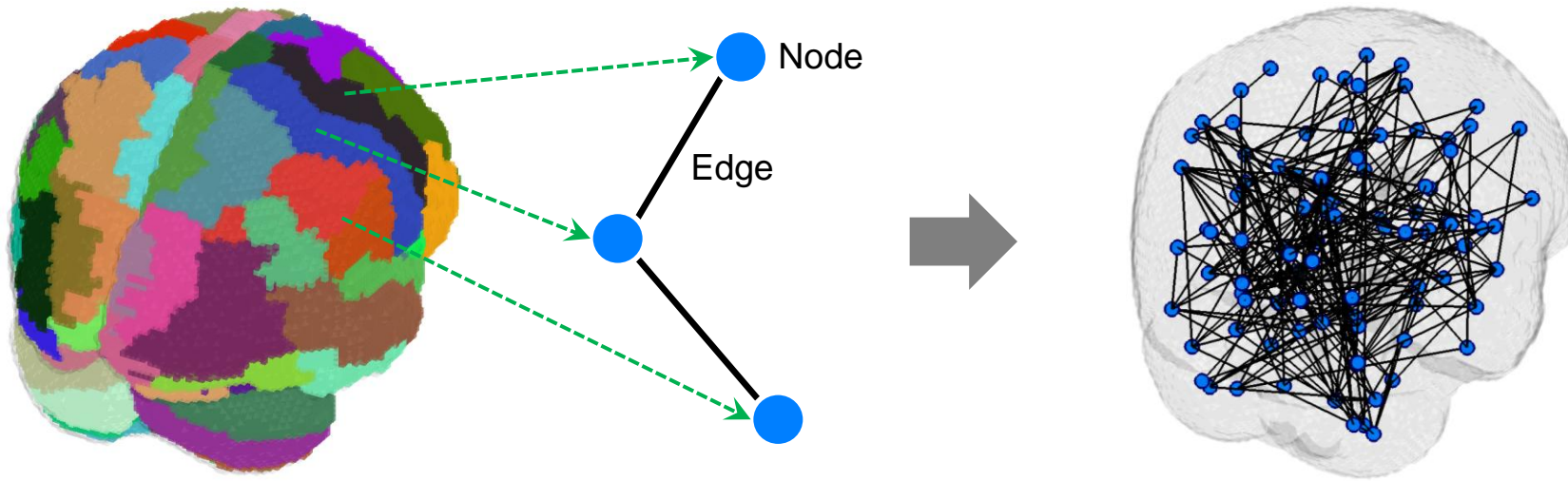
**Generated Streamlines**

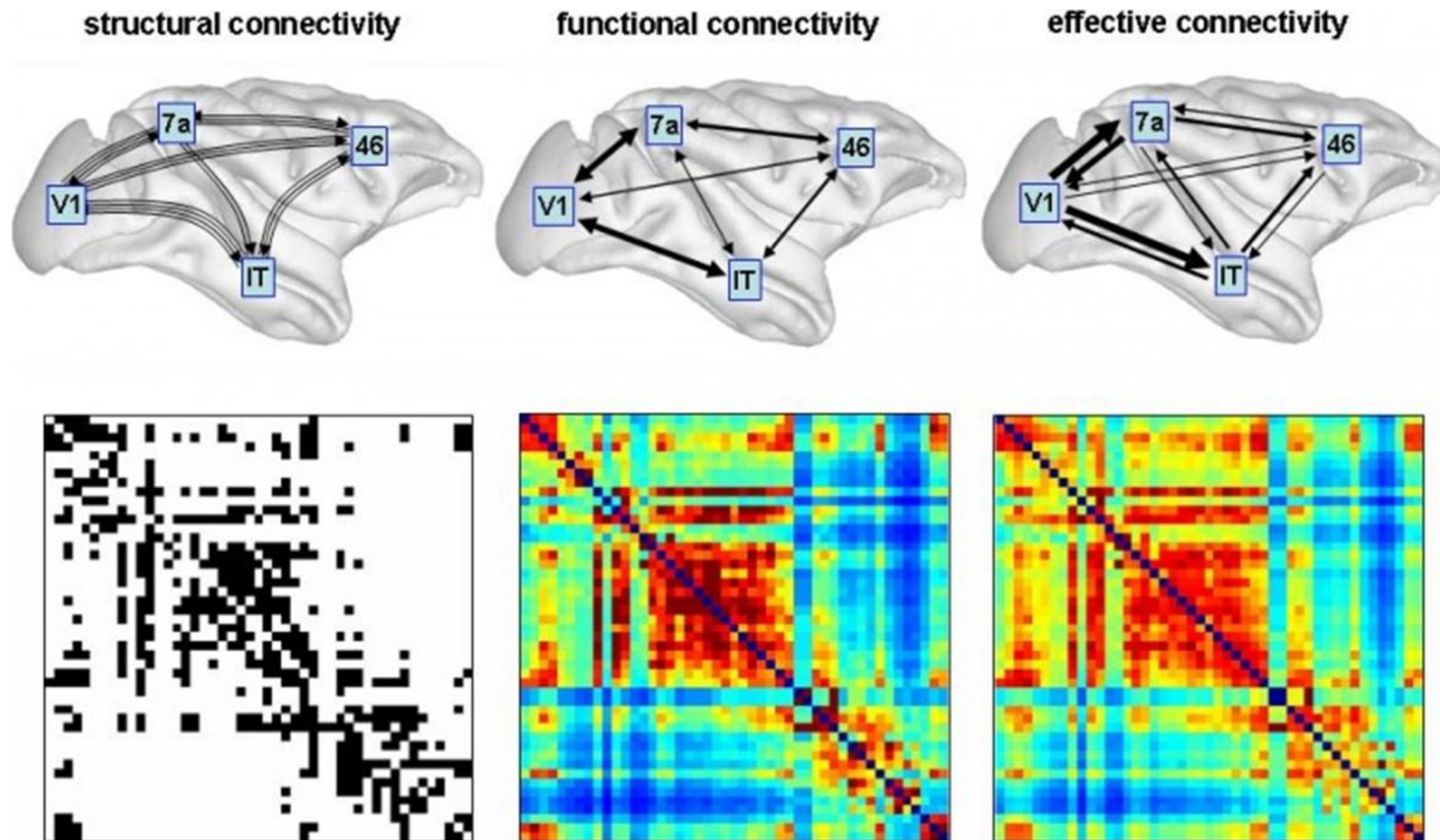


**Determination of White Matter Tracts**



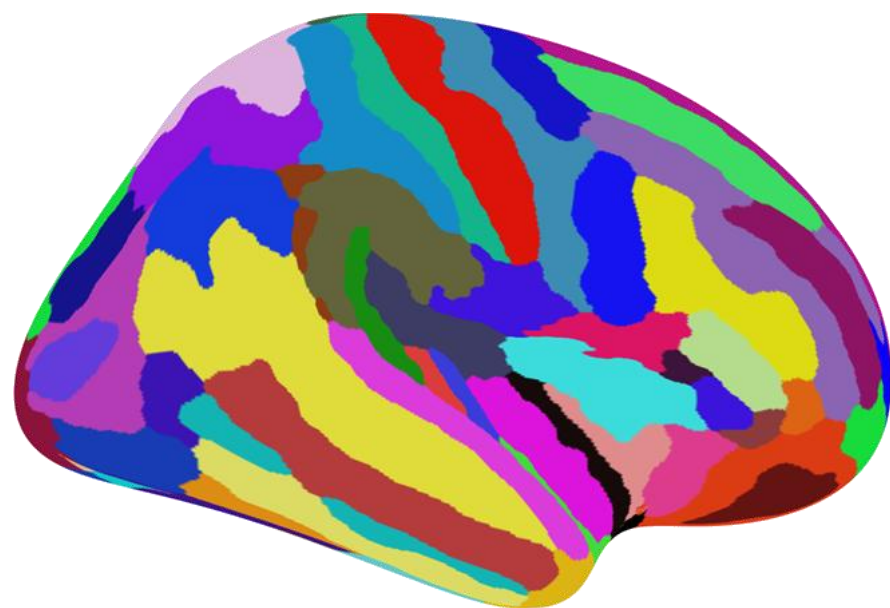
- Network
  - Set of nodes and edges
    - Nodes: pre-defined areas
    - Edges: connectivity (white matter streamlines) between areas



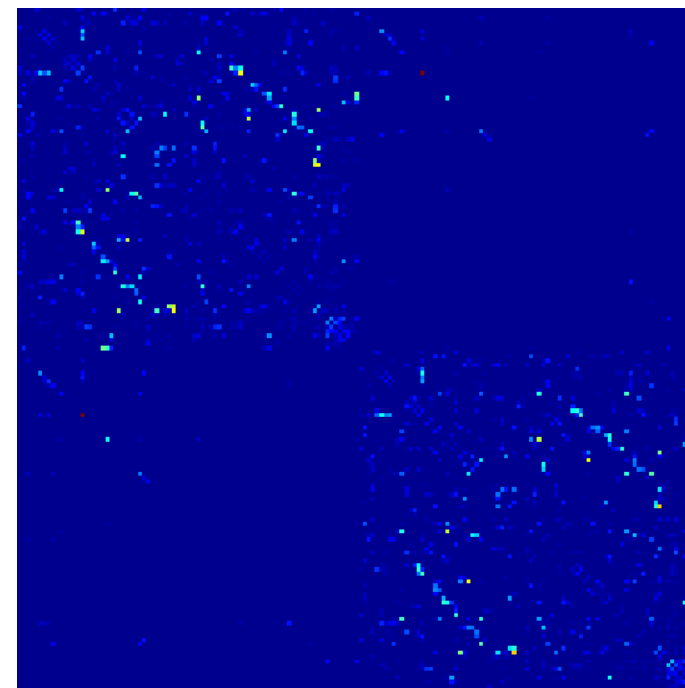


[Honey et al., 2007]

## Modes of Brain Connectivity

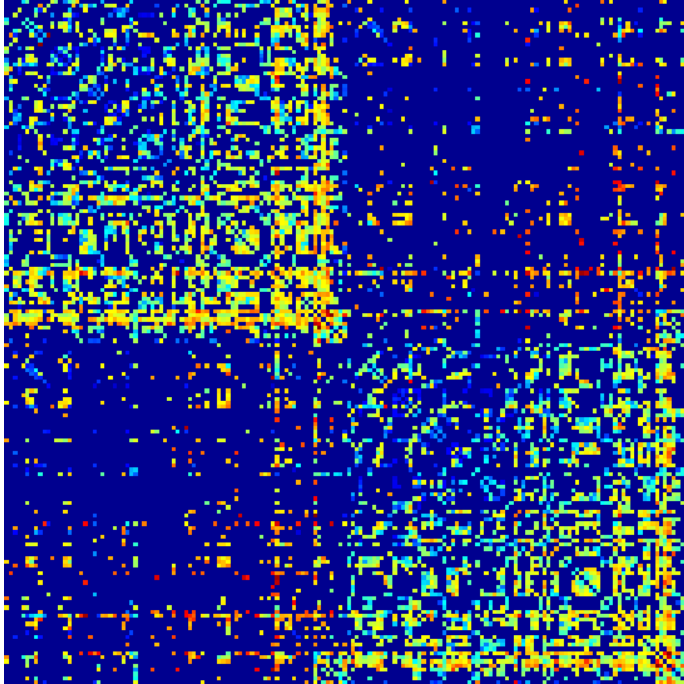


White matter streamlines

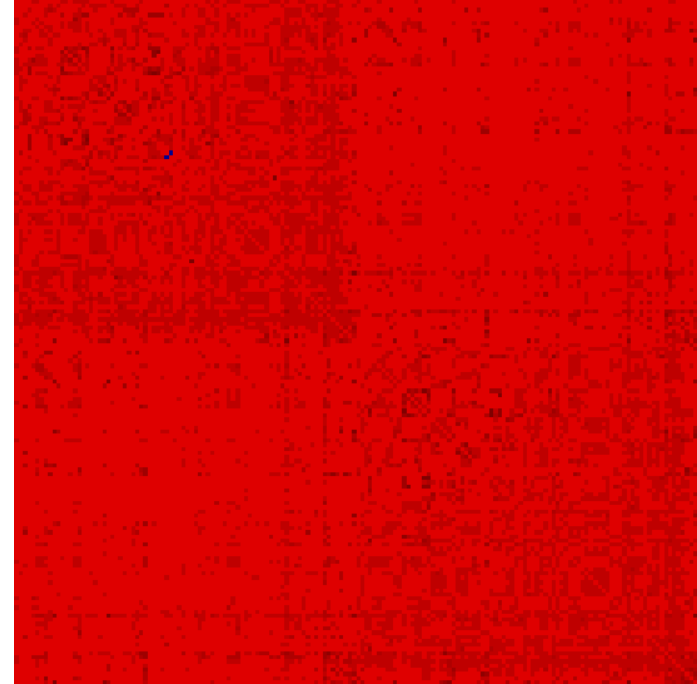


Streamline count

**Structural Network or Connectome**



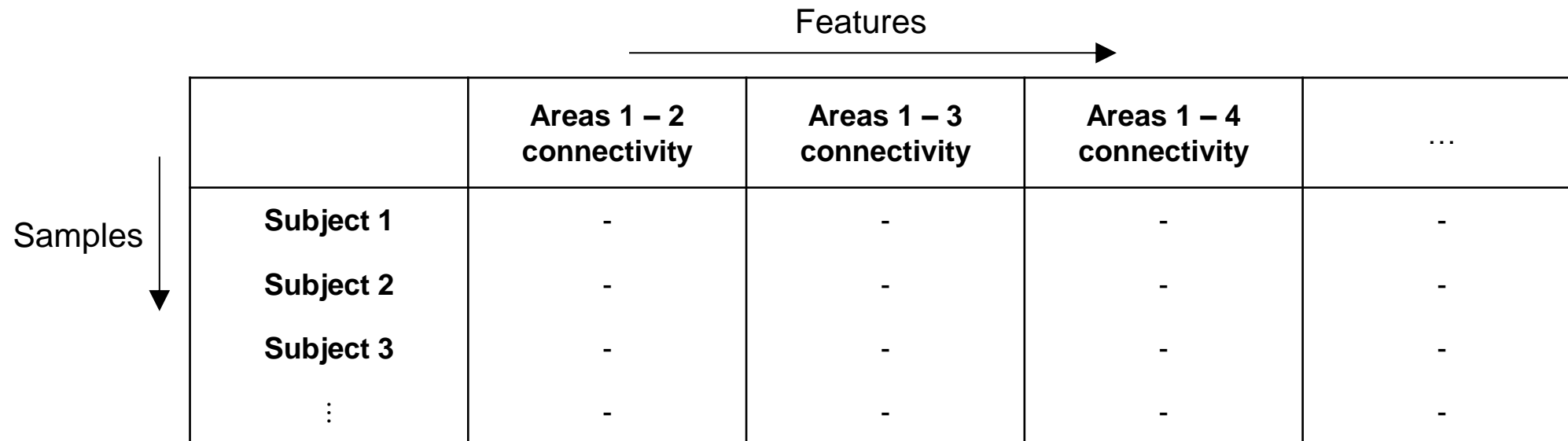
FA



MD

**Structural Network based on Diffusion Tensor Metrics**

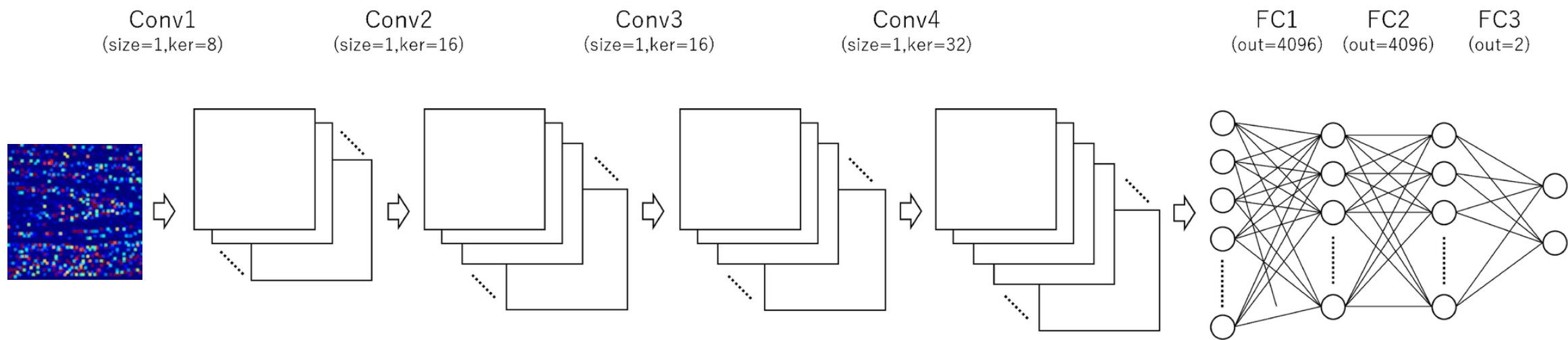
- Input to machine learning models
  - Table of area-to-area connectivity (white matter streamlines) values



The diagram shows a table representing area-to-area connectivity values. A horizontal arrow labeled 'Features' points to the right above the table. A vertical arrow labeled 'Samples' points downwards to the left of the table.

		Areas 1 – 2 connectivity	Areas 1 – 3 connectivity	Areas 1 – 4 connectivity	...
Samples	Subject 1	-	-	-	-
	Subject 2	-	-	-	-
	Subject 3	-	-	-	-
	⋮	-	-	-	-

- Structural network map

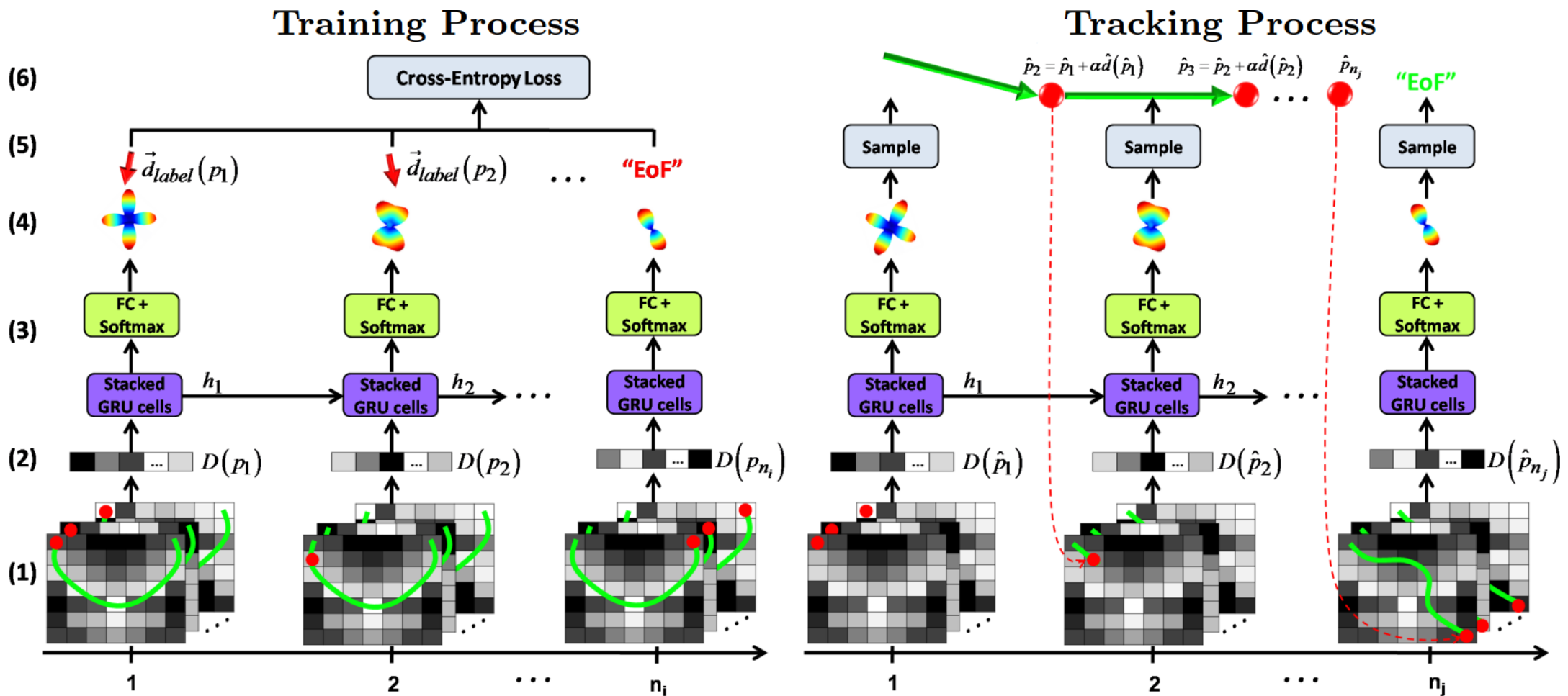


[Yasaka et al., 2021]

## Application of Deep Learning to Structural Network Maps

# Automated White Matter Tractography

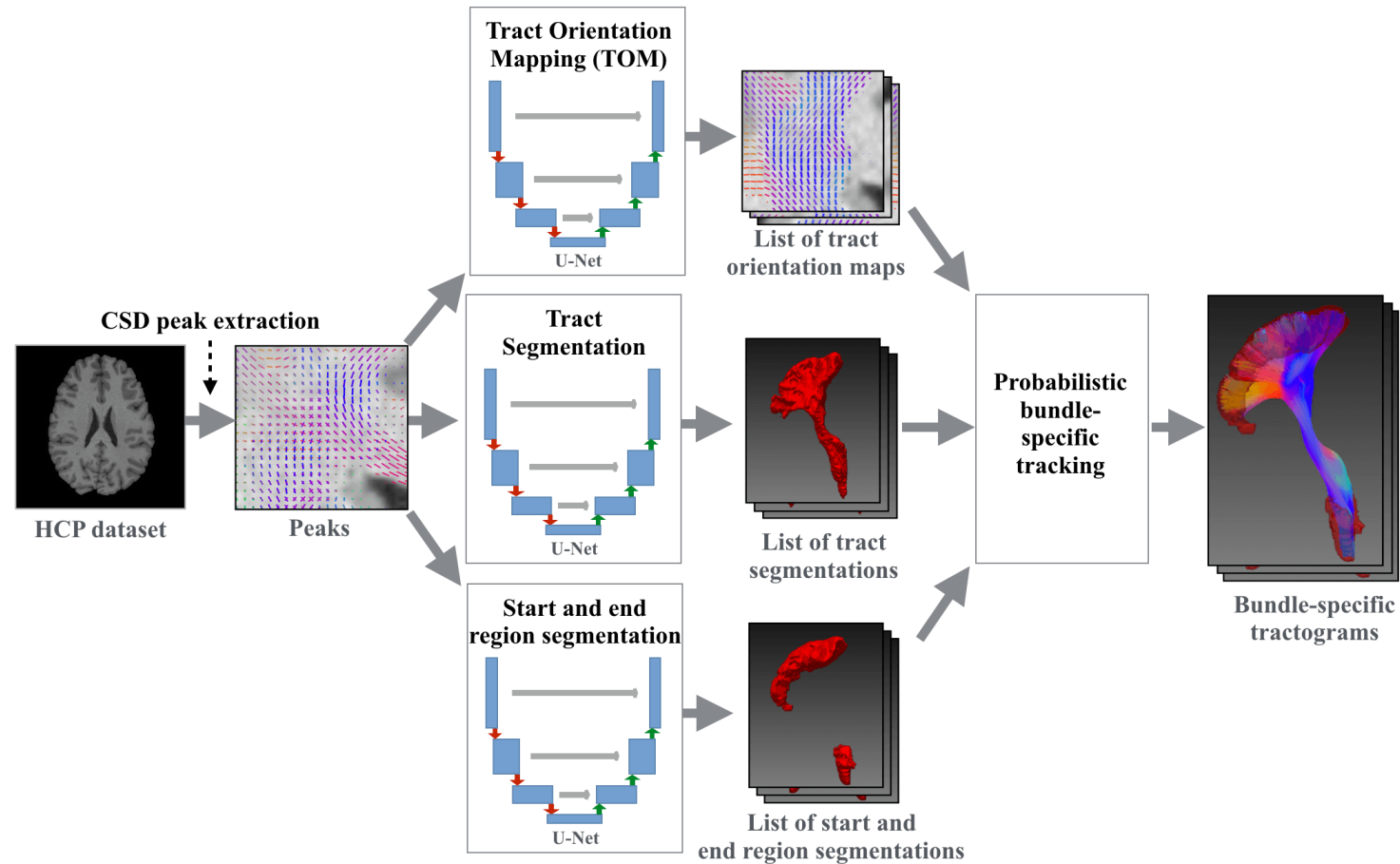
- Employs neural networks trained on large diffusion-weighted MRI datasets to identify white matter tracts
- Incorporates tissue segmentation to improve biological plausibility



[Benou & Riklin-Raviv, 2018; <https://github.com/itaybenou/DeepTract>]

## DeepTract: White Matter Tracking





[Wasserthal et al., 2018; <https://github.com/MIC-DKFZ/TractSeg>]

## TractSeg: White Matter Tract Segmentation