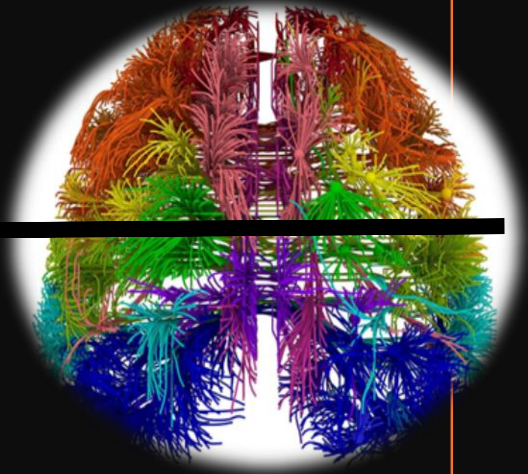
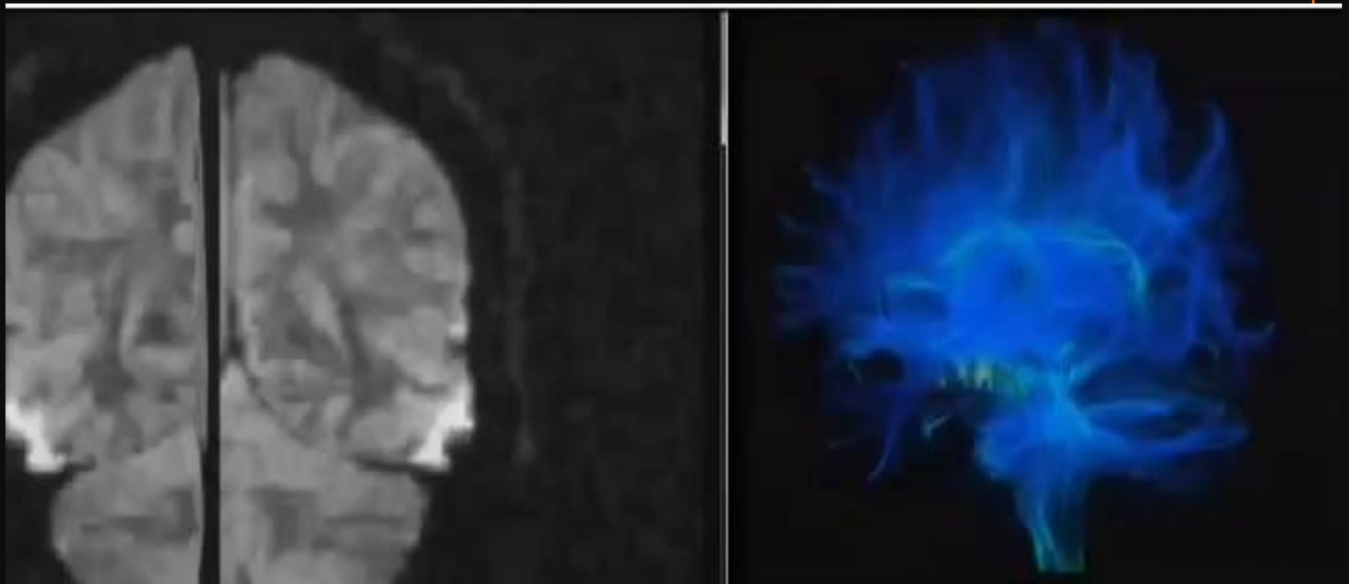
AI-Powered Tractography: Unveiling the Pathways of the Brain from Diffusion MRI

Mahdad Esmaeili, PhD.
Postdoc researcher at AI Virtanen institute
Eastern university of Finland.
Assistant professor of Biomedical
engineering department of Tabriz
university of medical science

"Nothing better defines the function of a neuron than its connections"
Marsel Mesulam (2006)



- **To better understand the brain, we need to understand its structure and connections, which fundamentally involve white matter**

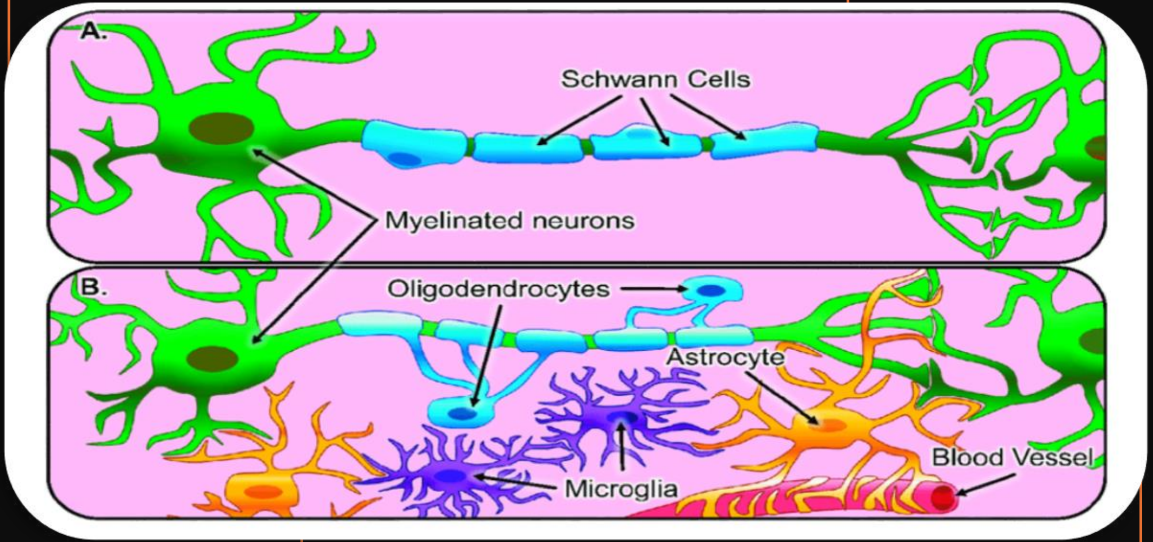


Microstructure of White Matter

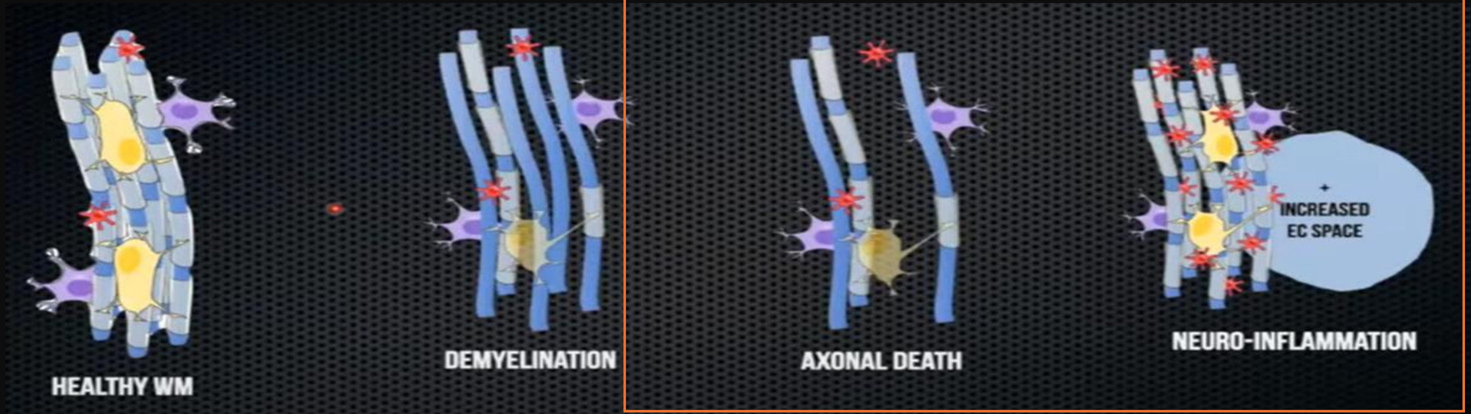
- White matter is **very unique Biologically** and Anatomically

- The dream is to have **biomarkers** or **quantitative measures** that can detect whether a bundle of axons is healthy, with healthy myelin and a supportive environment, or if there are **anomalies**:

- **Demyelination**
- **Axonal loss**
- **Axons swelling**
- **Neuroinflammation**

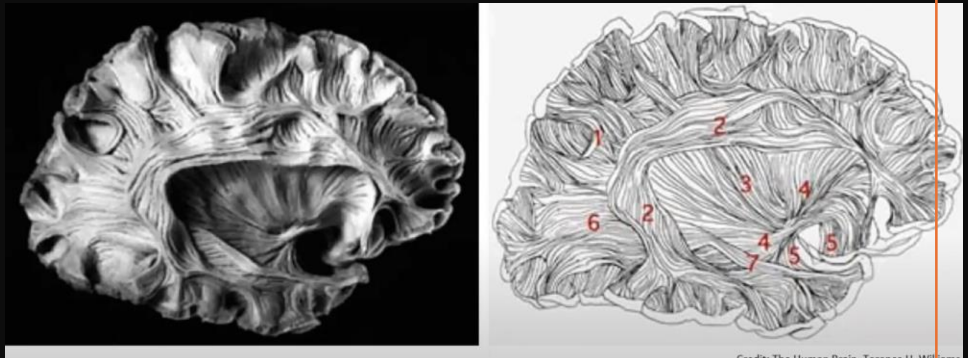


- *Figure adapted from 'Electrospun Fiber Scaffolds for Engineering Glial Cell Behavior to Promote Neural Regeneration*

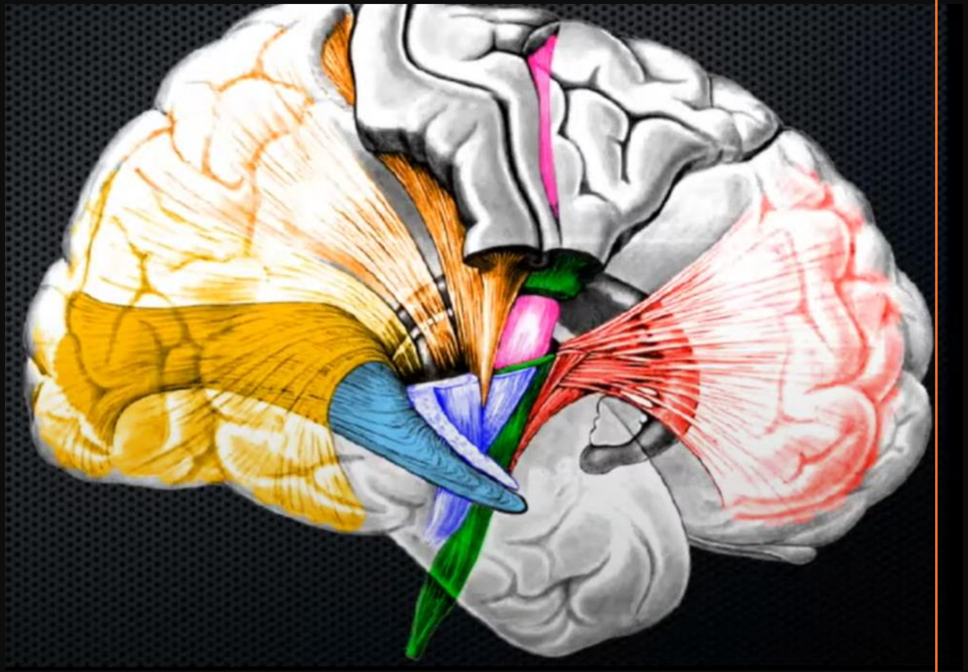


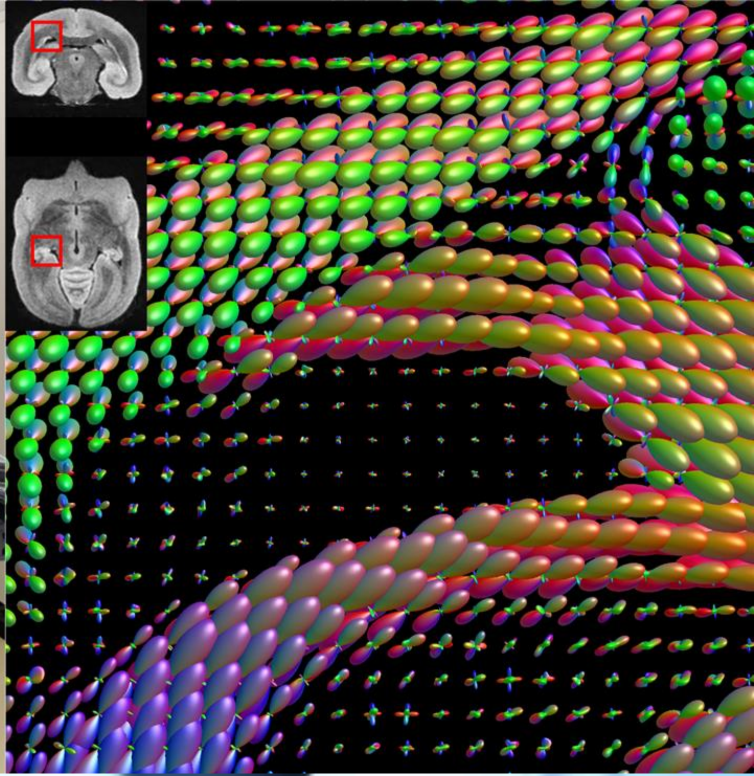
Macrostructure of White Matter

- White matter also has a **macrostructural organization**: axons organize themselves in **families** or **bundles** (fascicles)



Credit: The Human Brain. Terence H. Williams

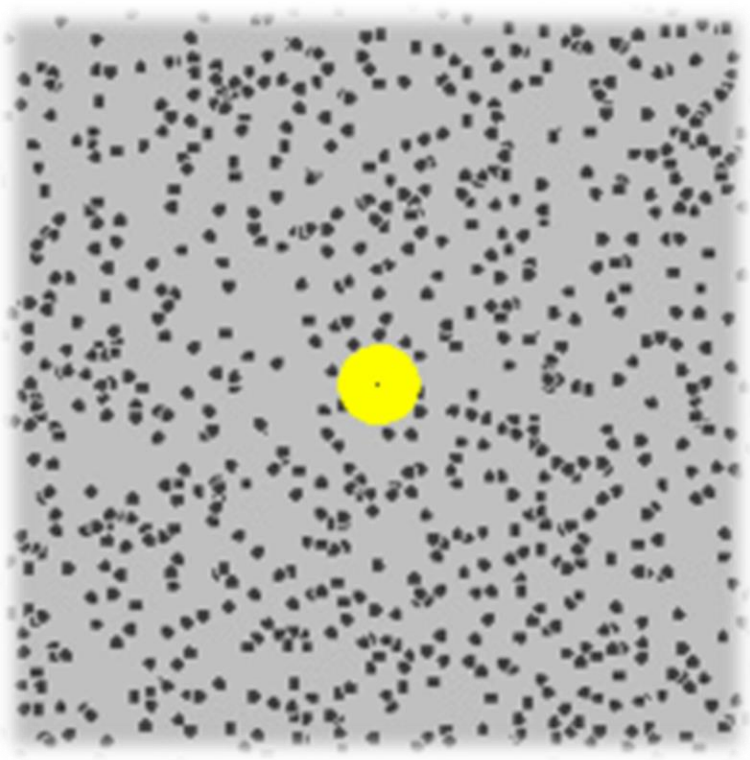




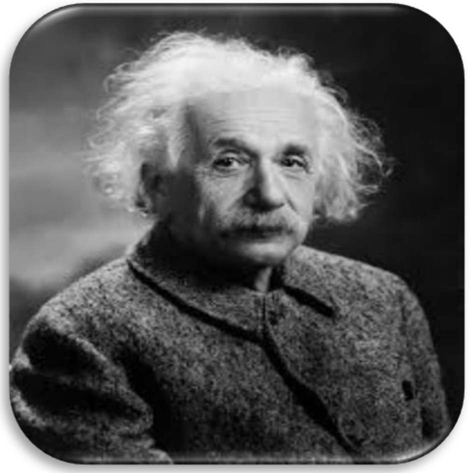
Why Diffusion

How do we **quantitatively** assess this complexity?

Diffusion is Essentially a R**andom** W**alk**



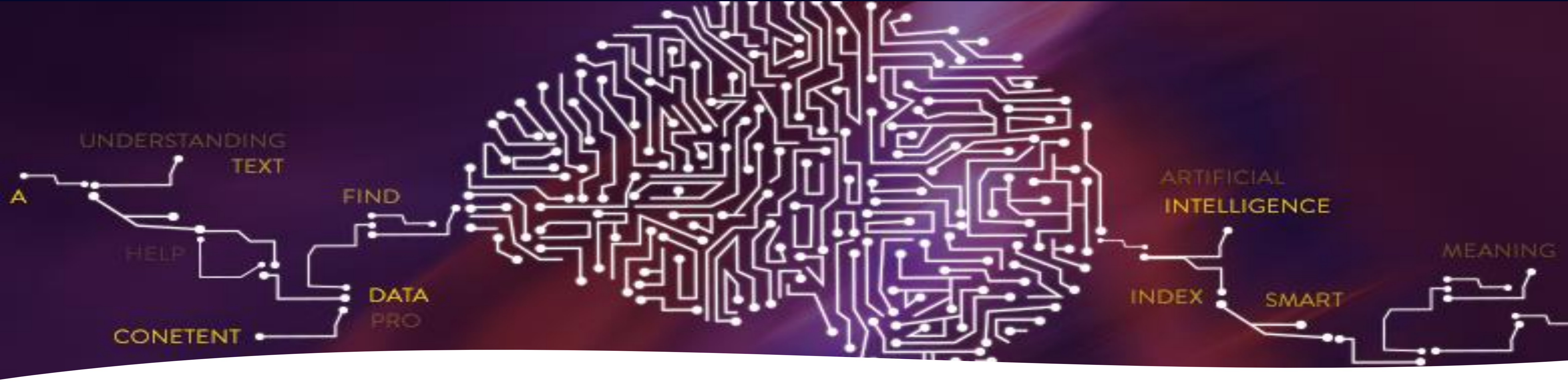
Robert Brown,1827
Brownian motion



Albert Einstein,1905
Derived the Diffusion Equation

Google Maps Analogy

Curtesy of G. Zhang & D Alexander (UC London)]



Challenges That Necessitate Machines

- **Number of Neurons**
- **Total Length of Axons**
- **Number of Synapses**
- **High Dimensionality of data**
- **Need for Precision**
- **Visualization and Interpretation**

The main idea is the Apparent Diffusion Coefficient (ADC)

Denis Le Bihan
1985

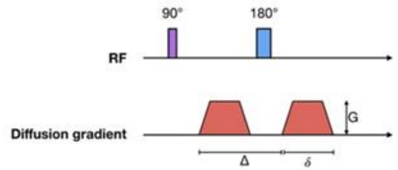
Le Bihan D, 1985
✓ *b factor*
✓ *ADC concept*

A key paper by **Denis Le Bihan** introduced **Diffusion-Weighted Imaging (DWI)** in the French Academy of Science

By acquiring enough data, we can find a **normal ADC** for brain tissue; any **tumor, stroke, or other abnormality** causes ADC to deviate from that norm.

b value

$$b = \gamma^2 G^2 \delta^2 (\Delta - \frac{\delta}{3})$$



γ = gyromagnetic ratio
G = magnitude of the two balanced DW gradient pulses
δ = width of the two balanced DW gradient pulses
Δ = time between the two balanced DW gradient pulses

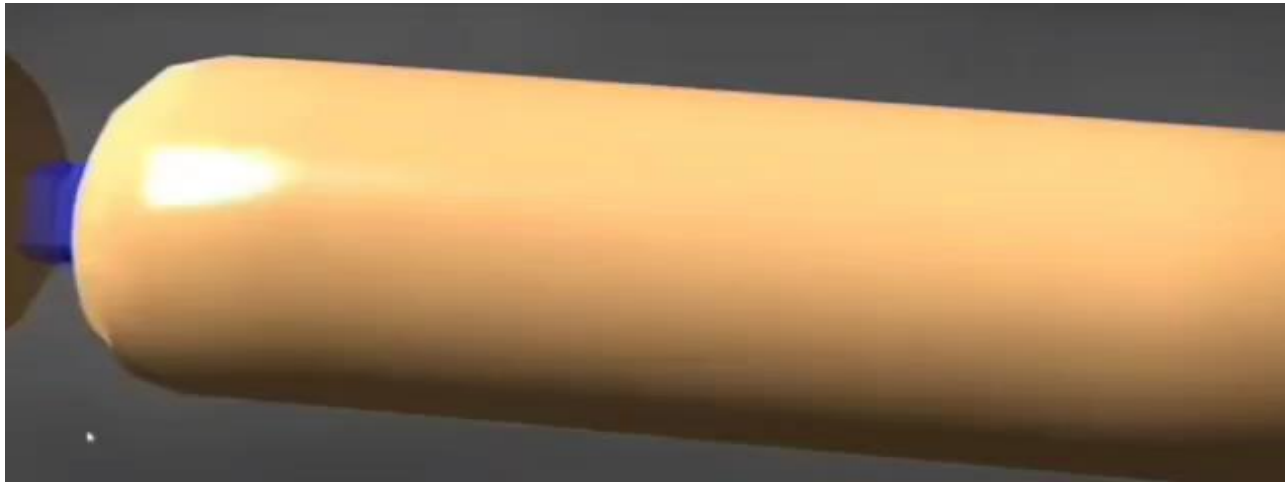
Relationship between signal of b = 0, DWI and ADC

$$S_{DWI} = S_{b=0} \times e^{(-b \times D)}$$

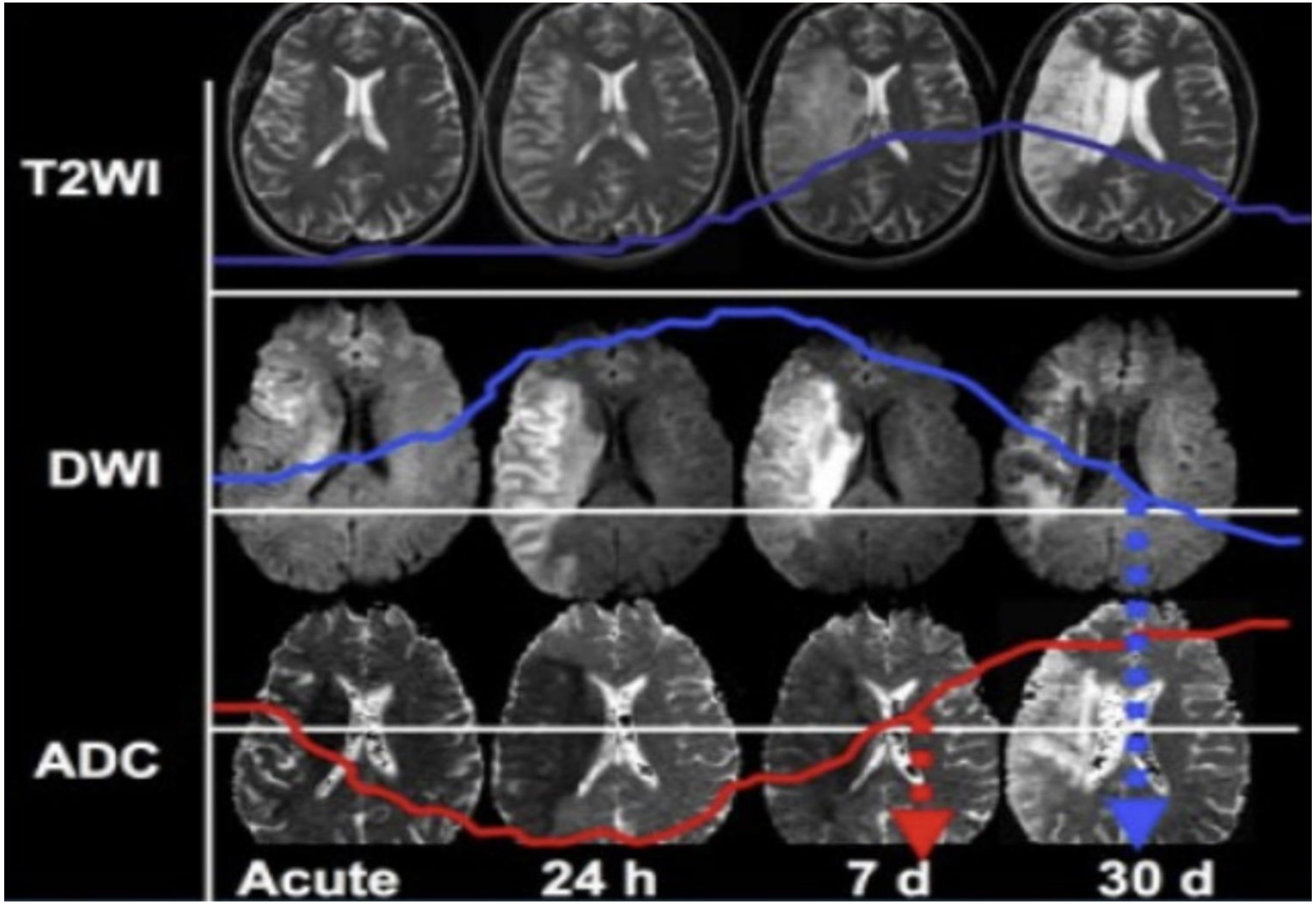
equivalent to...

$$D = -\frac{1}{b} \times \ln\left(\frac{S_{DWI}}{S_{b=0}}\right)$$

S_{DWI} = signal intensity of isotropic DWI
$S_{b=0}$ = signal intensity of b = 0
b = b value
D = apparent diffusion coefficient (ADC)

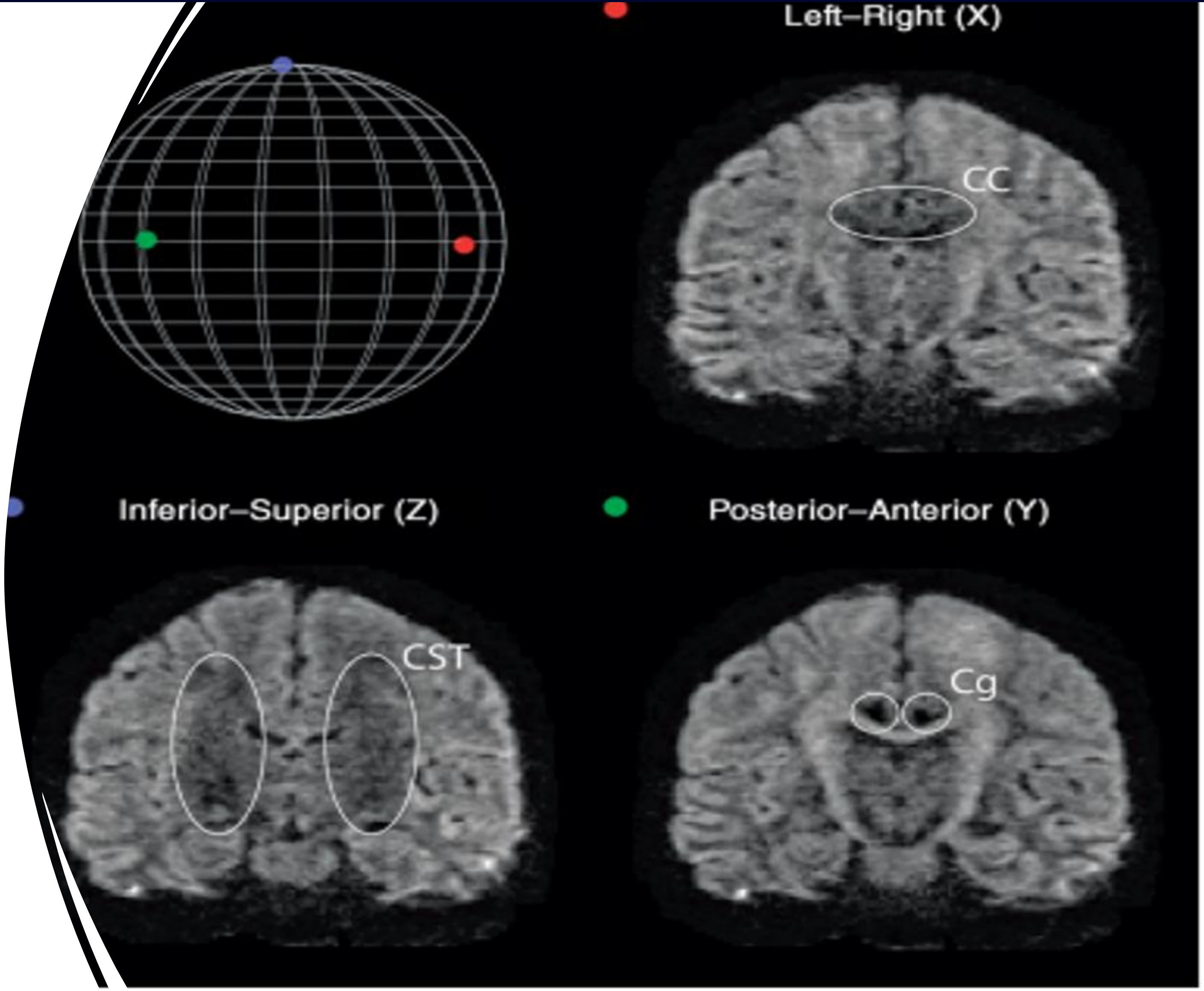


Stroke Imaging



Beyond ADC: Orientation and White Matter Organization

- Diffusion along X, Y, and Z directions. The signal in the left/right oriented corpus callosum is lowest when measured along X, while the signal in the inferior/superior oriented corticospinal tract is lowest when measured along Z.

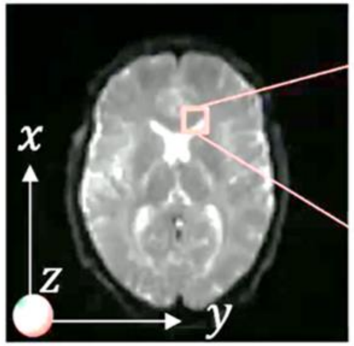


Diffusion Tensor Imaging (DTI)

- Diffusion Tensor Imaging (DTI) models diffusion in each voxel using a 3*3 tensor:

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

Diffusion Tensor



Peter Basser,1994

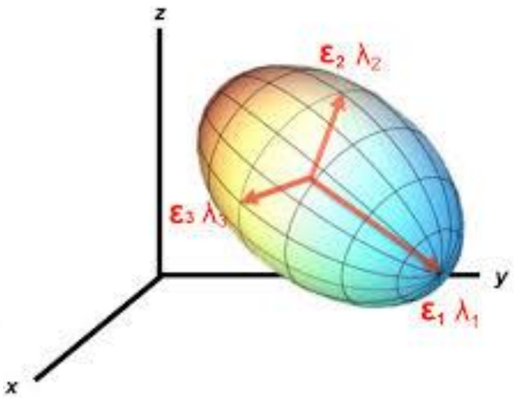
– AD, RD and MD can be more generally computed from eigen-value decomposition

$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix} = [\boldsymbol{v}_1 \quad \boldsymbol{v}_2 \quad \boldsymbol{v}_3] \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \begin{bmatrix} \boldsymbol{v}_1 \\ \boldsymbol{v}_2 \\ \boldsymbol{v}_3 \end{bmatrix}$$

$$AD = \lambda_1 \qquad RD = (\lambda_2 + \lambda_3)/2 \qquad MD = (\lambda_1 + \lambda_2 + \lambda_3)/3$$

$$FA = \sqrt{\frac{3}{2}} \cdot \frac{\sqrt{(\lambda_1 - \mathrm{MD})^2 + (\lambda_2 - \mathrm{MD})^2 + (\lambda_3 - \mathrm{MD})^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

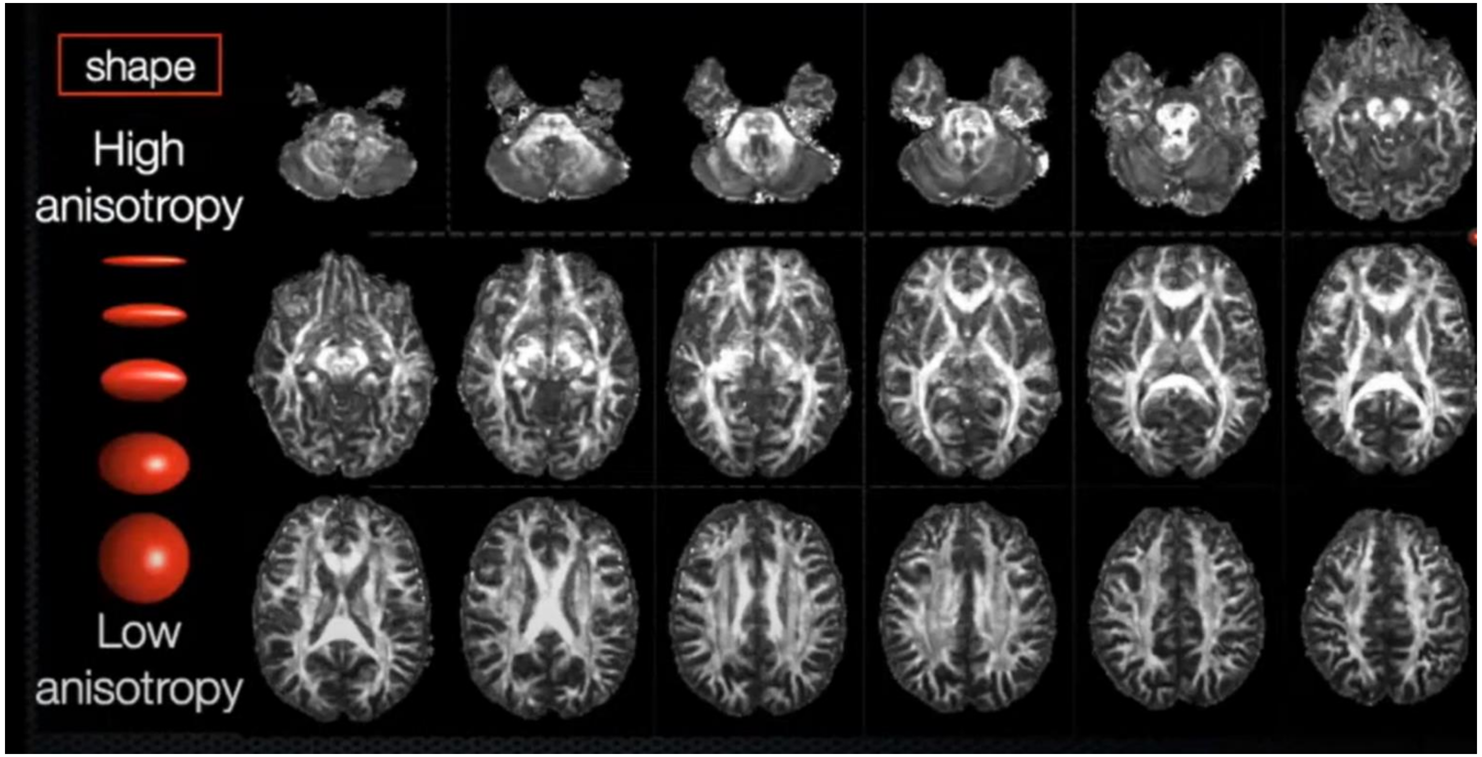
– Ellipsoid representation

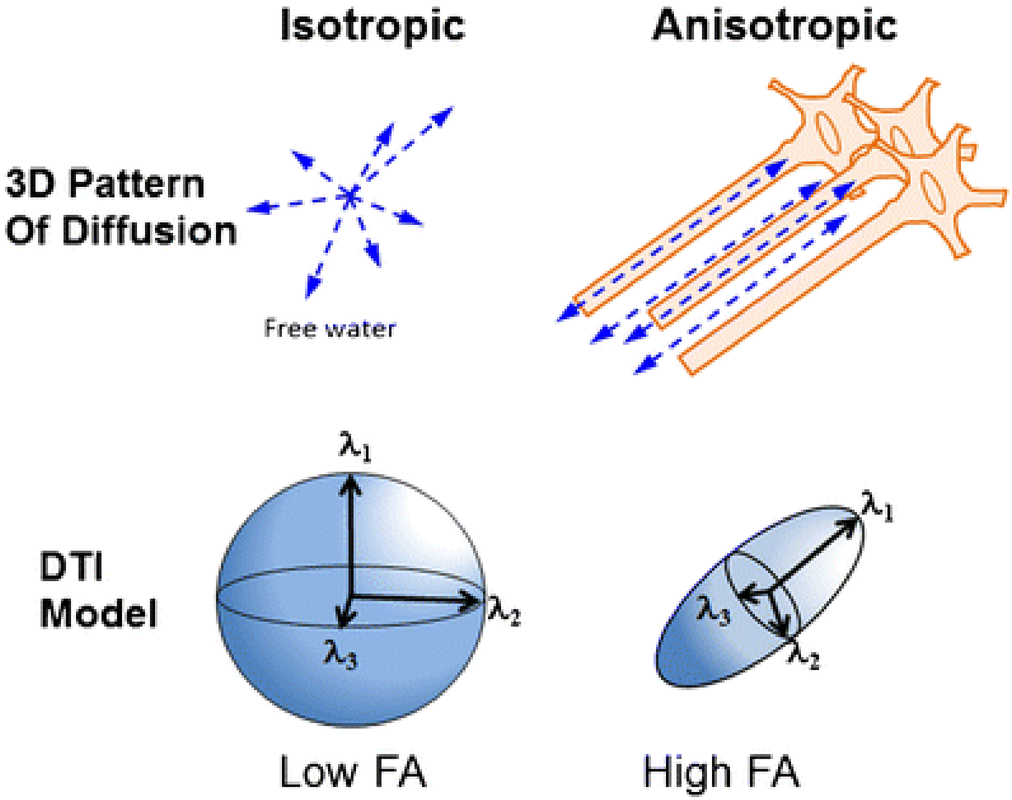


$$S(\mathbf{b}) = S_0 e^{-b\, \mathbf{g}^T \mathbf{D} \mathbf{g}},$$

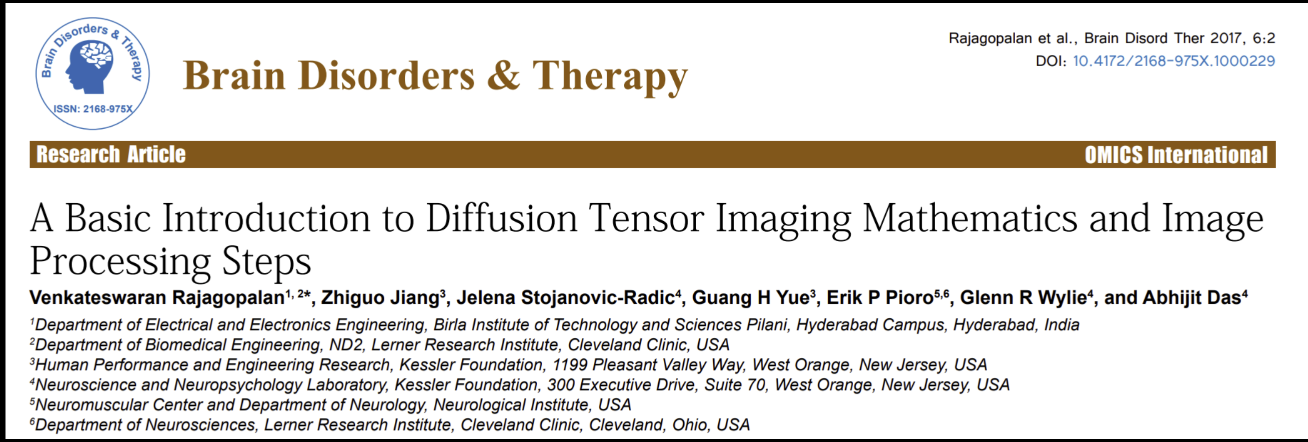
$$\mathbf{g} = [g_x, g_y, g_z]^T$$

Fractional Anisotropy (FA)





Limits of DTI



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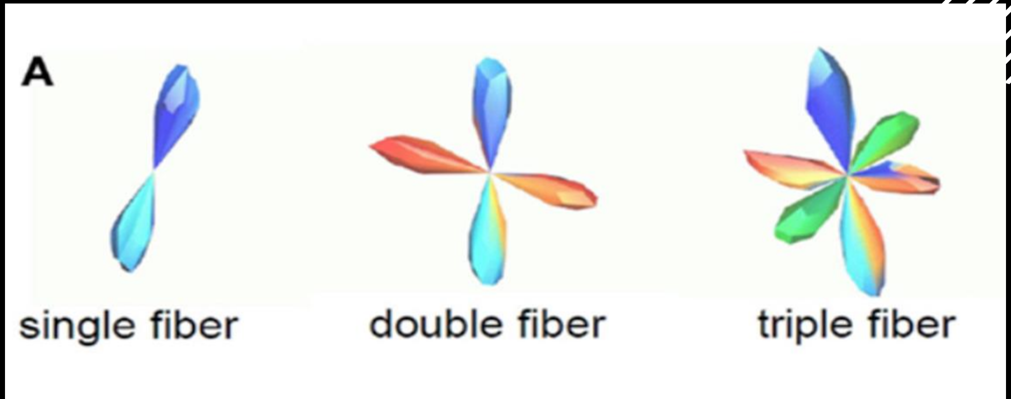
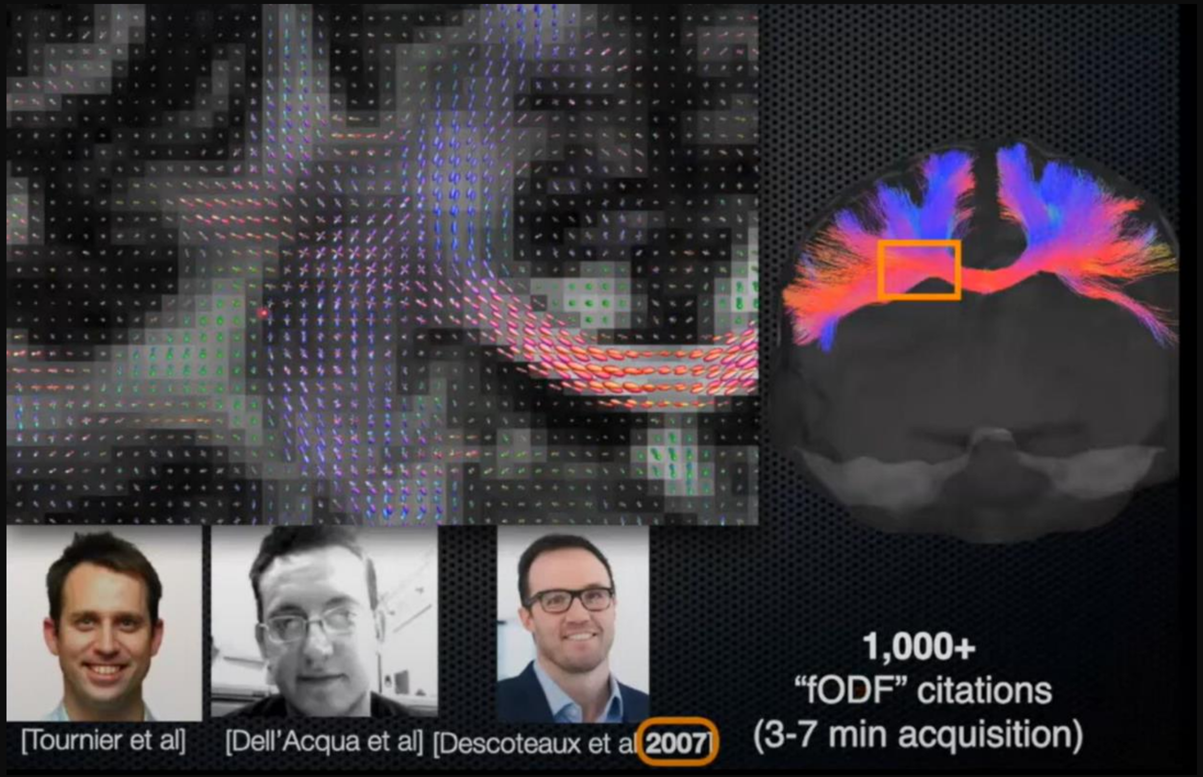
A Basic Introduction to Diffusion Tensor Imaging Mathematics and Image Processing Steps

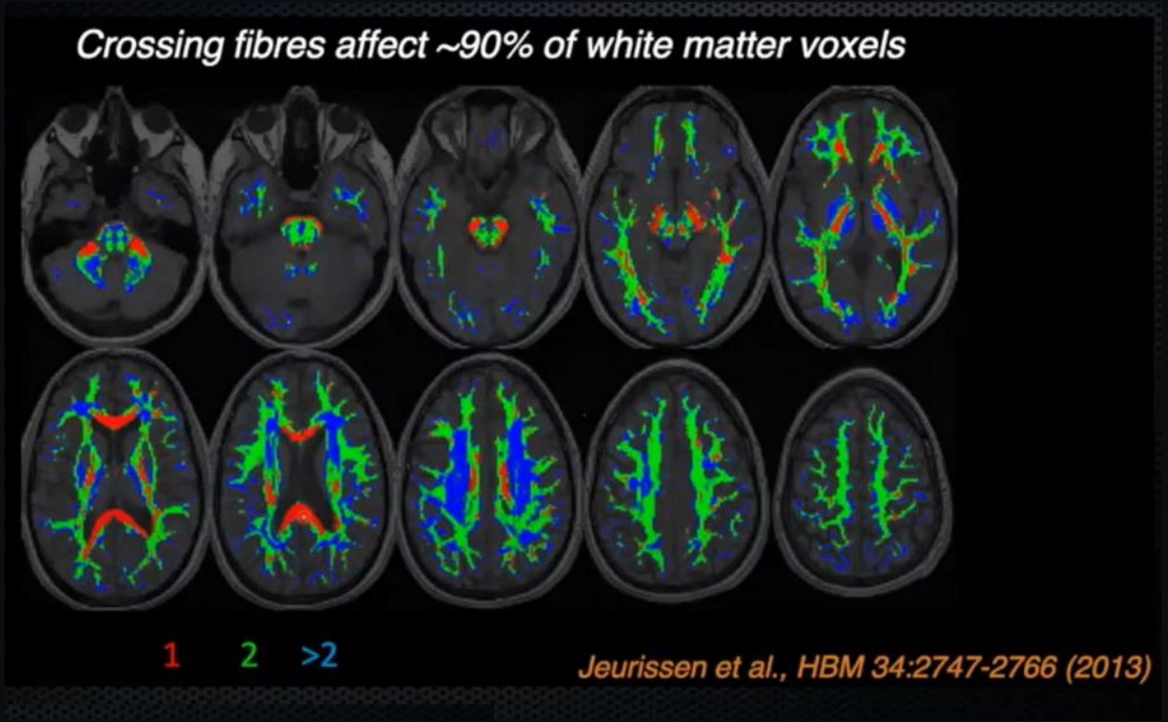
Venkateswaran Rajagopalan[1,2*], Zhiguo Jiang[3], Jelena Stojanovic-Radic[4], Guang H Yue[3], Erik P Pioro[5,6], Glenn R Wylie[4], and Abhijit Das[4]

[1]*Department of Electrical and Electronics Engineering, Birla Institute of Technology and Sciences Pilani, Hyderabad Campus, Hyderabad, India*
[2]*Department of Biomedical Engineering, ND2, Lerner Research Institute, Cleveland Clinic, USA*
[3]*Human Performance and Engineering Research, Kessler Foundation, 1199 Pleasant Valley Way, West Orange, New Jersey, USA*
[4]*Neuroscience and Neuropsychology Laboratory, Kessler Foundation, 300 Executive Drive, Suite 70, West Orange, New Jersey, USA*
[5]*Neuromuscular Center and Department of Neurology, Neurological Institute, USA*
[6]*Department of Neurosciences, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, USA*

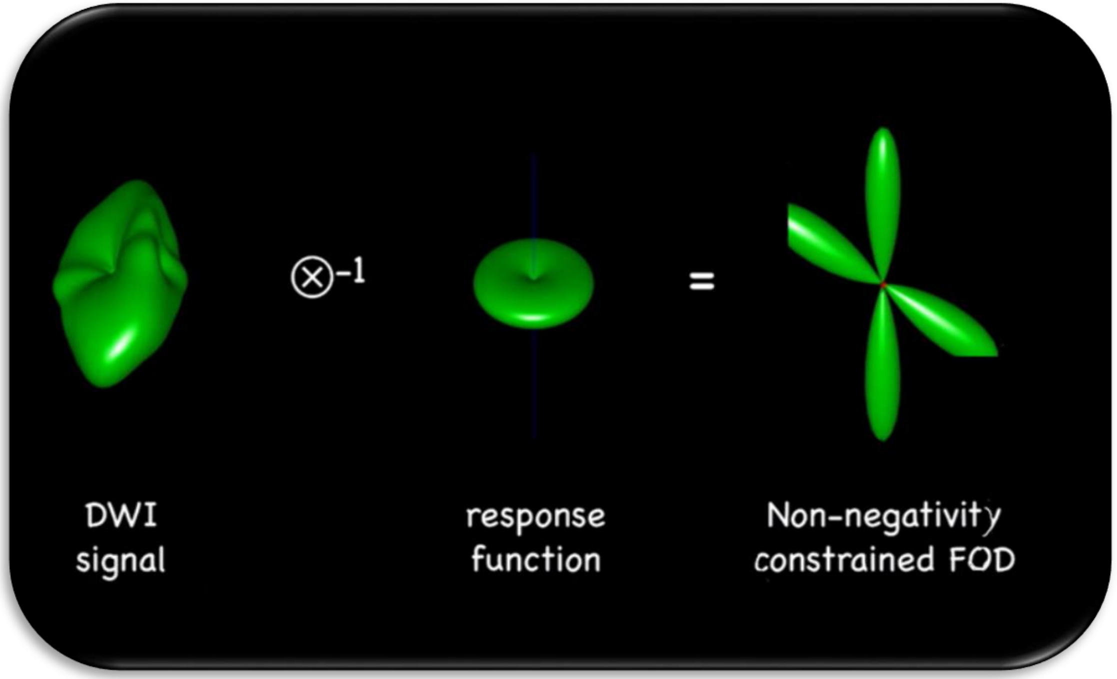


Crossing fibers everywhere





Constrained Spherical Deconvolution (CSD)



Mathematical Model:

$$S(\mathbf{q}) = \int_\Omega E(\mathbf{q}, \mathbf{r}) F(\mathbf{r}) d\mathbf{r},$$

where:

- $S(\mathbf{q})$: Measured diffusion signal.
- $E(\mathbf{q}, \mathbf{r})$: Single-fiber response function (kernel).
- $F(\mathbf{r})$: Fiber Orientation Distribution (FOD).

Model the Problem: The FOD is estimated by solving the optimization problem:

$$\mathbf{F} = \arg\min_{\mathbf{F}} \|\mathbf{S} - \mathbf{E}\mathbf{F}\|^2 + \lambda R(\mathbf{F}),$$

subject to:

$$F(\mathbf{r}) \geq 0 \quad \forall \mathbf{r}.$$

Instead of solving the optimization problem iteratively, the network approximates:

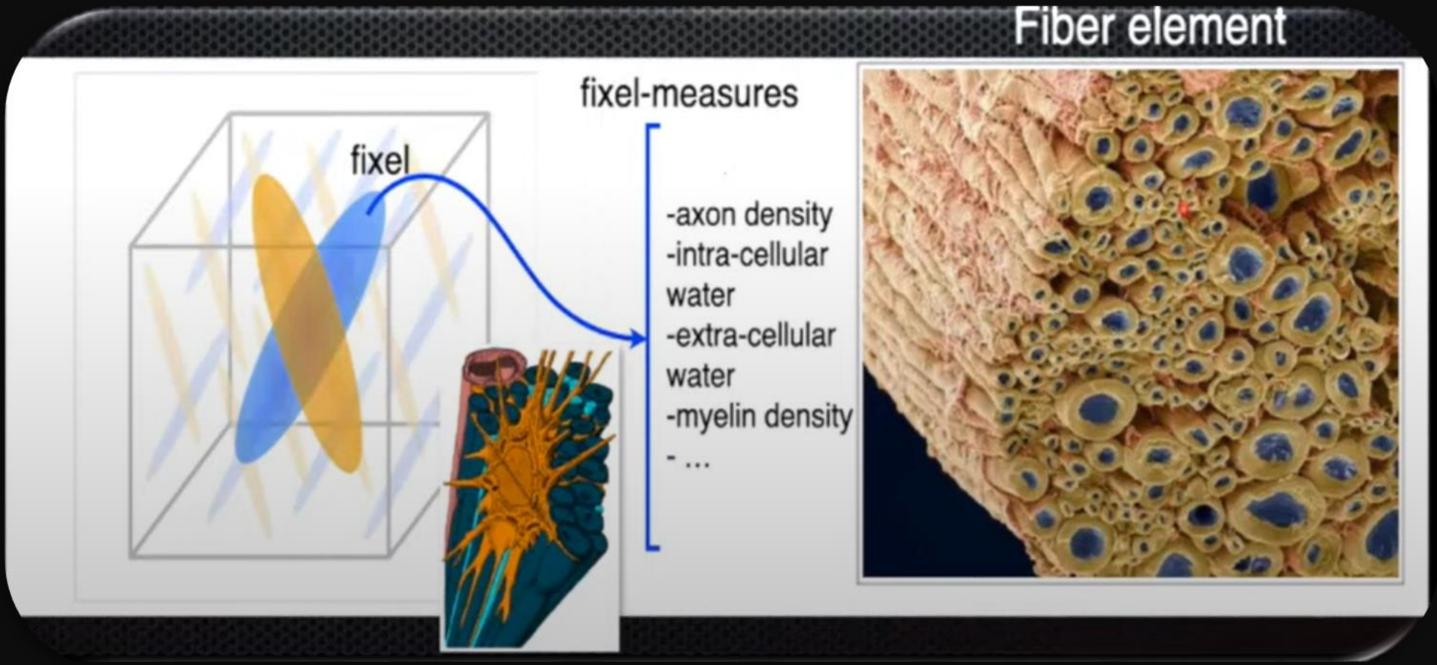
$$\mathbf{F} \approx f_{\text{NN}}(\mathbf{S}),$$

where f_{NN} is parameterized by neural network weights Θ learned by minimizing:

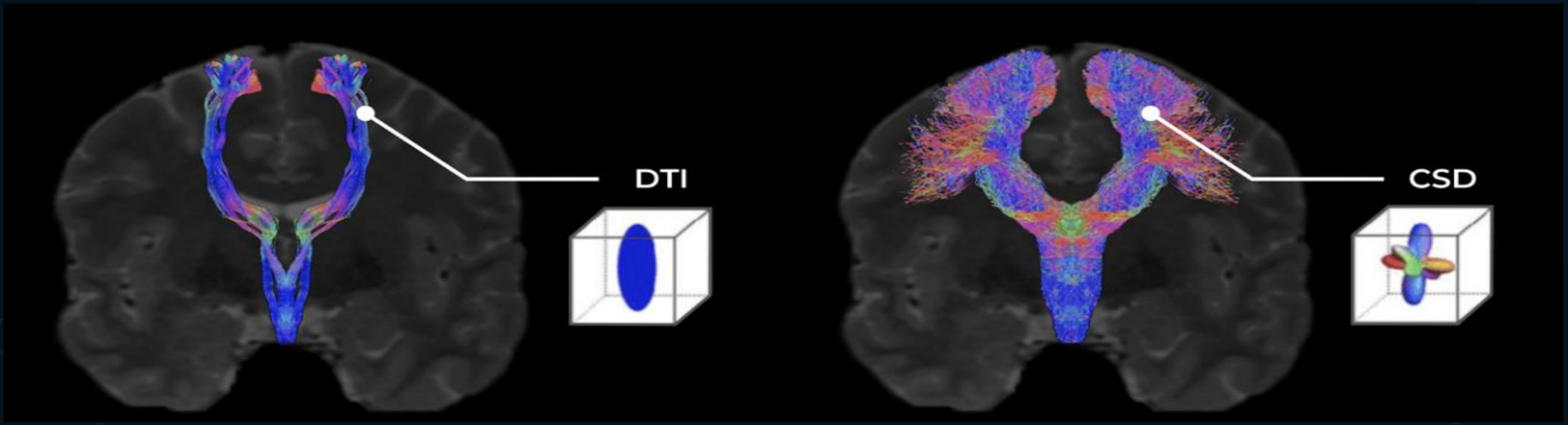
$$\mathcal{L}(\Theta) = \|\mathbf{F}_{\text{true}} - f_{\text{NN}}(\mathbf{S}; \Theta)\|^2 + \lambda R(f_{\text{NN}}(\mathbf{S}; \Theta)).$$

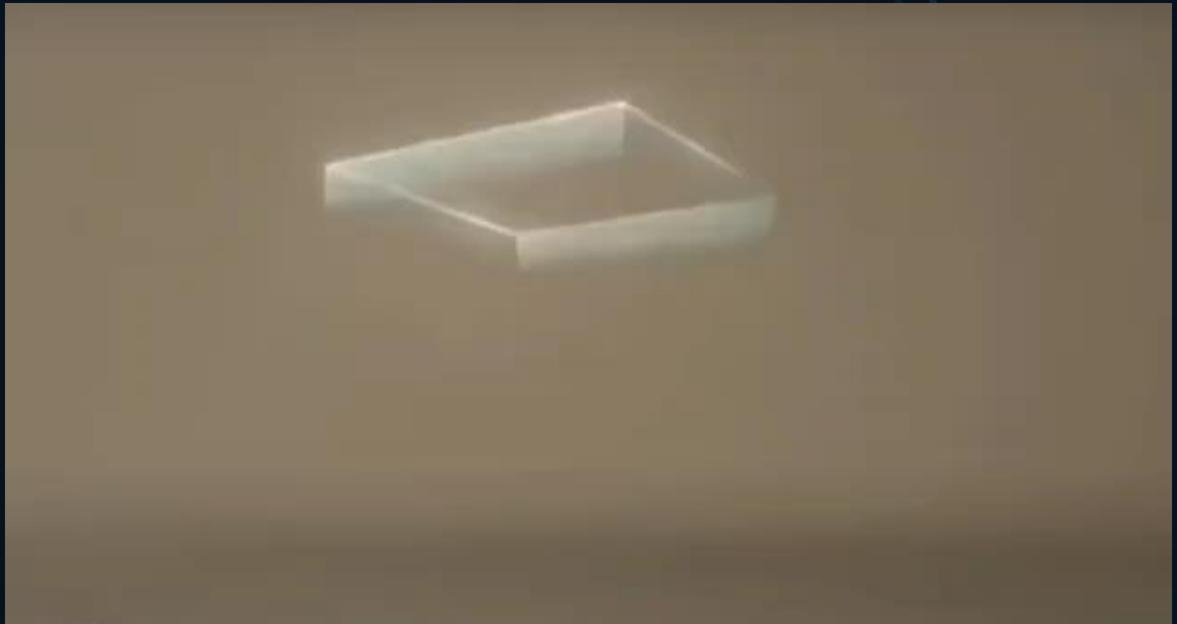
Fixel-Based Analysis (FBA)

- Pixel=picture element (2D)
- Voxel=Volume element (3D)
- Fixel=fiber element (5D)

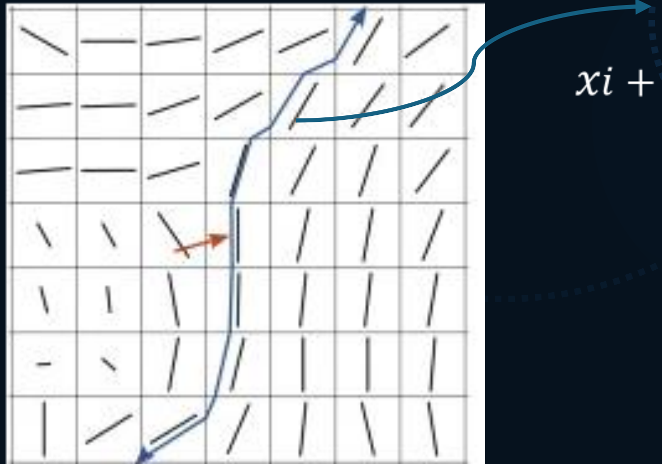


Tractography





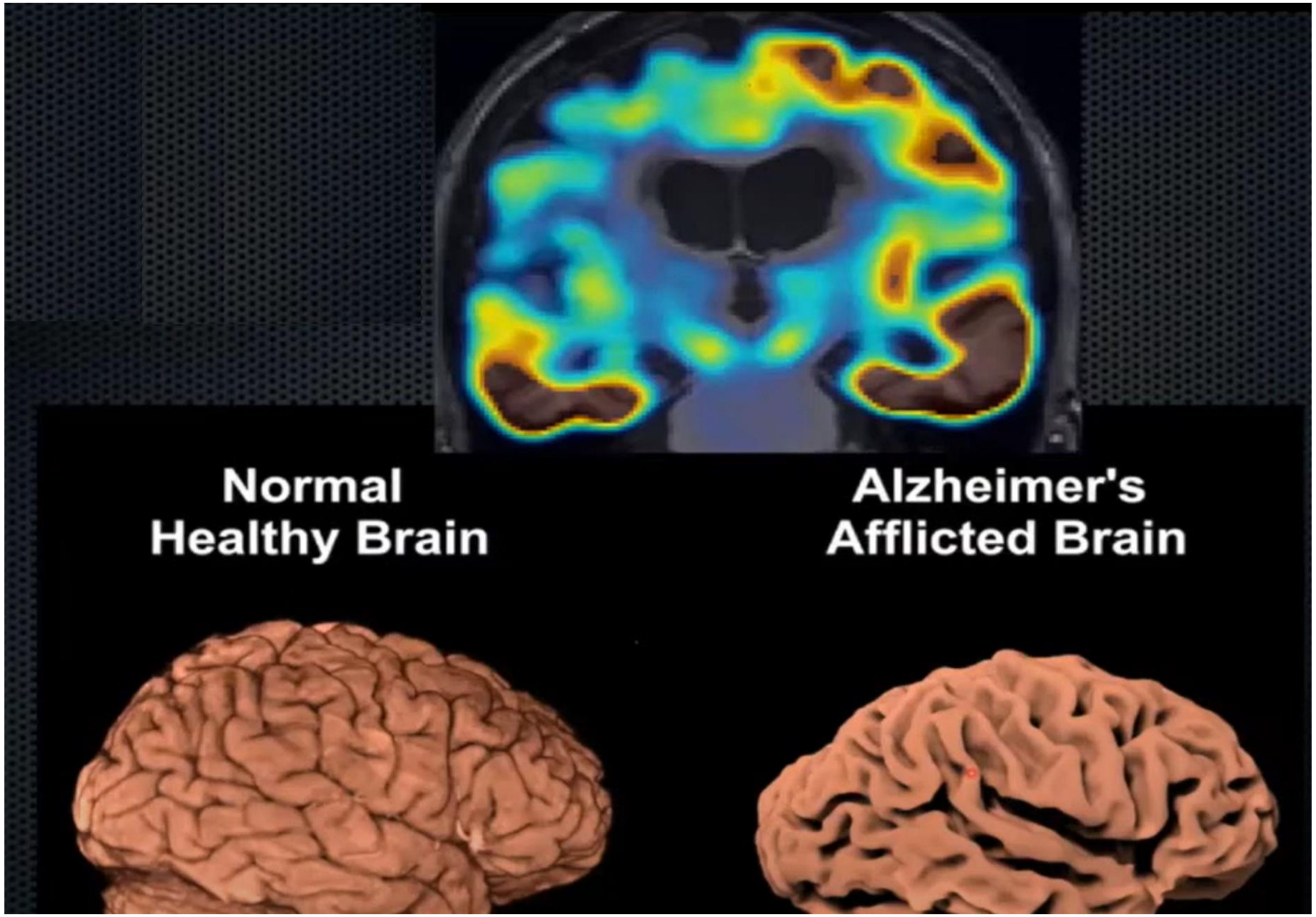
- **Tractography'** is a brain imaging technique that broadly describes the mapping of the location and direction of white matter bundles and their constituent fibers within the human brain



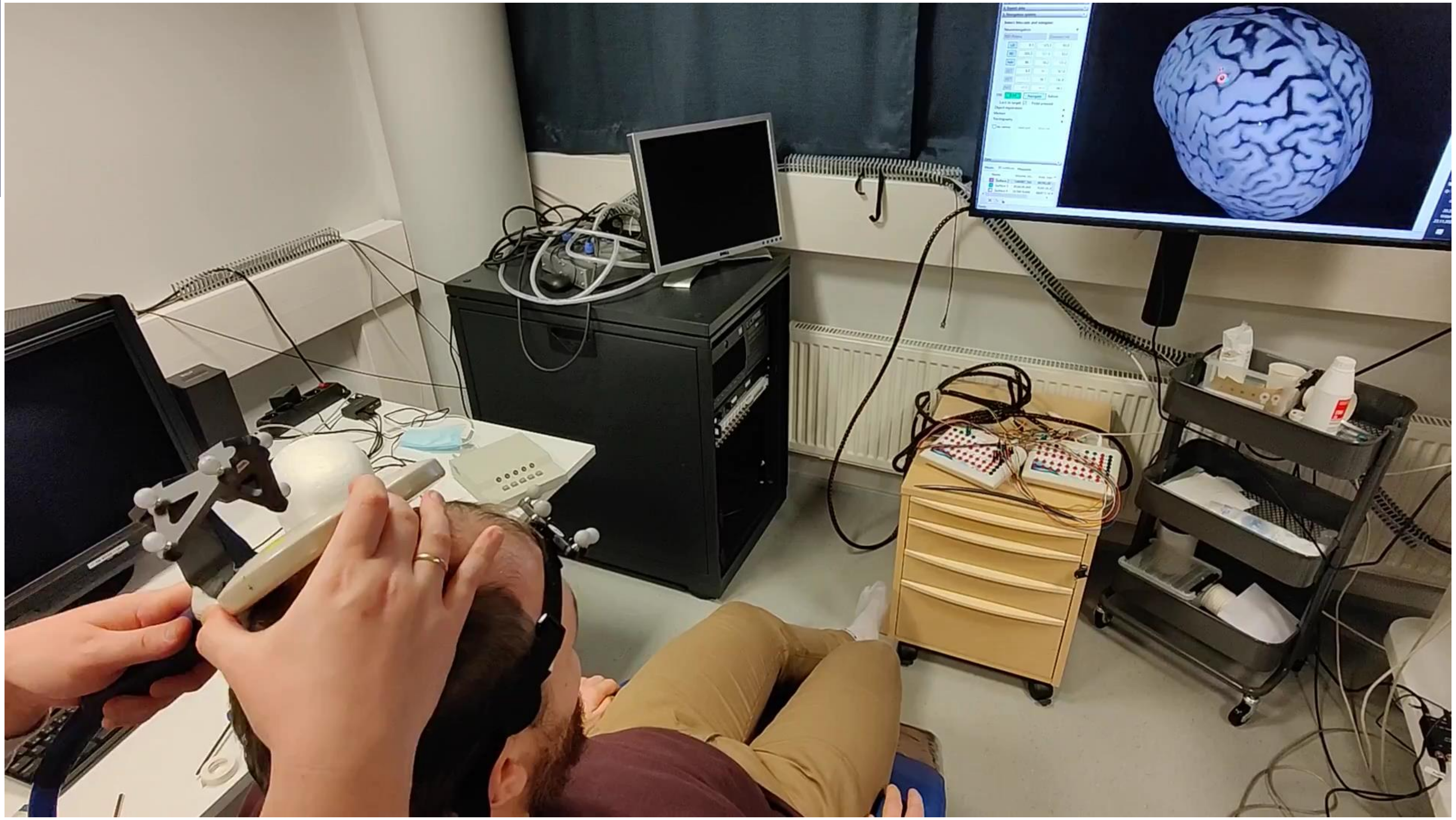
$$xi + 1 = xi + \Delta s \cdot di$$

Segmentation and Tractometry

Application of Tractography in Alzheimer’s Disease(AD)



Combining TMS and Tractography



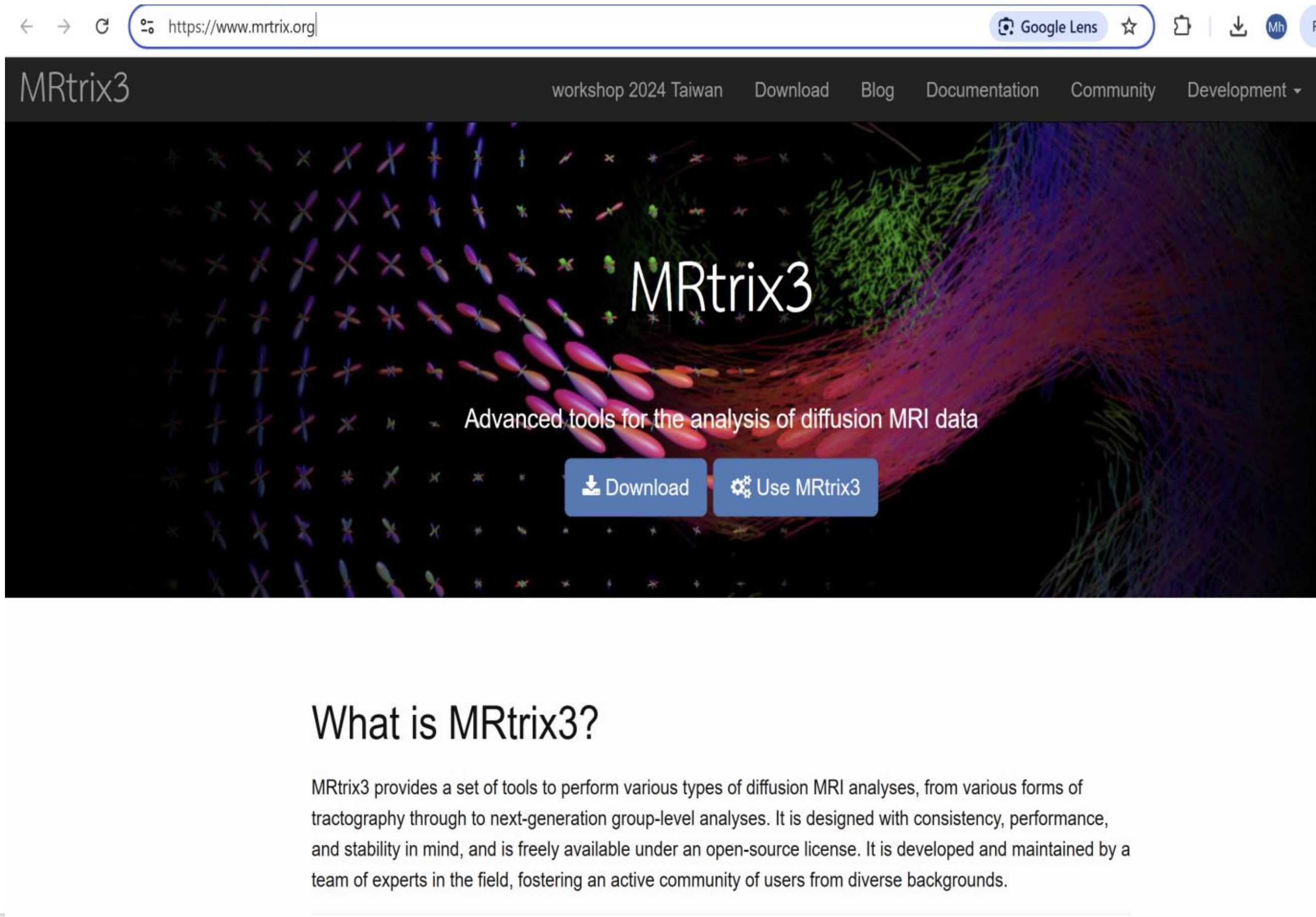
DIPY MRtrix3

Open-source Python software designed for computational anatomy.

Primarily focuses on diffusion MRI but also offers general medical imaging algorithms like denoising and registration.

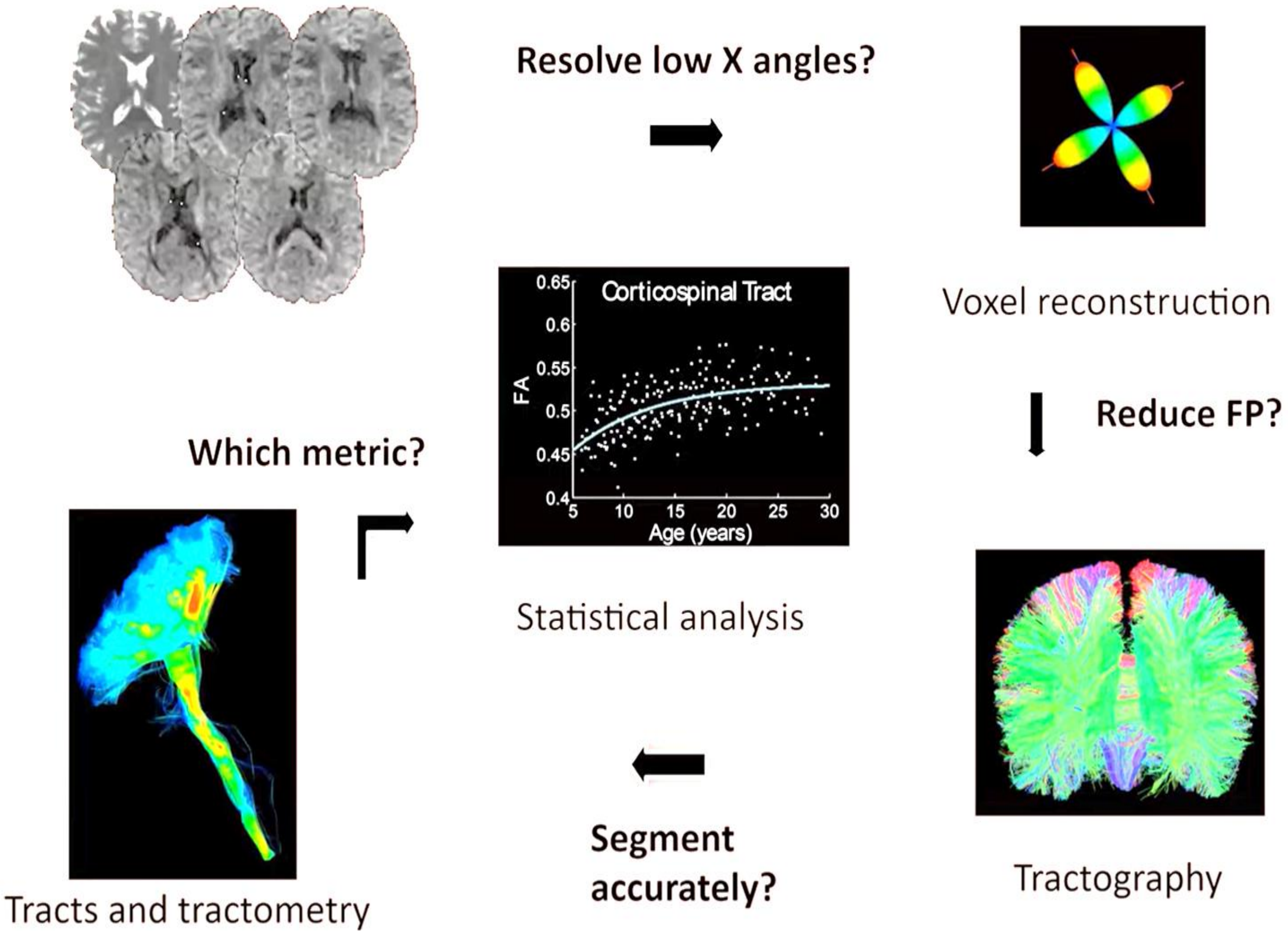
DIPY and MRtrix3 are global initiatives that foster collaboration among researchers across laboratories and countries

Aims to share cutting-edge code and expertise, accelerating progress in medical imaging research.



Use Case	Best Tool
High-performance tractography pipelines	MRtrix3
Interactive GUI for diffusion MRI analysis	MRtrix3 (`mrview`)
Flexible scripting and integration	DIPY
Teaching diffusion MRI principles	DIPY
Python-based workflows or pipelines	DIPY
Multi-modal connectomics	MRtrix3
Large-scale, multi-shell data	MRtrix3

Ongoing Research



Thank you for your attention ☺

Email:mahdad.esmaeili@uef.fi