Introduction to DTI

Pere-Pau Vázquez

Sources

- Source text (and some slides) come from: O’Donnell & Westin, National Alliance for Medical Imaging, D. Porter, TensorVis.org, Anna Vilanova...

Outline

- DTI basics
- Measuring DTI
- Displaying DTI
- Tractography
- Challenges
- Examples

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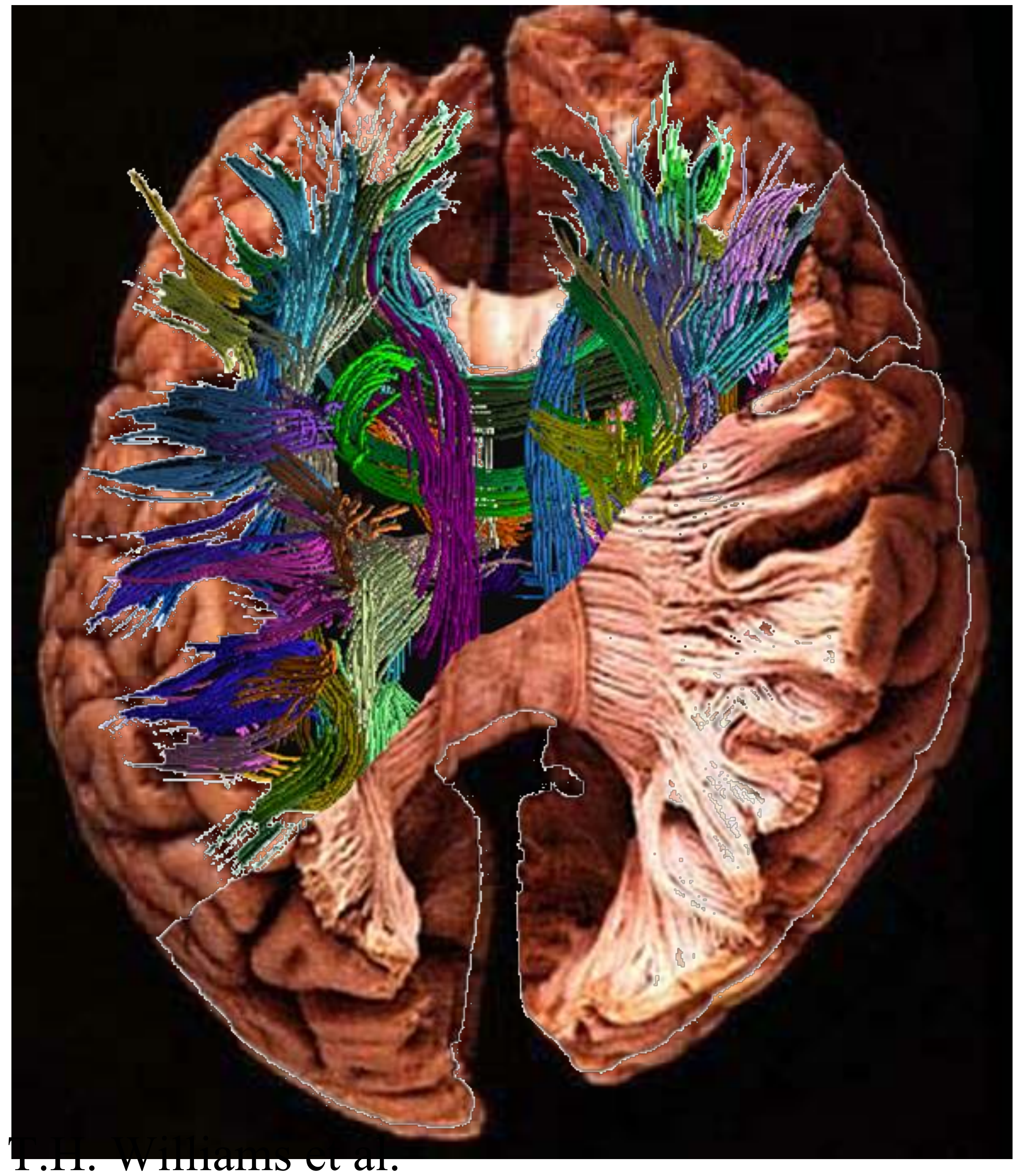
DTI basics

Motivation



T.H. Williams et al.

http://www.shands.org/

www.spiralnotebook.org/ mousehunt/

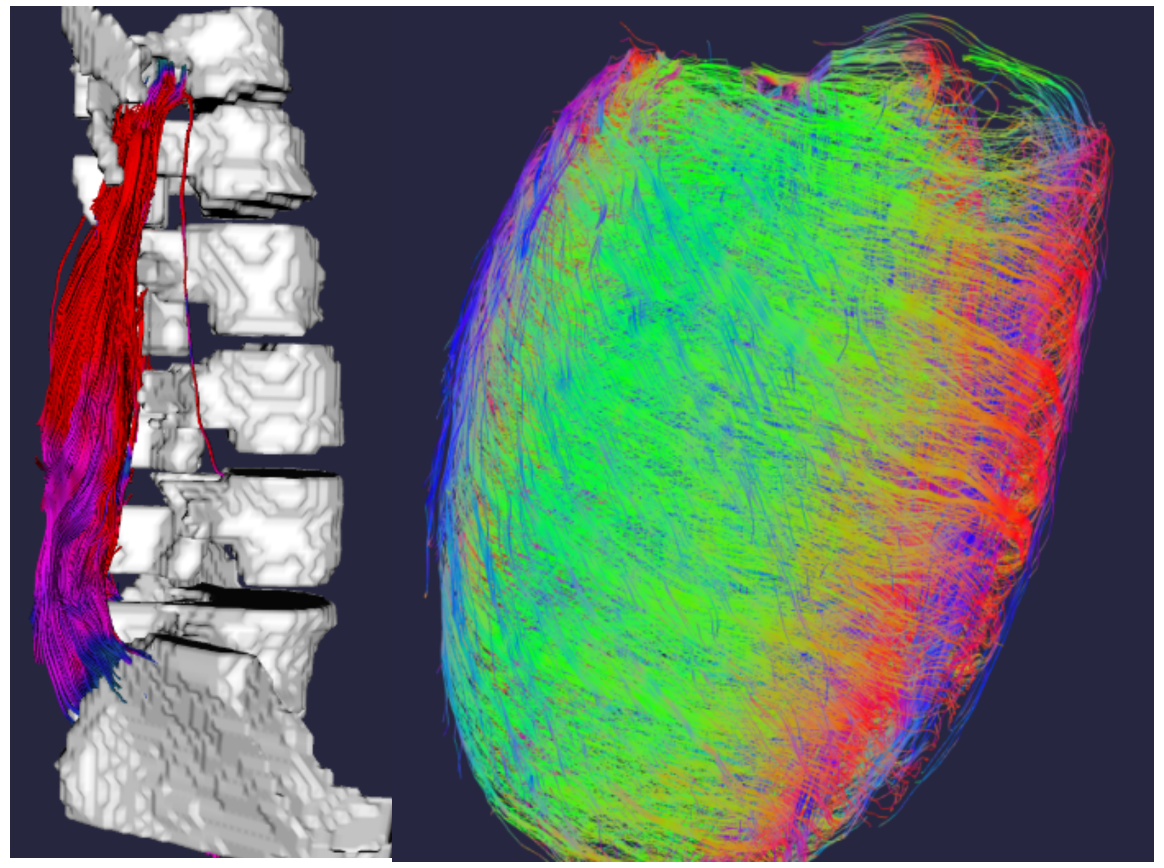
DTI basics

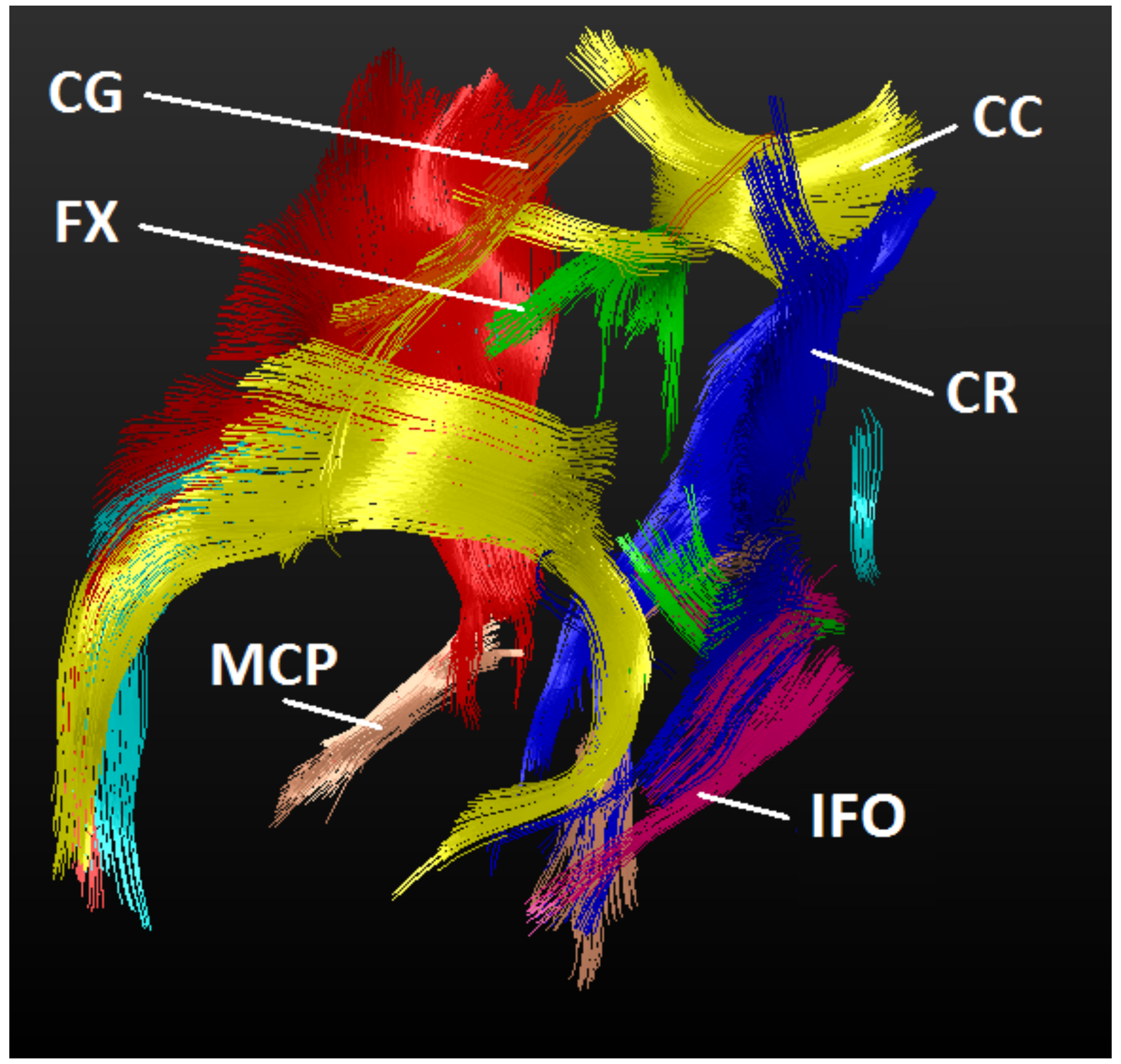
Applications:

- Understanding
    - Brain Development
    - Brain Injuries
    - Ischemic heart ...
- Diagnosis
    - Alzheimer
    - Multiple Sclerosis ...

Treatment

- Tumor Resection
- Epilepsy – Anterior Temporal Lobe Resection ...





DTI basics

- DTI: Diffusion Tensor magnetic resonance Imaging (commonly Diffusion Tensor Imaging)
  - Relatively new technology
  - Useful for imaging the white matter of the brain
  - Originally proposed for use in magnetic resonance imaging (MRI) by Peter Basser
  - DTI allows to get a rotationally invariant description of the shape of water diffusion
    - The invariance to rotation is crucial to enable the application of the DTI method to the complex anatomy of the fiber tracts in the human brain
    - Although these fibers are not well described in some places (e.g. crossings)

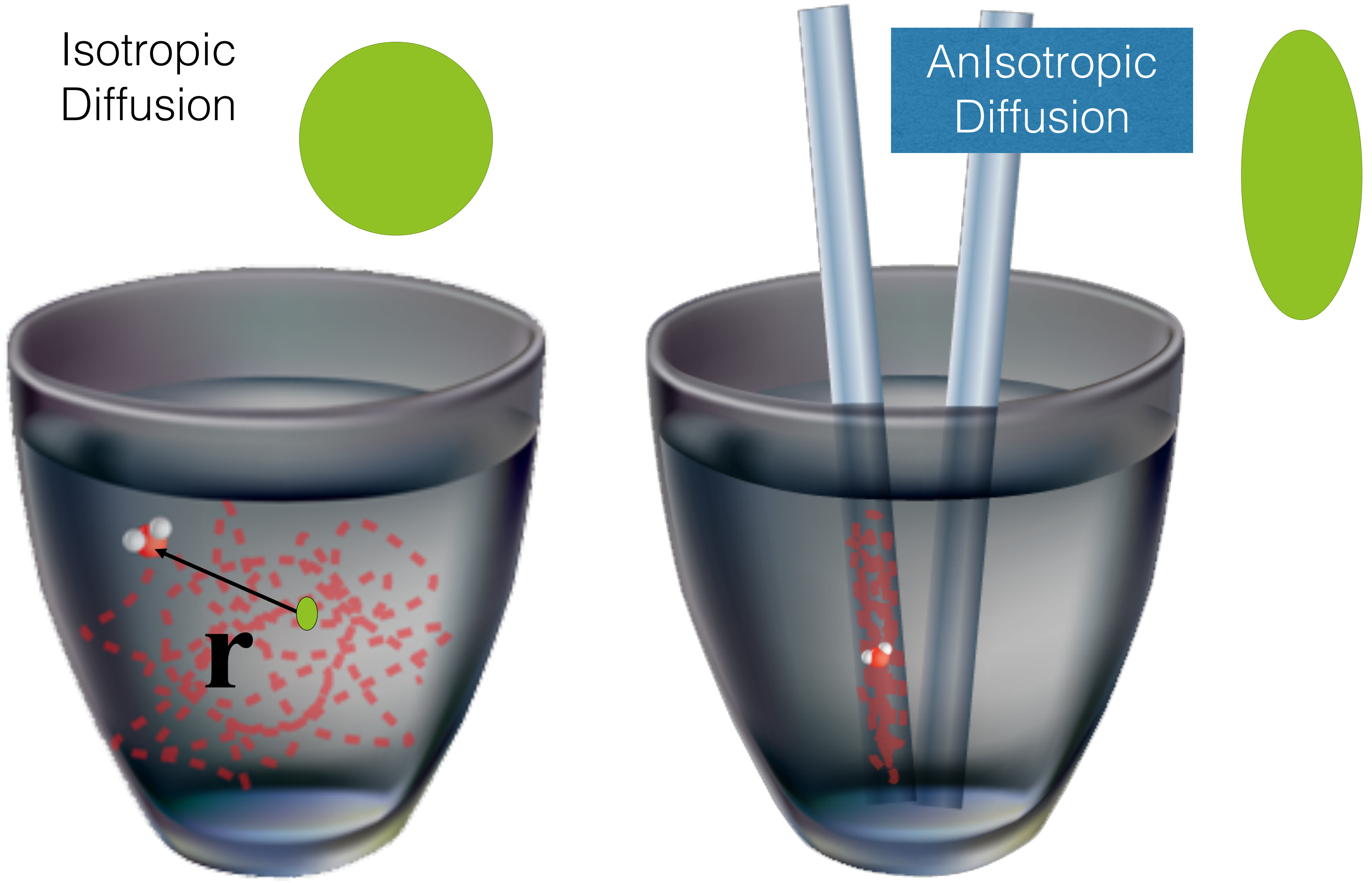
DTI basics

- DTI works by measuring the diffusion of water molecules
  - The measured quantity is the diffusivity or diffusion coefficient
    - A proportionality constant that relates diffusive flux to a concentration gradient
    - Has units of mm2/s
    - Diffusion measured in tissues varies with direction (anisotropic)
      - Pure water, for example, diffuses equally in all directions (isotropic)

DTI basics

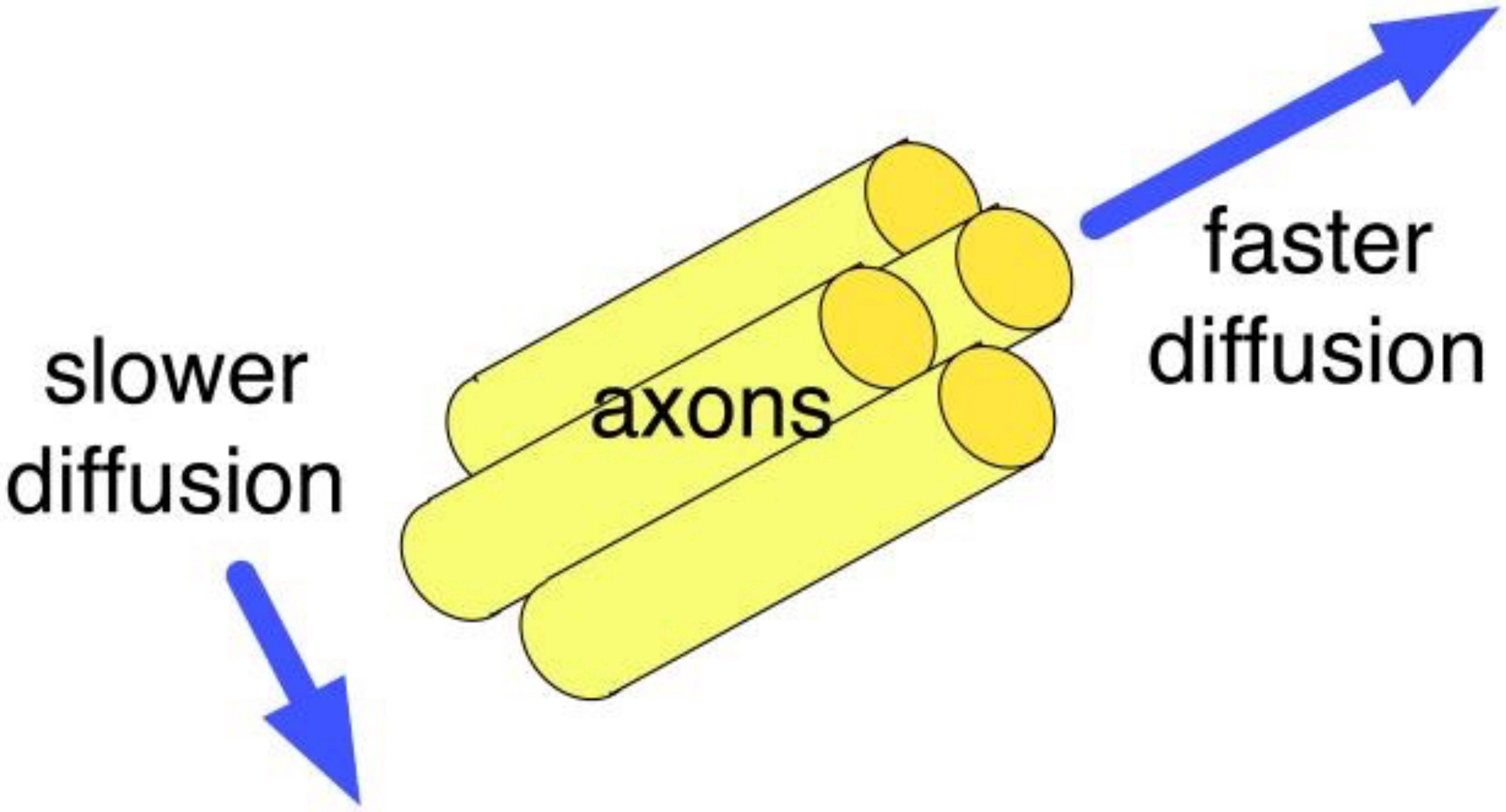
- DTI works by measuring the diffusion of water molecules
    - Measured macroscopic diffusion anisotropy is due to microscopic tissue heterogeneity
    - In the white matter of the brain, diffusion anisotropy is primarily caused by cellular membranes
        - With some contribution from myelination and the packing of the axons
        - Anisotropic diffusion can indicate the underlying tissue orientation

DTI basics



Background: Brownian Water Diffusion

DTI basics



DTI basics

- Diffusion is described in terms of the diffusion tensor (DT)
  - Describes the diffusion of water molecules using a Gaussian model
  - Technically, it is proportional to the covariance matrix of a three-dimensional Gaussian distribution that models the displacements of the molecules.
- The DT is a 3×3 symmetric, positive-definite matrix
  - It has 3 orthogonal (mutually perpendicular) eigenvectors
  - It also has three positive eigenvalues
  - The major eigenvector of the diffusion tensor points in the principal diffusion direction (the direction of the fastest diffusion)

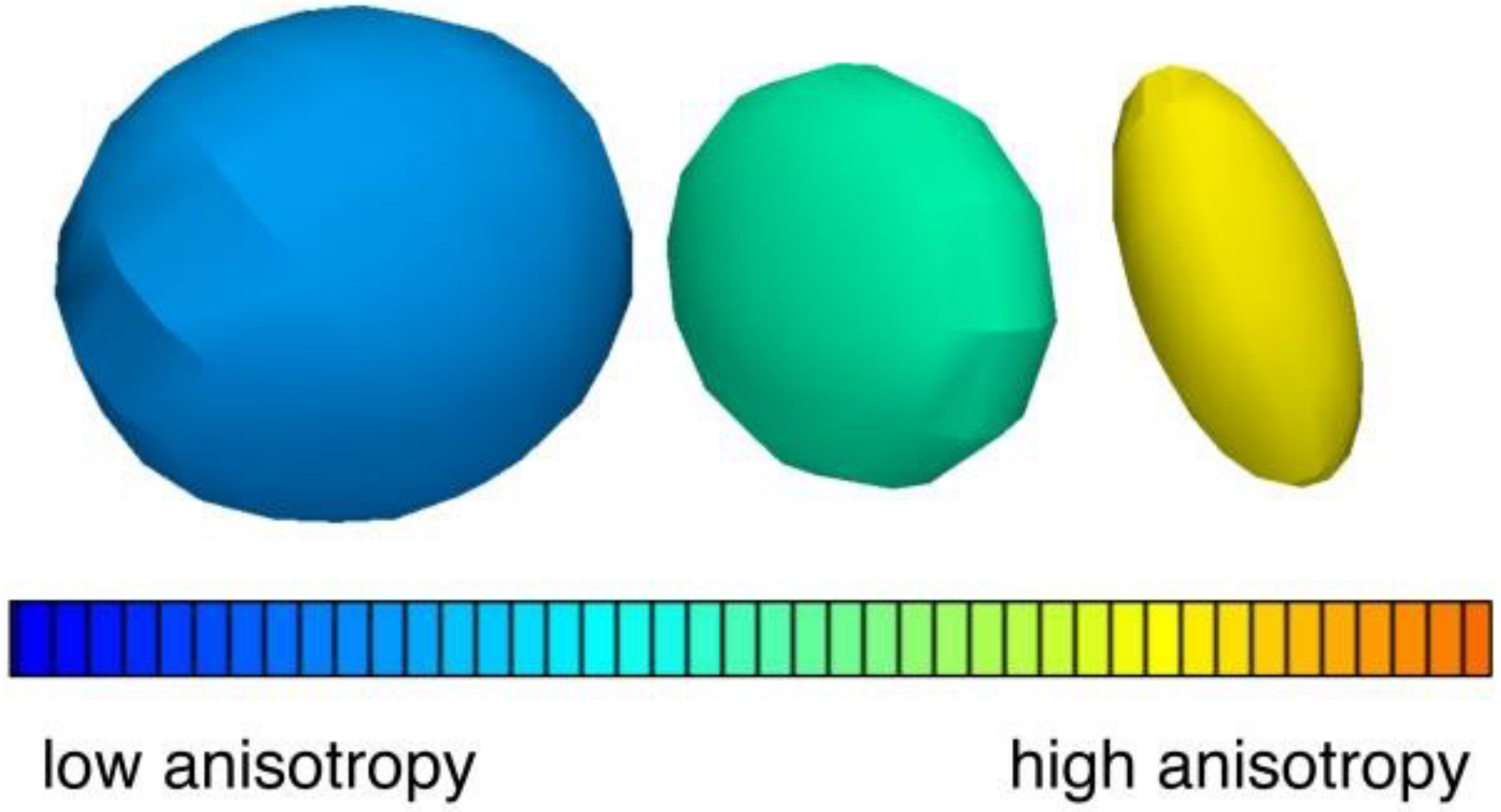
DTI basics

- The DT is a 3×3 symmetric, positive-definite matrix …
  - In anisotropic fibrous tissues the major eigenvector also defines the fiber tract axis of the tissue
  - Thus, the three orthogonal eigenvectors can be thought of as a local fiber coordinate system
    - This interpretation is only strictly true in regions where fiber tracts do not cross, fan, or branch

DTI basics

- The DT is a 3×3 symmetric, positive-definite matrix …
  - The three positive eigenvalues of the tensor ($\lambda 1, \lambda 2, \lambda 3$) give the diffusivity in the direction of each eigenvector
  - Together, the eigenvectors and eigenvalues define an ellipsoid that represents an isosurface of (Gaussian) diffusion probability
    - The axes of the ellipsoid are aligned with the eigenvectors and their lengths are sqrt($2\tau\lambda_i$)

DTI basics



DTI basics

- DTI improvements:
  - High angular resolution diffusion imaging (HARDI)
  - Magnetic resonance imaging (MRI) technique that can resolve locally more than one direction in the diffusion pattern of water molecules
  - Opens up the opportunity to display and track crossing fibers

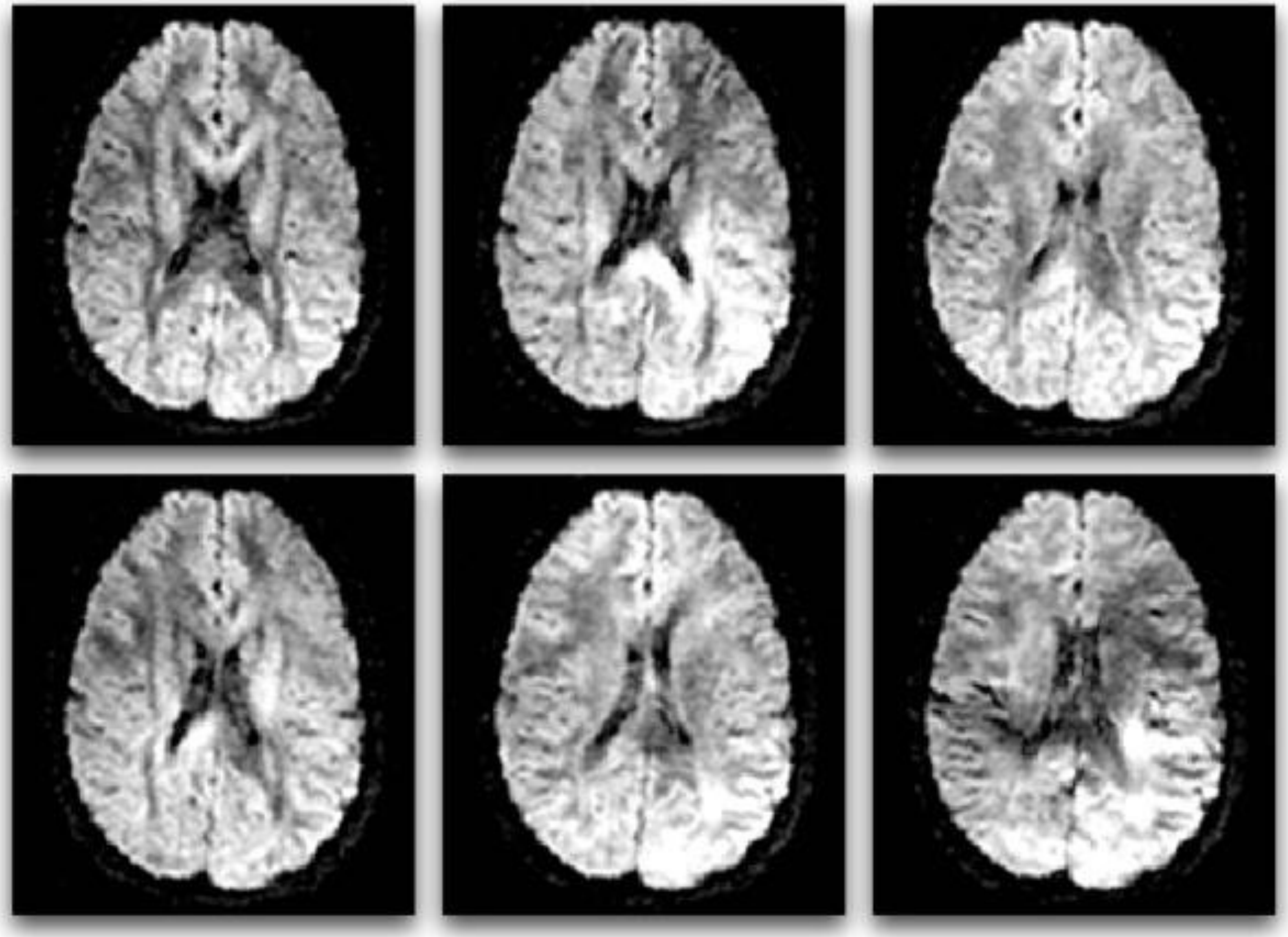
Outline

- *DTI basics*
- **Measuring DTI**
- Displaying DTI
- Tractography
- Challenges
- Examples

Measuring DTI

- To measure diffusion using MRI, magnetic field gradients are employed to create an image that is sensitized to diffusion in a particular direction
  - This process must be repeated in multiple directions to estimate the tensor
  - This will yield a three-dimensional diffusion model
- Diffusion imaging works by introducing extra gradient pulses whose effect “cancels out” for stationary water molecules, and causes a random phase shift for molecules that diffuse.
  - Due to their random phase, signal from diffusing molecules is lost
    - This loss of signal creates darker voxels (volumetric pixels)
    - White matter fiber tracts parallel to the gradient direction will appear dark in the diffusion-weighted image for that direction

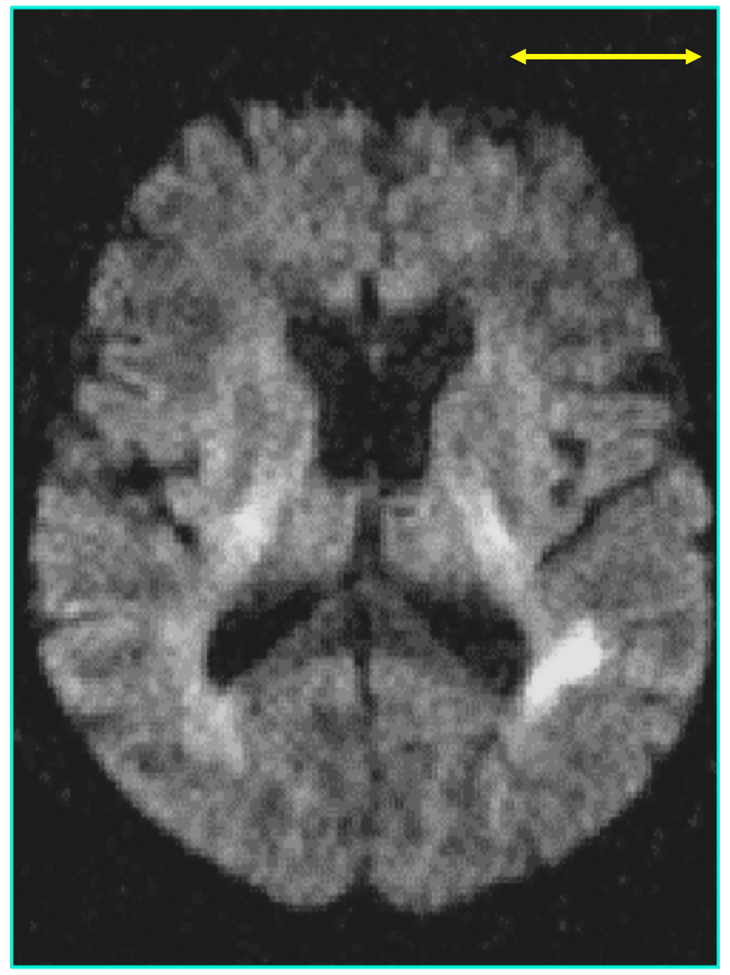
Measuring DTI



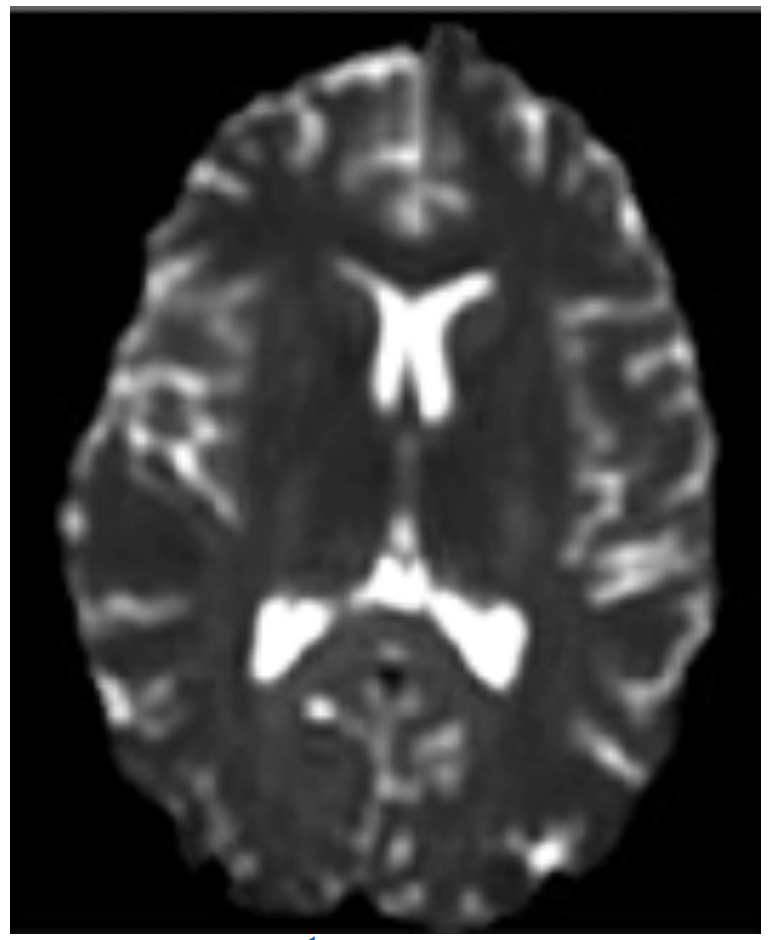
Measuring DTI

- To calculate the diffusion tensor, the decreased signal (Sk) is compared to the original signal (S0) by solving the Stejskal-Tanner (next slide)
    - This equation describes how the signal intensity at each voxel decreases in the presence of Gaussian diffusion

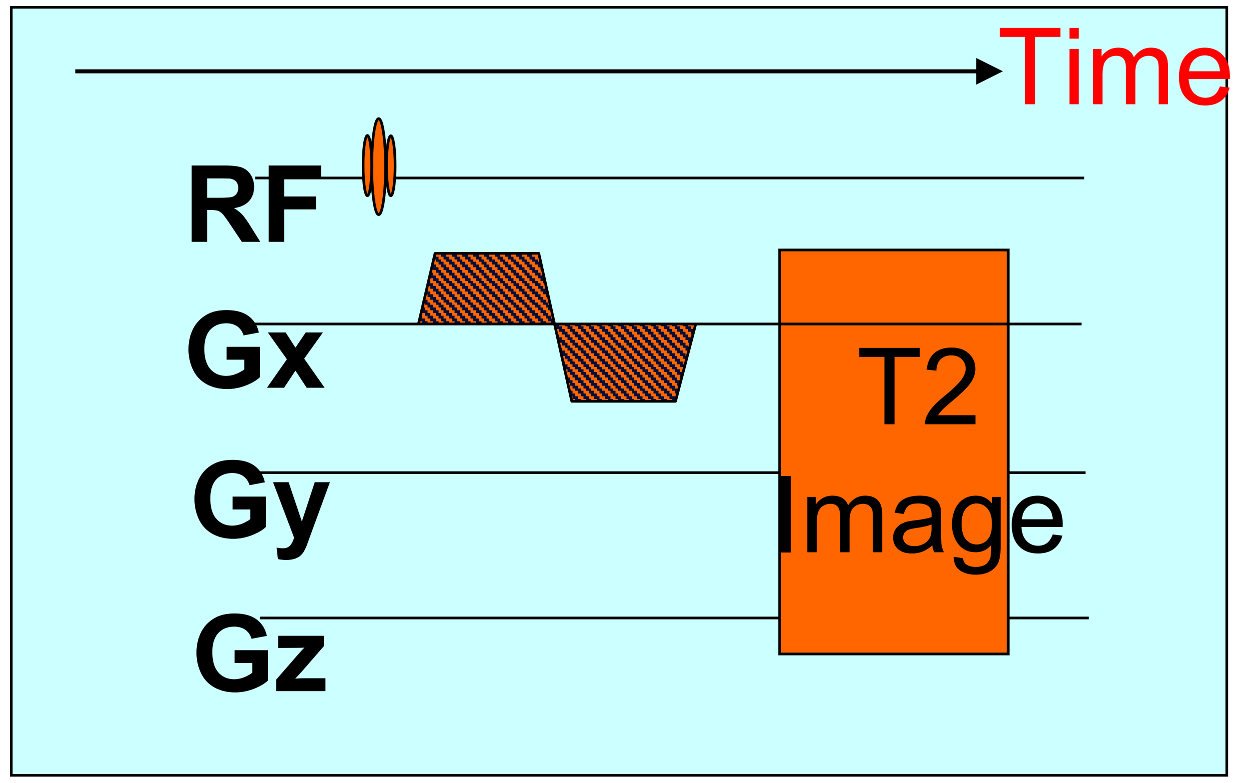
T2 + diffusion



T2



Sequence

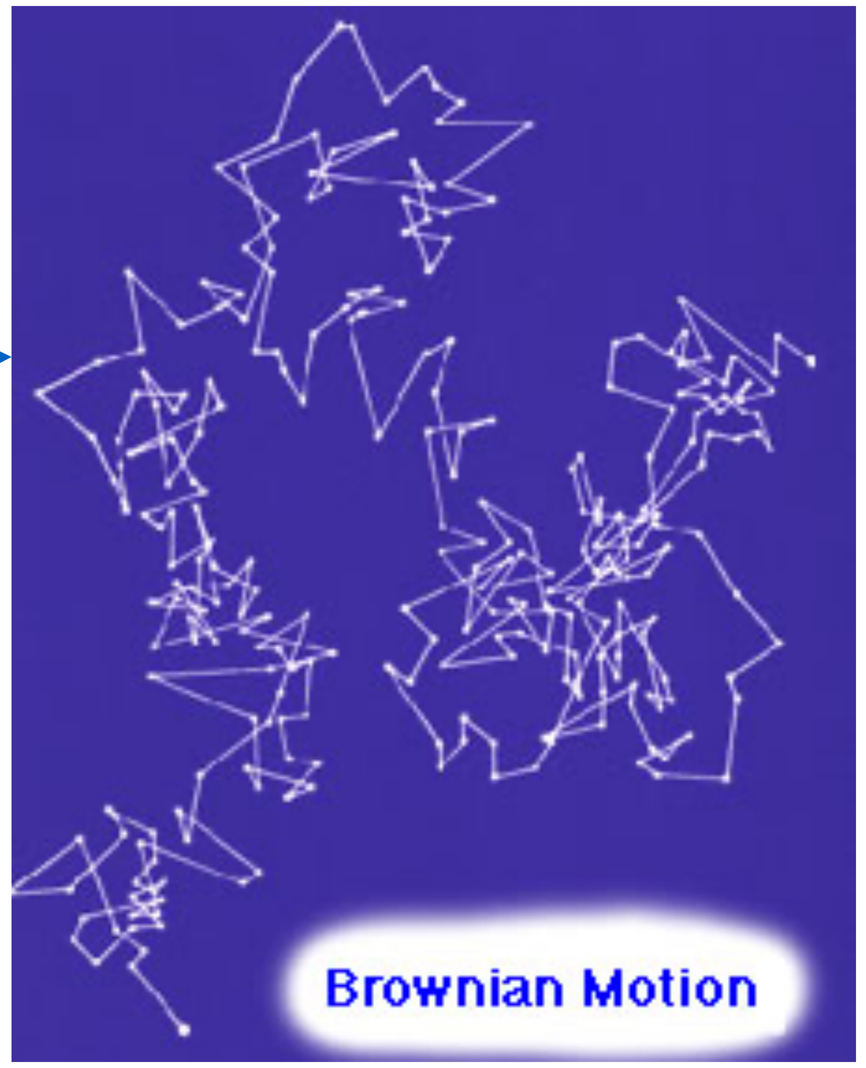


Excite

Measure
diffusion

Regular
T2 image

$$S = S_0 e^{-bD}$$



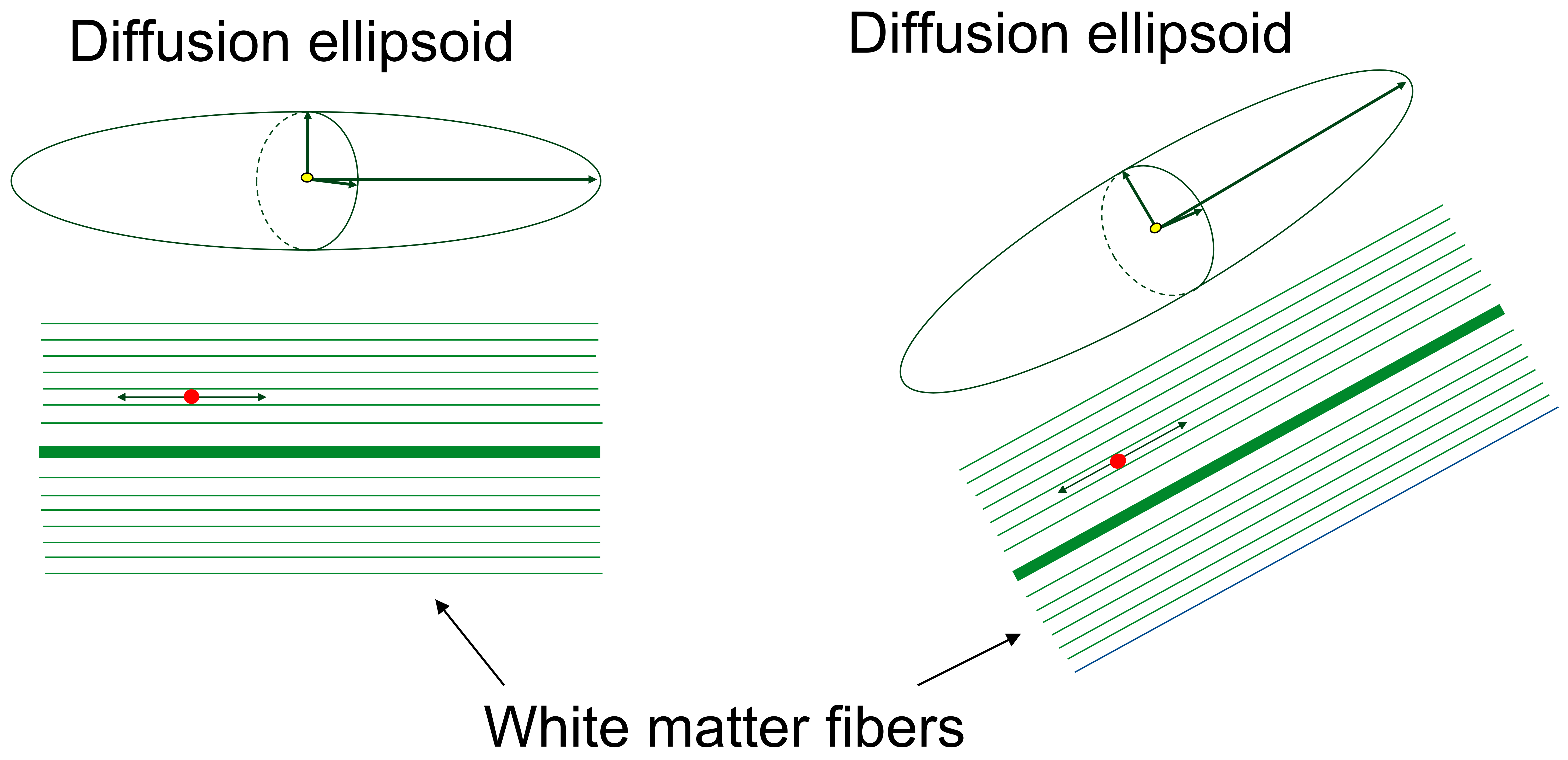
- S = measured signal
- S0 = signal without diffusion
- b = b factor (gradient strength)
- D = diffusion coefficient

Measuring DTI

- Obtaining a DTI
  - Measure water diffusion in at least 6 directions
  - Echo-planar imaging (fast acquisition)
  - Collecting small voxels (1.8 x 1.8 x 3mm), scanning takes about 10 minutes

Measuring DTI

Higher diffusion → lower signal

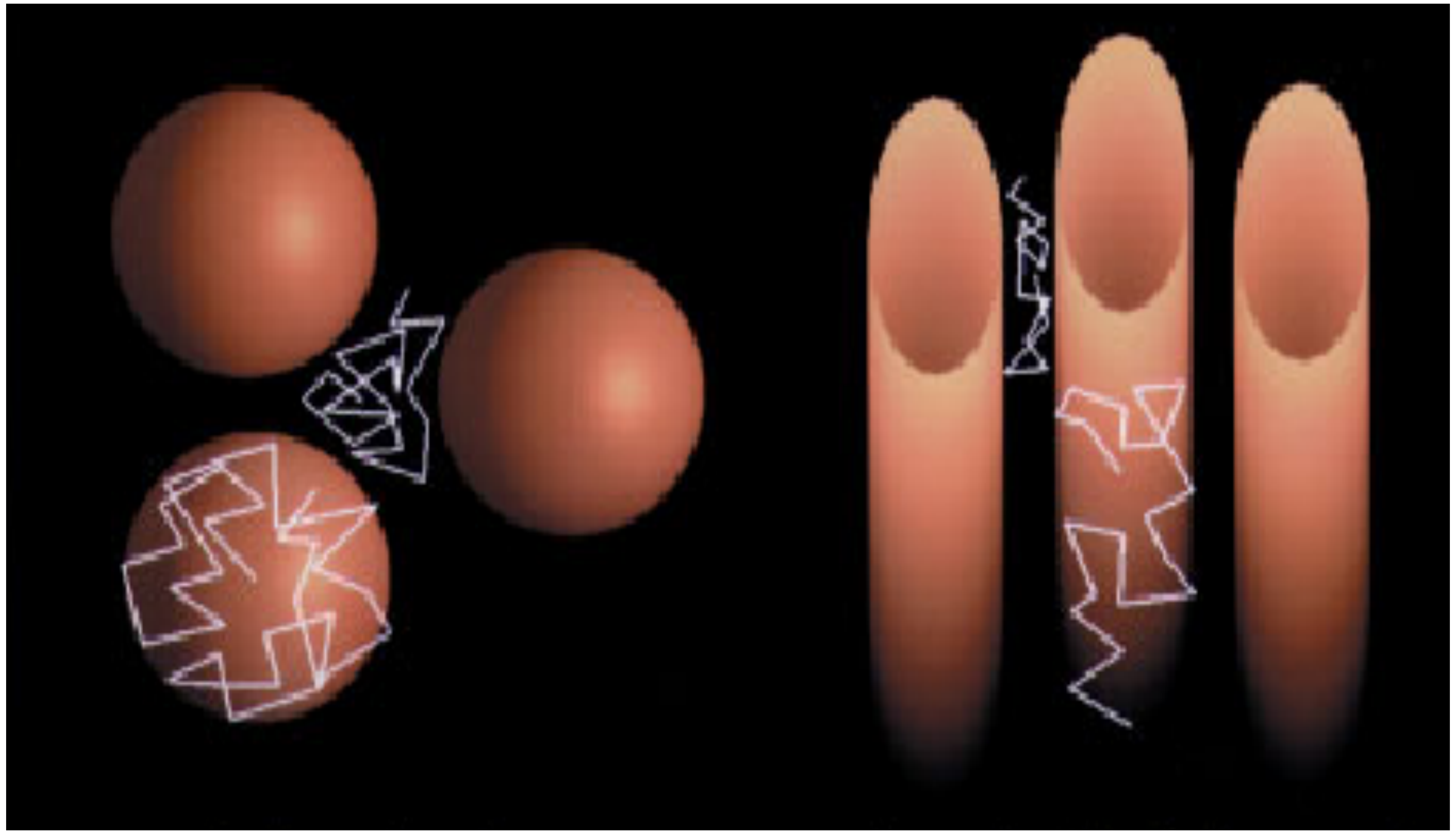


Useful for following white matter tracts in healthy brain

Measuring DTI

Higher diffusion -> lower signal

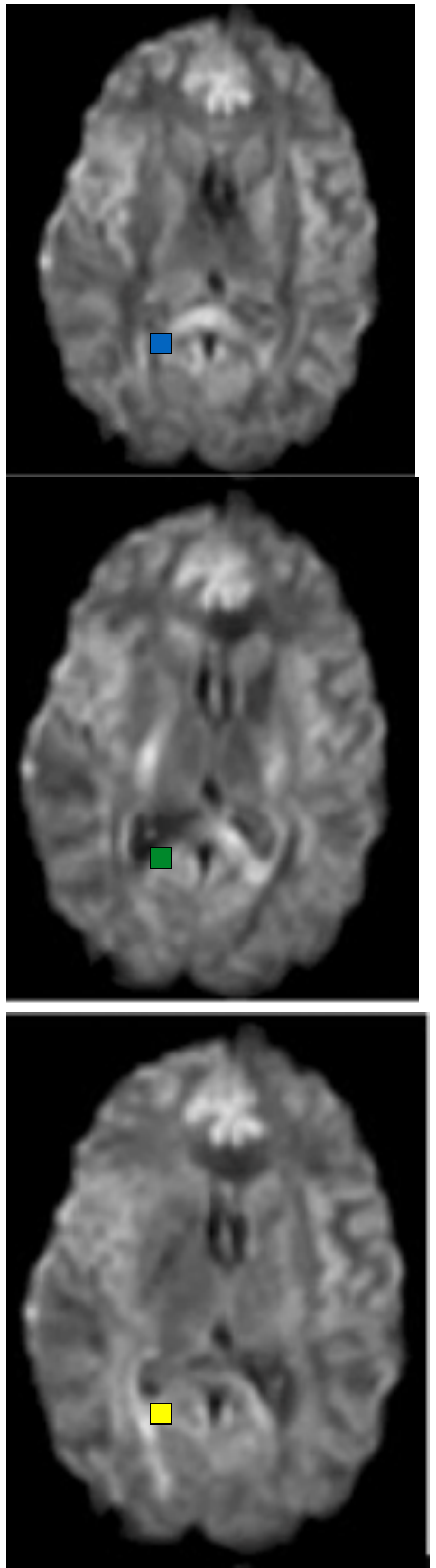
Water White matter fibers

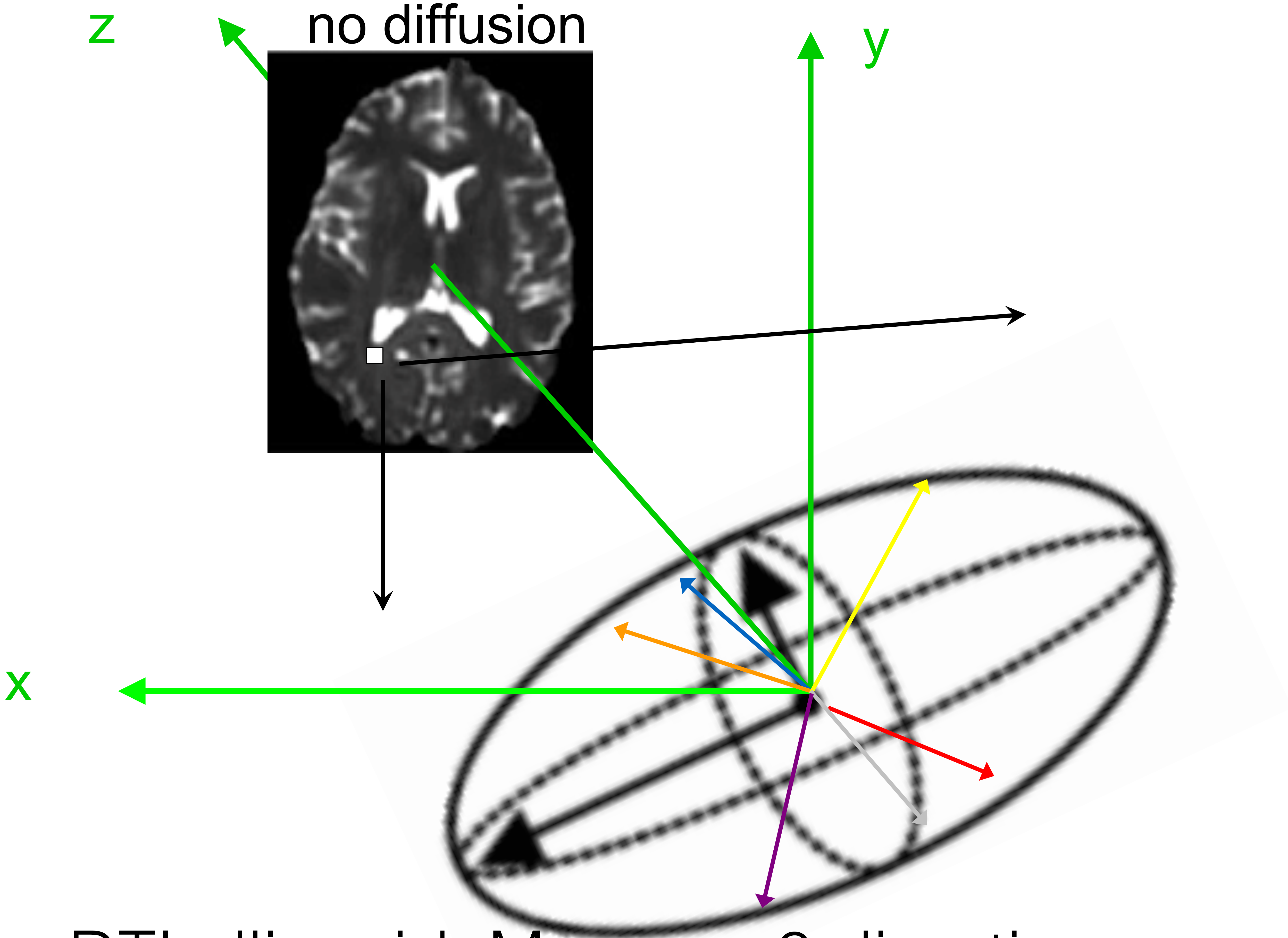


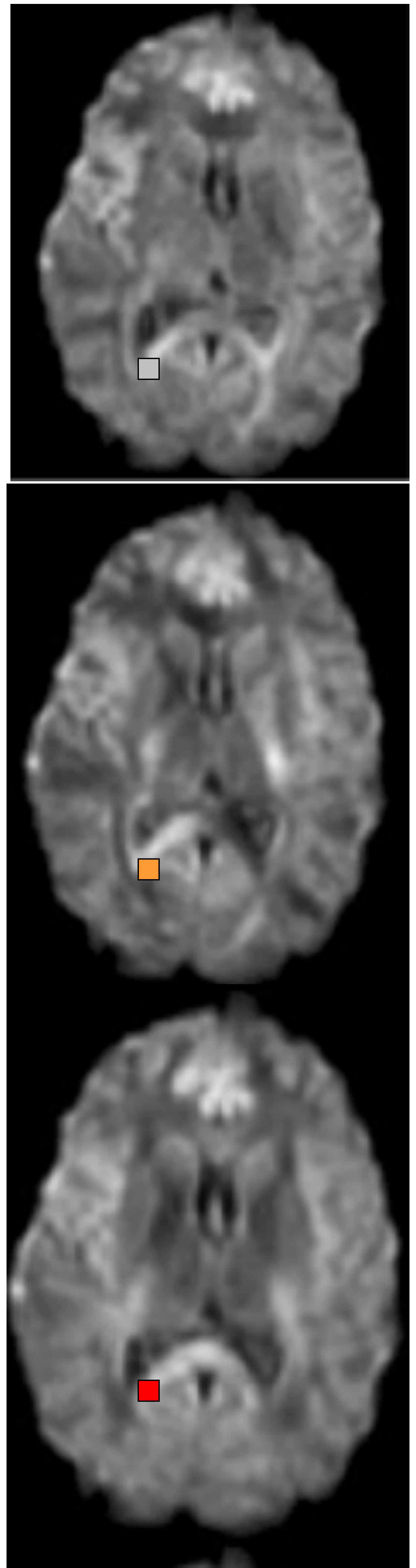
Isotropic Anisotropic

Adapted from: Beaulieu (2002). NMR in Biomed; 15:435-455

Measuring DTI







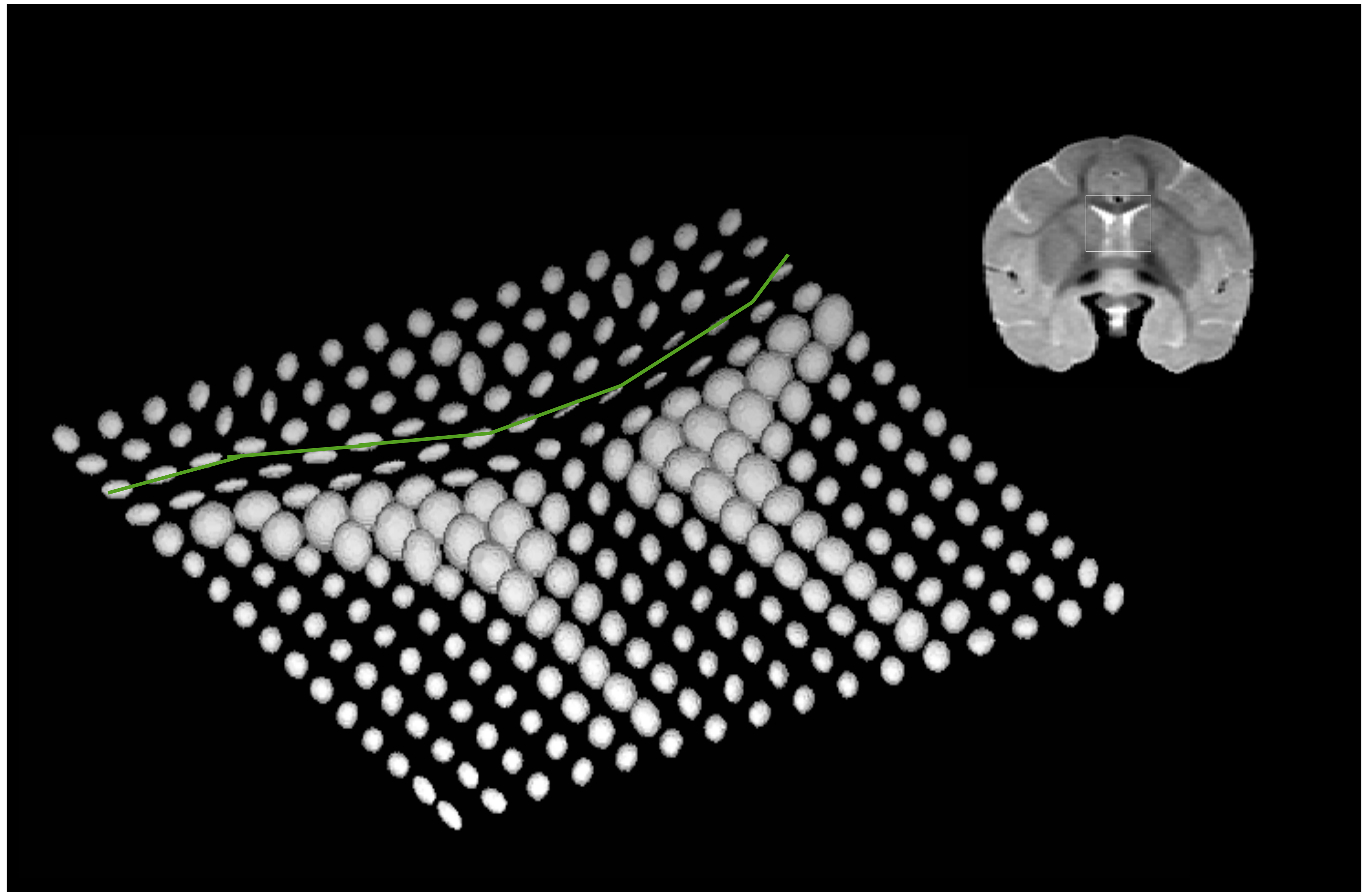
DTI ellipsoid: Measure 6 directions

Ellipsoid represents magnitude of diffusion in all directions by distance from center of ellipsoid to its surface.

Measuring DTI

Ellipsoid Image

Tract



Pierpaoli and Basser, Toward a Quantitative Assessment of Diffusion Anisotropy, Magn. Reson. Med, 36, 893-906 (1996)

Outline

- *DTI basics*
- *Measuring DTI*
- **Displaying DTI**
- Tractography
- Challenges
- Examples

Displaying DTI

- Different methods for display
    - Assign a scalar value per tensor
    - Assign 4 numbers (RGB and brightness) per tensor
    - Use glyphs
        - Small 3D representations of the major eigenvector or whole tensor
    - Visualize the white matter tracts as lines (aka spaghetti soup)
        - Requires to employ a process called tractography

Displaying DTI

- Single value per tensor
  - Commonly the average of the tensor's eigenvalues
    - Called Mean Diffusivity (MD)
  - These values evaluated per voxel
    - Related to the amount of water in the extracellular space
    - Clinically useful in early stroke detection because it is sensitive to the initial cellular swelling (cytotoxic edema) which restricts diffusion

Mean Diffusivity

$(\lambda 1 + \lambda 2 + \lambda 3)/3$

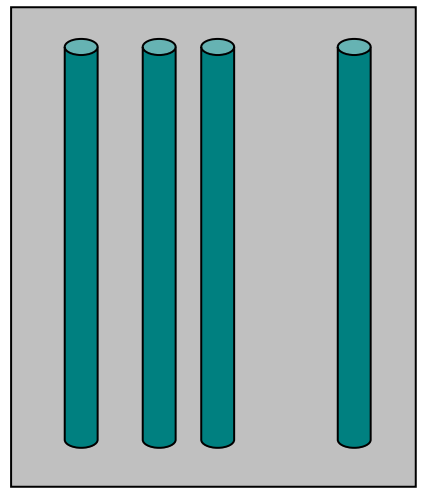
Addition of eigenvalues

Overall diffusion

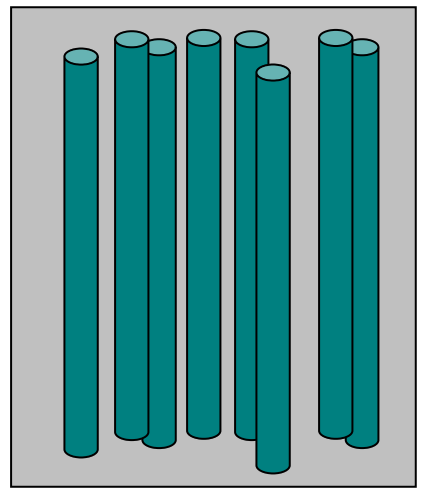
Interpreting Diffusivity and FA

Diffusivity and FA help determine the number, size and myelination of fibers, whereas only FA gives information about directionality.

Number of fibers

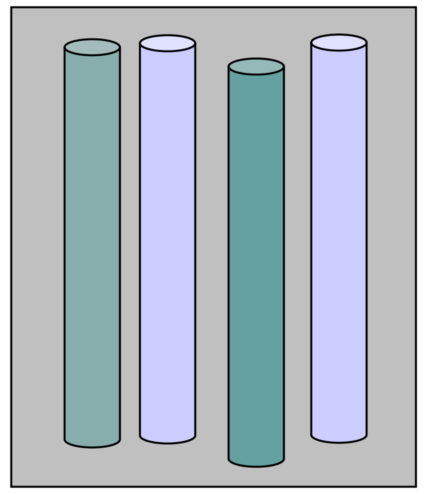


High Diffusivity
Low FA

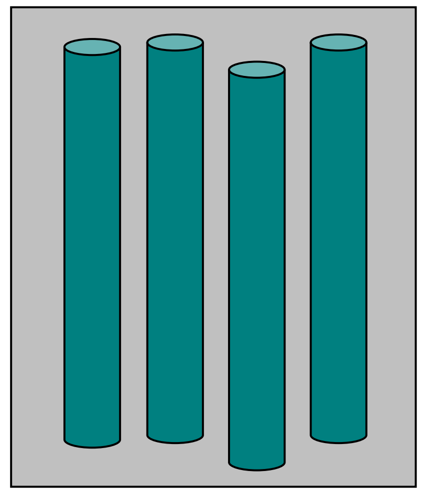


High FA
Low Diffusivity

Myelination of fibers

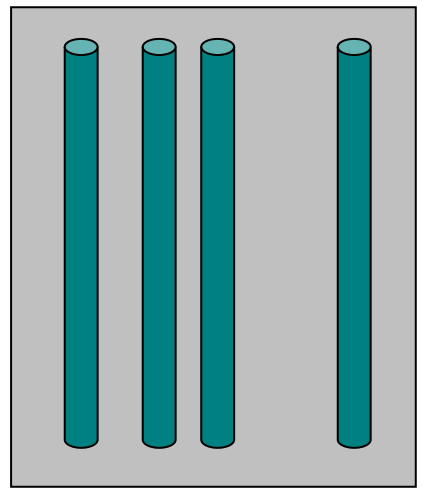


High Diffusivity
Low FA

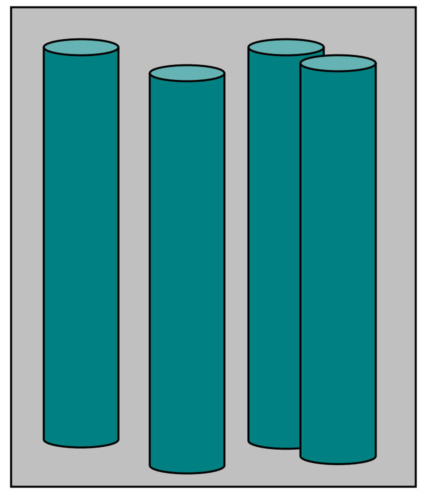


High FA
Low Diffusivity

Size of fibers

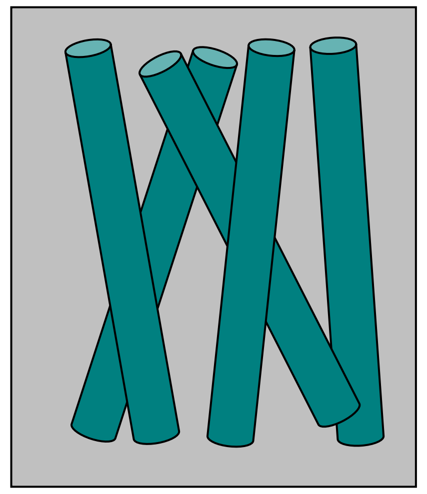


High Diffusivity
Low FA

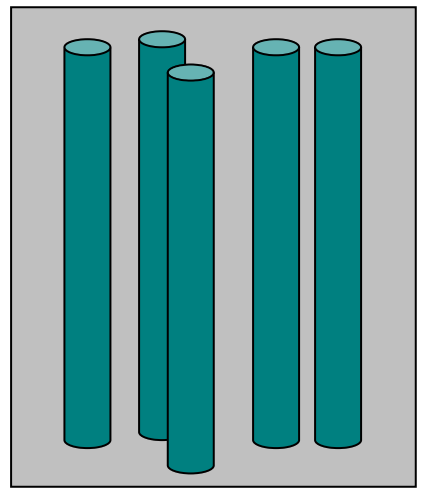


High FA
Low Diffusivity

Directionality of Fibers



Low FA
Same Diffusivity



High FA
Same Diffusivity

Displaying DTI

- Tensor anisotropy measures are ratios of the eigenvalues that are used to quantify the shape of the diffusion
  - Useful for describing the amount of tissue organization and for locating voxels likely to contain a single white matter tract
    - without crossing or fanning
    - The following measures are normalized and all range from 0 to 1, except for the mode, which ranges from −1 to +1.

Displaying DTI

- The most popular anisotropy measure is Fractional Anisotropy (FA)
  - Measures the fraction of the diffusion that is anisotropic
  - Can be thought of as the difference of the tensor ellipsoid’s shape from that of a perfect sphere
  - FA is basically a normalized variance of the eigenvalues

Displaying DTI

Fractional Anisotropy

$$\frac{\sqrt{(\lambda 1-\lambda 2)^2+(\lambda 2-\lambda 3)^2+(\lambda 1-\lambda 3)^2}}{\sqrt{2}\ \sqrt{\lambda 1^2+\lambda 2^2+\lambda 3^2}}$$

↓

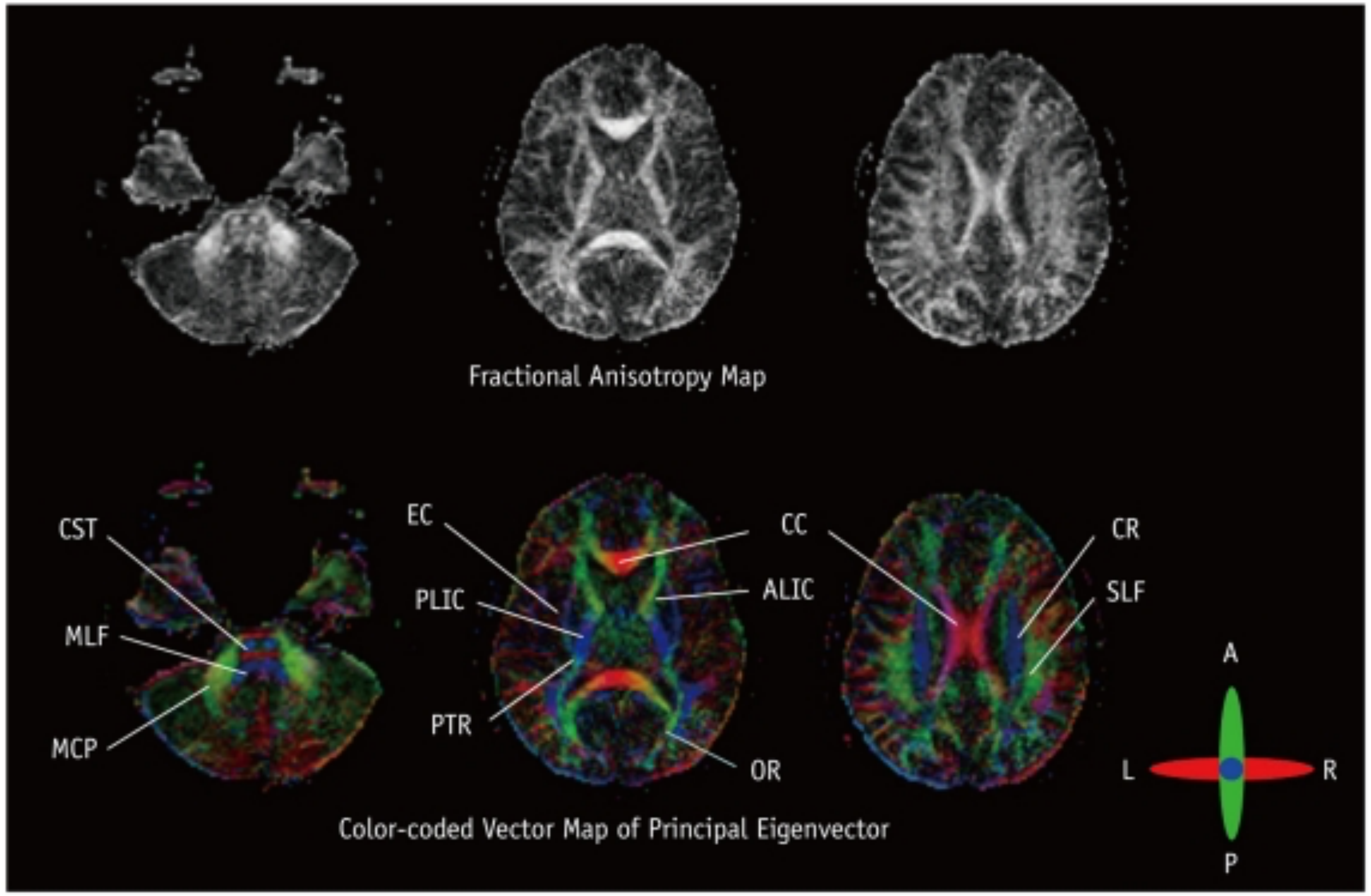
Difference in eigenvalues

↓

Directional diffusion

Displaying DTI

- FA is often considered a measure of “white matter integrity” though changes in FA may be caused by many factors.



Displaying DTI

- Other measures:
    - Linear (L), planar (P) and spherical (S) shape measures
        - Describe the shape of the diffusion

$$C_L = \frac{\lambda_1 - \lambda_2}{\lambda_1}$$

$$C_P = \frac{\lambda_2 - \lambda_3}{\lambda_1}$$

$$C_S = \frac{\lambda_3}{\lambda_1}$$

Displaying DTI

- Detecting fiber tracts is not always possible
  - Voxels with high planar or spherical measure may have a principal eigenvector not large enough to determine the underlying fiber tract direction
  - However, if the largest eigenvalue is much larger than the other two eigenvalues, the linear measure will be large, giving evidence for the presence of a single fiber tract

Displaying DTI

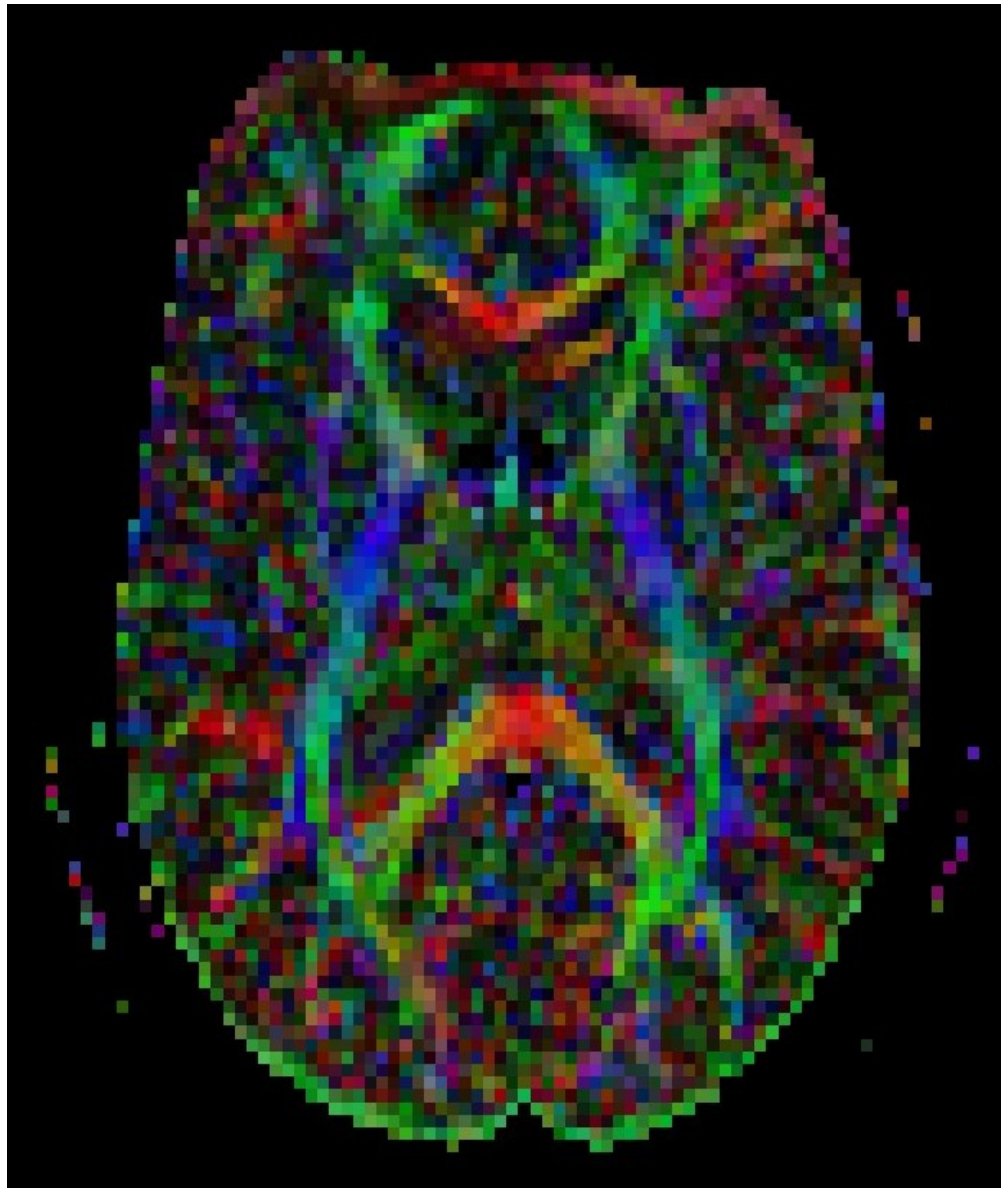
- Eigenvector fields can be visualized using a mapping to colors
  - A color scheme is used to represent the orientation of the major eigenvector
  - Blue: superior-inferior
  - Red: left-right
  - Green: anterior-posterior
  - To enhance visualization of the white matter and suppress information outside of it, the brightness of the color is usually controlled by tensor anisotropy (FA)

Eigenvector Based Visualization

$$\vec{e}_i = (x, y, z) \quad \text{map to } (R, G, B)$$

Pros and Cons

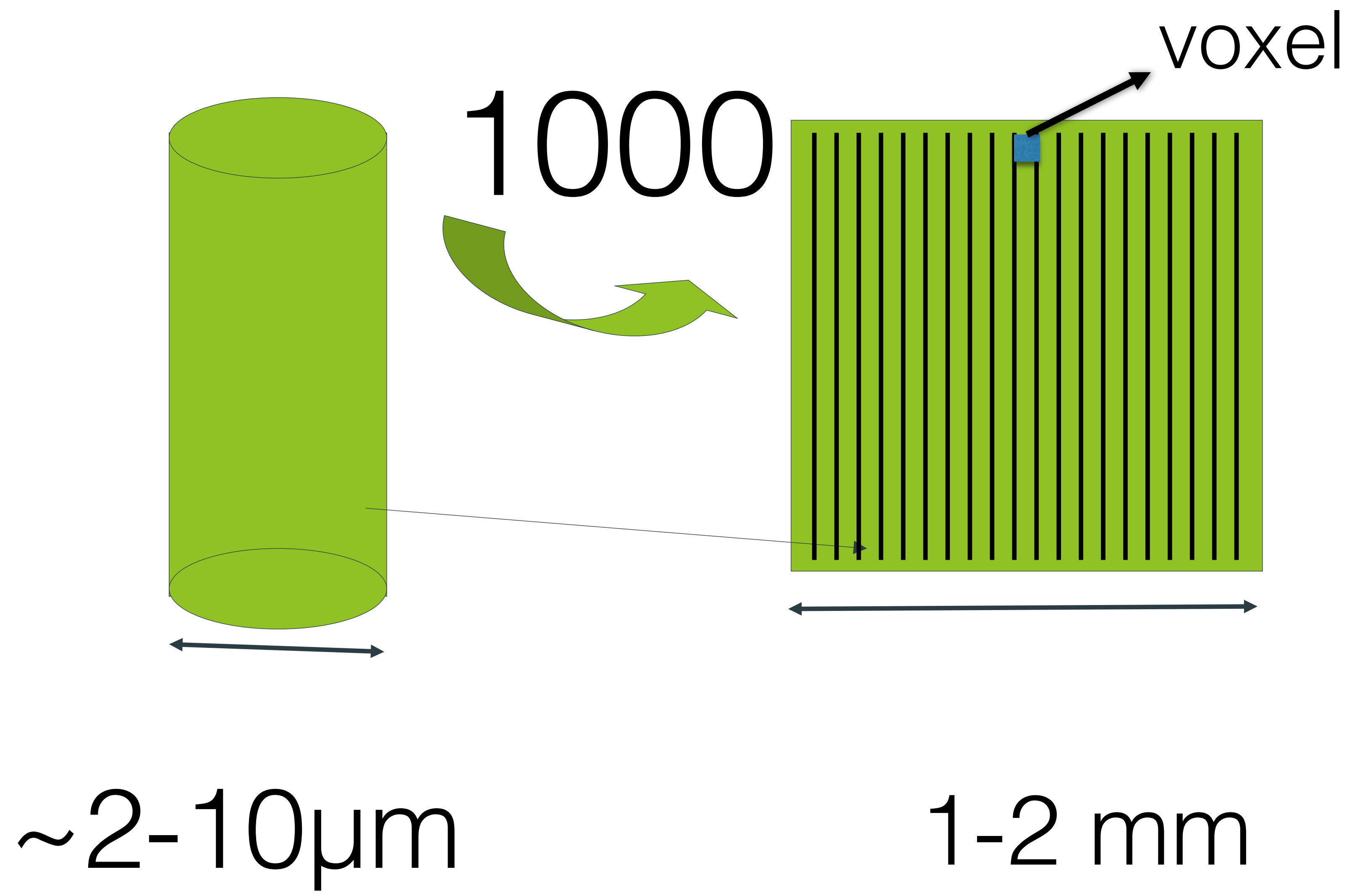
- ✓ Shows directional information
- ✓ Simple to implement
- ✗ Simplification to 3D
- ✗ Difficult to extract orientation information beyond (x,y,z)



Displaying DTI

Diffusion-Weighted MRI

- Fibers – Micrometers (~2-10μm)
- Scanner (MR) – Millimeters (~1-2 mm)



Tensor Visualization

Tensor Fields

- What data are we looking at?

data	description
2x2 matrix	2D tensor field
3x3 matrix	3D tensor field

Tensor Visualization

Why Do We Care?

If you're sitting at a cocktail party with a bunch of engineers, physicists, and mathematicians, and you want to start a heated debate,

Just ask out loud: "What is a tensor?"

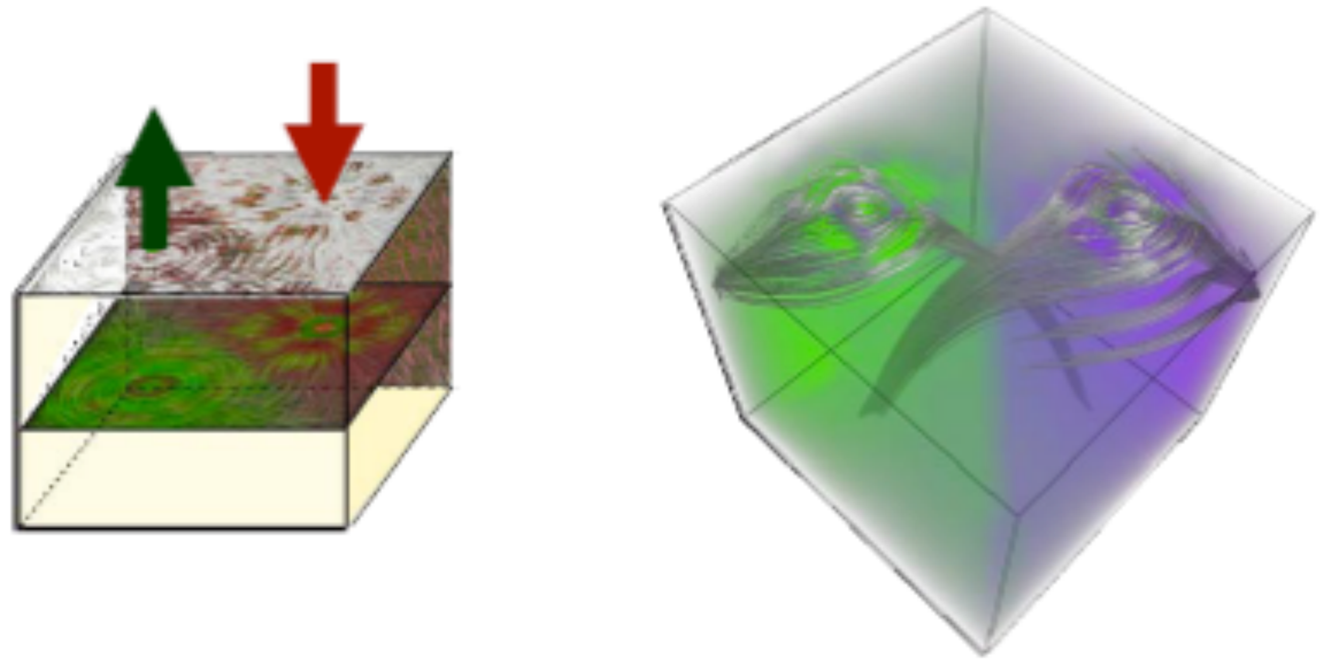
- One person will say that, for all practical purposes, a tensor is just a **fancy word for a matrix**.
- Then someone else will pipe up indignantly and insist that a tensor is a **linear transformation from vectors to vectors**.
- Yet another person will say that a tensor is an ordered **set of numbers that transform in a particular way upon a change of basis**.
- Other folks (like us) will start babbling about **"dyads" and "dyadics."**

[Brannon]

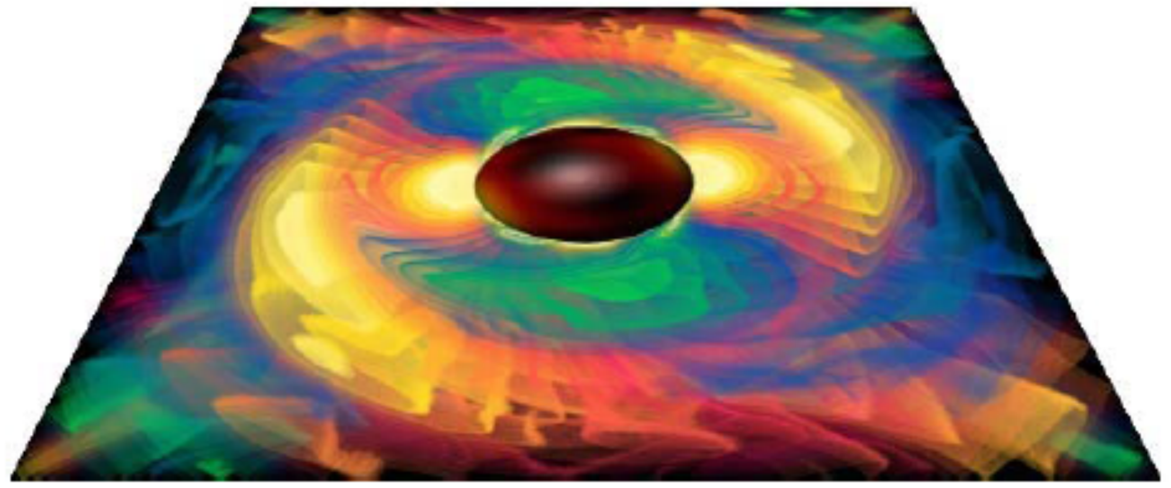
Courtesy of Ingrid Hotz IEEE Vis 2014 – tutorial tensor visualization – tensorvis.org

Tensor (field) Visualization

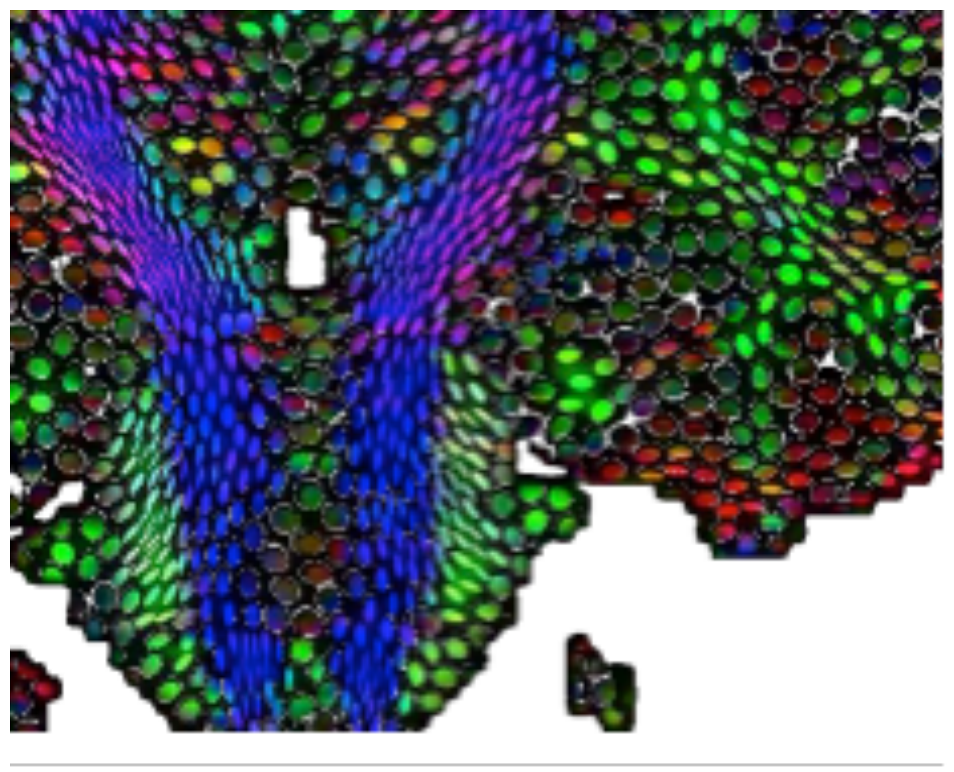
Material Sciences
(Stress tensor)



Metric tensor
(Simulation of General Relativity,
Curvature Tensor)



Medicine
(Diffusion tensor imaging: reconstruction
of fibrous structure)



Tensor (field) Visualization

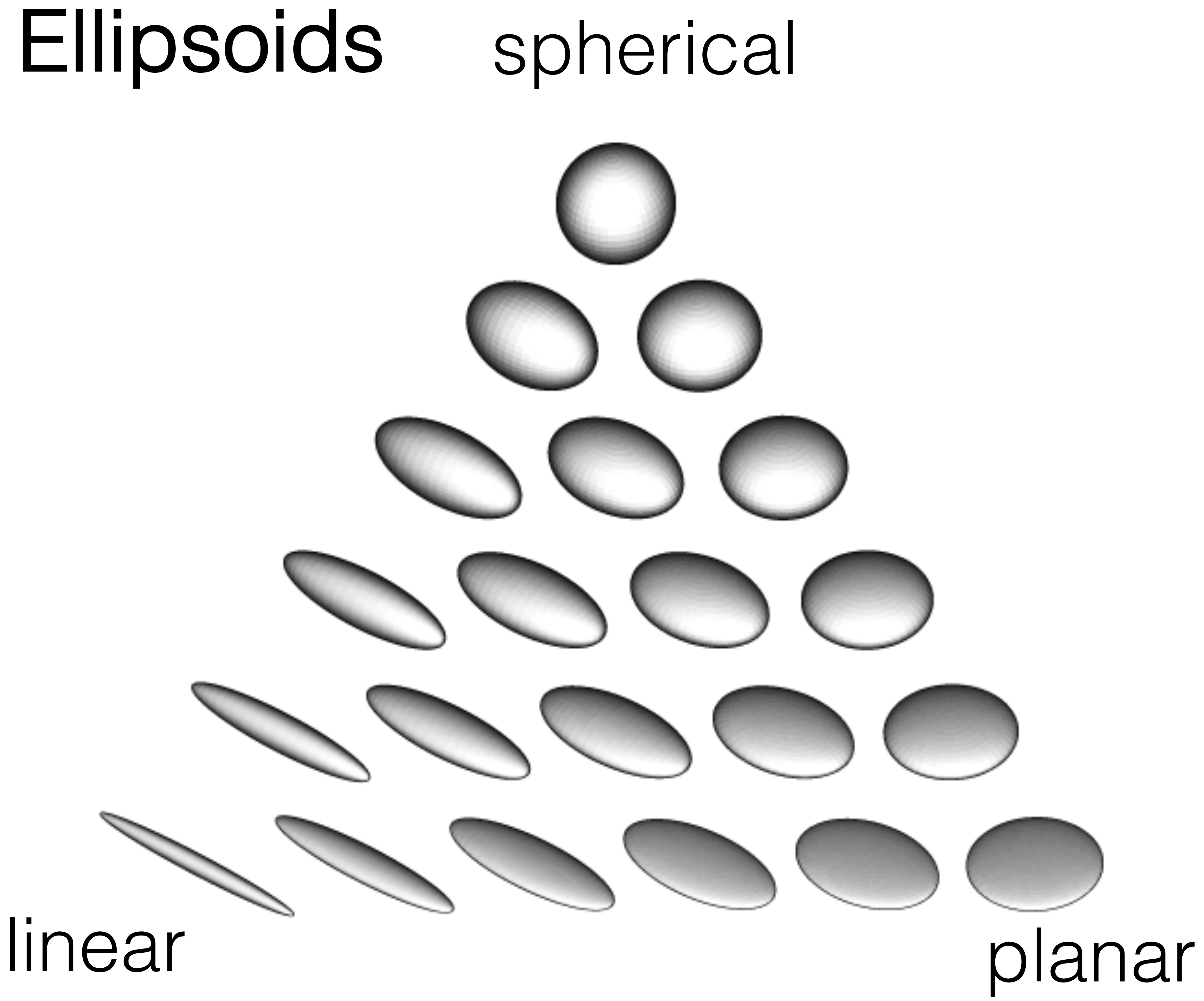
- Simplify to scalar fields (e.g. FA)
  - There are several values that can be extracted usually application dependent
    - “Easy” to visualize
    - Simplification 6D → 1D: loses information

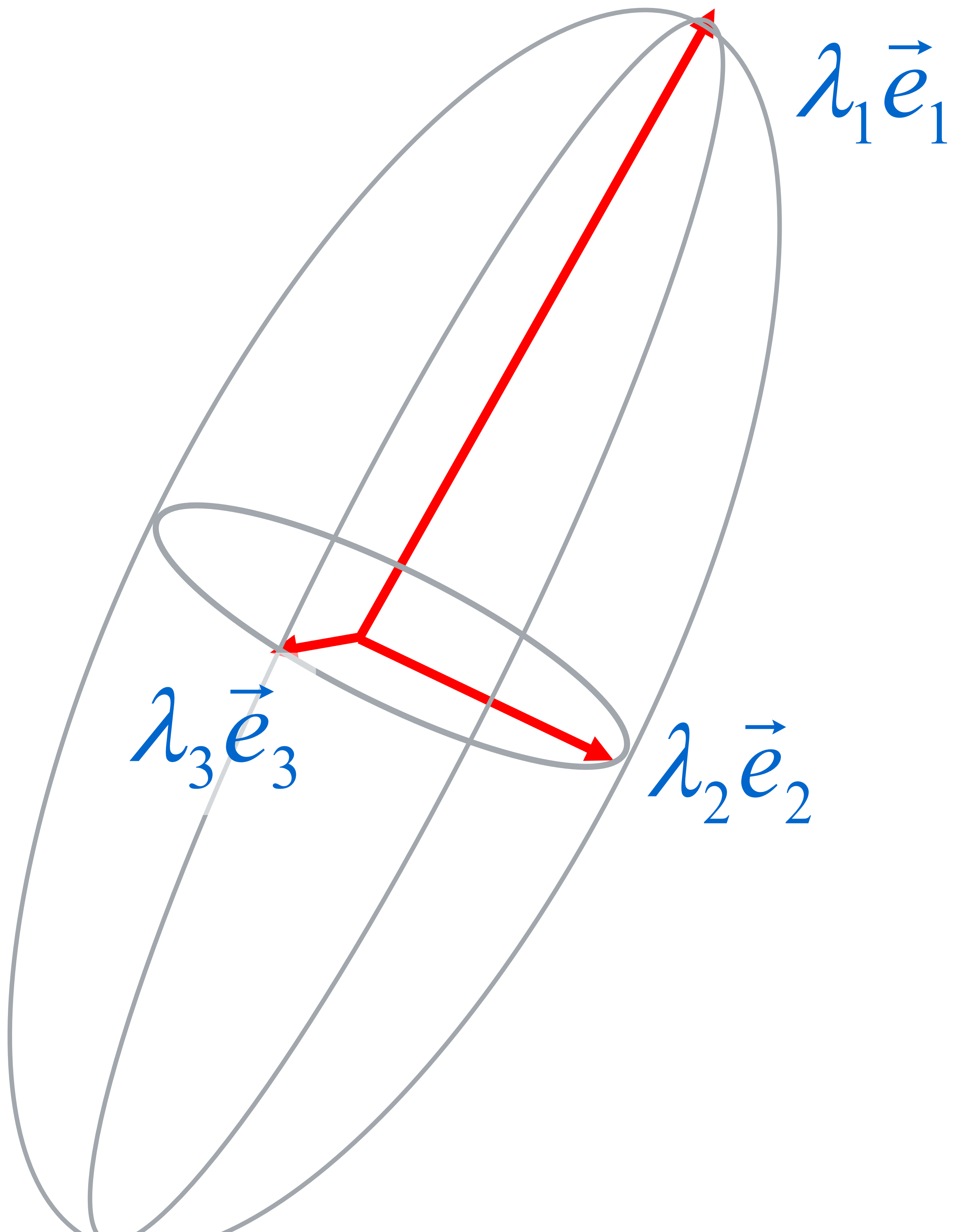
Glyph Representation

Shows local full information

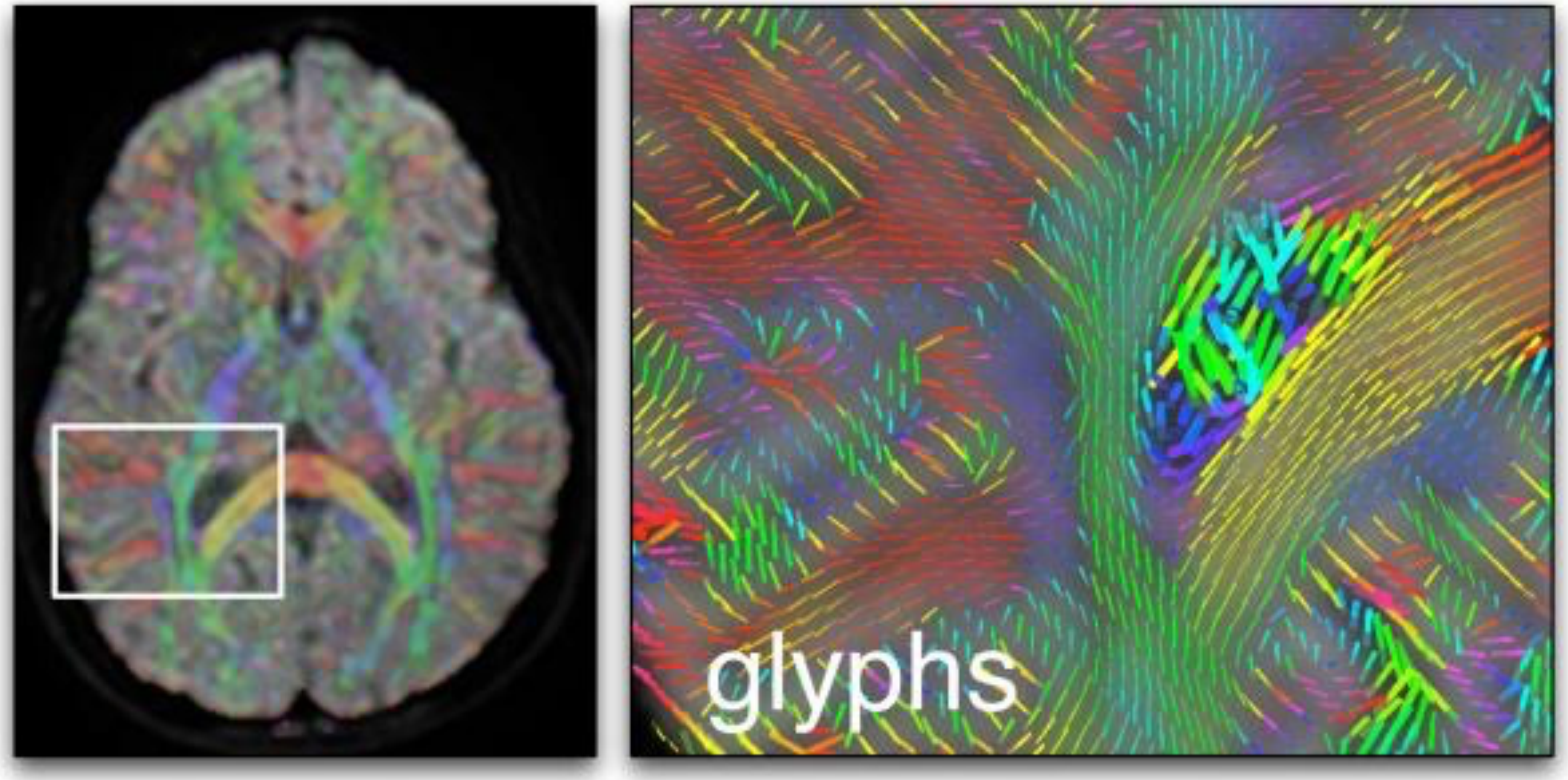
Symmetric positive-definite second-order tensors

Ellipsoids



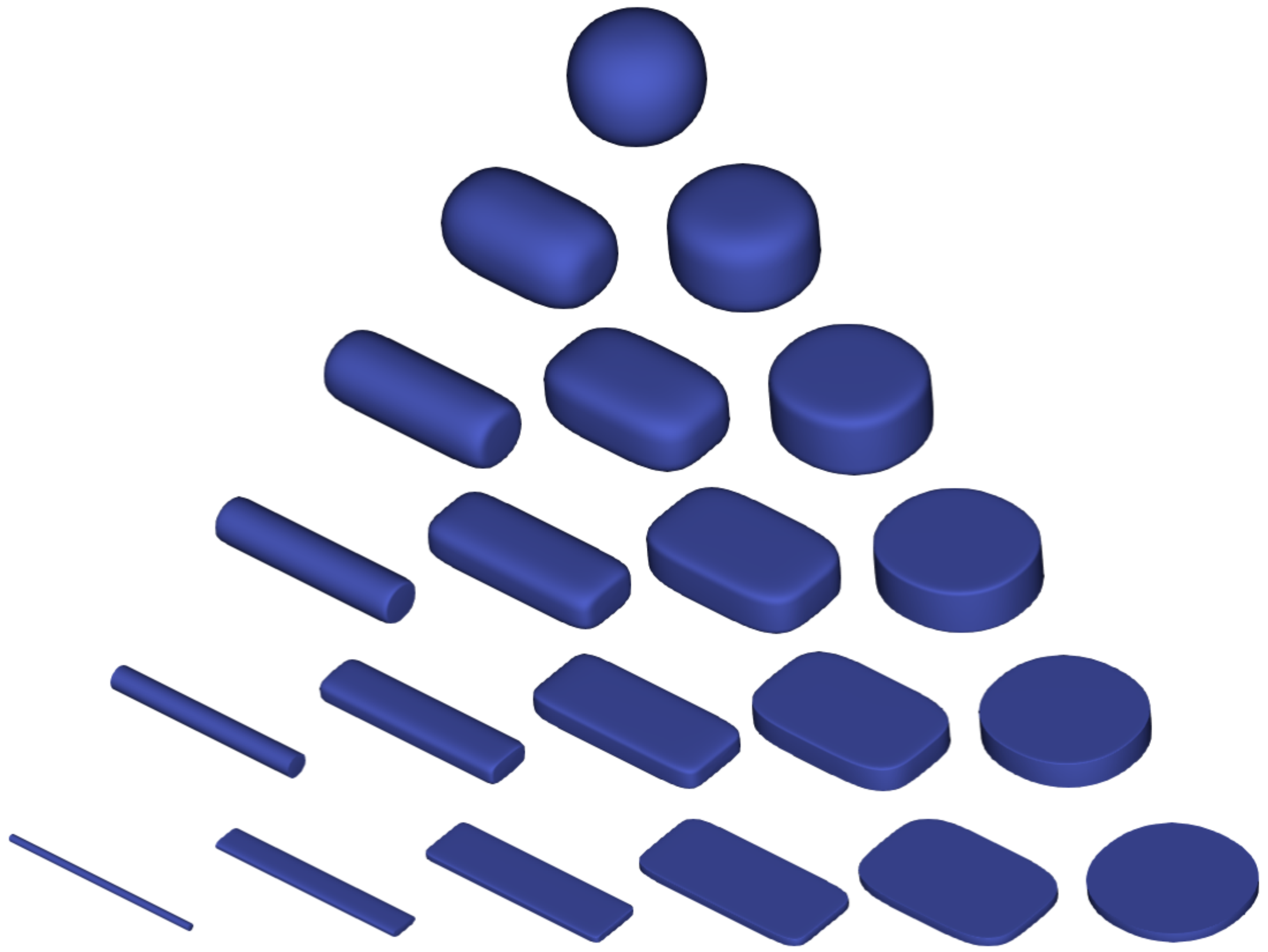


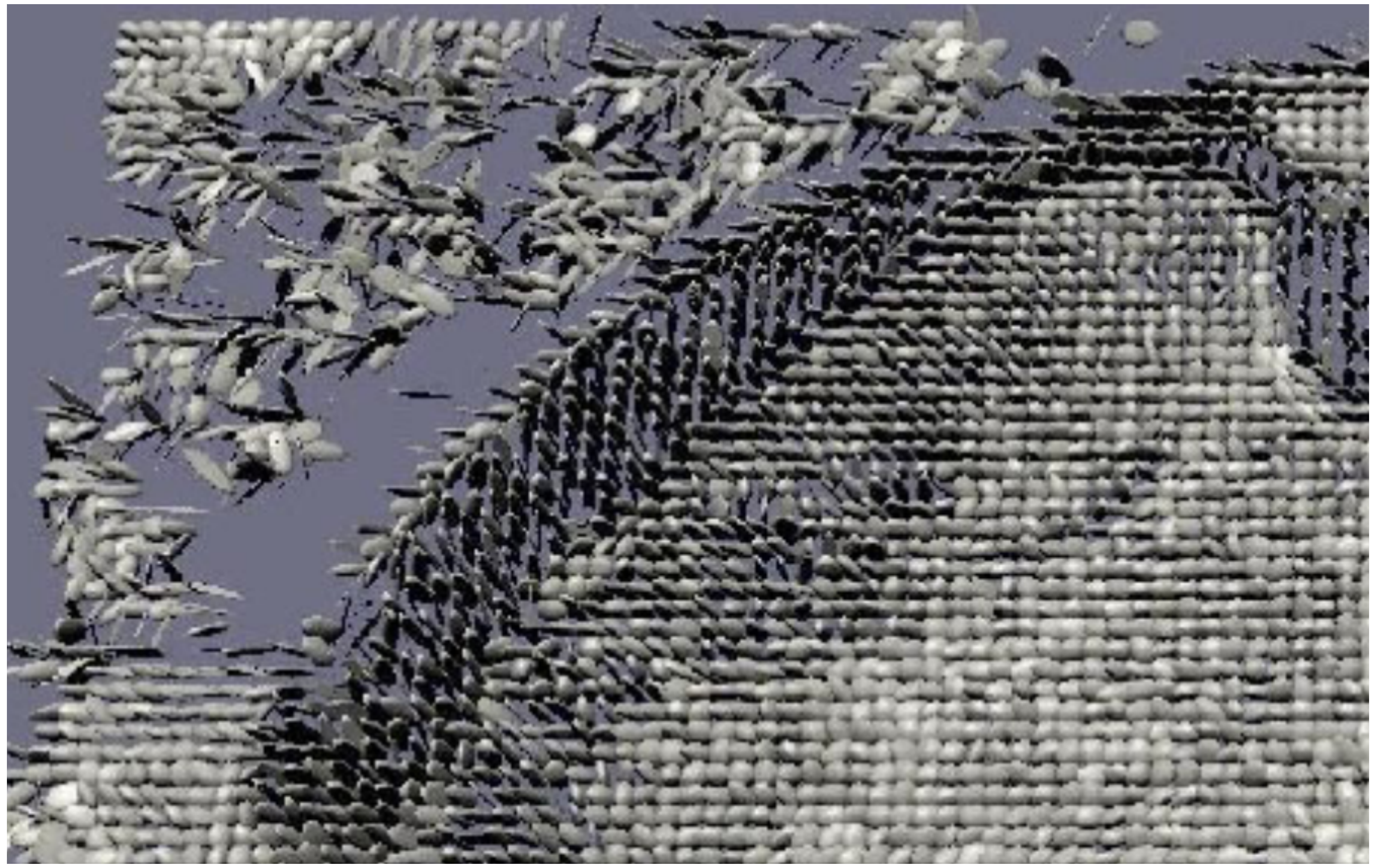
Displaying DTI



Displaying DTI

- Classical Glyphs

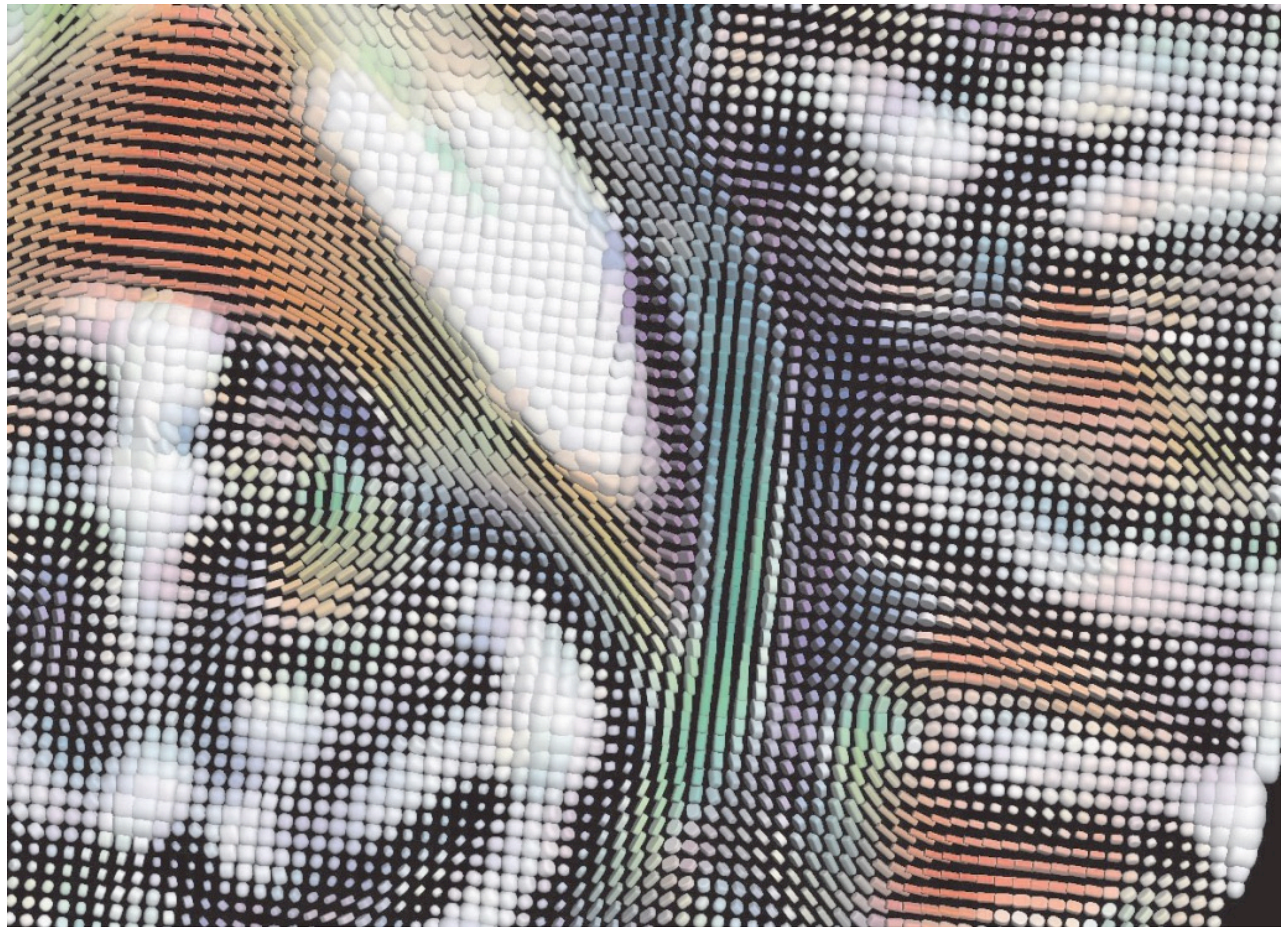




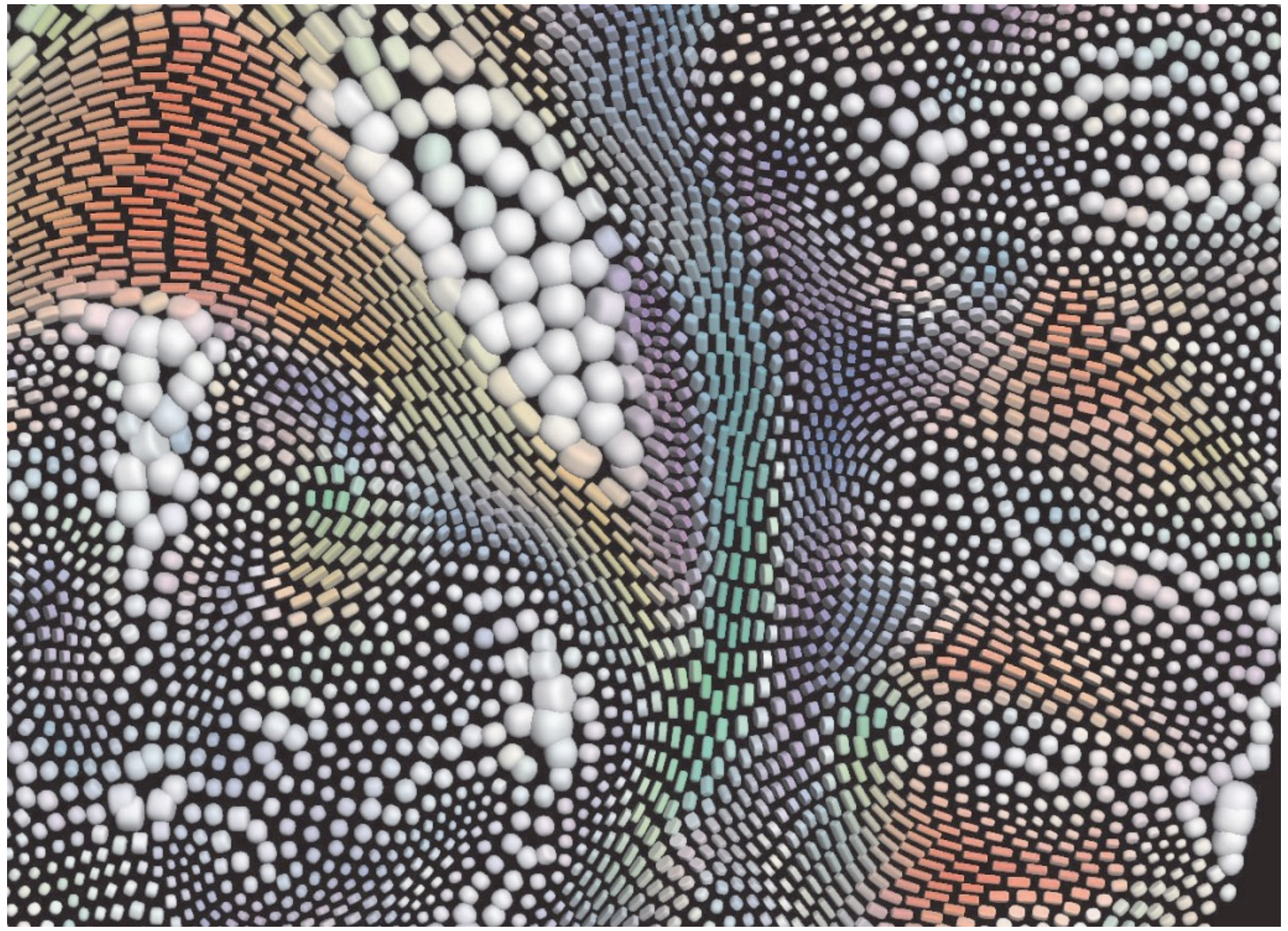
Glyph Packing

Grid structure can hide the real structure of the data

(Kindlmann and Westin 2006)



Grid structure



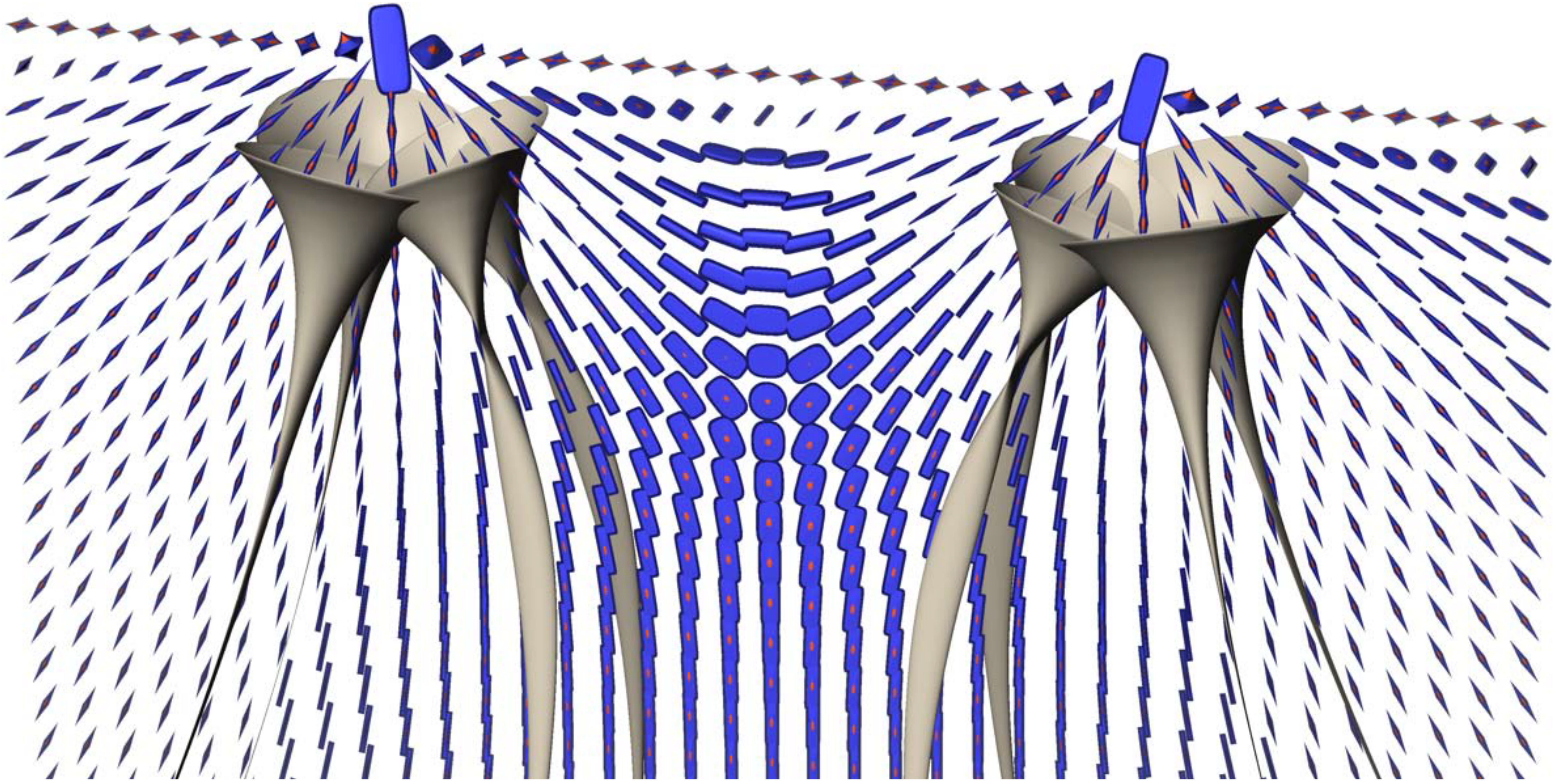
Glyph Packing
Interpolation is needed

Displaying DTI

- Drawing all glyphs may lead to important occlusion problems
    - Use glyphs only on selected slices
        - Vertically, horizontally or oblique

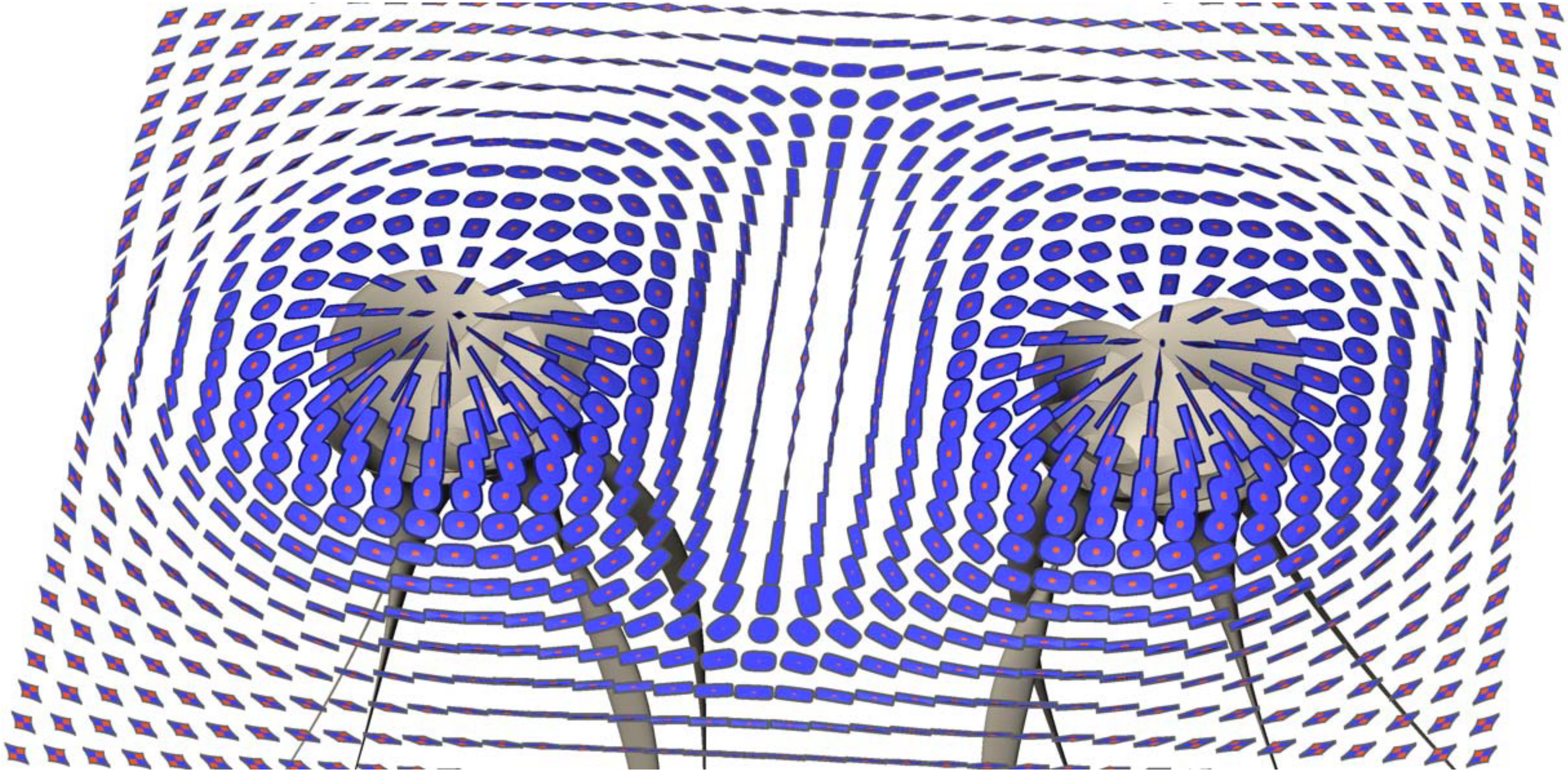
Displaying DTI

- Glyphs on a vertical cutting plane



Displaying DTI

- Glyphs on a horizontal cutting plane

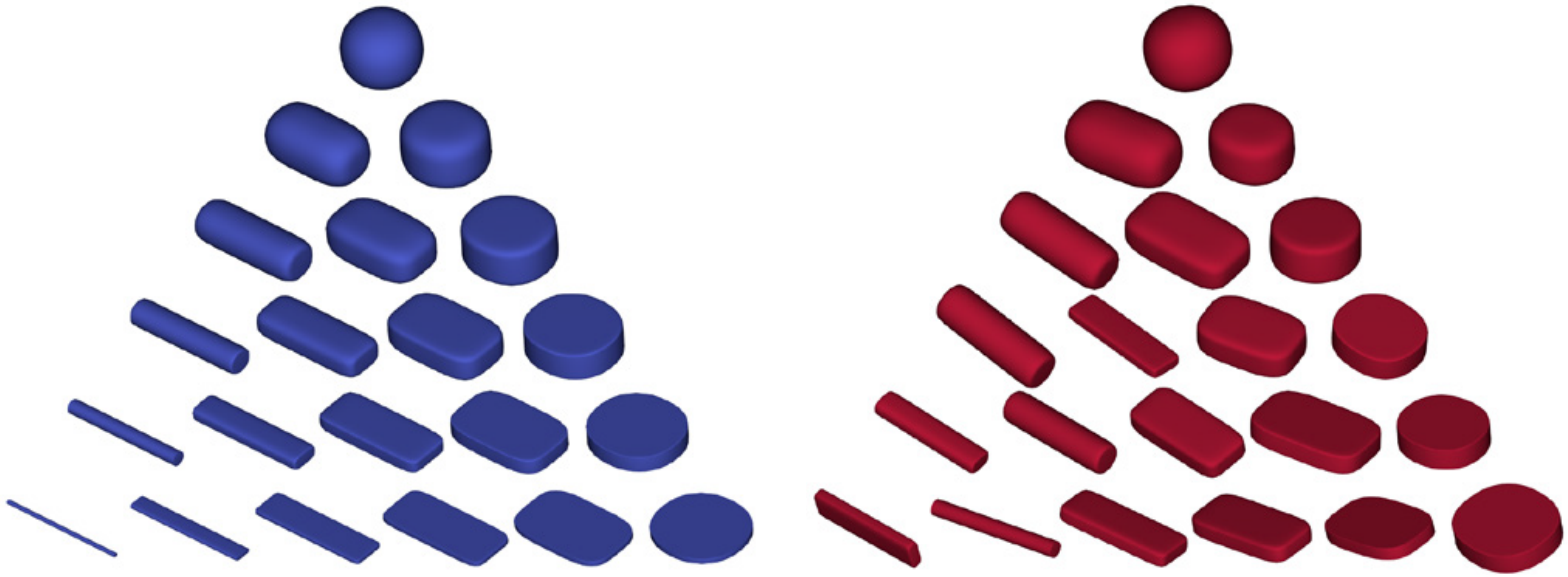


Displaying DTI

- Visual comparison is often necessary
  - To study the effects of acquisition parameters
  - To investigate the influence of pathologies on white matter structures
  - …
- Several alternatives:
  - Juxtaposition
  - Superposition
  - Superposition with transparency

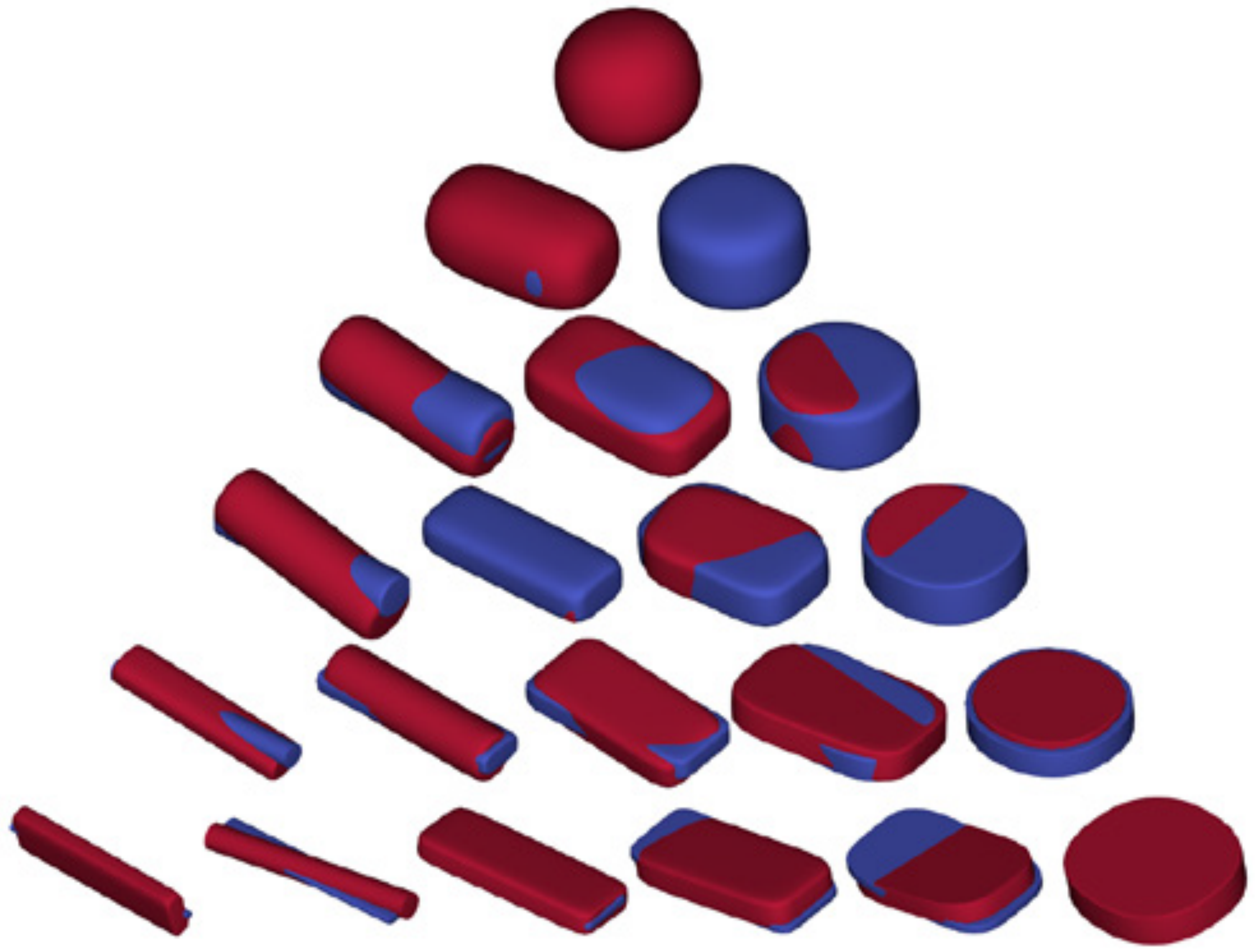
Displaying DTI

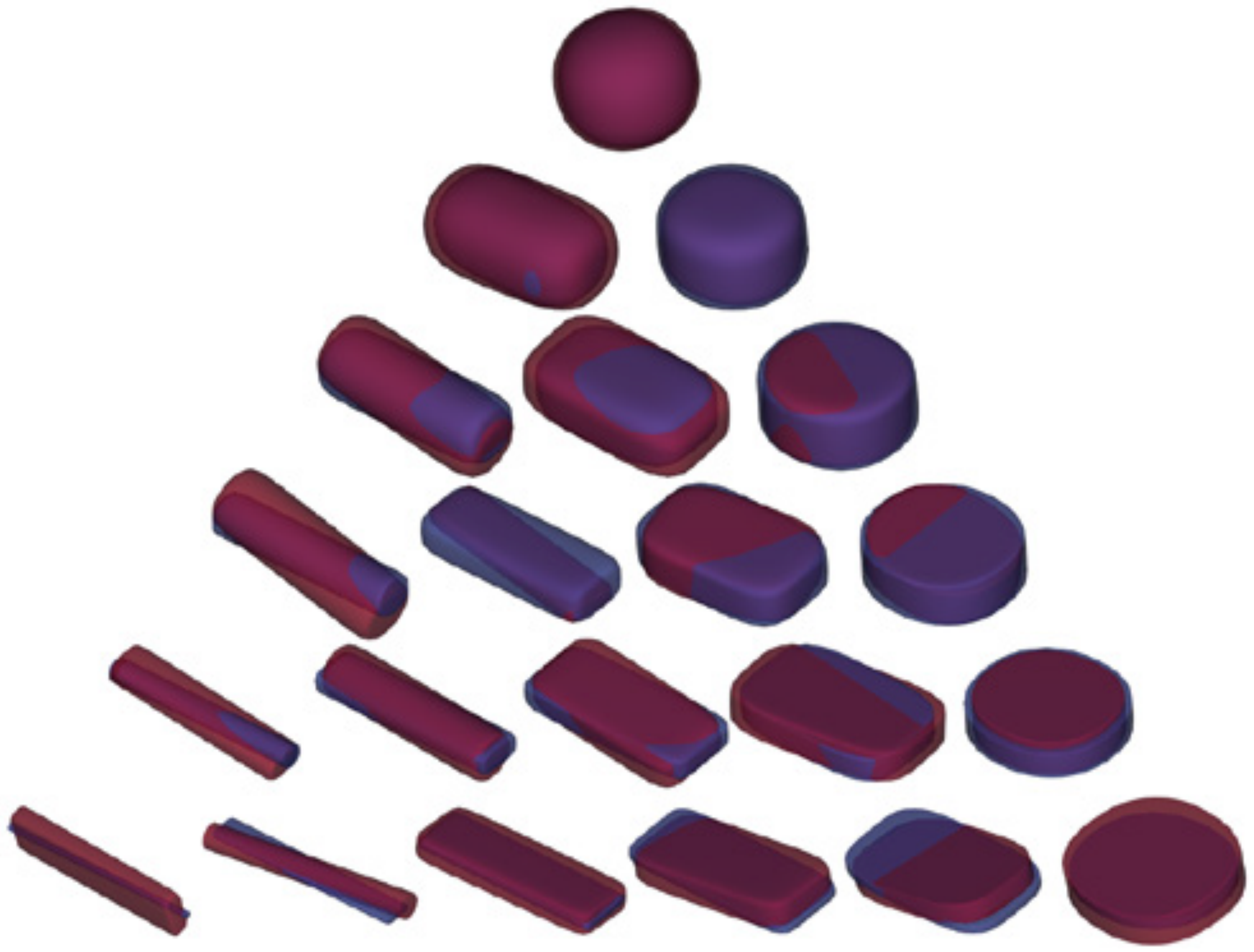
- Comparing glyphs. Juxtaposition
    - Hard to distinguish visual differences



Displaying DTI

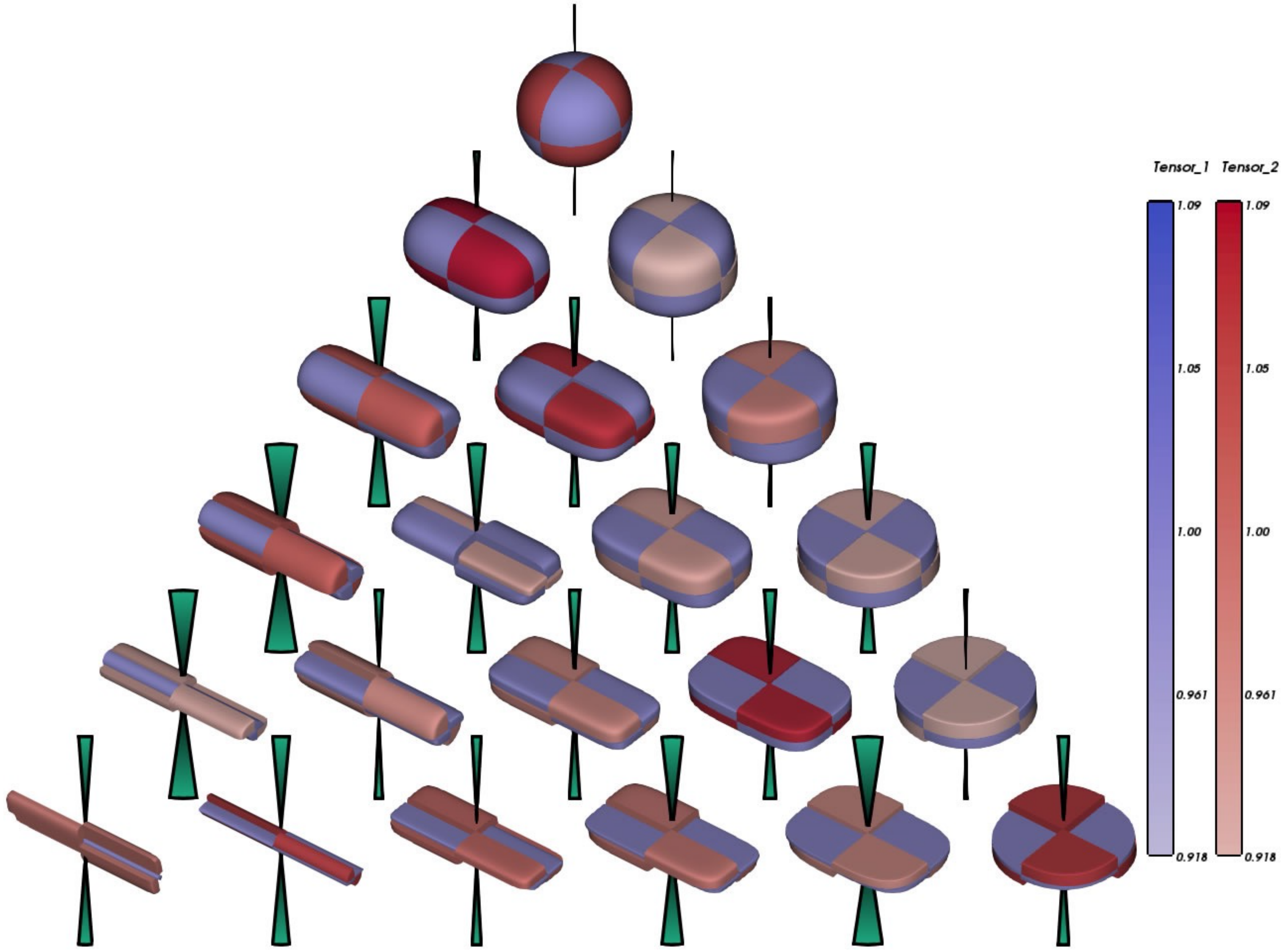
- Comparing glyphs. Superposition & superposition with transparency:
  - Occlusion & size may be a problem (one could be inside the other)
  - Difficult to determine the factors that differentiate them





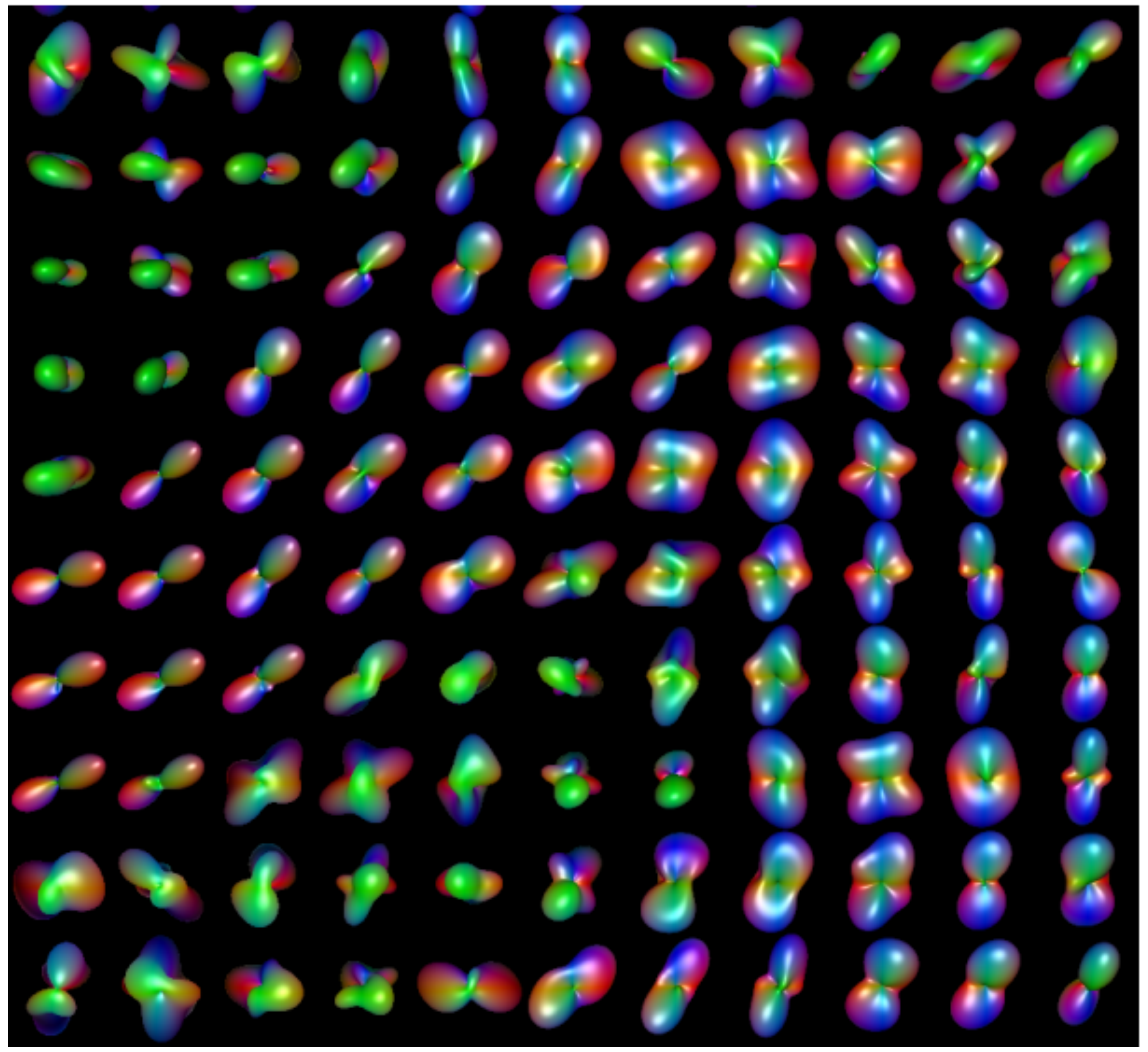
Displaying DTI

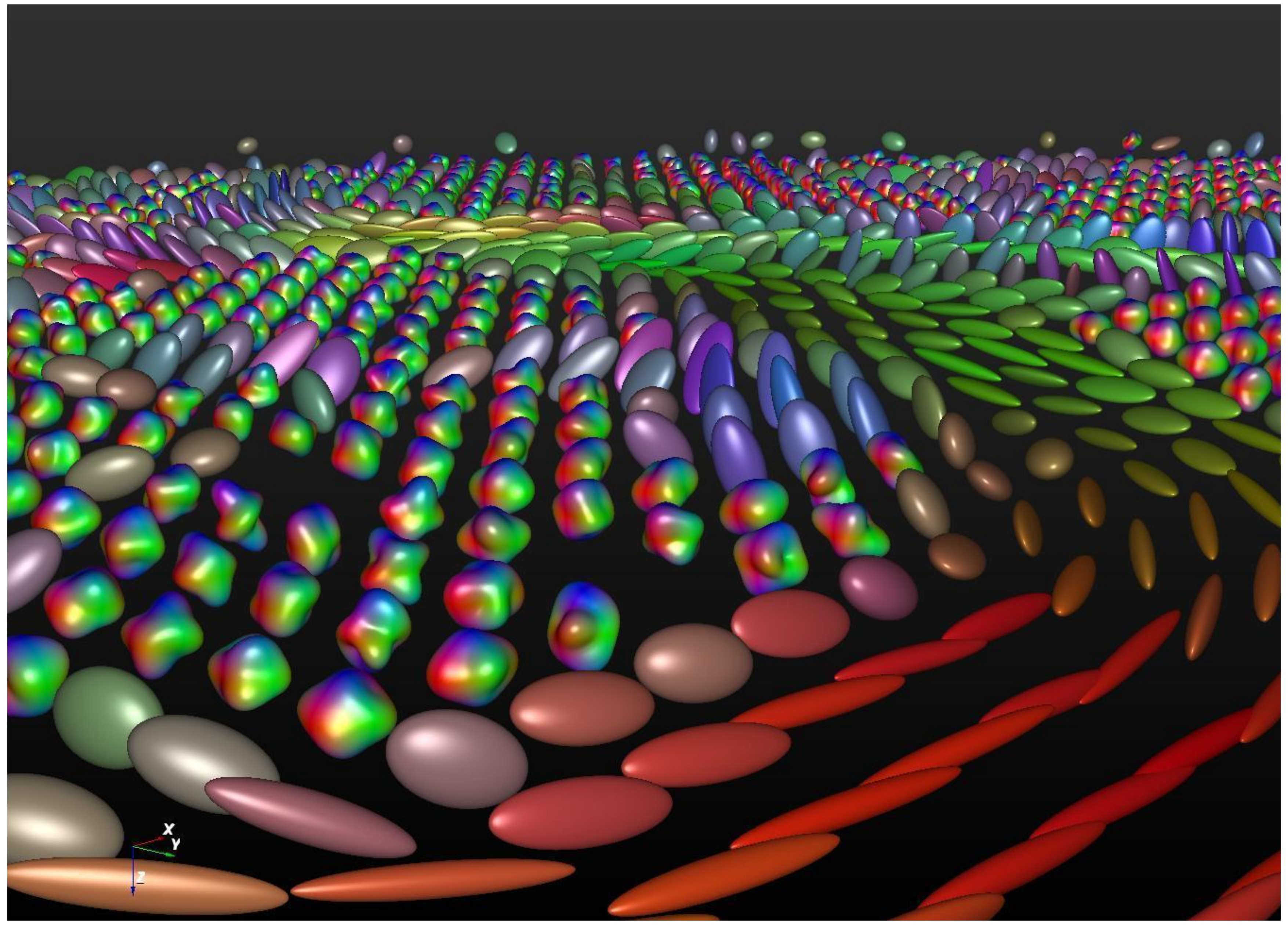
- Comparable glyphs
  - Align the glyphs
  - Divide the space in 4 quadrants
  - Use checkerboard analogy to display each element in one quadrant



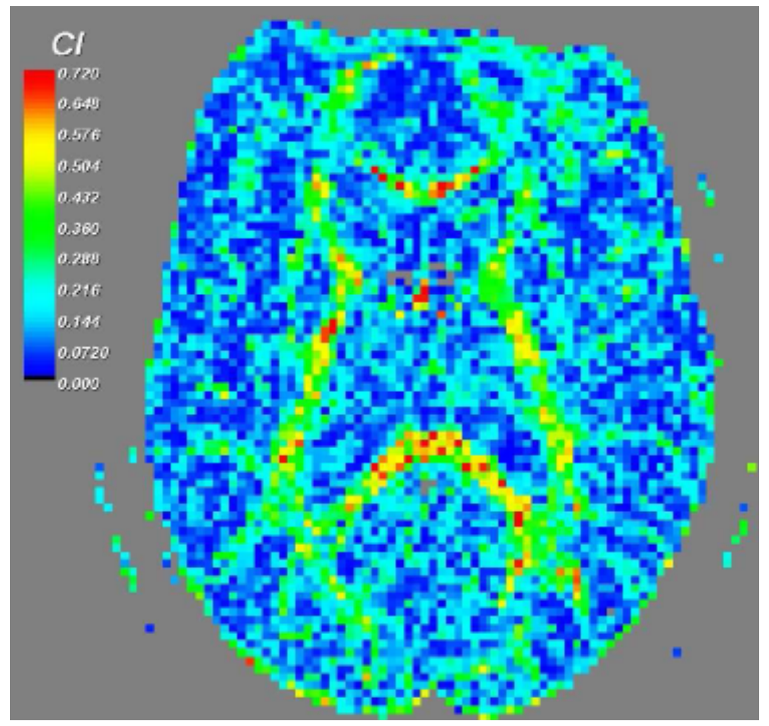
Displaying DTI

- Glyphs for HARDI
    - More complex shapes can also be used

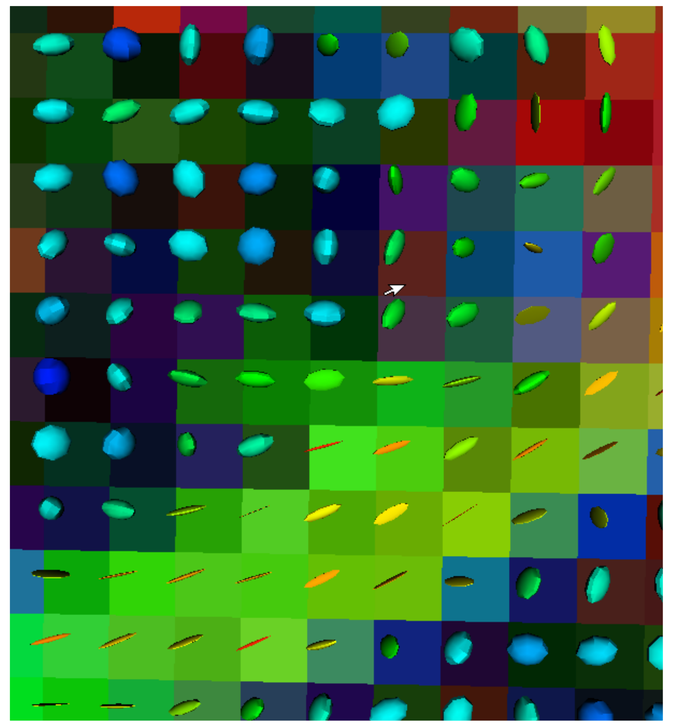




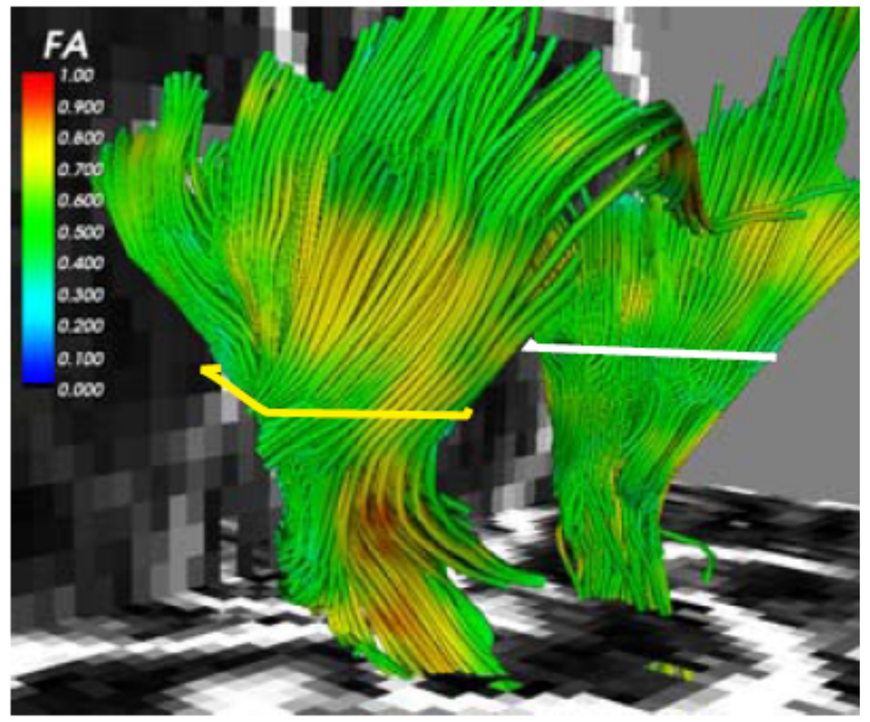
Displaying DTI



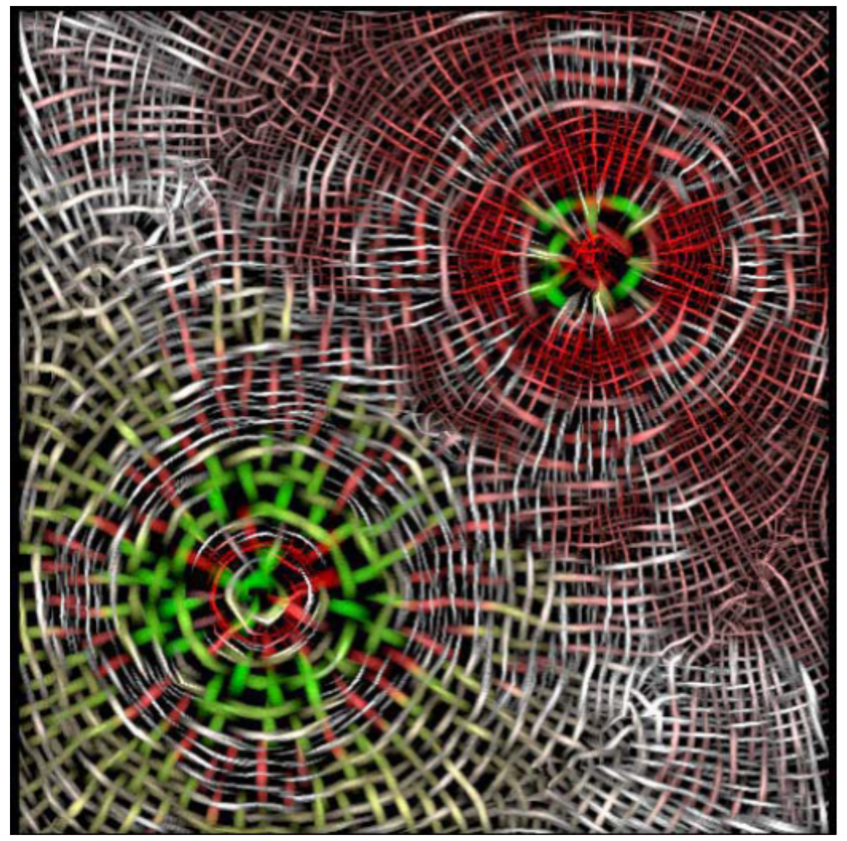
Scalar Fields



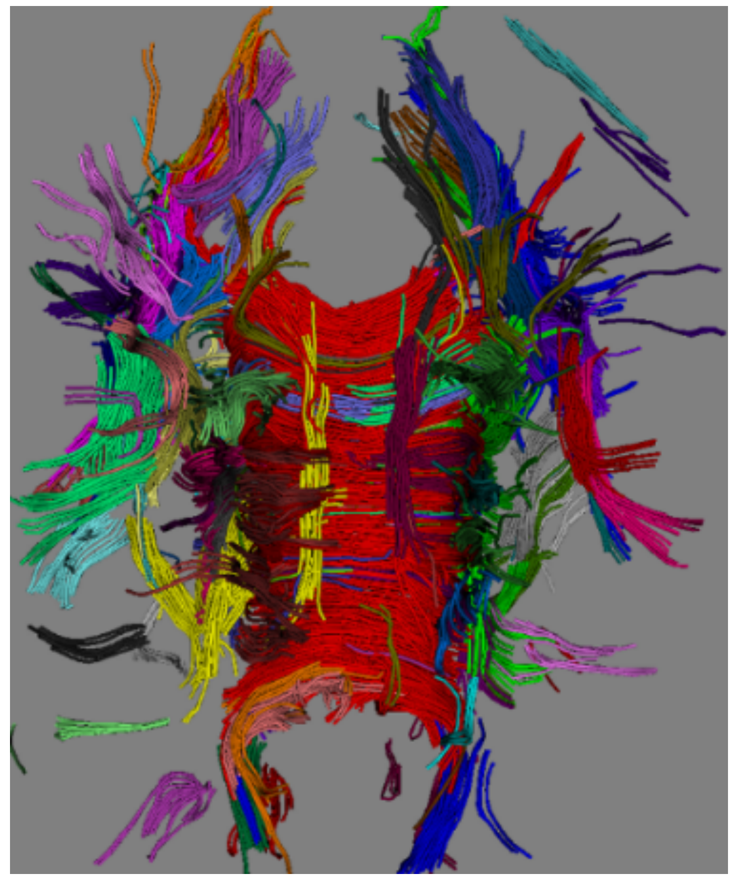
Glyphs



Tensor field lines



Texture



Segmentation

Outline

- DTI basics
- Measuring DTI
- Displaying DTI
- Tractography
- Challenges
- Examples

Tractography

- Estimation of the trajectories of fiber tracts in the white matter
  - Note the use of the word **estimation**
- Can then use this to address different diagnosis, surgery…
  - Problems with uncertainty

Tractography

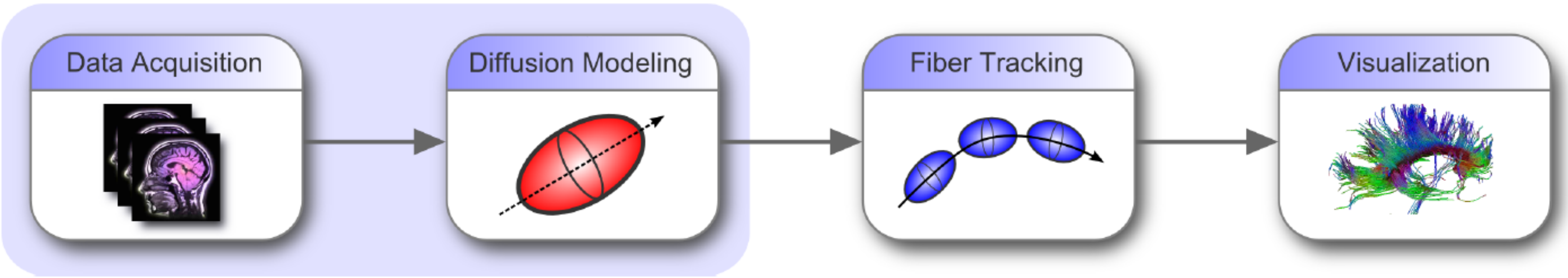
- General idea:
  - Use the diffusion tensor to track fibers along their whole length.
    - Starting from a seed region of interest (ROI)
      - Generally defined manually
    - Look for adjacent voxels whose main diffusion direction is in the continuity of the previous one

Tractography

- Most common approach is streamline tractography
  - Similar to hyperstreamlines tensor field visualization algorithm
  - Produces as output discrete curves or trajectories that are also called “tracts” (or “fibers” or “traces”)

Tractography

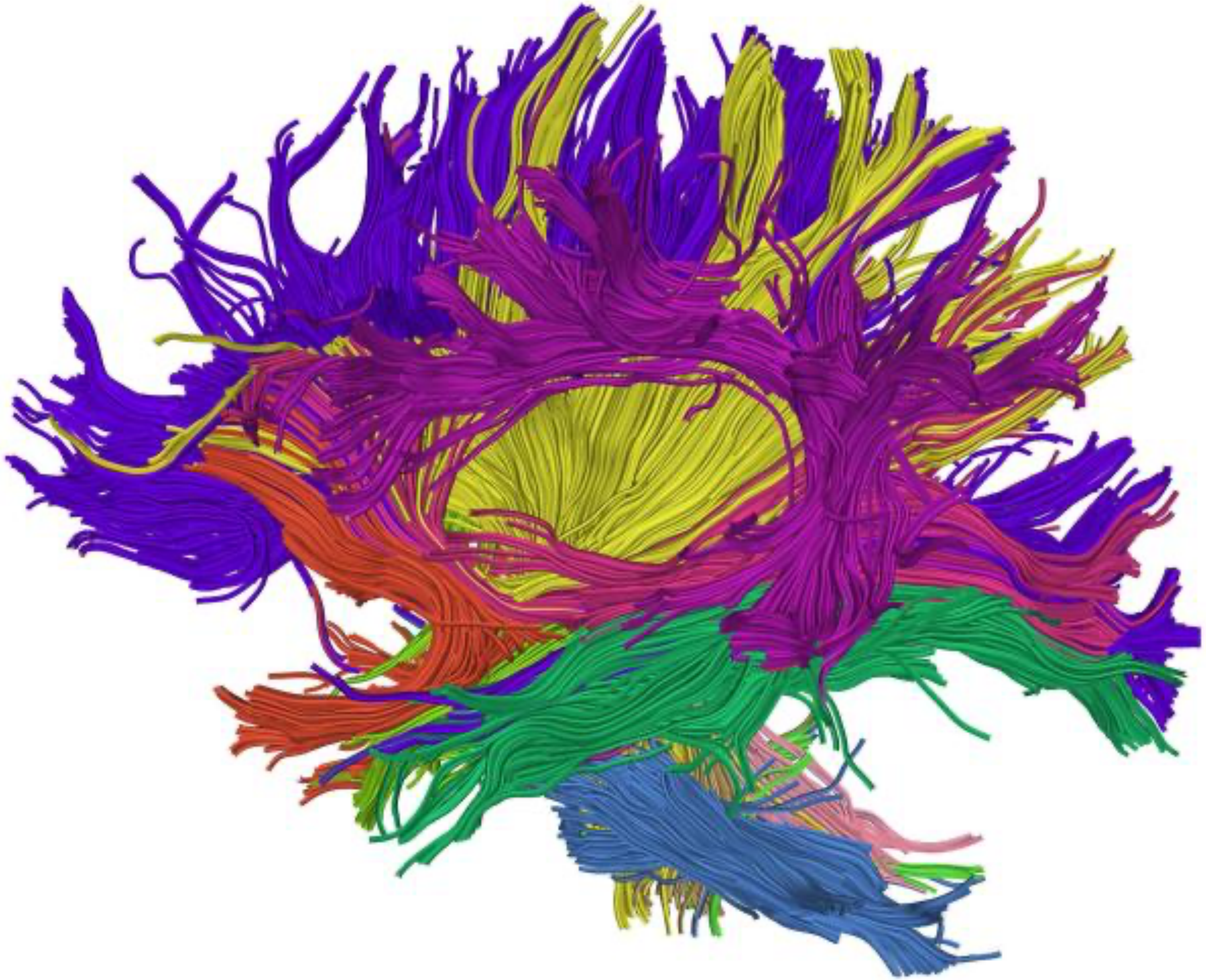
- Pipeline



Tractography

- Streamline tractography
  - Successive stepping in the direction of the principal eigenvector
    - Direction of fastest diffusion
    - Eigenvectors are tangent to the trajectory that is produced
      - Fixed step size of one millimeter or less (smaller than a voxel)
    - Calculated using Euler, second order Runge-Kutta, fourth order Runge-Kutta…

Tractography



Tractography

- Other methods exist:
  - Probabilistic tractography
  - Optimization methods (use graph theory or physical models
  - Region-growing and wavefront evolution methods
  - …

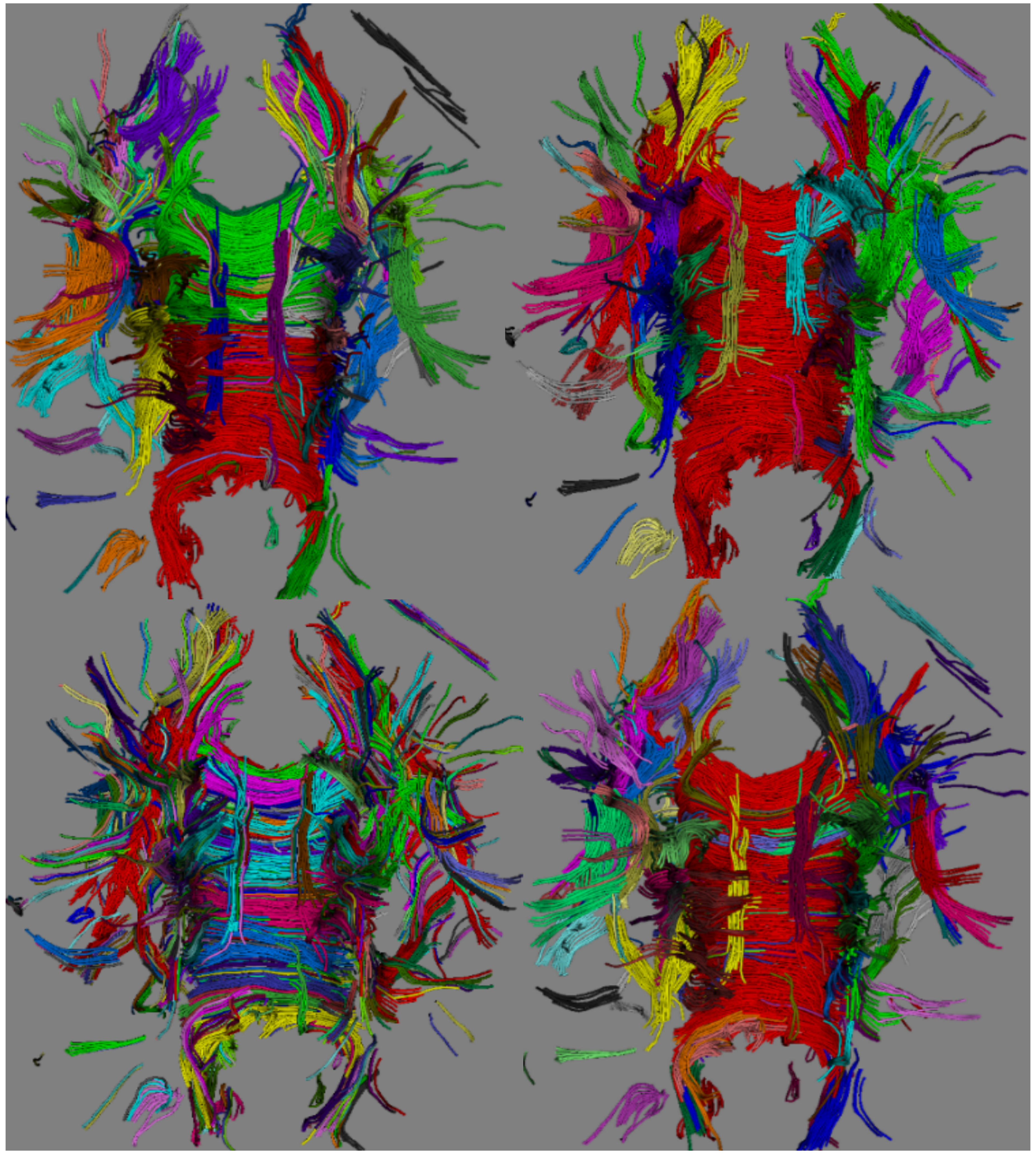
Tractography

- Problems:
  - May produce false positive and false negative results
    - Problems with crossings, partial volume effects…
  - Experiments have shown some clinical validations of accurate reconstruction using streamline tractography

Tractography

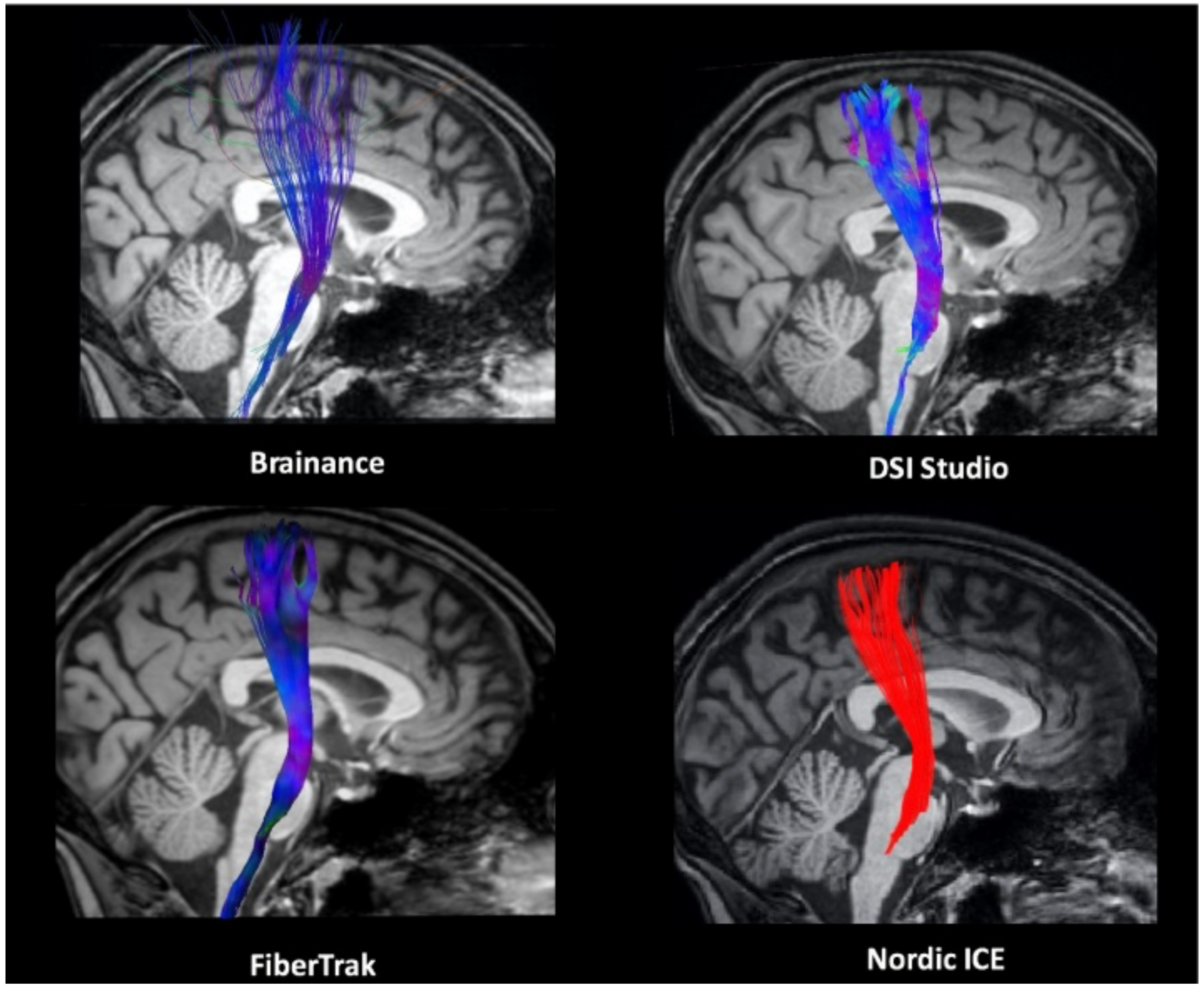
Seed point definition

- Region of interest
  - Biased
  - Not reproducible
  - Miss information
- Whole volume or dense visualization
  - Cluttering
- Clustering – bundle segmentation



Tractography

- Issues. Differences with software



Outline

- DTI basics
- Measuring DTI
- Displaying DTI
- Tractography
- Challenges
- Examples

Challenges

- Accurate results
- Illustrate uncertainty
- Better representation of glyphs (e.g. for comparison)

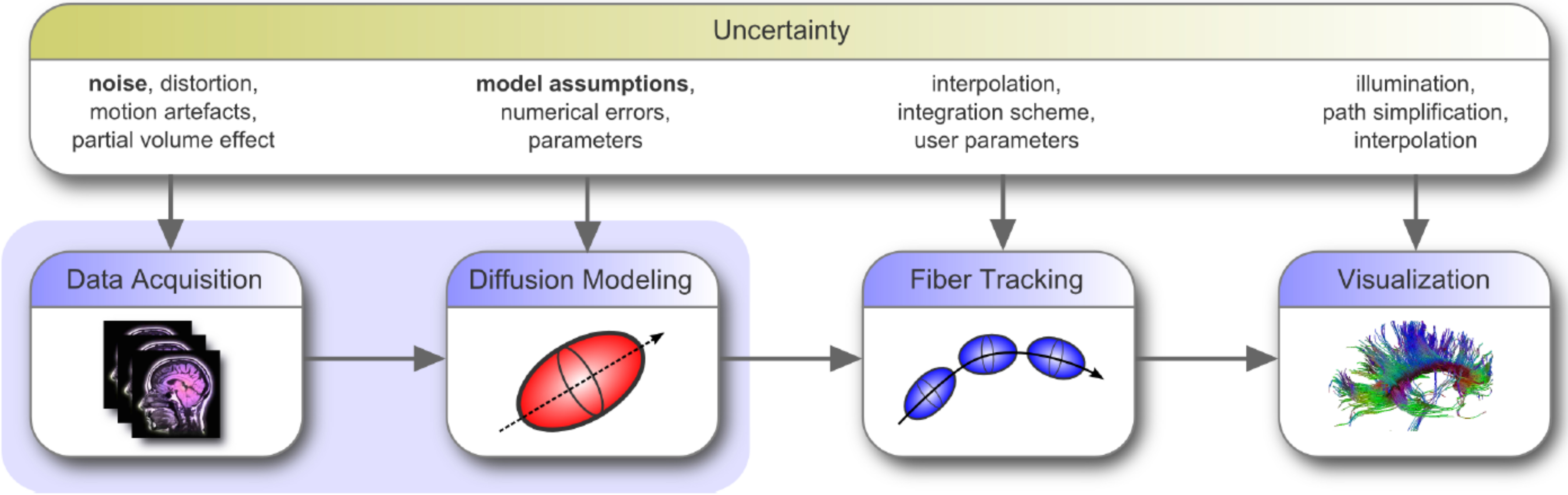
Outline

- DTI basics
- Measuring DTI
- Displaying DTI
- Tractography
- Challenges
- Examples

Examples. Uncertainty visualization

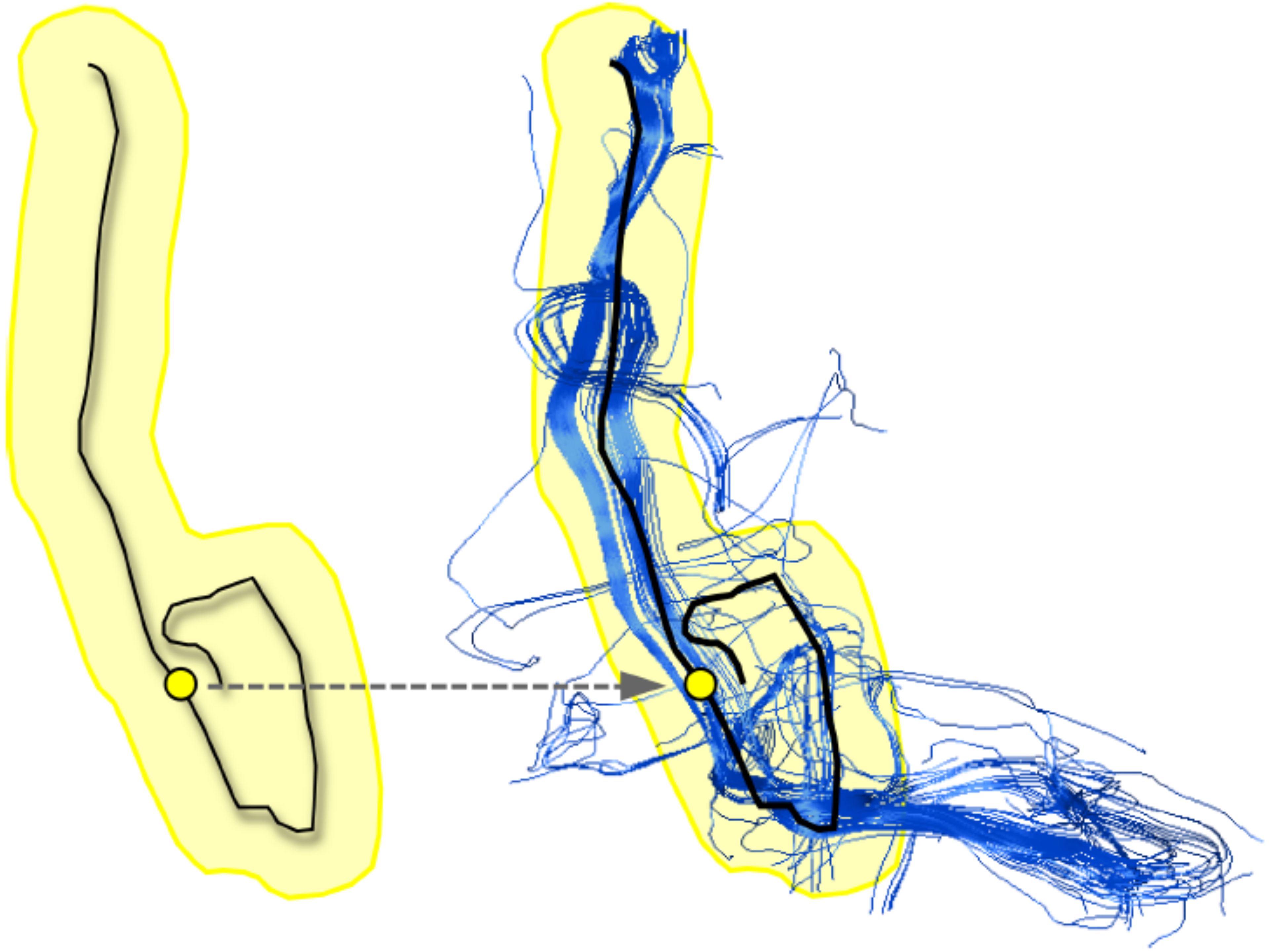
- Illustrative Uncertainty Visualization of DTI Fiber Pathways, R. Brecheisen B. Platel B.M. ter Haar Romeny A. Vilanova, The Visual Computer, 2012

Examples. Uncertainty visualization



Examples. Uncertainty visualization

- Problems with tractography:
  - Not exact method: many different fibers
  - May fall outside safety region

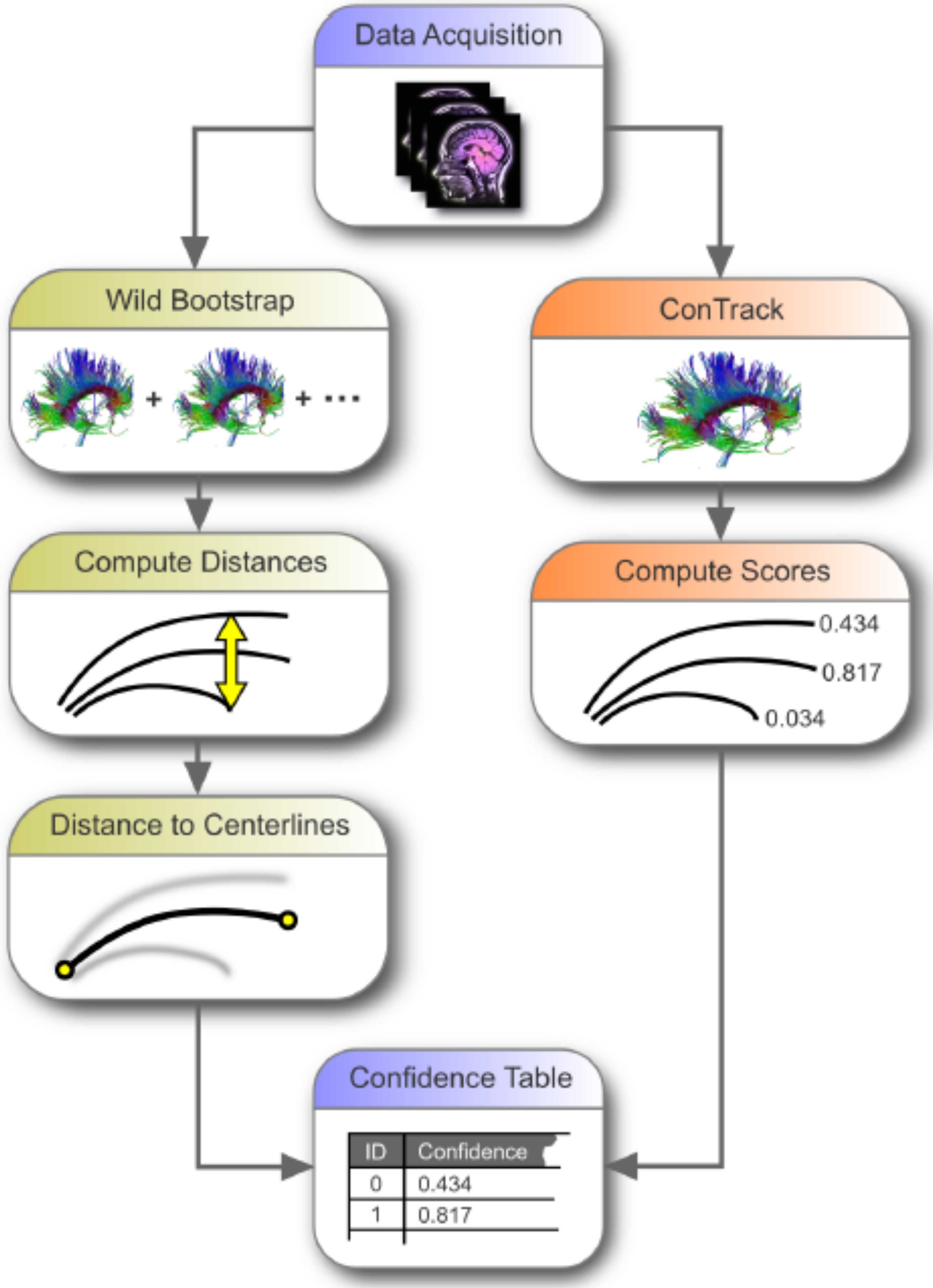


Examples. Uncertainty visualization

- Approximation:
    - Illustrate the uncertainty
    - Facilitate changing parameters interactively

Examples. Uncertainty visualization

- Pipeline:
  - Generate fibers
  - Generate confidences
  - Illustrate confidence

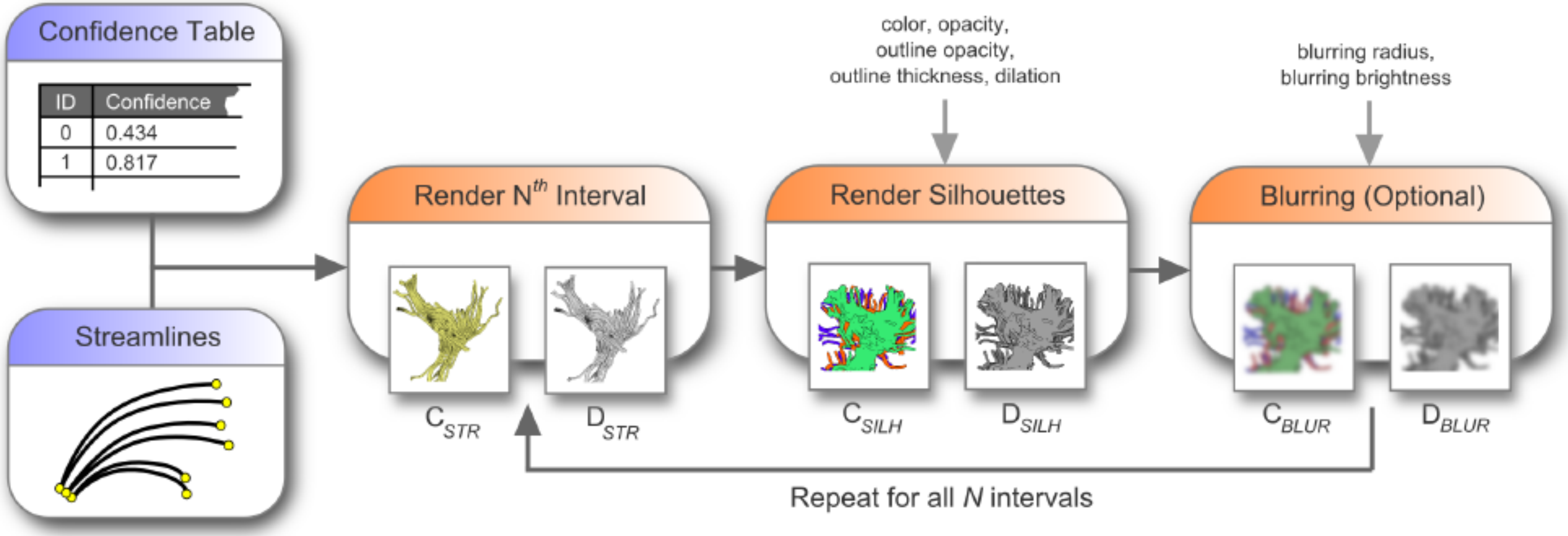


Examples. Uncertainty visualization

- Illustrate confidence intervals:
  - Step 1: Render most confident interval
    - Keep color and depth buffer
  - Step 2: Render subsequent intervals
    - Not overlapping (using stencil)
    - Reducing opacity
  - Step 3 (optional): Blur less confident intervals

Examples. Uncertainty visualization

- Overview



Examples. Uncertainty visualization

- Confidence exploration through interaction

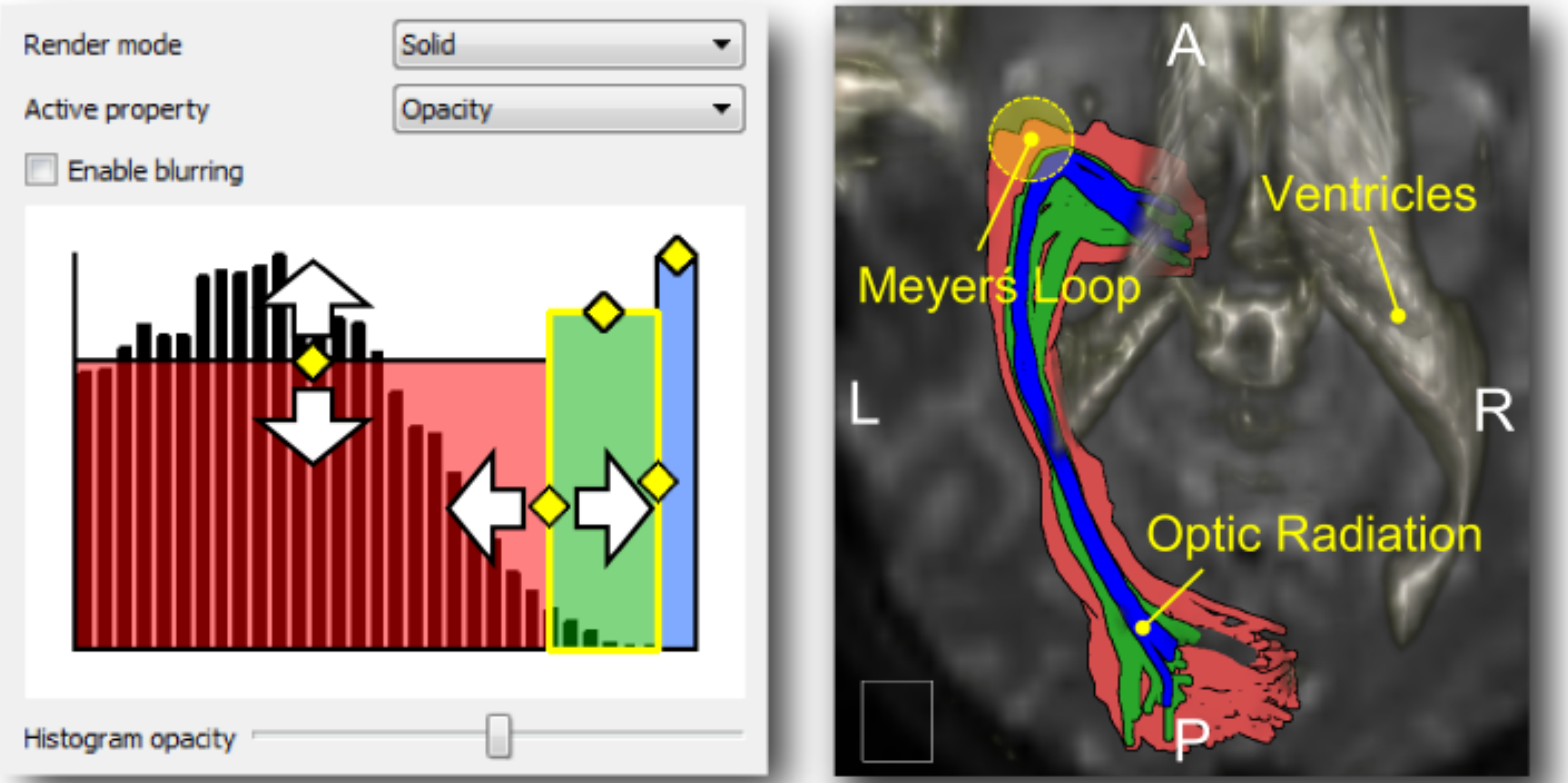
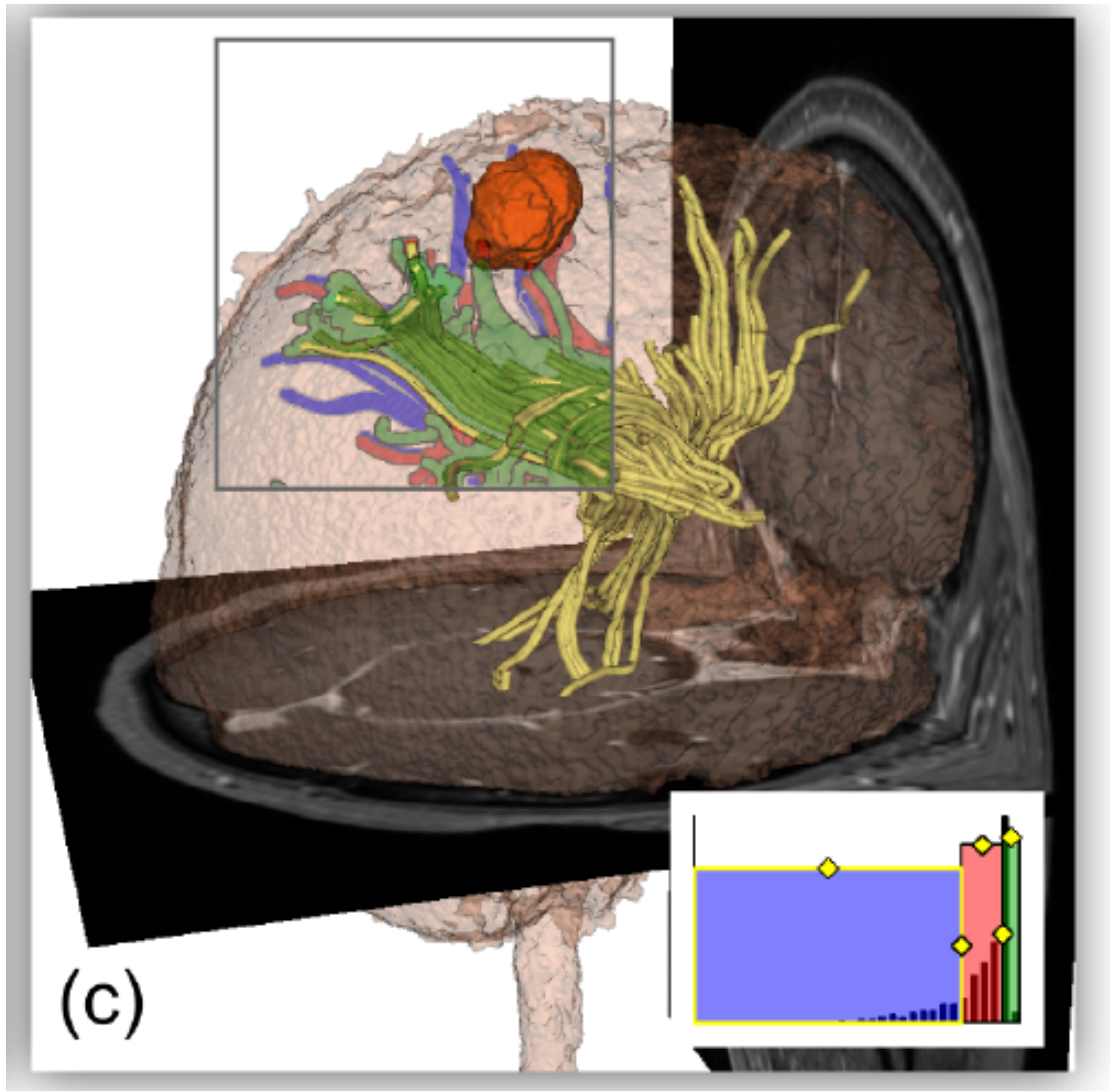


Fig. 6 Left: Confidence Histogram Widget with confidence values increase from left to right. White arrows indicate possible manipulation direction. Selected active property is 'Opacity'. Right: Corresponding confidence intervals of optic radiation fibers looping around ventricles.

Examples. Uncertainty visualization

- Example



Examples. Uncertainty visualization

- Tested with domain experts
- Three different scenarions
- Set of questions (Likert scale)

Examples. Uncertainty visualization

- Q1.1 What is the risk of a visual field deficit in anterior temporal lobe resection?
- Q1.2 How important is uncertainty visualization for anterior temporal lobe resections?
- Q1.3 What is the risk of resecting this particular low-grade glioma?
- Q1.4 How important is uncertainty visualization for low-grade glioma resection?
- Q1.5 What is the risk of resecting this particular intracerebral metastasis?
- Q1.6 To what extent would you discuss the uncertainty with the patient?

Examples. Uncertainty visualization

- Results

	User A	User B	User C
Q1.1	2	2	2
Q1.2	4	4	3
Q1.3	4	1	1
Q1.4	4	4	5
Q1.5	2	2	2
Q1.6	5	4	4

Examples. Uncertainty visualization

- Q2.1 To what extent does the standard fiber visualization give you more confidence in assessing risk of anterior temporal lobe resections?
- Q2.2 To what extent does the standard visualization give more confidence in assessing risk of resecting the given low-grade glioma?
- Q2.3 To what extent does the standard visualization give more confidence in assessing risk of resecting the given intracerebral metastasis?
- Q2.4 Which two visual styles do you prefer?
- Q2.5 Does our representation of uncertainty give you more confidence?
- Q2.6 How useful is it to show uncertainty only in a selected ROI?
- Q2.7 What is the overall rating of the potential use of our visualization?

Examples. Uncertainty visualization

- Results

	User A	User B	User C
Q2.1	4	2	3
Q2.2	3	2	2
Q2.3	1	1	1
Q2.4	Opacity	Outline	Opacity
	Lightness	-	Lightness
Q2.5	4	4	4
Q2.6	4	4	3
Q2.7	4	4	4

Introduction to DTI

Pere-Pau Vázquez