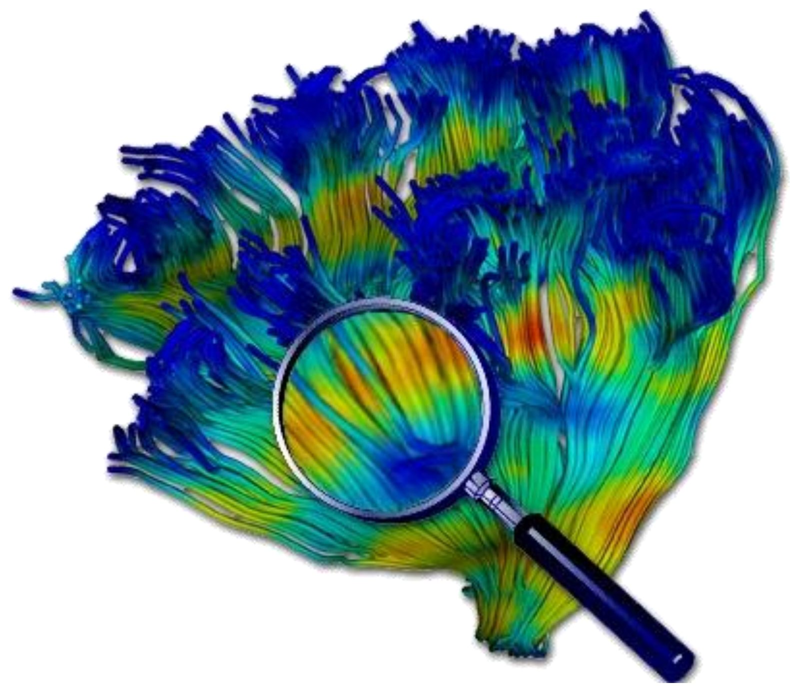
Diffusion Tensor Processing and Visualization

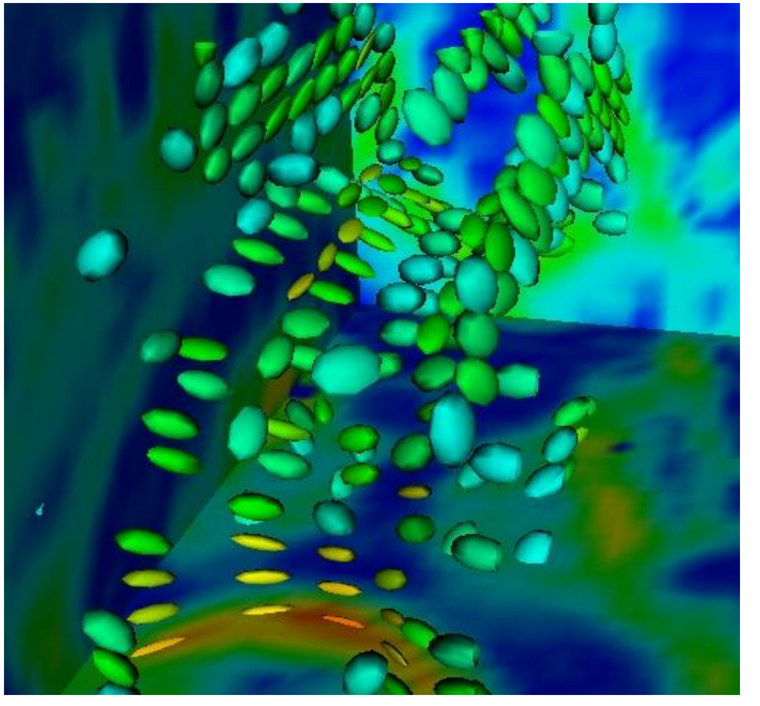


Guido Gerig
University of Utah
NAMIC: National Alliance for Medical Image Computing

Acknowledgments

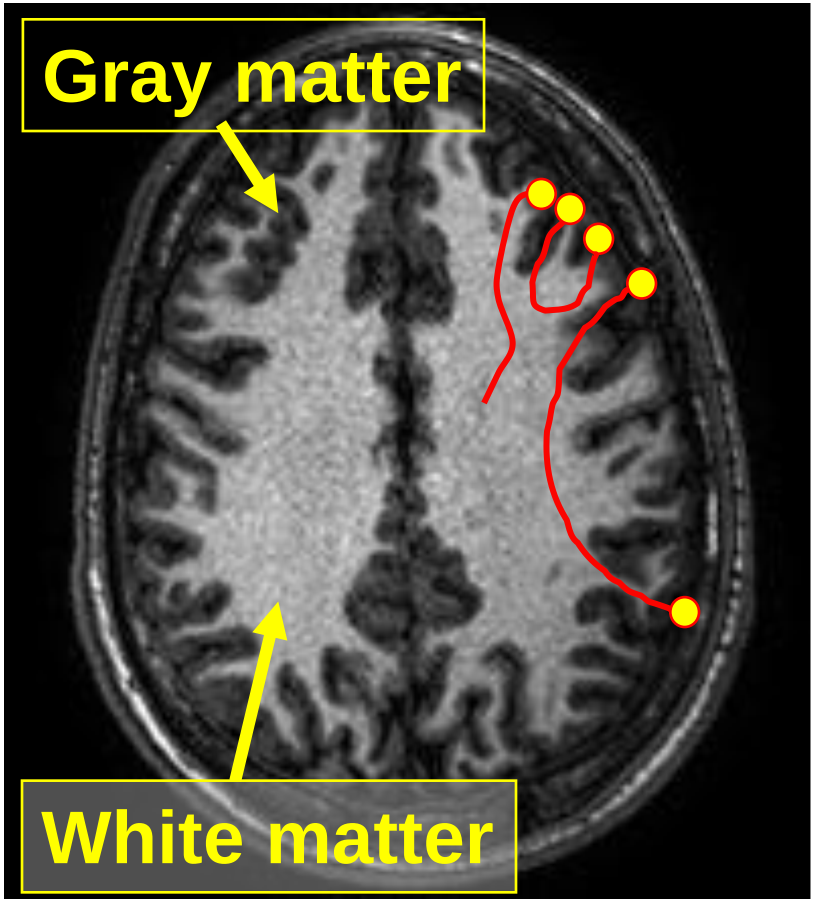
Contributors:

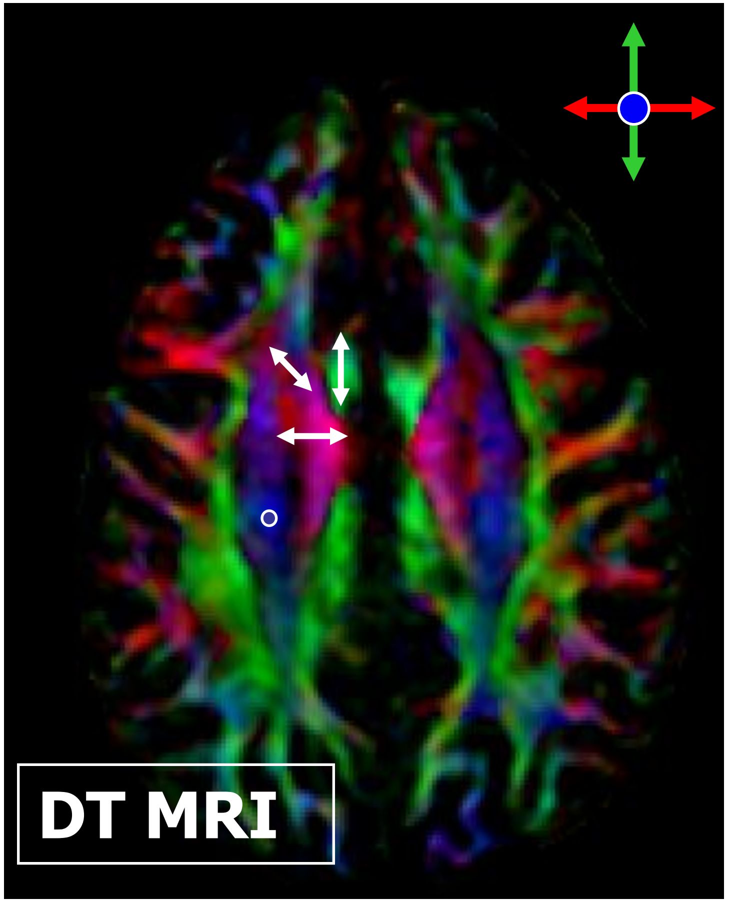
- C-F. Westin
- A. Alexander
- G. Kindlmann
- L. O'Donnell
- C. Goodlett
- J. Fallon
- R. Whitaker
- R. McKinstry



National Alliance for Medical Image Computing (NIH U54EB005149)

Diffusion Tensor Imaging (DT MRI) reveals White Matter Structure

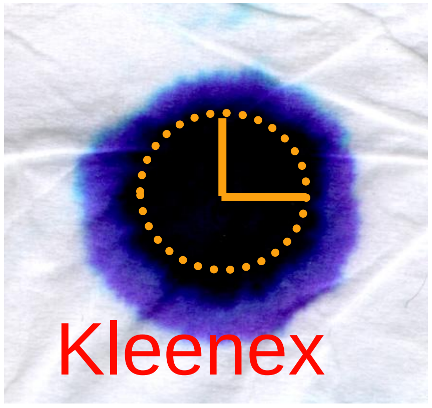


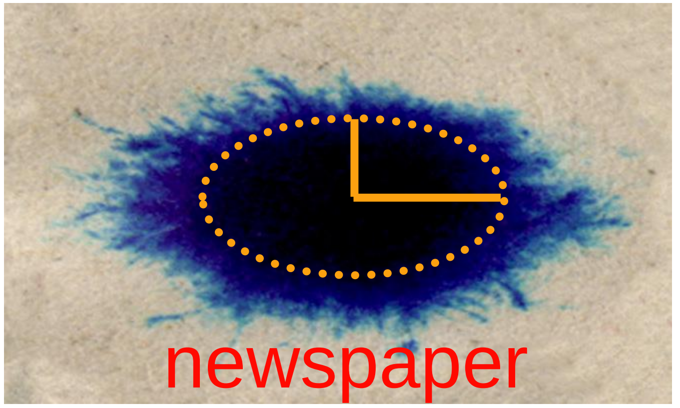


Courtesy of Susumu Mori, JHU

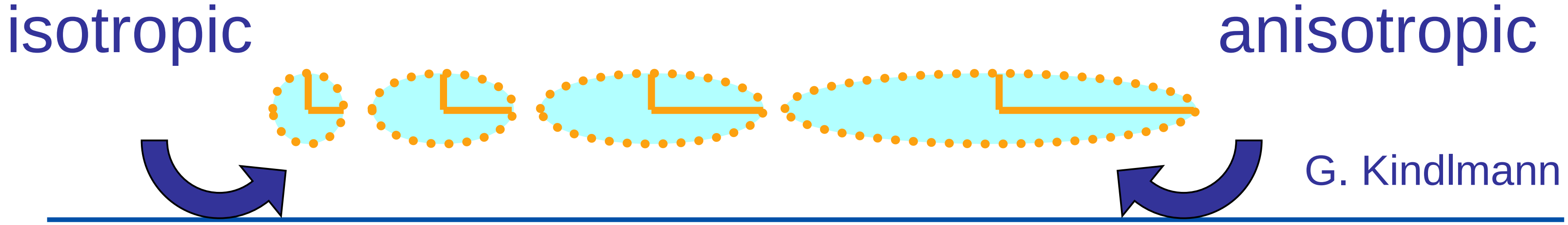
Diffusion in Biological Tissue

- Motion of water through tissue
- Sometimes faster in some directions than others





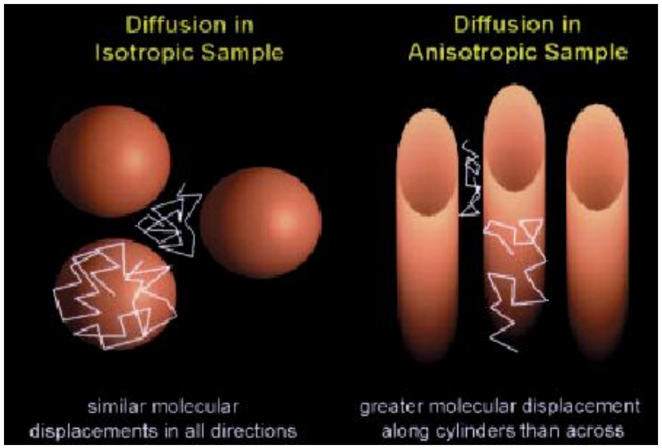
- <u>Anisotropy</u>: diffusion rate depends on direction



G. Kindlmann

Diffusion in White Matter

- Diffusion of water molecules



From Beaulieu[02]

- Reflects the underlying structure of the tissues
  - Faster diffusion along fibers than perpendicular to them
  - Water diffusion anisotropy used to track fibers, estimate white matter integrity
- Tensor model [Basser]
  - Determine the whole tensor to estimate diffusion anisotropy

The Physics of Diffusion

- Density of substance changes (evolves) over time according to a differential equation (PDE)

$$\frac{\partial \mu}{\partial t} = \nabla \cdot D \nabla \mu$$

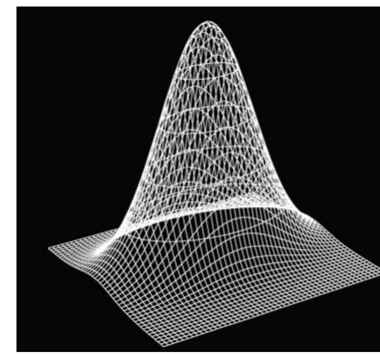
Change in density

Diffusion – matrix, tensor (2x2 or 3x3)

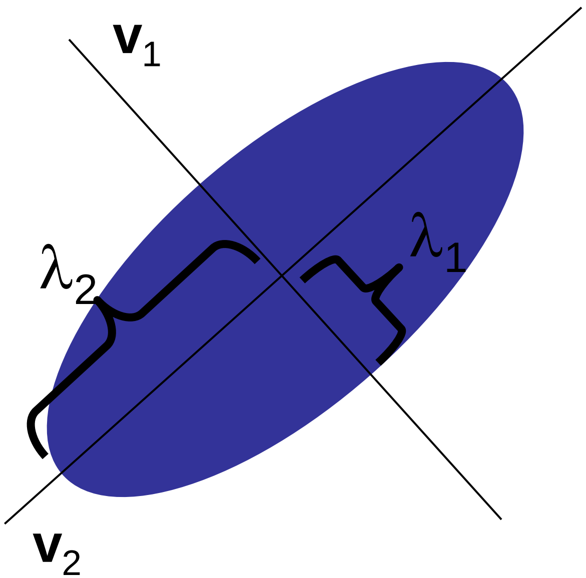
Derivatives (gradients) in space

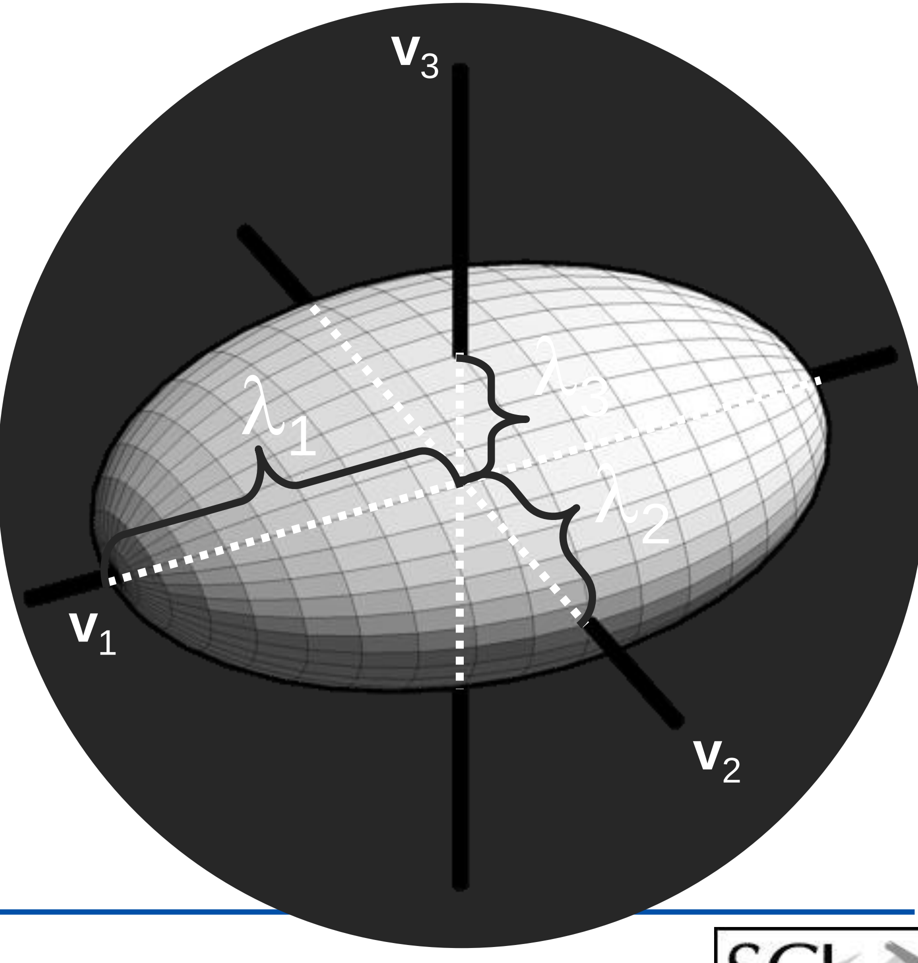
Solutions of the Diffusion Equation

- Simple assumptions
  - Small dot of a substance (point)
  - D constant everywhere in space
- Solution is a multivariate Gaussian
  - Normal distribution
  - “D” plays the role of the covariance matrix
- This relationship is not a coincidence
  - Probabilistic models of diffusion (random walk)



Eigen Directions and Values (Principle Directions)





Tensors From Diffusion-Weighted Images

- <u>Big</u> assumption
  - At the scale of DW-MRI measurements
  - Diffusion of water in tissue is approximated by Gaussian
    - Solution to heat equation with constant diffusion tensor
- Stejskal-**Tanner equation**
  - Relationship between the DW images and tensor D

$$S_k = S_0 e^{-b g_k^T D g_k}$$

Physical constants
Strength of gradient
Duration of gradient pulse
Read-out time

k[th] DW Image

Base image

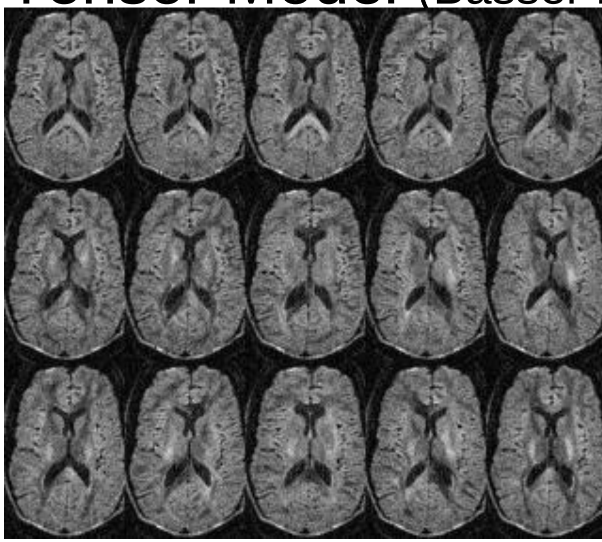
Gradient direction

DWI summary: Model

Single Tensor Model (Basser 1994)

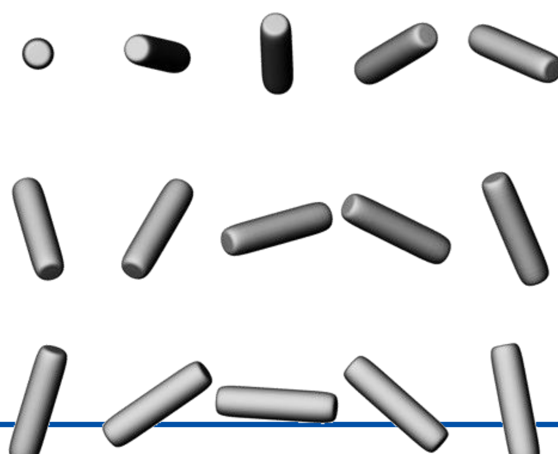
$$A_i = A_0 e^{-b\mathbf{g}_i^T \mathbf{D} \mathbf{g}_i}$$

A_i



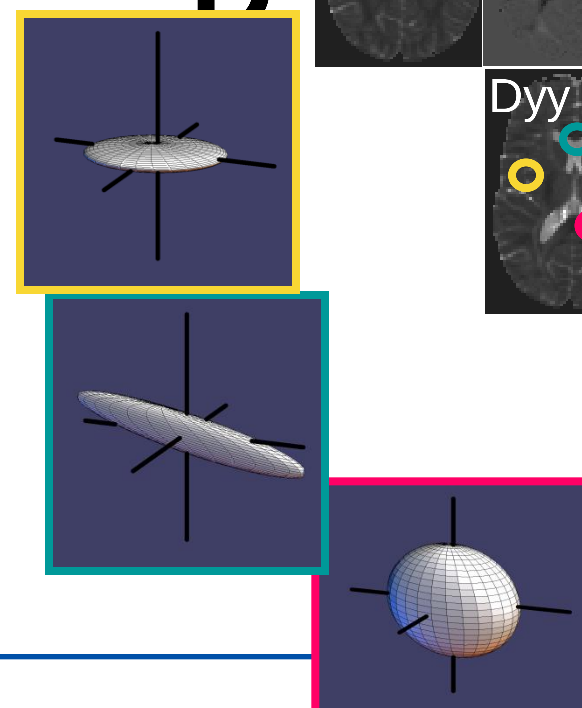
A_0

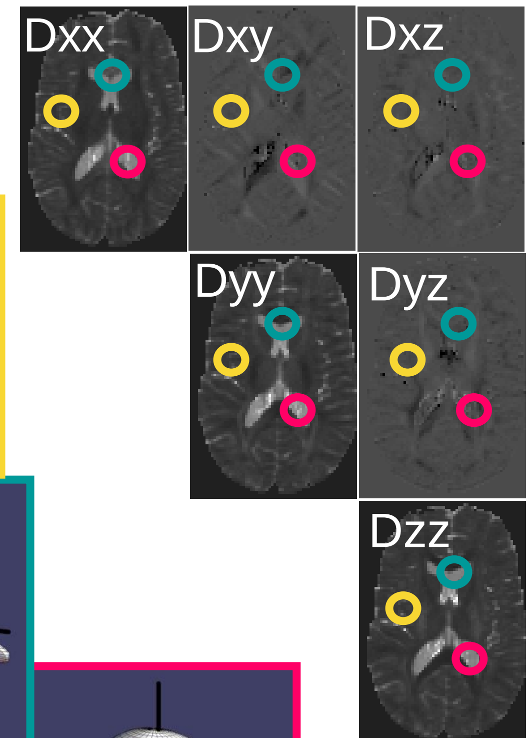
$\mathbf{g}_i$



Tensor estimation

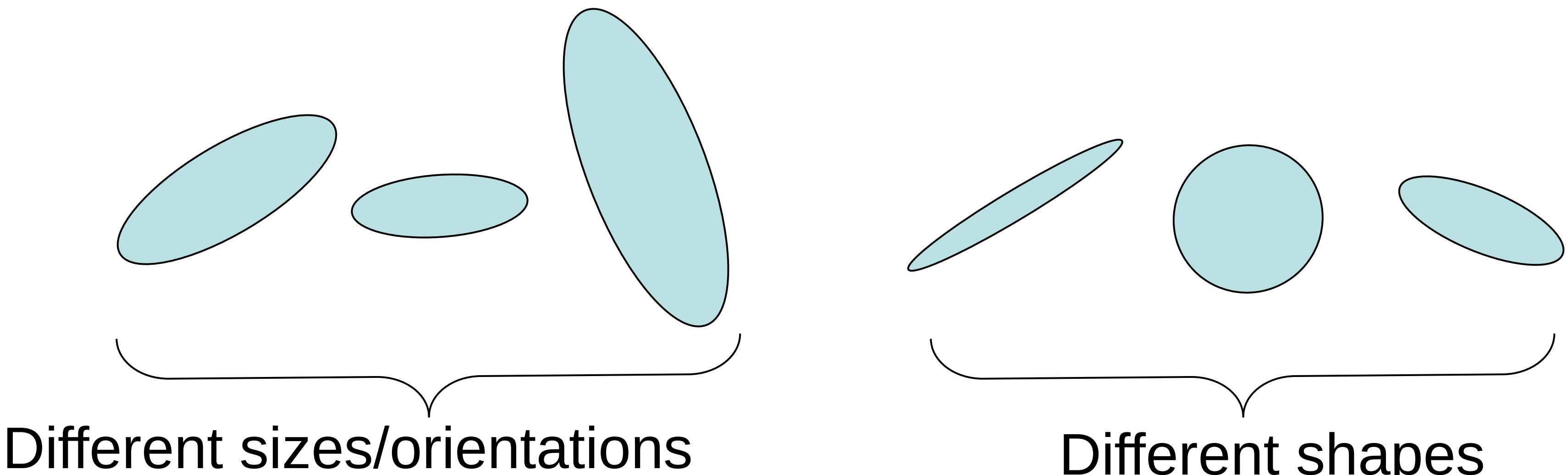
D





Shape Measures on Tensors

- Represent or visualization shape
- Quanitfy meaningful aspect of shape
- Shape vs size



Measuring the "Size" of a Tensor

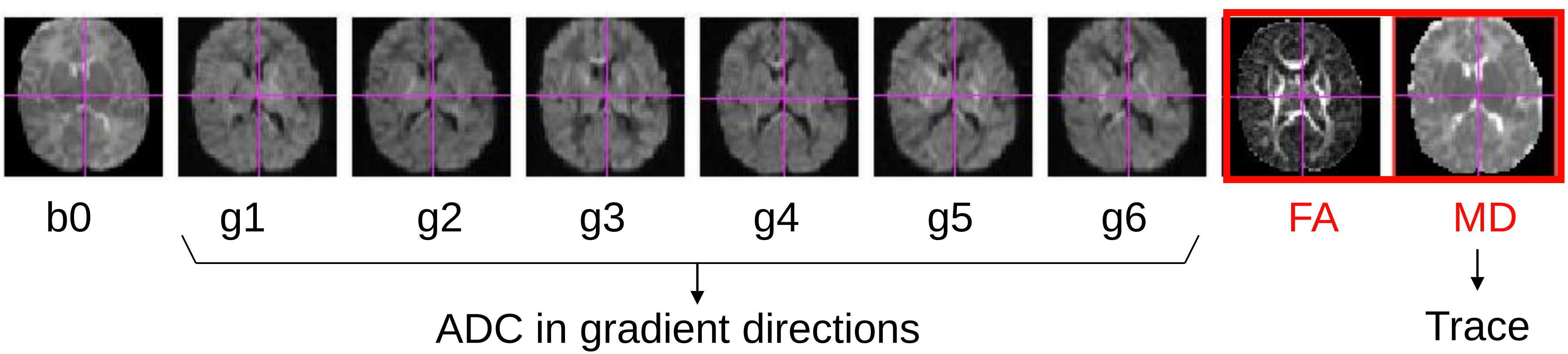
- Length – $(\lambda_1 + \lambda_2 + \lambda_3)/3$
  - $(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)^{1/2}$
- Area – $(\lambda_1 \lambda_2 + \lambda_1 \lambda_3 + \lambda_2 \lambda_3)$
- Volume – $(\lambda_1 \lambda_2 \lambda_3)$

Sometimes used.
Also called:
"Root sum of squares"
"Diffusion norm"
"Frobenius norm"

Generally used.
Also called:
"Mean diffusivity" <MD>
"Trace"

ADC versus Mean Diffusivity

- Apparent diffusion coefficient (ADC) measures diffusivity <u>in a specific direction</u>.
- Mean diffusivity (<MD>) is the trace of the diffusion tensor.
- Terms often not properly used, papers often cite ADC but actually mean <MD>

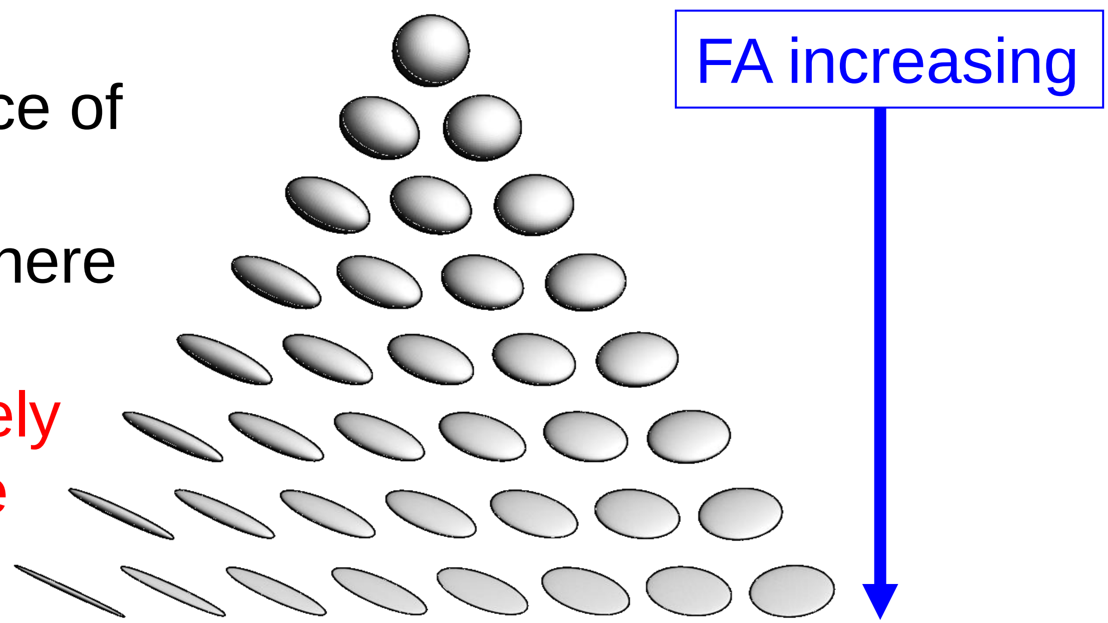


Reducing Shape to One Number
Fractional Anisotropy

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

Properties:

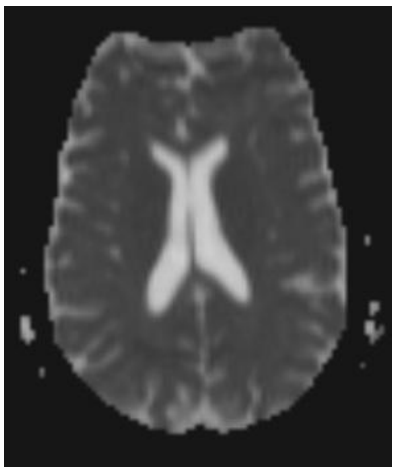
- Normalized variance of eigenvalues
- Difference from sphere
- Invariant to size
- FA does not uniquely characterize shape



Tensor size (MD) and shape (FA)

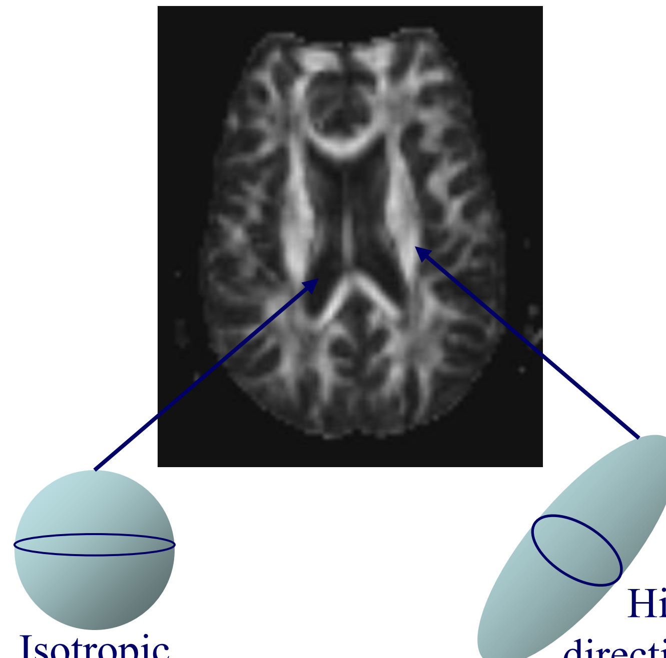
- Mean diffusivity (MD)

$$MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$



- Fractional anisotropy (FA)

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



Isotropic diffusion

Highly directional diffusion

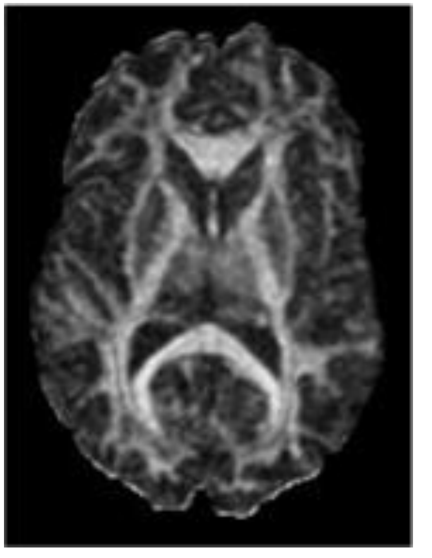
White matter — Cerebrospinal fluid

Low → **High**

0 → **1**

FA as an Indicator for White Matter

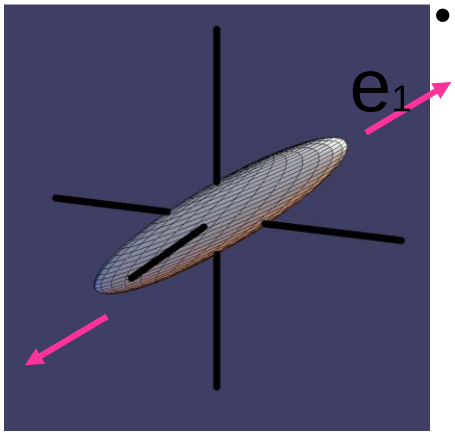
- Visualization – ignore tissue that is not WM
- Registration – Align WM bundles
- Tractography – terminate tracts as they exit WM
- Analysis
  - Axon density/degeneration/integrity
  - Myelin
- <u>Big question</u>
  - What physiological/anatomical property does FA measure?

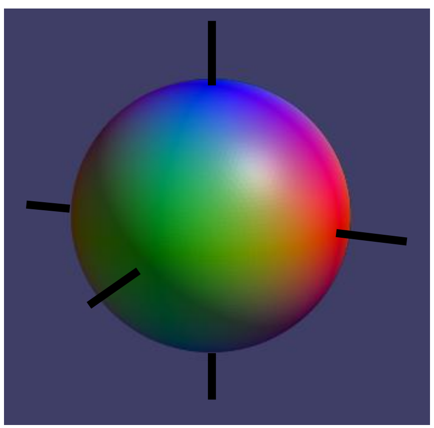


Visualizing Tensors: Direction and Shape

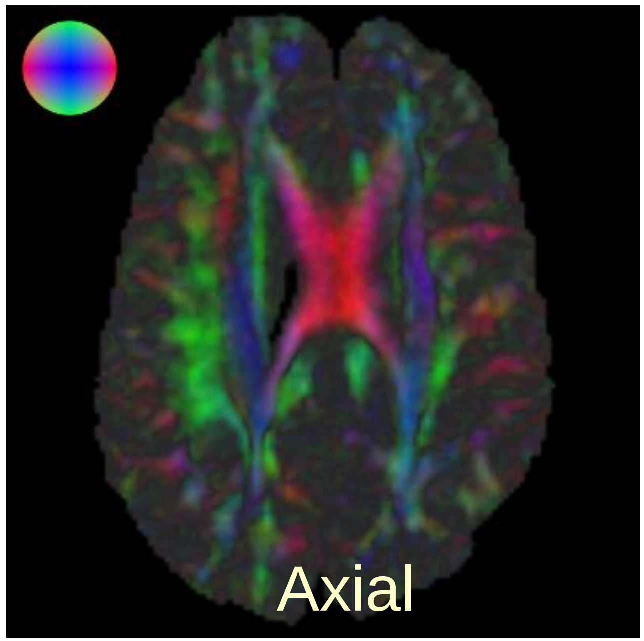
- Color mapping
- Glyphs

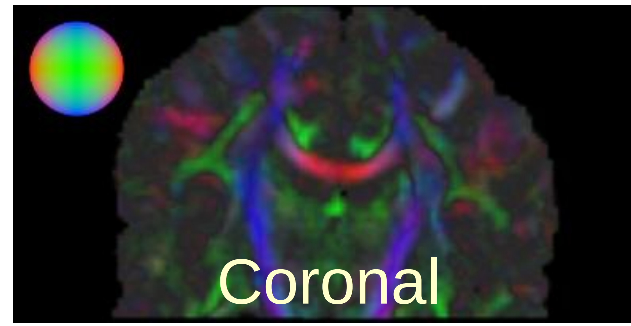
Coloring by Principal Diffusion Direction

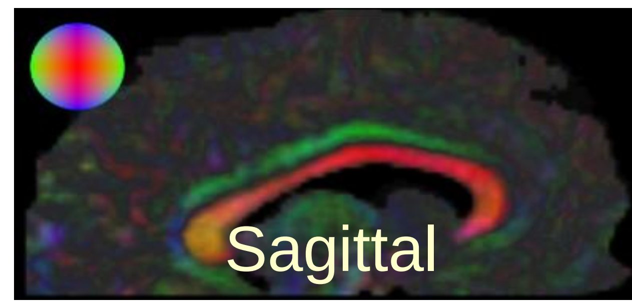




- Principal eigenvector, linear anisotropy determine color







$R = | \mathbf{e}_1 \cdot x |$

$G = | \mathbf{e}_1 \cdot y |$

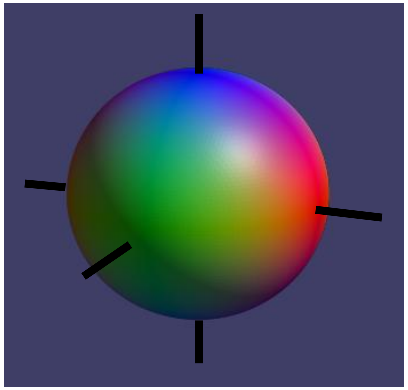
$B = | \mathbf{e}_1 \cdot z |$

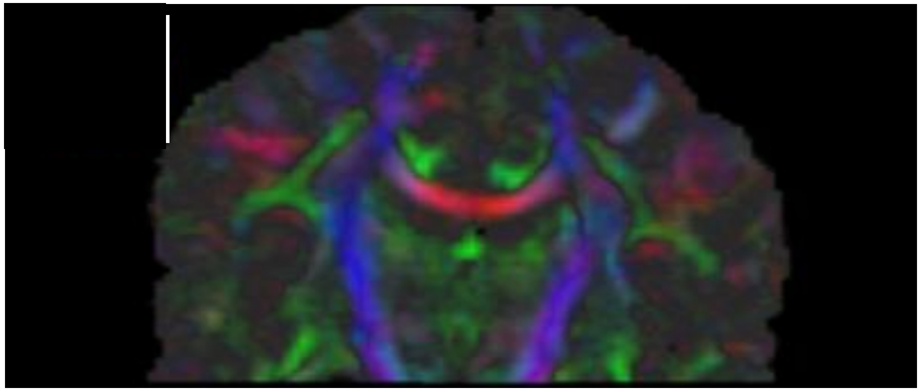
C. Pierpaoli, 1997

Slide G. Kindlmann

Issues With Coloring by Direction

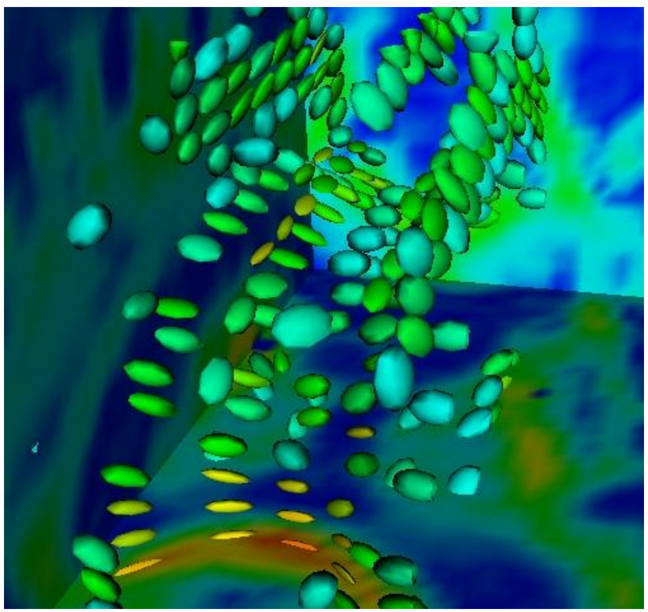
- Set transparency according to FA (highlight-tracts)
- Coordinate system dependent
- Primary colors dominate
  - Perception: saturated colors tend to look more intense
  - Which direction is “cyan”?
  - Coloring is not unique

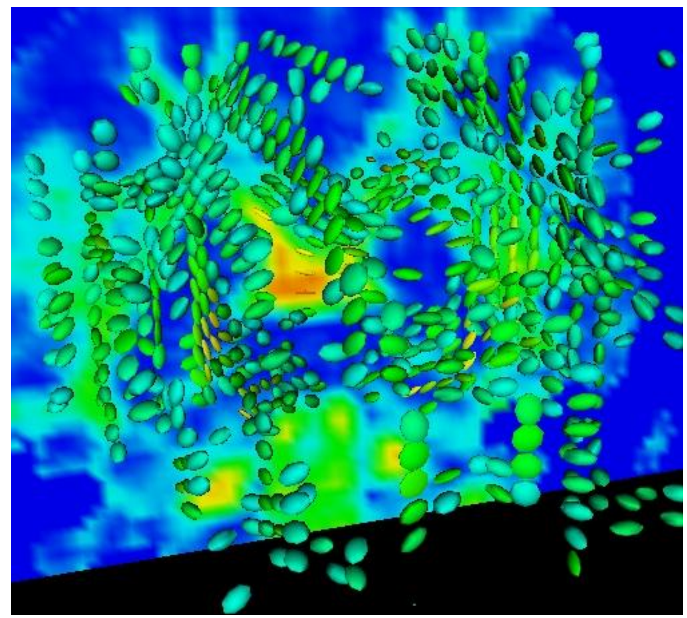




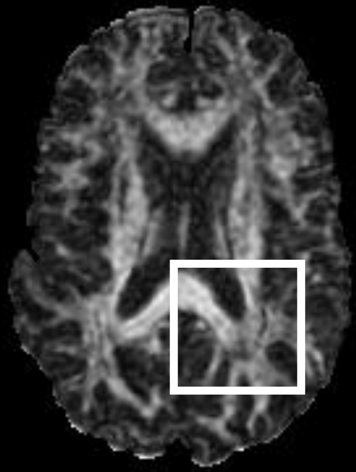
Visualization with Glyphs

- Density and placement based on FA or detected features
- Place ellipsoids on regular grid

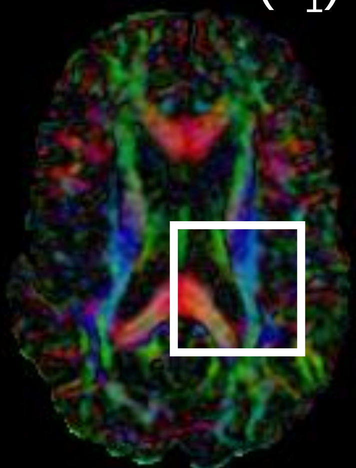


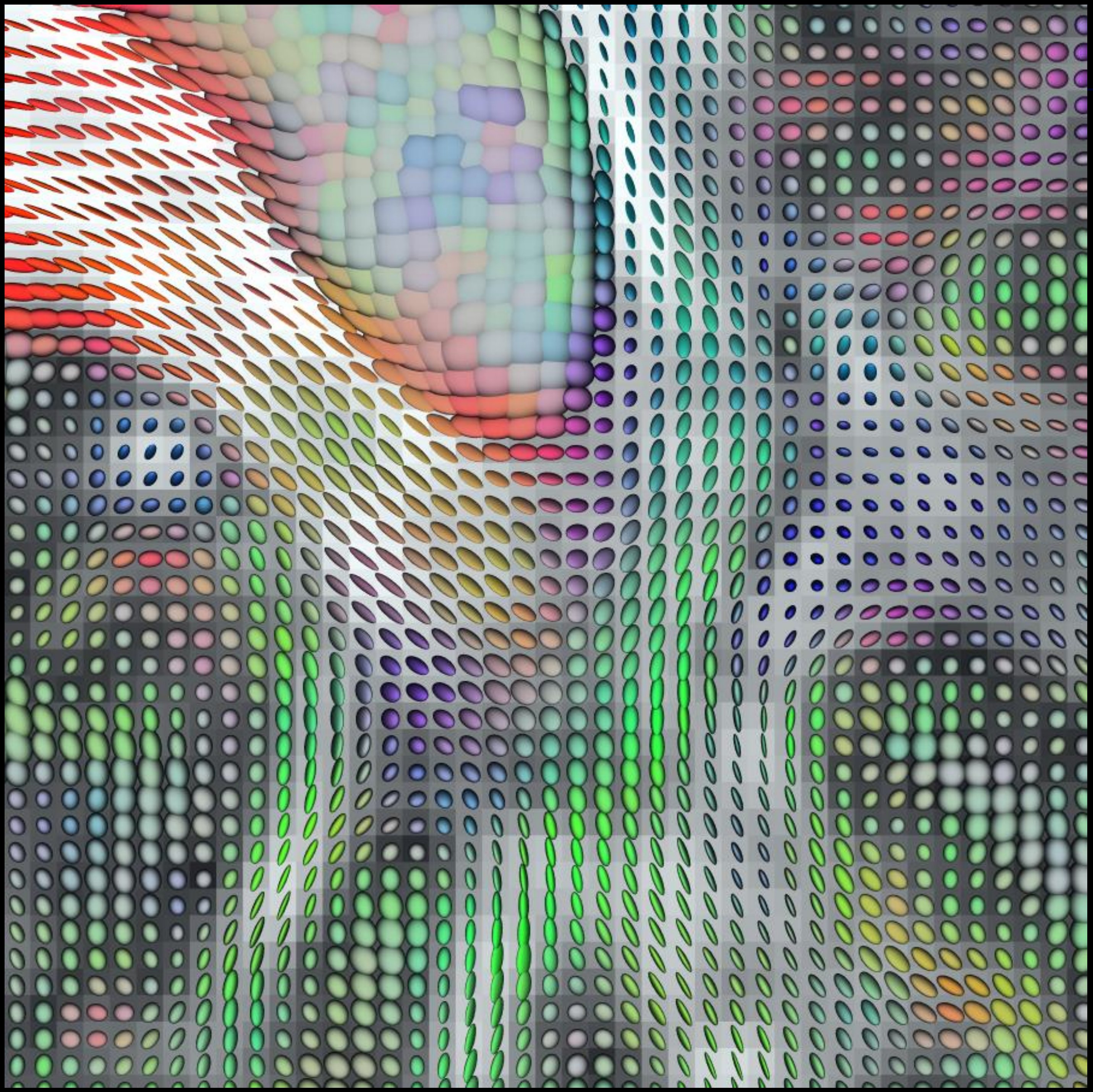


Backdrop: FA

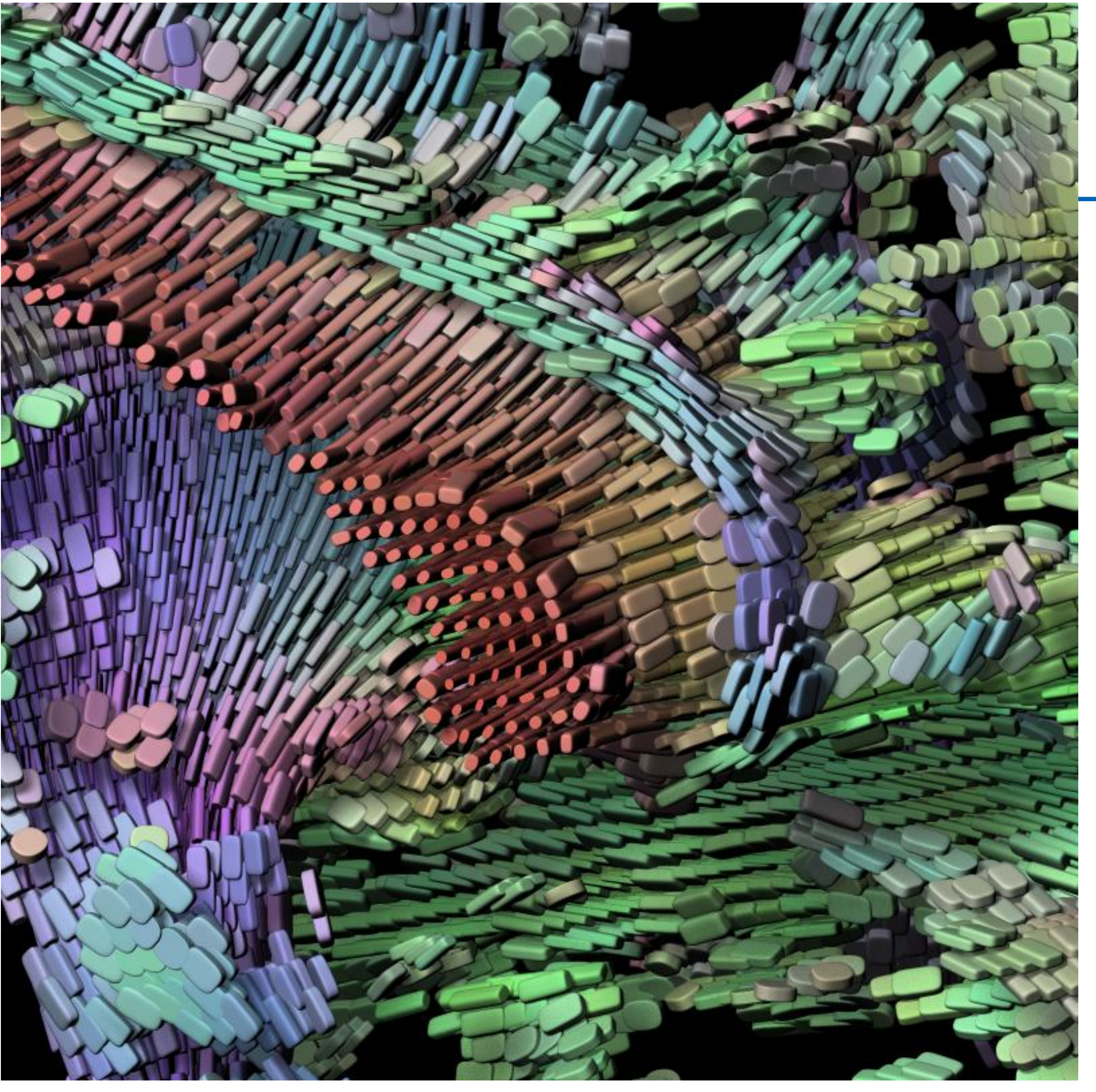


Color: RGB($\mathbf{e}_1$)



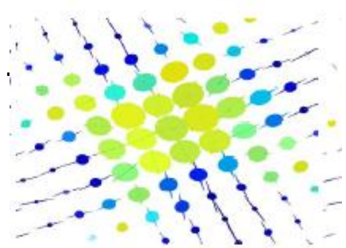


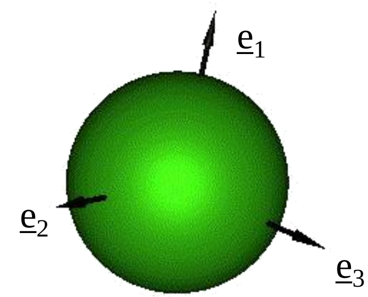
G. Kindlmann



Prolate vs. oblate: Why do we care?

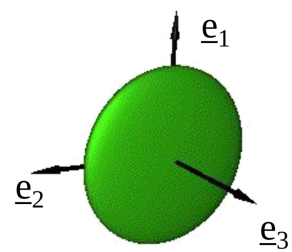
- Free diffusion (ventricles) shown as spheres.
- Intersecting tracts can't be properly modeled by a single tensor: Simplified disks in rank-1 tensors.
- Large tracts can be locally modeled by single tensors.





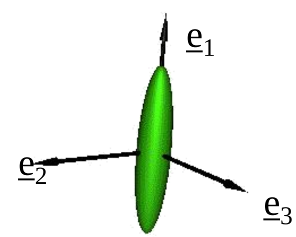
$\lambda_1 \approx \lambda_2 \approx \lambda_3$ - Isotropic

Prevalent in CSF and gray matter regions of the brain.



$\lambda_1 \approx \lambda_2 >> \lambda_3$ - Oblate

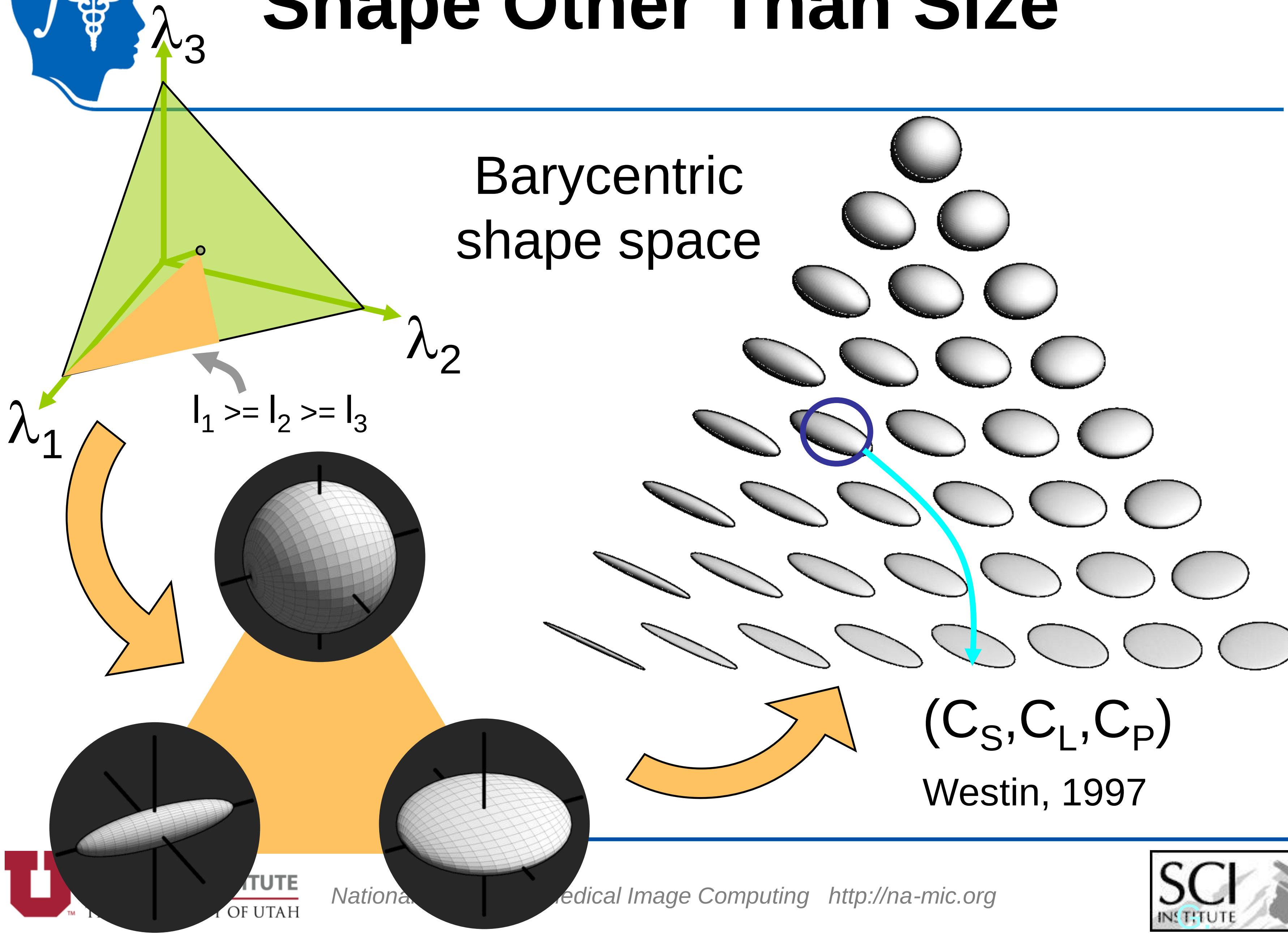
Arise in white matter regions.



$\lambda_1 >> \lambda_2 \approx \lambda_3$ - Prolate

Prevalent in white matter regions.

Shape Other Than Size

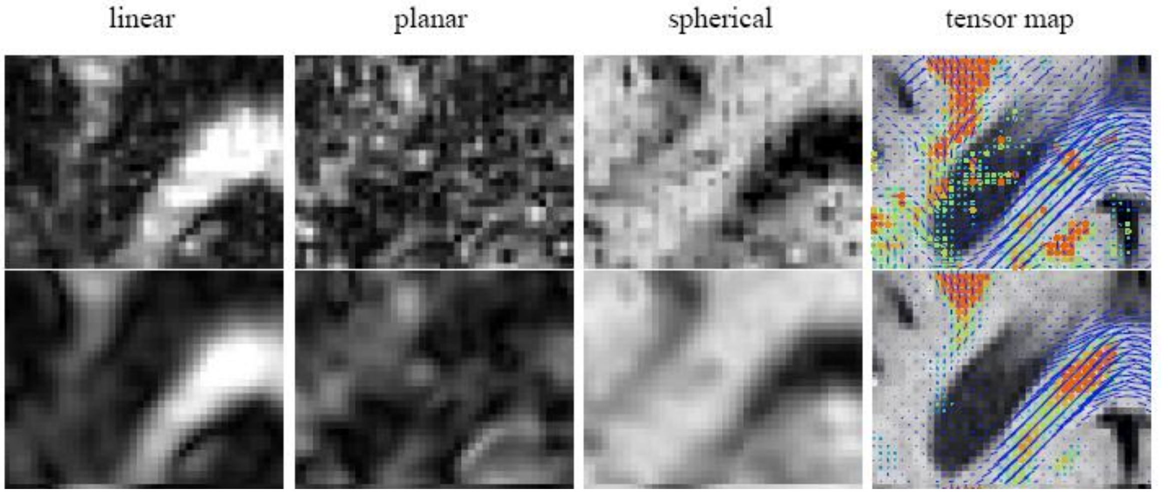


Shape Characterization: Westin

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

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

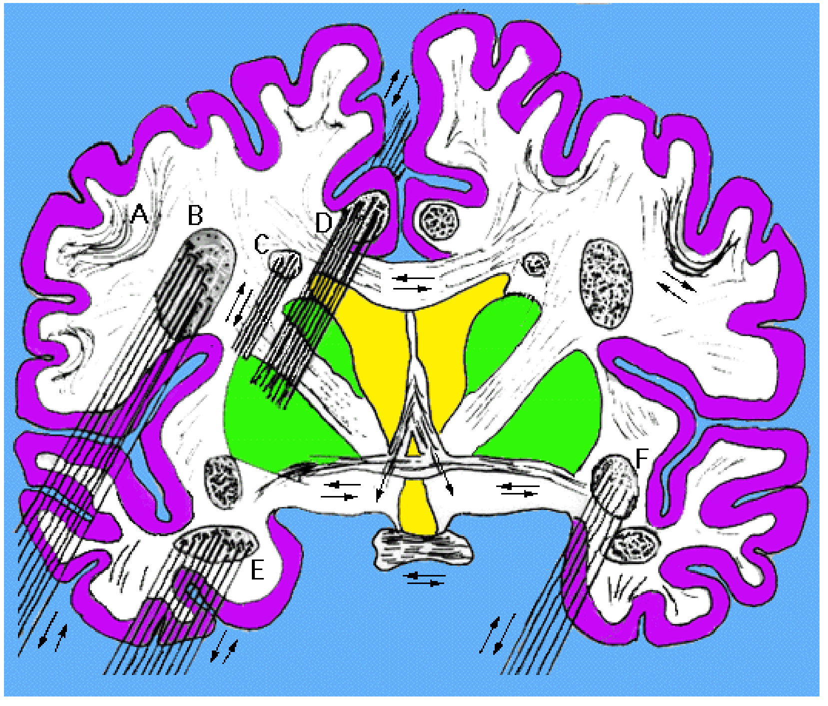
$$c_s = \frac{\lambda_3}{\lambda_1}$$



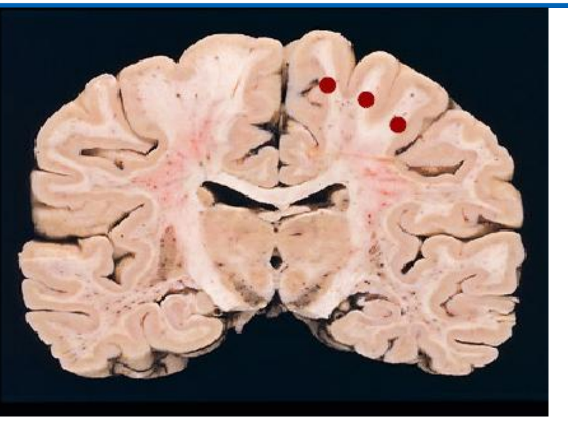
$$c_l + c_p + c_s = 1$$

Westin et al., MICCAI'99

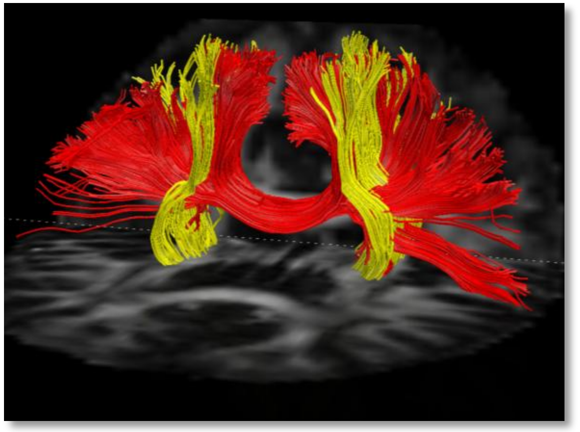
Dream: Connectivity?



Forebrain Fiber Bundles: General idea of where various fiber bundles are and regions they interconnnect or project to.

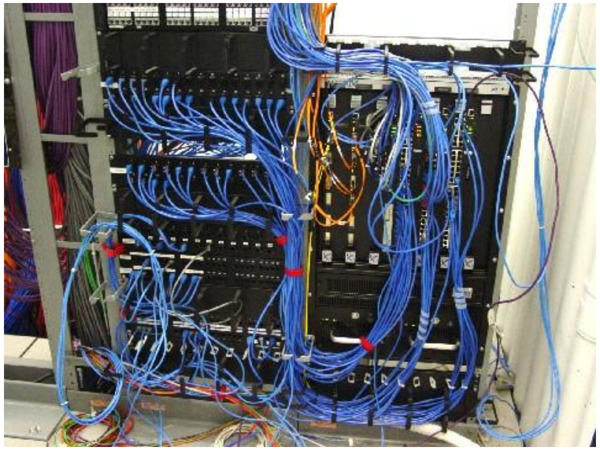


Source: Duke NeuroAnatomy Web Resources (Ch. Hulette)



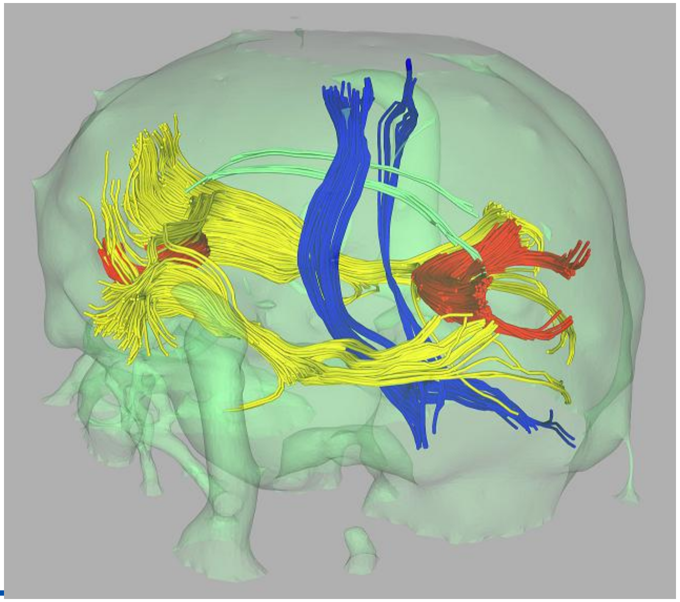
Tractography: Coronal view (Dell'Acqua et al. NeuroImage '10

Networking and Brain Connectivity

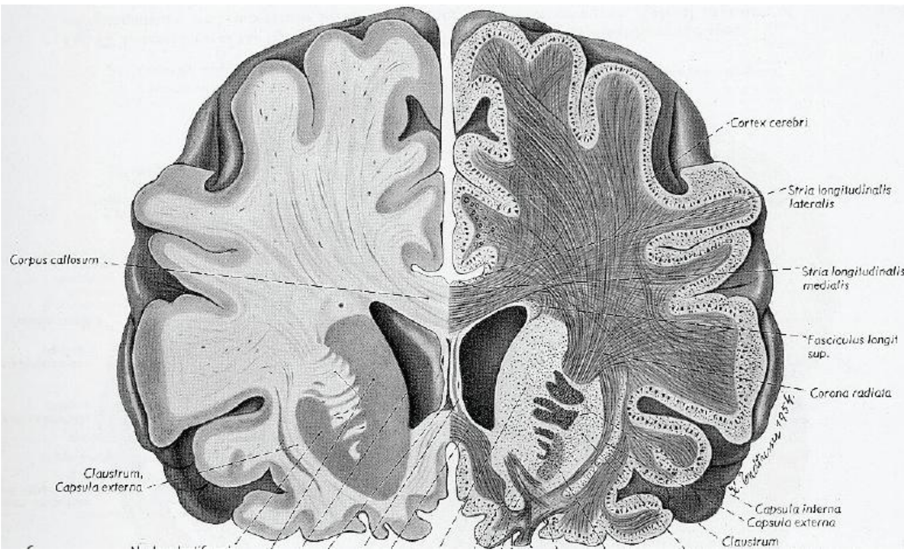



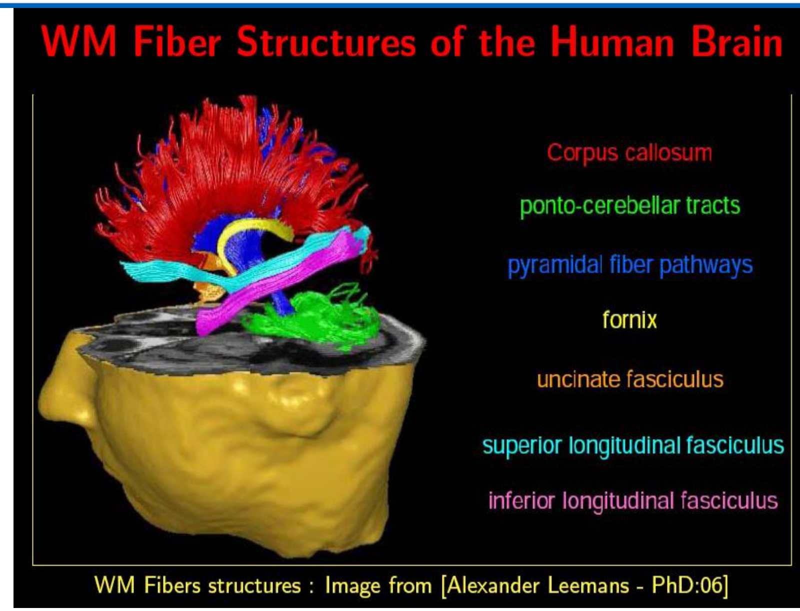
UNC Computer Science:
Network wire cabinets

Major Fiber Tracts extracted from DT MRI



White Matter Tracts





- In tractography fibers are traced, with the aim to visualize white matter tracts.
- The word “tractography” is not related to “tracking”, but to “tract”.
- White matter tract, white matter fasciculus

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Fiber Bundles via Tractography

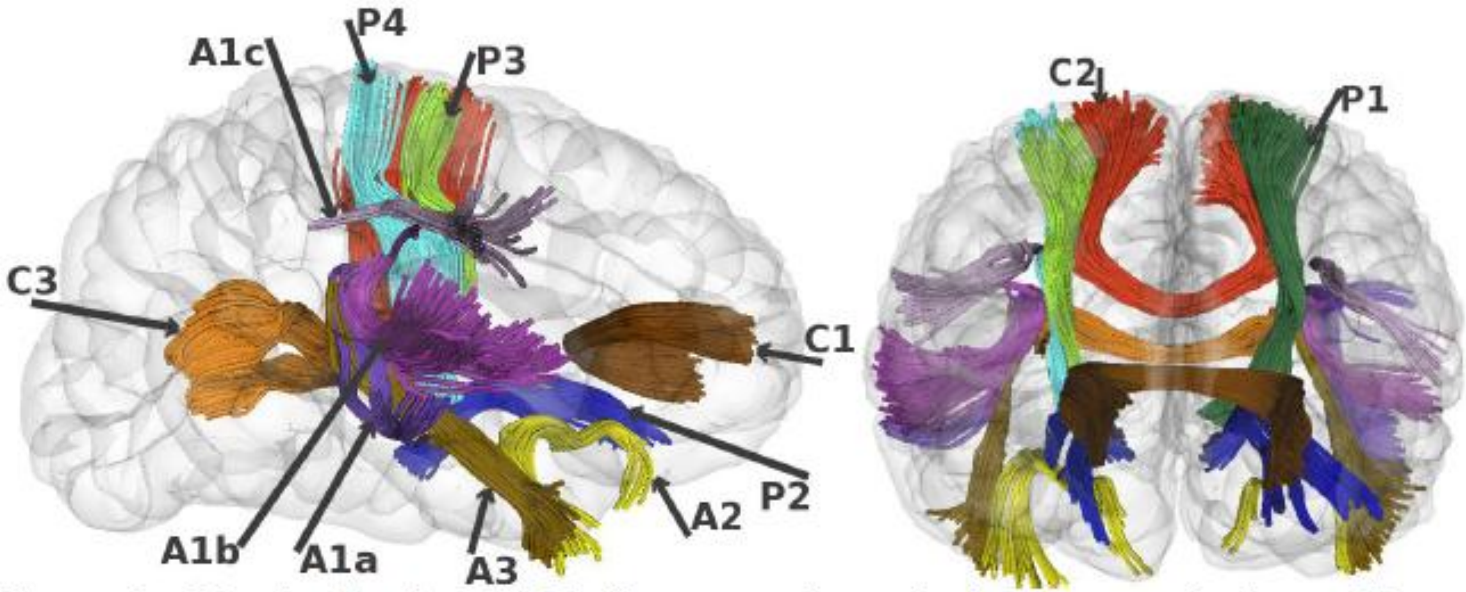
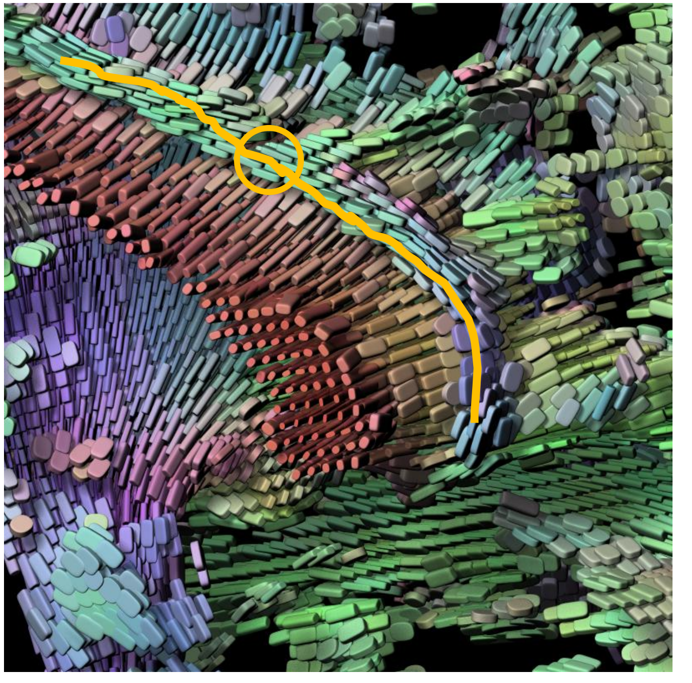


Figure 2. 3D visualization of 21 fiber tracts in sagittal and coronal views. C1, genu corpus callosum (CC); C2, body CC; C3, splenium CC. A1a, arcuate-inferior-temporal tract; A1b, arcuate-superior-temporal tract; A1c, arcuate-superior tract; A2, uncinate fasciculus; A3, inferior longitudinal fasciculus (ILF); P1, posterior limb internal capsule (PLIC); P2, anterior limb internal capsule (ALIC); P3, motor tract; P4 sensory tract.

Geng, Gilmore, Gerig et al., submitted

From Tensors to Connectivity?

- Study diffusivity in 3D tensor field
- Propagate principal diffusion direction originating at user-selected seed point
- Display paths as streamlines
- Measurement of FA and MD along path



DTI Tractography

Seed point(s)

Move marker in discrete steps and find next direction

Direction of principle eigen value

Going Beyond Voxels: Tractography

- Method for visualization/analysis
- Integrate vector field associated with grid of principle directions
- Requires
  - Seed point(s)
  - Stopping criteria
    - FA too low
    - Directions not aligned (curvature too high)
    - Neighborhood coherence
    - Leave region of interest/volume
- Many methods have been published during the past decade (Basser, Mori, Westin, Vermuri, Kindlmann, Lenglet, etc.)

White Matter Fiber Tract Atlases

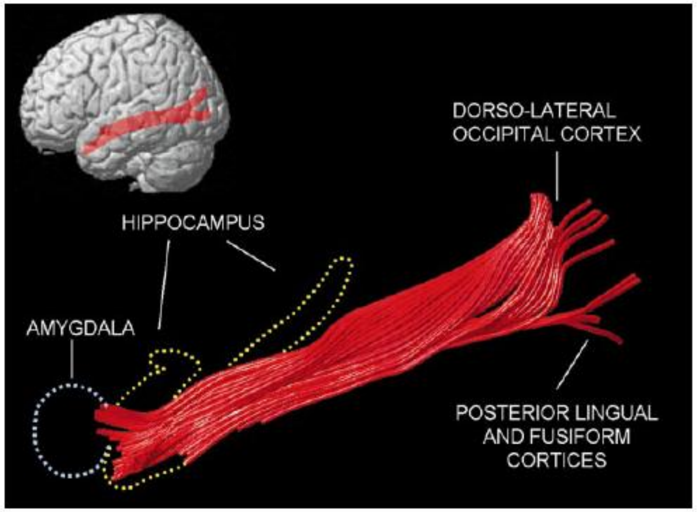


Fig. 7 Reconstruction of the ILF in the average DT-MRI data set. The long fibres originate from extrastriate areas of the occipital lobe and terminate in lateral temporal cortex and medial temporal cortex in the region of the amygdala and parahippocampal gyrus.

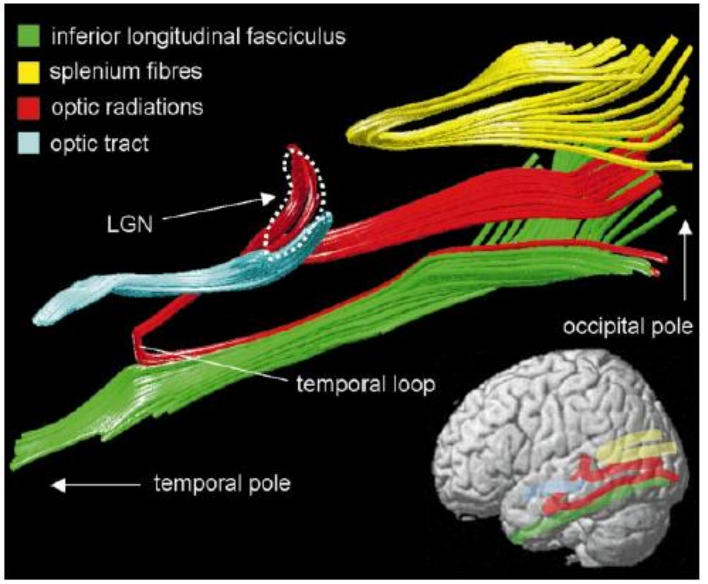
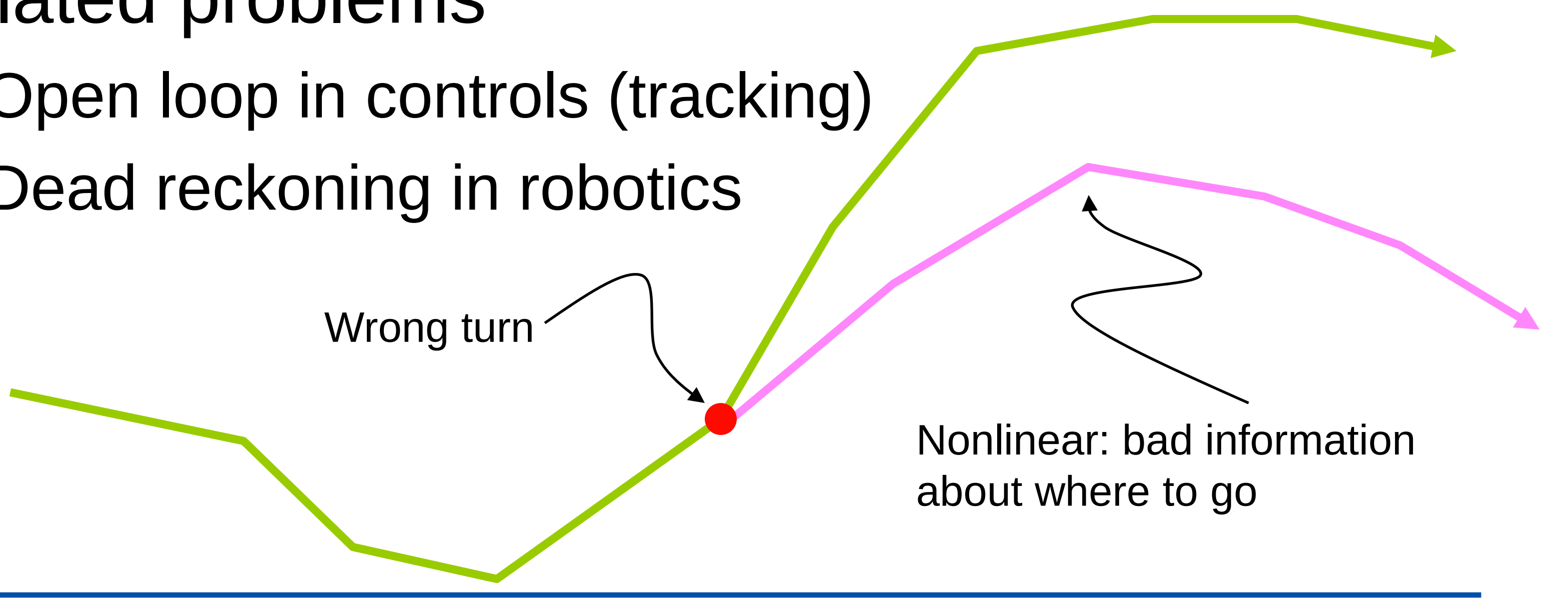


Fig. 2 Virtual *in vivo* dissection of the ILF and visual pathway of the right hemisphere (medial view) in the average brain data set. Splenial fibres connecting medial occipital regions are also shown. See text for explanation.

Catani et al., Occipito-temporal connections in the human brain, Brain 2003

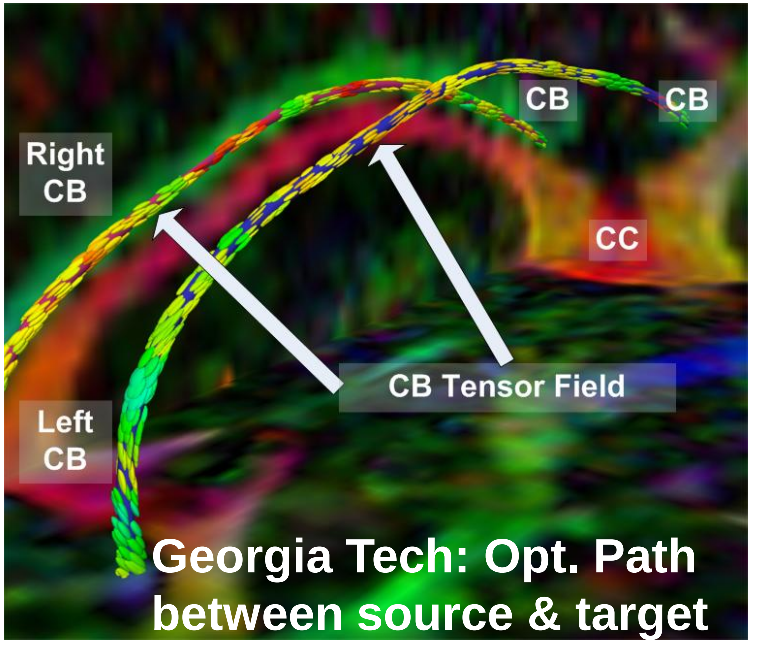
The Problem with Tractography
How Can It Work?

- Integrals of uncertain quantities are prone to error
  – Problem can be aggravated by nonlinearities
- Related problems
  – Open loop in controls (tracking)
  – Dead reckoning in robotics

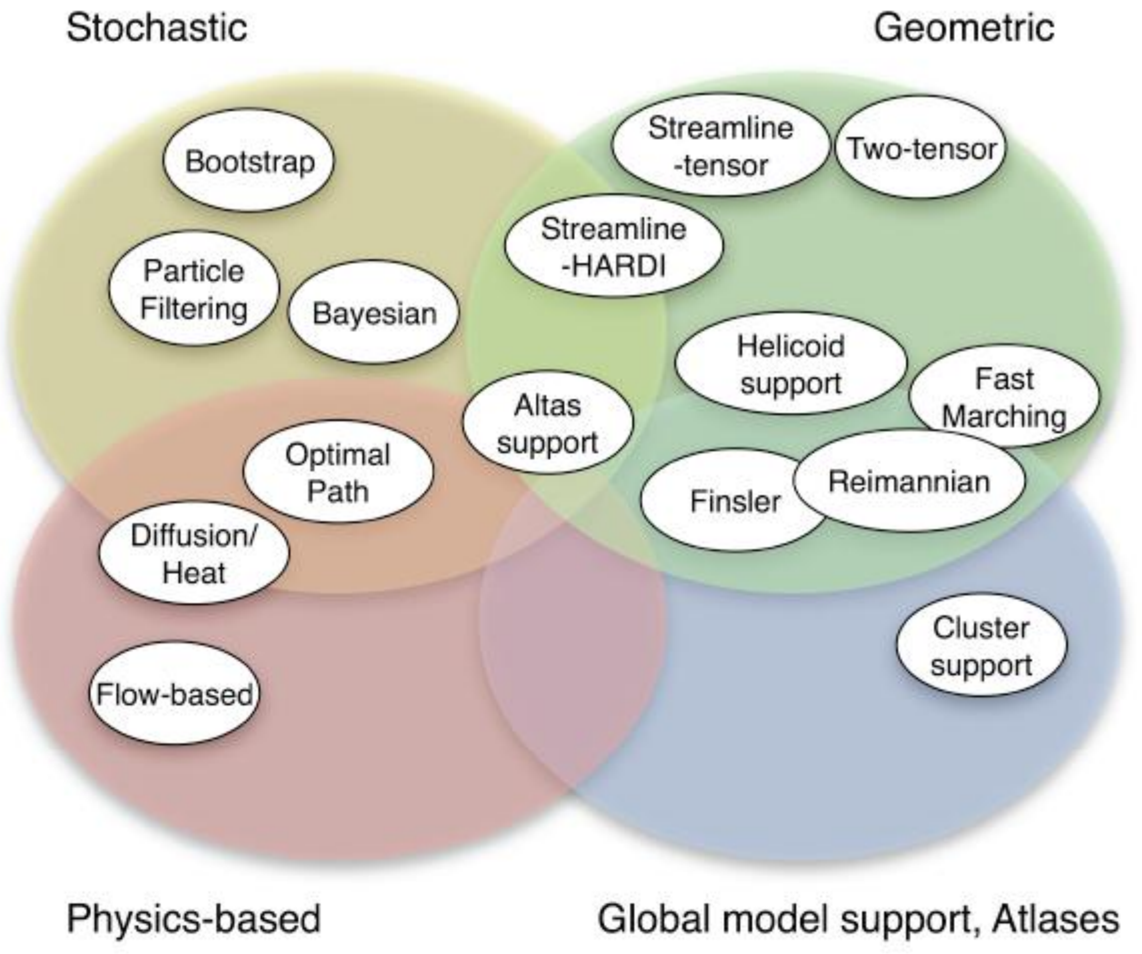


Alternative methods for tractography

- Tracking in vector-field of largest eigenvector
- Tracking in tensor field
- Probabilistic tractography
- Optimal path analysis
- Fiber tract by volumetric diffusion
- ….
- Variety of methods developed by NAMIC developers

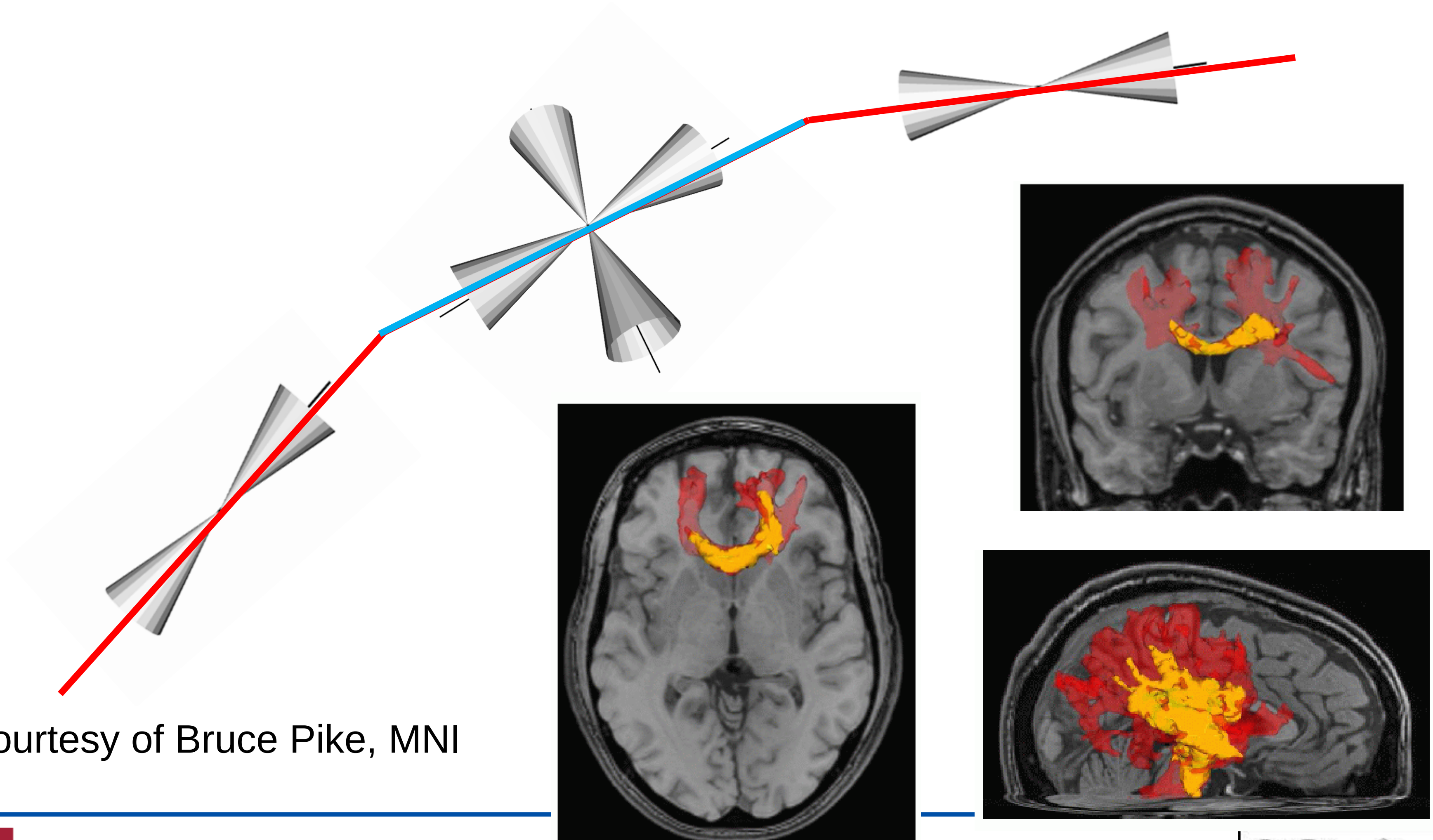


Diffusion MRI Tractography



Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

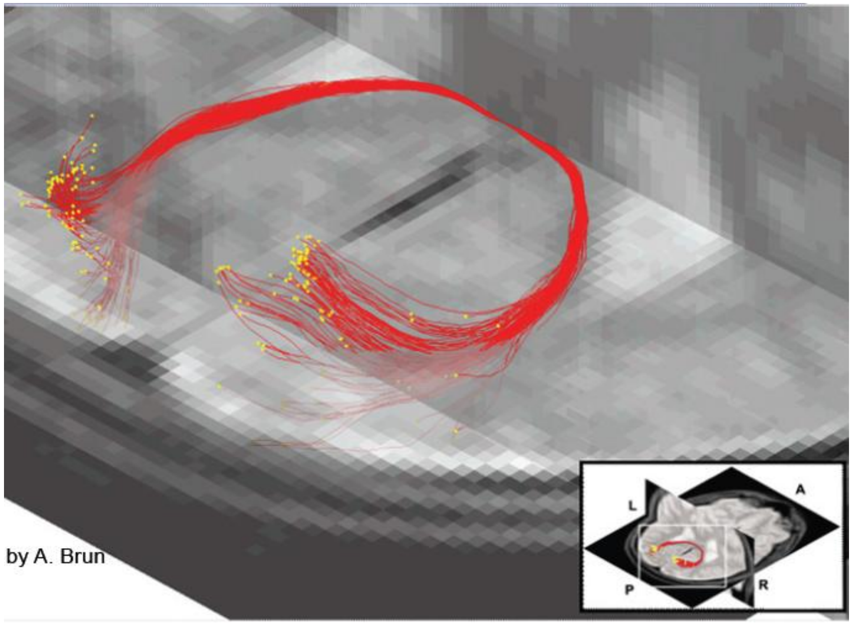
Tractography Incorporating Uncertainty



Courtesy of Bruce Pike, MNI

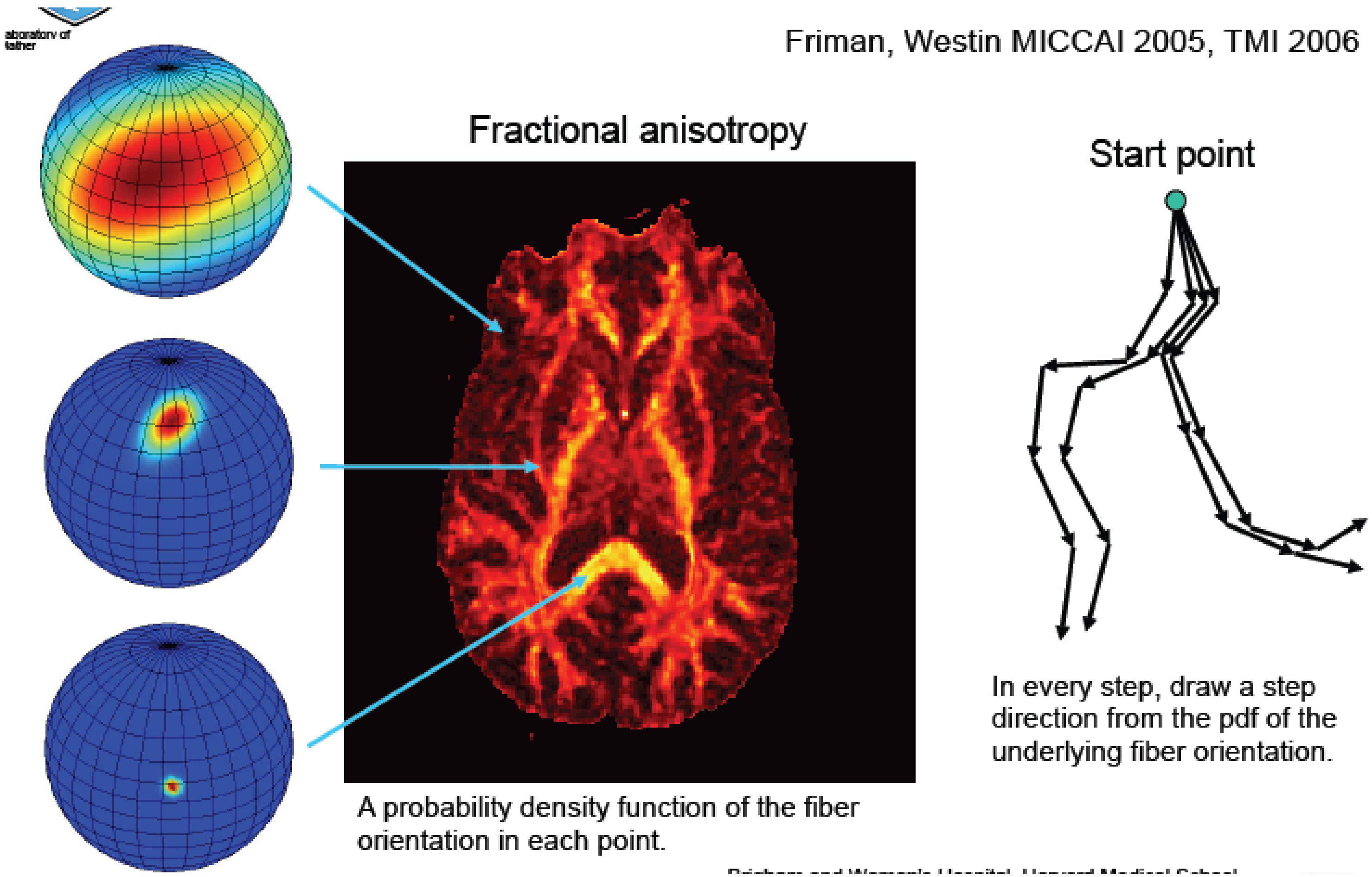
Stochastic Tractography

- Lazar, Alexander, **White Matter Tractography using Random Vector (RAVE) Perturbation, ISMRM 2002**
- D. Tuch, Diffusion MRI of complex tissue structure, Ph.D. dissertation, Harvard-MIT, 2002
- Brun, Westin, **Regularized Stochastic White Matter Tractography Using Diffusion Tensor MRI:** Monte Carlo, Sequential Importance Sampling and Resampling. MICCAI 2002.
- Zhang, Hancock, Goodlett and Gerig, **Probabilistic White Matter Fiber Tracking using, Particle Filtering and von Mises-Fisher Sampling**, Med Image Anal. 2009 Feb;13(1):5-18



Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

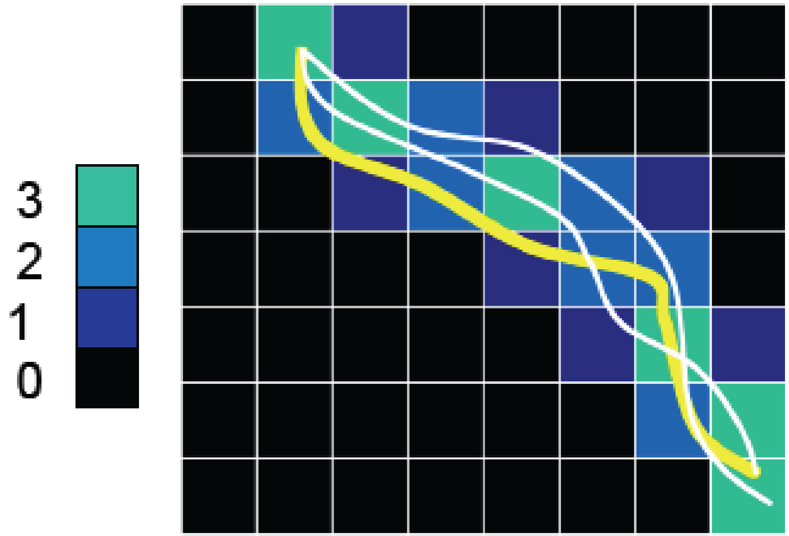
Stochastic Tractography



Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Probability of Connection

Given a large number of fibers, the probability of a connection between two voxels can be estimated



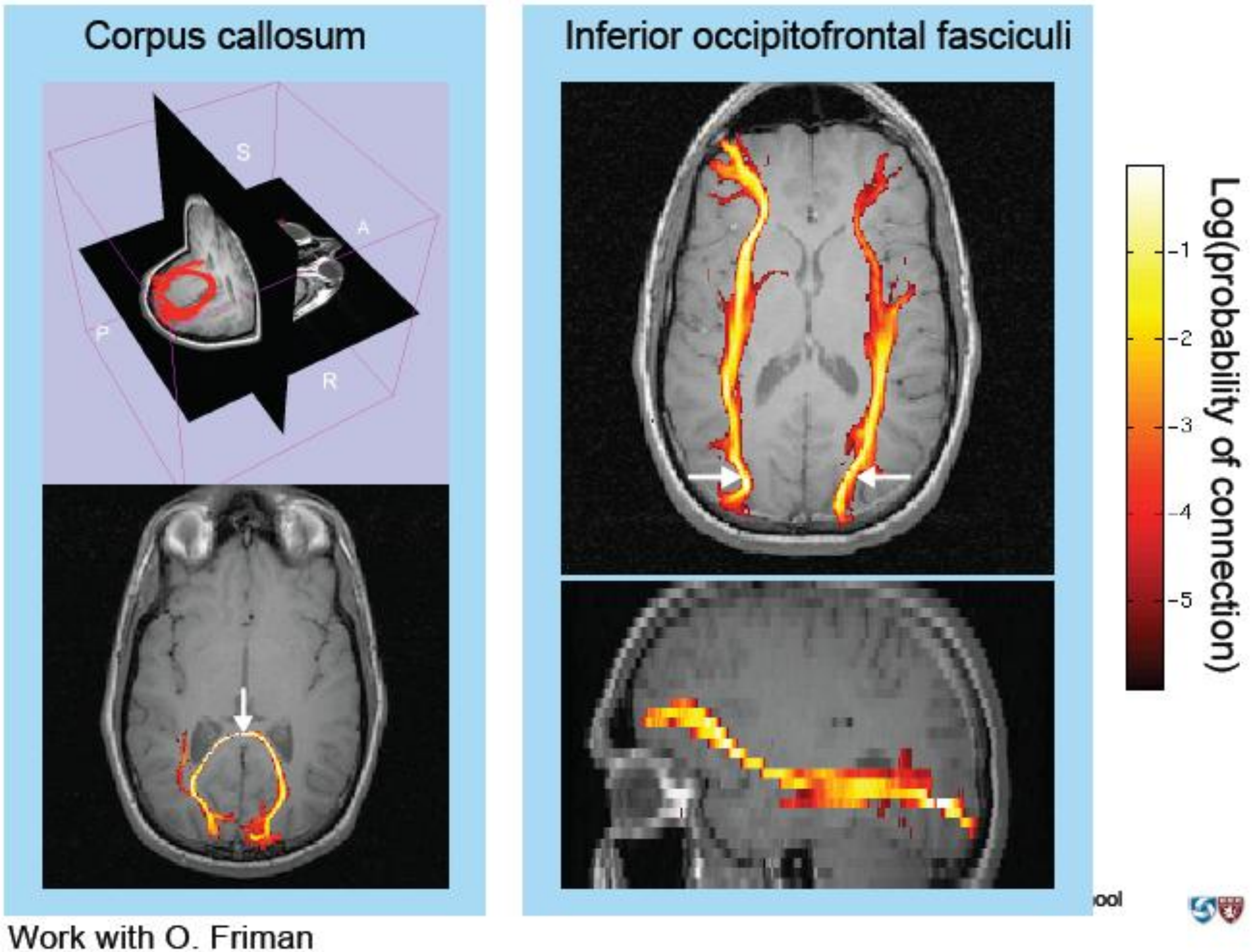
Probability density function: 1) Add the contribution from all paths, and 2) normalize the total sum of all voxels

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Tractography

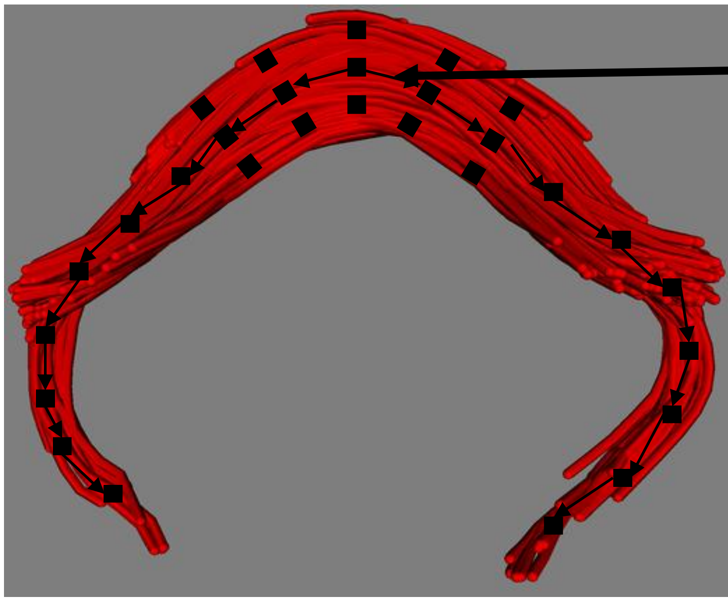
J. Fallon

Probability of Connection

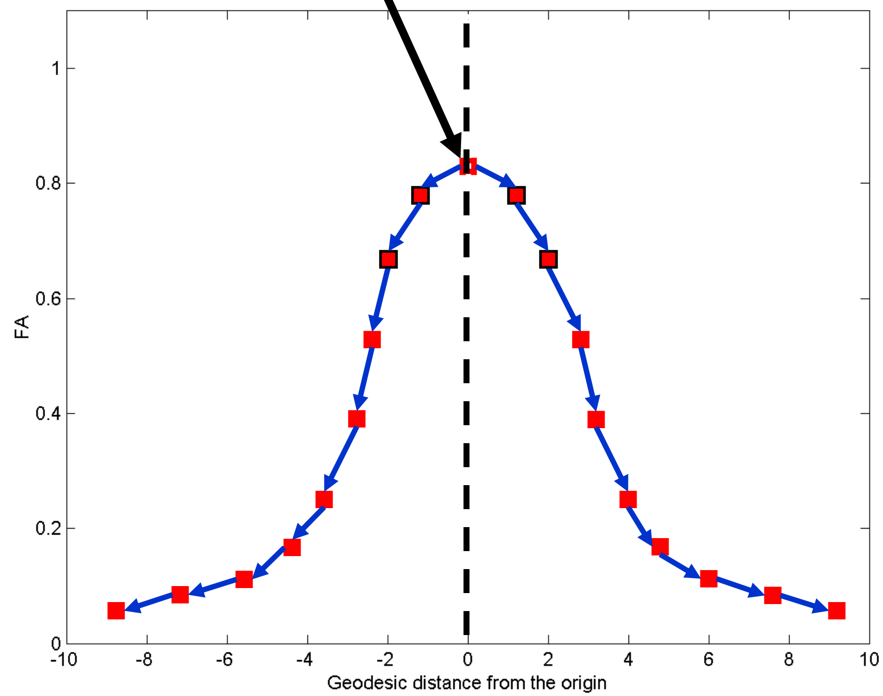


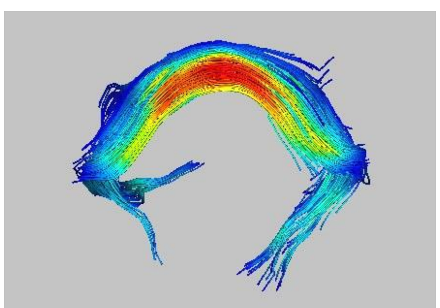
Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Modeling of fiber tracts

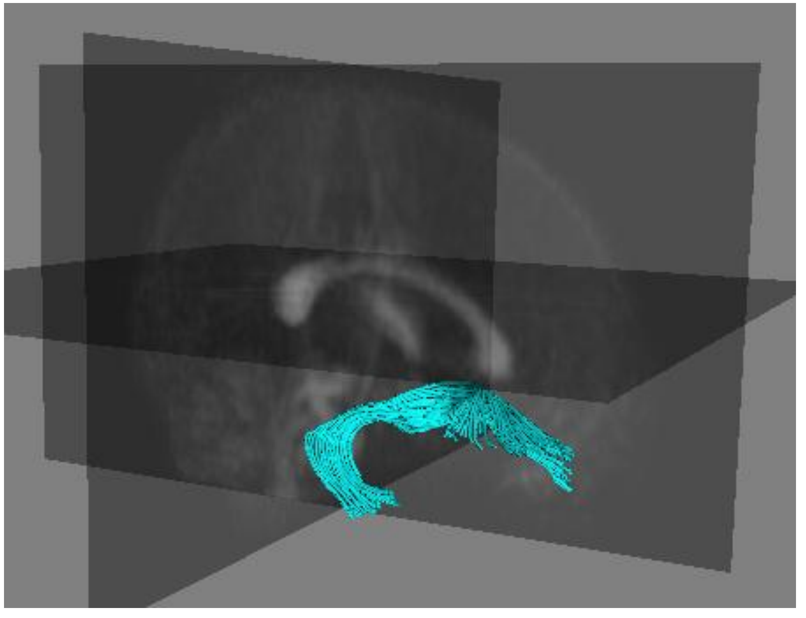


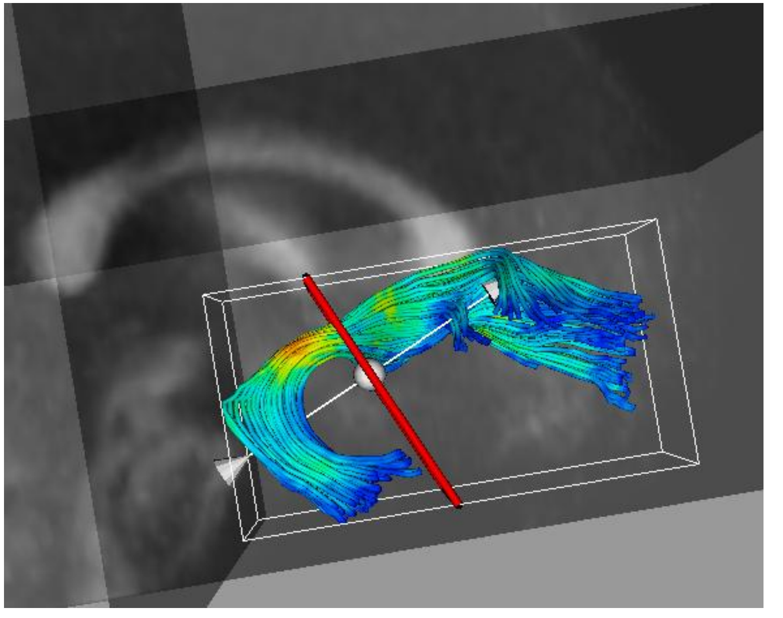
Origin (anatomical landmark)

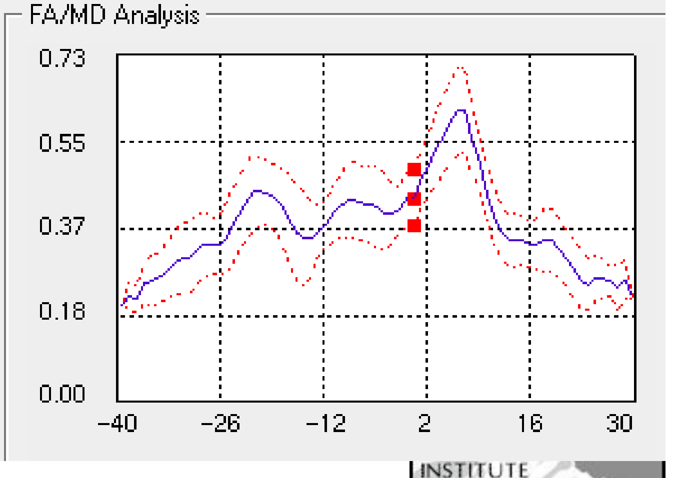




Example Uncinate Fasciculus

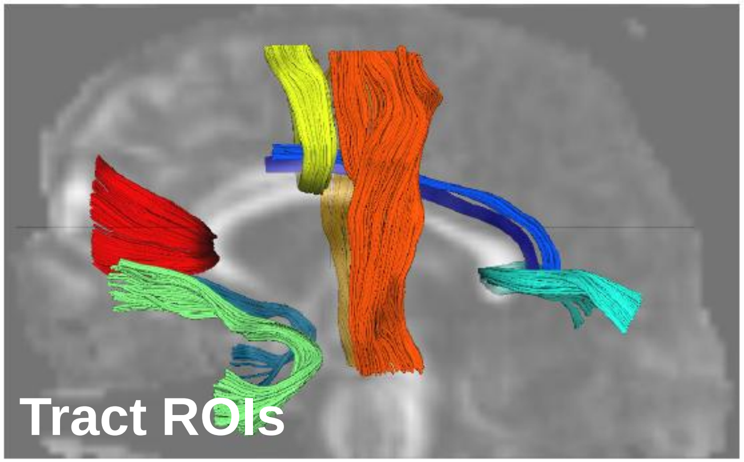


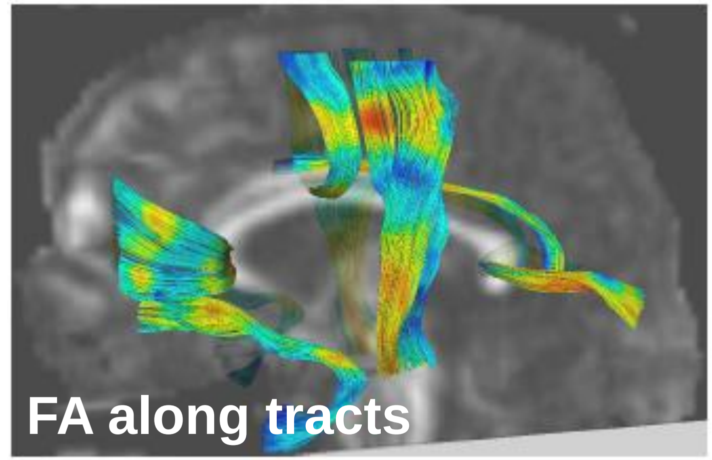


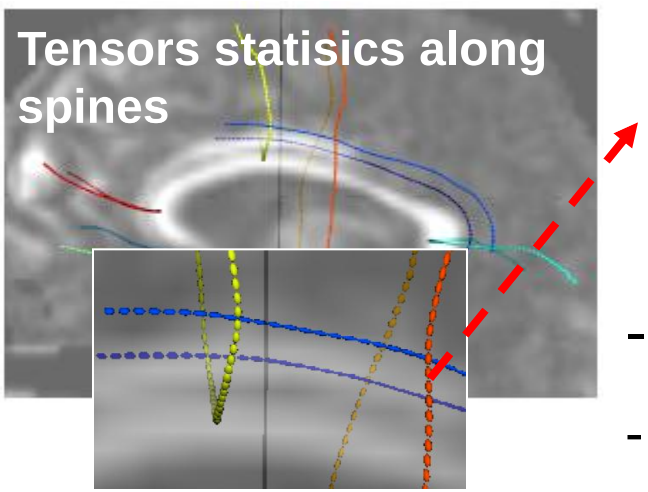


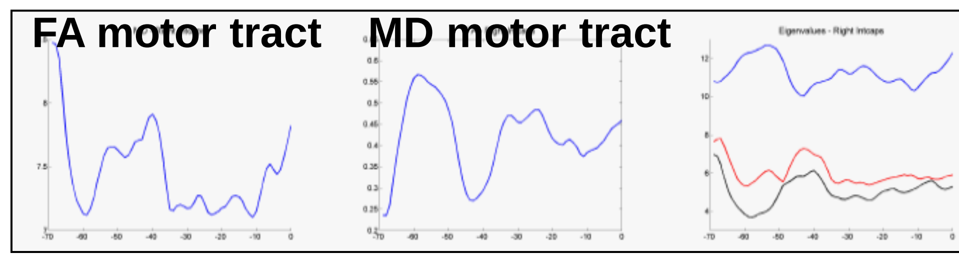
Corouge et al. *Fiber tract-oriented statistics for quantitative diffusion tensor MRI analysis*. Medical Image Analysis 2006.
FiberViewer software - http://www.ia.unc.edu/dev/

Quantitative Tractography



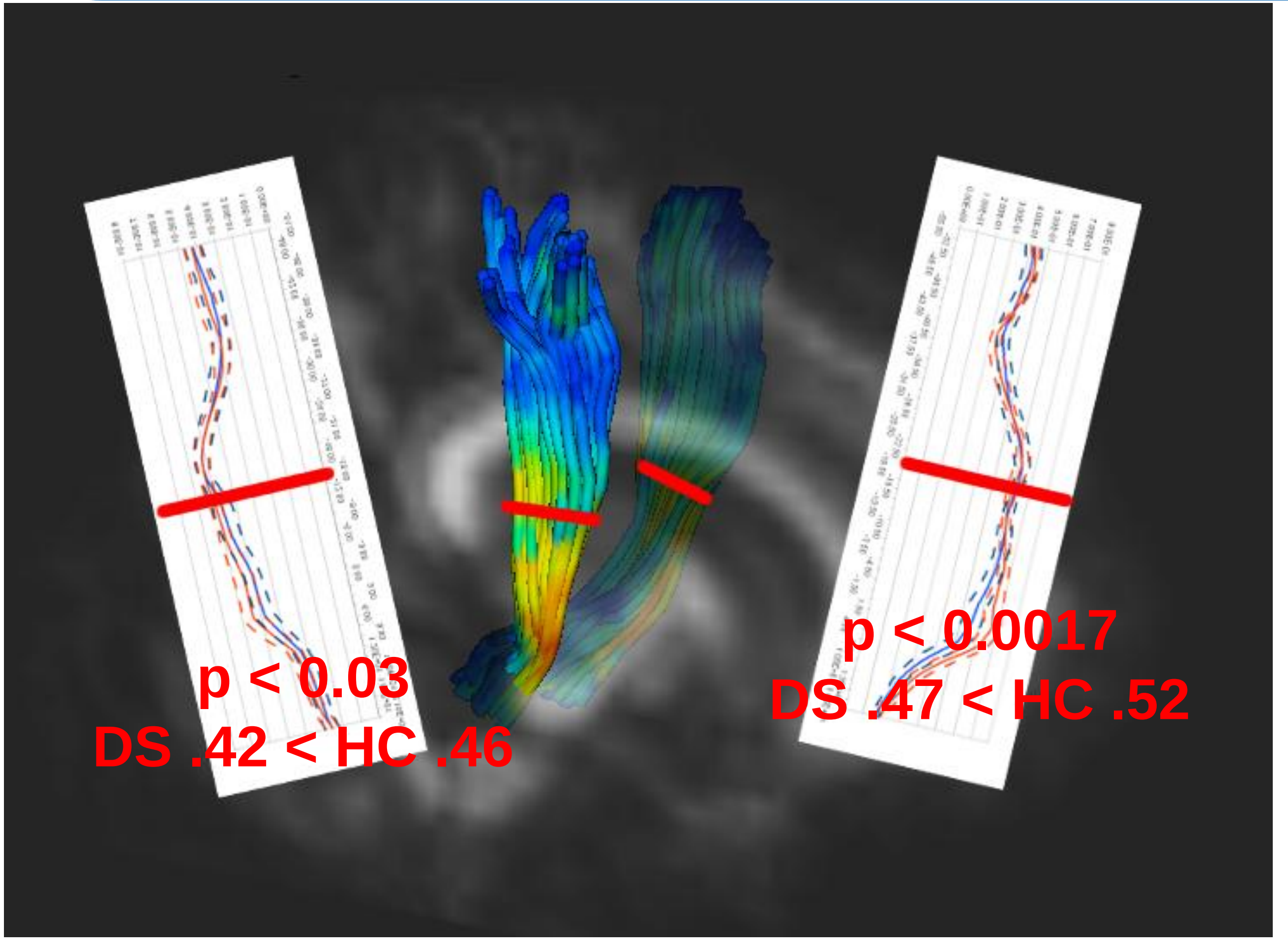






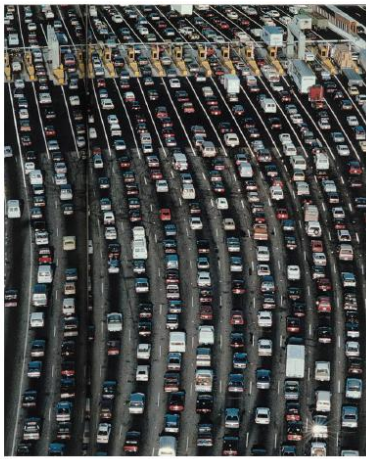
- Tractography for ROI definition
- Tensor-math. for statistics along tracts

Group testing of FA along motor tracts (Downs Syndrome vs. HC)



- **Center**: Left and right motor tracts, color-coded with FA (0 to 1 in blue to red)
- **Left and right**: FA as function of arc- length for HC (red) and DS (blue)

Summary: What do we measure?



- DWI measures <u>local</u> diffusivity pattern.
- Local diffusivity pattern is shaped by tissue type, axon structuring, myelination etc.
- Curves and streamlines from tractography are NOT AXONS but possible paths in vector/tensor field.
- "Fiber counting" scientifically questionable, # is method specific.
- DWI DOESN'T MEASURE AXONS or GLOBAL CONNECTIVITY !

Limitation of Tractograpy: Infer global structures from local estimates

We measure diffusion structure of local elements (2x2x2mm3) and make inference/guess about road network → axonal bundles.

- Voxel size: cubic mm
- Axon diameter: micrometers

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Ermerging New Techniques: HARDI, DSI, Q-Ball

Wendell JS Krieg, 1963

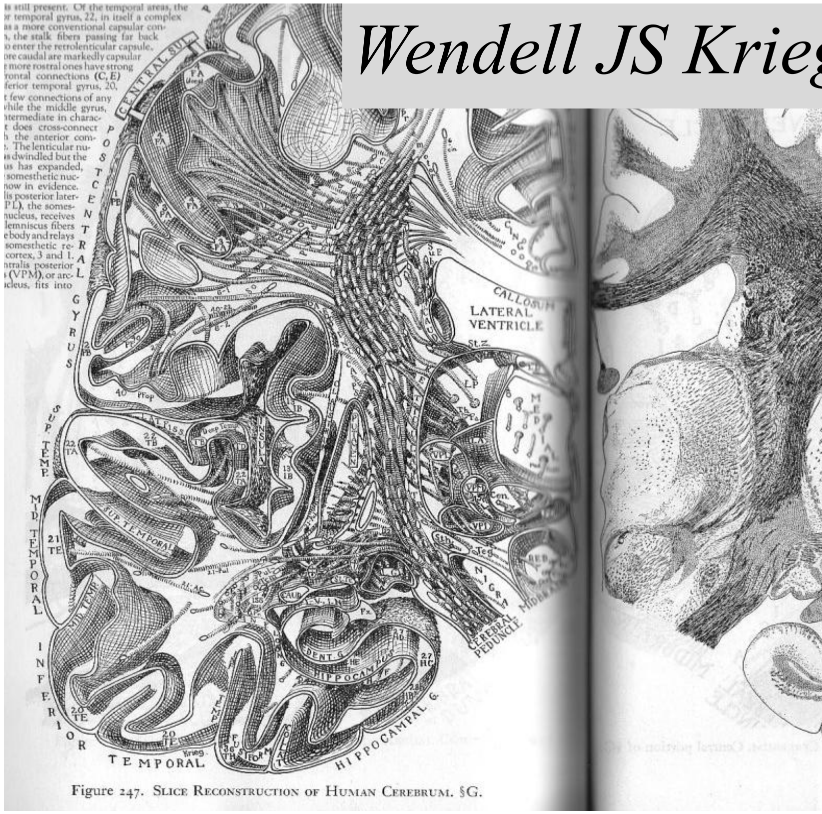
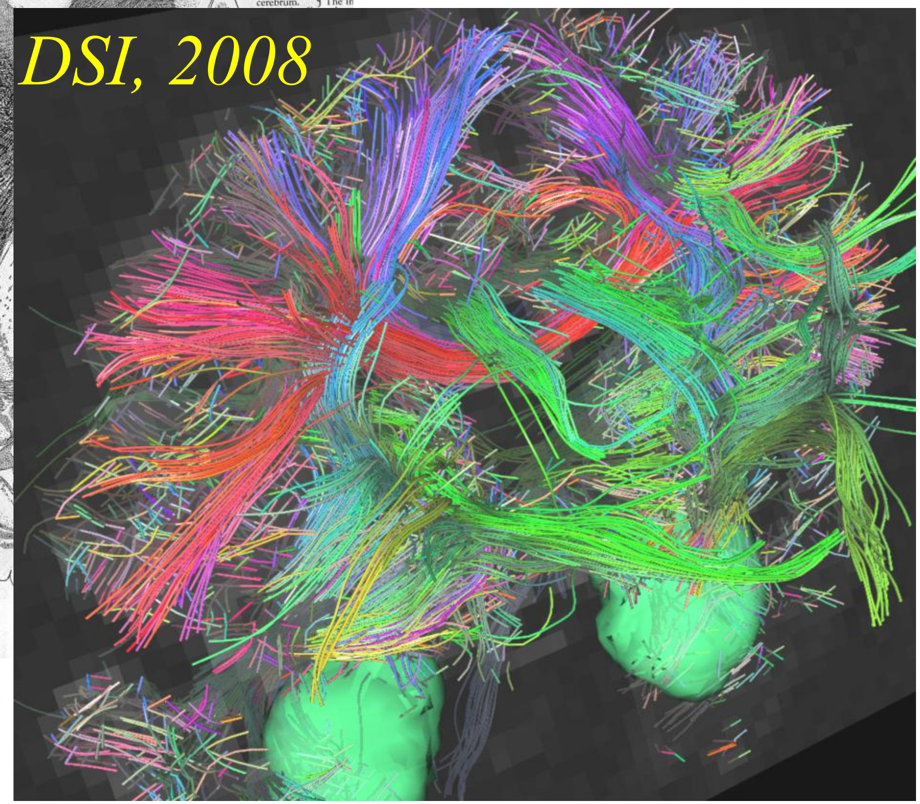


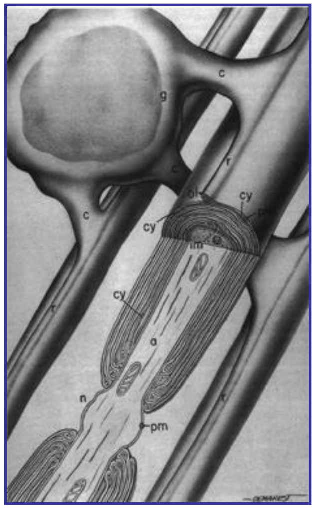
Figure 247. Slice Reconstruction of Human Cerebrum. §G.

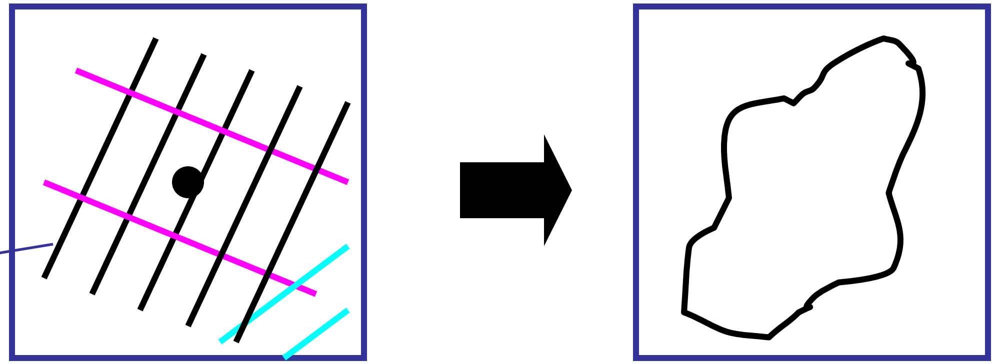
DSI, 2008



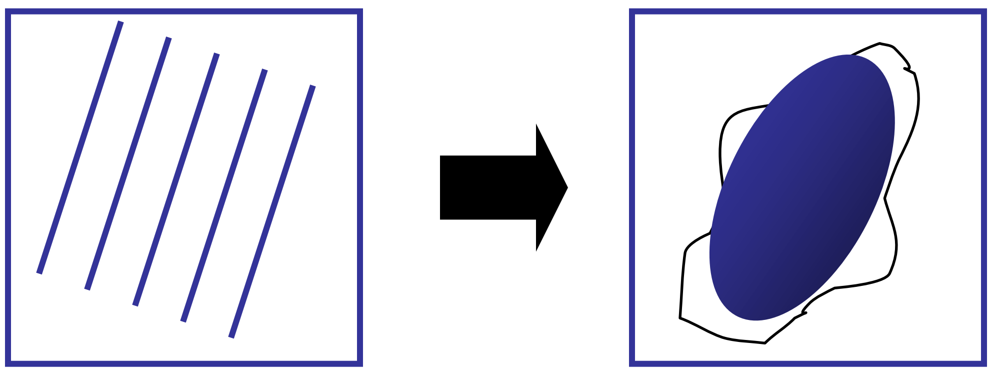
VJ Wedeen, R Wang, T Benner
MGH-Martinos Center,Harvard Medical School

Simplification and assumption





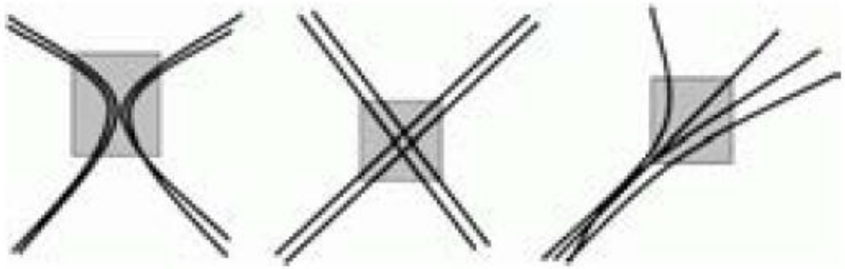
Orientational Diffusion Fct



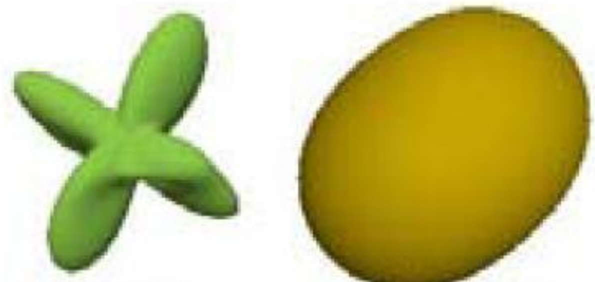
Diffusion ellipsoid

Courtesy of Susumu Mori, JHU

Limitations of the Diffusion Tensor Model

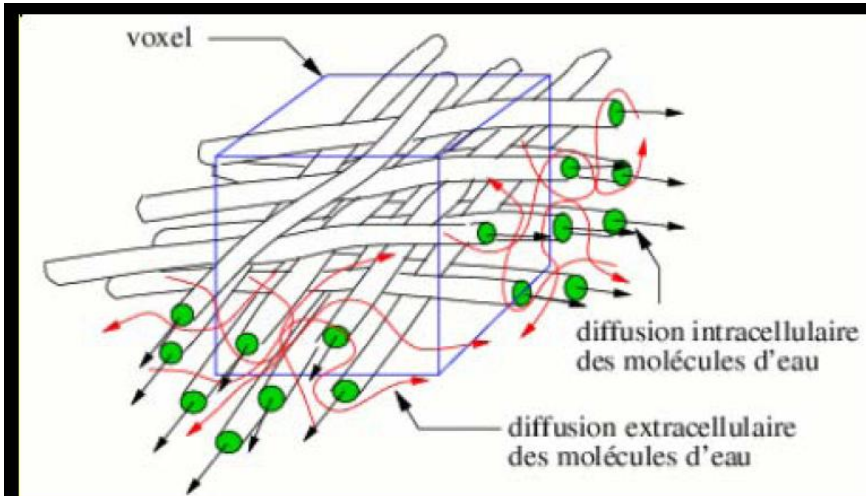


Kissing Crossing Splaying.



Diffusivity in a fiber crossing

2nd-order tensor approximation

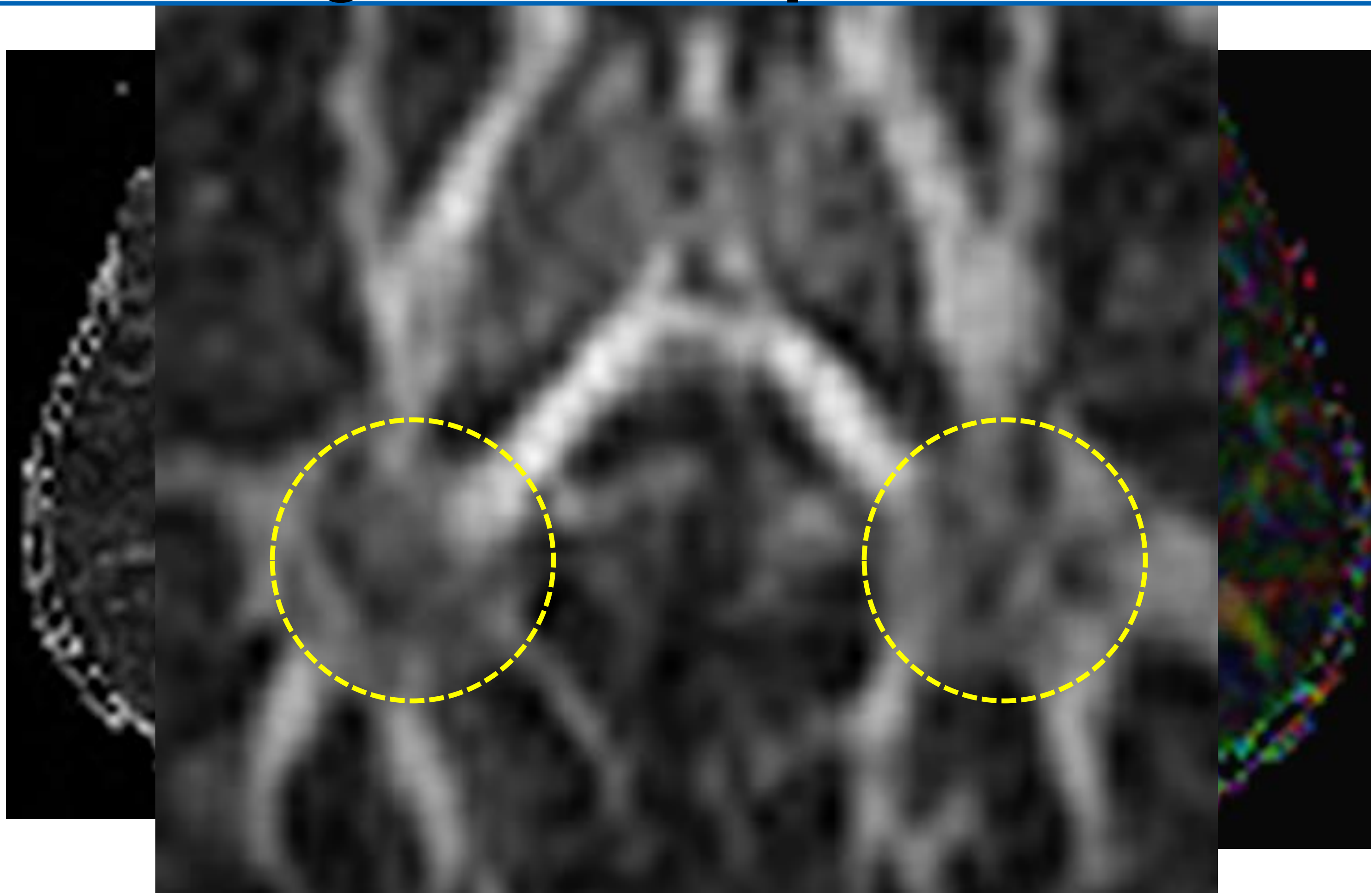


DTI fails when fiber bundles crosses within the same voxel

Non-Gaussian diffusion process - Image from [Poupon-PhD:99]

Courtesy B. Vemuri, MICCAI 2008 workshop

DTI with 12 directions & 2 averages
Crossing Fibers Dropout on FA



Courtesy R. McKinstry

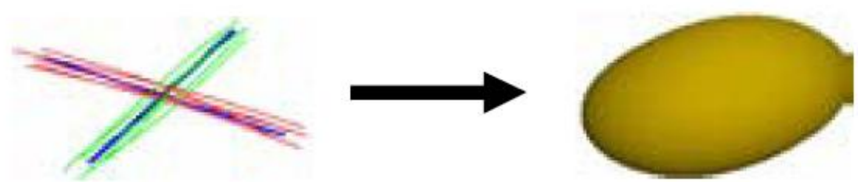
Motivation: Why higher order?

- 2nd order tensors are popular for representing the diffusivity profile in DW-MRI data sets.

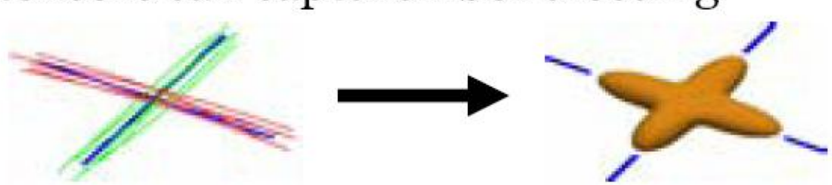
$$d(\mathbf{g}) = \mathbf{g}^T \mathbf{D} \mathbf{g}$$

$\mathbf{g} = [g_1\ g_2\ g_3]^T$ is the magnetic field gradient direction , $\mathbf{D}$ is the estimated tensor.

- 2nd order tensors fail to represent fibers crossings.

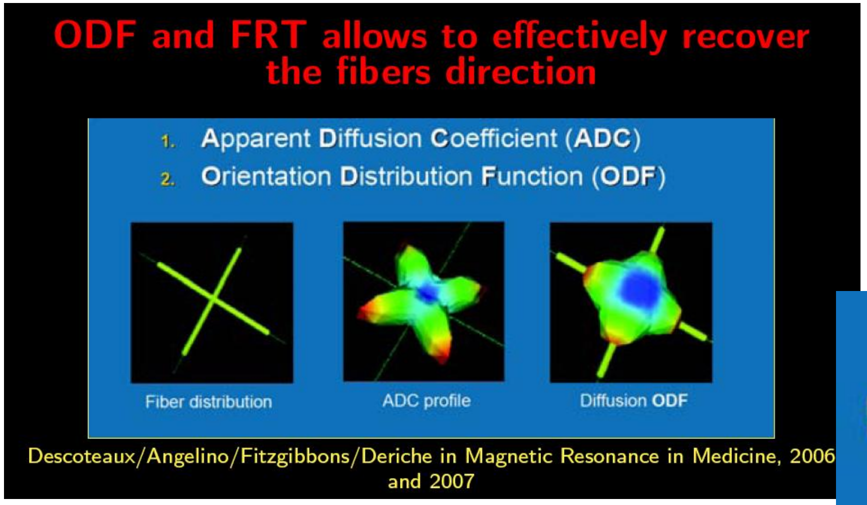


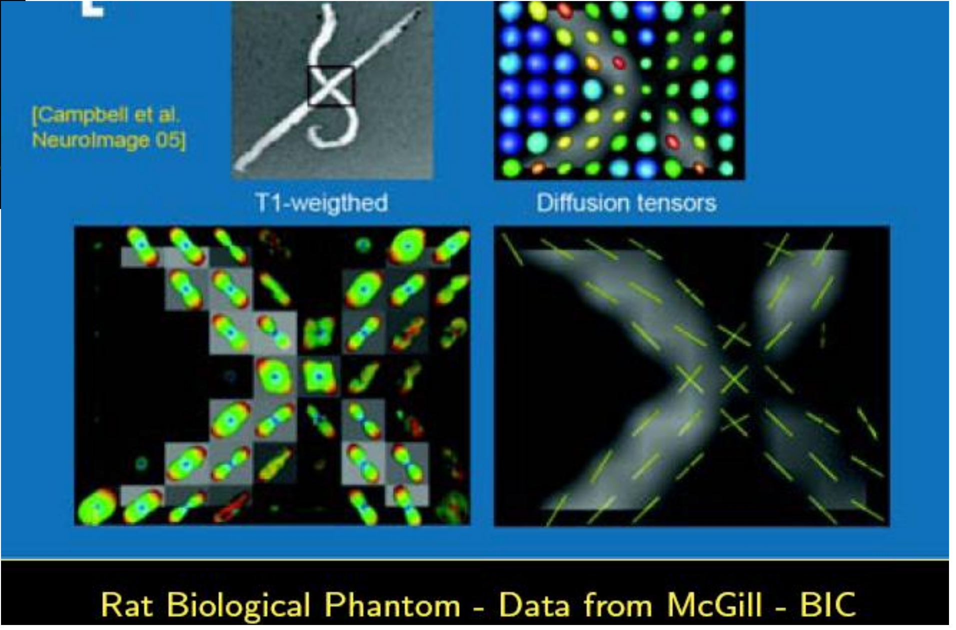
- Higher order tensors can capture fiber crossing geometry.



Courtesy Baba Vemuri, MICCAI 2008 workshop

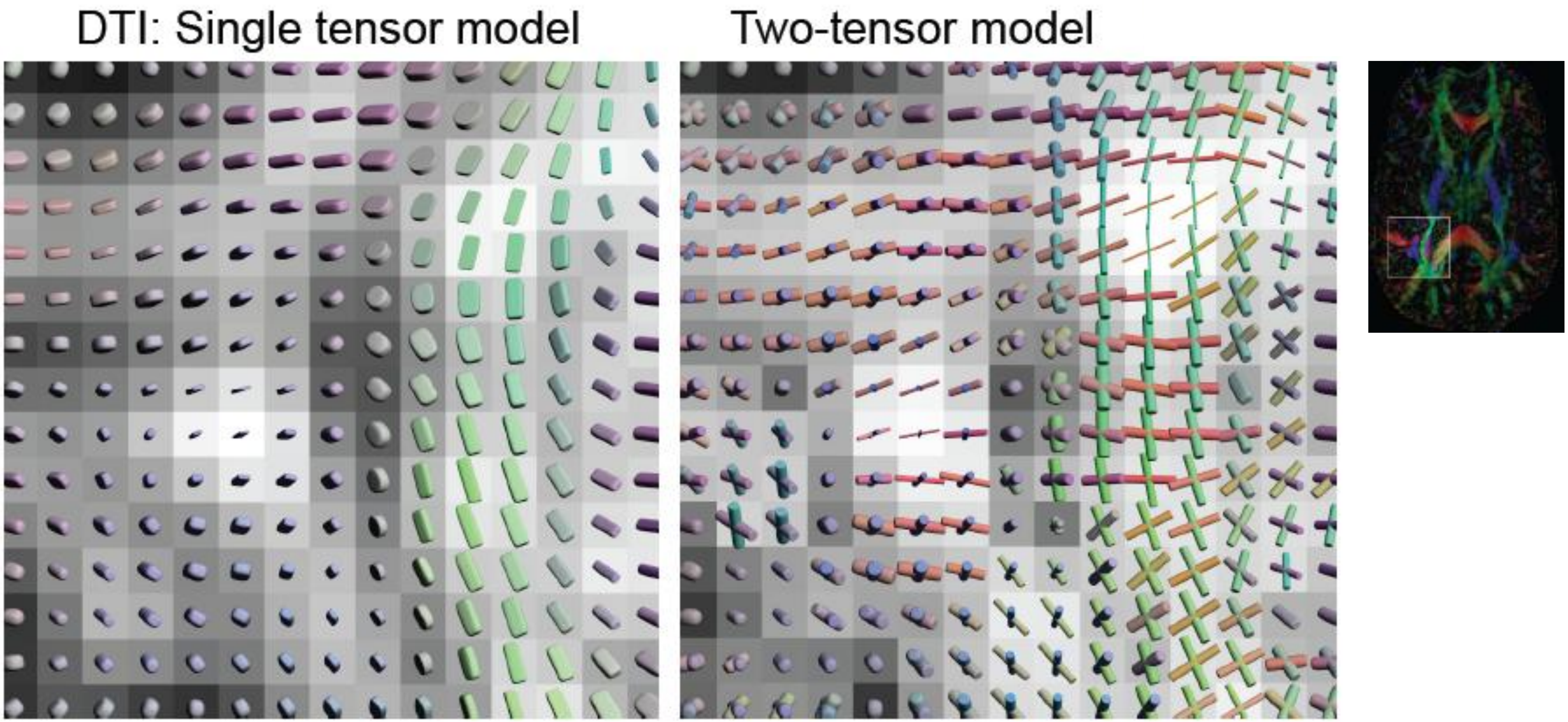
Orientation Distribution Function ODF





Courtesy Rachid Deriche, MICCAI 2008 workshop

Two Tensor Model (C-F Westin, S Peled, G Kindlmann)

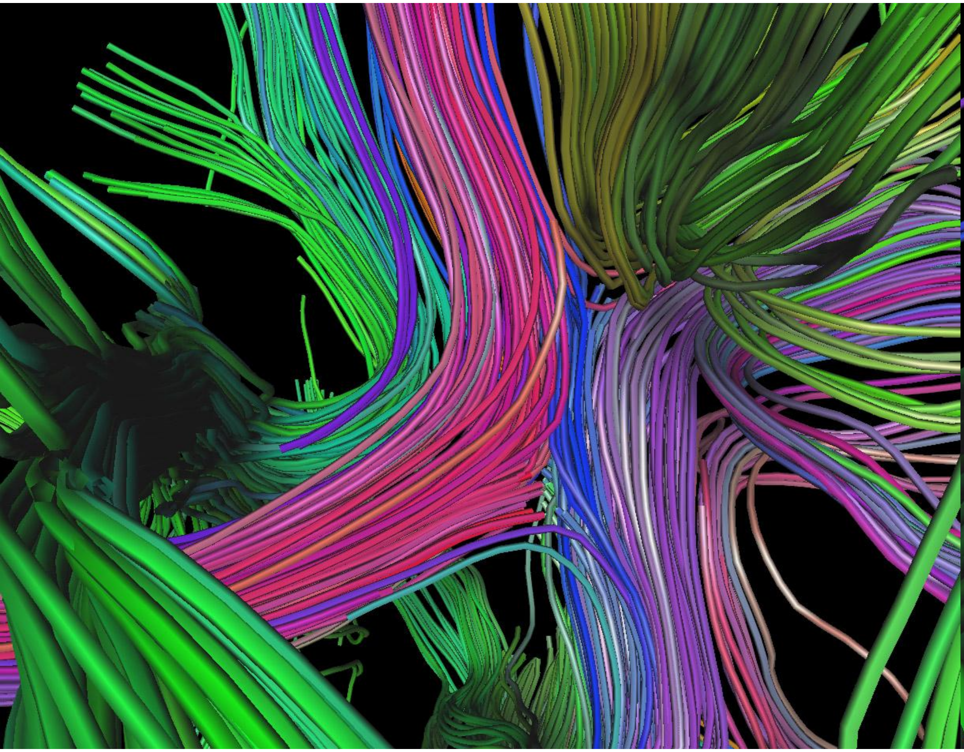


Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

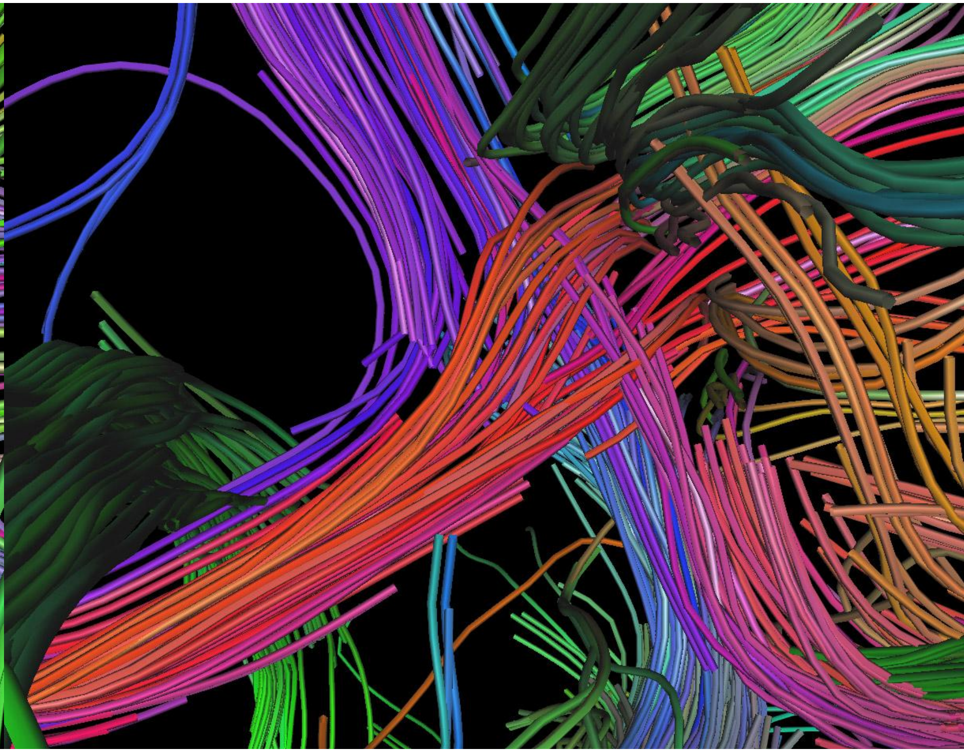
Centrum Semiovale

corpus callosum (red) & corticospinal tract (blue)

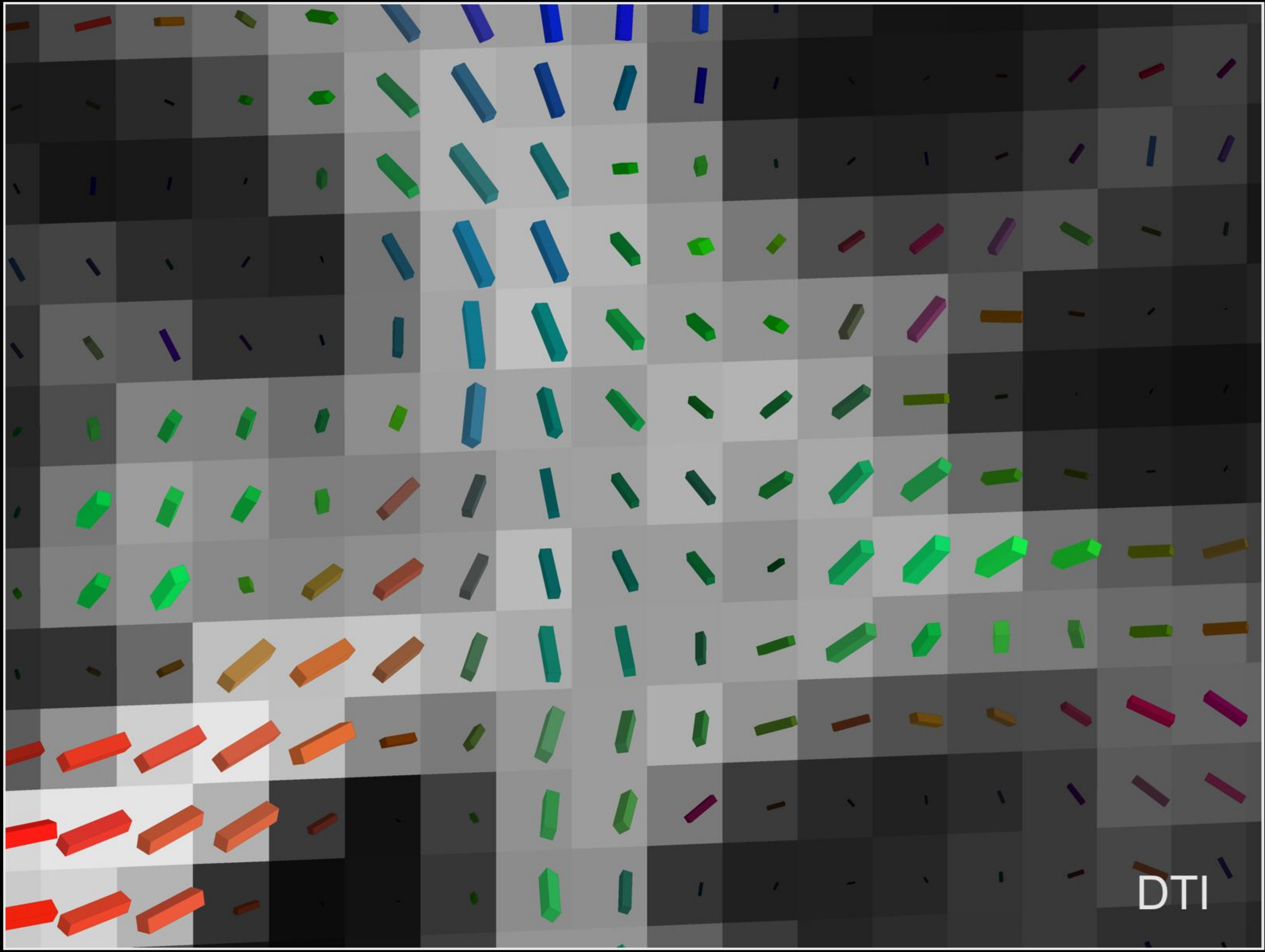
DTI



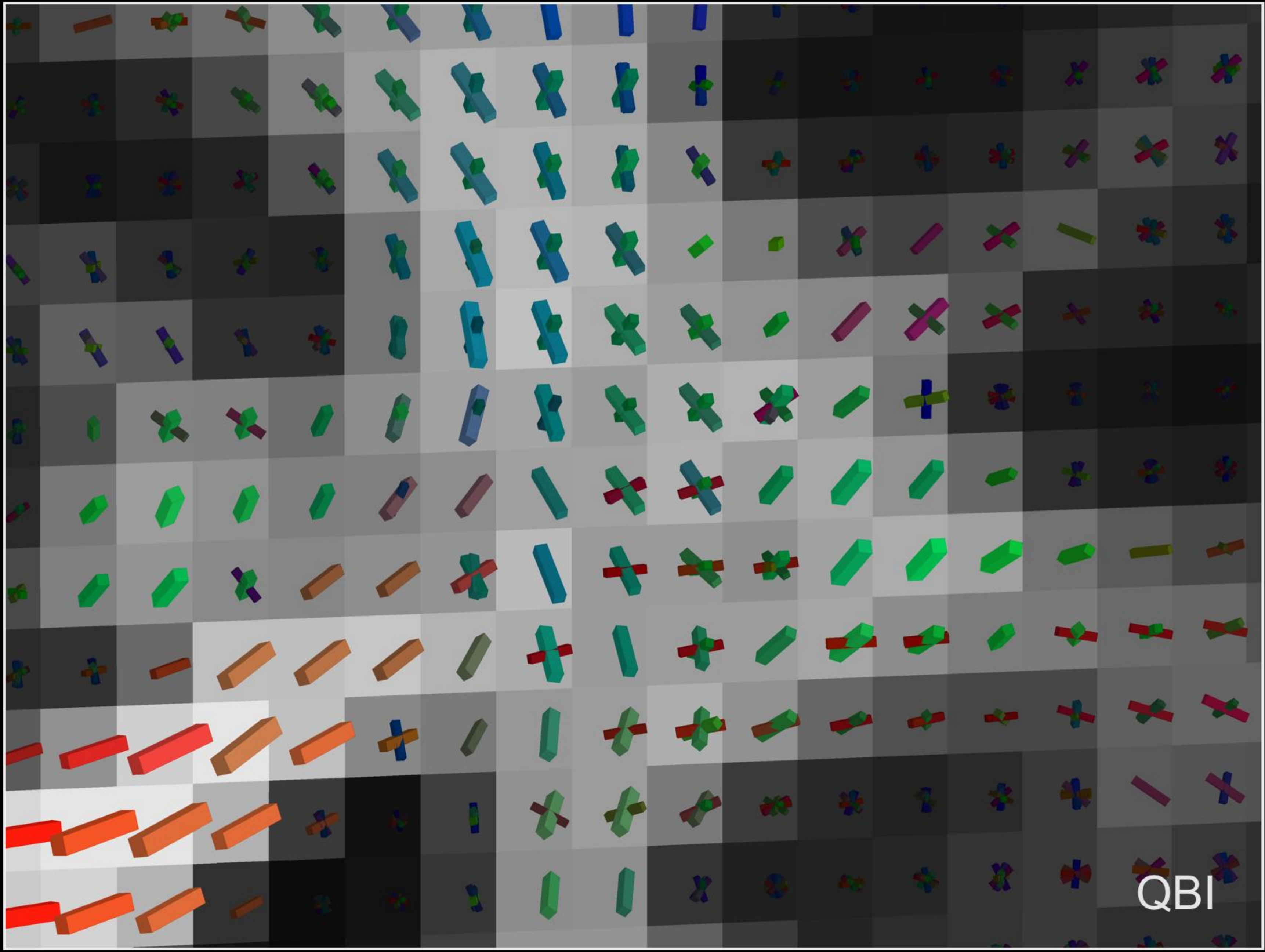
DSI



Wedeen / Wang /AGS / MGH - HST

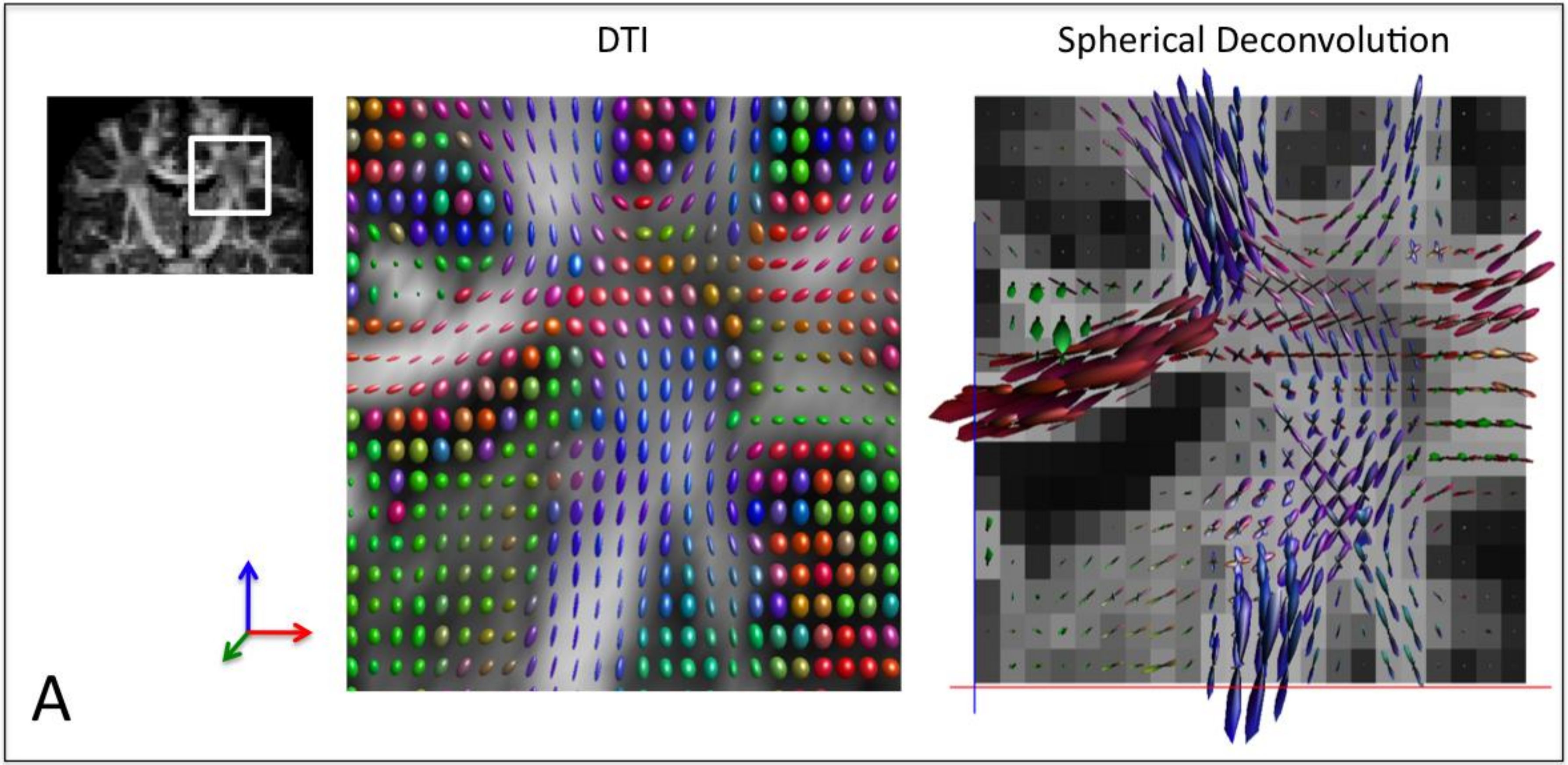


MGH / DT



MGH / DT

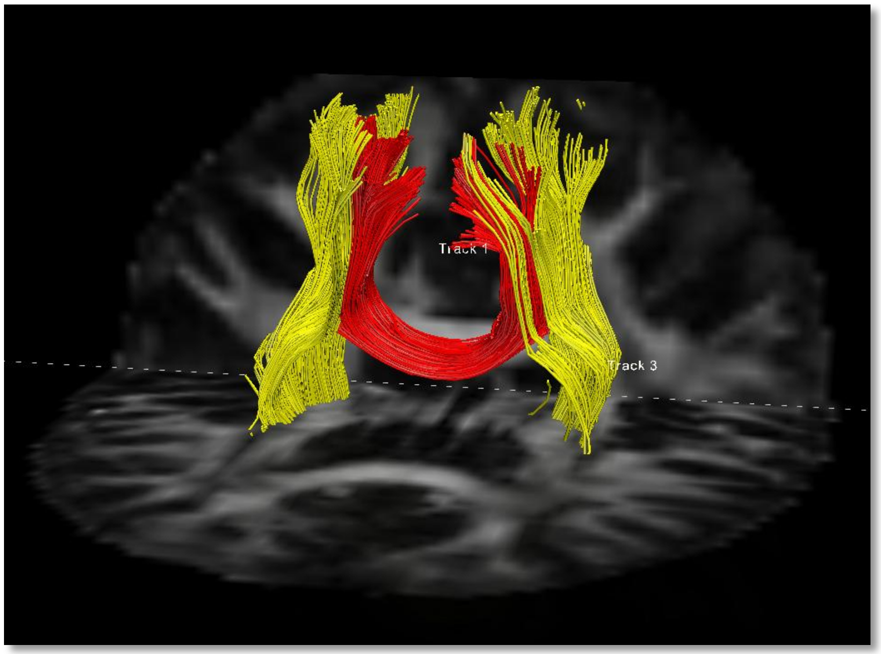
Spherical Deconvolution Tractography



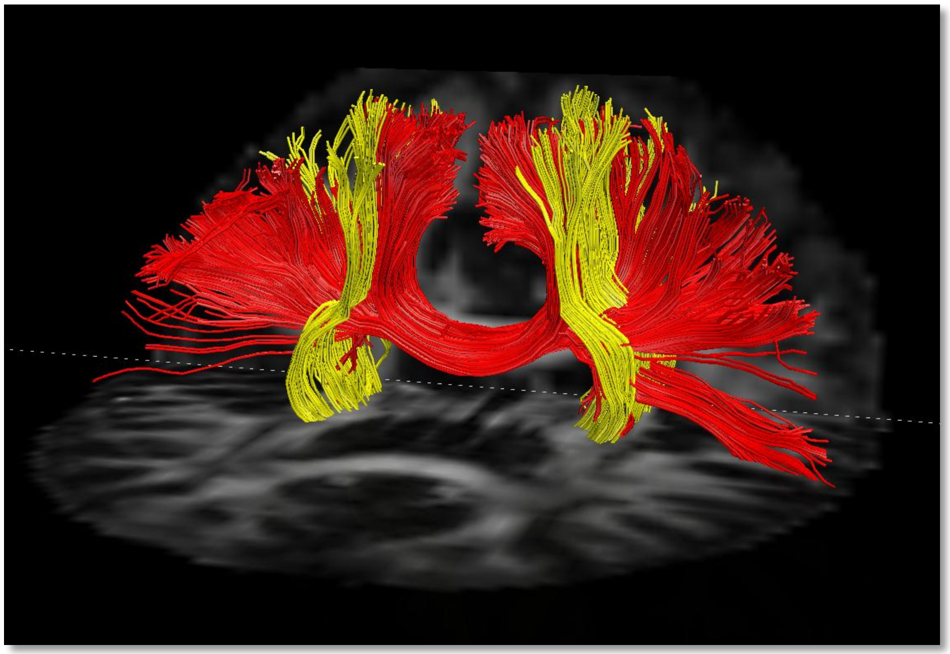
60 DW directions, Cardiac Gated, Scan time = 20 min, b = 3000 s/mm^2

Dell'Acqua et al. NeuroImage 2010

DTI Tractography



Spherical Deconvolution Tractography

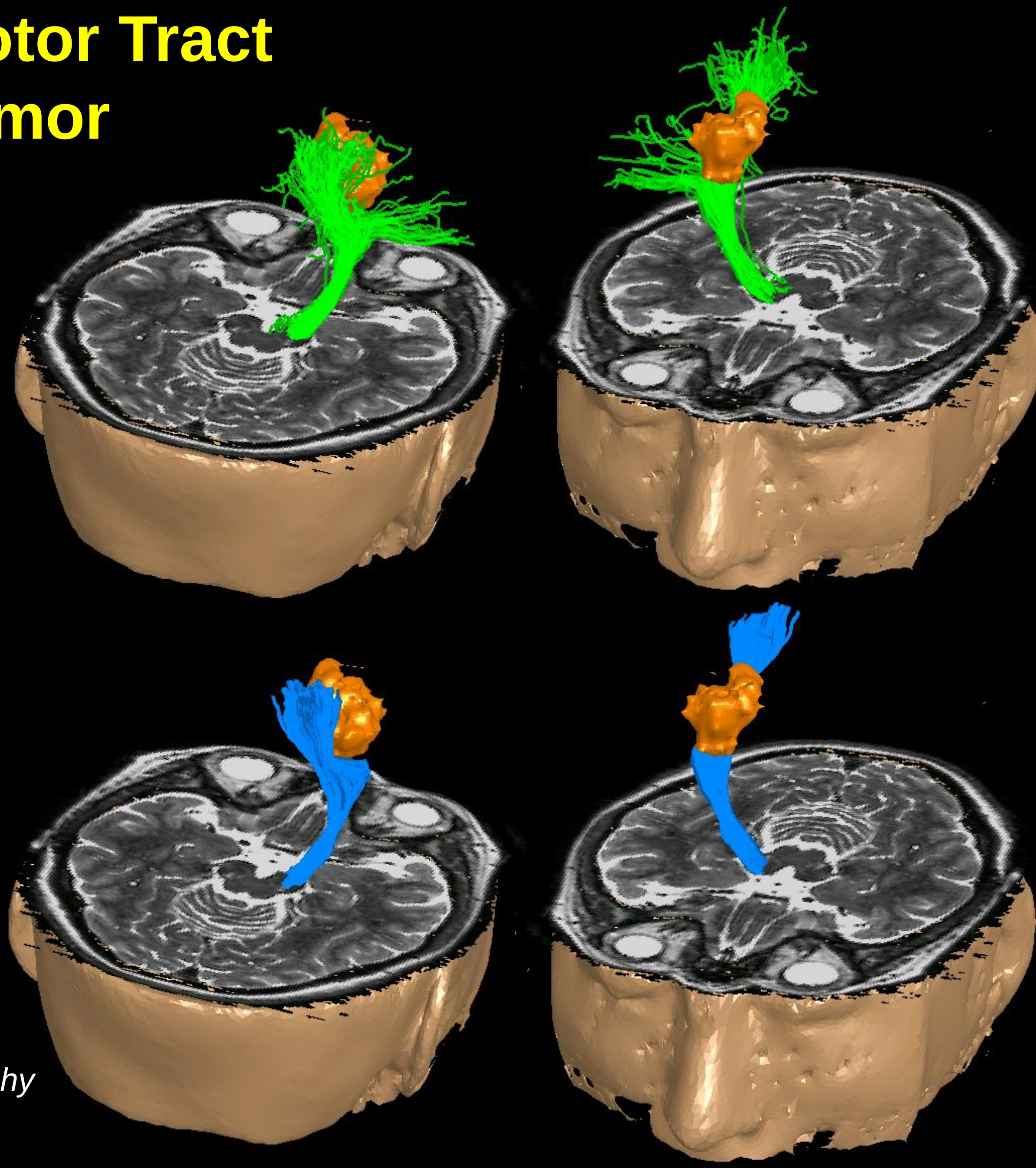


Close to standard DTI protocols →

60 DW dir, Cardiac Gated, **b=1500** s/mm^2

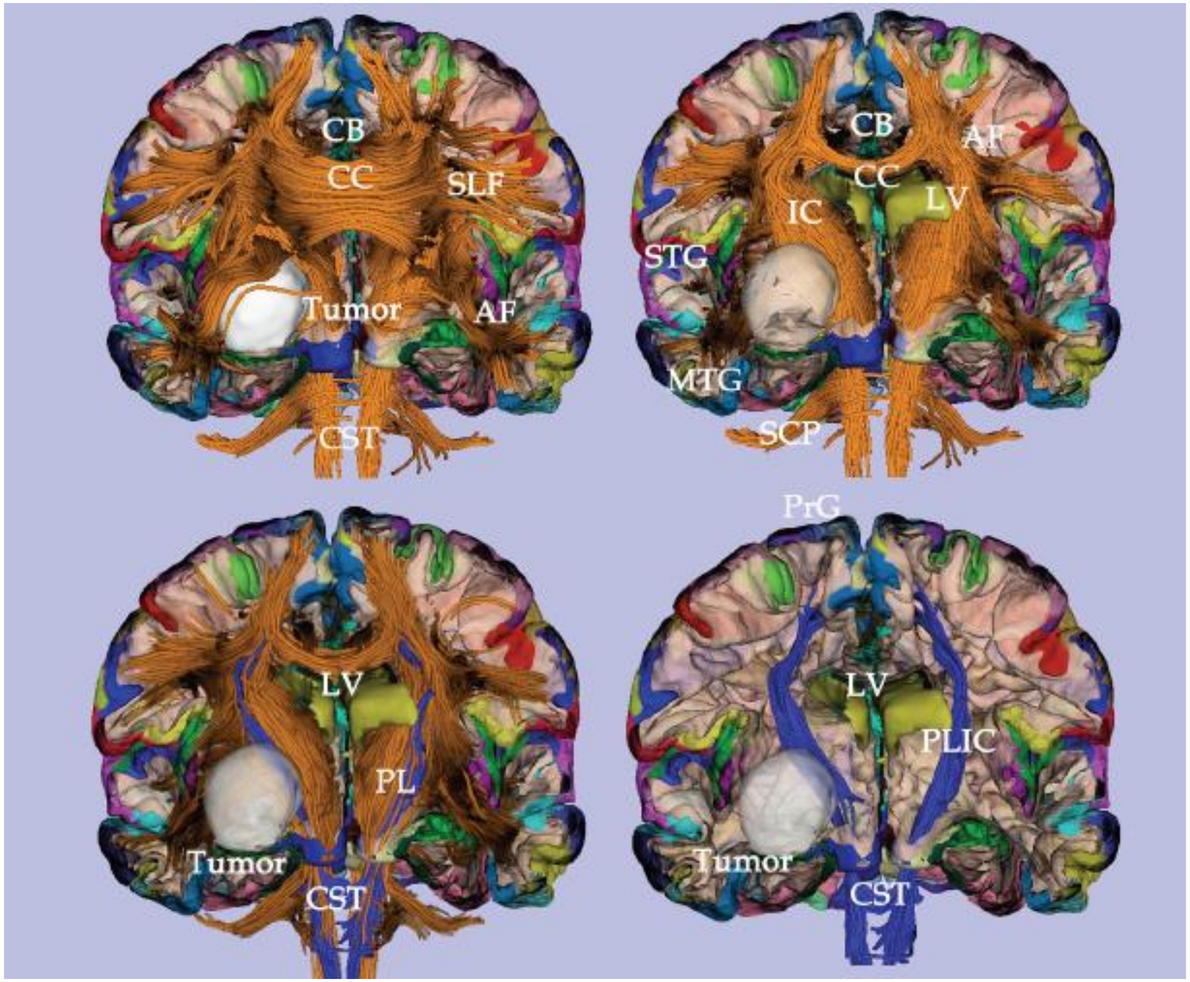
Dell'Acqua et al. NeuroImage 2010

Delineation of Motor Tract in Adult Brain Tumor Patient



J.I. Berman, *Diffusion MR Tractography as a Tool for Surgical Planning.* Mag. Res. Imag. Clinics of North America. 2009

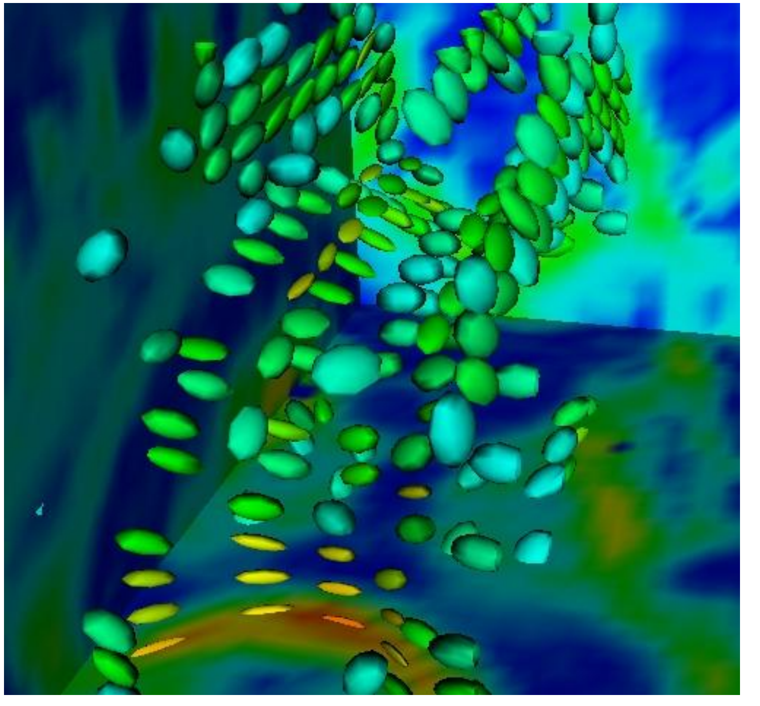
Brain Tumor Case



Tractography based on higher-order tensor models and modeling of crossings and disperging bundles is vital for neurosurgical applications.

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Acknowledgments



Contributors:

- C-F. Westin
- A. Alexander
- G. Kindlmann
- L. O'Donnell
- C. Goodlett
- J. Fallon
- R. Whitaker
- R. McKinstry

National Alliance for Medical Image Computing (NIH U54EB005149)