Diffusion Tensor Processing and Visualization

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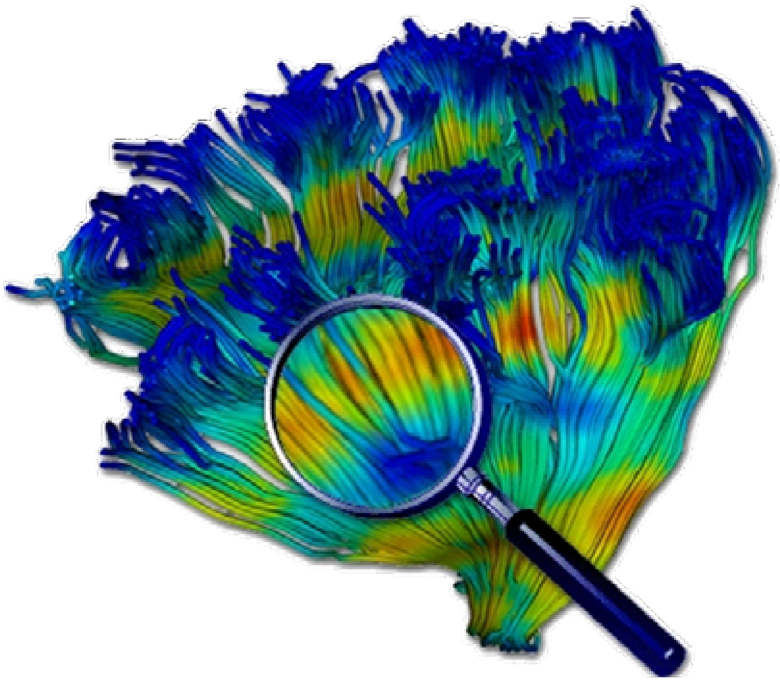
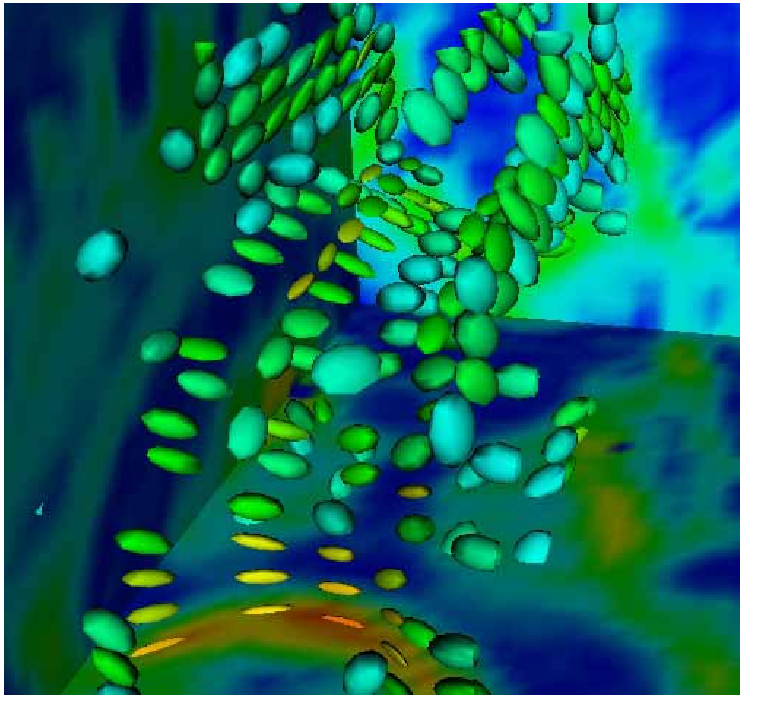
NAMIC: National Alliance for Medical Image Computing



Acknowledgments

Contributors:

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



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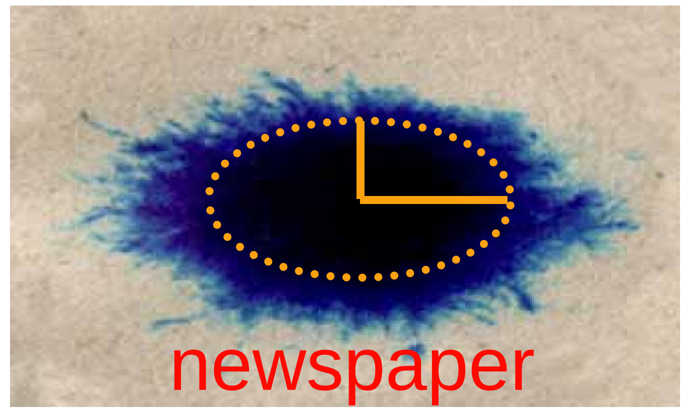
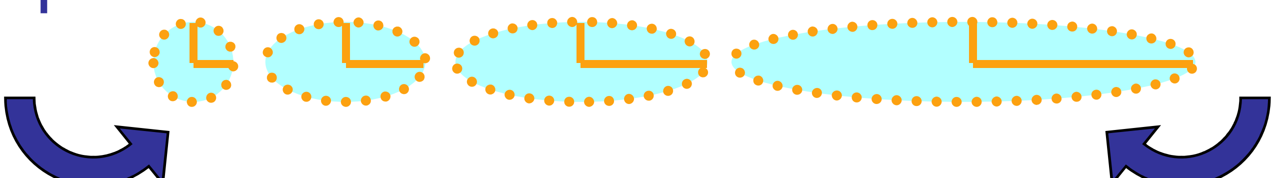
Diffusion in Biological Tissue

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



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

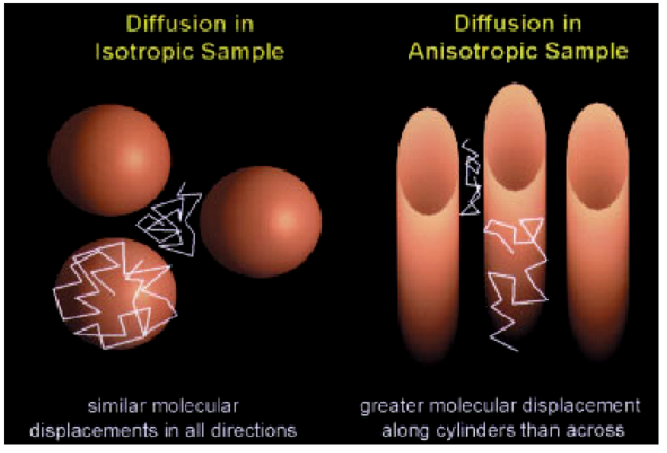
isotropic   anisotropic



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)

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

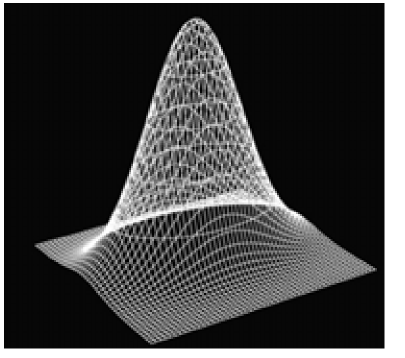
Change in density

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

Derivatives (gradients) in space

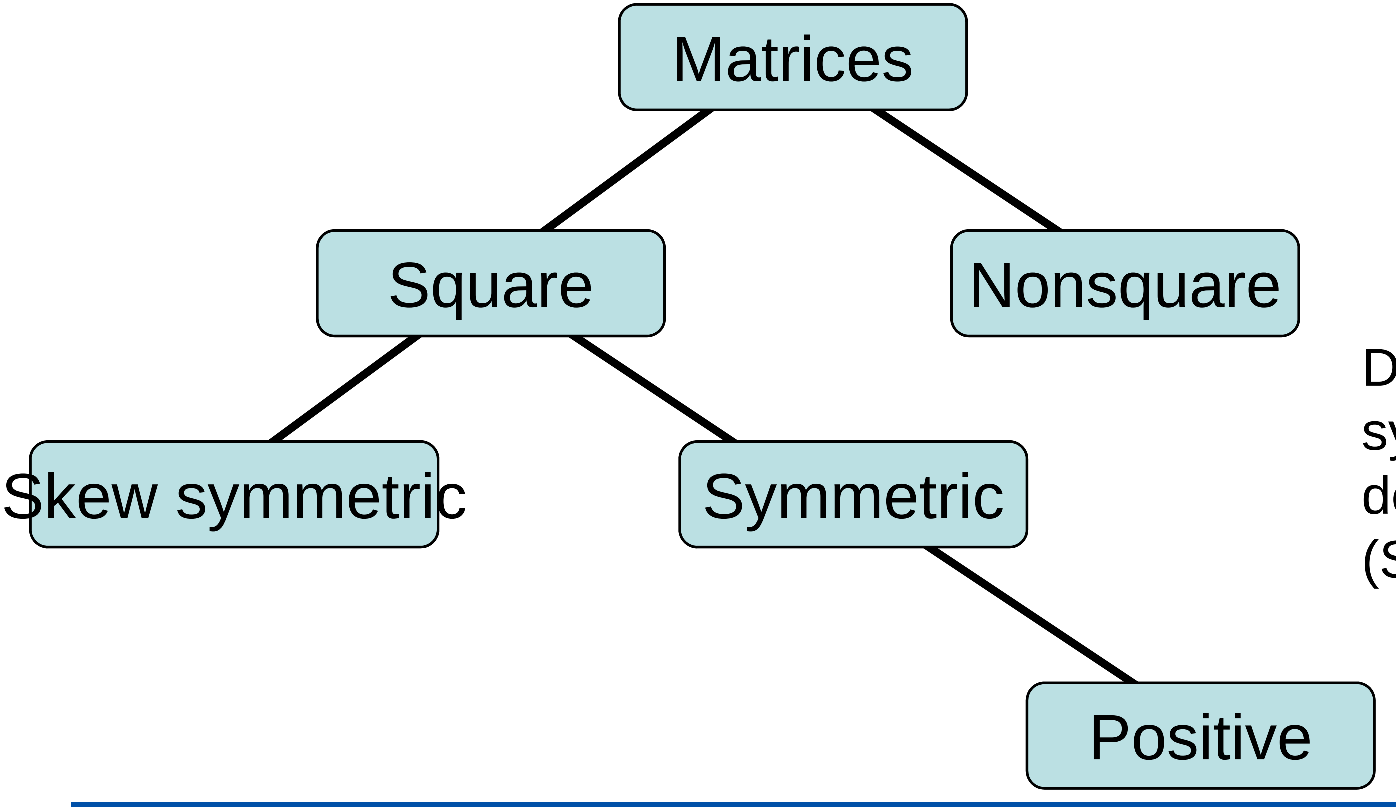
Solutions of the Diffusion Equation

- 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)



D Is A Special Kind of Matrix

- The universe of matrices



D is a "square, symmetric, positive-definite matrix" (SPD)

Properties of SPD

- Bilinear forms and quadratics

$$(x\ \ y\ \ z)\begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{12} & D_{22} & D_{23} \\ D_{13} & D_{23} & D_{33} \end{pmatrix}\begin{pmatrix} x \\ y \\ z \end{pmatrix} = k$$

$$(D_{11})x^2 + (2D_{21})xy + (2D_{31})xz + (D_{22})y^2 + (2D_{23})yz + (D_33)z^2 = k$$

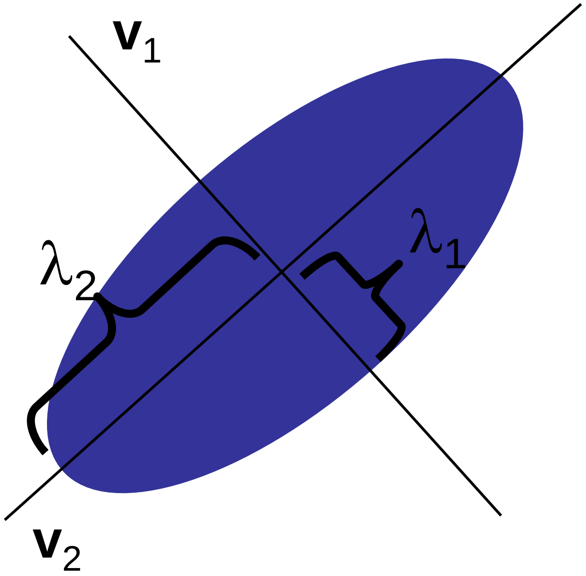
Quadratic equation – implicit equation for ellipse (ellipsoid in 3D)

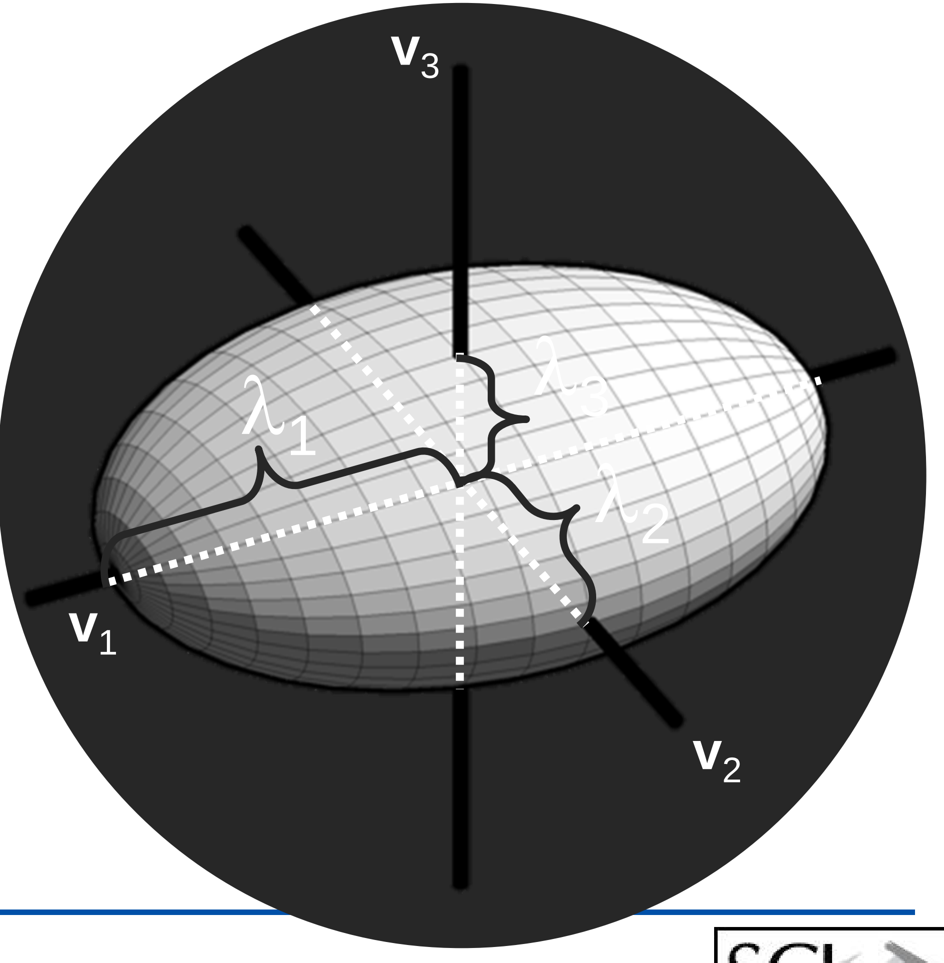
- Eigen Decomposition

$$D = R\Lambda R^{-1} = \begin{bmatrix} | & | & | \\ v_1 & v_2 & v_3 \\ | & | & | \end{bmatrix}\begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}\begin{bmatrix} - & v_1 & - \\ - & v_2 & - \\ - & v_3 & - \end{bmatrix}$$

  - Lambda – shape information, independent of orientation
  - R – orientation, independent of shape
  - Lambda's > 0

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 D

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

b: Physical constants, Strength of gradient, Duration of gradient pulse, Read-out time

S_k: k^{th} DW Image

S_0: Base image

g_k: Gradient direction

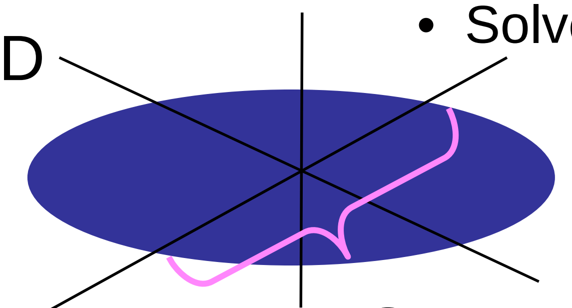
Tensors From Diffusion-Weighted Images

- Solving S-T for D
  - Take log of both sides

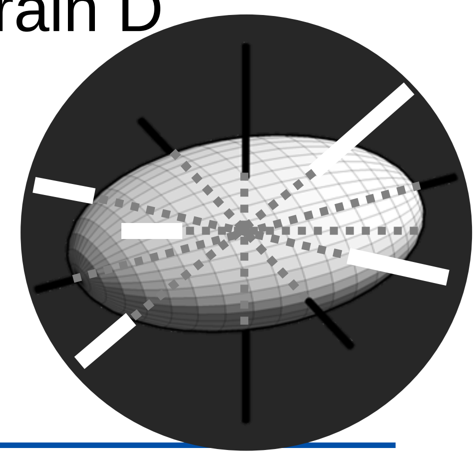
$$g_k^T D g_k = \frac{\log S_0 - \log S_k}{b}$$

  - Linear system for elements of D
  - Six gradient directions (3 in 2D) uniquely specify D
  - More gradient directions overconstrain D
    - Solve least-squares
      - » (constrain lambda>0)

2D



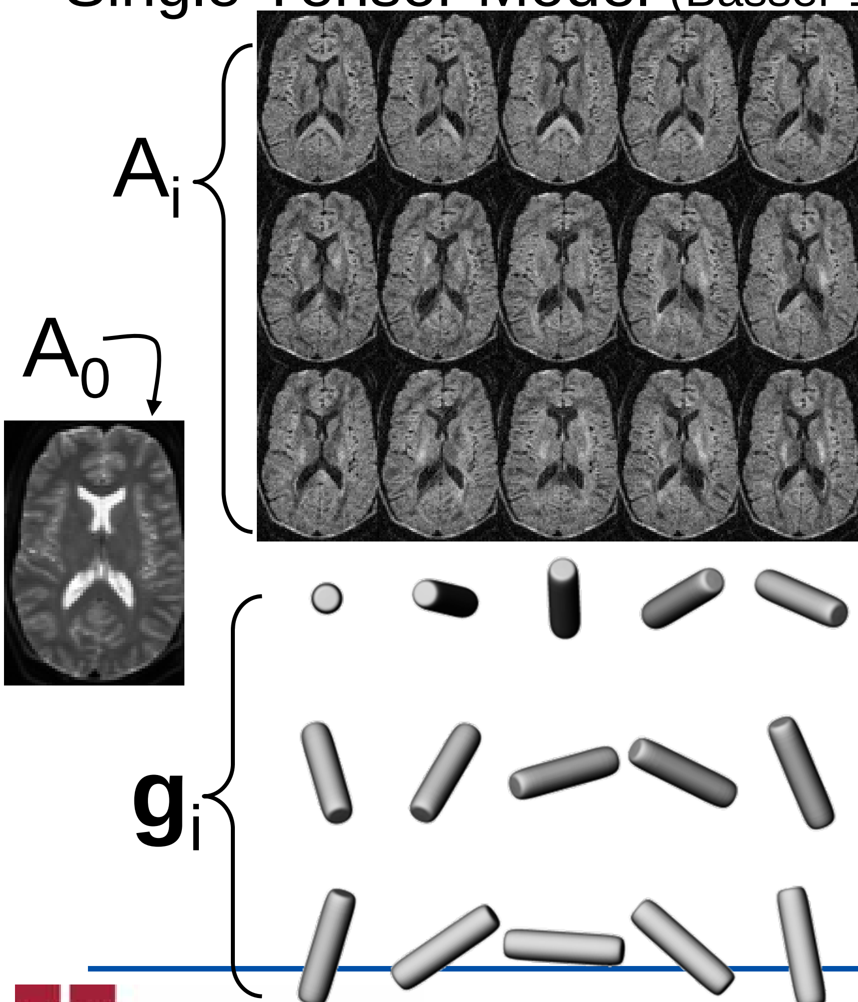
S-T Equation

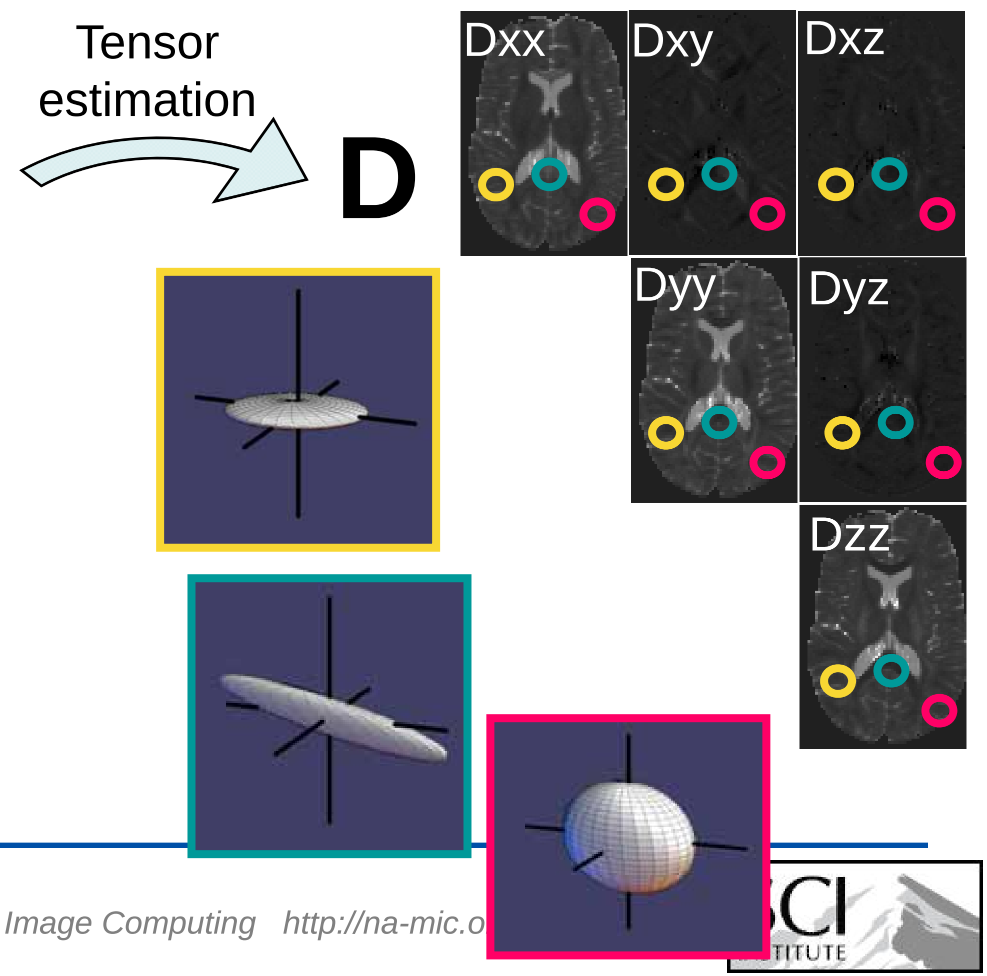


DWI summary: Model

Single Tensor Model (Basser 1994)

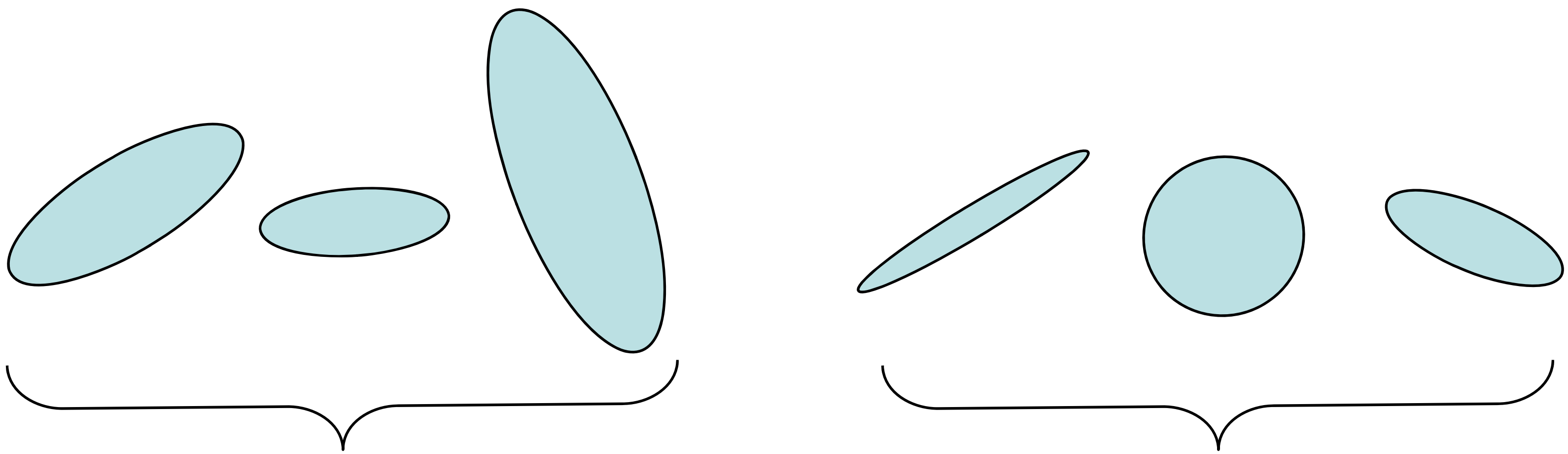
$$A_i = A_0 e^{-b\mathbf{g}_i^T \mathbf{D} \mathbf{g}_i}$$





Shape Measures on Tensors

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



Different sizes/orientations

Different shapes

Measuring the “Size” of a Tensor

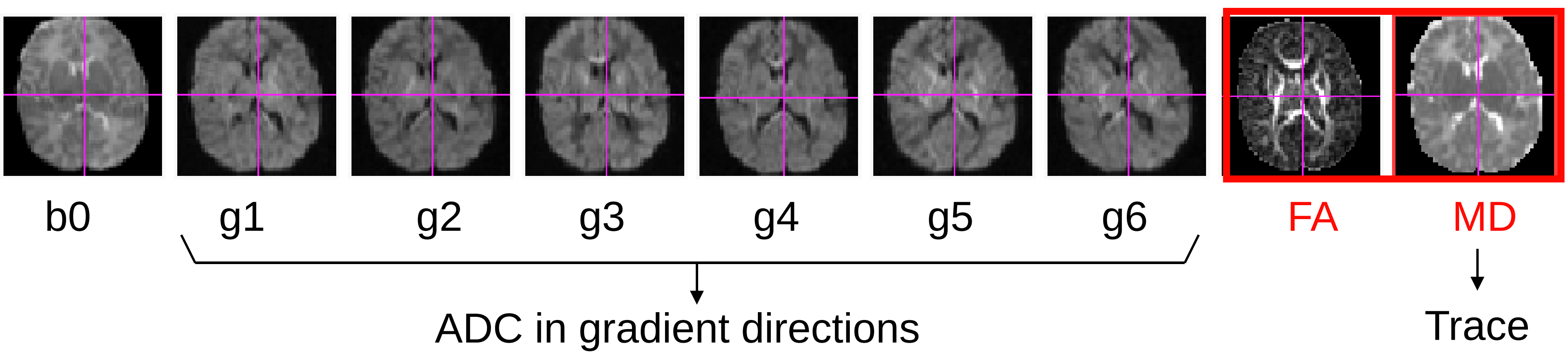
- Length – $(\lambda_1 + \lambda_2 + \lambda_3)/3$
  - $(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)^{1/2}$
- Area – $(\lambda_1 \lambda_2 + \lambda_1 \lambda_3 + \lambda_2 \lambda_3)$
- Volume – $(\lambda_1 \lambda_2 \lambda_3)$

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

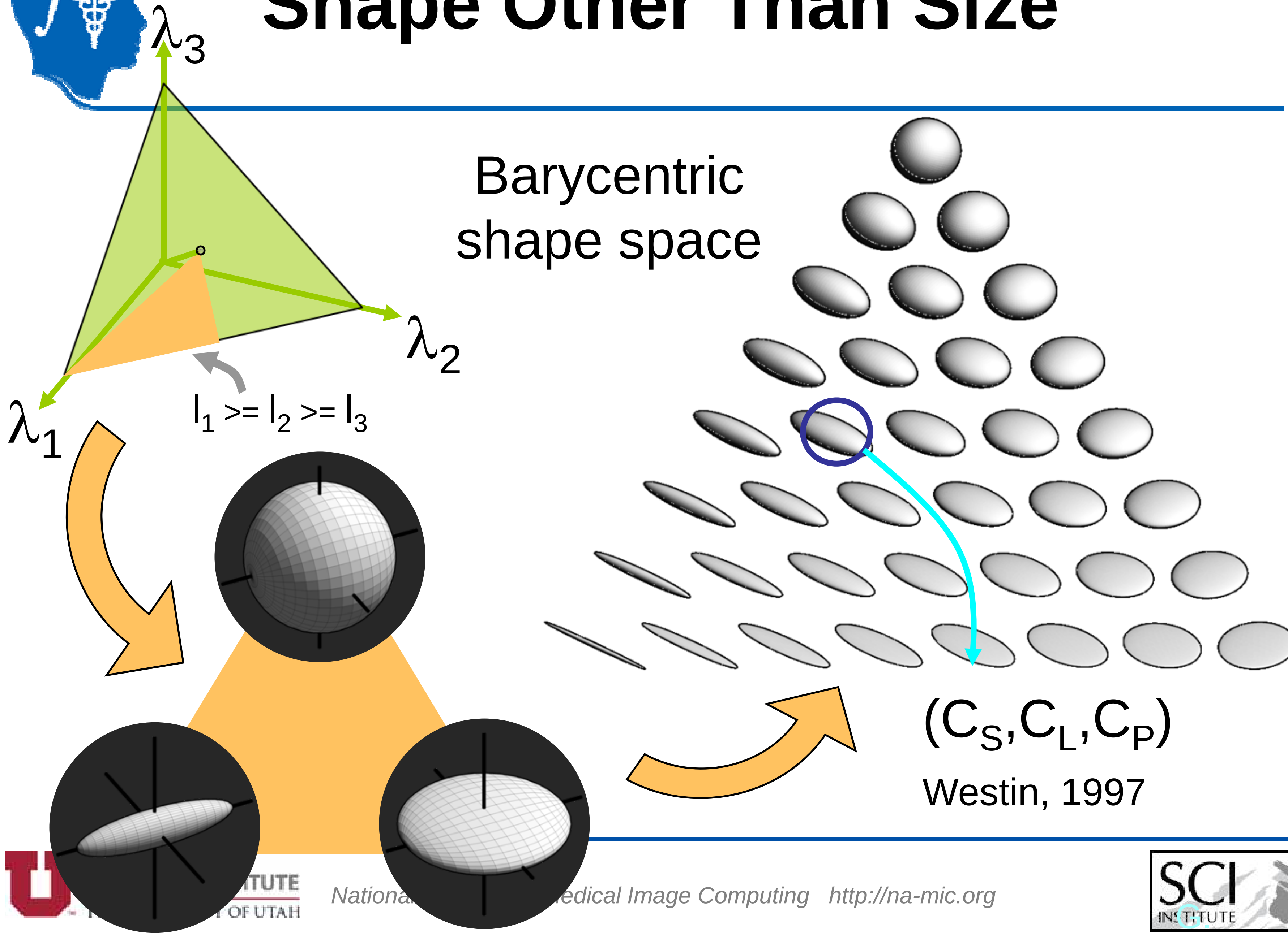
Generally used.
Also called:
“Mean diffusivity” <MD>
“Trace”

ADC versus Mean Diffusivity

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



Shape Other Than Size

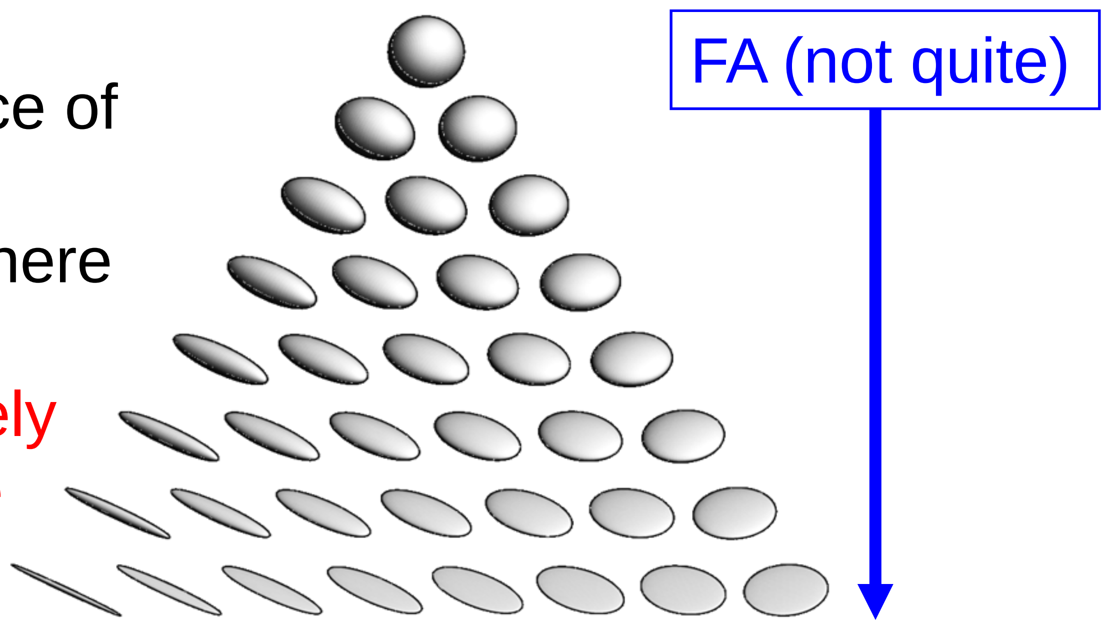


Reducing Shape to One Number
Fractional Anisotropy

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

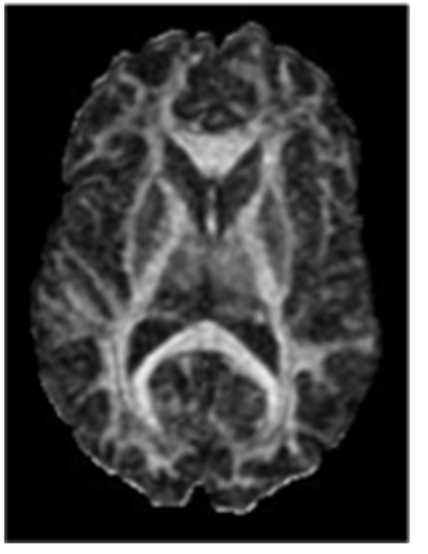
Properties:

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



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
  - Myelin

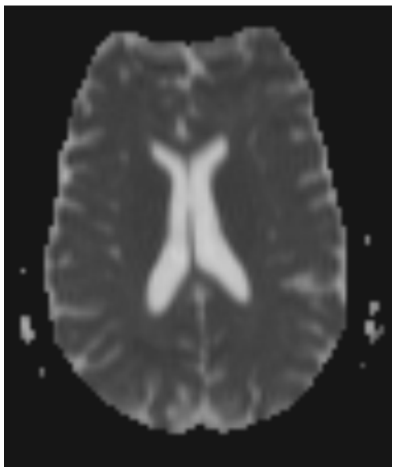


- <u>Big question</u>
  - What physiological/anatomical property does FA measure?

Tensor size (MD) and shape (FA)

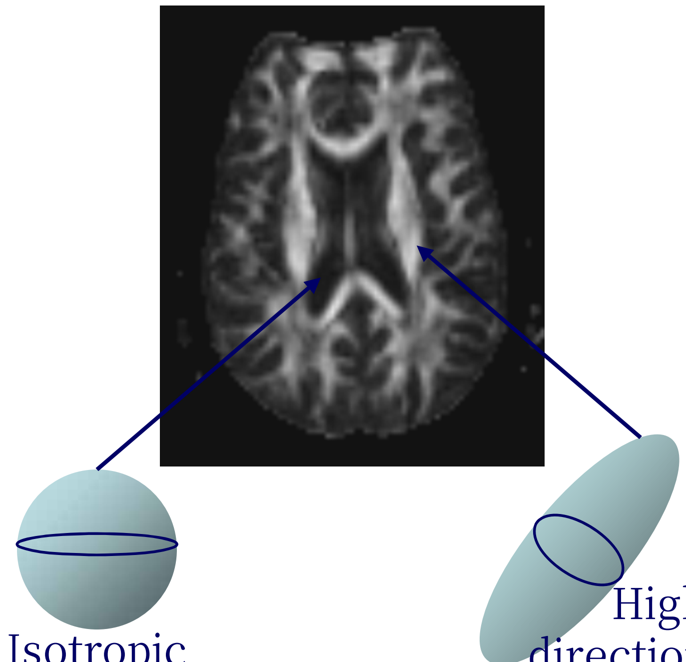
- Mean diffusivity (MD)

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



- Fractional anisotropy (FA)

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



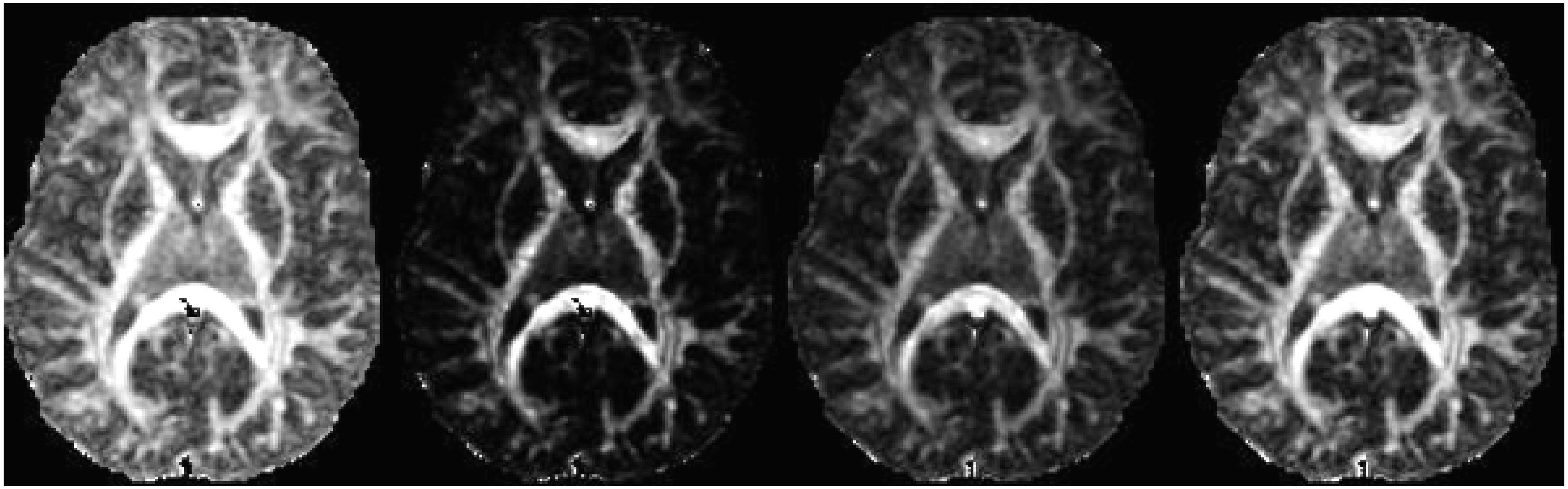
White matter → Cerebrospinal fluid

Low → High

0 → 1

Various Measures of Anisotropy

A_1 VF RA FA



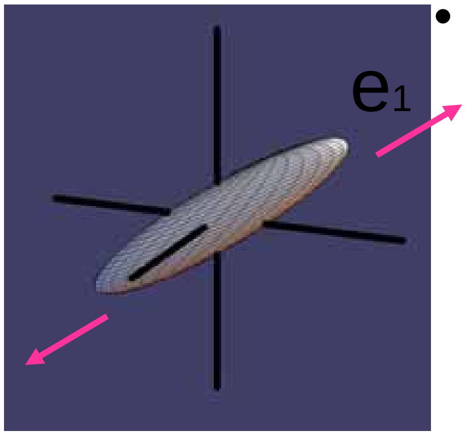
A. Alexander

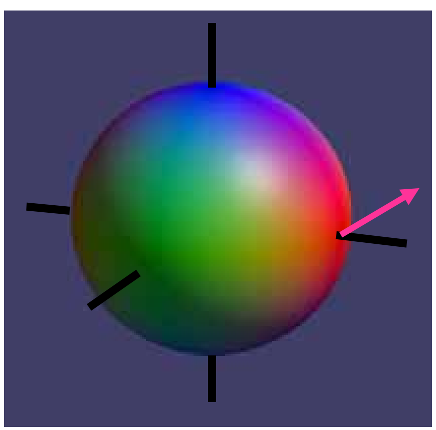
Visualizing Tensors: Direction and Shape

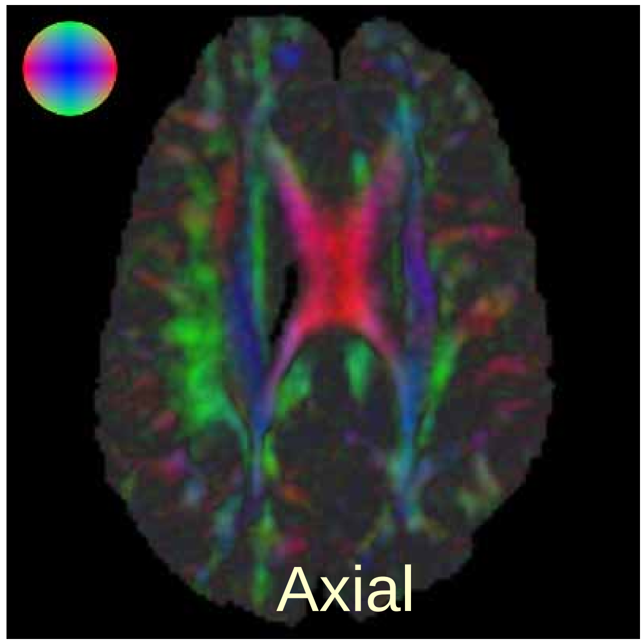
- Color mapping
- Glyphs

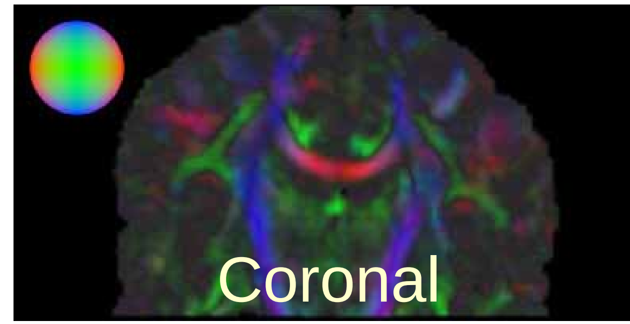
Coloring by Principal Diffusion Direction

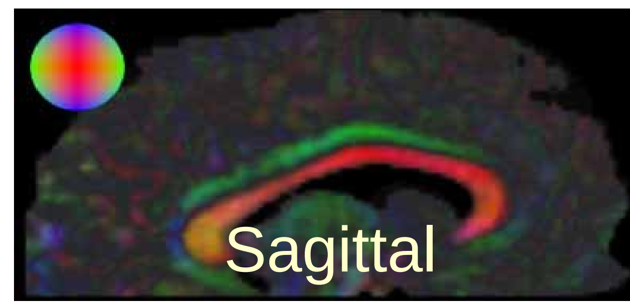
- Principal eigenvector, linear anisotropy determine color











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

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

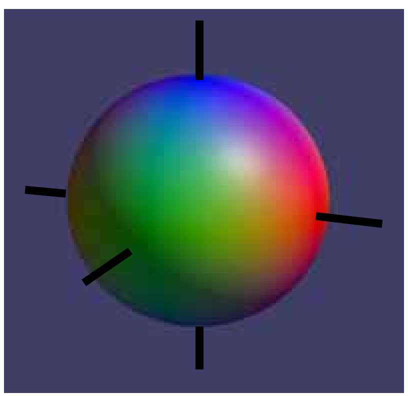
$B = | \mathbf{e}_1 \cdot z |$

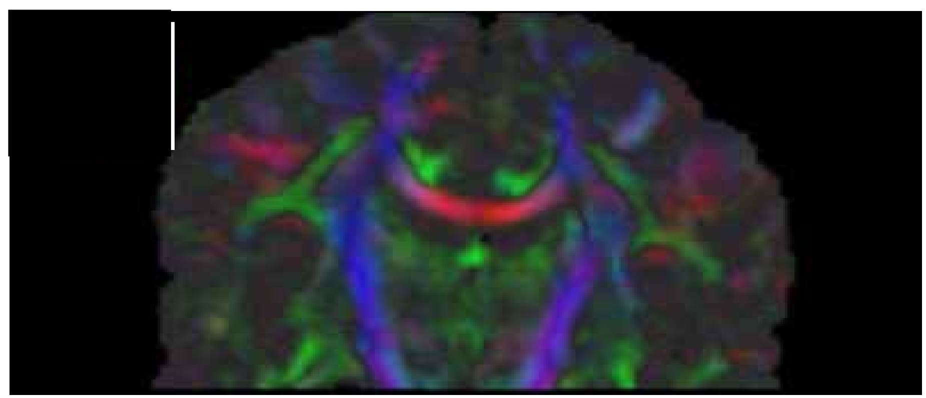
Pierpaoli, 1997

Slide G. Kindlmann

Issues With Coloring by Direction

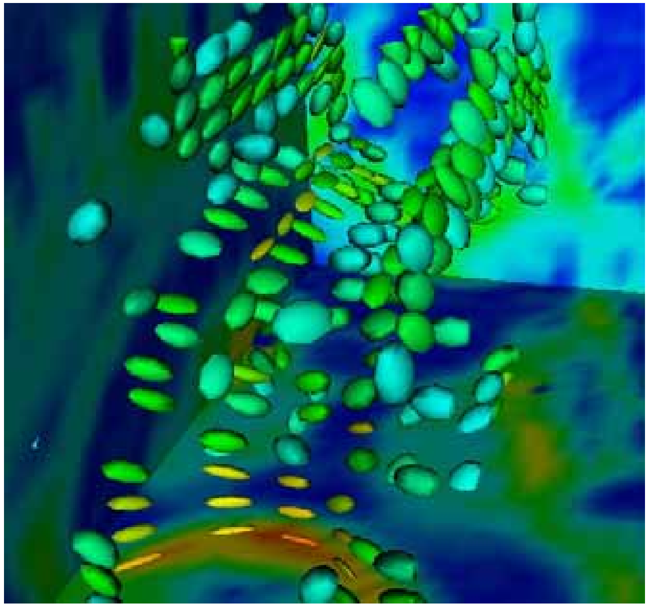
- Set transparency according to FA (highlight-tracts)
- Coordinate system dependent
- Primary colors dominate
  - Perception: saturated colors tend to look more intense
  - Which direction is “cyan”?
  - Coloring is not unique

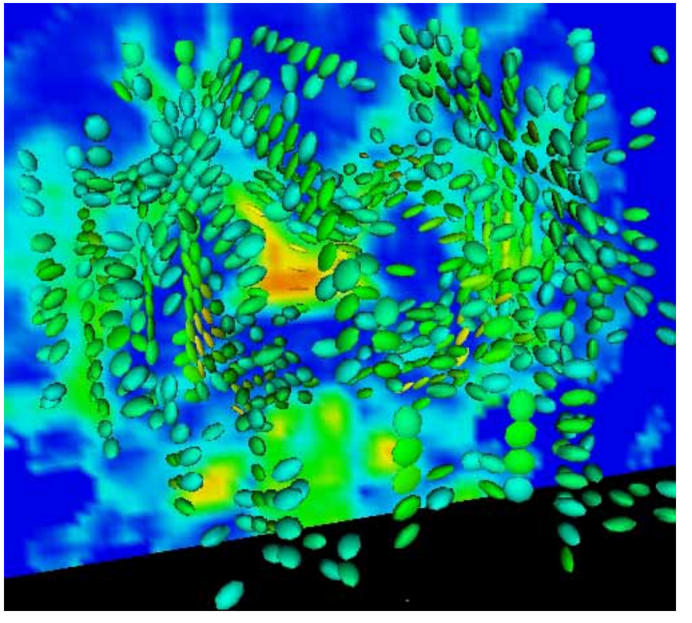




Visualization with Glyphs

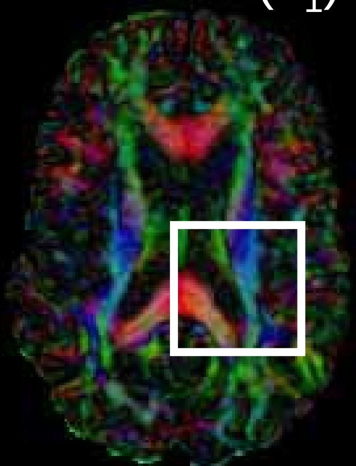
- Density and placement based on FA or detected features
- Place ellipsoids on regular grid



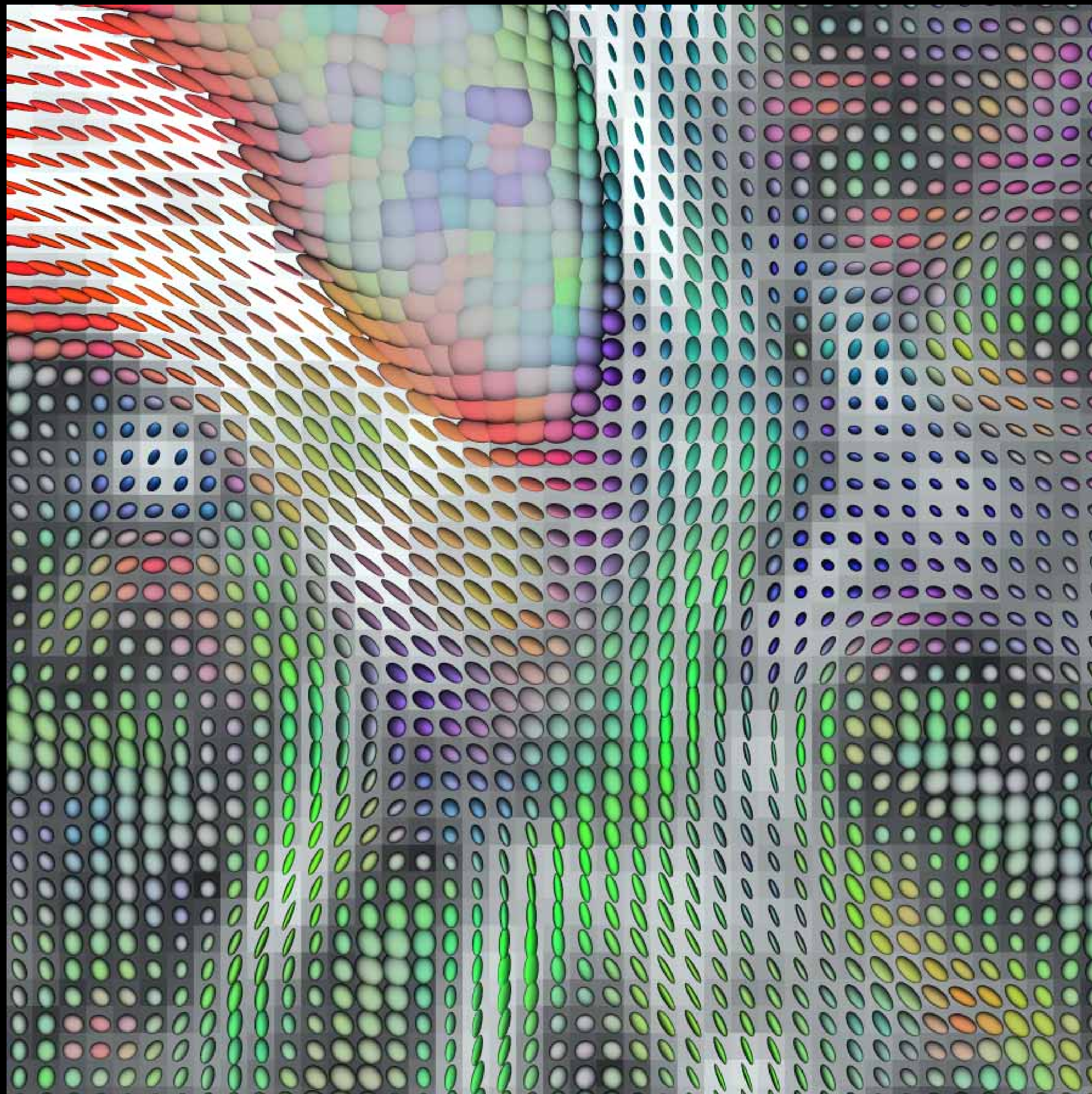


Backdrop: FA

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

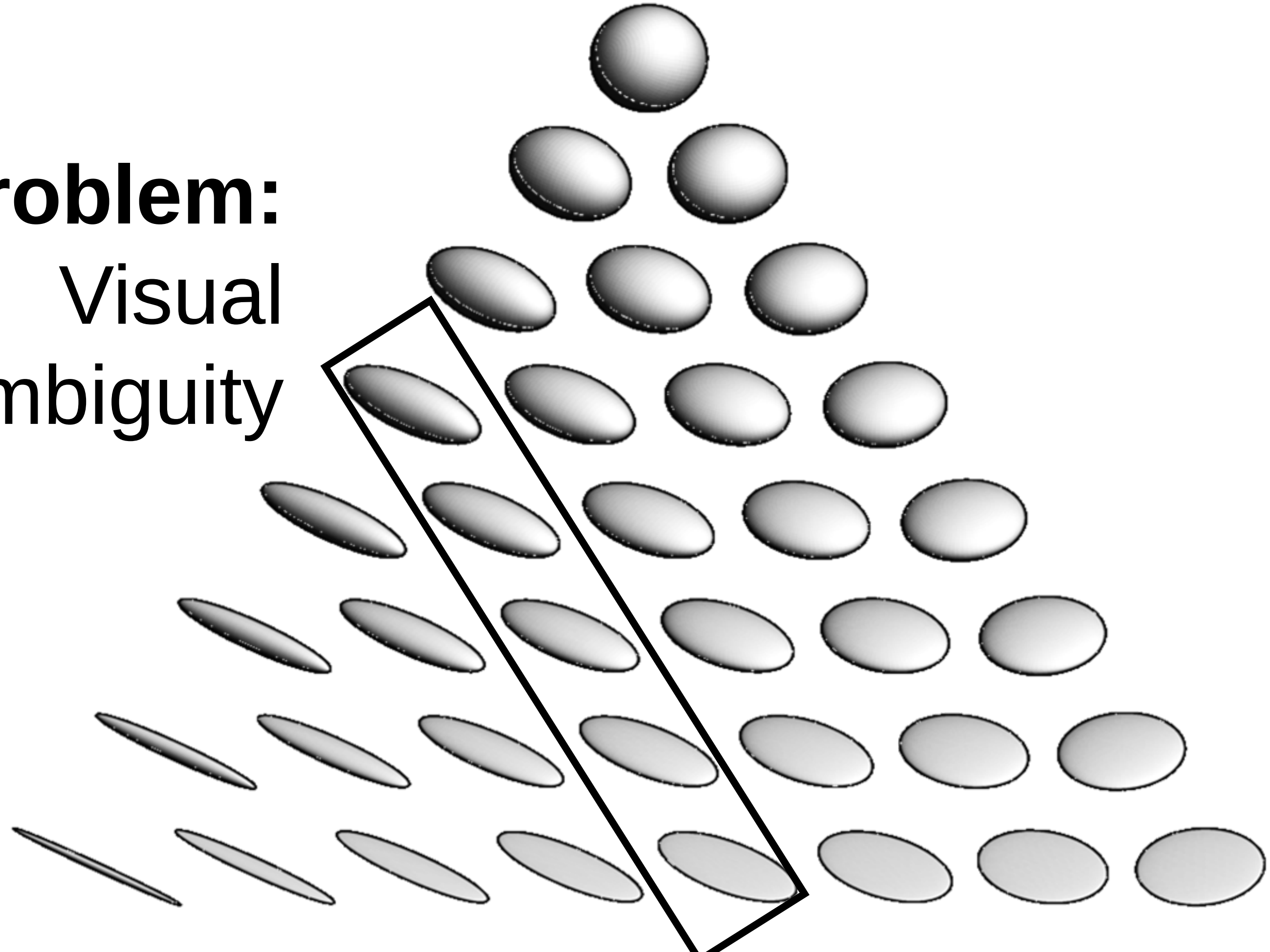


G. Kindlmann



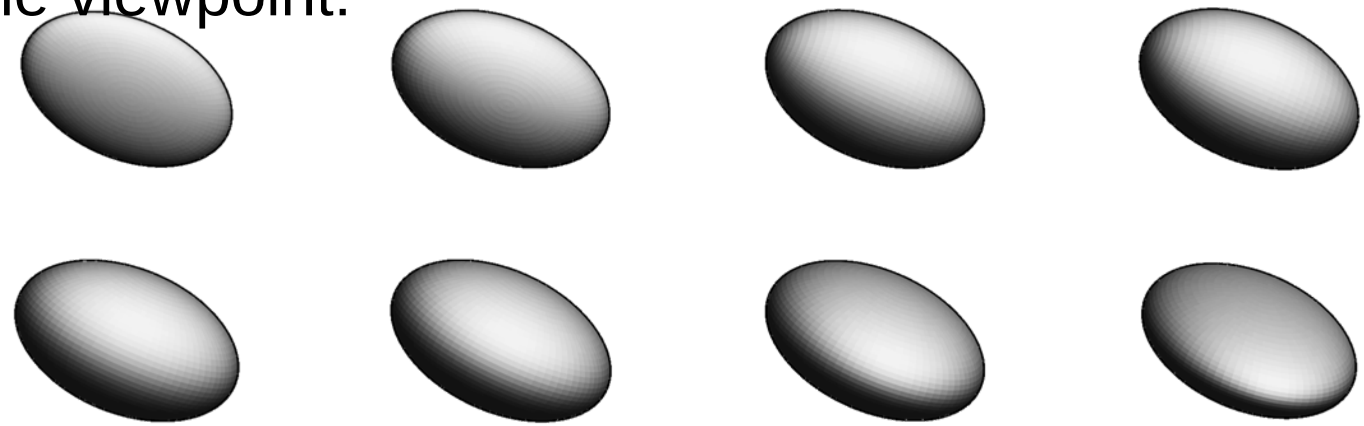
Glyphs: ellipsoids

Problem:
Visual ambiguity

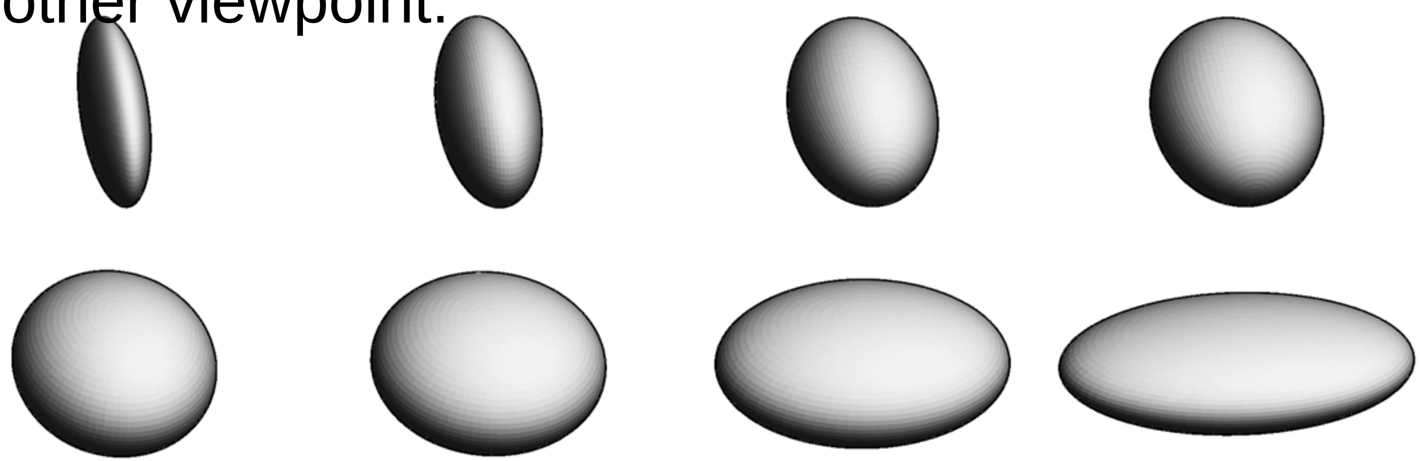


Worst case scenario: ellipsoids

one viewpoint:

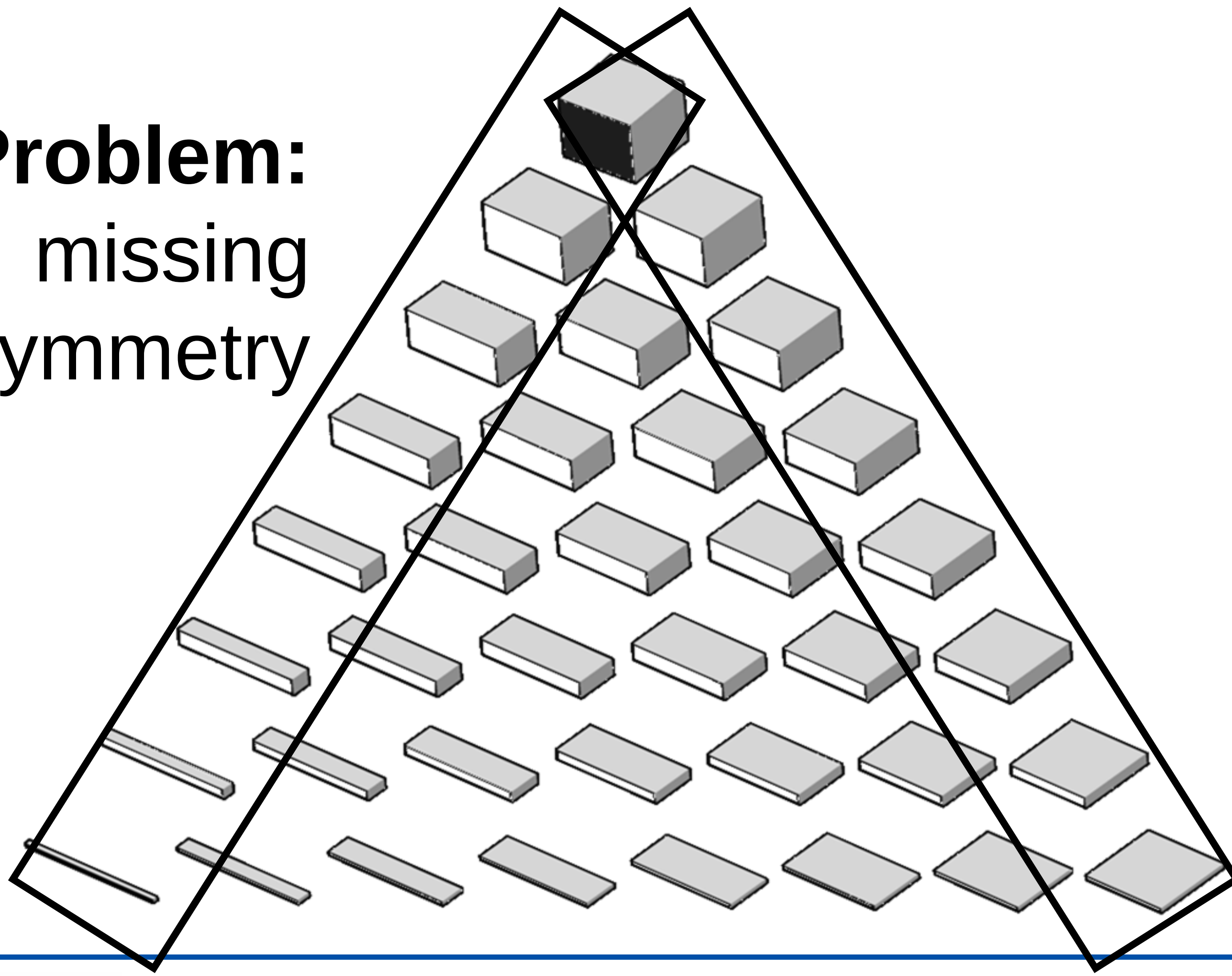


another viewpoint:



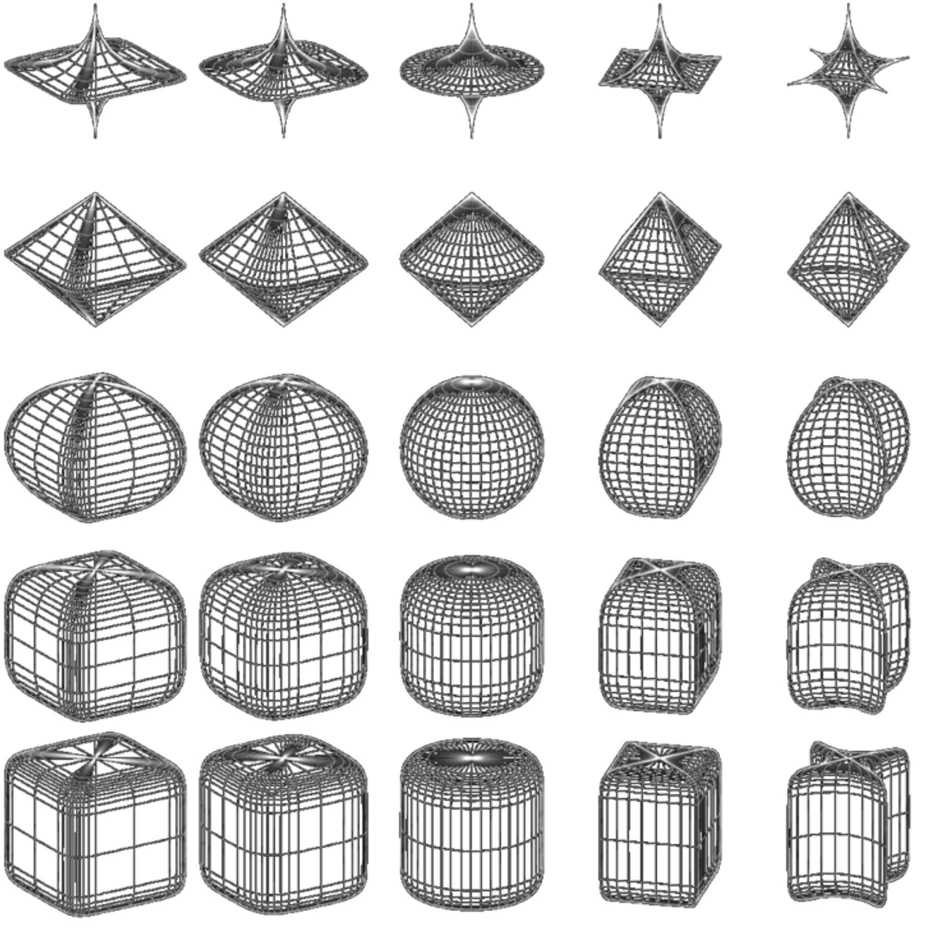
Glyphs: cuboids

Problem:
missing
symmetry

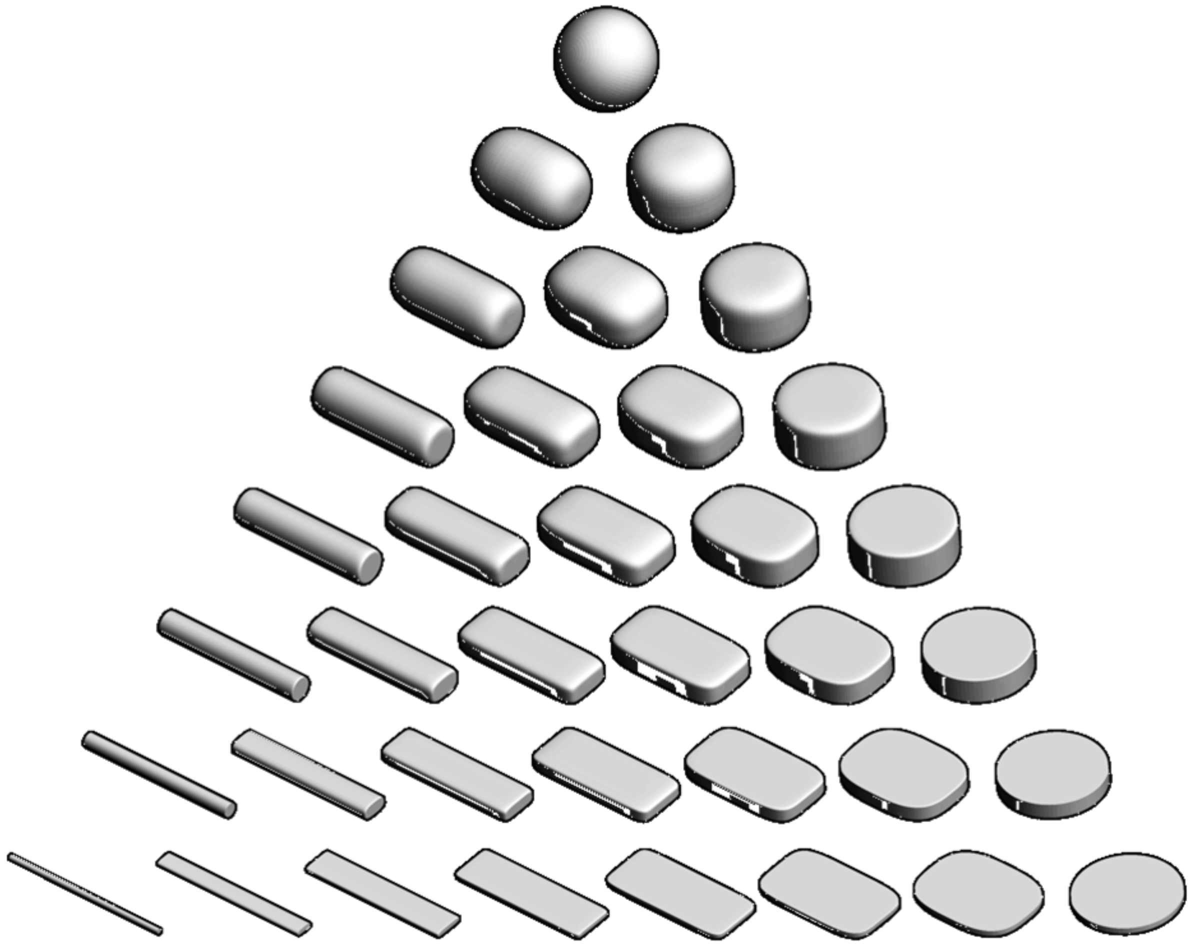


Superquadrics

Barr 1981



Superquadric Glyphs for Visualizing DTI
Kindlmann 2004



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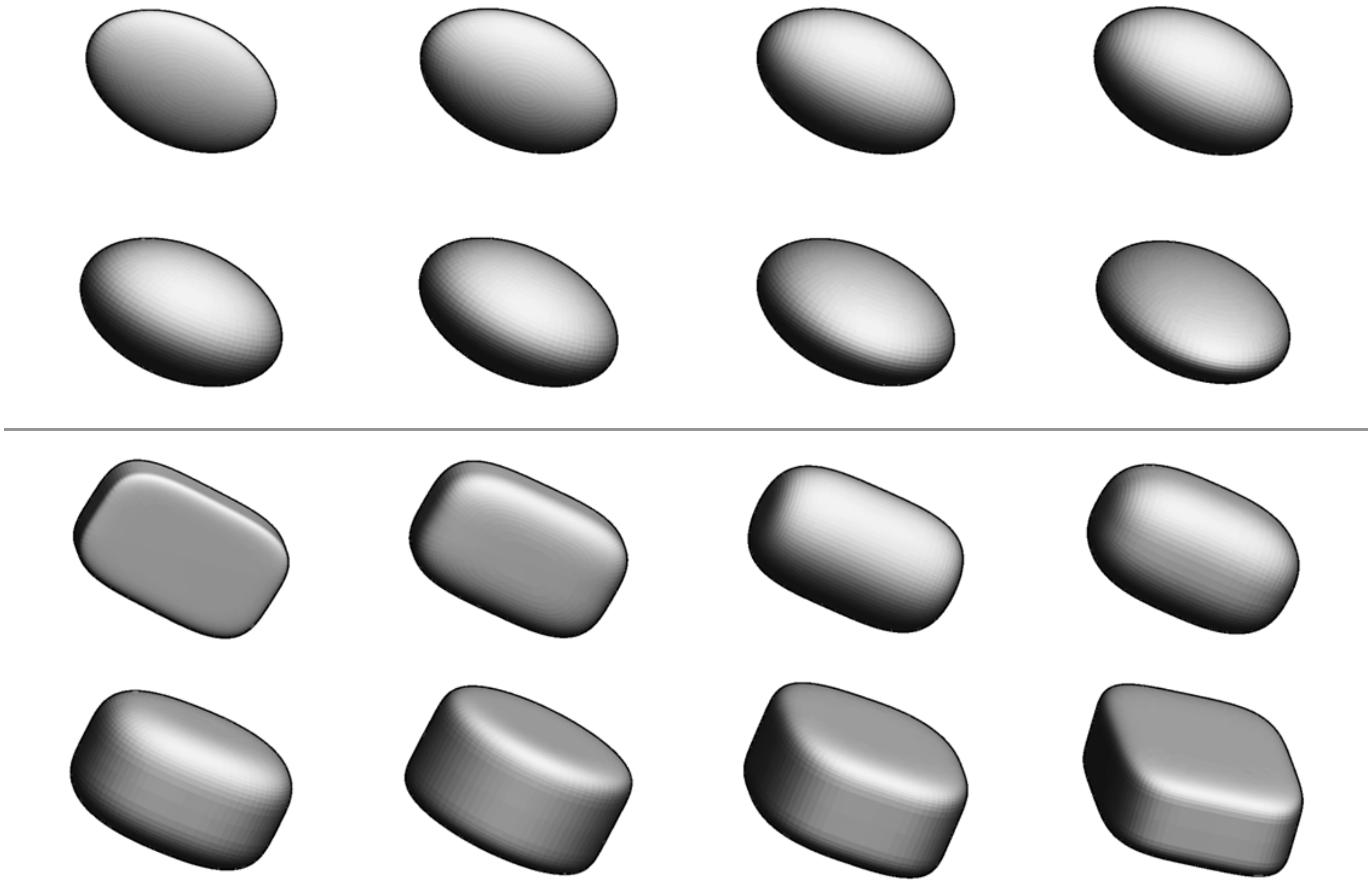
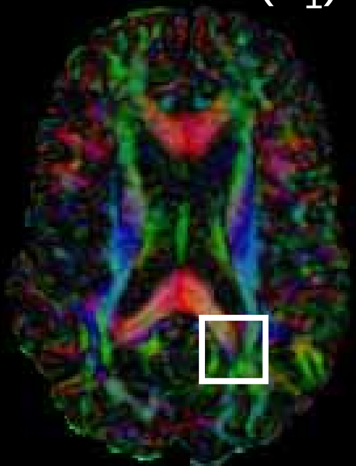
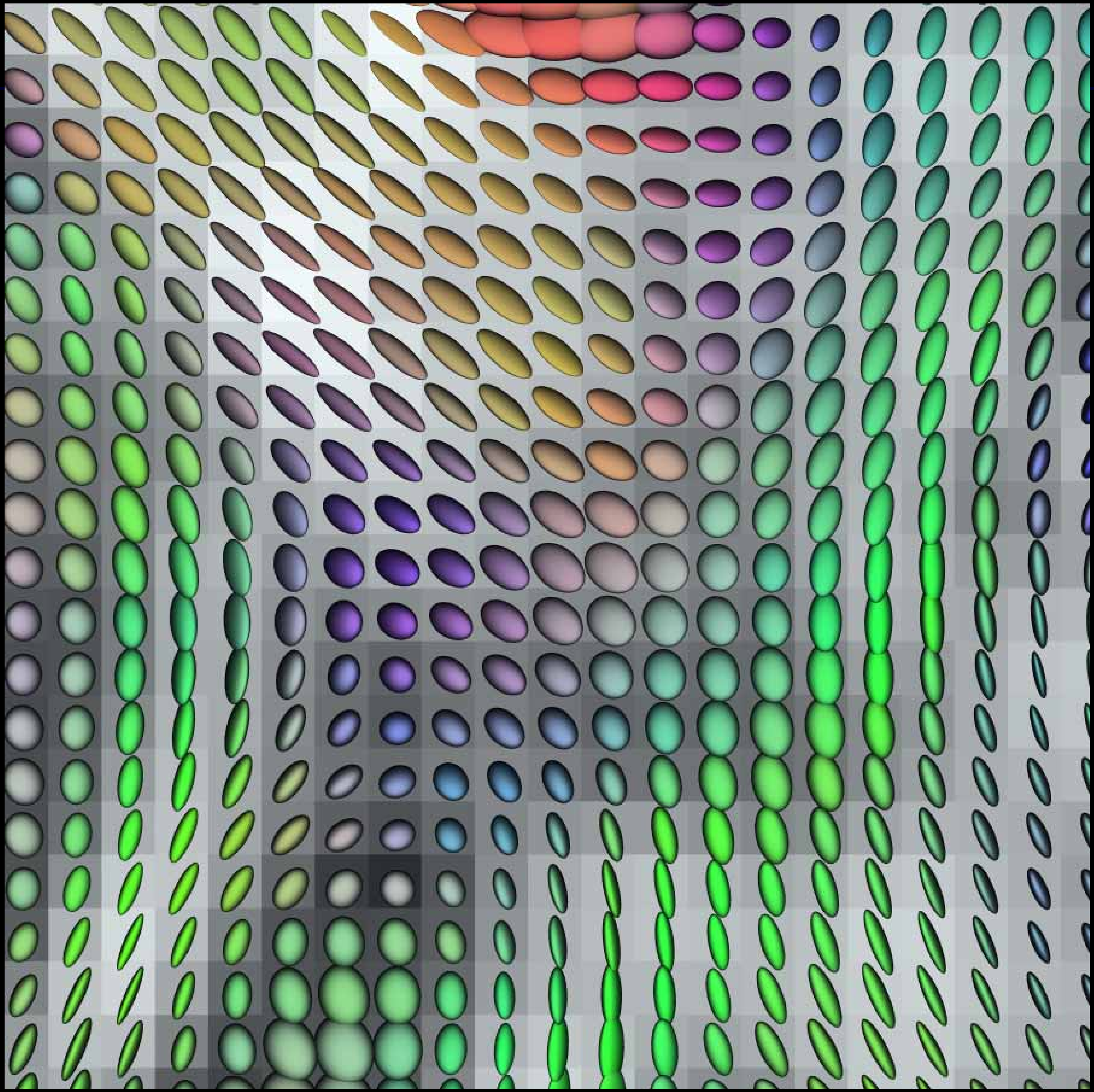
Worst case scenario, revisited



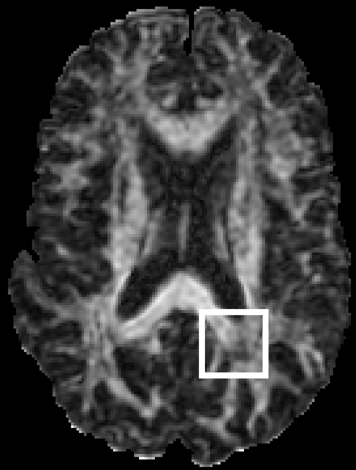
Backdrop: FA

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

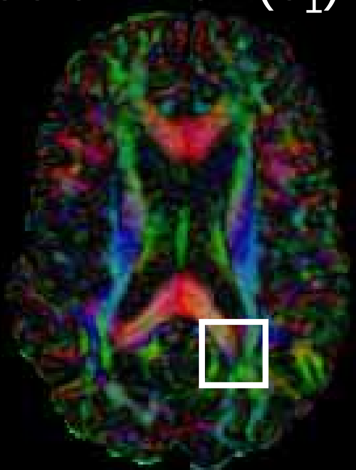


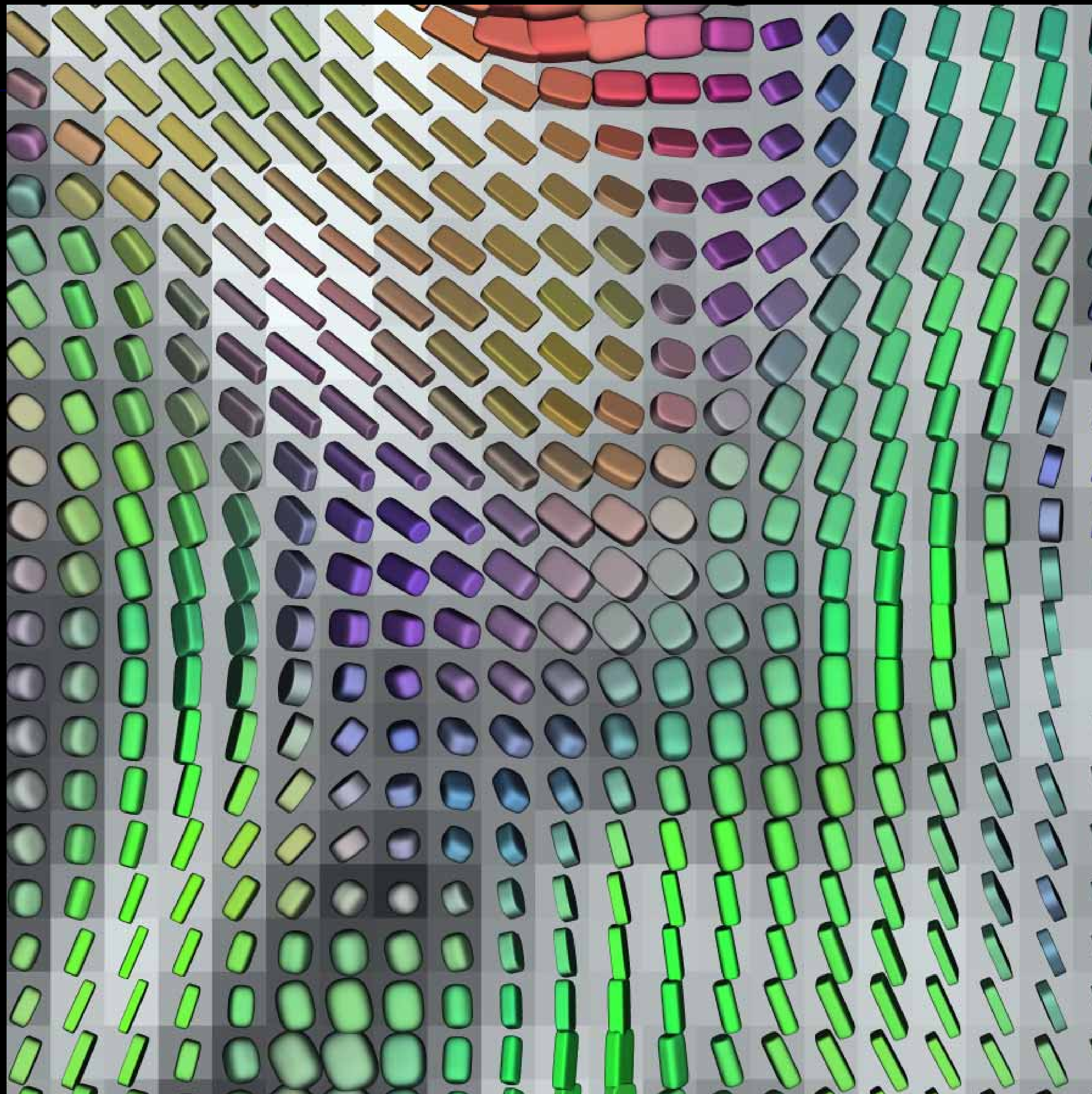


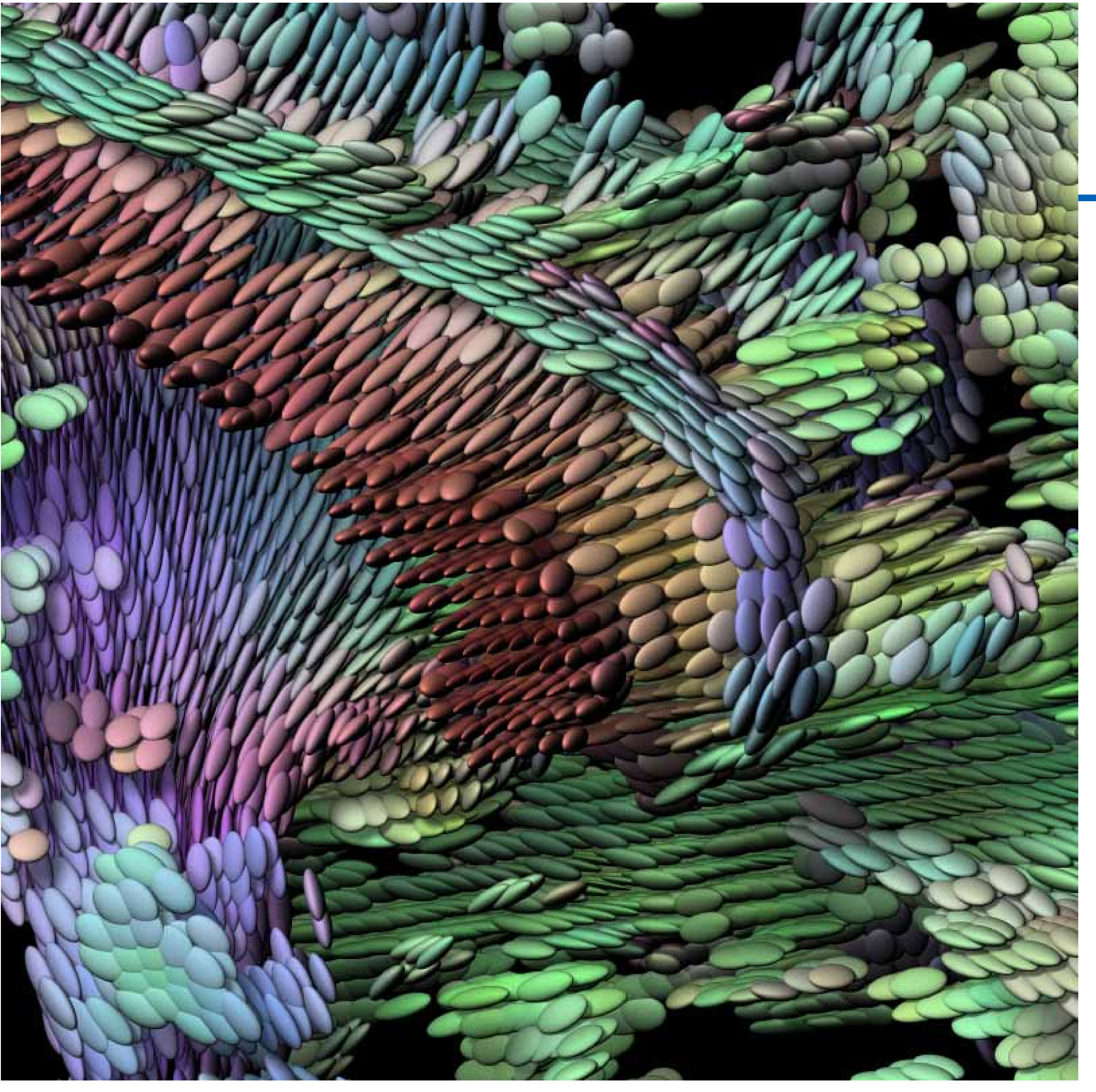
Backdrop: FA

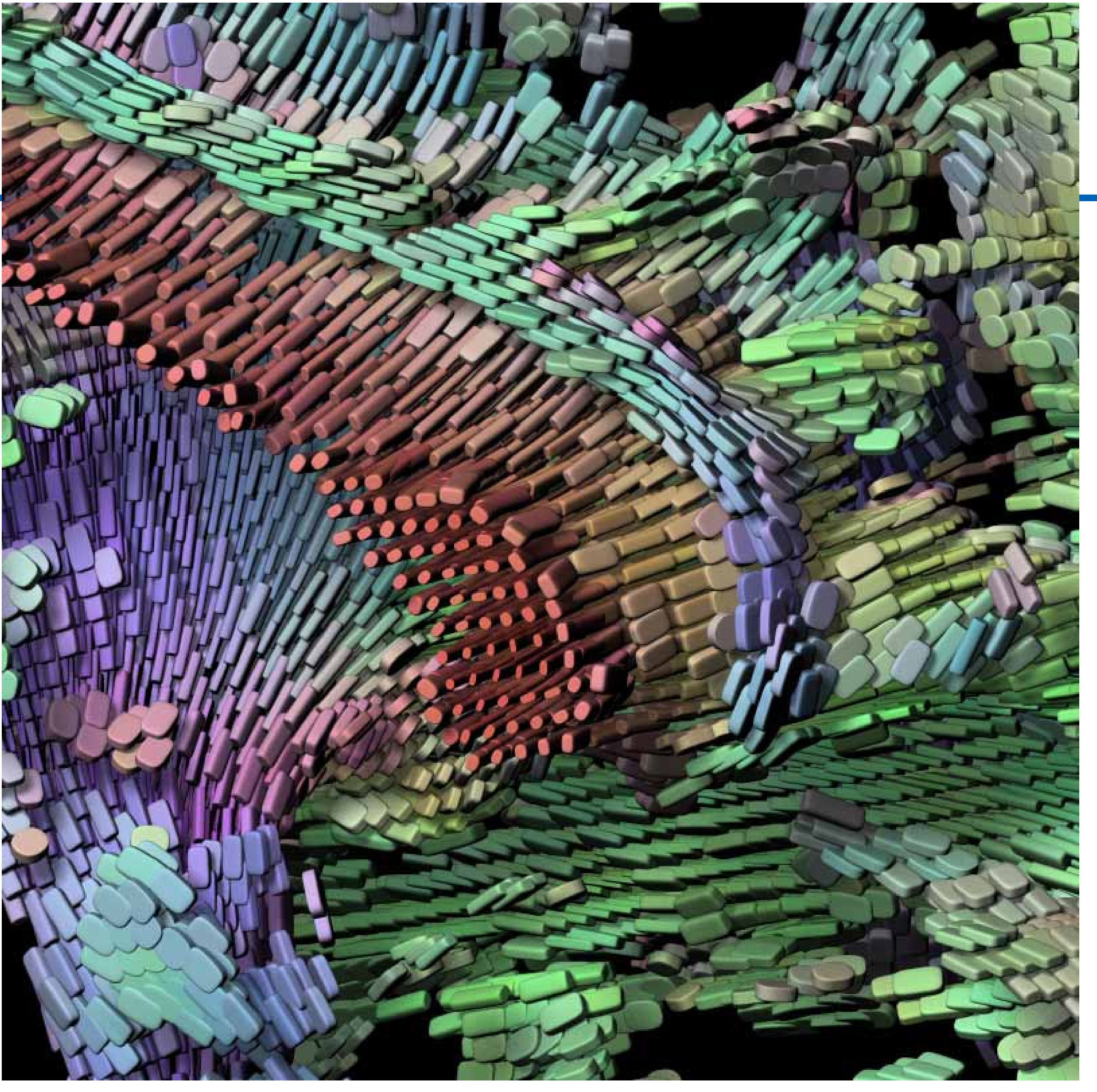


Color: RGB($\mathbf{e}_1$)



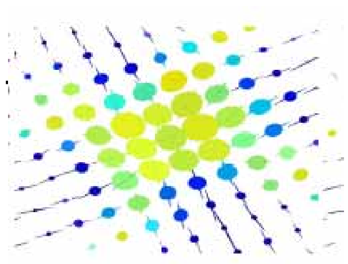




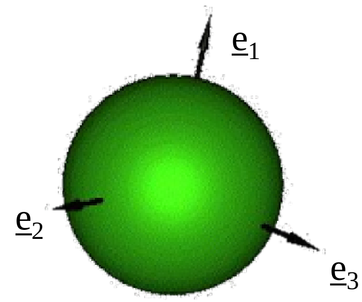


Why do we care?

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

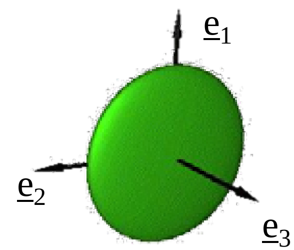


- Large tracts can be locally modeled by single tensors.



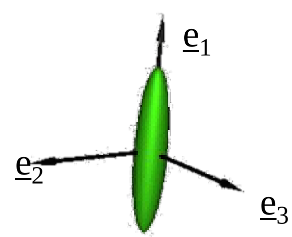
$\lambda_1 \approx \lambda_2 \approx \lambda_3$ - Isotropic

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.

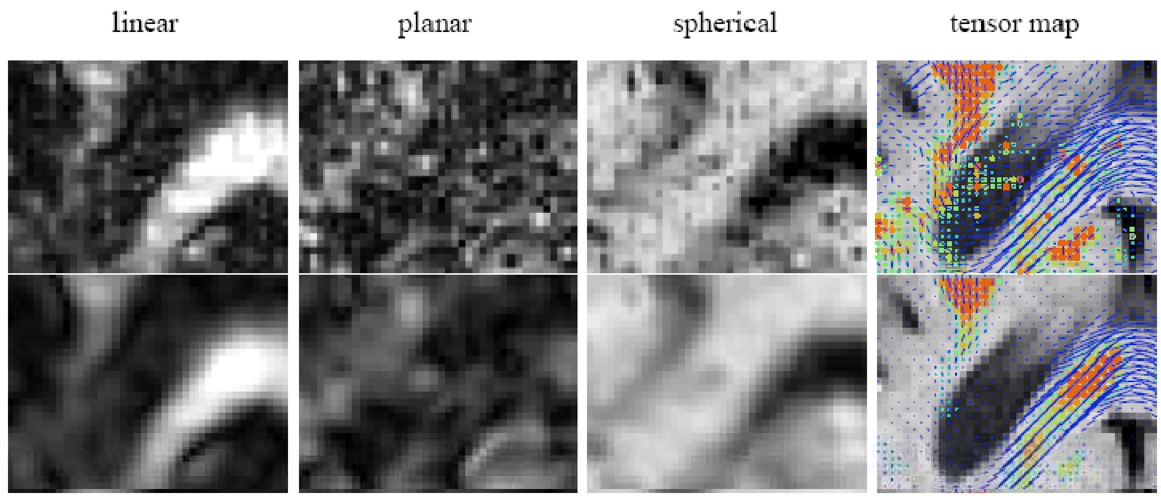
Shape Characterization: Westin

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

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

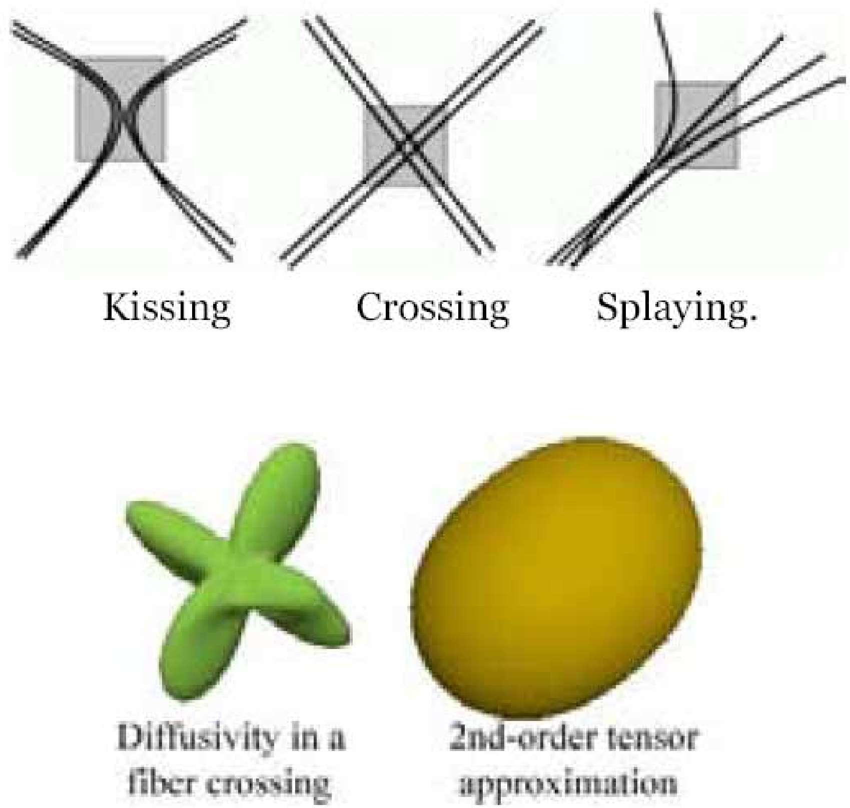
$$c_s = \frac{\lambda_3}{\lambda_1}$$

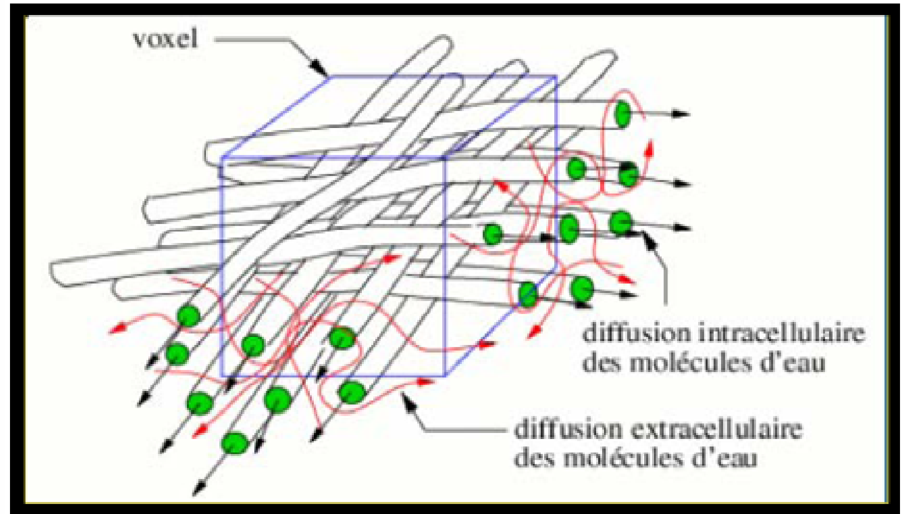
$$c_l + c_p + c_s = 1$$



Westin et al., MICCAI'99

Limitations of the Diffusion Tensor Model

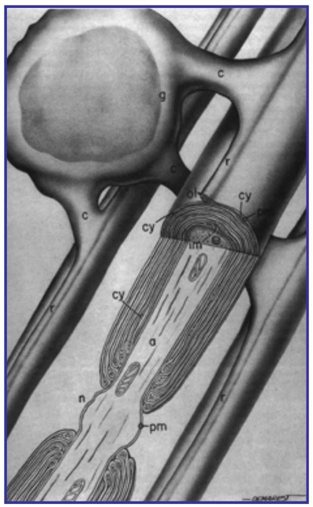


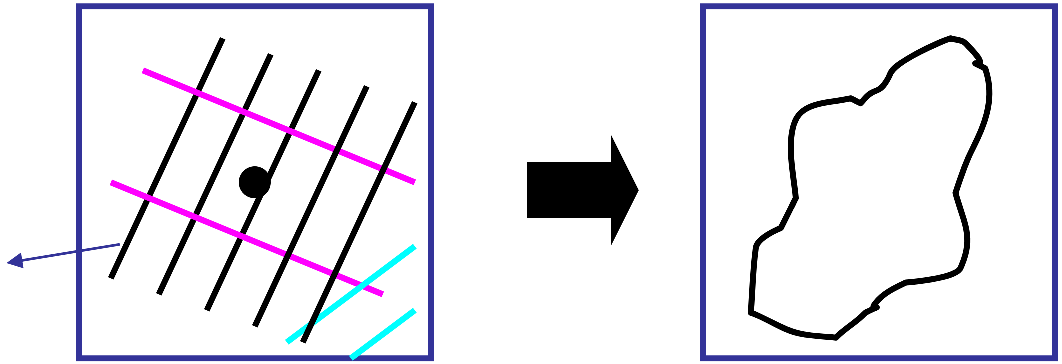


DTI fails when fiber bundles crosses within the same voxel
Non-Gaussian diffusion process - Image from [Poupon-PhD:99]

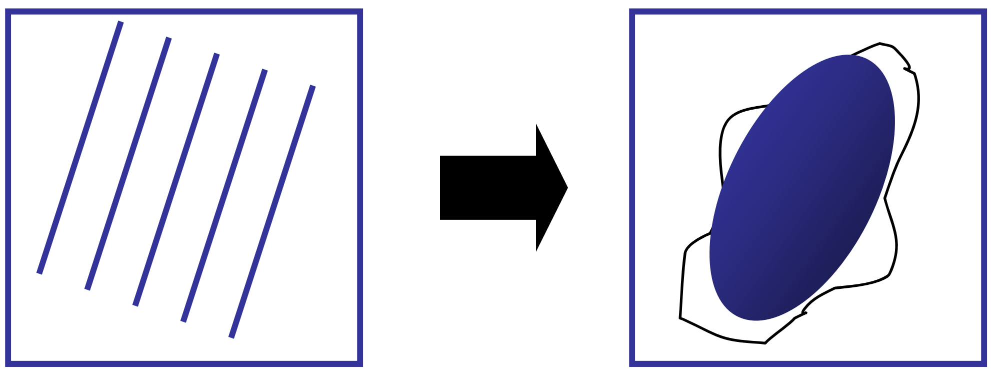
Courtesy B. Vemuri, MICCAI 2008 workshop

Simplification and assumption





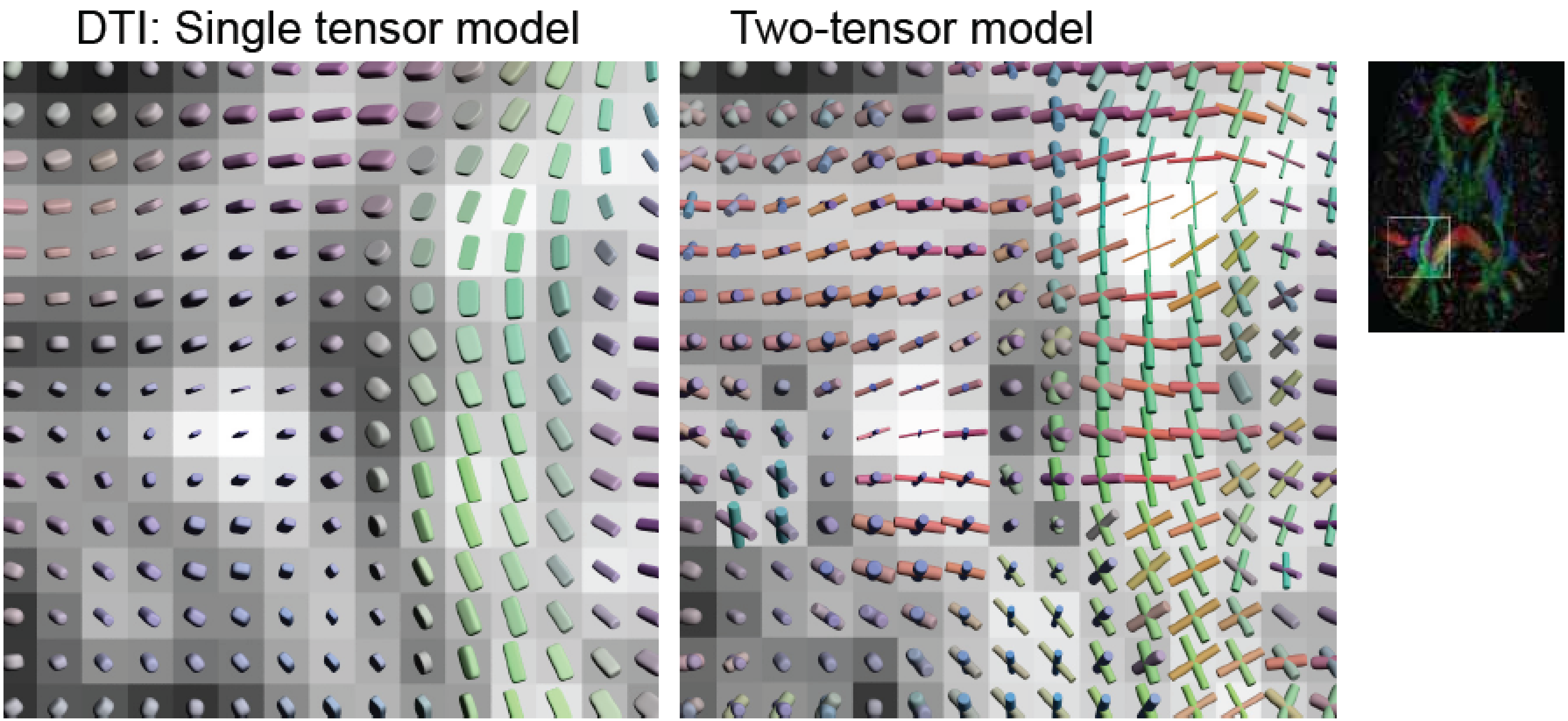
Orientational Diffusion Fct



Diffusion ellipsoid

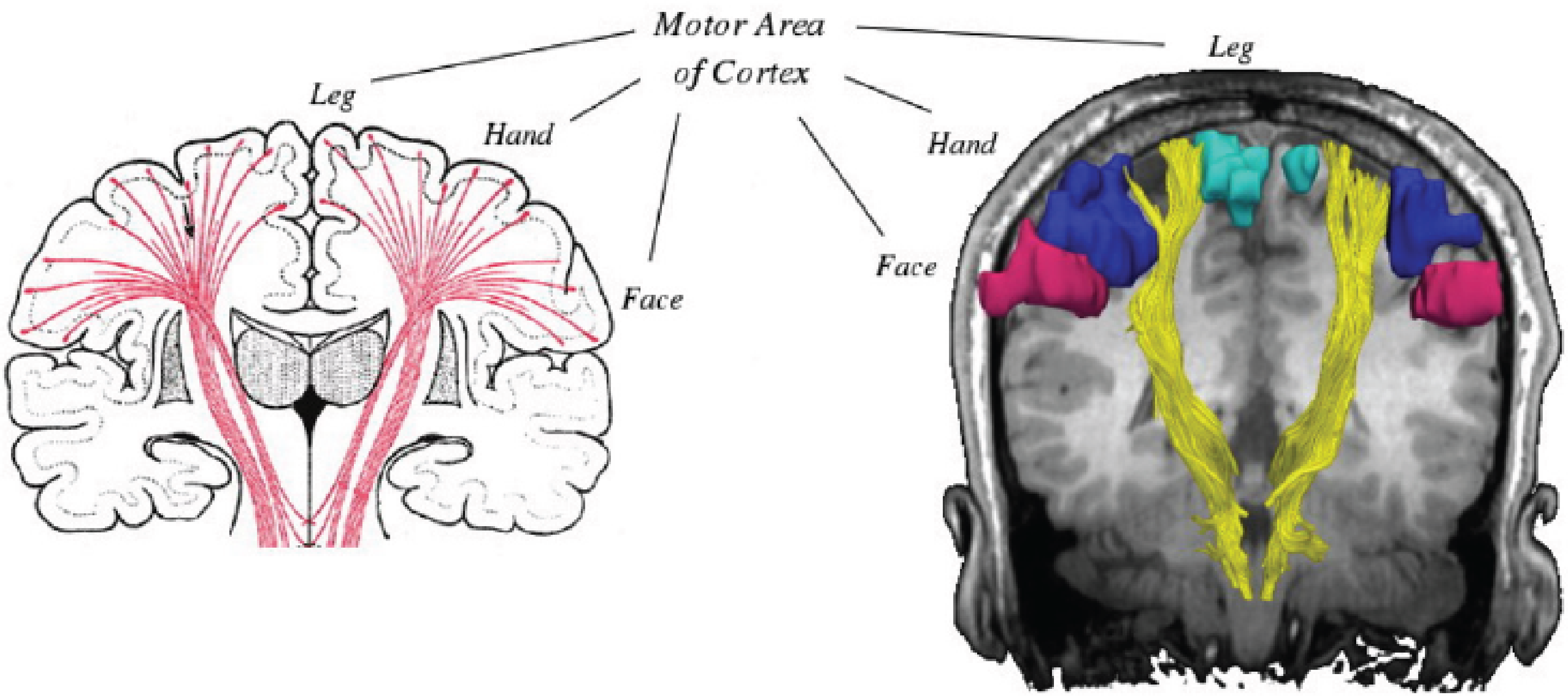
Courtesy of Susumu Mori, JHU

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



Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Tractography Corticospinal Tract

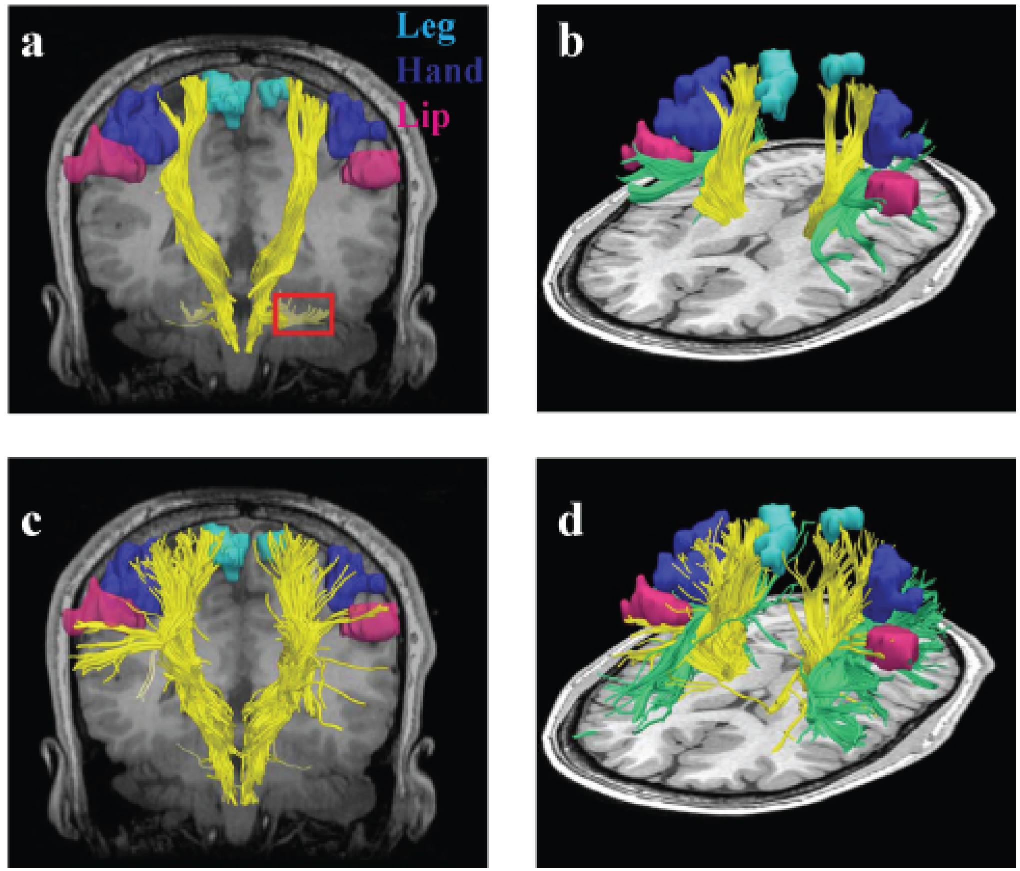


Provided by L O'Donnell

Results Two-Tensor Tractography

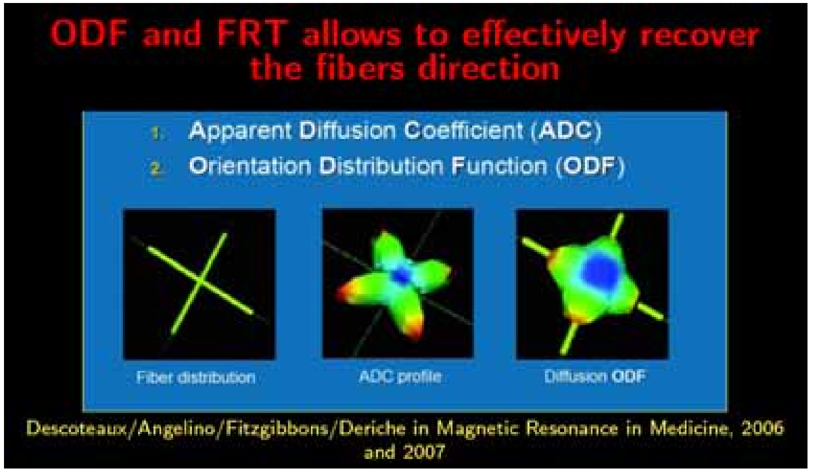
Single tensor model

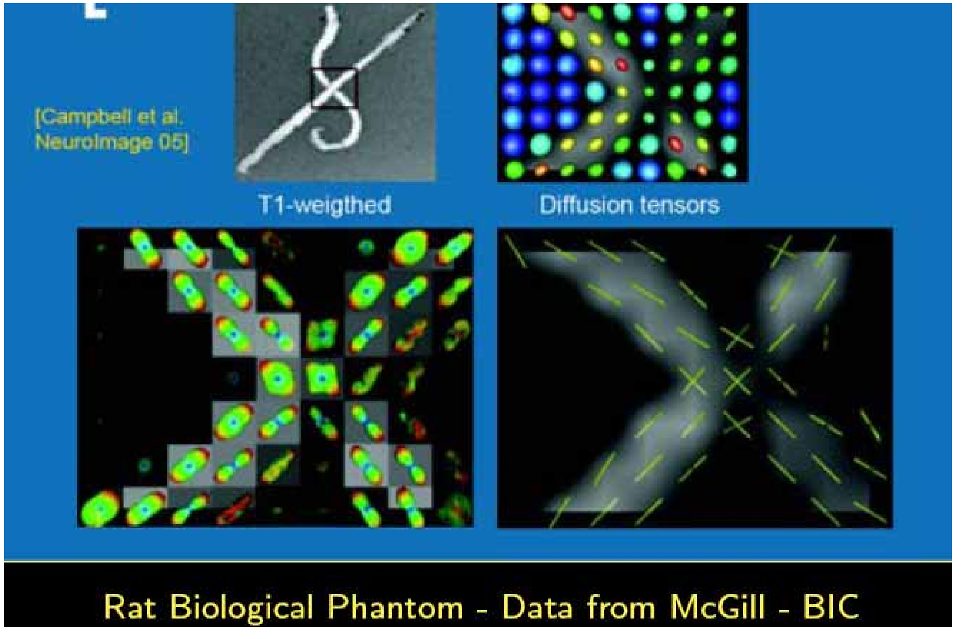
Two-tensor model



A Qazi, A Radmanesh, L O'Donnell, G Kindlmann, S Peled, S Whalen, C-F Westin, A J Golby. Resolving crossings in the corticospinal tract by two-tensor streamline tractography: method and clinical assessment using fMRI. NeuroImage 2008

Orientation Distribution Function ODF

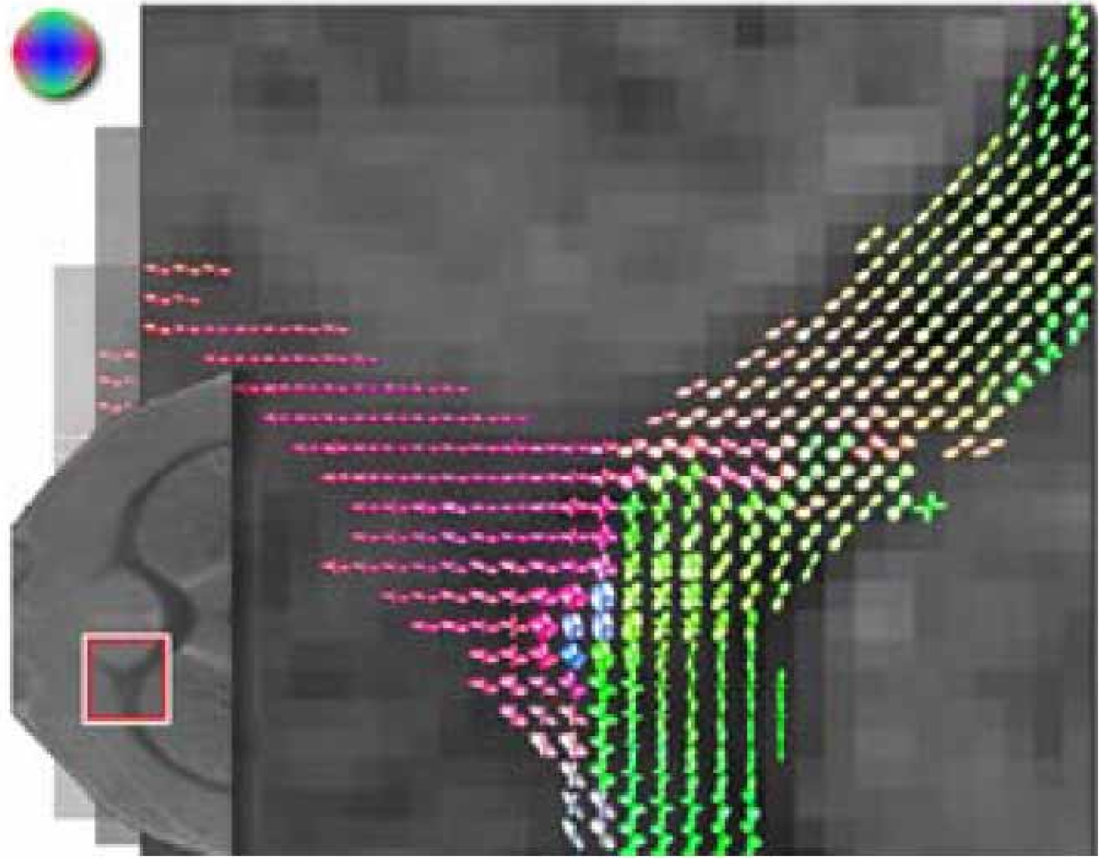




Courtesy Rachid Deriche, MICCAI 2008 workshop

Higher Order Tensor can capture fiber crossing geometry

- Excised full rat brain
- S_0 + HARDI (32 dir., B-value=1250 s/mm^2)
- Data provided by Drs Carney and Mareci

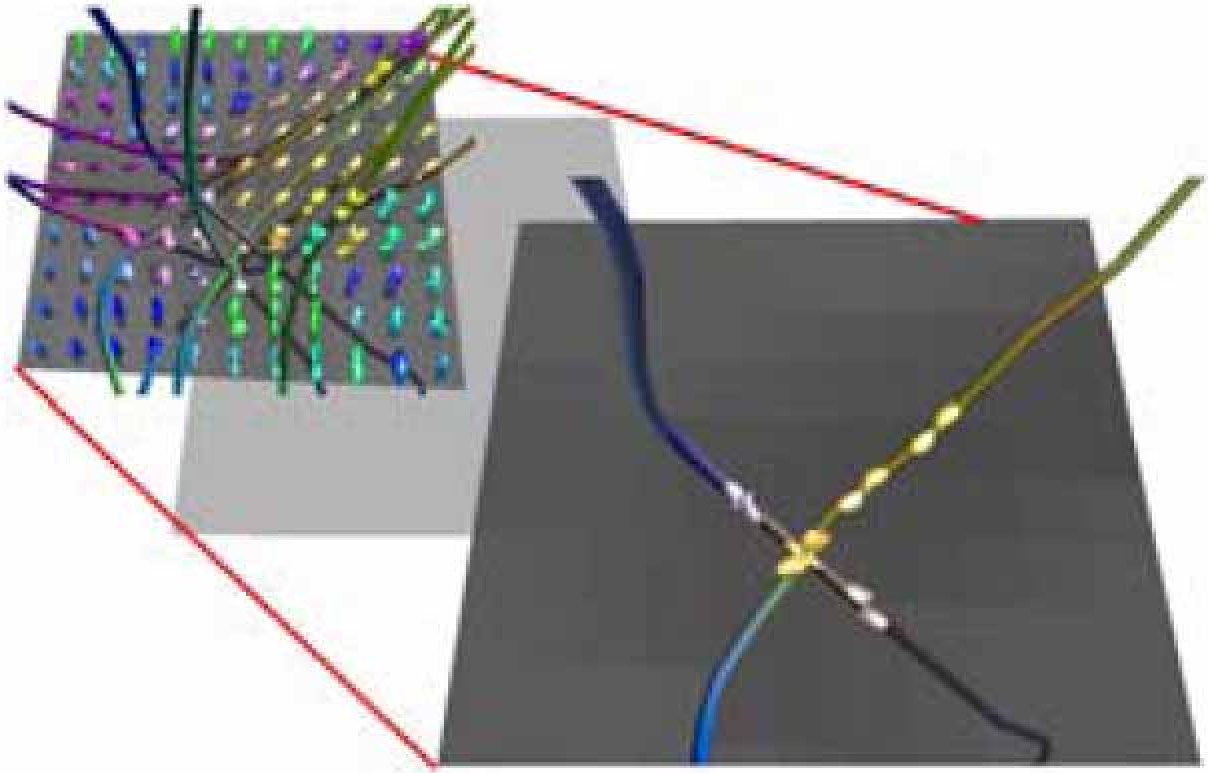


Junction of CC and singulum

Courtesy Baba Vemuri, MICCAI 2008 workshop

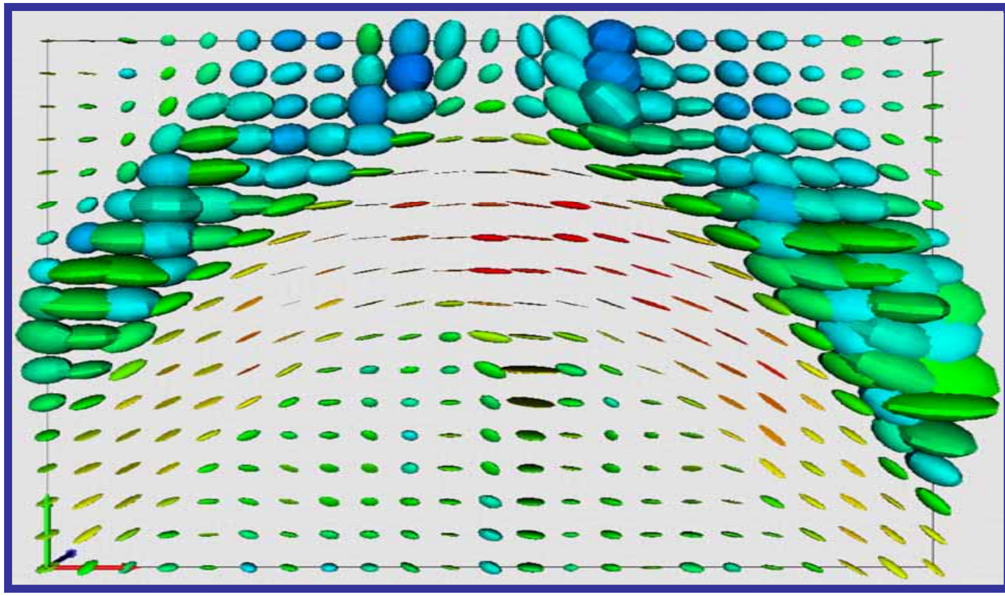
Higher Order Tensor can capture fiber crossing geometry

- Excised full rat brain
- S_0 + HARDI (32 dir., B-value=1250 s/mm^2)
- Data provided by Drs Carney and Mareci



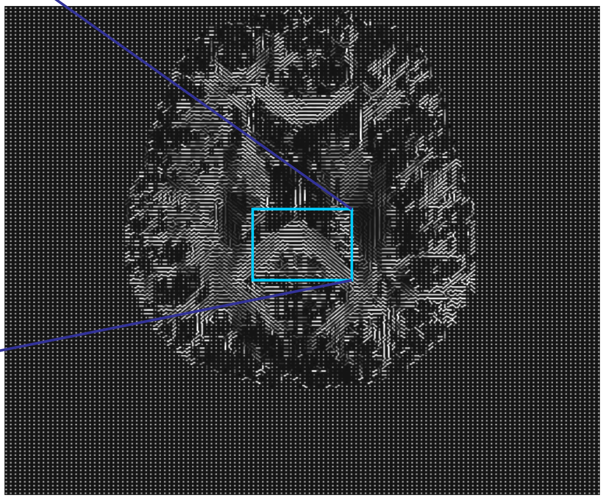
Courtesy Baba Vemuri, MICCAI 2008 workshop

Spatial Transformations of Diffusion Tensors



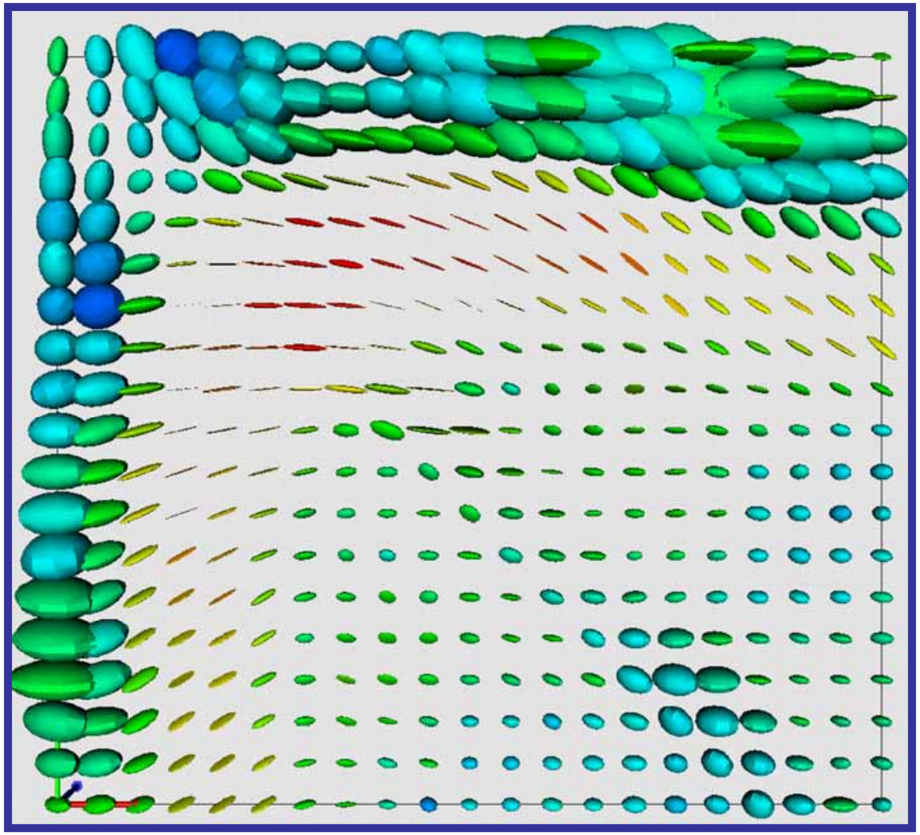
Warmer colors indicate higher anisotropy

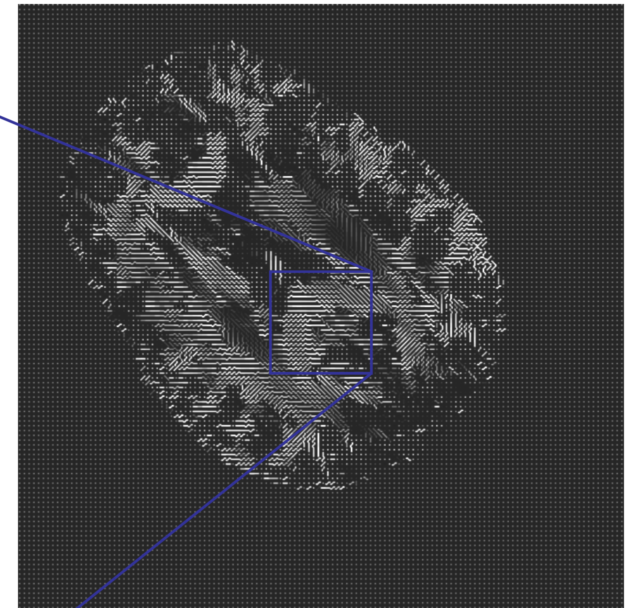
Principal diffusion directions in anisotropic regions of a DT-MR image slice



James Gee, Department of Radiology
University of Pennsylvania

Rotation without DT Reorientation



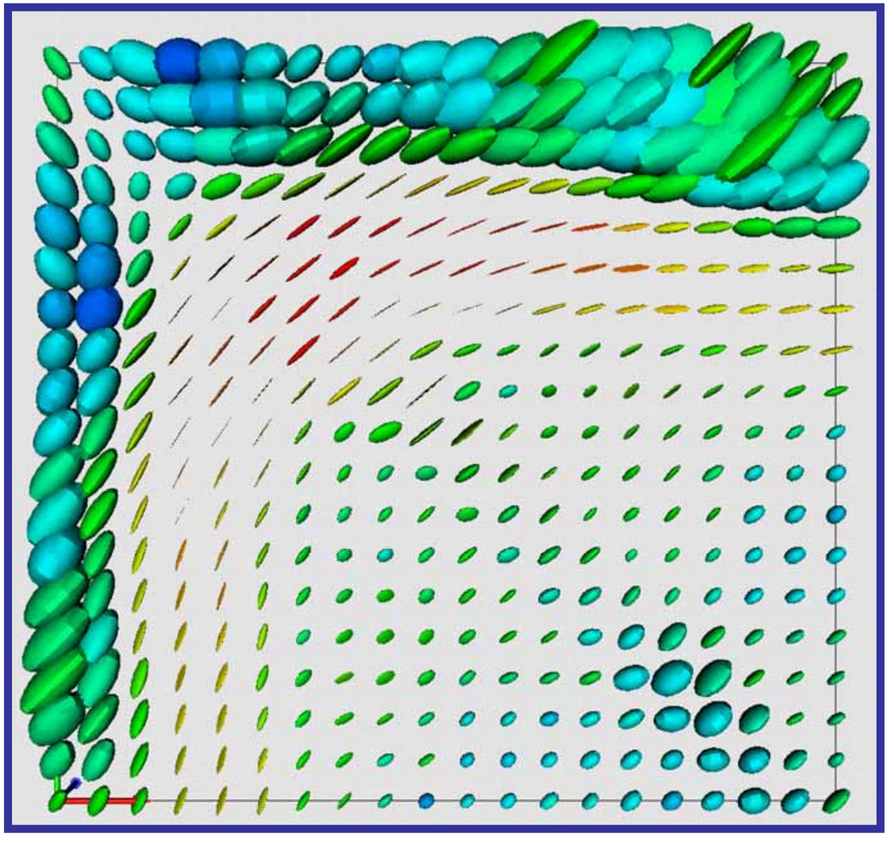


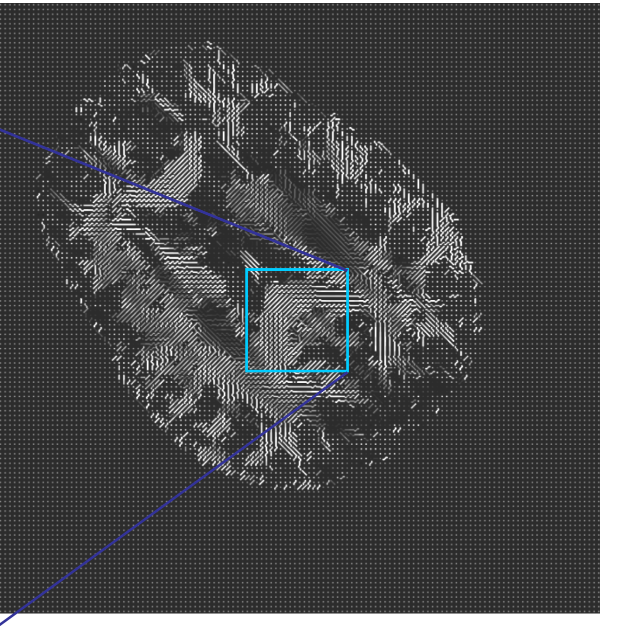
– Directional structure is lost.

– DTs orientations are no longer consistent with the anatomical structure of the image.

James Gee, Department of Radiology
University of Pennsylvania

Rotation with DT Reorientation



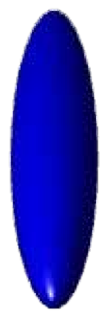


- $D \rightarrow R \cdot D \cdot R^T$.
- Directional structure preserved.
- DTs orientations remain consistent with the anatomy.

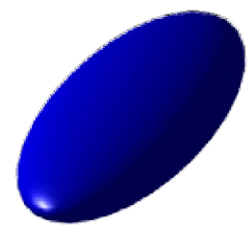
James Gee, Department of Radiology
University of Pennsylvania

Affine Tensor Transformations
(*Alexander et al, MICCAI 1999*)

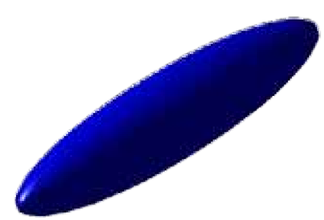
Original Tensor



Transformed Tensor



$D \rightarrow F \cdot D \cdot F^{T}$



$D \rightarrow R \cdot D \cdot R^{T}$

- For an affine transformation, , $D \rightarrow F \cdot D \cdot F^{T}$?
- No...

- We wish to preserve the shape of the DTs.
- But we must reorient them appropriately.
- Require R that reflects reorientation due to F.

Finite Strain Estimation

- Decompose F into:
  - Rigid rotation, R, and
  - Deformation, U:

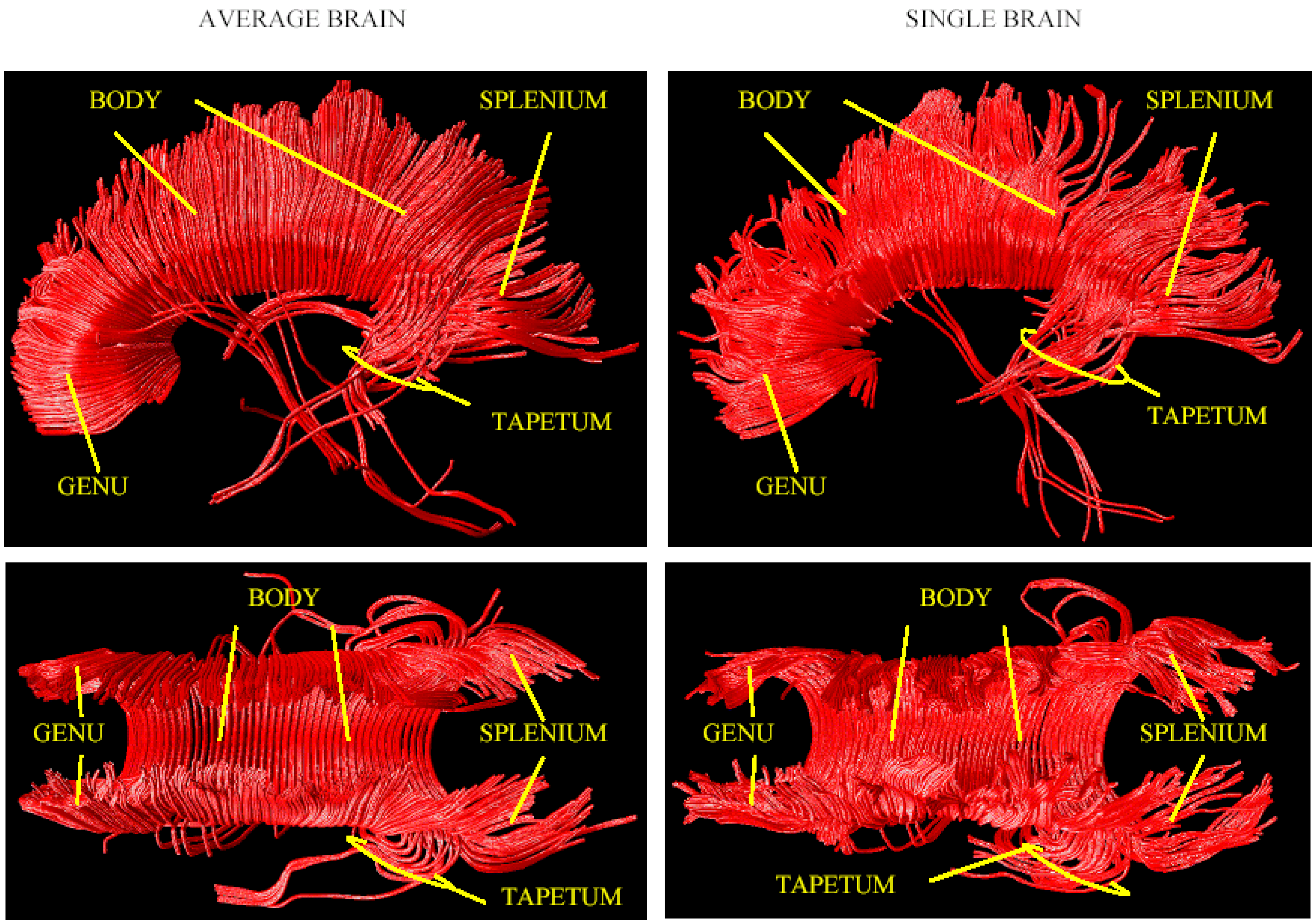
    $F = R \cdot U$

    $R = F \cdot (F^{T} \cdot F)^{-1/2}$
- Then reorient D using R:

  $D' = R \cdot D \cdot R^{T}$

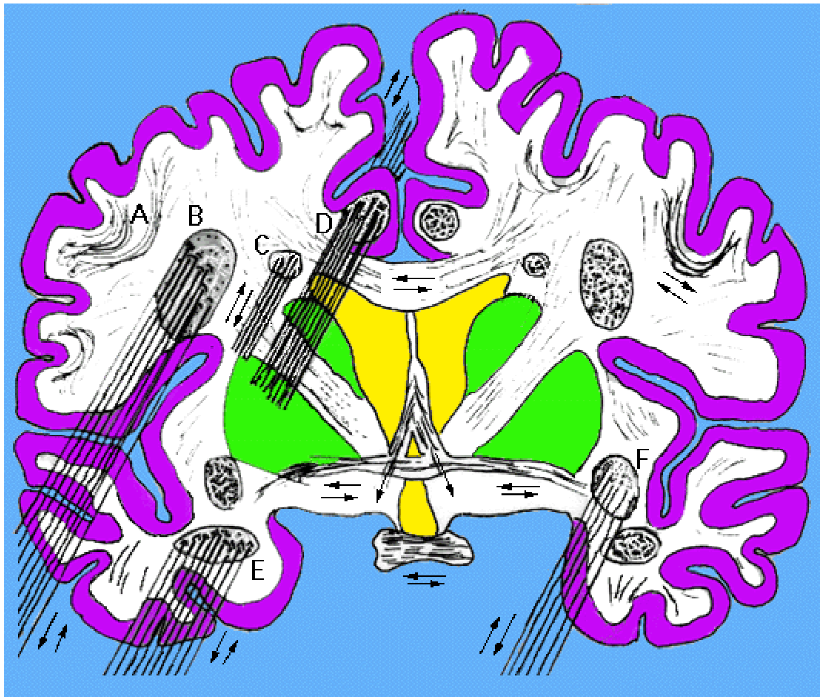
Mean Callosal Fiber Map

Diffusion Tensor Images Averaged over Ten Subjects

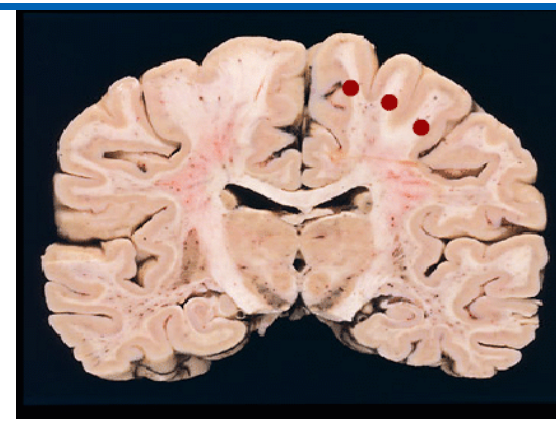


Jones et al, 2002

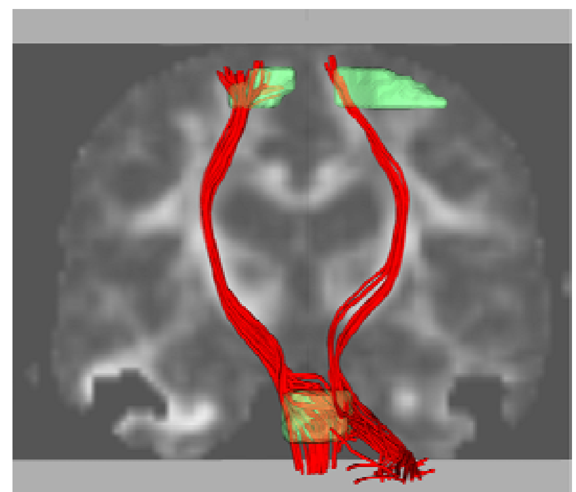
Dream: Connectivity?



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

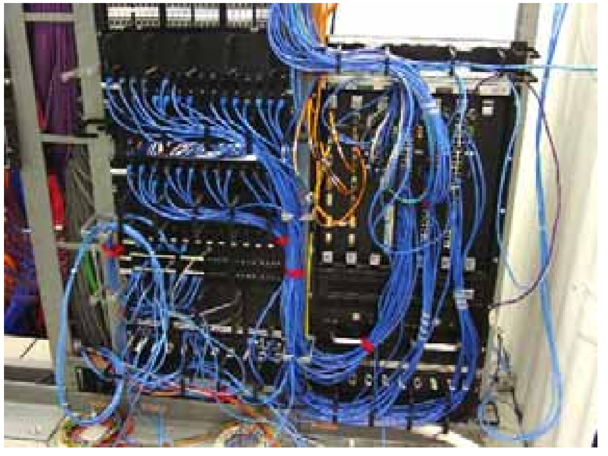


Source: Duke NeuroAnatomy Web Resources (Ch. Hulette)



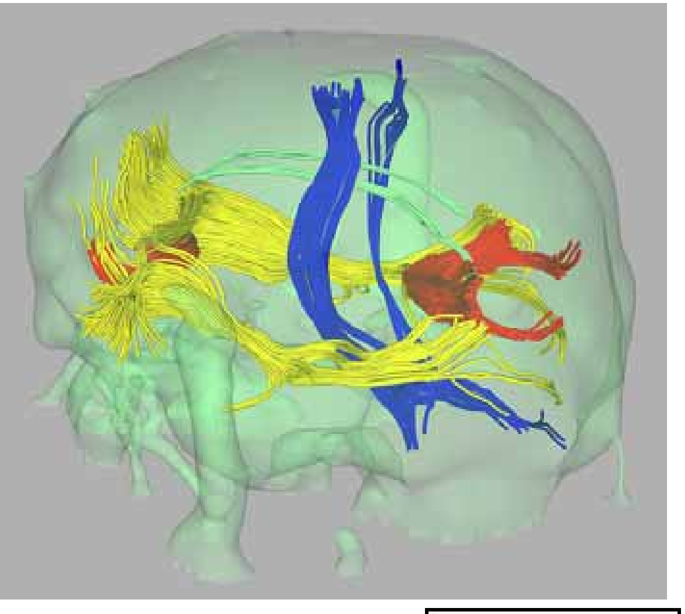
Tractography: Coronal view

Networking and Brain Connectivity

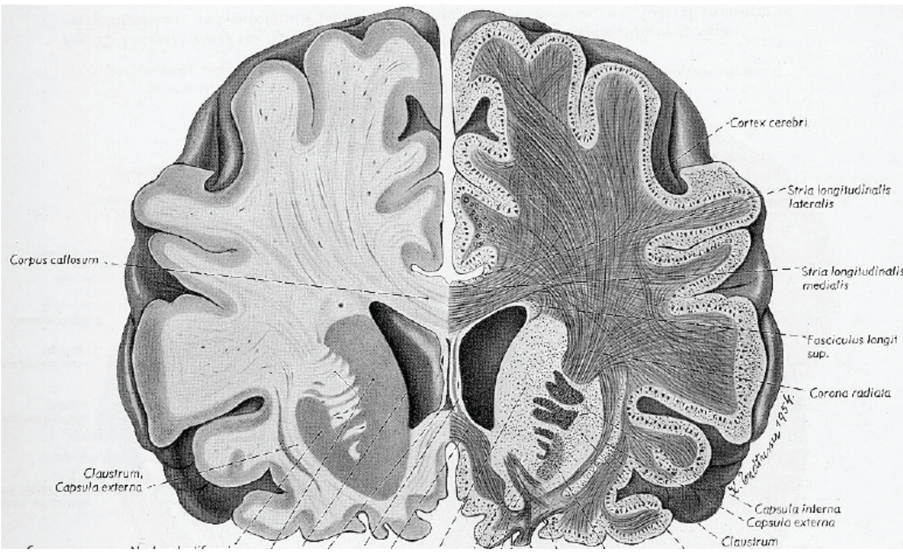


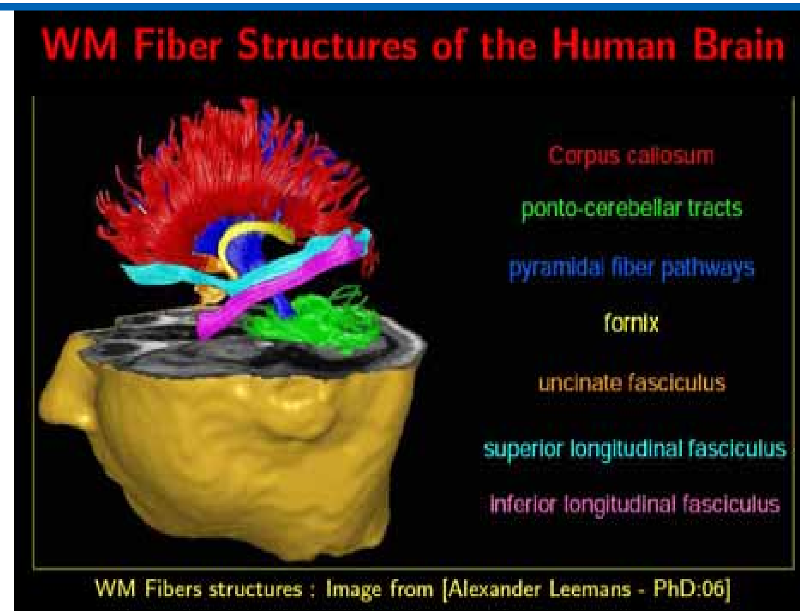
UNC Computer Science: Network wire cabinets

Major Fiber Tracts extracted from DT MRI



White Matter Tracts



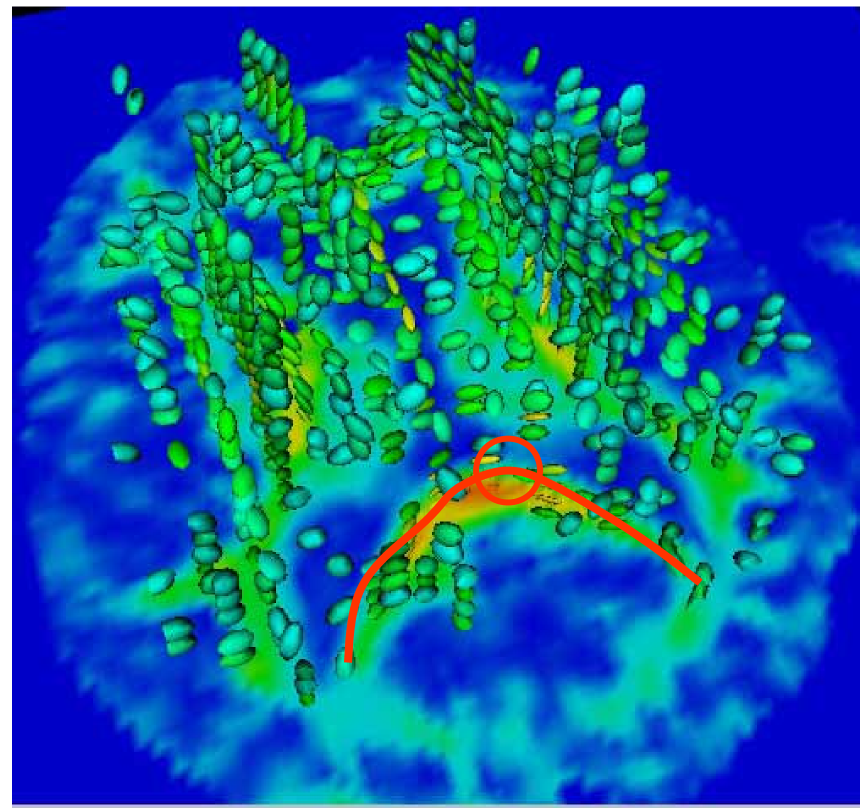


- In tractography fibers are traced, with the aim to visualize white matter tracts.
- The word “tractography” is not related to “tracking”, but to “tract”.
- White matter tract, white matter fasciculus

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

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

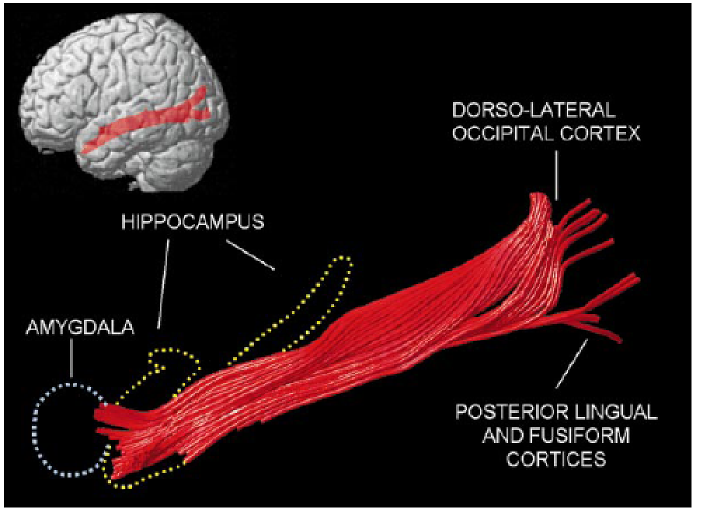


Fig. 7 Reconstruction of the ILF in the average DT-MRI data set. The long fibres originate from extrastriate areas of the occipital lobe and terminate in lateral temporal cortex and medial temporal cortex in the region of the amygdala and parahippocampal gyrus.

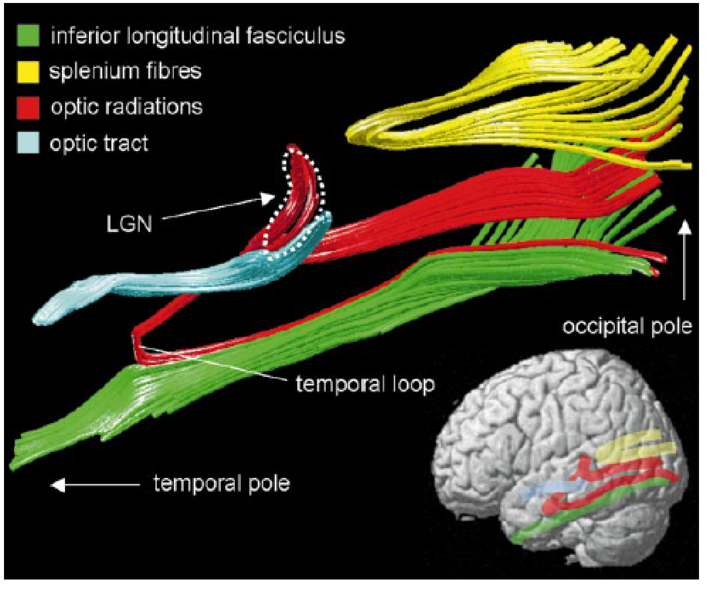
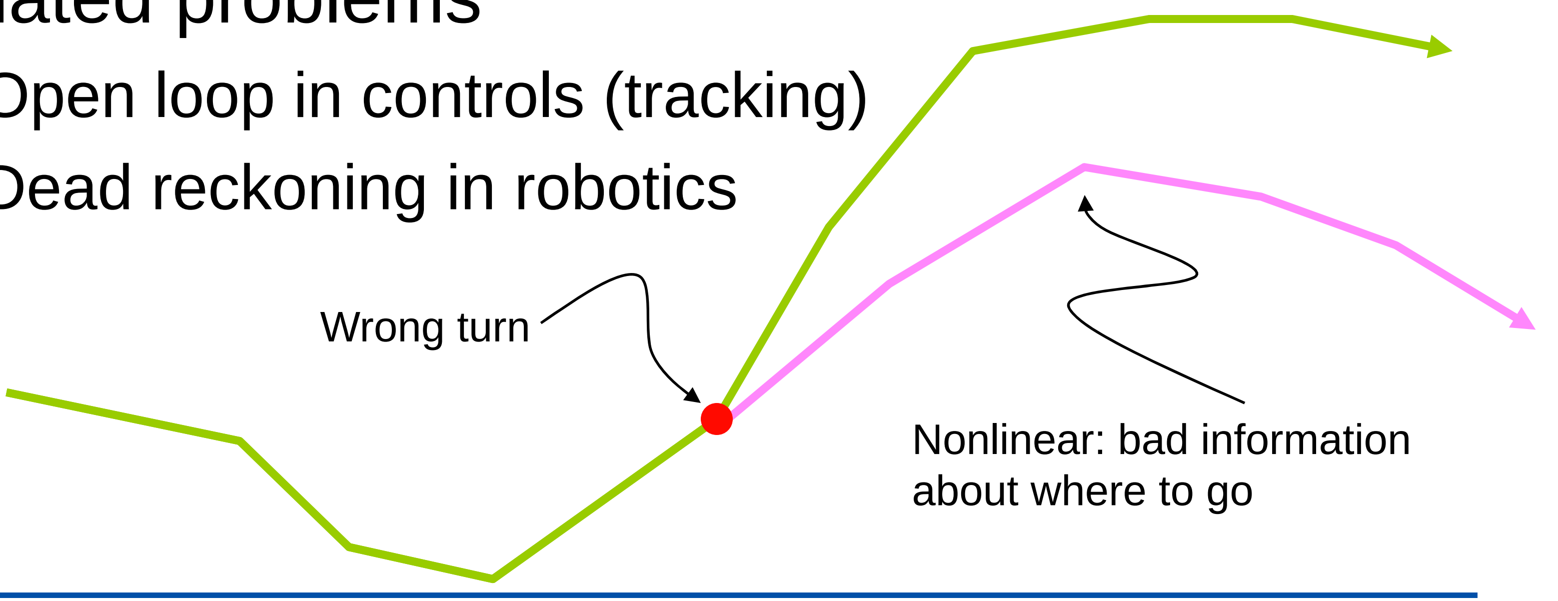


Fig. 2 Virtual *in vivo* dissection of the ILF and visual pathway of the right hemisphere (medial view) in the average brain data set. Splenial fibres connecting medial occipital regions are also shown. See text for explanation.

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

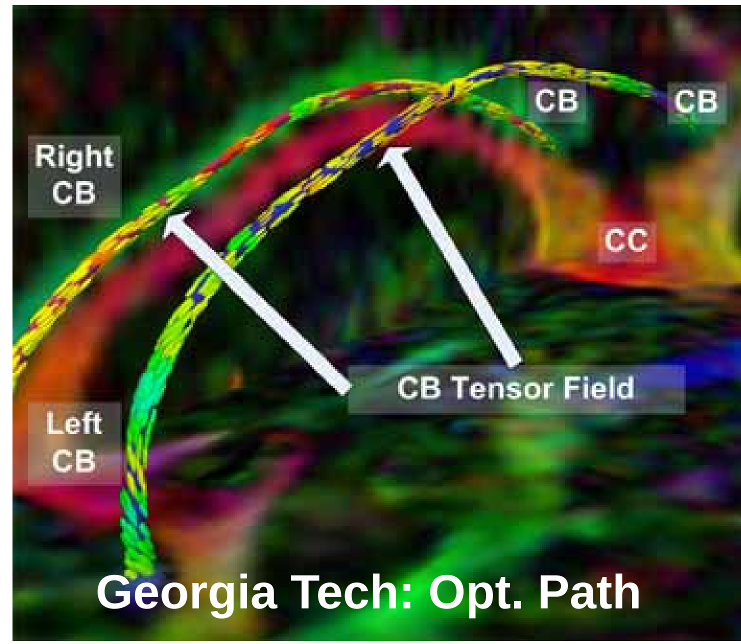
The Problem with Tractography
How Can It Work?

- 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



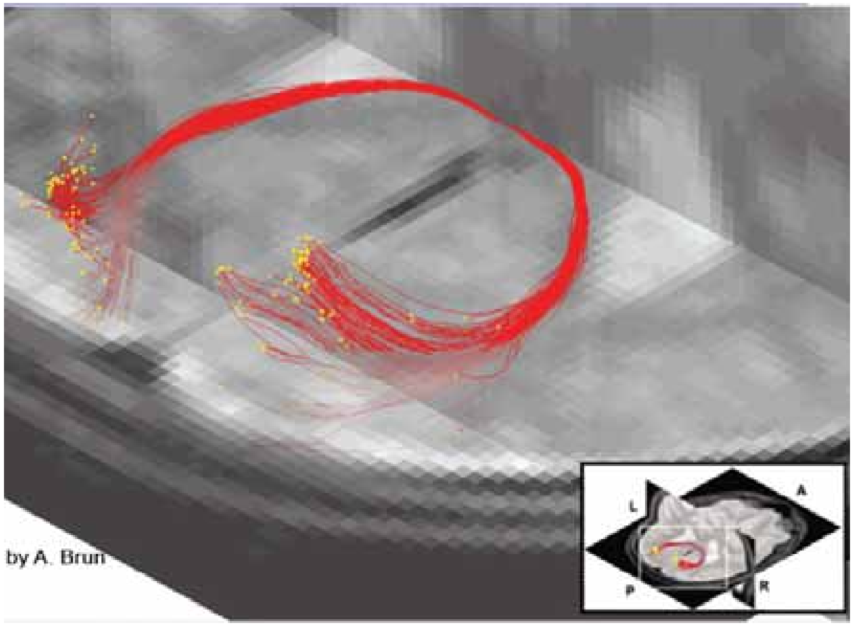
Alternative methods for tractography

- 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



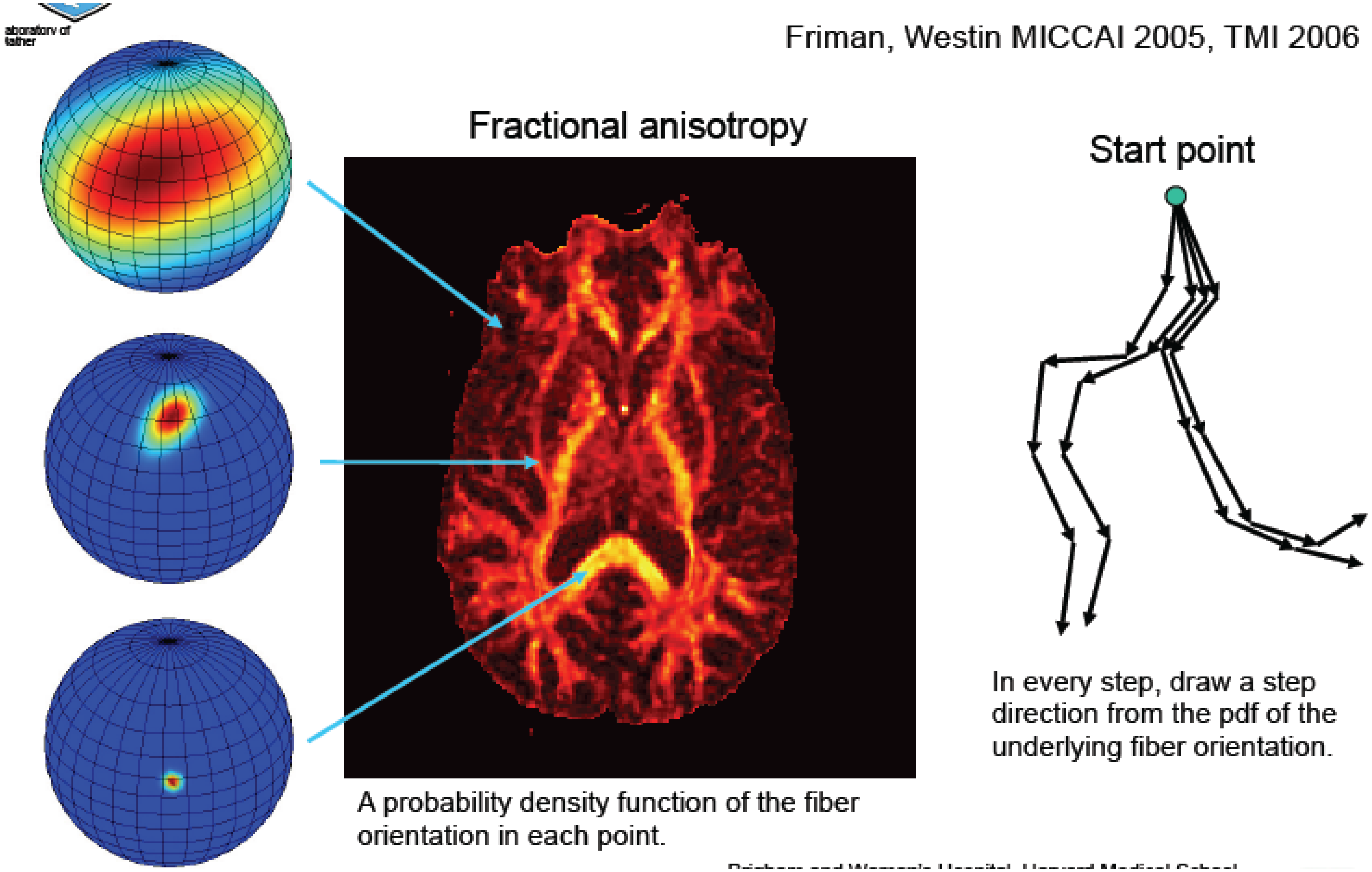
Stochastic Tractography

- 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

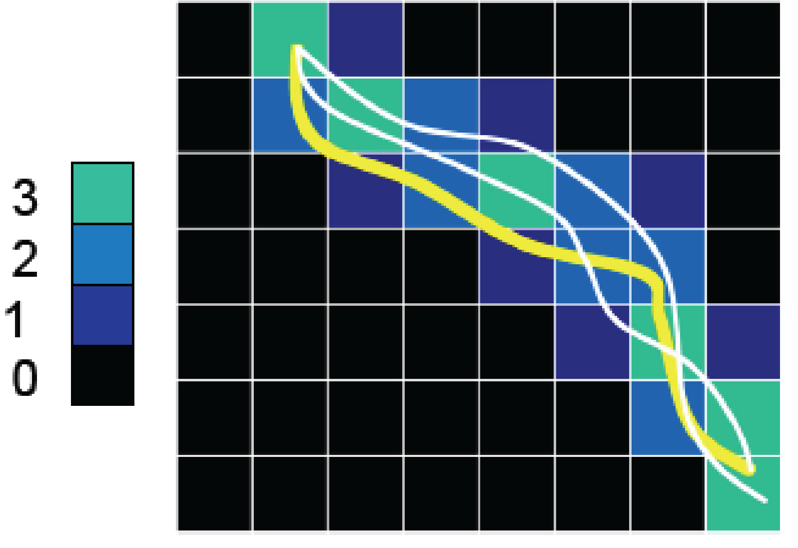
Stochastic Tractography



Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

Probability of Connection

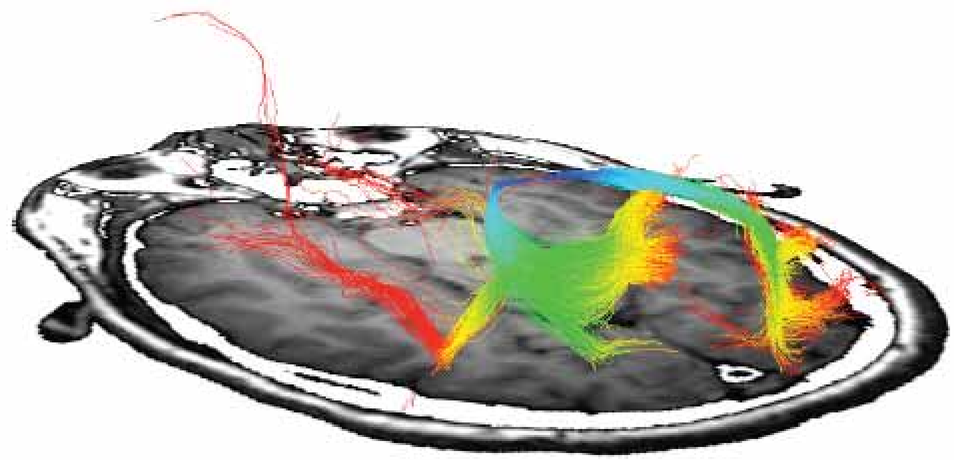
Given a large number of fibers, the probability of a connection between two voxels can be estimated



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

Probability of Connection

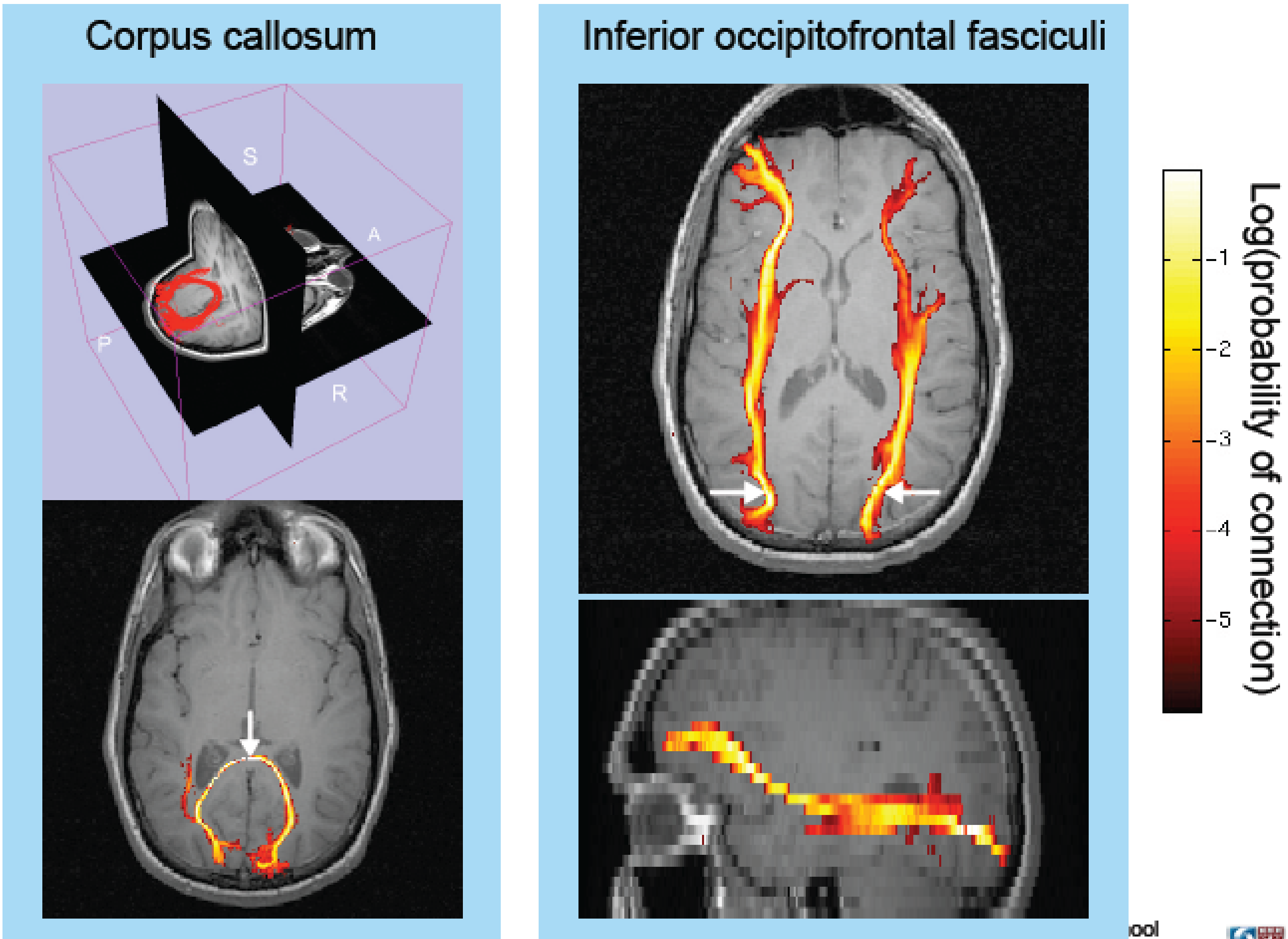


3,000 fiber samples initiated in the splenium of Corpus callosum. The coloring indicates the probability along each path to end up is a specific area.

Work with O. Friman

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

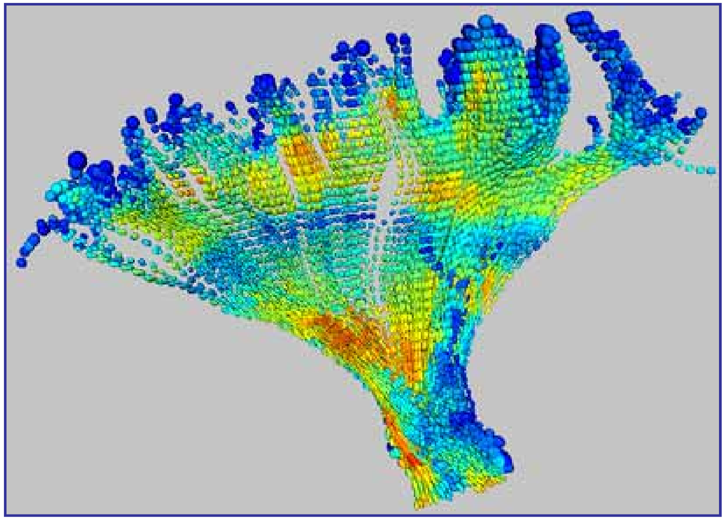
Probability of Connection



Work with O. Friman

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

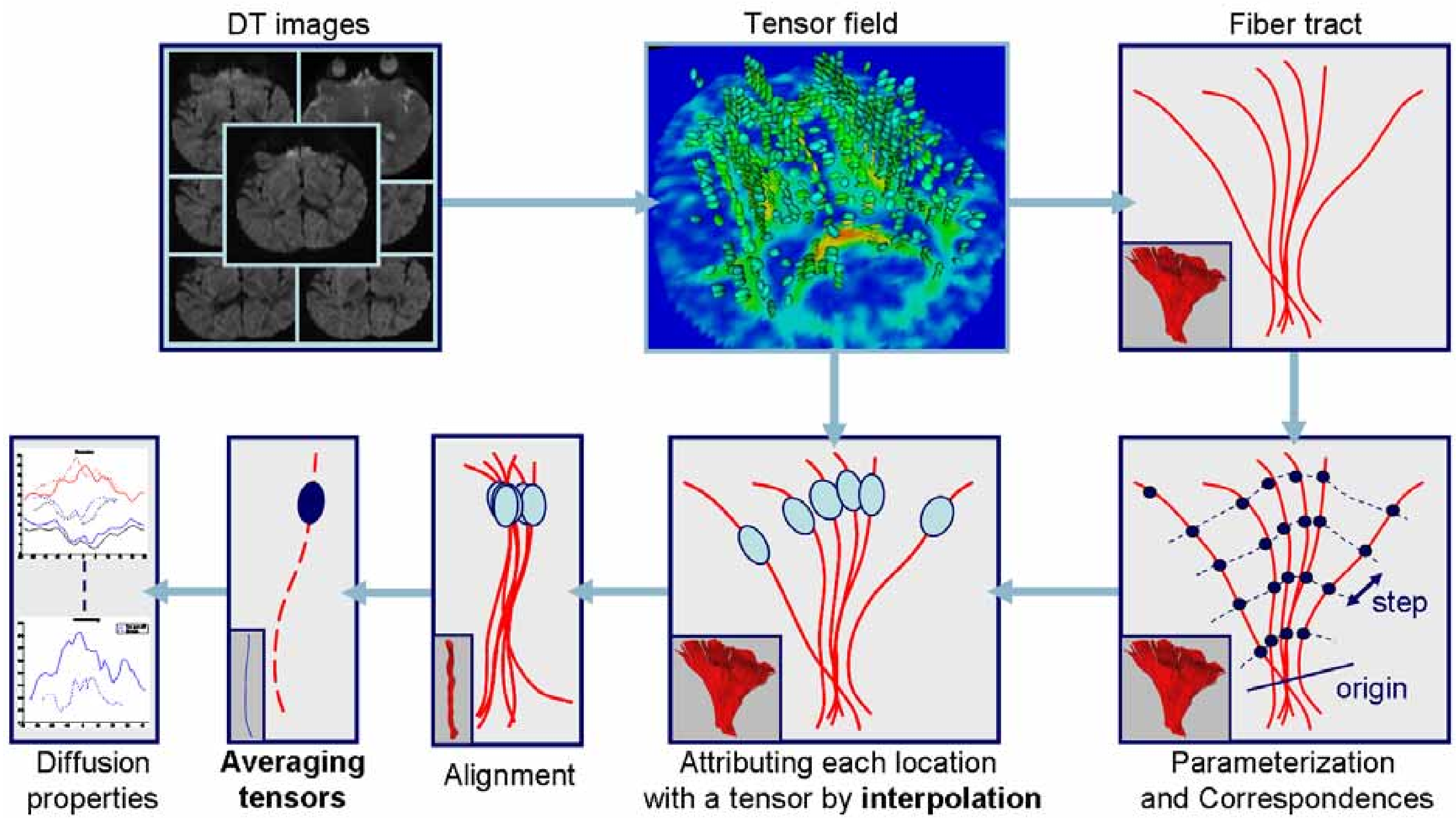
Quantitative Tractography: NAMIC Tool FiberViewer



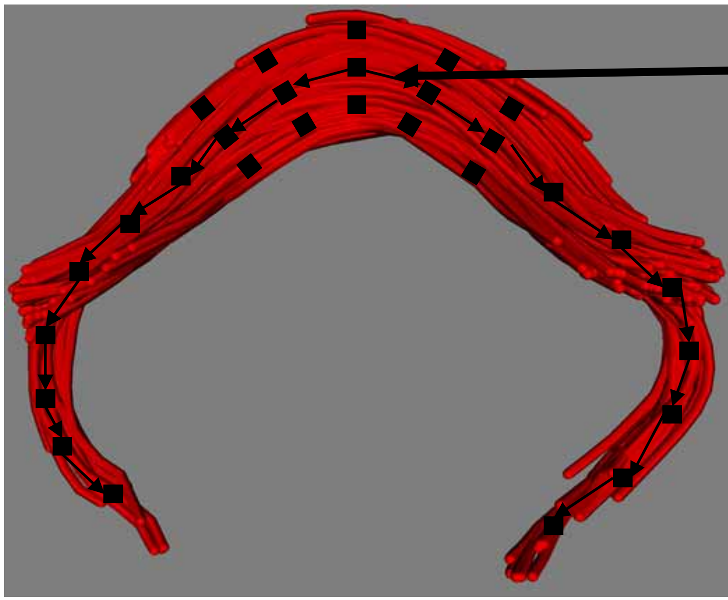
- Tractography results in selected fiber bundles of interest.
- Next step for clinical studies is geometrical and quantitative characterization.

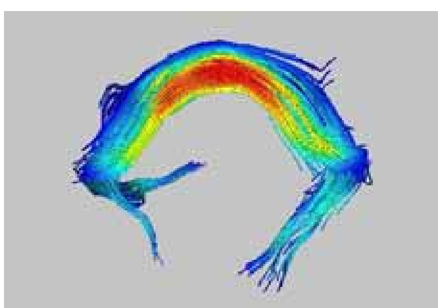
Fiber Tract-Oriented Statistics for Quantitative Diffusion Tensor MRI Analysis, Isabelle Corouge, P.Thomas Fletcher, Sarang Joshi, Sylvain Gouttard, Guido Gerig, Medical Image Analysis 10 (2006), 786 - 798

Fiber Tract Modeling and

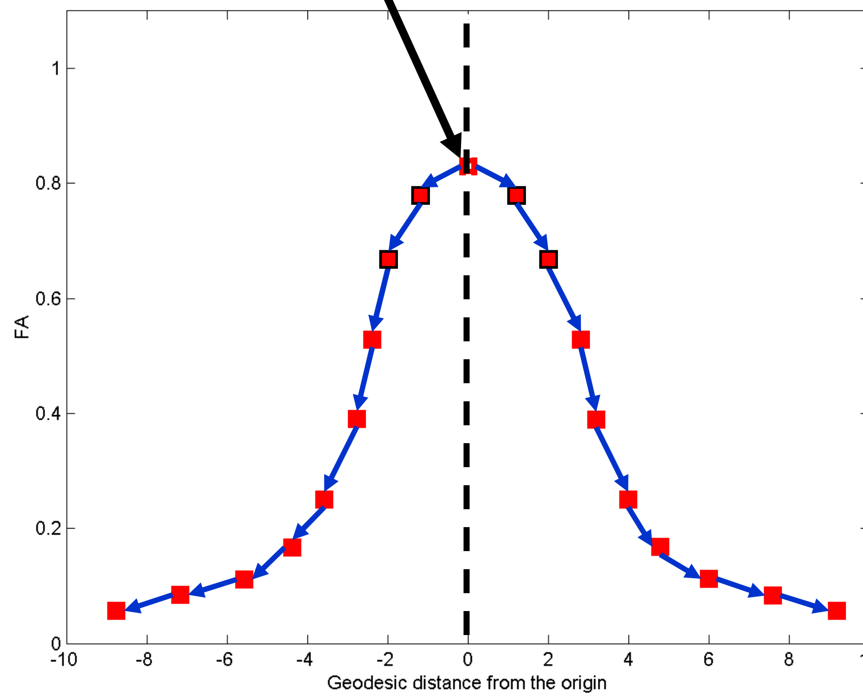


Processing of fiber tracts

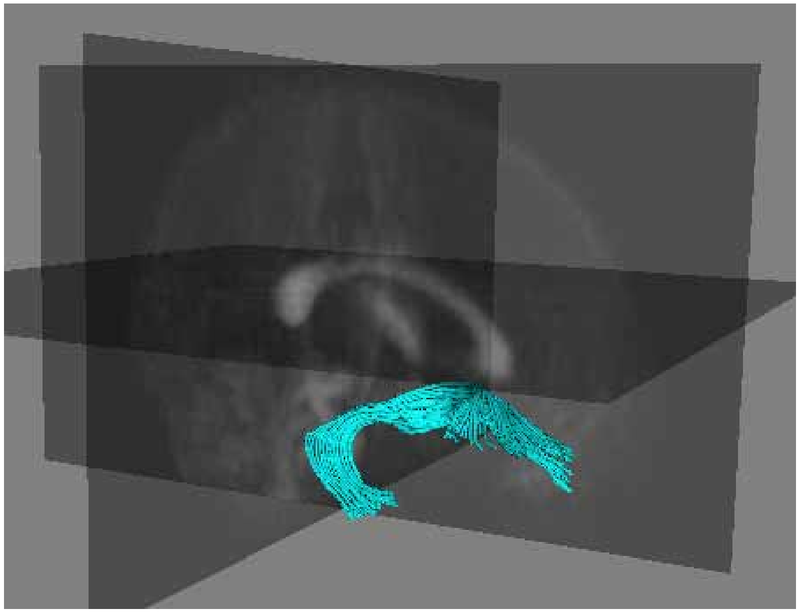


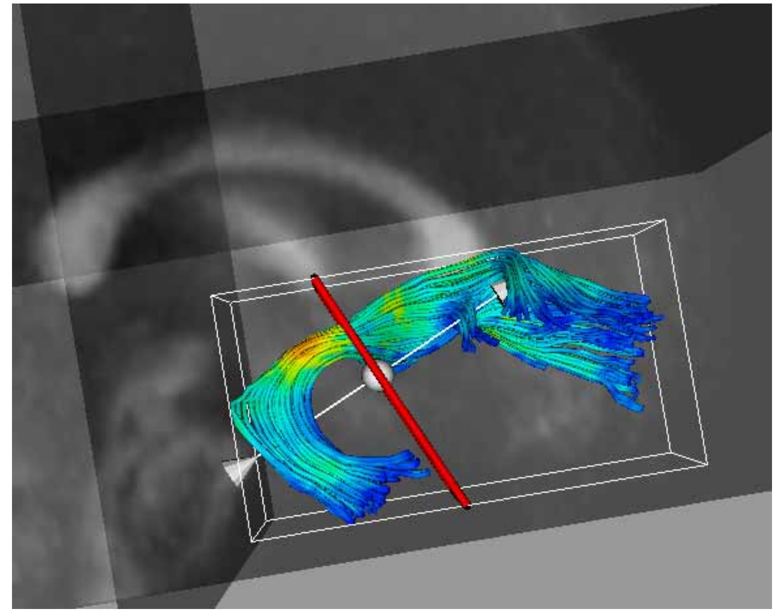


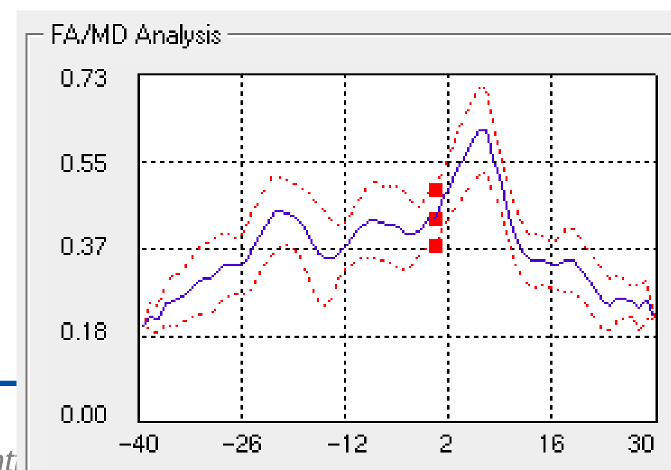
Origin (anatomical landmark)



Example Uncinate Fasciculus

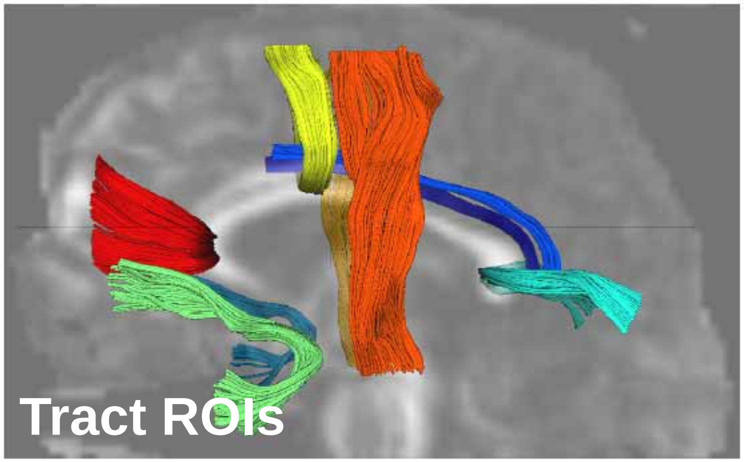


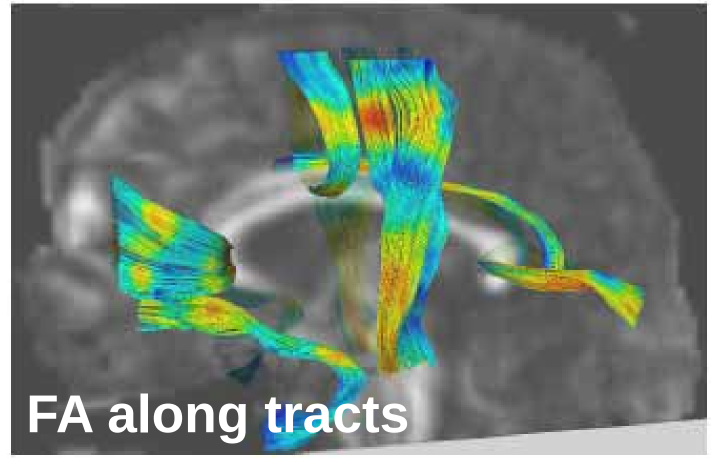


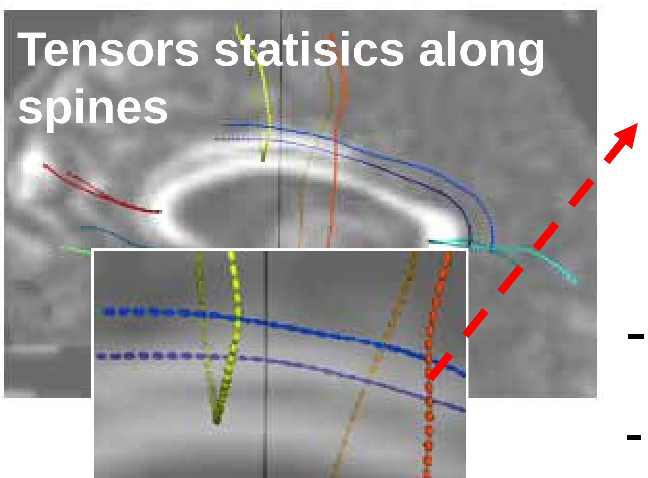


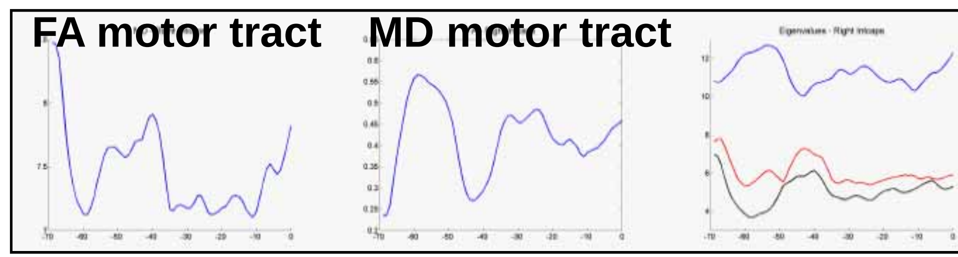
Corouge et al. *Fiber tract-oriented statistics for quantitative diffusion tensor MRI analysis*. Medical Image Analysis 2006.
FiberViewer software - http://www.ia.unc.edu/dev/

Quantitative Tractography



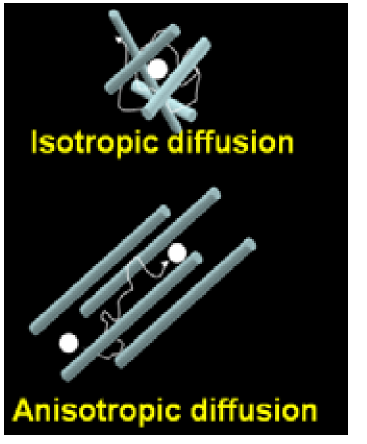






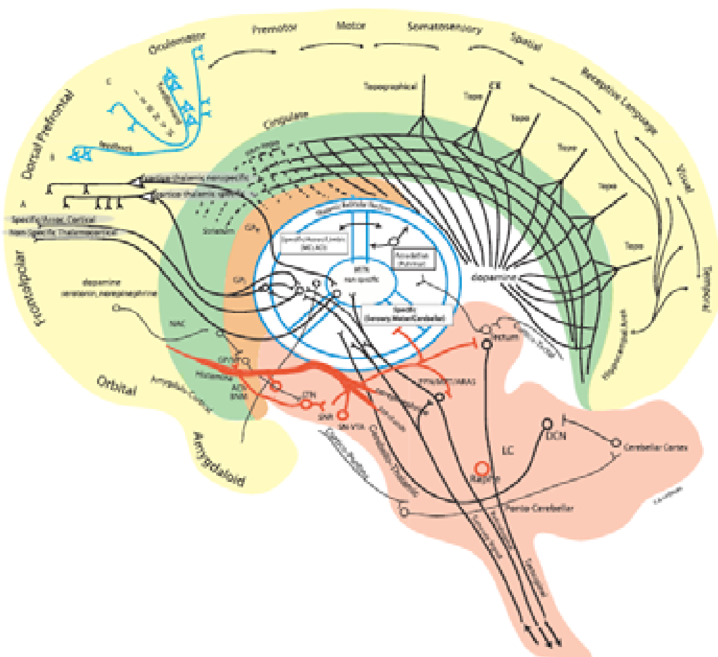
- Tractography for ROI definition
- Tensor-math. for statistics along tracts

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 !

Circuit -> Connectivity



Caution

- Do not "blindly" use the word "Connectivity" when applying DTI
- "Connectivity": Became forbidden C-word in some NIH study sections