Diffusion Tensor MRI Beyond Tractography

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Outline

Pictorial overview of DT-MRI data

Geomtric intuition for commonly studied tensor invariants

Three (non-tractography) methods of DTI analysis:

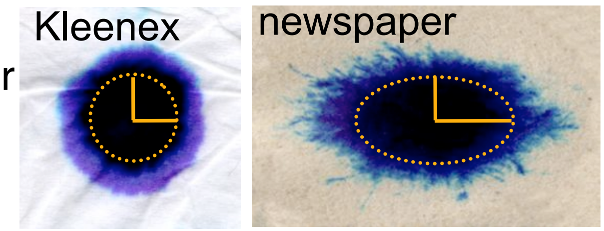
- Tract-based Spatial Statistics (Smith et al.)
- Tract-Specific Framework (Yushkevich, Zhang, Gee et al.)
- Anisotropy Creases (Kindlmann at al.)

Discussion & Conclusions

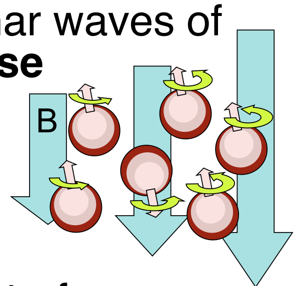
Diffusion & Diffusion weighting

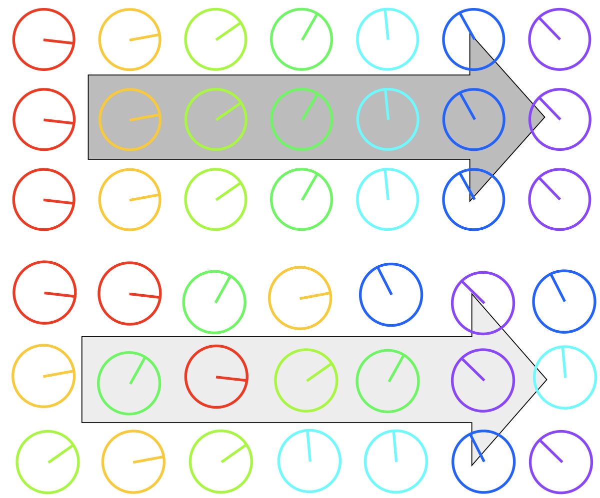
Diffusion: Brownian motion of one material through another

Anisotropy: diffusion rate depends on direction



Magnetic gradients create spatial planar waves of proton **phase**

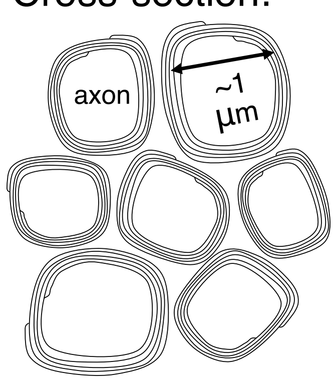




Destructive interference creates signal attenuation (diffusion-weighting) only along gradient direction

Indirect imaging of microstructure

Fiber bundle
Cross-section:



Microstructure of bundles directionally constrains water diffusion along fiber direction (LeBihan et al. 1985)

Intra- vs. extra-cellular diffusion

Diffusion lengths with the time-scale of MR measurement on order of 10µm

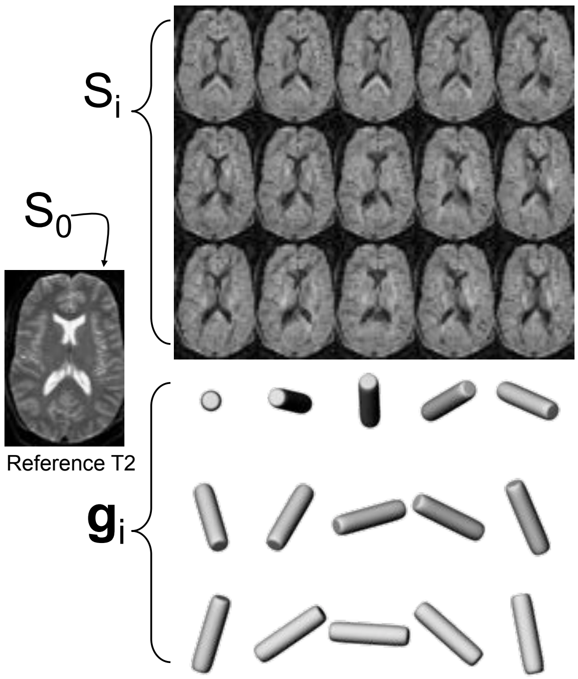
Apparent diffusion coefficient (ADC) measured for each gradient

Voxels on the order of 1mm

⇒ **Two to three orders of magnitude away from measuring axons**

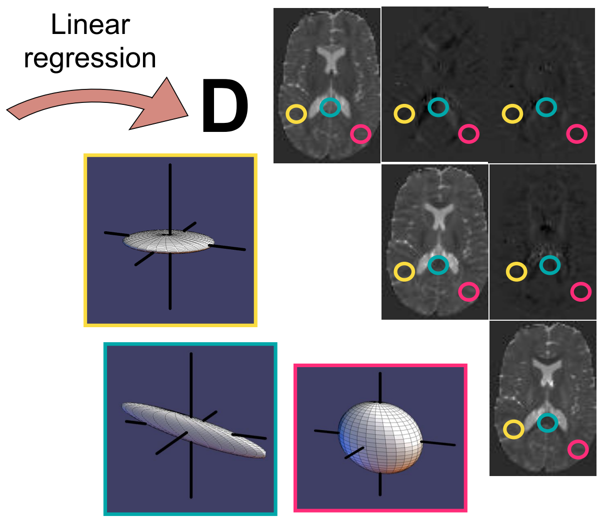
Diffusion-Weighted to Diffusion-Tensor

Diffusion-weighted MR data



Single Tensor Model (Basser et al. 1994)

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

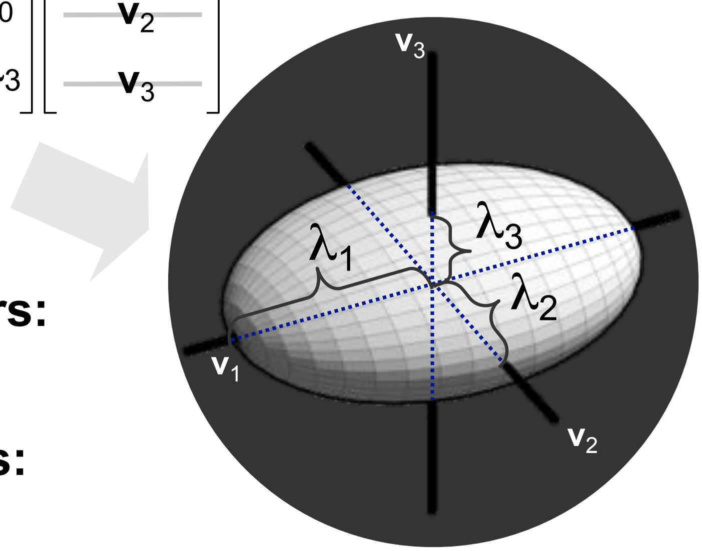


Single Tensor Model: only six degrees of freedom

Eigenvectors & eigenvalues

$$\mathbf{D} = \mathbf{R}\Lambda\mathbf{R}^{-1}$$

$$= \begin{bmatrix} \mathbf{v}_1 & \mathbf{v}_2 & \mathbf{v}_3 \end{bmatrix} \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \begin{bmatrix} \mathbf{v}_1 \\ \mathbf{v}_2 \\ \mathbf{v}_3 \end{bmatrix}$$

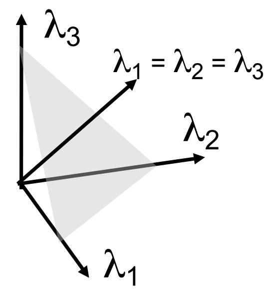


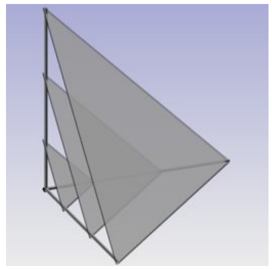
Eigenvectors: orientation

Eigenvalues: shape

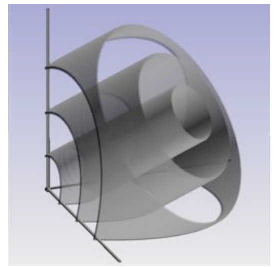
Tensor invariants describe shape

Can be understood as cylindrical or spherical coordinate system

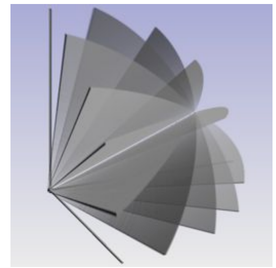




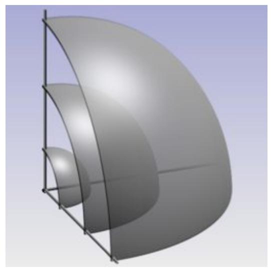
tr(**D**)



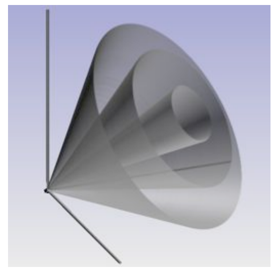
|**E**|



mode(**E**)
= det(**E**/|**E**|)
Mode measures
Linear vs. planar
anisotropy



|**D**|



|**E**|/|**D**| ~= FA
FA = **Fractional Anisotropy**

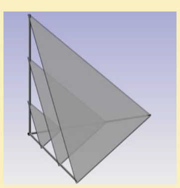
tr(**D**) = Dxx+Dyy+Dzz

|**D**| = sqrt(tr($\mathbf{D}^T\mathbf{D}$))

E = deviatoric(**D**)
= **D** - trace(**D**)***I**/3

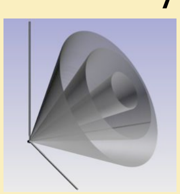
Biological meaning of tensor shape

Size: **bulk mean diffusivity MD** ("ADC")



- (ADC strictly speaking diffusivity along **one** direction)
- Roughly same across gray+white matter, high in CSF
- Indicator of acute ischemic stroke

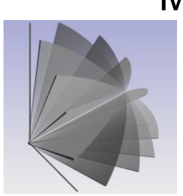
Anisotropy (e.g. FA): directional microstructure



- High in white matter, low in gray matter and CSF
- Increases with myelination, tends to decrease in diseases that damage white matter

Much diffusion-MRI-based neuroscience is about MD & FA

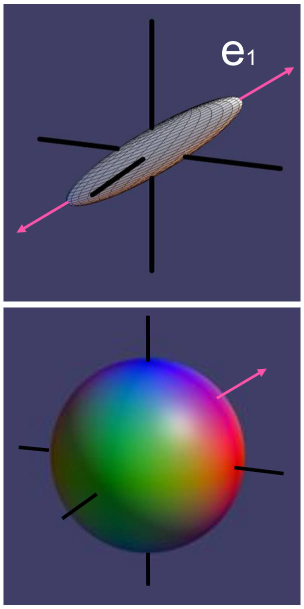
Mode: linear versus planar

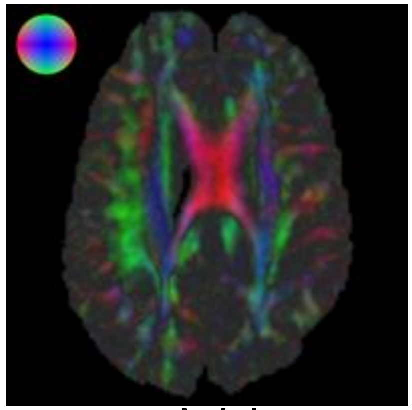


- Partial voluming of adjacent orthogonal structures
- Fine-scale mixing of diverse fiber directions
- Tensor fitting error increases with planarity (Tuch 2002)

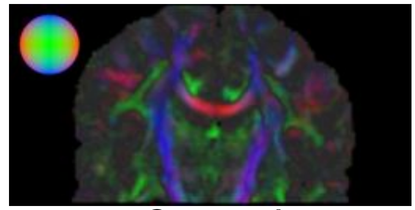
Principal eigenvector ~= axon direction

Standard RGB colormap

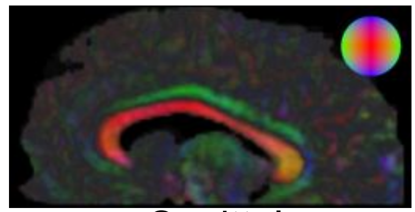




Axial



Coronal

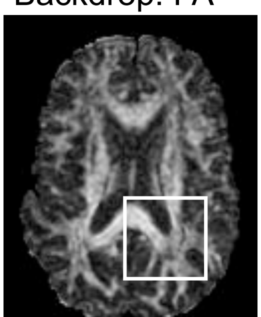


Sagittal

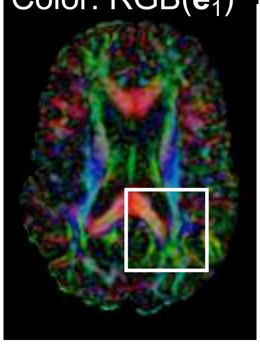
R=| $\mathbf{e}_1 \cdot x$ |
G=| $\mathbf{e}_1 \cdot y$ |
B=| $\mathbf{e}_1 \cdot z$ |

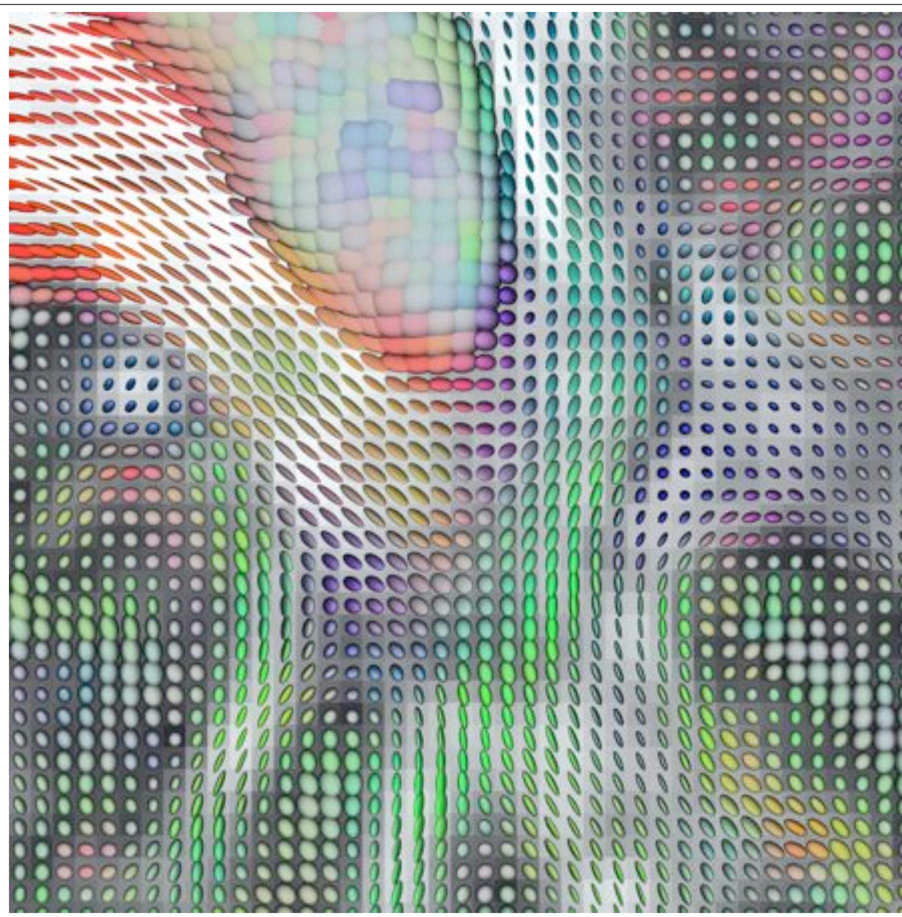
(Pajevic & Pierpaoli, 1999)

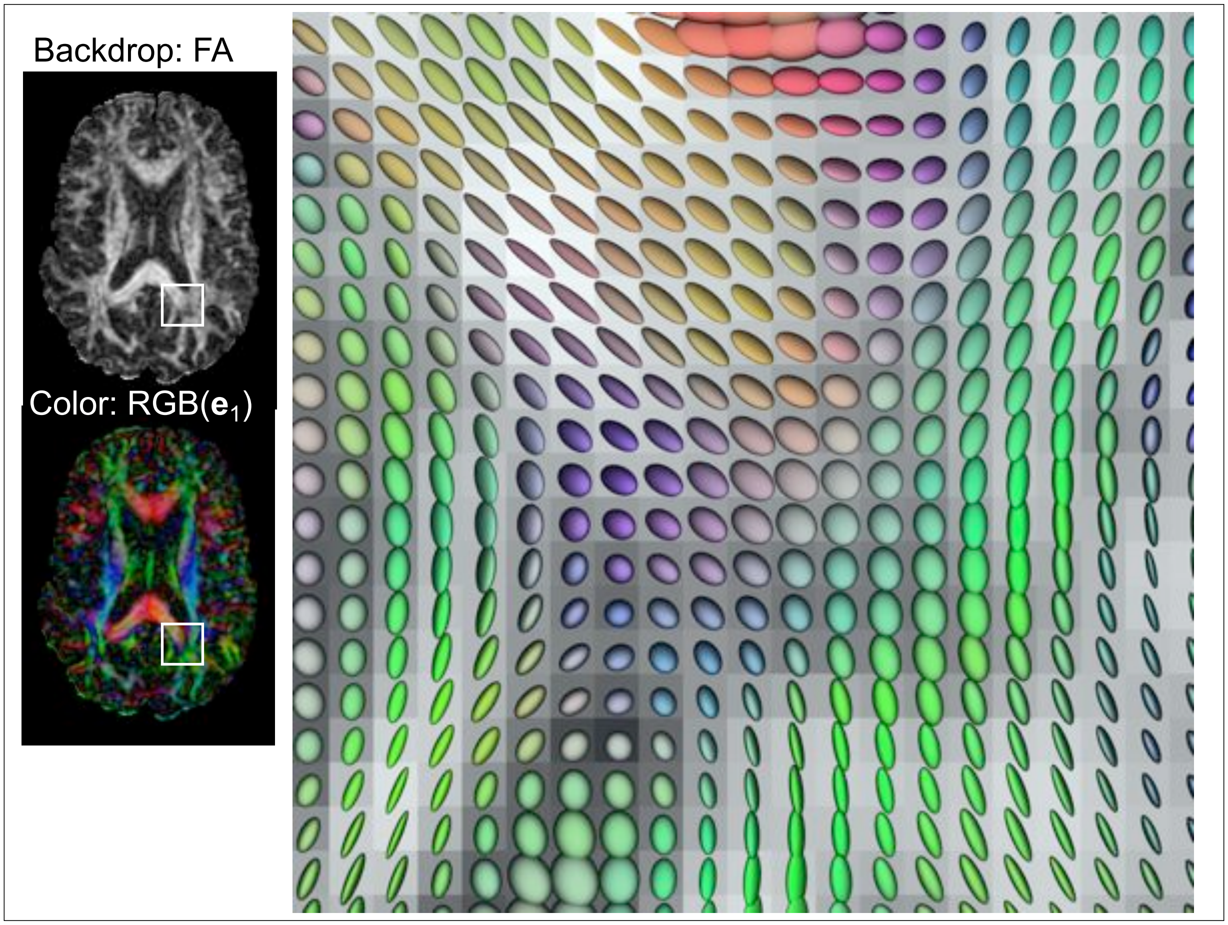
Backdrop: FA

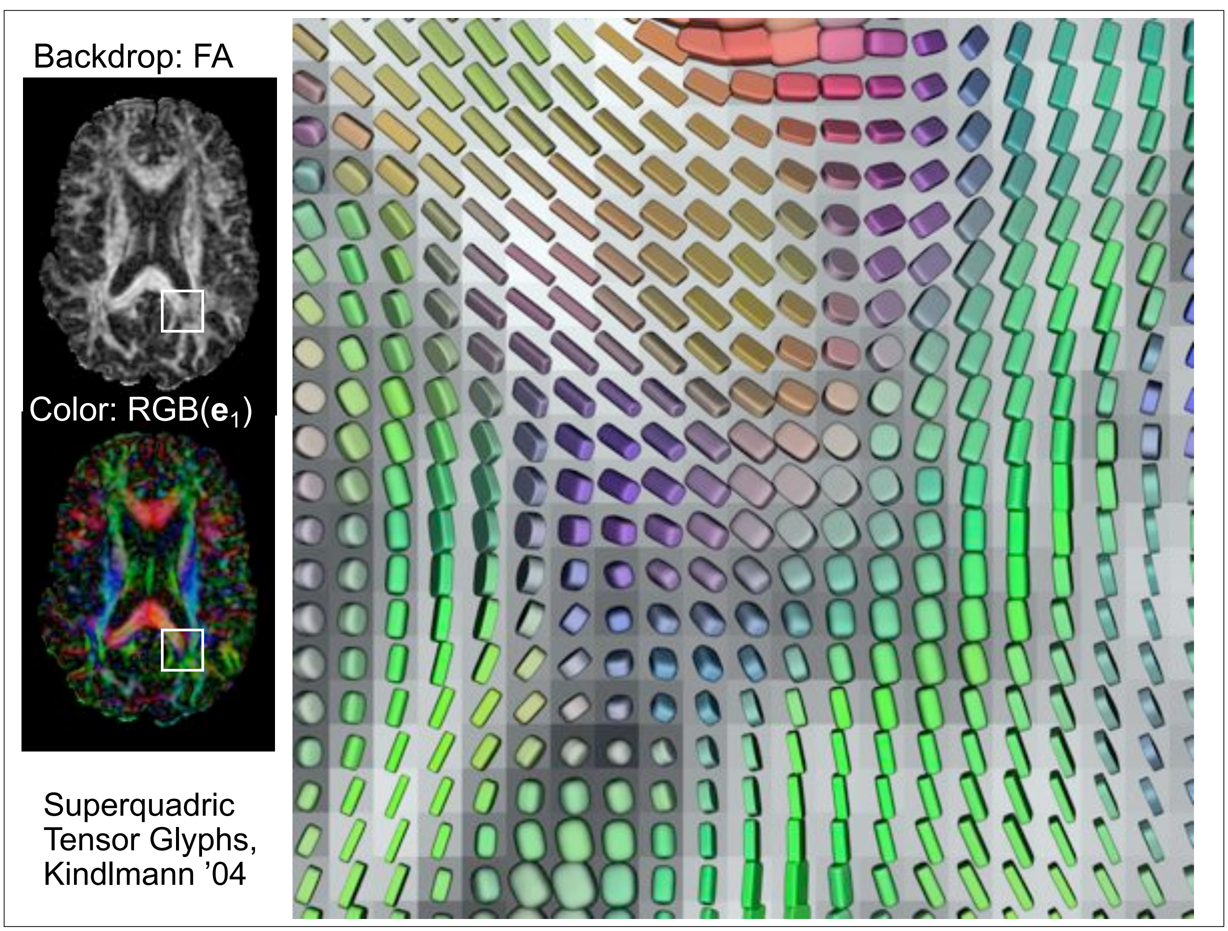


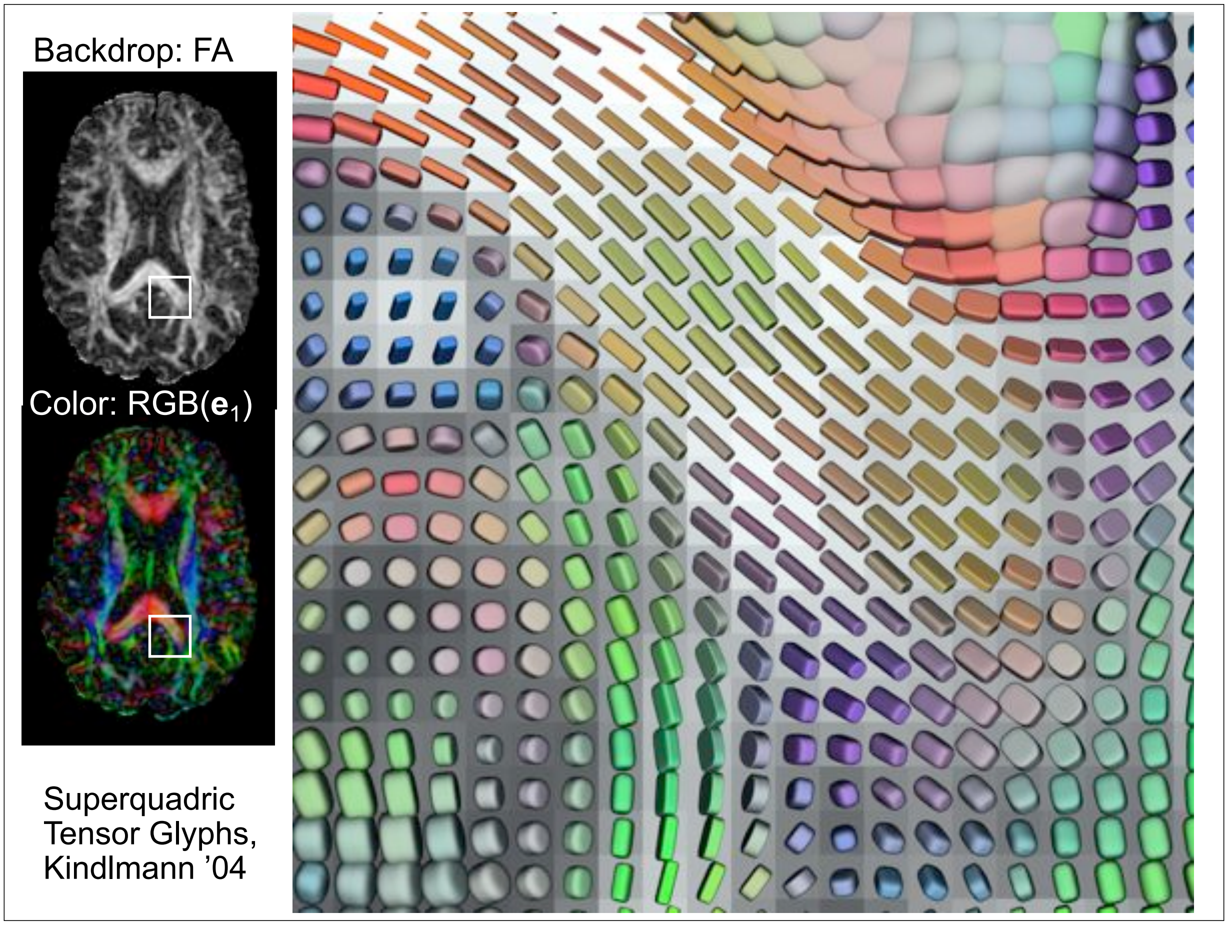
Color: RGB($\mathbf{e}_1$)






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


Backdrop: FA
Color: RGB($\mathbf{e}_1$)
Superquadric Tensor Glyphs, Kindlmann '04


Backdrop: FA
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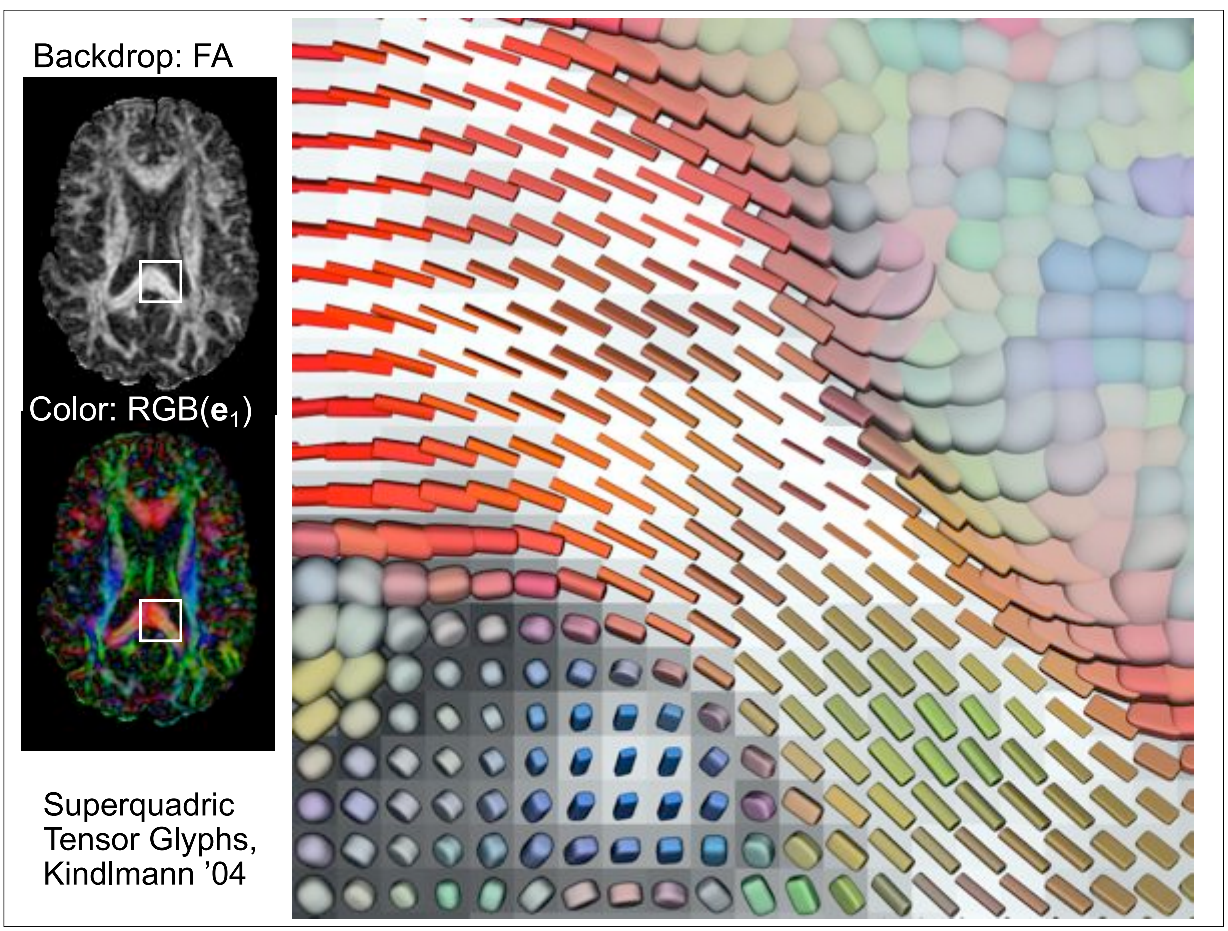
Superquadric Tensor Glyphs, Kindlmann '04


Backdrop: FA
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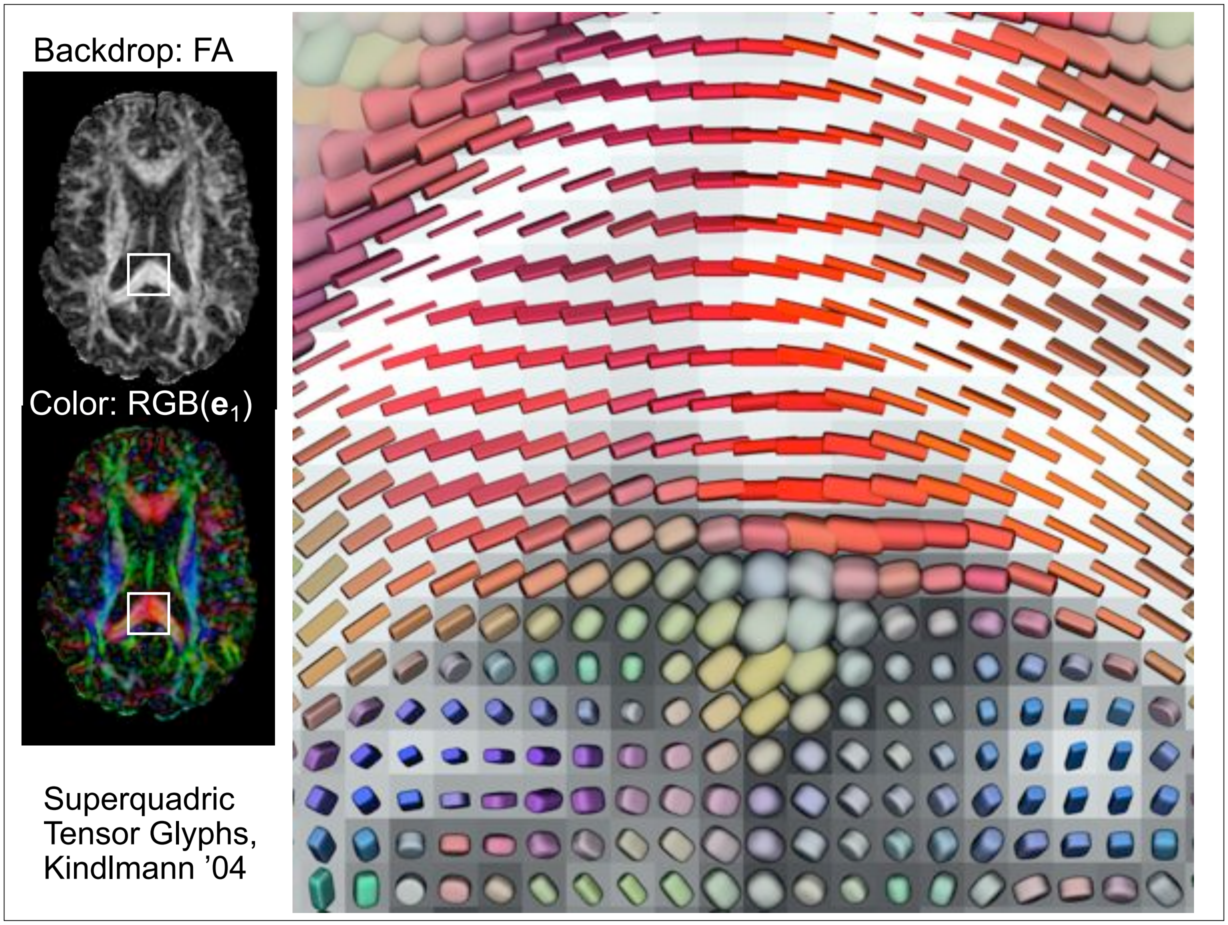
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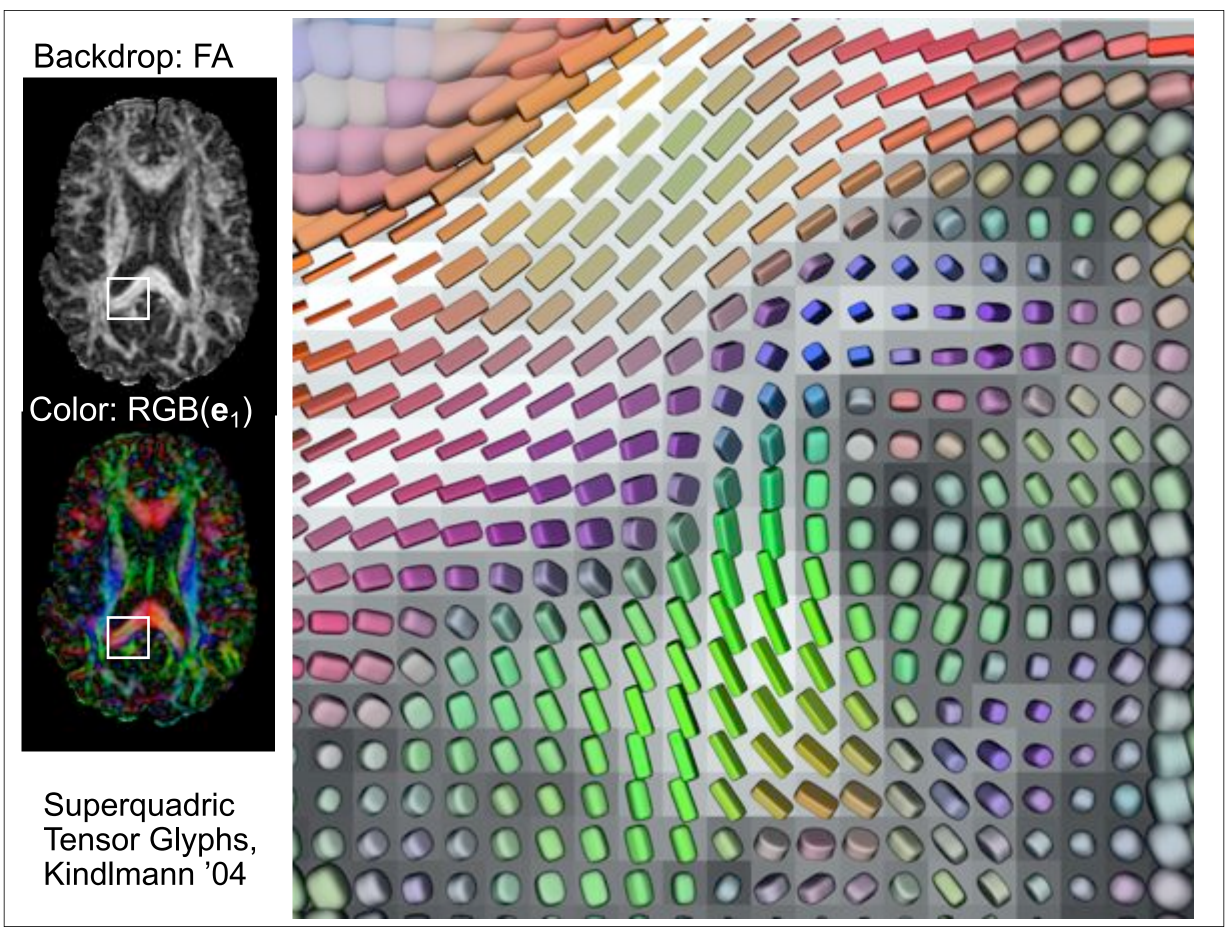
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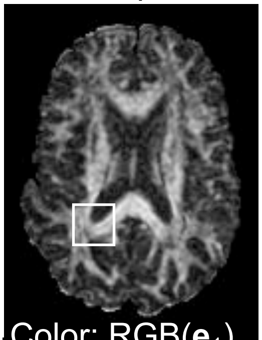
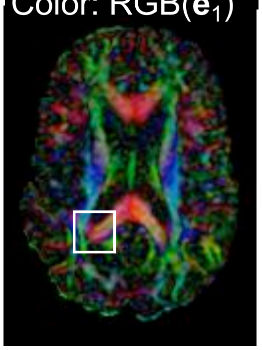
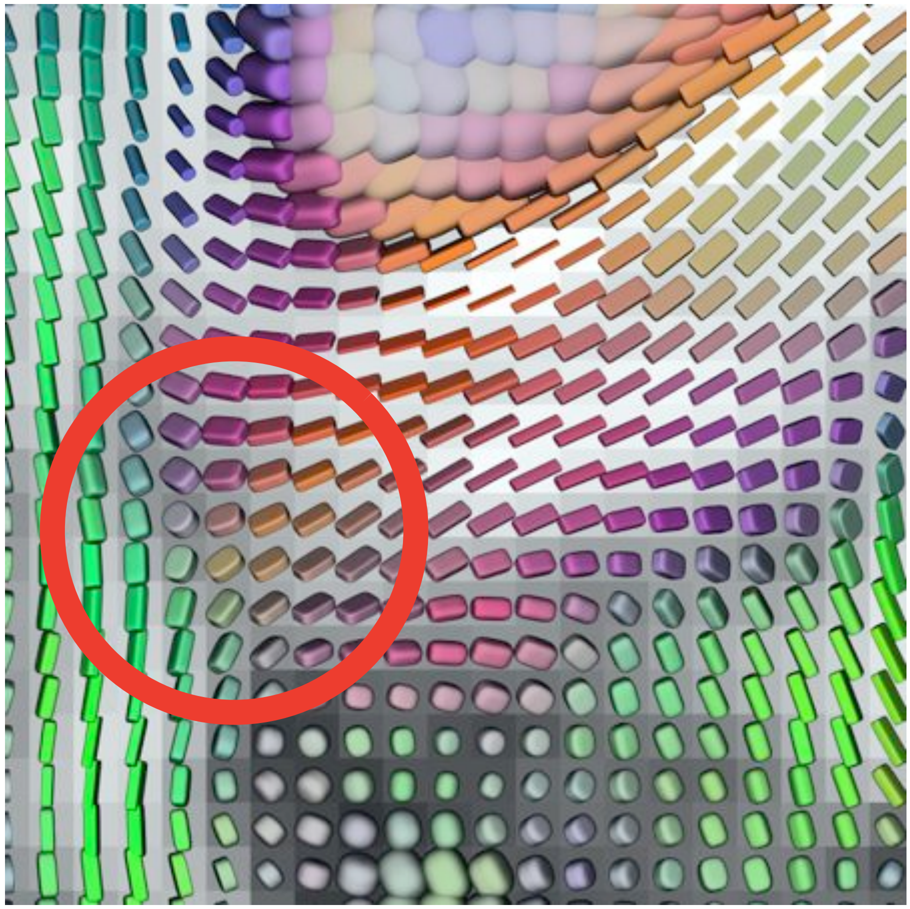


Color: RGB($\mathbf{e}_1$)

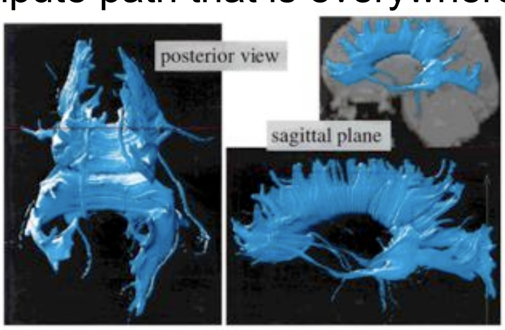




Superquadric Tensor Glyphs, Kindlmann '04

Tractography (deterministic) Basser et al. 1998

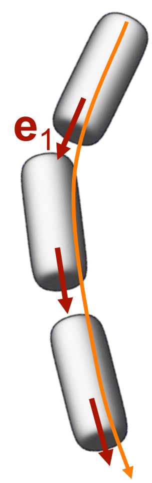
Compute path that is everywhere tangent to principal eigenvector



Idea: can compute paths of axons

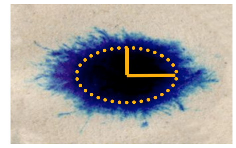
- Data too coarse
- Single-tensor model can't represent crossing or branching
- Selecting individual tracts requires manual editing or alignment with atlas
- Still used for large bundles

Probabilistic tractography and non-tensor models capture more complex architecture



Summarizing intro

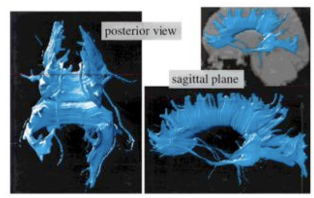
Diffusion MRI measures **anisotropy**



Anisotropy is a meaningful tissue propery

Anisotropy implies directionality

Tractography/Connectivity methods attempt to trace spatial patterns of directionality



Can also study anisotropy (FA) and other invariants themselves

Outline

Pictorial overview of DT-MRI data

Geomtric intuition for commonly studied tensor invariants

Three (non-tractography) methods of DTI analysis:

- Tract-based Spatial Statistics (Smith et al.)
- Tract-Specific Framework (Yushkevich, Zhang, Gee et al.)
- Anisotropy Creases (Kindlmann at al.)

Discussion & Conclusions

Tract-based Spatial Statistics (TBSS)

S M Smith, M Jenkinson, H Johansen-Berg, D Rueckert, T E Nichols, C E Mackay, K E Watkins, O Ciccarelli, M Z Cader, P M Matthews, and T E J Behrens. Tract-based spatial statistics: Voxelwise analysis of multi-subject diffusion data. NeuroImage, 31:1487–1505, 2006.

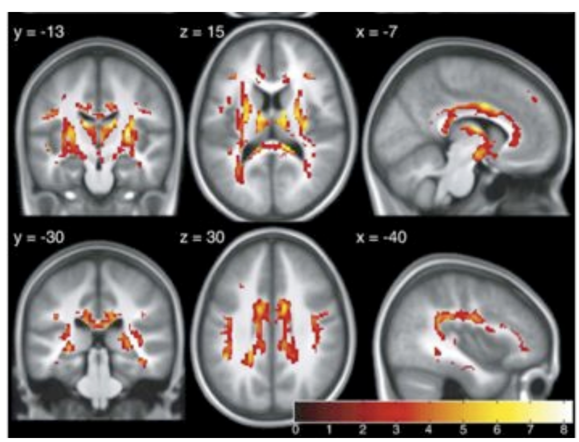
- For doing statistical tests on tensor invariants
- Conceptually close to Voxel-Based Morphometry (voxel-based, whole brain, automated)
- Computes a "skeleton" of group-mean FA image
- Voxel-based (raster) representation of skeleton
- Skeleton is reference manifold for projecting and doing statistics on registered single-subject FA
- Available in FSL: http://www.fmrib.ox.ac.uk/fsl/ http://www.fmrib.ox.ac.uk/fsl/tbss/index.html

TBSS compared to VBM

VBM: automated, simple, whole brain analysis
(Ashburner & Friston NeuroImage 2006)

VBM of FA sensitive to:

- Changes in WM alignment from registration
- Amount of smoothing (changes in FA levels vs volume of WM region, esp with thin tracts)

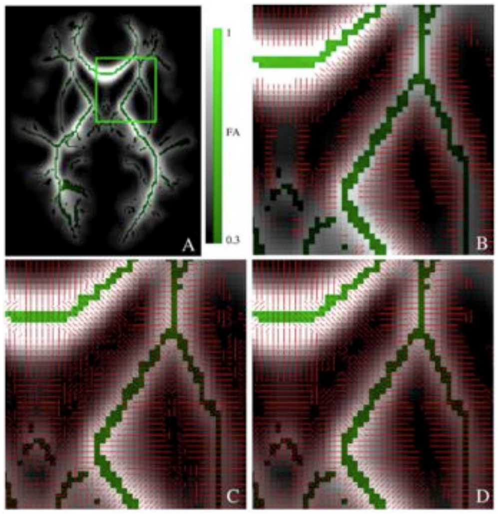


T R Vangberg, J Skranes, A M Dale, M Martinussen, A-M Brubakk, O Haraldseth. Changes in white matter diffusion anisotropy in adolescents born prematurely. NeuroImage 32:1538 – 1548 (2006)

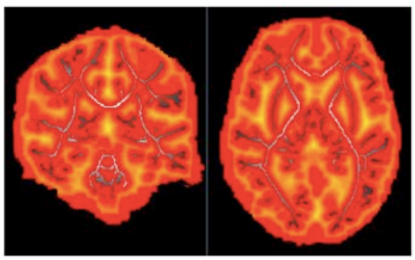
TBSS aims for robustness by using **skeleton**: avoids regions of low mean FA or high inter-subject variability

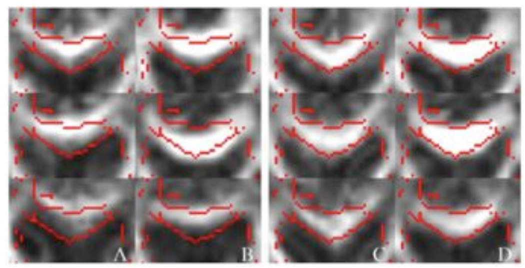
DT-MRI - Beyond Tractography ISMRM'11 "Functional & Anatomic Data Analysis: Principles & Practicalities"

Steps in TBSS

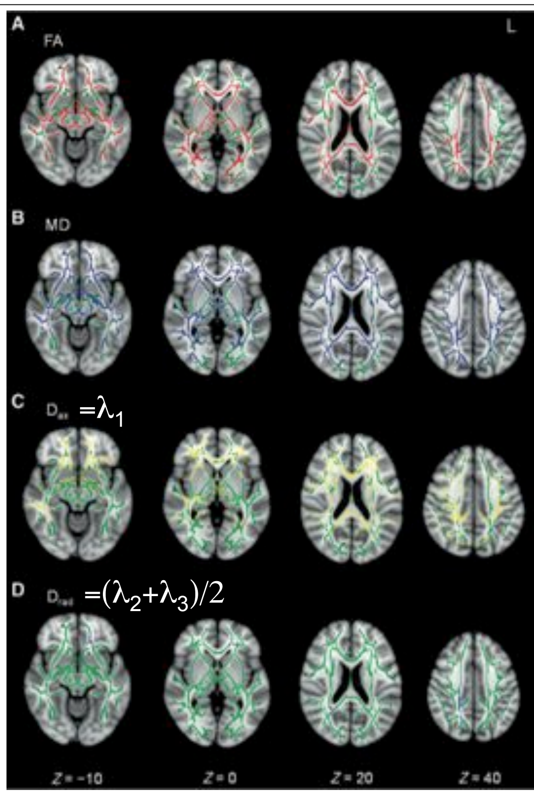


- Single-subject FA maps non-linear registered
- Mean FA image skeletonized by non-maximal supression (using either first or second derivatives)
- Single-subject FA maps projected into skeleton (with limit on distance of projection)
- GLM statistics on projected FA





Example of TBSS applied



DTI for TBI (Traumatic Brain Injury); indicates changes that are not prominent with structural imaging

Red: FA(cntl) > FA(TBI)

Blue: MD(cntl) < MD(TBI)

Yellow: D_{ax}(cntl) < D_{ax}(TBI)

(Blue: D_{rad}(cntl) < D_{rad}(TBI))

KM Kinnunen, R Greenwood, JH Powell, R Leech, PC Hawkins, V Bonnelle, MC Patel, SJ Counsell, DJ Sharp. White matter damage and cognitive impairment after traumatic brain injury. Brain 134:449–463 (2011)

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Discussion & Conclusions

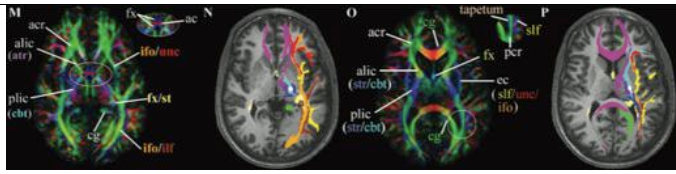
Tract-specific framework ("TSF")

PA Yushkevich, H Zhang, TJ Simon, JC Gee. Structure-specific statistical mapping of white matter tracts. NeuroImage, 41(2):448–461 (2008)

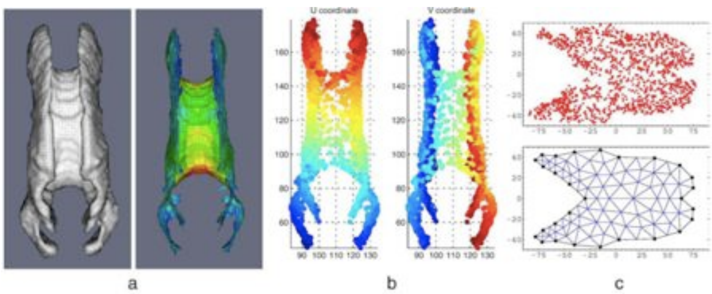
H Zhang, SP Awate, SR Das, JH Woo, ER Melhem, JC Gee, PA Yushkevich. A **tract-specific framework** for white matter morphometry combining macroscopic and microscopic tract features. Medical Image Analysis, 14(5):666–673 (2010)

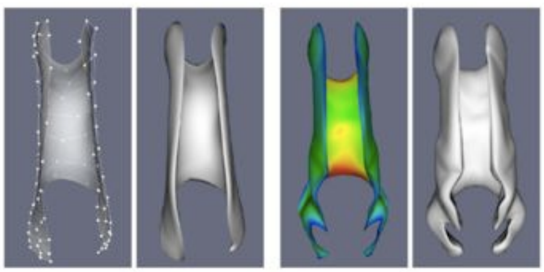
- Uses medial representations in **continuous** domain to **parameterize** representations of specific sheet-like tracts of interest
- Aims to increase sensitivity at cost of specificity
- Uses rasterizations of tractography to delineate tracts, then medial axis transform
- http://www.picsl.upenn.edu/Research/Research http://picsl.upenn.edu/Theme/DiffusionImaging

Steps in Tract-Specific Framework



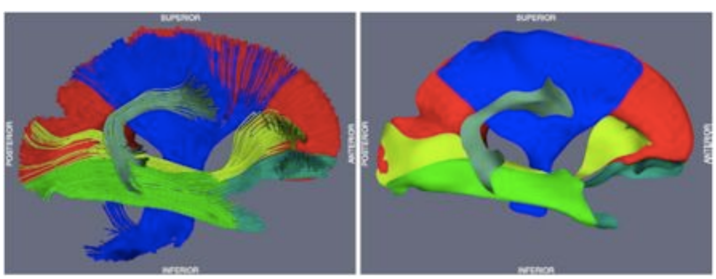
S Wakana, H Jiang, LM Nagae-Poetscher, PCM van Zijl, S Mori. Fiber tract-based atlas of human white matter anatomy. Radiology 30(1):77–87 (2004)



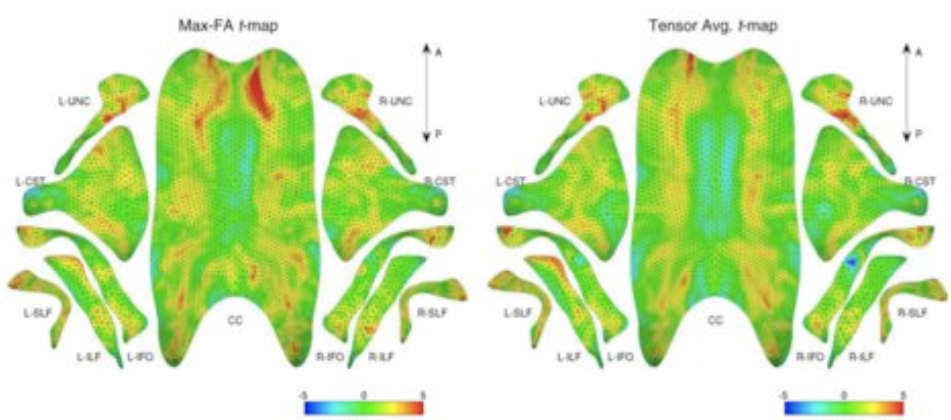


- Spatial normalization of all subjects' **tensor** images (including tensor reorientation)
- Tractography in tracts of interest according to Wakana et al.
- Rasterization processed by Voronoi pruning & manifold learning (Maximum Variance Unfolding) to recover low-DOF parameterization of underlying sheet
- Inverse Skeletonization optimizes fit of continuous medial representation of tractography (explicitly recovers tract thickness)

Using parametric representations



- Compute invariants and then project (like TBSS)
- Or average tensors and then compute invariants
- Leverage connection to known tract thickness



Out of image space, a real manifold: can connect to literature on cortical surface analysis

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Anisotropy Creases

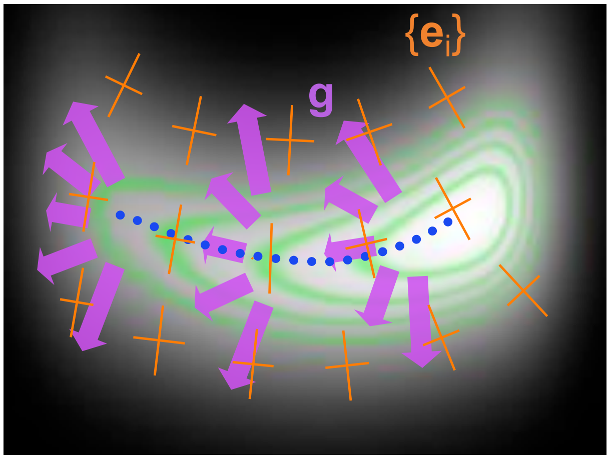
G Kindlmann, X Tricoche, C-F Westin. Delineating white matter structure in diffusion tensor MRI with anisotropy creases. Medical Image Analysis, 11(5):492–502, 2007

G Kindlmann, R San José, S M Smith, C-F Westin. Sampling and visualizing creases with scale-space particles. IEEE Trans. Vis. Comp. Graph., 15(6):1415–1424, 2009.

- Computes ridges of FA (like TBSS), but in the continuous domain (like TSF)
- Draws on basic Computer Vision
  - Ridge/valley feature definition
  - Scale-space for scale (blurring) selection
- Unlike TBSS & TSF: extracts features from single-subject scans, not group means
- Not (yet) used for group studies or available in tool

Differential Structure of image

Ridges & Valleys ("Creases") of **continuous** anisotropy map



"Ridges in Image and Data Analysis" Eberly '96

Constrained extremum

Gradient **g**

Hessian eigensystem $\mathbf{e}_i, \lambda_i$

Crease: **g** orthogonal to one or more $\mathbf{e}_i$

Eigenvalue gives **strength**

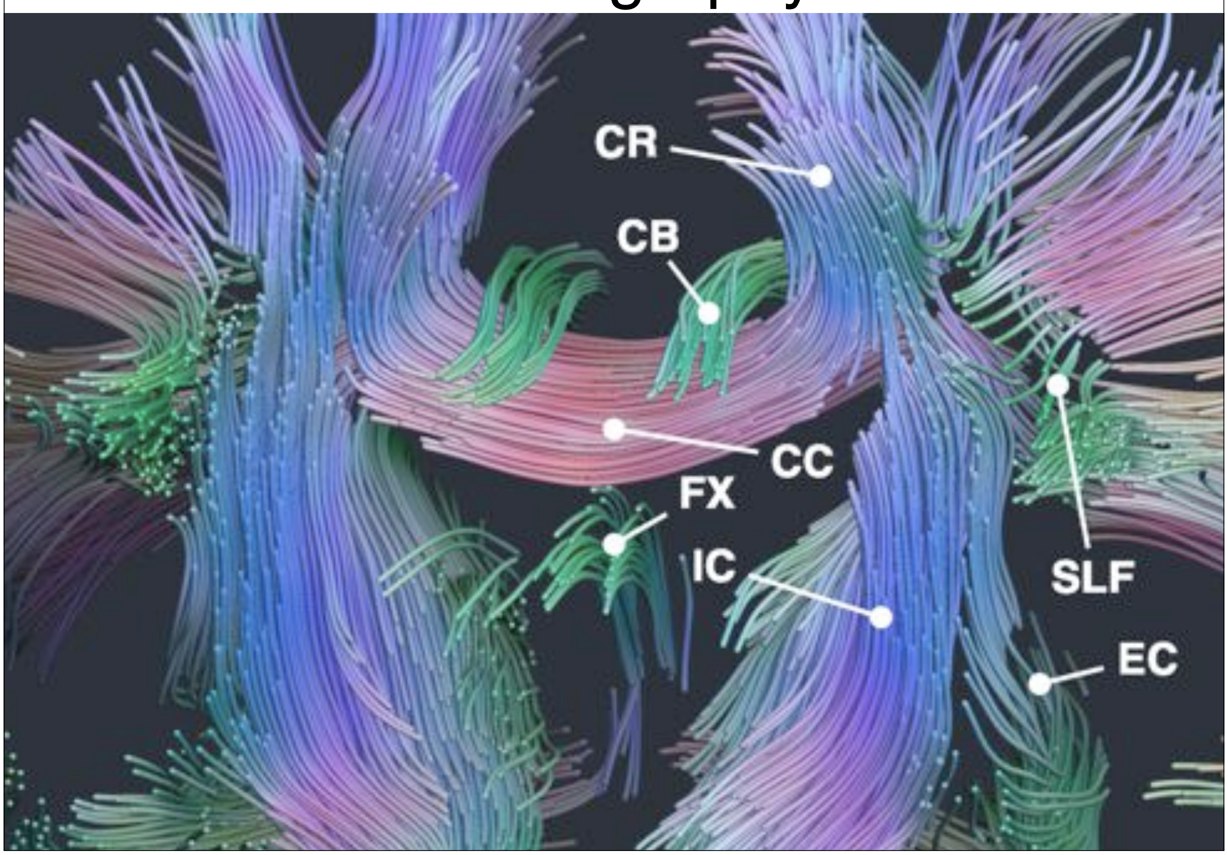
Ridge surface: $\mathbf{g} \cdot \mathbf{e}_3 = 0$; $\lambda_3 <$ thresh

Ridge line: $\mathbf{g} \cdot \mathbf{e}_3 = \mathbf{g} \cdot \mathbf{e}_2 = 0$; $\lambda_3, \lambda_2 <$ thresh

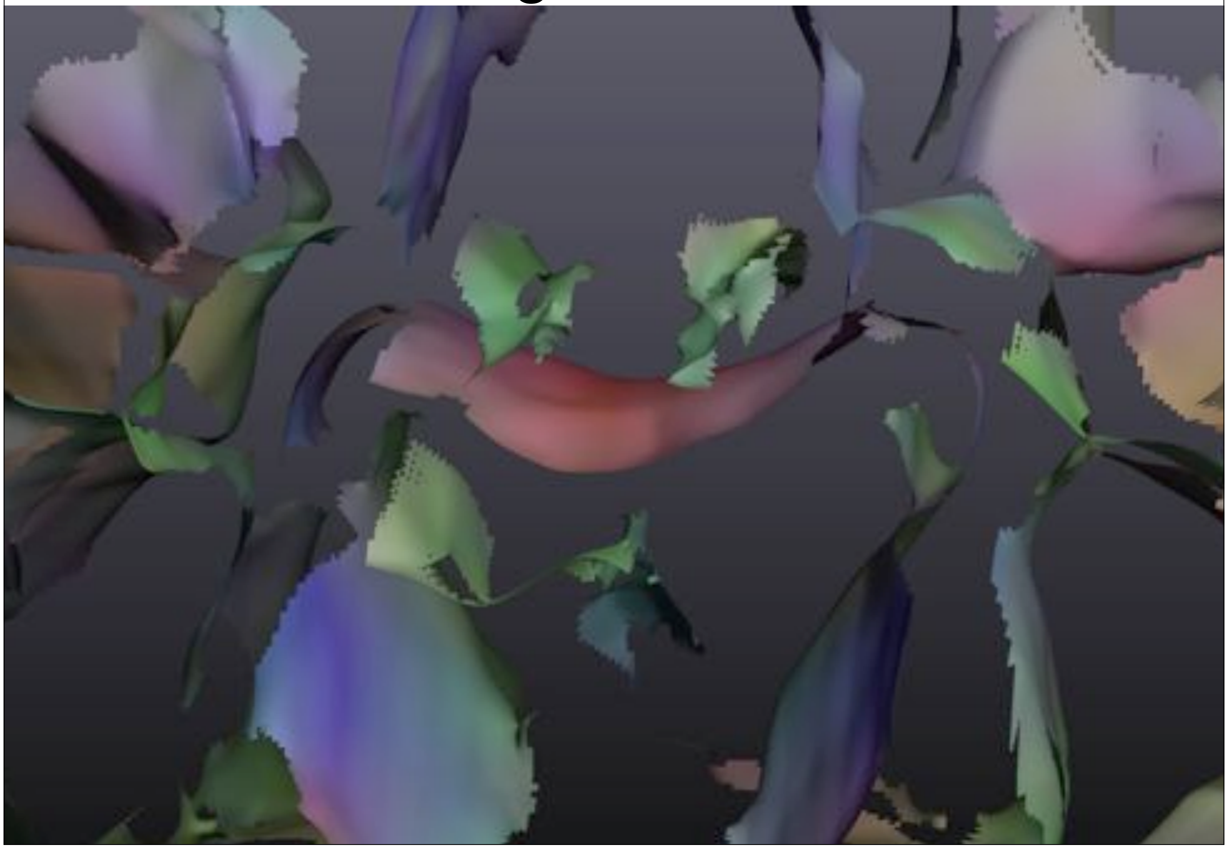
Valley surface: $\mathbf{g} \cdot \mathbf{e}_1 = 0$; $\lambda_1 >$ thresh

TBSS is a raster representation of the ridge surfaces of FA

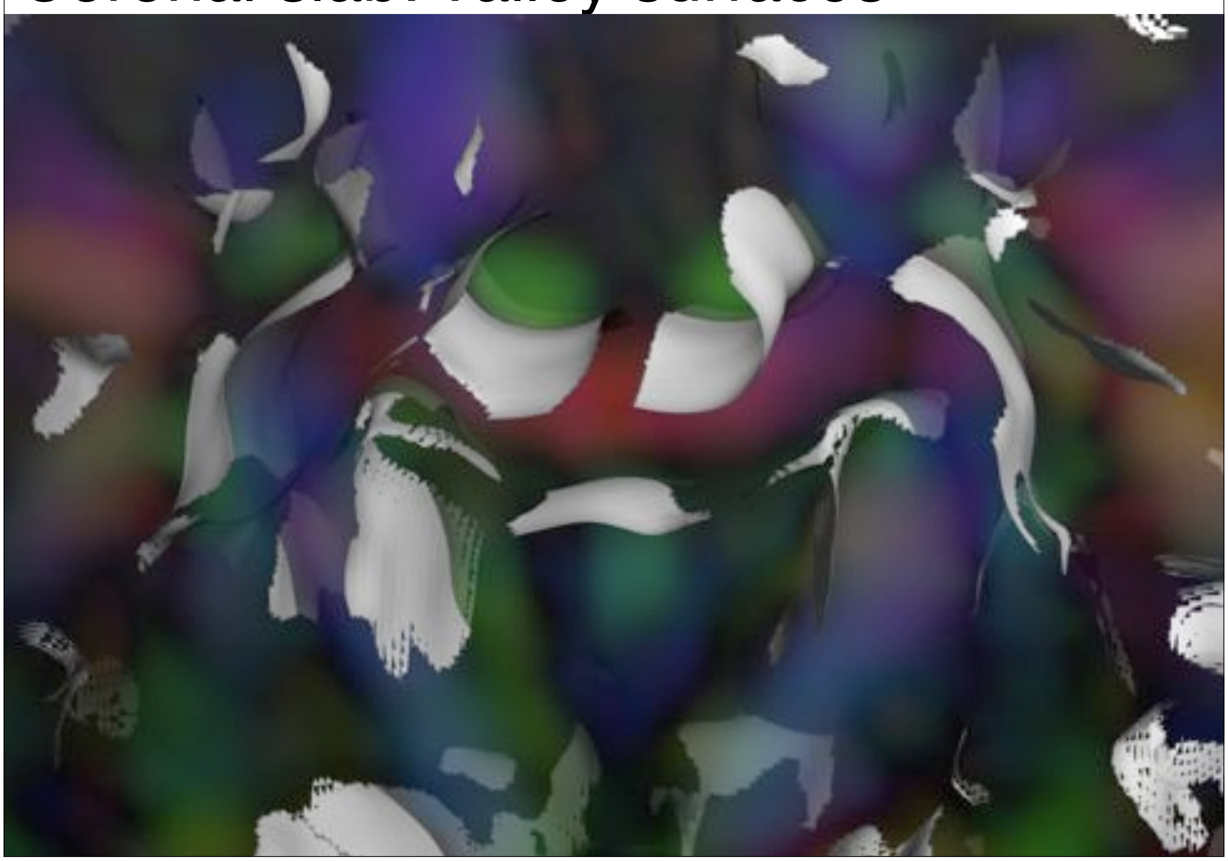
Coronal slab: tractography



Coronal slab: ridge surfaces



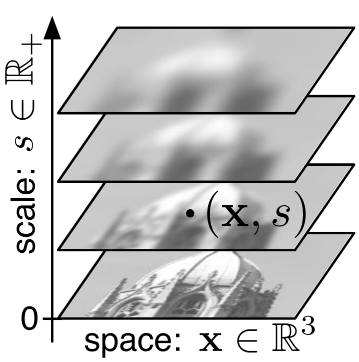
Coronal slab: valley surfaces

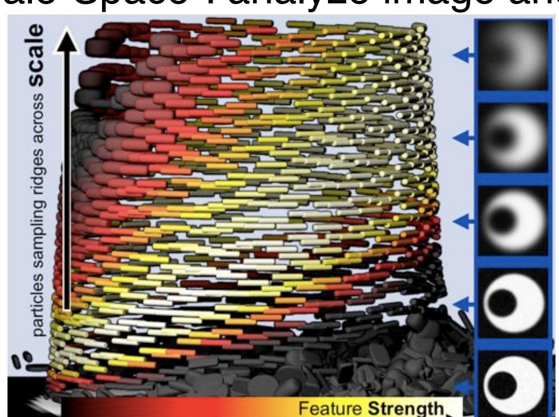


Coronal slab: tractography + valleys

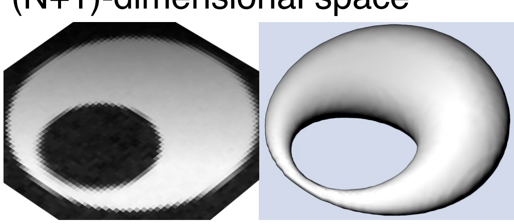
How to choose scale (amount of blurring)?

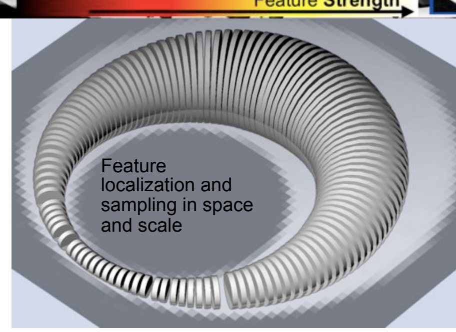
Computer vision notion of "Scale-Space": analyze image and all blurrings simultaneously





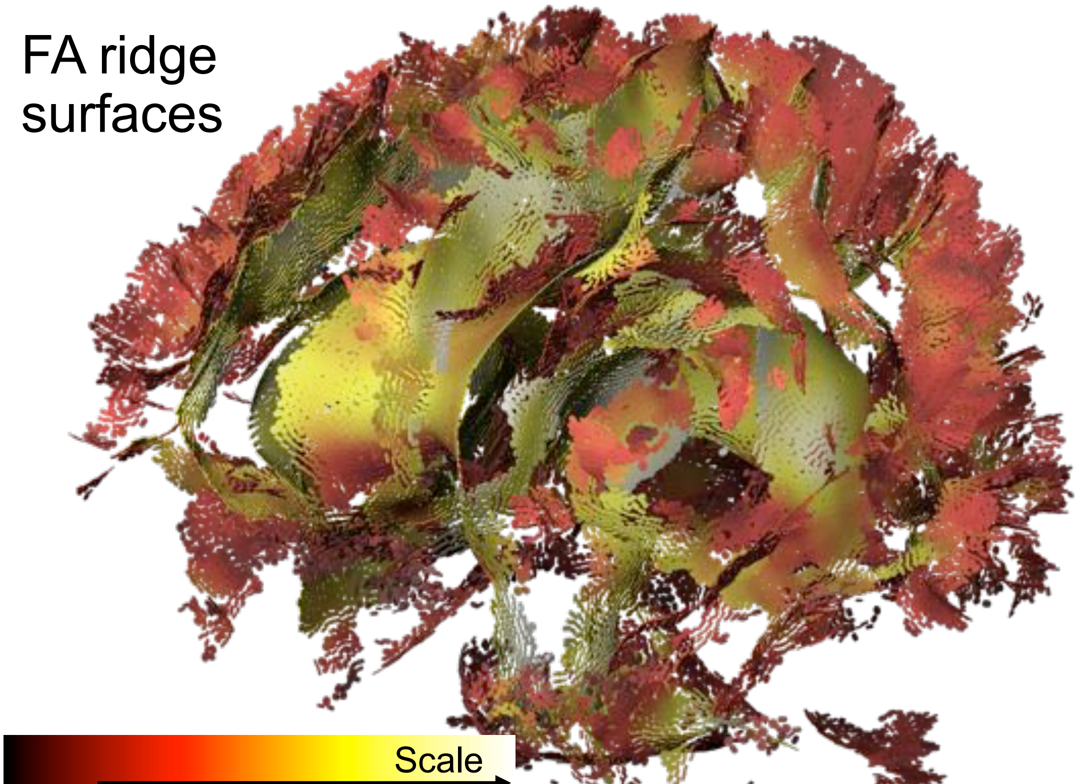
Features exist as manifolds in (N+1)-dimensional space



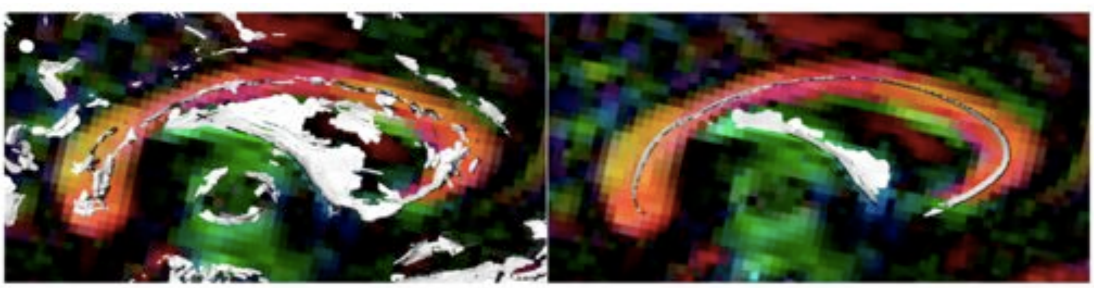


Brain DTI Results

FA ridge surfaces

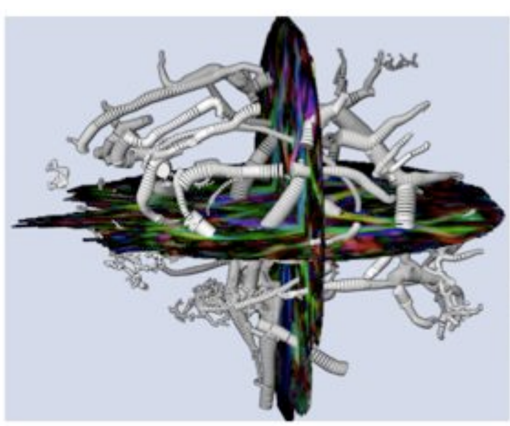


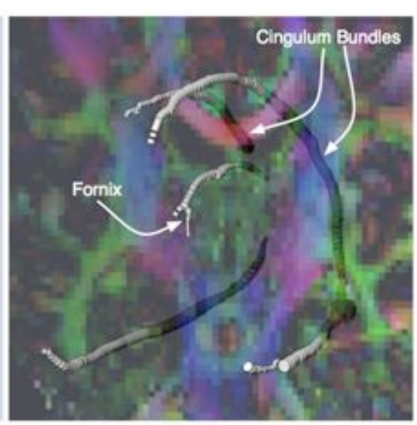
Brain DTI Results



Without Scale-Space With Scale-Space

FA ridge **lines**





Outline

Pictorial overview of DT-MRI data

Geomtric intuition for commonly studied tensor invariants

Three (non-tractography) methods of DTI analysis:

- Tract-based Spatial Statistics (Smith et al.)
- Tract-Specific Framework (Yushkevich, Zhang, Gee et al.)
- Anisotropy Creases (Kindlmann at al.)

Discussion & Conclusions

Discussion & Conclusions

Can use these examples to ponder space of DTI analysis ...

Role of Raster vs Continuous Representation

Represent “middle” only, or both middle and boundary

Exploratory vs Model-based Analysis

Interaction with Tractography

Role of Anisotropy (FA) Thresholding

Role of scale (blurring), and setting of scale

Role of Non-rigid Registration as means of learning correspondence (necessary?)

Basic question: How should we assess the correlation between mathematical features and anatomical features? (given reservations about single tensor model)

Thank you

Follow-up: glk@uchicago.edu