MICCAI Diffusion MRI Tutorial

Part 1: Diffusion MRI Analysis in Broad Strokes

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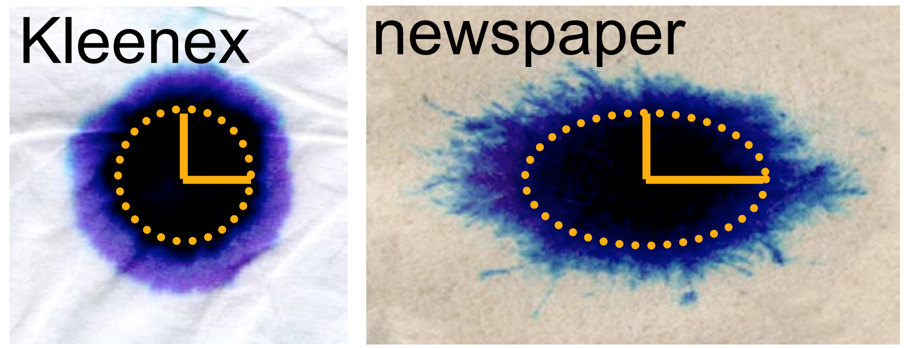
Overview

1. Diffusion Tensor MRI
2. Structural connectivity from diffusion MRI
3. White matter anatomy from connectivity

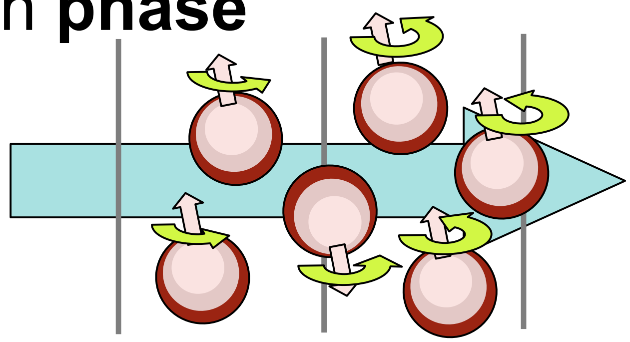
Diffusion-weighted MRI (DW-MRI)

Brownian motion of one material through another

Anisotropy: diffusion rate depends on direction



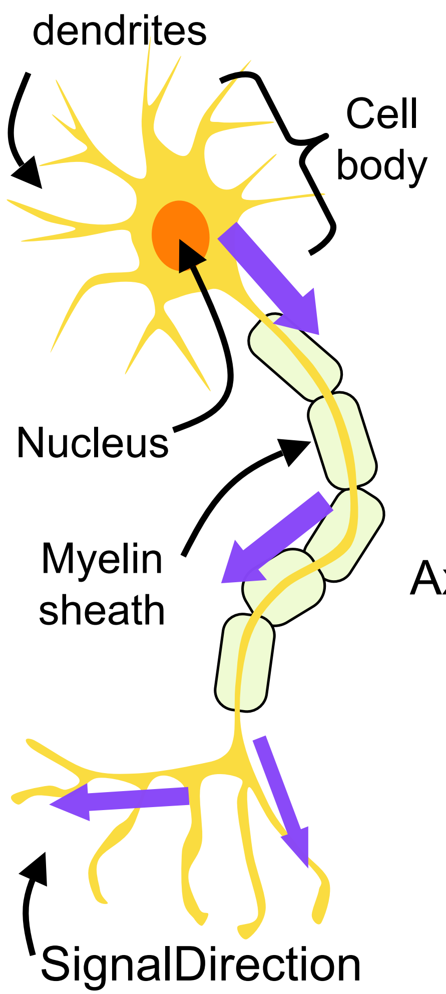
Magnetic gradients create spatial planar waves of proton **phase**



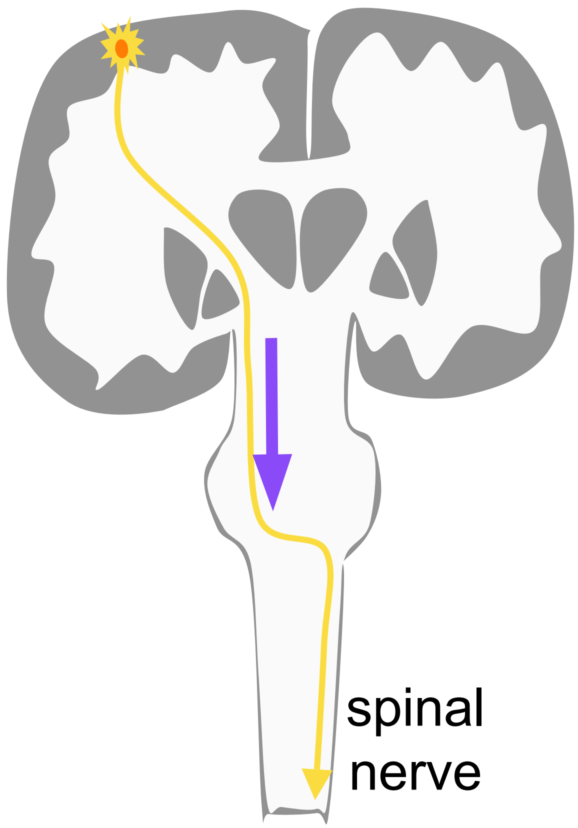
Destructive interference measures diffusion along gradient direction only

Underlying Biology (Simplified!)

Neuron:



Brain:

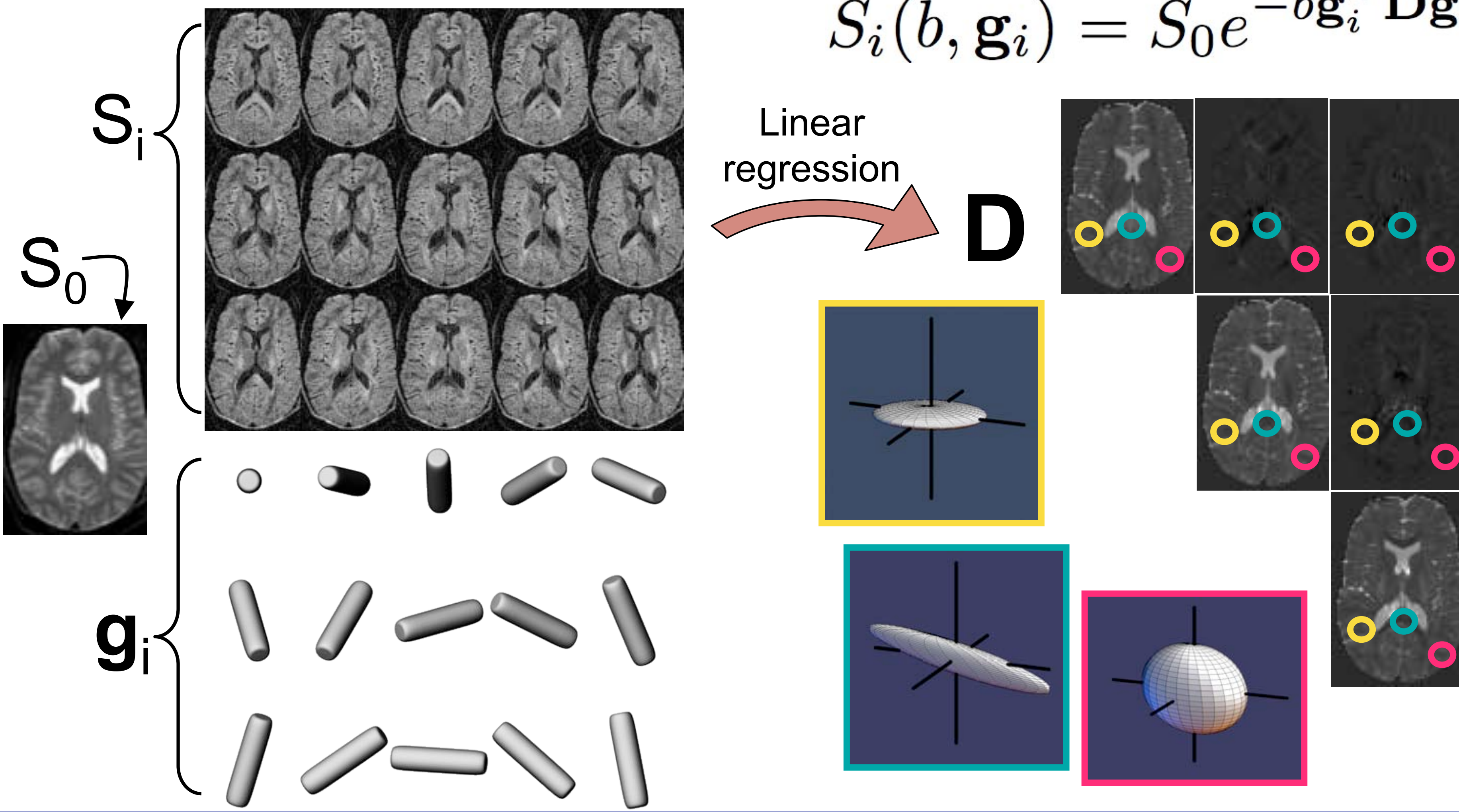


- Gray matter (cortex + nuclei): cell bodies
- White matter: axons
- Myelin sheath speeds signal conduction
- Axon + sheath = nerve fibers
- Major white matter pathways aggregate many fibers into bundles

Multiple DWI → Tensor Estimate

Single Tensor Model (Basser 1994)

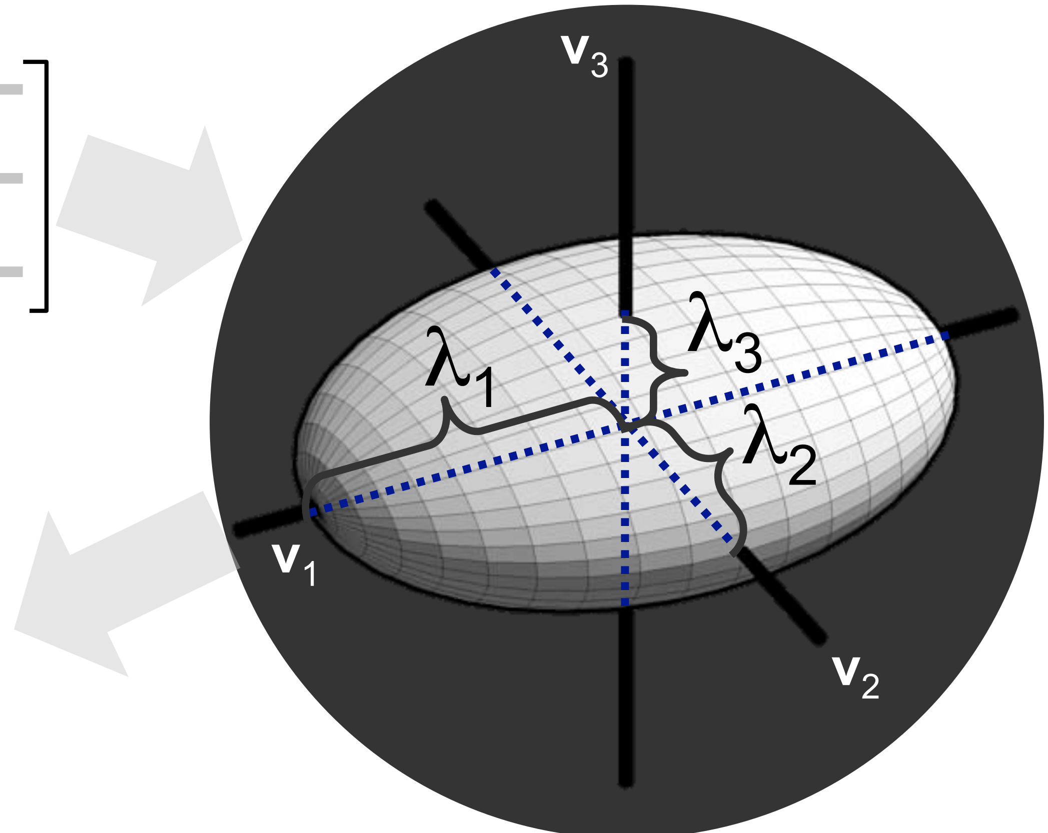
$$S_i(b, \mathbf{g}_i) = S_0 e^{-b\mathbf{g}_i^T \mathbf{D}\mathbf{g}_i}$$

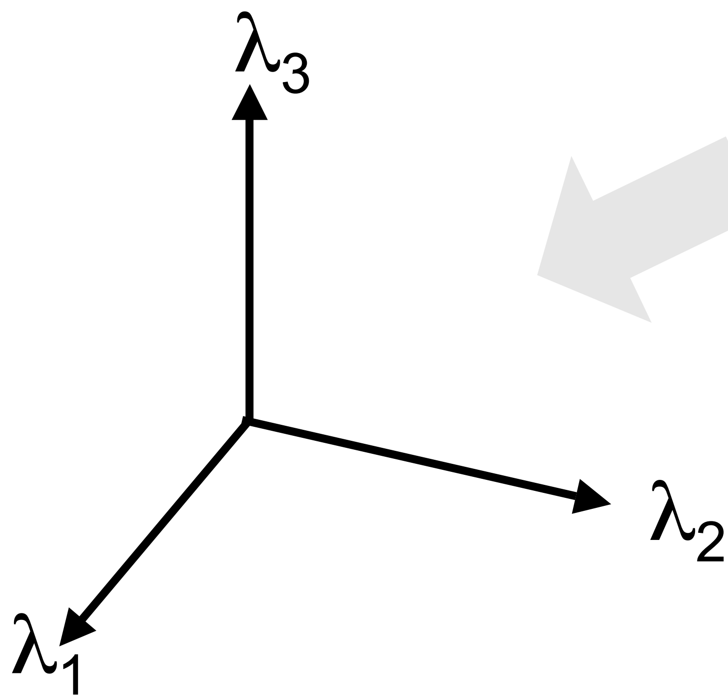


Eigenvalues == Shape

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

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

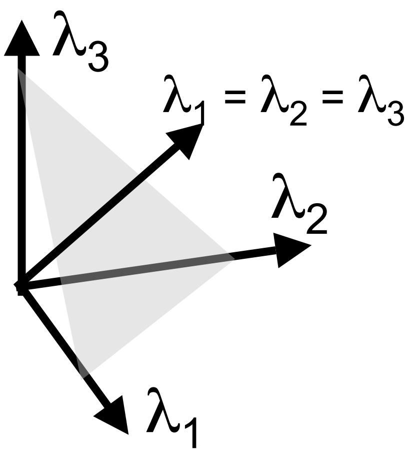


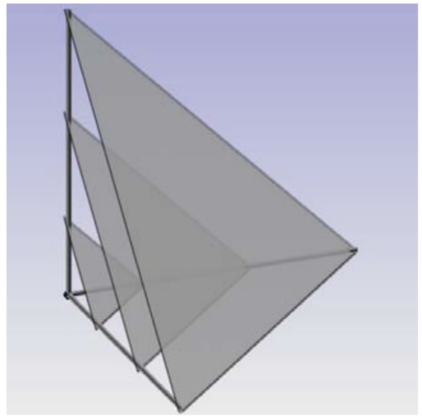


Tensor invariants as orthogonal shape parameterizations

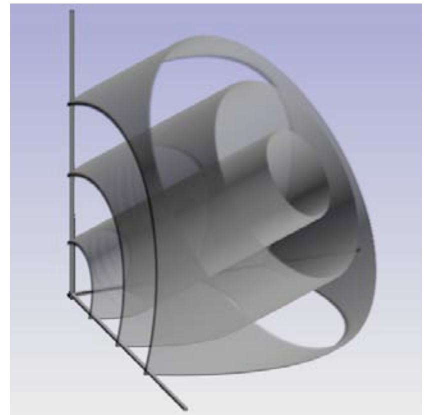
Cylindrical or spherical coordinates

(Ennis+Kindlmann 2005)

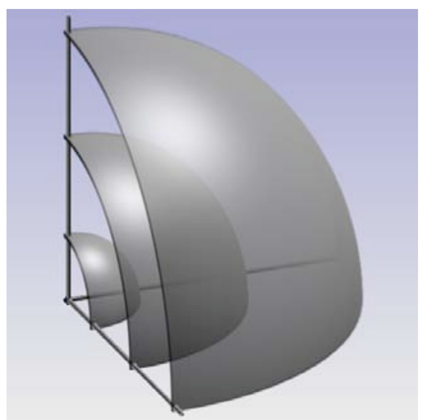




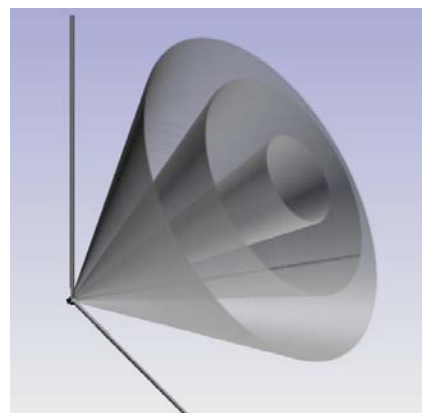
tr(**D**)



|**E**|

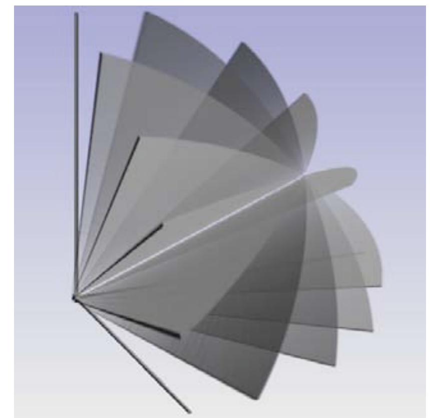


|**D**|



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

FA = **Fractional Anisotropy**



mode(**E**)

= det(**E**/|**E**|)

(Criscione ‘00)

Mode measures Linear vs. planar anisotropy

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

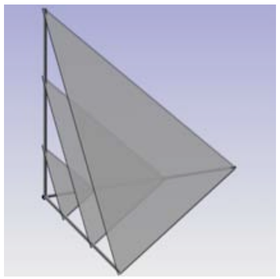
|**D**| = sqrt(tr($\mathbf{D}^T\mathbf{D}$))

E = deviatoric(**D**)

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

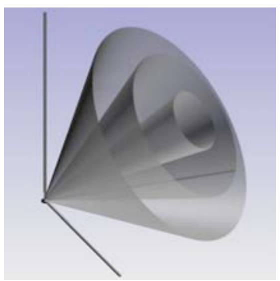
Biological Meaning of Tensor Shape

Size: **bulk mean diffusivity** (“ADC”)



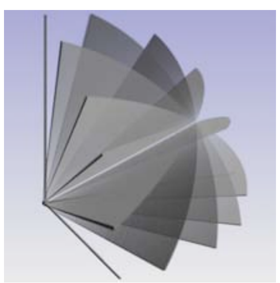
- ADC strictly speaking diffusivity along **one** direction
- Note: same across gray+white matter, high in CSF
- Indicator of acute ischemic stroke

Anisotropy (e.g. FA): directional microstructure



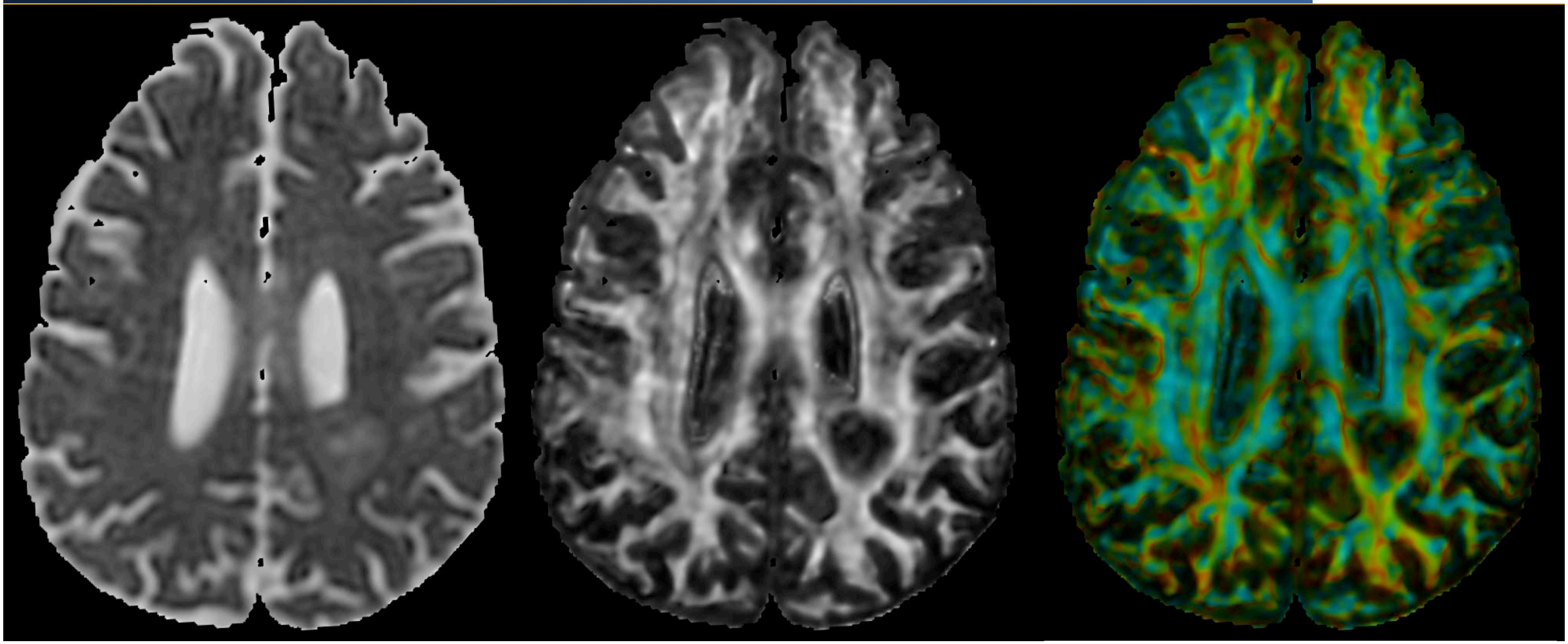
- High in white matter, low in gray matter and CSF
- Increases with myelination, decreases in some diseases (Multiple Sclerosis)

Mode: linear versus planar



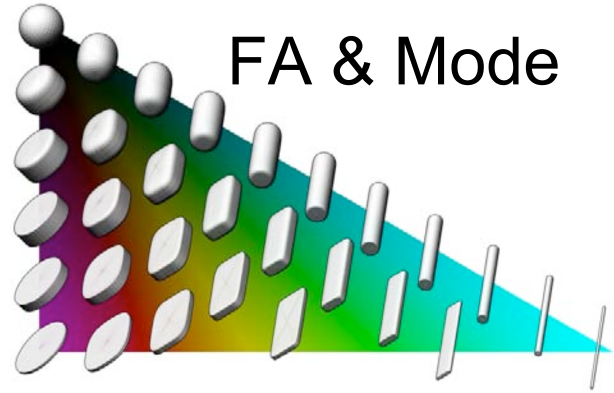
- Partial voluming of adjacent orthogonal structures
- Fine-scale mixing of diverse fiber directions
- Tensor fitting error increases with planarity (Tuch 2002)

Tensor shape on one slice



Trace

Fractional **A**nisotropy



FA & Mode

"Anisotropy" is a bivariate quantity

Overview

1. Diffusion Tensor MRI
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3. White matter anatomy from connectivity

"Connectivity" from dMRI

Examples of very different methods:

1. Principal Diffusion Direction (PDD) Tractography
2. Stochastic Methods, can model uncertainty
3. Geometric, Geodesic approaches

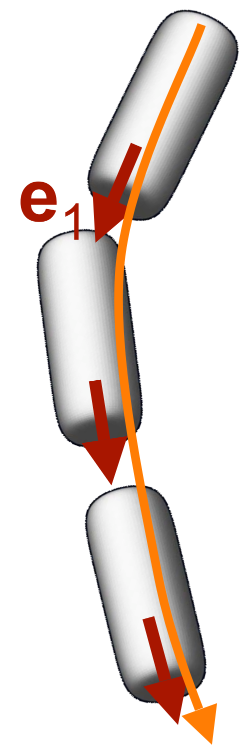
Fiber Tractography (Basser 1999)

Path integration along principal eigenvector

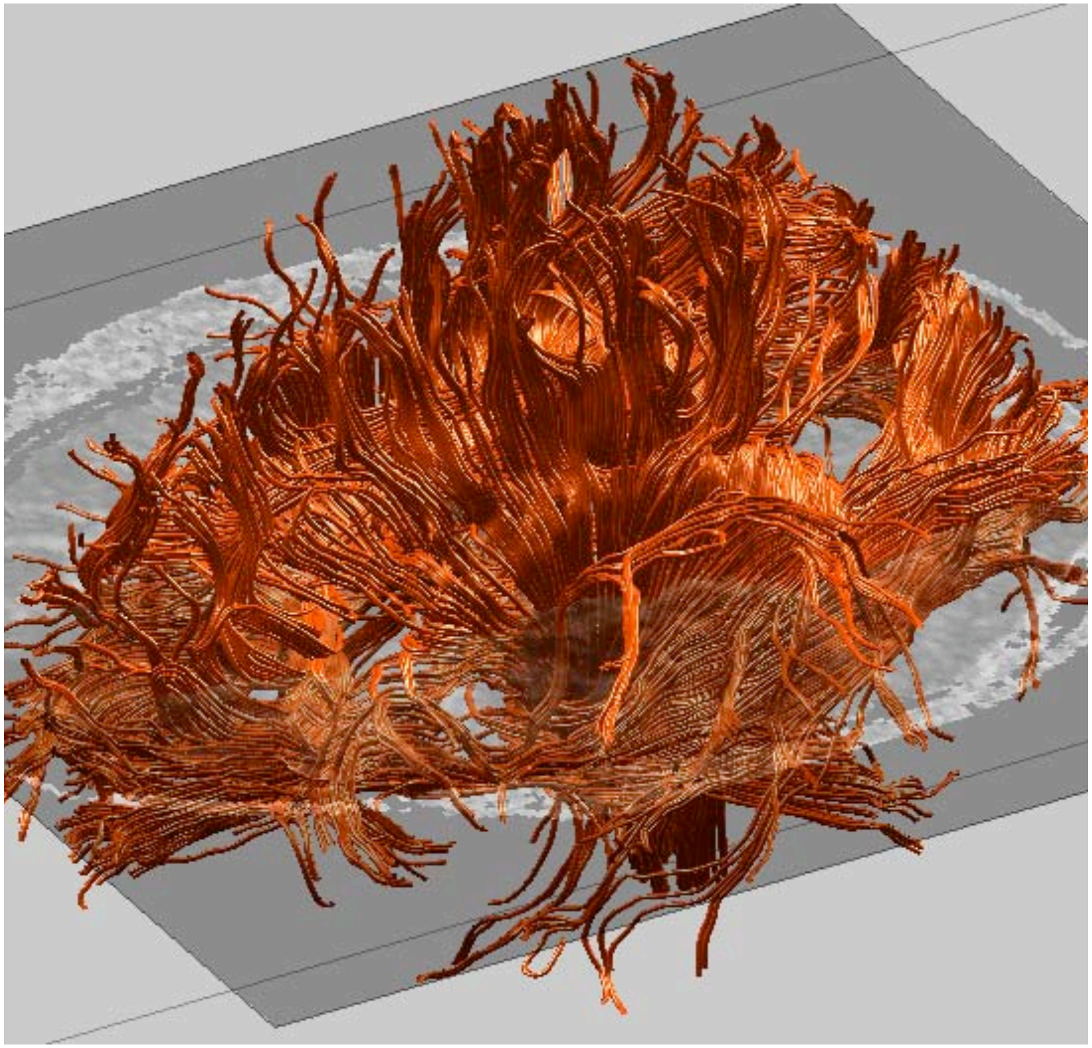
Idea/Fantasy: follow paths of individual axons!

- Reality: 2-3 orders of magnitude too coarse

Essentially same as simplified hyperstreamlines (Delmarcelle 1993)



Tractography



Fiber Tractography Issues

- Tensor Field Interpolation/Filtering
- Integration quality, step size
  - Eigensolve at every sample non-trivial
- Seedpoint selection determines path
- Termination criteria
- Parameter space → Reproducibility, Validation

"Connectivity" from dMRI

Examples of very different methods:

1. Principal Diffusion Direction (PDD) Tractography
2. Stochastic Methods, can model uncertainty
3. Geometric, Geodesic approaches

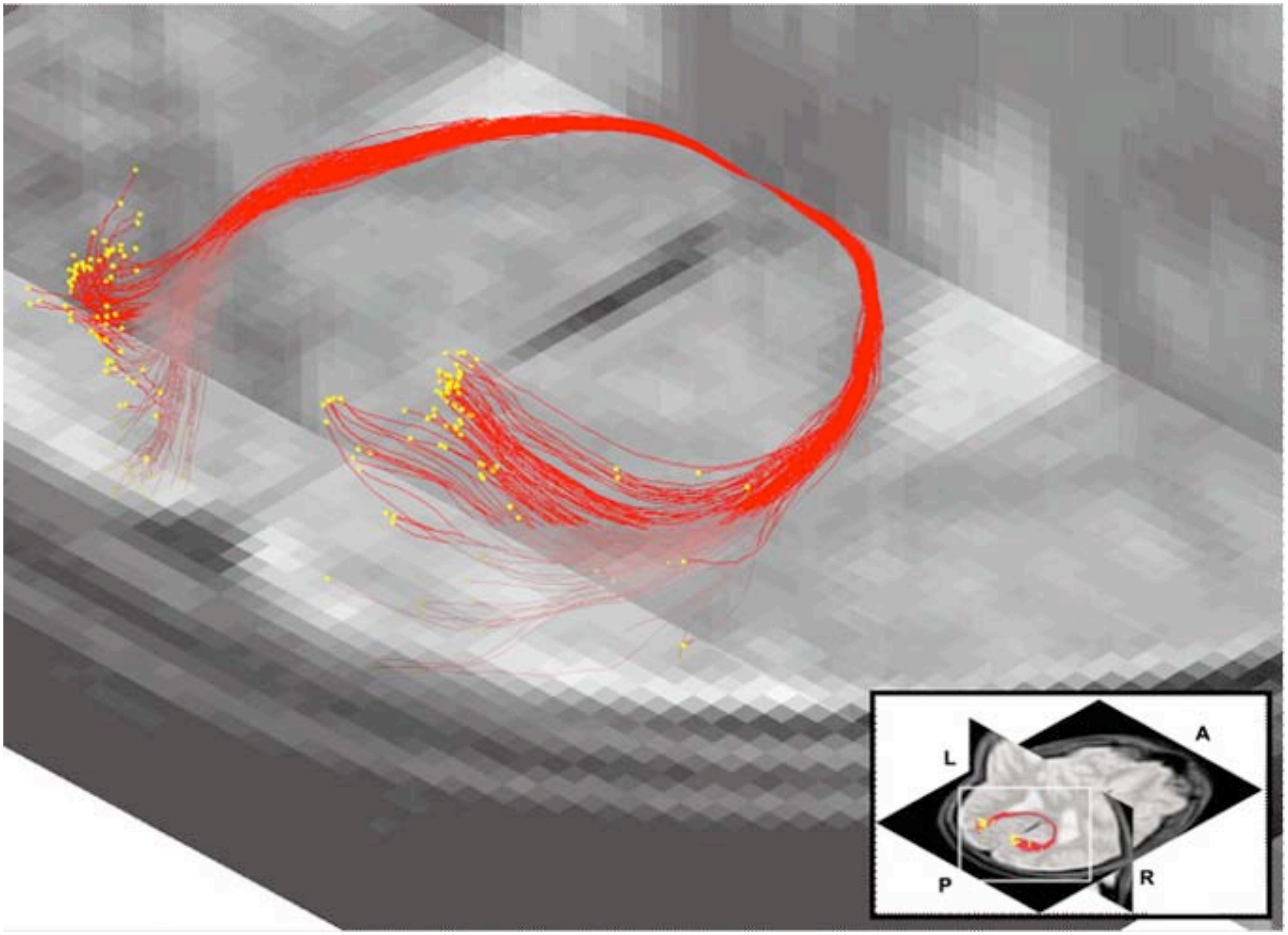
Stochastic Tractography

Brun, Westin, **Regularized Stochastic White Matter Tractography Using Diffusion Tensor MRI:** Monte Carlo, Sequential Importance Sampling and Resampling. MICCAI 2002.

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 Division of Health Sciences and Technology, 2002

Stochastic tractography: fiber distributions



Non-parametric approaches: Bootstrap

Pajevic and Basser, JMR 2003

Jones and Pierpaoli, MRM 2005

Lazar and Alexander, Neuroimage 2005

A drawback with non-parametric approaches is that they require a lot of data, and thereby also scanning times that may be unacceptable.

Parametric Approaches: Bayesian

Behrens, et al. *Characterization and propagation of uncertainty in diffusion-weighted MR imaging*,MRM 2003

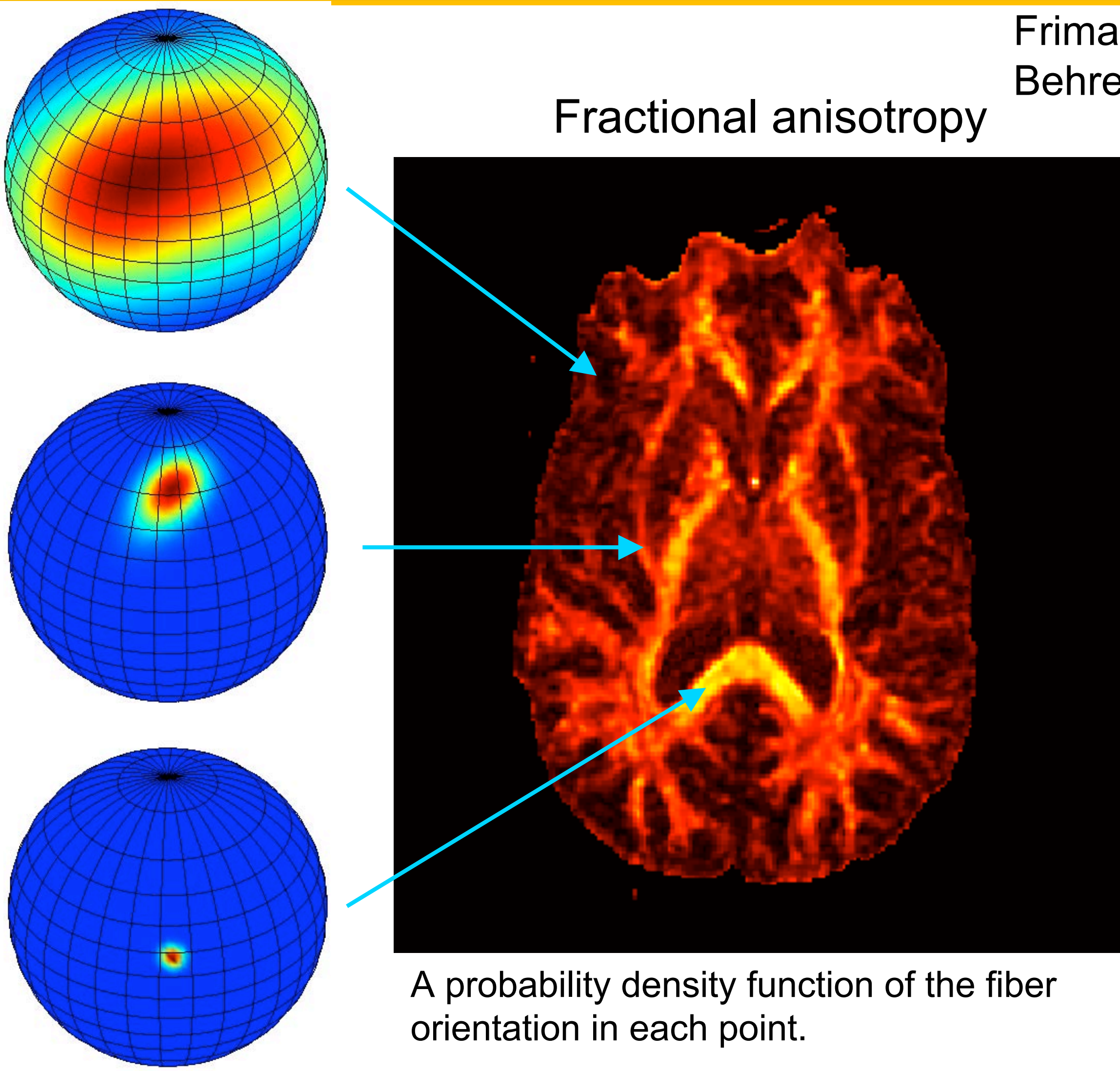
Friman, Westin. *Uncertainty in white matter tractography*, MICCAI 2005

Friman, Farneback, Westin. *A Bayesian Approach for Stochastic White Matter Tractography*, IEEE Trans Med Imaging 2006

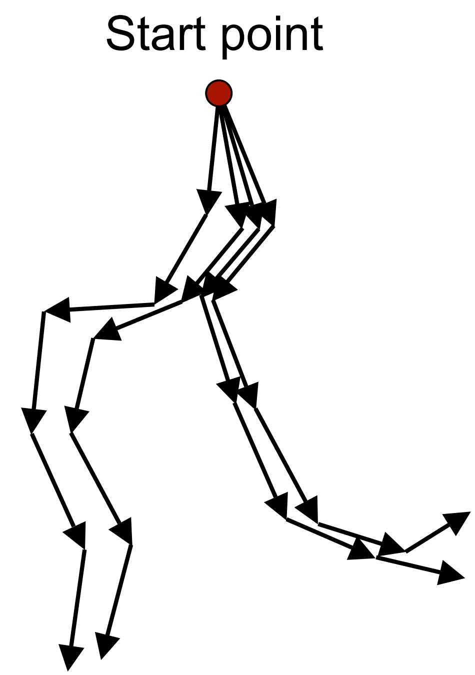
Stochastic tractography

Friman, Westin MICCAI 2005, TMI 2006
Behrens MRM 2003, Brun MICCAI 2002

Fractional anisotropy



A probability density function of the fiber orientation in each point.



In every step, draw a step direction from the pdf of the underlying fiber orientation.

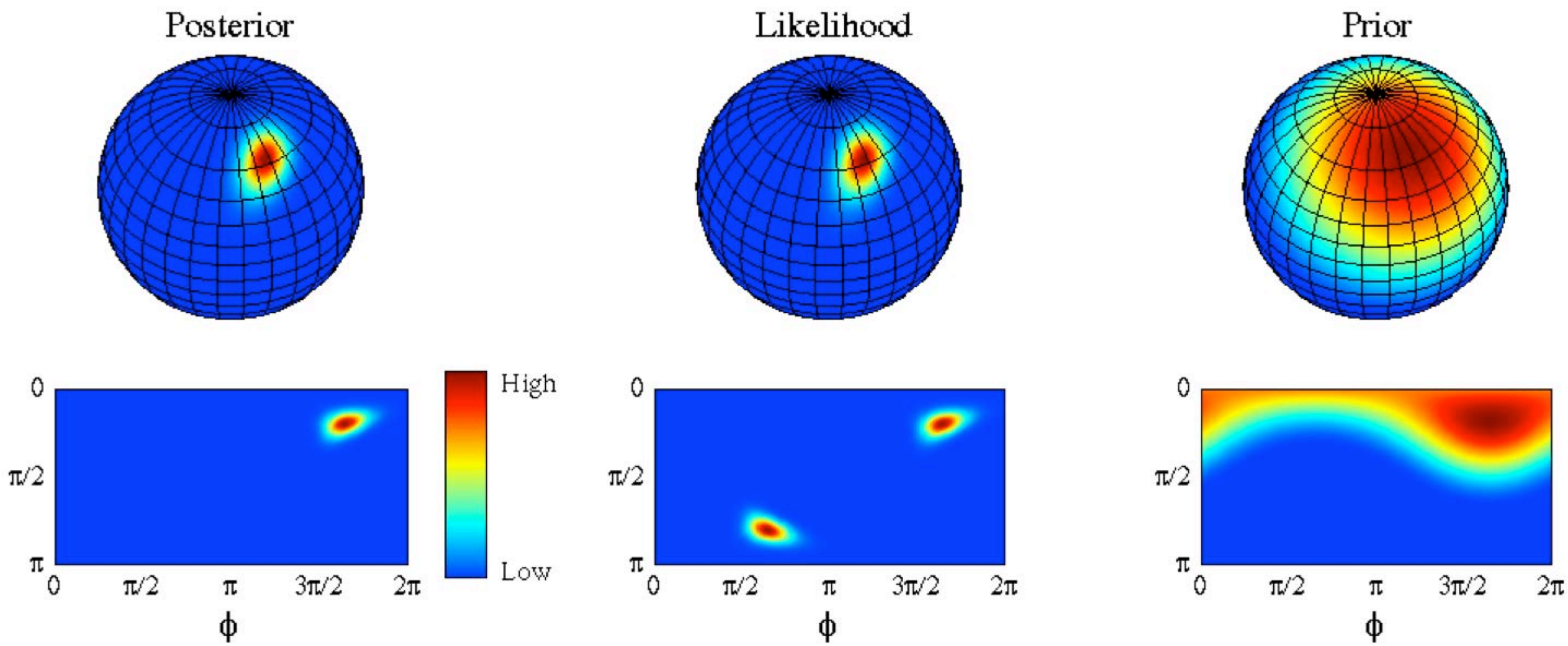
Bayesian Approach

Bayes' rule: $p(\mathbf{v}_k \mid \text{diffusion data}, \mathbf{v}_{k-1}) \propto p(\text{diffusion data} \mid \mathbf{v}_k)\, p(\mathbf{v}_k \mid \mathbf{v}_{k-1})$

Posterior distribution of next step direction $\mathbf{v}_k$ given the diffusion measurements and the previous step direction $\mathbf{v}_{k-1}$

Likelihood function of the diffusion measurements given an underlying fiber orientation $\mathbf{v}_k$. Models the noise and water diffusion.

Prior distribution of next step direction $\mathbf{v}_k$ given the previous step direction $\mathbf{v}_{k-1}$. Provides regularization of the fiber paths.



Constrained tensor model

Tensor model of local water diffusion:

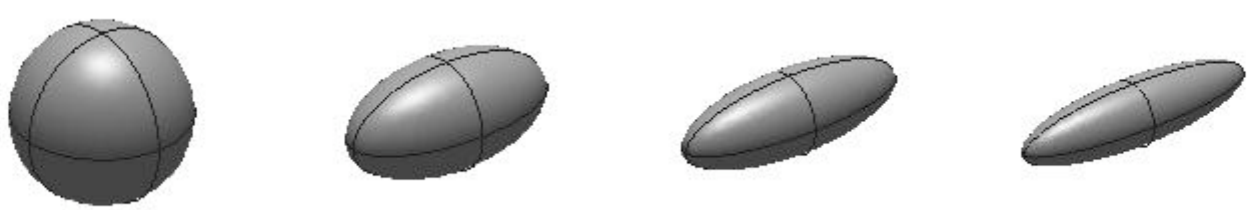
$$\mu_i = \mu_0 e^{-b_i \mathbf{g}_i^T \mathbf{D} \mathbf{g}_i}$$

Constrained tensor model where $\lambda_2 = \lambda_3$:

$$\mu_i = \mu_0 \underbrace{e^{-\alpha b_i}}_{\text{Isotropic}} \underbrace{e^{-\beta b_i \left(\mathbf{g}_i^T \mathbf{v}\right)^2}}_{\text{Anisotropic}}$$

Models the effect of a single underlying fiber bundle.

Multiple fiber orientations, and the oblate tensor case, will be reflected as increased uncertainty in the fiber orientation.



Constrained tensor model estimation

Constrained tensor model easy to estimate!

Baseline intensity, Isotropic diffusion, Anisotropic diffusion, Fiber direction

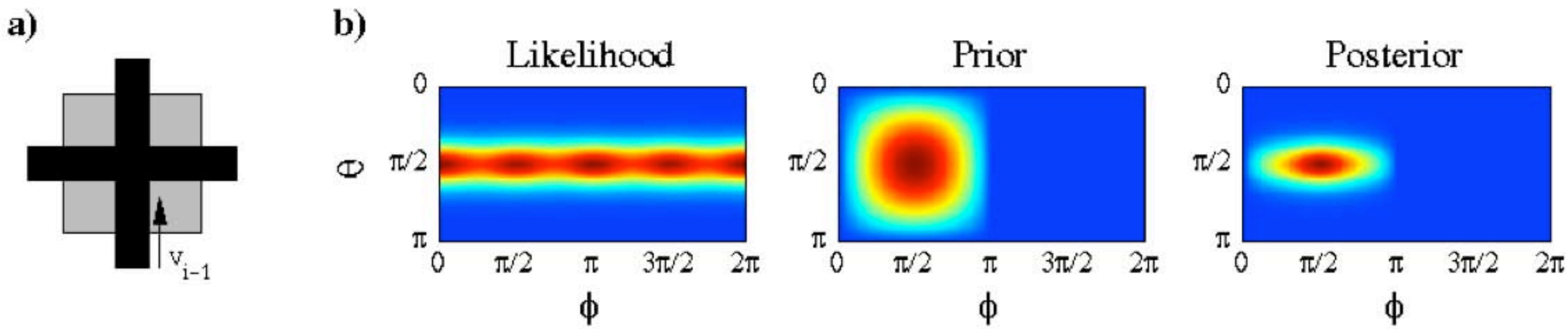
$$\mu_i = \mu_0 e^{-\alpha b_i} e^{-\beta b_i \left(\mathbf{g}_i^T \mathbf{v}\right)^2}$$

1. Estimate traditional tensor model which gives μ_0 and diffusion tensor

$$\mathbf{D} = \lambda_1 \mathbf{v}_1 \mathbf{v}_1^T + \lambda_2 \mathbf{v}_2 \mathbf{v}_2^T + \lambda_3 \mathbf{v}_3 \mathbf{v}_3^T, \quad \lambda_1 \geq \lambda_2 \geq \lambda_3$$

2. Set $\alpha = \frac{\lambda_2 + \lambda_3}{2}$ $\quad \beta = \lambda_1 - \alpha$ $\quad \mathbf{v} = \mathbf{v}_1$

Multiple fiber orientations



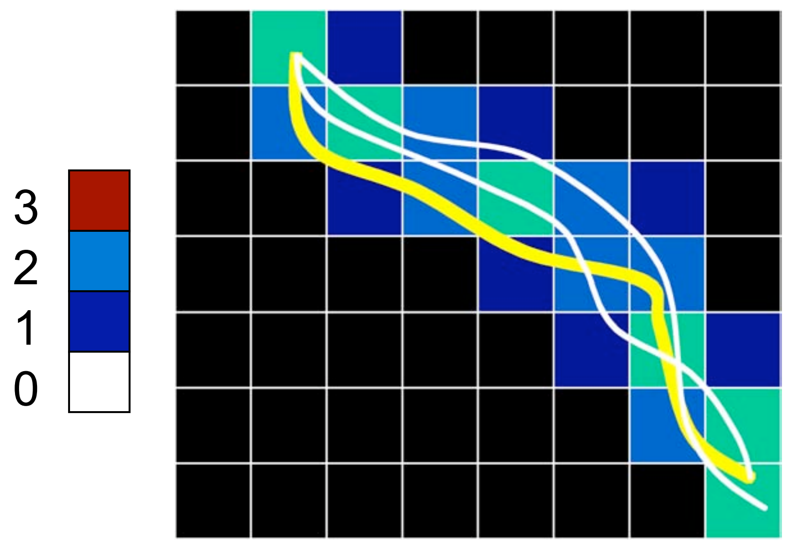
a) A schematic image of the fiber crossing used as basis for simulating diffusion measurements.

b) Assuming we are tracking the vertical fiber gives the prior above. The posterior is the produce of the prior and the likelihood.

The model miss-match results in increased uncertainty in the plane of crossing fibers.

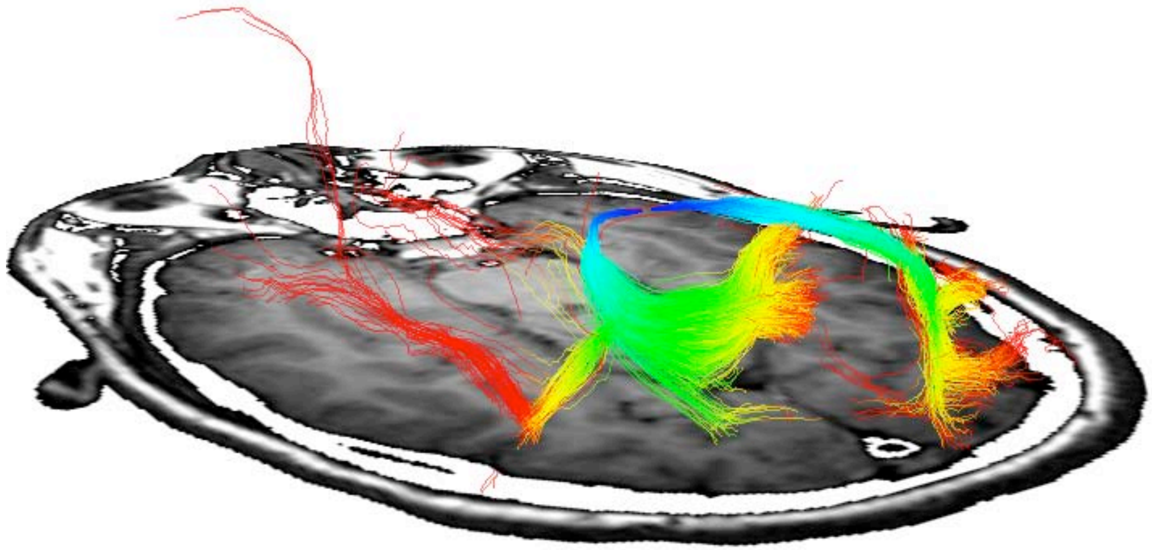
Probability of connection

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

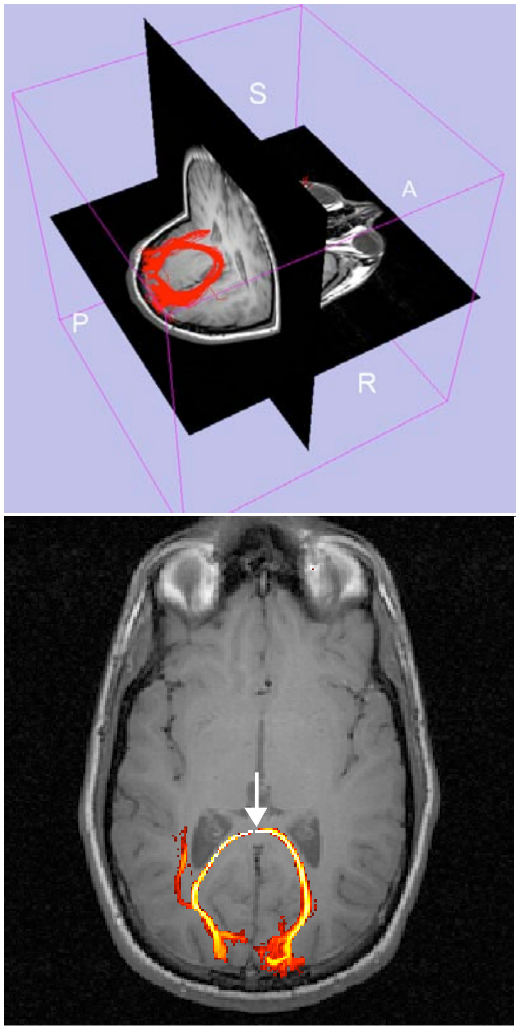
Stochastic tracking results



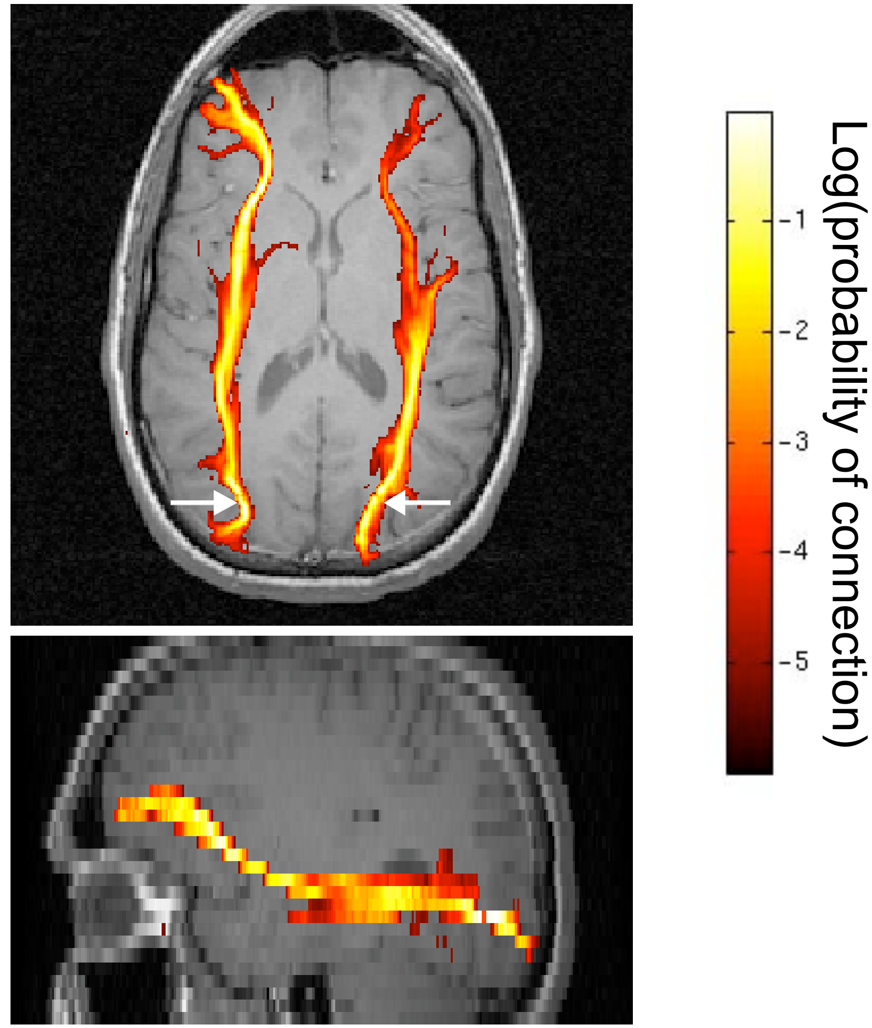
3,000 fiber samples initiated in the splenium of Corpus callosum. The coloring indicates the probability along each path to end up is a specific area.

Probability of connection

Corpus callosum



Inferior occipitofrontal fasciculi



Work with O. Friman

“Connectivity” from dMRI

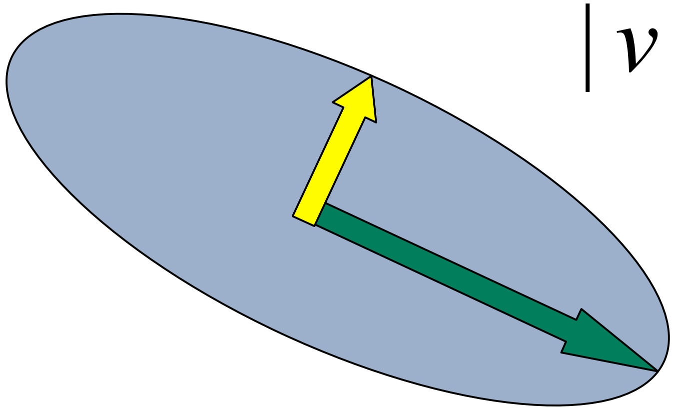
Examples of very different methods:

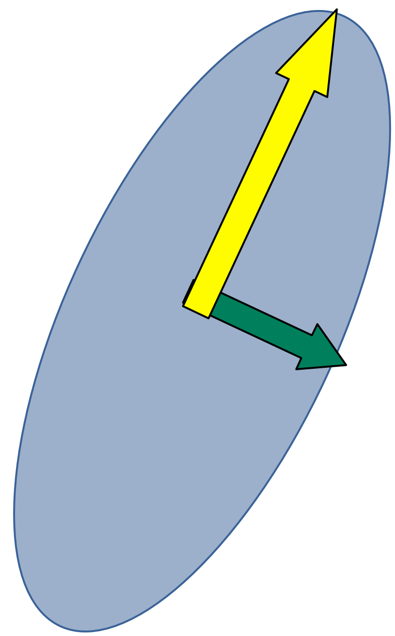
1. Principal Diffusion Direction (PDD) Tractography
2. Stochastic Methods, can model uncertainty
3. Geometric, Geodesic approaches

Geodesic Connectivity

Connectivity should be proportional to distance in some metric space.

$$|v|^2 = v^T G v$$





Diffusion Tensor, D Metric Tensor, $G = D^{-1}$

O'Donnell, Haker, Westin, MICCAI 2002

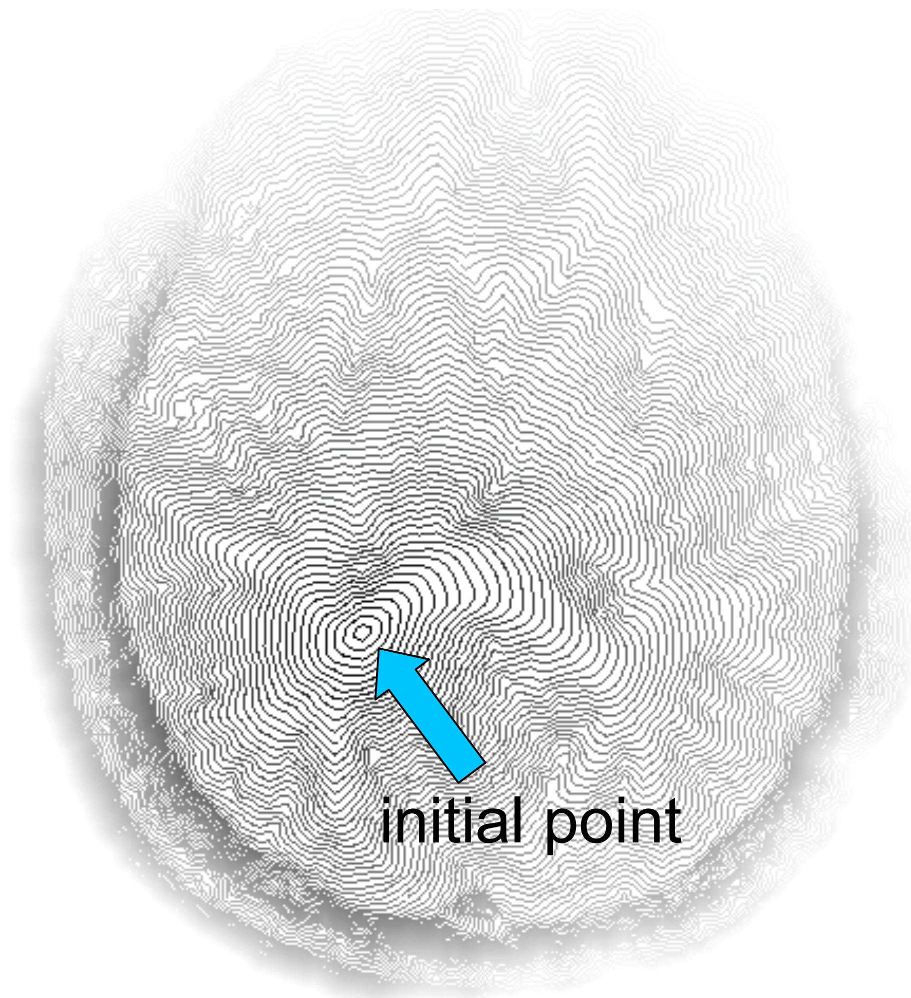
Riemannian Distance Map

Input: Riemannian metric tensor G.

Input: initial point

Output: geodesic paths.

Output: distances between points in the brain.

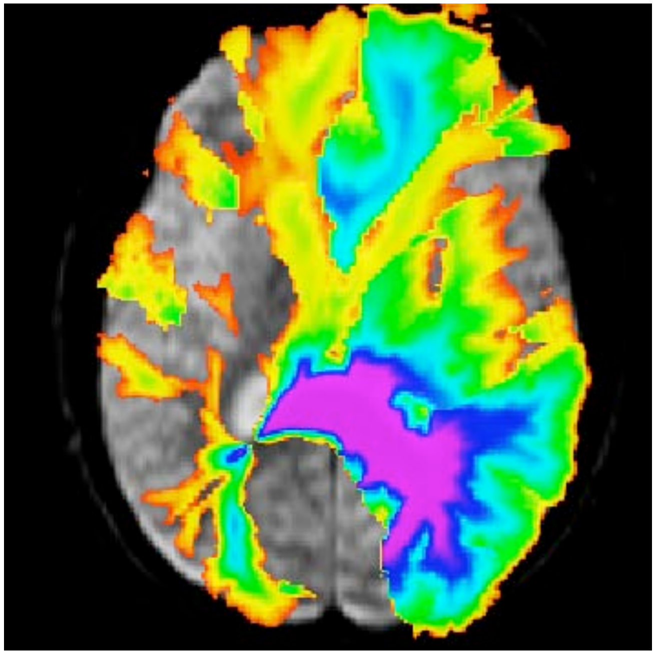


Color-coded Connectivity

The length of the shortest (geodesic) path between two points indicates connectivity.

One measure of connectivity:

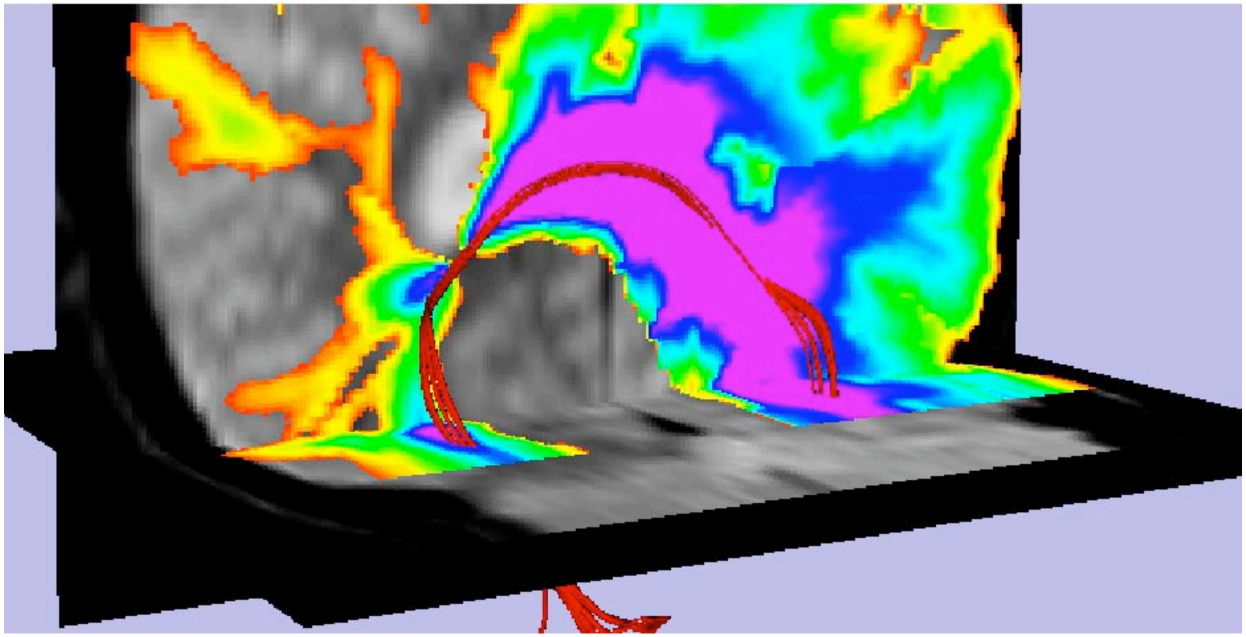
$$C = \frac{\text{Euclidean path length}}{G\text{-metric path length}}$$



Color-coded Connectivity

Computed connectivity measure in 3D

PDD Tractography visualization passes through highest-connectivity region.



Geodesic Connectivity

Geodesic connectivity based on the inverse diffusion tensor as Riemannian metric:

O'Donnell, Haker, Westin, MICCAI 2002

Lenglet, Deriche, Faugeras. Inferring White Matter Geometry from Diffusion Tensor MRI: Application to Connectivity Mapping, ECCV 2004

Fletcher, Tao, Jeong, Whitaker, A Volumetric Approach to Quantifying Region-to-Region White Matter Connectivity in Diffusion Tensor MRI, IPMI 2007

Geodesic Connectivity

What happens of the metric cannot be described by a tensor?

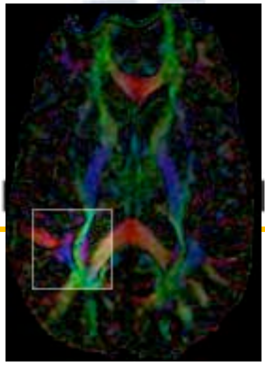
High Angular Diffusion Imaging (HARDI) data can be used for estimation of more complex diffusion profiles and cost functions.

Finsler geometry is a metric extension of Riemannian geometry.

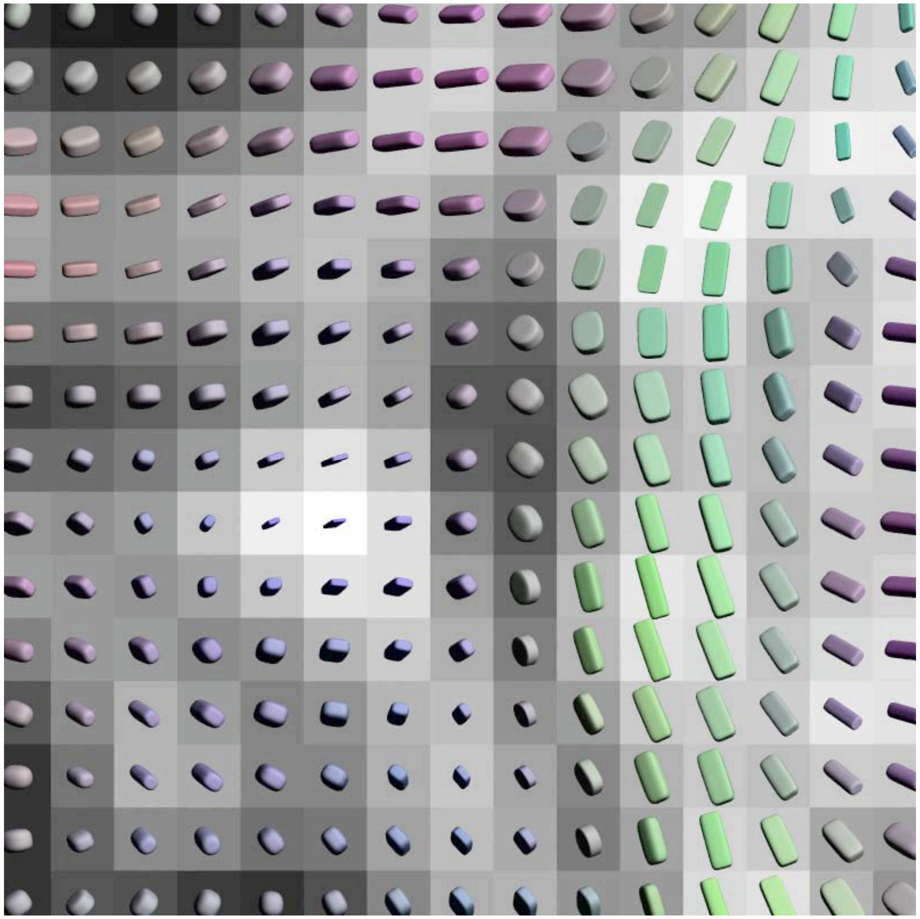
[Pichon05] Pichon, Westin, Tannenbaum "*A Hamilton-Jacobi-Bellman approach to high angular resolution diffusion tractography*", MICCAI 2005

[Melanakos07] Melonakos, Mohan, Niethammer, Smith, Kubicki, Tannenbaum, "*Finsler Tractography for White Matter Connectivity Analysis of the Cingulum Bundle*", MICCAI 2007

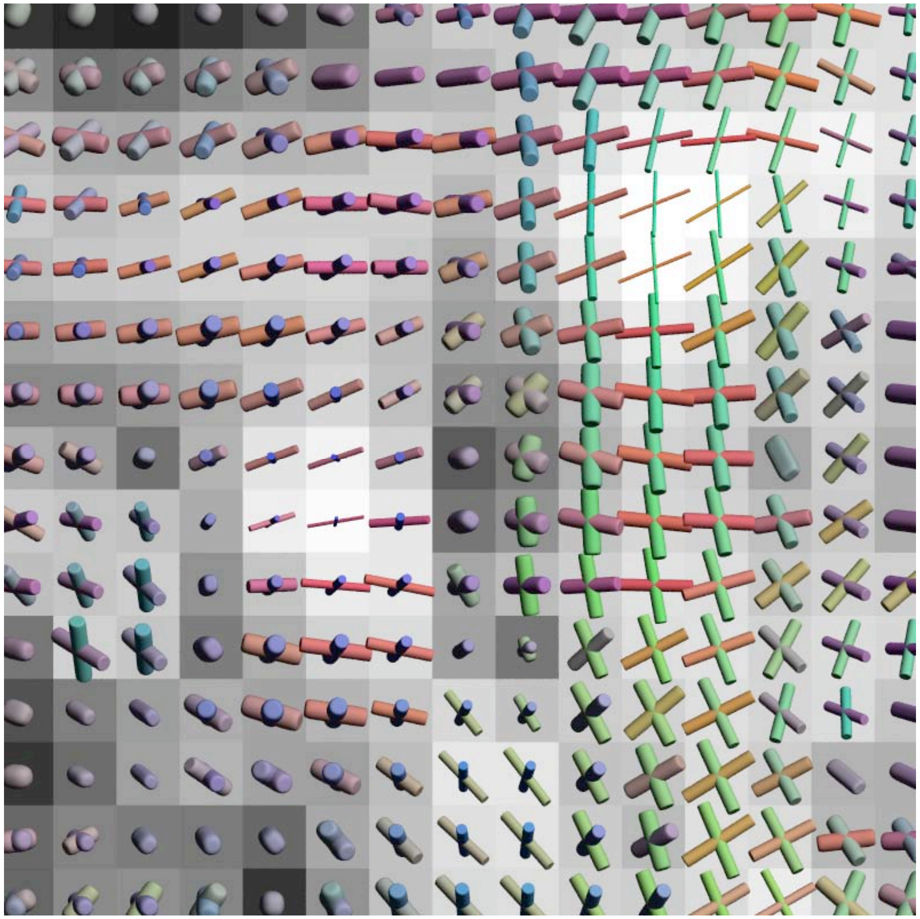
Modeling crossing tracts



DTI: Single tensor model



Two-tensor model



Overview

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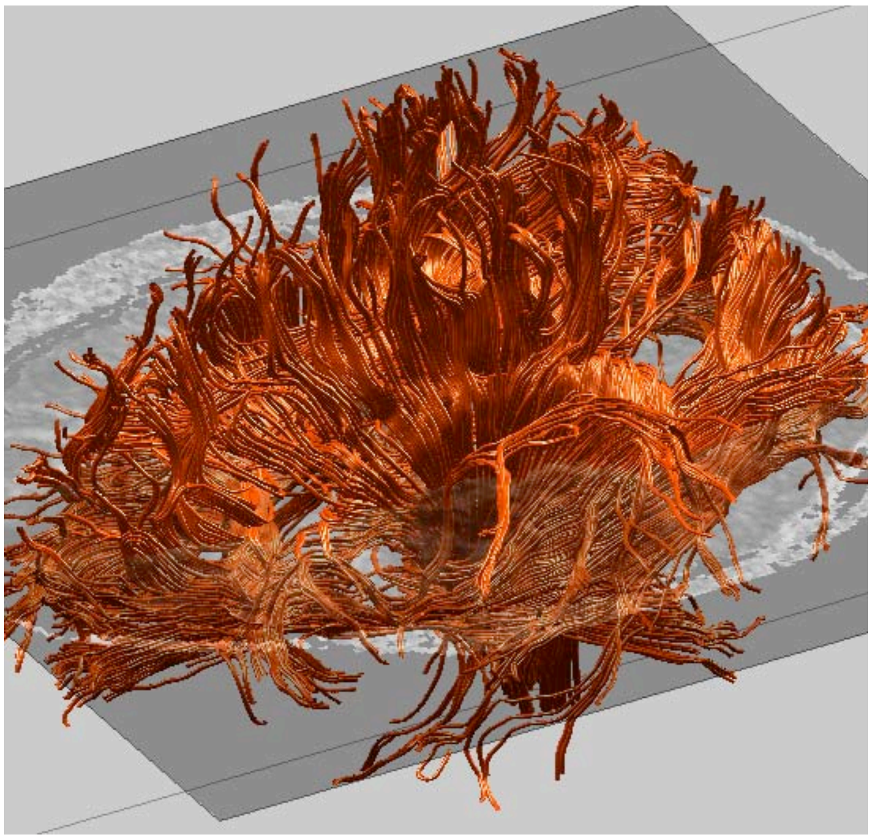
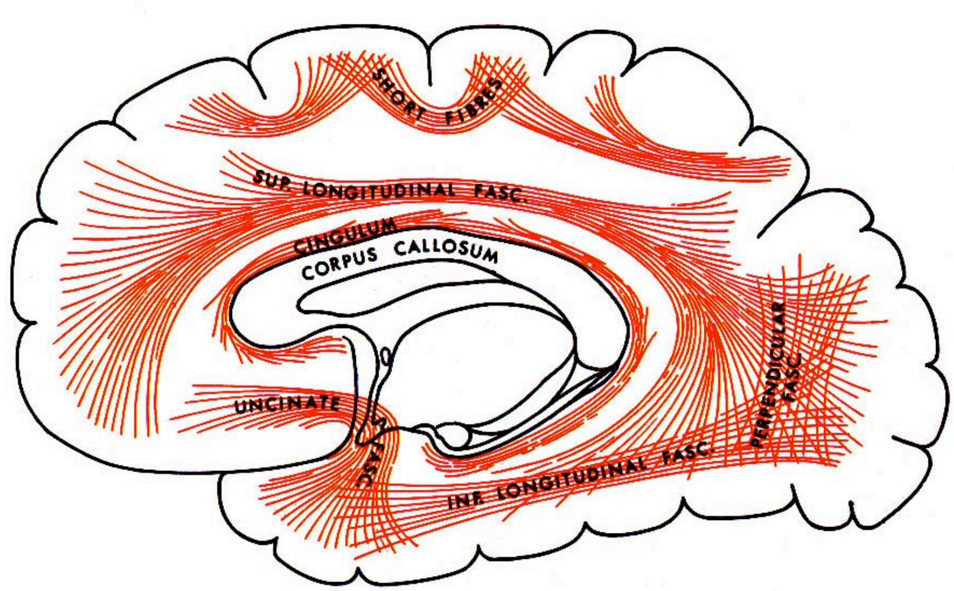
Segmentation challenge

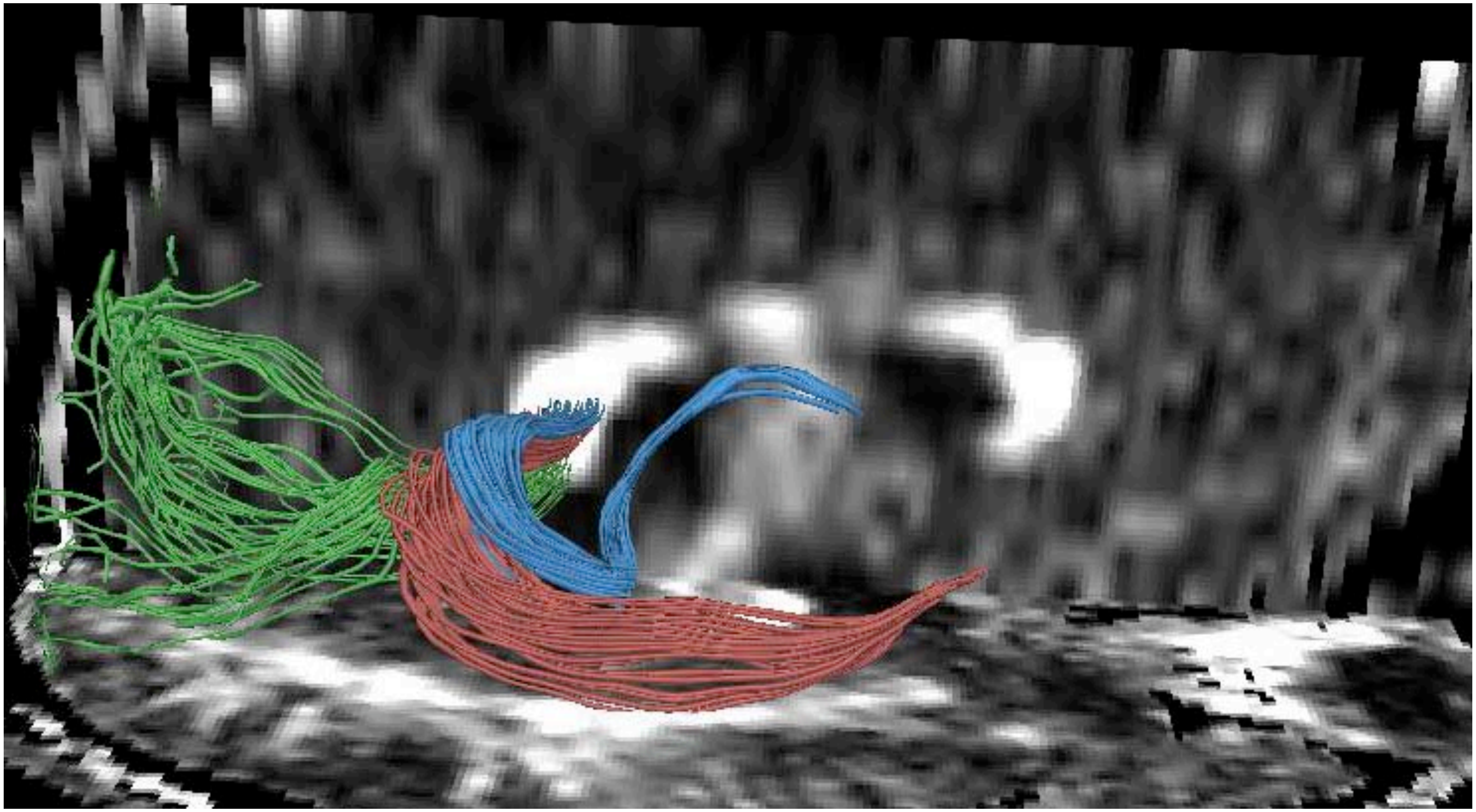
From DT-MRI tractography …





… to white matter tract models using **clustering**

Fibers to bundles



Splenium of the corpus callosum interconnecting different regions: occipital lobes (green), temporal lobes (red) and thalamus (blue).

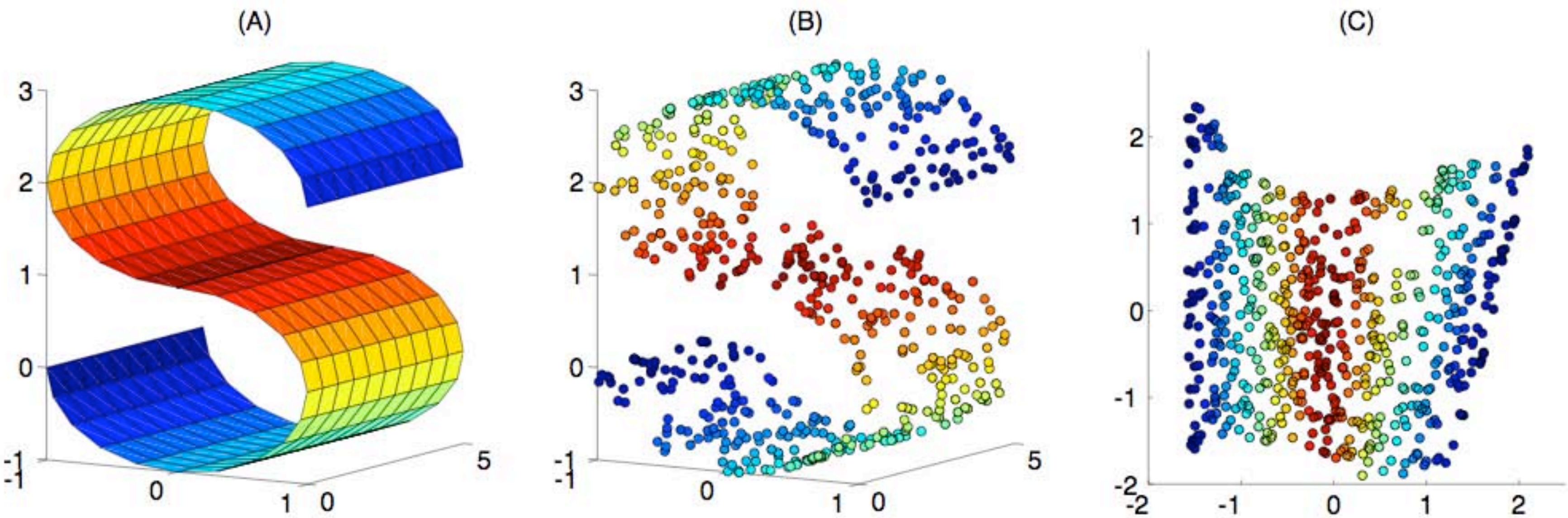
Provided by Marek Kubicki

Analysis by manifold learning

- Map data to a low-dimensional space
- Spectral methods to define manifold
- Try to preserve metric and topology

Provided by Anders Brun

Spectral methods to define manifold



Non-linear data reduction using locally linear embedding (LLE)

Images from Roweis and Saul, *Science* 2000

Spectral methods to define manifold

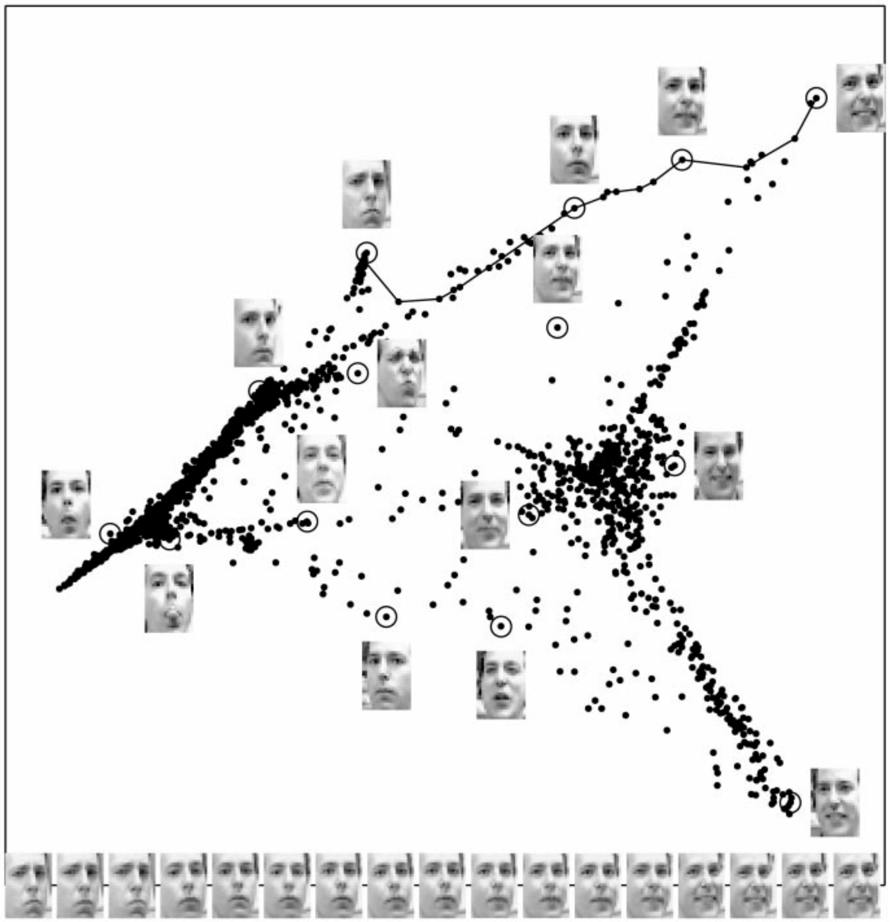


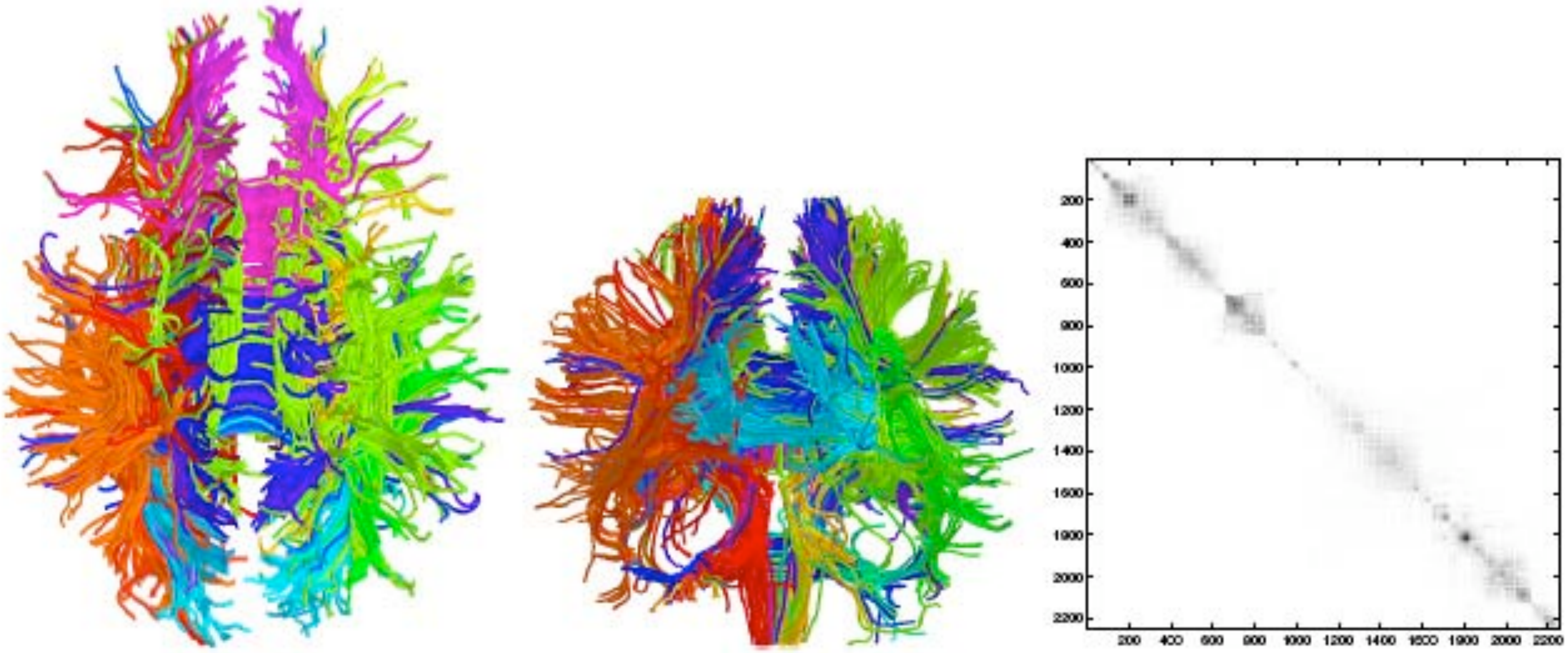
Image from Roweis and Saul, *Science* 2000

Images of faces mapped into the embedding space described by the first two coordinates of LLE

Spectral Method for Fiber Clustering

2004

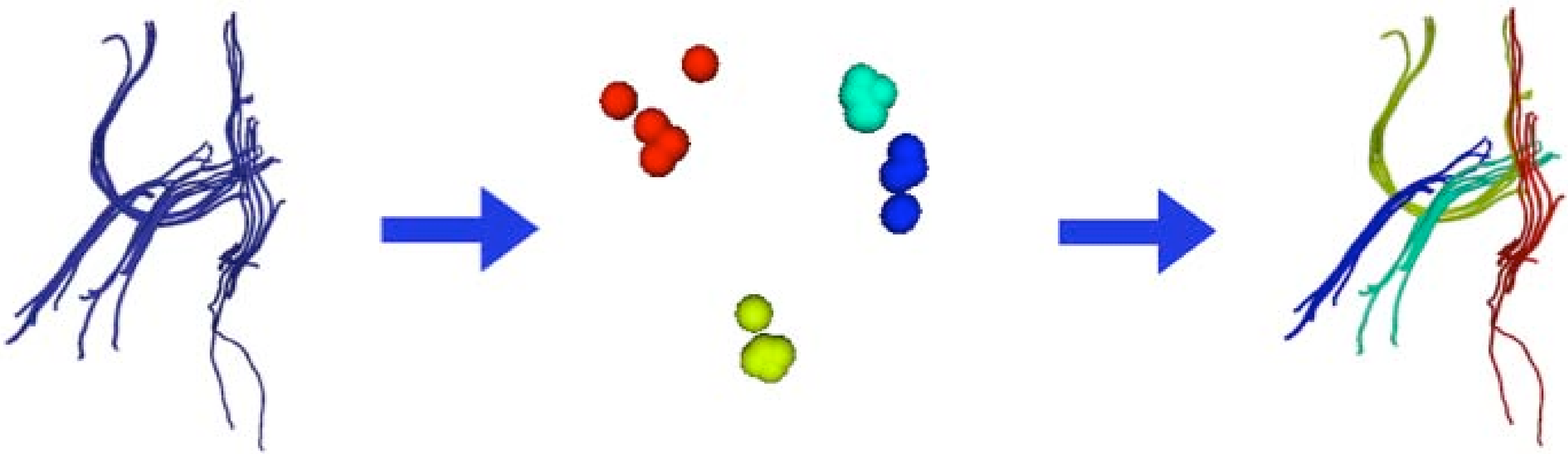
Fiber bundle clustering using spectral methods



- Pair-wise fiber affinities are inserted in a large matrix
- Eigenvectors of this matrix define manifold

Provided by A. Brun

Fiber Clustering

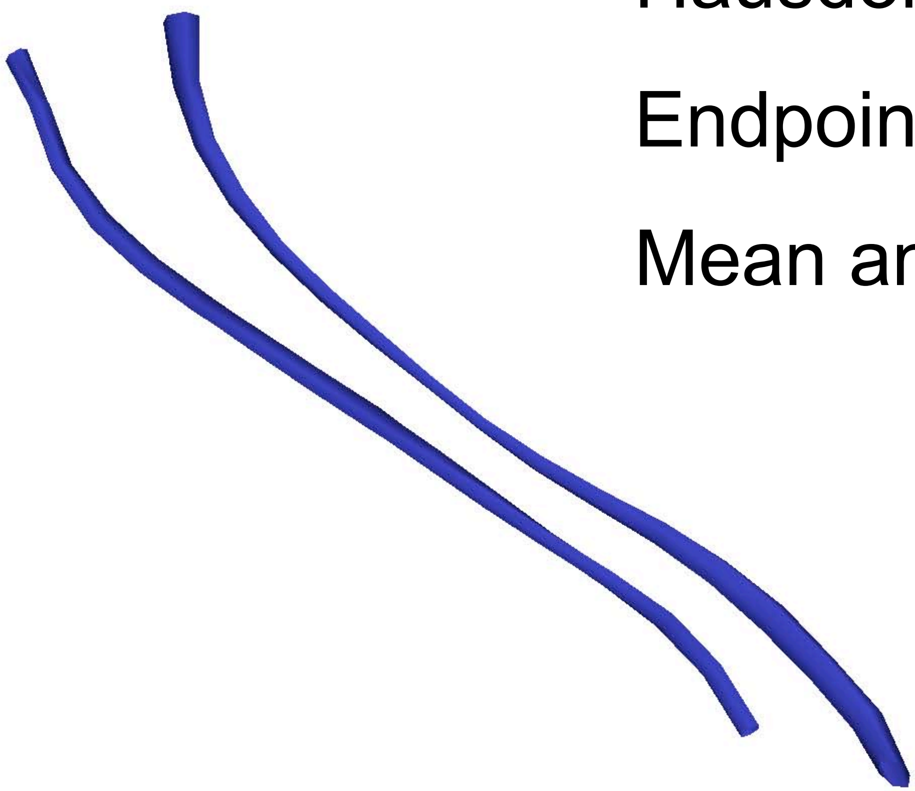


Traced fibers | High-dimensional feature space | Colored bundles

A clustering algorithm takes a number of traced fibers (left), extracts features from these fibers (middle), and produces a segmentation based on the similarity of the fibers (right).

O'Donnell MICCAI 2005

Defining fiber similarity



Hausdorff distance

Endpoint distance

Mean and covariance

Provided by L. O'Donnell

Population Clustering

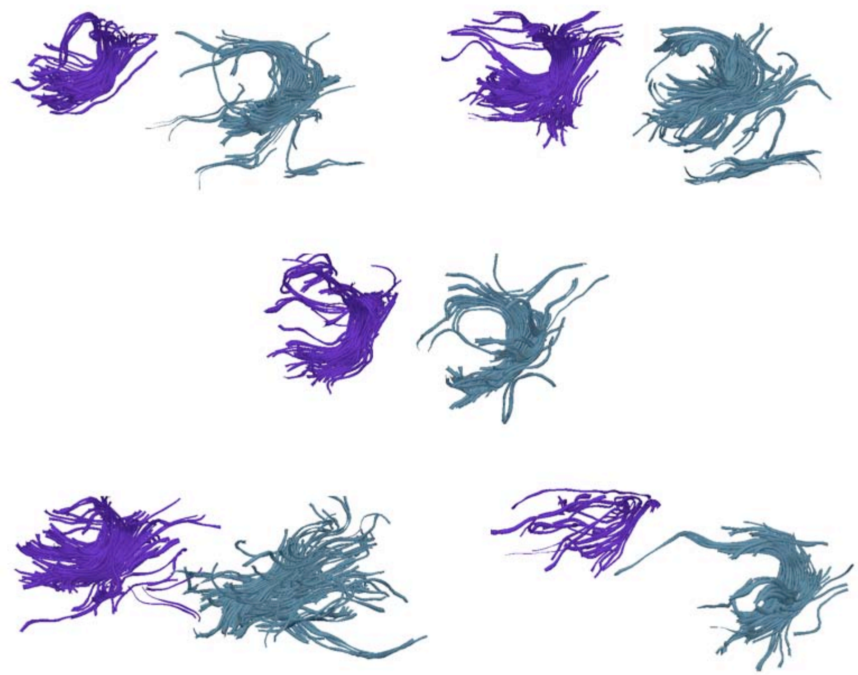
Five subject example

5,000-7,000 paths per subject

Automated generation of white matter ROIs

Work with L. O'Donnell

Selected clusters

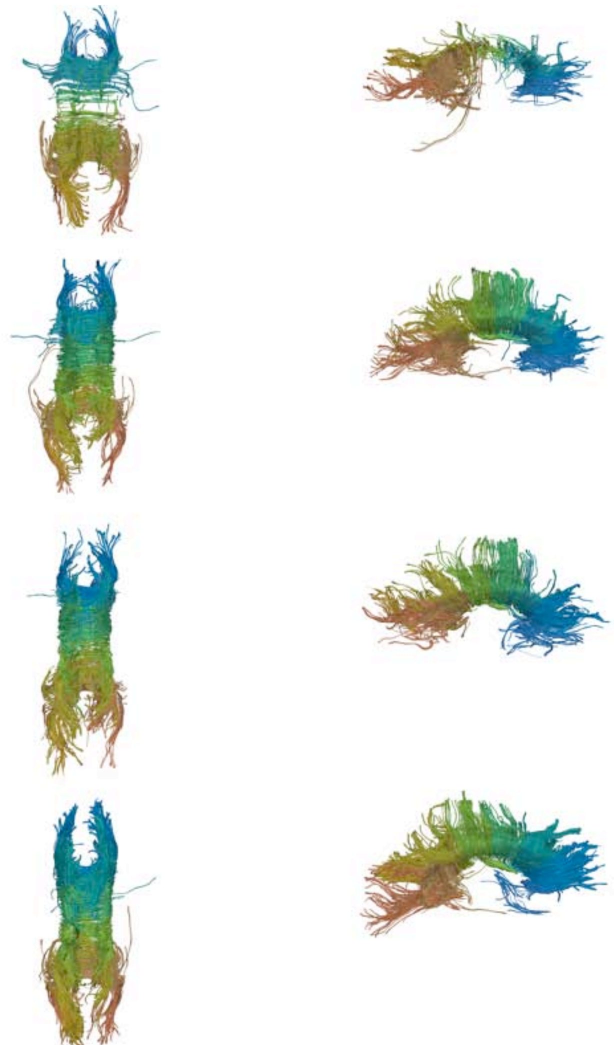


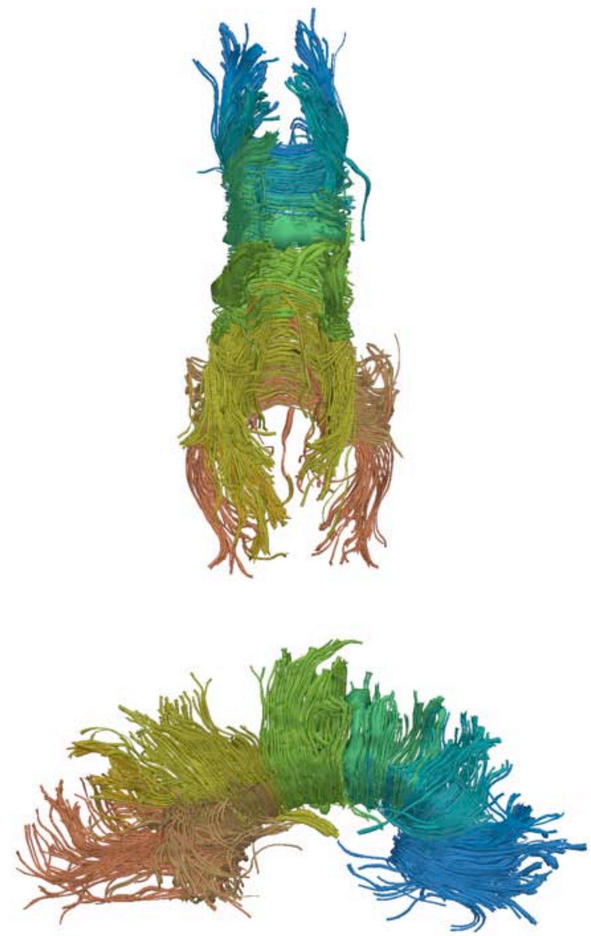
Cingulum bundles

Uncinate fasciculus

Work with L. O'Donnell

Selected clusters





Corpus callosum

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High-dimensional Fiber Atlas

Created using many subjects

In **embedding space**

High-dimensional

- 20 dimensions
- Not a voxel atlas

Automatic segmentation

- Project new subject tractography data to embedded atlas space

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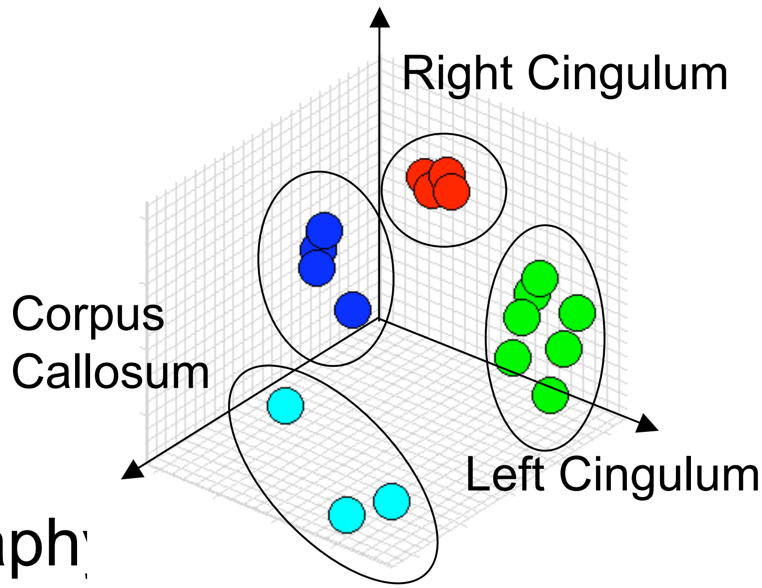


Example Atlas

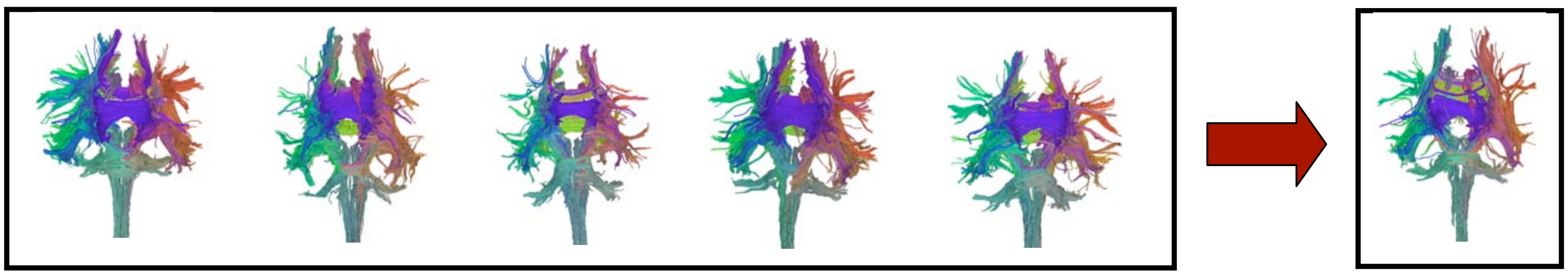
High-dimensional Fiber Atlas

Method for atlas creation

- Learns clusters from multiple subjects
- Incorporates expert labels

Automatic segmentation using atlas

- Label whole-brain tractography automatically



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Acknowlegements

Anders Brun, TechLic,

Lauren O'Donnell, PhD

Raul San-Jose Estepar, PhD

Ola Friman, PhD

Ron Kikinis, MD

Gordon Kindlmann, PhD

Marek Kubicki, MD,PhD

Hans Knutsson, PhD

Mahnaz Maddah, Msc

Marc Niethammer, PhD

Sharon Peled, PhD

Steve Pieper, PhD

Martha Shenton, PhD

Ulas Ziyan, MSc

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