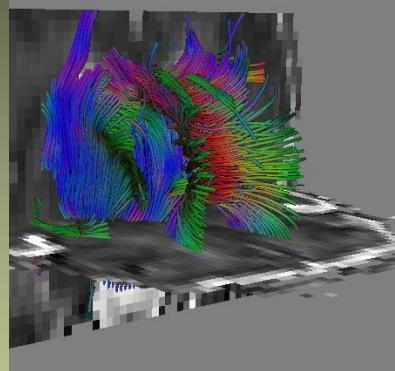
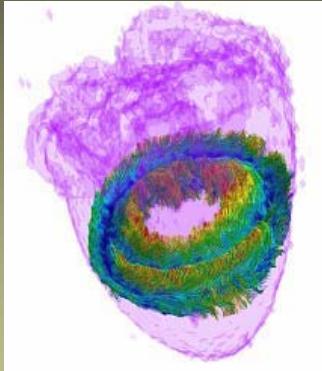
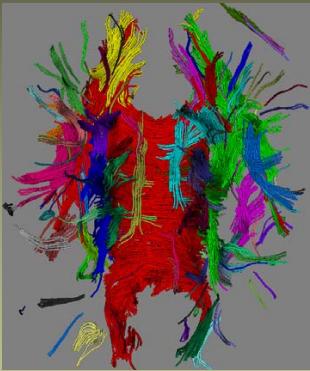
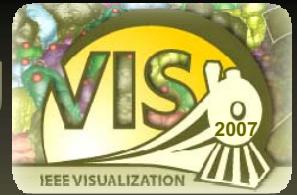


# Diffusion Tensor Imaging Visualization Techniques and Applications

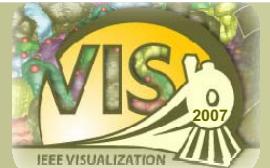


Anna Vilanova ([a.vilanova@tue.nl](mailto:a.vilanova@tue.nl))

BioMedical Image Analysis ([bmia.bmt.tue.nl](http://bmia.bmt.tue.nl))

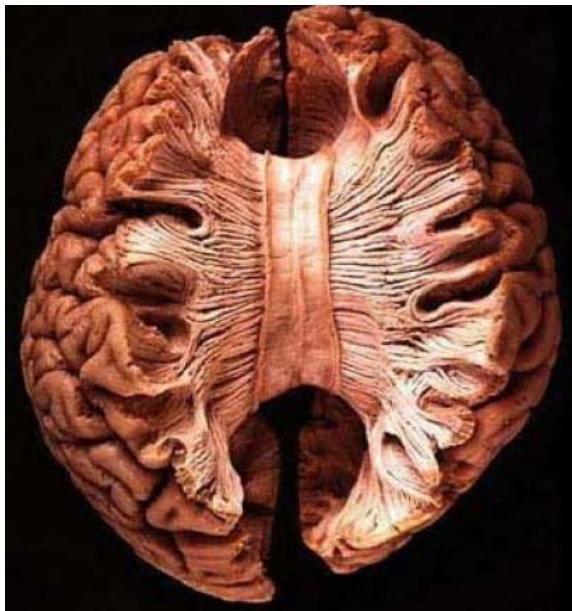
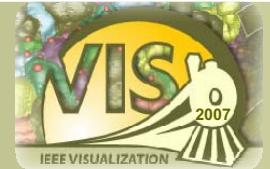
Eindhoven University of Technology, The Netherlands

## Overview

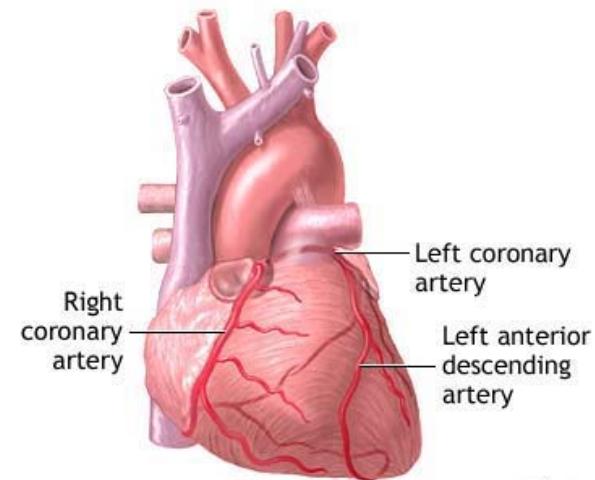


- Diffusion Tensor Imaging (DTI) data
- DTI visualization techniques
- Applications: newborn and ischemic heart
- Fiber clustering
- DTI segmentation

# Motivation



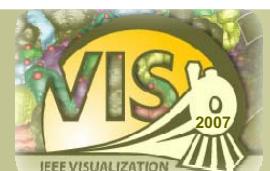
T.H. Williams et al.



©ADAM.

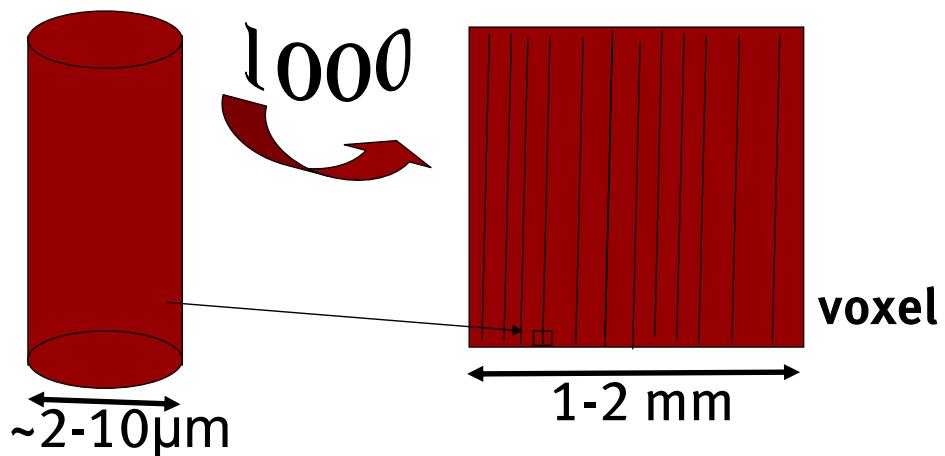
<http://www.shands.org/>

## Motivation MRI and Diffusion Tensor Imaging

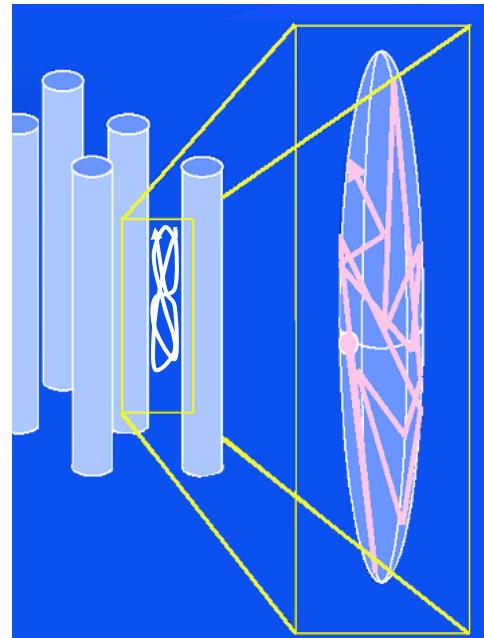
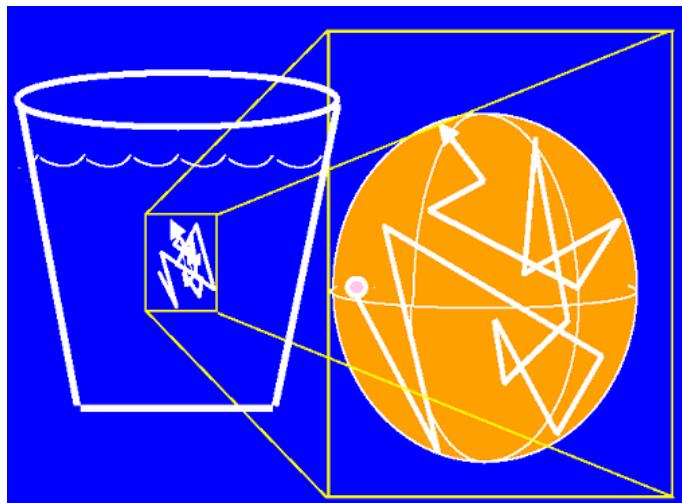


Fibers – Micrometers ( $\sim 2\text{-}10\mu\text{m}$ )

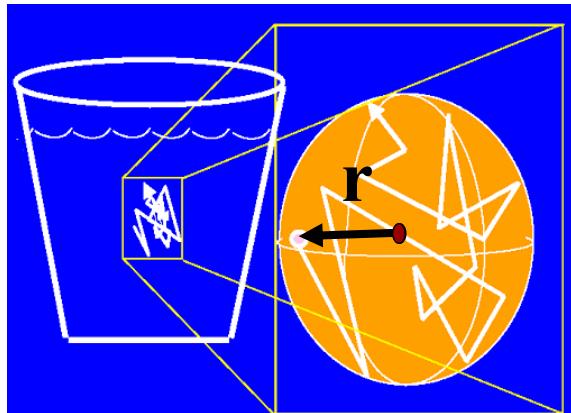
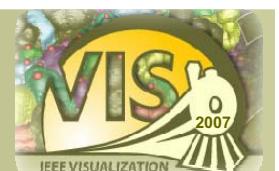
Scanner (MR) – Millimeters ( $\sim 1\text{-}2\text{ mm}$ )



# Water Diffusion Brownian Motion



## Fick's Law

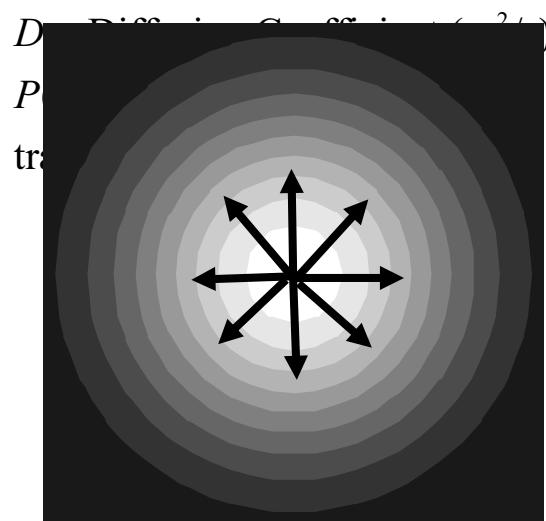


### Solution - 3D Gaussian

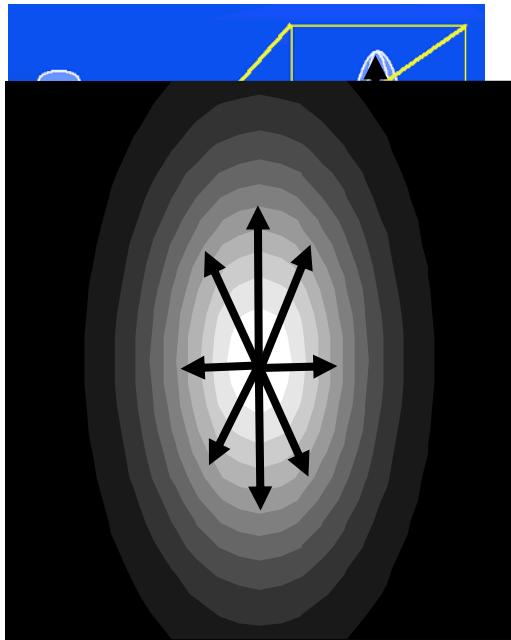
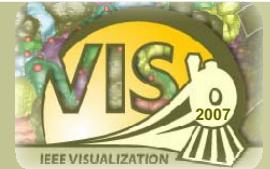
$$P(\mathbf{r}, t) = \frac{1}{(4\pi D t)^{3/2}} e^{-\frac{1}{4t} \mathbf{r}^2 D^{-1}}$$

$$\frac{\partial}{\partial t} P(\mathbf{r}, t) = D \cdot \nabla^2 P(\mathbf{r}, t)$$

$t$  Diffusion time



# Anisotropic Diffusion

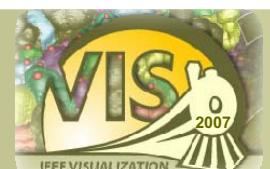


$$P(\mathbf{r}, t) = \frac{1}{(4\pi D t)^{3/2}} e^{-\frac{1}{4t} \mathbf{r}^2 D^{-1}}$$

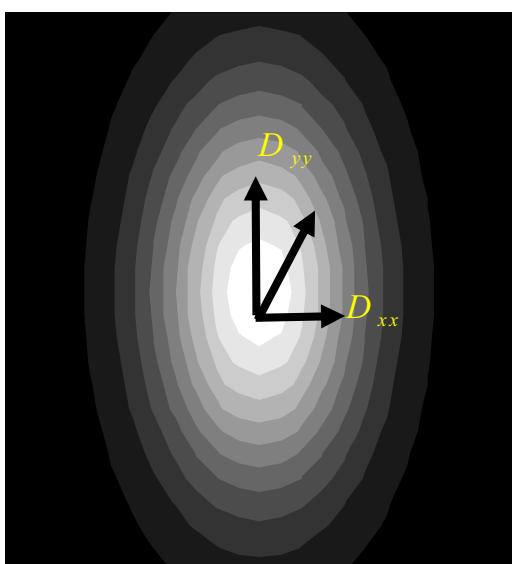
$$P_i(\mathbf{r}_i, t) = \frac{1}{(4\pi D_i t)^{3/2}} e^{-\frac{1}{4t} \mathbf{r}_i^2 D_i^{-1}}$$

$\mathbf{r}^2$  Indicates the distance squared of the vector  $\mathbf{r}$

## Anisotropic Diffusion – Diffusion Tensor



Diffusion Tensor



$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

$D_{ij} = D_{ji}$  **6 different values**

$$D_i = \mathbf{r}_i^t \mathbf{D} \mathbf{r}_i$$

$$P(\mathbf{r}, t) = \frac{1}{(4\pi |\mathbf{D}| t)^{3/2}} e^{-\frac{1}{4t} \mathbf{r}^t \mathbf{D}^{-1} \mathbf{r}}$$

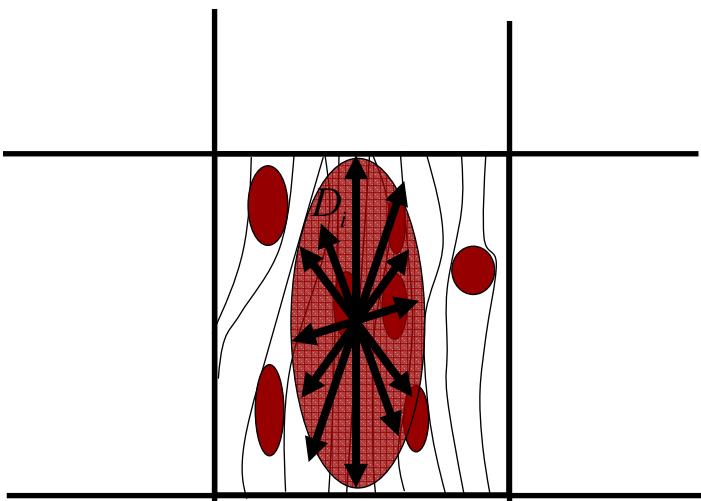
- Measure Diffusion Weighted signal  $S_i$  in a given direction
- Stejskal-Tanner relationship attenuation signal  $S_i$  to diffusion coefficient  $D_i$

$$S_i = S_0 e^{-bD_i} \quad \text{where } S_0 \text{ not diffusion weighted value}$$

b protocol parameter (diffusion time, ...)

$D_i$  is often called  $ADC_i$  (Apparent Diffusion Coefficient) – diffusion in a given direction

## MRI-Diffusion Measurement

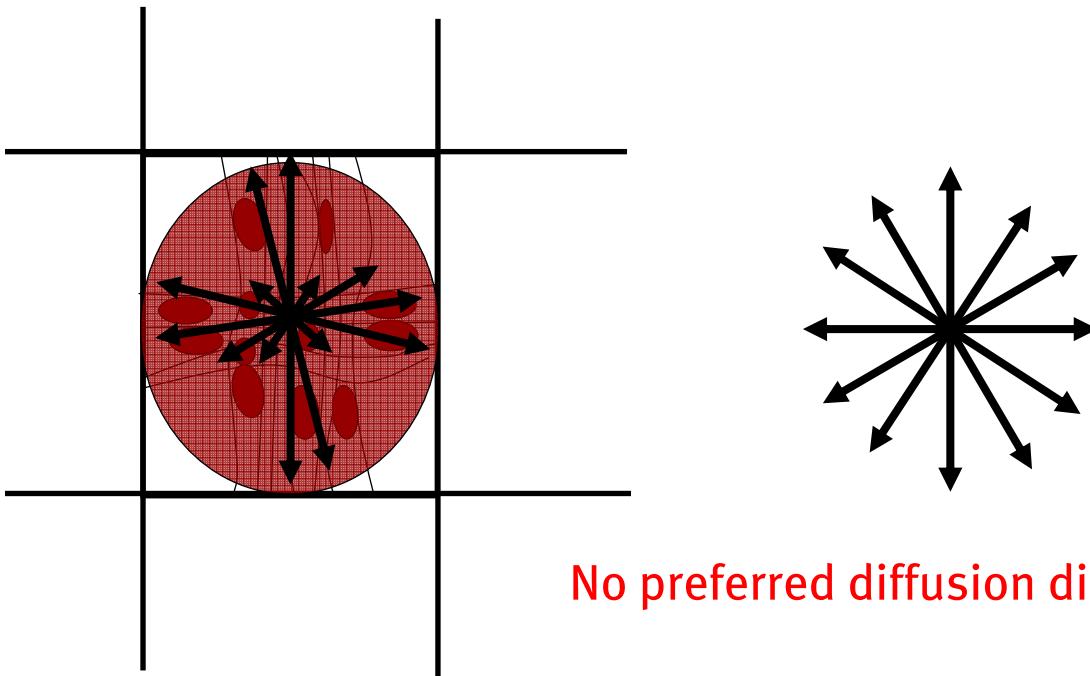
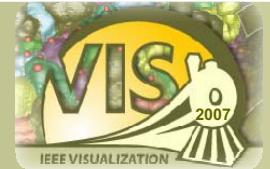


Measure  $ADC_i$  in a lot of directions (Minimum 6)

Fit  $\mathbf{D}$   
2nd Order Tensor  
Symmetric  
Positive Definite

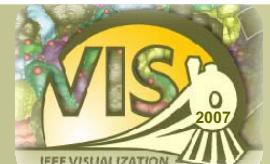
Assume Gaussian within a voxel

# What problems does the Gaussian model have?

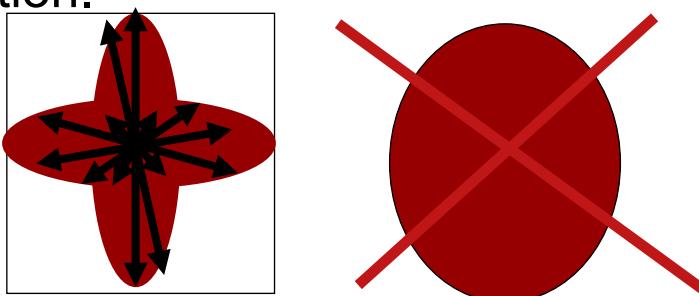


No preferred diffusion direction!

## Other models

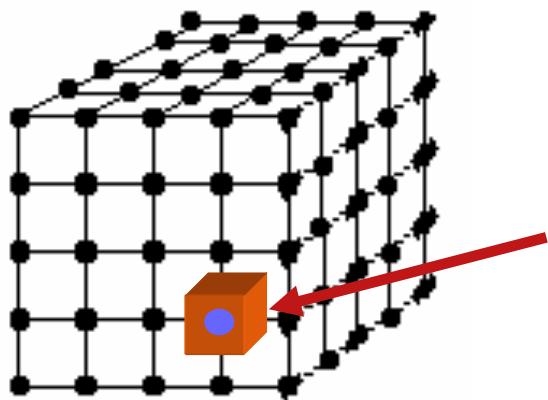
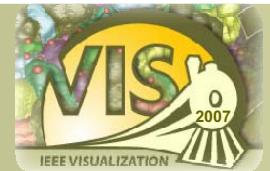


- HARDI - use other models for the probability density function.



- We will just talk about the Gaussian model!

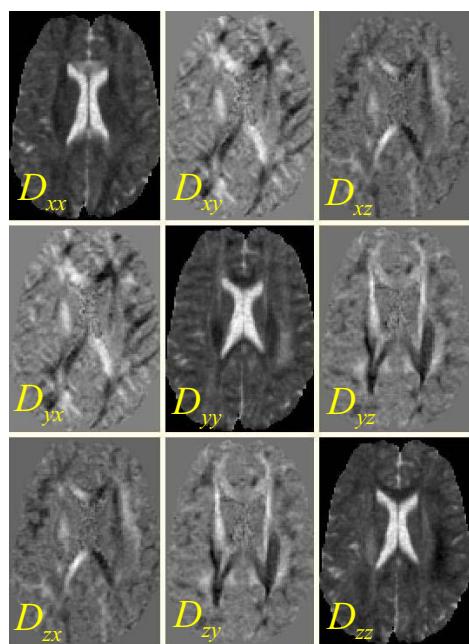
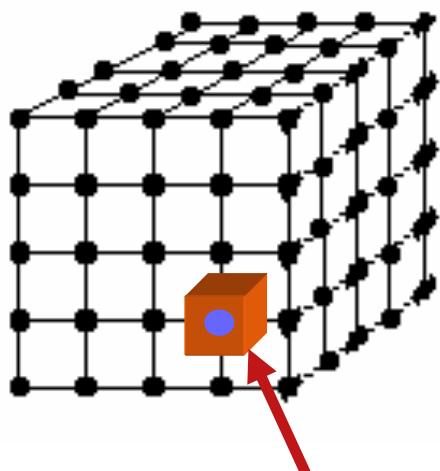
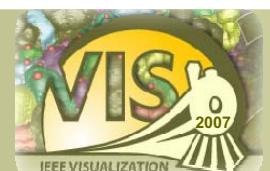
# Diffusion Tensor Imaging Visualization



$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

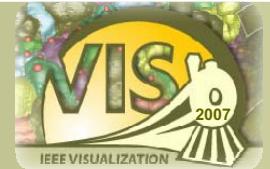
## How are we going to show this?

# Diffusion Tensor Imaging Visualization



$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

# Main diffusion directions



## Eigenanalysis

$$\mathbf{D}\vec{e}_i = \lambda_i \vec{e}_i \quad \det(\lambda \mathbf{I} - \mathbf{D}) = 0$$

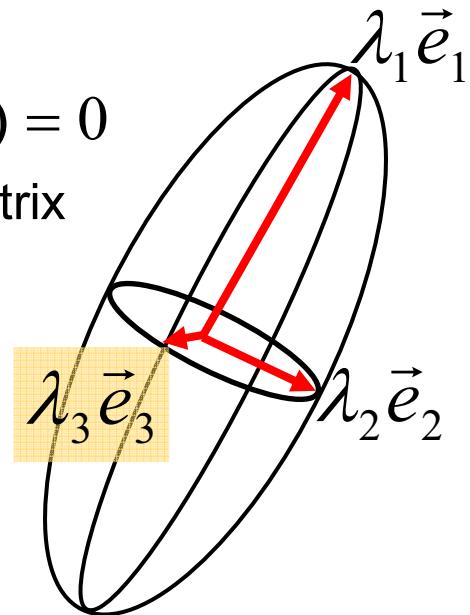
$\mathbf{I}$  identity matrix

## Eigenvalues

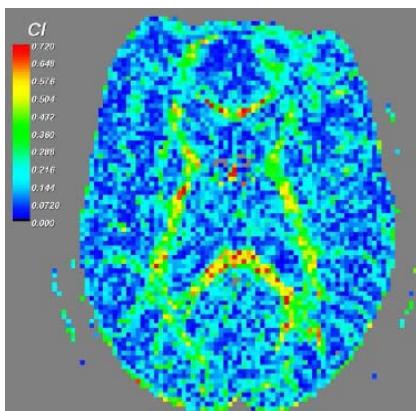
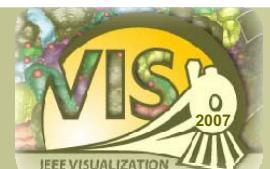
$$\lambda_1 \geq \lambda_2 \geq \lambda_3 \geq 0$$

## Eigenvectors

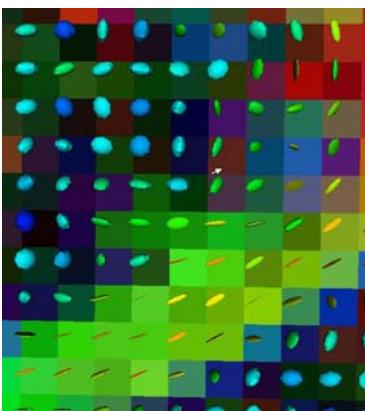
$$\vec{e}_1, \vec{e}_2, \vec{e}_3$$



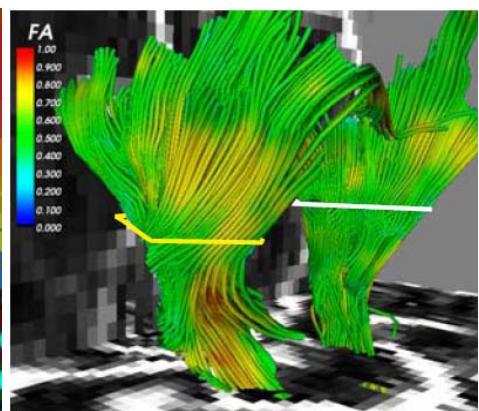
# DTI Visualization



Anisotropy Indices

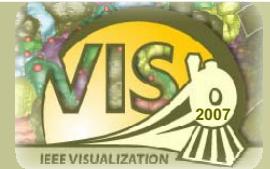


Glyphs



Fiber Tracking

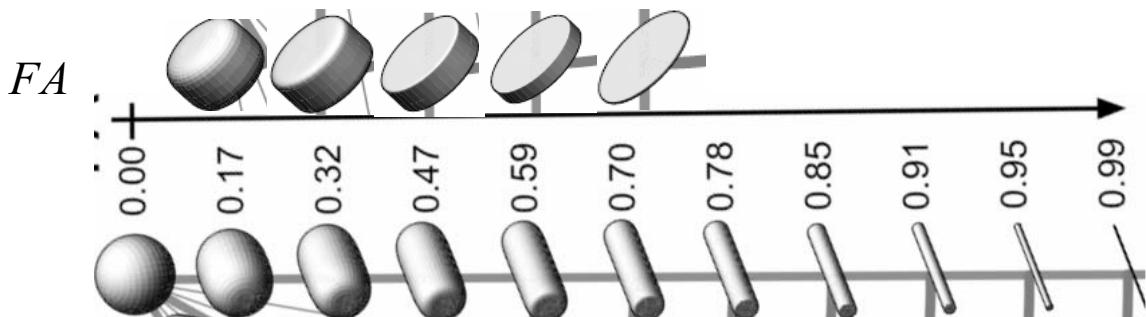
# Anisotropy indices



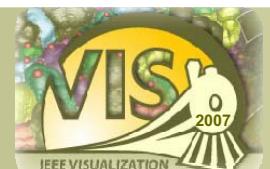
Index that indicates anisotropy

- Fractional Anisotropy

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



# Geometric Diffusion Measures



Isotropy:  $\lambda_1 \approx \lambda_2 \approx \lambda_3$

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

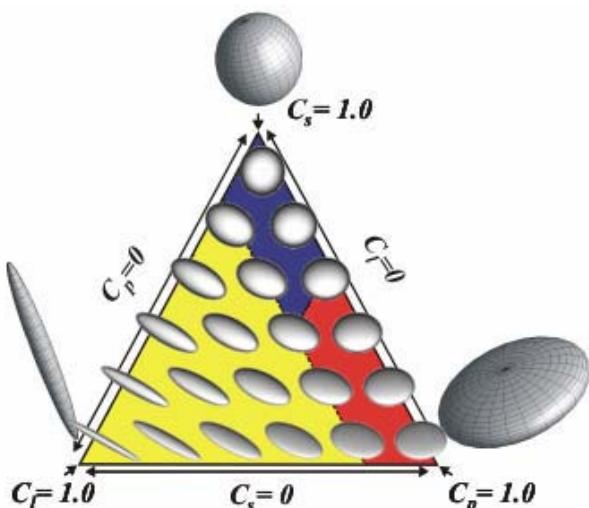
Anisotropy:

Linear  $\lambda_1 \gg \lambda_2 \approx \lambda_3$

$$C_l = \frac{\lambda_1 - \lambda_2}{\lambda_1 + \lambda_2 + \lambda_3}$$

Planar  $\lambda_1 \approx \lambda_2 \gg \lambda_3$

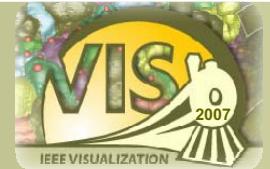
$$C_p = \frac{2(\lambda_2 - \lambda_3)}{\lambda_1 + \lambda_2 + \lambda_3}$$



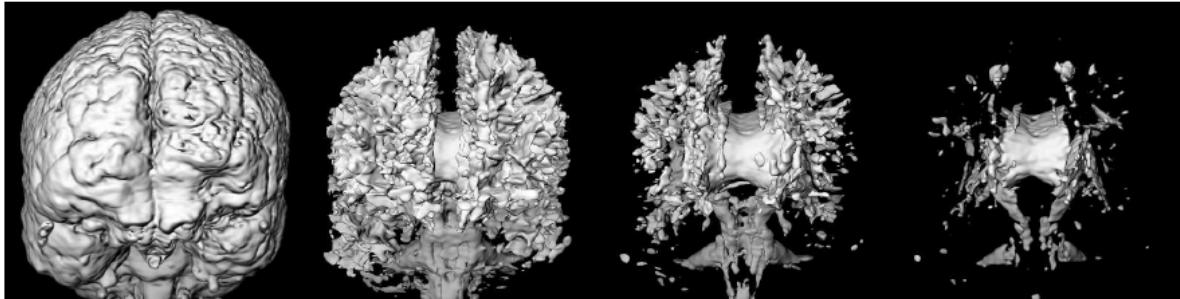
$$C_s + C_l + C_p = 1$$

[Westin et al. 97]

# Volume Rendering

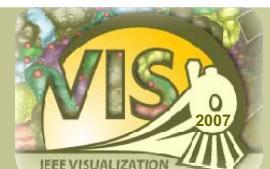


Scalar (e.g., Anisotropy index) [Kindlmann et al. 00]



FA = 0.0                  FA = 0.3                  FA = 0.5                  FA = 0.65  
Image from [Vilanova et al. 04]

## Anisotropy Indices



There are much more anisotropy indices:

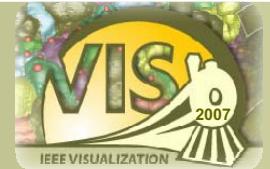
Relative anisotropy (RA), Mean diffusion, etc.

Pros and Cons

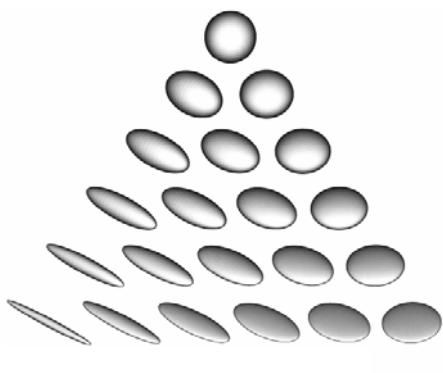
- ✓ “Easy” to visualize
- ✗ Simplification 6D → 1D

**That's a hell of a simplification!**

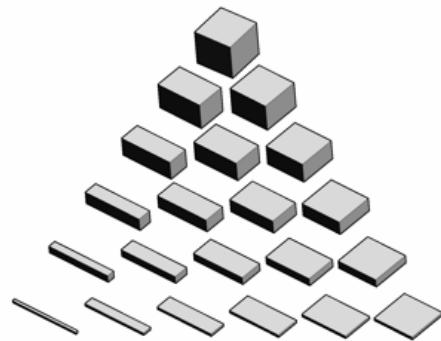
# Glyphs/Icons



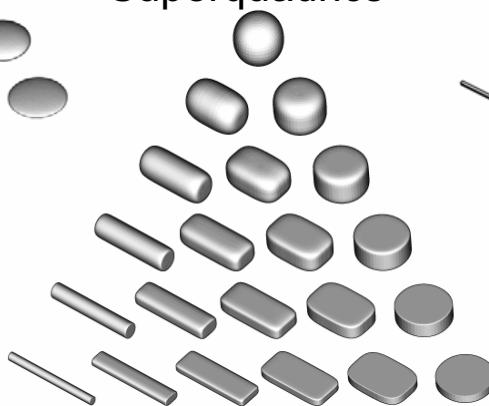
Ellipsoids



Cuboids

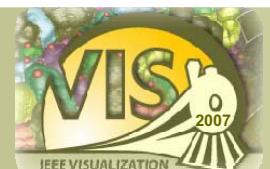


Superquadrics



[Kindlmann et al. 04]

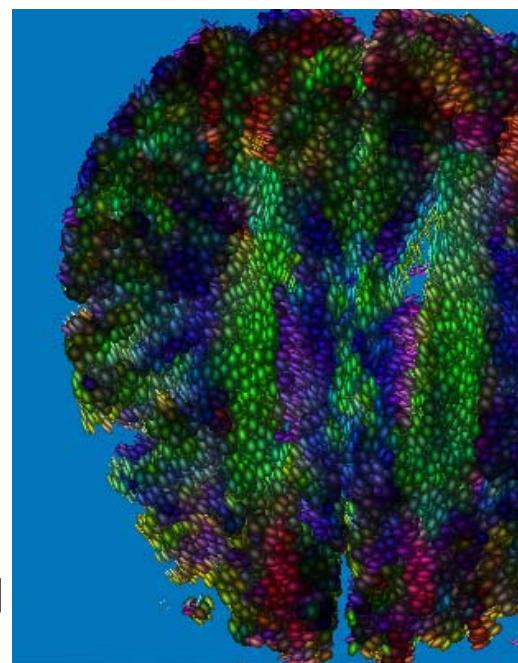
# Glyps/Icons



## Pros and Cons

- ✓ Shows 6D information
- ✗ Local information
- ✗ Cluttering extended to 3D

image from [Kondratieva et al. 05]  
[wwwcg.in.tum.de](http://wwwcg.in.tum.de)



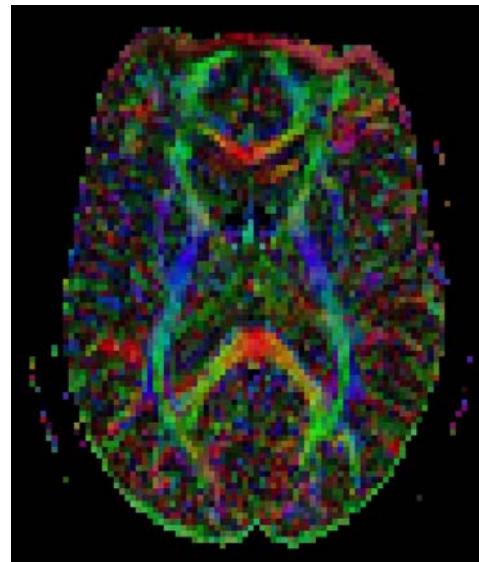
## Color Coding of the Main Diffusion Direction



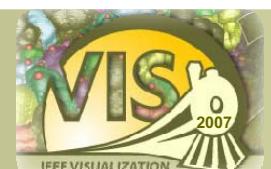
$$\vec{e}_1 = (x, y, z) \text{ map to } (R, G, B)$$

Pros and Cons

- ✓ Shows directional information
- ✓ Simple to implement
- ✗ Simplification 6D → 3D
- ✗ Difficult to extract fiber information



## Fiber Tracking *Streamline tracing*

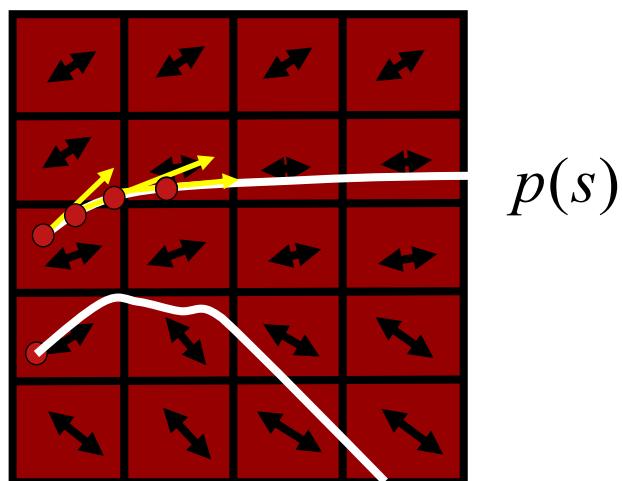


Streamline tracing

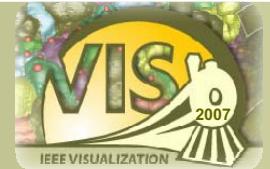
$$p(s) = \int \vec{e}_1(p(s)) ds \quad p(s) \text{ path with parameter } s$$

Integration scheme

- Euler Forward
- Runge Kutta
- etc.

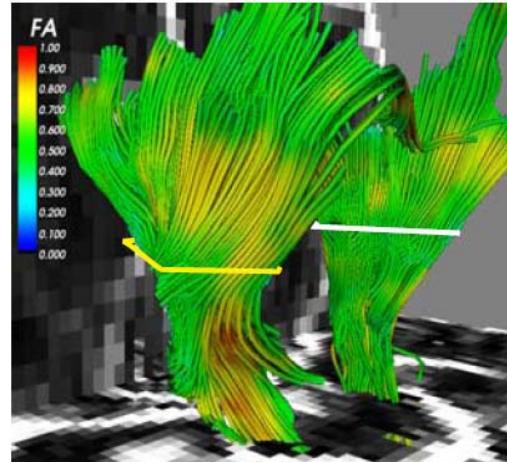


# Fiber Tracking Streamline Tracing

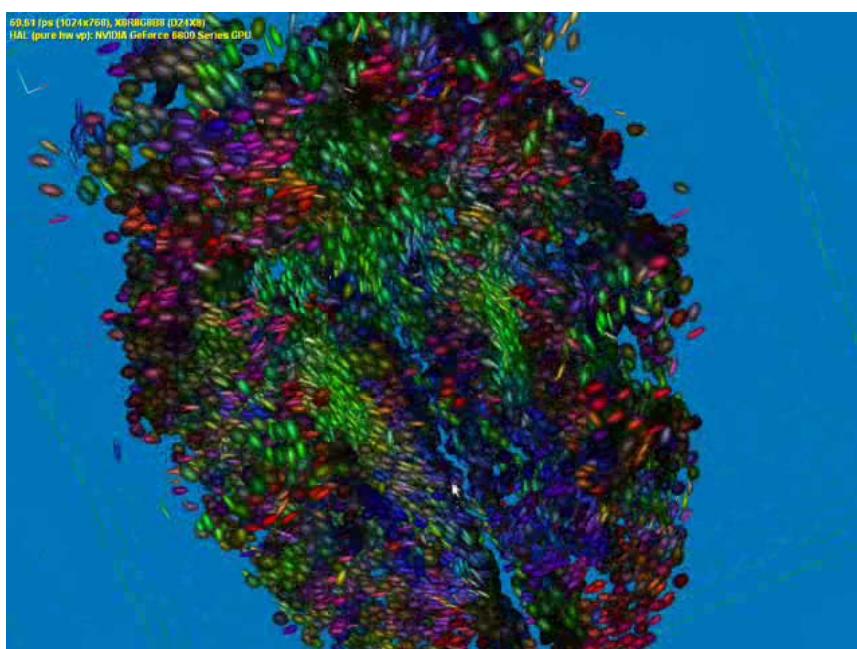


## Pros and Cons

- ✓ Analogy with fibers
- ✓ Shows global information
- ✗ Simplification 6D → 3D
- ✗ Problems with Crossing
- ✗ Seeding – Region of Interest
- ✗ Cluttering

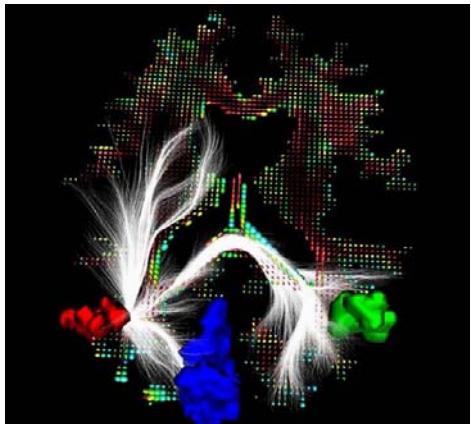


# Tracing Glyphs



Video from [Kondratieva et al. 05] [wwwcg.in.tum.de](http://wwwcg.in.tum.de)

# Other Fiber Tracking Techniques

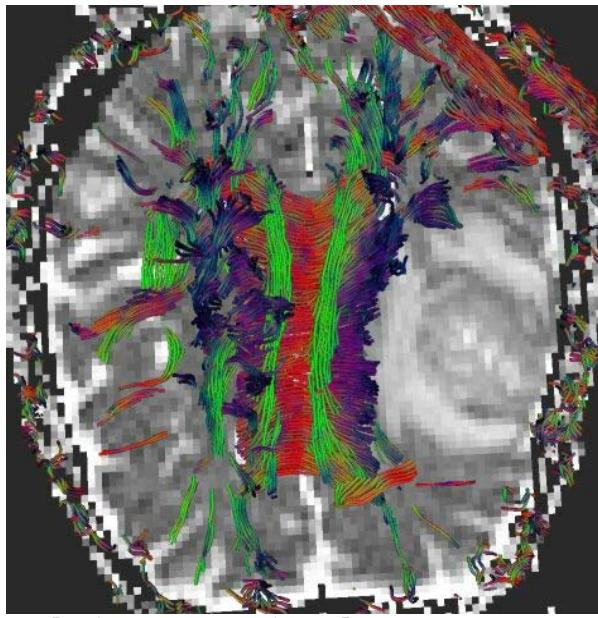
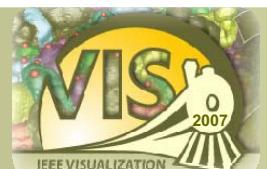


[N.Wotawa et al. 05] 02]

## Pros and Cons

- ✓ Analogy with fibers
- ✓ Shows global information
- ✗ Seeding – Initial and end
- ✗ Computational cost
- ✗ Cluttering

# Applications



[Vilanova et al. 04]

## Understanding

- Brain Development
- Brain Injuries
- Ischemic heart
- ...

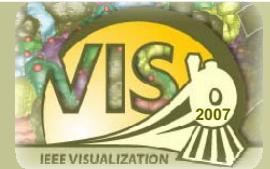
## Diagnosis

- Epilepsy
- Multiple Sclerosis
- ...

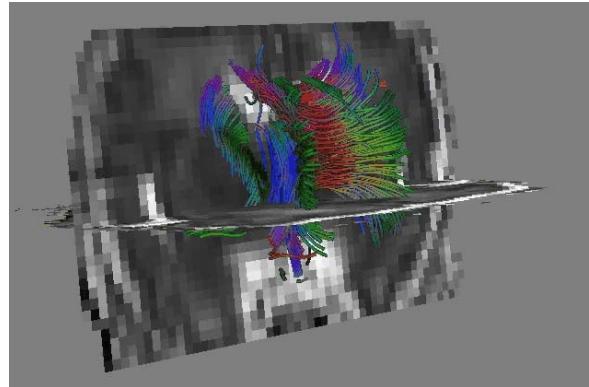
## Treatment

- Tumor resection
- ...

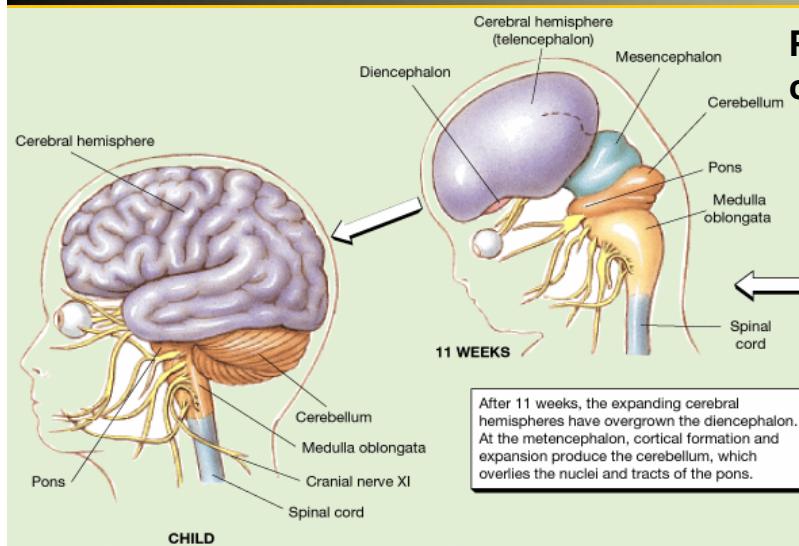
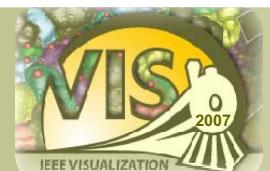
# DTI in the newborn brain



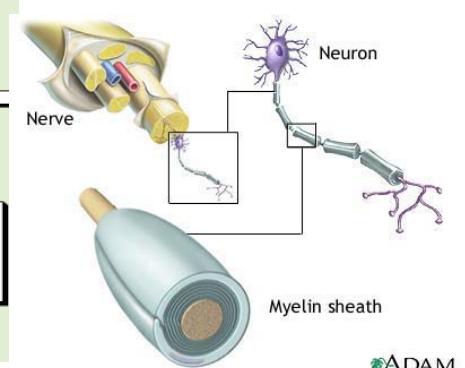
- DTI can reveal detailed anatomy of white matter development.
- Characterization of normal axonal growth of the white matter tracts.
- Understanding the extensive inhomogeneity of white matter injuries (e.g., hypoxic-ischemic regions)
- Reference standards for diagnostic radiology of premature newborns.
- Early detection can improve treatment



# Human brain development

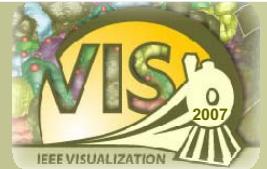


Picture from Prentice Hall -  
[cwx.prenticehall.com](http://www.cwx.prenticehall.com)



Brain myelination starts with 30 weeks of conception and it is not completed until the age 20-30

# Adult vs. Newborn

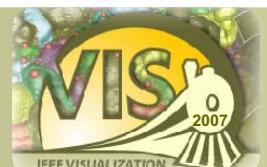


Acquisition Difference with Adults:

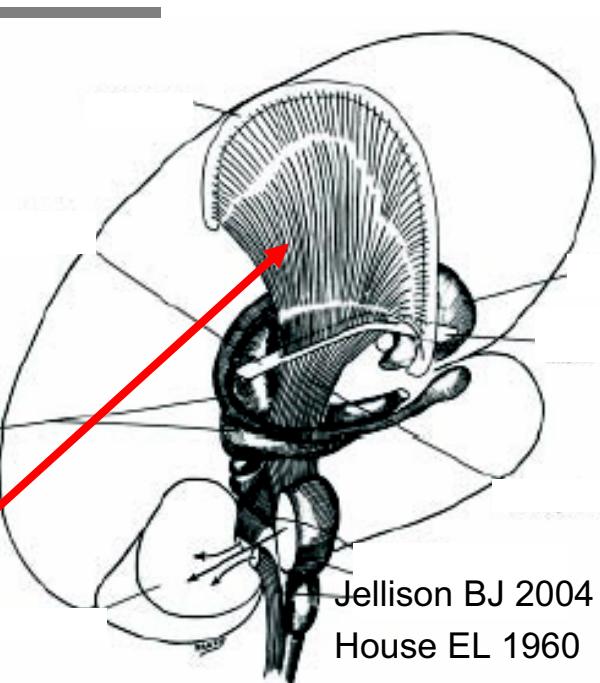
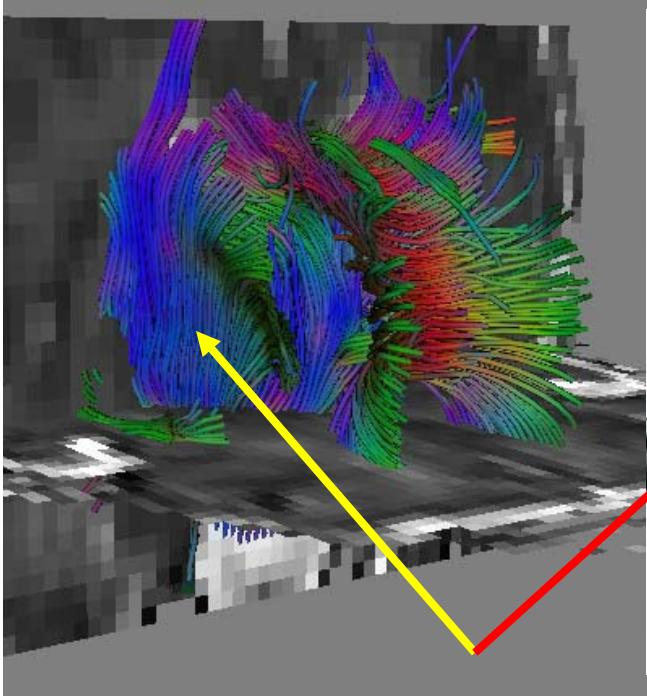


- Fibers are less myelinated → less anisotropy → lower signal intensity
- Motion artifacts can play a larger role (scan within 4 minutes full-term newborns)
- The size of the pre-term (and neonatal) brain is smaller than of an adult. Voxel contains more structures than in an adult.
- The signal strength decreases if the voxelsize decreases.

# Visualization DTI: fiber tracking

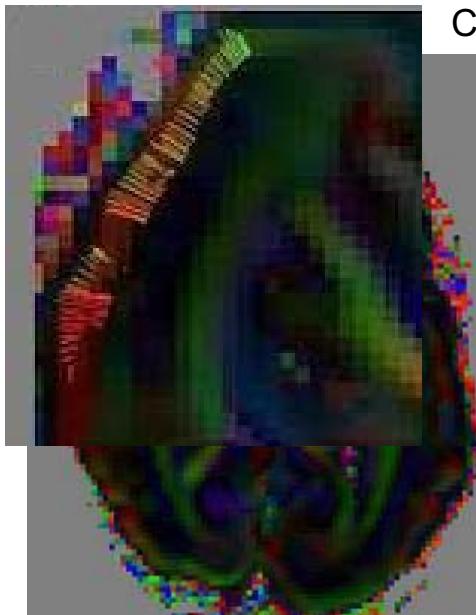
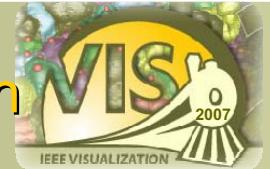


Full term newborn at day 6

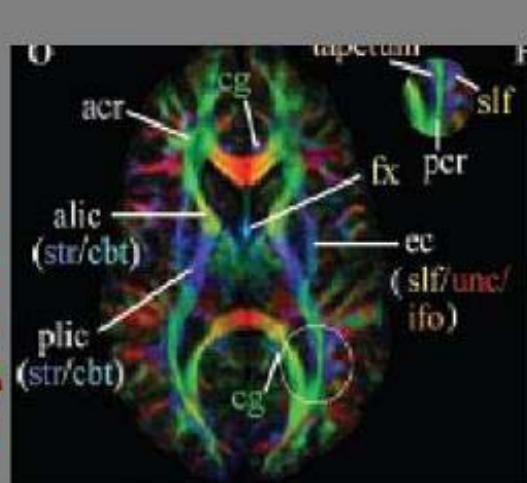


Jellison BJ 2004  
House EL 1960

## Example: Adult vs.Premature Newborn



Cortex with radial fibers



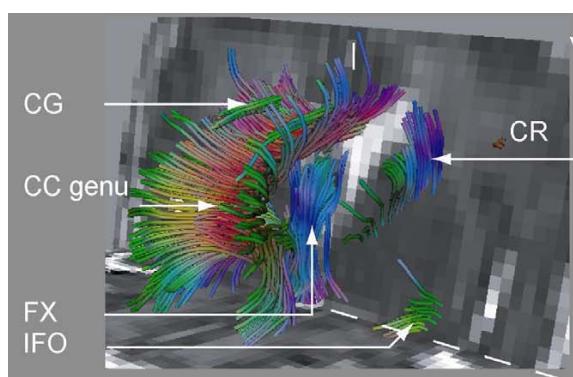
Atlas Wakana and Mori 2004

Premature Neonate (26 weeks)

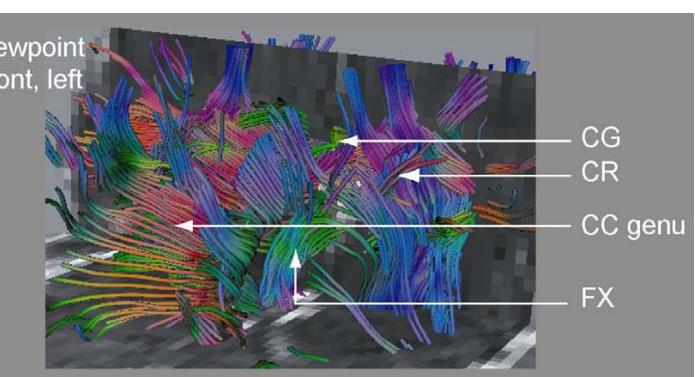
## Results: normal newborns (follow ups)



birth

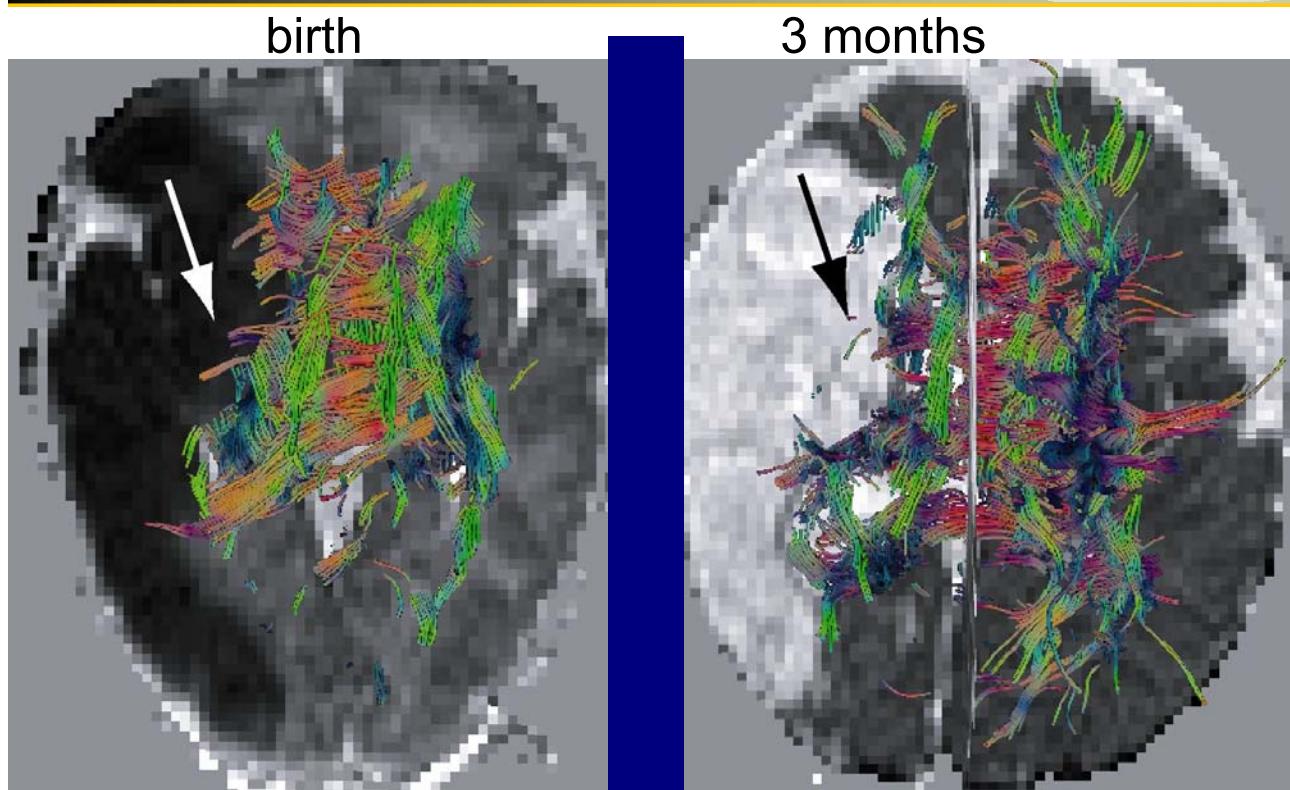
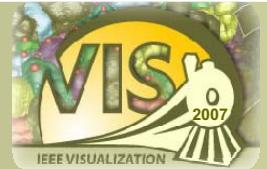


3 months

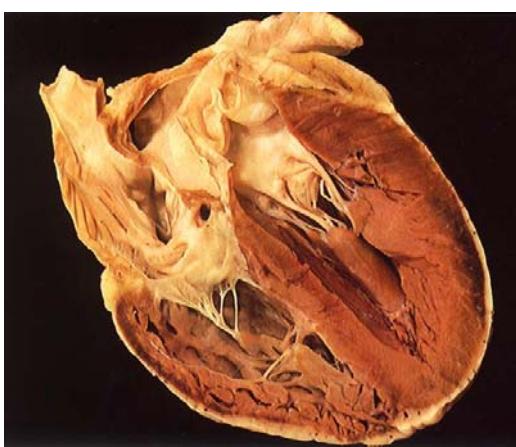
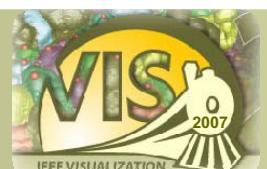


Which structures are developing and how?  
Quantification?

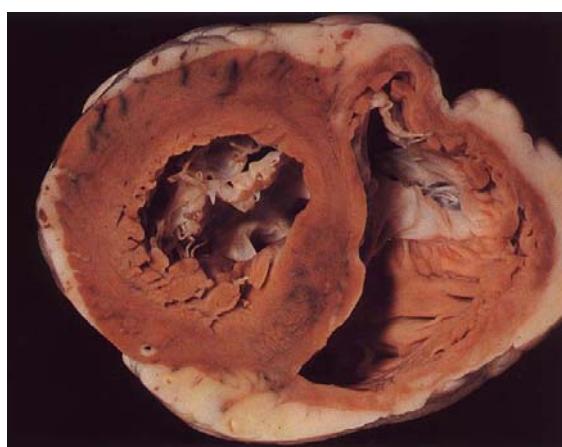
## Results: newborns with pathology



## Heart DTI visualization



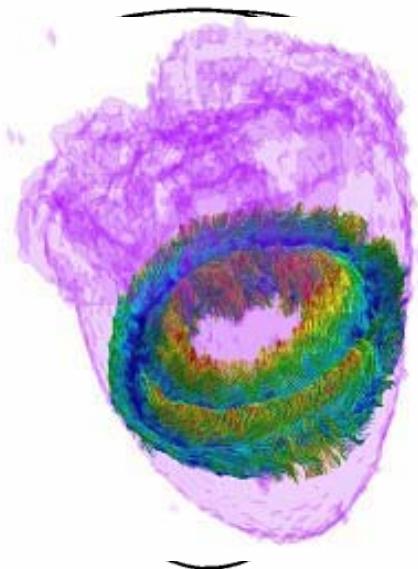
Sagittal section through the heart



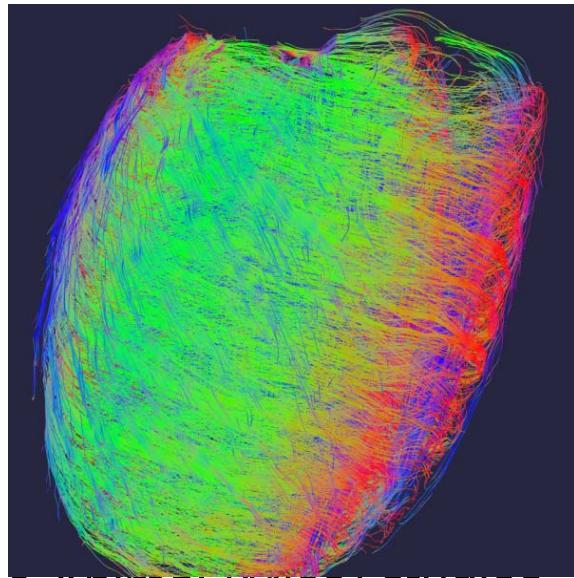
Short-axis section through the heart

[Anderson, 1980]

# Heart

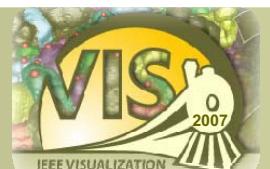


Model of Left Ventricle, depicting helix angle [Bovendeerd, 1992]

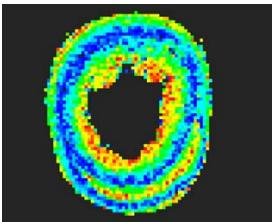


• Animal (mice) studies

## Visualization of the heart

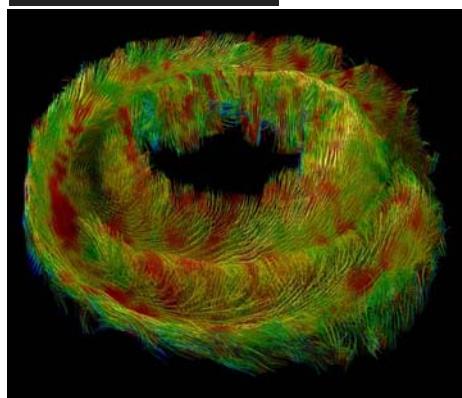
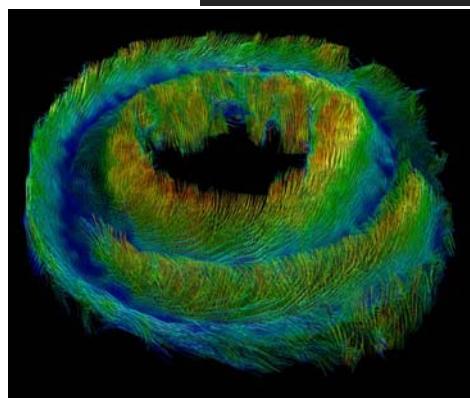
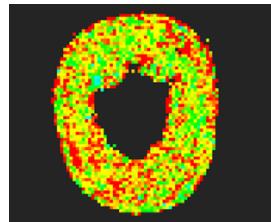


Hue color mapping



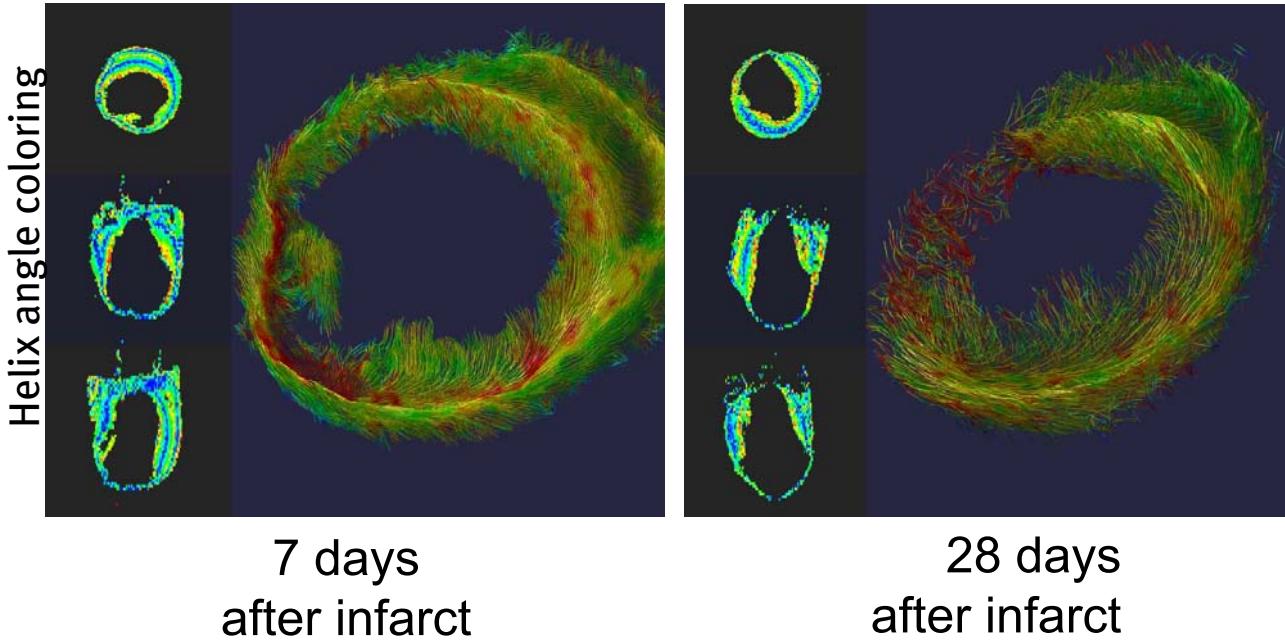
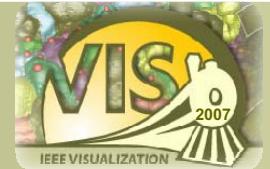
Helix Angle

Hue color mapping  
Fractional Anisotropy

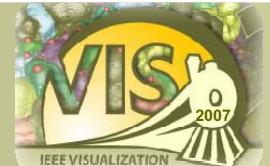


Illuminated lines + Shadows

# Fibers in a slice of ischemic mouse hearts



## Ischemic hearts

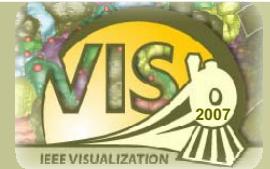


In ischemic areas:

- Heart-wall becomes thinner
- FA becomes higher (this was unexpected)
- More random fiber orientations

Conclusion: High FA and random fiber orientation probably caused by collagen fibers

# Cluttering

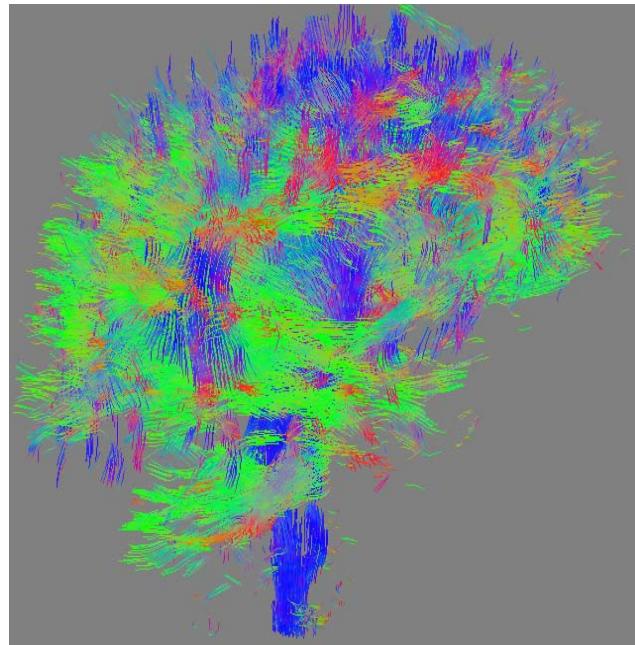


Seed point definition

- Region of interest
  - Biased
  - Not reproducible
  - Miss information
- Whole volume
  - Cluttering

Individual “fibers” are of no interest

Bundles structures are of interest



# Fiber Bundle

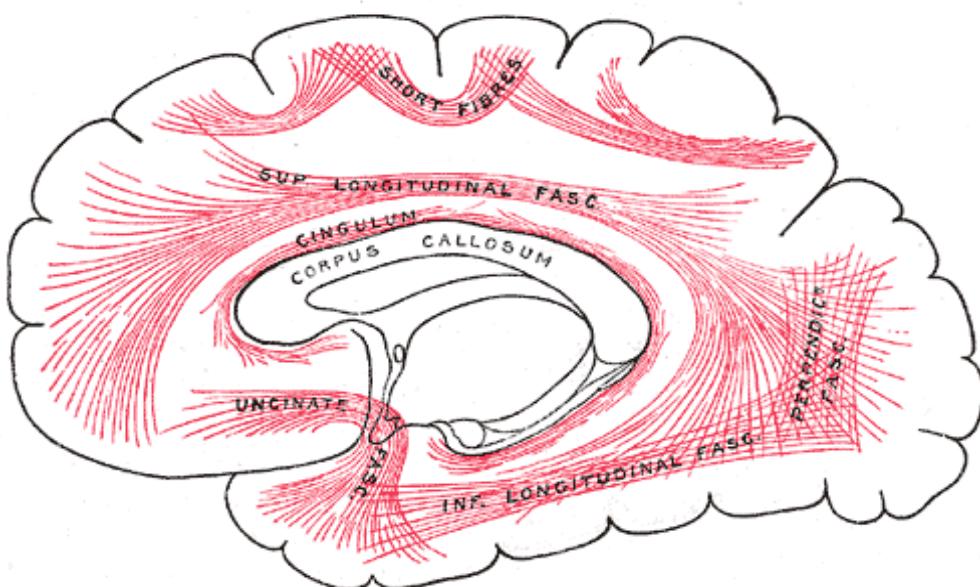
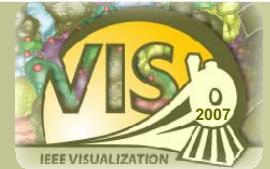


Image from Brun et al. 2003

# Fiber Clustering



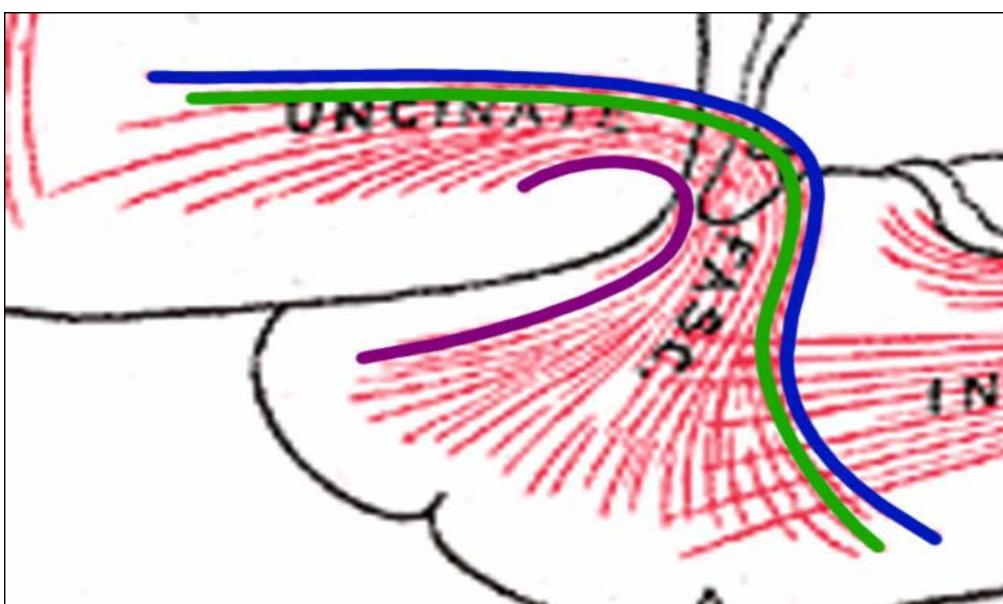
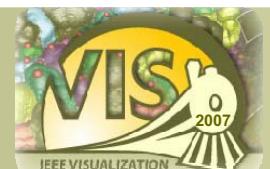
Group fibers together that are *similar*

Form fiber bundles that are meaningful

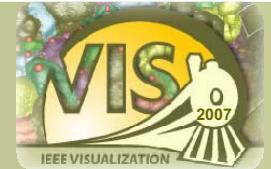
Two problems:

- How to measure similarity between fibers?
- How to define the groups of fibers?

# Fiber Bundle Properties



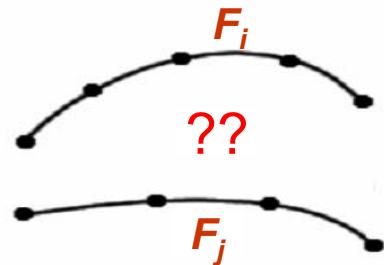
# A lot of possible combinations



Ding et al. 01, Shimony et al. 02, Zhang et al. 02, Brun et al. 03, Brun et al. 04, Corouge et al. 04, etc.

There are a lot of similarity measures :

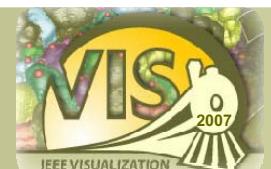
- Mean of closest points distance (Corouge et al. 04)
- Closest point distance (Corouge et al. 04)
- Hausdorff distance (Corouge et al. 04)
- End points distance (Brun et al. 03)
- ...



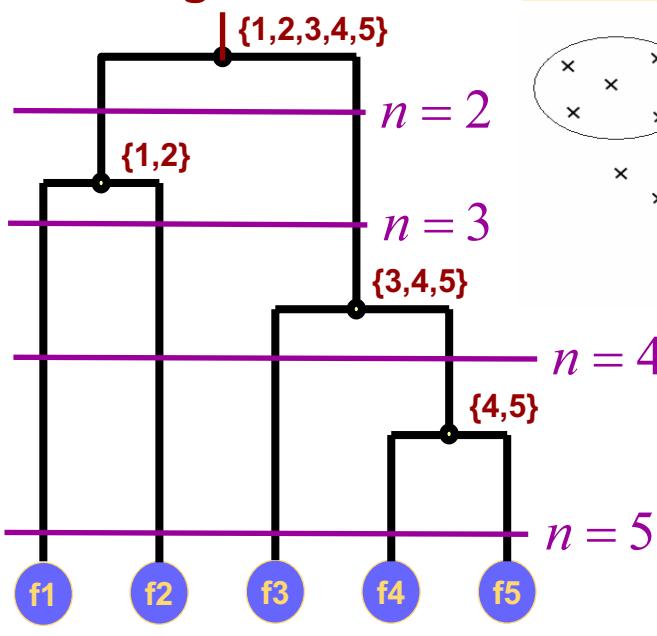
There are a lot of clustering algorithms:

- Hierarchical (Zhang et al. 02)
- Fuzzy c-means (Shimony et al. 02)
- Spectral clustering (O'Donnell and Westin 05)
- Shared nearest neighbor (Moberts et al. 05)
- ...

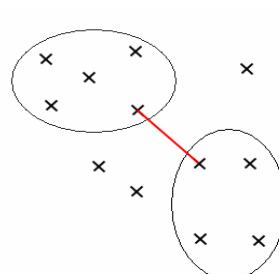
## Example: Hierarchical Clustering



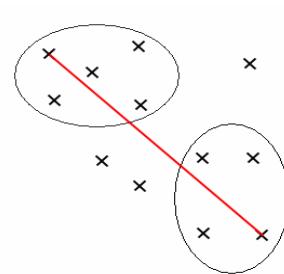
### Dendrogram



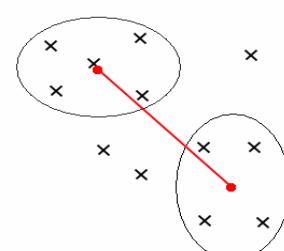
Single Link (HSL)



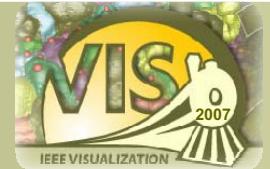
Complete Link (HCL)



Weighted Average(HWA)



# Validation

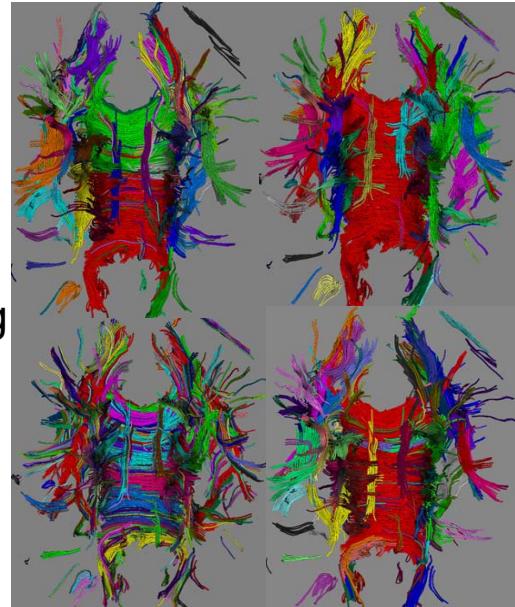


How do we know that ...

- ... a method is better than the other?
- ... a similarity measure is better than another?
- ... there is not a parameter setting giving better results?

Validation [Moberts et al. 05]

- Ground truth
- Comparison framework

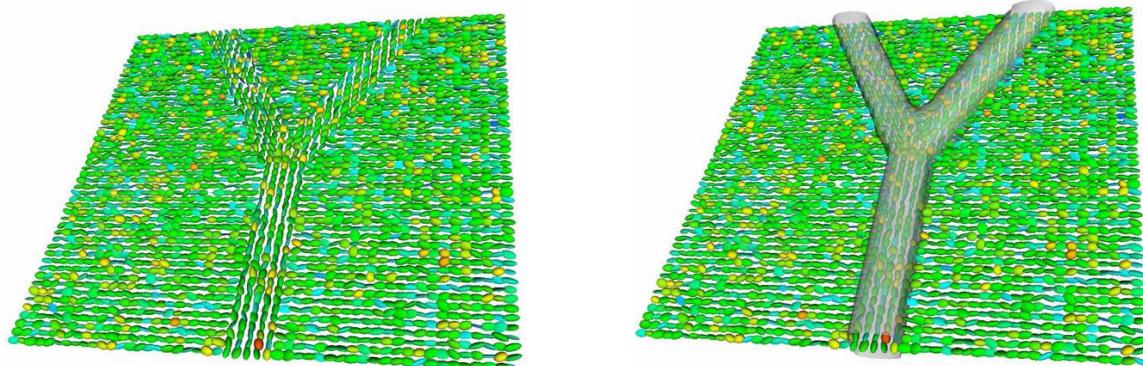


# Diffusion Tensor Imaging Segmentation



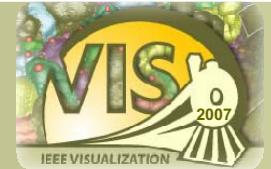
Fiber clustering depends on the fiber tracking algorithm and its parameter settings.

Can we directly segment the tensor fields (pdf)?



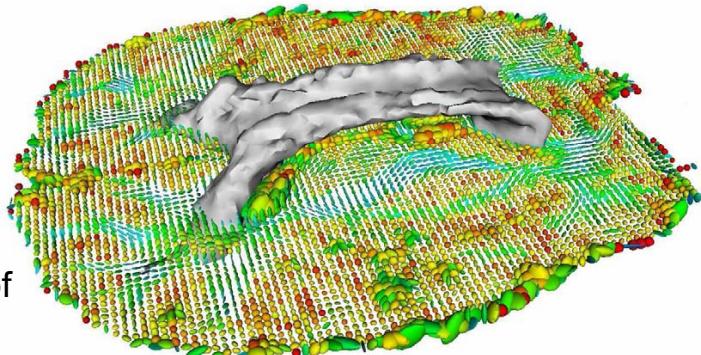
Images from [Lenglet et al. 04]

# Diffusion Tensor Imaging Segmentation



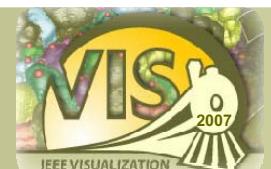
There exist several segmentation techniques for scalars:

- **Thresholding:** ordering of the tensors
- **Region based:** definition of homogeneity (e.g. Ziyani et al 06, Bartesaghi and Nadar 06)
- **Edge based:** definition of gradient in the tensor field
- **Deformable Models:** definition of forces and energies based on the tensor field (e.g., Lenglet et al 06, Wang et al. 05, Schultz et al. 06)
- ...



Corpus callosum segmentation  
using level sets technic  
Images from [Lenglet et al. 04]

## Tensor similarity or distance



You want to group diffusion tensors that are similar.

Given tensor A and B, How similar (different) are they?

- Linear Algebra- tensor is a 6D vector . Example:

$$d_{L2}(A, B) = \sqrt{\sum_{i=1}^3 \sum_{j=1}^3 (A_{ij} - B_{ij})^2}$$

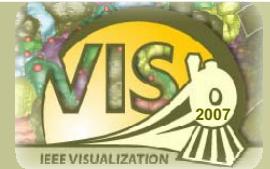
- Riemannian geometry- geodesic distance in the space of positive definite matrices.

$$d_g(A, B) = N(A^{-\frac{1}{2}} B A^{-\frac{1}{2}}) \quad N(D) = \sqrt{\sum_{i=1}^3 (\log(\lambda_i^D))^2}$$

Approximation Log-Euclidean distance

$$d_{LE}(A, B) = \sqrt{\text{tr}((\log(A) - \log(B))^2)}$$

## Tensor similarity or distance



- Probability density functions (pdf) – overlap of the pdf using A and B as covariant matrices of Gaussians

- Kullback-Leibler (KL) distance

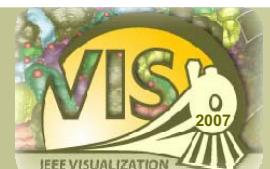
$$d_{KL}(A, B) = \frac{1}{2} \sqrt{\text{tr}(A^{-1}B + B^{-1}A) - 2n} \quad n \text{ is 3}$$

- Class separability Bhattacharvva bound

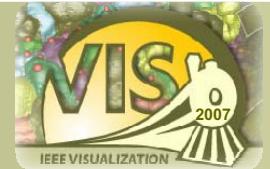
$$S_{Bhat}(A, B) = e^{-\frac{1}{2} \ln \left( \frac{\det(AB)/2}{\sqrt{\det(A)\det(B)}} \right)}$$

- Anisotropy Indices – use anisotropy indices FA, CI or any combination of those
- Angular differences – Use the angular difference between the main eigenvectors (dot product)

## DTI Segmentation

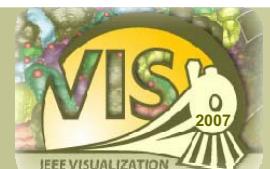


- What measure or method to use depends on the problem (e.g., bundle)
- Segmentation is an active field of research for scalar fields. Extension to tensor fields is a challenge
- These methods use the full information of the tensor and can be more robust and reproducible than fiber clustering techniques
- No much has been done in this field yet



- DiffusionTensor Imaging data
- DTI Visualization techniques
- Applications: newborn and ischemic heart
- Fiber clustering
- Diffusion tensor field segmentation

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