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Mathematik für Schlüsseltechnologien

Modeling the orientation distribution function by mixtures of angular central Gaussian distributions

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Outline

- Data properties
- Tensor model revisited
- Tensor mixture models
- Examples

- $P(\vec{r}, \vec{r}\,', \tau)$ - probability density for a particle (spin) to diffuse from position $\vec{r}\,'$ to $\vec{r}$ in time τ
- Aggregate over a voxel V

$$P(\vec{R}, \tau) = \int_{\vec{r}\,' \in V,\ \vec{R} = \vec{r} - \vec{r}\,'} P(\vec{r}, \vec{r}\,', \tau) p(\vec{r}\,') d\vec{r}\,',$$

$p(\vec{r}\,')$ is the initial probability density of particle location.

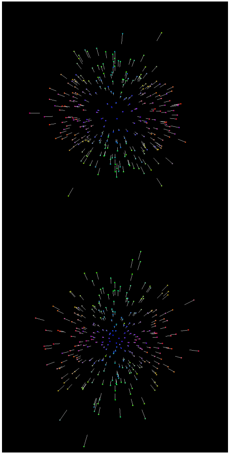
- Relates to the expected diffusion weighted signal $E(\vec{q}, \tau) = S(\vec{q}, \tau)/S_0$,

$$P(\vec{R}, \tau) = \int_{I\!R^3} E(\vec{q}, \tau)\, e^{-2\pi i \vec{q}\,\vec{R}} d\vec{q} = \mathcal{F}(E(\vec{q}, \tau)),$$

$$E(\vec{q}, \tau) = \int_{I\!R^3} P(\vec{R}, \tau)\, e^{2\pi i \vec{q}\,\vec{R}} d\vec{R} = \mathcal{F}^{-1}(P(\vec{q}, \tau)).$$

dMRI data in one voxel

140 gradients



Top: Data

Bottom: Apparent diffusion coefficient (ADC)

- Assumes homogeneity within a voxel
- Gaussian diffusion:

$$P(\vec{R},\tau) = P(r\vec{u},\tau) = \frac{1}{\sqrt{\det \mathcal{D}(4\pi\tau)^3}} \exp\left(-r^2 \frac{\vec{u}^T \mathcal{D}^{-1} \vec{u}}{4\tau}\right).$$

- Diffusion Tensor Model:

$$E(\vec{q},\tau) = E(q\vec{u},\tau) = e^{-b\vec{u}^T \mathcal{D}\vec{u}}$$

- Fully characterized by the Diffusion Tensor $\mathcal{D}$

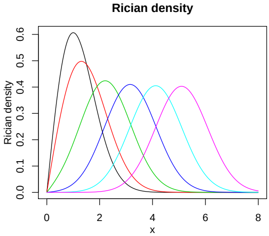
Noise:

- Measure $P(\vec{R},\tau)+\epsilon$ with $\epsilon \sim N(0,\sigma^2)$ (in K-Space)
- Noise:

$$S(\vec{u},\tau) \sim Rician(\zeta_i(\vec{u}),\sigma^2)$$

$$\zeta_i(\vec{u}) = \zeta_{i0} e^{-b\vec{u}^\top \mathcal{D}_i \vec{u}}$$

Rician densities



Estimation:

- Nonlinear regression with positivity constraints

$$\mathbf{R}(\zeta_i,\theta,\mathcal{D}) = \sum_j \frac{(\zeta_i(\vec{q}_j) - \theta\exp(-b\vec{q}_j^\top \mathcal{D}\vec{q}_j))^2}{\sigma^2_{j,i}}$$

$$\begin{pmatrix}\hat{\theta}_i \\ \hat{\mathcal{D}}_i\end{pmatrix} = \arg\min_{\theta,\mathcal{D}} \mathbf{R}(\hat{\zeta}_i,\theta,\mathcal{D})$$

- Mean diffusivity $Tr(\mathcal{D}) = \mu_1 + \mu_2 + \mu_3$
- Fractional anisotropy (FA)

$$FA = \sqrt{\frac{3}{2}}\sqrt{\frac{(\mu_1 - \langle\mu\rangle)^2 + (\mu_2 - \langle\mu\rangle)^2 + (\mu_3 - \langle\mu\rangle)^2}{\mu_1^2 + \mu_2^2 + \mu_3^2}}\ ,$$

- Geodesic anisotropy (GA) (Fletcher (2004), Corouge (2006))

$$GA = (\sum_{i=1}^{3}(log(\mu_i) - \overline{log(\mu)})^2)^{1/2}, \quad \overline{log(\mu)} = \frac{1}{3}\sum_{i=1}^{3} log(\mu_i)$$

- Bary-coordinates (characterizing spherical, planar and linear shape)

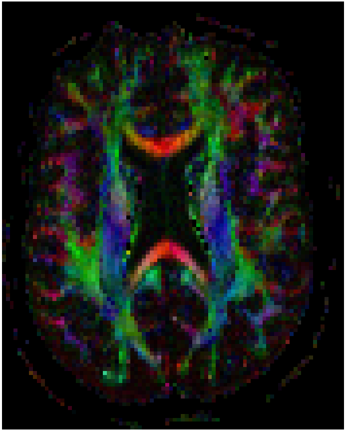
$$C_s = \frac{\mu_3}{\langle\mu\rangle} \quad C_p = \frac{2(\mu_2 - \mu_3)}{3\langle\mu\rangle} \quad C_l = \frac{(\mu_1 - \mu_2)}{3\langle\mu\rangle}$$

- Gray-valued map of mean diffusivity
- Color coded FA / GA maps
  - FA / GA coded as image intensity
  - Principal eigenvector $\vec{e}_1 = (e_{1x}, e_{1y}, e_{1z})$ color coded in RGB
  - Commonly used

$$(R, G, B) = (|e_{1x}|, |e_{1y}|, |e_{1z}|) \cdot FA$$

  - Better alternative

$$(R, G, B) = (e_{1x}^2, e_{1y}^2, e_{1z}^2) \cdot FA$$



Diffusion tensor model (DTI) Assumptions:

- anisotropic Gaussian diffusion

$$P(r\vec{u},\tau) = \frac{1}{\sqrt{|\mathcal{D}|(4\pi\tau)^3}} \exp\left(-r^2 \frac{\vec{u}^T \mathcal{D}^{-1}\vec{u}}{4\tau}\right)$$

- homogeneous fiber structure within a voxel

Reality: high percentage of voxel with fiber crossings or bifurcations

Consequences:

- Uninformative tensor estimates
- Reduction in FA
- Biased or non-existent directional information

Need a better description: Orientation density function Wedeen (2005), Aganj et.al.(2010)

$$\psi_{\vec{u}} = \int_0^\infty r^2 P(r\vec{u})dr,$$

Projection of $P(r\vec{u})$ onto the unit Sphere $\mathbb{S}^2$

Relation between $E(\vec{q})$ and $\psi_{\vec{u}} = \int_0^\infty r^2 P(r\vec{u})dr$

- Represent $\vec{q} = q\vec{u}$ by (q, θ, ϕ)
- The Fourier transform of $r^2 P(r\vec{q})$ is

$$\begin{aligned} -\bigtriangledown^2 E(\vec{q}) &= -\frac{1}{\vec{q}}\frac{\delta^2}{\delta\vec{q}^2}(qE) + \bigtriangledown_b^2 E \\ \bigtriangledown_b^2 E &= \frac{1}{q^2}\left[\frac{1}{\sin(\phi)}\frac{\delta}{\delta\theta}(\sin\theta\frac{\delta E}{\delta\theta}) + \frac{1}{\sin^2\theta}\frac{\delta^2 E}{\delta\phi^2}\right] \end{aligned}$$

- Funk-Radon transform (line integral over unit equator):
  for $f : R^3 \to R$ symmetric and $F(\vec{q})$ it's 3D Fourier transform

$$\int_0^\infty f(r\vec{q})dr = \frac{1}{8\pi^2}\iint_{\vec{u}^\perp} F(\vec{q})d^2\vec{q}$$

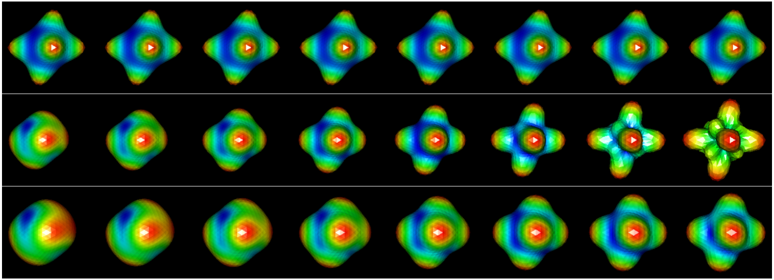
- In spherical coordinates (Q-Ball imaging, see Aganj et al. (2010)) $\theta \equiv \pi/2$

$$\psi(\vec{u}) = \frac{1}{4\pi} - \frac{1}{8\pi^2}\int_0^{2\pi}\int_0^\infty \frac{1}{q}\bigtriangledown_b^2 E dq d\phi = \frac{1}{4\pi} - \frac{1}{8\pi^2}\int_0^{2\pi}\bigtriangledown_b^2 ln(-lnE))d\phi$$

Expansion into spherical harmonics (fast) (Descoteaux et al., (2007), Aganj et al. (2010))

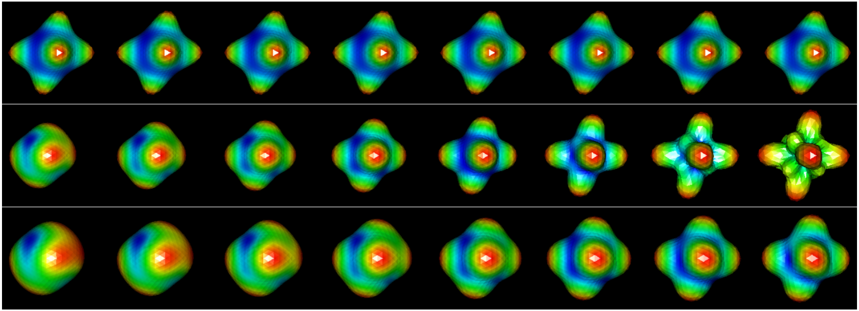
$$\ln(-\ln E(\vec{q}_i)) = \sum_{j=1}^{J} c_j Y_j(\vec{q}_i) \qquad \text{for } i = 1, \ldots, N$$

$$\psi(\vec{u}) = \frac{1}{2\sqrt{\pi}} Y_1(\vec{u}) - \frac{1}{16\pi^2} \sum_{j=2}^{J} 2\pi P_{k_j}(0) k_j(k_j+1) c_j Y_j(\vec{u})$$



Top: True ODF, Center: Q-ball direct, Bottom: Q-ball with regularization

- ODF via Funk-Radon transform is non-linear in E $(ln(-lnE))$
- Missing additivity for mixture distributions
- Reconstruction depends on b-value
- high-frequency artifacts (needs regularization)



Top: True ODF, Center: Q-ball direct, Bottom: Q-ball with regularization
b-value varying from left to right by a factor $\sqrt{2}$

- Elliptically symmetric distribution

$$P(\vec{R},\tau) = C_\tau (\det \mathcal{D})^{-1/2} h_\tau(\vec{R}^\top \mathcal{D}^{-1}\vec{R})$$

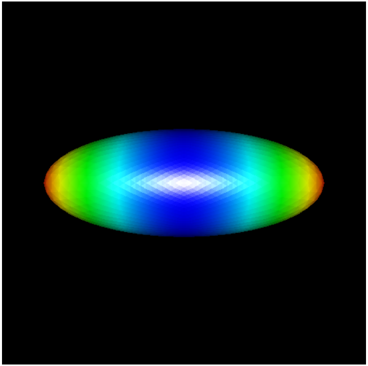
  with mean 0,
  tensor $\mathcal{D}$,
  function $h_\tau : R^+ \to R$ and
  normalization constant C_τ

- ODF

$$\psi(\vec{u}) = \frac{1}{4\pi\sqrt{\det \mathcal{D}}}\left(\vec{u}^T \mathcal{D}^{-1}\vec{u}\right)^{-3/2},$$

- angular central Gaussian distribution on the sphere.
- Special case: anisotropic Gaussian diffusion assumed for the tensor model.

Tensor ODF

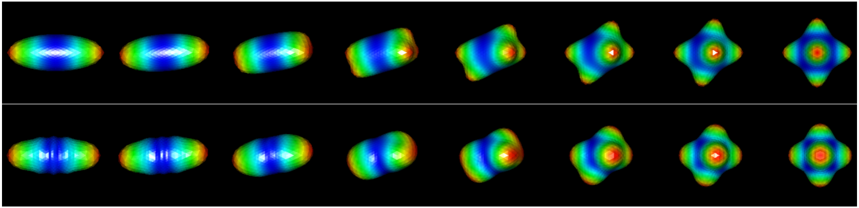


- Assume a mixture of fiber bundles in each voxel
- unknown number M of compartments
- Each fiber bundle can be described by a tensor model
- Model:

$$\mathrm{E}\,\frac{S(\vec{q})}{S_0} = \sum_m w_m \exp(-b\vec{q}^\top \mathcal{D}_m^{-1}\vec{q}) \quad \sum_m w_m = 1, \quad w_m \geq 0$$

- ODF-representation: Mixture of angular central Gaussian distributions

$$\psi(\vec{u},\tau) = (4\pi)^{-1} \sum_{m=1}^{M} w_m |\mathcal{D}_m|^{-1/2} (\vec{u}^\top \mathcal{D}_m^{-1}\vec{u})^{-3/2}$$



- Parameter identify-ability ? ..., need for model reduction
- Homogeneous geometry of fibers $\mapsto$ rotational symmetric (prolate) tensors of same eccentricities;

$$\mathcal{D}_m = \lambda_2 I_3 + (\lambda_1 - \lambda_2) d_m d_m^\top$$

- Model:

$$\begin{aligned} \mathrm{E}\,\frac{S(\vec{q})}{S_0} &= \sum_{m=1}^{M} w_m \exp(-b\vec{q}^{\,\top} \mathcal{D}_m \vec{q}), \qquad \sum_m w_m = 1, \quad w_m \geq 0 \\ &= \sum_m \tilde{w}_m \exp(-\theta(\vec{q}^{\,\top} d_m)^2) \qquad \tilde{w}_m \geq 0 \end{aligned}$$

with $w_m = \tilde{w}_m / \sum(\tilde{w}_m)$, $b\lambda_2 = \log(\sum(\tilde{w}_m))$ and $\theta = b(\lambda_1 - \lambda_2)$.

- Alternative model (with isotropic compartment):

$$\mathrm{E}\,\frac{S(\vec{q})}{S_0} = \tilde{w}_0 \exp(-\theta) + \sum_m \tilde{w}_m \exp(-\theta(\vec{q}^{\,\top} d_m)^2) \quad \tilde{w}_m \geq 0$$

Mixed Tensor Models II

- Separable nonlinear least squares problem with constraints on linear parameters.

$$min_{(\theta,d_1,\ldots d_M)} min_{\tilde{w}_m \geq 0} \sum_{j=1}^{N} \left(\frac{S(\vec{g_j})}{S_0} - \sum_{m=1}^{M} \tilde{w}_m \exp(-\theta(\vec{q}^\top d_m)^2) \right)^2$$

- Problem: difficult to solve for low SNR

How many components ?

- Model selection problem
- Nested models for orders $M = M_{max}, \ldots, 1$
- Order selected by BIC

$$Q(M) = \sum_{j=1}^{N} \left(\frac{S(\vec{g_j})}{S_0} - \sum_{m=1}^{M} \hat{\tilde{w}}_m \exp(-\hat{\theta}(\vec{q}^\top \hat{d}_m)^2) \right)^2 + \log(N)(3M+1)$$

- automatic reduction in case of zero weights

- Estimated model order M_{best}
- Mixture coefficients w_m estimate volume of compartments
- Partial volume corrected fractional anisotropy (PVC-FA):

$$\mathrm{FA} = \sqrt{\frac{3}{2}}\sqrt{\frac{(\lambda_1 - \langle\lambda\rangle)^2 + 2\cdot(\lambda_2 - \langle\lambda\rangle)^2}{\lambda_1^2 + 2\cdot\lambda_2^2}} = \frac{(\lambda_1 - \lambda_2)}{\sqrt{\lambda_1^2 + 2\cdot\lambda_2^2}}\ .$$

- Effective model order (EO):

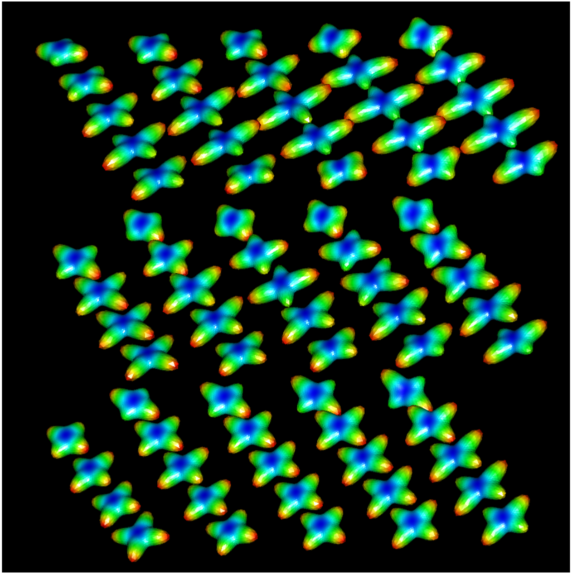
  For $w_1 \geq w_2 \geq \cdots \geq w_{M_{best}}$

$$\mathrm{EO} = \sum_{m=1}^{M_{best}-1} m^2(w_m - w_{m+1}) = \sum_{m=1}^{M_{best}} (2m-1)w_m\ .$$

Properties: $1 \leq \mathrm{EO} \leq M_{best}$, $\quad \mathrm{EO} = M_{best} \iff w_i \equiv 1/M_{best}$

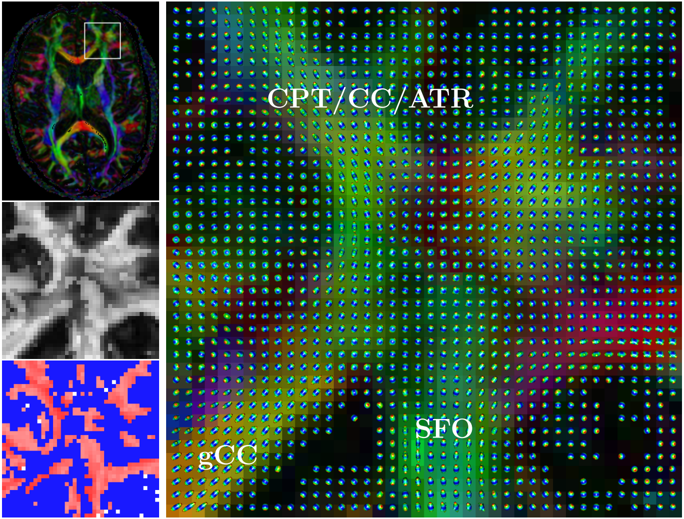
Data: (H.-U. Voss, Weill Cornell Medical College),

- 3.0 Tesla GE Signa Excite MRI Scanner
- 8 Channel receive only head coil
- $10 S_0$ images and 140 gradient directions
- $TE = 73.2ms, TR = 14s$
- 66 slices
- Acquisition matrix size: 128×128 zero filled to 256×256
- Voxelsize; $0.898 \times 0.898 \times 1.8mm^3$
- b-value $1000 \frac{s}{mm^2}$

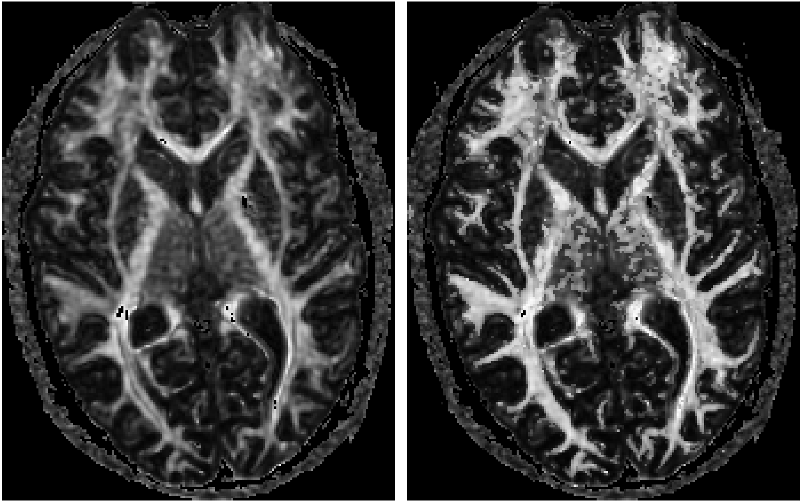


3D ODF: tensor mixtures
(exponentially scaled)

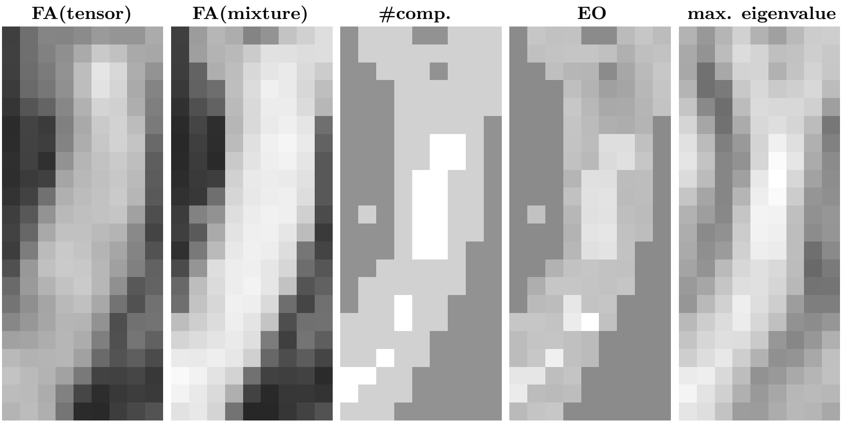
Tensor Mixture Models: Results



Color coded FA,
FA / PVC-FA,
effective order,
estimated tensor
mixtures



Tensor FA and PVC-FA



Results for a sub region, $M_{max} = 4$:

FA: range $(0, 1)$,

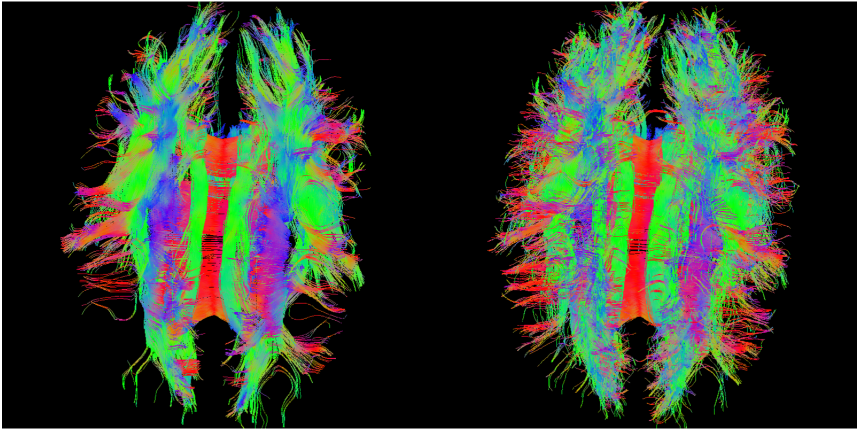
estimated number of mixture components: range $(0, 3)$,

effective order: range $(0, 2.8)$,

maximal eigenvalue (range $(0, 2.27)$)

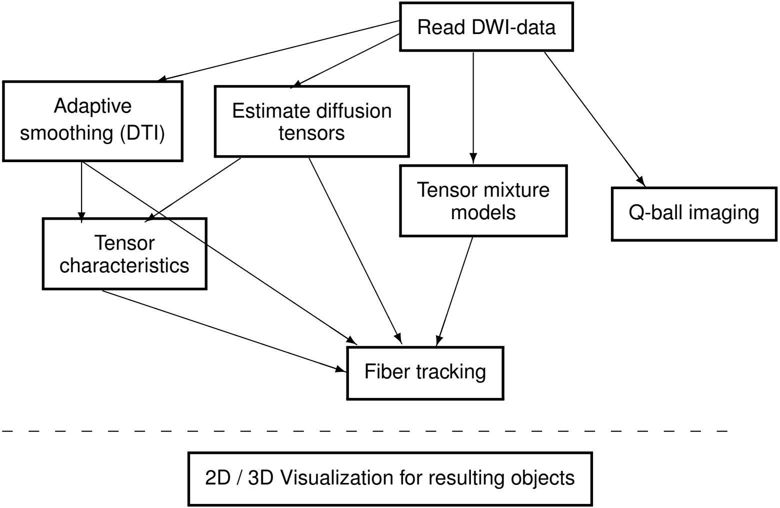
Fiber tracking results using a streamline algorithm

Fibers of length 80 or more



Left: Tensor model Right: Tensor Mixture Model with $M_{max} = 5$

Analyzing dMRI within the R statistical environment



```
> library(dti)
> gradients <- read.table("b-directions.txt")
> dwiobj <- readDWIdata(gradients, "data1", "NIFTI")
> dwiobj <- sdpar(dwiobj, 500, interactive = FALSE)
> dtiobj <- dtiTensor(dwiobj) # Tensor estimation
> dtiind <- dtiIndices(dtiobj) # Tensor characteristics
#  Smoothing
> dtiobj.smooth <- dti.smooth(dwiobj, hmax = 4) # Tensor estimation w. adapt. smoothing
> dtiind.smooth <- dtiIndices(dtiobj.smooth) # Tensor characteristics
> dwiobj.smooth <- dwi.smooth(dwiobj,kstar=12)
# Tensor Mixtures
> mtensobj <- dwiMixtensor(dwiobj, maxcomp = 4) # estimate tensor mixtures
> dwiqball8 <- dwiQball(dwiobj, order = 8, lambda = 2.5e-3) # Regularized Q-ball
# Fiber tracking
> tracks <- tracking(dtiobj, minfa = .266,maxangle=45) # Fiber tracking
> tracks <- reduceFibers(tracks, maxdist = .5) # remove redundant fibers
> tracksmt <- reduceFibers(tracking(mtensobj, minfa = .266,maxangle=45)) # Fiber tracking
# Visualization
> plot(dtiind.smooth, slice=45)
> show3d(mtensobj[36:45,36:45,41:45])
> show3d(selectFibers(tracksmt,minlength=100))
```

Collaborations

Joint Work with:

- Karsten Tabelow, Saskia Becker and Vladimir Spokoiny, WIAS and MATHEON
- Henning U. Voss, Weill Medical College, Cornell University
- Michael Deppe, University of Münster

Cooperation:

- Citigroup Biomedical Imaging Center, Weill Medical College, Cornell University
- University of Münster
- BNIC, Charité, Berlin
- Max-Plank Institute for Human Cognitive and Brain Sciences, Leipzig

R-Community:

- CRAN Task View: Medical Image Analysis
- Special volume 44 on Magnetic Resonance Imaging in R of *Journal of Statistical Software*

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