High Order Models in Diffusion MRI and Applications

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DTI



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GDTI











3-i













5-i











Introduction

- 1. Think Positive: 4th Order Symmetric Tensors
 - A Riemannian Approach
 - A Polynomial Approach (Ternary Quartic)
- Fast and Analytical EAP Approximation from a 4th Order Tensor
- 3. Geometric Features from Spherical Diffusion Functions
 - Maxima Extraction
 - Peak Fractional Anisotropy



Diffusion NMR 8-i



Stejskal-Tanner signal: a phenomenological approach

• Signal: $S = S_0 \exp(-bD)$ $S = S_0 \exp(-b \cdot \underbrace{\mathbf{g}^T \mathbf{D} \mathbf{g}}_{ADC})$



Diffusion NMR



Stejskal-Tanner signal: a phenomenological approach

Signal:
$$S = S_0 \exp(-bD)$$
 $S = S_0 \exp(-b \cdot \underbrace{\mathbf{g}^T \mathbf{D} \mathbf{g}}_{ADC})$

4 q-Space formalism: a random walk model

Solution Fourier Transform:
$$\frac{S(\mathbf{q}, \Delta)}{S_0} = \int P(\mathbf{r}, \Delta) e^{2\pi i \mathbf{q} \cdot \mathbf{r}} d\mathbf{r}$$

 $P(\mathbf{r}, \Delta)$: Ensemble Averate Propagator (EAP)



[Stejskal 1965, Callaghan 1993]



Stejskal-Tanner signal [Basser 1994]

$$\frac{S_i}{S_0} = \exp\left(-b\mathbf{g}_i^T \mathbf{D} \mathbf{g}_i\right)$$

Free diffusion / Gaussian diffusion [Basser 1994]

$$P(\mathbf{r},t) = \frac{1}{\sqrt{|\mathbf{D}|(4\pi t)^3}} \exp\left(-\frac{\mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}}{4t}\right)$$





Higher Order Description 11-i

$$\underbrace{S(\mathbf{q},\Delta)}{S_0} = \int P(\mathbf{r},\Delta) e^{2\pi i \mathbf{q}.\mathbf{r}} d\mathbf{r} \longrightarrow \underbrace{S(\mathbf{q},\Delta)}_{\mathbf{F}} e^{2\pi i \mathbf{q}.\mathbf{r}} d\mathbf{r}$$



Higher Order Description 12-i











Strong *b*-values

[Callaghan 1993, Wedeen 2000]



Higher Order Description 14-i



- S Function: Sphere -> Sphere [Tuch 2004]
- Angular information
- Analytical Expression (Spherical Harmonics)

[Anderson 2005, Hess 2006, Descoteaux 2007]



Higher Order Description 15-i

Spherical Harmonics Q-Ball Imaging (QBI) E(q) Funk-Radon Transform Acquisition q-space Signal ∞ $P(r\hat{u})dr$ **Diffusion Tensor Imaging (DTI)** Stejskal-Tanner Fourier $ADC = \mathbf{g}^T \mathbf{D} \mathbf{g}$ Transform Gaussian Gaussian $\overline{S(\mathbf{q},\Delta)} =$ Radial $P(\mathbf{r},\Delta)e^{2\pi i\mathbf{q}.\mathbf{r}}d\mathbf{r}$ S_0 Integral EAP Acquisition $\frac{\text{ODF}}{P(r\hat{u})r^2dr}$ Fast Fourier Transform steiskal-tannet **Diffusion Spectrum Imaging (DSI)** Fast Fourier Transform q-Space Extrapolation $ADC = D_{i_1 i_2 \dots i_k} g_{i_1} g_{i_2} \dots g_{i_k}$ Stejskal-Tanner Generalized DTI-1 Higher Order Tensor q-Space

High Order Cartesian Tensors

[Ozarslan 2003, 2004]



1. Think Positive 16-i



1. Think Positive: High Order Symmetric Tensors



2. EAP Approximation 17-i



2. Analytical EAP Approximation from a 4th Order Tensor



3. Geometric Features 18-i



3. Geometric Features from Spherical Diffusion Functions



- Research at INRIA Sophia Antipolis Méditerranée:
- DTI with positivity constraint (*tensors*):
 - > Riemannian Metric: Odyssée, Asclepios

[Pennec 2006, Lenglet 2006]

- > Log-Euclidean Metric: Asclepios [Arsigny 2006]
- Analytical QBI (high order models): Odyssée [Descoteaux 2008]

Explore *high order Cartesian tensor models*



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Context 2-1





Motivation 3-1

A Diffusion is a physical process: Positive DTI

Riemannian Metric: [Bachelor'05, Moakher'05, Pennec'06, Lenglet'06]

$$d(\mathbf{D}_1, \mathbf{D}_2)_{Rm} = \sqrt{tr(ln^2(\mathbf{D}_1^{-1/2}\mathbf{D}_2\mathbf{D}_1^{-1/2}))}$$

S Log-Euclidean Metric: [Arsigny 2006]

$$d(\mathbf{D}_1, \mathbf{D}_2)_{LE} = \sqrt{tr(\{ln(\mathbf{D}_1) - ln(\mathbf{D}_2)\}^2)}$$

DTI limited to Gaussian diffusion

 $ADC = \mathbf{g}^T \mathbf{D} \mathbf{g} = g_1^2 d_{11} + g_2^2 d_{22} + g_3^2 d_{33} + \dots 2$ nd order polynomial



Generalized DTI 4-1

[Ozarslan 2003]

$$ADC = D_{j_1 j_2 \dots j_k} g_{j_1} g_{j_2} \dots g_{j_k} = \sum_{j_1=1}^3 \sum_{j_2=1}^3 \dots \sum_{j_k=1}^3 D_{j_1 j_2 \dots j_k} g_{j_1} g_{j_2} \dots g_{j_k}$$

- Higher Order symmetric Tensors
- Complex ADC profile





Generalized DTI 5-1

[Ozarslan 2003]

$$ADC = D_{j_1 j_2 \dots j_k} g_{j_1} g_{j_2} \dots g_{j_k} = \sum_{j_1=1}^3 \sum_{j_2=1}^3 \dots \sum_{j_k=1}^3 D_{j_1 j_2 \dots j_k} g_{j_1} g_{j_2} \dots g_{j_k}$$

Higher Order symmetric Tensors

Complex ADC profile



Complex ADC





Generalized DTI 6-1

$$ADC = D_{j_1 j_2 \dots j_k} g_{j_1} g_{j_2} \dots g_{j_k} = \sum_{j_1=1}^3 \sum_{j_2=1}^3 \dots \sum_{j_k=1}^3 D_{j_1 j_2 \dots j_k} g_{j_1} g_{j_2} \dots g_{j_k}$$

Higher Order symmetric Tensors

Complex ADC profile



Complex ADC







K Isometric mapping: Matrix -> Vector

$$\mathbf{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} \qquad \qquad \mathbf{d} = \begin{bmatrix} D_{xx} \\ D_{yy} \\ D_{zz} \\ \sqrt{2}D_{xy} \\ \sqrt{2}D_{xz} \\ \sqrt{2}D_{yz} \end{bmatrix}$$

A Major+Minor symmetry: 4th order 3D -> 6D Matrix:

$$\mathcal{A} = \begin{pmatrix} \begin{pmatrix} A_{xx}^{A} & A_{xy}^{A} & A_{xz}^{A} & A_{xx}^{A} & A_{xx$$



8-1

Isometric mapping: Matrix -> Vector

$$\mathbf{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} \qquad \qquad \mathbf{d} = \begin{bmatrix} D_{xx} & D_{yy} \\ D_{yy} \\ D_{zz} \\ \sqrt{2}D_{xy} \\ \sqrt{2}D_{xz} \\ \sqrt{2}D_{yz} \end{bmatrix}$$

X Major+Minor symmetry: 4th order 3D -> 6D Matrix:



Athena GDTI-4: A Riemannian Approach 9-1

GDTI 4th order Stejskal-Tanner equation: [Moakher 2006]

$$-\frac{1}{b}\ln\left(\frac{S_i}{S_0}\right) = \widehat{A}_{j_1j_2j_3j_4}g_{j_1}g_{j_2}g_{j_3}g_{j_4} = \mathbf{d}_i^T\widehat{\mathbf{A}}\mathbf{d}_i \qquad \mathbf{d}_i = \mathbf{g}_i \times \mathbf{g}_i$$

a **GDTI-4: A Riemannian Approach** ¹⁰⁻¹

GDTI 4th order Stejskal-Tanner equation: [Moakher 2006]

$$-\frac{1}{b}\ln\left(\frac{S_i}{S_0}\right) = \widehat{A}_{j_1j_2j_3j_4}g_{j_1}g_{j_2}g_{j_3}g_{j_4} = \mathbf{d}_i^T\widehat{\mathbf{A}}\mathbf{d}_i \qquad \mathbf{d}_i = \mathbf{g}_i \times \mathbf{g}_i$$

 \bigstar Riemannian gradient descent on Sym_6^+

$$\widehat{\mathbf{A}}_{t+1} = \widehat{\mathbf{A}}_t^{\frac{1}{2}} \exp\left(-\epsilon \cdot \widehat{\mathbf{A}}_t^{\frac{1}{2}} \left[\sum_{i=1}^N \left(\frac{1}{b} \ln\left(\frac{S_i}{S_0}\right) + \mathbf{d}_i^T \widehat{\mathbf{A}} \mathbf{d}_i\right) \cdot (\mathbf{d}_i \mathbf{d}_i^T)\right] \widehat{\mathbf{A}}_t^{\frac{1}{2}}\right) \widehat{\mathbf{A}}_t^{\frac{1}{2}}$$

Guarantees positive definiteness: $ADC = \mathbf{d}_i^T \widehat{\mathbf{A}} \mathbf{d}_i > 0$

• Estimate totally symmetric: $\widehat{\mathbf{A}} \longrightarrow \widehat{\mathbf{A}}^s$

GDTI-4: A Riemannian Approach ¹¹⁻¹

GDTI 4th order Stejskal-Tanner equation: [Moakher 2006]

$$-\frac{1}{b}\ln\left(\frac{S_i}{S_0}\right) = \widehat{A}_{j_1j_2j_3j_4}g_{j_1}g_{j_2}g_{j_3}g_{j_4} = \mathbf{d}_i^T\widehat{\mathbf{A}}\mathbf{d}_i \qquad \mathbf{d}_i = \mathbf{g}_i \times \mathbf{g}_i$$

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Guarantees positive definiteness: $ADC = \mathbf{d}_i^T \widehat{\mathbf{A}} \mathbf{d}_i > 0$

• Estimate totally symmetric: $\widehat{\mathbf{A}} \longrightarrow \widehat{\mathbf{A}}^s$

 $\widehat{\mathbf{G}} \text{ Riemannian constraint is too strong} \\ \mathbf{d}^T \widehat{\mathbf{A}} \mathbf{d} > 0 \ \forall \mathbf{d} \in \mathbf{R}^6$



Results: Real Data 12-1

(81 dirs)	LS	SH	RM
Positive	181757	249263	249352
Negative	67595	89	0

249352 estimated tensors. ADC along 81 dirs





Real data: [Poupon 2006]



Results: Phantom Data 13-1

Rat phantom data:

[Campbell 2005]

(a) Layout
(b),(c) GDTI → EAP
(d) ODF-SA





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Riemannian approach on GDTI won't permit:

Unreachable tensors (swelling effect?)

X Matrix representation has to be *rank-defficient*



A Polynomial Approach 16-1

[Barmpoutis 2007,2009, Ghosh 2009]

🔆 A Homogeneous Polynomial

 $ADC = \sum_{j_1=1}^{3} \sum_{j_2=1}^{3} \sum_{j_3=1}^{3} \sum_{j_4=1}^{3} D_{j_1 j_2 j_3 j_4} g_{j_1} g_{j_2} g_{j_3} g_{j_4} = \sum_{m+n+p=4}^{3} D_{mnp} g_1^m g_2^n g_3^p$

Ternary Quartics: think positive

Theorem (Hilbert 1888)

A *non-negative* real ternary quartic form f(x, y, z) is the sum of three squares of quadratic forms.



A Polynomial Approach 17-1

[Barmpoutis 2007,2009, Ghosh 2009]

🔆 A Homogeneous Polynomial

 $ADC = \sum_{j_1=1}^{3} \sum_{j_2=1}^{3} \sum_{j_3=1}^{3} \sum_{j_4=1}^{3} D_{j_1 j_2 j_3 j_4} g_{j_1} g_{j_2} g_{j_3} g_{j_4} = \sum_{m+n+p=4}^{3} D_{mnp} g_1^m g_2^n g_3^p \ge \mathbf{0}$

Ternary Quartics: think positive

Theorem (Hilbert 1888)

A *non-negative* real ternary quartic form f(x, y, z) is the sum of three squares of quadratic forms.

$$\overleftarrow{\mathbf{\mathsf{Gram Matrix}}}$$

$$ADC = (\mathbf{v}^T \mathbf{q}_1)^2 + (\mathbf{v}^T \mathbf{q}_2)^2 + (\mathbf{v}^T \mathbf{q}_3)^2 = \mathbf{v}^T \mathbf{Q} \mathbf{Q}^T \mathbf{v} = \mathbf{v}^T \mathbf{G} \mathbf{v}$$

$$\mathbf{v} = [g_1^2, g_2^2, g_3^2, g_1 g_2, g_1 g_3, g_2 g_3]^T, \quad \mathbf{Q} : 6 \times 3, \quad \mathbf{G} : Rank - 3$$


[Ghosh 2009]

Stejskal-Tanner equation:

$$\frac{1}{b} \ln \left(\frac{S_i}{S_0} \right) = (\mathbf{v}^T \mathbf{q}_1)^2 + (\mathbf{v}^T \mathbf{q}_2)^2 + (\mathbf{v}^T \mathbf{q}_3)^2$$
$$= [\mathbf{q}_1^T, \mathbf{q}_2^T, \mathbf{q}_3^T] \begin{bmatrix} \mathbf{v} \mathbf{v}^T & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{v} \mathbf{v}^T & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{v} \mathbf{v}^T \end{bmatrix} \begin{bmatrix} \mathbf{q}_1 \\ \mathbf{q}_2 \\ \mathbf{q}_3 \end{bmatrix} = \mathbf{Q}^T \mathbf{V} \mathbf{Q}$$



[Ghosh 2009]

Stejskal-Tanner equation:

$$\begin{aligned} -\frac{1}{b} \ln \left(\frac{S_i}{S_0} \right) &= (\mathbf{v}^T \mathbf{q}_1)^2 + (\mathbf{v}^T \mathbf{q}_2)^2 + (\mathbf{v}^T \mathbf{q}_3)^2 \\ &= [\mathbf{q}_1^T, \mathbf{q}_2^T, \mathbf{q}_3^T] \begin{bmatrix} \mathbf{v} \mathbf{v}^T & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{v} \mathbf{v}^T & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{v} \mathbf{v}^T \end{bmatrix} \begin{bmatrix} \mathbf{q}_1 \\ \mathbf{q}_2 \\ \mathbf{q}_3 \end{bmatrix} = \mathbf{Q}^T \mathbf{V} \mathbf{Q} \end{aligned}$$

Non-linear optimization:

$$\nabla E(\mathbf{Q}) = \sum_{i=1}^{N} \left(\frac{1}{b} \log \left(\frac{S_i}{S_0} \right) + \mathbf{Q}^T \mathbf{V}_i \mathbf{Q} \right) \left(\mathbf{V}_i + \mathbf{V}_i^T \right) \mathbf{Q}$$

Guarantees non-negativeness: $ADC \ge 0$

Solves the correct problem

Results: Synthetic Data 20-1















Results: Real Data 21-1



Real data: [Poupon 2006]





Results: Real Data 22-1

(81 dirs)	LS	SH	RM	TQ
Positive	181757	249263	249352	249352
Negative	67595	89	0	0

249352 estimated tensors. ADC along 81 dirs

(987 tensors)	LS	Rm	TQ
Estimation	6s	35s	102s

Time for estmating 987 tensors





[Ghosh 2008]

- 4th order 3D tensor -> 2nd order 6D tensor
- Guarantees Positive Definiteness
- Solves over-constrained problem
- 🔆 A Polynomial Approach

[Ghosh 2009]

- Hilbert's theorem on Ternary Quartics
- Solves the correct problem
- Guarantees non-negativeness



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Context 2-2





Ensemble Average Propagator

3-2

[Ozarslan-2004]





Ensemble Average Propagator

4-2

[Ozarslan-2004]







Motivation



5-2



Modified GDTI 6-2

$$E(\mathbf{q})_{k} = e^{-\frac{4\pi^{2}|\mathbf{q}|^{2}t}{\sum_{m+n+p=k} D_{mnp}g_{1}^{m}g_{2}^{n}g_{3}^{p}}} t = (\Delta - \frac{\delta}{3}); \quad \mathbf{g} = \frac{\mathbf{q}}{|\mathbf{q}|}}$$

Radial: order-2 Angular: order-k



Modified GDTI 7-2

$$E(\mathbf{q})_{k} = e^{-4\pi^{2}|\mathbf{q}|^{2}t} \sum_{m+n+p=k} D_{mnp}g_{1}^{m}g_{2}^{n}g_{3}^{p} \qquad t = (\Delta - \frac{\delta}{3}); \quad \mathbf{g} = \frac{\mathbf{q}}{|\mathbf{q}|}$$

Radial: order-k1 Angular: order-k2

Generalize separation of radial & angular

$$E(\mathbf{q})_{k1,k2} = e^{-4\pi^2 \alpha |\mathbf{q}|^{k_1} t \sum_{m+n+p=k_2} D_{mnp} g_1^m g_2^n g_3^p} \\ = e^{-4\pi^2 \alpha |\mathbf{q}|^{k_1-k_2} t \sum_{m+n+p=k_2} D_{mnp} q_1^m q_2^n q_3^p}$$

 $\alpha = 1m^{2-k1}$



Modified GDTI 8-2

$$E(\mathbf{q})_{k} = e^{-4\pi^{2}|\mathbf{q}|^{2}t} \sum_{m+n+p=k} D_{mnp}g_{1}^{m}g_{2}^{n}g_{3}^{p} \qquad t = (\Delta - \frac{\delta}{3}); \quad \mathbf{g} = \frac{\mathbf{q}}{|\mathbf{q}|}$$

Radial: order-k1 Angular: order-k2

Generalize separation of radial & angular

$$E(\mathbf{q})_{k,k} = e^{-4\pi^2 \alpha t} \sum_{m+n+p=k} D_{mnp} q_1^m q_2^n q_3^p$$

$$\bigstar$$
 Homogeneous polynomial over \mathbb{R}^3 when k1=k2=k



Taylor Expansion9-2

 $E(\mathbf{q})_{k,k} = e^{\left(-4\pi^2 \alpha t \sum D_{mnp} q_1^m q_2^n q_3^p\right)}$



Taylor Expansion10-2

$$E(\mathbf{q})_{k,k} = e^{\left(-4\pi^2 \alpha t \sum D_{mnp} q_1^m q_2^n q_3^p\right) + 2\pi^2 \beta (q_1^2 + q_2^2 + q_3^2)} \times e^{-2\pi^2 \beta (q_1^2 + q_2^2 + q_3^2)}$$

 $\beta = 1m^2$



Taylor Expansion11-2

$$E(\mathbf{q})_{k,k} = e^{\left(-4\pi^{2}\alpha t \sum D_{mnp}q_{1}^{m}q_{2}^{n}q_{3}^{p}\right) + 2\pi^{2}\beta(q_{1}^{2} + q_{2}^{2} + q_{3}^{2})} \times e^{-2\pi^{2}\beta(q_{1}^{2} + q_{2}^{2} + q_{3}^{2})} \\ = h(\mathbf{q})e^{-2\pi^{2}\beta(q_{1}^{2} + q_{2}^{2} + q_{3}^{2})}$$



Taylor Expansion12-2

$$E(\mathbf{q})_{k,k} = e^{\left(-4\pi^2\alpha t \sum D_{mnp}q_1^m q_2^n q_3^p\right)}$$

$$= h(\mathbf{q})e^{-2\pi^2\beta(q_1^2+q_2^2+q_3^2)}$$

X Taylor expansion:
$$h_n(\mathbf{q}) = \sum_{l+s+u < n} C_{l,s,u} q_1^l q_2^s q_3^u$$

$$E(\mathbf{q})_{k,k}^{(n)} = \left(\underbrace{\sum_{l+s+u < n} C_{l,s,u} q_1^l q_2^s q_3^u}_{\mathbf{Polynomial}}\right) e^{-2\pi^2 \beta (q_1^2 + q_2^2 + q_3^2)}$$



EAP Approximation 13-2

$C_{l,s,u}q_1^l q_2^s q_3^u \times e^{-2\pi^2\beta(q_1^2+q_2^2+q_3^2)}$

Separable monomial



$$C_{l,s,u}q_1^lq_2^sq_3^u \times e^{-2\pi^2\beta(q_1^2+q_2^2+q_3^2)}$$

- Separable monomial
- **Fourier Transform (1D)**

$$\mathbf{F}\{x^n e^{-2\pi^2 x^2}\}(t) = \left(\frac{i}{2\pi}\right)^n He_n(t) \frac{1}{\sqrt{2\pi}} e^{\frac{-t^2}{2}}$$

🔆 Hermite Polynomial

$$P(\mathbf{r})_{k,k}^{(n)} = e^{\frac{-1}{2\beta}(r_1^2 + r_2^2 + r_3^2)} \times \left(\sum_{l+s+u < n} i^{l+s+u} C_{l,s,u} He_l(r_1) He_s(r_2) He_u(r_3) \right)$$



EAP Approximation 15-2

$$E(\mathbf{q})_{k,k} = e^{\left(-4\pi^{2}\alpha t \sum D_{mnp}q_{1}^{m}q_{2}^{n}q_{3}^{p}\right)}$$

$$E(\mathbf{q})_{k,k}^{(n)} = \left(\sum_{l+s+u < n} \frac{C_{l,s,u}}{C_{l,s,u}}q_{1}^{l}q_{2}^{s}q_{3}^{u}\right)e^{-2\pi^{2}\beta(q_{1}^{2}+q_{2}^{2}+q_{3}^{2})}$$

$$P(\mathbf{r})_{k,k}^{(n)} = e^{\frac{-1}{2\beta}(r_{1}^{2}+r_{2}^{2}+r_{3}^{2})} \times \left(\sum_{l+s+u < n} i^{l+s+u}C_{l,s,u}He_{l}(r_{1})He_{s}(r_{2})He_{u}(r_{3})\right)$$



Implementation 16-2

 $\checkmark P(\mathbf{r})_{4.4}^{(5)}$

Symbolic computation + code generation (Maple)

pdf = -std::pow(0.3141592654e1, 0.3e1 / 0.2e1) * (-0.35e2 + (double) (16 * std::abs(b) * M(3, 3)) + (double) (8 * std::abs(b) * M(2, 0)) + (double) (16 * std::abs(b) * M(4, 4)) + (double) (8 * std::abs(b) * M(0, 2)) - std::pow(vX[0], 0.4el) - 0.2el * std::pow(vX[0], 0.2el) * std::pow(vX[2], 0.2el) + 0.8el * (double) std::abs(b) * (double) M(1, 0) * std::pow(vX[0], 0.2el) * std::pow(vX[1], 0.2el) + 0.8el * (double) std::abs(b) * (double) M(0, 1) * std::pow(vX[0], 0.2el) * std::pow(vX[1], 0.2e1) + 0.16e2 * (double) std::abs(b) * (double) M(3, 3) * std::pow(vX[0], 0.2e1) * std::pow(vX[1], 0.2el) - 0.48e2 * (double) std::abs(b) * (double) M(0, 0) * std::pow(vX[0], 0.2el) - 0.8el * (double) std::abs(b) * (double) M(1, θ) * std::pow(vX[θ], θ.2el) - θ.8el * (double) std::abs(b) * (double) M(0, 1) * std::pow(vX[0], 0.2e1) - 0.2e1 * std::pow(vX[0], 0.2e1) * std::pow(vX[1], 0.2e1) + 0.8e1 * sqrt(0.2e1) * vX[2] * vX[0] * (double) std::abs(b) * (double) M(1, 4) * std::pow(vX[1], 0.2el) + 0.8el * sqrt(0.2el) * vX[2] * (double) std::abs(b) * (double) M(1, 5) * std::pow(vX[1], 0.3el) + 0.16e2 * vX[2] * vX[0] * (double) std::abs(b) * (double) M(5, 3) * std::pow(vX[1], 0.2el) -0.16e2 * (double) std::abs(b) * (double) M(3, 3) * std::pow(vX[0], 0.2e1) + 0.14e2 * std::pow(vX[1], 0.2el) - std::pow(vX[1], 0.4el) - 0.24e2 * sqrt(0.2el) * vX[0] * (double) std::abs(b) * (double) M(1, 3) * vX[1] + 0.8el * sqrt(0.2el) * vX[0] * (double) std::abs(b) * (double) M(1, 3) * std::pow(vX[1], 0.3el) - 0.24e2 * sqrt(0.2el) * vX[0] * (double) std::abs(b) * (double) M(3, 1) * vX[1] + 0.8e1 * sqrt(0.2e1) * vX[0] * (double) std::abs(b) * (double) M(3, 1) * std::pow(vX[1], 0.3el) + 0.8el * sqrt(0.2el) * vX[2] * vX[1] * (double) std::abs(b) * (double) M(0, 5) * std::pow(vX[0], 0.2el) - 0.24e2 * sqrt(0.2el) * vX[2] * (double) std::abs(b) * (double) M(4, 0) * vX[0] + 0.16e2 * vX[2] * vX[1] * (double) std::abs(b) * (double) M(3, 4) * std::pow(vX[0], 0.2e1) + 0.8el * sqrt(0.2el) * vX[1] * (double) std::abs(b) * (double) M(0, 3) * std::pow(vX[0], 0.3el) -0.24e2 * sqrt(0.2e1) * vX[1] * (double) std::abs(b) * (double) M(0, 3) * vX[0] + 0.8e1 * sqrt(0.2e1) * vX[1] * (double) std::abs(b) * (double) M(3, 0) * std::pow(vX[0], 0.3e1) - 0.24e2 * sqrt(0.2e1) * vX[1] * (double) std::abs(b) * (double) M(3, 0) * vX[0] + (double) (8 * std::abs(b) * M(1, 2)) + (double) (8 * std::abs(b) * M(2, 1)) + (double) (16 * std::abs(b) * M(5, 5)) + (double) (24 * std::abs(b) * M(0, 0)) + (double) (24 * std::abs(b) * M(1, 1)) + (double) (24 * std::abs(b) * M(2, 2)) + (double) (8 * std::abs(b) * M(1, 0)) + (double) (8 * std::abs(b) * M(0, 1)) - 0.8e1 * (double) $std::abs(b) \neq (double) M(0, 1) \neq std::bow(vX[11, 0, 2e1) = 0, 16e2 \neq (double) std::abs(b)$

Compiled C-code





Multi-tensor model with diagonal:

 $[1390, 355, 355] \times 10^{-6} \ mm^2/s$





Synthetic Dataset - 2 18-2

🛧 DTI





Synthetic Dataset - 2 19-2

🛧 DTI



2562 vertices



Synthetic Dataset - 2 20-2



G-DTI with Numerical Fourier Transform

⋠ 162 vertices

✓ 30 x 30 voxels

Time: ~ 10 mins



Synthetic Dataset - 2 21-2





Synthetic Dataset - 2 22-2

G-DTI with EAP approximation







Effects of the Approximation 23-2













[Anwander-2008]



Human Brain 25-2





Human Brain 26-2





Take Home Messages 27-2

[Ghosh 2010]

✓ Full EAP recovered



Efficient implementation

Polynomial approximation can cause negative values



Introduction

1. Think Positive: 4th Order Symmetric Tensors

- A Riemannian Approach
- A Polynomial Approach (Ternary Quartic)
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- 3. Geometric Features from Spherical Diffusion Functions
 - Maxima Extraction
 - Peak Fractional Anisotropy









Spherical Functions play a central role in Diffusion MRI

DTI Spherical Function: Diffusion Ellipsoid

$$\frac{\mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}}{2t} = 1$$



Geometric Characteristics:

Spectral Decomposition (Fast & Easy)



Tractography Fractional Anisotropy Other scalars (biomarkers)


DTI has limitations in regions with fiber-crossings

Other Spherical Functions (SF) in dMRI:

- Orientation Distribution Function (ODF)
- Siber Orientation Density (FOD)
- PASMRI/MESD
- DOT, ADC ... etc...



Geometric Characteristics? Maxima, minima ...?



5-3

$$\longrightarrow \frac{S(\mathbf{q})}{S_0} = \int P(\mathbf{r}, \Delta) e^{i\mathbf{q}\cdot\mathbf{r}} d\mathbf{r}; \quad \mathbf{q} = \gamma \delta g \mathbf{u} \longrightarrow \mathbf{q}$$

V ODF-Tuch: [Tuch Thesis] $\Psi_T(\hat{u}) = \int_0^\infty P(r\hat{u})dr$ **ODF-Solid Angle:** $\Psi_{SA}(\hat{u}) = \int_0^\infty P(r\hat{u})r^2dr$ (True marginal distribution) [Wedeen 2000, Aganj 2010, Vega 2010]

Spherical Harmonics: [Descoteaux 2007]



$$\Psi(\theta,\phi) = \sum_{j=1}^{N} \underbrace{2\pi P_{d(j)}(0)c_j}_{f_j} Y_j(\theta,\phi)$$



Stationary Points (*extrema*) of a Spherical Function (SF)

- Homogeneous Polynomial (HP) representation
- Constrained Optimization formulation
 - System of HPs
- Categorize extrema: maxima, minima, saddle-points
- Principal curvatures at extrema: $\kappa_1 \kappa_2$



1. Change of Basis 7-3

⅔ 3 equivalent bases to represent a SF:





1. H.P. Representation

8-3

Tensor basis to HP basis:

$$A_{j_1 j_2 \dots j_d} g_{j_1} g_{j_2} \dots g_{j_d} = \sum_{i_1 + i_2 + i_3 = d} A_{i_1 i_2 i_3} g_1^{i_1} g_2^{i_2} g_3^{i_3}$$

(Re-ordering of terms)

$$\checkmark \quad \text{ODF as a HP:} \quad \begin{array}{l} \mathbb{P}_{\Psi}(\mathbf{x} = [x_1, x_2, x_3]^T) = \sum_{i_1 + i_2 + i_3 = d} A_{i_1 i_2 i_3} x_1^{i_1} x_2^{i_2} x_3^{i_3} \\ (||\mathbf{x}||_2 = 1) \end{array}$$



9-3

Non-linear Polynomial optimization:

$$F(\mathbf{x}, \lambda) = P(\mathbf{x}) - \lambda \left(\|\mathbf{x}\|_2^2 - 1 \right).$$

(Lagrange Multipliers)

System of HPs:
$$\nabla F$$
: $\frac{\partial F}{\partial x_1} = \frac{\partial F}{\partial x_2} = \frac{\partial F}{\partial x_3} = \|\mathbf{x}\|_2^2 - 1 = 0$

Polynomial system solver: Finds all extrema
 (Find all real roots)
 [Mourrain 2009]

Athena 2. Subdivision Poly. System Solver 10-3

[Mourrain 2009]

Convert HP to Bernstein Basis: $p(x) = \sum_{i=0}^{a} c_i B_i^d(x; a, b)$

(exact arithmetic)

(in the interval [a,b])

Theorem (Descartes Rule 1D)

The number of real roots of p(x) in]a,b[is bounded by the number V(c) of sign changes of $\mathbf{c} = (c_i)_{i=0..d}$, and is equal modulo 2.(exclusion test V(c)=0 no roots)

Analytically bracket / Numerically refine roots

ALL real roots (extrema) found by exclusion



3. Bordered Hessian 11-3

$$\overline{H}_{(m+n)\times(m+n)}[F(\mathbf{x},\lambda)] = \begin{pmatrix} \frac{\partial^2 F}{\partial x_1 \partial x_1} & \cdots & \frac{\partial^2 F}{\partial x_1 \partial x_n} & \frac{\partial g_1}{\partial x_1} & \cdots & \frac{\partial g_m}{\partial x_1} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{\partial^2 F}{\partial x_n \partial x_1} & \cdots & \frac{\partial^2 F}{\partial x_n \partial x_n} & \frac{\partial g_1}{\partial x_n} & \cdots & \frac{\partial g_m}{\partial x_n} \\ \\ & & & & & \\ \frac{\partial g_1}{\partial x_1} & \cdots & \frac{\partial g_1}{\partial x_n} & 0 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \frac{\partial g_m}{\partial x_1} & \cdots & \frac{\partial g_m}{\partial x_n} & 0 & \cdots & 0 \end{pmatrix}$$



3. Bordered Hessian 12-3





3. Bordered Hessian ¹³⁻³



X Maximum: $(-1)^m |\overline{H}_r[F(\mathbf{x}, \lambda)]| > 0; r = m + 1, ..., n,$

Minimum: $(-1)^r |\overline{H}_r[F(\mathbf{x}, \lambda)]| > 0 \quad (m = 1 \ n = 3)$







Glyph-colour: red: high anisotropy, blue: low anisotropy Lines: thick-green: Maxima, thin-blue: Saddle points, green: Minima. a) 1-fiber b) 2-fibers c) 3-fibers



Synthetic Data 15-3





Synthetic Data 16-3





Synthetic Data 17-3





(Synthetic data)

How good was the estimation?

- Take ground truth directions {*d*_{*i*}} and generate *signal*
- Estimate ODF-Ts from signal \bigcirc
- Compute maxima of ODF-Ts: {*d'i*} \bigcirc
- Compute (F= ODF as HP): $||\nabla F(d)|| \& ||\nabla F(d')||$

 $||\nabla F(d)||$: estimation $||\nabla F(d')||$: maxima error

extraction error

	$ang(d,d^{'})^{o}$		$ abla { m F}(d^{'}) $		$ abla \mathrm{F}(d) $	
	m	V	m	V	m	V
1-Fib	0.01	4.22e-05	2.07e-11	1.5e-21	4.9e-04	9.17e-08
2-Fib _{90°}	0.025	3.85e-05	5.58e-11	1.76e-21	3.6e-03	2.48e-06

m = mean, v = variance

Noise-free 100 simulations (each)



Compare Discrete Mesh Search 19-3

(Human brain data)

$\|\nabla F(d)\|$: HP maxima error $\|\nabla F(d')\|$: Discrete mesh search (DS) maxima error

Comparison of error in Discrete Search method (DS)





Human Brain 20-3

[Anwander 2007]





Human Brain 21-3

[Anwander 2007]







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[Bloy 2008]

✤ ODF in Cartesian coordinates:

 $\Psi: [\Psi(\theta,\phi)sin(\theta)cos(\phi), \ \Psi(\theta,\phi)sin(\theta)sin(\phi), \ \Psi(\theta,\phi)cos(\theta)]^T$

- **Form-I** : *e, f, g*
 - Form-II: E, F, G



Principal Curvatures:

$$K = \frac{eg - f^2}{EG - F^2}$$
$$H = \frac{eG - 2fF + gE}{2(EG - F^2)}$$

$$\kappa_1 = H + \sqrt{H^2 - K}$$

$$\kappa_2 = H - \sqrt{H^2 - K}$$





24-3

Compute bio-marker from SFs (ODF) using geometric characteristics

K Ellipsoidal: Peak FA ✓ ODF Peak FA: (Tuch & SA) $\begin{array}{c}
\kappa_{1} \kappa_{2} \\
\mathcal{F} \\
\mathcal{F} \\
\widetilde{\kappa}_{i} \\
\widetilde{\mathcal{F}} \\
= \\
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(Analytical ODF model)

 $\operatorname{FA}(\Lambda_x(\kappa_1,\kappa_2,\mathcal{F}),\Lambda_y(\kappa_1,\kappa_2,\mathcal{F}),\Lambda_z(\kappa_1,\kappa_2,\mathcal{F}))$



Peak Fractional Anisotropy

✓ ODF-Tuch: PFA-T

$$\Psi_T = \frac{1}{Z} \sqrt{\frac{1}{\frac{x^2}{\Lambda_x} + \frac{y^2}{\Lambda_y} + \frac{z^2}{\Lambda_z}}}$$

$$\widetilde{\kappa_1} = \frac{Z\sqrt{\Lambda_x}}{\Lambda_y}; \ \widetilde{\kappa_2} = \frac{Z\sqrt{\Lambda_x}}{\Lambda_z}; \ \widetilde{\mathcal{F}} = \frac{\sqrt{\Lambda_x}}{Z}$$

$$\Psi_{SA} = \frac{1}{4\pi\sqrt{\Lambda_x\Lambda_y\Lambda_z}} \left(\frac{1}{\frac{x^2}{\Lambda_x} + \frac{y^2}{\Lambda_y} + \frac{z^2}{\Lambda_z}}\right)^{\frac{3}{2}}$$

$$\widetilde{\kappa_{1}} = \frac{4\pi\Lambda_{y}(3\Lambda_{x} - 2\Lambda_{z})}{\Lambda_{x}\sqrt{\Lambda_{y}\Lambda_{z}}}; \ \widetilde{\kappa_{2}} = \frac{4\pi\Lambda_{z}(3\Lambda_{x} - 2\Lambda_{y})}{\Lambda_{x}\sqrt{\Lambda_{y}\Lambda_{z}}}$$
$$\widetilde{\mathcal{F}} = \frac{\Lambda_{x}^{3/2}}{4\pi\sqrt{\Lambda_{x}\Lambda_{y}\Lambda_{z}}}$$

Total PFA:

 $\text{TotalPFA} = \sum_{i=1}^{N} \mathcal{F}_{i} \cdot \text{PFA}_{i}.$ i=1



Results: PFA 26-3



Colour coded DTI eigenvector weighted by FA Colour coded ODF-T main-maximum weighted by PFA-T Colour coded ODF-SA main-maximum weighted by PFA-SA



Results: Total-PFA



Total-PFA

No. Maxima



Green: single fiber, high anisotropy Red: multiple fibers, high anisotropy Orange: multiple "fibers", low anisotropy



Results: Total-PFA

28-3





[Ghosh 2008b, Ghosh2011]





Peak Fractional Anisotropy (PFA): a new bio-marker



Extend Streamline & Tensorline tractography to any spherical function with maxima-extraction

• PFA as a stopping criterion in tractography?

Conclusion and Perspectives





DTI



High Order Models in Diffusion MRI and Applications



[Ghosh 2008, Ghosh 2009]

- Generalized DTI: Higher Order Cartesian Tensors (HOTs) Positive Diffusion Constraint
 - So 3D 4th Order tensors -> 6D 2nd Order tensors Riemannian metric for symmetric positive definite matrices
 - Positive-definiteness; solves constrained problem
 - Polynomial Interpretation of HOTs Hilbert's theorem on Ternary Quartics
 Positive-semi-definiteness; solves correct problem
- Analytical approximation of EAP from HOTs
 - Closed-form formulation
 - Efficient implementation

[Ghosh 2010]



Conclusion & Perspectives

[Ghosh 2008b, Ghosh 2011, Ghosh 2011b]

- Geometric Features from Spherical Diffusion functions
 - All maxima found from any kind of spherical function
 - Peak Fractional Anistropy (PFA): a new bio-marker
 - Streamline & Tensorline tractography for any kind of spherical function
 - **Perspectives**:
 - Alternate Cartesian tensor (& coordinates) approach
 - Cartesian Fourier Transform
 - Cartesian descriptors: Kurtosis, Cumulants...

Members of the Jury: Dr. Peter Basser Dr. Baba Vemuri Dr. Habib Benali Dr. Pierre Comon Dr. Rachid Deriche Dr. Nikos Paragios

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High Order Models in Diffusion MRI and Applications



Tractography

DTI Streamline: tractography [Basser 2000]

$$\frac{d\mathbf{r}(s)}{ds} = \mathbf{t}(s) = \epsilon_1(\mathbf{r}(s)),$$



ODF Streamline: tractography

$$\frac{d\mathbf{r}(s)}{ds} = \eta_{\theta_{min}}(\mathbf{r}(s)), \quad \mathbf{r}(0) = \eta_{max}(0)$$







DTI Tensorline: [Weinstein 1999, Lazar 2003]

$$\mathbf{v}_{\text{out}} = f\epsilon_1 + (1-f)((1-g)\mathbf{v}_{\text{in}} + g\mathbf{D}\cdot\mathbf{v}_{\text{in}})$$





DTI Tensorline: [Weinstein 1999, Lazar 2003]

$$\mathbf{v}_{\text{out}} = f\epsilon_1 + (1 - f)((1 - g)\mathbf{v}_{\text{in}} + g\mathbf{D} \cdot \mathbf{v}_{\text{in}})$$

ODF Tensorline:

$$\mathbf{v}_{\text{out}} = f\eta_{\theta_{min}} + (1-f)\mathbf{v}_{\text{in}}$$

- Euclidean interpolation
- ↓ 0.5mm step-length
- Stopping Criterion: 0.87mm Radius of Curvature



Results: DTI Tractography





seeds: Corpus Callosum



Results: ODF-SA Tensorline



seeds: Corpus Callosum


Results: ODF-SA Tensorline



blue: Cortico-Spinal Tract green: Superior Longitudinal Fasciculus red: Corpus Callosum





[C. Poupon et al. 2008]

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Spacing: 3x3x3 b = 1500s/mm^2 64 DWIs + T0 ODF-Tuch



[C. Poupon et al. 2008]







[C. Poupon et al. 2008]

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化合合体 计 方法	

Spacing: 3x3x3 b = 1500s/mm^2 64 DWIs + T0 ODF-Tuch



[C. Poupon et al. 2008]

