# Computational Diffusion MRI : Models, Algorithms and Applications



#### Rachid DERICHE

#### Odyssée Project Team INRIA Sophia Antipolis - Méditerranée Research Center

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# INRIA



**Eight Research Centers** 

#### **Computational Neurosciences** Measuring, Modeling and simulating

- Single and assemblies of neurons, Cortical columns and areas
- The human brain anatomical connectivity
- The functioning of the human brain through its electrical activity

#### and some of its Applications

- Clinical Brain Research
- Brain Computer Interface
- Computational and biological vision.



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## Anatomy of Cerebral White Matter (I)



 Frontal forceps 2. Corpus callosum commissural fibers 3. Short arcuate fibers 4. Occipital forceps 5. Indusium griseum 6. Medial longitudinal stria 7. Lateral longitudinal stria

Corpus Callosum and its radiation (images from [Williams-etal:97])

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#### Anatomy of Cerebral White Matter (II)



Images from [Williams-etal97]

I. Short arcuate bundles, 2. Superior longitudinal fasciculus, 3. External capsule,

 Inferior occipitofrontal fasciculus, 5. Uncinate fasciculus, 6. Sagittal stratum, 7. Inferior longitudinal fasciculus

Short and Long Association tracts in the right hemisphere (images from [Williams-etal:97])

Corticostriate Pathway: From all parts of the cerebral cortex to the striatum

### WM Fiber Structures of the Human Brain



Corpus callosum

ponto-cerebellar tracts

pyramidal fiber pathways

fornix

uncinate fasciculus

superior longitudinal fasciculus

inferior longitudinal fasciculus

WM Fibers structures : Image from [A.Leemans-PhD:06]

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#### **Diffusion MRI**

- MRI introduced by Paul C. Lauterbur and Peter Mansfield in 1973, jointly Nobel Prize in Physiology/Medicine - 2003.
- DMRI is a recent imaging modality that measures, in vivo and non-invasively, the random motion of water molecules in biological tissues
- The random motion of water molecules reflects the structure and the architecture of the biological tissues
- Pioneering and related contributions discussed by Denis Le Bihan (cras:85,ismrm:85), Moseley (bmr:84), Merboldt (mjmr:85)...

#### Diffusion Tensor MRI and beyond...

- Water Diffusion is anisotropic : Formalism of Diffusion Tensor (DT-MRI) introduced by Peter Basser in 1994 to correct the scalar model (Basser-Mattiello-LeBihan:94,J Magn Reson B)
- Important invariant quantities can be extracted (Eigenvalues, Trace, Det, FA..)
- High Angular Resolution Diffusion Imaging (DSI, Q-Ball, tuch-mrm:2002)

### From Images to WM Fibers through DMRI

# Estimation and Regularization

Diffusion Tensors from noisy DWI Images (tschumperle-deriche:pami:2005;lenglet-deriche:jmiv:06)

# Connectivity

How to recover the geometric description of the anatomical connectivity between brain areas ? (descoteaux-deriche:tmi:08)

# Segmentation

How to recover a set of coherently oriented white matter fibers population? (lenglet-deriche:tmi:2006;jmiv:06, wassermann-deriche:biomed:08)

# Q-Ball Imaging

How to deal with HARDI data and Fibers Crossings (descoteaux-deriche:mrm:06;mrm:07;jmiv:08)

## **Diffusion MRI : Basic Principles I**

- Diffusion can be measured using a magnetic field B<sub>0</sub>, two RF and gradient pulses that magnetically label moving water molecules
- ► The scanner applies first a constant magnetic field B<sub>0</sub> over the sample tissue
- The spins of the water molecule align along B<sub>0</sub> and causes a net magnetization of the sample

# **A MRI Scanner**



The scanner applies a constant magnetic field  $B_0$ 

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#### **Diffusion MRI Image Formation**



Acquisition of several raw images under different magnetic fields.

# **Diffusion MRI : Basic Principles II**

► A 90 degree RF pulse followed after a time  $\Delta$  with a 180 degrees RF pulse with a gradient strength G induces a phase shift proportional to the spin displacement :  $\delta(\phi) = \gamma \delta G.(\mathbf{r} - \mathbf{r}_0)$ 

► The total magnetization encodes the displacement for moving spins  $\frac{S}{S} = \int_{-\infty}^{+\infty} e^{i\gamma\delta \mathbf{G}.(\mathbf{r}-\mathbf{r}_0)} P(\mathbf{r} \mid \mathbf{r}_0, \delta) d\mathbf{r} d\mathbf{r}_0$ 

► For free diffusion in an homogeneous domain, there is a close form distribution

# DT-MRI Image Formation (I)

For free diffusion in an homogeneous domain, the probability to find a spin initially at r<sub>0</sub> at position r after a time interval Δ is :

$$P(\mathbf{r} \mid \mathbf{r_0}, \Delta) = \frac{1}{\sqrt{(4\pi\Delta)(det(\mathbf{D}))}} e^{-(\frac{(\mathbf{r}-\mathbf{r_0})^{\mathbf{t_0}-1}(\mathbf{r}-\mathbf{r_0})}{4\Delta})}$$

Combining the equations, we obtain :

 $\frac{S}{S_0} = e^{-\gamma^2 \delta^2 (\Delta - \delta/3) \mathbf{G}^t \mathbf{D} \mathbf{G}}$   $\blacktriangleright \text{ With } \mathbf{G} = \mid \mathbf{G} \mid \mathbf{g} \text{ and } b = (\gamma \mid \mathbf{G} \mid \delta)^2 (\Delta - \frac{\delta}{3})$   $\frac{S}{S_0} = e^{-b\mathbf{g}^t \mathbf{D} \mathbf{g}}$ 

### **DT-MRI Image Formation (II)**

Diffusion described by D<sub>(x,y,z)</sub>, an SPD 3 \* 3 matrix, which explains through the Stejskal-Tanner equation the measurements S<sub>k</sub> obtained :

$$\forall (x, y, z), \qquad \qquad S_{k_{(x, y, z)}} = S_{0_{(x, y, z)}} e^{-bg_{k}^{\,\prime} \mathbf{D}_{(x, y, z)}g_{k}}$$

The diffusion Tensors can be visualized as ellipsoids :





# **DT-MRI Processing**



Diffusion tensors estimated from CMRR data

# DT-MRI Images : Direct estimation of the tensors

Direct estimation (Westin etal:02) :

$$\mathbf{D} = \sum_{k=1}^{6} -\frac{1}{b} \ln \left( \frac{S_k}{S_0} \right) \, g_k g_k^{\mathsf{T}}$$

- ► [⊕] S<sub>0</sub> and at least six non-colinear diffusion gradient directions, i.e 7 images are then theoretically sufficient.
- ▶ [⊖] Results are very sensitive to noise.
- ▶ [⊖] Positive definiteness of the tensors is not insured.

#### **DT-MRI Images : Least square estimation**

When n > 7 raw images are available, D can be retrieved by a least square method :

$$\min_{\mathbf{D}} \sum_{k=1}^{n} \left( -\frac{1}{b} \ln \left( \frac{S_{k}}{S_{0}} \right) - g_{k}^{T} \mathbf{D} g_{k} \right)^{2} \quad \Rightarrow \quad \left\{ \begin{array}{l} AX = b \\ \hat{X} = (A^{T} A)^{-1} A^{T} b \end{array} \right.$$

- [+] Least square methods are more robust to noise, by using all the raw image informations.
- ▶  $[\ominus]$  Positive definiteness of the tensors is not insured.

# Reprojection of the tensors is needed for both estimation methods.

#### Variational approaches for tensor estimation & regularization

Estimation

Minimize the criterion, in the constrained tensor space :

$$\min_{\mathbf{D}\in\mathrm{P}(3)}\int_{\Omega}\sum_{k=1}^{n}\psi\left(\left|\ln\left(\frac{S_{0}}{S_{k}}\right)-g_{k}^{T}\mathbf{D}g_{k}\right|\right)+\alpha\;\phi(\|\nabla\mathbf{D}\|)\;d\Omega$$

Regularization

Minimize the following regularisation functional f, as :

$$\min_{X \in \textit{ConstrainedSpace}} f(X) = \int_{\Omega} \phi(\|\nabla_{\Omega} X\|) + \frac{\alpha}{2} (X - X_0)^2 \ d\Omega$$

### The Corpus Callosum regularized



#### Characterizing Tissue Microstructure





## **Towards Anatomical Connectivity Mapping**

- The water diffusion in many regions of the white matter is highly anisotropic
- The orientation of the principale eigenvector u(.) of D represents the predominant axonal direction of white matter fiber, represented by a 3D curve c(t)

## **Streamlines Propagation**

#### Classical streamlines estimation expected to coincide with neural paths



#### Whole brain tractography [8000 fibers / 5 min] Euler, Runge-Kutta integration scheme with DTI interpolation

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#### Fibers as geodesics in the white matter

- Use the entire tensor information and see the White matter as a surface with a metric given by D<sup>-1</sup>
- We can compute a distance function \u03c6 in the intrinsic white matter as :

$$|\nabla \phi|^2 = \frac{\partial \phi}{\partial x_i} \frac{\partial \phi}{\partial x_j} g^{ij} = 1, \qquad (1)$$

Fibers can be extracted individually as geodesics in  $\phi$ 

## **Tractography: Real Dataset**



### **Diffusion Tensor MRI Segmentation**

- Given a DT-MRI volumic image I
- Evolve an initial surface S to segment I using all the information provided by the Diffusion tensor..



#### Corpus-Callosum

Cortico-Spinal Tract

# Level-set based segmentation using the GAR framework





Scalar



Color



Texture



Color + Texture

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# DTI Segmentation and Surface Evolution (I)

- Use the Kullback-Liebler divergence to measure the distance between Gaussian distributions and induce a distance between Diffusion tensors [Wang-Vemuri:04]
- Tensor distance as the square root of the J-divergence, a symmetrized version of the KL Divergence:

$$d(\mathsf{T}_1,\mathsf{T}_2) = \frac{1}{2}\sqrt{tr(\mathsf{T}_1^{-1}\mathsf{T}_2 + \mathsf{T}_2^{-1}\mathsf{T}_1) - 2n}$$

Closed form expression for the mean µ of a set of T
 Euclidean 0 and Euclidean 1 and Euclidean 2
 Euclidean 0 and J-Divergence 1 and J-Divergence 2

# DTI Segmentation and Surface Evolution (II)

• The geodesic distance between any two fixed mean and m-variate normal distributions  $\Sigma_1$  and  $\Sigma_2$  wis shown to be :

$$\mathcal{D}(\Sigma_1,\Sigma_2) = \sqrt{rac{1}{2} ext{tr}( \log^2(\Sigma_1^{-1/2}\Sigma_2\Sigma_1^{-1/2}))} = \sqrt{rac{1}{2}\sum_{i=1}^m \log^2(\eta_i)}$$

where  $\eta_i$  denote the *m* eigenvalues of the matrix  $\Sigma_1^{-1/2} \Sigma_2 \Sigma_1^{-1/2} \in S^+$ .

Properties of D: D is indeed a distance on S<sup>+</sup> and exhibits nice properties.

Geodesic 1 and Geodesic 2

# On DTI Distance, Gradient, Mean and beyond...

Euclidean	J-divergence	Geodesic
$\operatorname{tr}\left((A-B)(A-B)^{T}\right)$	$\frac{1}{4}\left( \mathrm{tr}\left( A^{-1}B + B^{-1}A  ight) - 6  ight)$	$\frac{1}{2}$ tr (log <sup>2</sup> (A <sup>-1/2</sup> BA <sup>-1/2</sup> )
A-B	$\frac{1}{4}(B^{-1}-A^{-1}BA^{-1})$	$A \log (B^{-1}A)$
$rac{1}{N}\sum_{i=1}^{N}\Sigma_{i}$	$V^{-1/2} \left( U^{1/2} V U^{1/2}  ight)^{1/2} V^{-1/2}$ with $U = rac{1}{N} \sum_{i=1}^{N} \Sigma_i$ and $V = rac{1}{N} \sum_{i=1}^{N} \Sigma_i^{-1}$	Algorithm

Lenglet/Rousson/Deriche "Statistics on the Manifold of Multivariate Normal Distributions: Theory and Application to Diffusion Tensor MRI Processing", Journal of Mathematical Imaging and Vision, 2006 Lenglet/Rousson/Deriche "DTI Segmentation by Statistical Surface Evolution", IEEE Transactions on Medical Imaging, 2006

### Algorithm for Mean of tensors

Algorithm 1 Riemannian estimation of the mean diffusion tensor

**Require**:  $\{\Sigma_i\} \in S^+(3), i = 1, \dots N$  and *nit*, the number of iterations

**Ensure**:  $\overline{\Sigma}_g$ , the mean tensor

1: 
$$M \leftarrow \mathscr{I}$$
  
2: for  $k = 1$  to *nit* do  
3:  $V \leftarrow \mathbb{O} \{3 \times 3 \text{ zero matrix}\}$   
4: for  $i = 1$  to N do  
5:  $V \leftarrow \log(\Sigma_i^{-1}M)$   
6: end for  
7:  $V = (1/N)MV$   
8:  $M \leftarrow M^{1/2} \exp(-M^{-1/2}VM^{-1/2})M^{1/2}$   
9: end for  
10: Return M

#### Further results : On the Geodesic

► The geodesic starting from  $\Sigma(t_1) \in S^+$  in the direction  $\dot{\Sigma}(t_1) = \Sigma(t_1)^{1/2} X \Sigma(t_1)^{1/2}$  with  $\dot{\Sigma}(t_1), X \in S = TS^+$  is given by:

$$\Sigma(t) = \Sigma(t_1)^{1/2} \exp{(tX)} \Sigma(t_1)^{1/2} \in S^+, \, \forall t \in [t_1, t_2]$$



(a): Geodesic Interpolation (b) : Euclidean Interpolation

#### **DTI Segmentation on Real Data**

Segmentation of the corpus callosum in real DTI:





#### **Euclidean Distance**

J-Divergence



#### Geodesic Distance

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### **Limitations of DTI**



DTI fails when fiber bundles crosses within the same voxel Non-Gaussian diffusion process - Image from [Poupon-PhD:99]

#### HARDI : High Angular Resolution Diffusion Imaging



► Use of N gradient directions : 162, 252 ..

Process all discrete noisy data on the sphere using SH

$$S(\Theta_i, \Phi_i) = \sum_{j=1}^R c_j Y_j(\Theta_i, \Phi_i)$$
 or  $S = BC$ 

# **Solving for SH Coefficients**

- Classical LS : Minimize (S BC)<sup>t</sup>(S BC)
- Smooth solution on the sphere : Laplace-Beltrami regularization
- $\blacktriangleright$  Minimize  $E({f S})=\int_{\sigma}(\Delta_b{f S})^2d\sigma$
- SH obey the PDE :  $\Delta_b \mathbf{S} + I(I+1)\mathbf{S} = 0$

# **Solving for SH Coefficients**

New criterion :

 $E(\mathbf{S}) = (\mathbf{S} - \mathbf{BC})^t (\mathbf{S} - \mathbf{BC}) + \lambda \mathbf{C}^t \mathbf{LC}$ 

L is the R × R matrix with entries l<sup>2</sup><sub>j</sub>(l<sub>j</sub> + 1)<sup>2</sup> along the diagonal (l<sub>j</sub> is the order associated with the j<sup>th</sup> coefficient).
 Closed form solution :

$$\mathbf{C} = (\mathbf{B}^t \mathbf{B} + \lambda \mathbf{L})^{-1} \mathbf{B}^t \mathbf{S}$$

Smooth solution on the sphere with a penalty for higher order term.

#### **Attenuation and Diffusion MRI Signal** The attenuation of the MRI signal is given by : $S(g) = S_0 exp(-bD(g))$



Red : not attenuated - Blue : highly attenuated

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#### **Q-Ball Imaging** ODF can be computed directly from HARDI $\Psi(\mathbf{u}) = \int_0^\infty P(\alpha.\mathbf{u})d\alpha$



Integral over the perpendicular equator = Funk Radon Transform  $G[f(\mathbf{w})](\mathbf{u}) = \int \delta(\mathbf{u}^t \mathbf{w}) f(\mathbf{w}) d\mathbf{w} \equiv ODF$ 

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#### Analytical ODF ODF can be computed analytically from SH coefficients

$$\Psi(\mathbf{u}) = \sum_{j=1}^{R} 2\pi P_{\ell_j}(0) c_j Y_j(\mathbf{u}).$$

where  $P_{\ell}(0)$  the Legendre polynomial of degree  $\ell$  evaluated at 0,

$$P_\ell(0) = \left\{ egin{array}{ccc} 0 & \ell ext{ odd} \ (-1)^{\ell/2} rac{1\cdot 3\cdot 5\cdots (\ell-1)}{2\cdot 4\cdot 6\cdots \ell} & \ell ext{ even} \end{array} 
ight.$$

Fast speed-up factor of 15 with classical QBI Validated against ground truth and classical QBI

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# Funck Radon Transform (I)



FRT is the line integral along the equator plane

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# Funck Radon Transform (II)



FRT allows to effectively recover the fibers direction

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#### ODF and FRT allows to effectively recover the fibers direction



Descoteaux, Deriche et al in "Magnetic Resonance in Medicine", 2007



Rat Biological Phantom - Data from McGill - BIC

# Real Data : Crossing between the CC, CST and SLF..)





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# HARDI : Reconstruction and Processing



Descoteaux/Deriche : IEEE TMI:2008, JMIV:2008

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# ODF Segmentation based on SH (I)

• Dissimilarity measure: L2 norm of SH coefficients difference

$$\begin{aligned} \langle \psi, \psi' \rangle &= \int_{S^2} \psi(r) \cdot \psi'(r) dr = \int_{S^2} \left( \sum_{i=1}^R c_i Y_i(r) \right) \left( \sum_{i=1}^R c_i' Y_i(r) \right) dr = \sum_{i=1}^R c_i \cdot c_i' \\ &\Rightarrow \| \psi - \psi' \|^2 = \sum_{i=1}^R (c_i - c_i')^2 \end{aligned}$$

• Assumption of Gaussian distribution for SH coefficients:



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## **ODF Segmentation based on SH (II)**







Corpus-Callosum

Cortico-Spinal Tract

Biol. Phantom

Descoteaux/Deriche " HARDI MRI Segmentation Using Region-Based Statistical Surface Evolution". Journal of Mathematical Imaging in Vision, in press 2008

## Deterministic vs Probabilistic Tractography

- Efficient
- Vulnerable to initialization
- Vulnerable to principal direction
- Output: streamlines



- Slower
- Robust to initialization
- Accounts for uncertainty in principal direction
- Output: quantitative connectivity map



Descoteaux, Deriche et al "IEEE Transactions in Medical Imaging", 2008. In press.

#### Extracting ODF Maxima as Stationary Points of Constrained Homogeneous Polynomial



Workshop MICCAI-CDMRI, Sept. 10, 2008 (with A.Ghosh, E. Tsigaridas etal)

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## White Matter Fibers Clustering

- Data Given a set of tensors, fibers, define a distance and an affinity matrix
- **Embedding** : N-Cuts, Laplacian EigenMaps, Diffusion Maps.
- Clustering : K Means..





Wassermann/Descoteaux/Deriche." Diffusion Maps Clustering for MR Q-Ball Imaging Segmentation." International Journal on Biomedical Imaging, 2008.

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#### Application : Detection of multiple pathways in the spinal cord using q-ball imaging

- Application to an ex vivo spinal cord of one cat using a 3T scanner, 100 directions and b-values varying from 1000 to 3000 s/mm2.
- QBI can retrieve crossing fibre information, where the diffusion tensor imaging approach is constrained to a single diffusion direction.
- First study demonstrating the benefits of QBI in observing longitudinal, commissural and dorso-ventral fibres in the spinal cord.
- First step towards in vivo characterization of the healthy and injured spinal cord using HARDI/Q-Ball

### **DW-MRI of Spinal Cord Injury**



## Tractography of the Cat Spinal Cord



Tractography



Crossing fibers that are not taken into account using the tensor model → Need for a less constraining approach

Cohen-Adad et al, Neuroimage, 40, 685-697, 2007

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# Q-Ball Imaging of the Spinal Cord (I)



DTI

Q-Ball

Cohen-Adad, Descoteaux et al, Neuroimage, 42, 739-749, 2008

# Q-Ball Imaging of the Spinal Cord (II)



Cohen-Adad, Descoteaux et al, Neuroimage, 42, 739-749, 2008

## Q-Ball Imaging of the Spinal Cord (III)





Cohen-Adad, Descoteaux et al, Neuroimage, 42, 739-749, 2008

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- ▶ NIH NICHD Bethesda ( P.Basser/C.Pierpaoli/E.Ozarslan)
- Some algorithms are plugins of the BrainVisa Software package (SHFJ-IFR 49) and Slicer3D.
- The INRIA Odyssée Geodesic Connectivity Mapping Library http://gcm.gforge.inria.fr/index.html

## **Recent Publications/Acknowledgments**

- Lenglet/Rousson/Deriche/ "DTI Segmentation by Statistical Surface Evolution", IEEE Transactions on Medical Imaging, 2006
- Lenglet/Rousson/Deriche/Faugeras "Statistics on the Manifold of Multivariate Normal Distributions: Theory and Application to Diffusion Tensor MRI Processing", Journal of Mathematical Imaging and Vision, 2006
- Descoteaux/Angelino/Fitzgibbons/Deriche "ADC from HARDI: Estimation and Applications", Magnetic Resonance in Medicine, 2006
- Descoteaux/Angelino/Fitzgibbons/Deriche "Regularized, Fast, and Robust Analytical Q-Ball Imaging", Magnetic Resonance in Medicine, 2007
- Descoteaux/Deriche/Knosche/Anwander "Deterministic and Probabilistic Tractography Based on Complex Fiber Orientation Distributions" IEEE Transactions in Medical Imaging, 2008. In press.
- Wassermann/Descoteaux/Deriche."Diffusion Maps Clustering for Magnetic Resonance Q-Ball Imaging Segmentation." International Journal on Biomedical Imaging, 2008.
- Related work on Fibers Clustering with D.Wassermann and on High Order Tensors with A.Ghosh Miccai:08 and Workshops on Sept. 10th
- Other related papers : http : //www sop.inria.fr/odyssee/en/rachid.deriche

#### $\epsilon v \chi \alpha \rho \iota \sigma \tau \omega!$



ερωτησεις?

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