Diffusion Tensor Processing and Visualization

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Acknowledgments

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National Alliance for Medical Image Computing
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Diffusion in Biological Tissue

- Motion of water through tissue
- Sometimes faster in some directions than others

- **Anisotropy**: diffusion rate depends on direction

Kleenex newspaper

isotropic anisotropic

G. Kindlmann
Diffusion in White Matter

• Diffusion of water molecules

  - Faster diffusion along fibers than perpendicular to them
  - Water diffusion anisotropy used to track fibers, estimate white matter integrity

• Reflects the underlying structure of the tissues

  - From Beaulieu[02]

• Tensor model [Basser]

  - Determine the whole tensor to estimate diffusion anisotropy

From Beaulieu[02]
The Physics of Diffusion

- Density of substance changes (evolves) over time according to a differential equation (PDE)

\[ \frac{\partial \mu}{\partial t} = \nabla \cdot D \nabla \mu \]

- Change in density
- Diffusion – matrix, tensor (2x2 or 3x3)
- Derivatives (gradients) in space
Solutions of the Diffusion Equation

• Simple assumptions
  – Small dot of a substance (point)
  – $D$ constant everywhere in space
• Solution is a multivariate Gaussian
  – Normal distribution
  – “$D$” plays the role of the covariance matrix
• This relationship is not a coincidence
  – Probabilistic models of diffusion (random walk)
D Is A Special Kind of Matrix

- The universe of matrices

D is a “square, symmetric, positive-definite matrix” (SPD)
Properties of SPD

- Bilinear forms and quadratics

\[
\begin{pmatrix}
D_{11} & D_{12} & D_{13} \\
D_{12} & D_{22} & D_{23} \\
D_{13} & D_{23} & D_{33}
\end{pmatrix}
\begin{pmatrix}
x \\
y \\
z
\end{pmatrix}
= k
\]

\[
(D_{11})x^2 + (2D_{21})xy + (2D_{31})xz + (D_{22})y^2 + (2D_{23})yz + (D_{33})z^2 = k
\]

Quadratic equation – implicit equation for ellipse (ellipsoid in 3D)

- Eigen Decomposition

\[
D = R\Lambda R^{-1} =
\begin{pmatrix}
\lambda_1 & 0 & 0 \\
0 & \lambda_2 & 0 \\
0 & 0 & \lambda_3
\end{pmatrix}
\]

- Lambda – shape information, independent of orientation
- R – orientation, independent of shape
- Lambda’s > 0
Eigen Directions and Values (Principle Directions)
Tensors From Diffusion-Weighted Images

- **Big assumption**
  - At the scale of DW-MRI measurements
  - Diffusion of water in tissue is approximated by Gaussian
    - Solution to heat equation with constant diffusion tensor
- **Stejskal-Tanner equation**
  - Relationship between the DW images and D
    \[
    S_k = S_0 e^{-b g_k^T D g_k}
    \]
    - Physical constants
    - Strength of gradient
    - Duration of gradient pulse
    - Read-out time

\[ k^{th} \text{ DW Image} \quad \text{Base image} \quad \text{Gradient direction} \]
Tensors From Diffusion-Weighted Images

• Solving S-T for D
  – Take log of both sides
  – Linear system for elements of D
  – Six gradient directions (3 in 2D) uniquely specify D
  – More gradient directions overconstrain D

\[ g_k^T D g_k = \frac{\log S_0 - \log S_k}{b} \]

• Solve least-squares
  » (constrain lambda>0)
DWI summary: Model

Single Tensor Model (Basser 1994)

\[ A_i = A_0 e^{-b g_i^T D g_i} \]

A_0

A_i

g_i

Tensor estimation

D

Dxx

Dxy

Dxz

Dyy

Dyz

Dzz
Shape Measures on Tensors

- Represent or visualization shape
- Quanify meaningful aspect of shape
- Shape vs size

Different sizes/orientations

Different shapes
Measuring the “Size” of a Tensor

- **Length** – \((\lambda_1 + \lambda_2 + \lambda_3)/3\)
  
  \(- (\lambda_1^2 + \lambda_2^2 + \lambda_3^2)^{1/2}\)

- **Area** – \((\lambda_1 \lambda_2 + \lambda_1 \lambda_3 + \lambda_2 \lambda_3)\)

- **Volume** – \((\lambda_1 \lambda_2 \lambda_3)\)

Sometimes used. Also called:

- “Root sum of squares”
- “Diffusion norm”
- “Frobenius norm”

Generally used. Also called:

- “Mean diffusivity” \(<\text{MD}>\)
- “Trace”
ADC versus Mean Diffusivity

- Apparent diffusion coefficient (ADC) measures diffusivity in a specific direction.
- Mean diffusivity ($<\text{MD}>$) is the trace of the diffusion tensor.
- Terms often not properly used, papers often cite ADC but actually mean $<\text{MD}>$

ADC in gradient directions Trace

b0  g1  g2  g3  g4  g5  g6  FA  MD

Trace
Shape Other Than Size

Barycentric shape space

\[ (C_S, C_L, C_P) \]
Westin, 1997
Reducing Shape to One Number
Fractional Anisotropy

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

Properties:
- Normalized variance of eigenvalues
- Difference from sphere
- Invariant to size
- FA does not uniquely characterize shape
FA as an Indicator for White Matter

- Visualization – ignore tissue that is not WM
- Registration – Align WM bundles
- Tractography – terminate tracts as they exit WM
- Analysis
  - Axon density/degeneration
  - Myelin
- Big question
  - What physiological/anatomical property does FA measure?
Tensor size (MD) and shape (FA)

- Mean diffusivity (MD)
  \[ MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3} \]

- Fractional anisotropy (FA)
  \[ FA = \frac{1}{\sqrt{2}} \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}} \]

White matter

Cerebrospinal fluid

Isotropic diffusion

Highly directional diffusion

Low

High

0

1

National Alliance for Medical Image Computing   http://na-mic.org
Various Measures of Anisotropy

A₁, VF, RA, FA

A. Alexander
Visualizing Tensors: Direction and Shape

- Color mapping
- Glyphs
Coloring by Principal Diffusion Direction

- Principal eigenvector, linear anisotropy determine color

\[ R = |e_1 \cdot x| \]
\[ G = |e_1 \cdot y| \]
\[ B = |e_1 \cdot z| \]

Pierpaoli, 1997

Slide G. Kindlmann
Issues With Coloring by Direction

- Set transparency according to FA (highlight-tracts)
- Coordinate system dependent
- Primary colors dominate
  - Perception: saturated colors tend to look more intense
  - Which direction is “cyan”?
  - Coloring is not unique
Visualization with Glyphs

- Density and placement based on FA or detected features
- Place ellipsoids on regular grid
Backdrop: FA

Color: RGB($e_1$)

G. Kindlmann
Glyphs: ellipsoids

Problem: Visual ambiguity
Worst case scenario: ellipsoids

one viewpoint:

another viewpoint:
Glyphs: cuboids

Problem:
missing symmetry
Superquadrics
Barr 1981
Superquadric Glyphs for Visualizing DTI
Kindlmann 2004
Worst case scenario, revisited
Backdrop: FA

Color: RGB($e_1$)
Why do we care?

- Free diffusion (ventricles) shown as spheres.
- Intersecting tracts can’t be properly modeled by a single tensor: Simplified disks in rank-1 tensors.
- Large tracts can be locally modeled by single tensors.

\[ \lambda_1 \approx \lambda_2 \approx \lambda_3 \] - Isotropic
Prevailing in CSF and gray matter regions of the brain.

\[ \lambda_1 \approx \lambda_2 \gg \lambda_3 \] - Oblate
Arise in white matter regions.

\[ \lambda_1 \gg \lambda_2 \approx \lambda_3 \] - Prolate
Prevailing in white matter regions.
Shape Characterization: Westin

\[
C_l = \frac{\lambda_1 - \lambda_2}{\lambda_1}, \quad C_p = \frac{\lambda_2 - \lambda_3}{\lambda_1}, \quad C_s = \frac{\lambda_3}{\lambda_1}
\]

\[C_l + C_p + C_s = 1\]

Westin et al., MICCAI’99
Limitations of the Diffusion Tensor Model

Kissing, Crossing, Splaying.

Diffusivity in a fiber crossing, 2nd-order tensor approximation.

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

Courtesy B. Vemuri, MICCAI 2008 workshop
Simplification and assumption

Orientational Diffusion Fct

Diffusion ellipsoid

Courtesy of Susumu Mori, JHU
Two Tensor Model (C-F Westin, S Peled, G Kindlmann)

DTI: Single tensor model

Two-tensor model

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop
Tractography Corticospinal Tract

Provided by L O’Donnell
Results Two-Tensor Tractography

Single tensor model

Two-tensor model

Orientation Distribution Function ODF

ODF and FRT allows to effectively recover the fibers direction

1. Apparent Diffusion Coefficient (ADC)
2. Orientation Distribution Function (ODF)

Fiber distribution
ADC profile
Diffusion ODF

Descoteaux/Angelino/Fitzgibbons/Deriche in Magnetic Resonance in Medicine, 2006 and 2007

Rat Biological Phantom - Data from McGill - BIC

Courtesy Rachid Deriche, MICCAI 2008 workshop
Higher Order Tensor can capture fiber crossing geometry

- Excised full rat brain
- $S_0 + \text{HARDI (32 dir., B-value}=1250 \text{ s/mm}^2$)
- Data provided by Drs Carney and Mareci

Courtesy Baba Vemuri, MICCAI 2008 workshop

Junction of CC and singulum
Higher Order Tensor can capture fiber crossing geometry

- Excised full rat brain
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Courtesy Baba Vemuri, MICCAI 2008 workshop
Spatial Transformations of Diffusion Tensors

Warmer colors indicate higher anisotropy

Principal diffusion directions in anisotropic regions of a DT-MR image slice

James Gee, Department of Radiology
University of Pennsylvania
Rotation without DT Reorientation

- Directional structure is lost.
- DTs orientations are no longer consistent with the anatomical structure of the image.

James Gee, Department of Radiology
University of Pennsylvania
Rotation with DT Reorientation

- $D \rightarrow R \cdot D \cdot R^T$.
- Directional structure preserved.
- DTs orientations remain consistent with the anatomy.

James Gee, Department of Radiology
University of Pennsylvania
Affine Tensor Transformations  
(Alexander et al, MICCAI 1999)

• For an affine transformation, \( D \rightarrow F \cdot D \cdot F^T \)?  
• No...

Finite Strain Estimation  
• Decompose \( F \) into:  
  • Rigid rotation, \( R \), and  
  • Deformation, \( U \):  
    \[
    F = R \cdot U \\
    R = F \cdot (F^T \cdot F)^{-1/2}
    \]
• Then reorient \( D \) using \( R \):  
  \[
  D' = R \cdot D \cdot R^T
  \]
Mean Callosal Fiber Map
Diffusion Tensor Images Averaged over Ten Subjects

Jones et al, 2002
Dream: Connectivity?

Forebrain Fiber Bundles: General idea of where various fiber bundles are and regions they interconnect or project to.

Source: Duke NeuroAnatomy
Web Resources (Ch. Hulette)

Tractography: Coronal view
Networking and Brain Connectivity

Major Fiber Tracts extracted from DT MRI

UNC Computer Science: Network wire cabinets
White Matter Tracts

- In tractography fibers are traced, with the aim to visualize white matter tracts.
- The word “tractography” is not related to “tracking”, but to “tract”.
- White matter tract, white matter fasciculus

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop
From Tensors to Connectivity?

- Study diffusivity in 3D tensor field
- Propagate principal diffusion direction originating at user-selected seed point
- Display paths as streamlines
- Measurement of FA and MD along path
DTI Tractography

Seed point(s)

Move marker in discrete steps and find next direction

Direction of principle eigen value
Going Beyond Voxels: Tractography

• Method for visualization/analysis
• Integrate vector field associated with grid of principle directions
• Requires
  – Seed point(s)
  – Stopping criteria
    • FA too low
    • Directions not aligned (curvature too high)
    • Neighborhood coherence
    • Leave region of interest/volume
• Many methods have been published during the past decade (Basser, Mori, Westin, Vermuri, Kindlmann, Lenglet, etc.)
White Matter Fiber Tract Atlases

Catani et al., Occipito-temporal connections in the human brain, Brain 2003
The Problem with Tractography
How Can It Work?

- Integrals of uncertain quantities are prone to error
  - Problem can be aggravated by nonlinearities
- Related problems
  - Open loop in controls (tracking)
  - Dead reckoning in robotics
Alternative methods for tractography

- Tracking in vector-field of largest eigenvector
- Tracking in tensor field
- Probabilistic tractography
- Optimal path analysis
- Fiber tract by volumetric diffusion
- 
  - Variety of methods developed by NAMIC developers

Georgia Tech: Opt. Path
Stochastic Tractography

- Zhang, Hancock, Goodlett and Gerig, Probabilistic White Matter Fiber Tracking using, Particle Filtering and von Mises-Fisher Sampling, Med Image Anal. 2009 Feb;13(1):5-18

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop
Stochastic Tractography

Fractional anisotropy

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

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

Friman, Westin MICCAI 2005, TMI 2006

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop
Probability of Connection

Given a large number of fibers, the probability of a connection between two voxels can be estimated.

Probability density function: 1) Add the contribution from all paths, and 2) normalize the total sum of all voxels.

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop
Probability of Connection

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

Work with O. Friman

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop
Probability of Connection

Corpus callosum

Inferior occipitofrontal fasciculi

Log(probability of connection)

Work with O. Friman

Courtesy Carl-Fredrik Westin, MICCAI 2008 workshop

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Quantitative Tractography: NAMIC Tool

FiberViewer

• Tractography results in selected fiber bundles of interest.

• Next step for clinical studies is geometrical and quantitative characterization.

Fiber Tract-Oriented Statistics for Quantitative Diffusion Tensor MRI Analysis, Isabelle Corouge, P.Thomas Fletcher, Sarang Joshi, Sylvain Gouttard, Guido Gerig, Medical Image Analysis 10 (2006), 786 - 798
Fiber Tract Modeling and Analysis

1. DT images
2. Tensor field
3. Fiber tract
4. Diffusion properties
5. Averaging tensors
6. Alignment
7. Attributing each location with a tensor by interpolation
8. Parameterization and Correspondences
Processing of fiber tracts

Origin (anatomical landmark)
Example Uncinate Fasciculus

Quantitative Tractography

- Tractography for ROI definition
- Tensor-math. for statistics along tracts
Summary: What do we measure?

- DWI measures local diffusivity pattern.
- Local diffusivity pattern is shaped by tissue type, axon structuring, myelination etc.
- Curves and streamlines from tractography are NOT AXONS but possible paths in vector/tensor field.
- “Fiber counting” scientifically questionable, # is method specific.
- DWI DOESN’T MEASURE AXONS or GLOBAL CONNECTIVITY!
Circuit -> Connectivity

Caution

• Do not “blindly” use the word “Connectivity” when applying DTI

• “Connectivity”: Became forbidden C-word in some NIH study sections