Diffusion Tensor MRI
Beyond Tractography

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Outline

Pictorial overview of DT-MRI data
Geomtric intuition for commonly studied tensor invariants

Three (non-tractography) methods of DTI analysis:
  • Tract-based Spatial Statistics (Smith et al.)
  • Tract-Specific Framework (Yushkevich, Zhang, Gee et al.)
  • Anisotropy Creases (Kindlmann at al.)

Discussion & Conclusions
**Diffusion & Diffusion weighting**

**Diffusion**: Brownian motion of one material through another

**Anisotropy**: diffusion rate depends on direction

Magnetic gradients create spatial planar waves of proton phase

Destructive interference creates signal attenuation (diffusion-weighting) only along gradient direction

**Indirect imaging of microstructure**

Microstructure of bundles directionally constrains water diffusion along fiber direction (LeBihan et al. 1985)

Intra- vs. extra-cellular diffusion

Diffusion lengths with the time-scale of MR measurement on order of 10μm

**Apparent** diffusion coefficient (ADC) measured for each gradient

Voxels on the order of 1mm

⇒ **Two to three orders of magnitude** away from measuring axons
**Diffusion-Weighted to Diffusion-Tensor**

**Diffusion-weighted MR data**

**Single Tensor Model** (Basser et al. 1994)

\[ S_i(b, g_i) = S_0 e^{-b g_i^T D g_i} \]

Linear regression

**Single Tensor Model**: only six degrees of freedom

**Eigenvectors & eigenvalues**

\[ D = R \Lambda R^{-1} \]

\[ = \begin{bmatrix} v_1 & v_2 & v_3 \end{bmatrix} \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \begin{bmatrix} v_1 \\ v_2 \\ v_3 \end{bmatrix} \]

**Eigenvectors**: orientation

**Eigenvalues**: shape
Tensor invariants describe shape

Can be understood as cylindrical or spherical coordinate system

\[ \lambda_3 \]
\[ \lambda_1 = \lambda_2 = \lambda_3 \]

\[ \text{tr}(D) = D_{xx} + D_{yy} + D_{zz} \]
\[ |D| = \sqrt{\text{tr}(D^T D)} \]
\[ E = \text{deviatoric}(D) = D - \text{trace}(D)^* I/3 \]

\[ \text{mode}(E) \]
\[ \frac{|E|}{|D|} \sim FA \]
\[ FA = \text{Fractional Anisotropy} \]

Biological meaning of tensor shape

Size: bulk mean diffusivity MD (“ADC”)
- (ADC strictly speaking diffusivity along one direction)
- Roughly same across gray+white matter, high in CSF
- Indicator of acute ischemic stroke

Anisotropy (e.g. FA): directional microstructure
- High in white matter, low in gray matter and CSF
- Increases with myelination, tends to decrease in diseases that damage white matter

Much diffusion-MRI-based neuroscience is about MD & FA

Mode: linear versus planar
- Partial voluming of adjacent orthogonal structures
- Fine-scale mixing of diverse fiber directions
- Tensor fitting error increases with planarity (Tuch 2002)
Principal eigenvector \(\approx\) axon direction

Standard RGB colormap

\[
\begin{align*}
R &= |e_1 \cdot x| \\
G &= |e_1 \cdot y| \\
B &= |e_1 \cdot z|
\end{align*}
\]

(Pajevic & Pierpaoli, 1999)
Superquadric Tensor Glyphs, Kindlmann '04
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Tractography (deterministic) Basser et al. 1998

Compute path that is everywhere tangent to principal eigenvector

Idea: can compute paths of axons

- Data too coarse
- Single-tensor model can’t represent crossing or branching
- Selecting individual tracts requires manual editing or alignment with atlas
- Still used for large bundles

Probabilistic tractography and non-tensor models capture more complex architecture
Summarizing intro

Diffusion MRI measures **anisotropy**

Anisotropy is a meaningful tissue property
Anisotropy implies directionality

Tractography/Connectivity methods attempt to trace spatial patterns of directionality

**Can also study anisotropy (FA) and other invariants themselves**

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### Tract-based Spatial Statistics (TBSS)


- For doing statistical tests on tensor invariants
- Conceptually close to Voxel-Based Morphometry (voxel-based, whole brain, automated)
- Computes a “skeleton” of group-mean FA image
- Voxel-based (raster) representation of skeleton
- Skeleton is reference manifold for projecting and doing statistics on registered single-subject FA

### TBSS compared to VBM

VBM: automated, simple, whole brain analysis
(Ashburner & Friston NeuroImage 2006)

VBM of FA sensitive to:
- Changes in WM alignment from registration
- Amount of smoothing (changes in FA levels vs volume of WM region, esp with thin tracts)

TBSS aims for robustness by using **skeleton**: avoids regions of low mean FA or high inter-subject variability

Steps in TBSS

- Single-subject FA maps non-linear registered
- Mean FA image skeletonized by non-maximal suppression (using either first or second derivatives)
- Single-subject FA maps projected into skeleton (with limit on distance of projection)
- GLM statistics on projected FA

Example of TBSS applied

DTI for TBI (Traumatic Brain Injury); indicates changes that are not prominent with structural imaging

Red: FA(cntl) > FA(TBI)
Blue: MD(cntl) < MD(TBI)
Yellow: $D_{ax}(cntl) < D_{ax}(TBI)$
(Blue: $D_{rad}(cntl) < D_{rad}(TBI)$)

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Tract-specific framework ("TSF")


• Uses medial representations in continuous domain to parameterize representations of specific sheet-like tracts of interest
• Aims to increase sensitivity at cost of specificity
• Uses rasterizations of tractography to delineate tracts, then medial axis transform
• http://www.picsl.upenn.edu/Research/Research
  http://picsl.upenn.edu/Theme/DiffusionImaging
Steps in Tract-Specific Framework

- Spatial normalization of all subjects’ tensor images (including tensor reorientation)
- Tractography in tracts of interest according to Wakana et al.
- Rasterization processed by Voronoi pruning & manifold learning (Maximum Variance Unfolding) to recover low-DOF parameterization of underlying sheet
- Inverse Skeletonization optimizes fit of continuous medial representation of tractography (explicitly recovers tract thickness)


Using parametric representations

- Compute invariants and then project (like TBSS)
- Or average tensors and then compute invariants
- Leverage connection to known tract thickness

Out of image space, a real manifold: can connect to literature on cortical surface analysis

DT-MRI - Beyond Tractography ISMRM'11 "Functional & Anatomic Data Analysis: Principles & Practicalities"
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Anisotropy Creases


• Computes ridges of FA (like TBSS), but in the continuous domain (like TSF)
• Draws on basic Computer Vision
  • Ridge/valley feature definition
  • Scale-space for scale (blurring) selection
• Unlike TBSS & TSF: extracts features from single-subject scans, not group means
• Not (yet) used for group studies or available in tool
**Differential Structure of image**

Ridges & Valleys (“Creases”) of **continuous** anisotropy map

“Ridges in Image and Data Analysis”
Eberly ’96

Constrained extremum

Gradient $\mathbf{g}$

Hessian eigensystem $\mathbf{e}_i, \lambda_i$

**Crease**: $\mathbf{g}$ orthogonal to one or more $\mathbf{e}_i$

Eigenvalue gives **strength**

Ridge surface: $\mathbf{g} \cdot \mathbf{e}_3 = 0$; $\lambda_3 < \text{thresh}$

Ridge line: $\mathbf{g} \cdot \mathbf{e}_3 = \mathbf{g} \cdot \mathbf{e}_2 = 0$; $\lambda_3, \lambda_2 < \text{thresh}$

Valley surface: $\mathbf{g} \cdot \mathbf{e}_1 = 0$; $\lambda_1 > \text{thresh}$

**TBSS** is a raster representation of the ridge surfaces of FA

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**Coronal slab: tractography**
Coronal slab: ridge surfaces

Coronal slab: valley surfaces
Coronal slab: tractography + valleys

How to choose scale (amount of blurring)?

Computer vision notion of “Scale-Space”: analyze image and all blurrings simultaneously

Features exist as manifolds in (N+1)-dimensional space

DT-MRI - Beyond Tractography  
ISMRRM'11 “Functional & Anatomic Data Analysis: Principles & Practicalities”
Brain DTI Results

FA ridge surfaces

Without Scale-Space   With Scale-Space

FA ridge lines
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Can use these examples to ponder space of DTI analysis ...
  Role of Raster vs Continuous Representation
  Represent “middle” only, or both middle and boundary
  Exploratory vs Model-based Analysis
  Interaction with Tractography
  Role of Anisotropy (FA) Thresholding
  Role of scale (blurring), and setting of scale
  Role of Non-rigid Registration as means of learning correspondence (necessary?)
  Basic question: How should we assess the correlation between mathematical features and anatomical features? (given reservations about single tensor model)
Thank you

Follow-up: glk@uchicago.edu