Tract-Specific Analysis for DTI of Brain White Matter

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The Whole-Brain Approach to Population Analysis





From Simon et al., Neuroimage, 2005

Why Focus on Structures?

- Evaluate specific a priori hypotheses
- Reduce confounding effects of surrounding structures
- Enable structures to be normalized independently
- Increase the level of detail
- Present findings in the context of anatomy





Structure-Specific Coordinate Systems



Talairach space: a coordinate system for the whole brain



A shape-based coordinate system for the corpus callosum in 2D



A three-dimensional shapebased coordinate system

Structure-Specific Normalization

Geometrical Correspondence





Motivation:

Anatomical correspondences may not be always continuous across structures

Motivation:

In the absence of strong intensity features, structures may be better normalized on the basis of shape cues

Preliminaries



A specialized method for DTI registration and template-building



A surface-based framework for DTI population studies

Normalization with Diffeomorphisms



A Diffeomorphic Deformation



$$\phi(\mathbf{x}, t) = x + \int_0^1 v(\phi(\mathbf{x}, t), t) dt$$

$$\int \text{Discretize } v(\mathbf{x}, t) \text{ and integrate at sub-voxel resolution}$$

$$\phi(\mathbf{x}, t) = x + \int_0^1 \underbrace{\bullet \quad v(\mathbf{x}, dt) \quad v(\mathbf{x}, 2dt) \quad v(\mathbf{x}, 1)}_{\phi(\mathbf{x}, dt) \quad v(\mathbf{x}, 2dt)} dt$$

 $\phi(x,t)$ is a path of diffeomorphisms and gives a smooth curve at each voxel

Optimization is performed by manipulating v at each x and t

Symmetric Normalization with Diffeomorphisms

Find
$$\phi(x,t) = x + \int_0^{0.5} v_1(\phi(x,t),t)dt + \int_{0.5}^1 v_2(\phi(x,t),t)dt$$

gradients wrt / gradients wrt /

with $\phi_1(x, 0.5)I = \phi_2(x, 0.5)J$ and $\phi(x, 1) = \phi_2^{-1}(\phi_1(x, 0.5), 0.5)$



A Symmetric Normalization Diffeomorphic Deformation



Extension to Symmetric Population Studies Optimal Template Construction

Find the template and set of transformations that gives the "smallest" parameterization of the dataset:

$$\begin{split} \sum_{i} \inf_{\phi_1^i} & \inf_{\phi_2^i} \int_{t=0}^1 \{ \|v_1^i\|_L^2 + \|v_2^i\|_L^2 \} dt + \\ & \int_{\Omega} \omega \overline{I(\phi_1^i(0.5))} - J_i(\phi_2^i(0.5))|^2 d\Omega. \\ & \text{where } \forall i, \phi_1^i(0) = \psi \overline{I(\phi_1^i(x,1))} = J_i, \\ & \text{and each pairwise problem is solved with} \\ & \text{SyN} \text{ (see equation 1 and 2).} \end{split}$$





Varying the geometric origin of the study is fundamental to minimizing the total distance between the template and the population

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Steps in Template Construction for Lesioned Brains Benefit of Shape Update



Initial Template Later Template Shape Update to the Previous Template

Comparison with Appearance Averaging Only Need for Shape Update



Intensity averaging does not fully correct blurring caused by mismatch during initialization

This problem becomes more severe with more complex shapes or worse initialization

SyN finds the theoretical result for the **mean shape and appearance**

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Example SyN Templates



Example DTI Template



Spatial Transformations Need for DT Reorientation



No Reorientation



With Reorientation



Tensors are re-located but not reoriented Tensors are correctly re-located and reoriented

Affine Tensor Transformations

Original Tensor



Transformed

Tensor

 $D \rightarrow F \cdot D \cdot F^{\mathrm{T}}$

For an affine transformation, (F,t), $D \rightarrow F \cdot D \cdot F^{\mathsf{T}}$?

No...

We wish to preserve the shape of the DTs

- But we must reorient them appropriately
- Require *R* that reflects reorientation due to F

 $D \rightarrow R \cdot D \cdot R^{\mathrm{T}}$

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*:

 $D' = R \cdot D \cdot R^T$

Affine Tensor Transformations

Original Tensor



Transformed

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 $\phi(x,1)I = J$

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Piece-wise Affine DTI Registration

- Task-Driven Evaluation Study:
 - White matter changes in ALS
 - Cross-sectional design (8 patients, 8 controls)
- Key Findings:
 - Increased sensitivity of detected FA changes with full-tensor registration
 - Reduced susceptibility to false positives due to shape confounds



Deformable registration of FA images to an external template using SPM2 Population-Specific Atlas via diffeomorphic registration of FA images Population-Specific Atlas via registration of full diffusion tensors

Tensor SyN Captures Large Deformations



Tensor SyN vs SyN on FA



Template DT

Tensor SyN registration

SyN registration on FA

Tract-Specific Analysis Framework





Tract-Based Analysis in the Literature

Curve-Based

Skeleton-Based



Curve-based tract representation (Corouge et al., *MedIA*, '06)



Skeleton-based white matter representation (Smith et al., *Neuroimage*, '06)

Surface-Based Tract Representation



Expert-Driven Tract Labeling



ROI delineation



Fiber selection

corpus callosum (CC) corticospinal tract (CST) inferior longitudinal fasciculus (ILF) superior longitudinal fasciculus (SLF) inferior fronto-occipital fasciculus (IFO) uncinate fasciculus (UNC)



Surface representation



Six sheet-like fasciculi

Tracking and Labeling on the Surface







Tract-Wise Statistical Mapping



Dimensionality Reduction



Model and fibers



Subject FA Maps

Tract-wise t-map

Flattening for White Matter Tracts



3D t-statistic map



Results shown are ADC difference maps from a 22q11.2 deletion syndrome study (Tony J. Simon, PI)

2D FWER-controlled cluster analysis

L-ILF

L-IFO

R-IFO R-ILF

ADC cluster z-score