A Riemannian Framework for Detecting Stimulus-Relevant

Fiber Pathways

uroscience

brain

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Outline

Motivation Mathematical Framework Experimental Results



Motivation: Fiber Clustering



There is evidence for Functional Networks in the Human Brain's White Matter

The purpose of fiber clustering is to cluster white matter fibers extracted from tractography into **similar and meaningful** fiber bundles

The clustering of white matter fiber tracts has significant implications for understanding how the brain works



Motivation: BOLD Signals Encode Neural Activity

- Functional MRI based on blood oxygenation level-dependent (BOLD) contrast is well established as a neuroimaging technique for detecting neural activity in the cortex of the human brain.
- Recent studies have shown that variations of BOLD signals in white matter are also related to neural activities both in resting state and under functional loading.
- Fiber tracts have been studied as open curves with different physical features (shape, scale, orientation and position).
- Fiber clustering becomes more meaningful by combining physical features and the BOLD signals associated with them to find stimulus-relevant pathways.





Outline

Motivation
Mathematical Framework
Experimental Results



- We have developed a comprehensive framework for analyzing and clustering white matter fibers that can incorporate both physical properties of fibers and BOLD signals associated with fibers.
- We propose a proper metric on the product space of shapes and functions to compare, align, and summarize white matter fibers.



Elastic Shape Analysis of Open Curves

We consider fiber tracts as 3D open curves and adopt square-root velocity function (SRVF) of curves proposed by Srivastava et al.

- Let $\beta: [0,1] \to \mathbb{R}^3$ denote a curve, the SRVF is $q(t) = \frac{\dot{\beta}(t)}{\sqrt{|\dot{\beta}(t)|}}$
- The distance in the shape space, called the shape metric, is given by:

 $d_{\mathcal{S}}([q_1], [q_2]) = inf_{(\gamma, O) \in \Gamma \times SO(3)} \|q_1 - O(q_2 \circ \gamma) \sqrt{\dot{\gamma}}\| \text{ where } \Gamma = \{\gamma \colon [0, 1] \to [0, 1] | \gamma(0) = 0, \gamma(1) = 1\}$

The optimal re-parametrization is solved by dynamic programming

 $\gamma^* = \operatorname{argmin}_{\gamma \in \Gamma}(\|q_1 - O^*(q_2 \circ \gamma)\sqrt{\dot{\gamma}}\|).$



Elastic Analysis of Trajectories of Functions

We consider BOLD signals associated with fiber tracts as trajectory of functions, and adopt squareroot slope function (SRSF) of functions proposed by Tucker et al.

- Let f be a real-valued function in [0, 1], the SRSF is defined as $q_f(t) = sign(\dot{f}(t)) \sqrt{|\dot{f}(t)|}$
- A trajectory of functions can now be expressed as a trajectory of SRSFs.
- Let α denote a smooth trajectory of SRSFs. We define a representation called the trajectory square-root vector field (TSRVF) according to: $h_{\alpha}(t) = \frac{\dot{\alpha}(t)}{\sqrt{|\dot{\alpha}(t)|}}$
- The distance between two trajectories is given by: $d_h([h_{\alpha_1}], [h_{\alpha_2}]) = inf_{\gamma \in \Gamma}(\int_0^1 |h_{\alpha_1}(t) h_{\alpha_2}(\gamma(t))\sqrt{\dot{\gamma}(t)}|^2 dt)^{\frac{1}{2}}$

• Solve the correspondence by:
$$\gamma^* = argmin_{\gamma \in \Gamma}((\int_0^1 |h_{\alpha_1}(t) - h_{\alpha_2}(\gamma(t))\sqrt{\dot{\gamma}(t)}|^2 dt)^{\frac{1}{2}}).$$



Joint Framework of Analyzing Shapes and Functions

- Define a metric on the product space, which is a weighted sum of d_S and d_h
- Let the pair (β, ω) denote a curve and a trajectory of BOLD signals associated with it.

 $d((\beta_1, \omega_1), (\beta_2, \omega_2)) = \phi_1 d_{\mathcal{S}}([q_1], [q_2]) + \phi_2 d_h([h_{\alpha_1}], [h_{\alpha_2}])$

Solve the optimal correspondence by

$$\gamma_* = argmin_{\gamma_* \in \Gamma}(\phi_1 d_{\mathcal{S}}(q_1, O^*(q_2 \circ \gamma_*) \sqrt{\dot{\gamma}_*}) + \phi_2 d_h(h_{\alpha_1}, (h_{\alpha_2} \circ \gamma_*) \sqrt{\dot{\gamma}_*})).$$

• Choice of Weights: ϕ_1 and ϕ_2 determine the contributions of shapes of fiber tracts and BOLD signals associated with the tracts, respectively. They are chosen by combining the clustering results with the anatomical structure.



Outline

Motivation
 Mathematical Framework
 Experimental Results



Data Acquisition

- Full brain MRI data were acquired from 10 healthy right-handed adult volunteers.
- We have imposed two different stimuli including motor and touch, denoted as MR and TR, and measured BOLD signals under three scenarios, including resting state (RS), MR and TR.
- The ROIs of probabilistic tracking which are a combination of PSC and MC are defined using Brodmann areas.



- 1, 2, 3: Primary somatosensory cortex (PSC)
- 4, 6: Motor Cortex (MC)



Data Acquisition

- The obtained fibers can be divided into three groups:
 - PSC connecting PSC
 MC connecting MC
 Cross-connecting
- The cross-connecting fibers mostly locate on the boundary area between PSC and MC (red)
- Each fiber is sampled equally with 100 points and each BOLD signal includes 145 timestamps.





Choice of Weights

- Apply the K-Means to cluster fibers based on the distance matrix computed by proposed metric.
- Different weights will lead to different clusters.



 $\phi_1 = 1, \phi_2 = 0$



 $\phi_1=10, \phi_2=1$



 $\phi_1 = 1, \phi_2 = 1$





Choice of Weights

- Select the optimal weights by comparing correlations, temporal variations and power spectra between stimuli and BOLD signals.
- Combining the anatomical structure and clustering results, we know MR activates red and blue clusters, and TR activates green and red clusters.
- Finally choose $\phi_1 = 1$ and $\phi_2 = 10$

TABLE I: Comparison of correlations between BOLD signals and stimuli under different combinations of ϕ_1 and ϕ_2 .

Different states	ϕ_1	ϕ_2	Green clus- ter	Red cluster	Blue cluster
MR	1	1	0.348	0.377	0.454
MR	10	1	0.339	0.361	0.431
MR	1	10	0.355	0.490	0.437
MR	1	0	0.467	0.369	0.296
TR	1	1	0.472	0.255	0.281
TR	10	1	0.375	0.212	0.271
TR	1	10	0.474	0.467	0.276
TR	1	0	0.465	0.253	0.274
RS	1	1	0.171	0.195	0.194
RS	10	1	0.189	0.192	0.171
RS	1	10	0.193	0.180	0.168
RS	1	0	0.109	0.124	0.176



Choice of Weights

- Power spectra of TR (black) and BOLD signals in clusters using FFT
- TR evokes red and green fibers





Comparison of Temporal Variations

• BOLD signals under TR (left) exhibit much clearer periodic pattern than under RS (right).





Comparison with Different Methods



Shape analysis only



Shape analysis and FPCA



Our method



Comparison with Different Methods

- We compute correlations for all 10 subjects under MR, TR and RS. Table below reports the averages of correlations for MR and TR.
- Based on the anatomical structure, MR evokes red & blue clusters, TR evokes red & green clusters. Therefore, MR is expected to have the lowest correlation in green, and TR is expected to have the lowest correlation in blue.

Different clusters under	Green	Red clus-	Blue clus-
MR	cluster	ter	ter
Shape analysis [10], [15]	0.280	0.370	0.264
Shape analysis and FPCA	0.281	0.309	0.276
Our method	0.256	0.308	0.389
Different clusters under	Green	Red clus-	Blue clus-
TR	cluster	ter	ter
Shape analysis [10], [15]	0.271	0.405	0.283
Shape analysis and FPCA	0.361	0.251	0.391
Our method	0.422	0.309	0.235



Statistical Testing

- In the end, the mean correlations are converted to Fisher's Z-scores for statistical testing.
- The two-tailed, paired students t-tests are used to evaluate differences between green cluster versus red & blue clusters for MR, differences between green & red clusters versus blue cluster for TR.
- In both cases, the p-values are less than 0.0001, which indicates the clustering results by our method are very significant.



Conclusion

We have developed a comprehensive framework for analyzing and clustering stimulus-relevant whiter matter fibers.

The proposed model can be used to analyze multimodality data. Our framework has correctly identified clusters with different stimuli, which agrees with the anatomical structure.

In future, we aim to obtain the functional structure in task state by clustering whole-brain FMRI signals.





