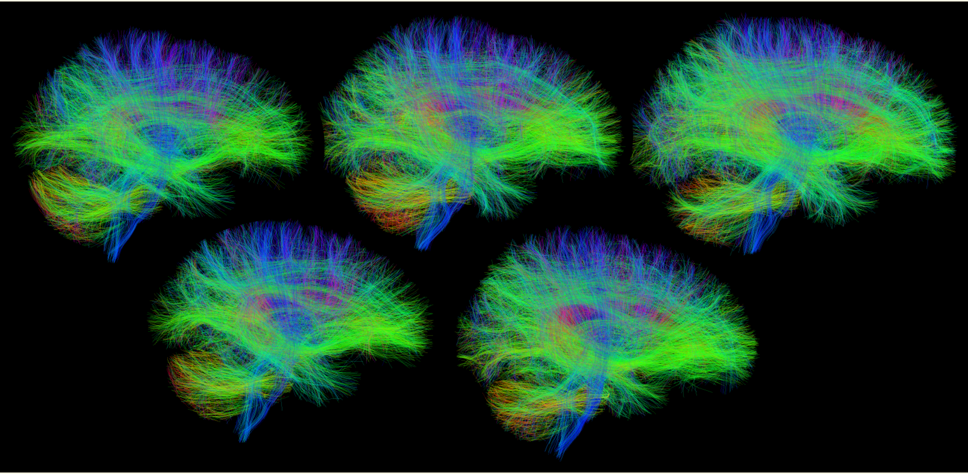
Structural Connectome Atlas Construction in the Space of Riemannian Metrics

Kris Campbell [1] Haocheng Dai [1] Zhe Su [2]
Martin Bauer [3] P. Thomas Fletcher [4] Sarang Joshi [1,5]

[1]School of Computing, Scientific Computing and Imaging Institute, Univ of Utah
[2]Department of Neurology, Univ of California Los Angeles
[3]Department of Mathematics, Florida State Univ
[4]Electrical & Computer Engineering, Univ of Virginia
[5]Department of Bioengineering, Univ of Utah

www.sci.utah.edu

How do we statistically analyze a population of connectomes?



Tractography provided by [Zhang et al. 2018]

Structural Connectome Atlas

Structural connectome: structural network of the brain

- white matter pathways between brain regions

Goal: Construct connectome atlas from tractography data

Purpose: Statistically quantify the geometric variability of structural connectivity across a population

Existing Methods

Register DWI to anatomical template[1]

- Euclidean average of diffusion tensors at each voxel
- No directionality information considered

Register q-space diffusion image to anatomical template[2]

- Averages spin-distribution function (SDF) at each voxel
- Considers directionality information
- No consistency of long-range white matter connections

Register tractography, then cluster into fiber bundles[3]

- Considers long-range connections
- Computationally expensive

[1] [Mori et al. 2008]
[2] [Yeh et al. 2018]
[3] [Zhang et al. 2018]

Our Contributions

Represent tractography fibers as geodesics of a metric, that is, as a point on the infinite-dimensional manifold of Riemannian metrics

Diffeomorphism-invariant Ebin metric to compute distances and geodesics between connectomes

Diffeomorphic Metric Registration of connectomes

Method to estimate atlas of connectomes

Structural Connectomes as Riemannian Metrics

Goal: Find a metric whose geodesics match the tractography as defined by a vector field, V

Inverse diffusion tensor metric[4]: $\tilde{g} = D(x)^{-1}$

- Geodesics capture essence of the tractography
- Deviates from tractography in high curvature areas

Estimate locally-adaptive metric[5]: $g_\alpha = e^{\alpha(x)}\tilde{g}$

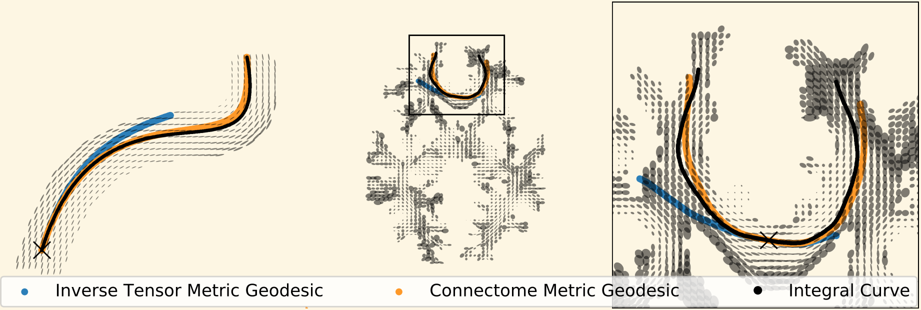
- Chosen so that geodesics of the metric match tractography

Minimize $$F(\alpha) = \int_M \|\operatorname{grad}\alpha - 2\nabla_V V\|_{\tilde{g}}^2 dx$$

by solving $\Delta_{\tilde{g}}\alpha = 2\operatorname{div}_{\tilde{g}}(\nabla_V V)$ for α

[4] [O'Donnell et al. 2002]
[5] [Hao et al. 2014]

Tractography-based Metric Estimation



Geodesics for a synthetic tensor field (left) and a subject's connectome metric from the Human Connectome Project (center) with a detailed view of the geodesics in the corpus callosum (right).

Manifold of Metrics

$g \in \mathrm{Met}(M)$, space of smooth Riemannian metrics on M

$\mathrm{Diff}(M)$ acts on $\mathrm{Met}(M)$ via pullback, $\varphi \in \mathrm{Diff}(M)$:

$$(g, \varphi) \mapsto \varphi^* g = g(T\varphi\cdot, T\varphi\cdot)$$

Geodesics w.r.t. g are mapped via φ to geodesics w.r.t. $\varphi^* g$

Equip $\mathrm{Met}(M)$ with Ebin metric

Ebin Metric (Metric on Metrics)

Ebin metric[6] is the integral of point-wise metrics on SPD:

$$G_g^E(h,k) = \int_M \mathrm{Tr}\left(g^{-1}hg^{-1}k\right) \mathrm{vol}(g)$$

- $h, k \in T_g \operatorname{Met}(M)$, $\mathrm{vol}(g)$ - induced volume density of g

Invariant under the action of $\mathrm{Diff}(M)$

$$G_g(h,k) = G_{\varphi^* g}(\varphi^* h, \varphi^* k)$$

Explicit point-wise formulas for geodesics and distances

[6] [Ebin 1970]

Geodesics[7] with Respect to Ebin Metric

Distance is the integral of point-wise distances on SPD:

$$\mathrm{dist}_{\mathrm{Met}}(g_0, g_1)^2 = \frac{16}{n} \int_M \left(\alpha(x)^2 - 2\alpha(x)\beta(x)\cos\left(\theta(x)\right) + \beta(x)^2\right) dx$$

Geodesic $g(x,t)$ between $g_0(x), g_1(x)$:

$$g(x,t) = \begin{cases} \left(q^2 + r^2\right)^{\frac{2}{n}} g_0 \exp\left(\frac{\arctan(r/q)}{\kappa} k_0\right) & 0 < \kappa < \pi, \\ q^{\frac{4}{n}} g_0 & \kappa = 0, \\ \left(1 - \frac{\alpha+\beta}{\alpha} t\right)^{\frac{4}{n}} g_0 1_{\left[0, \frac{\alpha}{\alpha+\beta}\right]} + \left(\frac{\alpha+\beta}{\beta} t - \frac{\alpha}{\beta}\right)^{\frac{4}{n}} g_1 1_{\left[\frac{\alpha}{\alpha+\beta}, 1\right]} & \kappa \geq \pi, \end{cases}$$

where:

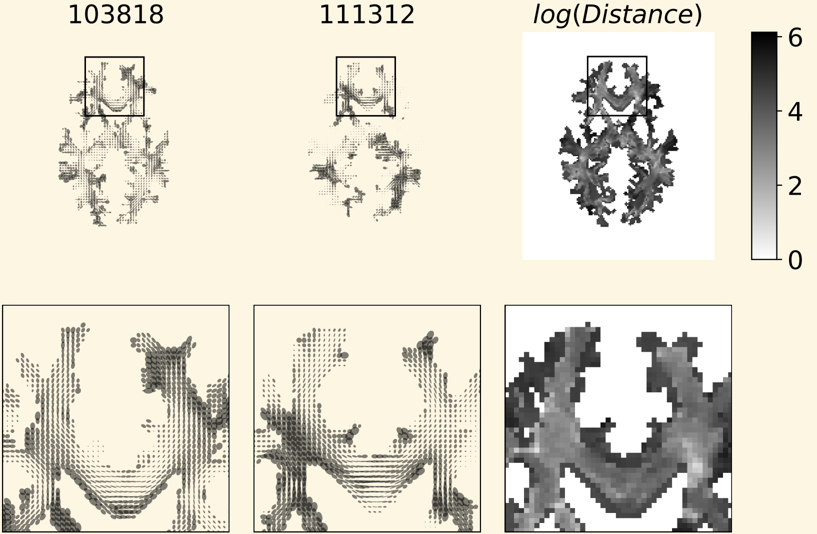
$$\alpha(x) = \sqrt[4]{\det(g_0(x))}, \quad \beta(x) = \sqrt[4]{\det(g_1(x))}, \quad \theta(x) = \min\{\pi, \kappa(x)\}$$

$$k(x) = \log\left(g_0^{-1}(x) g_1(x)\right), \quad k_0(x) = k(x) - \frac{\mathrm{Tr}(k(x))}{n} \mathrm{Id}, \quad \kappa(x) = \frac{\sqrt{n\,\mathrm{Tr}(k_0(x)^2)}}{4}$$

$$q(t,x) = 1 + t\left(\frac{\beta(x)\cos(\kappa(x)) - \alpha(x)}{\alpha(x)}\right), \quad r(t,x) = \frac{t\beta(x)\sin(\kappa(x))}{\alpha(x)}.$$

[7] [Gil-Medrano, Michor 1991], [Clarke 2013]

Geodesic Distance of Connectome Metric



Diffeomorphic Metric Registration

Recall Diff(M) acts on Met(M)) via pullback:

$$(g, \varphi) \mapsto \varphi^* g = g(T\varphi \cdot, T\varphi \cdot)$$

Ebin metric induces right-invariant distance on Diff(M)

$$\mathrm{dist}^2_{\mathrm{Diff}}(\mathrm{id}, \varphi) = \mathrm{dist}^2_{\mathrm{Met}}(g, \varphi^* g)$$

Register two connectomes by finding φ that minimizes:

$$E(\varphi) = \inf_{\varphi \in \mathrm{Diff}(M)} \mathrm{dist}^2_{\mathrm{Diff}}(\mathrm{id}, \varphi) + \lambda \, \mathrm{dist}^2_{\mathrm{Met}}(g_0, \varphi^* g_1)$$

Connectome Atlas Building

Explicit distance used in registration formulation to minimize

$$\hat{g} = \underset{g,\varphi_i}{\operatorname{argmin}} \sum_{i=1}^{N} \mathsf{dist}^2_{\mathsf{Diff}}(\mathsf{id}, \varphi_i) + \lambda\, \mathsf{dist}^2_{\mathsf{Met}}(g, \varphi_i^* g_i)$$

Alternating algorithm implemented in PyTorch:

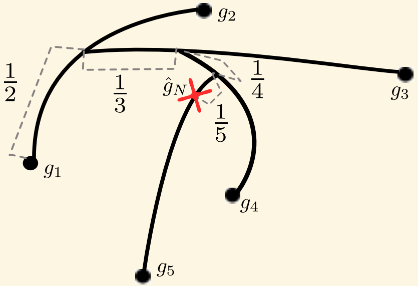
1. Estimate Fréchet mean
2. Register each connectome to current mean estimate
   - Gradient flow to optimize
   - only 2 iterations of metric matching each time to avoid overfitting early

Recursive[8] Fréchet Mean of Connectomes

Fréchet mean, $\hat{g}$, of metrics $g_1, \ldots, g_N$, minimizes:

$$\hat{g} = \underset{g}{\operatorname{argmin}} \sum_{i=1}^{N} \mathrm{dist}^2_{\mathrm{Met}}(g, g_i)$$

Requires only N geodesic calculations in total



[8] [Ho et al. 2013]

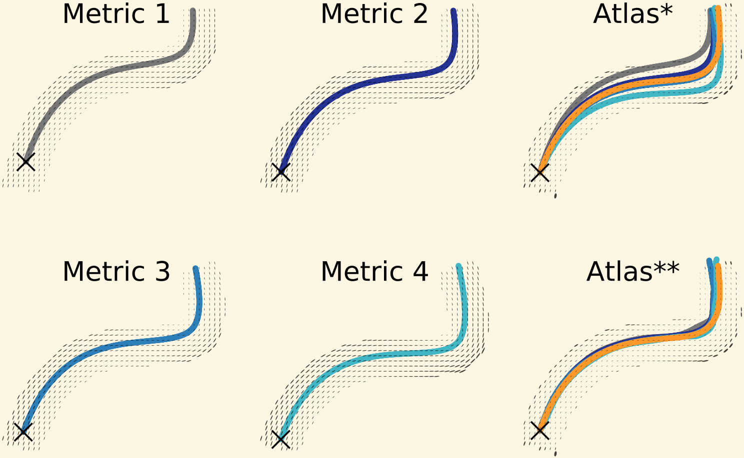
Synthetic Data

Generate vector fields with integral curves from a family of parameterized cubic functions

400 iterations, $\lambda = 100$, learning rate $\epsilon = 5$

Algorithm behaves well when $1/\epsilon$ is approx equal to energy

Atlas of Synthetic Tractograms



* Subject geodesics not deformed to atlas

** Subject geodesics deformed to atlas

Real Data

Subjects from Human Connectome Project (HCP)[9]

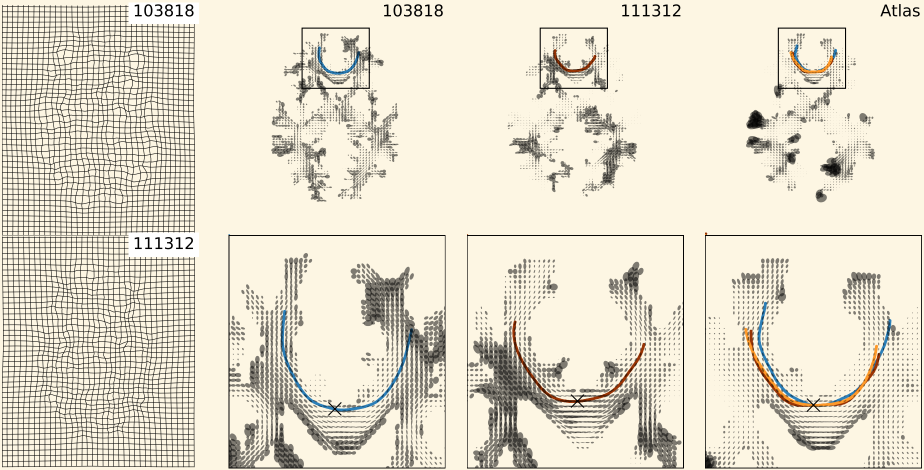
Estimate diffusion tensors for b -value = 1000 using FSL's `dtifit`

5000 iterations, $\lambda = 100$, learning rate $\epsilon = 1$

λ balances magnitude of diffeomorphisms from each connectome metric to the atlas

[9] [Van Essen et al. 2013]

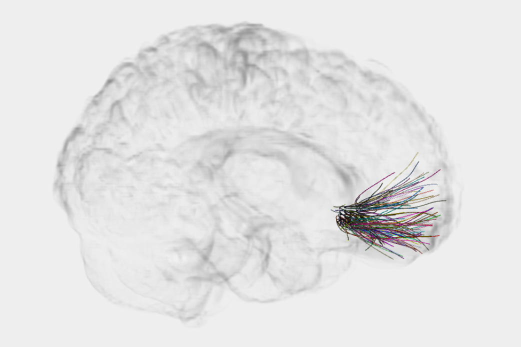
Example HCP Structural Connectome Atlas



Future Work

Statistical analysis

- Median, principal geodesic analysis, regression
- Robustness of connectome atlases



Conclusions

Novel framework for statistical analysis of structural connectomes

Represent tractography fibers as geodesics of a metric, that is, as a point on the manifold of Riemannian metrics

Explicitly compute distances and geodesics between connectomes using diffeomorphism-invariant Ebin metric

Diffeomorphic Metric Registration framework to register connectomes

Structural connectome atlas building algorithm

This research is supported by NSF grants DMS-1912037, DMS-1953244, DMS-1912030 and NIH/NIAAA award R01-AA026834.

Supplemental Materials

Connectome Atlas Supplement