Structural Connectome Atlas Construction
in the Space of Riemannian Metrics

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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*
**Goal:** Find a metric whose geodesics match the tractography as defined by a vector field, $\mathbf{V}$

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 $F(\alpha) = \int_M ||\text{grad} \alpha - 2 \nabla \mathbf{V}||_{\tilde{g}}^2 \, dx$

by solving $\Delta_{\tilde{g}} \alpha = 2 \text{div}_{\tilde{g}} (\nabla \mathbf{V})$ for $\alpha$

\(^4\)[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

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

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

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

Geodesics w.r.t. \( g \) are mapped via \( \varphi \) to geodesics w.r.t. \( \varphi^*g \)

Equip \( \text{Met}(M) \) with Ebin metric
Ebin Metric (Metric on Metrics)

Ebin metric\(^6\) is the integral of point-wise metrics on SPD:

\[
G^E_g(h, k) = \int_M \text{Tr} \left( g^{-1} h g^{-1} k \right) \text{vol}(g)
\]

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

**Invariant** under the action of Diff\((M)\)

\[
G_g(h, k) = G_{\phi^*g}(\phi^*h, \phi^*k)
\]

**Explicit** point-wise formulas for geodesics and distances

\(^6\)[Ebin 1970]
Geodesics\textsuperscript{7} with Respect to Ebin Metric

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

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

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

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

where:

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

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

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

\textsuperscript{7}[Gil-Medrano, Michor 1991], [Clarke 2013]
Geodesic Distance of Connectome Metric

103818

111312

$log(Distance)$
Diffeomorphic Metric Registration

Recall $\text{Diff}(M)$ acts on $\text{Met}(M))$ via pullback:

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

Ebin metric induces right-invariant distance on $\text{Diff}(M)$

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

Register two connectomes by finding $\varphi$ that minimizes:

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

**Explicit** distance used in registration formulation to minimize

\[
\hat{g} = \arg\min_{g, \varphi_i} \sum_{i=1}^{N} \text{dist}_{\text{Diff}}^2(\text{id}, \varphi_i) + \lambda \text{dist}_{\text{Met}}^2(g, \varphi^*_i g_i)
\]

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
Recursive⁸ Fréchet Mean of Connectomes

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

\[
\hat{g} = \arg \min_g \sum_{i=1}^{N} \text{dist}_{\text{Met}}^2(g, g_i)
\]

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

Metric 1
Metric 2
Metric 3
Metric 4
Atlas*
Atlas**

* 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 \(\epsilon = 1\)

\(\lambda\) 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.

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Supplemental Materials
Connectome Atlas Supplement