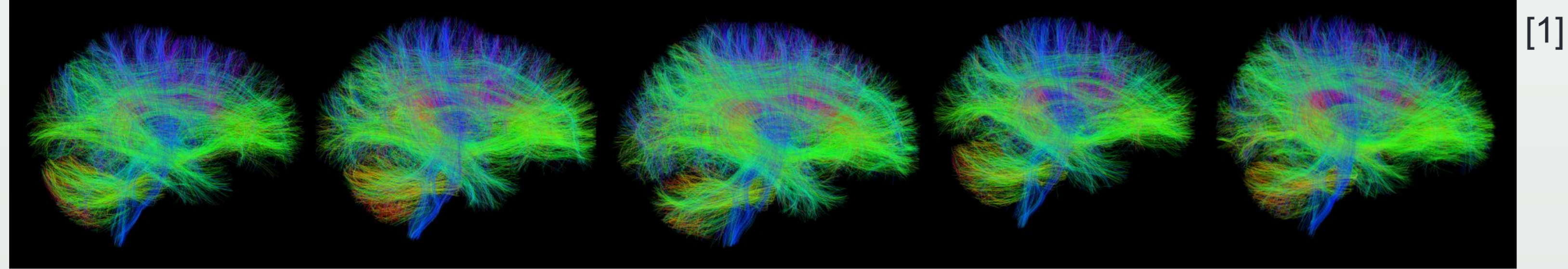


## How to statistically analyze a population of connectomes?



- We propose a method of analyzing connectomes by representing tractography fibers as geodesics of a Riemannian metric, that is, as points on an infinite-dimensional manifold.
- We equip the Riemannian manifold with diffeomorphism-invariant Ebin metric to compute distances and geodesics between connectomes.
- We develop a Diffeomorphic Metric Registration framework to register connectomes
- We apply object-oriented statistical analysis to define an atlas as the Fréchet mean of a population of Riemannian metrics.

## METHODS

1. Estimate a locally-invariant metric,  $g_\alpha = e^{\alpha(x)} \tilde{g}$ , conformal to the inverse-diffusion tensor metric,  $\tilde{g} = D(x)^{-1}$  and whose geodesics match the tractography as defined by a vector field,  $V$ , by minimizing [2]:

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

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

2. Equip the infinite-dimensional space of all Riemannian metrics with a diffeomorphism-invariant Riemannian metric, called the Ebin metric [3], which is the integral of point-wise metrics on SPD:

$$G_g^E(h, k) = \int_M \text{Tr}(g^{-1} h g^{-1} k) \text{vol}(g),$$

where  $h, k \in T_g \text{Met}(M)$ ,  $\text{vol}(g)$  the induced volume density of the metric  $g$ .

Distance is integral of point-wise distances on SPD:

$$\text{dist}_{\text{Met}}(g_0, g_1)^2 = \frac{16}{n} \int_M (a(x)^2 - 2a(x)b(x) \cos(\theta(x)) + b(x)^2) dx$$

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

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

$$\alpha(x) = \sqrt[n]{\det(g_0(x))} \quad \beta(x) = \sqrt[n]{\det(g_1(x))}$$

$$k(x) = \log(g_0^{-1}(x)g_1(x)) \quad \theta(x) = \min\{\pi, \kappa(x)\}$$

$$k_0(x) = k(x) - \frac{\text{Tr}(k(x))}{n} \text{Id} \quad \kappa(x) = \frac{\sqrt{n \text{Tr}(k_0(x)^2)}}{4}$$

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

$$r(t, x) = \frac{t\beta(x) \sin(\kappa(x))}{\alpha(x)}$$

3. Define “distance” of diffeomorphism  $\varphi$  to the identity, Ebin metric induces right-invariant distance on  $\text{Diff}(M)$ :

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

4. Register two connectomes by finding  $\varphi$  that minimizes  $E(\varphi)$ :

$$E(\varphi) = \inf_{\varphi \in \text{Diff}(M)} \text{dist}_{\text{Diff}}^2(\text{id}, \varphi) + \lambda \text{dist}_{\text{Met}}^2(g_0, \varphi^* g_1) \quad (\text{Algorithm 1})$$

5. Build atlas,  $\hat{g}$ , of metrics  $g_1, \dots, g_N$  by finding  $g$  and  $\varphi_1, \dots, \varphi_N$  that minimize:

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

$V$  - vector field,  $\text{div}$  - Riemannian divergence,  $\Delta$  - Laplace-Beltrami operator,  $\text{id}$  - identity mapping,  $g$  - metric,  $E$  - energy function,  $n$  - metric dimension,  $*$  - pull back operation

### Algorithm 1 Inexact Metric Matching Algorithm

**Inputs:**

source and target metric  $g_0, g_1$

**Initialize:**

learning rate  $\epsilon$ ; weight parameter  $\lambda$ ; max iteration  $\text{MaxIter}$   
 $\varphi, E \leftarrow \text{id}, 0$

**for** iteration = 0 :  $\text{MaxIter}$  **do**

$\varphi^* g_1 \leftarrow (d\varphi)^T (g_1 \circ \varphi) (d\varphi)$

$E \leftarrow \text{EbinEnergy}(\varphi^* g_1, g_0, \lambda)$

$v \leftarrow -\Delta^{-1}(E. \text{grad})$

$\psi \leftarrow \text{id} + \epsilon v$

$\varphi \leftarrow \psi \circ \varphi$

**end for**

**return**  $\varphi$

### Algorithm 2 Atlas Building Algorithm

**Inputs:**

sample metric fields list  $G$

**Initialize:**

max iteration times  $\text{MaxIter}$

**for** iteration = 0 :  $\text{MaxIter}$  **do**

$g_{\text{mean}} \leftarrow \text{FréchetMean}(G)$

**for**  $i = 0 : \text{len}(G)$  **do**

$\varphi \leftarrow \text{MetricMatching}(g_{\text{mean}}, G[i])$

$G[i] \leftarrow \varphi^* G[i]$

**end for**

**end for**

**return**  $g_{\text{mean}}$

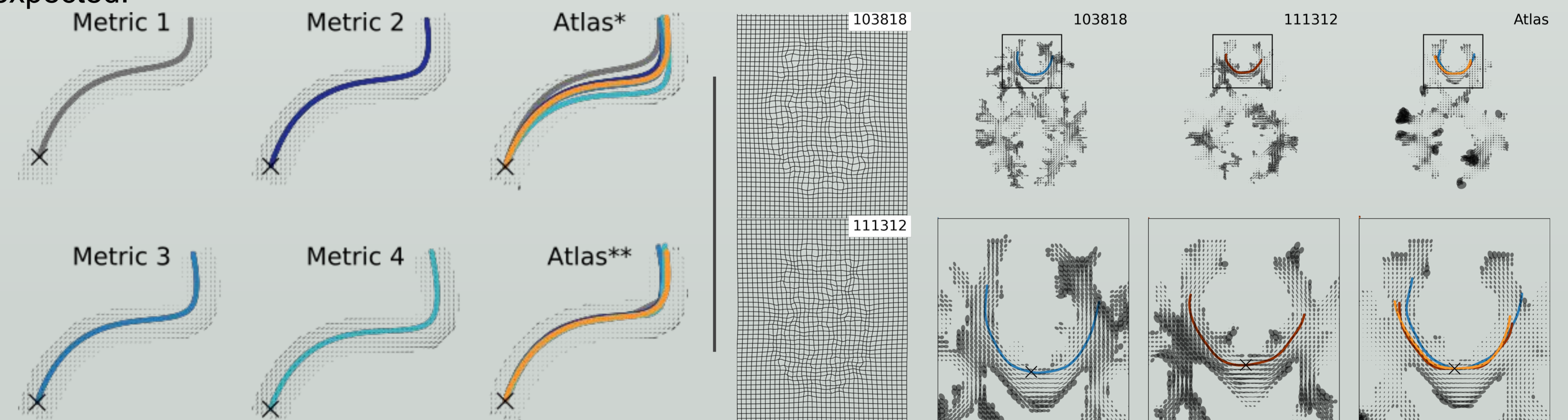
## RESULTS

**Hypothesis:** The geodesic on atlas metric field should be the average of the geodesics on sample metric fields.

**Data:** Generated vector fields whose central integral curves are a family of parameterized cubic functions; a subset of subjects from the Human Connectome Project Young Adult (HCP) dataset.

**Evaluation:** We first estimated the adaptive metric conformal to the inverse-tensor metric. After finding the connectome metric for each subject, we ran atlas building Algorithm 2 to estimate the atlas shown in right column of each figure. Then, we map the geodesics of the individual connectome metrics to atlas space and compare with the atlas geodesic.

**Conclusion:** The atlas geodesic is nicely centered in the middle of the undeformed individual geodesics as expected.



orange: geodesic of atlas metric; other colors: geodesics of sample metrics.

\*undeformed geodesics of sample metrics. \*\*geodesics of sample metrics deformed into atlas space.

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