Modeling the Shape of the Brain Connectome via Deep Neural Networks

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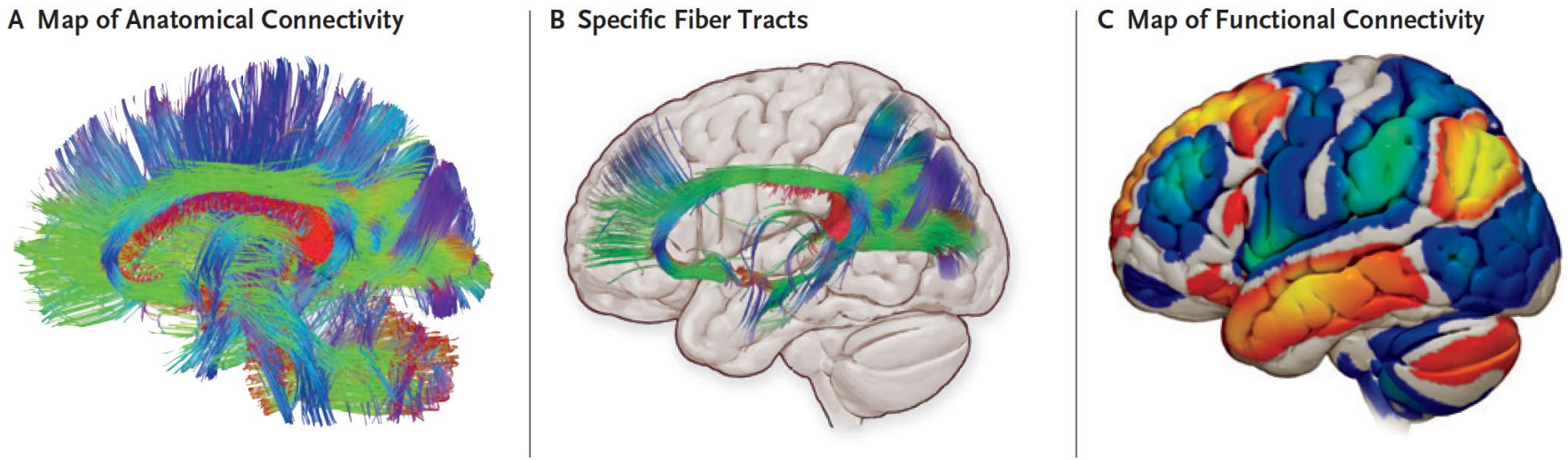
What is brain connectome?

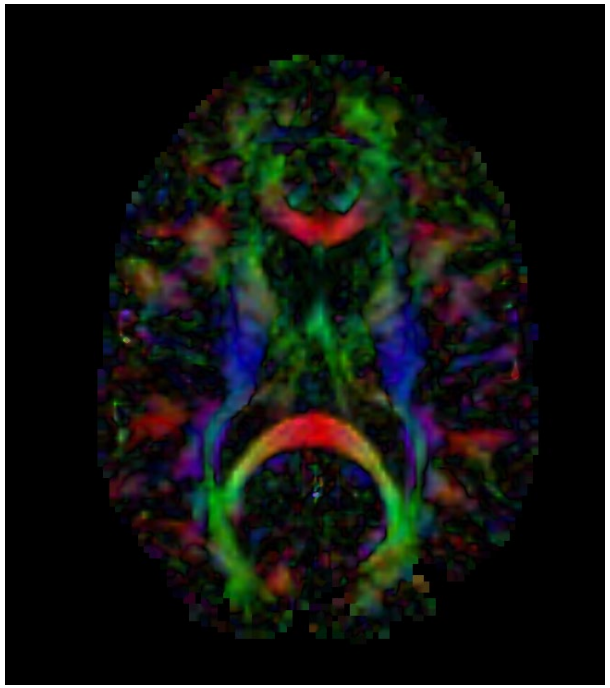
A comprehensive map of neuronal connections



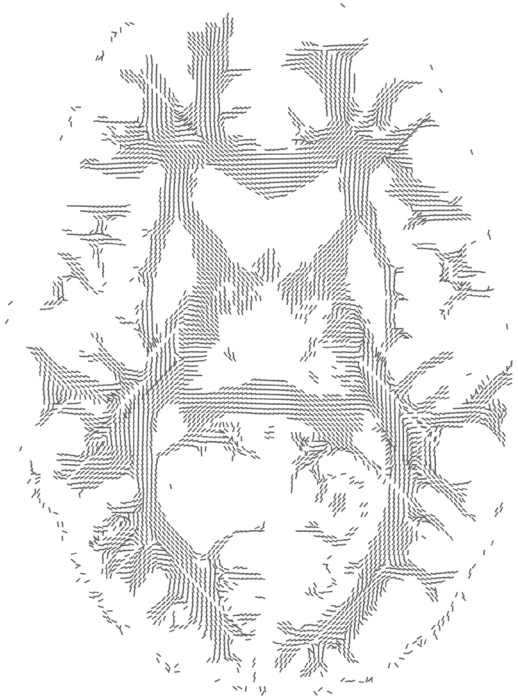
Tractography

Fox MD, 2018

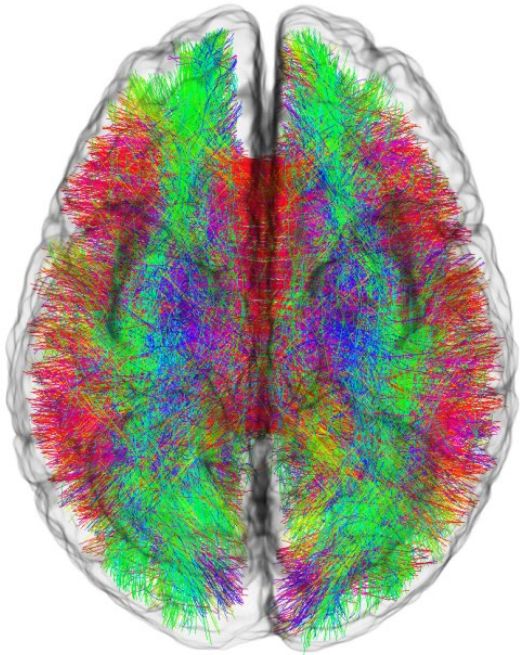
How do we infer tractography?



Diffusion MRI



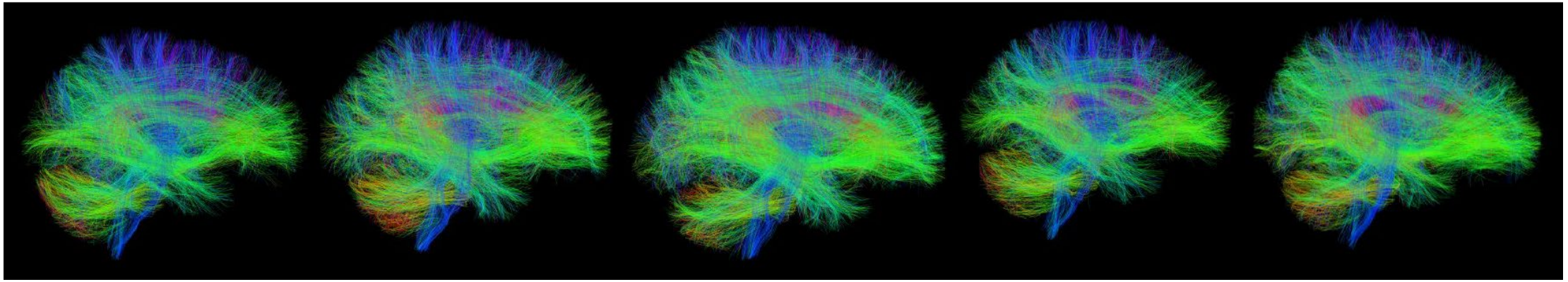
Vector Field



Tractography

Campbell KM, Dai H et al., 2022

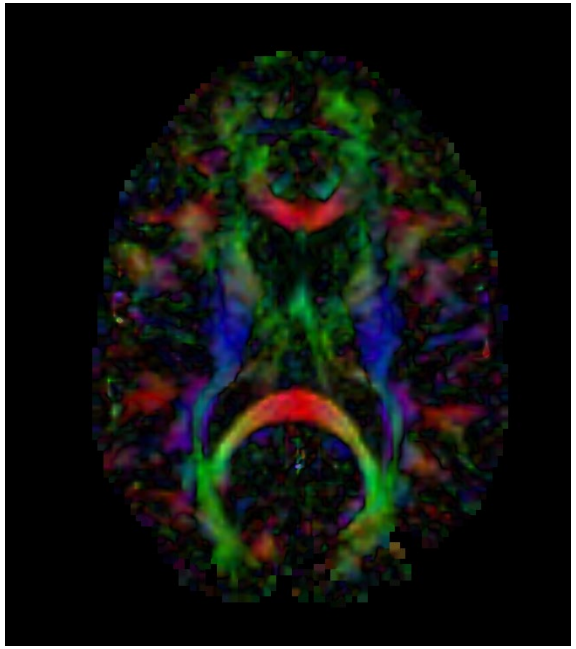
How do we statistically analyze a population of connectomes?



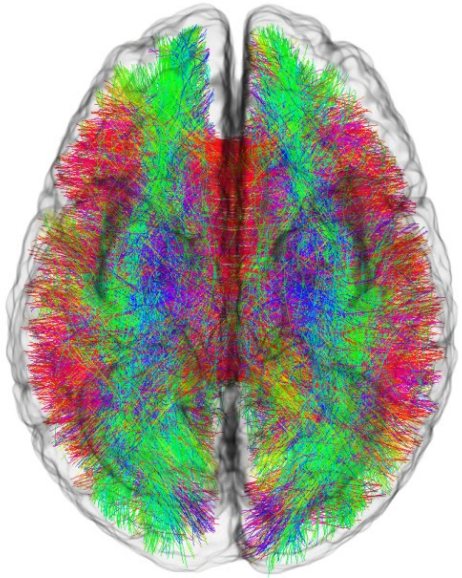
Construct connectome **Riemannian manifold** atlas from tractography data to statistically quantify the geometric variability of structural connectivity across a population.

Zhang et al. 2018

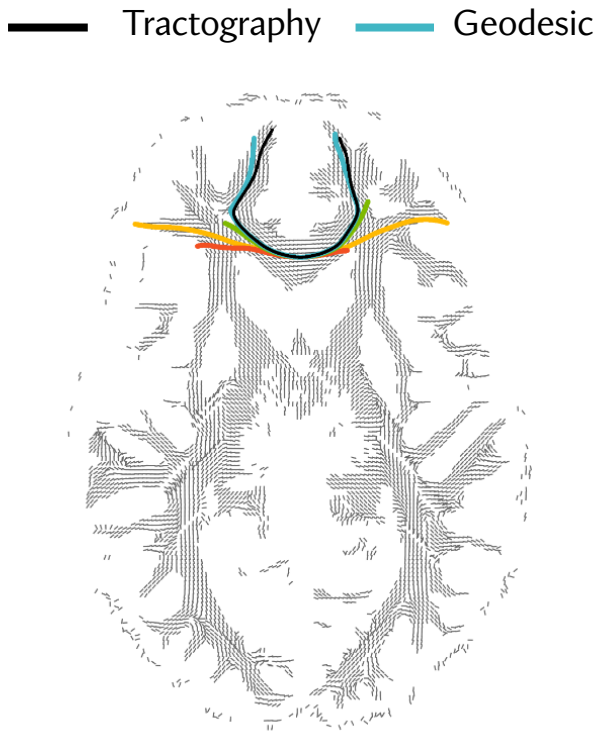
Geodesic Tractography



Diffusion MRI

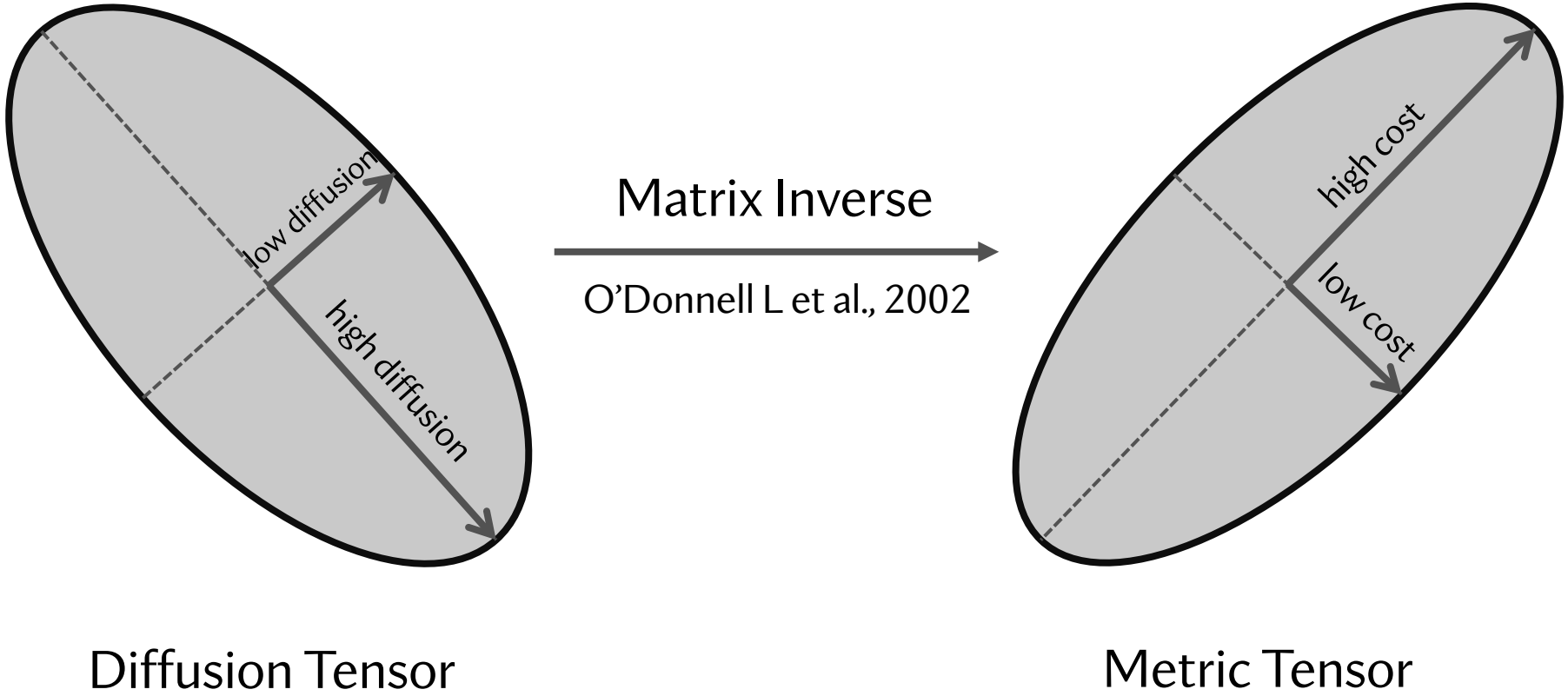


Tractography



Riemannian Manifold

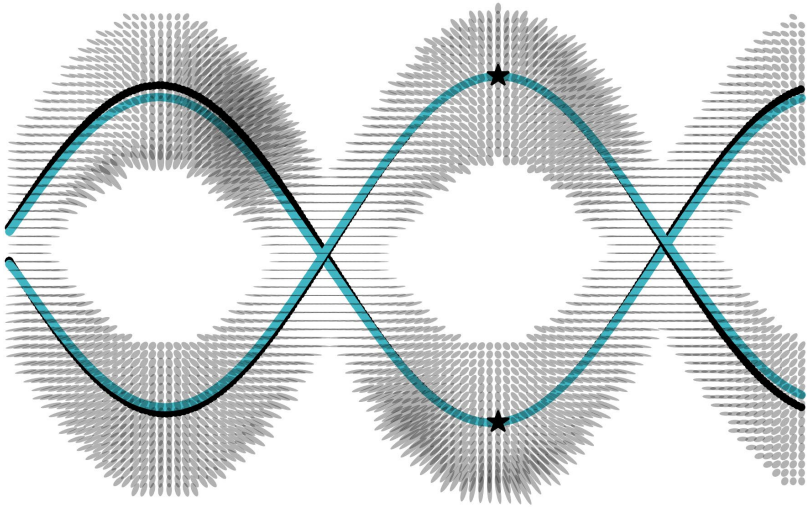
Related Work



Diffusion Tensor

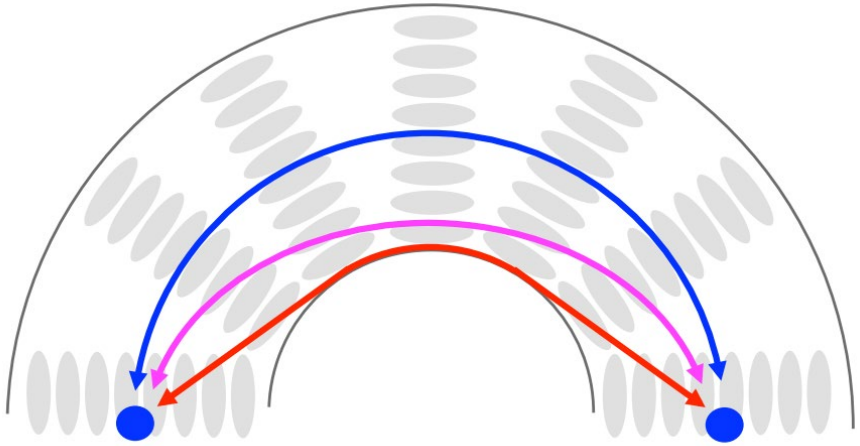
Metric Tensor

Pros and Cons of Geodesic Tractography



Advantage of geodesic tractography

- Can find tracts between two endpoints;
- A tool of studying geometry of the brain.



Disadvantage of previous geodesic tractography

- Easy deviation in high-curvature area (does not take neighbor metric variation into consideration);
- Unable to characterize crossing fibers

Hao et al., 2011

What is a metric tensor?

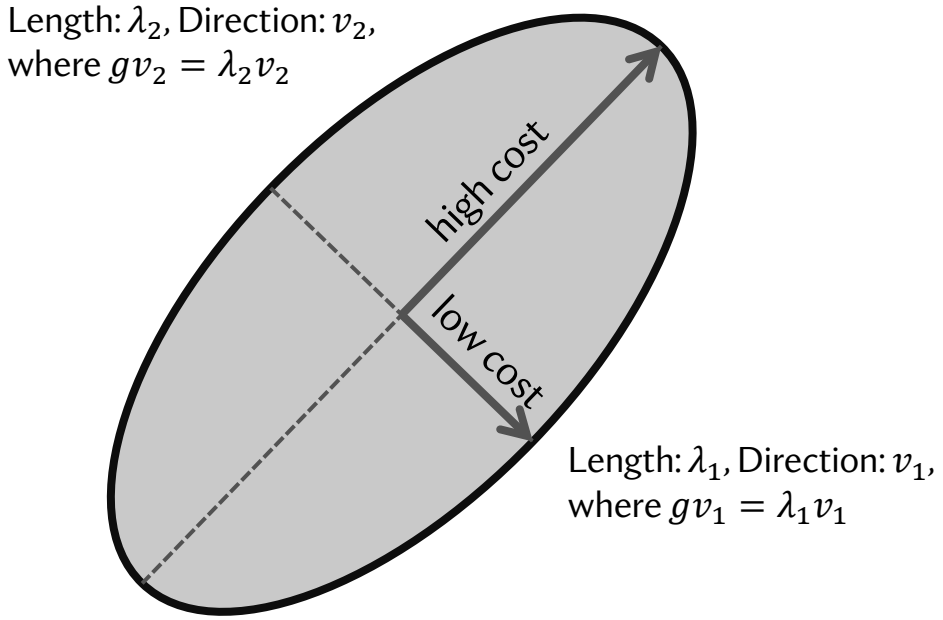
Metric tensor defines how we calculate the inner product under a given space.

$$g(u, v) = u^T g v,$$
$$g(v, v) = \|v\| = v^T g v,$$

where $g \in \mathbb{R}^{n \times n}$, n is the dimension of the space.

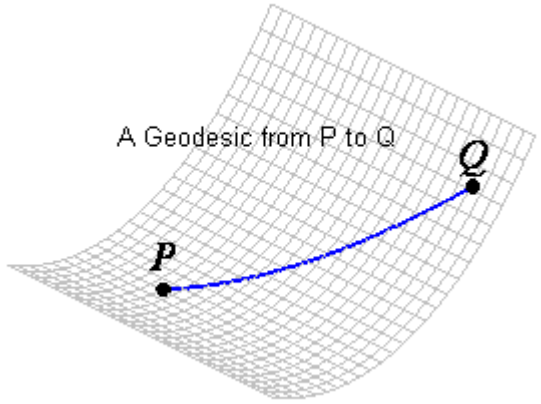
Euclidean metric	$g = I$
Riemannian metric	g can be any SPD matrix

Visualization of metric tensor



The axis of the ellipsoid is regulated by the eigenvector and eigenvalue of the metric tensor.

What is a geodesic?



The speed of a geodesic on a Riemannian manifold is constant, i.e. the tangential acceleration of a geodesic is zero.

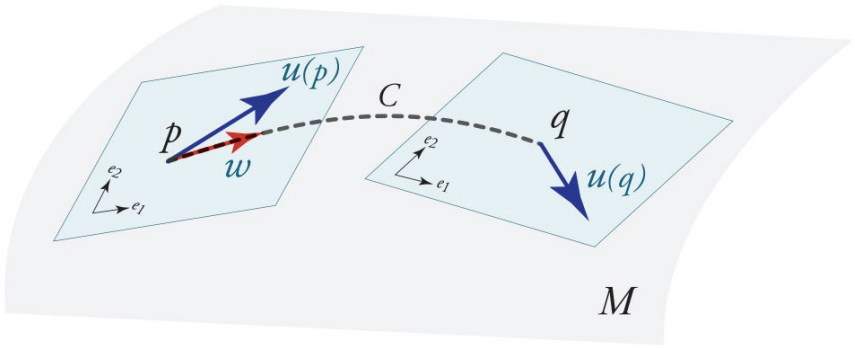
To compute geodesic curves, we need to find curves where the acceleration vector is normal to the space, namely

$$\nabla_{\dot{\gamma}} \dot{\gamma} = 0$$

holds along the curve γ, where ∇ is called covariant derivative, or Levi-Civita connection.

Knisley JR, 2001

What is covariant derivative?



Intuitively, covariant derivative

$$\nabla_w u$$

is a rate of change vector at u of a vector field in the direction of w, taking changes of the coordinate system into account.

Covariant derivative is the generalization of the directional derivative. It provides a connection between tangent spaces in a curved space.

Liu B et al., 2016

Estimating Riemannian Metrics from Geodesics

Explicitly, covariant derivative $\nabla_{\mathcal{V}}^{g}\mathcal{V}$ can be written as

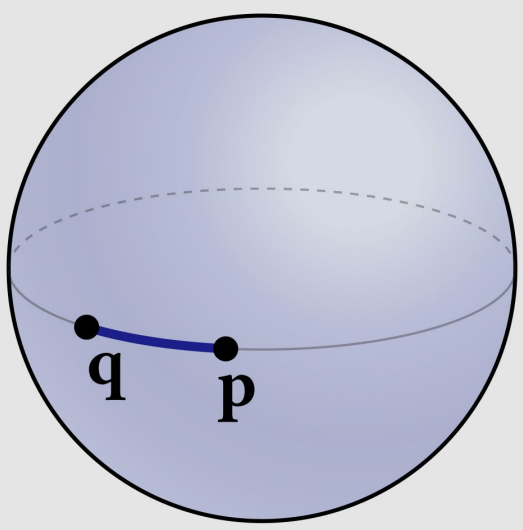
$$\nabla_{\mathcal{V}}^{g}\mathcal{V} = \sum_k \left(\sum_i v^i \frac{\partial v^k}{\partial x^i} + \sum_{i,j} \Gamma_{ij}^k v^i v^j \right) e_k. \quad (4)$$

A vector field $\mathcal{V}$ is called a geodesic vector field if and only if it satisfies the equations

$$\nabla_{\mathcal{V}}^{g}\mathcal{V} = 0, \text{(unit)}$$
$$\nabla_{\mathcal{V}}^{g}\mathcal{V} = \sigma\mathcal{V}, \text{(non-unit)}$$

where $\mathcal{V} = v^i e_i$ with $e_i = \frac{\partial}{\partial x^i}$ being the i-th basis vector, and $\sigma = \frac{\nabla_{\mathcal{V}}\mathcal{V}^T\mathcal{V}}{\mathcal{V}^T\mathcal{V}}$.

How is geodesic related to Riemannian metric?



As shown by Spivak, a critical curve for

$$L(\gamma) = \int_0^1 \frac{1}{2} \|\dot{\gamma}(t)\|^2 dt \quad (1)$$

is also a critical curve for

$$L(\gamma) = \int_0^1 \|\dot{\gamma}(t)\| dt. \quad (2)$$

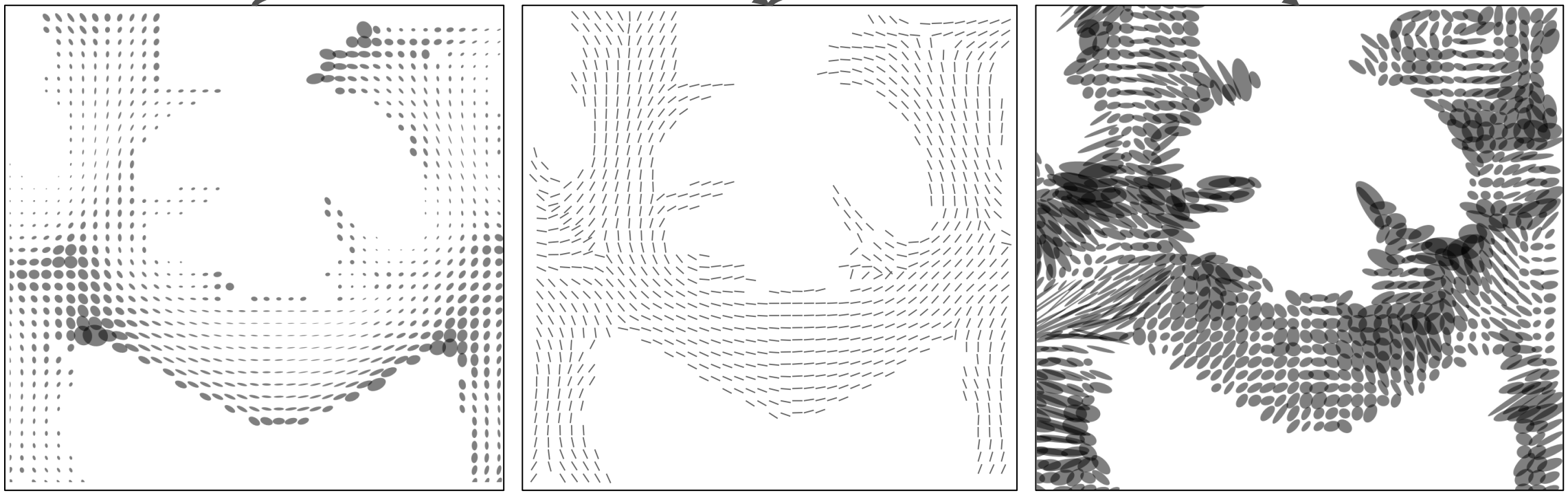
The only difference is that the geodesic that minimizes (1) has a constant speed.

Spivak M. A comprehensive introduction to differential geometry. Publish or Perish, Incorporated; 1970.

Estimating Riemannian Metrics from Geodesics

SOTA tractography method

Metric Estimation via Neural Network



A. DWMRI

B. Tangent Vector of Tractography

C. Riemannian Metric Field

Estimating Riemannian Metrics from Geodesics

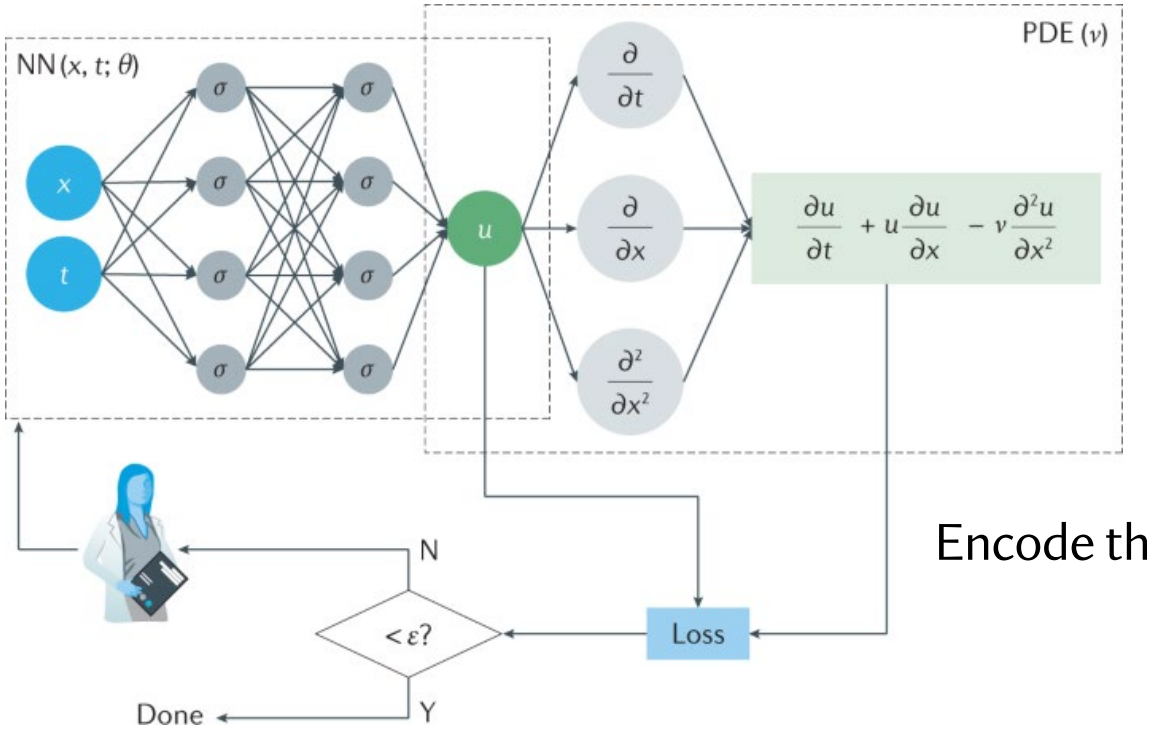
Objective function: Given vector fields $\mathcal{V}_i \in \mathfrak{X}(M), i \in \{1, \dots, m\}$ find the Riemannian metric g on M that minimizes the energy functional

$$E(g) = \sum_i^m \left\| \nabla^{\mathrm{g}}_{\mathcal{V}_i} \mathcal{V}_i - \sigma_i \mathcal{V}_i \right\| + \alpha \cdot Reg(g),$$

where $\sigma_i = \frac{\nabla_{\mathcal{V}_i} \mathcal{V}_i^T \mathcal{V}_i}{\mathcal{V}_i^T \mathcal{V}_i}$.

Physics-Informed Neural Networks (PINNs)

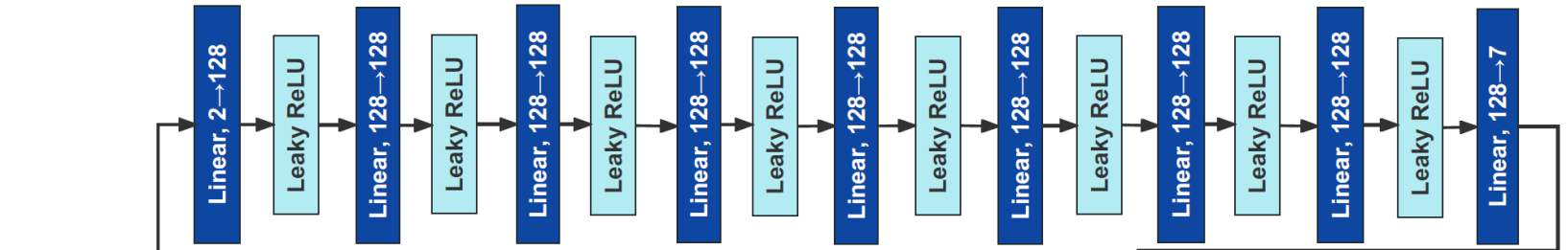
Leverage AutoGrad in PyTorch or TensorFlow to calculate derivative



Encode the inverse problem into loss function

Karniadakis GE, 2021

Architecture: Baseline MLP



Output: Symmetric Matrix Batch (distinct entries)
b × 7

Eigen Composition

Rodrigues' Rotation Formula

PDS Matrix Batch
b × 3 × 3

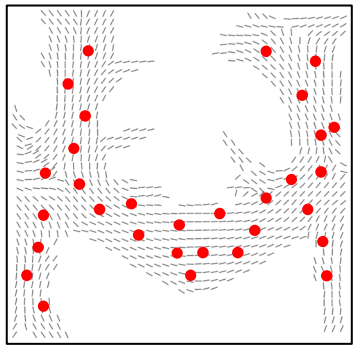
Input: 3D Coordinate Batch
b × 3

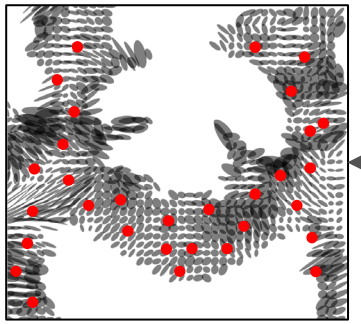
Derivative of PDS Matrix Batch
w.r.t Input by Autograd

Vector Field and Corresponding
Derivative by Central Finite Difference

Loss Function:

$$\sum_i \left\| \nabla^g_{\mathbf{v}_i} \mathbf{v}_i - \sigma \cdot \mathbf{v}_i \right\|_2$$

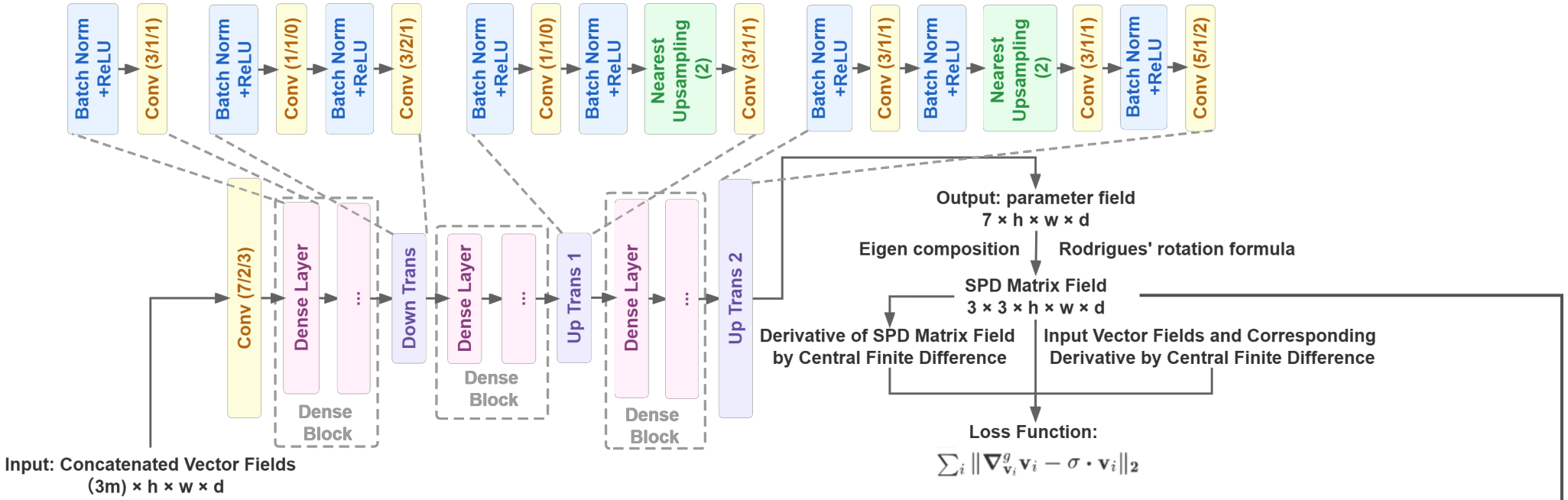


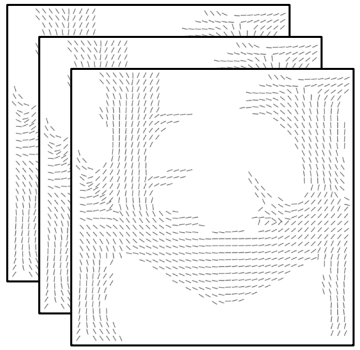


Recap: $\nabla^g_{\mathcal{V}} \mathcal{V} = \sum_k \left(\sum_i v^i \frac{\partial v^k}{\partial x^i} + \sum_{i,j} \Gamma^k_{ij} v^i v^j \right) e_k$

$$\Gamma^k_{ij} = \frac{1}{2} \left(\frac{\partial g_{ik}}{\partial x^j} + \frac{\partial g_{jk}}{\partial x^i} - \frac{\partial g_{ij}}{\partial x^k} \right)$$

Architecture: CEDNN

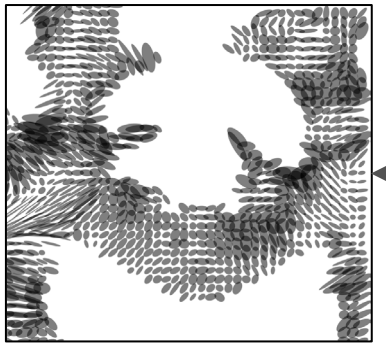




Multiple vector fields describe crossing fibers.

*2D example only for illustration purpose.

One metric field accommodates multiple crossing fibers.



SPD Metric Matrix Composition

Matrix Exponential

$$e^S = \sum_{k=0}^{\infty} \frac{1}{k!} S^k$$

$$S = \begin{bmatrix} u_1 & u_2 & u_3 \\ u_2 & u_4 & u_5 \\ u_3 & u_5 & u_6 \end{bmatrix}$$

*In implementation, eigen composition is 5 times faster than matrix exponential.

Eigen Composition

Orthogonal

$$g = R \Lambda R^T$$

Positive eigenvalues

We formulate orthogonal matrix through Rodrigues rotation formula:

$$R = I + \sin(\theta)\, K + \cos(1 - \theta)\, K^2$$

$$I = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, \qquad K = \begin{bmatrix} 0 & -u_1 & u_2 \\ u_1 & 0 & -u_3 \\ -u_2 & u_3 & 0 \end{bmatrix},$$

$$\theta = u_4, \qquad \Lambda = \begin{bmatrix} \exp(u_5) & 0 & 0 \\ 0 & \exp(u_6) & 0 \\ 0 & 0 & \exp(u_7) \end{bmatrix}$$

Geodesic Shooting

Algorithm 1 Geodesic Shooting

Require: Vector field $\mathbf{v} : M \to \mathbb{R}^n$; Christoffel symbol $\Gamma_{ij}^k : M \to \mathbb{R}$ based on metric $g : M \to \mathbb{R}^{n \times n}$; starting point $\gamma\left(\frac{0}{T}\right) \in M$; proper step size ϵ, η.

$\dot{\gamma}\left(\frac{0}{T}\right) = \mathbf{v}\left(\gamma\left(\frac{0}{T}\right)\right)$ ▷ Linearly interpolate $\mathbf{v}$

$\gamma\left(\frac{1}{T}\right) = \gamma\left(\frac{0}{T}\right) + \epsilon \cdot \dot{\gamma}\left(\frac{0}{T}\right)$

for $t = 2 : T$ **do**

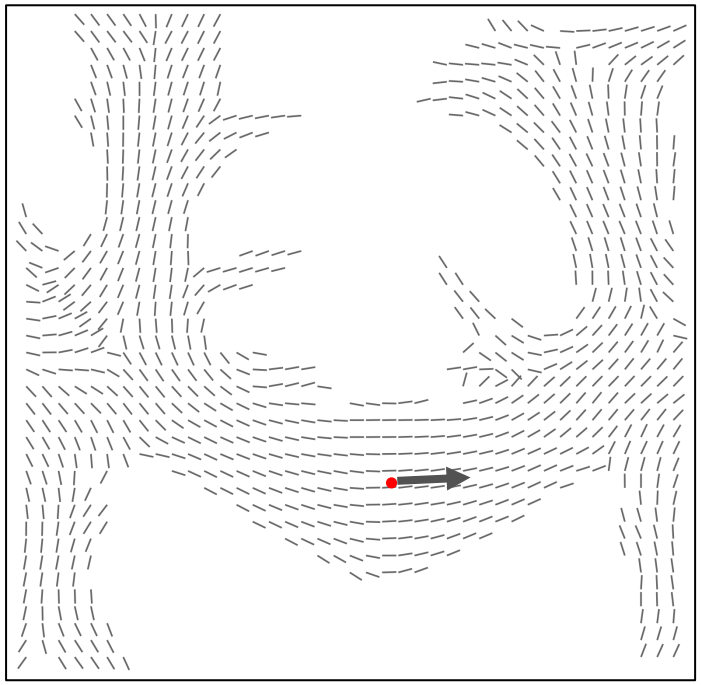
$\ddot{\gamma}^k\left(\frac{t-2}{T}\right) = -\Gamma_{ij}^k\left(\gamma\left(\frac{t-2}{T}\right)\right) \cdot \dot{\gamma}^i\left(\frac{t-2}{T}\right) \cdot \dot{\gamma}^j\left(\frac{t-2}{T}\right) + \sigma \cdot \dot{\gamma}^k\left(\frac{t-2}{T}\right)$ ▷ Linearly interpolate Γ_{ij}^k

$\dot{\gamma}\left(\frac{t-1}{T}\right) = \dot{\gamma}\left(\frac{t-2}{T}\right) + \eta \cdot \ddot{\gamma}\left(\frac{t-2}{T}\right)$

$\gamma\left(\frac{t}{T}\right) = \gamma\left(\frac{t-1}{T}\right) + \epsilon \cdot \dot{\gamma}\left(\frac{t-1}{T}\right)$

end for

return γ



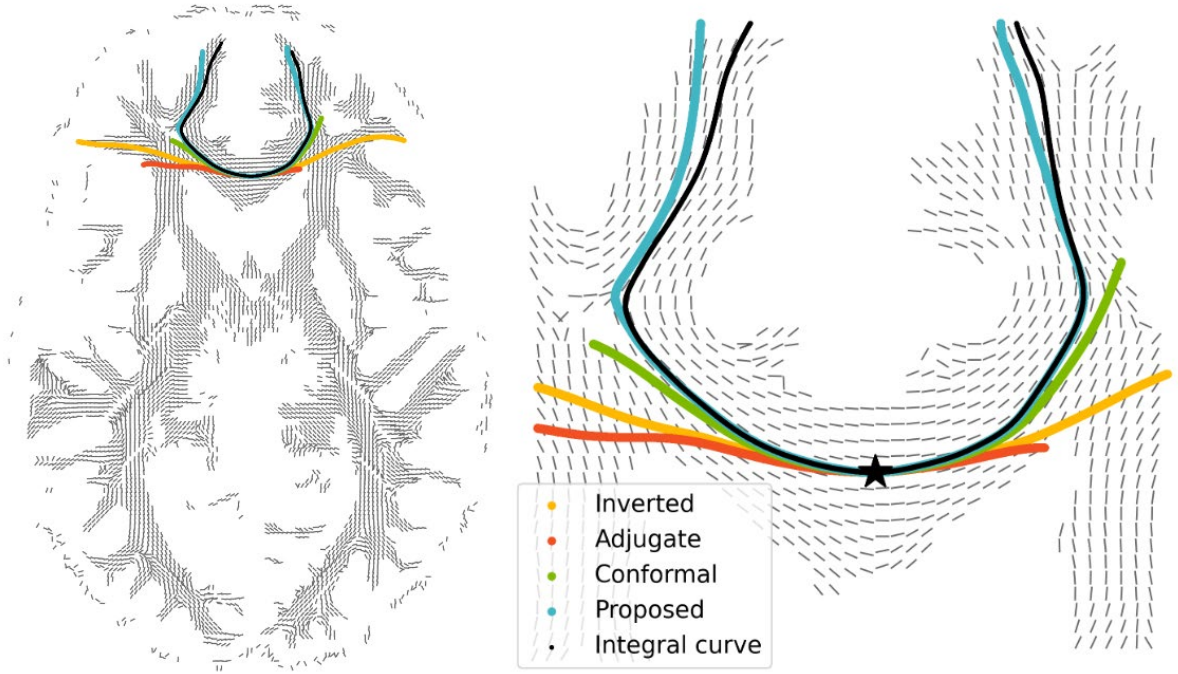
- Starting point: $\gamma(0)$
- Initial shooting direction: $\mathcal{V}(\gamma(0))$

Geodesic equation (non-unit) recap: $\ddot{\gamma}^k + \Gamma_{ij}^k \dot{\gamma}^i \dot{\gamma}^j = \sigma \cdot \dot{\gamma}^k$

Christoffel symbol recap: $\Gamma_{ij}^k = \frac{1}{2}\left(\frac{\partial g_{ik}}{\partial x^j} + \frac{\partial g_{jk}}{\partial x^i} - \frac{\partial g_{ij}}{\partial x^k}\right)$

Experiment 1: 2D Brain Slices

Inverted	O'Donnell et al., 2002	Take the inverse of the diffusion tensor as metric
Adjugate	Fuster et al., 2016	Take the adjugate of the diffusion tensor as metric
Conformal	Hao et al., 2011	Apply scalar field modulation to inverted diffusion tensor



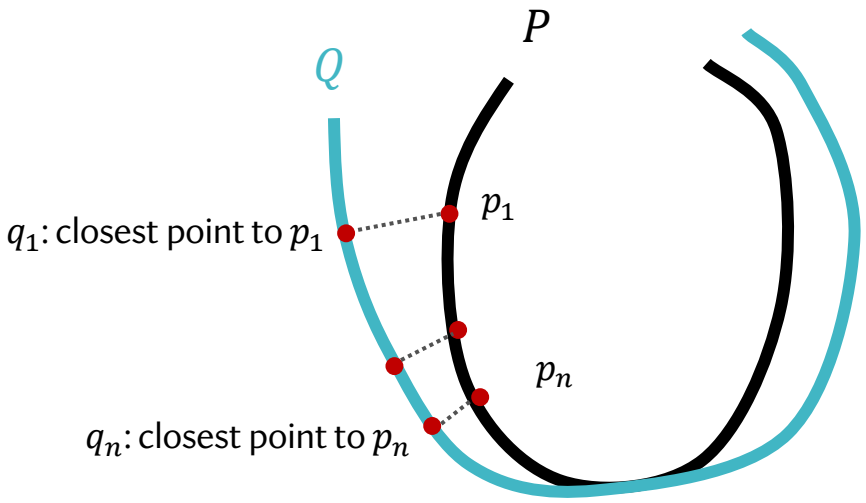
38 HCP brain subjects, 400 seed points on each subject, 15200 pairs of geodesics and tractography in total

Experiment 1: 2D Brain Slices

Mean min errors:

$$Error(P,Q) = \frac{1}{|P|}\sum_{p\in \mathrm{P}} min_{q\in Q}\|p-q\|_2\,,$$

where *P denotes a tractography* and *Q our geodesic tractography* curve starting at the same seed point.



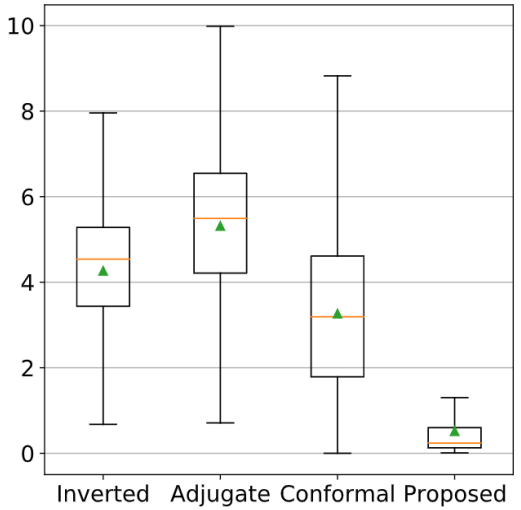


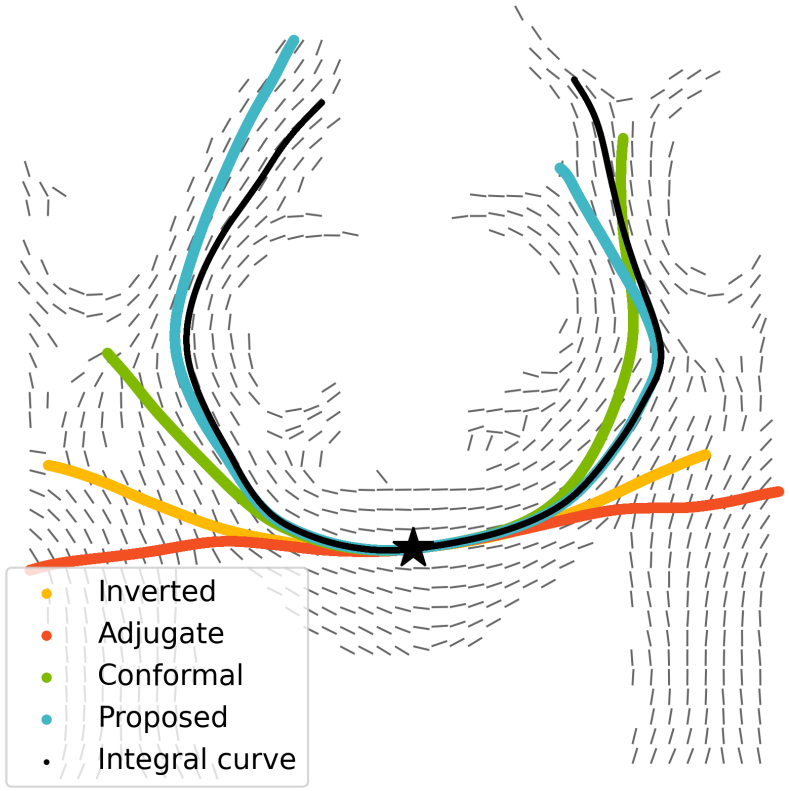
Table 1: Mean and median of mean min errors across different methods over 38 HCP subjects.

Methods	Mean	Median
Inverted	4.2660	4.5393
Adjugate	5.3153	5.4906
Conformal	3.2658	3.1915
Proposed	**0.5172**	**0.2388**

▲ mean of the mean min errors distribution

▬ median of the mean min errors distribution

Experiment 1: 2D Brain Slices



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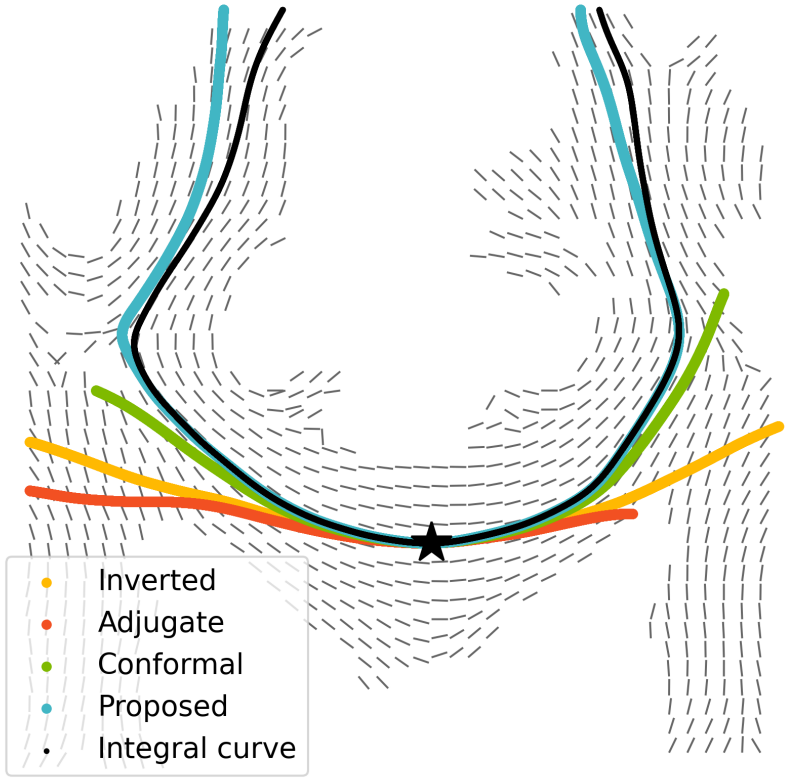

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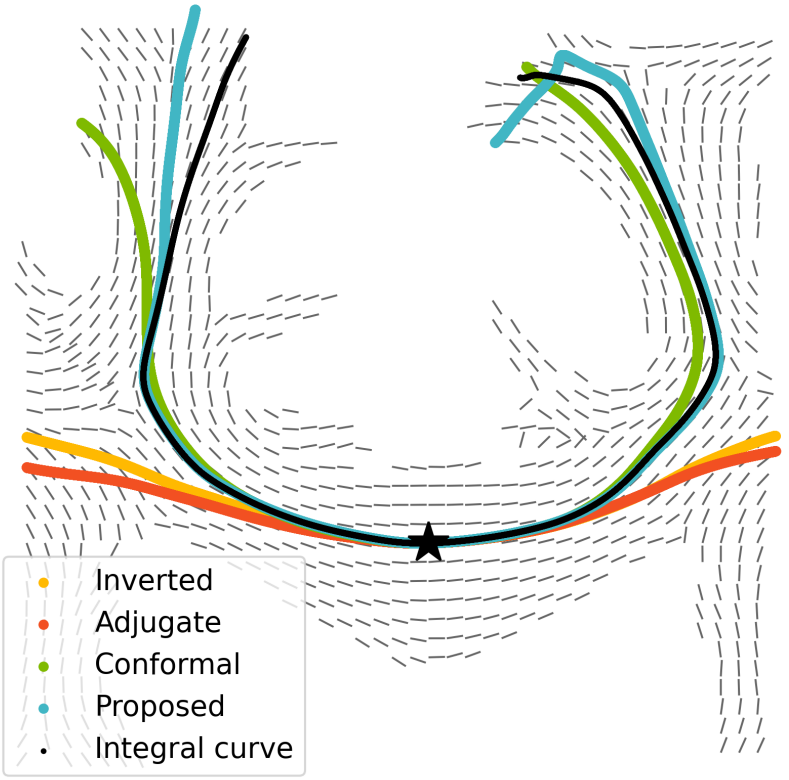

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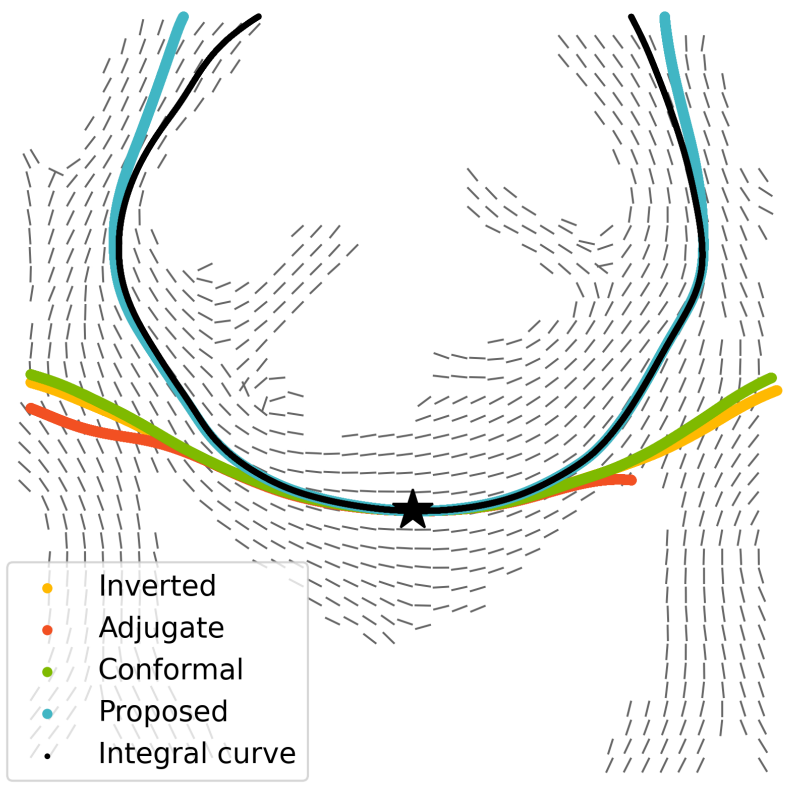
Experiment 1: 2D Brain Slices



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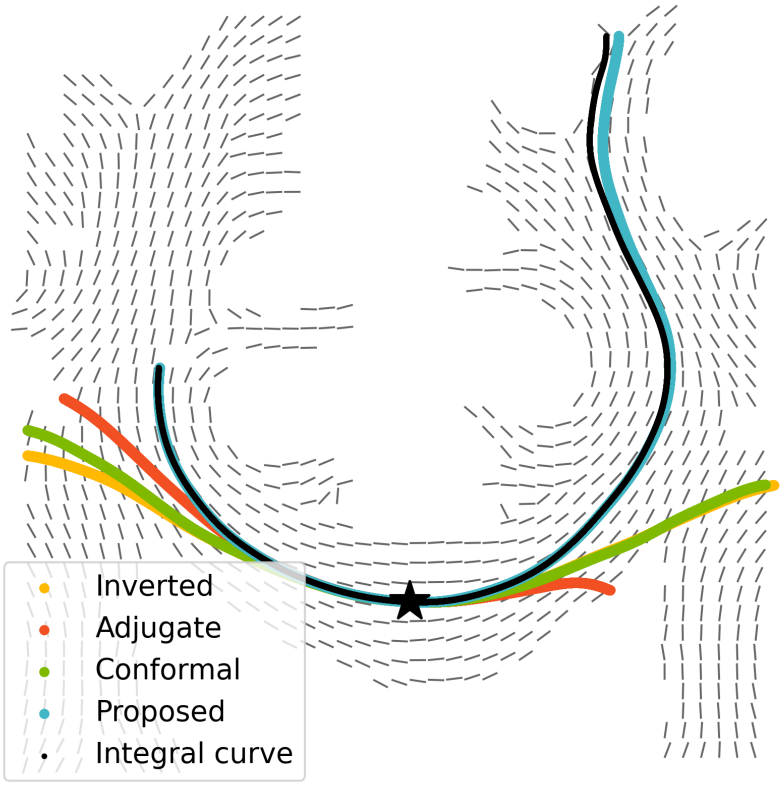

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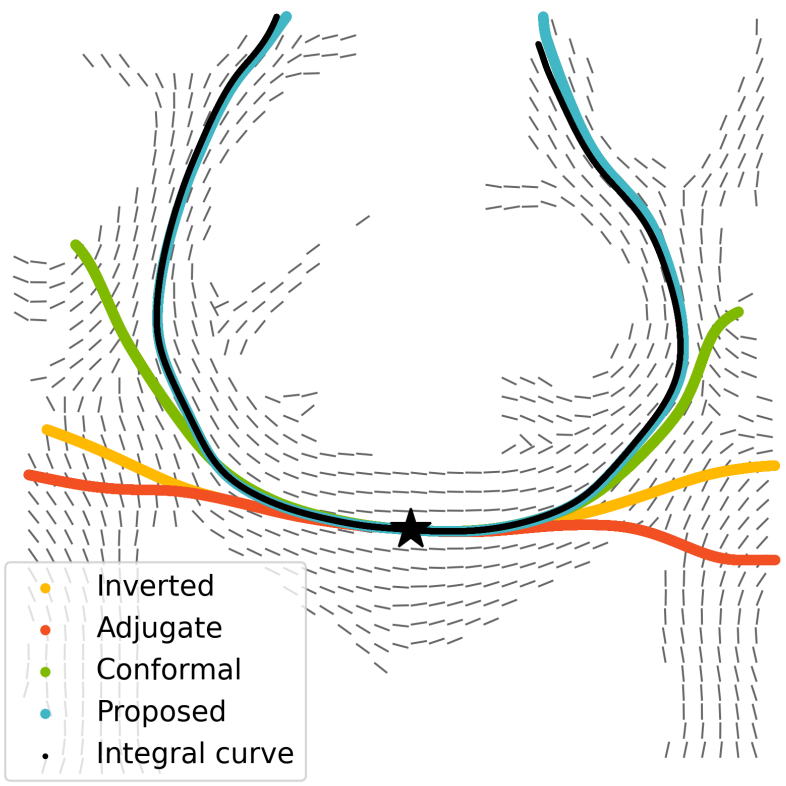

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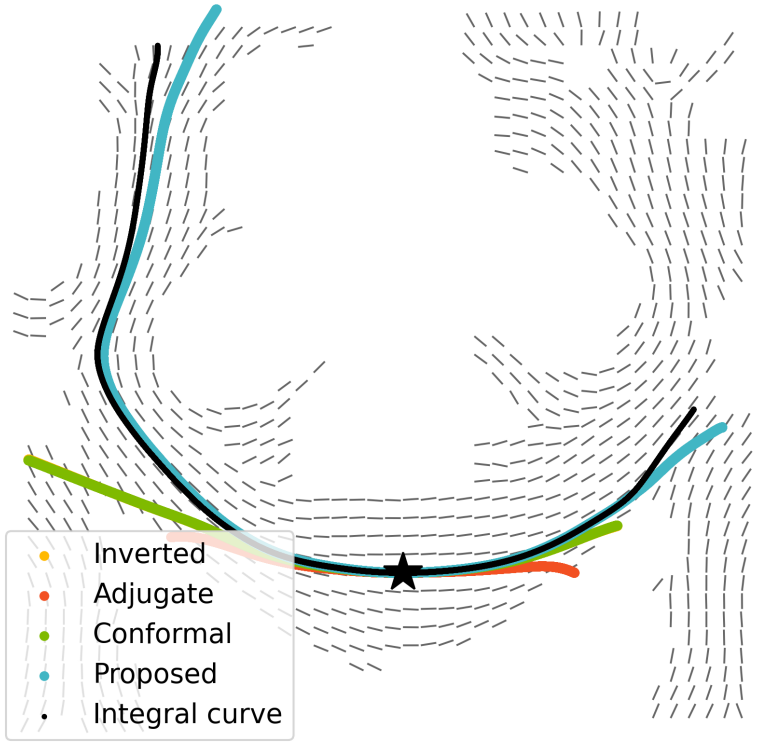
Experiment 1: 2D Brain Slices



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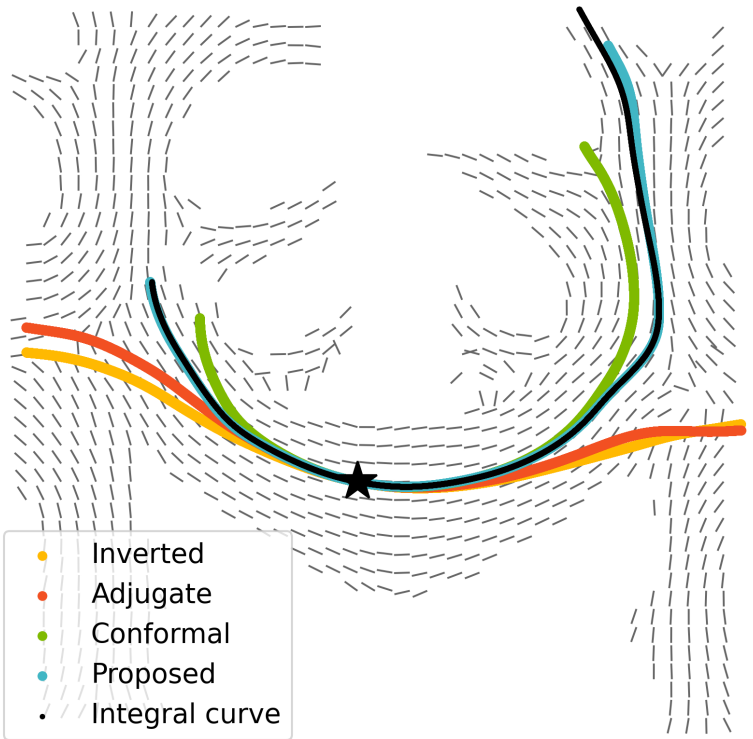

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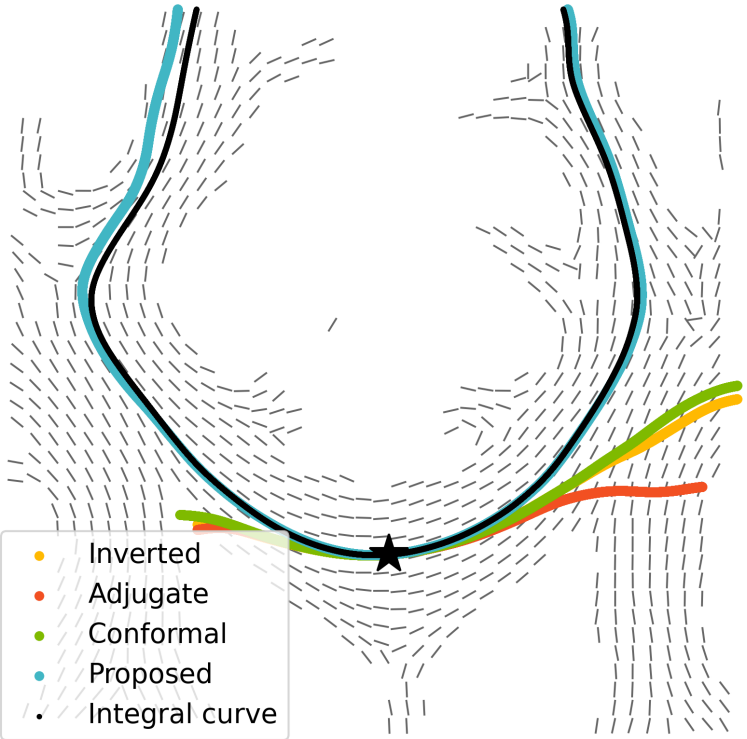

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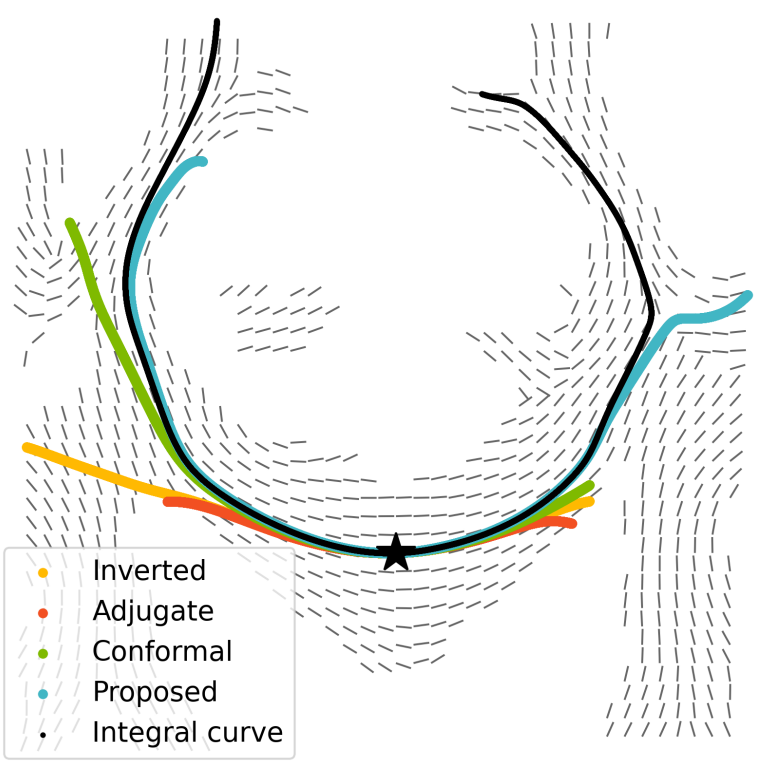
Experiment 1: 2D Brain Slices



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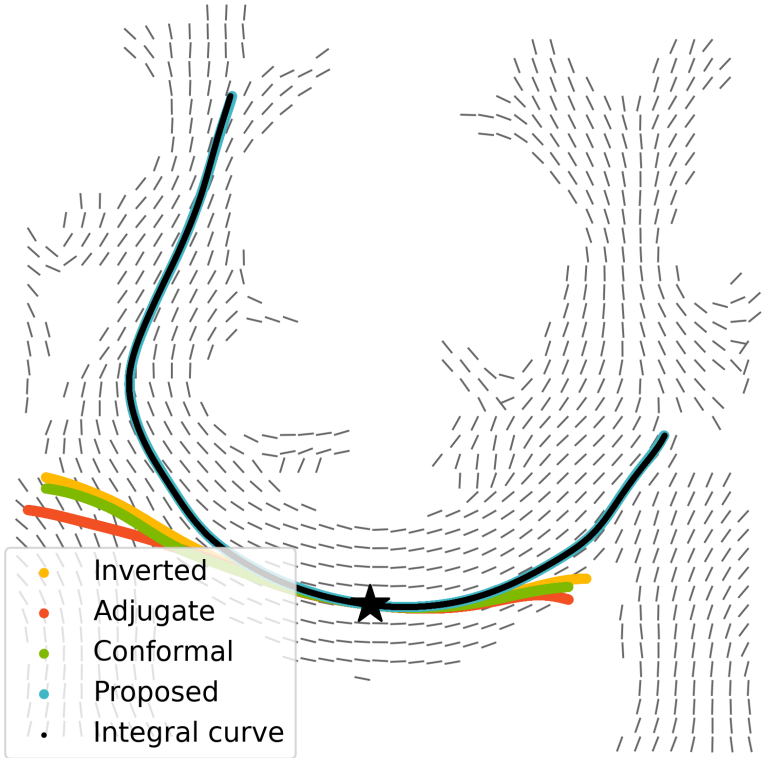
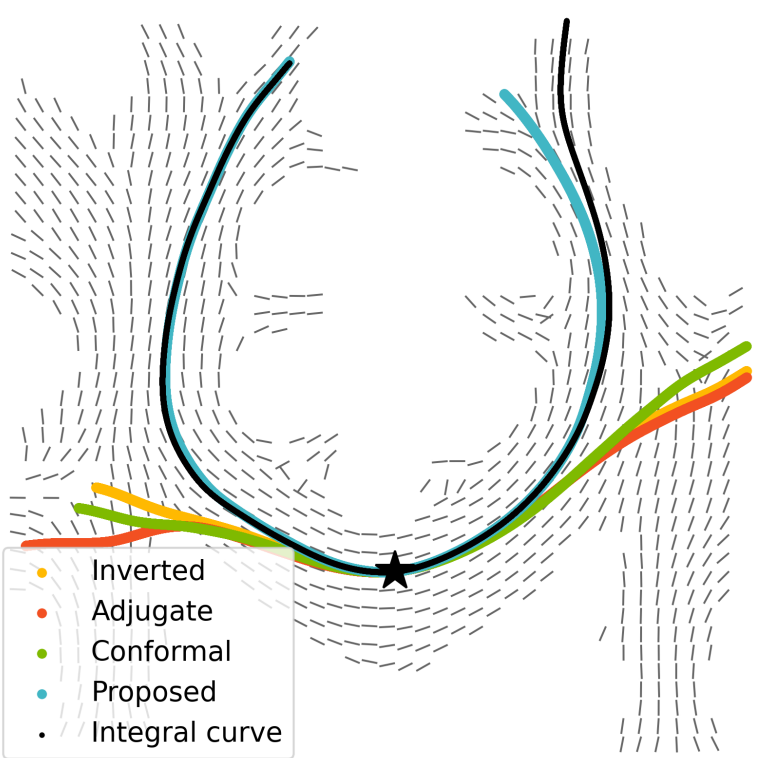
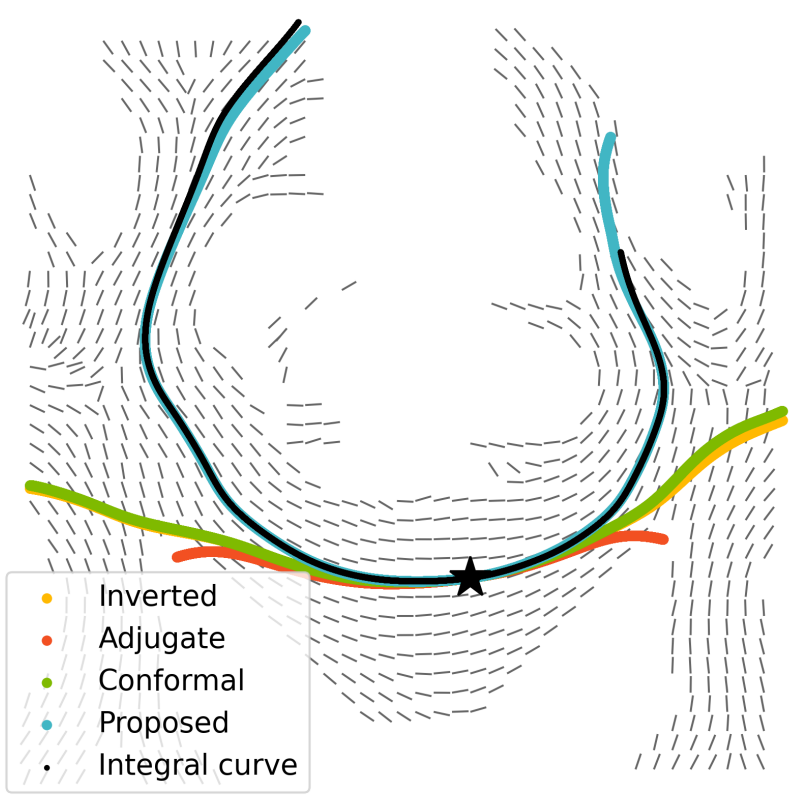


102816

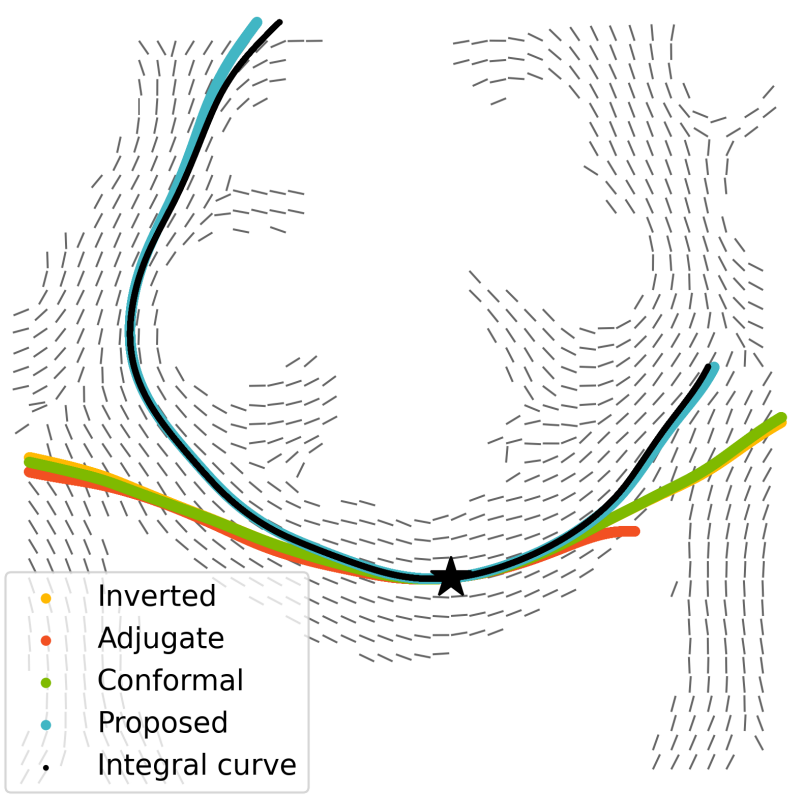


103515

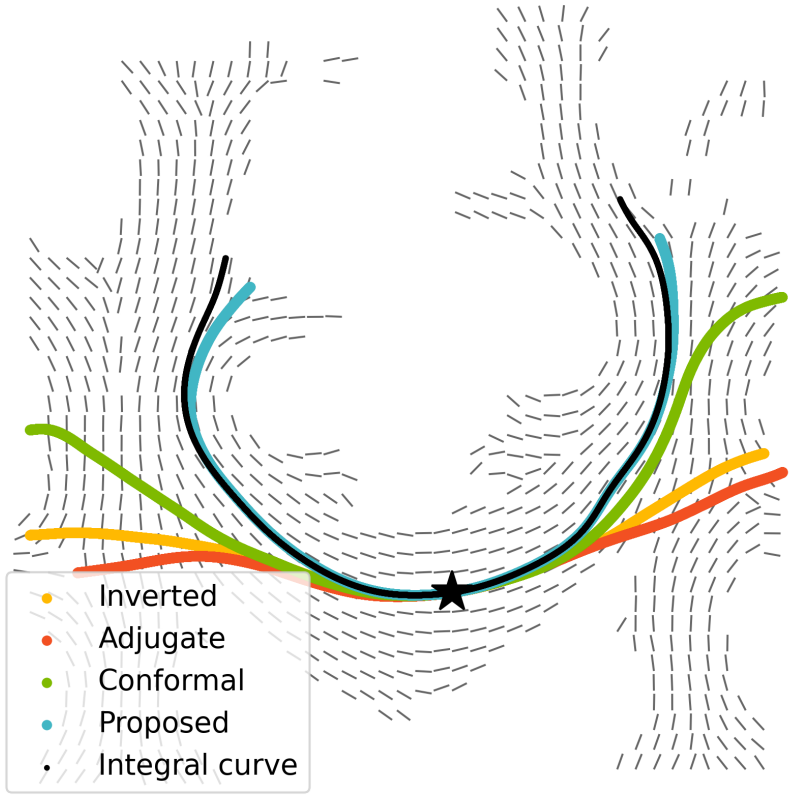
Experiment 1: 2D Brain Slices



104012

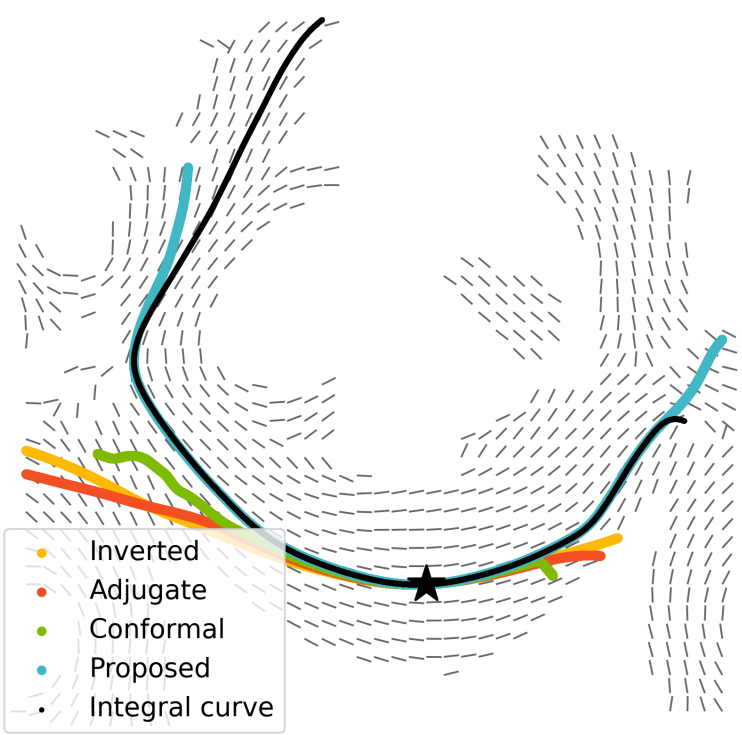


105216

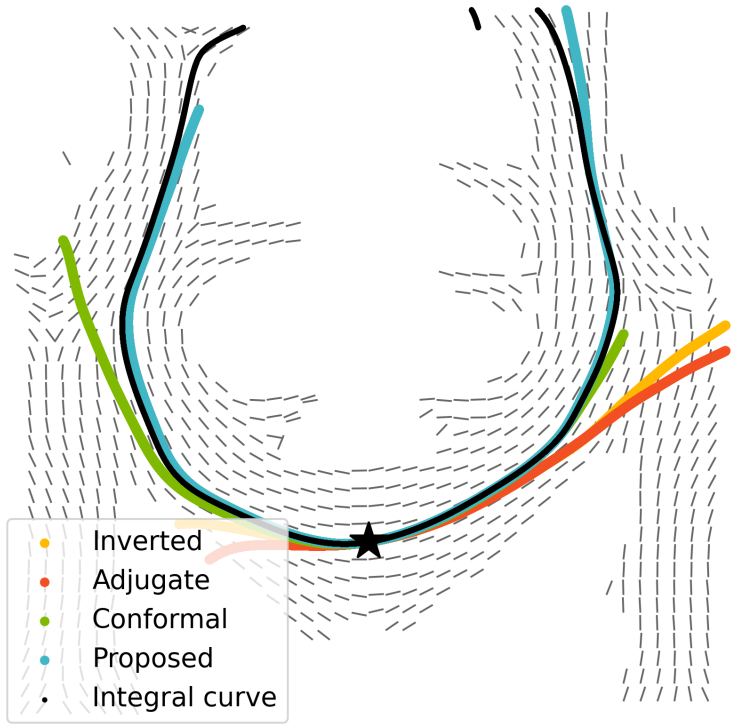


107018

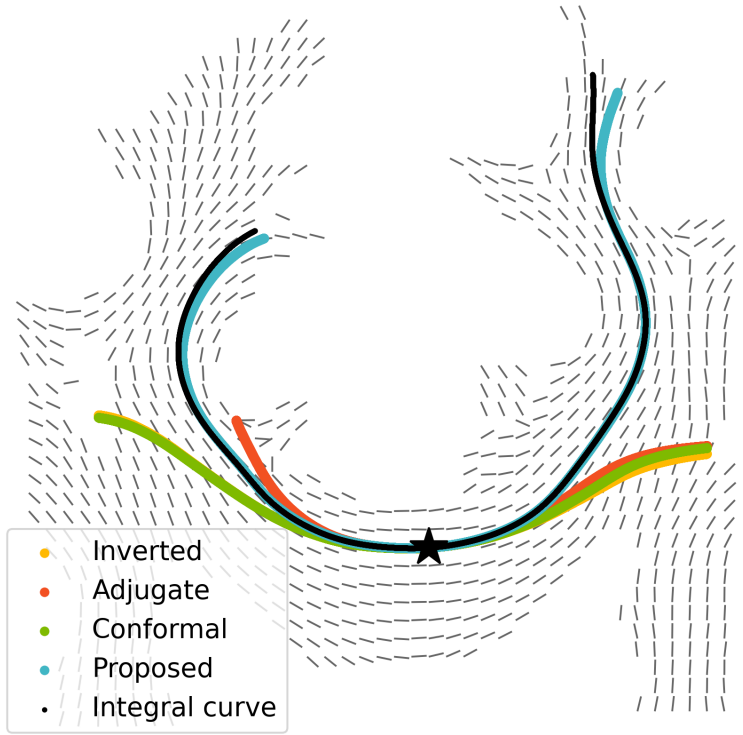
Experiment 1: 2D Brain Slices



108323

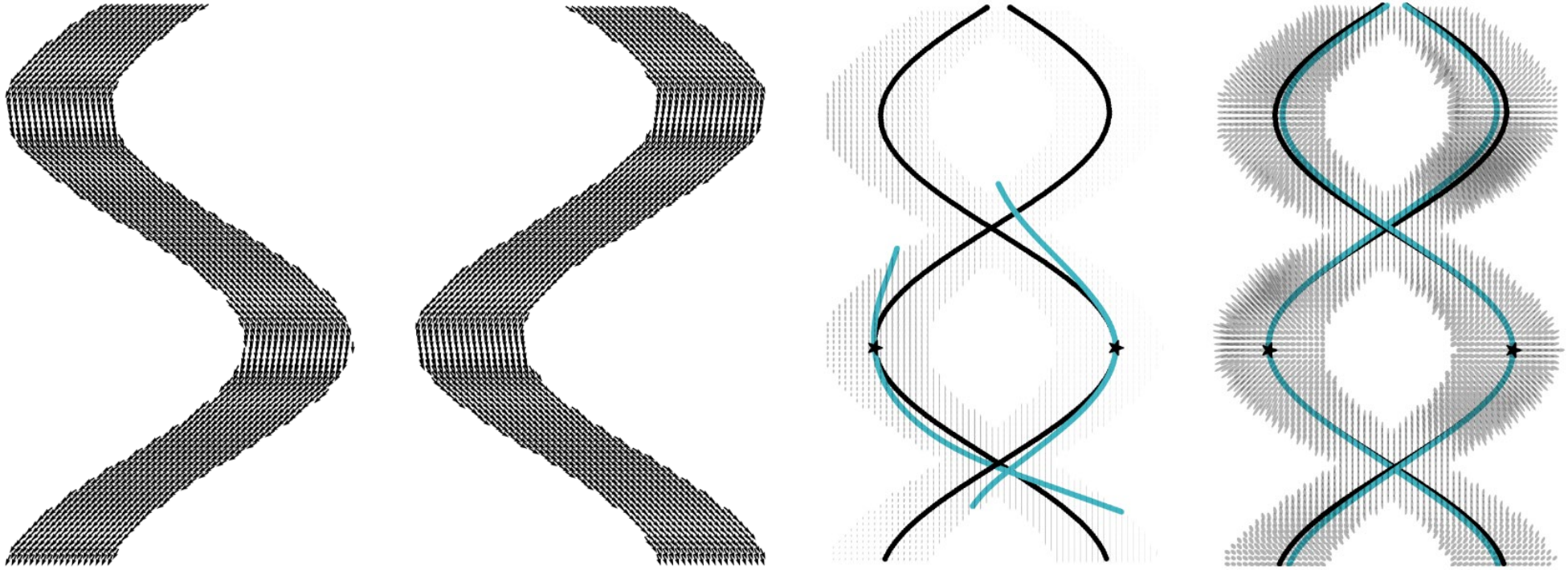


109123



107321

Experiment 2: 2D Synthetic “Braid”



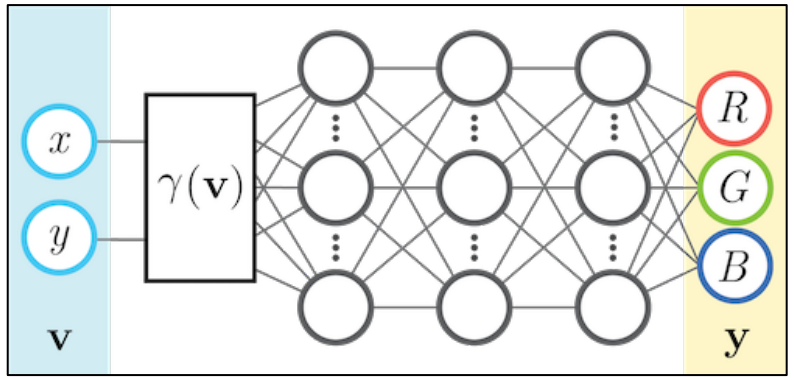
(a) vector field $\mathbf{v}_1$ (b) vector field $\mathbf{v}_2$ (c) metric g^P (d) metric g^C

By MLP
(0.7M params)

By CEDNN
(0.7M params)

Experiment 2: 2D Synthetic “Braid”

Fourier feature

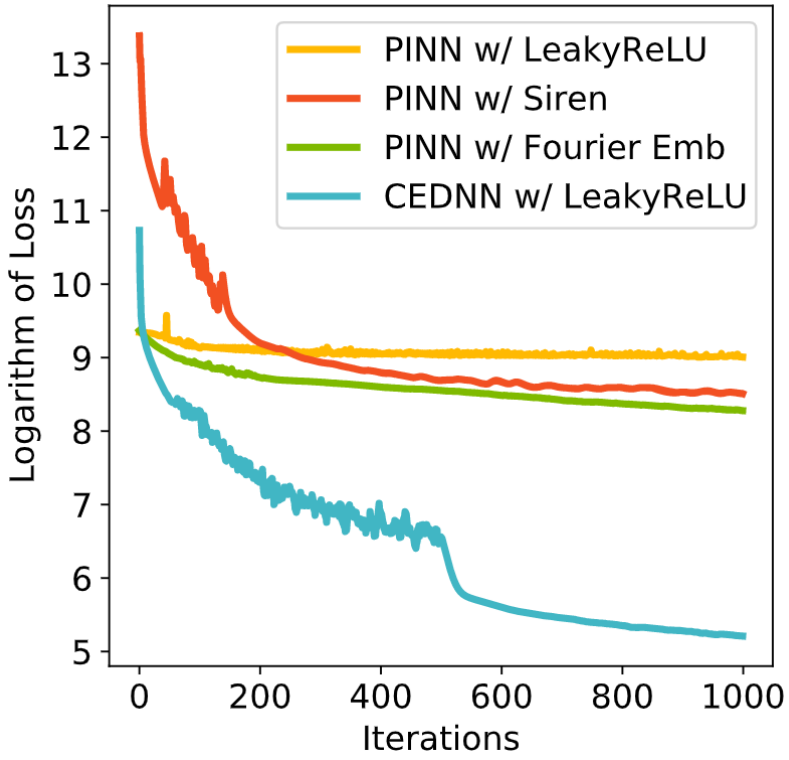


Tancik M et al., 2020

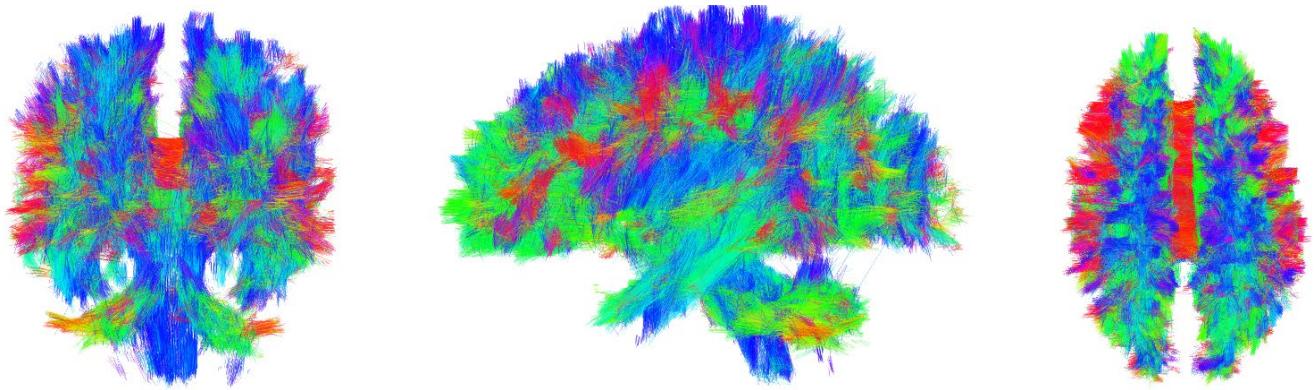
SIREN activation function

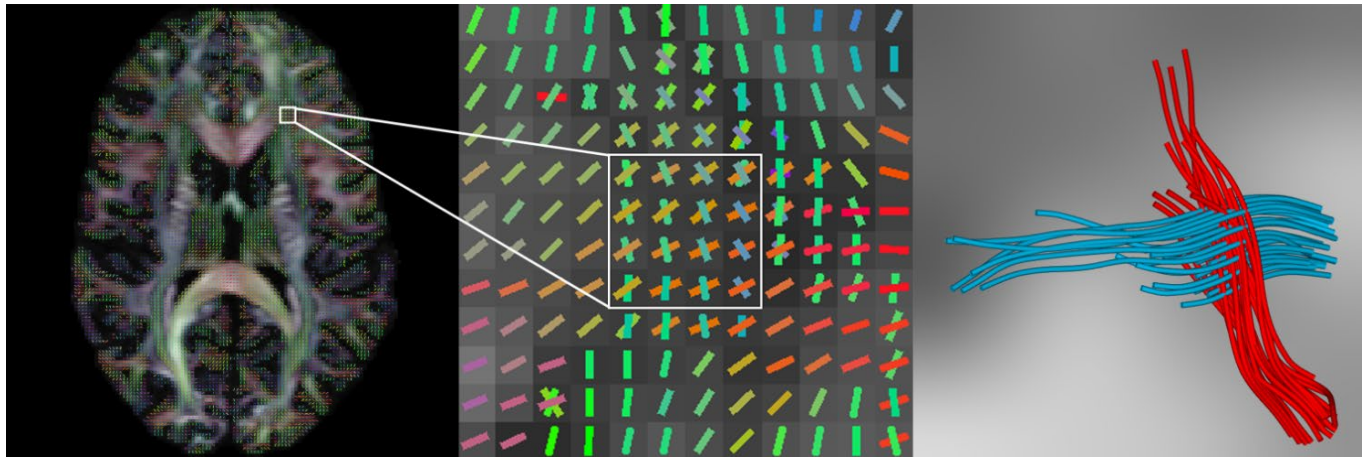
$$\mathbf{x}_i \mapsto \phi_i\left(\mathbf{x}_i\right) = \sin\left(\mathbf{W}_i\mathbf{x}_i + \mathbf{b}_i\right)$$

Sitzmann V et al., 2020



Experiment 3: 3D Brains





Conclusions

1. We proposed to estimating a Riemannian metric of the brain manifold via deep neural network for the first time.

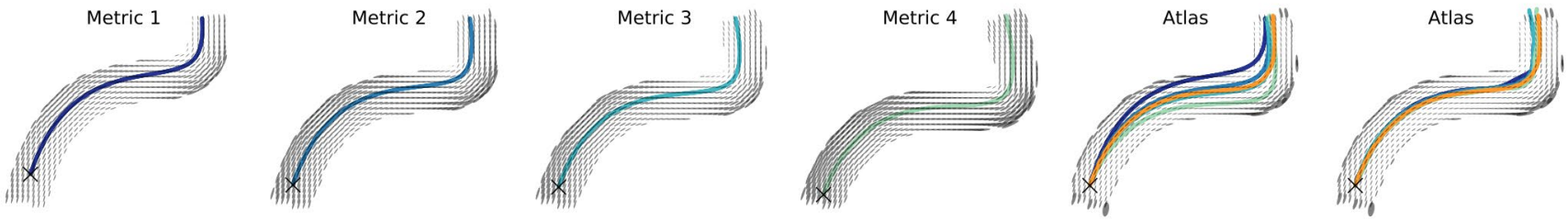
2. We show that our proposed method outperforms any of the previously proposed methods in geodesic tractography by a large margin.

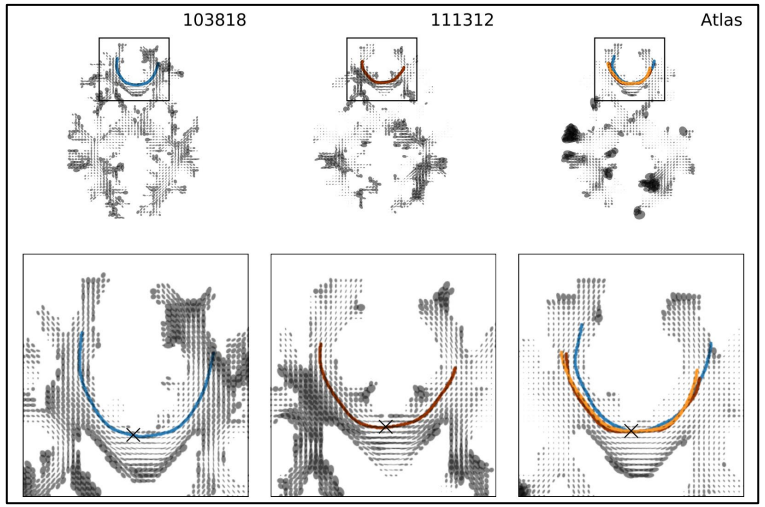
3. In addition, our approach solves the long-standing issue of these previous methods: the inability to recover crossing fibers with high fidelity.

4. One limitation of the proposed method is that the generalization ability of the trained model to the unseen data is relatively weak.

Future Work

With the ability to robustly and efficiently model the white matter of the brain as a Riemannian manifold, one can directly apply geometrical statistical techniques such as statistical atlas construction, principal geodesic analysis to precisely study the variability and differences in white matter architecture.





Campbell KM, Dai H et al., 2021

Scan the QR code for more project details

Derivation of σ

$$
\begin{aligned}
\nabla^g_{\mathbf{v}} \frac{\mathbf{v}}{\|\mathbf{v}\|_g} &= \nabla^g_{\mathbf{v}}\mathbf{v} \cdot \frac{1}{\|\mathbf{v}\|_g} + \mathbf{v} \cdot \nabla^g_{\mathbf{v}} \frac{1}{\|\mathbf{v}\|_g} \\
&= \frac{\nabla^g_{\mathbf{v}}\mathbf{v}}{\|\mathbf{v}\|_g} + \mathbf{v} \cdot \nabla^g_{\mathbf{v}} \langle \mathbf{v}, \mathbf{v} \rangle_g^{-\frac{1}{2}} \\
&= \frac{\nabla^g_{\mathbf{v}}\mathbf{v}}{\|\mathbf{v}\|_g} + \mathbf{v} \cdot \left(-\frac{1}{2}\right) \cdot \langle \mathbf{v}, \mathbf{v} \rangle_g^{-\frac{3}{2}} \cdot \nabla^g_{\mathbf{v}} \langle \mathbf{v}, \mathbf{v} \rangle \\
&= \frac{\nabla^g_{\mathbf{v}}\mathbf{v}}{\|\mathbf{v}\|_g} - \frac{1}{2}\mathbf{v} \cdot \langle \mathbf{v}, \mathbf{v} \rangle_g^{-\frac{3}{2}} \cdot (\langle \nabla^g_{\mathbf{v}}\mathbf{v}, \mathbf{v} \rangle_g + \langle \mathbf{v}, \nabla^g_{\mathbf{v}}\mathbf{v} \rangle_g) \\
&= \frac{\nabla^g_{\mathbf{v}}\mathbf{v}}{\|\mathbf{v}\|_g} - \mathbf{v} \cdot \langle \mathbf{v}, \mathbf{v} \rangle_g^{-\frac{3}{2}} \cdot \langle \nabla^g_{\mathbf{v}}\mathbf{v}, \mathbf{v} \rangle_g \\
&= 0
\end{aligned}
$$

$$
\begin{aligned}
\frac{\nabla^g_{\mathbf{v}}\mathbf{v}}{\|\mathbf{v}\|_g} &= \mathbf{v} \cdot \langle \mathbf{v}, \mathbf{v} \rangle_g^{-\frac{3}{2}} \cdot \langle \nabla^g_{\mathbf{v}}\mathbf{v}, \mathbf{v} \rangle_g \\
\nabla^g_{\mathbf{v}}\mathbf{v} &= \mathbf{v} \cdot \langle \mathbf{v}, \mathbf{v} \rangle_g^{-1} \cdot \langle \nabla^g_{\mathbf{v}}\mathbf{v}, \mathbf{v} \rangle_g \\
\nabla^g_{\mathbf{v}}\mathbf{v} &= \boxed{\frac{\langle \nabla^g_{\mathbf{v}}\mathbf{v}, \mathbf{v} \rangle_g}{\|\mathbf{v}\|_g^2}} \cdot \mathbf{v}
\end{aligned}
$$

σ