Longitudinal Principal Manifold Estimation

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Overview

We developed longitudinal Principal Manifold Estimation to obtain smooth, longitudinally meaningful estimates of manifolds over time. We used this method to reach smooth estimates of manifolds underlying subcortical structures in individuals with Alzheimer's disease.

Background

- Alzheimer's disease (AD) is a progressive neurodegenerative condition that causes atrophy in certain structures in the brain.
- Longitudinal magnetic resonance imaging (MRI) data is used to model trajectories of change in brain regions of interest.
- Image segmentation approaches to extract subcortical structures from neuroimages for analysis are applied to individual scans independently, resulting in variability in the shape and volume estimates of these structures.
- We developed a manifold learning-based approach to obtaining smooth estimates of subcortical surfaces to mitigate the effects of spurious variability on biomarker estimates.

Longitudinal Principal Manifold Estimation

- Longitudinal principal manifold estimation uses smoothing splines to estimate a smooth surface that minimizes the mean squared distance plus within-time point and between-time point roughness penalties :

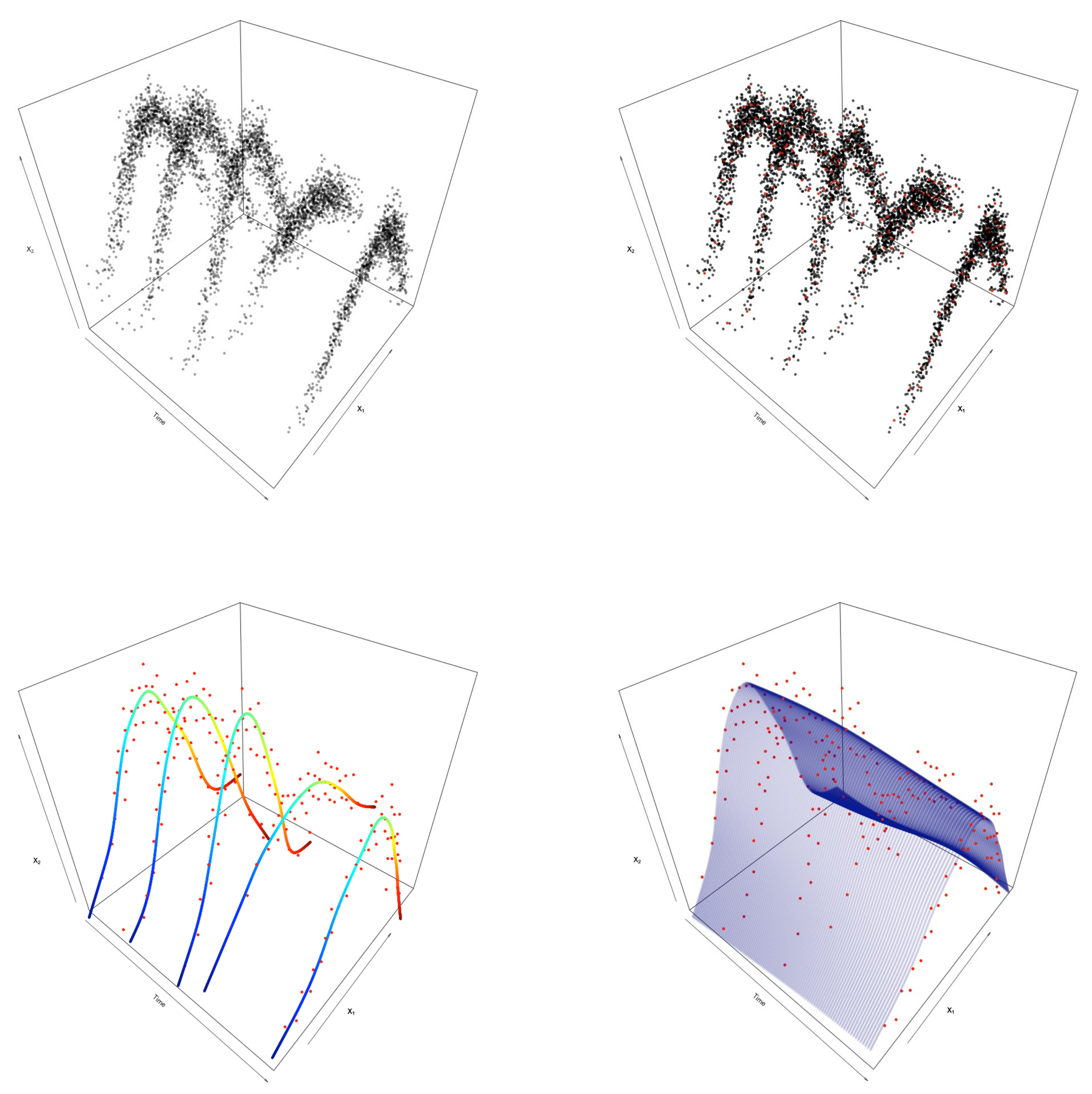
$$\mathcal{K}_{\lambda,\gamma,\mathbb{P}}(F) = \int_{\mathbb{R}} \mathbb{E}\left\|\boldsymbol{X}_t - f_t\left(\pi_{f_t}(\boldsymbol{X}_t)\right)\right\|_{\mathbb{R}^D}^2 \, dt + \int_{\mathbb{R}} \lambda_t \cdot \|\nabla^{\otimes 2} f_t\|_{L^2(\mathbb{R}^d)}^2 \, dt + \gamma \cdot \int_{\mathbb{R}} \left\| \frac{\partial^2}{\partial t^2} f_t \right\|_{L^2(\mathbb{R}^d)}^2 dt$$

The LPME algorithm consists of four steps:

1. Sample Size Reduction: k-means clustering is used to represent the full dataset as a mixture of k components, with $k \ll N$.
2. Initialization: Principal manifold estimation (PME) algorithm is applied to data at the first time point to obtain parameterizations for all mixture components. These initial parameterizations are used to fit PME estimates independently at each individual time point t, yielding function coefficients $\boldsymbol{s}_t, \boldsymbol{\alpha}_t$.
3. Fitting: For given smoothing parameter γ, a smoothing spline is used to smooth over the PME model coefficients, yielding time-varying coefficients $\left(\boldsymbol{s}_\gamma(t), \boldsymbol{\alpha}_\gamma(t)\right)$.
4. Tuning: Leave-one-out cross-validation is used to select the value of γ that minimizes the empirical Mean Squared Distance:

$$MSD(\gamma) = \frac{1}{T}\sum_{t=1}^{T}\frac{1}{I_t}\sum_{i=1}^{I_t}\|x_{i,t} - f_\gamma^{(t)}(t, \pi_{f_\gamma^{(t)}}(x_{i,t}))\|^2$$

LPME Algorithm Steps



Funding and Key References

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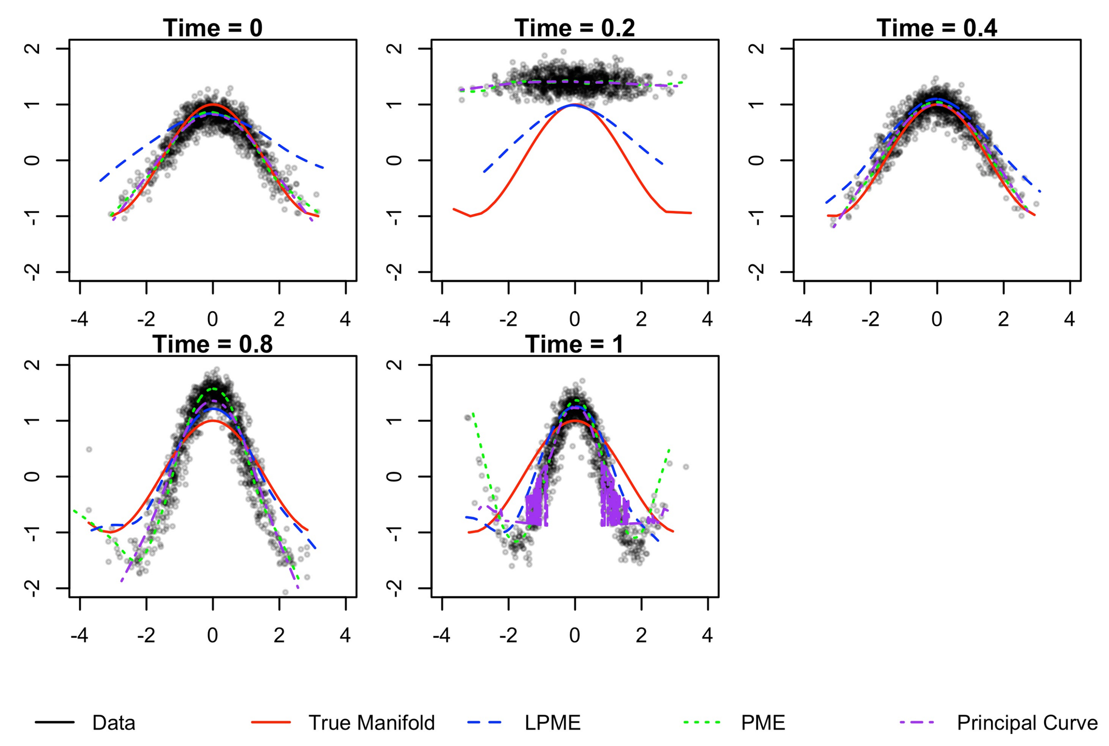
Meng, Kun and Ani Eloyan (2021). "Principal Manifold Estimation via Model Complexity Selection". *Journal of the Royal Statistical Society: Series B (Statistical Methodology).*

Simulations



- We used simulated datasets to compare the LPME algorithm to the PME and Principal Curve/Surface algorithms fit independently at each time point.
- We use PME, LPME, and Principal Curves/Surfaces to recover the true values of the embedded manifold used to generate the data with varying levels of noise introduced between time points.
- We measure performance using the mean squared distance between the estimated function values and the true values:

$$MSD = \frac{1}{N}\sum_{i=1}^{N}\left\|Y_i - f^*\left(\pi_{f^*}(X_i)\right)\right\|.$$

- Simulations used eight manifolds with differing intrinsic and embedded dimensions to generate data.

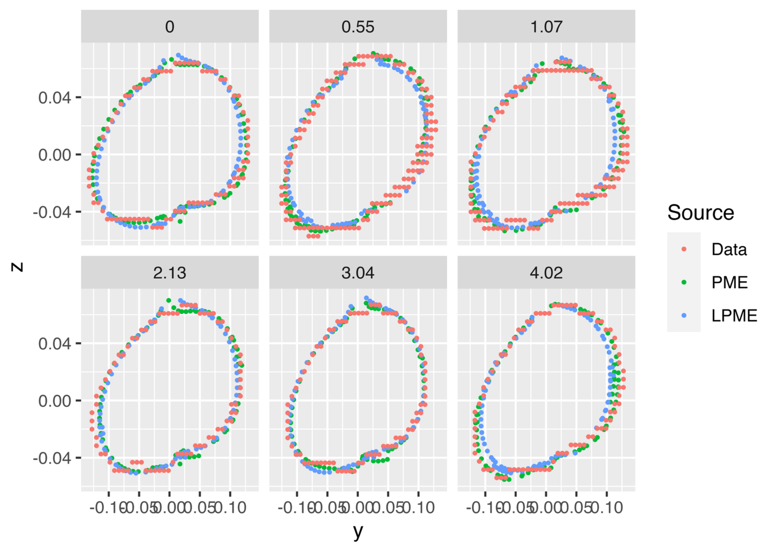
Simulation Results

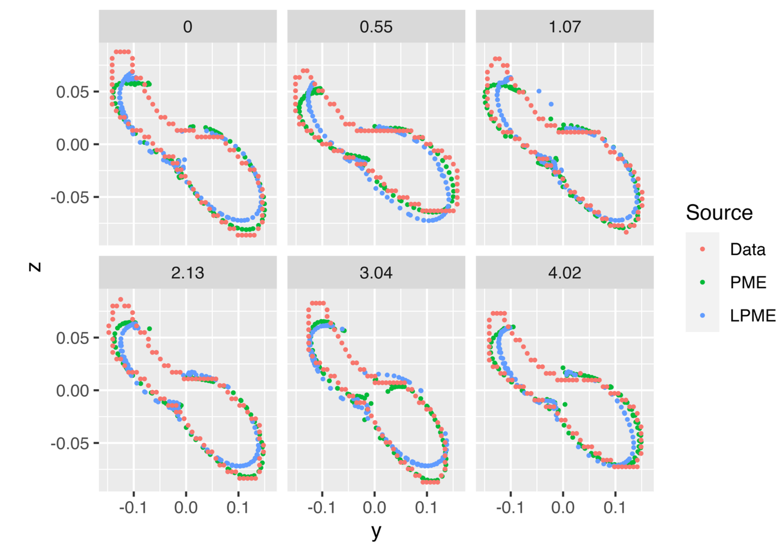
Simulation Case	Data	LPME	PME	PC/PS
1	0.146 (0.233)	**0.074 (0.122)**	0.131 (0.258)	0.118 (0.206)
2	0.467 (0.665)	**0.248 (0.516)**	0.516 (0.750)	0.564 (0.419)
3	0.291 (0.601)	**0.239 (0.564)**	0.317 (0.640)	0.264 (0.584)
4	4.26 (21.2)	**3.29 (13.0)**	4.23 (21.1)	4.22 (21.2)
5	0.895 (1.33)	**0.584 (1.08)**	0.894 (1.36)	0.821 (1.22)
6	0.284 (1.06)	**0.273 (0.891)**	0.316 (1.04)	0.557 (0.387)
7	0.145 (0.552)	2.96 (4.65)	6.92 (1.17)	**1.58 (0.514)**
8	0.110 (0.325)	**0.074 (0.208)**	0.115 (0.331)	0.172 (0.234)

MSD comparison to true values, Median (IQR). The lowest algorithm-specific median (IQR) are highlighted in bold. LPME shows the smallest deviations from the true values in most simulation cases.

ADNI Results

- The PME and LPME algorithms were fit to the surfaces of the thalami and hippocampi of participants in the Alzheimer's Disease Neuroimaging Initiative (ADNI).
- Cartesian coordinates were augmented with spherical coordinates to enable fitting to self-intersecting structures.
- PME and LPME capture the shape of the thalamus (left) well, with LPME yielding smaller variations between estimates across time points.
- Both PME and LPME are unable to adequately capture the irregular shape of the hippocampus (right).





Conclusion

- LPME demonstrates performance improvements over naïve application of alternative approaches in simulated datasets using several underlying manifolds.
- In applications, LPME is capable of fitting closely to regularly shaped subcortical structures but struggles to accurately estimate irregularly shaped manifolds.
- Work to approximate volumes of subcortical structures from LPME and PME estimates is ongoing.
- Further development of the data augmentation approach used to enable fitting to self-intersecting structures may yield improved results for irregular manifolds.