Executive summary: Trajectory inference via Mean-field Langevin in path space

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1 Paper Details

Title:
Lénaïc Chizat, Stephen Zhang, Matthieu Heitz, and Geoffrey Schiebinger. "Trajectory Inference via Mean-field Langevin in Path Space" *NeurIPS*, 2022. [arxiv link]

2 Repository

Code is provided at `https://github.com/zsteve/mfl` for reproducing the main experiments and implementing the Mean-Field Langevin (MFL) method on trajectory inference tasks.

3 High-level Problem

We have snapshots of a population evolving over time (for example, cells at different stages of development). We want to reconstruct a continuous trajectory or stochastic process explaining how points (cells) move from earlier snapshots to later snapshots.

- The snapshots come from unknown time marginals of some underlying diffusion, but each individual trajectory is not directly observed.
- The paper adopts a nonparametric framework, treating the *law on paths* as the unknown to be estimated.
- By placing a relative-entropy regularization (with respect to Brownian motion), the method yields an estimator that smoothly interpolates between the observed timepoints.

4 Intuition behind the Technique

- **Min-Entropy Estimator.** The authors build on earlier work which proposed a "min-entropy" criterion: out of all candidate distributions on paths that fit the data, pick the one with minimal Kullback–Leibler divergence from Brownian motion in path space.

- **Reduction to Schrödinger Bridges.** Although the unknown is an entire continuous-time law P over paths, one can reduce the problem to working with discrete marginals $\{\mu_t\}_{t=1}^{T}$ and entropic optimal transport (a.k.a. Schrödinger bridges) between consecutive timepoints.

- **Mean-Field Langevin (MFL).** Instead of discretizing space on a fixed grid, the paper proposes a "particle" approach. Multiple point clouds evolve via gradient descent on an entropy-regularized objective, with the gradient involving repeated Schrödinger-bridge computations (via Sinkhorn).

5 Method Outline

1. **Formulate an Objective in Path Space:**

$$\min_{P \in \mathcal{P}(\Omega)} \sum_{i=1}^{T} \lambda \, \mathrm{Fit}_\sigma(P_{t_i}, \, \hat{\mu}_{t_i}) \; + \; \tau \, \mathrm{KL}\big(P \,\|\, W_\tau\big),$$

   where W_τ is Brownian motion on $[0, 1]$ in the domain X (possibly with reflecting boundary), and Fit_σ is a smooth cost enforcing P_{t_i} to match the observed snapshot $\hat{\mu}_{t_i}$.

2. **Reduced Form / Markovian Representation:** Show that the entropy term decomposes through time and can be expressed as *coupled entropic optimal transports* plus a differential entropy over marginals.

3. **Mean-Field Gradient Flow:** Propose a McKean–Vlasov SDE whose equilibrium is the minimizer of the above objective. Particles at each time index i diffuse with a drift that depends on the gradient of the objective, while the entire set of time-indexed measures is coupled via Schrödinger bridges.

6 Results and Examples

- **Synthetic Bifurcation in 10D:** The authors simulate a stochastic process with branching potential in a 10-dimensional space. They show that the MFL approach recovers smooth trajectories from limited snapshots, outperforming a static grid-based method called gWOT, especially with very few samples at intermediate times.

- **Single-Cell Reprogramming:** On a real dataset of reprogramming cells, MFL demonstrates improved reconstruction of intermediate cell states relative to naive interpolation of snapshots. They measure performance via an Energy Distance to a large "ground-truth" pool of cells.

- **Branching Extension:** The method can incorporate a prior growth rate $g(t, x)$ in unbalanced Schrödinger bridges so that the mass of the population can increase or decrease over time. This is beneficial for branching processes in biology.

7 Some Additional Background

7.1 Mean-Field Langevin (MFL)

The classical *Langevin dynamics* is a gradient descent in distribution space. The authors show how to adapt it to a non-linear PDE system that couples multiple time-slices. Convergence guarantees to the global minimizer follow from recent theoretical work on entropic gradient flows.

7.2 Complexity and Implementation

- **Iteration:** Each MFL iteration updates particle locations using noisy gradient descent.

- **Inner Sinkhorn Solve:** The gradient wrt. the entropic OT terms requires computing Schrödinger bridges. Each step thus calls Sinkhorn repeatedly (one for each pair of consecutive times).

- **Convergence Guarantees:** Under compactness assumptions and mild technical conditions, MFL converges at a rate exponential in iteration if an additional small entropy ε is added (simulated annealing can remove that ε).

8 Application Outlook

- **Cell Trajectory Inference:** Potentially quite powerful for single-cell data, especially in cases where snapshot coverage at intermediate times is sparse.

- **General Diffusion Models:** The approach is relevant to any scenario of partial dynamic data, bridging multiple timepoints or states, with a preference for smoothly entropic couplings.