A093 · FlowMap: GeometryConsistent Embedding of RNA Velocity for Interpretable Cellular Trajectories

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RNA velocity estimates short-term gene-expression changes in individual cells, providing directional information about cellular state transitions. Geometrically, it defines a high-dimensional vector field on an intrinsically low-dimensional cell-state manifold. Yet existing approaches typically construct embeddings from gene expression alone and project velocity afterward, which can distort or destabilize inferred trajectories. We present FlowMap, a manifold-learning framework that jointly embeds cell states and RNA velocity while preserving their geometric relationship. FlowMap reconstructs a smooth cell-state manifold and constrains velocity to its local tangent geometry, yielding coherent and interpretable representations of cellular dynamics. Across simulated and real datasets, FlowMap recovers continuous developmental progressions, branching processes, cyclic behaviors, and stable states. The unified representation enables analysis of gene-expression programs along developmental flows and identifies regions where trajectories redirect during fate specification. FlowMap further decomposes trajectory curvature to distinguish bending imposed by the underlying manifold from active redirection of cellular dynamics. This analysis highlights transitional progenitor states, early lineage biases, and transcriptional programs associated with emerging fate decisions. The reconstructed geometry also reveals convergent and divergent regions associated with developmental commitment and pausing. Finally, FlowMap extends to spatial transcriptomics, allowing transcriptional dynamics to be interpreted in tissue context. Together, FlowMap provides a principled framework for visualizing and interpreting cellular dynamics from single-cell and spatial genomic data.

FlowMap: Geometry–Dynamics Consistent Embedding of RNA Velocity for Interpretable Cellular Trajectories

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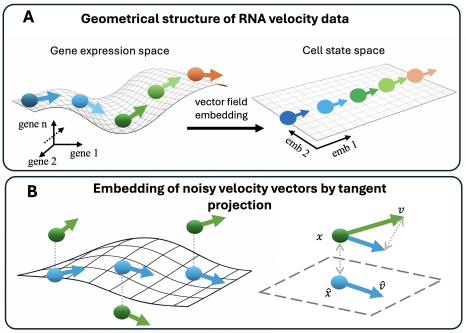
Background. RNA velocity estimates short-term changes in gene expression, providing a directional signal for cellular state transitions. Geometrically, these measurements define a high-dimensional vector field over an intrinsically low-dimensional cell-state manifold. Most workflows, however, construct an expression embedding first and add velocity afterward through neighborhood smoothing or transition probabilities. Because the embedding lacks an explicit differentiable connection to gene-expression space, projected velocities may point in directions that are inconsistent with the local manifold, producing embedding-dependent artifacts and obscuring developmental structure.

Method. We introduce **FlowMap**, a manifold-learning framework that jointly represents cellular states and RNA velocity. FlowMap first constructs a velocity-aware phase distance that combines expression proximity with relative progression along the local flow. It then reconstructs the embedding using a smooth spline map $\psi : \mathbb{R}^d \to \mathbb{R}^p$ from latent coordinates to gene-expression space. The Jacobian $J_\psi(y)$ defines the tangent space of the reconstructed manifold at each cell, and an observed gene-space velocity v is mapped to the intrinsic velocity $u = J_\psi(y)^+ v$. This removes off-manifold components while retaining changes supported by cellular state variation.



FlowMap geometry. RNA velocity defines a vector field on a cell-state manifold (A); FlowMap projects noisy gene-space velocities onto locally supported tangent directions (B).

Results. Across simulated linear, branching, and cyclic systems, FlowMap preserved trajectory geometry and improved directional agreement, smoothness, and neighborhood fidelity relative to conventional embedding and velocity-visualization pipelines. In FUCCI-labeled cell-cycle data, FlowMap recovered the expected cycle, with embedding-derived angular position agreeing with experimental phase (circular correlation = 0.60). Reconstruction selectively retained trajectory-consistent programs: 33 curated cell-cycle genes achieved global $R^2 = 0.37$ for expression and $R^2 = 0.24$ for velocity, substantially exceeding results across all highly variable genes. In pancreatic endocrinogenesis, FlowMap identified locally dominant dynamical programs that differed from genes selected by differential expression or kinetic significance alone.

The differentiable representation further supports second-order analysis of developmental flow. We decomposed acceleration into flow, surface, and steering components, separating bending imposed by manifold geometry from active redirection within the manifold. In clonal hematopoiesis, localized steering curvature identified transitional progenitors with early lineage biases supported by fate probabilities and lineage-associated gene programs. In B-cell differentiation, negative Ricci curvature marked divergent, low-velocity transition regions. In spatial mouse organogenesis, FlowMap related gene-expression gradients to local transcriptional flow while retaining tissue coordinates, distinguishing developmental programs from positional signals. Together, FlowMap provides a principled, interpretable framework for cellular dynamics across single-cell and spatial transcriptomic data.