Title: Topology guided geometric diffusion on evolving graph sequences

Abstract:

We introduce FoamFormer, a topology-aware geometric learning framework for single-cell transcriptomics that adapts concepts from epithelial tissue mechanics and foam dynamics to model cellular state transitions in scRNA-seq data. Cells are represented as nodes in transcriptomic k-nearest-neighbor graphs constructed in latent spaces such as PCA or learned embeddings, where local connectivity patterns encode the geometry of the transcriptional manifold. To quantify topological reorganization across developmental or pseudotemporal stages, we define a Topological Earth Mover (TEM) distance based on optimal transport between distributions of local graph motifs, enabling principled measurement of transcriptional rewiring. We further introduce a composite TEM score to identify transitional cellular states by integrating motif deviation, local manifold incoherence, clustering instability, neighborhood entropy, bridge centrality, and graph curvature. In particular, degree-corrected Forman–Ricci curvature highlights bottlenecks, branching regions, and lineage bifurcations associated with developmental commitment and rare intermediate populations. Since scRNA-seq lacks explicit spatial tracking, classical morphogenetic events such as neighbor exchanges are reformulated as motif rewiring processes between pseudotime windows, allowing dynamic topological transitions to be quantified without spatial measurements. Beyond descriptive analysis, FoamFormer provides a framework for evaluating graph neural network embeddings through topology-preserving criteria and offers an interpretable bridge between geometric deep learning, optimal transport, and transcriptomic manifold analysis for studying cellular organization, differentiation, and fate dynamics.

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