Learning Biochemically Accurate Models of Gene Regulatory Dynamics from Single-Cell Multi-Omic Data

Modeling the temporal gene expression changes that drive cell fate transitions in differentiation and reprogramming is a fundamental goal of molecular biology. The state-of-the-art experimental technologies for measuring single-cell gene expression and epigenomic state can only measure each cell at one time point, requiring sophisticated computational approaches to reconstruct gene regulatory dynamics. Toward this goal, we developed VeloVAE, a deep neural network that uses single-cell sequencing data to learn the parameters of a chemical master equation coupled over thousands of genes. We also extended VeloVAE to incorporate paired single-cell epigenome and expression data and model spatial coupling among neighboring cells within a tissue. Our work lays a foundation for biochemically accurate predictive models of cell fate transitions in healthy and diseased cells.

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