A Unified Approach for Integrating Spatial and Single-cell Transcriptomics Data Using Deep Generative Models

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The rapid emergence of spatial transcriptomics (ST) technologies is revolutionizing our understanding of tissue spatial architecture and their biology. Current ST technologies based on either next generation sequencing (seq-based approaches) or fluorescence in situ hybridization (image-based approaches), while providing hugely informative insights, remain unable to provide spatial characterization at transcriptome-wide single-cell resolution, limiting their usage in resolving detailed tissue structure and detecting cellular communications. To overcome these limitations, we developed SpatialScope, a unified approach to integrating scRNA-seq reference data and ST data that leverages deep generative models. With innovation in model and algorithm designs, SpatialScope not only enhances seq-based ST data to achieve single-cell resolution, but also accurately infers transcriptome-wide expression levels for image-based ST data. We demonstrate the utility of SpatialScope through comprehensive simulation studies and then apply it to real data from both seq-based and image-based ST approaches. SpatialScope provides a spatial characterization of tissue structures at transcriptome-wide single-cell resolution, greatly facilitating the downstream analysis of ST data, such as detection of cellular communication by identifying ligand-receptor interactions from seq-based ST data, localization of cellular subtypes, and detection of spatially differently expressed genes. This is joint work with Xiaomeng Wan, Jiashun Xiao, Sindy Tam, Mingxuan Cai, Ryohichi Sugimura, Yang Wang, Xiang Wan, Zhixiang Lin, and Angela Wu.