University of California, Irvine
Statistics Seminar

Characterizing the Brain Regulatory Grammar at a Single-cell Resolution to Highlight Disease-driving Genetic and Epigenetic Dysregulations

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The recent advances in single-cell sequencing technologies provide unprecedented opportunities to decipher the multi-scale gene regulatory grammars at diverse cellular states. Here, we will introduce our computational efforts to decipher cell-type-specific gene regulatory grammar using large-scale single-cell multi-omics data. First, we developed a deep generative model, named SAILER, to learn the low-dimensional latent cell representations from single-cell epigenetic data for accurate cell state characterization. SAILER adopted the conventional encoder-decoder framework and imposed additional constraints for biologically robust cell embeddings invariant to confounding factors. Then, we will introduce DIRECT-NET, an efficient method to discover cis-regulatory elements and construct regulatory networks using single-cell multi-omics data. Unlike existing methods requiring extensive functional genomic data, DIRECT-NET can build cell-type-specific gene regulatory networks from individual genomes without any auxiliary data. Finally, we applied our methods on 1.3 million single nuclei from post-mortem brain samples and discovered key genetic and epigenetic changes in brain disorders.