Merging Dynamic State Models with Single-Cell Pseudotime Trajectories and Cell Fates in HIV-Associated Atherosclerosis

Boolean network models are used to interpret cell signaling dynamics. scBONITA (single-cell Boolean Omics Network Invariant-Time Analysis) is a programmatic tool that uses single-cell RNA-seq data to generate executable Boolean models of intracellular signaling pathways. Previous research applied scBONITA to peripheral blood mononuclear cells from individuals with HIV (PLWH) to analyze immune signaling dysregulation in HIV-associated atherosclerosis (Palshikar et al., 2022). The analysis identified pathway-specific attractors/steady states and cell-type–specific alterations, most notably in $CD8^+$ T cells and monocytes. Boolean network models describe system evolution in terms of state transition graphs under synchronous updating rules, each of which generates distinct dynamic behaviors. By examining gene expression along pseudotime trajectories that terminate in regions corresponding to attractor states, we can better understand how signaling states evolve over time. The state dynamics framework of scBONITA2, a next-generation version currently in development infers the pseudotime in a pathway and cell-type specific manner.This approach lays the foundation for personalized simulations of immune responses in disease contexts. In this project, we integrate trajectory inference algorithms with scBONITA2's pseudotime framework. We present our results using PAGA-DPT and CellRank to map pseudotime development and fate probabilities onto Boolean attractor landscapes computed by scBONITA2. This integration allows us to visualize and cluster the temporal development of gene expression alongside signaling network dynamics. Together, these tools establish a new framework to study immune cell heterogeneity and reveal regulatory mechanisms relevant to patient-specific HIV-associated atherosclerosis.

Citation:

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