Nonparametric Bayesian analysis of dynamic protein-networks in heterogeneous cell populations

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The reconstruction of cellular biochemical networks is fundamentally limited by the number of intracellular species, particularly proteins, that can be co-measured in the same cell. Consequently, cell-to-cell variability in unmeasured proteins can lead to completely different observed relations between the same measured proteins. Attempts to infer such relations in a heterogeneous cell population can yield uninformative average relations if only one underlying biochemical network is assumed. To address this, we developed a method that recursively couples an iterative unmixing process with a Bayesian analysis of each unmixed subpopulation.

Our approach enables to identify the number of distinct cell subpopulations, unmix their corresponding observations and resolve the dynamic network structure of each subpopulation. Using synthetic time-series protein expression data we assess the performance of the method. We demonstrate that the presented method can identify better than clustering approaches the number of subpopulations within a mixture of observations, thus resolving correctly the statistical relations between the proteins.