Discriminative Modeling of Cell Signaling as Bayesian Networks

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Abstract. Recent developments in high-throughput technologies have been very helpful towards understanding the molecular abnormalities observed in disease conditions such as cancer. High-throughput experiments, which provide transcriptome-wide expression information for a cell give better insight into understanding the differences of biological processes between normal and pathological conditions. Instead of examining each gene individually, considering the interactions between genes in a pathway would be more effective for understanding cellular events as a whole. Group of genes that chemically act together in a particular cellular process to perform certain functions in a cell is defined as a cellular signaling pathway. In this study, our aim is to represent the signaling pathway as a probabilistic model to analyze the behavior of the final activity processes in the pathway over high-throughput microarray experiment data obtained from normal and cancer samples. In order to model the pathway probabilistically, we used Bayesian Networks (BNs) that are most suitable for representing the probabilistic knowledge in a graph-like structure. In our Bayesian Network model, the gene products in the pathway denote the nodes of the network and the relations between the genes denote the edges of the network. The expression values of the genes, which are continuous values, stand for the random variables representing the nodes. In the first phase of the study, we considered the discrete case and discretized the continuous expression values in order to construct the Conditional Probability Tables (CPTs) of the BNs. We modeled two Bayesian Networks, one with normal samples and the other with cancer samples, to verify whether the BNs trained using the samples from these two cases (normal vs. cancer) can distinguish a test sample of a specific case. We first tested our model on a small pathway and obtained promising results. Our further purpose is to improve the model for larger pathways with different datasets from various cancer types.