

# Cell cycle and protein complex dynamics in discovering signaling pathways

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Signaling pathways are responsible for the regulation of cell processes, such as monitoring the external environment, transmitting information across membranes, and making cell fate decisions. Given the increasing amount of biological data available and the recent discoveries showing that many diseases are related to the disruption of cellular signal transduction cascades, *in silico* discovery of signaling pathways in cell biology has become an active research topic in past years. However, reconstruction of signaling pathways remains a challenge mainly because of the need for systematic approaches for predicting causal relationships, like edge direction and activation/inhibition among interacting proteins in the signal flow. We propose an approach for predicting signaling pathways that integrates protein interactions, gene expression, phenotypes, and protein complex information. Our method first finds candidate pathways using a directed-edge-based algorithm and then defines a graph model to include causal activation relationships among proteins, in candidate pathways using cell cycle gene expression and phenotypes to infer consistent pathways in yeast. Then, we incorporate protein complex coverage information for deciding on the final predicted signaling pathways. We show that our approach improves the predictive results of the state of the art using different ranking metrics.