**Dynamical systems modeling and gene regulatory network structure analysis reveals Hap4's role in regulating the response to cold shock in *Saccharomyces cerevisiae***

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A gene regulatory network (GRN) is a set of transcription factors which regulates the level of expression of genes encoding other transcription factors. The dynamics of a GRN show how gene expression in the network changes over time. A MATLAB software package called GRNmap uses ordinary differential equations to model the dynamics of medium-scale GRNs and estimates production rates, expression thresholds, and regulatory weights for each transcription factor in the network based on DNA microarray data. Microarray data were obtained from a *Saccharomyces cerevisiae* strain deleted for the Hap4 transcription factor and subjected to cold shock at 13°C for 15, 30, and 60 minutes. A modified ANOVA showed that 1794 genes had a log2 fold change significantly different than zero at any of the time points. These genes were submitted to the YEASTRACT database to determine which transcription factors regulated them. From this, we generated a database-derived candidate GRN of 15 genes and 28 edges as well as random networks of similar size. GRNmap was used to estimate the production rates, expression thresholds, and regulatory weights for these networks. Gephi was used to analyze the networks’ structures in terms of the node in- and out-degrees, eccentricity, and betweenness centrality. We found that the random networks had different degree distributions than the database-derived network. Also, Hap4 had a different betweenness centrality value in the random networks, which affected the estimated parameter values, helping us further understand its role in the cold shock response in yeast.

Keywords: *Saccharomyces cerevisiae*, Hap4, gene regulatory network, dynamical systems modeling