**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 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 candidate GRN of 15 genes and 28 edges. GRNmap was used to estimate the production rates, expression thresholds, and regulatory weights for this network. Forward simulation of the model showed a good fit with the experimental data. The program Gephi was then used to analyze the network structure in terms of the weighted node in- and out-degrees, eccentricity, betweenness centrality, closeness centrality, and clustering coefficients. From this analysis we have gained further insight into Hap4's role in the gene regulatory network that controls the cold shock response in yeast.

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