**Mathematical Modeling of Six Database-Derived Gene Regulatory Networks Identifies Key Regulators and Network Properties Controlling the Early Response to Cold Shock in Saccharomyces cerevisiae**

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A gene regulatory network (GRN) is a group of transcription factors that control the level of expression of genes encoding other transcription factors. Dynamics of GRNs illustrate how expression in the network changes over time. GRNmap, a MATLAB software package, uses differential equations to model the dynamics of medium-scale GRNs. The software estimates production rates, expression thresholds, and regulatory weights for each transcription factor in the network based on microarray data. Microarray data was obtained from a cold shock experiment where wild-type budding yeast, *Saccharomyces cerevisiae*, and five strains from which the transcription factors Cin5, Gln3, Hap4, Hmo1, and Zap1 were deleted were subjected to cold shock at 13°C for 15, 30, and 60 minutes. Six related GRNs, which ranged from 14-17 genes and 25-35 edges, were constructed using data from the YEASTRACT database. GRNmap was then used to estimate production rates, expression thresholds, and regulatory weights for each of these GRNs. Forward simulation of the model showed a good fit to the experimental data**,** particularly in comparison to 30 random networks with the same genes and number of edges. Multiple regression analysis of the database-derived and random networks demonstrated that factors with high eigenvector centrality, such as Gcn4 and Yhp1, contributed significantly to accurate modeling of experimental data. Systematic analysis of edges further indicated conserved motifs including an early coherent type I feed forward loop (FFL), an activating regulatory chain, and symmetrical incoherent type I FFLs terminating on the paralogs Yhp1 and Yox1.

Keywords: *Saccharomyces cerevisiae*, cold shock, gene regulatory network, transcription factors, dynamical systems modeling, eigenvector centrality, network motifs