

# Mathematical Modeling of the Transcriptional Network Controlling the Environmental Stress Response in *Saccharomyces cerevisiae*

Kam D. Dahlquist<sup>1\*</sup>, Stephanie Kuelbs<sup>2</sup>, Nathan C. Wanner<sup>3</sup>, Ben G. Fitzpatrick<sup>2</sup>, Erika Camacho<sup>4</sup>

<sup>1</sup>Department of Biology, Loyola Marymount University, 1 LMU Drive, Los Angeles, California 90045 USA

<sup>2</sup>Department of Mathematics, Loyola Marymount University, 1 LMU Drive, Los Angeles, California 90045 USA

<sup>3</sup>Biomathematics Graduate Program, North Carolina State University, Box 8203, Raleigh, NC 27695-8203 USA

<sup>4</sup>Department of Applied Mathematical Sciences and Applied Computing, New College of Interdisciplinary Arts & Sciences, Arizona State University, Mail Code 0852, P.O. BOX 37100, Phoenix, AZ 85069-7100 USA

\*email: kdahlquist@lmu.edu

Recently, genome-wide location analysis has determined the relationships between transcription factors and their target genes on a global scale in budding yeast, *Saccharomyces cerevisiae* (Lee *et al.*, 2002; Harbison *et al.*, 2004). While these data have identified properties of the network topology, they do not reveal the dynamics of the behavior of the network. Using differential equations, we have modeled how the concentrations of proteins in the cell changes over time for a subset of a real gene expression network of twenty-one transcription factors controlling the environmental stress response in yeast. The differential equations governing the rate of change of concentration for each gene in the network were based on Vu and Vohradsky (2007). A weight parameter determined how each transcription factor affects the transcriptional and translational rate of its target gene. The weights were optimized to experimentally derived gene expression data from yeast exposed to the environmental stress of cold shock (Schade *et al.*, 2004). We then used the model to generate a simulated gene expression dataset giving the steady-state concentrations of each protein after a period of time has elapsed. The simulated data determined which transcription factors have a greater impact on the overall dynamics of the network. Then each gene in the network was systematically deleted *in silico* to determine how the steady-state concentrations of the proteins in the network changed after the deletions. Finally, the simulated data was used to make predictions tested by laboratory experiments.

## References

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