Dynamic environments reveal specialized roles in the HOG network

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***Short Abstract* — The ability of biological systems to grow and survive depends upon the detection of specific environmental signals and the organization of adequate physiological responses. At the cellular level, information from the environment is processed using molecular networks that orchestrate an appropriate response, which often includes changes in gene expression. The high osmolarity glycerol (HOG) pathway in yeast serves as a prototype signaling system for eukaryotes. Its main function is to sense changes in osmotic pressure and coordinate a wide range of molecular processes that lead to the adaptation of cell volume. The signaling properties of the HOG pathway have been widely studied both experimentally and theoretically. An integrative framework, however, that connects the dynamic properties of the pathway with its Y-shaped structure and its ability to process information is still missing. Using novel microfluidic experiments and mathematical modeling, we are determining how the two branches of the HOG network combine to allow both a response at short times to enable survival and at longer times to enable adaptation in dynamic environments.**

***Keywords* — cell signaling, HOG pathway, microfluidics, mathematical modeling.**

I. Introduction

The High Osmolarity Glycerol (HOG) pathway in yeast (*Saccharomyces cerevisiae*) serves as a prototype system for MAPK signaling in eukaryotes. Its main function is to respond to hyper-osmotic shocks by driving a wide range of molecular processes that lead to the adaptation of cellular volume. The pathway consists of two input branches (SLN1 and SHO1) that activate Pbs2 (MAPKK). Subsequent activation of Hog1 (MAPK) by Pbs2 enables regulation of glycerol levels in various ways; for example, activating regulatory enzymes in glycolysis but also up-regulating the expression of enzymes required for glycerol production (Gpd1) and glycerol import (Stl1). Although the signaling properties of the HOG pathway have been widely studied both experimentally and theoretically [1-4] an integrative framework that connects the dynamic properties of the HOG pathway to its ability to process information is still missing.

II. Results

Using microfluidic experiments and mathematical modeling, we are determining how the two branches of the HOG network combine to allow cellular response both at short times—to enable survival to severe shocks—but also at longer times—to enable better adaptation to dynamic environments.

Using a novel design of the ALCATRAS microfluidic device [5] we measure single-cell signaling responses and fitness dynamics under various dynamic environments. We find that ste11 mutant cells (only SLN1 branch active) do better under sudden, step-like hyper-osmotic shocks, while, skk1 mutant cells (only SHO1 branch active) adapt better in slowly varying environments. Therefore, our results indicate that the SLN1 branch is essential when response speed is important, while the SHO1 branch allows precise cellular adaptation to gradually fluctuating environments.

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