Information processing in single yeast cells: from signal transduction to gene expression

Neuert, G[1], and van Oudenaarden, A[1]

Short Abstract — How cells sense their environment using signal transduction pathways and respond to environmental changes by regulating gene expression is a key problem in systems biology. Here we investigate the coupling dynamics between signal transduction and gene expression in *Saccharomyces cerevisiae* yeast cells. The research focus on the high-osmolarity glycerol (HOG) signal transduction pathway, which is one of the mitogen-activated protein kinase (MAPK) pathways in bakers yeast. We are studying single yeast cells to understand variability in signal transduction and gene expression.

Keywords — mitogen-activated protein kinase (MAPK) signal transduction pathway**,** high-osmolarity glycerol, stochastic gene expression, single cells

I. Purpose

The mitogen-activated protein kinase (MAPK) pathways, which are evolutionarily conserved from yeast to mammals, provide an excellent model to study how signal transduction is coupled to gene expression. The MAPK pathways play important roles in regulating diverse cellular processes including pheromone signaling, metabolism, differentiation, proliferation and apoptosis [1-4]. Our research focus on the high-osmolarity glycerol (HOG) MAPK pathway in single, *Saccharomyces cerevisiae* yeast cells [5, 6]. During the last few decades, the components and regulatory network of this pathway have been elucidated via genetic and biochemical assays performed on large populations of yeast cells. However, surprisingly little is known about the detailed coupling dynamics of signal transduction and gene expression in individual cells. After osmotic shock, homogenous Hog1 kinase dynamics were measured in all cells. However, in the subsequent gene expression of *STL1*, a gene that encodes for a glycerol proton symporter of the plasma membrane, we observed that one subpopulation of cells exhibits no gene expression at all (OFF-population), whereas another subpopulation of cells show gene expression over a wide range of expression levels (ON-population). Further, the ratio of the two subpopulations of cells remained constant despite changes in osmolyte concentration from 0.3 M to 0.6 M NaCl. We also observed that the mean expression level of the ON-population increased with increasing osmolyte concentration. To test the hypothesis that the two subpopulations have a random origin, we performed single cell time-lapse experiments using repetitive osmotic shocks. These experiments indicated that switching between gene expression levels after subsequent osmotic shocks was random and uncorrelated.

[1] Department of Physics, Massachusetts Institute of Technology, Cambridge, MA 02139, USA, E-mail: gneuert@mit.edu

References

[1] Chang, L. and M. Karin, *Mammalian MAP kinase signaling cascades.* Nature, 2001. **410**(6824): p. 37-40.

[2] Johnson, G.L. and R. Lapadat, *Mitogen-activated protein kinase pathways mediated by ERK, JNK, and p38 protein kinases.* Science, 2002. **298**(5600): p. 1911-2.

[3] Morrison, D.K. and R.J. Davis, *Regulation of MAP kinase signaling modules by scaffold proteins in mammals.* Annu Rev Cell Dev Biol, 2003. **19**: p. 91-118.

[4] O'Rourke, S.M., I. Herskowitz, and E.K. O'Shea, *Yeast go the whole HOG for the hyperosmotic response.* Trends in genetics : TIG, 2002. **18**(8): p. 405-12.

[5] Hohmann, S., *Osmotic stress signaling and osmoadaptation in yeasts.* Microbiology and molecular biology reviews : MMBR, 2002. **66**(2): p. 300-72.

[6] Mettetal, J.T., D. Muzzey, C. Gomez-Uribe, and A. van Oudenaarden, *The Frequency Dependence of Osmo-Adaptation in Saccharomyces cerevisiae.* Science, 2008. **319**(5862): p. 482-484.