Dynamic Pheromone Gradient Sensing in Yeast

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***Short Abstract* — We analyze yeast's ability to cope with dynamic pheromone gradients. *S. cerevisiae* cells are exposed to time-varying pheromone gradient signals generated by a microfluidic device. Fluorescence microscopy is used for the tracking and analysis of cell morphology and cell polarization. To interpret our findings, we consider models that couple cell morphology to polarization of the actin cytoskeleton.**

***Keywords* — yeast, pheromone, gradient, fluorescence microscopy, microfluidics, actin**

I. Introduction

S. cerevisiae has become a key model eukaryotic organism, owing in part to ease of genetic manipulation and high growth rate. Many of the mechanisms that regulate cell polarity in yeast (via the actin cytoskeleton) are conserved in higher eukaryotes [1,2]. The yeast mating response provides one path to understanding regulation of cell polarity.

Haploid yeast cells can exist in one of two types. Different types will fuse (mate) into a diploid cell when in proximity to one another [3]. This mating response is directed by mutual pheromone signaling and, among other things, leads to the reorientation of cell growth along the complementary type's pheromone gradient [4].

Most studies of yeast have focused on static pheromone gradients (e.g. see [5]). Instead, we seek to explore the response of yeast cells to dynamic perturbation, probing yeast's ability to cope with a fluctuating environment. The usefulness of dynamic perturbation has recently been verified in the context of mRNA degradation regulation in the GAL network [6].

II. Methods and Preliminary Results

A. Experimental

A microfluidic device [7] from a previous study [8] has been modified to generate dynamic gradients. This new device allows a pheromone gradient across a 150 μm-wide cell trap to be switched in direction with a response time of approximately 30 s. Cells within the device are imaged with fluorescence microscopy, providing time-resolved data for cell morphology and polarization.

We find that yeast's response to a dynamic gradient of intermediate strength exhibits at least two different phases. The early phase concerns the transition from isotropic (or weakly anisotropic) growth to highly polarized growth. Gradient sensing is rapid (approx. 15-30 min.) in this phase. Imposed gradient switching slower than this rapid timescale leads to many cells polarized along a common direction, while faster gradient switching leads to a weaker correlation of the cell polarization across the population.

The subsequent late phase is instead characterized by slow (2-3 hr.) adaptation of cell polarization to the gradient (related to "locking", see [9]). Here, we find cells can "wiggle" with the switching gradient, leading to wavy cell morphologies. Other phenomena are seen to occur only in very long cells, such as bipolar growth (growth at both ends of an elongated cell) and occasional jumping of cell polarization between ends of a cell.

B. Theoretical

A simple model, based on a reduced version of the redistribution model in [10], has been used to minimally explain certain aspects of the experimental system, including "locking" and "wigglers". One advantage of this approach is that the bifurcation between isotropic and anisotropic growth due to pheromone exposure is given in terms of the ratio of two natural timescales.

However, the simple model is inadequate for a description of cells with arbitrary cell morphology, so we also seek to validate a more general two-dimensional model that explicitly includes polarization of the actin cytoskeleton. Actin polarization is here determined by a free energy functional similar to that used in liquid crystals. Phenomena seen only in long cells, e.g. stable bipolar growth, are explained in terms of an actin cytoskeleton correlation length. Reduction of the model to one dimension makes the condition for bistable growth more transparent.

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