Polarized Stochastic Amplification During Mating in *Saccharomyces cerevisiae*

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We have developed a spatial stochastic model of polarisome formation in mating yeast, focusing on the tight localization of proteins on the membrane. This new model is built on simple mechanistic components, but is able to achieve a highly polarized phenotype even in relatively shallow input gradients. Preliminary results highlight the need for spatial stochastic modeling because deterministic simulation fails to achieve a sharp break in symmetry.

One of the best-studied examples of cell polarization is the growth of the mating projection during yeast mating. Yeast cells localize specific proteins to the front of the cell in response to a spatial gradient of mating pheromone secreted by a partner [1]. The spatial sensing and response exhibit remarkable sensitivity, dynamic range, and robustness. A single molecular entity located at the front of the cell, termed the polarisome, helps to organize structural, transport, and signaling proteins [2]. The function of the polarisome is well-conserved in eukaryotes, and analogous scaffold complexes may be responsible for such diverse structures as focal adhesions and the synapse [3].

Prior work has produced deterministic (PDE) mathematical models that described the spatial dynamics of yeast cell polarization in response to spatial gradients of mating pheromone [4], as well as addressing the trade-off between amplification and tracking [5]. In these models a special mechanism (e.g. high cooperativity) is needed to match the characteristic punctate of the polarisome.

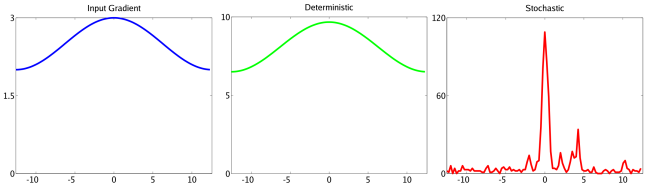

Figure 1: Model input and output. Left (blue) input gradient. Middle (green) deterministic output. Right (red) stochastic output. The horizontal is membrane location; the vertical is molecule count.

Noise plays an increasingly acknowledged role in intra- and intercellular signal transduction, protein interaction networks, and gene regulation [6], and as such, work has been done on simple models of the system's components. Specifically, models of self recruitment [7] and actin nucleation and directed transport [8] have highlighted the important role of spatial stochastics in initiating polarization in the absence of an external cue.

In this work, we present a model that combines directed transport and self recruitment, while focusing on three molecular species: Bni1 (a formin that nucleates actin [9]), Spa2, and actin. The mechanism and rate constants in this model are based on evidence from the literature [2,9-10] and experiments in Yi's group. None of the terms in the model require cooperativity.

Given a relatively shallow low level input, the model stochastically produces sharp polarization. However, when simulated deterministically, the model produces a very shallow slope that provides gradient matching (Fig. 1). We show that the deterministic simulation provides the mean of many stochastic realizations, yet fails to capture the spike in protein levels on the membrane within a given realization.

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