

# 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 with a relatively shallow input gradient. Preliminary results highlight the need for spatial stochastic modeling and simulation to reproduce experimental observations.

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 synapses [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]. Noise plays an increasingly acknowledged role in intra- and intercellular signal transduction, protein interaction networks, and gene regulation [6], and as such, increased focus has been placed on developing stochastic models of biological systems. Recently, models of self-recruitment [7] and actin nucleation and directed transport [8] have highlighted the important role of spatial stochastics in initializing and maintaining polarization in the absence of an external cue.

In this work, we present a model that combines gradient-sensing, directed transport and self-recruitment and also focuses on three molecular species: Bni1 (a formin that nucleates actin [9]), Spa2 (a scaffold protein), and actin. The mechanisms and rate constants in this model are based on evidence from the literature [2,9-10] and experiments.

Stochastic simulation of our model reproduces the sharp polarization seen in experiments, whereas deterministic simulation fails to achieve tight spatio-temporal localization. In addition, stochastic simulation is required to balance tight polarization and the dynamic searching behavior that allows for the tracking of the input cue. We show that spatial stochastic models are necessary to reproduce these biological phenomena with mechanisms that are simple and biologically relevant.

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