

Dynamic Polarized Response of Yeast to Microfluidically Generated α -factor Gradients

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Orienting oneself in the environment and to external stimuli is a fundamental aspect of an organism's existence. Many mechanisms to achieve these types of sensing have evolved; including the widespread utilization of G-protein coupled receptor systems. The budding yeast *S. cerevisiae* is confronted with this task in its haploid state during mating with the opposite mating type to form a diploid cell. Mating pheromone is secreted and diffuses outward from the cell to be detected by potential mates, which in turn polarize and form a mating projection. In order to explore how cells sense their environment and create a polarized response, a combination of microfluidic techniques, live imaging, and computational modeling were used to explore yeast **a**-cells after exposure to spatial gradients of α -factor.

Yeast cells have the capability of faithfully detecting shallow gradients (**Figure 1**). Mutations in the pheromone response pathway result in a decrease in their broad dynamic range. Additionally, alternative mating strategies are employed to improve and optimize the accuracy of gradient sensing and projection steering. When polarized cells are exposed to a gradient, or the gradient's direction is switched 180°, yeast cells must make a decision to either bend the existing mating projection or to make a new one, which is dependent on mating factor concentration.

Computational modeling techniques (**Figure 2**) were employed to explore receptor and mating pathway dynamics and their influence on the cell's ability to maintain their ability to sense spatial differences in ligand concentrations and changes in their environment.

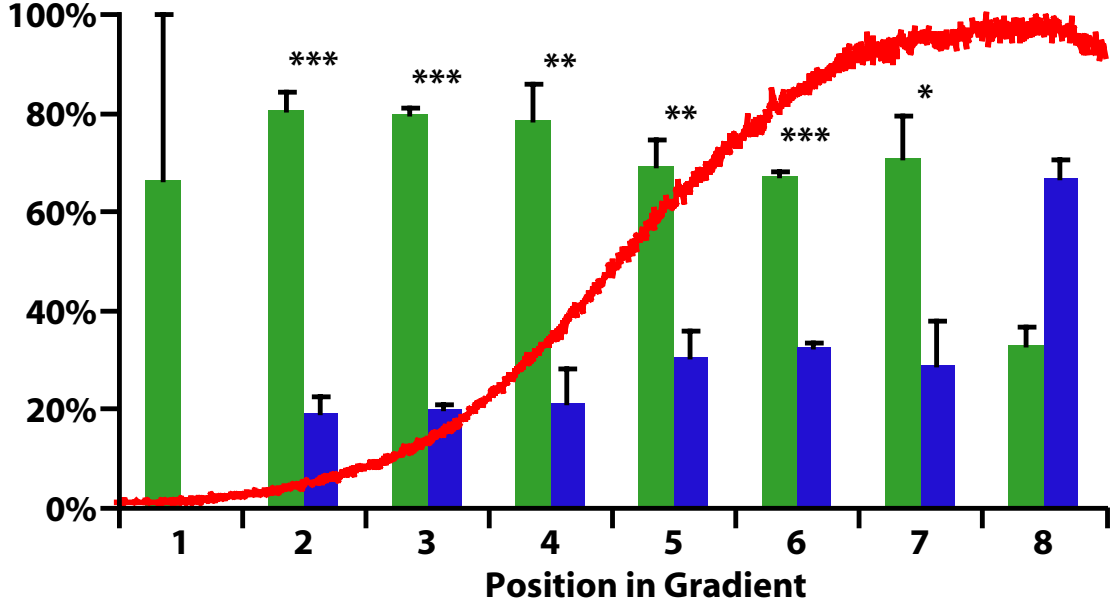


Figure 1.

The cell chamber is divided into eight cross-sections, where the slope and average alpha factor concentration changes. A significant (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$) percent of shmooing cells (bar1 Δ) align (■) with the gradient (0 - 100nM) (—) when compared to those that do not (■) after four hours.

$$\frac{\partial [R]}{\partial t} = D_m \nabla_m^2 [R] + k_{Rs} + k_{Rsp} - k_{Ri} [R] - k_{Ra} [R][L] + k_{Rd} [RL]$$

$$\frac{\partial [RL]}{\partial t} = D_m \nabla_m^2 [RL] + k_{Ra} [R][L] - k_{Rd} [RL] - k_{Rd} [RL]$$

$$\frac{\partial [G]}{\partial t} = D_m \nabla_m^2 [G] + k_{Gd} [G_d][G_b] - k_{Ga} [RL][G]$$

$$\frac{\partial [G_a]}{\partial t} = D_m \nabla_m^2 [G_a] + k_{Ga} [G][RL] - k_{Gad} [G_a]$$

$$k_{Rsp} \propto \frac{[RL]_{bin}}{[RL]_{cell}}$$

$$[G_d] = [G_o] - [G] - [G_a]$$

$$[G_b] = [G_o] - [G]$$

Figure 2.

We modeled the response of an **a**-cell to α -factor. In the heterotrimeric G-protein cycle, the peptide pheromone α -factor (L) binds the α -factor receptor (R) to form the active receptor complex (RL). The RL species catalyzes the activation of the heterotrimeric G-protein (G) to form active α -subunit (G_a) and free $G\beta\gamma$ (G_b). G_a is deactivated to form inactive α -subunit (G_d), which binds to $G\beta\gamma$ to reform the heterotrimer.