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Background

Haploid *Saccaromyces cerevisiae* cells (budding yeast) exist in two mating types (a and α), which communicate via secreted pheromones. In a cells, α-factor pheromone triggers a fate decision to switch from normal growth to mating behavior, including induction of gene transcription and cell cycle arrest. In addition, when the cell cycle machinery commits cells to division, it blocks pheromone response. Given that the pheromone pathway and the cell cycle machinery can inhibit each other, we decided to study at the single cell level how *S.cerevisiae* makes the cell fate choice of dividing or preparing to mate using a combination of experimentation and modeling.

Material and Methods

Experimentally, we monitored, by time-lapse fluorescent microscopy, yeast stimulated with different concentrations of α factor. We determined the appearance of morphological changes (mating projection vs budding) and measured the expression of a pheromone-inducible YFP reporter. In addition, we developed a low-dimensional mathematical model that captures the interaction between the pheromone pathway and the cell cycle. We represented the activity of the pheromone pathway with species “F” and that of the cell cycle by species “C”. F represents the overall level of activation of the signaling pathway. C represents the G1 Cdk1 complex Cdc28/Cln2. C inhibits F and F inhibits C. C negatively modulated the latter inhibition. We also included positive and negative feedbacks originating in F.

Results

At high pheromone concentrations, cells exhibited a strong and stable pheromone response. However, we found cells that initiated pheromone response and arrested the cell cycle but, after some time, they turned off pheromone response and resumed cell division. This behavior required functional Cdk1. The frequency of “switching cells” decreased as the concentration of pheromone tested increased. Our mathematical model accounts for the two coexistence of switching and non-switching cells. Identical cells (represented by a single set of parameter values) will have different behaviors when their initial conditions (e.g. F and C values at the time of pheromone stimulation) lie on opposite sides of a dynamical separatrix. In this case, two cells with very similar initial conditions (similar F and C in the model) will display nearly identical initial dynamics, yet eventually they will diverge.

Conclusions

We present a low-dimensional model that suggests a possible mechanism underlying a cell fate decision system as the interplay between pheromone response pathway and cell cycle. In this scenario, small variations in the key components trigger totally different responses.