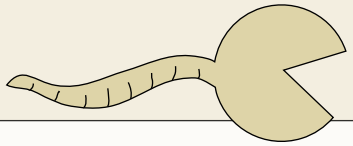
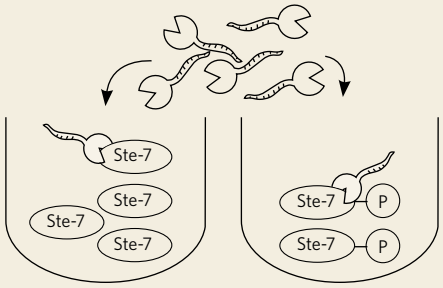
The Molecular Sciences Institute's new tools

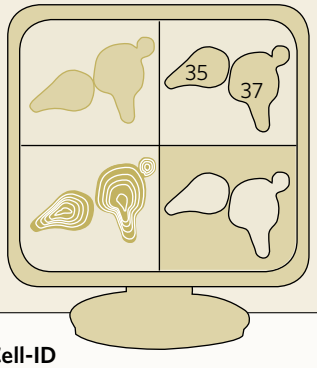
In some sense, MSI's investigation of the α pheromone pathway in yeast has served as a sharpening stone for numerous quantitative tools. Under certain circumstances, the signaling pathway leads to changes that allow the yeast to grow a protrusion, or shmoo, in the direction of the pheromone and a potential mate. The tools, some of which are presented here, have given researchers insight into the workings of the signaling pathway, but they are also finding application in the real world.



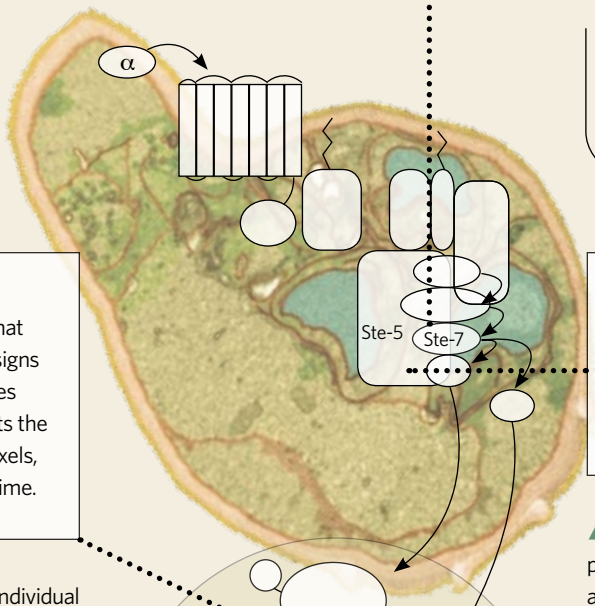
Tadpoles
A detector protein bound to a tail of DNA that amplifies a target molecule's signal to detectable levels.

◀ Researchers wanted a way to count the number of modified proteins in the α pheromone pathway. But the low numbers of such proteins made it difficult to get a precise count using typical methods. They realized that if they lysed the yeast cells and separated their protein of choice, Ste-7, by its modification state – phosphorylation, in this case – then they could count the number of proteins in each pool (see below) using tadpoles. **Other application**: Can count low levels of indicator molecules for disease diagnostics.

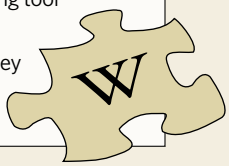




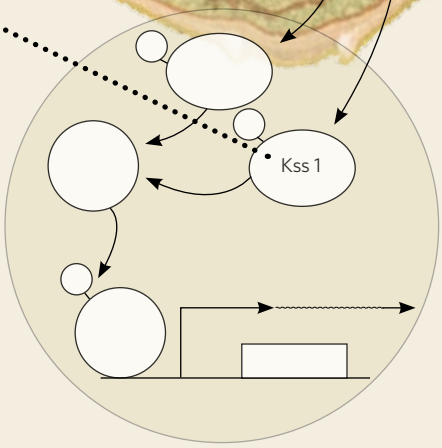
Cell-ID
An open-source software program that locates the yeast cell's perimeter, assigns each cell a tracking number, calculates volume with contour lines, and counts the fluorescence intensity of enclosed pixels, to follow molecular changes in real-time.



YeastPheromoneModel.org. - Wiki
A Wikipedia based modeling tool that lets researchers keep track of their changes as they tinker with the model.



▲ Using a wiki to look at the yeast pheromone pathway in silico (see below), researchers built a model that revealed a reason for the unusually low levels of one of the proteins in the pathway, Ste5, the scaffold protein. The model predicted that Ste5 was low in order to make the system more sensitive to changes in pheromone concentration. **Other application**: A simple tool for modelers studying other protein interactions.



▲ Researchers wanted to look at individual yeast cells, and how they reacted to different levels of alpha pheromone over time. But available microscopy software programs didn't combine all of the necessary tools. So a program called Cell-ID was built to monitor each cell as it was exposed to pheromones. Researchers noticed that at low pheromone concentrations, yeast cells have varied responses, at times completing the pathway to initiate a shmoo, at times not. That decision is regulated by the Kss1 MAP kinase. However, at high levels, the majority of cells shmoo (see below). **Other application**: Can track single-cell responses in real-time for high-throughput drug screens.