**Figure 1.** **Signal transduction pathways controlling pheromone induced responses.**

**Figure 2.** **Memory in the pheromone transcriptional response.** When stimulated with a 90 minute pulse of pheromone GFP with a half-life of seven minutes continues to be expressed after stimulus is removed, and dually phosphorylated MAPKs (Kss1 and Fus3) decrease rapidly (A). The duration of memory, measured as the length of time after stimulus is removed until the transcriptional response reaches its maximum, decreases with increasing pulse duration (B). A simple linear model (C) is unable to capture the different durations of memory, as shown by the model traces (green in D-F) compared to the experimental data (black in D-F). Other pulse durations can be found in Figure S1.

I am unsure as to how to include the constant and constant mutants in this. It would be nice to have a panel showing the MAPK and GFP response to constant pheromone in one panel (I don’t have that data, but I imagine it exists) and another panel showing the WT, far1D, and pSTE5-STE12 on one plot in another panel. But that leaves the top row one panel short.

**Figure 3.** **Model and evolutionary algorithm.** Diagram showing the seven species in the model and their relationships (A). Small icons adjacent to arrows represent a protein affecting that rate. The model is fit to experimental data using an evolutionary algorithm illustrated in panel B. Many individual parameter sets are simulated and the parameter sets are selected and undergo crossover and mutation leading to another generation of parameter sets. Over generations the difference between the experimental data and simulations , quantified as the total absolute error, decreases (C).

**Figure 4.** **Model fits to periodic data.** The best fitting 2.5% of parameter (green) to six periodic experimental data sets (black). The same parameters sets fit to constant and single pulse can be found in Figure S2.

**Figure 5. Predicting low dose data**. The parameter sets shown in figure 4 were used to predict pathway dynamics at lower doses of pheromone (10 nM)**.** The predictions (blue lines) are compared to the experimental low (black triangles) and high (black circles and green lines) dose data for three stimulation profiles. (Other other stimulation profiles can be found in Figure S3).

**Figure S1. Fits of simple model to single pulse and constant data.** The simple linear model (Figure 2C) is used to fit experimental data (black). The top 2.5% of fits are shown for six different stimulation profiles.

**Figure S2. Model fits to constant and single pulse data.** The best fitting 2.5% of parameter (green) to experimental data sets (black) including five single pulse experimental data sets and constant data sets for wildtype, far1D, and pSTE5-STE12.