

## **MAPK-dependent negative feedback in yeast pheromone response regulates system information transmission**

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### **Abstract**

**Haploid *Saccharomyces cerevisiae* yeast cells use a prototypic GPCR-MAPK signaling system to measure and transmit the concentration of extracellular mating pheromone secreted by yeast cells of the opposite mating type. Precise measurement and transmission of pheromone concentration is important for cells to determine the direction toward and suitability of mating partners. Here, we identify a rapid non-transcriptional negative feedback, mediated by the MAPK Fus3, which improves the ability of cells to measure and respond to different doses of pheromone. The feedback adjusts the dose-responses downstream responses so that they match the dose-responses of receptor-pheromone binding. We propose that this feedback-mediated “dose-response alignment” increases both the range of doses over which the cells can respond to changes in receptor occupancy, and the precision of their responses. Our work reveals a new molecular mechanism for regulating signal intensity in cell signaling systems, and suggests how concepts from pharmacology, noise and variation in signaling, and information theory can aid study and understanding how signaling systems transmit information.**