Local Pheromone Release from Dynamic Polarity Sites Underlies Cell-Cell Pairing during Yeast Mating

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Cell pairing is central for many processes, including immune defense, neuronal connection or sexual reproduction. How does a cell precisely orient towards a partner, especially when faced with multiple choices? During conditions of nitrogen starvation, the model eukaryote *S. pombe* (fission yeast) undergoes sexual sporulation. Because fission yeast are non-motile, contact between opposite mating types is accomplished by polarizing growth, via the Rho GTPase Cdc42, in each mating type towards the selected mate, a process known as shmooing. We used a combination of computational modeling and experiments to show that Cdc42- GTP polarization sites are also zones of pheromone secretion and signaling. Simulations of pair formation through a fluctuating Cdc42-GTP zone show that the combination of local pheromone release, short pheromone decay length, and local sensing leads to efficient pair formation. Experimentally we found that Cdc42-GTP polarization sites contain the M-factor transporter Mam1, the general secretion machinery, which underlies P-factor secretion, and Gpa1, suggesting that these are sub-cellular zones of pheromone secretion and signaling. Pairing efficiency is reduced in absence of the P-factor protease, as predicted by the simulations with longer pheromone decay lengths. Increasing zone pheromone sensitivity in simulations leads to reduction in pairing efficiency. This result matches experimental observations of cells lacking the predicted GTPase-activating protein for Ras, which exhibit stabilized zones at reduced pheromone levels.