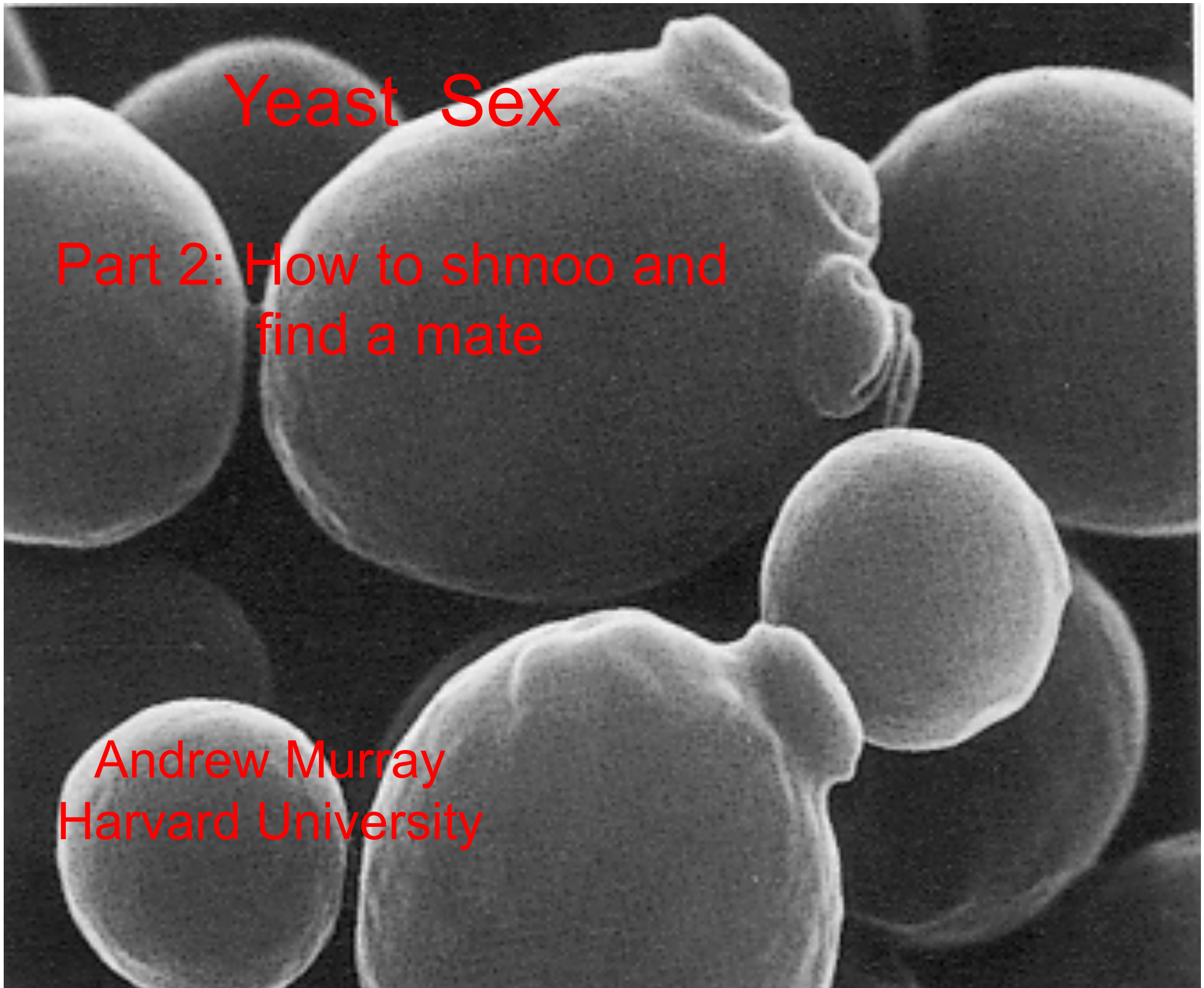


Yeast Sex

Part 2: How to shmoo and find a mate

Andrew Murray
Harvard University



Our heros



Chinlin Guo



Matthieu Piel

People are complicated, yeast are simple

Peeps
(Homo sapiens)

vs.

Yeasties
(Saccharomyces cerevisiae)

Doubling time = 20 yrs

Doubling time = 90 min

50 trillion cells

1 cell

DNA = 6 billion bases

DNA = 12 million bases

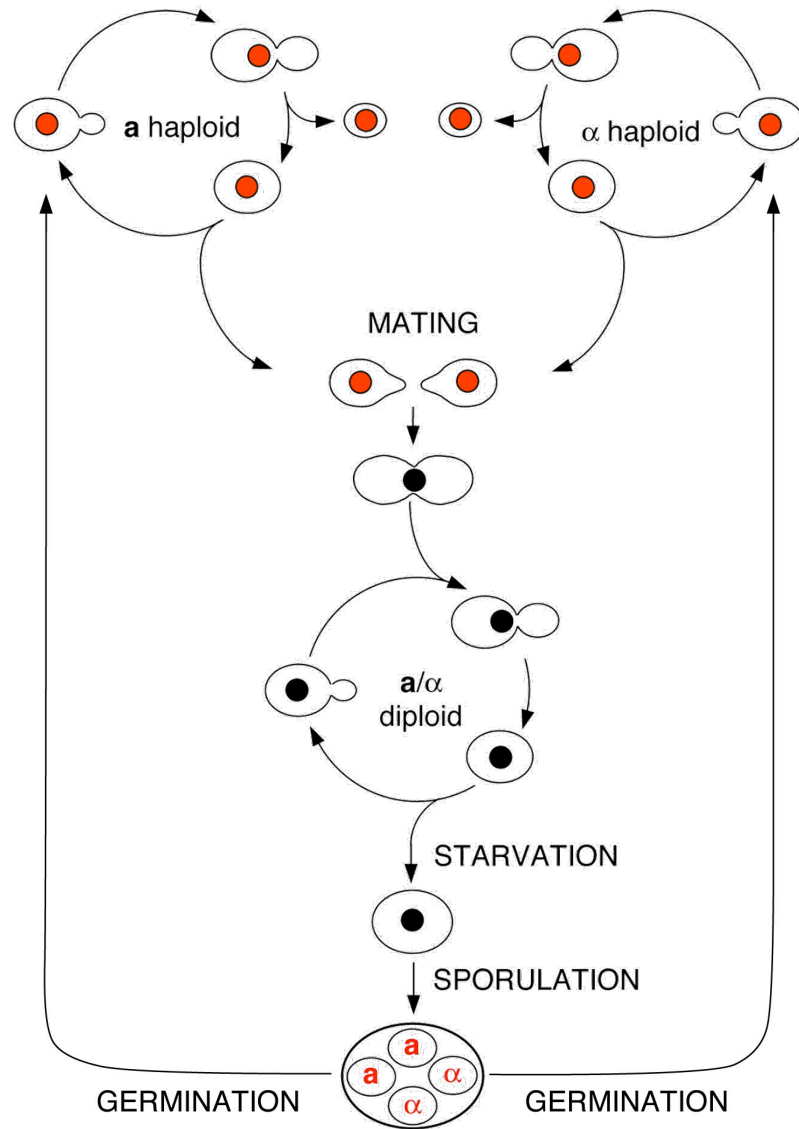
Limits on experiments

Anything goes
genetic manipulation
forced mating
EXTREME survivor

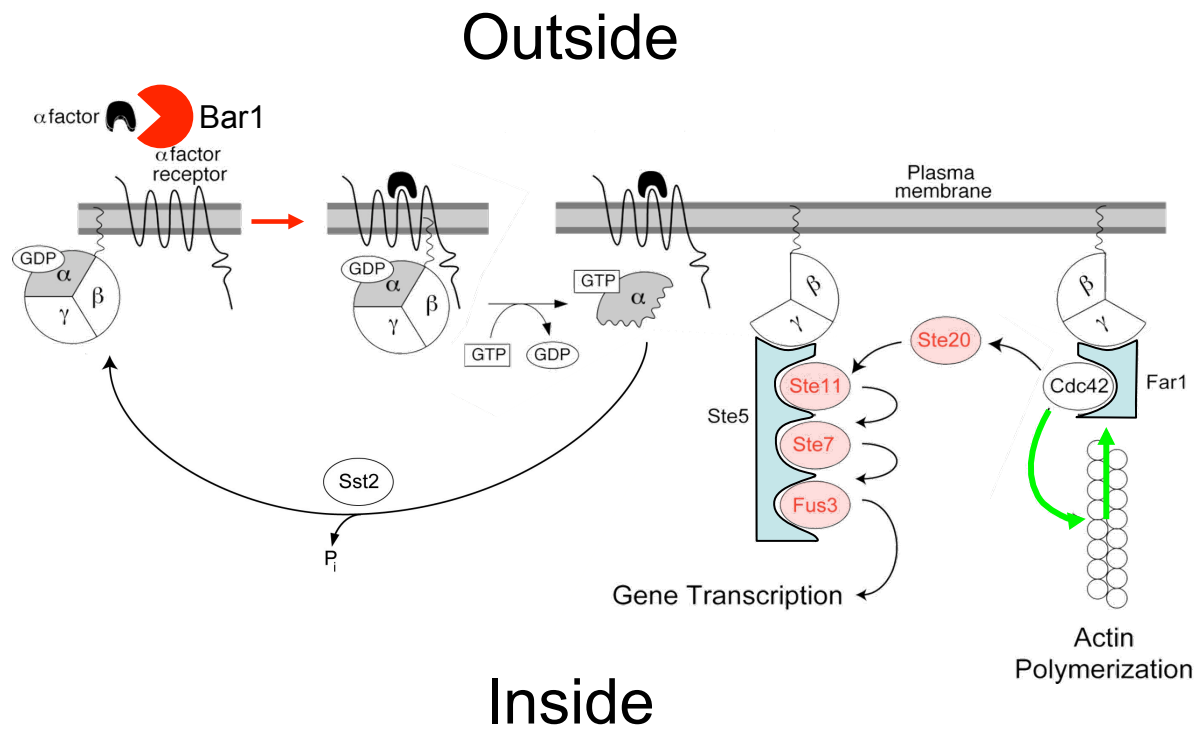
Sex!

Sex!

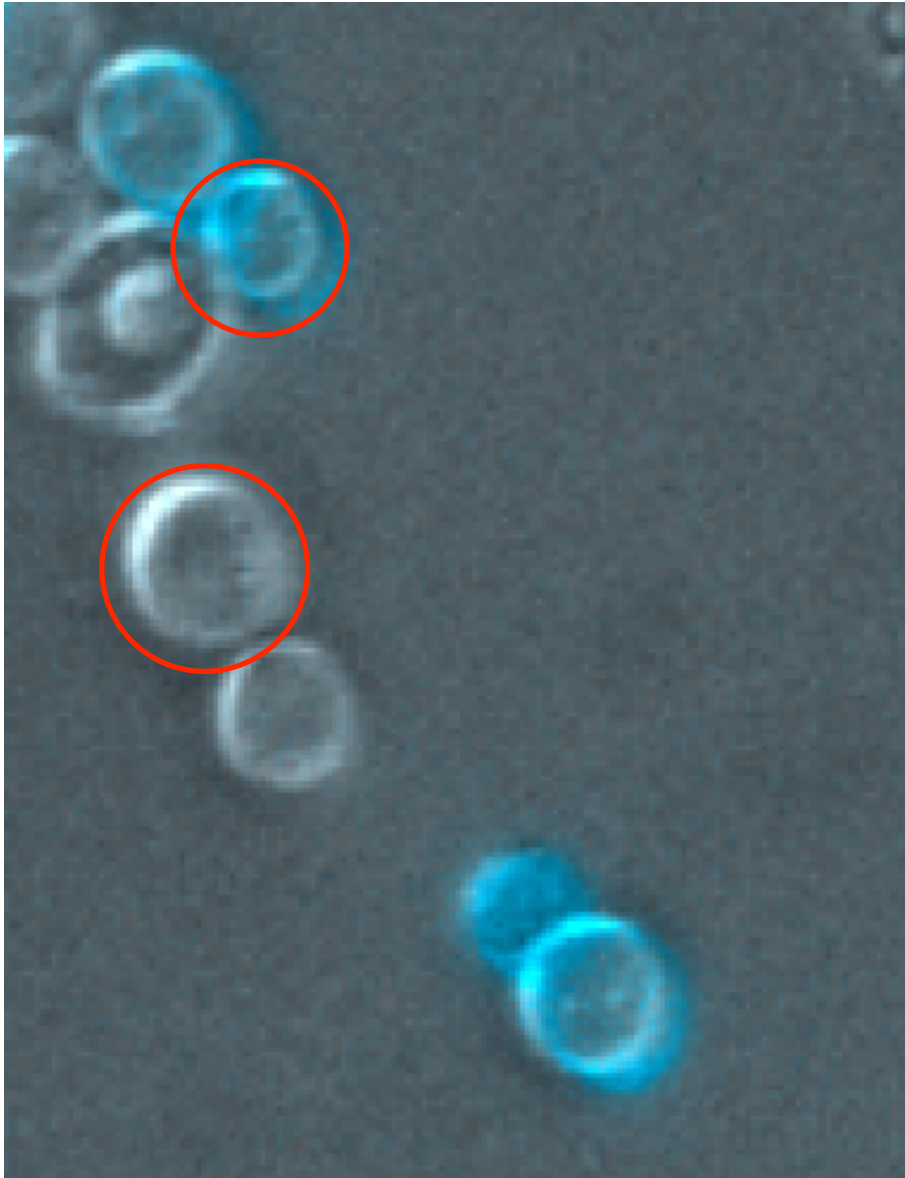
The life cycle of budding yeast



A molecular view of sexual signaling

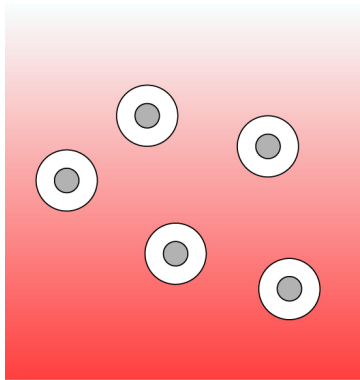


A night at the yeast singles bar

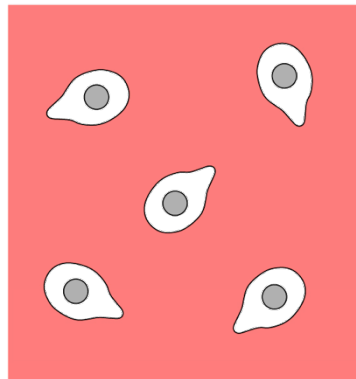
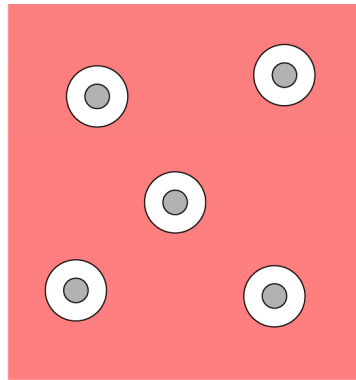


Shmooing is independent of gradients

Chemotropism

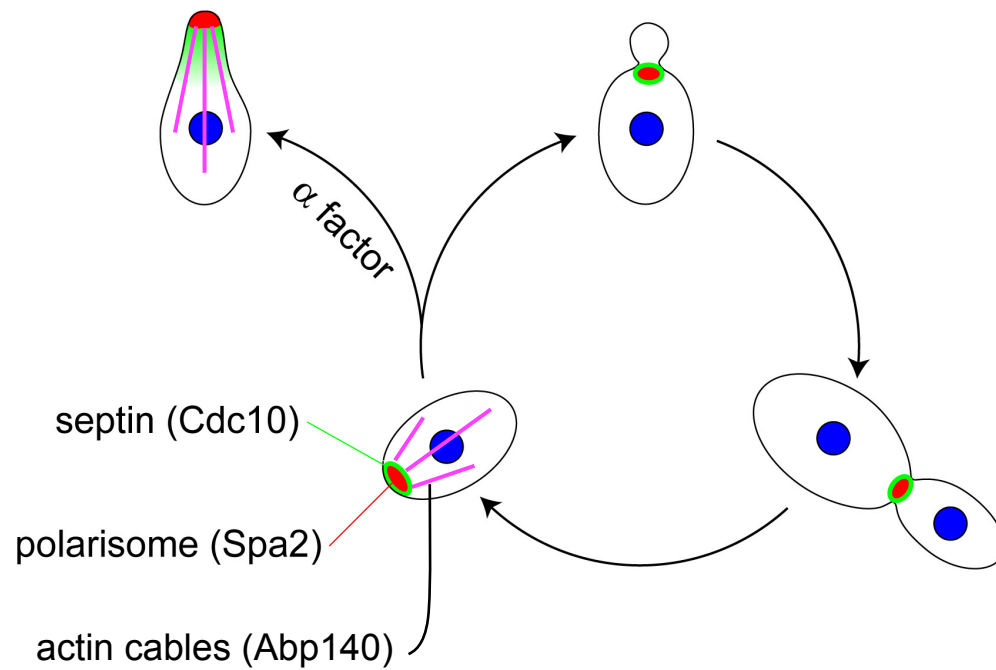


Symmetry breaking

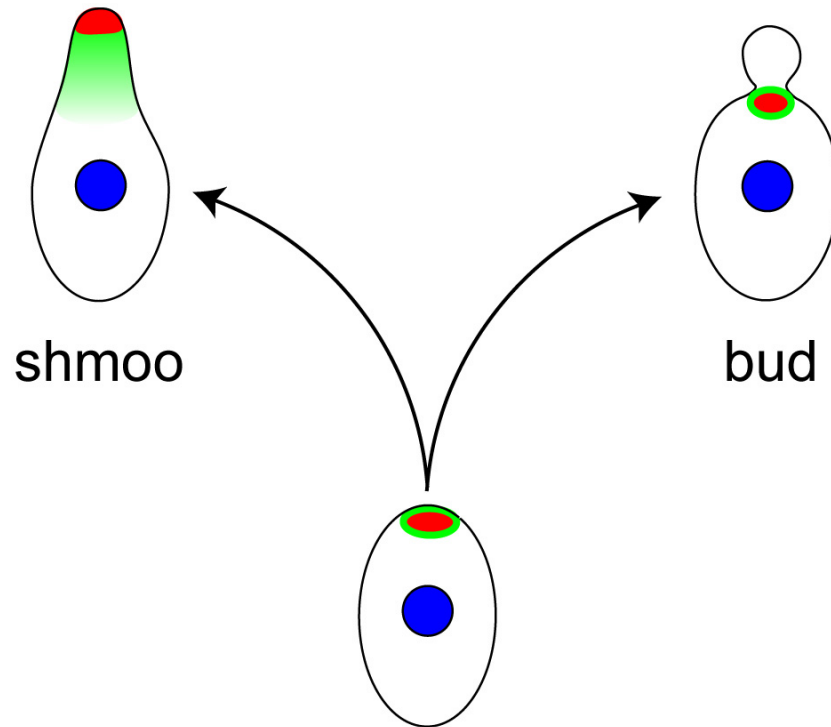


Pheromone concentration

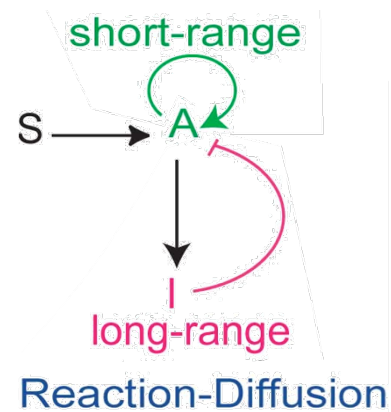
How to study polarization: polarity markers



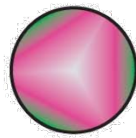
Model 1: Pre-existing marks



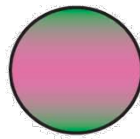
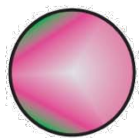
Model 2: lateral inhibition



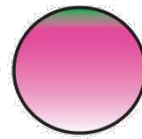
weak stimulation



strong stimulation



?

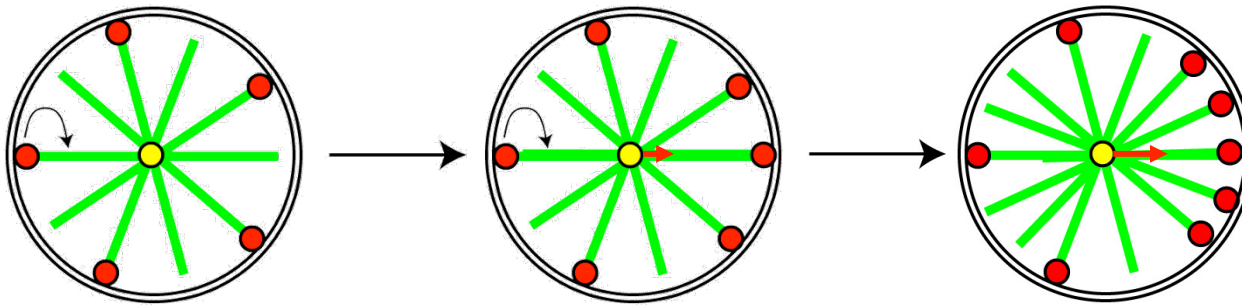


active zones repel each other

Model 3: Global Integration

- Cytoskeletal polymer (actin)
- Active signaling stimulates actin polymerization
- Inactive signaling molecules in/on vesicles

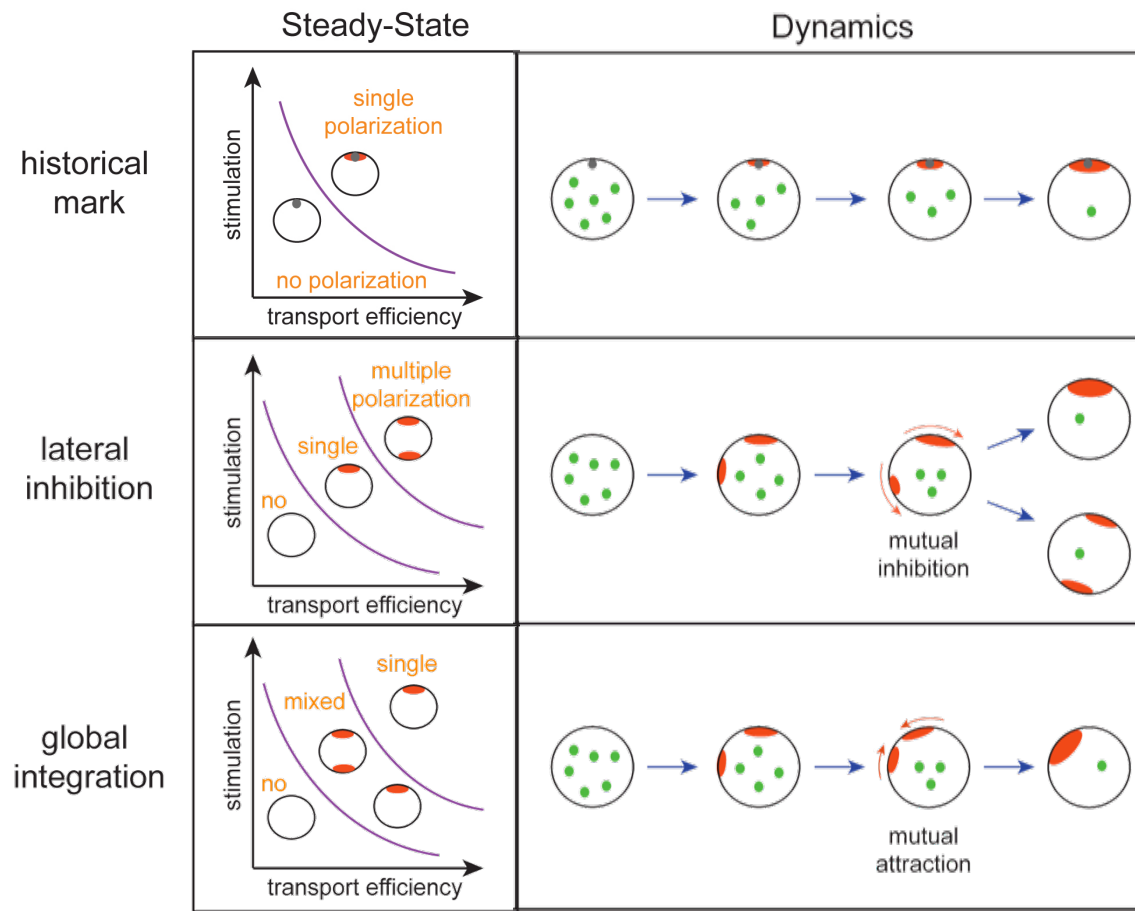
Transport is **distributive**: bind, move, fall off, bind, move,...



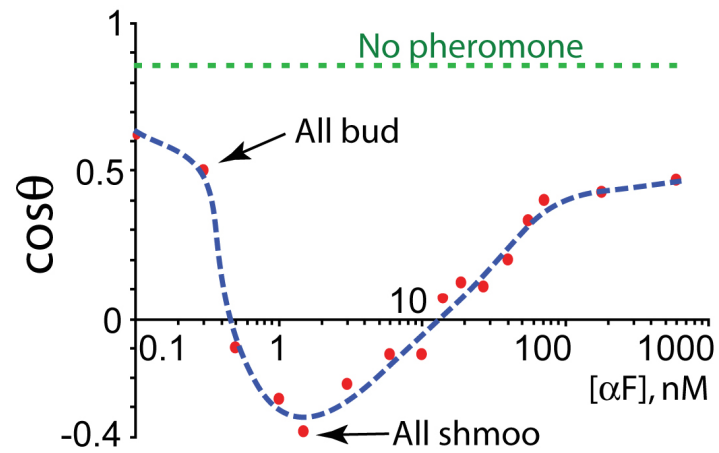
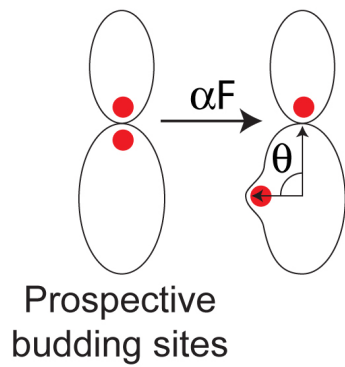
Pro: robust polarization along a single axis

Con: drive to polarize → fragile gradient detection

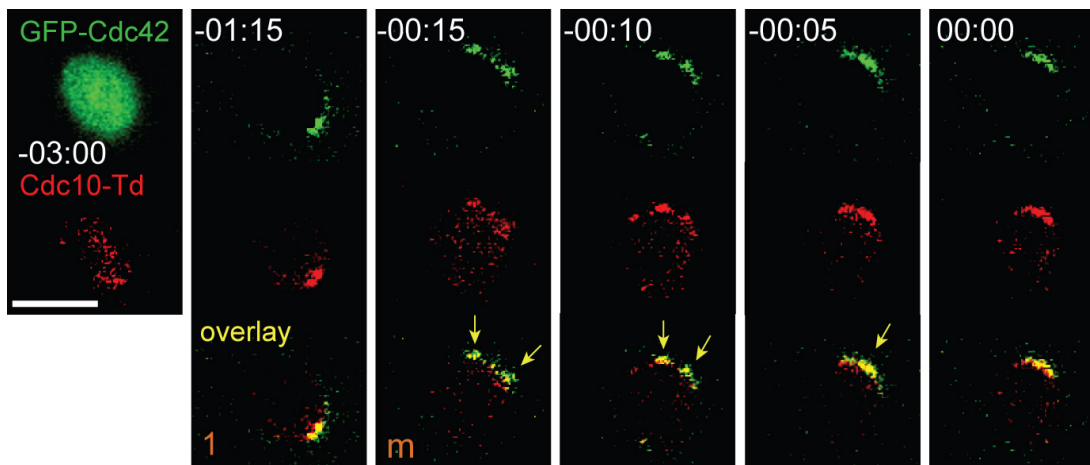
The three models compared



Cells don't shmoo from presumptive bud sites



Patches merge in weakly stimulated (2 nM α F) cells



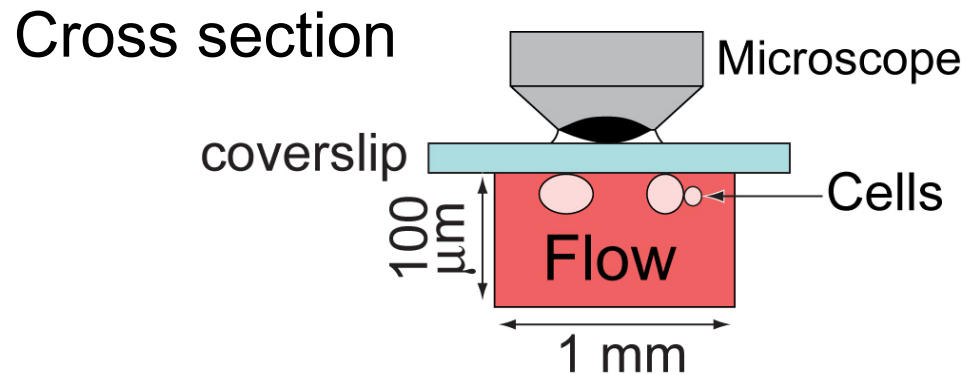
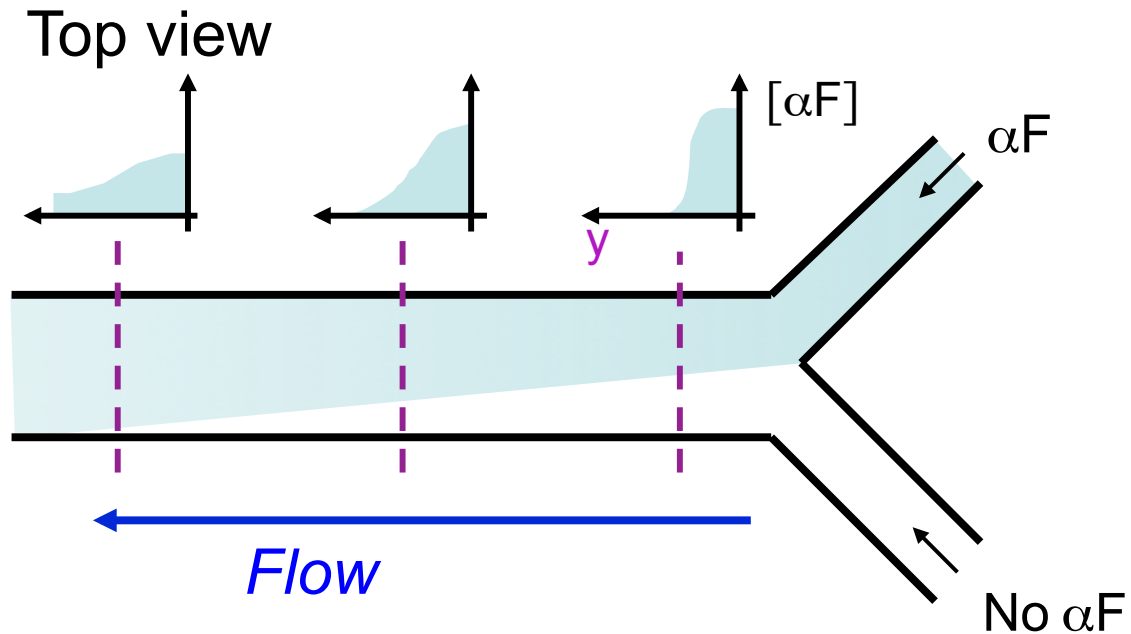
Only a single patch in strongly
(10 nM α F) stimulated cells



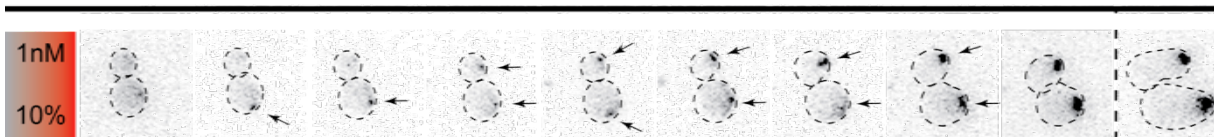
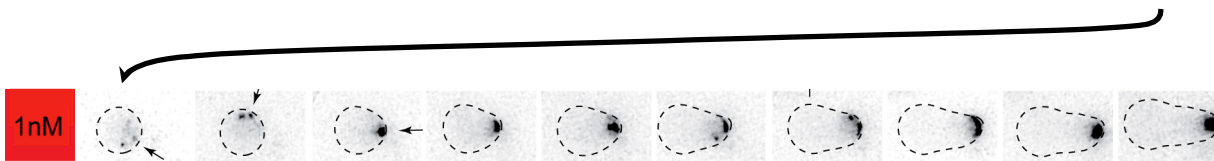
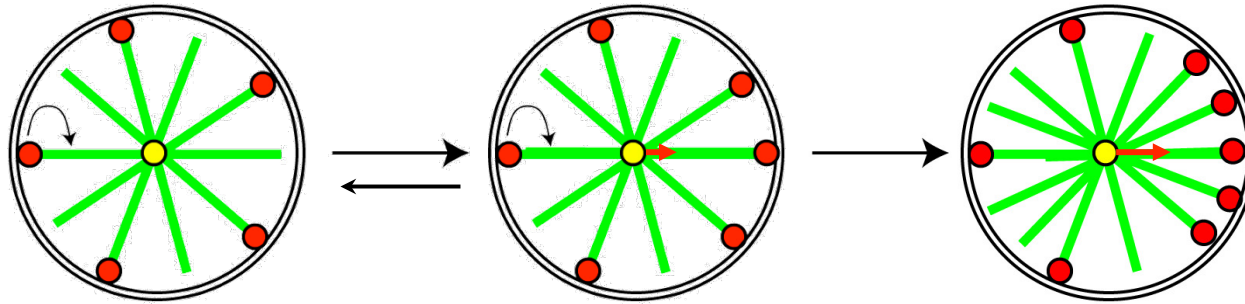
Spa2-YFP

How robust is
gradient detection?

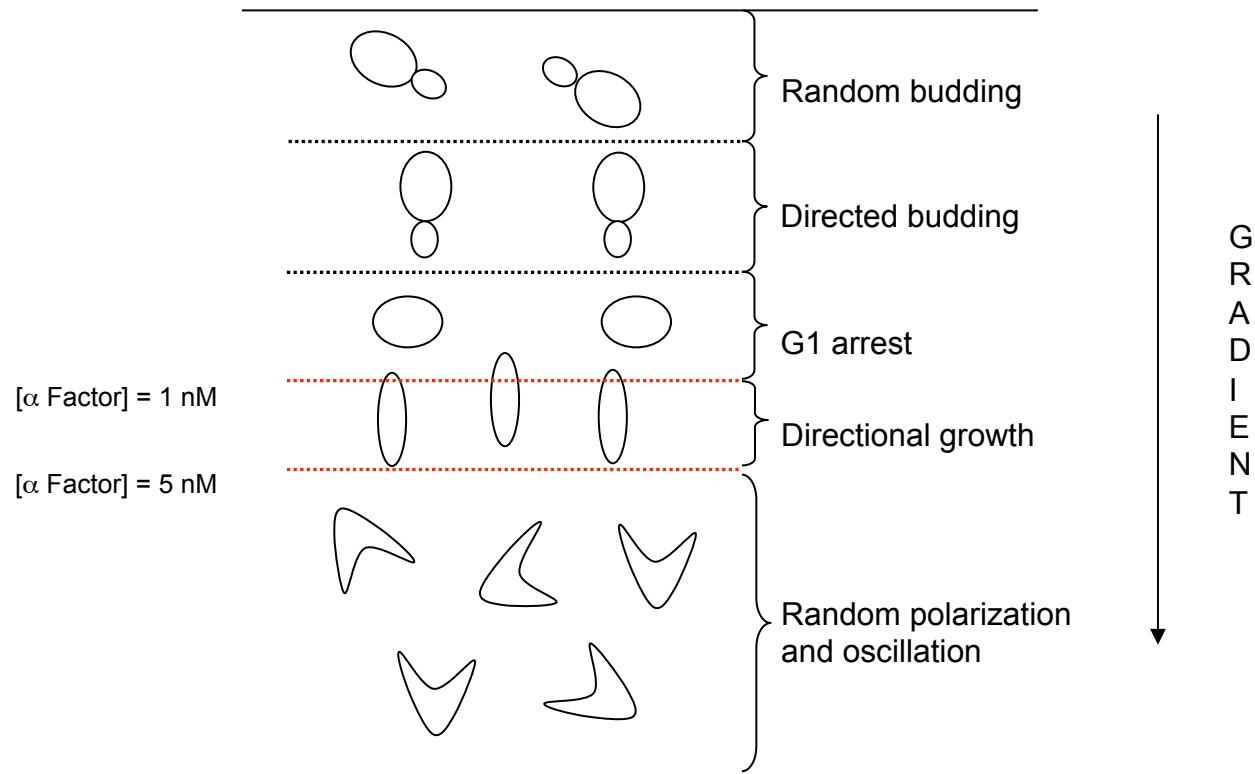
Microfluidics yields controlled pheromone gradients



Global integration implies a polarization threshold

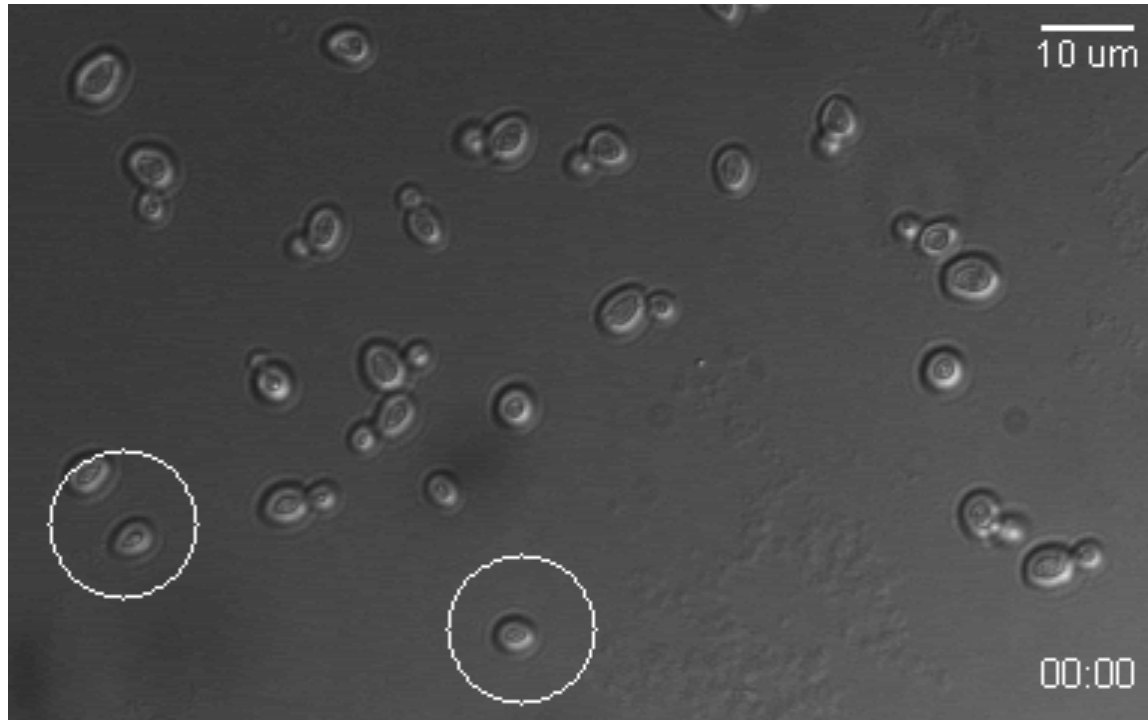


Cellular response depends on $[\alpha F]$: summary



Cellular response depends on pheromone levels

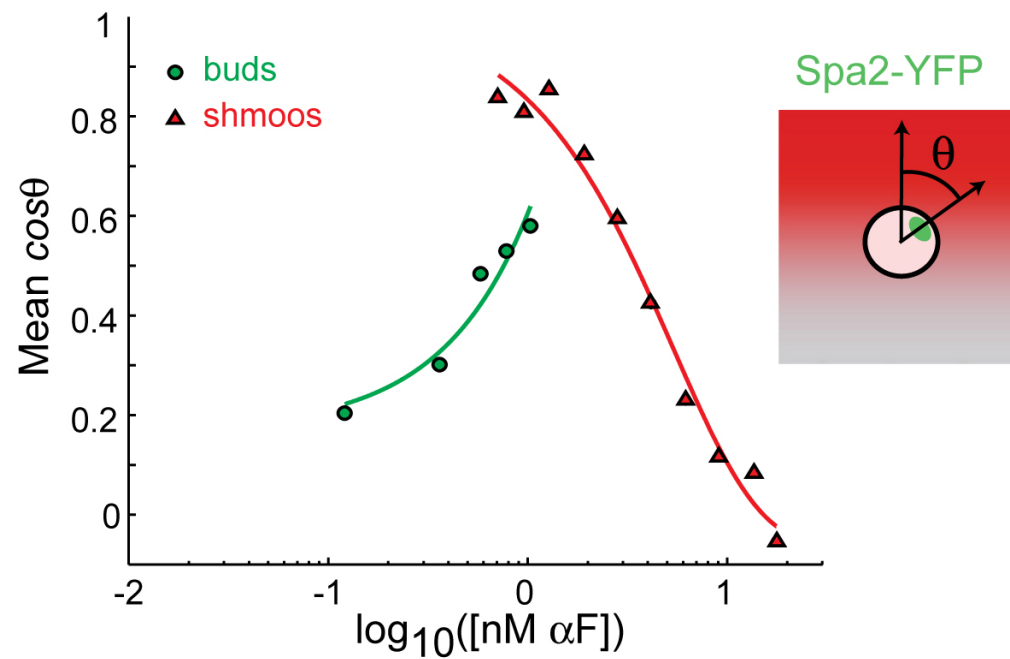
High
[α F]



Low
[α F]

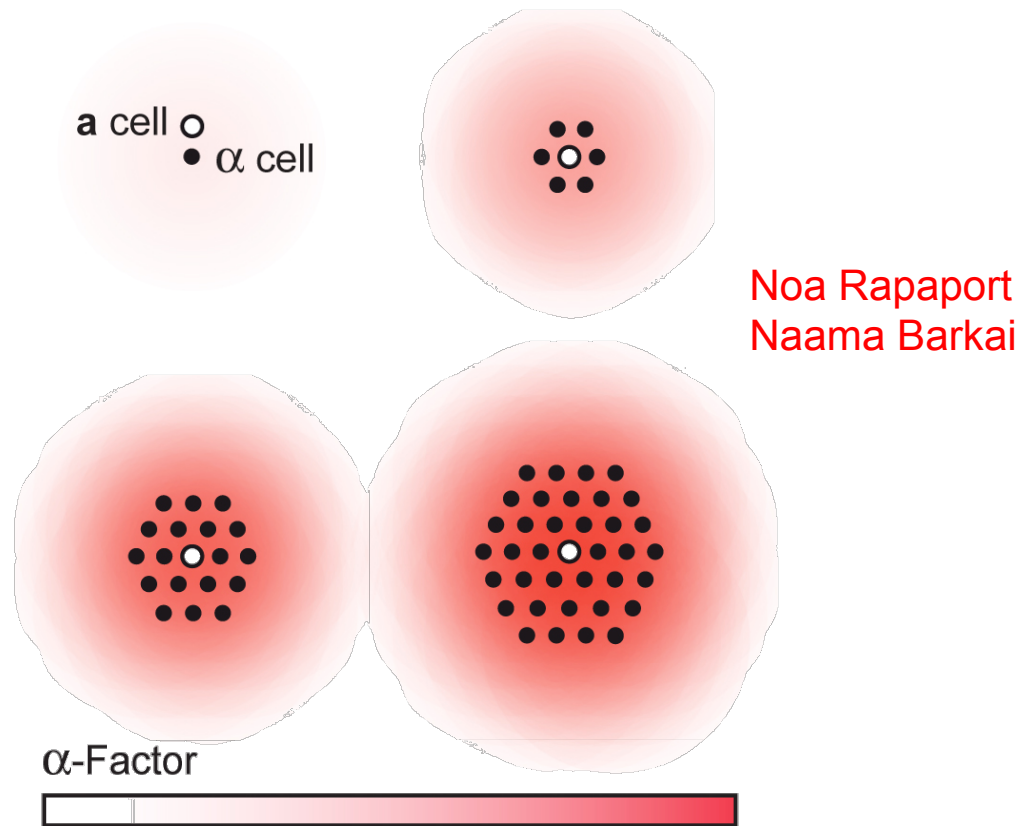
←
Flow

Cells only detect a narrow range gradients



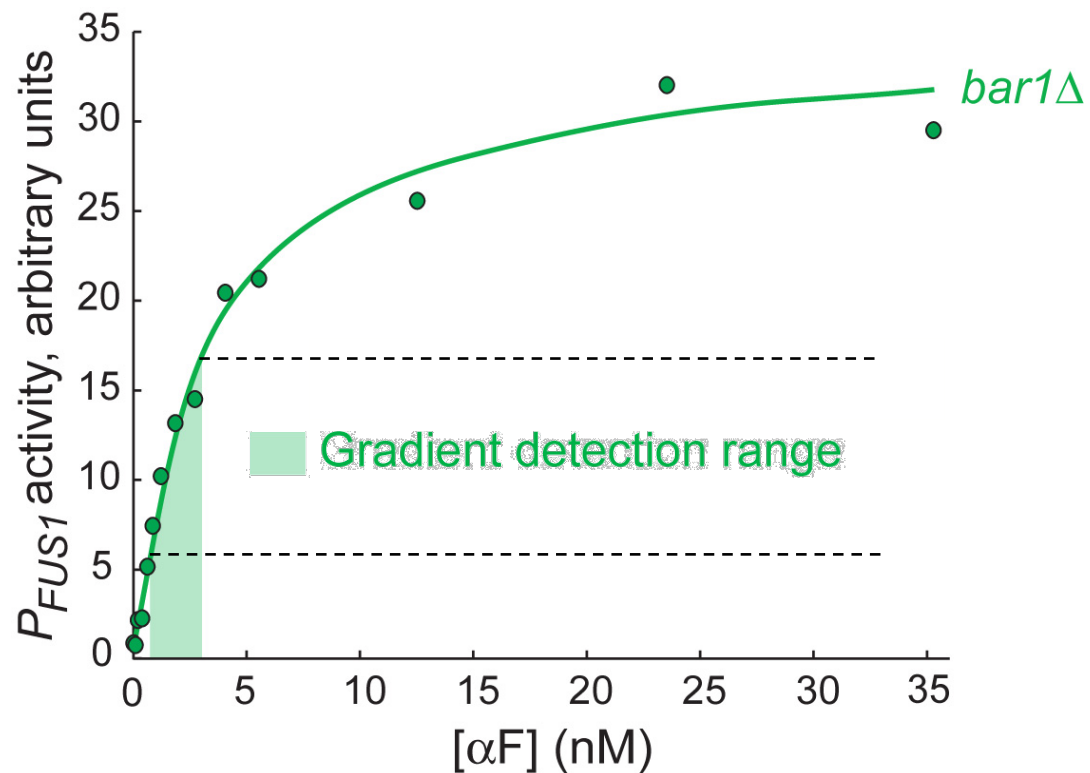
How do cells mate
robustly?

Local concentration should depend on cell number

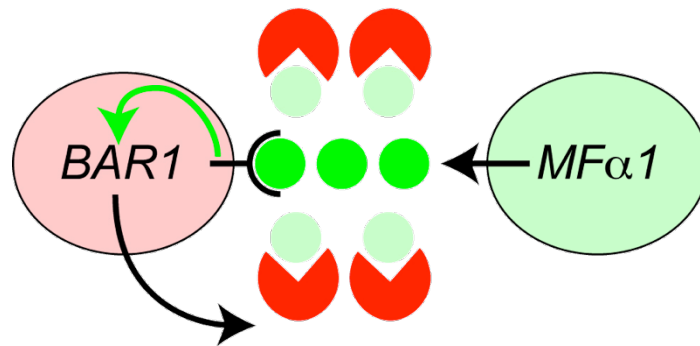
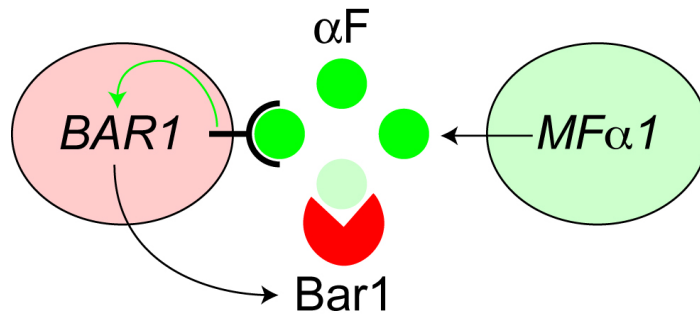


One cell's pheromone contribution depends on $1/r$
Number of contributing cells in a ring depends on r
Each ring contributes the same amount of α factor

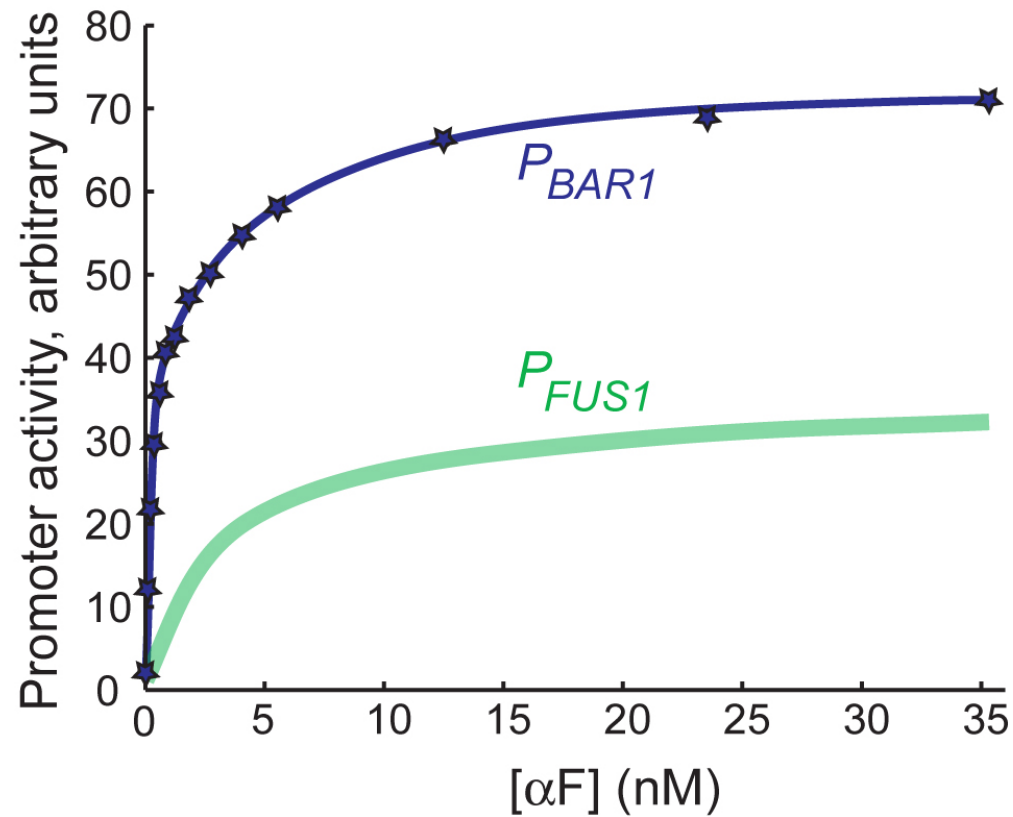
Gene induction as a surrogate for $[\alpha \text{ factor}]$



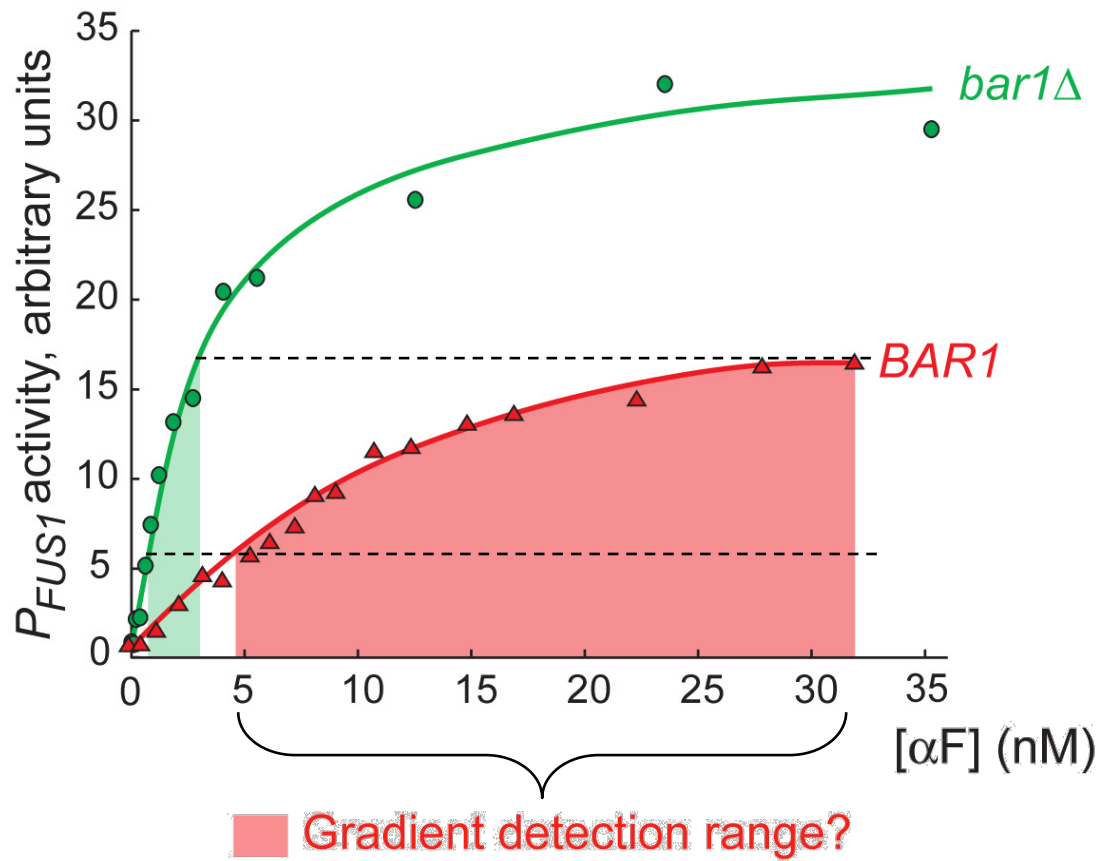
A scheme to control α factor concentration



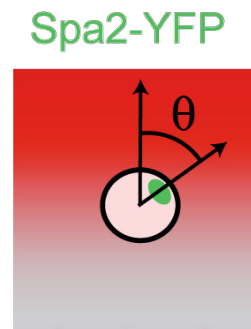
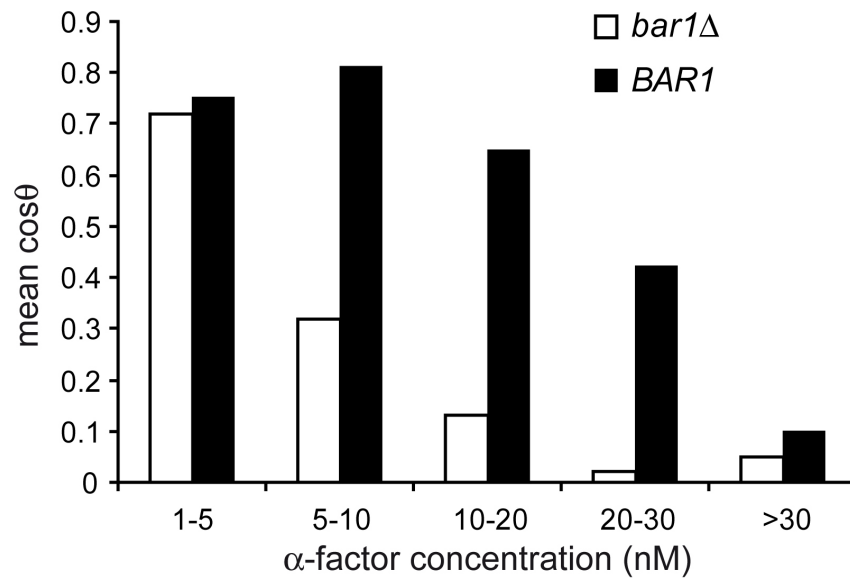
The *BAR1* promoter is regulated



Bar1 controls α factor concentration at the cell surface



BAR1 cells detect gradients robustly



Thanks

Chinlin Guo
Matthieu Piel
Joana Sa

Noa Rapaport
Naama Barkai

Justin Jiang
George Whitesides

