Engineering Yeast to Play Conway's Game of Life
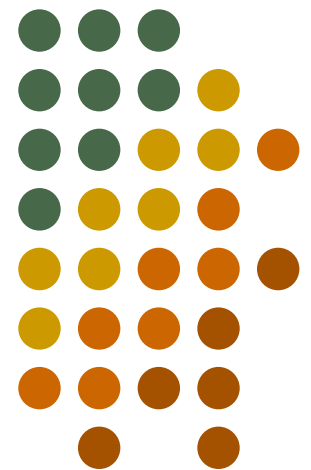
Elizabeth Bendler[1]

Ming-Tang Chen[2]
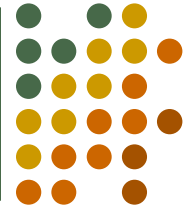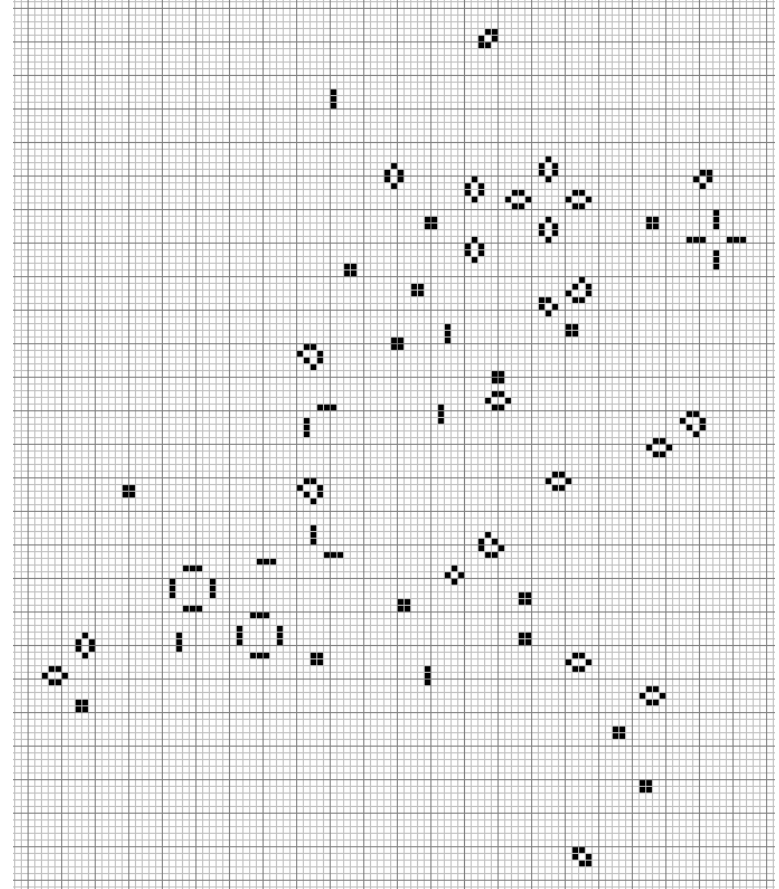
Ron Weiss[2]

03/12/2006
[1]Drew University, [2]Princeton University

Motivation

- **Behavioral study**
  - Test boundaries of what may be predictable in biological systems
  - Compare behavior between implementations
- **Applications**
  - Population control for fermentation processes
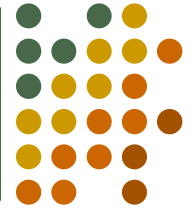 - Development in higher eukaryotes (e.g. tissue engineering, organ regeneration)
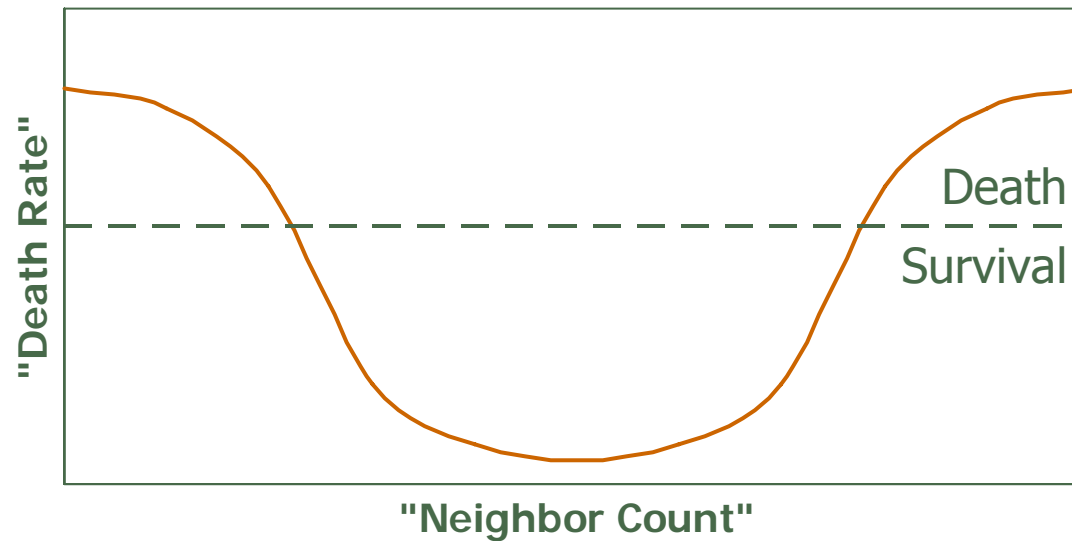
What is Conway's Game of Life?

- Infinite grid
- Four simple rules
  - <2–loneliness–death
  - 2 or 3–"happy"–survival
  - >3–overcrowded–death
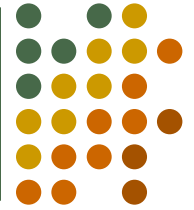 - Empty location bounded by 3 neighbors–birth
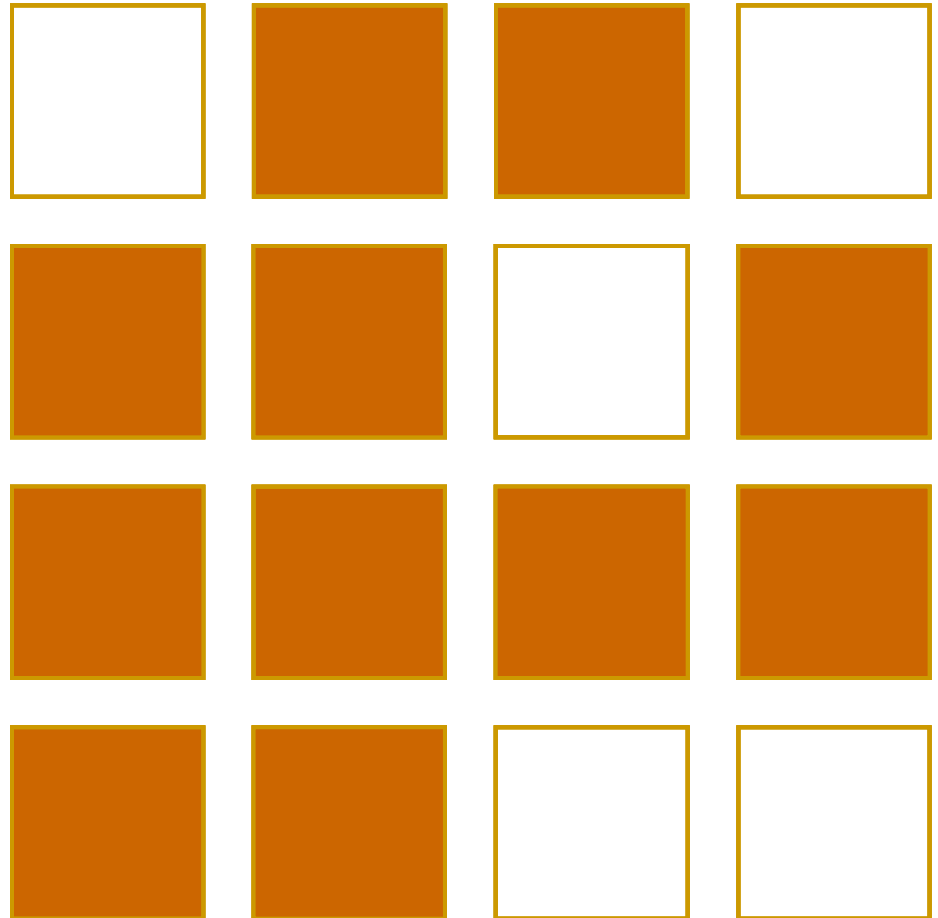
Design goals

- Artificial cell-cell communication allows yeast to detect nearby population densities
- Killing mechanism to control cell lysis/death
- Population density-band detect circuit
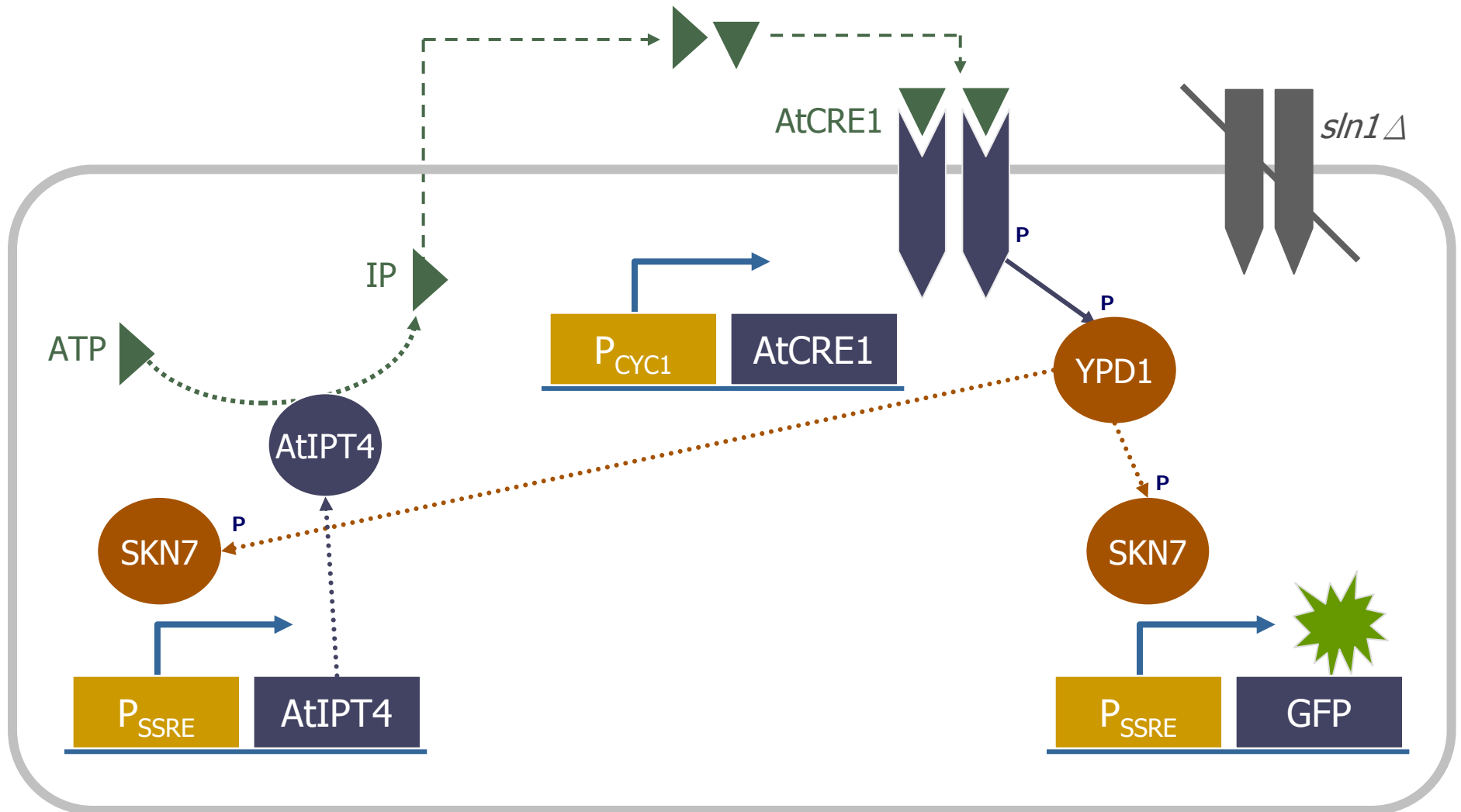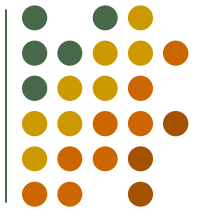
Non-deterministic pattern formation

- Stochastic spatiotemporal simulations
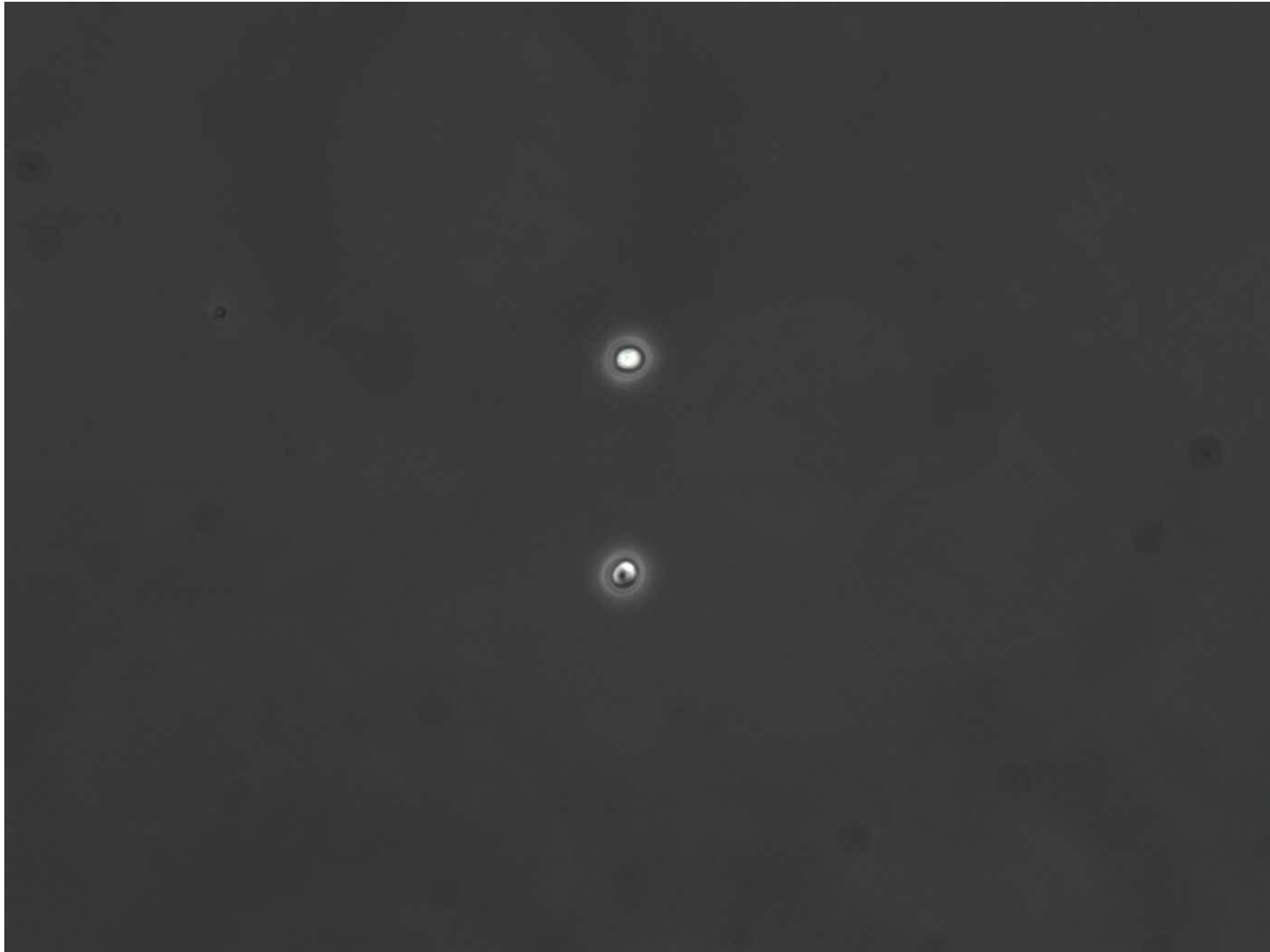- Same initial conditions
- Global behavior appears to be unpredictable
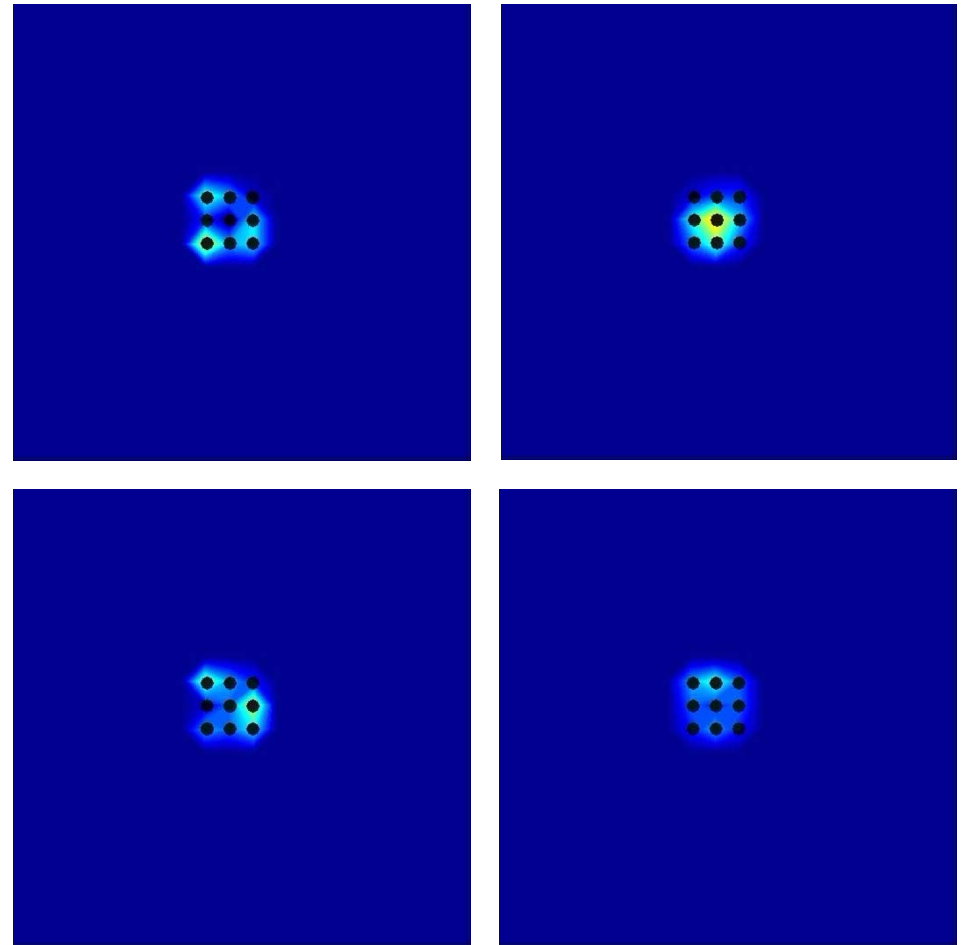
Simulations: Subhayu Basu

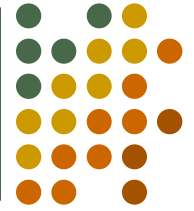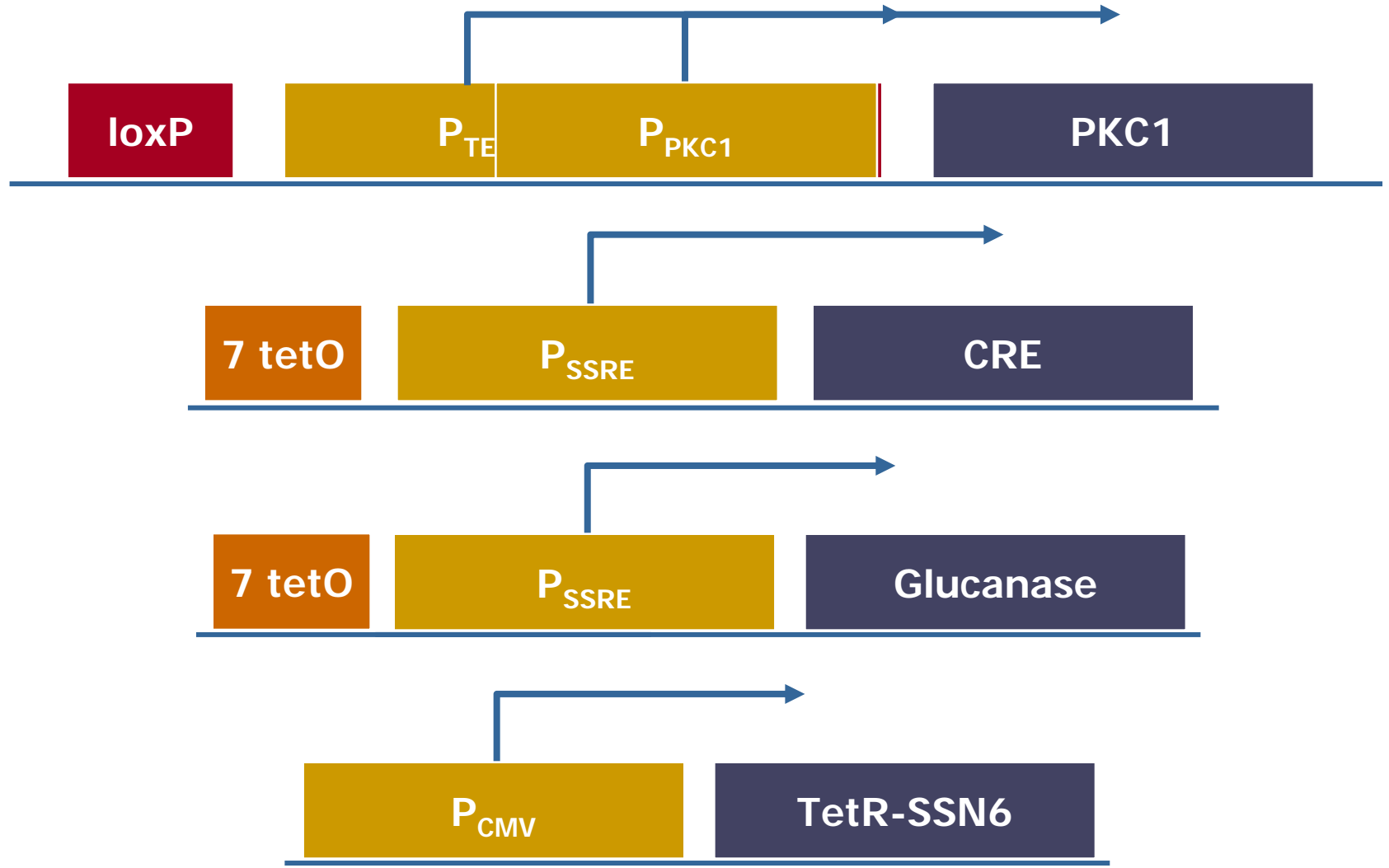# Artificial quorum sensing in yeast
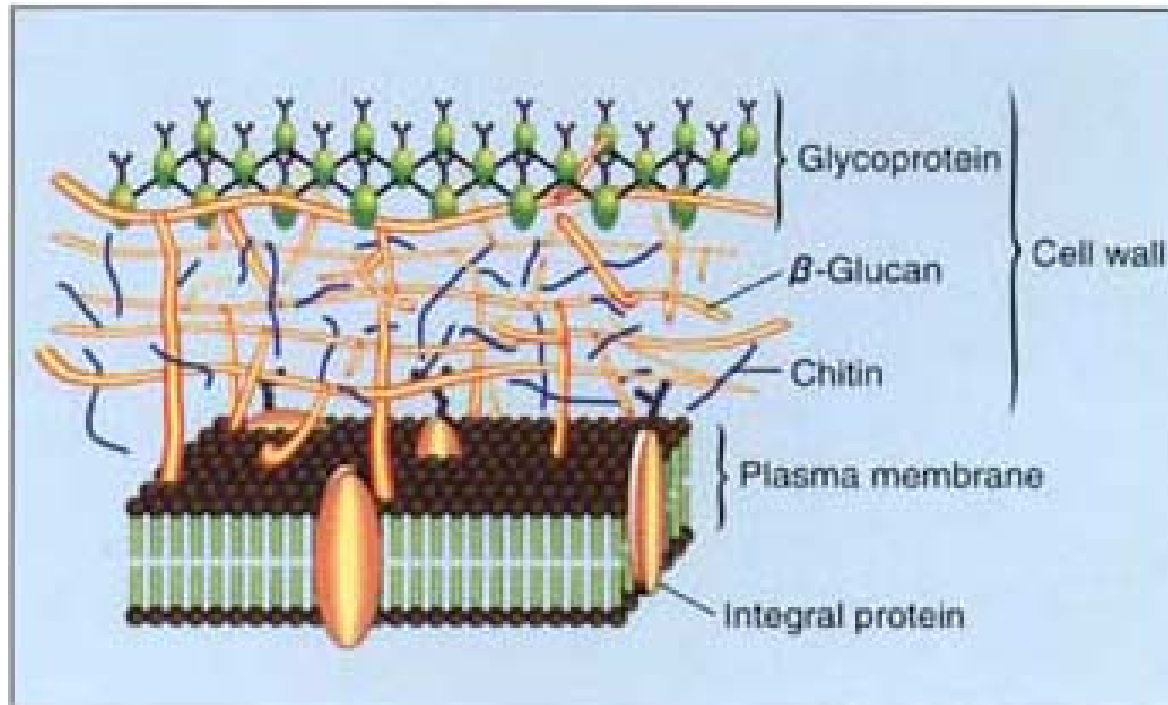

Chen & Weiss, 2005 NBT
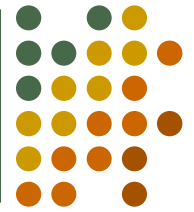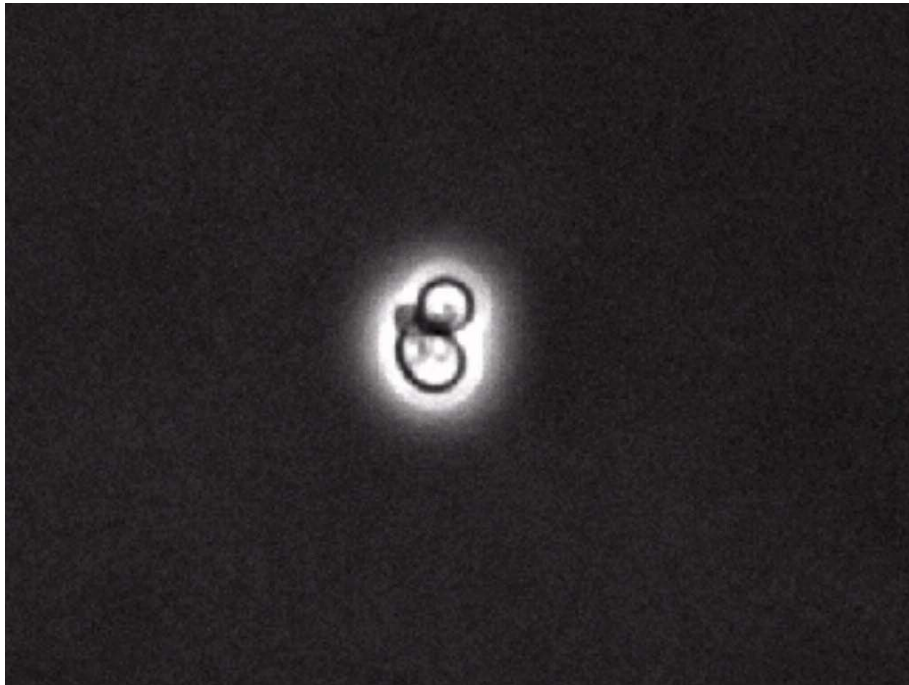
Quorum sensing

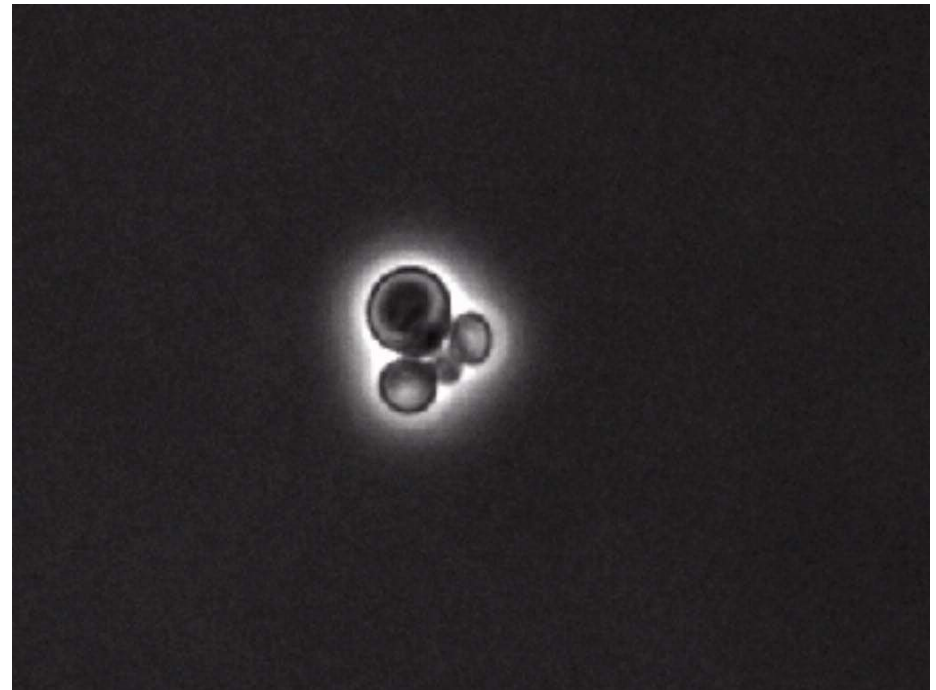# High threshold design

Diagram of yeast cell wall

Demonstration of high threshold

Cell death

Lysis

Demonstration of high threshold
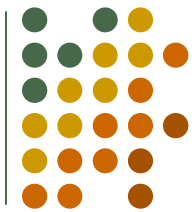
Negative control w/o IP
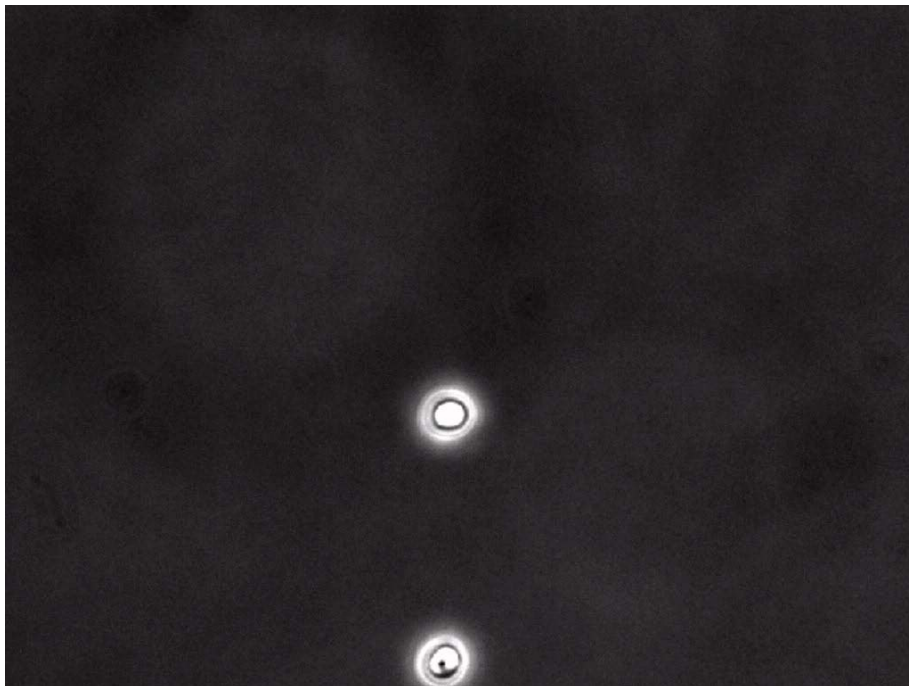
Positive control w/ IP

Demonstration of high threshold

Growth over a two day period
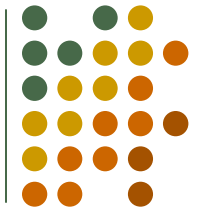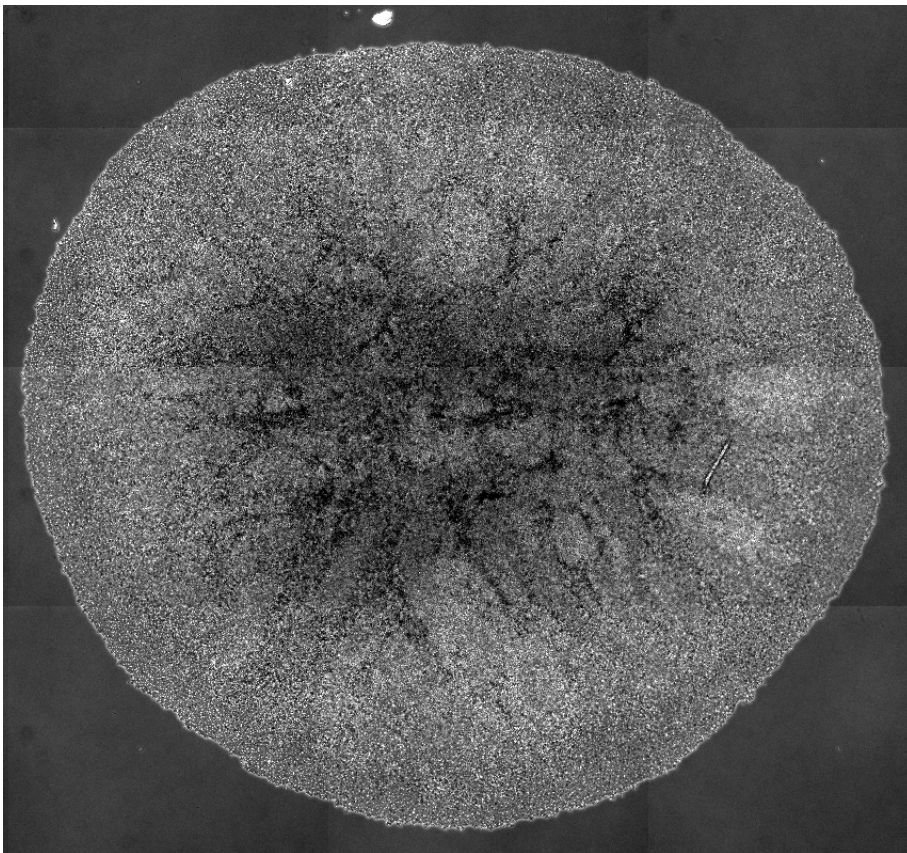
Negative control w/o IP

Positive control w/ IP
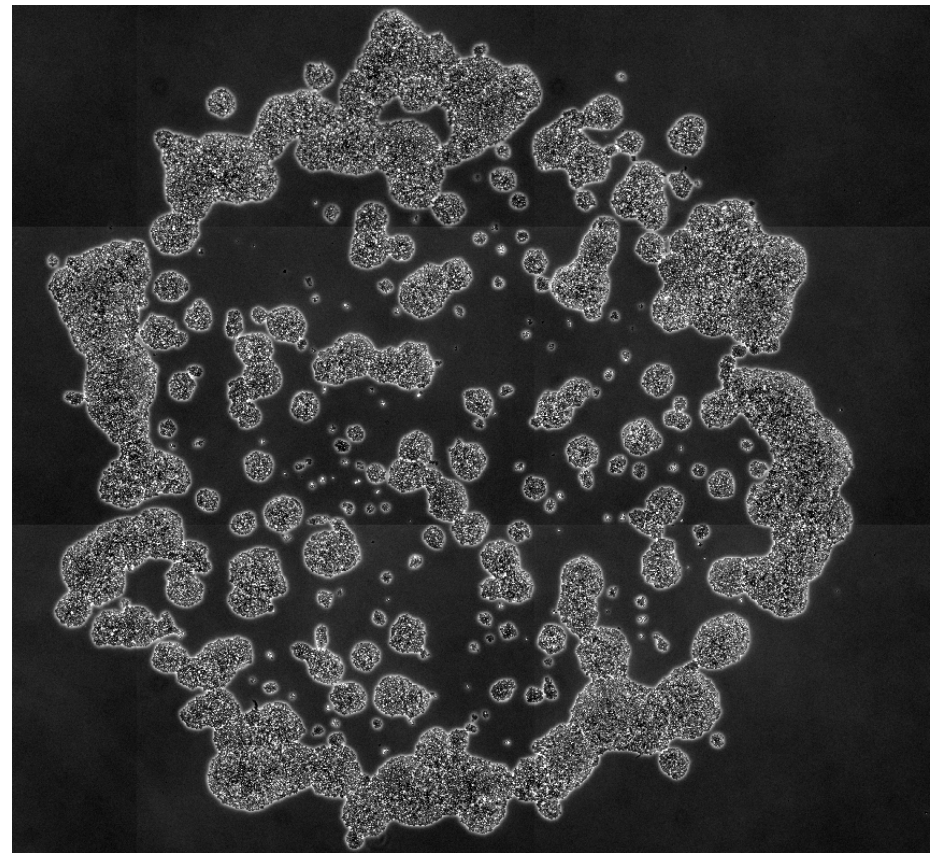
Future work–low threshold

loxP	P$_{TEF}$	loxP	PKC1

7 tetO	Gal1 UAS (4 Gal4 binding sites)	8 LexA	TATA	CRE

P$_{TR\text{-}SSRE}$	LexA-SSN6

[CRE] vs [IP]
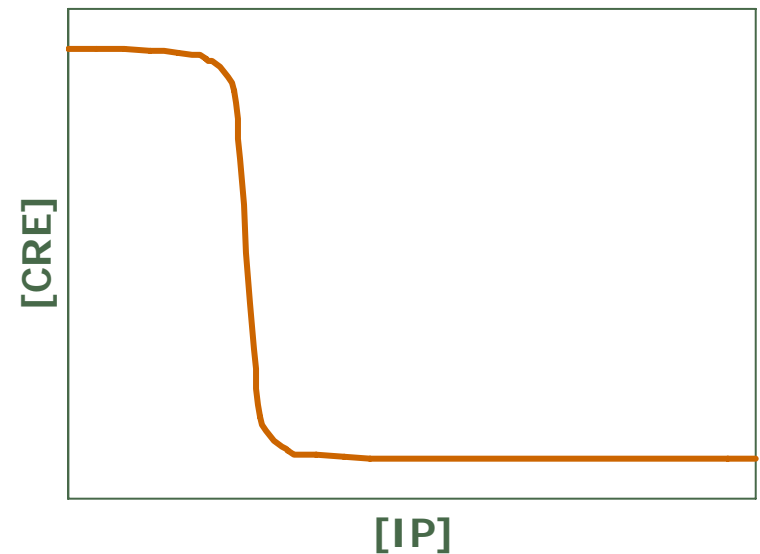
Future work (cont'd)
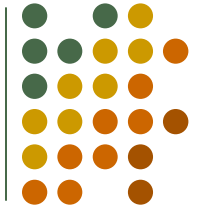
- System integration
  - Stability
    - Adjust plasmid copy number to fine tune system dynamics
    - Possibility of integrating more elements into chromosome
- Killing efficiency
  - $P_{SSRE} \rightarrow P_{TR\text{-}SSRE}$
    - Elevated expression levels
  - Change expression levels of glucanase

Conclusions

- Quorum sensing strain of yeast
- Self-initiate death at sufficiently high population densities
- Develop a low threshold system
- More efficient cell death

Acknowledgements

- Institute for Biological Engineering
- iGEM and MIT
- Professor Ron Weiss
- Members of Weiss Lab
  - Professor Yoram Gerchman
  - Subhayu Basu
  - Sairam Subramanian

Complete circuit design

| P~CMV~ | TetR-SSN6 |

| P~TR-SSRE~ | LexA-SSN6 |

| loxP | Leu | P~GPD~ | loxP | PKC1 |

| 7 tetO | P~TDH3-UAS~ | LexA site | P~GAL1-TATA~ | CRE |

| 7 tetO | P~SSRE~ | CRE |