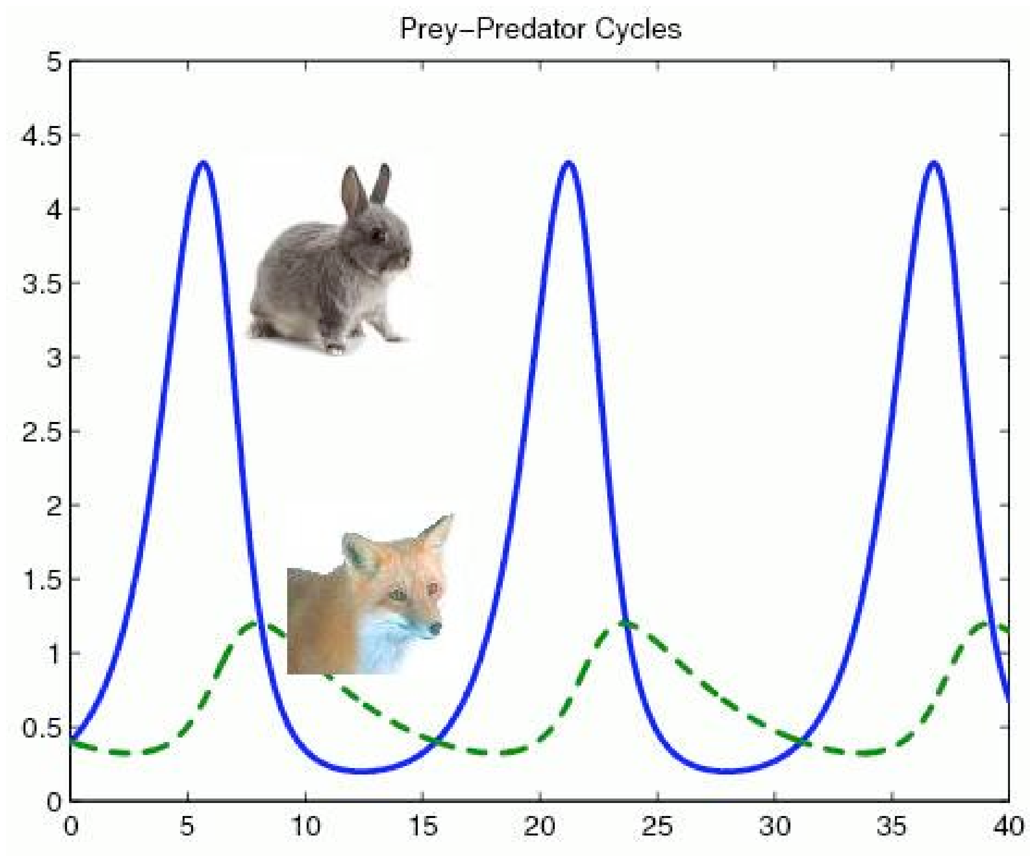
A synthetic E.coli predator-prey ecosystem

FK Balagaddé, H Song, J Ozaki,
CH Collins, M Barnet, FH Arnold,
SR Quake, L You
Molecular Systems Biology
4:187 (2008)

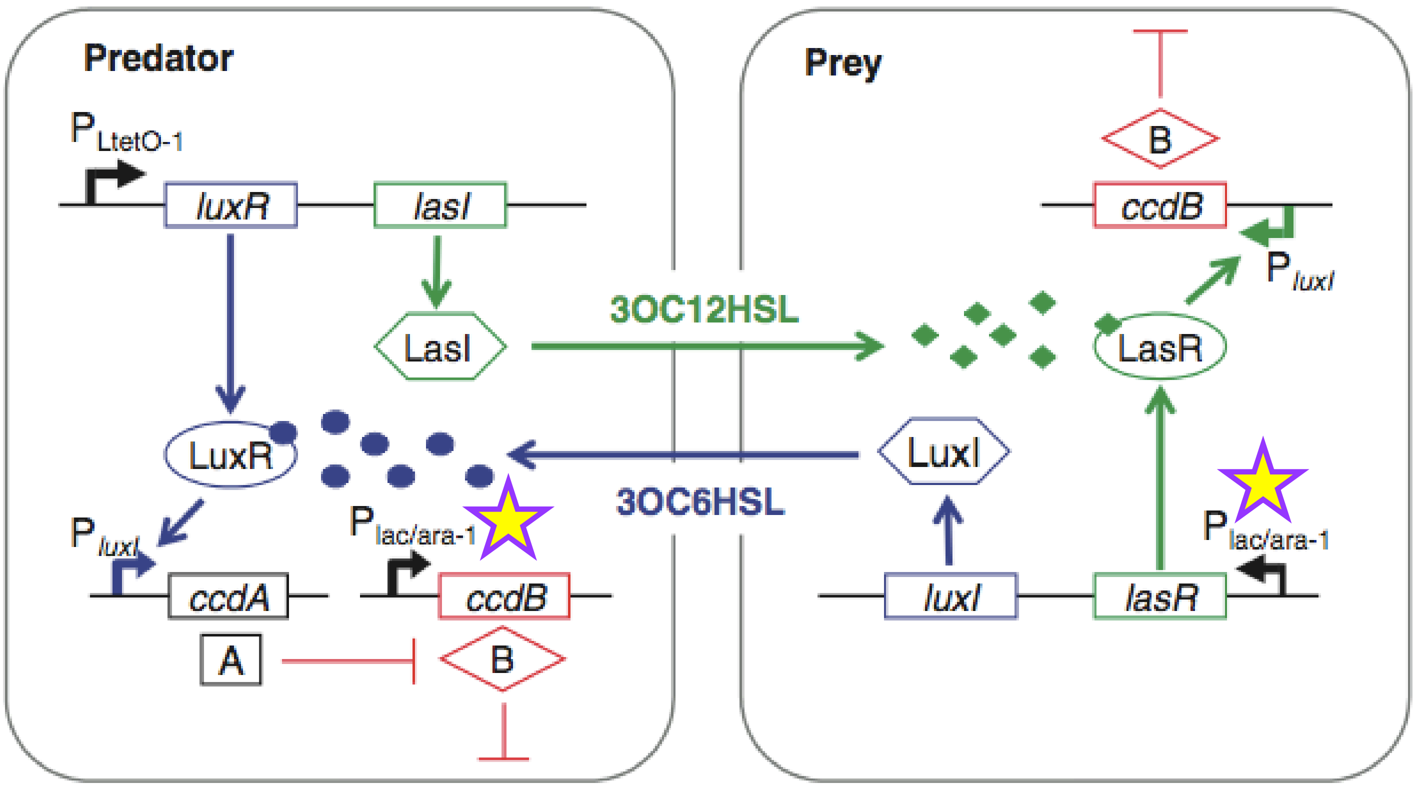
Presented by Kelly Drinkwater
20.385 Week 13
May 5, 2010

Predator-prey oscillation



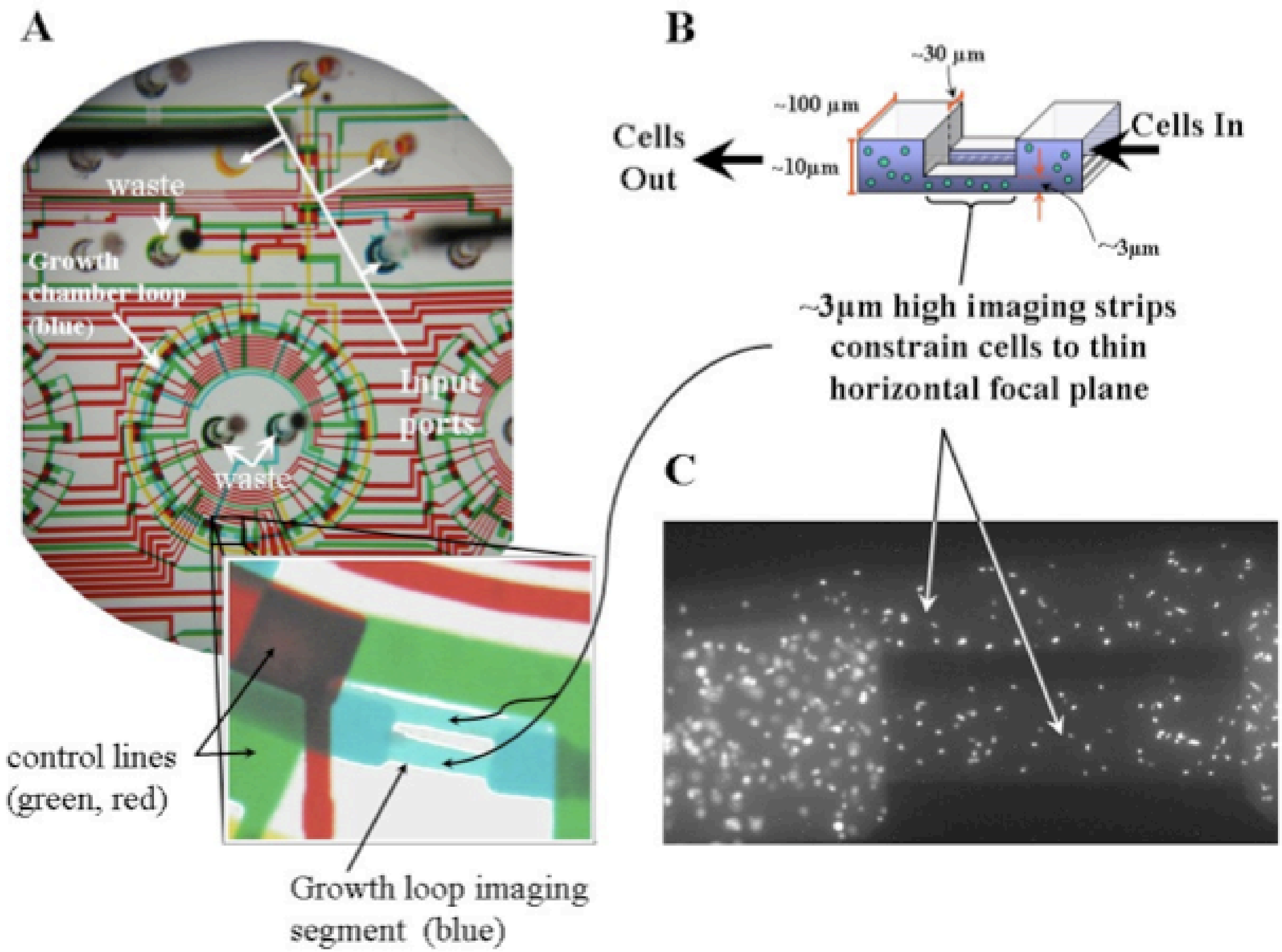
Frank Hoppensteadt. "Prey-Predator Cycles".
<http://www.scholarpedia.org/article/Predator-prey_model>

Translating into E.coli using AHL signals

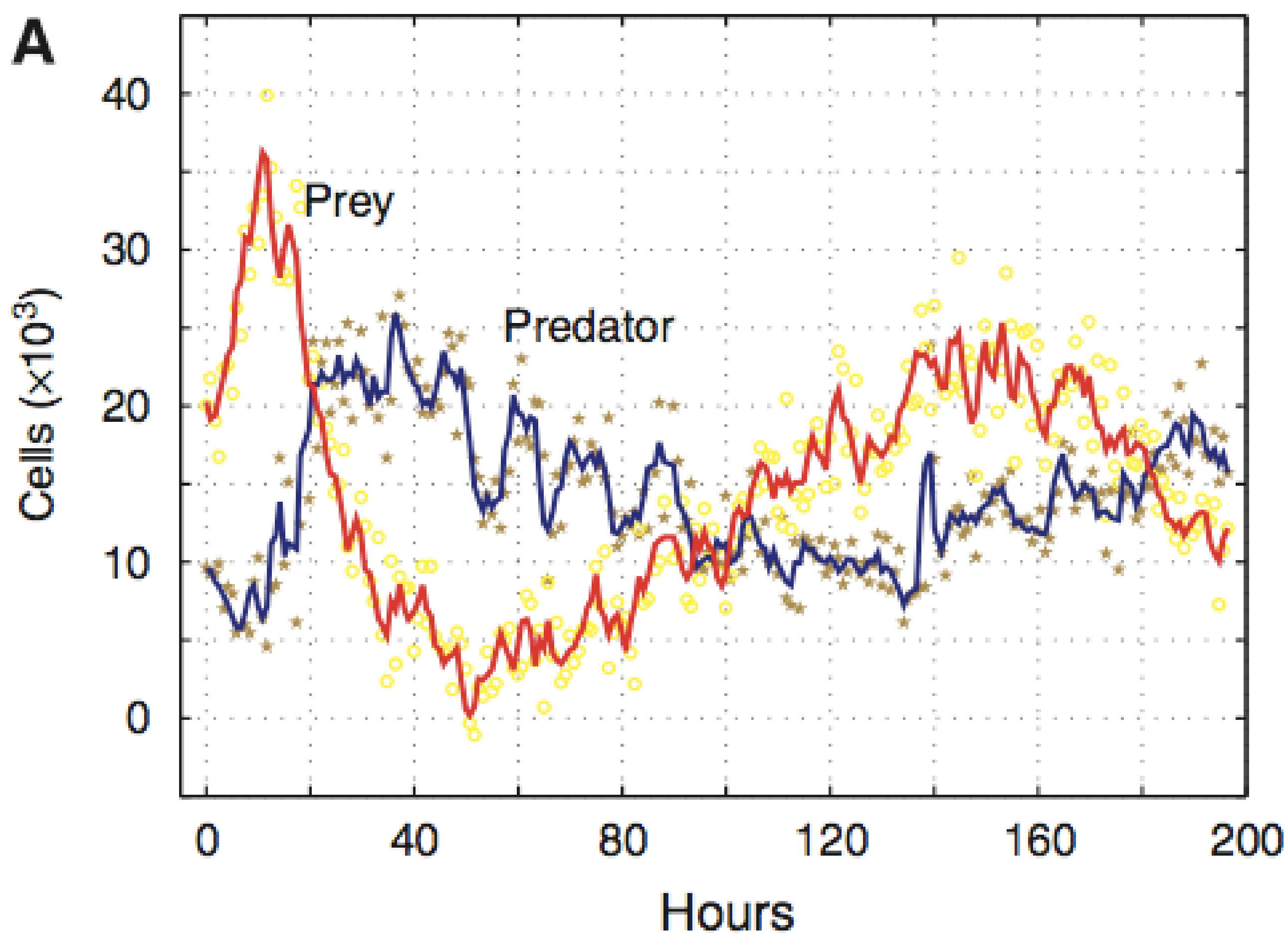


Note IPTG induction of cooperation at $P_{lac/ara-1}$ ☆

Microchemostats

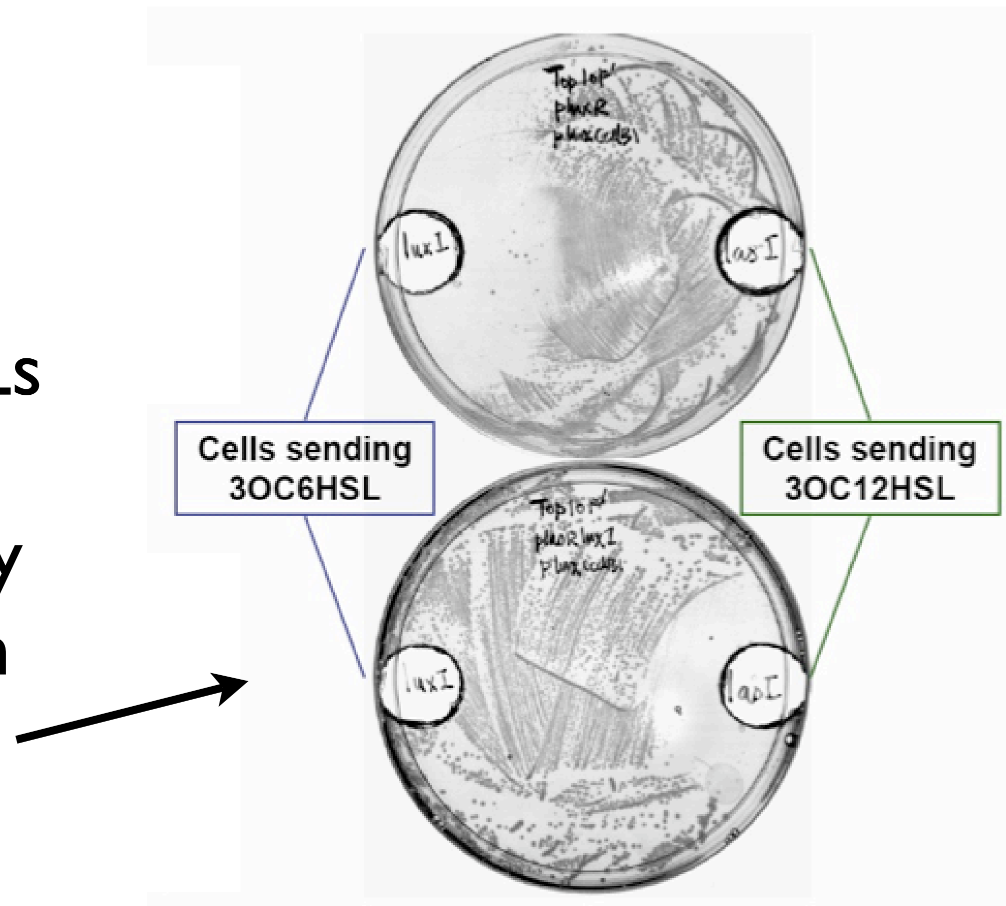


It oscillates!



First round of assumptions

- Logistic cell growth
- First-order decay
- Constant synthesis of AHLs
- Simplified kinetics
- No basal promoter activity
- Ignore diffusion in medium
- No crosstalk AHL1/AHL2



Quasi-steady-state assumptions

- mRNA, LuxR, LasR, and ccdB are steady
- QSSA really means "changes fast compared to gene regulation & cell growth"
- Further QSSAs changed qualitative behavior, killed oscillation completely.

Final simplified diffEQ model

$$\frac{dc_1}{dt} = k_{c1}c_1\left(1 - \frac{c_1 + c_2}{c_{max}}\right) - d_{c1}c_1\frac{K_1}{K_1 + A_{e2}{}^{\beta}} - Dc_1 + \varepsilon \cdot \xi$$

$$\frac{dc_2}{dt} = k_{c2}c_2\left(1 - \frac{c_1 + c_2}{c_{max}}\right) - d_{c2}c_2\frac{A_{e1}{}^{\beta}}{K_2 + A_{e1}{}^{\beta}} - Dc_2 + \varepsilon \cdot \xi$$

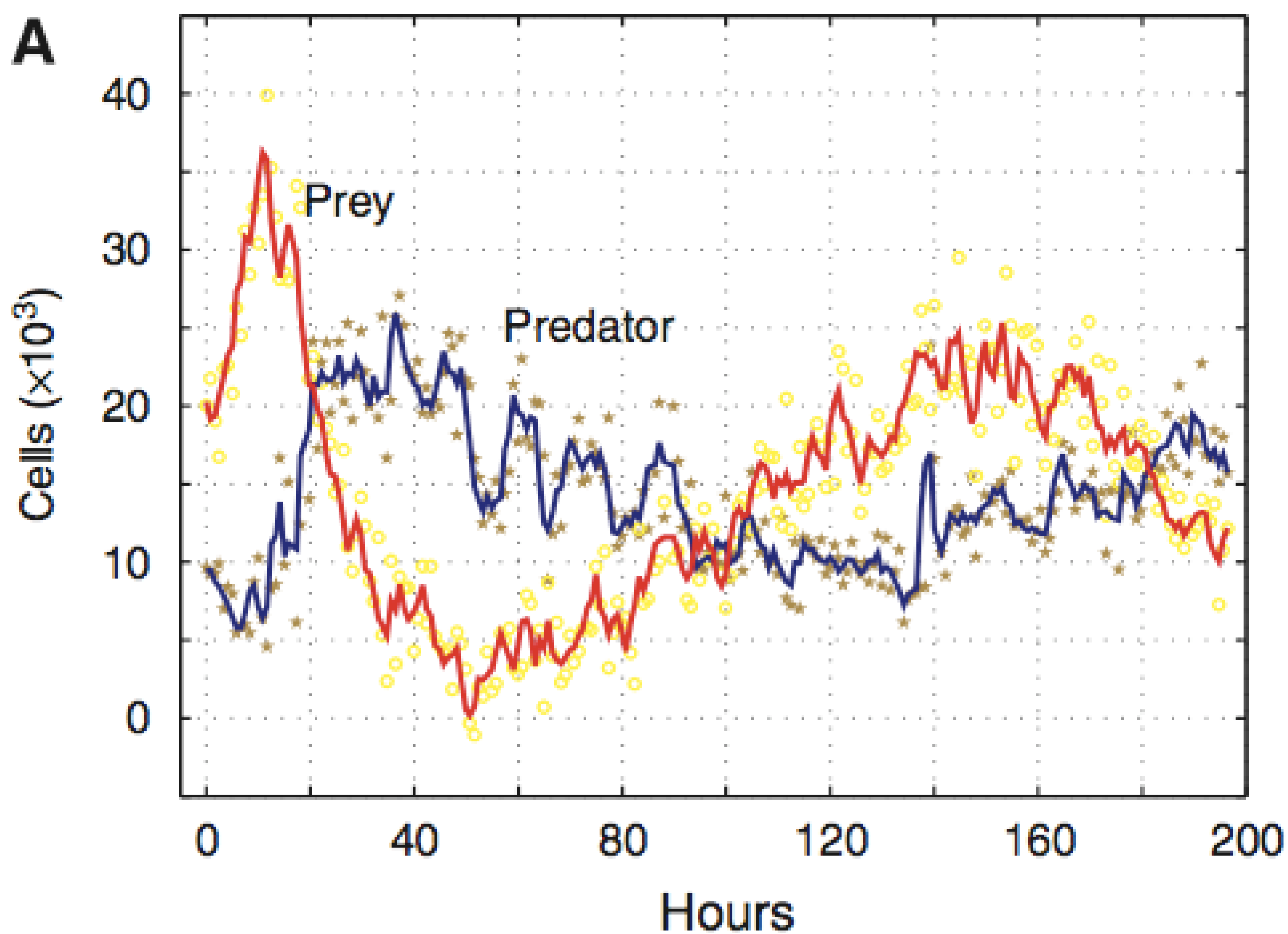
$$\frac{dA_{e1}}{dt} = k_{A1}c_1 - (d_{Ae1} + D)A_{e1} + \varepsilon \cdot \xi$$

$$\frac{dA_{e2}}{dt} = k_{A2}c_2 - (d_{Ae2} + D)A_{e2} + \varepsilon \cdot \xi$$

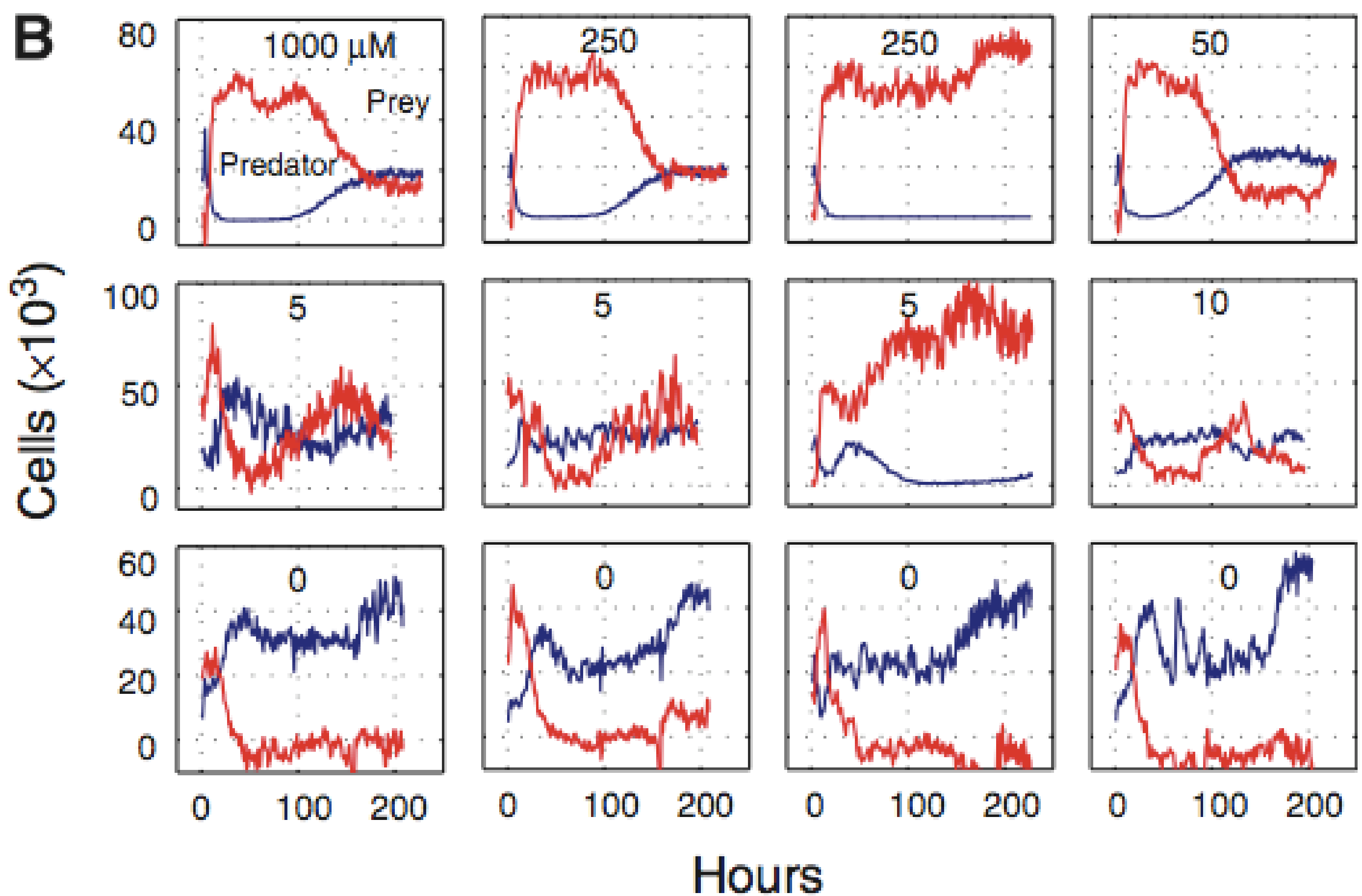
Noise terms

- c_1 = predators
- c_2 = prey
- A_{e1} = predator signal
- A_{e2} = prey signal
- d_{ci} = cell death rate const
- K_1 = regulator synthesis
- β = cooperativity
- D = dilution rate
- k_{Ai} = signal synthesis
- d_{Aei} = signal decay

Recall...

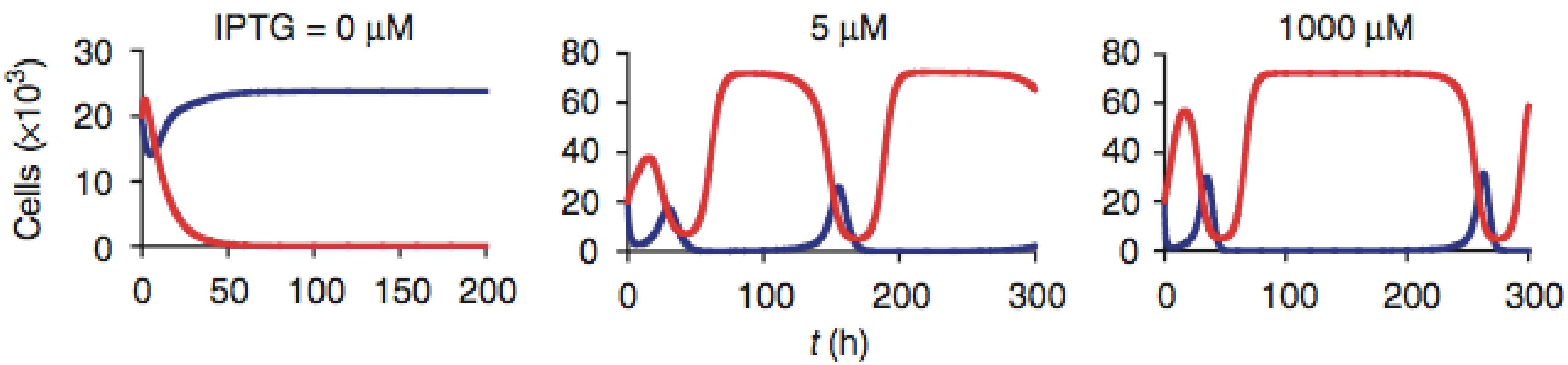


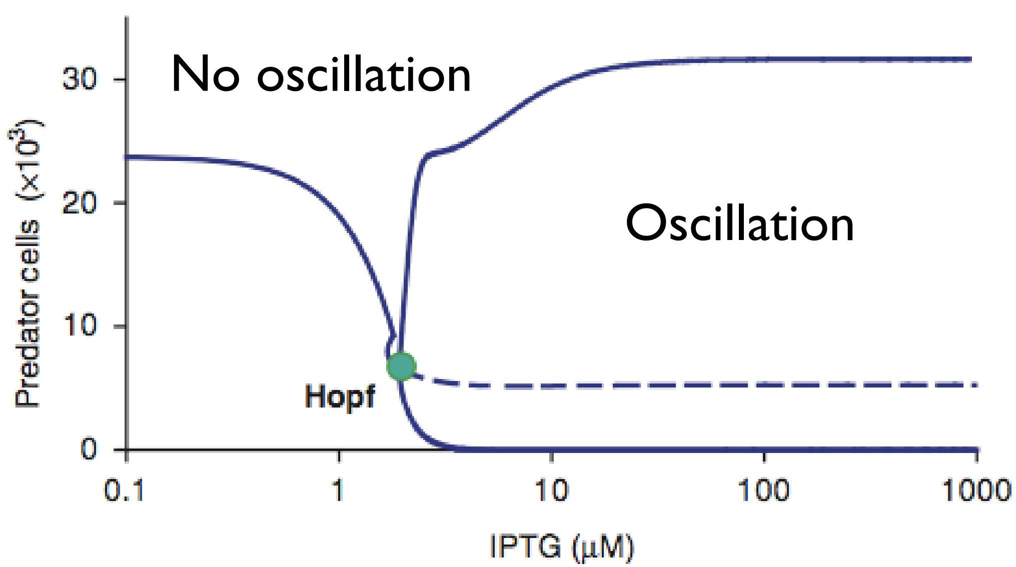
IPTG changes system behavior



Modeling effect of IPTG

(Predator, Prey)





Hopf bifurcation: system eigenvalue crosses imaginary axis, qualitative behavior change

System is not stable in cells

- Hard to avoid: ccdB exerts strong evolutonary pressure
- Makes time-courses short and messy due to microchemostat
- Lesson: Kill-switch design is hard

Contributions

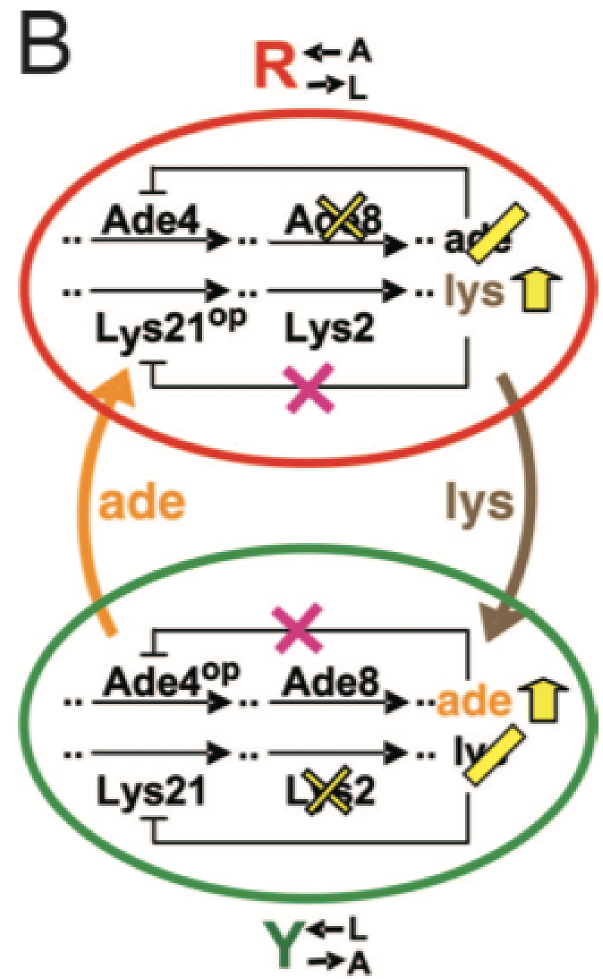
- Constructed working predator-prey system
- Pioneered use of microchemostat
- Modeled system behavior under different conditions

Synthetic cooperation in engineered yeast populations

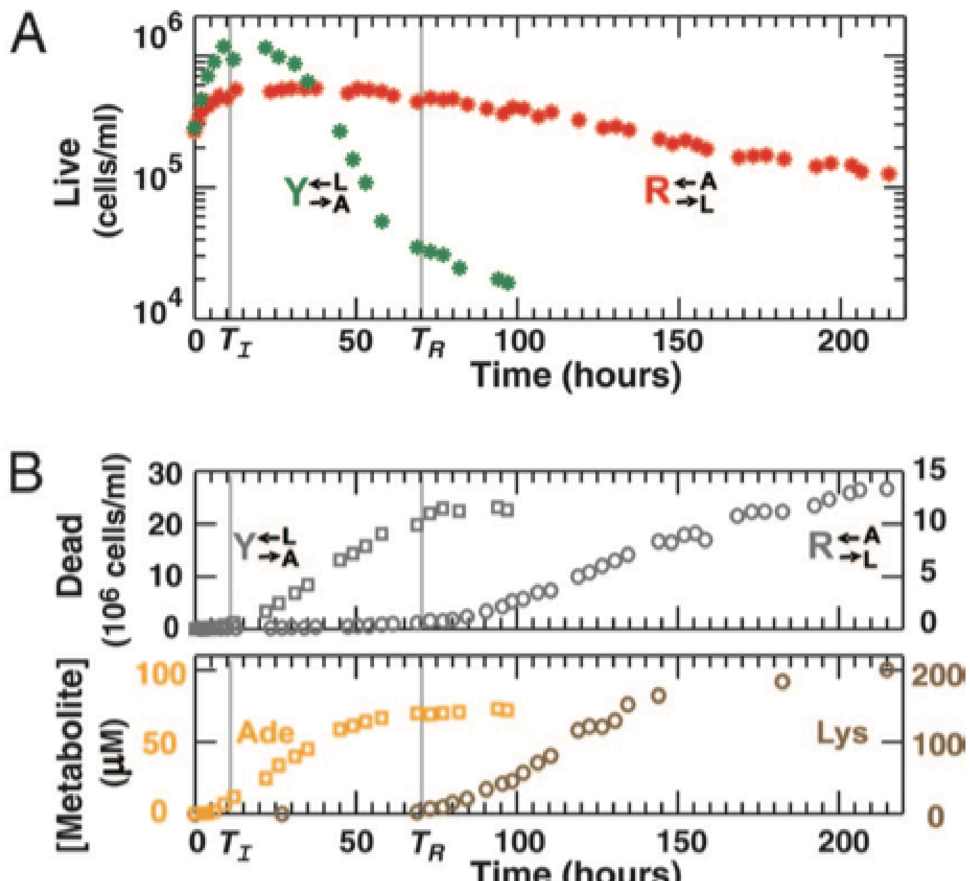
W Shou, S Ram, JMG Vilar
PNAS 104:6 (2007)

CoSMO

- Big contribution: STABILITY
- Auxotrophy-based codependence (recommended to my 20.20 group)
- Useful basis for many kinds of cooperative systems

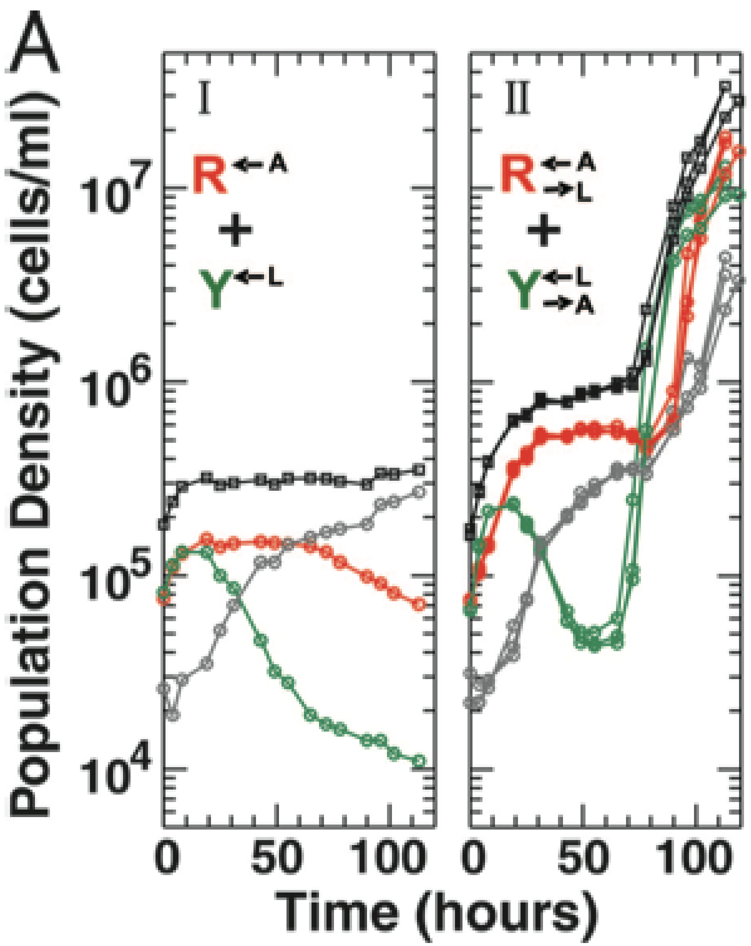


Problem: nutrients release w/ cell death



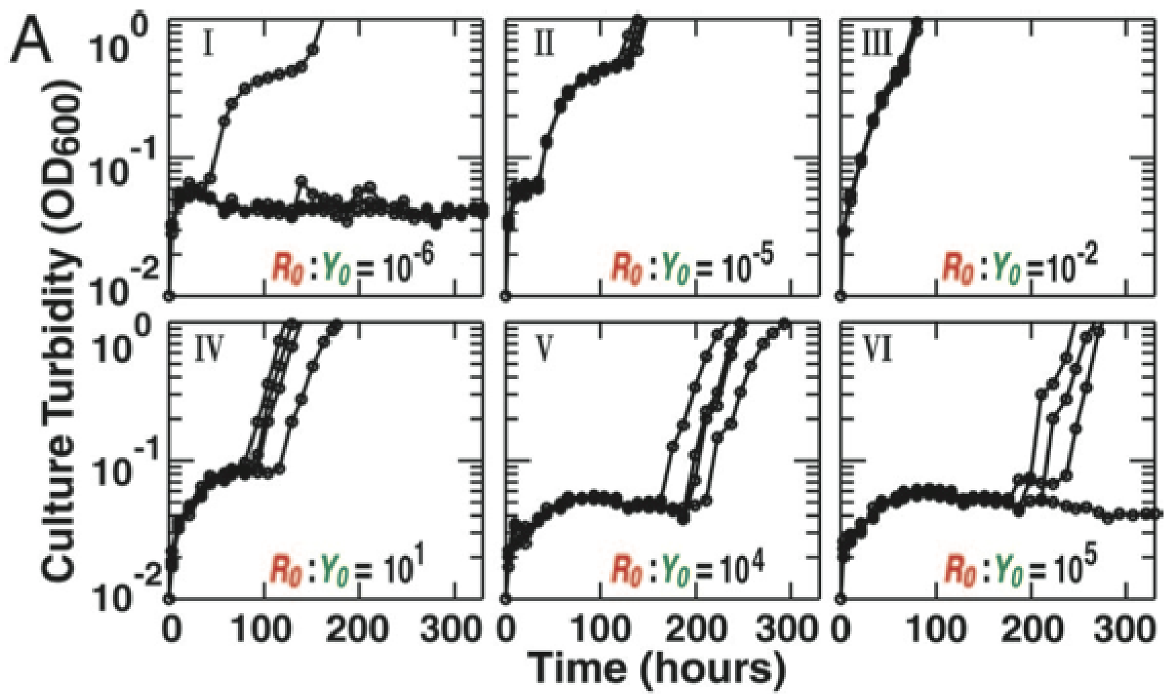
Why not export metabolites??

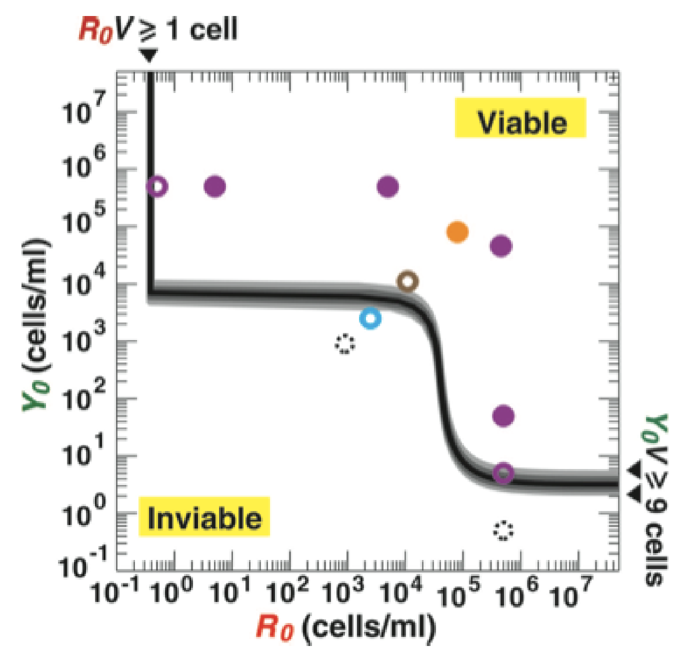
But it still seems to work



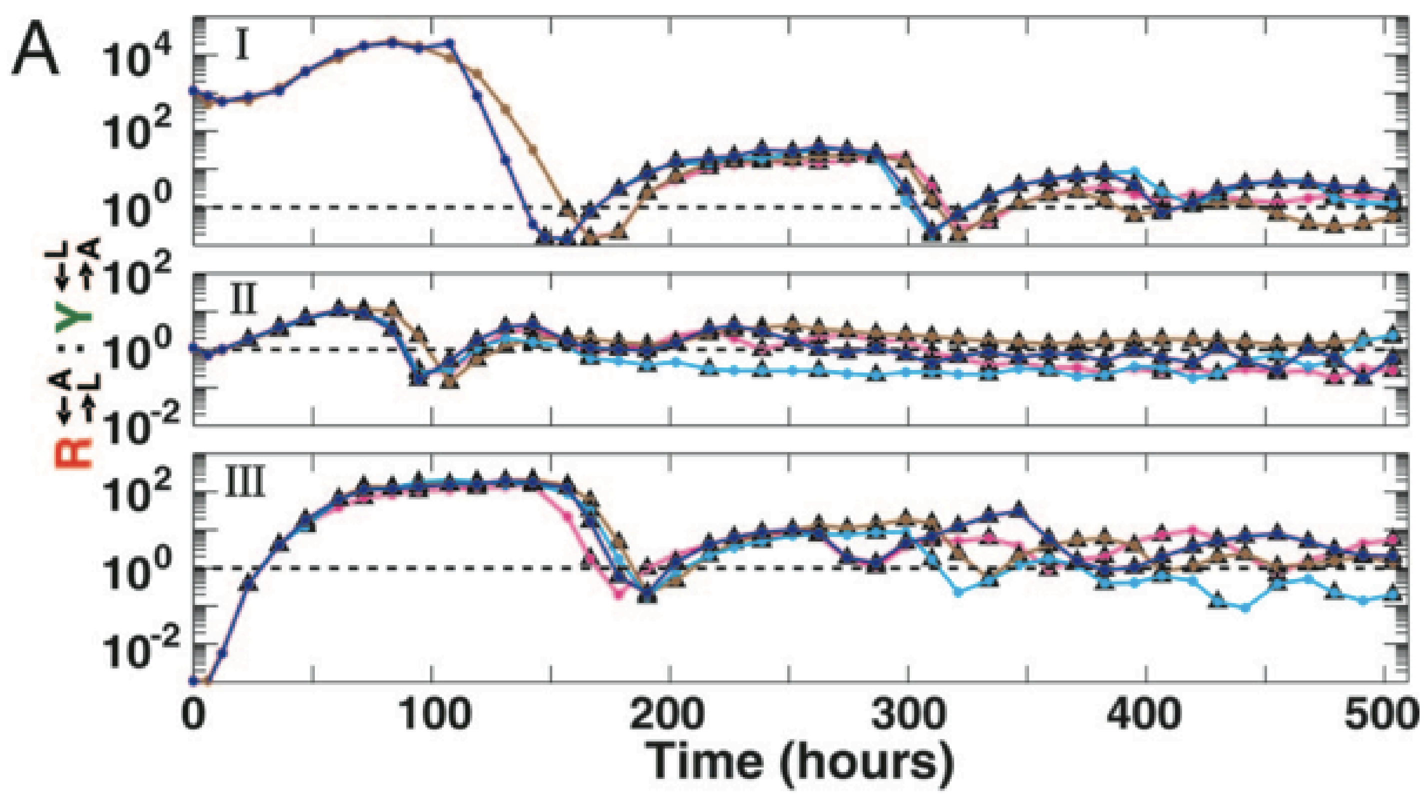
+ overproduction of Ade/Lys

Viability depends on initial conditions



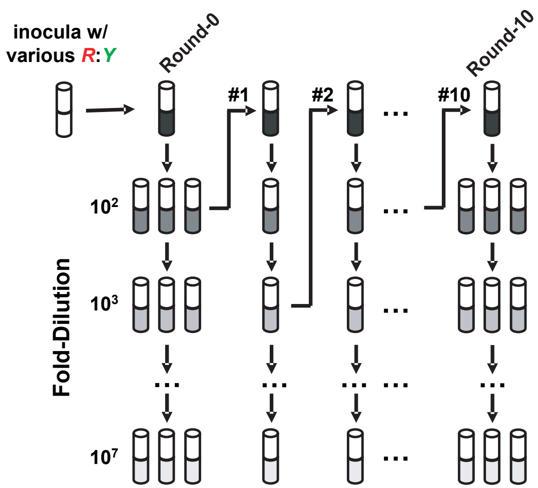


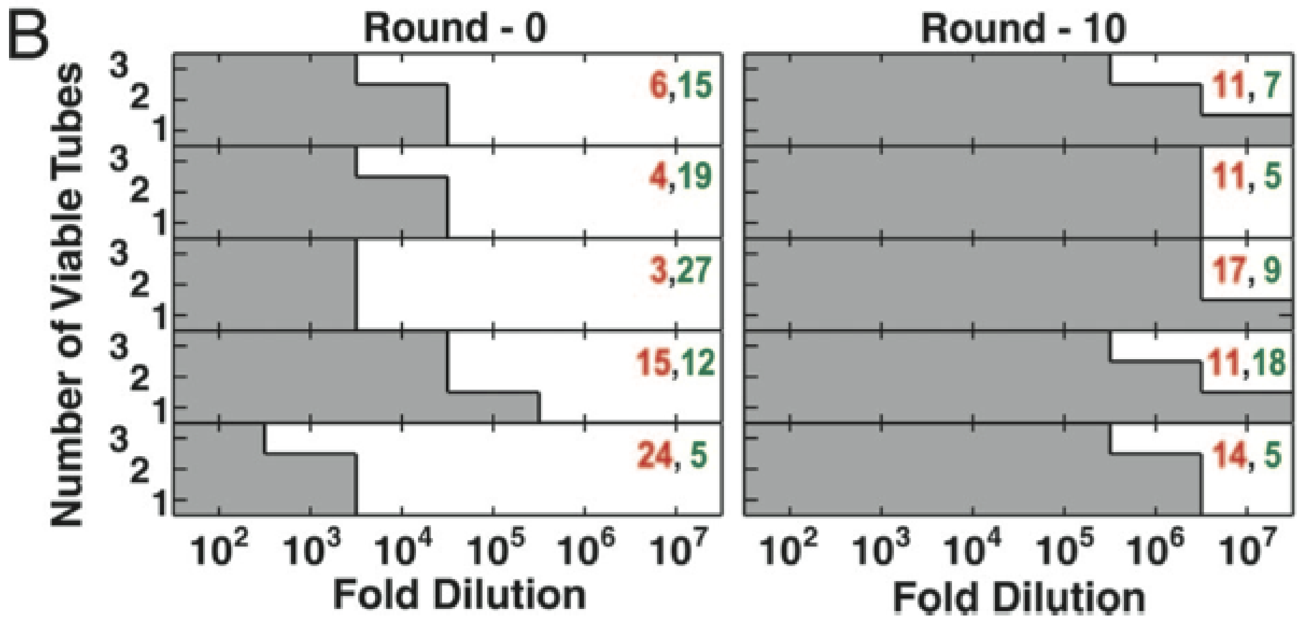
Population ratio stabilizes near 1:1



Range:
~1:5 - 5:1

Increased robustness over long term





How? Evolved better metabolite sharing?

Contributions

- Built symmetrically cooperating yeast system
- Stable over the long term
- Derived constraints on viable initial conditions
- Demonstrated convergence to a small population ratio

Considerations for biofuels project

- Use auxotrophy-based codependence instead of inducer-based (evolutionarily stable)
- Tune final population ratio for best nutrient recycling
- Take care with initial conditions, possibly supplement cultures at first
- Self-regulation strictly necessary?
  (Probably still a good idea)