Day 2

A brief intro to social dilemmas ... and how bacteria and humans solve them

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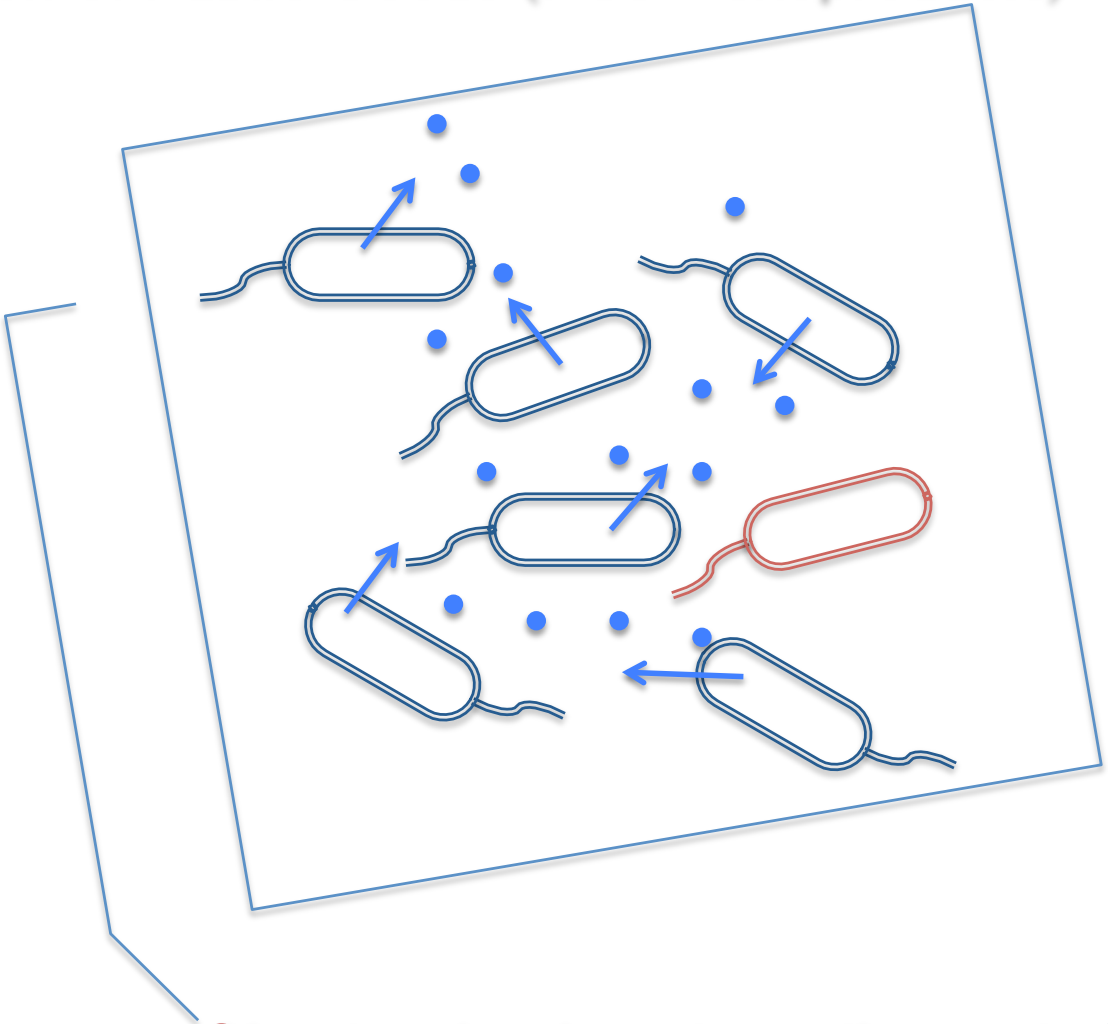
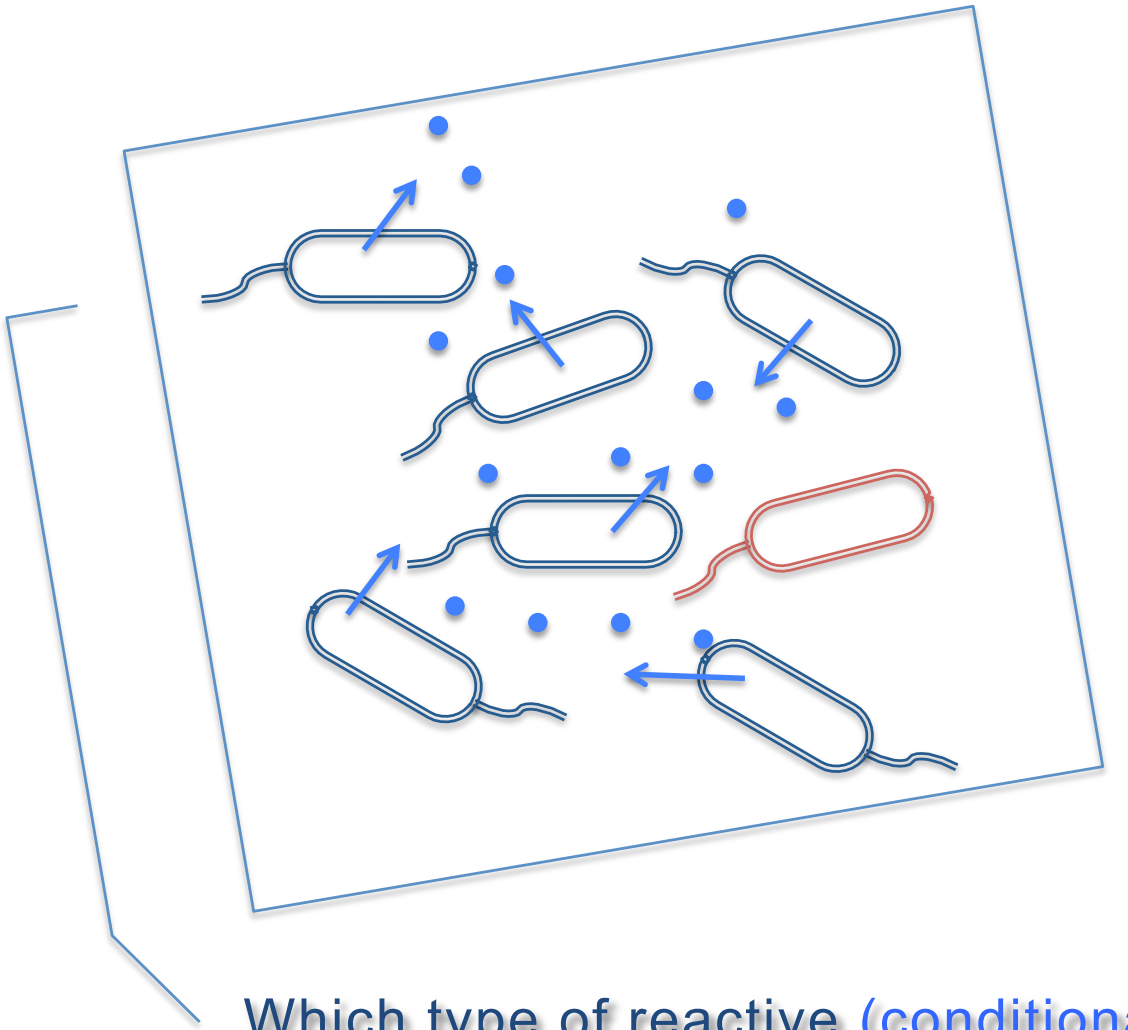
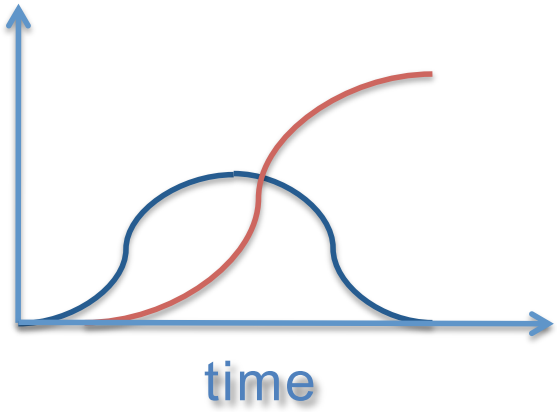
The most common form of social behavior in microbes is the production of Public Goods (PGs – exoproducts)



Cheats who do not pay the cost of producing PGs can benefit of that produced by other cells





Which type of reactive (conditional) strategies are implemented by bacteria?

Phenotypic plasticity in response not only to a ecological but to a social environment

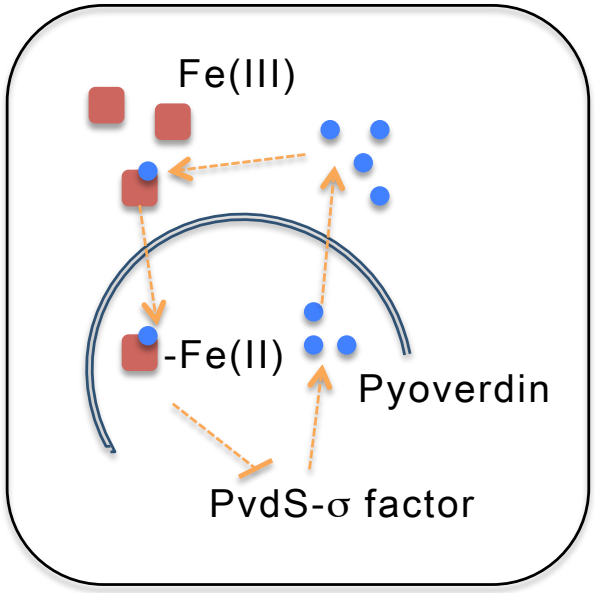
Conditional cooperation in *Pseudomonas aeruginosa*

The Biology

-most iron in the environment is in the insoluble Fe(III) form

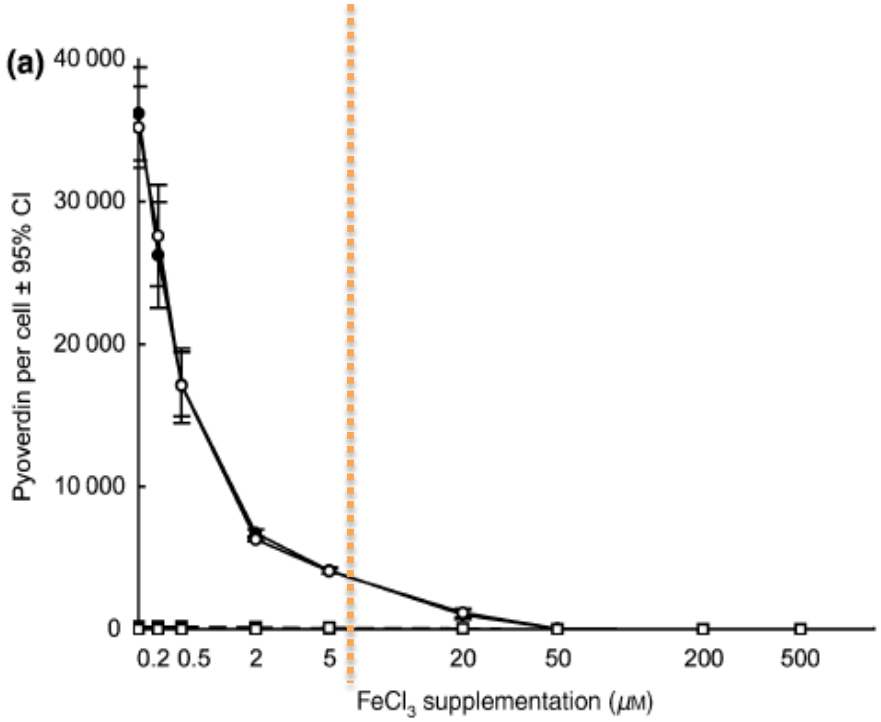
-microbes release siderophores to scavenge iron (forming soluble complexes that can be transported through the membrane)

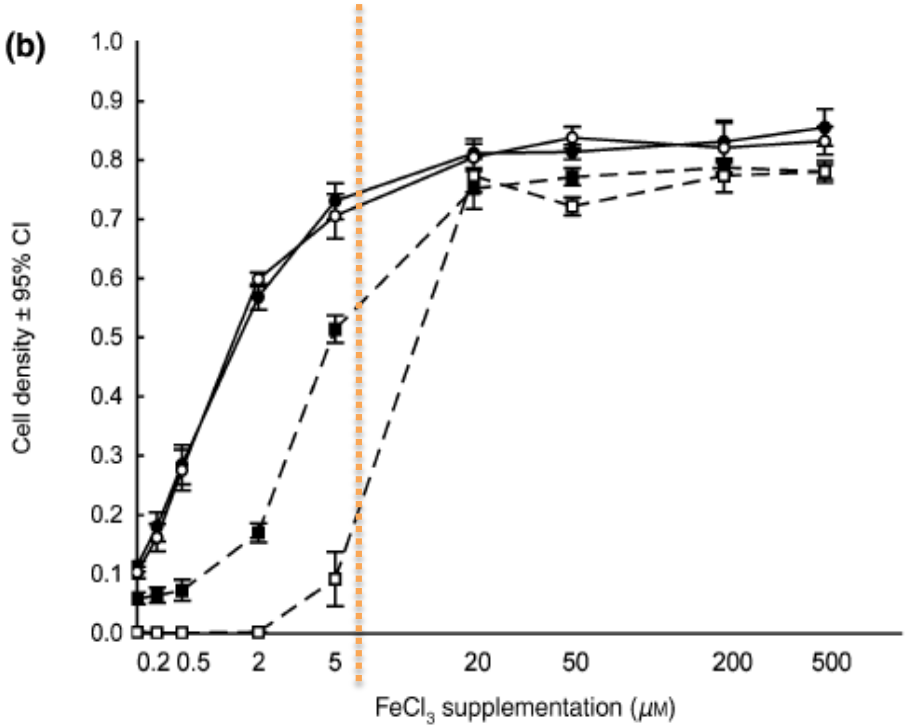
-pyoverdin production is a cooperative behaviour



-facultative production of pyoverdin (proximate mechanism)

Cells adjust pyoverdin production in response to iron availability





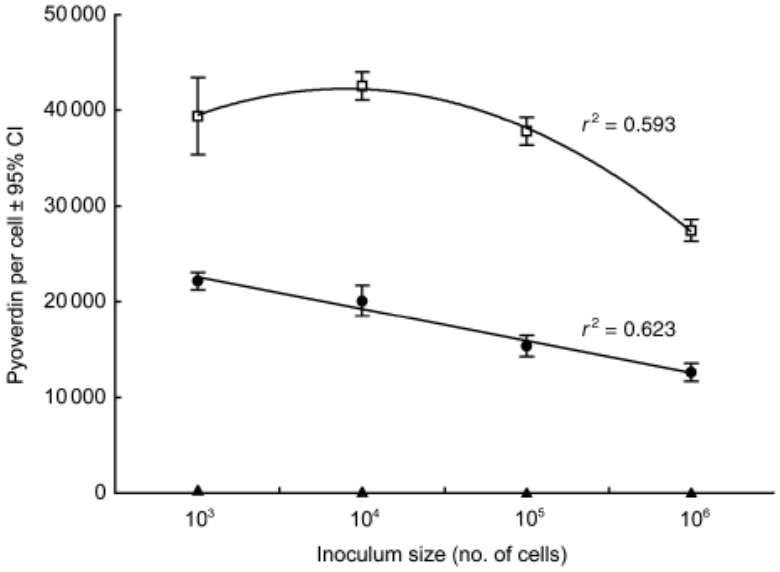
-pyoverdin fluoresces green

-adding different quantities of $FeCl_3$

- ● wild-type
- ○ pch- (secondary low-affinity syderophore)
- ■ pvd- (no pyoverdin)
- □ pvd-/pch-

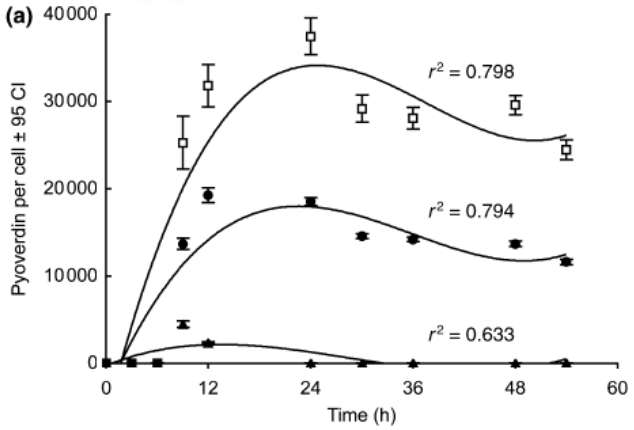
Kümmerli R. *et al*, J. Evol. Biol. 22 (2009) 589

Cells adjust pyoverdin production in response to cell density



wild-types in 0μM (squares) 0.5μM (circles) or 50μM (triangles) environments

pyoverdin



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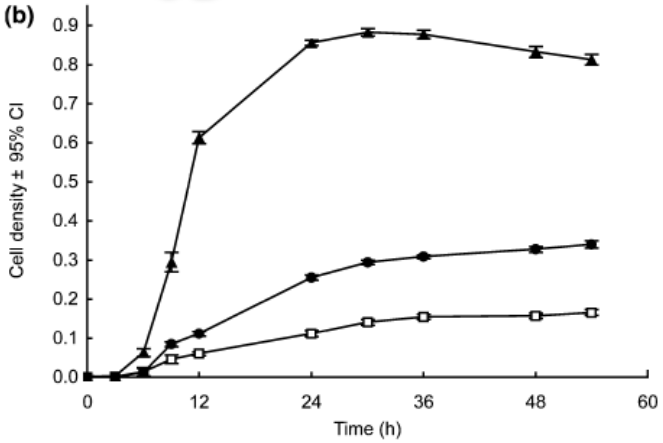
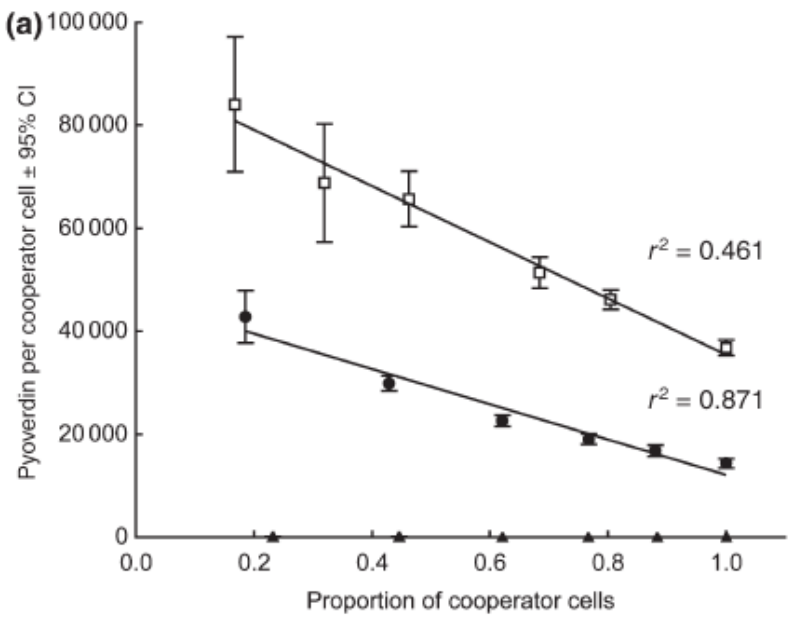
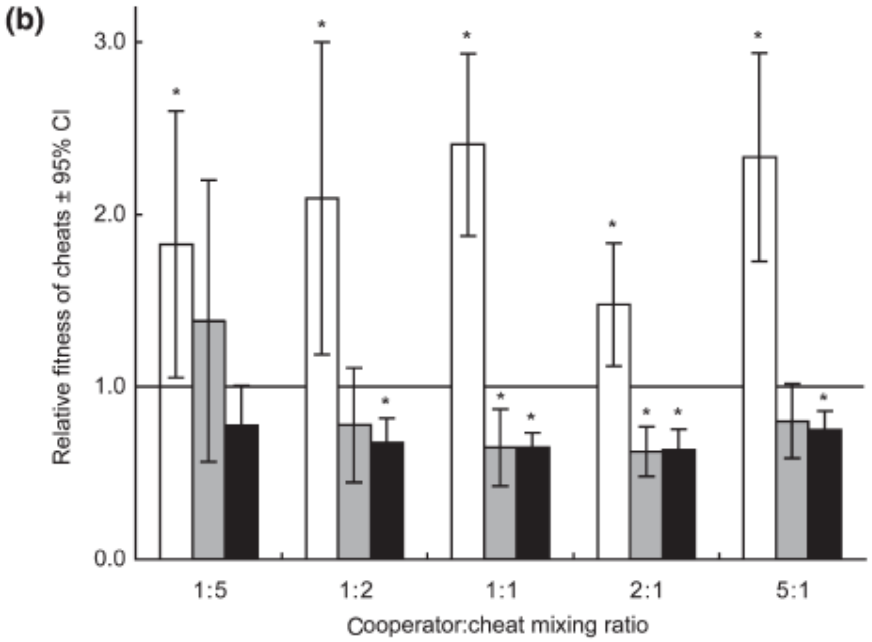


Cells adjust pyoverdin production in response to cheats





0μM (squares and open bars) 0.5μM (circles and grey bars) or 50μM (triangles and black bars) environments

What type of exoproducts are regulated by Quorum Sensing?

- Virulence factors

- Nutrient scavenging molecules (siderophores)

- Structural compounds for biofilm growth

- Surfactans to facilitate movement

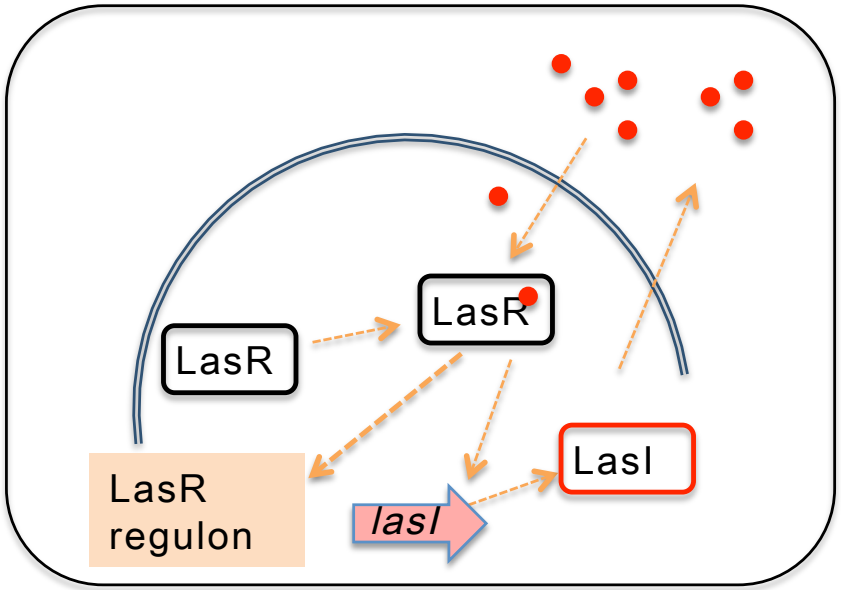
6-10% *Pseudomonas aeruginosa* genome regulated by QS
lasI/lasR system; the 'signal blind' mutant does not pay the
Cost of producing the public good (*lasI*)

Pleiotropy stabilizes *Pseudomonas aeruginosa* cooperation

The Biology

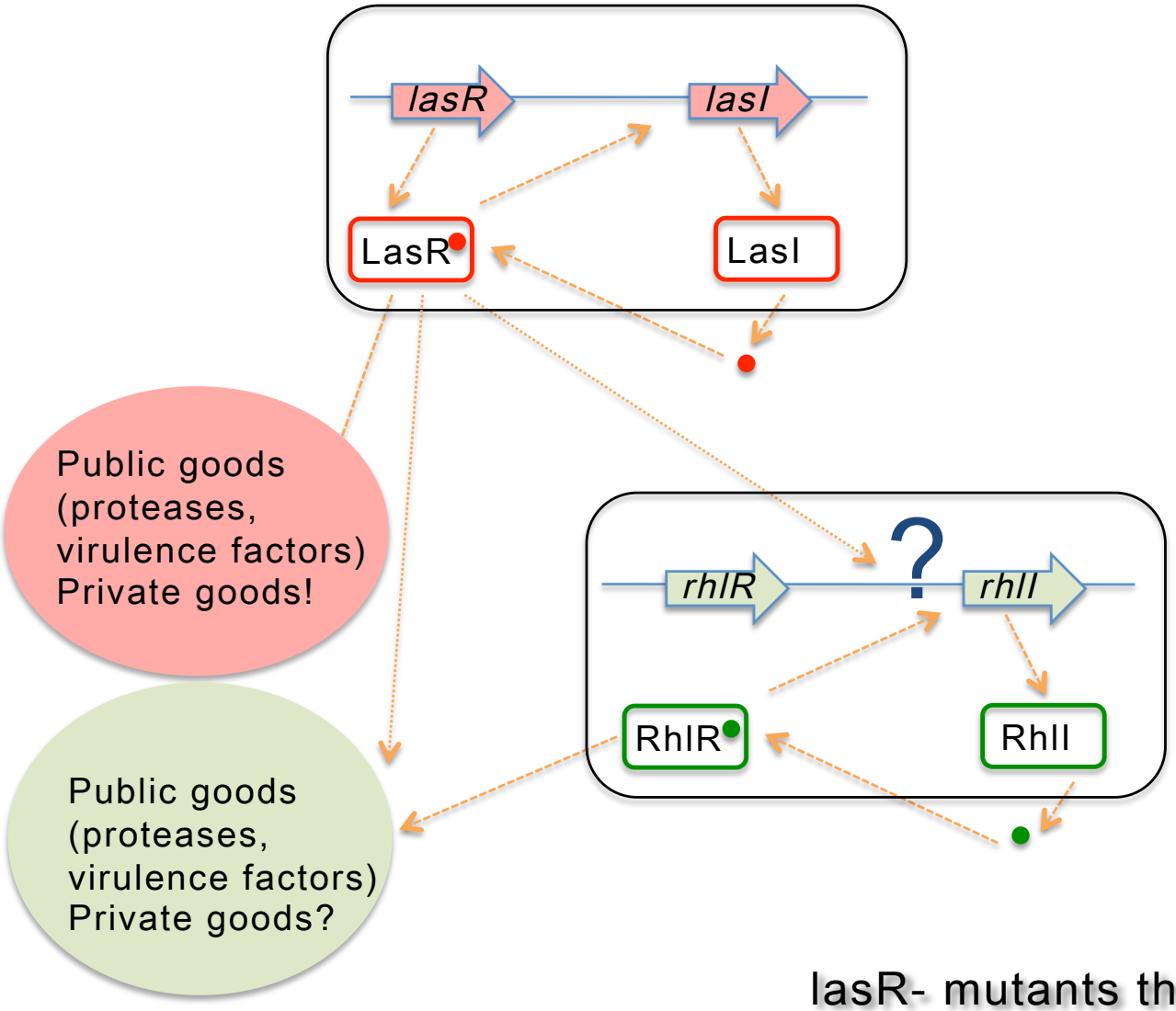
-Acyl-homoserine lactone (AHL) quorum sensing is a form of cell-cell communication that allows bacteria to monitor their population density

-a number of genes become activated when populations reaches a threshold density; this mainly includes a variety of public goods (e.g., extracellular proteases) but also some private ones (e.g., metabolic enzymes)



-LasR/LasI system

The quorum-sensing based public/private good hierarchy
Pseudomonas aeruginosa

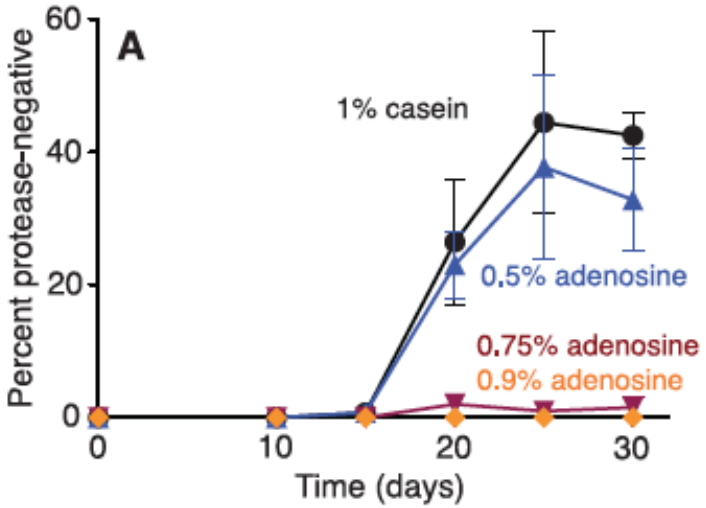


lasR- mutants the ones appearing more often

Metabolic incentives to cooperate

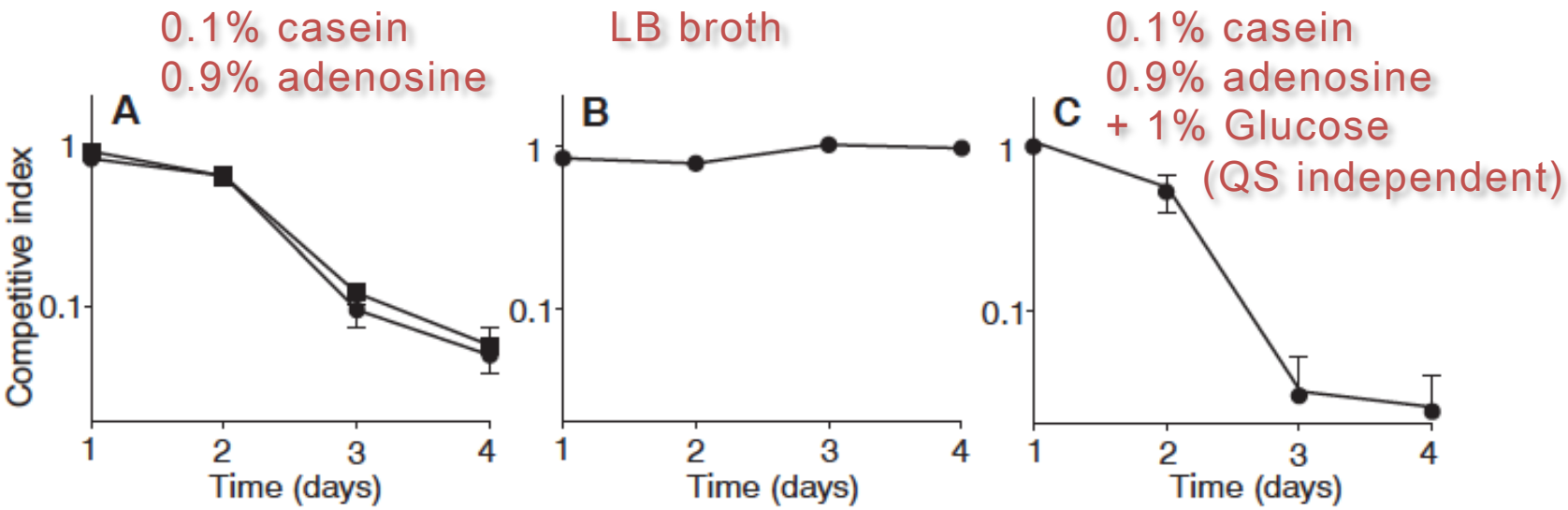
Could the obligate pairing of public and private goods restrict the ability of social cheaters to invade the population?

Growth in casein as the sole source of carbon requires proteases
Adenosine restrains emergence of social cheaters (protease-negative; LasR-null mutantions)



Dandekar A. *et al*, Science 338 (2012) 264

Adenosine reduces the relative fitness of LasR mutants



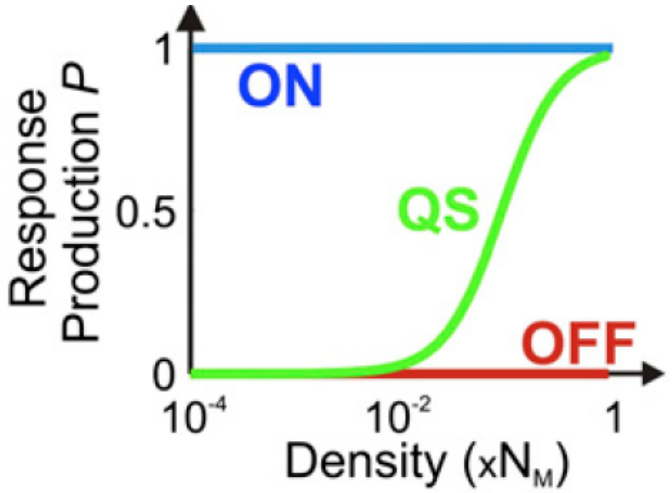
Competitive-index:
Cheater:wild_type final ratio compared with initial ratio

Quorum sensing as 'collective cognition'

Benefit of QS-control of exoproducts: to delay production of costly exoproducts until reaching enough density, i.e., benefit is density dependent

Imagine three alternative strategies:

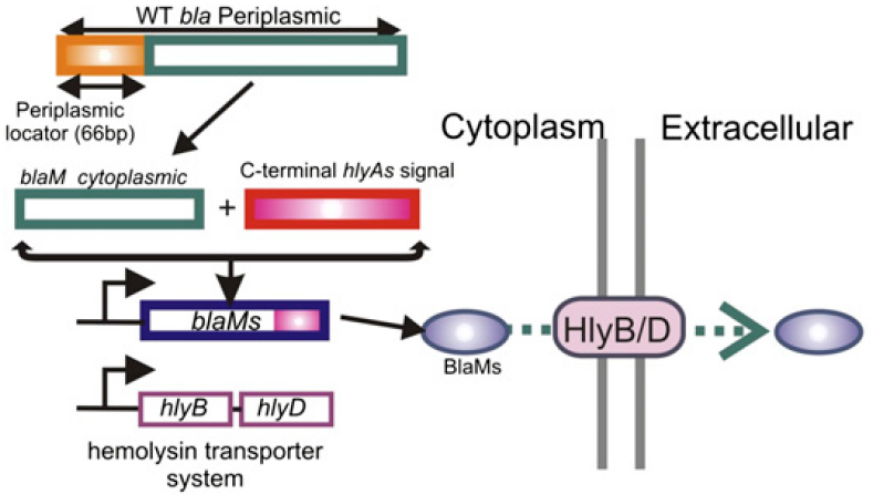
OFF	not to produce the exoenzyme
ON	always produce the exoenzyme at high rate
QS	produce the exoenzyme at sufficiently high density



Pai A. *et al*, PNAS 338 (2012) 109, 19810

Synthetic circuit

-exoenzyme: BlaMs, exoenzyme
to degrade β-lactam antibiotics
(e.g., penicillin, cephalosporins, ...)

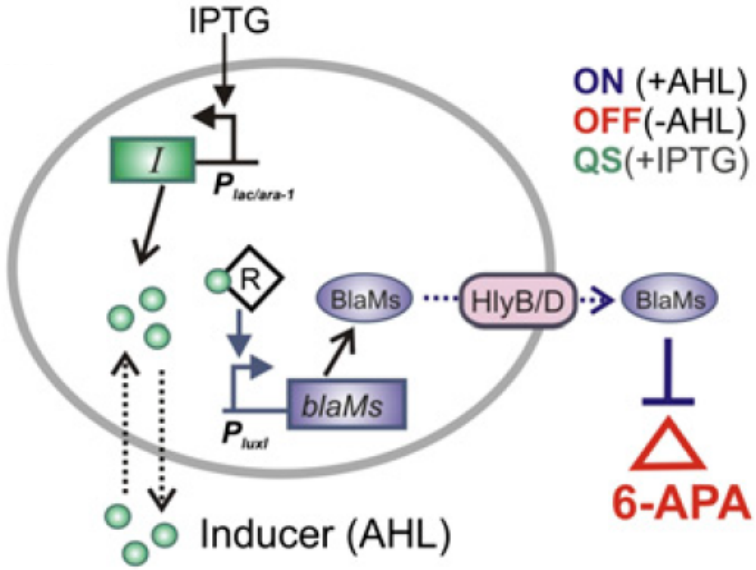


strategies:

OFF

ON

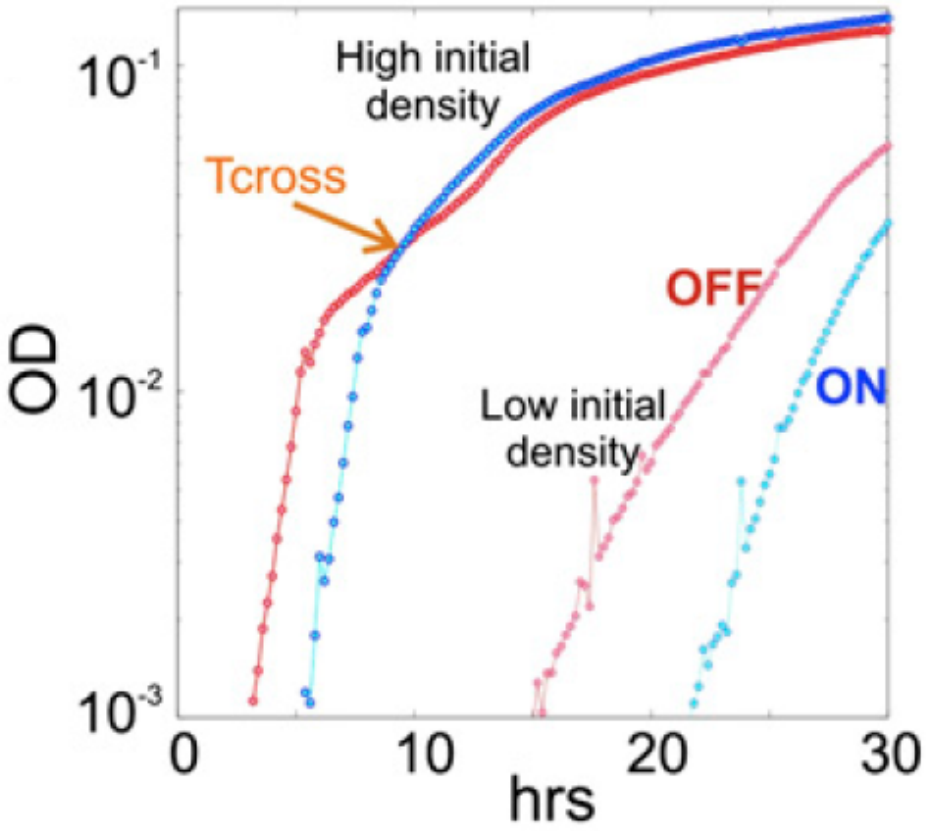
QS



ON (+AHL)
OFF(-AHL)
QS(+IPTG)

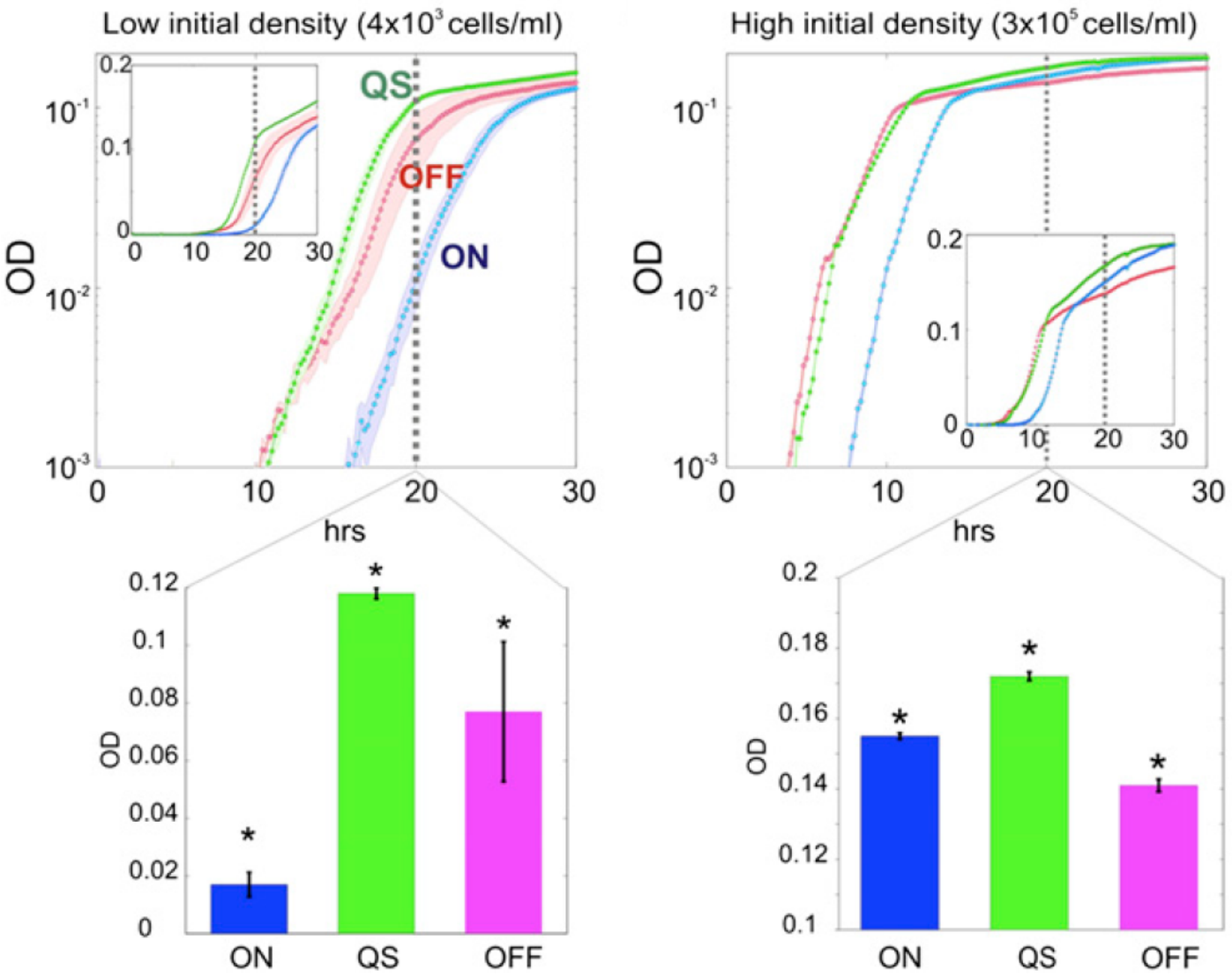
6-APA 6-aminopenicillanicacid

Exoenzyme production is beneficial ONLY
at sufficiently high density



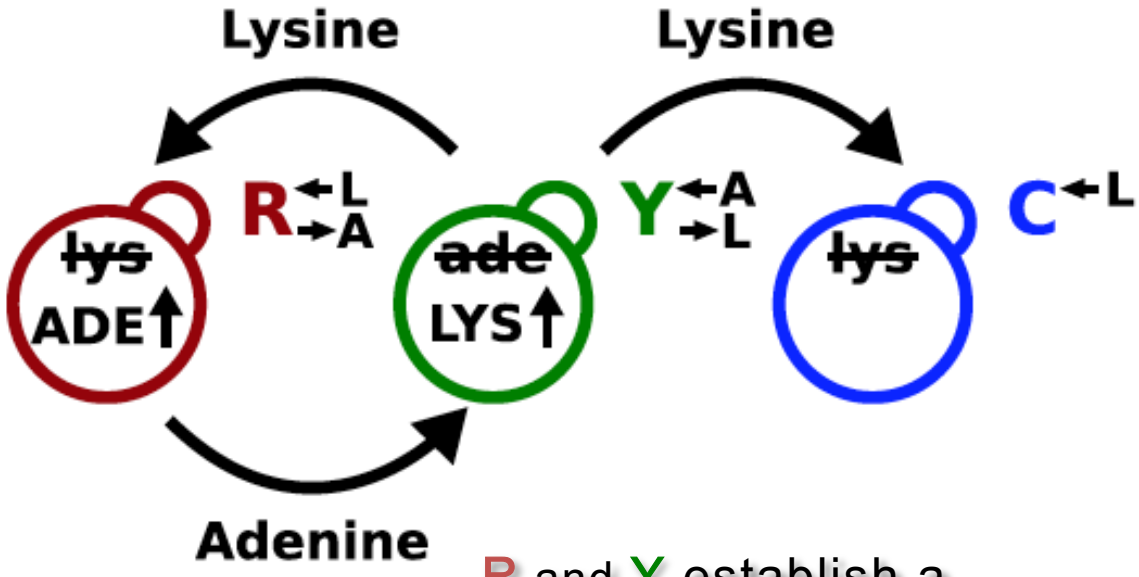
25 μg/ml 6-APA

Density-dependent activation through QS



Yeast cooperator-cheater engineered system

- Red strain: requires Lysine and overproduces Adenine (that is released into the medium)
- Green strain: requires Adenine and overproduces Lysine (that is released into the medium
- Blue (cheater) strain: only takes Lysine

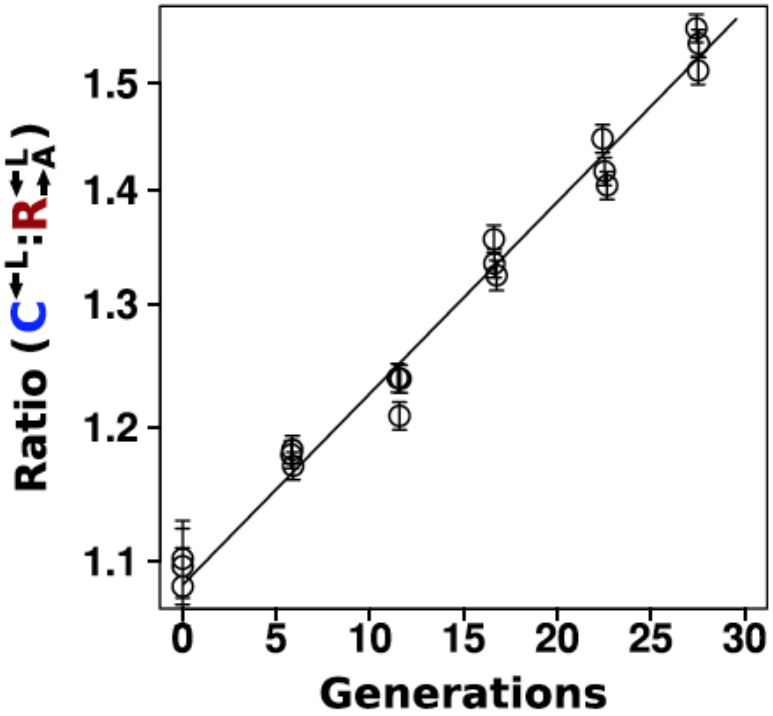


R and Y establish a mutualistic system

Waite A. *et al*, PNAS 109 (2012) 19079

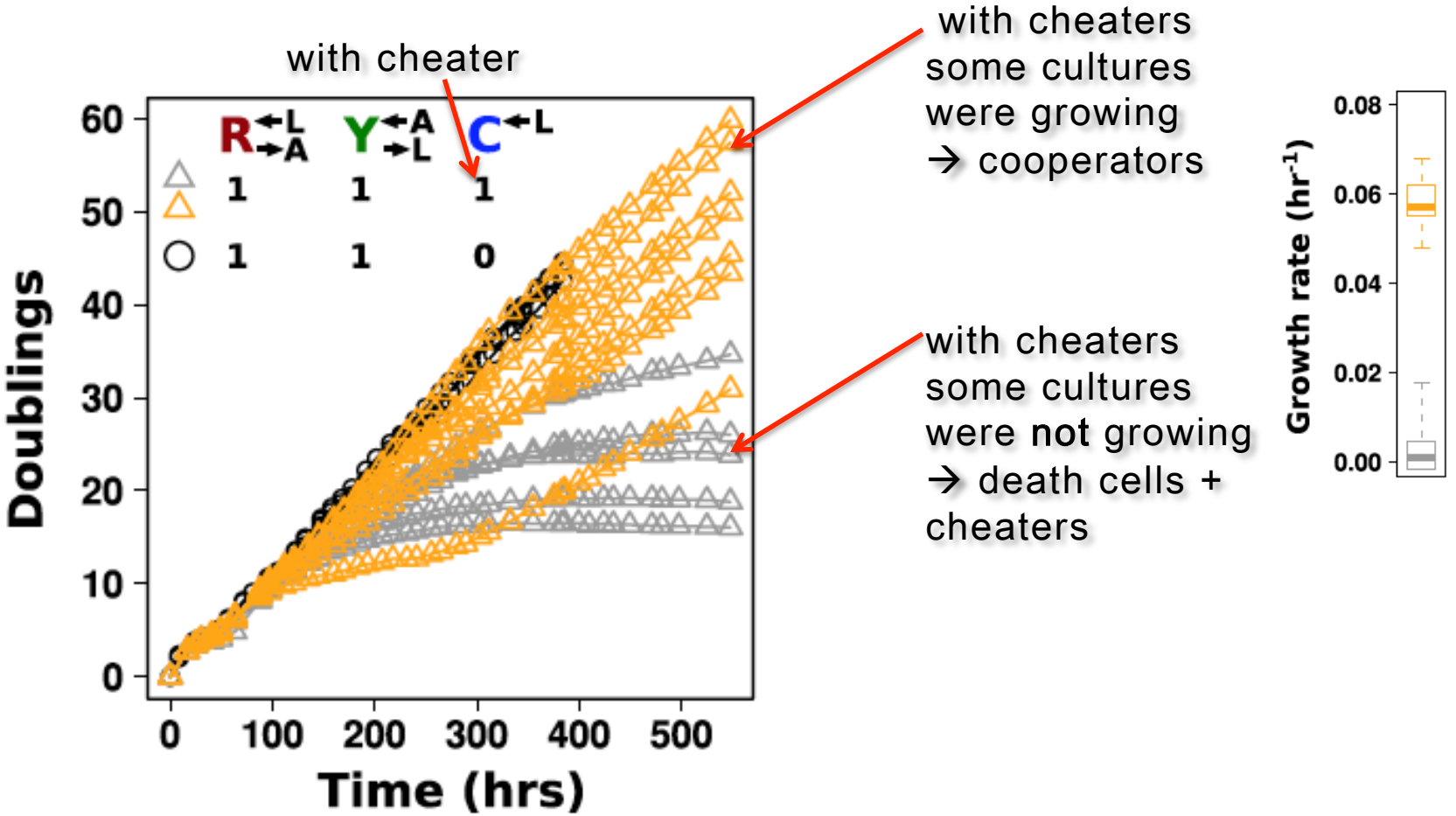
Cheaters are fitter than cooperators

- media with non-limiting lysine
- this measures the cost of adenine overproduction (metabolic overproduction carries a significant cost)



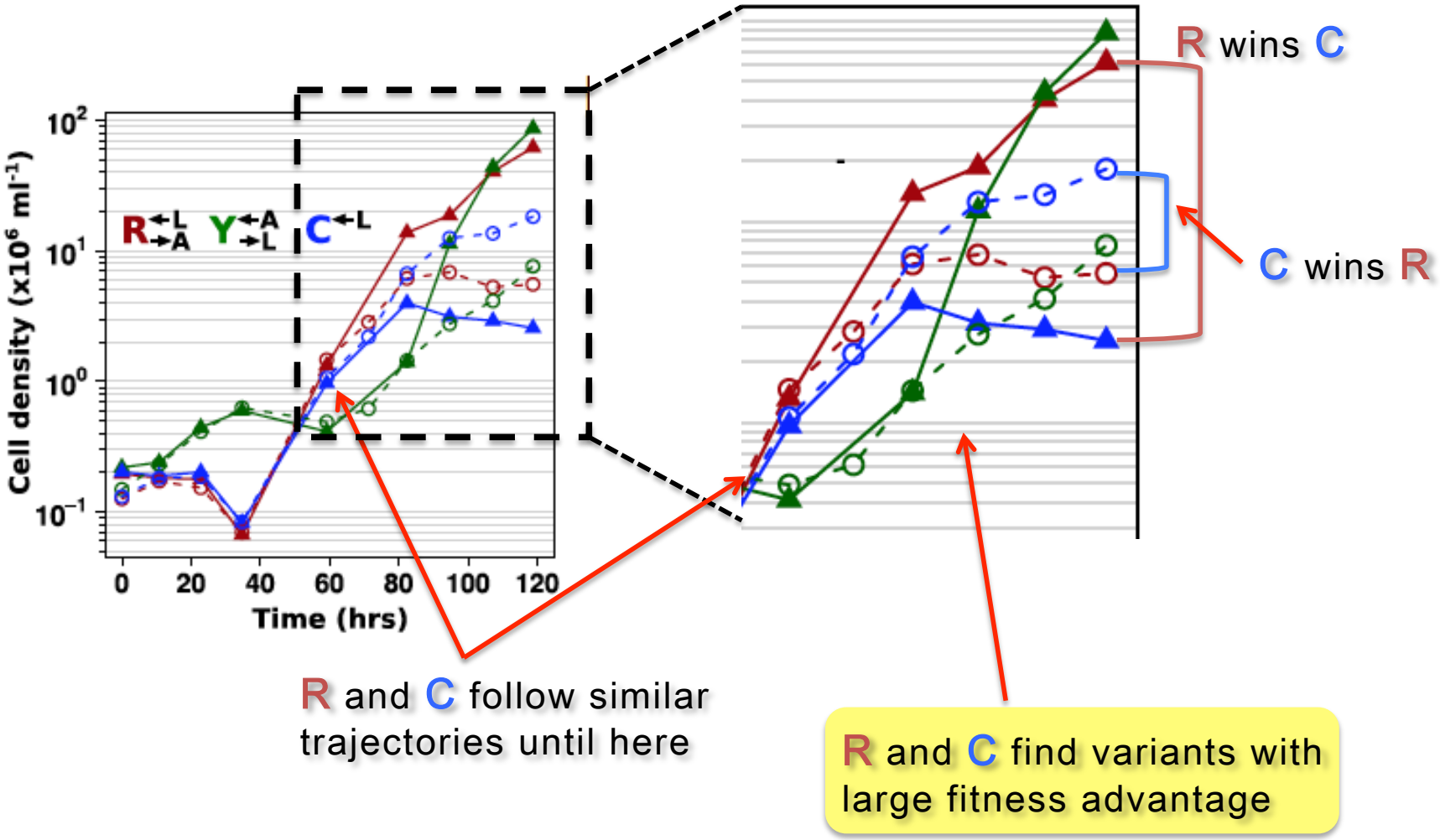
Grown in SD supplemented with non-limiting lysine

Stochastic cheater outcome in initially identical cooperator-cheater co-cultures

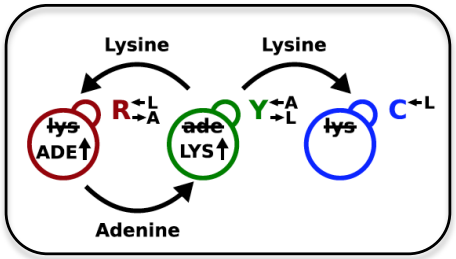


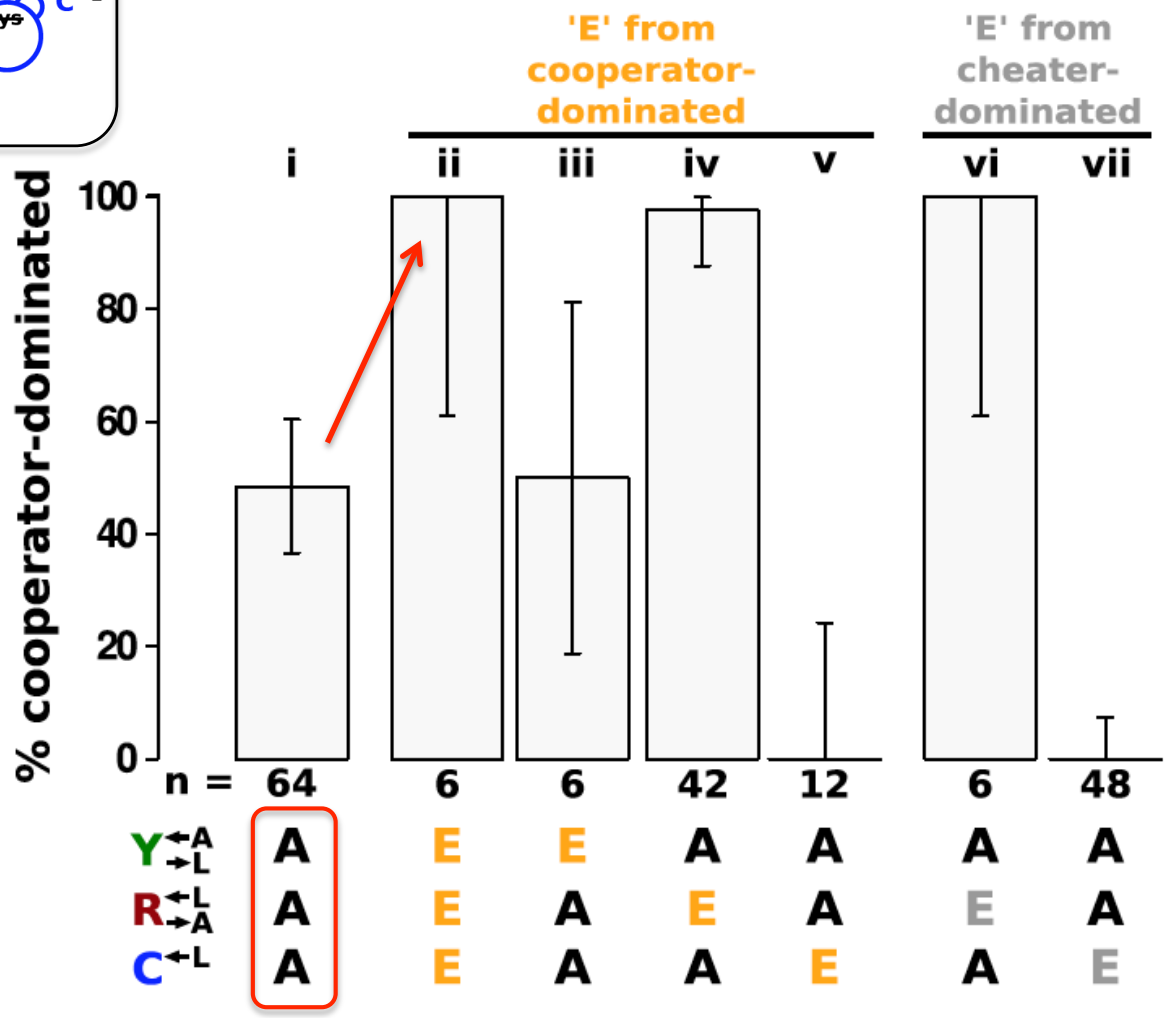
Grown in SD; ratios 1:1:1 or 1:1:0

Extremely fit mutations (enhancing nutrient transport) drive stochastic cooperator dominance



Evolved cooperators and cheaters are superior to ancestors





Mutations in a small set of genes involved in Nutrient Transport

Bacterial exoproducts become public goods

It is always better to be reactive!

Sometimes private goods save public goods

You should properly “tune” when to produce a public good

Adaptation to a given environment can influence social interactions