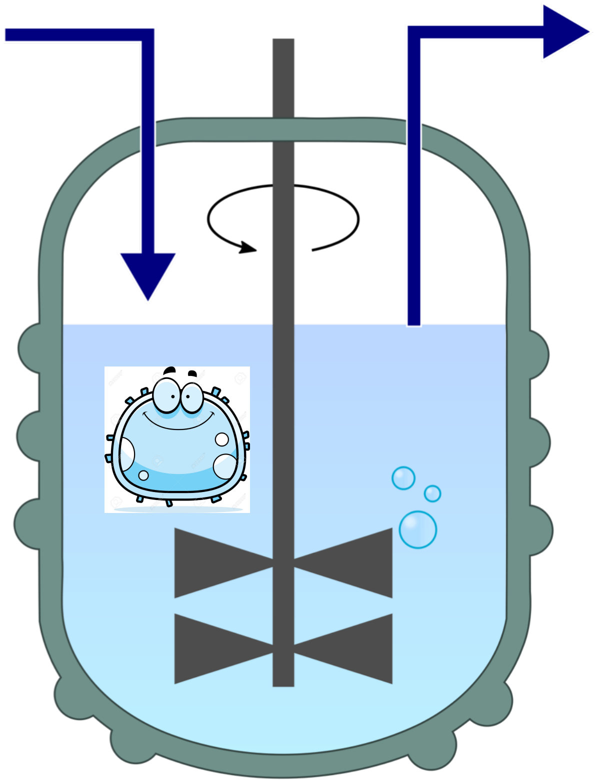
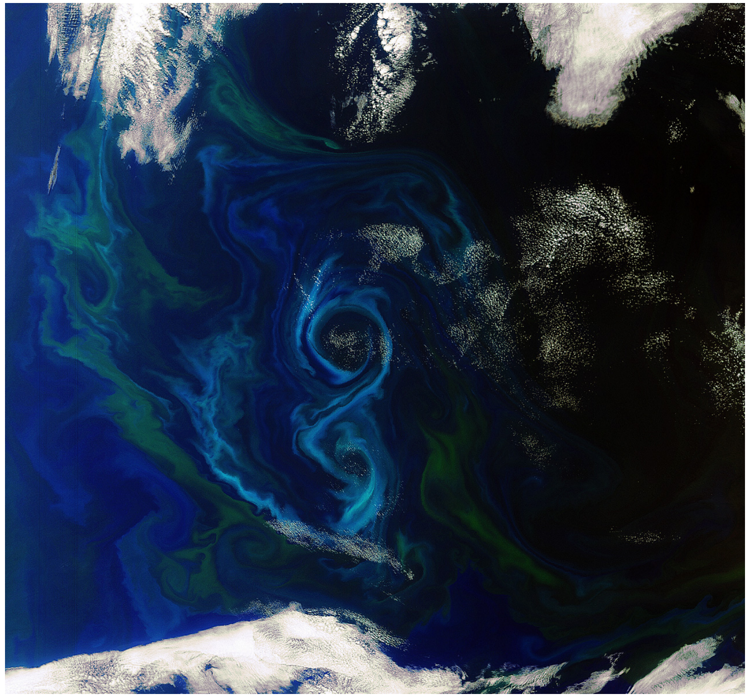
A View of Resource Competition Models: Chemostat, Nutrient Limitations and Self-building Spatial Heterogeneity



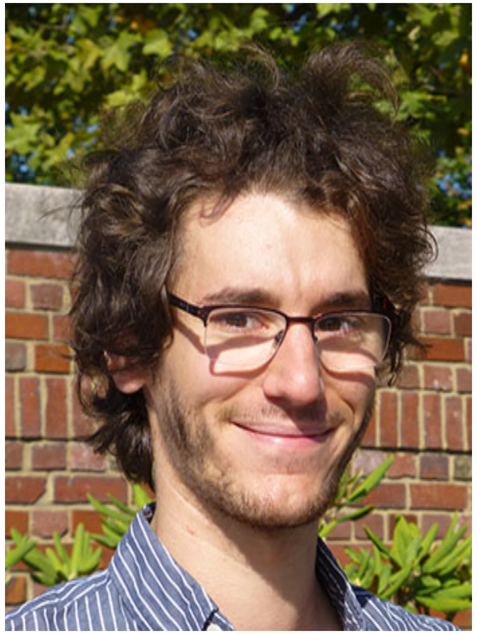
Zhiyuan Li

ICTP, 2018



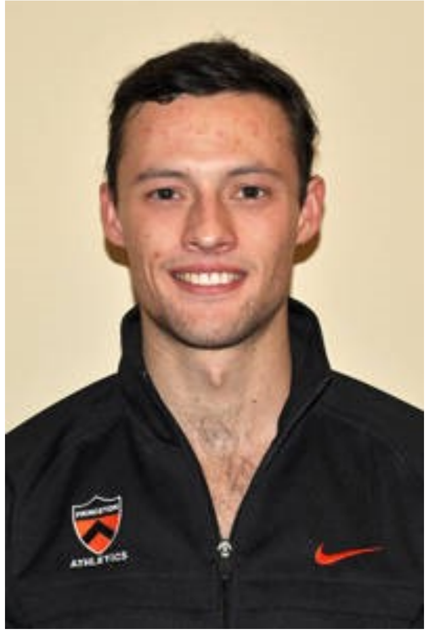
Acknowledgment

Ned S. Wingreen



Pierre Ronceray

Sophia Hsin-Jung Li

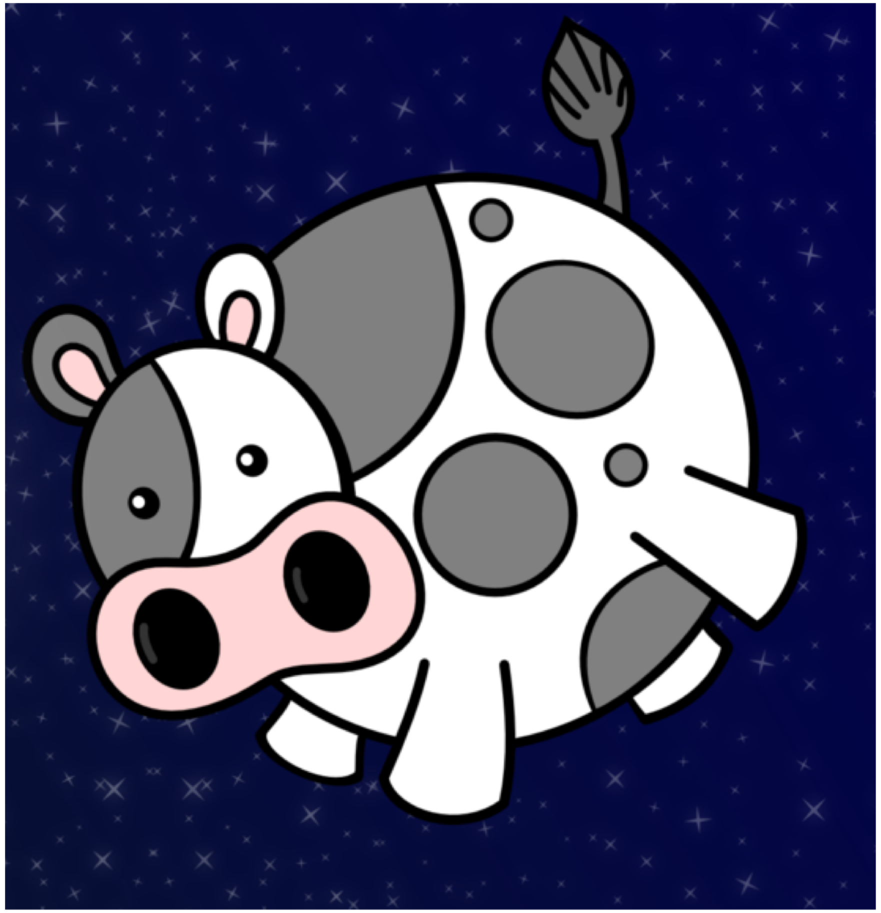


Christopher G. King

PRINCETON CENTER FOR THEORETICAL SCIENCE

What does theoretician do in biology

Assume a spherical cow in a vacuum…



Paradox of the plankton

Competitive exclusion principle:
The number of species stably coexisting cannot exceed the number of resources

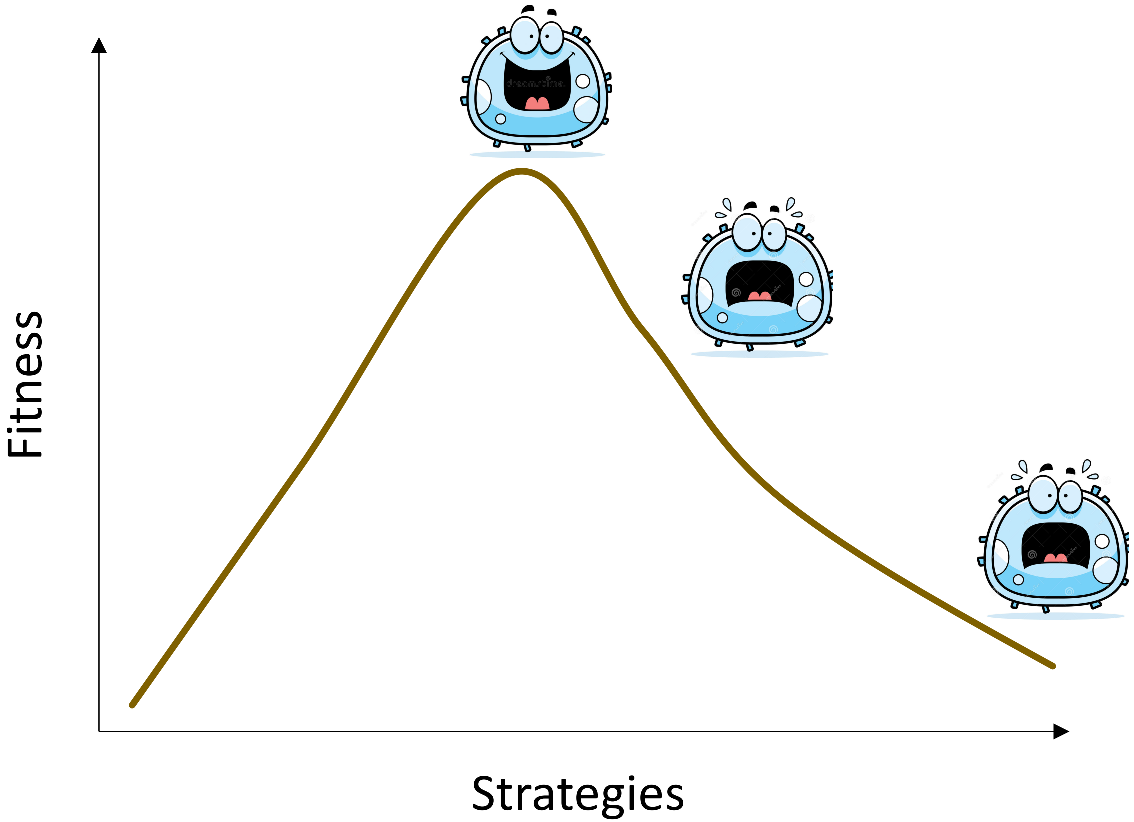
Real world
Tremendous diversity

A giant *E. coli* in a vacuum: fixed growth rate

E.coli:

mass/cell: ~ 10^{-12} g
doubling rate: ~ 20 min
after 51 hours: ~ 6 solar mass

“Winner takes all” in a fixed fitness landscape



Outline

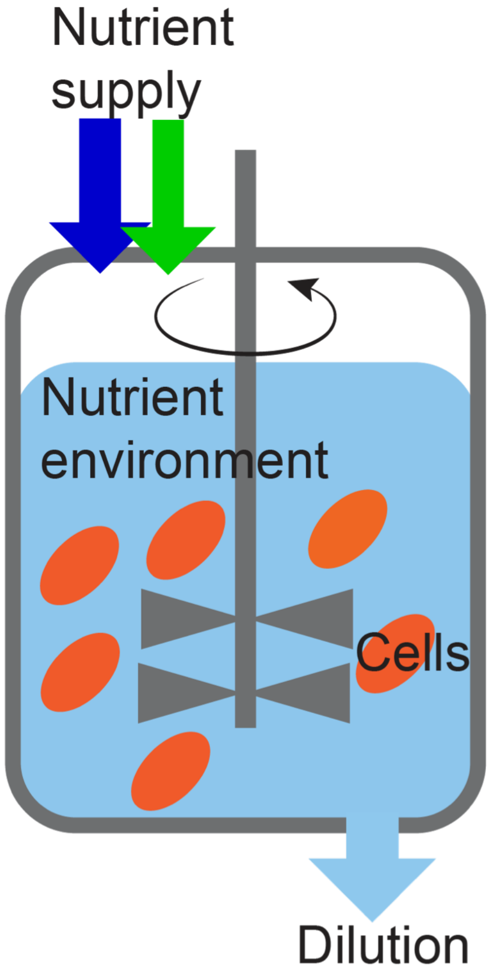
Species shape their environments.

1. Visual framework for resource competition models in general.
2. Controllables in chemostat experiment.
3. Rule of invasion.
    1. Multistability.
    2. Mutual invasibility.
    3. Oscillation.
4. “Super species” and local optimal strategies.
5. Emergence of spatial heterogeneity.

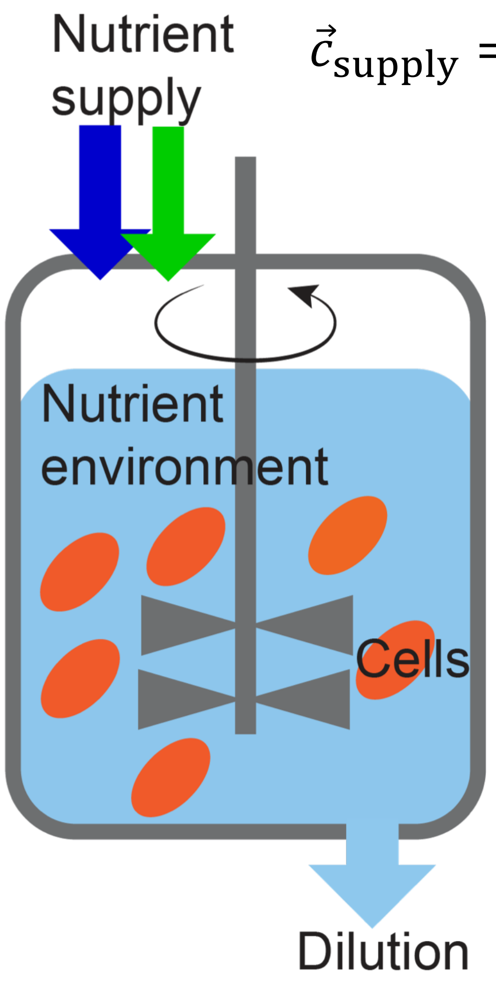
The simplest ecosystem: chemostat

Cell mass

Nutrient
concentration
In environment



Cell growth in a chemostat: species creates the balance point



$\vec{c}_{\text{supply}} = \{c_{1,\text{supply}}, c_{2,\text{supply}}, \dots\}$

$\vec{c} = \{c_1, c_2, \dots c_P\}$

M

d

Assume:

Growth rate: $g = g(\vec{c})$,

non-decreasing with $\forall c_i$.

Intake rate per biomass: $I_i = I_i(\vec{c})$,

non-decreasing with c_i.

Dynamic Equations:

Cell growth:

$$\frac{dM}{dt} = M * (g(\vec{c}) - d)$$

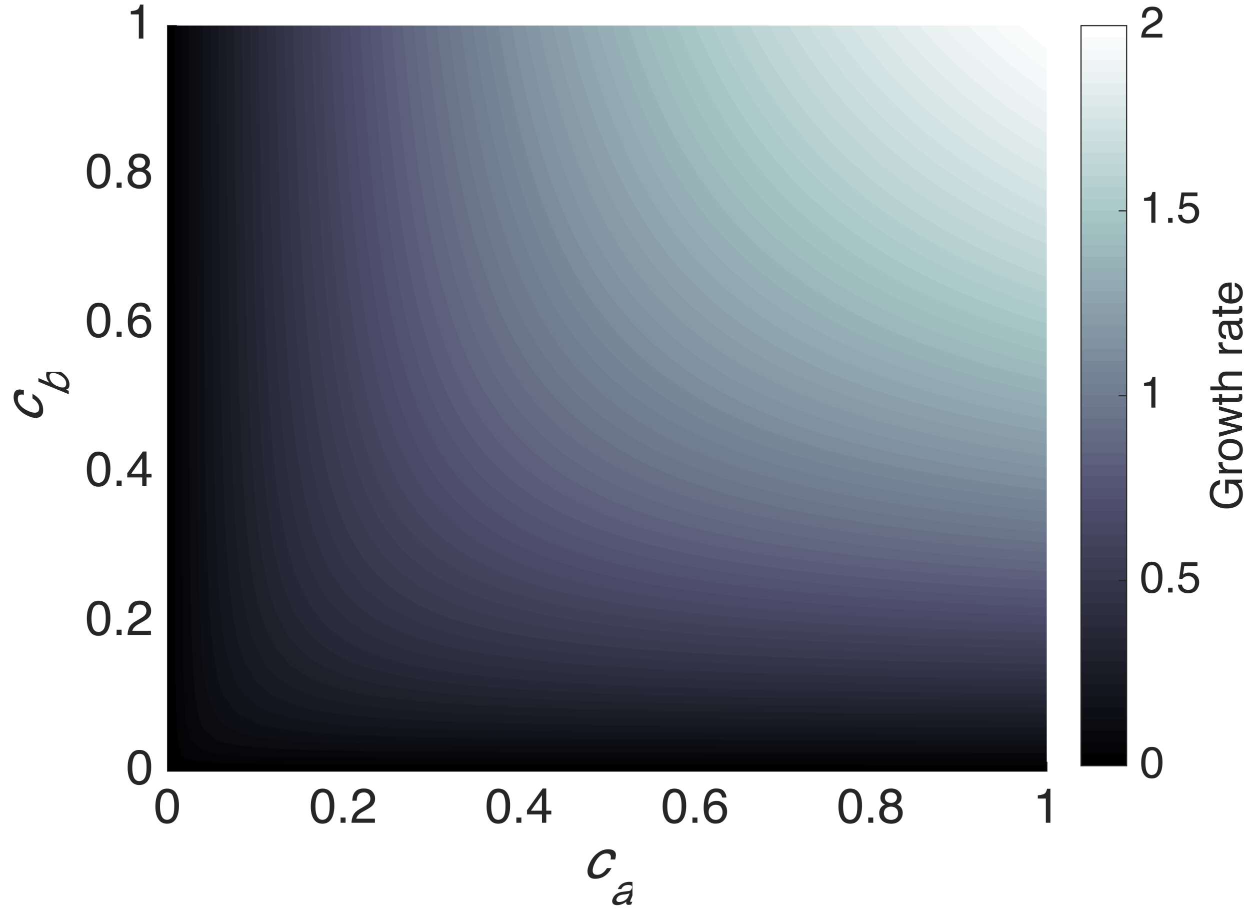
Nutrient consumption:

$$\frac{dc_i}{dt} = d * \left(c_{i,\text{supply}} - c_i\right) - M * I_i\,(\vec{c})$$

Visualization in the nutrient space: Growth contours

Cell growth :

$$g = g(\vec{c})$$

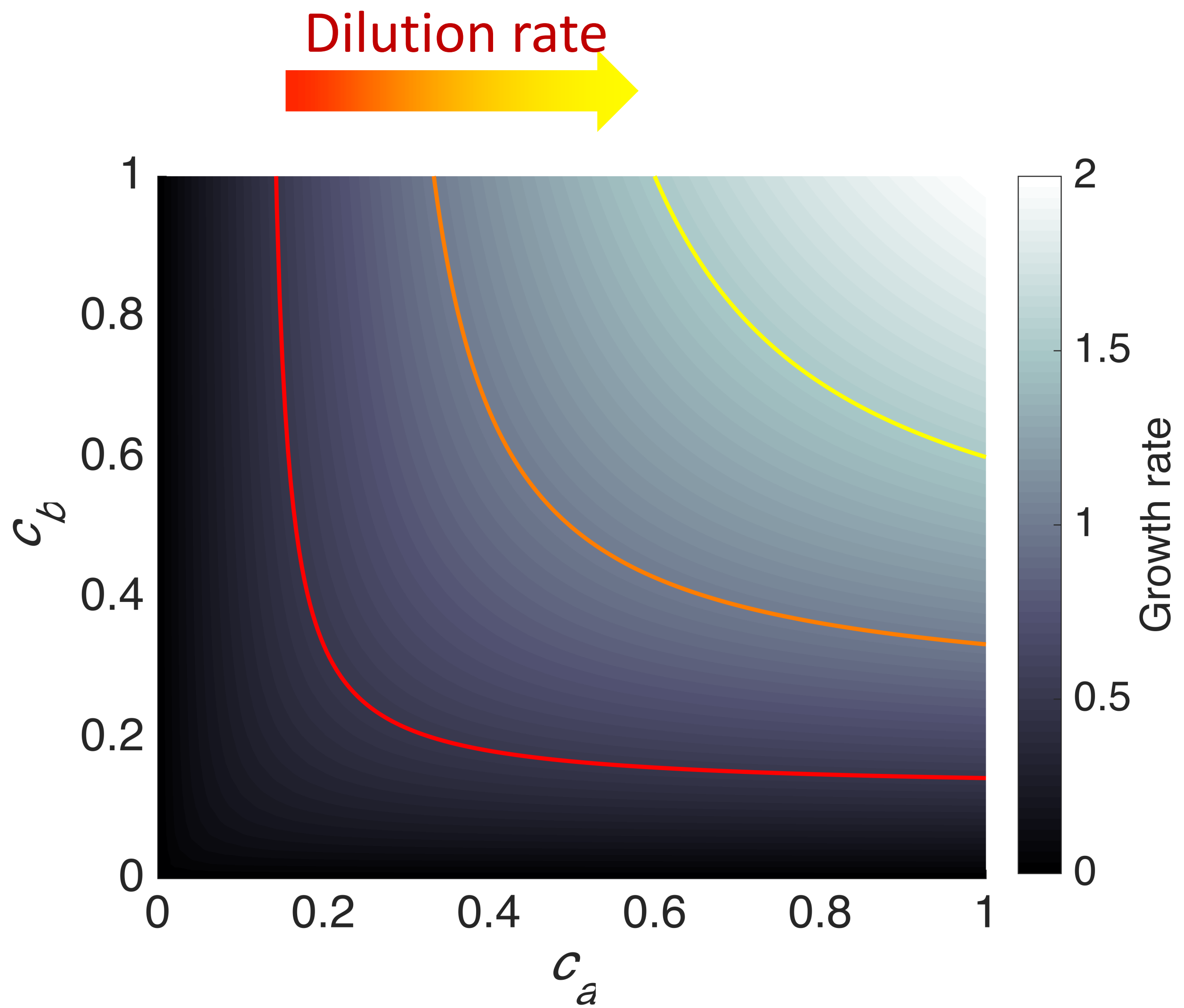


Visualization in the nutrient space: Growth contour

Balance of growth and dilution:

$$\frac{dM}{dt} = M * (g(\vec{c}) - d) = 0$$

$$=> g(\vec{c}) = d$$



Visualization in the nutrient space: Flux balance curve

Nutrient influx, dilution and consumption:

$$\frac{dc_i}{dt} = d * \left(c_{i,\text{supply}} - c_i\right) - M * I_i\,(\vec{c}) = 0$$

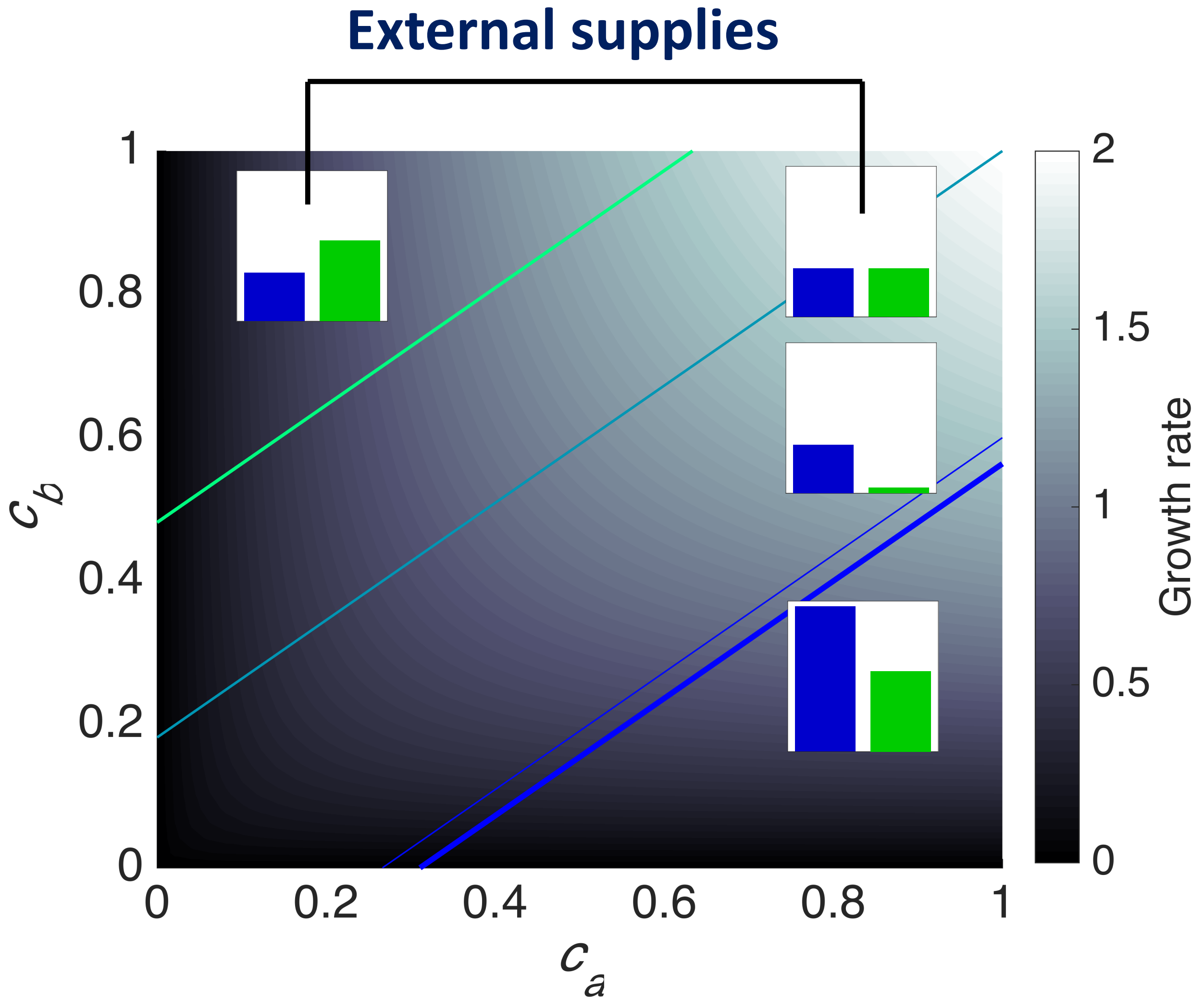
P types of nutrients

=> P equations

=> P+1 variables

(P c_i concentrations + M)

=> 1 dimensional curve



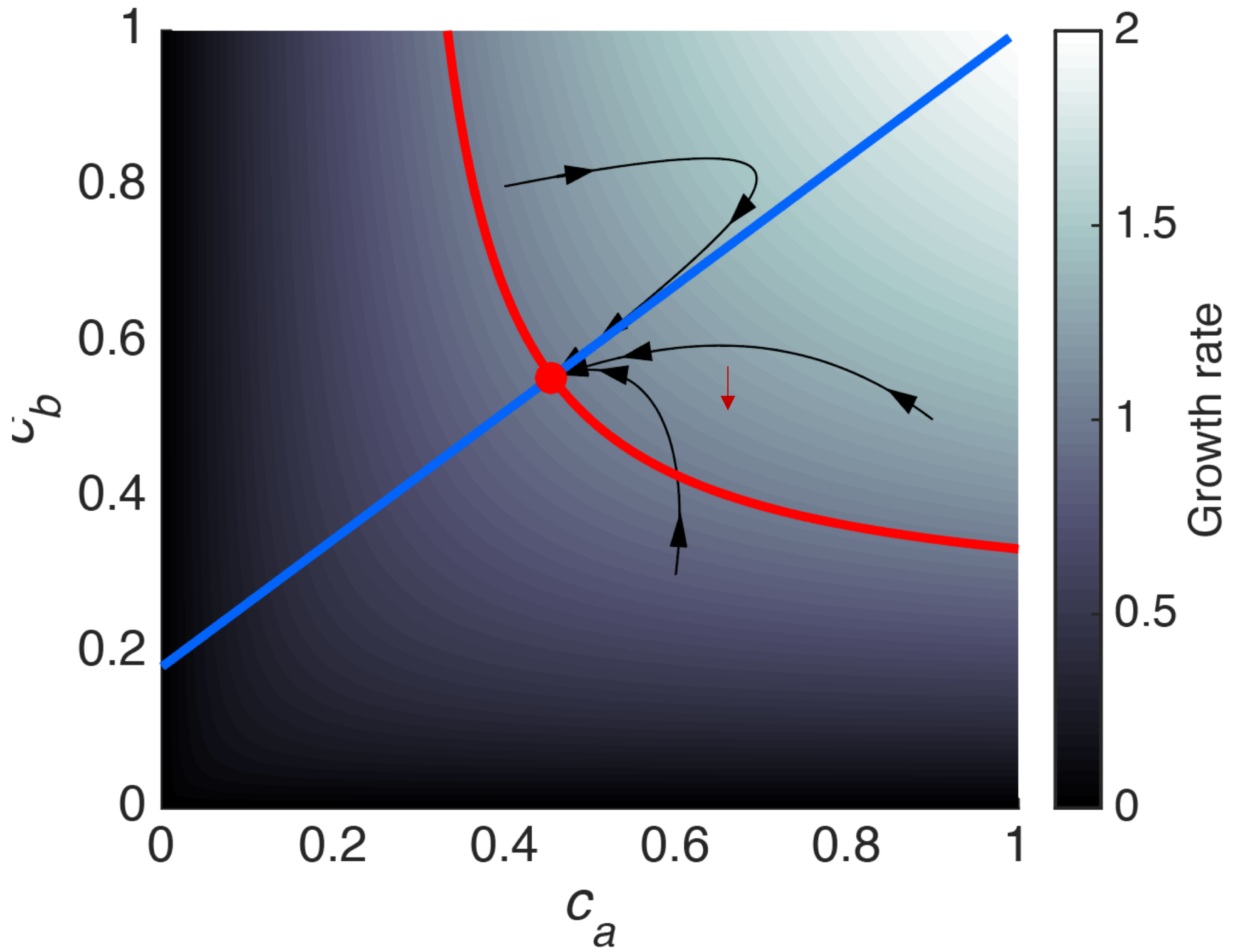
Visualization in the nutrient space: Species creates its own environment

Growth contour:

$$g(\vec{c}) = d$$

Flux balance curve:

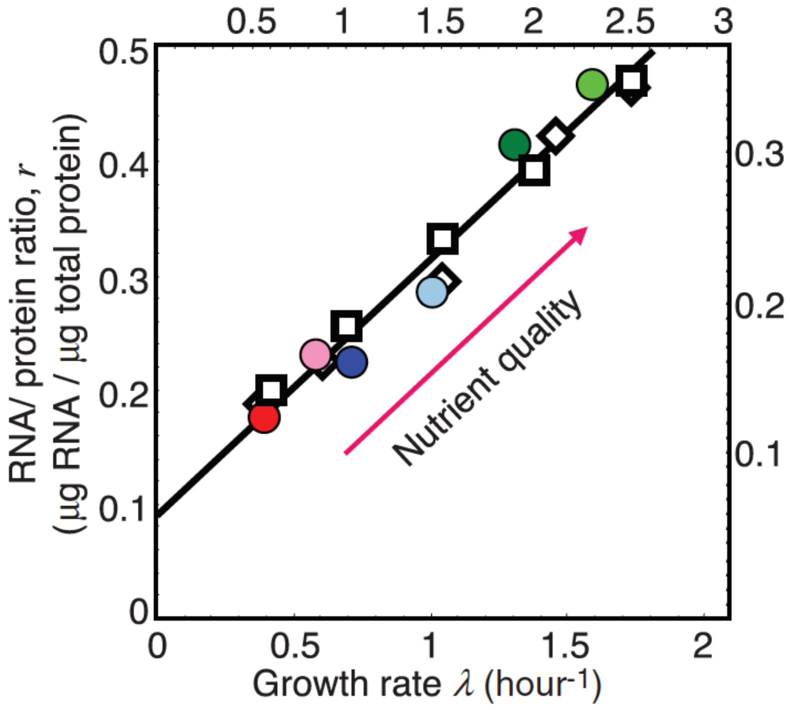
$$d * \left(c_{i,\text{supply}} - c_i\right) - M * I_i\,(\vec{c}) = 0$$



A diversion to experiments…

Previous Observation:

Linear growth law between RNA-to-Protein ratio and growth rate.

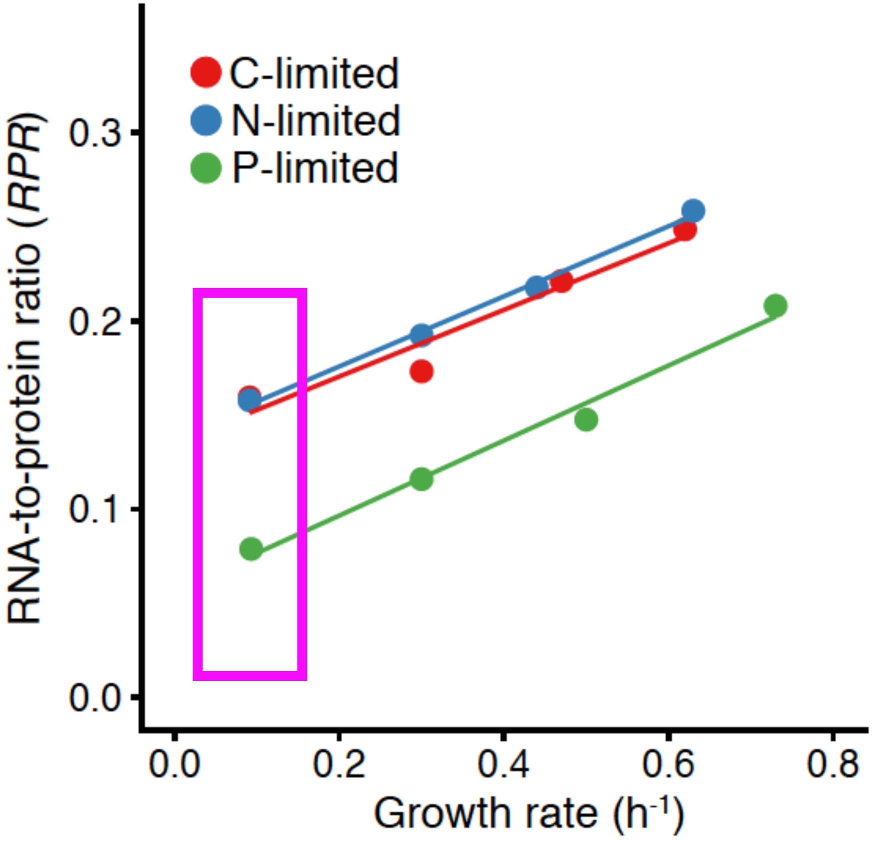


Scott et al (2010) Interdependence of Cell Growth and Gene Expression

Our observation: Ribosome abundance depends on nutrient-limitation

Experiment system:
E. coli in chemostat

Observation:
Cells under P-limitation have fewer ribosomes



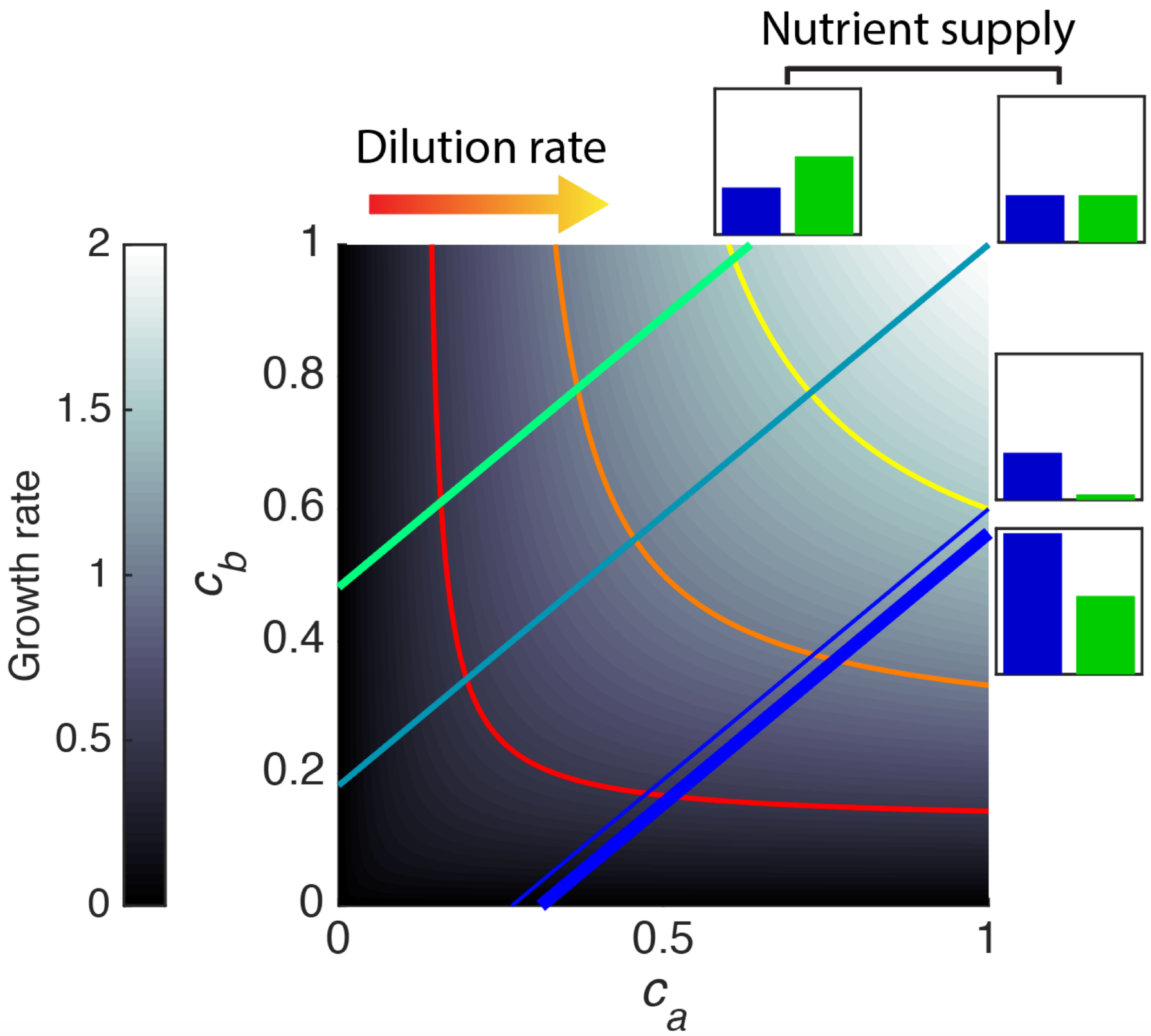
Nutrient supplies in chemostat experiment.

When cell has a fixed composition w_a and w_b:

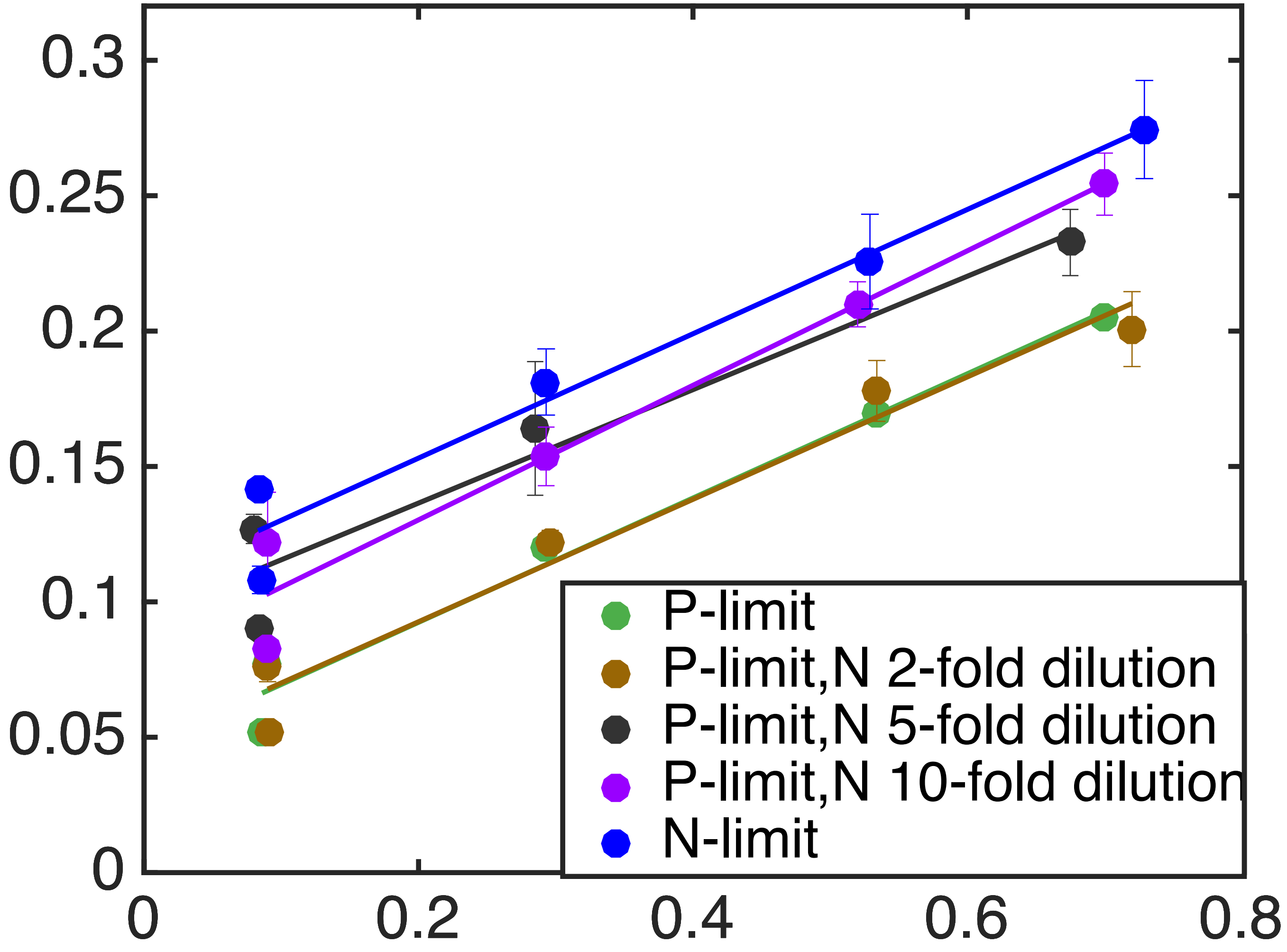
$$d * \left(c_{a,\text{supply}} - c_i\right) = M * (g * w_a)$$
$$d * \left(c_{b,\text{supply}} - c_i\right) = M * (g * w_b)$$

Flux balance curve is determined by the relative difference between nutrient supplies:

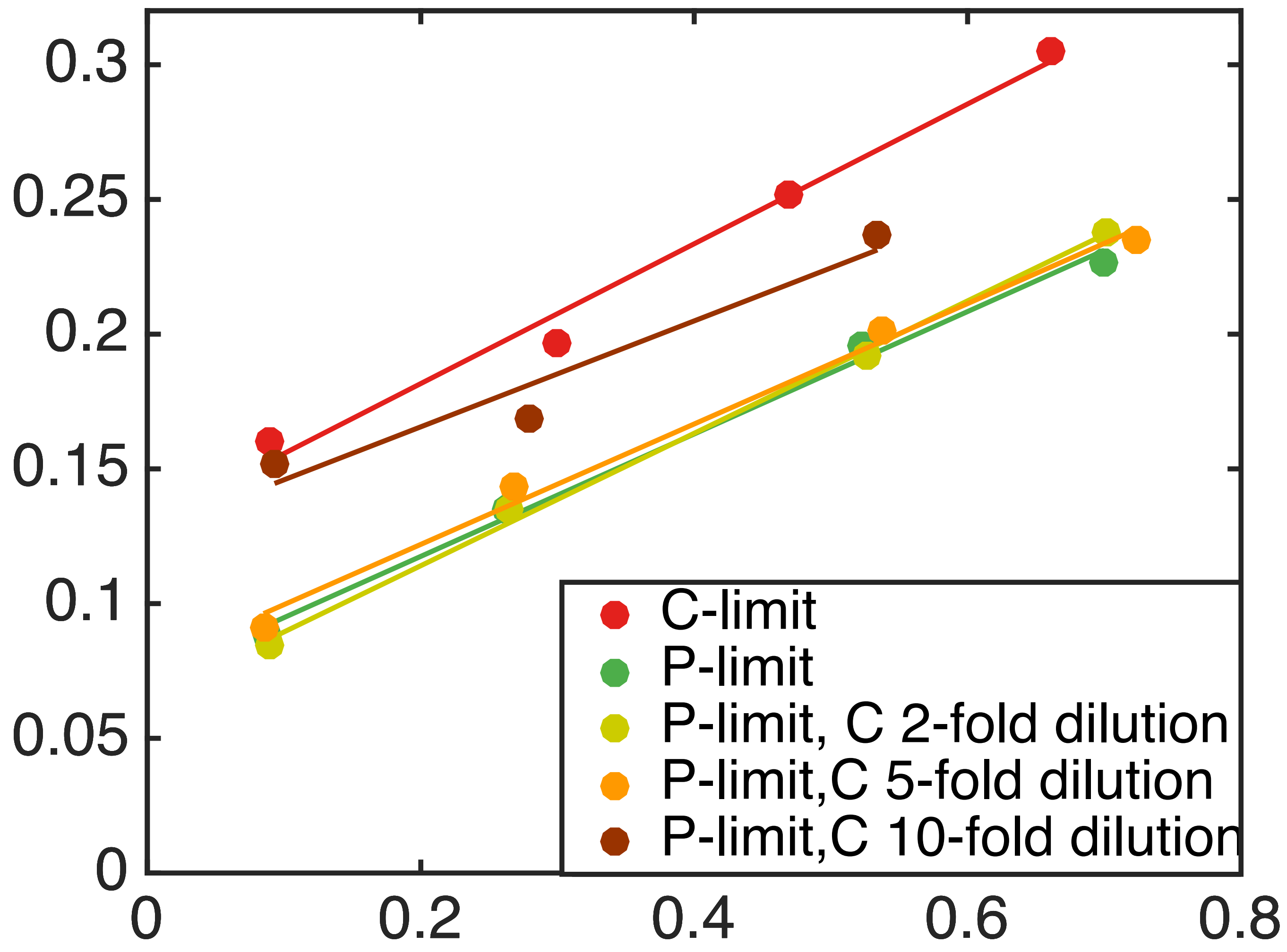
$$\frac{c_{a,\text{ supply}} - c_a}{w_a} = \frac{c_{b,\text{ supply}} - c_b}{w_b}$$



Relative changes in the supply shifts the RNA/Protein ratio-growth rate relationship



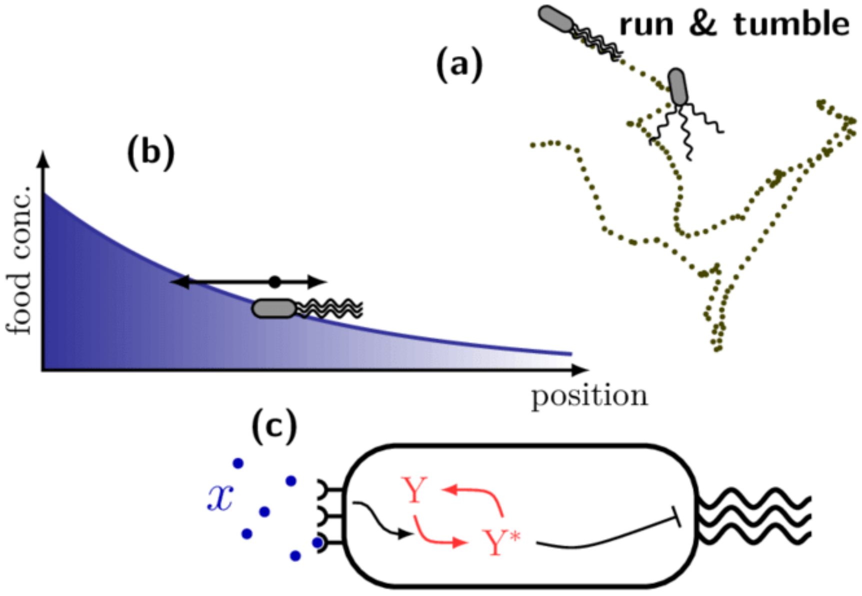
Relative changes in the supply shifts the RNA/Protein ratio-growth rate relationship



Brief summary on chemostat controllables

Difficult to experimentally distinguish :

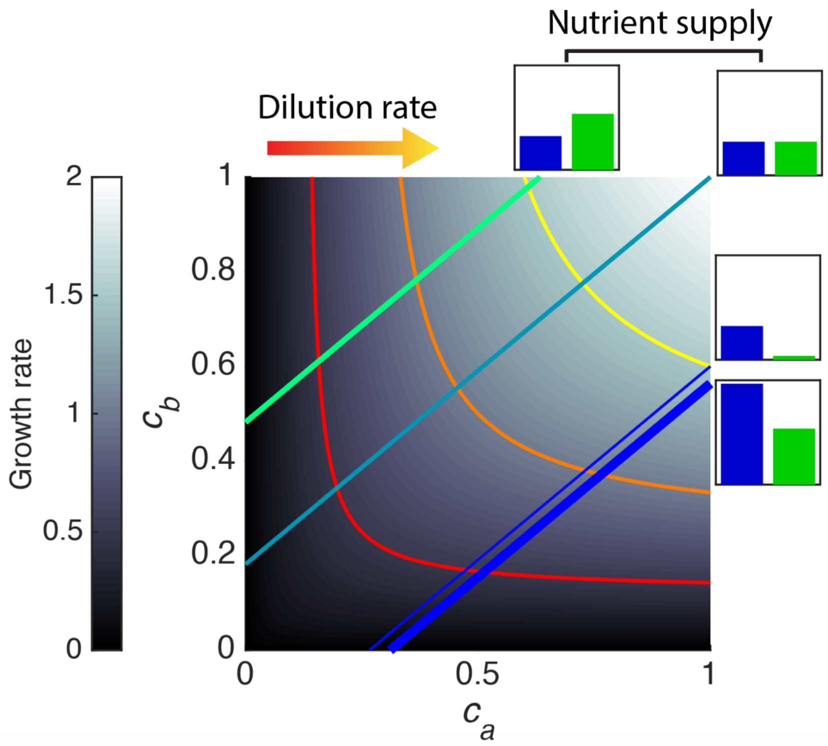
Cells perceive relative changes in nutrient environment by intra-cellular regulations



David Hartich, 2017

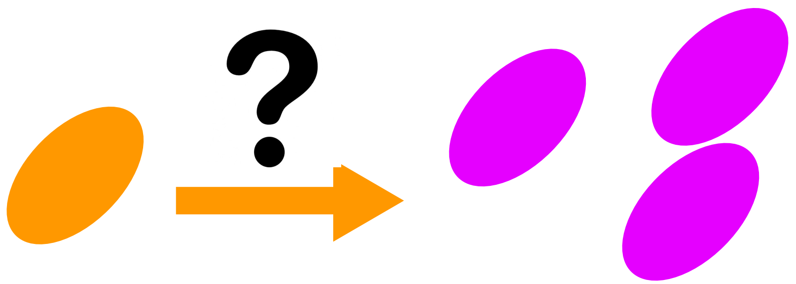
OR

Cells create same nutrient environment out of different nutrient supplies

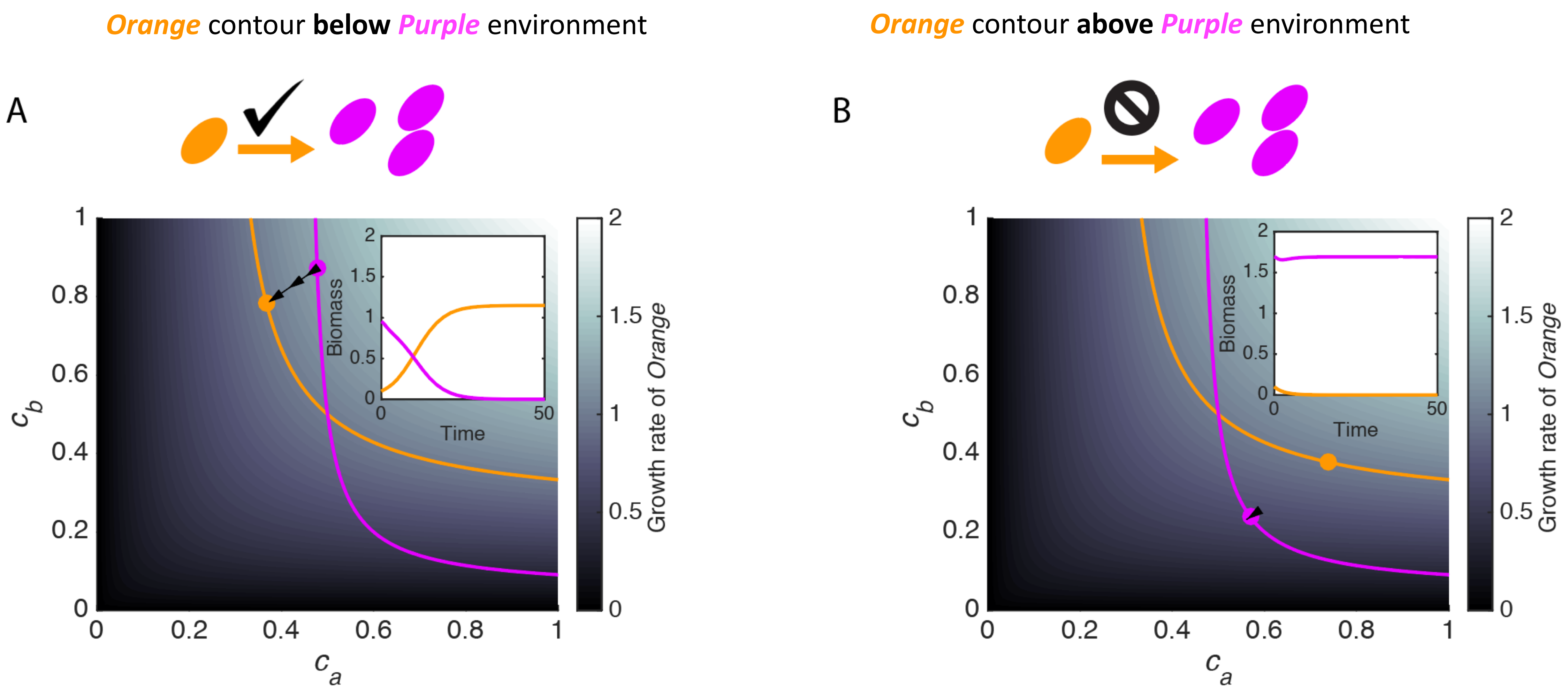


Two species competition dynamics

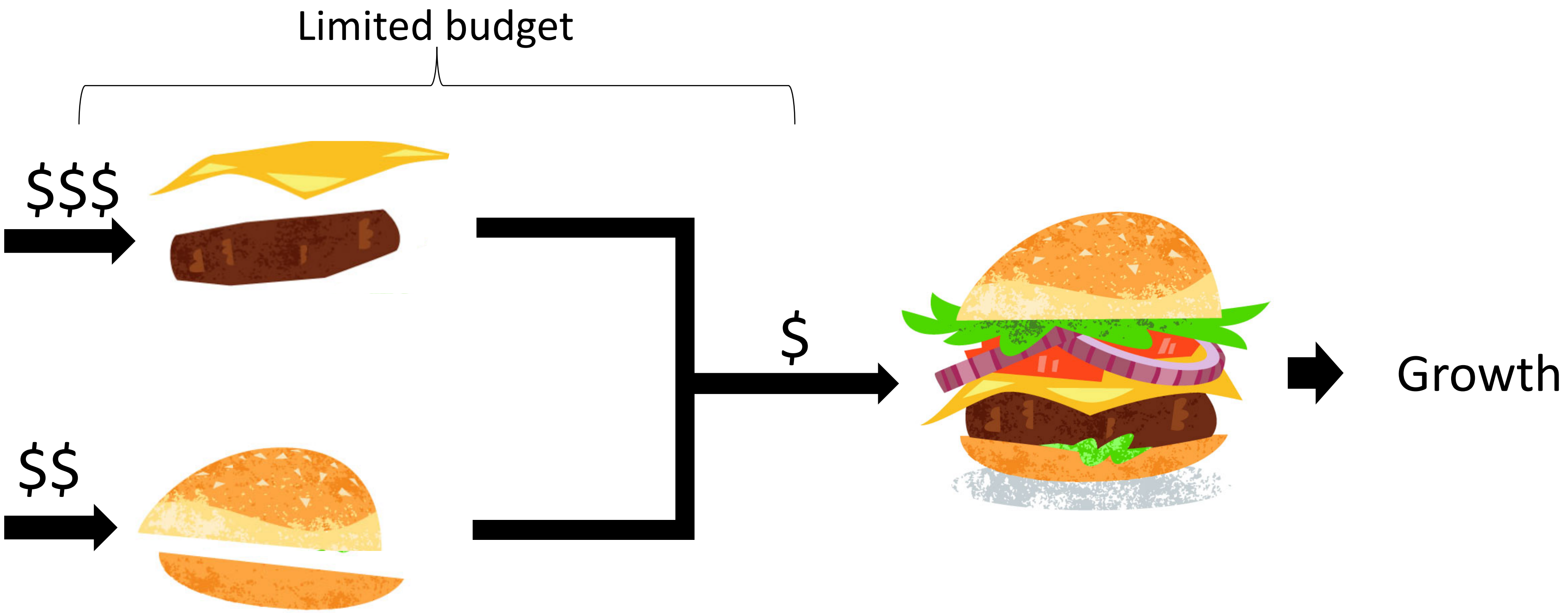
Invasion:
Introducing small amount of species *Orange* to a chemostat occupied by species *Purple* in steady state. If *Orange* can increase its number, we call it a successful invasion; otherwise, unsuccessful.



Rule of invasion



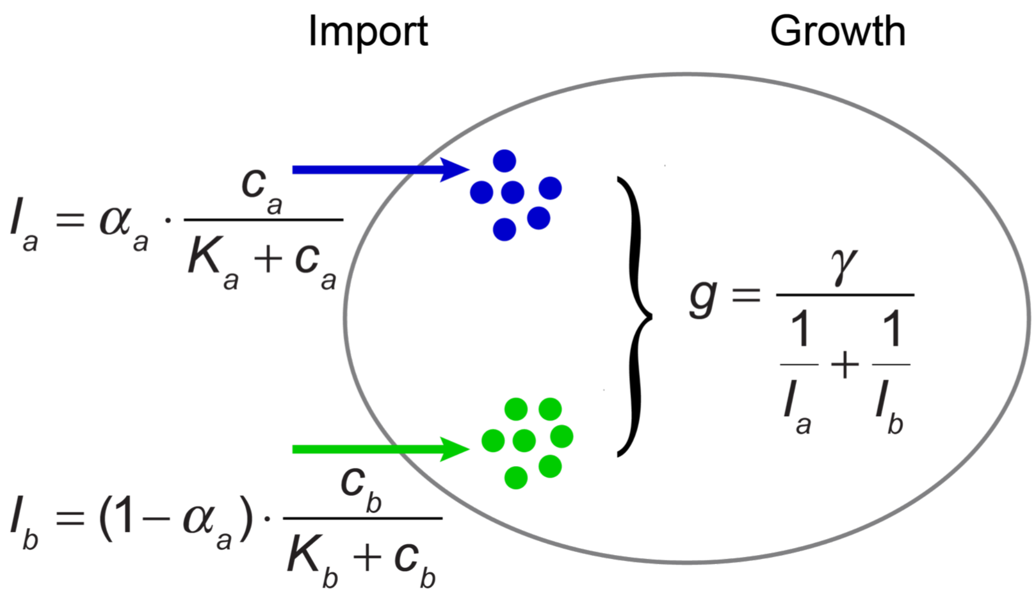
Metabolic trade-offs and regulatory strategy

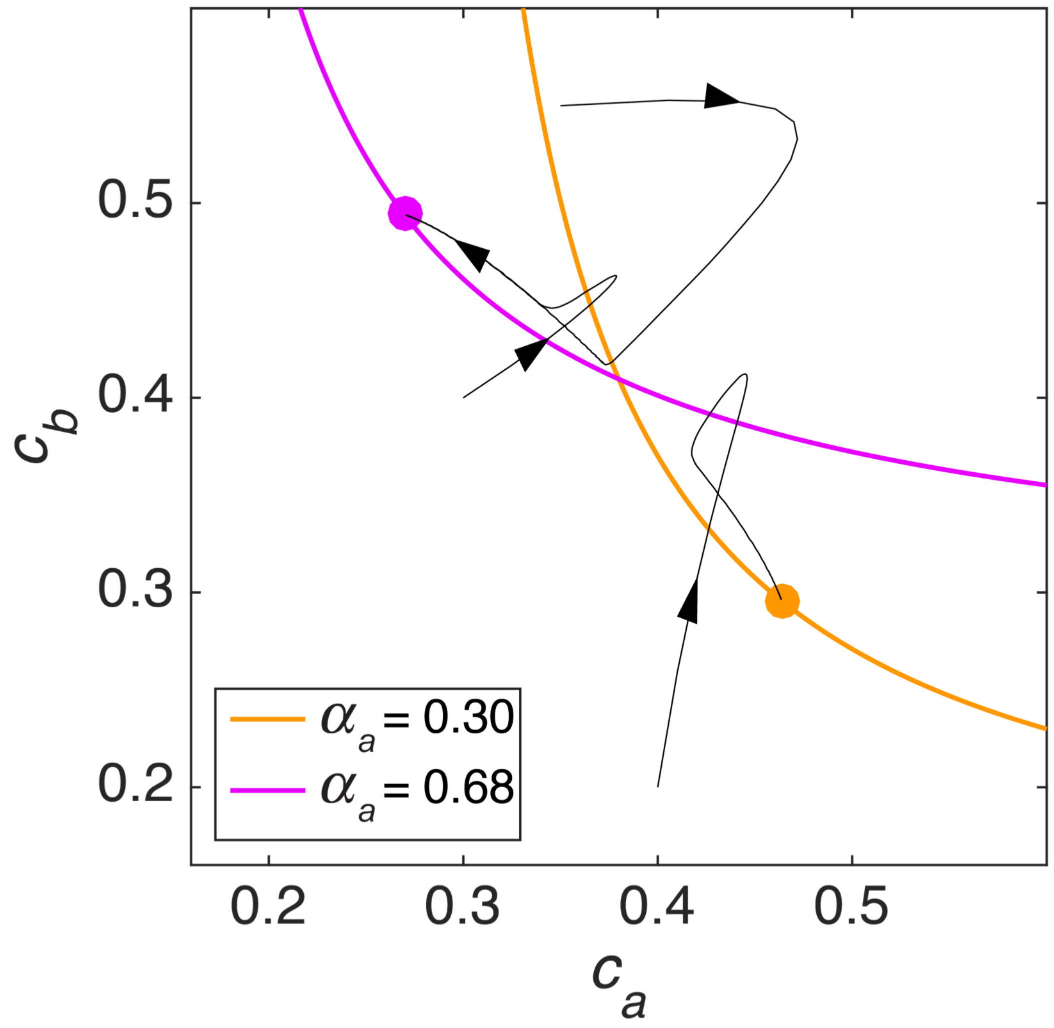


Regulatory strategy $\vec{\alpha} = \{\alpha_1,\ \alpha_2 \ldots\}$: allocation of resources into different cellular functions

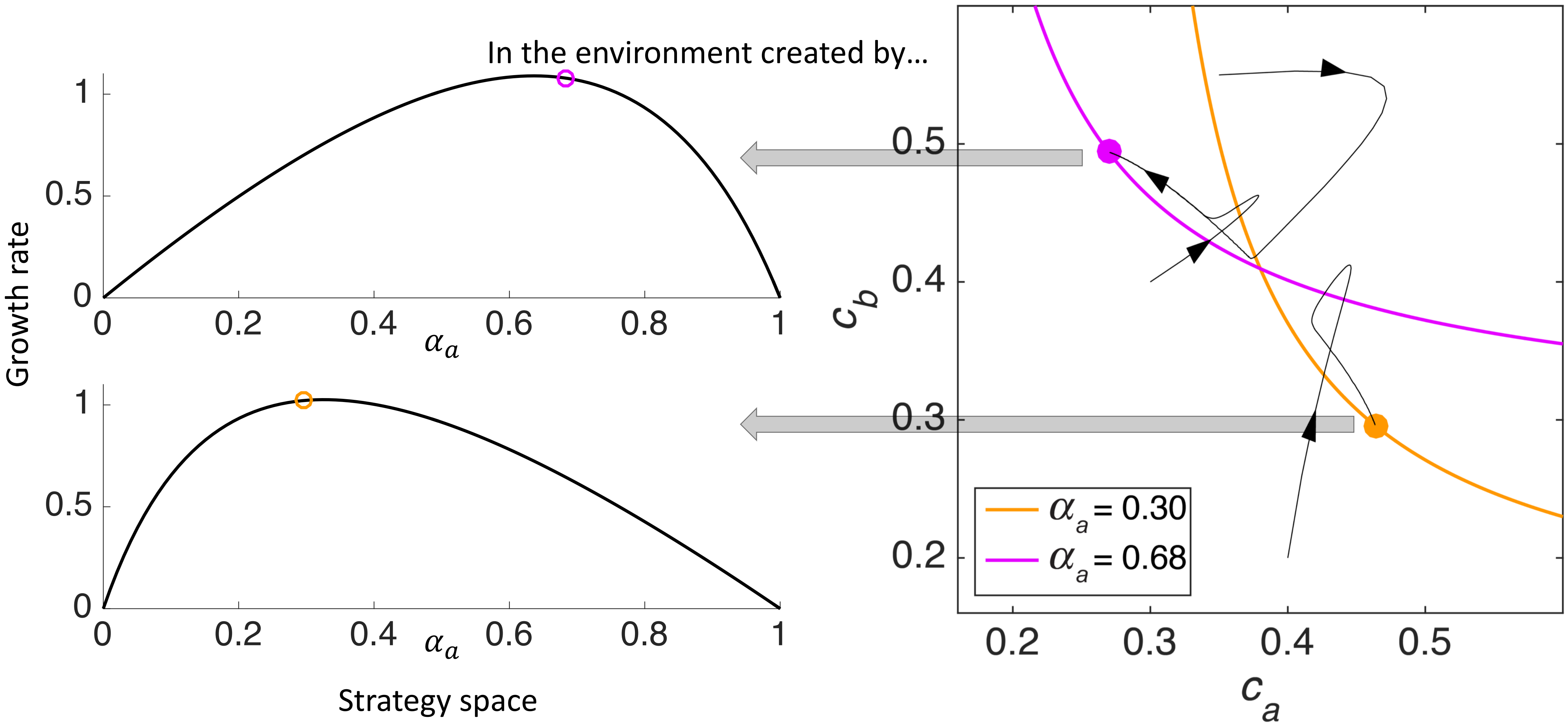
α_j : the fraction of proteins/energies that is allocated to the *j*-th cellular function

Examples of bistability

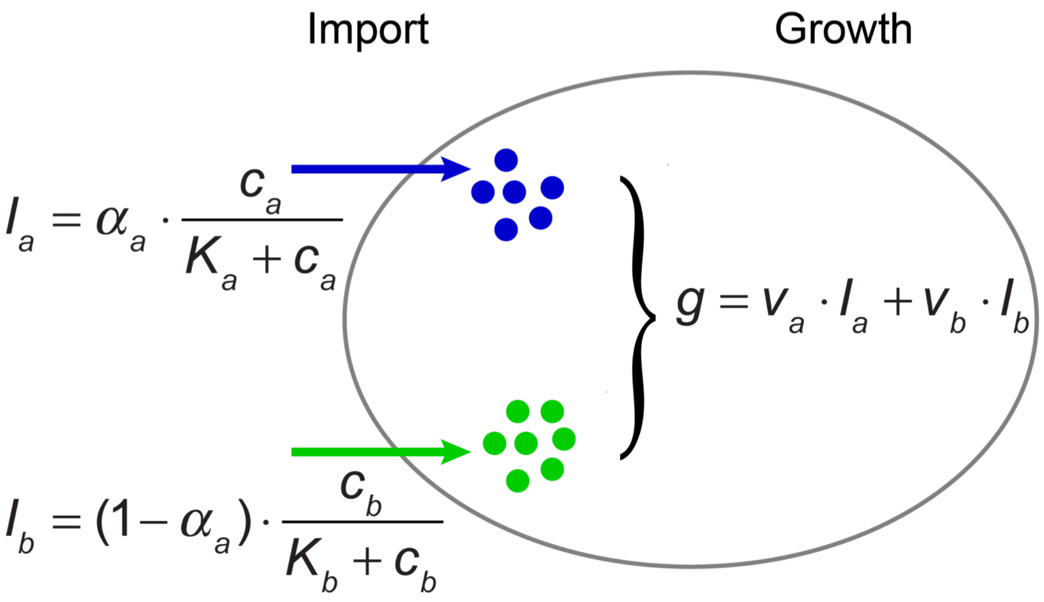


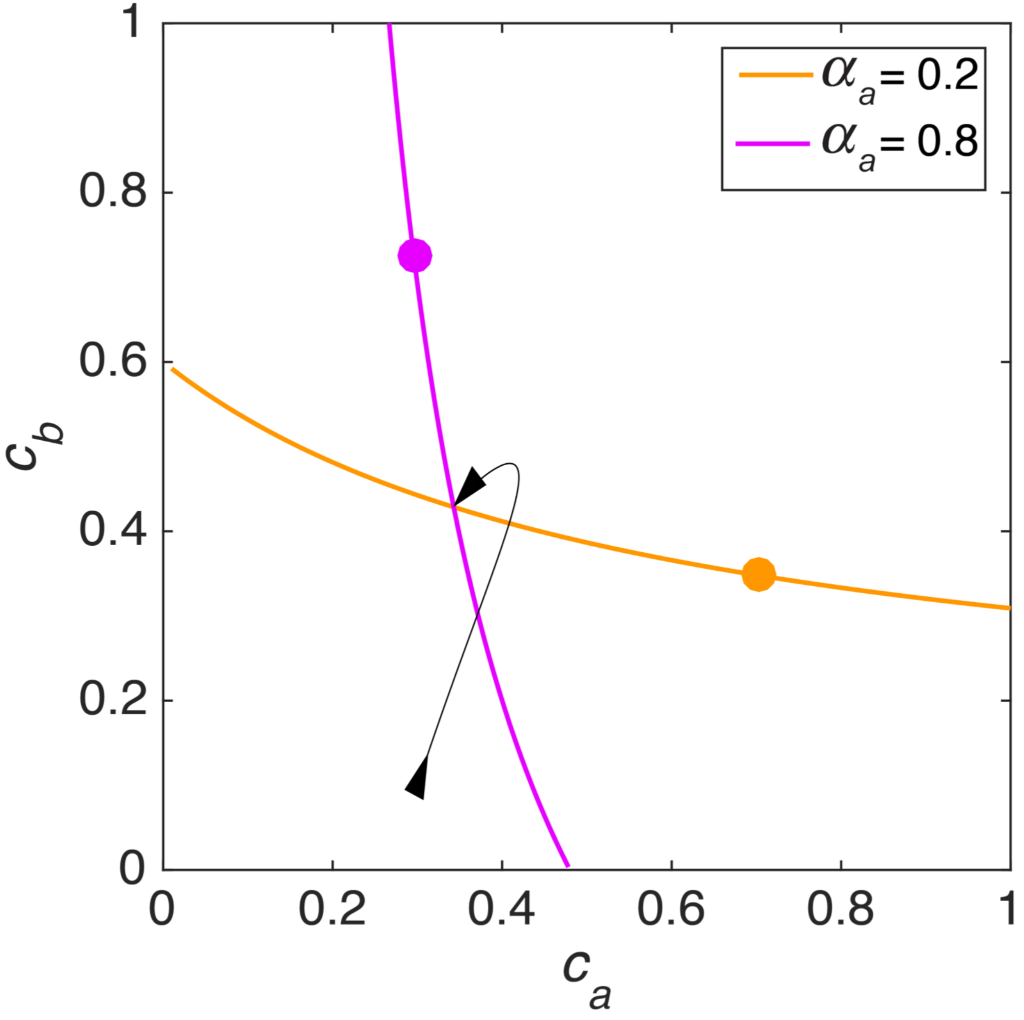


How to achieve bistability:
Species creates an environment that favors itself

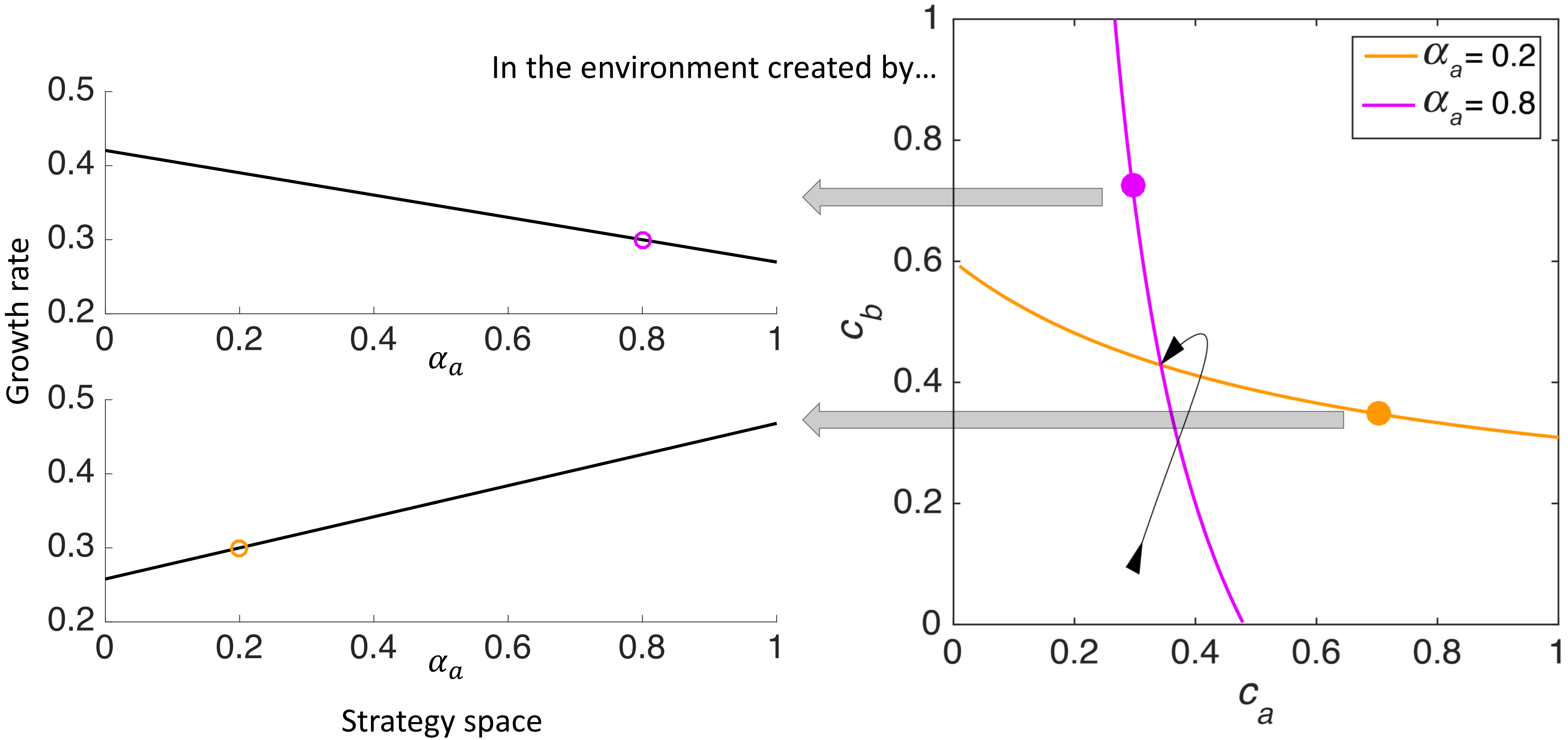


Examples of mutual invasion





How to obtain achieve mutual invasion: Species creates an environment that favors the other

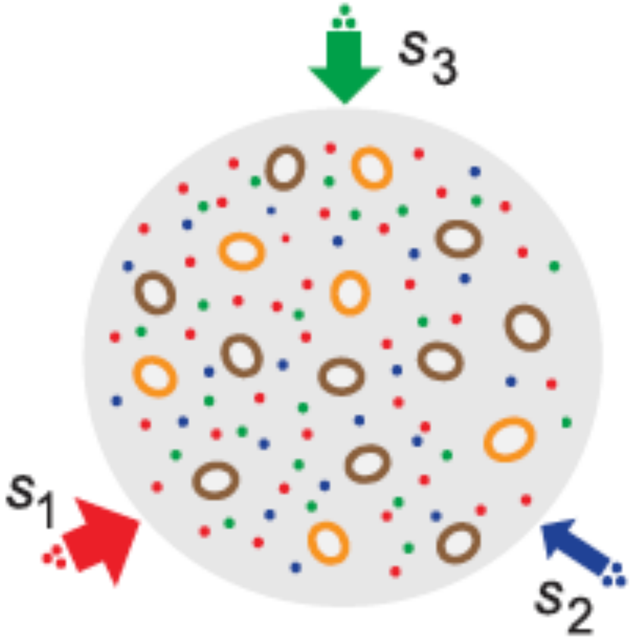


Metabolic Trade-Offs Promote Diversity in a Model Ecosystem

PRL **118**, 028103 (2017)

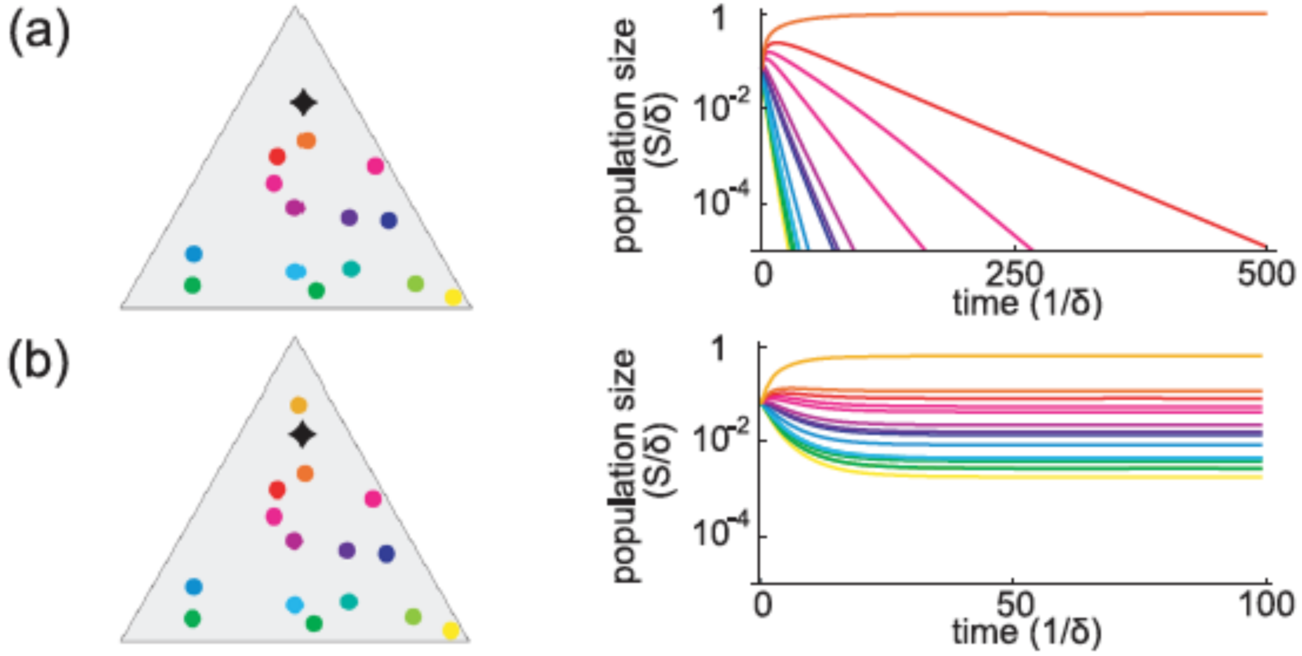
Anna Posfai,[1] Thibaud Taillefumier,[2] and Ned S. Wingreen[1,3]

Trade-offs:

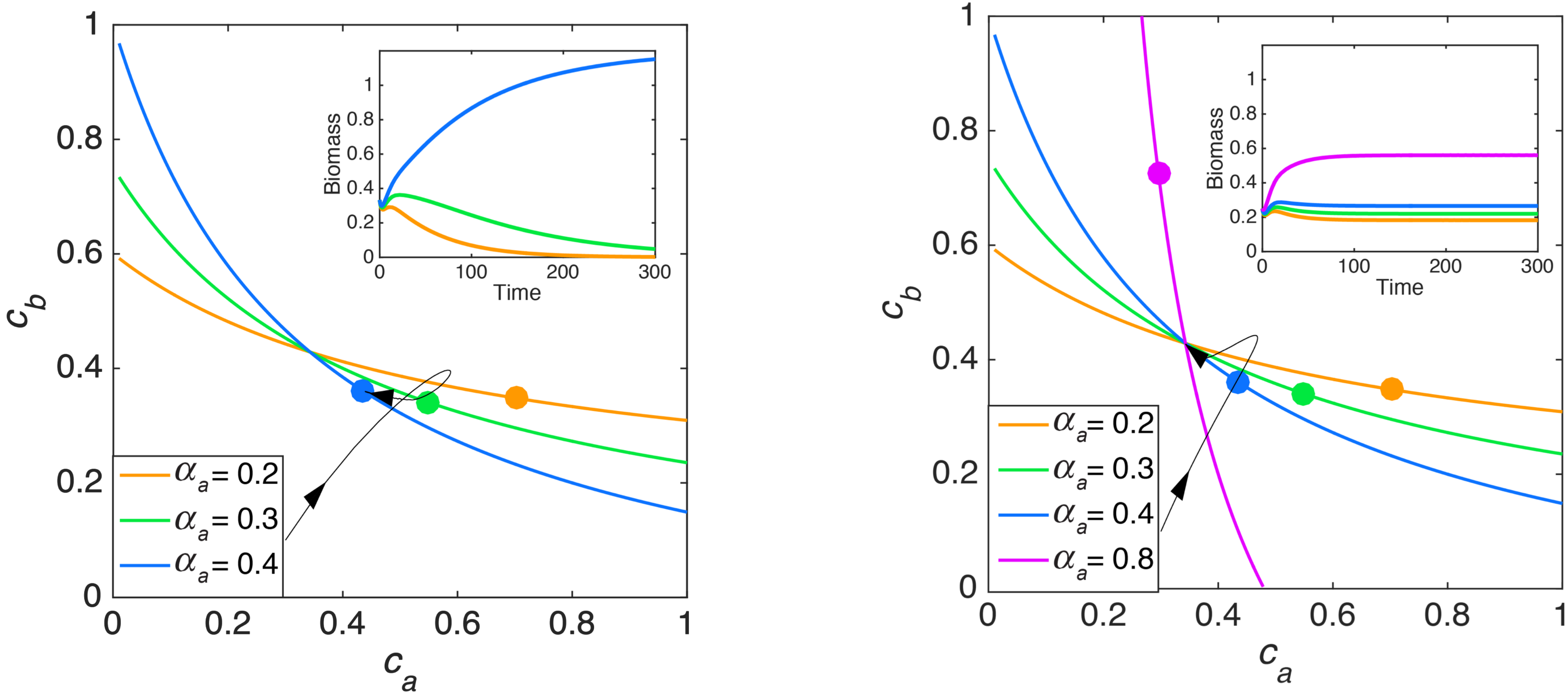


Result:

Unlimited number of species can co-exist under this model setting, if there are “keystone species” to maintain the ecosystem.



How metabolic trade-offs permit unlimited coexistence



letters to nature

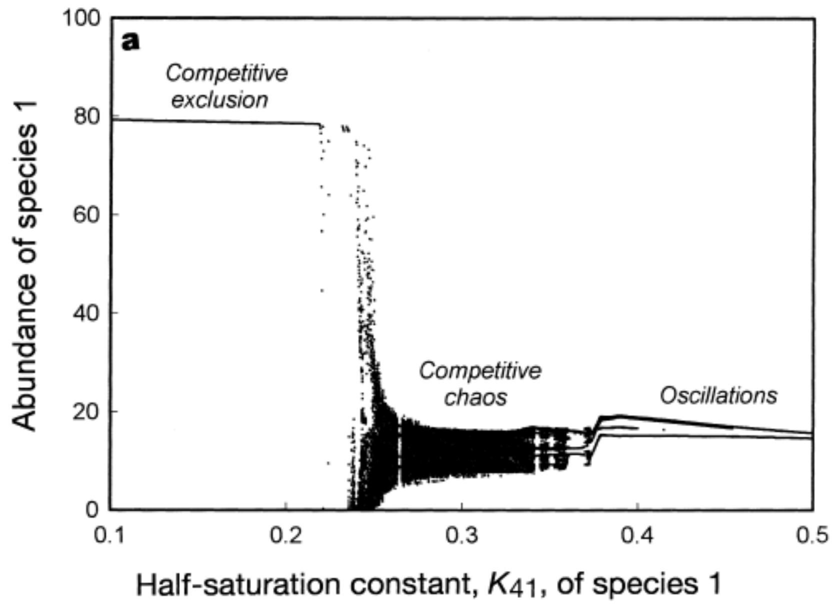
Biodiversity of plankton by species oscillations and chaos

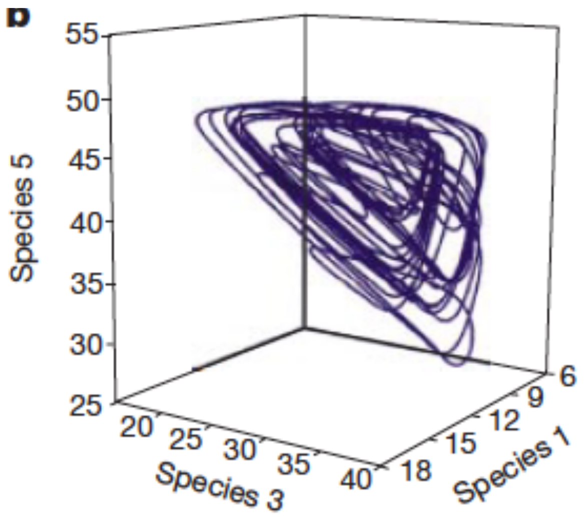
Jef Huisman*†‡ & Franz J. Weissing§

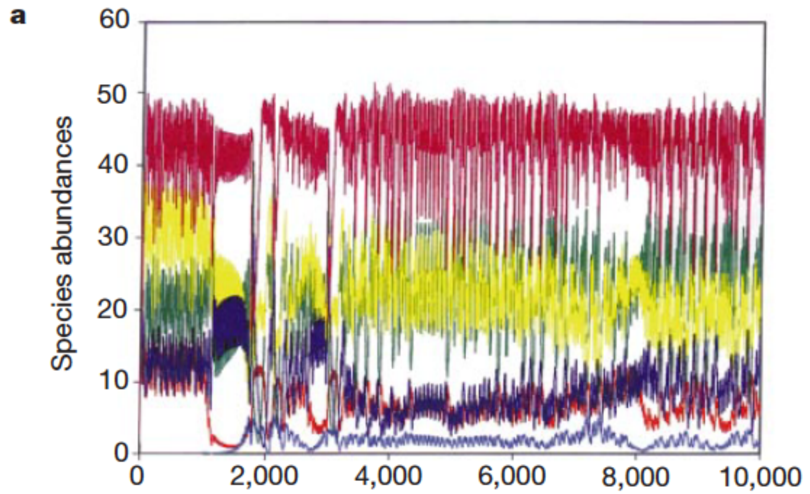
$$\frac{\mathrm{d}N_i}{\mathrm{d}t} = N_i(\mu_i(R_1, \ldots, R_k) - m_i) \quad i = 1, \ldots, n \qquad (1)$$

$$\frac{\mathrm{d}R_j}{\mathrm{d}t} = D(S_j - R_j) - \sum_{i=1}^{n} c_{ji}\mu_i(R_1, \ldots, R_k)N_i \quad j = 1, \ldots, k \qquad (2)$$

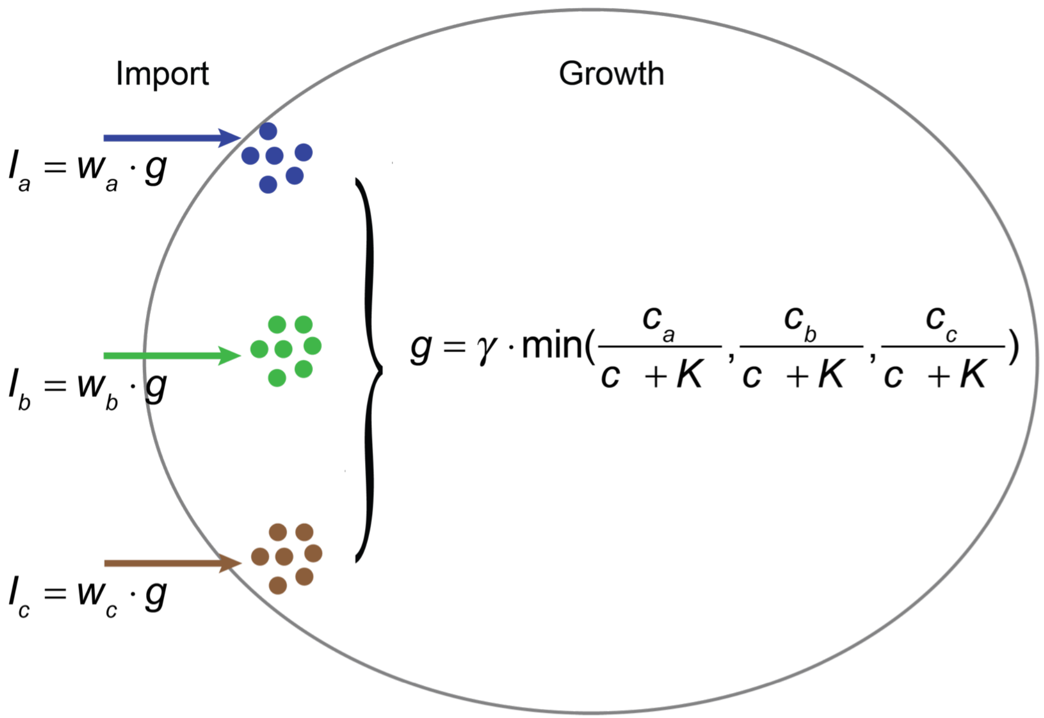
$$\mu_i(R_1, \ldots, R_k) = \min\left(\frac{r_i R_1}{K_{1i} + R_1}, \ldots, \frac{r_i R_k}{K_{ki} + R_k}\right) \qquad (3)$$

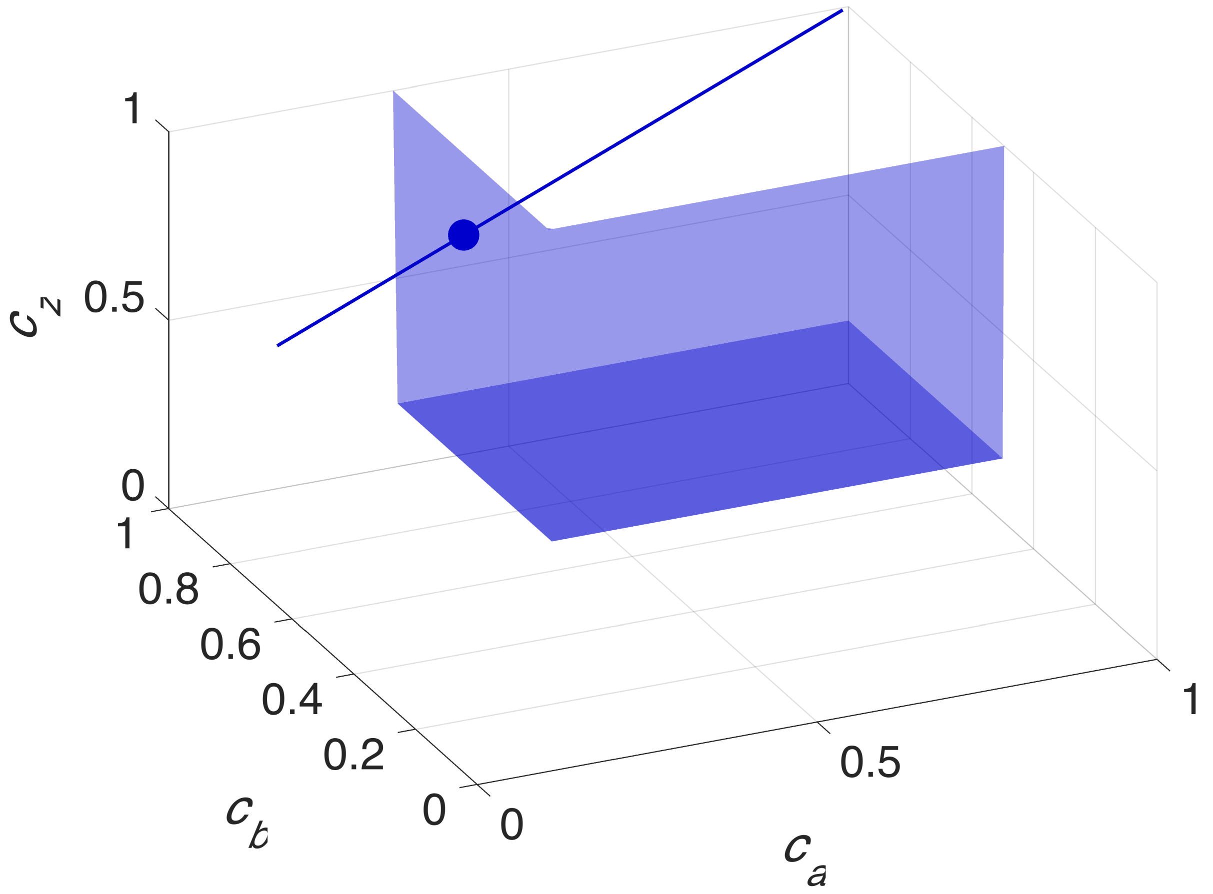




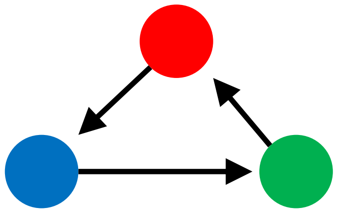


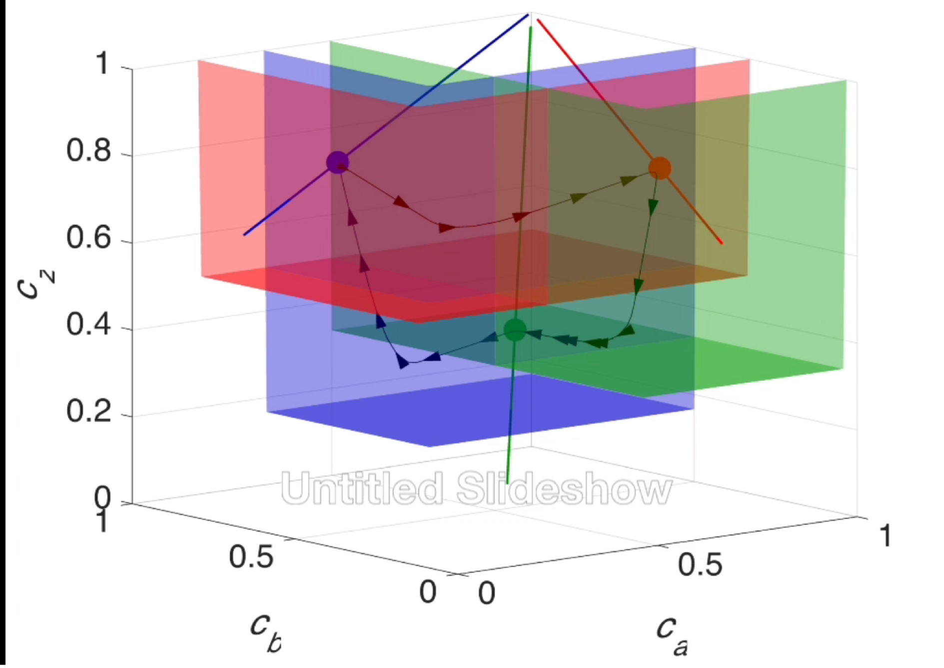
Rock-paper-scissors invasion loop

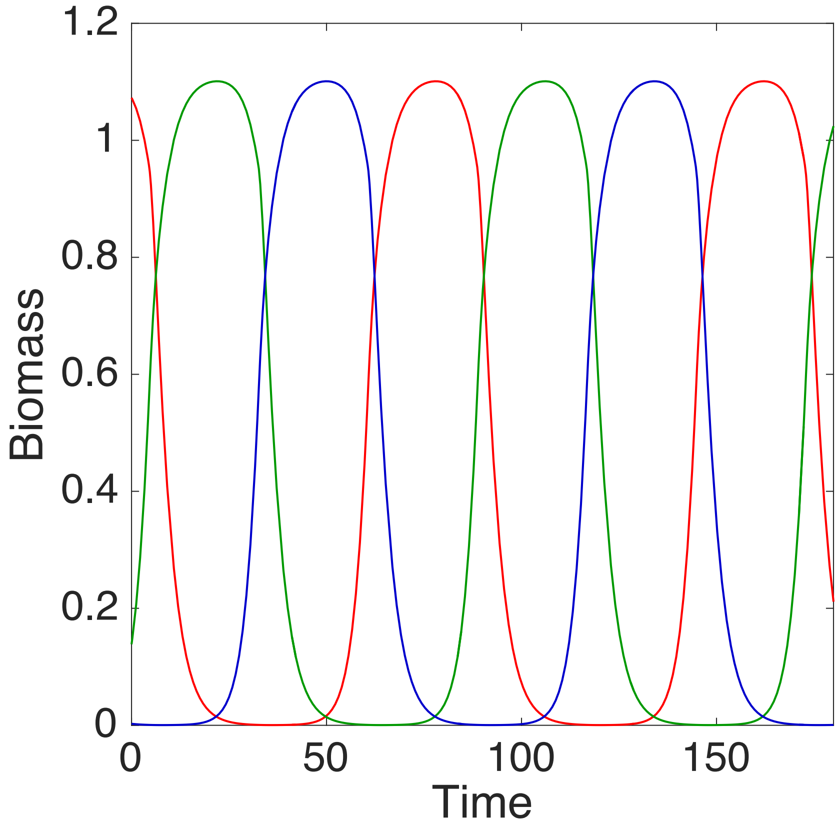




Rock-paper-scissors invasion loop







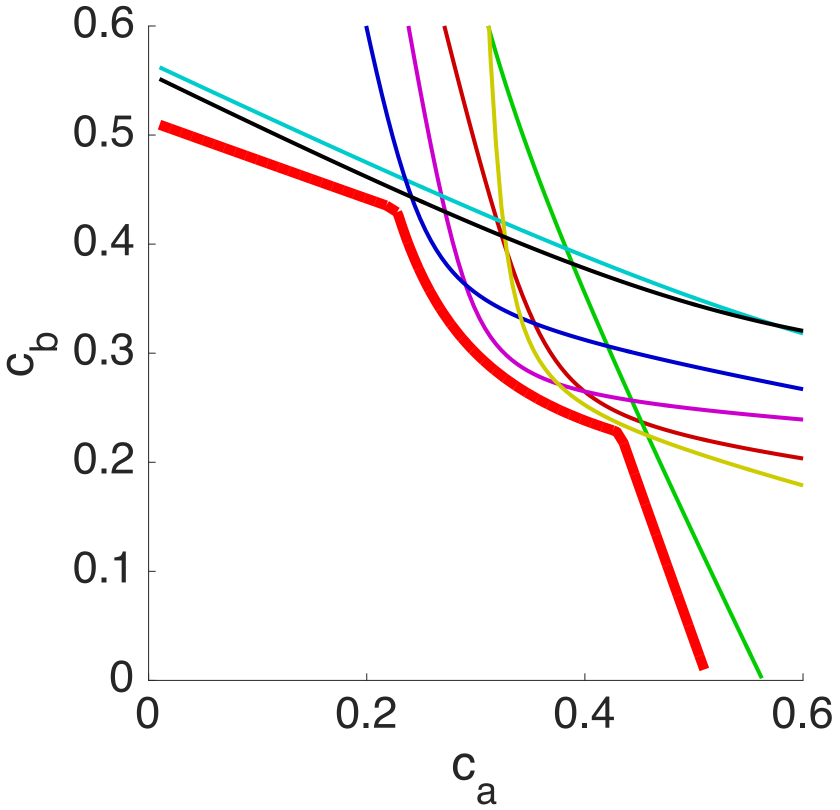
Brief summary on the rule of invasion and intransitivity of fitness

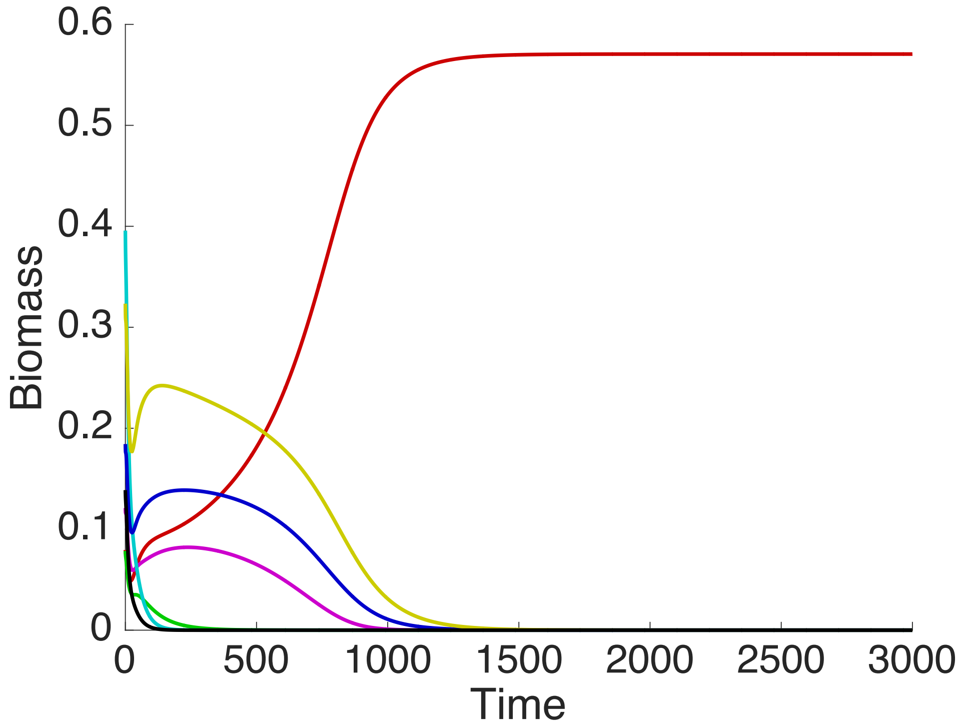
- Regardless of model details, the outcome of species *Orange* invading species *Purple* only depends on the relative position of *Orange* contour and *Purple* environment
- Cross of two growth contours allows intransitivity of fitness, leading to rich population dynamics

The “superspecies” resistant to any invasion

Superspecies: the hypothetic speices with the most inclusive growth contour that no any other species could create an environment below it. It is equivalent to:

$$\mathrm{Max}(g|\vec{c}).$$





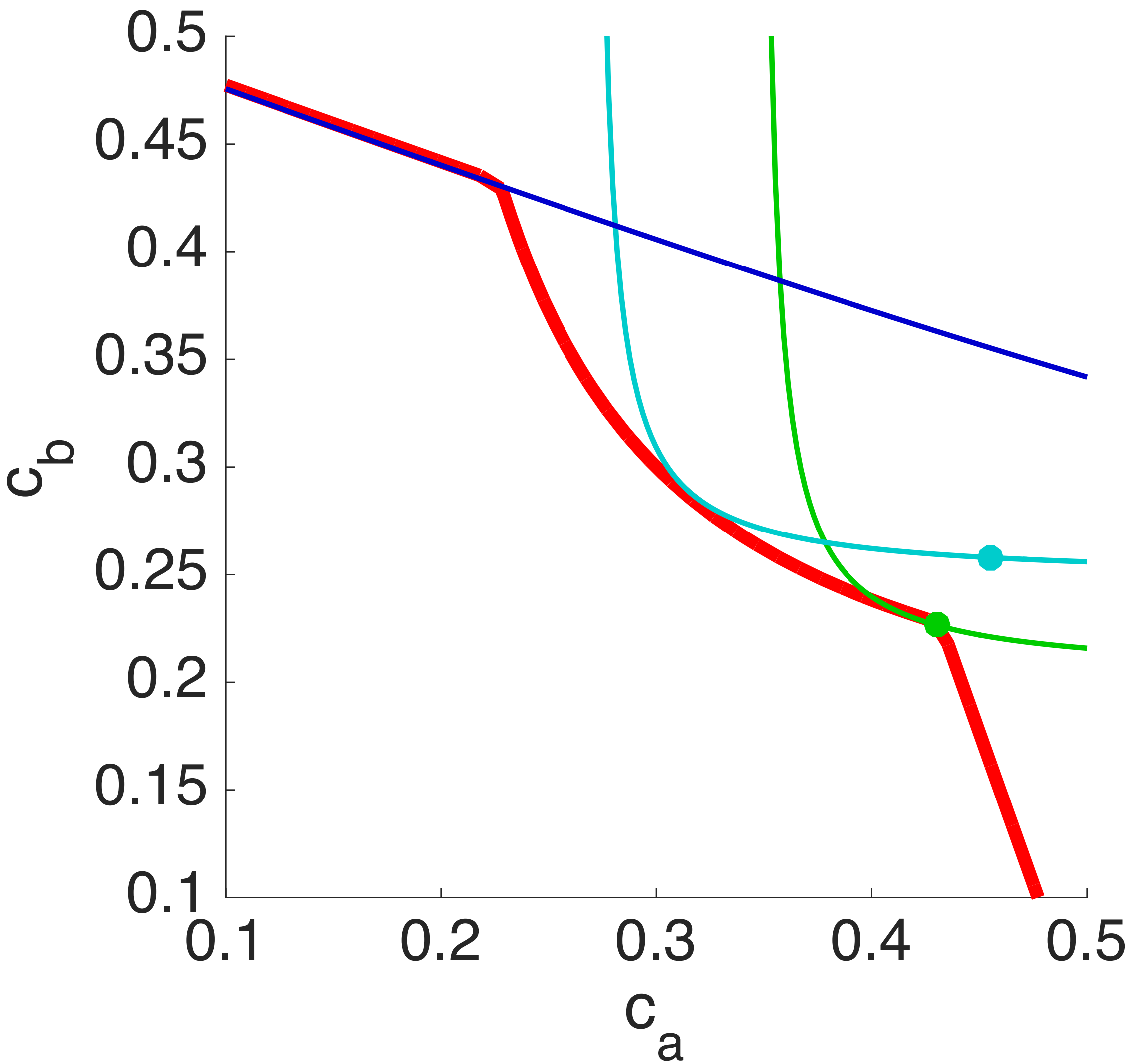
Fixed strategy, “local optimal”, and non-transitivity of fitness

Superspecies:

Variable $\vec{f}_{opt}$ to ensure $g(\vec{c}, \vec{f}_{opt}) \geq g(\vec{c}, \forall \vec{f})$ under any supply condition

“Local optimized species”:

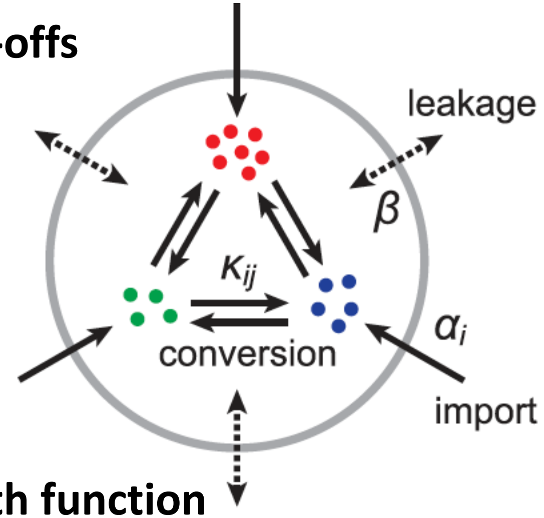
- Fixed $\vec{f}$ = $\vec{f}_{opt}(\vec{c}_{\text{supply}})$, for the $\vec{c}_{\text{supply}}$ it encounters most frequently
- Partially overlaps with the growth contour of the superspecies



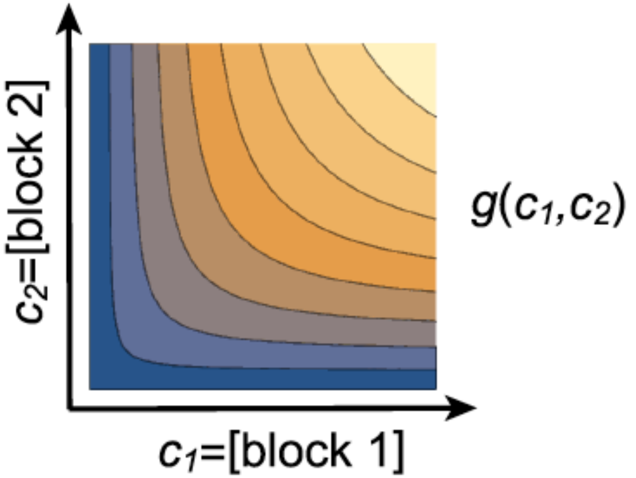
Microbial consortia at steady supply

Thibaud Taillefumier[1,2,3], Anna Posfai[1], Yigal Meir[4], Ned S Wingreen[1,5*]

Trade-offs

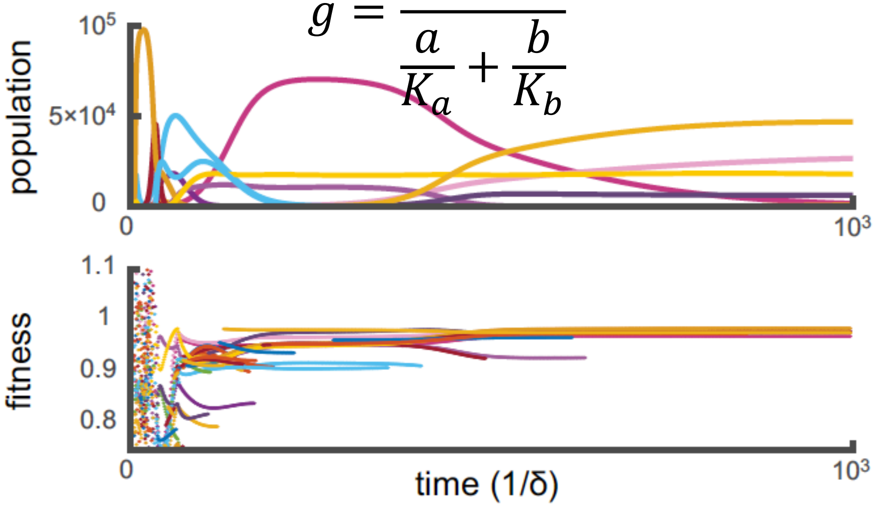


Growth function

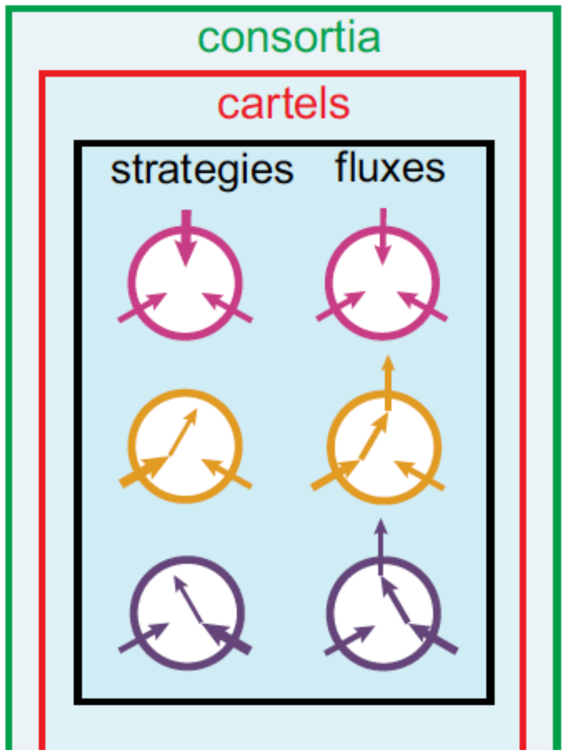


Method: silico-evolution for searching the group of "optimal species", and theoretical analysis

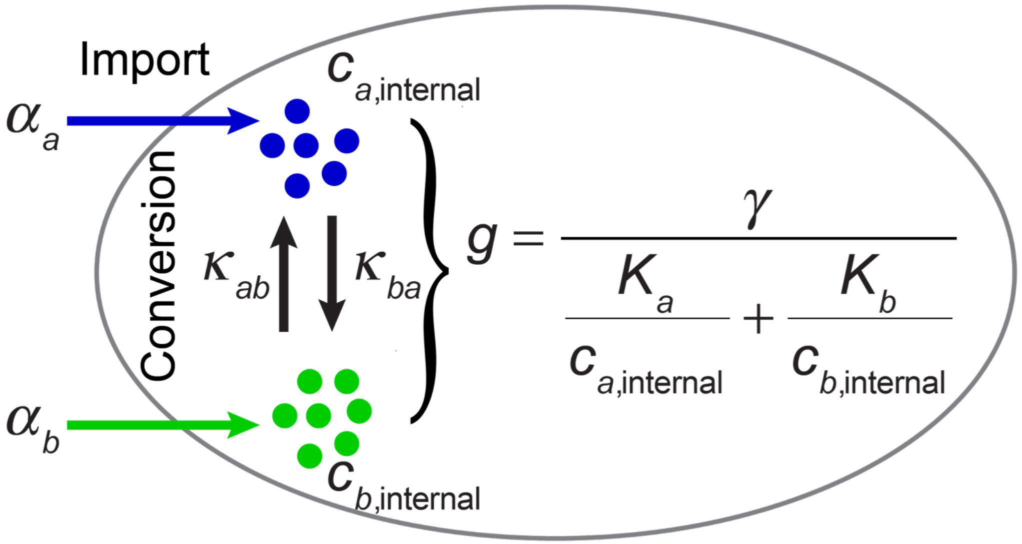
$$g = \frac{V}{\frac{a}{K_a} + \frac{b}{K_b}}$$

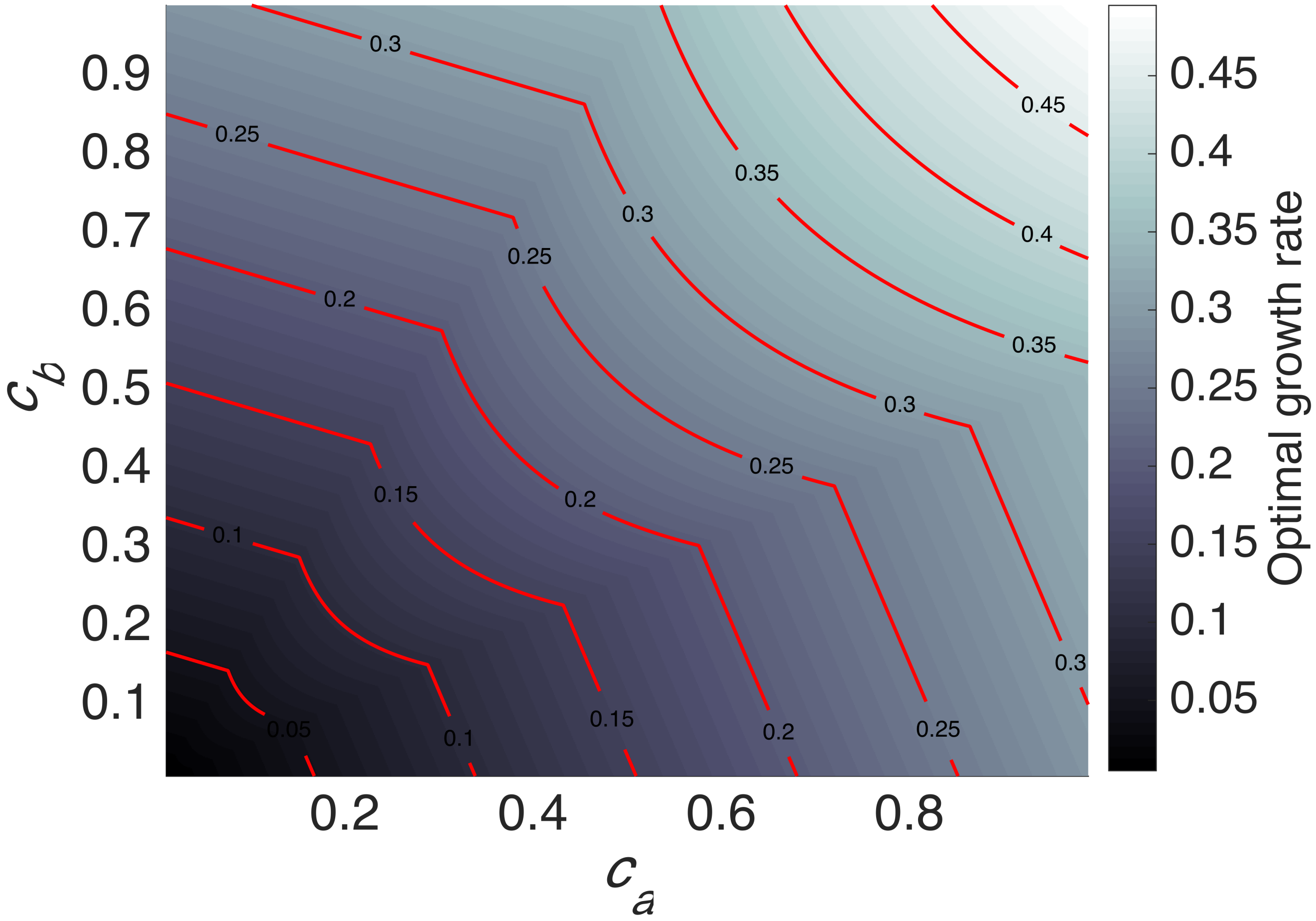


Result:
Under certain nutrient supply condition, species with distinct metabolic strategies can co-exist as the non-invadeable consortia

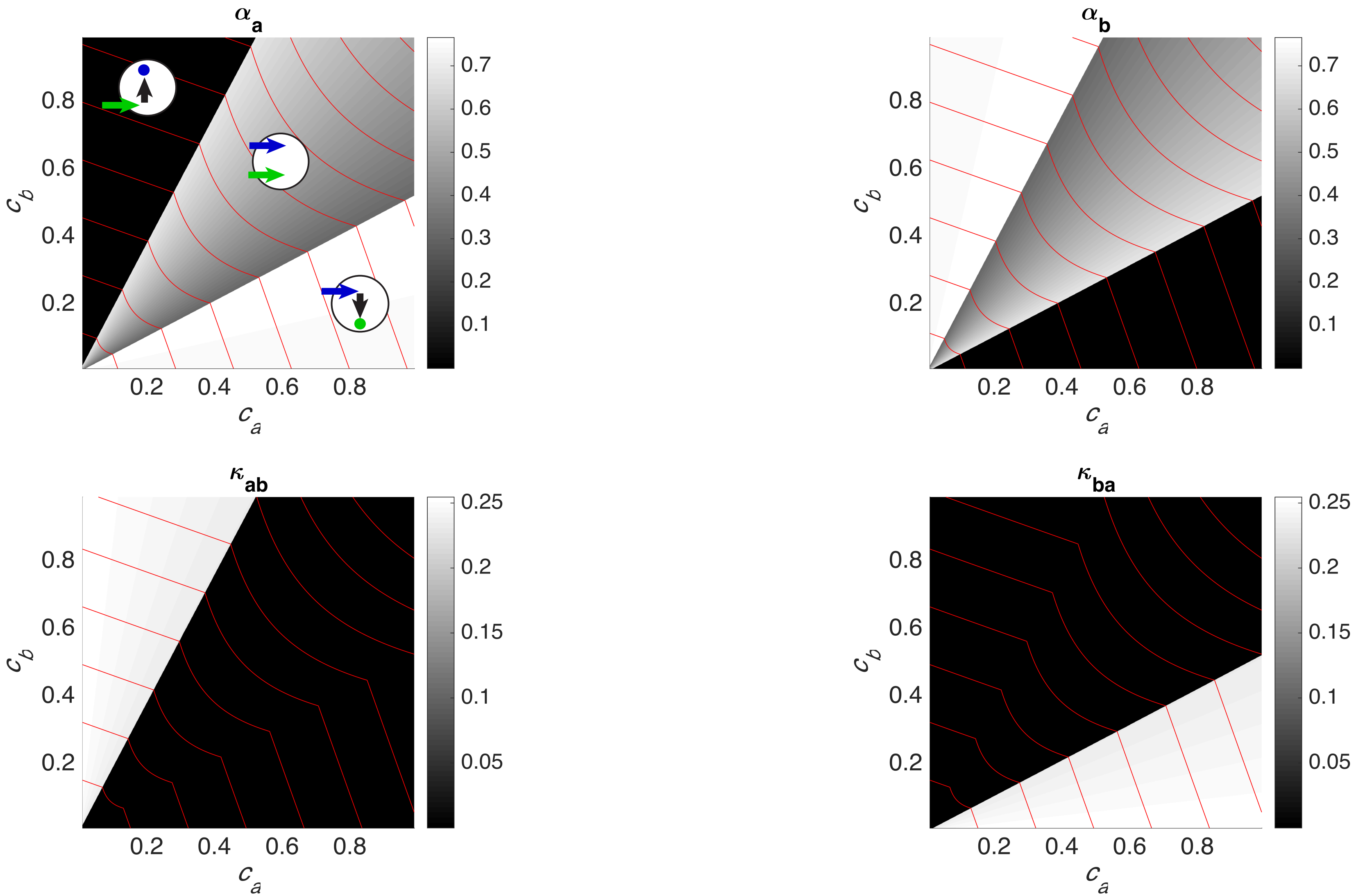


Optimal growth rate for a import/conversion model

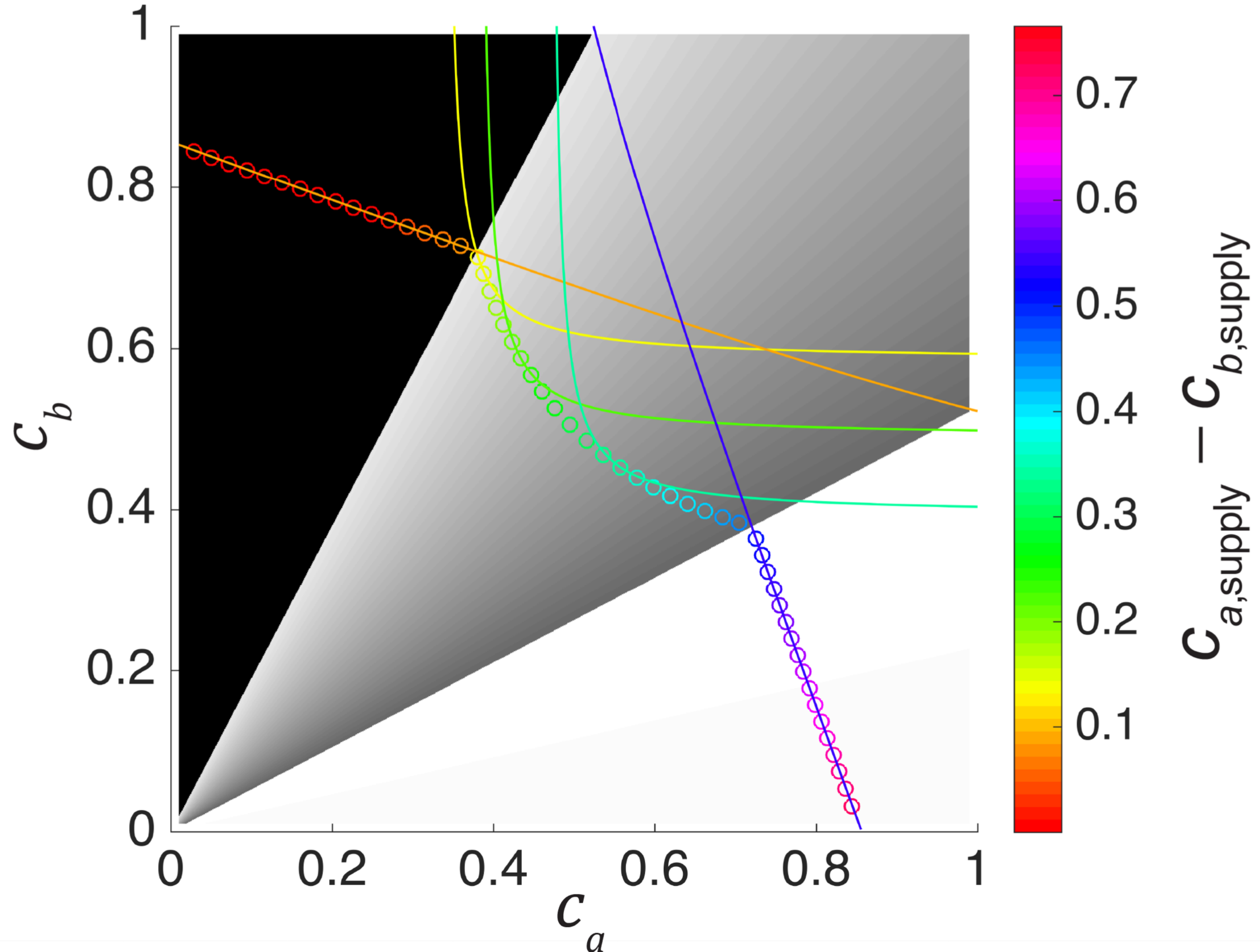


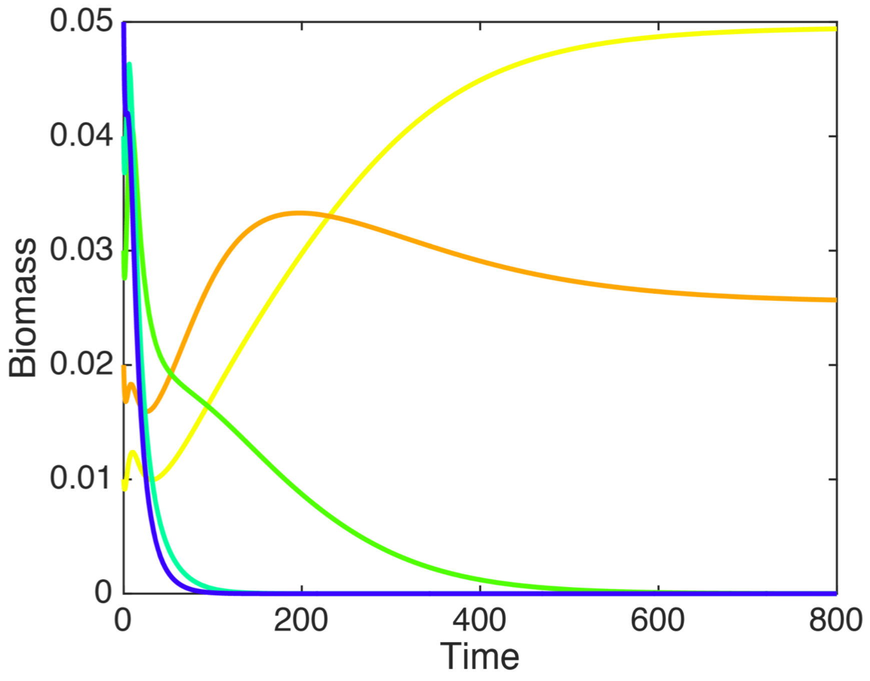


Three sectors of optimal strategies for an import/conversion model

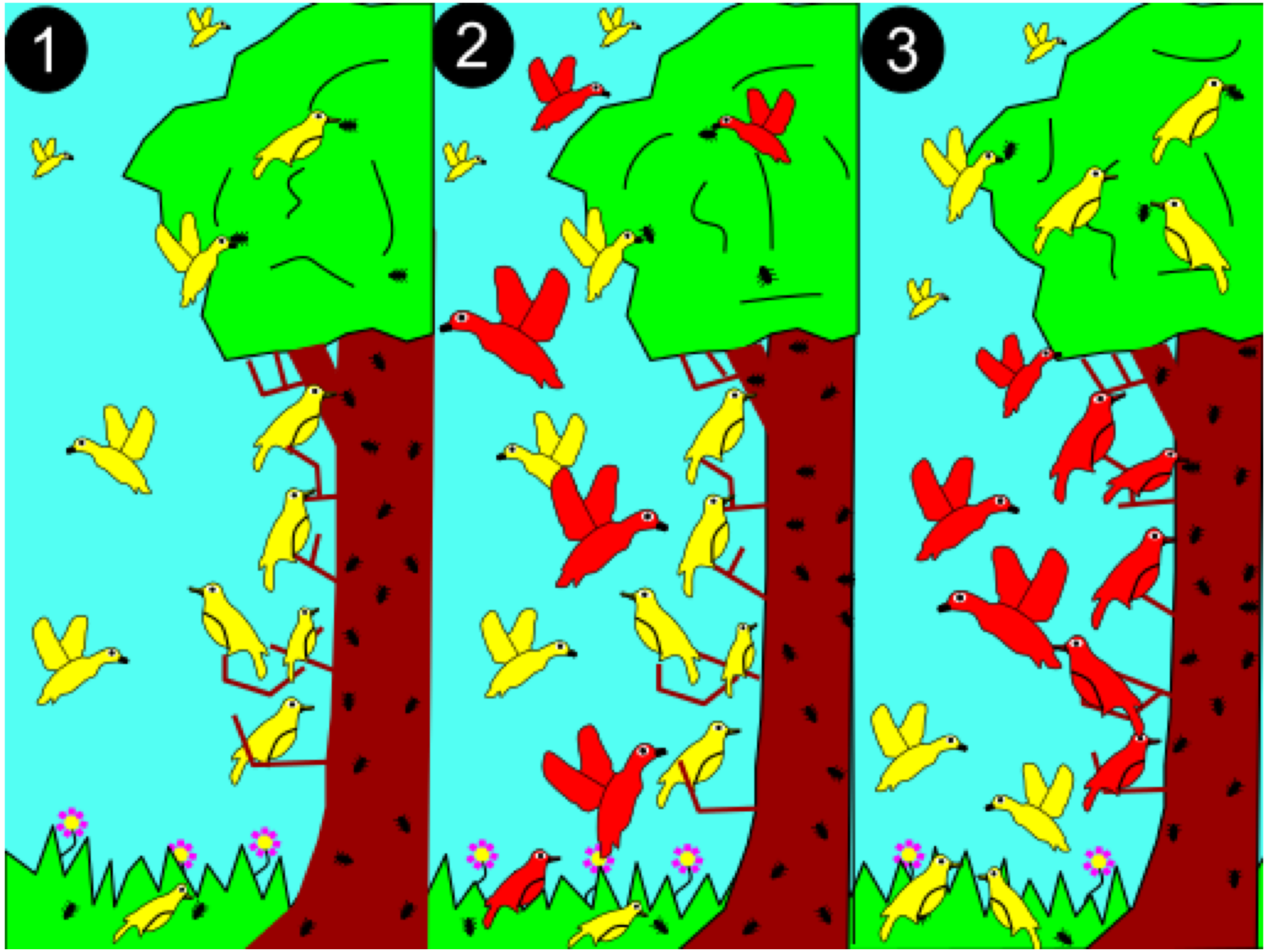


Joint locally optimal strategies and cartels

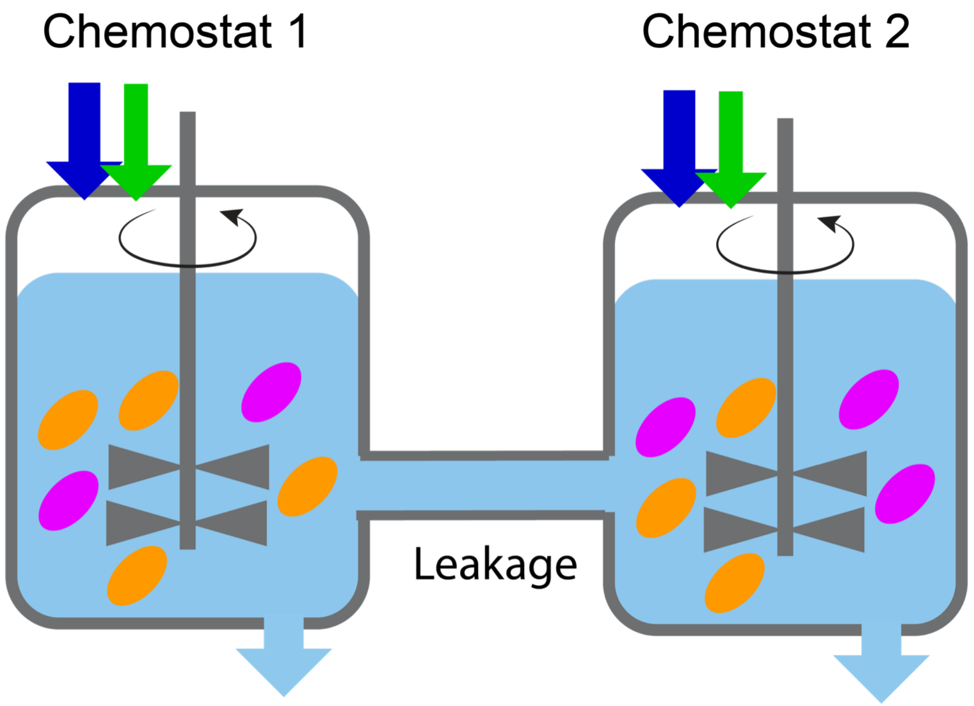


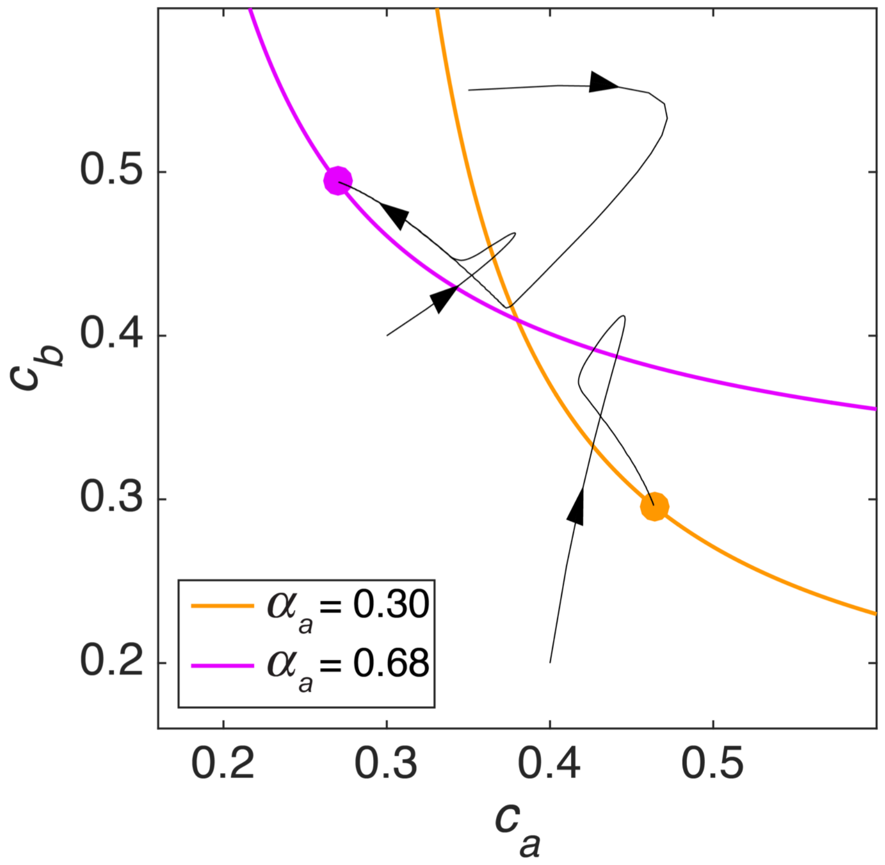


One solution for plankton paradox: Spatial heterogeneity

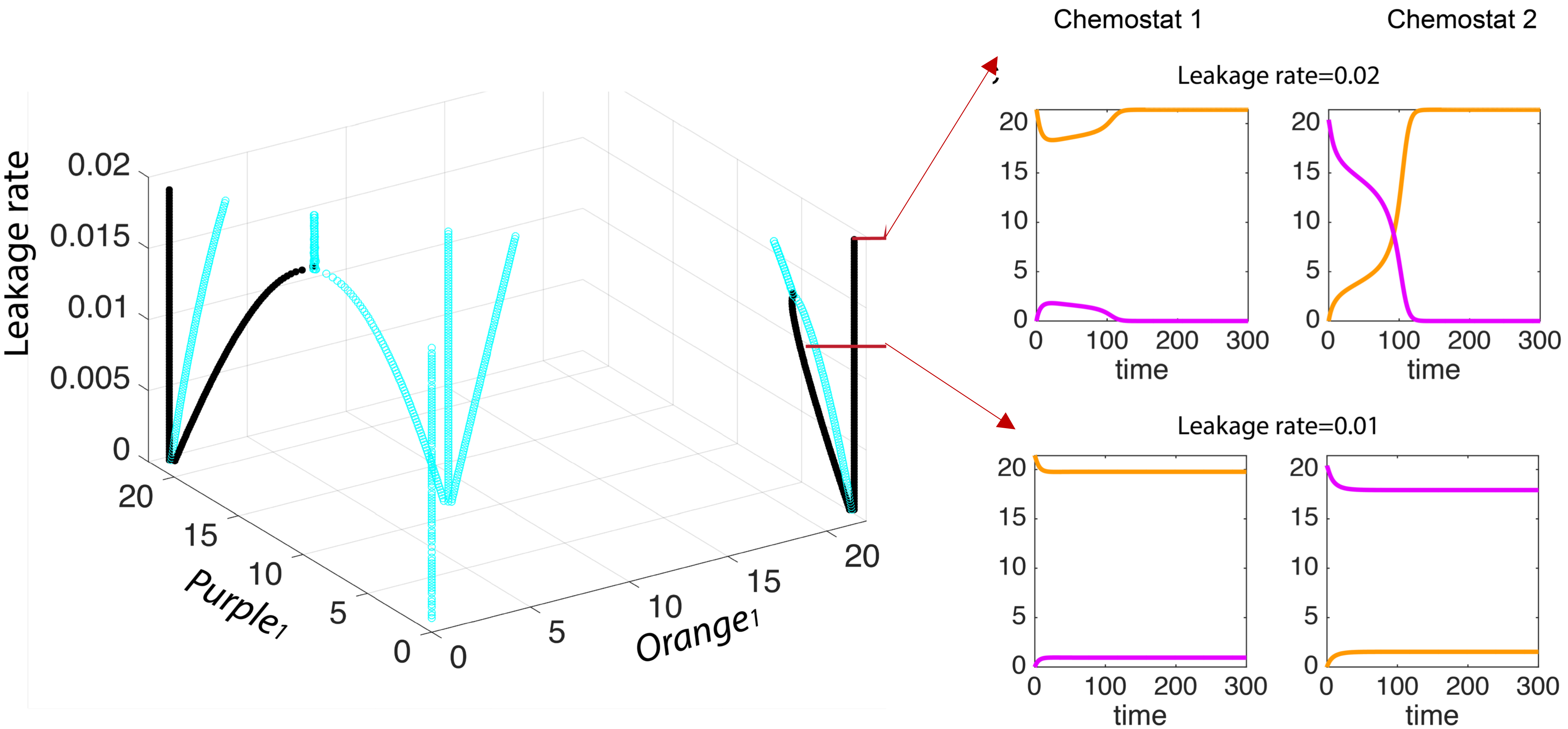


Spatial heterogeneity can emerge out of homogeneous external condition

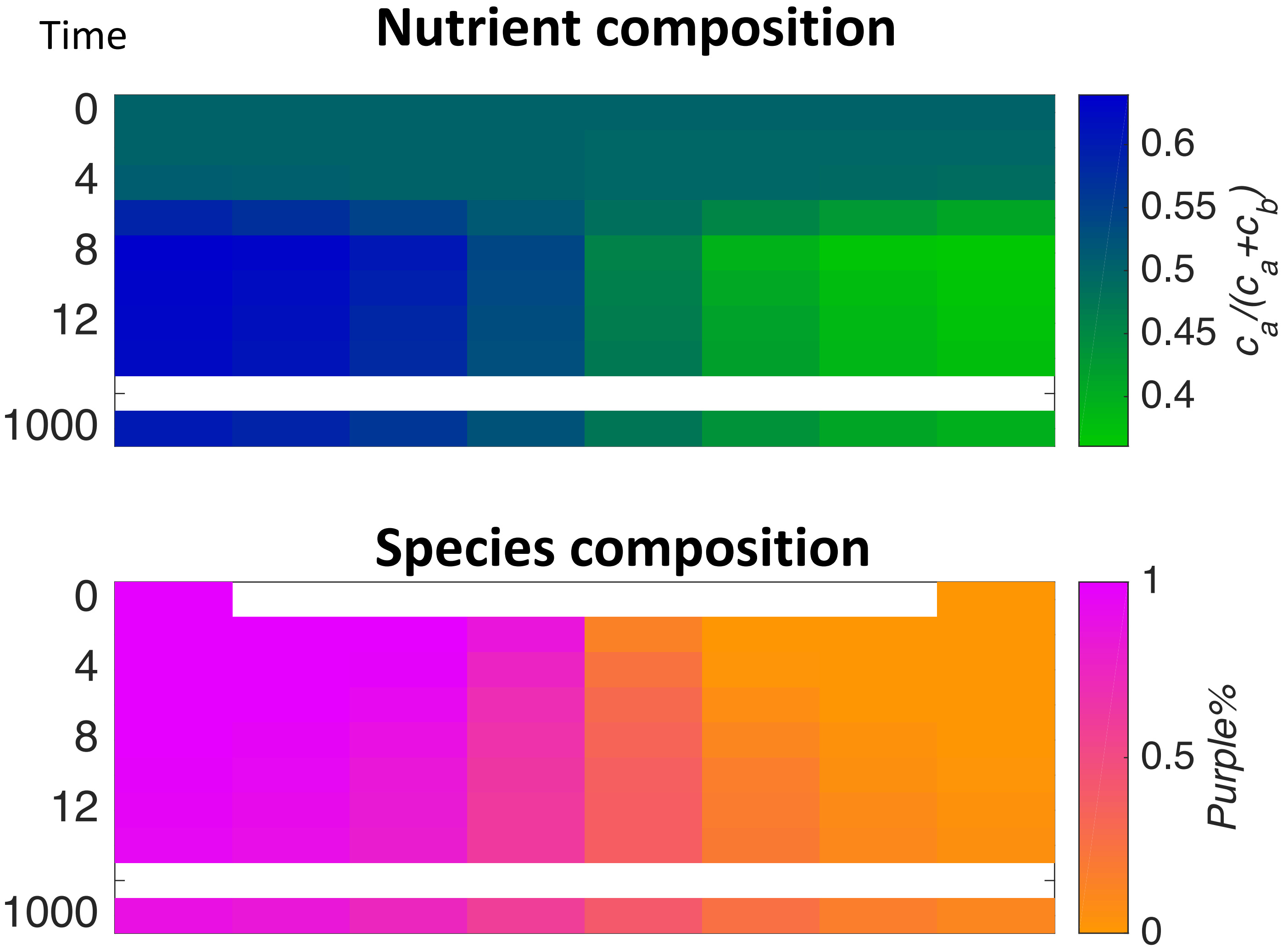




Spatial heterogeneity can emerge out of homogeneous external condition



Formation of spatial gradient by chain of chemostats



Summary

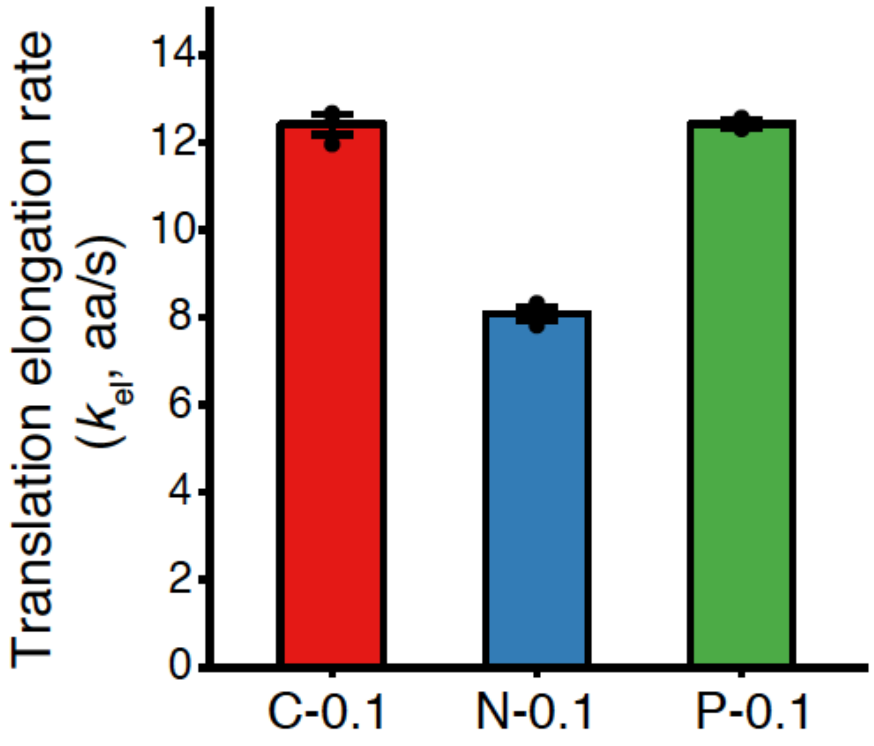
- By growth and consumption, species create their **own environment**.
- The environment shaped by one species may be inviting or prohibiting to another species, leading to the **non-transitivity of fitness**.
- This none-transitivity of fitness can lead to **rich ecosystem dynamics.**
- We constructed an **intuitive and generalizable** mathematical framework that clarifies the relationship of previous resource-competition models, and provides insight into the stability of spontaneously spatially structured communities.

Thanks!

"Fitness Trampoline"

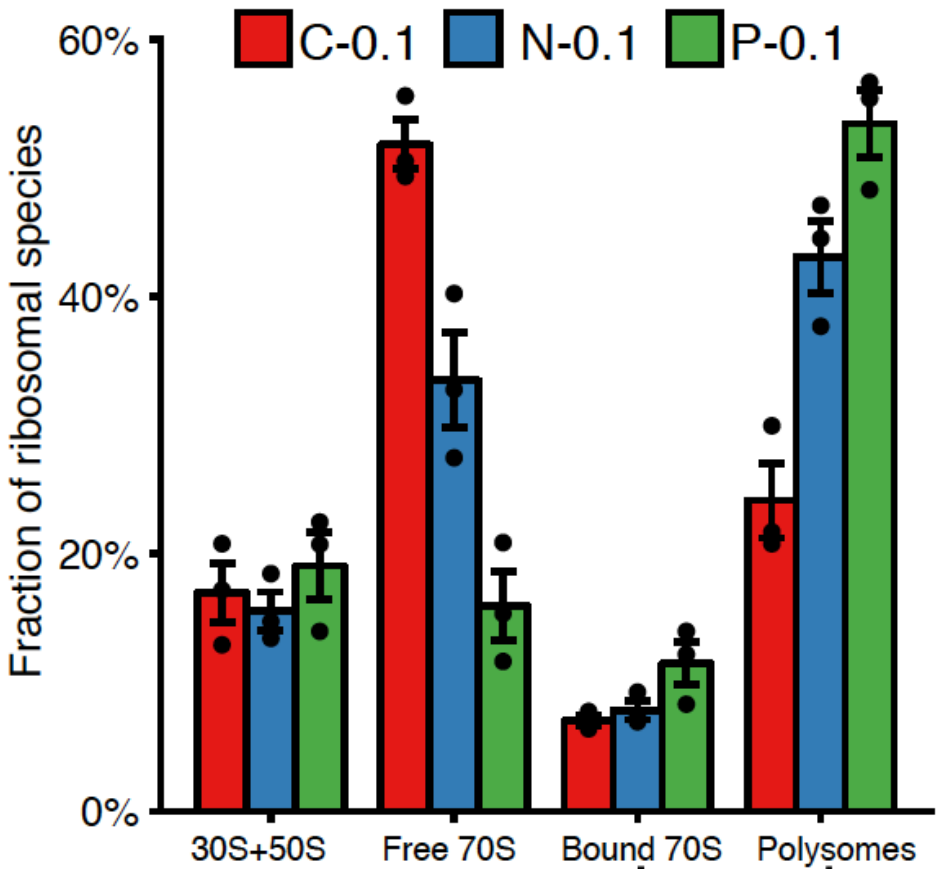
What are ribosomes doing

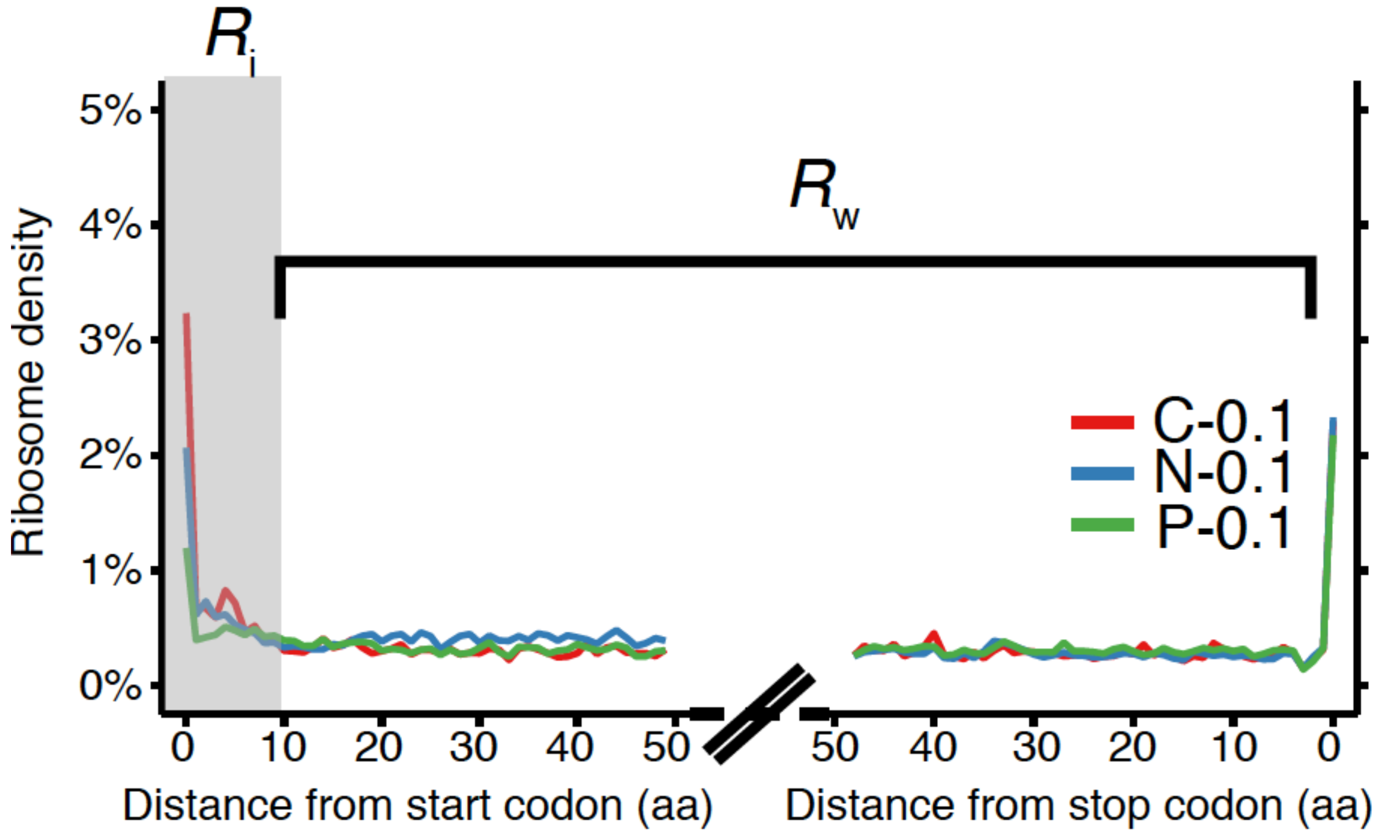
Different Elongation Rates



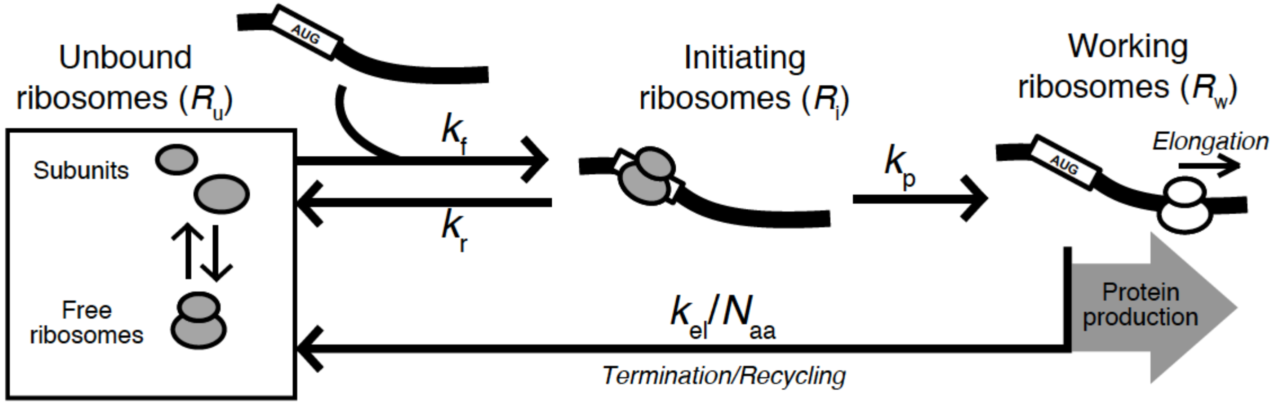
What are ribosomes doing

Different fraction of working ribosomes



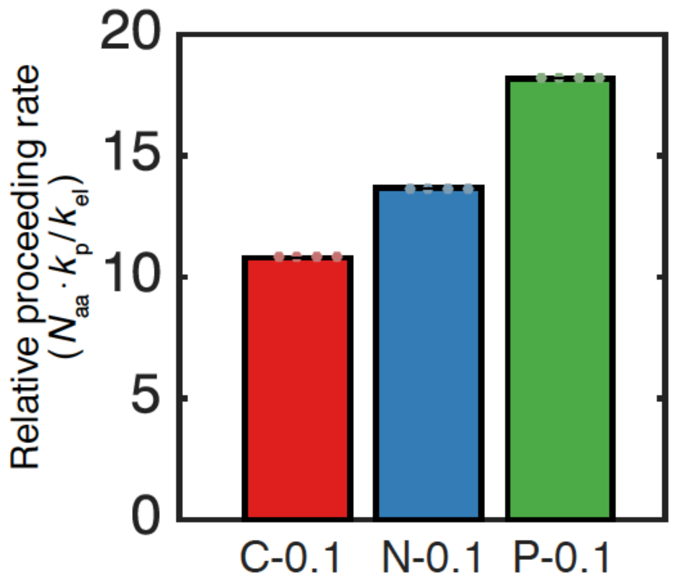


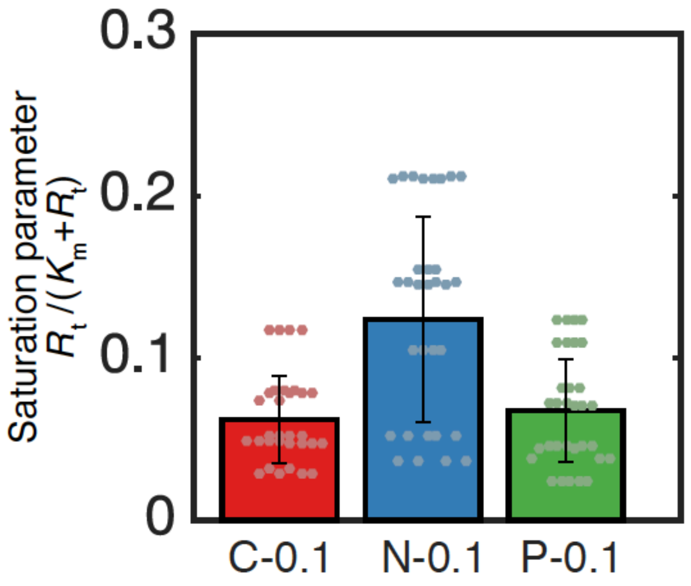
Model the ribosome dynamics



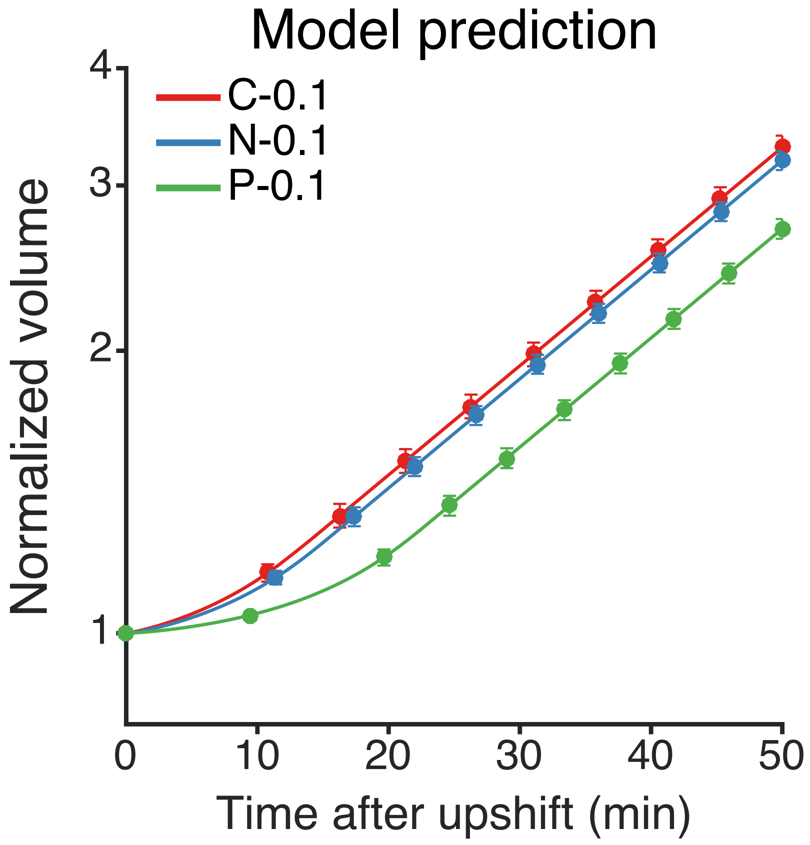
$$E + S \underset{k_r}{\overset{k_f}{\rightleftharpoons}} ES \xrightarrow{k_{cat}} E+P$$

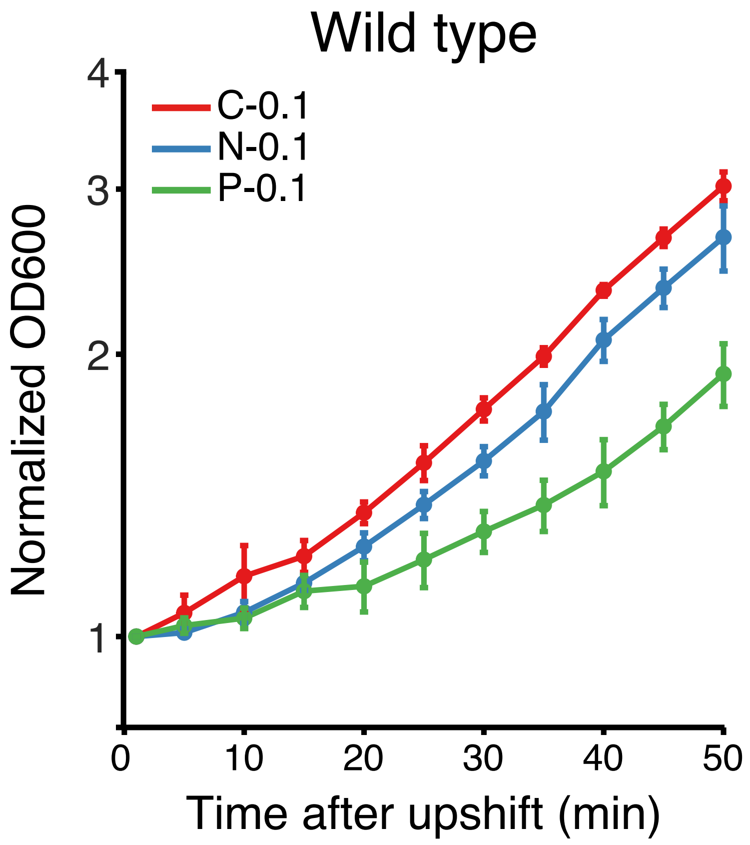
$$K_m = \frac{k_r + k_{cat}}{k_f}$$





Predicted and experimental growth rate upon nutrient upshift





Summary: Diverse ribosomal behaviors achieve the same growth rate