

PHYS 239
Spatiotemporal Dynamics in Biological Systems
Winter 2022

Solution of Homework #3

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1. Proteome allocation and the Monod growth law

In class we went over key elements of the proteome allocation analysis for bacterial growth. In this problem, you will work them out step-by-step using a concrete example, for the growth of E. coli on lactose as the sole carbon source. From a few assumptions, we will obtain quantitatively the growth rate and the expression of the lac operon for different concentrations of lactose, i.e., Monod's growth law and the phenomenon of catabolite repression.

In the following, all quantities correspond to amount contained in 1-mL of exponentially growing culture at optical density (OD) = 1, referred to as "OD· mL" for short. 1 OD· mL of culture corresponds to $10^8 \sim 10^9$ bacterial cells depending on the specific culturing condition. We will refrain from using per cell quantity because the amount per cell can vary 10x due to change of cell size in different growth conditions (including for cells grown in different lactose concentrations to be studied here). Instead, amount per OD· mL is more invariant. In particular, 1 OD· mL of culture contains a total dry mass of ~ 0.5 mg and total cytoplasmic water content of ~ 1 mg (or 1 μ L in volume) for most conditions characterized. The total protein content in OD· mL varies moderately, from 0.3 mg at fast growth to 0.4 mg at slow growth. For simplicity, we will take total protein per OD· mL to be 0.35 mg.

Definition of symbols to be used below: N_X and M_X are, respectively, the number and mass of protein X per OD· mL culture. $M = 0.35$ mg is the total mass of cellular proteins per OD· mL of culture. m_X is the molecular weight of protein X . $\phi_X \equiv M_X/M$ is the mass fraction of protein X among all cellular proteins; it is referred to as the "proteome fraction", a measure of "protein abundance".

- (a)** *Conversion between proteome fraction and concentration: The average intracellular concentration of a protein X , denoted as $[X]$, can be taken as the number of proteins in OD· mL, N_X , divided by the total cytoplasmic water volume in OD· mL, V . Derive a relation between the concentration $[X]$ and the proteome fraction ϕ_X in terms of the molecular weight m_X . For typical proteins 300 aa in length, find its concentration in μ M if the proteome fraction is 1‰ (part per thousand). You can take the average mass of an amino acid to be 110 Daltons.*

[Note: Below we will only refer to protein concentrations as proteome fractions. It turns out that the latter is more readily obtained experimentally, e.g., by proteomics or by ribosome-profiling. It is also a natural quantity to work with in models.

The above exercise is meant to let you know that you can always convert proteome fraction to a more familiar concentration unit, e.g., μM .]

Solution

From the definition of $[X]$ we have:

$$[X] = \frac{N_X}{V}$$

Furthermore, since m_X is the molecular weight of protein X we also have:

$$N_X = \frac{M_X}{m_X}$$

Therefore:

$$[X] = \frac{1}{V} \cdot \frac{M_X}{m_X}$$

If we now multiply and divide by M :

$$\begin{aligned} [X] &= \frac{1}{V} \cdot M \cdot \frac{1}{M} \cdot \frac{M_X}{m_X} = \frac{M_X}{M} \cdot \frac{1}{m_X} \cdot \frac{M}{V} = \frac{\phi_X}{m_X} \cdot \frac{M}{V} = \frac{\phi_X}{m_X} \cdot 0.35 \frac{\text{mg}}{\mu\text{L}} \Rightarrow \\ &\Rightarrow [X] = \frac{\phi_X}{m_X} \cdot 0.35 \frac{\text{mg}}{\mu\text{L}} \end{aligned}$$

Now, since the average mass of an amino acid is 110 Da, we have that 1 mole of amino acids will weight 110 grams, and so the molecular weight m_X of protein X will be:

$$m_X = L_X \frac{110 \text{ g}}{1 \text{ mol}} = L_X \frac{0.11 \text{ mg}}{1 \mu\text{mol}}$$

where L_X is the length of the protein (in number of amino acids). Therefore:

$$[X] = \frac{\phi_X}{L_X} \cdot \frac{1 \mu\text{mol}}{0.11 \text{ mg}} \cdot \frac{0.35 \text{ mg}}{1 \mu\text{L}} \approx \frac{\phi_X}{L_X} \cdot \frac{1 \mu\text{mol}}{1 \mu\text{L}} \cdot 3 = \frac{\phi_X}{L_X} \cdot 3 \text{ M} = \frac{\phi_X}{L_X} \cdot 3000 \text{ mM}$$

If we now use $\phi_X = 1\% = 10^{-3}$ and $L_X = 300$:

$$[X] \approx \frac{10^{-3}}{300} \cdot 3000 \text{ mM} = 10^{-2} \text{ mM} = 10 \mu\text{M}$$

- (b) *Protein synthesis flux by ribosomes: Let J_R denote the flux of protein synthesis, in unit of # aa polymerized per OD· mL of culture. For a culture growing exponentially at the specific rate r , this is just $r \cdot M$ (with the total protein mass M expressed in # aa/(OD· mL)). Molecularly, protein synthesis flux can be written as the product of the ribosome elongation rate (denoted as ϵ) and N_R , the total number of ribosomes per OD· mL of culture. [Here we have assumed that all ribosomes are engaged in translation at the same speed. This turns out to be a reasonably good approximation, breaking down only at very slow growth.]*

i. Show that the above leads to the growth law

$$\phi_R = \frac{r}{k_R} \tag{1}$$

where $\phi_R \equiv M_R/M$ is the proteome fraction of ribosomal proteins, M_R being the total mass of r-proteins per OD· mL of culture. Express k_R in terms of ϵ and m_R , the weight of all r-proteins in a ribosome.

- ii. Adding up all r -proteins in the ribosome of *E. coli* gives 7336 aa. However, for the ribosomes to do its job, many helper proteins such as elongation factors are also needed. These proteins add up to another 60% in mass. Thus, we can take the “molecular weight” of an effective ribosome as $m_R = 1.6 \times 7336$ aa. Further using the measured elongation rate of $\epsilon = 16$ aa/s, find the value of k_R in unit of h^{-1} .
- iii. What is the theoretical maximum growth rate if a cell contains only ribosomes? What is the corresponding doubling time? [Note the factor of $\ln 2$ in the conversion.] The fastest doubling time observed for *E. coli* is ~ 17 min, when the culture contains many nutrient ingredients including all amino acids and nucleotides. What is the corresponding ribosomal fraction ϕ_R at this fastest growth rate? The remaining fraction of the proteome (ϕ_Q) found at the fastest growth rate, are comprised of obligatory proteins needed for house-keeping functions. Empirically, ϕ_Q is found to be approximately growth-rate independent even though ϕ_R changes according to Eq. (1).

Solution

- i. From its definition, we have:

$$J_R = rM \qquad J_R = \epsilon N_R = \epsilon \frac{M_R}{m_R}$$

Therefore:

$$r = \frac{\epsilon}{m_R} \cdot \frac{M_R}{M} \Rightarrow \phi_R = \frac{r}{k_R} \quad \text{where} \quad k_R = \frac{\epsilon}{m_R}$$

- ii. We have:

$$k_R = \frac{\epsilon}{m_R} = \frac{16 \text{ aa/s}}{1.6 \times 7336 \text{ aa}} \approx 1.4 \cdot 10^{-3} \text{ s}^{-1} = 1.4 \cdot 10^{-3} \cdot 3600 \text{ h}^{-1} \approx 5 \text{ h}^{-1}$$

- iii. If a cell only contains ribosomes we have $\phi_R = 1$, so that $r_{\max} = k_R = 5 \text{ h}^{-1}$. The corresponding doubling time is $\tau_{\max} = \ln 2 / r_{\max} \approx 0.14 \text{ h} \approx 8 \text{ min}$.

The fastest observed growth rate is $r_{\text{fastest}} = \ln 2 / 17 \text{ min} \approx 2.45 \text{ h}^{-1}$, and its corresponding ribosomal fraction is $\phi_R = 2.45 \text{ h}^{-1} / 5 \text{ h}^{-1} \approx 0.5 = 50\%$. Therefore, $\phi_Q = 50\%$.

- (c) **Carbon uptake flux:** Consider growth of *E. coli* in minimal medium with a single carbon source, without the supplement of amino acid and other substances. Let J_C denote the flux of carbon uptake, in unit of # substrate molecule taken up per time per OD · mL. Molecularly, this can be written as the product of ω_E , the specific rate of the uptake enzyme E , and N_E , the number of uptake enzymes per OD · mL of culture.

- i. Express J_C in term of the proteome fraction of the uptake enzyme, $\phi_E = M_E / M$, and the molecular weight of the uptake enzyme, m_E .
- ii. The condition of flux balance can be stated as $J_R = Y \cdot J_C$, where the yield Y represents the conversion factor from the substrate molecule to aa. Using flux balance and the expression you obtained above for J_R and J_C , derive the relation $\phi_E = r / k_E$ and find an expression for the parameter k_E in terms of the molecular parameters (ω_E , m_E) and the yield Y .
- iii. Consider the case where lactose is the sole carbon substrate. 1 g of lactose is known to produce 0.5 g of dry mass. Based on the protein:dry mass ratio given above, work out the value of Y for lactose. Express it in unit of # aa/lactose molecule and in OD/mM lactose.
- iv. Given that the specific uptake rate for the lactose transporter (LacY, the lac permease, 417aa in length) is $\omega_E = 3/s$ in saturating lactose concentration, write down the value of k_E for lactose uptake in unit of h^{-1} .

Solution

i. We have:

$$J_C = \omega_E N_E = \omega_E \frac{M_E}{m_E} \cdot \frac{M}{M} = \frac{\omega_E}{m_E} \phi_E M$$

ii. By using $J_R = rM$ and the expression of J_C found above, we have:

$$rM = Y \frac{\omega_E}{m_E} \phi_E M \Rightarrow \phi_E = \frac{r}{k_E} \quad \text{where} \quad k_E = Y \frac{\omega_E}{m_E}$$

iii. By definition:

$$Y = \frac{0.5 \text{ g dry mass}}{1 \text{ g lactose}}$$

With the data provided at the beginning, the protein:dry mass ratio is $0.35/0.5 = 0.7$. Therefore:

$$Y = \frac{0.5 \cdot 0.7 \text{ g protein mass}}{1 \text{ g lactose}} = \frac{0.35 \text{ g protein mass}}{1 \text{ g lactose}}$$

Since the mass of an amino acid is 110 Da, we have that 1 mol aa = 110 g; therefore, 0.35 g of protein mass are equal to $(0.35/110) \text{ mol} \approx 3.2 \text{ mmol}$ of amino acids. On the other hand, the molecular weight of lactose is 342.3 g, and so 1 g of lactose is equal to 2.9 mmol of lactose. Therefore:

$$Y = \frac{0.35 \text{ g protein mass}}{1 \text{ g lactose}} \approx \frac{3.2 \text{ mmol aa}}{2.9 \text{ mmol lactose}} \approx 1.1 \frac{\text{aa}}{\text{lactose molecule}}$$

On the other hand, since $1 \text{ OD} \cdot \text{mL} = 0.5 \text{ g dry mass}$:

$$Y = \frac{0.5 \text{ g dry mass}}{1 \text{ g lactose}} \approx \frac{1 \text{ OD} \cdot \text{mL}}{1 \text{ g lactose}} = \frac{1 \text{ OD}}{1 \text{ g lactose/mL}} \approx \frac{1 \text{ OD}}{2.9 \text{ mmol lactose/mL}} \approx 0.34 \frac{\text{OD}}{\text{mM lactose}}$$

iv. Plugging all the numbers, we get:

$$\begin{aligned} k_E = Y \frac{\omega_E}{m_E} &= \frac{0.35 \text{ g mass}}{1 \text{ g lactose}} \cdot \frac{3/\text{s}}{417 \cdot \frac{110 \text{ g mass}}{1 \text{ mol lactose}}} = \frac{0.35 \text{ g mass}}{2.9 \cdot 10^{-3} \text{ mol lactose}} \cdot \frac{3/\text{s}}{417 \cdot \frac{110 \text{ g mass}}{1 \text{ mol lactose}}} = \\ &= \frac{0.35 \cdot 3}{2.9 \cdot 10^{-3} \cdot 417 \cdot 110} \text{ s}^{-1} \approx 7.9 \cdot 10^{-3} \text{ s}^{-1} \approx 28.4 \text{ h}^{-1} \end{aligned}$$

where we have computed m_E from the length of the protein similarly to what was done above.

(d) The lactose transporter is one of a suite of “carbon catabolic proteins” expressed when E. coli is short of carbon supply. The other proteins include beta-galactosidase (LacZ) which degrades lactose into glucose and galactose (which then enter central metabolism), and other enzymes not specific to lactose degradation. Let the proteome fraction of all these carbon catabolic proteins be ϕ_C . Since the expression of LacY is co-regulated with these other catabolic proteins and thus have the same growth-rate dependences, we can take the proteome fraction of LacY, ϕ_E , to be a fixed portion α_E of ϕ_C . This leads to

$$\phi_C = \frac{r}{k_C} \quad (2)$$

where $k_C = \alpha_E k_E$

For cells grown in minimal medium without the supplement of amino acids, etc., another significant fraction of the proteome is comprised of anabolic proteins, e.g., enzyme for biosynthesis of amino acids. Let the total proteome fraction of these enzymes be ϕ_A . Empirically, a linear relation between the growth rate r and ϕ_A similar to Eqs. (1) and (2) has been found,

$$\phi_A = \frac{r}{k_A} \quad (3)$$

with a coefficient k_A . It turns that numerically, $k_A \approx k_R$.

Finally, there is the constraint that sum of all proteome fractions add up to 1, i.e.,

$$\phi_R + \phi_C + \phi_A = \phi_{\max} \quad (4)$$

where $\phi_{\max} \equiv 1 - \phi_Q$, with ϕ_Q being the fraction of obligatory proteins encountered in **(b)**.

- i. Combine Eqs. (1)-(4) to show that the growth rate depends on the parameter k_C as

$$r = r_C \frac{k_C}{k_C + k_{RA}} \quad (5)$$

Express the lumped parameter r_C and k_{RA} in terms of k_R and ϕ_{\max} and find their values. How would you interpret the meaning of r_C and how would you test this experimentally? Explain the sense by which the ratio $k_C:k_{RA}$ is regarded as a measure of “carbon quality”.

- ii. For *E. coli* growing on saturating concentration of lactose, the growth rate is found to be $\sim 1/h$. Find the corresponding value of k_C . What is the ratio $k_C:k_{RA}$ for lactose? Find the proteome fraction ϕ_R , ϕ_A , ϕ_C during growth on lactose.
- iii. Based on the value of k_E you calculated in **(c)**, what share of catabolic proteins is *LacY*? What fraction of the entire proteome is *LacY*?
- iv. *E. coli* is found to grow on saturating glycerol at rate $\sim 0.7/h$ and on saturating galactose at rate $\sim 0.35/h$. What are the corresponding carbon quality index? Based on the development above, give two distinct molecular causes by which a substance may be of poor carbon quality.

Solution

- i. By plugging Eqs. (1)-(3) into Eq. (4) we get:

$$\phi_{\max} = \frac{r}{k_R} + \frac{r}{k_C} + \frac{r}{k_A} \approx \frac{r}{k_R} + \frac{r}{k_C} + \frac{r}{k_R}$$

where we have used the fact that $k_A \approx k_R$. Therefore:

$$r = \phi_{\max} \left(\frac{2}{k_R} + \frac{1}{k_C} \right)^{-1} = \phi_{\max} \frac{k_C k_R}{2k_C + k_R} = \phi_{\max} \frac{k_R}{2} \cdot \frac{k_C}{k_C + \frac{k_R}{2}}$$

and so we have:

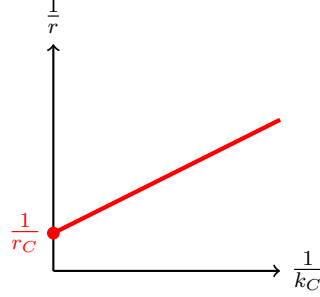
$$r_C = \phi_{\max} \frac{k_R}{2} \approx 0.5 \frac{5 \text{ h}^{-1}}{2} = 1.25 \text{ h}^{-1} \quad k_{RA} = \frac{k_R}{2} \approx \frac{5 \text{ h}^{-1}}{2} = 2.5 \text{ h}^{-1}$$

The parameter r_C is the maximum possible growth rate that *E. coli* can sustain on any single carbon source. One way we can test this experimentally is by growing *E. coli* in several different carbon sources, and for

each one of them measure r , ϕ_R and ϕ_C , so that we can estimate k_R and k_C ¹. The expression for r as a function of k_C can be rewritten as:

$$r = r_C \frac{k_C}{k_C + k_R} \Rightarrow \frac{1}{r} = \frac{1}{r_C} + \frac{k_R}{2r_C} \cdot \frac{1}{k_C}$$

Therefore, if we plot $1/r$ against $1/k_C$ we should get a straight line whose intercept is $1/r_C$:



which is also known as *Lineweaver-Burke plot*. Therefore, by performing a simple linear fit of the data plotted this way we can get a value for r_C .

By using Eqs. (1) and (2), the ratio k_C/k_{RA} can also be rewritten in this way:

$$\frac{k_C}{k_{RA}} = \frac{k_C}{k_R/2} = \frac{\chi/\phi_C}{\frac{1}{2} \cdot \chi/\phi_R} = 2 \frac{\phi_R}{\phi_C}$$

(notice that this expression is independent of the growth rate). Therefore, this ratio gives a measure of how much of the proteome is allocated to catabolic proteins with respect to ribosomal proteins. In particular, if $k_C/k_{RA} \ll 1$ we have $\phi_C \gg \phi_R$, i.e. cells need to produce *a lot* of catabolic proteins to grow; therefore, we can say that the “quality” of the carbon source is low (because it requires a great effort to import/catabolize). On the other hand, if $k_C/k_{RA} \gg 1$ we have $\phi_C \ll \phi_R$ and so very little catabolic proteins will be necessary to import enough carbon to grow; we can therefore say that in this case the “quality” of the carbon source is high.

ii. Solving Eq. (5) for k_C we obtain:

$$k_C = \frac{r k_{RA}}{r_C - r} = \frac{r k_R}{k_R \phi_{\max} - 2r} = \frac{1 \text{ h}^{-1} \cdot 5 \text{ h}^{-1}}{5 \text{ h}^{-1} \cdot 0.5 - 2 \cdot 1 \text{ h}^{-1}} = 10 \text{ h}^{-1}$$

Therefore, the carbon quality index for glucose is:

$$\frac{k_C}{k_{RA}} = \frac{k_C}{k_R/2} = \frac{10 \text{ h}^{-1}}{5 \text{ h}^{-1}/2} = 4$$

Finally:

$$\phi_R = \frac{r}{k_R} = \frac{1 \text{ h}^{-1}}{5 \text{ h}^{-1}} = \frac{1}{5} = 20\%$$

¹Notice that, since $k_C \propto k_E$, we can alternatively measure ϕ_E to estimate k_E and use it instead of k_C .

$$\phi_A = \frac{r}{k_A} = \frac{r}{k_R} = \frac{1 \text{ h}^{-1}}{5 \text{ h}^{-1}} = \frac{1}{5} = 20\%$$

$$\phi_C = \frac{r}{k_C} = \frac{1 \text{ h}^{-1}}{10 \text{ h}^{-1}} = \frac{1}{10} = 10\%$$

and so $\phi_R = \phi_A = 20\%$ while $\phi_C = 10\%$.

iii. From the definition given above, the share of catabolic proteins that are LacY is given by:

$$\alpha_E = \frac{k_C}{k_E} = \frac{10 \text{ h}^{-1}}{28.4 \text{ h}^{-1}} \approx 35\%$$

and therefore the fraction of the entire proteome occupied by LacY is:

$$\phi_E = \alpha_E \phi_C \approx 35\% \cdot 10\% = 3.5\%$$

iv. First of all, we call:

$$r_{\text{glyc}} = 0.7 \text{ h}^{-1} \quad r_{\text{gal}} = 0.35 \text{ h}^{-1}$$

the growth rates on glycerol and galactose, respectively. Since we know the value of k_R for *E. coli*, we can estimate the protein fractions occupied by ribosomes when growing on glycerol and galactose:

$$\phi_R^{\text{glyc}} = \frac{r_{\text{glyc}}}{k_R} = \frac{0.7 \text{ h}^{-1}}{5 \text{ h}^{-1}} \approx 14\% \quad \phi_R^{\text{gal}} = \frac{r_{\text{gal}}}{k_R} = \frac{0.35 \text{ h}^{-1}}{5 \text{ h}^{-1}} \approx 7\%$$

Then, since $k_A \approx k_R$, we have:

$$k_{RA} = \frac{k_R}{2} = 2.5 \text{ h}^{-1} \quad \phi_A^{\text{glyc}} = \phi_R^{\text{glyc}} = 14\% \quad \phi_A^{\text{gal}} = \phi_R^{\text{gal}} = 7\%$$

and since $\phi_{\text{max}} = 50\%$:

$$\phi_C^{\text{glyc}} = \phi_{\text{max}} - \phi_R^{\text{glyc}} - \phi_A^{\text{glyc}} = 22\% \quad \phi_C^{\text{gal}} = \phi_{\text{max}} - \phi_R^{\text{gal}} - \phi_A^{\text{gal}} = 36\%$$

we have:

$$k_C^{\text{glyc}} = \frac{r_{\text{glyc}}}{\phi_C^{\text{glyc}}} = \frac{0.7 \text{ h}^{-1}}{22\%} \approx 3.2 \text{ h}^{-1} \quad k_C^{\text{gal}} = \frac{r_{\text{gal}}}{\phi_C^{\text{gal}}} = \frac{0.35 \text{ h}^{-1}}{36\%} \approx 1 \text{ h}^{-1}$$

Therefore, the carbon quality indexes of glycerol and galactose are, respectively:

$$\frac{k_C^{\text{glyc}}}{k_{RA}} \approx \frac{3.2 \text{ h}^{-1}}{2.5 \text{ h}^{-1}} \approx 1.3 \quad \frac{k_C^{\text{gal}}}{k_{RA}} \approx \frac{1 \text{ h}^{-1}}{2.5 \text{ h}^{-1}} \approx 0.4$$

There can be two molecular causes by which a substance may be of poor carbon quality: it may be difficult to import into the cell and/or it could be difficult to catabolize (i.e., difficult to break down into precursors for protein synthesis). In fact, from what we have seen in the problems above we have:

$$k_C = \alpha_E k_E = \alpha_E \cdot Y \frac{\omega_E}{m_E}$$

If a substance is difficult to import into the cells then the ratio ω_E/m_E (i.e., the specific uptake rate per molecular weight of the importer proteins) will be small; in this case, therefore, the value of k_C will be low and as a consequence also the quality index of the substance will be low. On the other hand, if a substance is difficult to catabolize, its yield Y will be low and again as a consequence k_C will be small.

- (e) To derive the Monod growth law, we consider the lactose concentration in the medium to be maintained at a constant value $[L]$. Then the lactose uptake rate per LacY molecule is given by the Michaelis-Menten kinetics as

$$\omega_E([L]) = \omega_E \frac{[L]}{[L] + K_E} \quad (6)$$

where $\omega_E = 3/s$ is the uptake rate used above, and K_E is the equilibrium binding constant of lactose to LacY. Express k_C in terms of $\omega_E([L])$ and use it in Eq. (5) to derive the Monod growth law:

$$r([L]) = r_0 \frac{[L]}{[L] + K_M} \quad (7)$$

where r_0 is the growth rate under saturating concentration of lactose as given by Eq. (5). Express the Monod constant for lactose, K_M , in terms of K_E and the basic parameters of the growth laws in Eqs. (1)-(4). Find the value of the Monod constant if $K_E = 0.3$ mM. Can you explain why the Monod constant is much smaller than the binding constant K_E ?

Solution

First of all, we have:

$$k_C([L]) = \alpha_E k_E([L]) = \alpha_E \frac{Y}{m_E} \omega_E([L]) = \underbrace{\frac{\alpha_E Y \omega_E}{m_E}}_{k_C} \frac{[L]}{[L] + K_E}$$

where k_C is the value we have found before for saturating concentrations of lactose, i.e. $k_C = 10 \text{ h}^{-1}$. Therefore:

$$\begin{aligned} r([L]) &= r_C \frac{k_C([L])}{k_C([L]) + k_{RA}} = r_C k_C \frac{[L]}{[L] + K_E} \cdot \frac{1}{k_C \frac{[L]}{[L] + K_E} + k_{RA}} = \\ &= r_C k_C \frac{[L]}{[L] + K_E} \cdot \frac{1}{\frac{k_C[L] + k_{RA}([L] + K_E)}{[L] + K_E}} = r_C k_C \frac{[L]}{[L](k_C + k_{RA}) + k_{RA}K_E} = \\ &= \frac{r_C k_C}{k_C + k_{RA}} \cdot \frac{[L]}{[L] + K_E \frac{k_{RA}}{k_C + k_{RA}}} \end{aligned}$$

we therefore have:

$$r_0 = \frac{r_C k_C}{k_C + k_{RA}} \quad K_M = K_E \frac{k_{RA}}{k_C + k_{RA}}$$

and by substituting $r_C = \phi_{\max} k_R/2$ and $k_{RA} = k_R/2$:

$$r_0 = \phi_{\max} \frac{k_R k_C}{k_R + 2k_C} \quad K_M = K_E \frac{k_R}{k_R + 2k_C}$$

If $K_E = 0.3$ mM, we have:

$$K_M = 0.3 \text{ mM} \cdot \frac{5 \text{ h}^{-1}}{5 \text{ h}^{-1} + 2 \cdot 10 \text{ h}^{-1}} = \frac{1}{5} \cdot 0.3 \text{ mM} = 0.06 \text{ mM} = 60 \mu\text{M}$$

The reason why the Monod constant K_M is much smaller than the binding constant K_E is that at lower concentrations of lactose² the cells readjust their proteome in order to express more lac permeases. This way the carbon influx does not decrease by the same amount of the permease import rate.

For example, if the external concentration of lactose is $[L] = K_E = 300 \mu\text{M}$, we will have $\omega_E([L]) = \omega_E/2$, i.e. every lac permease on the cell membrane will be importing lactose molecules at a rate that is half of the rate at saturating concentrations of lactose (i.e., ω_E). To compensate this, cells reallocate their proteome to produce more lac permeases, and as a result the growth rate is $r = r_0[L]/([L] + K_M) = r_0 \cdot 300 \mu\text{M}/(300 \mu\text{M} + 60 \mu\text{M}) \approx 0.83 \cdot r_0$. Therefore, even if the lactose permease import rate has decreased by 50%, the growth rate has decreased by only 17%.

(f) Solve for $\phi_C([L])$, the fraction of catabolic proteins at different lactose concentration $[L]$. Show that

$$\phi_C([L]) = \phi_C^{\max} \left(1 - \frac{r([L])}{r_C} \right) \quad (8)$$

and give the value of ϕ_C^{\max} . Eq. (8) describes a linear decline in the abundance of catabolic proteins with increasing growth rate, referred to as the “C-line”. It is a quantitative statement of the phenomenon of “catabolite repression” ubiquitous in microbiology, wherein the expression of catabolic enzymes is inhibited in medium with improved carbon availability. Explain in your own words why should cells reduce the catabolic proteins when carbon is more available.

Solution

From Eq. (4) we can write:

$$\phi_C([L]) = \phi_{\max} - \phi_R([L]) - \phi_A([L]) = \phi_{\max} - \frac{r([L])}{k_R/2}$$

which we can write as:

$$\phi_C([L]) = \phi_C^{\max} \left(1 - \frac{r([L])}{r_C} \right) \quad \text{with} \quad \phi_C^{\max} = \phi_{\max} \quad r_C = \phi_{\max} \frac{k_R}{2}$$

When carbon is more available, cells should reduce the expression of catabolic proteins because they need less permeases to import the same amount of carbon. Furthermore, if they did *not* reduce catabolic proteins in these conditions, they would be able to import a lot of carbon and convert it into precursors for the synthesis of amino acids, but they would not have enough proteins to convert these precursors into amino acids and then put them together to produce proteins.

In other words, when carbon is more available it becomes easier to import it, and the cellular processes that limit growth in this case are no longer catabolism, but anabolism and protein synthesis.

2. Competition for nutrient

Two species described by densities $\rho_1(t)$ and $\rho_2(t)$ grow on the same nutrient source, of concentration $n(t)$. Suppose the growth rate of species i is given by the Monod growth law, $r_i(n) = r_{i,0} \cdot n/(n + K_i)$, the death rate is given by μ_i , and the nutrient influx is j_0 . Find a criterion on the physiological parameters ($r_{i,0}$, K_i , μ_i) in order for species i to survive in the steady state.

²This is true in general for any carbon source: the cells will readjust their proteome in order to produce more permeases.

Solution

The equations of the system are:

$$\dot{\rho}_1 = \rho_1 \left(r_{1,0} \frac{n}{n + K_1} - \mu_1 \right) \quad \dot{\rho}_2 = \rho_2 \left(r_{2,0} \frac{n}{n + K_2} - \mu_2 \right) \quad \dot{n} = j_0 - \frac{\rho_1 r_1}{Y_1} - \frac{\rho_2 r_2}{Y_2}$$

Suppose species 1 survives, and species 2 goes to extinction. From the equation for ρ_1 at steady state we have:

$$\begin{aligned} \dot{\rho}_1 = \rho_1^* \left(r_{1,0} \frac{n_1^*}{n_1^* + K_1} - \mu_1 \right) = 0 \quad \rho_1^* > 0 \quad \Rightarrow \quad r_{1,0} \frac{n_1^*}{n_1^* + K_1} = \mu_1 \quad \Rightarrow \\ \Rightarrow \quad \frac{r_{1,0}}{\mu_1} = 1 + \frac{K_1}{n_1^*} \quad \Rightarrow \quad \frac{1}{n_1^*} = \frac{1}{K_1} \left(\frac{r_{1,0}}{\mu_1} - 1 \right) \end{aligned}$$

Where n_1^* is the steady-state resource concentration when only species 1 is present.

Similarly, if we assume that species 2 survives and species 1 goes to extinction we have:

$$\frac{1}{n_2^*} = \frac{1}{K_2} \left(\frac{r_{2,0}}{\mu_2} - 1 \right)$$

where again n_2^* is the steady-state resource concentration when only species 2 is present.

Now, let's consider the case where species 1 survives and species 2 is going to extinction. In this case when $n = n_1^*$ we need $\dot{\rho}_2(n_1^*) < 0$ (the population of species 2 will always decrease until $\rho_2^* = 0$). Therefore:

$$\begin{aligned} \dot{\rho}_2 = \rho_2 \left(r_{2,0} \frac{n_1^*}{n_1^* + K_2} - \mu_2 \right) < 0 \quad \Rightarrow \quad r_{2,0} \frac{n_1^*}{n_1^* + K_2} < \mu_2 \quad \Rightarrow \quad \frac{r_{2,0}}{\mu_2} < 1 + \frac{K_2}{n_1^*} \quad \Rightarrow \\ \Rightarrow \quad \frac{r_{2,0}}{\mu_2} - 1 < \frac{K_2}{n_1^*} \left(\frac{r_{1,0}}{\mu_1} - 1 \right) \quad \Rightarrow \quad \frac{1}{K_2} \left(\frac{r_{2,0}}{\mu_2} - 1 \right) < \frac{1}{K_1} \left(\frac{r_{1,0}}{\mu_1} - 1 \right) \end{aligned}$$

This condition can be rewritten as:

$$\frac{1}{K_2} \left(\frac{r_{2,0}}{\mu_2} - 1 \right) < \frac{1}{K_1} \left(\frac{r_{1,0}}{\mu_1} - 1 \right) \quad \Rightarrow \quad \frac{1}{n_2^*} < \frac{1}{n_1^*} \quad \Rightarrow \quad n_1^* < n_2^*$$

Therefore, species 1 survives if $n_1^* < n_2^*$. By symmetry, species 2 will survive when $n_2^* < n_1^*$. In general, if we have N species in this system the only one that will survive is the species with the lowest value of n_i^* . The ecological meaning of this condition is that the species that will outcompete all the others is the one that uses the resource most efficiently, because it is the species that leaves the lowest steady-state concentration of resource in the environment, thus making it harder for other species to keep up with its own growth.

3. MacArthur's model of resource competition

MacArthur's model applied to 2-species (of densities ρ_1, ρ_2) and 2 nutrients (of concentrations n_A, n_B) is

$$\dot{\rho}_1 = (v_{1A}n_A + v_{1B}n_B) \cdot \rho_1 - \mu_1\rho_1 \quad (9)$$

$$\dot{\rho}_2 = (v_{2A}n_A + v_{2B}n_B) \cdot \rho_2 - \mu_2\rho_2 \quad (10)$$

$$\dot{n}_A = \gamma_A n_A \cdot \left(1 - \frac{n_A}{K_A}\right) - (v_{1A}\rho_1 + v_{2A}\rho_2)n_A \quad (11)$$

$$\dot{n}_B = \gamma_B n_B \cdot \left(1 - \frac{n_B}{K_B}\right) - (v_{1B}\rho_1 + v_{2B}\rho_2)n_B \quad (12)$$

where $v_{i\alpha}$ is the consumption matrix indicating the uptake preference of species i for nutrient α , μ_i is the death rate of species i , and γ_α is the generation rate, K_α is the concentration scale of nutrient α in the habitat. (The yield factor has been omitted.)

- (a) Assume the existence of a non-trivial steady state with n_A^* , n_B^* , ρ_1^* , ρ_2^* all being non-zero. From $\dot{\rho}_i/\rho_i = 0$ in Eqs. (9) and (10), show that in the limit the death rate $\mu_i \rightarrow 0$, the steady state concentrations $n_\alpha \rightarrow 0$. Using this result in Eqs. (11) and (12), show that $\dot{n}_\alpha/n_\alpha = 0$ lead to the following equation for the steady state densities

$$\begin{pmatrix} v_{1A} & v_{2A} \\ v_{1B} & v_{2B} \end{pmatrix} \cdot \begin{pmatrix} \rho_1 \\ \rho_2 \end{pmatrix} = \begin{pmatrix} \gamma_A \\ \gamma_B \end{pmatrix}$$

Solution

From Eqs. (9) and (10) at steady state we have:

$$\begin{cases} \mu_1 = v_{1A}n_A^* + v_{1B}n_B^* \\ \mu_2 = v_{2A}n_A^* + v_{2B}n_B^* \end{cases} \Rightarrow n_A^* = \frac{\mu_1 v_{2B} - \mu_2 v_{1B}}{v_{1A}v_{2B} - v_{1B}v_{2A}} \quad n_B^* = \frac{\mu_1 v_{2A} - \mu_2 v_{1A}}{v_{1B}v_{2A} - v_{1A}v_{2B}}$$

Therefore, we will have $n_\alpha^* \rightarrow 0$ if $\mu_i \rightarrow 0$.

From Eqs. (11) and (12) at steady state we have:

$$\begin{cases} \gamma_A(1 - n_A^*/K_A) = v_{1A}\rho_1^* + v_{2A}\rho_2^* \\ \gamma_B(1 - n_B^*/K_B) = v_{1B}\rho_1^* + v_{2B}\rho_2^* \end{cases}$$

and in the limit $n_\alpha^* \rightarrow 0$ this reduces to:

$$\begin{cases} \gamma_A = v_{1A}\rho_1^* + v_{2A}\rho_2^* \\ \gamma_B = v_{1B}\rho_1^* + v_{2B}\rho_2^* \end{cases} \Rightarrow \begin{pmatrix} v_{1A} & v_{2A} \\ v_{1B} & v_{2B} \end{pmatrix} \cdot \begin{pmatrix} \rho_1^* \\ \rho_2^* \end{pmatrix} = \begin{pmatrix} \gamma_A \\ \gamma_B \end{pmatrix}$$

- (b) Write down the solution of the above matrix equation for ρ_1^* and ρ_2^* . Show that the feasibility condition, i.e., $\rho_1^* > 0$ and $\rho_2^* > 0$, can be written as two conditions between the environmental parameters γ_A , γ_B , and $m_i \equiv v_{iB}/v_{iA}$, which describes the nutrient preference of species i . Plot the “ecological phase diagram” in the space (γ_A, γ_B) , marking clearly the region of coexistence, and the region of dominance/extinction.

Solution

By simply solving the linear system:

$$\begin{cases} \gamma_A = v_{1A}\rho_1^* + v_{2A}\rho_2^* \\ \gamma_B = v_{1B}\rho_1^* + v_{2B}\rho_2^* \end{cases} \Rightarrow \rho_1^* = \frac{v_{2B}\gamma_A - v_{2A}\gamma_B}{v_{1A}v_{2B} - v_{1B}v_{2A}} \quad \rho_2^* = \frac{v_{1B}\gamma_A - v_{1A}\gamma_B}{v_{1B}v_{2A} - v_{1A}v_{2B}}$$

Therefore, we have $\rho_1^* > 0$ when:

$$\begin{cases} v_{2B}\gamma_A > v_{2A}\gamma_B \\ v_{1A}v_{2B} > v_{1B}v_{2A} \end{cases} \quad \text{or} \quad \begin{cases} v_{2B}\gamma_A < v_{2A}\gamma_B \\ v_{1A}v_{2B} < v_{1B}v_{2A} \end{cases} \Rightarrow \begin{cases} m_2 > \gamma_B/\gamma_A \\ m_1 < m_2 \end{cases} \quad \text{or} \quad \begin{cases} m_2 < \gamma_B/\gamma_A \\ m_1 > m_2 \end{cases}$$

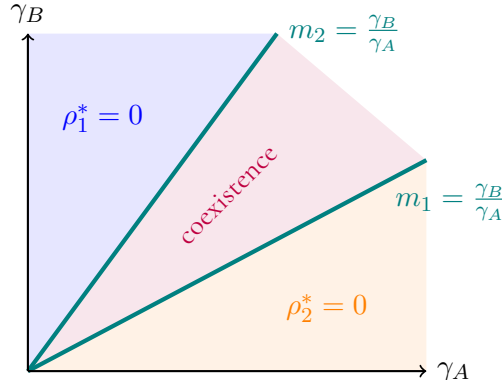
Similarly, we have that $\rho_2^* > 0$ when:

$$\begin{cases} m_1 > \gamma_B/\gamma_A \\ m_1 > m_2 \end{cases} \quad \text{or} \quad \begin{cases} m_1 < \gamma_B/\gamma_A \\ m_1 < m_2 \end{cases}$$

Therefore, putting together these results, we have:

$$\begin{aligned} m_1 < \frac{\gamma_B}{\gamma_A} < m_2 & \quad \text{when } m_1 < m_2 \\ m_2 < \frac{\gamma_B}{\gamma_A} < m_1 & \quad \text{when } m_1 > m_2 \end{aligned}$$

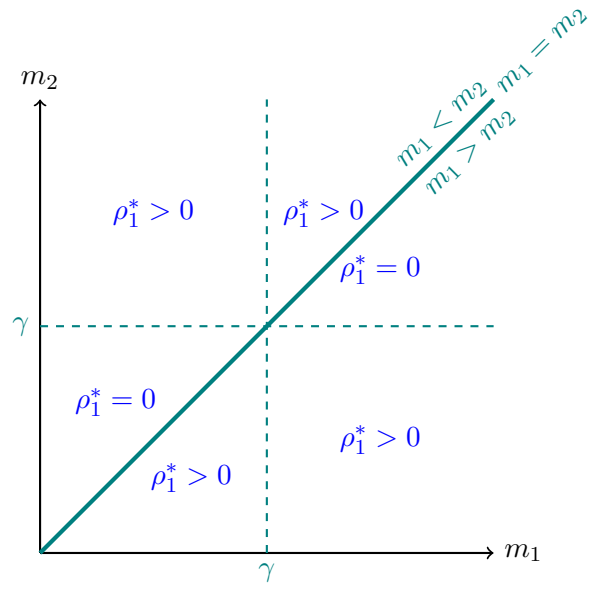
Therefore, the “ecological phase diagram” in (γ_A, γ_B) space looks like this (in the case $m_1 < m_2$):



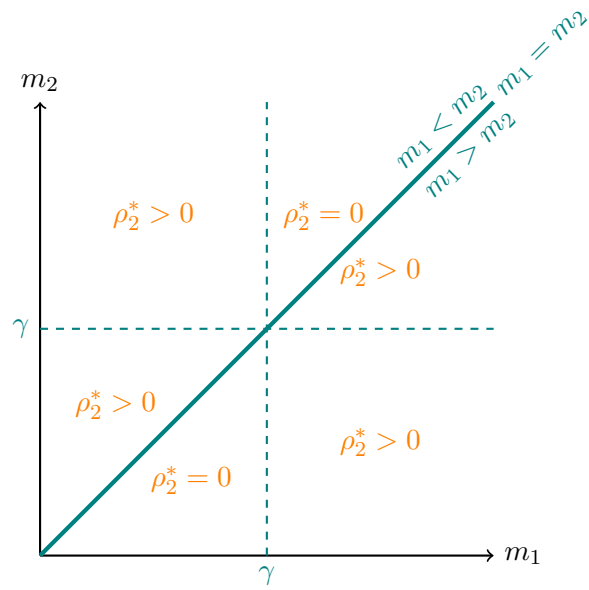
- (c) For a fixed environment parameterized by $\gamma \equiv \gamma_B/\gamma_A$ (which indicates the relative nutrient availability), plot the “physiological phase diagram” in the space (m_1, m_2) by indicating which regions of this space give coexistence, and which regions give dominance of species 1 or 2.

Solution

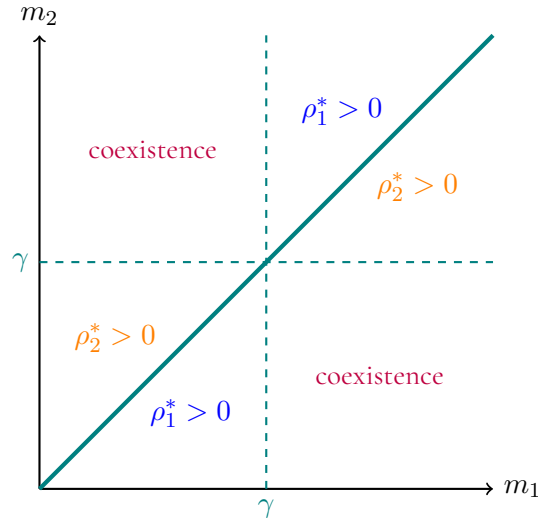
By looking at the conditions found above, in the (m_1, m_2) space we have that $\rho_1^* > 0$ and $\rho_1^* = 0$ when:



Similarly, for ρ_2^* we have:



Therefore, the “physiological phase diagram” in (m_1, m_2) space looks like this:



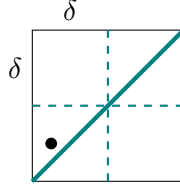
- (d) What is the ‘optimal’ value of m_1 that species 1 should take on to maximize its existence (i.e., survival) if it expects species 2 to take on a random value of m_2 ? or if it expects species 2 to take on the ‘optimal’ value of m_2 ? If the m values of both species are close to this ‘optimal’ value, what would be the probability that one species becomes extinct if the environmental parameter γ can take on a value within a finite range δ about a mean value, $\bar{\gamma}$ with equal probability? [Assume the environment can vary rapidly while m_i , determined by genetics, is frozen over the scale of environmental variation.] What range of m_i should each species i take on to maximize its existence in a fluctuating environment if it can coordinate with the other species which is also interested in maximizing its existence? What danger is there if the other species ‘cheats’? [Note: Your response to (d) is not expected to be quantitative.]

Solution

The “optimal” value that m_1 should take to maximize the survival of species 1 is γ in both cases.

Let’s now consider the case $m_1, m_2 \approx \gamma$ and the environmental parameter can take value within a finite range δ around its mean value $\bar{\gamma}$. As the hint suggest, we can assume that the point (m_1, m_2) that describes the species is fixed and γ changes rapidly. In this case there are three possibilities: we either end up in one of the two “quadrants” where coexistence is possible, or we end up in one branch of the two “half-quadrants” where one of the species goes to extinction. Let’s consider for example species 1: the probability that species 1 goes extinct as γ changes will be proportional to the angles occupied by the quadrant $\rho_2^* > 0$, and since each quadrant is spanned by an angle of 45° , the probability of going extinct is $2 \cdot 2 \cdot 45/360 = 1/2$ (alternatively, we can compute this probability as the complementary of the probability of both species coexisting, i.e. $1 - 2 \cdot 90/360 = 1 - 1/2 = 1/2$).

A more formal way to see the same thing is the following. If we fix $(m_1^*, m_2^*) \approx (\gamma, \gamma)$ and then we let the environmental parameter γ vary within a range δ , we can “zoom in” the physiological phase diagram:



and the system now will be in a point (e.g., the one shown in the figure above) that can be thought of as randomly drawn in this square. Therefore, the probability that (for example) species 1 will go extinct will be equal to the ratio between the area inside that square where $\rho_1^* = 0$ and the total area of the square. Since $\rho_1^* = 0$ in two right triangles of base and height δ , the probability of extinction is:

$$\frac{2 \cdot \delta^2/2}{(2\delta)^2} = \frac{\delta^2}{4\delta^2} = \frac{1}{4}$$

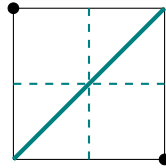
If the species want to maximize their existence in a fluctuating environment and can coordinate with each other, they should set their m_i so that the system will end up surely in one of the two “quadrants” where coexistence is possible, i.e.:

$$m_1 < \gamma < m_2 \quad \text{or} \quad m_2 < \gamma < m_1$$

For example, if $\gamma \in [\bar{\gamma} - \delta, \bar{\gamma} + \delta]$, they should set:

$$\begin{cases} m_1 = \bar{\gamma} + \delta \\ m_2 = \bar{\gamma} - \delta \end{cases} \quad \text{or} \quad \begin{cases} m_1 = \bar{\gamma} - \delta \\ m_2 = \bar{\gamma} + \delta \end{cases} \quad (13)$$

which, referring to the “zommed in” figure shown above, means putting the system in either of these two points:



Finally, if one of the two species “cheats” (i.e., it doesn’t coordinate with the other as discussed above) there is the risk that either one of the two species will go extinct³.

4. Competition for essential nutrients

The dependence of the growth of bacterial species i on two essential nutrients A and B is given by

$$r_i(n_A, n_B) = \left[\frac{1}{v_{iA}n_A} + \frac{1}{v_{iB}n_B} \right]^{-1} \quad (14)$$

where $v_{i\alpha}$ is the single-nutrient consumption efficiency (when the other nutrient is in saturation) and n_α is the concentration of nutrient α as in Problem #2. Unlike substitutable nutrients, the uptake of nutrient α by species i is given by $r_i \cdot \rho_i / Y_\alpha$,

³Notice: even the species that is cheating can go extinct: a cheater can drive itself to extinction, if it doesn’t cheat in the “right” way!

where ρ_i is the density of species i , and Y_α is the yield of either species for nutrient α . This leads to the following set of consumer-resource equations

$$\begin{aligned}\dot{\rho}_1 &= r_1(n_A, n_B) \cdot \rho_1 - \mu\rho_1 \\ \dot{\rho}_2 &= r_2(n_A, n_B) \cdot \rho_2 - \mu\rho_2 \\ \dot{n}_A &= \mu(n_A^0 - n_A) - r_1(n_A, n_B) \frac{\rho_1}{Y_{1,A}} - r_2(n_A, n_B) \frac{\rho_2}{Y_{2,A}} \\ \dot{n}_B &= \mu(n_B^0 - n_B) - r_1(n_A, n_B) \frac{\rho_1}{Y_{1,B}} - r_2(n_A, n_B) \frac{\rho_2}{Y_{2,B}}\end{aligned}$$

for a chemostat-based system where μ is the dilution rate and n_α^0 is the inflow concentration of nutrient α . In this problem, you will derive the feasibility conditions for this system using Tilman's graphical approach.

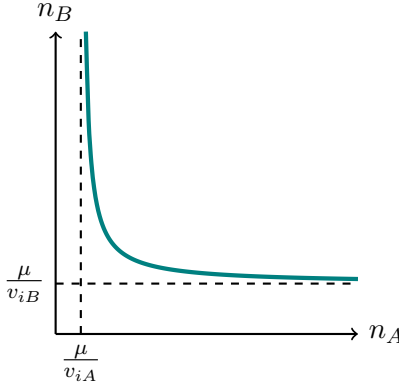
- (a) Without solving the equations algebraically, sketch the conditions for $\dot{\rho}_i = 0$ in the (n_A, n_B) plane. Indicate the location of (n_A^*, n_B^*) where both ρ_1 and ρ_2 are finite. On the plot, also mark the point (n_A^0, n_B^0) which is proportional to the nutrient inflow. Next, find an algebraic expression for n_A^* , n_B^* in terms of the environmental and physiological parameters. [Hint: You can first use the matrix inversion formula for n_α^{-1} .]

Solution

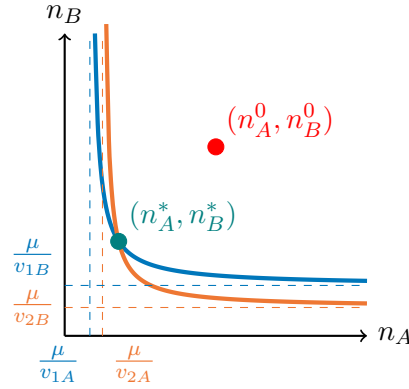
From $\dot{\rho}_i = 0$ we have:

$$\frac{1}{v_{iA}n_A} + \frac{1}{v_{iB}n_B} = \frac{1}{\mu} \Rightarrow n_B = \frac{v_{iA}}{v_{iB}} \cdot \frac{n_A}{\frac{v_{iA}n_A}{\mu} - 1}$$

which is a hyperbola that looks like this:



Therefore, putting together the two species we will have, for example:



where we have also shown the point proportional to nutrient inflow.

In order to find the algebraic expression of n_A^* and n_B^* , we start from $\dot{\rho}_i = 0$ as above:

$$\begin{cases} \frac{1}{v_{1A}} \cdot \frac{1}{n_A^*} + \frac{1}{v_{1B}} \cdot \frac{1}{n_B^*} = \frac{1}{\mu} \\ \frac{1}{v_{2A}} \cdot \frac{1}{n_A^*} + \frac{1}{v_{2B}} \cdot \frac{1}{n_B^*} = \frac{1}{\mu} \end{cases} \Rightarrow \begin{pmatrix} \frac{1}{v_{1A}} & \frac{1}{v_{1B}} \\ \frac{1}{v_{2A}} & \frac{1}{v_{2B}} \end{pmatrix} \begin{pmatrix} \frac{1}{n_A^*} \\ \frac{1}{n_B^*} \end{pmatrix} = \begin{pmatrix} \frac{1}{\mu} \\ \frac{1}{\mu} \end{pmatrix}$$

If we now call M the matrix on the left and use the inversion formula, we get:

$$\begin{pmatrix} \frac{1}{n_A^*} \\ \frac{1}{n_B^*} \end{pmatrix} = \frac{1}{\det M} \begin{pmatrix} \frac{1}{v_{2B}} & -\frac{1}{v_{1B}} \\ -\frac{1}{v_{2A}} & \frac{1}{v_{1A}} \end{pmatrix} \begin{pmatrix} \frac{1}{\mu} \\ \frac{1}{\mu} \end{pmatrix}$$

where:

$$\det M = \frac{1}{v_{1A}v_{2B}} - \frac{1}{v_{1B}v_{2A}} \Rightarrow \frac{1}{\det M} = \frac{v_{1A}v_{1B}v_{2A}v_{2B}}{v_{1B}v_{2A} - v_{1A}v_{2B}}$$

Therefore, we get:

$$\frac{1}{n_A^*} = \frac{1}{\mu} \cdot \frac{v_{1A}v_{2A}(v_{1B} - v_{2B})}{v_{1B}v_{2A} - v_{1A}v_{2B}} \quad \frac{1}{n_B^*} = \frac{1}{\mu} \cdot \frac{v_{1B}v_{2B}(v_{2A} - v_{1A})}{v_{1B}v_{2A} - v_{1A}v_{2B}}$$

and thus:

$$n_A^* = \mu \cdot \frac{v_{1B}v_{2A} - v_{1A}v_{2B}}{v_{1A}v_{2A}(v_{1B} - v_{2B})} \quad n_B^* = \mu \cdot \frac{v_{1B}v_{2A} - v_{1A}v_{2B}}{v_{1B}v_{2B}(v_{2A} - v_{1A})}$$

- (b) Show the balance of nutrient fluxes at (n_A^*, n_B^*) graphically using a vector relation among the nutrient influx \vec{J}_0 and the consumption fluxes \vec{J}_1, \vec{J}_2 , as done in class. Describe the condition for coexistence graphically, and write down the corresponding algebraic expression involving the constraint on n_A^0, n_B^0 .

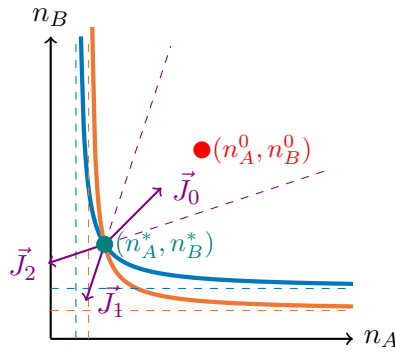
Solution

We can rewrite the equations for \dot{n}_A and \dot{n}_B as follows:

$$\begin{cases} \dot{n}_A = \mu(n_A^0 - n_A) - r_1(n_A, n_B) \frac{\rho_1}{Y_{1,A}} - r_2(n_A, n_B) \frac{\rho_2}{Y_{2,A}} \\ \dot{n}_B = \mu(n_B^0 - n_B) - r_1(n_A, n_B) \frac{\rho_1}{Y_{1,B}} - r_2(n_A, n_B) \frac{\rho_2}{Y_{2,B}} \end{cases} \Rightarrow$$

$$\Rightarrow \begin{pmatrix} \dot{n}_A \\ \dot{n}_B \end{pmatrix} = \underbrace{\mu \begin{pmatrix} n_A^0 - n_A \\ n_B^0 - n_B \end{pmatrix}}_{:= \vec{J}_0} - \underbrace{\rho_1 \begin{pmatrix} r_1/Y_{1,A} \\ r_1/Y_{1,B} \end{pmatrix}}_{:= \vec{J}_1} - \underbrace{\rho_2 \begin{pmatrix} r_2/Y_{2,A} \\ r_2/Y_{2,B} \end{pmatrix}}_{:= \vec{J}_2}$$

Therefore, the consumption fluxes \vec{J}_1 and \vec{J}_2 point in directions with slopes $Y_{1,B}/Y_{1,A}$ and $Y_{2,B}/Y_{2,A}$, respectively. If we use $(n_A, n_B) = (n_A^*, n_B^*)$, the system looks like this:



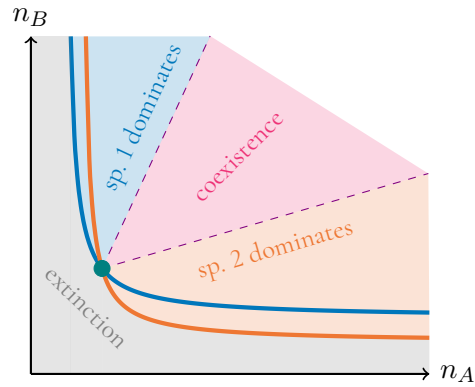
Where we have also highlighted the directions along which \vec{J}_1 and \vec{J}_2 lie, i.e. the lines passing through (n_A^*, n_B^*) and with slopes $Y_{1,B}/Y_{1,A}$ and $Y_{2,B}/Y_{2,A}$. Coexistence will be possible if the slope of \vec{J}_0 , i.e. $(n_B^0 - n_B^*)/(n_A^0 - n_A^*)$, lies between the slopes of these two lines:

$$\frac{Y_{2,B}}{Y_{2,A}} < \frac{n_B^0 - n_B^*}{n_A^0 - n_A^*} < \frac{Y_{1,B}}{Y_{1,A}}$$

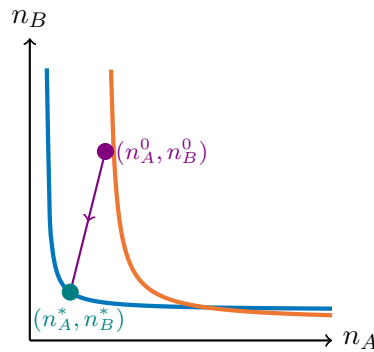
- (c) Show graphically what happens if (n_A^0, n_B^0) lies outside of the constraint, and write down the algebraic expression for the steady-state concentrations n_A^* , n_B^* and densities ρ_1^* , ρ_2^* corresponding to the two types of outcomes that would arise.

Solution

Referring to the figure above, if (n_A^0, n_B^0) lies outside of the coexistence region we can have either one or both species going to extinction. In particular, if (n_A^0, n_B^0) lies between the blue hyperbola and the direction of \vec{J}_1 species 1 will dominate, and conversely species 2 will outcompete species 1 if (n_A^0, n_B^0) ; finally, if (n_A^0, n_B^0) lies below the two hyperbolas, both species will go to extinction:



Let's assume for example that (n_A^0, n_B^0) lies in the area where species 1 dominates (the case for species 2 is symmetrical). The point will follow \vec{J}_1 and thus move along the line passing through (n_A^0, n_B^0) with the same slope as \vec{J}_1 . At the steady state, (n_A^*, n_B^*) will lie on the intersection between this line and the nullcline $\dot{\rho}_1 = 0$:



Therefore, can find n_A^*, n_B^* by finding the intersection of these two curves. The nullcline $\dot{\rho}_1 = 0$ is:

$$\frac{1}{v_{1A}n_A} + \frac{1}{v_{1B}n_B} = \mu$$

On the other hand, the line along which the system moves is:

$$n_B = q + m \cdot n_A$$

where $m = Y_{1,B}/Y_{1,A}$ (the slope of \vec{J}_1) and q can be found from the fact that the line passes through (n_A^0, n_B^0) :

$$n_B^0 = q + \frac{Y_{1,B}}{Y_{1,A}}n_A^0 \quad \Rightarrow \quad q = n_B^0 - \frac{Y_{1,B}}{Y_{1,A}}n_A^0$$

Therefore, the point (n_A^*, n_B^*) can be found by solving:

$$\frac{1}{v_{1A}n_A^*} + \frac{1}{v_{1B}n_B^*} = \mu \quad n_B^* = q + m \cdot n_A^*$$

This can be done, for example, by taking the reciprocal of the equation of the line:

$$\frac{1}{n_B^*} = \frac{1}{1 + mn_A^*}$$

and substituting in the equation of the nullcline:

$$\frac{1}{v_{1A}n_A^*} + \frac{1}{v_{1B}(1 + mn_A^*)} = \mu \Rightarrow \mu = \frac{v_{1B}(1 + mn_A^*) + v_{1A}n_A^*}{v_{1A}v_{1B}n_A^*(q + mn_A^*)} \Rightarrow$$

$$\Rightarrow \mu v_{1A}v_{1B}m \cdot (n_A^*)^2 + (\mu v_{1A}v_{1B}q - v_{1B}m - v_{1A})n_A^* - v_{1B}q = 0 \Rightarrow$$

$$\Rightarrow n_A^* = \frac{1}{2\mu m v_{1A}v_{1B}} \left(v_{1B}m + v_{1A} - \mu q v_{1A}v_{1B} + \sqrt{(\mu q v_{1A}v_{1B} - v_{1B}m - v_{1A})^2 + 4\mu m q v_{1A}v_{1B}^2} \right)$$

(which is the only acceptable solution, since the other one is negative). Substituting in the equation for the straight line we get $n_B^* = q + m \cdot n_A^*$.

Finally, from the equation for $\dot{\rho}_1$ at steady state we get:

$$\rho_1(r_1(n_A^*, n_B^*) - \mu) = 0 \Rightarrow r_1(n_A^*, n_B^*) = \mu \quad (15)$$

and therefore, from the equation for \dot{n}_A :

$$\mu(n_A^0 - n_A^*) - r_1(n_A^*, n_B^*) \frac{\rho_1^*}{Y_{1,A}} \Rightarrow \rho_1^* = Y_{1,A}(n_A^0 - n_A^*)$$

as stated above, the case where species 2 dominates is symmetrical, so:

$$n_A^* = \frac{1}{2\mu m v_{2A}v_{2B}} \left(v_{2B}m + v_{2A} - \mu q v_{2A}v_{2B} + \sqrt{(\mu q v_{2A}v_{2B} - v_{2B}m - v_{2A})^2 + 4\mu m q v_{2A}v_{2B}^2} \right)$$

$$\text{where:} \quad m = \frac{Y_{2,B}}{Y_{2,A}} \quad q = n_B^0 - \frac{Y_{2,B}}{Y_{2,A}} n_A^0$$

and furthermore:

$$\rho_2^* = Y_{2,A}(n_A^0 - n_A^*)$$

- (d) Describe and explain the difference of the behavior obtained here compared to the ones obtained in class for two substitutable nutrients.

Solution

In the case of substitutable resources, if we inflow of either of the two resources is very large, one of the two species will dominate (according to their preferences). This happens because the nullclines intersect the axes and therefore the area in the (n_A, n_B) space where both species go to extinction is finite. Here, however, this is not true for essential resources: since the nullclines are now hyperbolas with non-trivial asymptotes (i.e., the asymptotes are not the axes, see also the representation of the system in point (a)) the area where extinction is possible extends to infinity. This means that even if we put a very large amount of one resource, let's say resource A for example, it is not guaranteed that species 2 will dominate (if we refer to the phase diagrams plotted above). In fact, since both resources are essential species 2 also needs a minimum supply of resource 1 to grow. If this supply is not provided, species 2 will not be able to dominate the system even though resource A is very abundant.