Cross-feeding explorations

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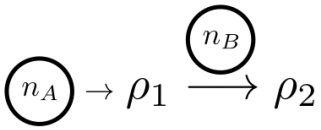
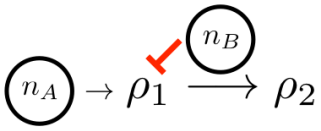
1 Cross-feeding Scenarios

There are a few cross-feeding mechanisms to look into:

(a) commensalism



(b) syntrophy



(c) mutualism

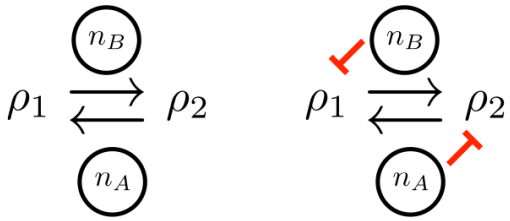


Figure 1: Schematics for the three cross-feeding mechanisms.

As we suggested in the grant, we plan to look at these three system with spatial structure.

General notations: Numeral subscripts are for species and letter subscripts are for nutrients. $\rho_{1,2}$ are the population density and $n_{A,B}$ are the nutrient concentration.

1.1 Commensalism:

In this case, ρ_1 grows on a primary nutrient, n_A, and excretes n_B, which is used by ρ_2 as nutrient. The accumulation of n_B has *no* toxic effect on either species, hence the interaction is *commensal*. For simplicity, let's assume n_A is from the substrate and is very abundant. Its diffusion effect is thus negligible.

Accounting for the cell division, cell diffusion, nutrient production, consumption and diffusion, the dynamics can

be described in the following equations:

$$\frac{\partial \rho_1}{\partial t} = \lambda_1(n_A)\rho_1 + D_1 \cdot \nabla^2 \rho_1, \quad \lambda_1(n_A) = \lambda_1^* \frac{n_A}{n_A + K_A} \approx \lambda_1^* \tag{1}$$

$$\frac{\partial \rho_2}{\partial t} = \lambda_2(n_B)\rho_2 + D_2 \cdot \nabla^2 \rho_2, \quad \lambda_2(n_B) = \lambda_2^* \frac{n_B}{n_B + K_B} \tag{2}$$

$$\frac{\partial n_B}{\partial t} = \gamma \rho_1 - \lambda_2(n_B)\rho_2 / Y_B + D_B \cdot \nabla^2 n_B \tag{3}$$

$\lambda_{1,2}$ are the growth rates which depend on nutrient availability in a Monod-like manner, and $\lambda_{1,2}^*$ are the maximal growth rate when nutrients are abundant. $D_{1,2}$ are the cell diffusion coefficients. $D_1 \simeq D_2$. Eq.(3) describes the nutrient dynamics: the first term is the nutrient production by ρ_1, the second is the consumption by ρ_2 with Y_B the yield, and the last is the diffusion. Given that the nutrient molecules are much smaller than the cells, $D_B \gg D_{1,2}$

1.2 Syntrophy:

The main difference between syntrophy and the above commensal scenario is that now the accumulation of n_B is toxic to ρ_1. The equations are:

$$\frac{\partial \rho_1}{\partial t} = \lambda_1(n_A, n_B)\rho_1 + D_1 \cdot \nabla^2 \rho_1, \quad \lambda_1(n_A) = \lambda_1^* \frac{n_A}{n_A + K_A} \cdot \frac{1}{1 + n_B/K_{tB}} \approx \lambda_1^* \frac{1}{1 + n_B/K_{tB}} \tag{4}$$

$$\frac{\partial \rho_2}{\partial t} = \lambda_2(n_B)\rho_2 + D_2 \cdot \nabla^2 \rho_2, \quad \lambda_2(n_B) = \lambda_2^* \frac{n_B}{n_B + K_B} \tag{5}$$

$$\frac{\partial n_B}{\partial t} = \gamma \rho_1 - \lambda_2(n_B)\rho_2 / Y_B + D_B \cdot \nabla^2 n_B \tag{6}$$

K_{tB} indicates the toxicity of the accumulation of n_B and γ is the production rate of n_B by ρ_1.

1.3 Mutualism:

In the mutualism case where the excretants are neutral to both species, the equations are:

$$\frac{\partial \rho_1}{\partial t} = \lambda_1(n_A)\rho_1 + D_1 \cdot \nabla^2 \rho_1, \quad \lambda_1(n_A) = \lambda_1^* \frac{n_A}{n_A + K_A} \tag{7}$$

$$\frac{\partial \rho_2}{\partial t} = \lambda_2(n_B)\rho_2 + D_2 \cdot \nabla^2 \rho_2, \quad \lambda_2(n_B) = \lambda_2^* \frac{n_B}{n_B + K_B} \tag{8}$$

$$\frac{\partial n_A}{\partial t} = \gamma_A \rho_2 - \lambda_1(n_A)\rho_1 / Y_A + D_A \cdot \nabla^2 n_A \tag{9}$$

$$\frac{\partial n_B}{\partial t} = \gamma_B \rho_1 - \lambda_2(n_B)\rho_2 / Y_B + D_B \cdot \nabla^2 n_B \tag{10}$$

Similarly the set of equation where the accumulation of excretants are *toxic* is:

$$\frac{\partial \rho_1}{\partial t} = \lambda_1(n_A)\rho_1 + D_1 \cdot \nabla^2 \rho_1, \quad \lambda_1(n_A) = \lambda_1^* \frac{n_A}{n_A + K_A} \cdot \frac{1}{1 + n_B/K_{tB}} \tag{11}$$

$$\frac{\partial \rho_2}{\partial t} = \lambda_2(n_B)\rho_2 + D_2 \cdot \nabla^2 \rho_2, \quad \lambda_2(n_B) = \lambda_2^* \frac{n_B}{n_B + K_B} \cdot \frac{1}{1 + n_A/K_{tA}} \tag{12}$$

$$\frac{\partial n_A}{\partial t} = \gamma_A \rho_2 - \lambda_1(n_A)\rho_1 / Y_A + D_A \cdot \nabla^2 n_A \tag{13}$$

$$\frac{\partial n_B}{\partial t} = \gamma_B \rho_1 - \lambda_2(n_B)\rho_2 / Y_B + D_B \cdot \nabla^2 n_B \tag{14}$$

2 kMC algorithm on 2d lattice

All scenarios will be simulated on an $L \times L$ two-dimensional square lattice with lattice constant a and periodic boundary condition. Each lattice site can hold *at most* one single cell (either species 1 or 2) and can hold as many nutrient molecules (n_B) as possible.

When cells (or nutrient) **diffuse**, they are placed in one of the 4 nearest-neighbor sites, provided that it is empty in case of the cell.

When cells **divide**, the daughter cell is placed in one of the 4 nearest-neighbor sites, provided that it is empty.

2.1 Algorithm for Commensalism and Syntrophy:

Assume n_A is in unlimited supply. Initially the system contains one of each type of cell, placed in the center of the lattice.

#	process	rate	notes
1	cell 1 divide	$k_1 = \lambda_1 \rho_1$	$\lambda_1 = \lambda_1^*$; $\lambda_1 = \lambda_1^* \frac{1}{1+n_B/K_{tB}}$
2	cell 1 excrete n_B	$k_2 = \gamma \rho_1$	
3	cell 1 diffuse	$k_3 = \frac{D_1}{a^2}\rho_1$	
4	cell 2 divide	$k_4 = \lambda_2 \rho_2$	$\lambda_2 = \lambda_2^* \frac{n_B}{n_B + K_B}$
5	cell 2 take up n_B	$k_5 = \frac{\lambda_2}{Y_B}\rho_2$	
6	cell 2 diffuse	$k_6 = \frac{D_2}{a^2}\rho_2$	
7	nutrient diffuse	$k_7 = \frac{D_B}{a^2} n_B$	
		$k_0 = \sum_{i=1}^{7} k_i$	

1. Initialize the system with one of each type of cell, placed in the center of the lattice.
2. Generate a random number r_1 from a uniform random distribution in $[0, 1)$, and if it is $\sum_{i=1}^{j-1} k_i < r_1 k_0 < \sum_{i=1}^{j} k_i$, then reaction j is chosen to take place.
3. Afterwards the time is increased by $\Delta t = -\frac{\ln r_2}{k_0}$, where r_2 is also drawn from a uniform random distribution in $[0, 1)$.
4. The process is repeated until T_{MAX}.

Parameters: The lattice spacing a is chosen to be the typical length of a bacterium cell $a = 1\mu$m; $\lambda_1 \approx \lambda_2 = 0.5\mathrm{hr}^{-1} = 1.3 \times 10^{-4}\mathrm{s}^{-1}$;

The following are estimated:
1 OD$= 10^9$ cells/ ml.
Excretion rate $\gamma = 10\mu\mathrm{M/OD/hr} \approx 1.5 \times 10^3 \mathrm{s}^{-1}$; Biomass yield $Y_B = 0.1$ OD/mM $\approx 10^{-13} - 10^{-12}$.
Diffusion coefficients for cell: $D_1 \approx D_2 \approx 1 - 10\ \mu\mathrm{m}^2/s$; diffusion coefficient of nutrient $D_A = D_B = 600\ \mu\mathrm{m}^2/s$

2.2 Algorithm for Mutualism without and with toxicity:

#	process	rate	notes
1	cell 1 divide	$k_1 = \lambda_1 \rho_1$	$\lambda_1 = \lambda_1^* \frac{n_A}{n_A + K_A}$; $\lambda_1 = \lambda_1^* \frac{n_A}{n_A + K_A} \cdot \frac{1}{1 + n_B/K_{tB}}$
2	cell 1 excrete n_B	$k_2 = \gamma_B \rho_1$	
3	cell 1 take up n_A	$k_3 = \frac{\lambda_1}{Y_A} \rho_1$	
4	cell 1 diffuse	$k_4 = \frac{D_1}{a^2} \rho_1$	
5	cell 2 divide	$k_5 = \lambda_2 \rho_2$	$\lambda_2 = \lambda_2^* \frac{n_B}{n_B + K_B}$; $\lambda_2(n_B) = \lambda_2^* \frac{n_B}{n_B + K_B} \cdot \frac{1}{1 + n_A/K_{tA}}$
6	cell 2 excrete n_A	$k_6 = \gamma_A \rho_2$	
7	cell 2 take up n_B	$k_7 = \frac{\lambda_2}{Y_B} \rho_2$	
8	cell 2 diffuse	$k_8 = \frac{D_2}{a^2} \rho_2$	
9	nutrient diffuse	$k_9 = \frac{D_B}{a^2} n_B$	
		$k_0 = \sum_{i=1}^{9} k_i$	

1. Initialize the system with one of each type of cell, placed in the center of the lattice.
2. Generate a random number r_1 from a uniform random distribution in $[0, 1)$, and if it is $\sum_{i=1}^{j-1} k_i < r_1 k_0 < \sum_{i=1}^{j} k_i$, then reaction j is chosen to take place.
3. Afterwards the time is increased by $\Delta t = -\frac{\ln r_2}{k_0}$, where r_2 is also drawn from a uniform random distribution in $[0, 1)$.
4. The process is repeated until T_{MAX}.

2.3 Quantities of interest:

Per page 12 of our proposal, we devised two metrics to quantify the radial asymmetry of the colony formed. We define a roughness metric through the peripheral radial profile $\Delta R(\theta) = R(\theta)/\overline{R} - 1$, where $R(\theta)$ is the colony radius at angle θ and $\overline{R}$ is the average colony radius. Additionally, we can quantify the population diversity at the expanding colony front, with a diversity metric, $\Delta\rho(\theta) = |\rho_{\mathrm{A}}[R(\theta)] - \rho_{\mathrm{B}}[R(\theta)]| / (\rho_{\mathrm{A}}[R(\theta)] + \rho_{\mathrm{B}}[R(\theta)])$. The angular diversity profile $\Delta\rho(\theta)$ for colonies with cross-feeding is markedly different from the neutral case

Additionally, we can visually investigate the colony pattern in the neutral and beneficial mutualism cases.