II C. CR model: Symbiosis

- So far, nutrient is directly supplied by env.
- Here, we consider nutrient generated by the organisms themselves, as excretant (II C1) or by breaking down the environment (II C2)

→ incomplete survey to illustrate diff. classes of behaviors

1. Effect of Metabolic exchange (crossfeeding)

a) Commensalism:

$n_A \rightarrow \rho_1 \rightarrow n_B \rightarrow \rho_2$

[Specie 2 depends on species 1 but has no effect on 1]

$$\dot{\rho}_1 = r_1(n_A)\rho_1 - \mu\rho_1$$

$$\dot{\rho}_2 = r_2(n_B)\rho_2 - \mu\rho_2$$

$$\dot{n}_A = \mu(n_A^0 - n_A) - r_1(n_A)\rho_1/Y_A$$

$$\dot{n}_B = \gamma\rho_1 - \mu n_B - r_2(n_B)\rho_2/Y_B$$

↑ production of nutrient B by sp. 1

γ can be GR-dependent

Growth rate: take linear approx $r_i \simeq \nu_{i\alpha} n_\alpha$

ρ_1 not affected by ρ_2

→ dynamics of ρ_1 same as before

$\dot{\rho}_1 = 0 \quad \nu_{1A} n_A^* = \mu$

$\dot{n}_A = 0 \quad \mu(n_A^0 - n_A^*) = \underbrace{\nu_{1A} n_A^*}_{\mu} \rho_1^* / Y_A$

$\rightarrow \begin{cases} n_A^* = \mu/\nu_{1A} \\ \rho_1^* = (n_A^0 - n_A^*) Y_A \end{cases}$

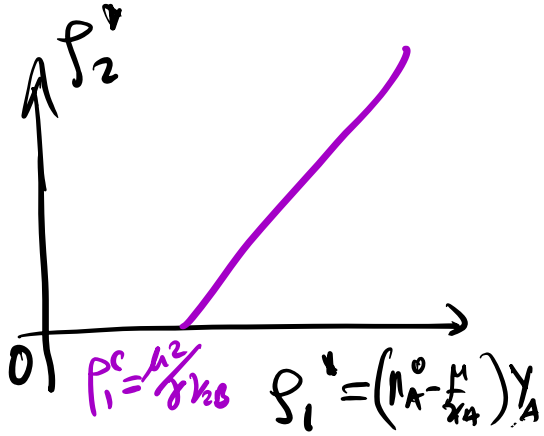
(Stable fixed pt)

Next, n_B and ρ_2:

$\dot{\rho}_2/\rho_2 = 0 \quad \nu_{2B} n_B^* = \mu.$

$\dot{n}_B = 0 \quad \gamma \rho_1^* = \mu n_B^* + \mu \rho_2^* / Y_B$

$\rightarrow \begin{cases} n_B^* = \mu/\nu_{2B} \\ \rho_2^* = \frac{\gamma}{\mu} Y_B \rho_1^* - n_B^* Y_B \end{cases}$

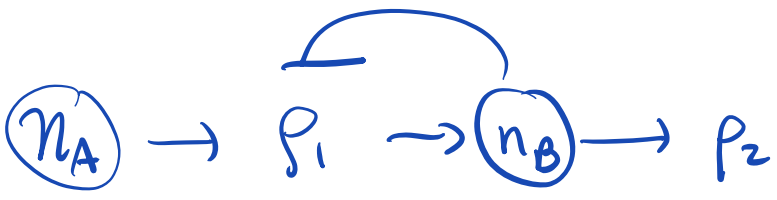


- Species 2 just passively follows species 1.
- threshold: $\rho_2^* = 0$ if $\gamma \rho_1^* \leq \mu n_B^*$ or $(n_A^0 - \frac{\mu}{\nu_{1A}}) Y_A \cdot \gamma \leq \mu^2/\nu_{2B}$

excretion ≤ dilution or $\mu \geq \sqrt{n_A^0 Y_A \gamma \cdot \nu_{2B}}$

b) Mutualism (two species benefit each other)

example:



- n_B is toxic to ρ_1 (e.g. acetate, ethanol)
- removal of n_B benefits both ρ_1 and ρ_2

growth inhibition by B

$$\dot{\rho}_1 = r_1(n_A, n_B)\,\rho_1 - \mu\rho_1$$

try $r_1 = \frac{\nu_{1A} n_A}{1 + n_B/K_I}$ (details depends on inhibitory mech)

$$\dot{\rho}_2 = r_2(n_B)\,\rho_2 - \mu\rho_2$$

$$\dot{n}_A = \mu(n_A^0 - n_A) - r_1(n_A, n_B)\,\rho_1/Y_A$$

$$\dot{n}_B = \gamma\rho_1 - \mu n_B - r_2(n_B)\rho_2/Y_B; \quad r_2(n_B) = \nu_{2B} n_B .$$

Q: under what condition does sp2 make a qualitative difference to ρ_1? (e.g. shift the boundary of washout region)

First, find effect of n_B on ρ_1 (ρ_2 not involved)

$$\mu = r_1(n_A^*, n_B^*); \quad \rho_1^* = (n_A^0 - n_A^*)\cdot Y_A = n_A^0 Y_A\left(1 - \frac{n_A^*}{n_A^0}\right)$$

$$\mu = \frac{\nu_{1A} n_A^*}{1 + n_B^*/K_I}$$

$$n_A^* = \frac{\mu}{\nu_{1A}}(1 + n_B^*/K_I)$$

$$\rho_1^* = n_A^0 Y_A\left[1 - \frac{\mu}{\nu_{1A} n_A^0}\left(1 + \frac{n_B^*}{K_I}\right)\right]$$

$n_A^0 Y_A = \rho_1^0$; $\frac{\mu}{\nu_{1A} n_A^0} = \eta$

Recall simple chemostat ($n_B = 0$):

$$\rho_1 = \rho_1^0 \cdot (1 - \eta); \text{ wash out at } \eta = 1$$

→ inhibition by B:

increases η + shift boundary of washout?

* if $\rho_2 = 0$, $\dot{n}_B = 0 \rightarrow n_B^* = \frac{\gamma}{\mu}\rho_1^*$

$$\rightarrow \frac{\rho_1^*}{\rho_1^0} = 1 - \eta\cdot\left(1 + \frac{\gamma}{\mu K_I}\rho_1^*\right),$$

$$\frac{\rho_1^*}{\rho_0} = \frac{1-\eta}{1 + \frac{\eta\gamma}{\mu K_I}\rho_0} = \frac{1-\eta}{1 + \gamma\gamma_A/K_I\nu_{1A}}$$

$\Rightarrow$ washout limit (where $\rho_1^* \to 0$) is still $\eta = 1$ for finite K_I.

$\rightarrow$ inhibition by B only leads to reduced value of ρ_1^* no qualitative change, e.g. shift of washout boundary

$\rightarrow$ because ρ_1^* (hence n_B^*) is small near washout. (toxicity of B reduced as ρ_1^* reduced)

* if $\rho_2 \neq 0$, $\dot{\rho}_2/\rho_2 = 0$: $\nu_{2B} n_B^* = \mu$

$$\rho_1 = \rho_1^0\left[1 - \underbrace{\eta\cdot\left(1 + \frac{\mu}{\nu_{2B}K_I}\right)}_{\eta' > \eta}\right] = \rho_1^0\left[1 - \eta - \eta^2\frac{\nu_{2A}n_A^0}{\nu_{2B}K_I}\right]$$

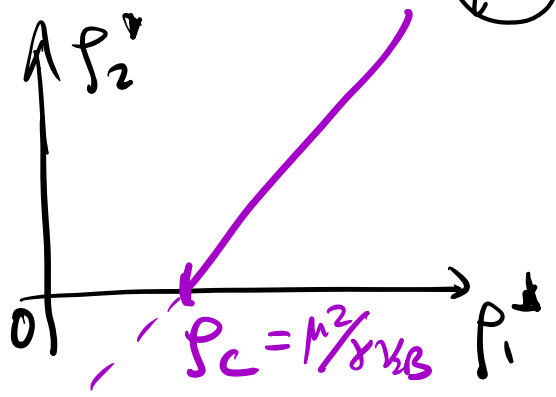
$\rightarrow$ increase of η

(but ρ_2 is supposed to help?!)

* For what range of parameters is $\rho_2^* > 0$?

$n_B = 0$: $\rho_2^* \propto \frac{\gamma Y_B}{\mu}(\rho_1^* - \rho_c)$

- doesn't involve toxicity of B



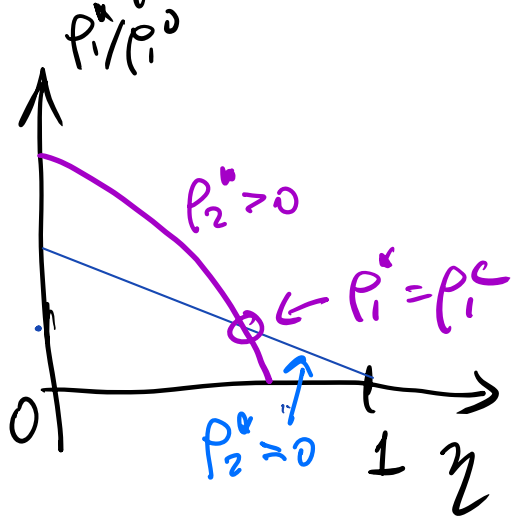
⇒ as ρ_1^* is reduced towards 0 by B, $\rho_2 = 0$

thus sp2 cannot affect the washout boundary of sp1

→ work out the quantitative effect of inhibition for $\rho_2 \neq 0$

$\rho_2 \neq 0$ $\quad \frac{\rho_1^*}{\rho_1^0} = 1 - \eta - \eta^2 \frac{\nu_{iA} n_A^0}{\nu_B K_I}$

$\rho_2 = 0$ $\quad \frac{\rho_1^*}{\rho_1^0} = \frac{1-\eta}{1 + \frac{\gamma Y_A}{\nu_A K_I}}$



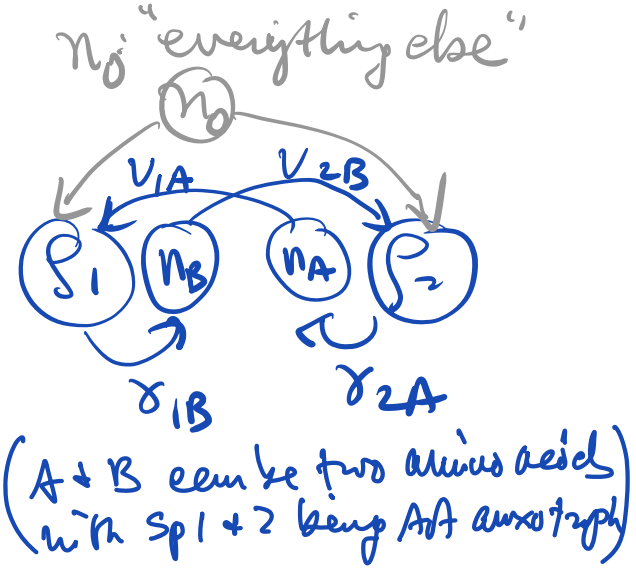
⇒ moderate increase of ρ_1^* due to sp 2 far from washout limit; no qualitative change!

⇒ result of batch culture growth quite different from chemostat due to higher density (HW)

c) Mutualism: Complementary cross feeding

Consider chemostat setting:

$$\dot{\rho}_1 = \gamma_{1A} n_A \rho_1 - \mu \rho_1$$
$$\dot{\rho}_2 = \gamma_{2B} n_B \rho_2 - \mu \rho_2$$
$$\dot{n}_A = \gamma_{2A} \rho_2 - \mu n_A - \gamma_{1A} n_A \rho_1$$
$$\dot{n}_B = \gamma_{1B} \rho_1 - \mu n_B - \gamma_{2B} n_B \rho_2$$



(A & B could be two amino acids with sp 1 & 2 being Aux auxotroph)

(Assume infinite supply of n_0; setting $Y_\alpha = 1$)

Assume rapid eq of crossfeeding metabolites:

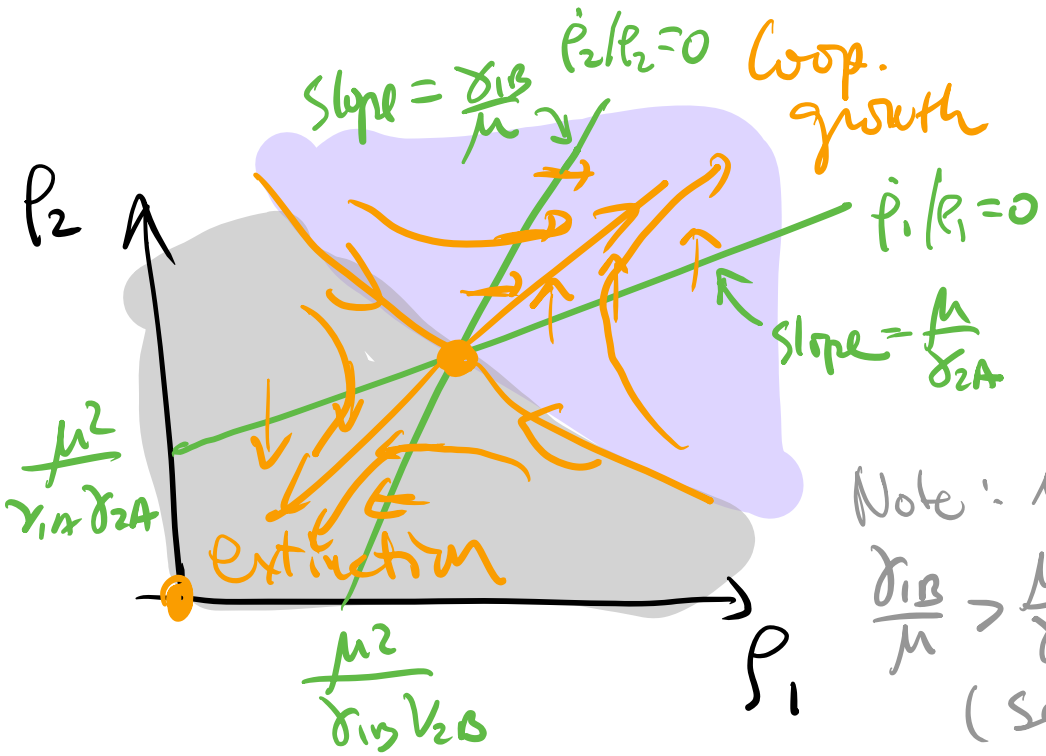
$$\left.\begin{aligned}\dot{n}_A &= 0 \\ \dot{n}_B &= 0\end{aligned}\right\} \quad n_A = \frac{\gamma_{2A}\rho_2}{\mu + \gamma_{1A}\rho_1}, \quad n_B = \frac{\gamma_{1B}\rho_1}{\mu + \gamma_{2B}\rho_2}$$

Insert into eqns for ρ_1, ρ_2:

$$\begin{cases} \dot{\rho}_1 = \gamma_{1A} \dfrac{\gamma_{2A}\rho_1\rho_2}{\mu + \gamma_{1A}\rho_1} - \mu\rho_1 \\ \dot{\rho}_2 = \gamma_{2B} \dfrac{\gamma_{1B}\rho_1\rho_2}{\mu + \gamma_{2B}\rho_2} - \mu\rho_2 \end{cases}$$

$$\dot{\rho}_1/\rho_1 = 0 \rightarrow \gamma_{1A}\gamma_{2A}\rho_2 = \mu(\mu + \gamma_{1A}\rho_1)$$

$$\dot{\rho}_2/\rho_2 = 0 \rightarrow \gamma_{2B}\gamma_{1B}\rho_1 = \mu(\mu + \gamma_{2B}\rho_2)$$



Note: requires

$\frac{\gamma_{1B}}{\mu} > \frac{\mu}{\gamma_{2A}}$ or $\gamma_{1B}\gamma_{2A} > \mu$

(see below)

Allee effect: must exceed critical density before reaping benefit.

In the growth phase, need $n_A^* > 0$, $n_B^* > 0$.

$$\begin{cases} \dot{n}_A = \gamma_{2A}\rho_2 - \mu n_A - \gamma_{1A} n_A \rho_1 \\ \dot{n}_B = \gamma_{1B}\rho_1 - \mu n_B - \gamma_{2B} n_B \rho_2 \end{cases}$$

Does the system support simple exponential growth?
(need $n_A^* = \text{const}$, $n_B^* = \text{const}$, $\rho_1 \sim e^{\lambda t}$, $\rho_2 \sim e^{\lambda t}$)

$$\begin{cases} \dot{n}_A = 0 \\ \dot{n}_B = 0 \end{cases} \Rightarrow \begin{cases} n_A^* = \dfrac{\gamma_{2A}\rho_2(t)}{\mu + \gamma_{1A}\rho_1(t)} \\ n_B^* = \dfrac{\gamma_{1B}\rho_1}{\mu + \gamma_{2B}\rho_2} \end{cases} \to \begin{cases} \dfrac{\gamma_{2A}}{\gamma_{1A}} b \\ \dfrac{\gamma_{1B}}{\gamma_{2B}} b^{-1} \end{cases}, \quad b = \frac{\rho_2^*(t)}{\rho_1^*(t)}$$

requires $\rho_1^* \sim e^{\lambda t}$, $\rho_2^* \sim e^{\lambda t}$

from $\dot{\rho}_1 = \nu_{1A} n_A \rho_1 - \mu \rho_1$

$\dot{\rho}_2 = \nu_{2B} n_B \rho_2 - \mu \rho_2$

$$\Rightarrow \begin{cases} \lambda = \nu_{1A} n_A^* - \mu = \gamma_{2A} \cdot b - \mu \\ \lambda = \nu_{2B} n_B^* - \mu = \gamma_{1B} \cdot b^{-1} - \mu \end{cases} \Big\} \; \gamma_{2A} \cdot b = \gamma_{1B} \cdot b^{-1}$$

$$b = \sqrt{\frac{\gamma_{1B}}{\gamma_{2A}}};$$

$$n_A^* = \frac{\gamma_{2A}}{\nu_{1A}} \cdot b = \frac{\sqrt{\gamma_{2A}\gamma_{1B}}}{\nu_{1A}} \rightarrow r_1 = \nu_{1A} n_A^* = \sqrt{\gamma_{2A}\gamma_{1B}}$$

$$n_B^* = \frac{\gamma_{1B}}{\nu_{2B}} b^{-1} = \frac{\sqrt{\gamma_{2A}\gamma_{1B}}}{\nu_{2B}} \rightarrow r_2 = \nu_{2B} n_B^* = \sqrt{\gamma_{2A}\gamma_{1B}} \Big\} r$$

$\rightarrow \lambda > 0$ requires $r > \mu$ or $\sqrt{\gamma_{2A}\gamma_{1B}} > \mu$

(due to dilution at rate μ)

- exp growth allowed due to infinite supply of n_0
- coop. growth set by physiological parameter (γ_{iA} ν_{jB})

$\rightarrow$ Strategy of coop: optimize resource allocation

(trade off between γ and ν)