IIC. CR model: Symbiosis

- So far, nutrient is directly supplied by env.
- Here, we consider nutrient <u>generated</u> by the organisms themselves, as excretant (IIC1) or by breaking down the environment (IIC2)

→ incomplete survey to illustrate diff. classes of behaviors

1. Effect of Metabolic exchange (crossfeeding)

a) Commensalism:

$$n_A \to \rho_1 \to n_B \to \rho_2$$

[species 2 depends on species 1 but has <u>no effect</u> 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 n_B by ρ_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 $\rightarrow$ dynamics of ρ_1 as before

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

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

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

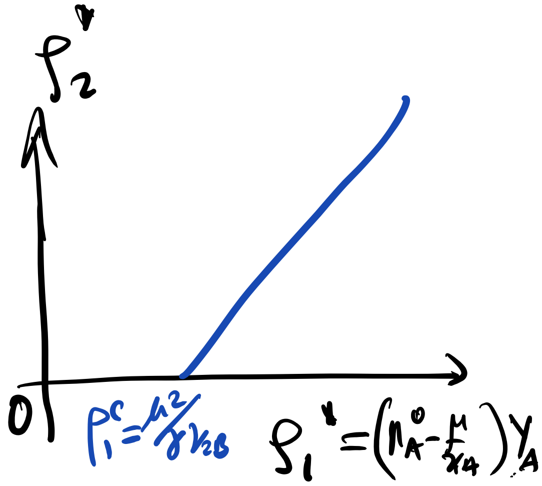
(Stable fixed pt)

Now, n_B and ρ_2:

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

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

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



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

  excretion $\le$ dilution $\qquad$ or $\mu \ge \sqrt{n_A^0 Y_A \gamma \cdot \nu_{2B}}$

b) Mutualism (two species benefit each other)

example:

$$\begin{tikzcd} n_A \arrow[r] & \rho_1 \arrow[r] & n_B \arrow[r] \arrow[l, bend right] & \rho_2 \end{tikzcd}$$

- 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 n_B

$$\dot\rho_1 = r_1(n_A, n_B)\rho_1 - \mu\rho_1$$

try $r_1 = \dfrac{\nu_{1A} n_A}{1 + n_B/K_I}$

(details depends on inhibitory mech)

$$\dot\rho_2 = r_2(n_B)\rho_2 - \mu\rho_2$$

$$\dot n_A = \mu\cdot(n_A^0 - n_A) - r_1(n_A, n_B)\rho_1/Y_A$$

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

Q: under what condition does ρ_2 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)

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

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

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

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

recall simple chemostat ($n_B = 0$):

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

→ inhibition by B:

increase η + shift boundary of washout?

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

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

$$\frac{\rho_1^*}{\rho_0} = \frac{1-\eta}{1+\frac{\eta\gamma}{\mu K_I}} = \frac{1-\eta}{1+\gamma/K_I \nu_{1A} n_A^0}$$

⇒ washout limit (when $\rho_1 \to 0$) is still $\eta=1$ for finite K_I.

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

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

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

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

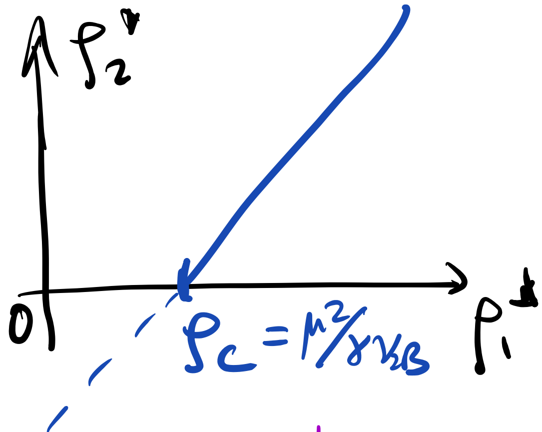
$$\eta\frac{\mu}{\nu_{2B}K_I} = \eta^2\frac{\nu_{1A}n_A^0}{\nu_{2B}K_I}$$

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

→ increase of η
(but ρ_2 is supposed to help?!)

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

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



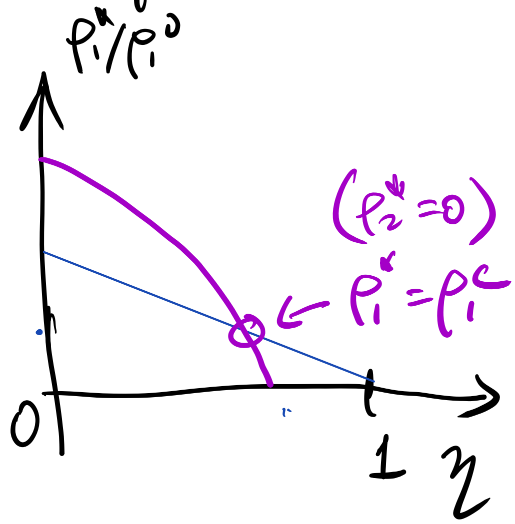
- doesn't involve toxicity of B

⇒ as ρ_1^* is reduced (by B), ρ_2 becomes negligible (cannot affect washout boundary)

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

$\rho_2 \neq 0$: $$\frac{\rho_1^*}{\rho_1^0} = 1 - \eta - \eta^2 \frac{\nu_{IA} n_A^0}{\nu_{IB} K_I}$$

$\rho_2 = 0$: $$\frac{\rho_1^*}{\rho_1^0} = \frac{1-\eta}{1 + \frac{\gamma}{\nu_{IA} n_A^0 K_I}}$$

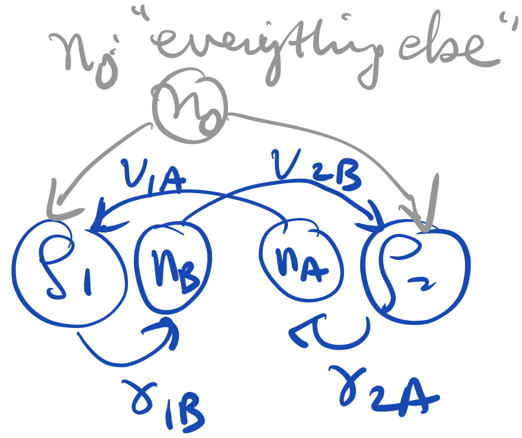


⇒ moderate increase of ρ_1^* due to sp 2 far from washout limit; no qualitative change!

⇒ result of batch culture growth very different due to higher density (HW)

c) Mutualism: Complementary cross feeding

Consider chemostat setting:



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

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

$$\dot{n}_A = \gamma_{2A} \rho_2 - \mu n_A - \nu_{1A} n_A \rho_1$$

$$\dot{n}_B = \gamma_{1B} \rho_1 - \mu n_B - \nu_{2B} n_B \rho_2$$

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

Assume rapid eq of crossfeeding metabolites:

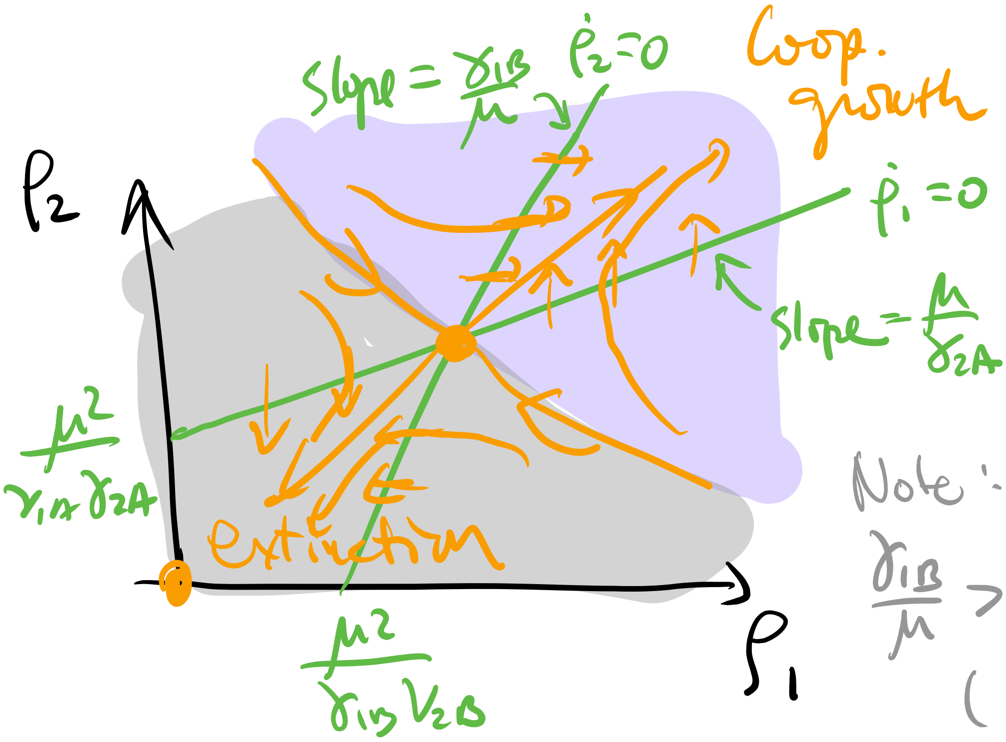
$$\left.\begin{array}{l} \dot{n}_A = 0 \\ \dot{n}_B = 0 \end{array}\right\} \quad n_A = \frac{\gamma_{2A} \rho_2}{\mu + \nu_{1A} \rho_1}, \quad n_B = \frac{\gamma_{1B} \rho_1}{\mu + \nu_{2B} \rho_2}$$

Insert into eqns for ρ_1, ρ_2:

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

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

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



Note: requires $\frac{\gamma_{1B}}{\mu} > \frac{\mu}{\gamma_{2A}}$ or $\sqrt{\gamma_{1B}\gamma_{2A}} > \mu$ (see below)

Allee effect: must exceed critical density before reaping benefit.

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

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

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

$$n_A^* = \frac{\gamma_{2A}\rho_2(t)}{\mu + \gamma_{1A}\rho_1(t)} \rightarrow \frac{\gamma_{2A}}{\gamma_{1A}} b, \quad b = \frac{\rho_2^*(t)}{\rho_1^*(t)}$$

$$n_B^* = \frac{\gamma_{1B}\rho_1}{\mu + \gamma_{2B}\rho_2} \rightarrow \frac{\gamma_{1B}}{\gamma_{2B}} b^{-1}$$

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

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

$$\Rightarrow \left\{ \begin{array}{l} \lambda = \nu_{1A} n_A^* - \mu = \gamma_{2A} \cdot b - \mu \\ \lambda = \nu_{2B} n_B^* - \mu = \gamma_{1B} \cdot b^{-1} - \mu \end{array} \right\} \gamma_{2A} \cdot b = \gamma_{1B} \cdot b^{-1}$$

$$\boxed{\begin{array}{l} b = \sqrt{\dfrac{\gamma_{1B}}{\gamma_{2A}}}; \\ n_A^* = \dfrac{\gamma_{2A}}{\nu_{1A}} \cdot b = \dfrac{\sqrt{\gamma_{2A}\gamma_{1B}}}{\nu_{1A}} \\ n_B^* = \dfrac{\gamma_{1B}}{\nu_{2B}} b^{-1} = \dfrac{\sqrt{\gamma_{2A}\gamma_{1B}}}{\nu_{2B}} \end{array}}$$

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

$\rightarrow r_2 = \nu_{2B} n_B^* = \sqrt{\gamma_{2A}\gamma_{1B}}$

$\} \; r$

$\rightarrow$ $\lambda > 0$ 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 parameters ($\gamma_{i\alpha}$ $\nu_{j\beta}$)

$\rightarrow$ Strategy of coop: optimize resource allocation

(trade off between γ and ν)