Modèles multi-étapes

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La réalité?

$$\begin{aligned} \frac{dX_{ch}}{dt} &= -DX_{ch} + Y_{ch}f_0\left(S_{ch}, S_{H_2}\right)X_{ch} - k_{dec,ch}X_{ch} \\ \frac{dX_{ph}}{dt} &= -DX_{ph} + Y_{ph}f_1\left(S_{ph}, S_{H_2}\right)X_{ph} - k_{dec,ph}X_{ph} \\ \frac{dX_{H_2}}{dt} &= -DX_{H_2} + Y_{H_2}f_2\left(S_{H_2}\right)X_{H_2} - k_{dec,H_2}X_{H_2} \\ \frac{dS_{ch}}{dt} &= D\left(S_{ch,in} - S_{ch}\right) - f_0\left(S_{ch}, S_{H_2}\right)X_{ch} \\ \frac{dS_{ph}}{dt} &= D\left(S_{ph,in} - S_{ph}\right) + \frac{224}{208}\left(1 - Y_{ch}\right)f_0\left(S_{ch}, S_{H_2}\right)X_{ch} \\ - f_1\left(S_{ph}, S_{H_2}\right)X_{ph} \\ \frac{dS_{H_2}}{dt} &= \left(S_{H_2,in} - S_{H_2}\right) + \frac{32}{224}\left(1 - Y_{ph}\right)f_1\left(S_{ph}, S_{H_2}\right)X_{ph} \\ - \frac{16}{208}f_0\left(S_{ch}, S_{H_2}\right)X_{ch} - f_2\left(S_{H_2}\right)X_{H_2} \end{aligned}$$

Chlorophenol degradation

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- $S_{\rm ch}$ and $X_{\rm ch}$ are the chlorophenol substrate and biomass concentrations
- $S_{\rm ph}$ and $X_{\rm ph}$ those for phenol and $S_{\rm H_2}$ and $X_{\rm H_2}$ those for hydrogen
- $Y_{\rm ch},~Y_{\rm ph}$ and $Y_{\rm H2}$ are the yield coefficients,
- $224/208 \left(1-Y_{\rm ch}\right)$ represents the part of chlorophenol degraded to phenol,
- + 32/224 (1 $Y_{\rm ph})$ represents the part of phenol that is transformed to hydrogen

Growth functions take Monod form with hydrogen inhibition acting on the phenol degrader.

$$\begin{split} f_{0}\left(S_{\rm ch}, S_{\rm H_{2}}\right) &= \frac{k_{m, {\rm ch}}S_{\rm ch}}{K_{S, ch} + S_{\rm ch}} \frac{S_{H_{2}}}{K_{S, {\rm H_{2}, c}} + S_{{\rm H_{2}}}} \\ f_{1}\left(S_{\rm ph}, S_{{\rm H_{2}}}\right) &= \frac{k_{m, {\rm ph}}S_{\rm ph}}{K_{S, {\rm ph}} + S_{\rm ph}} \frac{1}{1 + \frac{S_{{\rm H_{2}}}}{K_{i, {\rm H_{2}}}}}, \quad f_{2}\left(S_{{\rm H_{2}}}\right) = \frac{k_{m, {\rm H_{2}}}S_{{\rm H_{2}}}}{K_{S, {\rm H_{2}}} + S_{{\rm H_{2}}}} \end{split}$$

Wade et al. 2015

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Stabilité des équilibres Diagramme opératoire

- 2 Modèle à deux étapes
- 3 Commensalisme Modèle AM2
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- **5** Anaerobic digestion
- 6 Maintenance
- Modèle à 3 étapes

Chemostat



Chemostat : $S_1 \xrightarrow{\mu_1(\cdot)} X_1$ $\begin{cases} \dot{S}_1 = D(S_1^{in} - S_1) - k_1\mu_1(S_1)X_1 \\ \dot{X}_1 = -DX_1 + \mu_1(S_1)X_1 \end{cases}$

- S_1 : concentration of substrate
- X₁ : concentration of bacteria
- S_1^{in} : input concentration of substrate
- D = Q/V : Dilution rate
- k₁ : stoichiometric coefficient
- $\mu_1(\cdot)$: specific growth functions









Le bactogène-chemostat

Review	Continuous culture – making a comeback?
	Paul A. Hoskisson ¹ and Glyn Hobbs ²
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The system and term chemostat were invented by Novick & Szilard (1950), although simultaneously and independently the 'bactogène', a virtually identical device, was developed by Monod (1950). The basis of both is that the specific growth rate of an organism, relative to its theoretical maximum, is governed by the external substrate concentration of a limiting nutrient.

Chemostat : Stabilité des équilibres



Détermination des équilibres



Détermination des équilibres



$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$



Portrait de phase

 $\dot{s} = -\mu(s)x + D(s_{in} - s)$ $\dot{x} = \mu(s)x - Dx$





Stabilité des équilibres (Monod)

$$\begin{cases} \dot{s} = D(s_{in} - s) - \mu(s)x \\ \dot{x} = (\mu(s) - D)x \end{cases}$$

• $\mu(S) = \frac{\mu_{max}S}{K+S}$ • $(\mu(s) - D)x = 0 \Longrightarrow x = 0 \text{ or } \mu(s) = D$ (thus $s = s^*$)

•
$$D(s_{in}-s)-\mu(s)x=0 \Longrightarrow s=s_{in} \text{ or } x=x^*=s_{in}-s^*$$

- $E_0 = (s_{in}, 0)$ (washout) always exists
- $E_1 = (s^*, x^*)$ exists if and only if $s_{in} > s^* \Longleftrightarrow \mu(s_{in}) > D$

Steady-state	Existence condition	Stability condition
E ₀	Always exists	$\mu(s_{in}) < D$
E_1	$\mu(s_{in}) > D$	Stable if it exists

Stabilité des équilibres (Haldane)

$$\begin{cases} \dot{s} = D(s_{in} - s) - \mu(s)x \\ \dot{x} = (\mu(s) - D)x \end{cases}$$

•
$$\mu(S) = \frac{mS}{K+S+S^2/K_i}$$

•
$$(\mu(s) - D)x = 0 \Longrightarrow x = 0 \text{ or } \mu(s) = D,$$

$$(\text{thus } s = s_1^* \text{ or } s = s_2^*, \ s_1^* < s_2^*)$$

•
$$D(s_{in} - s) - \mu(s)x = 0 \Longrightarrow s = s_{in} \text{ or } x = x_1^* \text{ or } x = x_2^*$$

$$(x_1^* = s_{in} - s_1^*, \ x_2^* = s_{in} - s_2^*)$$

•
$$E_0 = (s_{in}, 0) \text{ (washout) always exists}$$

• $E_i = (s_i^*, x_i^*)$ exists if and only if $s_i^* < s_{in}$

Steady-state	Existence condition	Stability condition
E ₀	Always exists	$s_{in} > s_2^*$
E ₁	$s_{in}>s_1^*$	Stable if it exists
E_2	$s_{in} > s_2^*$	Unstable if it exists

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Chemostat : Diagramme opératoire

Apart from the two operating (or control) parameters, which are the inflowing substrate s_{in} and the dilution rate D, that can vary, all others have biological meaning and are fixed depending on the organisms and substrate considered

Diagramme opératoire



region	E ₀	E_1
$(s_{in}, D) \in \mathcal{I}_0$	S	
$(s_{in}, D) \in \mathcal{I}_1$	U	S

region	E ₀	E_1	E_2
$(s_{in}, D) \in \mathcal{J}_0$	S		
$(s_{in}, D) \in \mathcal{J}_1$	U	S	
$(s_{in},D)\in\mathcal{J}_2$	S	S	U

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Chemostat Modèle à deux étapes



Mixed culture :

$$S_1 \xrightarrow{\mu_1(\cdot)} X_1 + S_2, \quad S_2 \xrightarrow{\mu_2(\cdot)} X_2$$

$$\begin{cases} \dot{S}_1 = D(S_1^{in} - S_1) - k_1 \mu_1(\cdot) X_1 \\ \dot{X}_1 = -DX_1 + \mu_1(\cdot) X_1 \\ \dot{S}_2 = -DS_2 + k_3 \mu_1(\cdot) X_1 - k_2 \mu_2(\cdot) X_2 \\ \dot{X}_2 = -DX_2 + \mu_2(\cdot) X_2 \end{cases}$$

- S_1 , S_2 : concentrations of substrate and product
- X_1 , X_2 : concentrations of bacteria
- S_1^{in} : input concentration of substrate
- D : Dilution rate
- k_1 , k_2 , k_3 : steochiometric coefficients (inverses of yields)
- $\mu_1(\cdot)$, $\mu_2(\cdot)$: specific growth functions

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Chemostat Modèle à deux étapes Commensalisme

État d'animaux ou de végétaux vivant associés à d'autres espèces et profitant de leurs aliments sans leur porter préjudice. http://www.cnrtl.fr/definition/commensalisme

Commensalism

'Two populations of microorganisms which grow in a mixed culture and interact in such a way that one population (the commensal population) depends for its growth on the other population and thus benefits from the interaction while the other population (the host) is not affected by the growth of the commensal population constitutes an example of commensalism.'

$$\mu_1(\cdot) = \mu_1(S_1), \quad \mu_2(\cdot) = \mu_2(S_2)$$

are monotone increasing (Monod) or can exhibit a maximum if the growth is inhibited at high substrate concentrations (Haldane)

 $\begin{cases} \dot{S}_1 = D(S_1^{in} - S_1) - k_3 \mu_1(S_1) X_1 \\ \dot{X}_1 = -DX_1 + \mu_1(S_1) X_1 \\ \dot{S}_2 = -DS_2 + k_1 \mu_1(S_1) X_1 - k_2 \mu_2(S_2) X_2 \\ \dot{X}_2 = -DX_2 + \mu_2(S_2) X_2 \end{cases}$

Stephanopoulos 1981

Commensalism

$$\begin{cases} \dot{S}_1 = D(S_1^{in} - S_1) - k_3\mu_1(S_1)X_1 \\ \dot{X}_1 = -DX_1 + \mu_1(S_1)X_1 \\ \dot{S}_2 = -DS_2 + k_1\mu_1(S_1)X_1 - k_2\mu_2(S_2)X_2 \\ \dot{X}_2 = -DX_2 + \mu_2(S_2)X_2 \end{cases}$$

- Solve the first and second equations for S_1 , X_1
- Use this result is the remaining equations to find S_2 , X_2
- Consequently S₁ and X₁ are the same in pure and mixed culture experiments
- In contrast to this, synthrophic associations exhibit a mutual dependance of the two members of the food chain

Reilly 1974, Stephanopoulos 1981, Bernard et al. 2001, Benyahia et al. 2012

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Chemostat Modèle à deux étapes Commensalisme : Modèle AM2

Modèle AM2

$$\begin{cases} \dot{S}_{1} = D(S_{1}^{in} - S_{1}) - k_{3}\mu_{1}(S_{1})X_{1} \\ \dot{X}_{1} = -\alpha DX_{1} + \mu_{1}(S_{1})X_{1} \\ \dot{S}_{2} = D(S_{2}^{in} - S_{2}) + k_{1}\mu_{1}(S_{1})X_{1} - k_{2}\mu_{2}(S_{2})X_{2} \\ \dot{X}_{2} = -\alpha DX_{2} + \mu_{2}(S_{2})X_{2} \\ \mu_{1}(S_{1}) = \frac{m_{1}S_{1}}{K_{1} + S_{1}}, \quad \mu_{2}(S_{2}) = \frac{m_{2}S_{2}}{K_{2} + S_{2} + S_{2}^{2}/K_{i}} \end{cases}$$

$$0 = D(S_1^{in} - S_1) - k_3 \mu_1(S_1) X_1$$
(6)

$$0 = (\mu_1(S_1) - \alpha D) X_1$$
 (7)

$$0 = D(S_2^{in} - S_2) + k_1 \mu_1(S_1) X_1 - k_2 \mu_2(S_2) X_2$$
 (8)

$$0 = (\mu_2(S_2) - \alpha D) X_2$$
 (9)

Bernard et al. 2001, Benyahia et al. 2012



Fig. 2. Diagram summarizing the equilibria of system (1)-(4). Hence, the system has at most six equilibrium points, see Proposition 1.

Journal of Process Control 22 (2012) 1008-1019



Bifurcation and stability analysis of a two step model for monitoring anaerobic digestion processes *

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B. Benyahia^{a,b,*}, T. Sari^{b,c}, B. Cherki^a, J. Harmand^{b,d}

AM2 : steady-states

- $E_1^0 = (S_{1in}, 0, S_{2in}, 0)$, washout of X_1 and X_2 .
- $E_1^i = (S_{1in}, 0, S_2^{i*}, X_2^i)$, i = 1, 2, washout of X_1 but not of X_2 .
- $E_2^0 = (S_1^*, X_1^*, S_{2in}^*, 0)$, washout of X_2 but not of X_1 .
- $E_2^i = (S_1^*, X_1^*, S_2^{i*}, X_2^{i*}), i = 1, 2$, coexistence of X_1 and X_2 .

where

$$\mu_{1}(S_{1}) = \alpha D \iff S_{1} = S_{1}^{*}$$

$$\mu_{2}(S_{2}) = \alpha D \iff S_{2} = S_{2}^{1*} \text{ or } S_{2} = S_{2}^{2*}, \quad S_{2}^{1*} < S_{2}^{2*}$$

$$S_{2in}^{*} = S_{2in} + \frac{k_{2}}{k_{1}} \left(S_{1in} - S_{1}^{*} \right), \quad X_{1}^{*} = \frac{1}{k_{1}\alpha} \left(S_{1in} - S_{1}^{*} \right)$$

$$X_{2}^{i} = \frac{1}{k_{3}\alpha} \left(S_{2in} - S_{2}^{i*} \right), \quad X_{2}^{i*} = \frac{1}{k_{3}\alpha} \left(S_{2in}^{*} - S_{2}^{i*} \right), \quad i = 1, 2$$

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AM2 : Existence and Stability of steady states

If $S_{1in} < S_1^*$ then we have 3 sub-cases :

Condition	E_{1}^{0}	E_{1}^{1}	E_{1}^{2}
$S_{2in} < S_2^{1*} < S_2^{2*}$	S		
$S_2^{1*} < S_{2in}^{-} < S_2^{-2*}$	U	S	
$S_2^{1*} < S_2^{2*} < S_{2in}^{-}$	S	S	U

If $S_{1in} > S_1^*$ then we have 6 sub-cases :

Condition	E_{1}^{0}	E_{1}^{1}	E_{1}^{2}	E_{2}^{0}	E_{2}^{1}	E_{2}^{2}
$\overline{S_{2in} < S_{2in}^* < S_2^{1*} < S_2^{2*}}$	U			S		
$S_{2in} < S_2^{1*} < S_{2in}^* < S_2^{2*}$	U			U	S	
$S_{2in} < S_2^{1*} < S_2^{2*} < S_{2in}^{*}$	U			S	S	U
$S_2^{1*} < S_{2in} < S_{2in}^* < S_2^{2*}$	U	U		U	S	
$S_2^{1*} < S_{2in} < S_2^{2*} < S_{2in}^*$	U	U		S	S	U
$S_2^{1*} < S_2^{2*} < S_{2in} < S_{2in}^*$	U	U	U	S	S	U

AM2 : Operating diagram



region	E_{1}^{0}	E_{2}^{0}	E_{2}^{1}	E_{2}^{2}
$(S_{1in}, D) \in \mathcal{I}_0$	S			
$(S_{1in},D)\in\mathcal{I}_1$	U	S		
$(S_{1in}, D) \in \mathcal{I}_2$	U	U	S	
$(S_{1in},D)\in\mathcal{I}_3$	U	S	S	U

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Chemostat Modèle à deux étapes Commensalisme Syntrophie

syntrophe, adj.[En parlant d'une souche de bactéries ou de champignons] Qui n'est capable de se développer sur un milieu nutritif minimal que quand elle est associée à une autre (d'apr. Méd. Biol. t. 3 1972).

syntrophie, subst. fém. Aptitude de deux cellules ou de deux souches bactériennes à être syntrophes (d'apr. Méd. Biol. t. 3 1972).

http://www.cnrtl.fr/definition/syntrophie

Syntrophy

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$$\begin{cases} \dot{S}_1 &= D(S_1^{in} - S_1) - k_3 \mu_1(S_1, S_2) X_1 \\ \dot{X}_1 &= \mu_1(S_1, S_2) X_1 - D X_1 \\ \dot{S}_2 &= k_1 \mu_1(S_1, S_2) X_1 - D S_2 - k_2 \mu_2(S_2) X_2 \\ \dot{X}_2 &= \mu_2(S_2) X_2 - D X_2 \end{cases}$$

- The first organism is inhibited by high concentrations of the product S_2
- Therefore, the extent to which the substrate S_1 is degraded by the organism X_1 depends on the efficiently of the removal of the product S_2 by the bacteria X_2
- Bistability cannot occur

Wilkinson et al. 1974, Kreikenbohm & Bohl 1986, Burchard 1994, El Hajji et al. 2011, Harvey et al. 2014

Syntrophic associations

Wilkinson et al. 1974 : Use the following growth functions

$$\mu_1(S_1, S_2) = \frac{m_1 S_1}{\kappa_1 + S_1} \frac{1}{1 + S_2/L_2}, \quad \mu_2(S_2) = \frac{m_2 S_2}{\kappa_2 + S_2}$$

• Kreikenbohm & Bohl 1986 : Use the same μ_2 and the following μ_1

$$\mu_1(S_1, S_2) = \begin{cases} \frac{m_1(S_1 - S_2/L_2)}{K_1 + S_1 + K_3 S_2} & \text{if } S_1 - S_2/L_2 > 0\\ 0 & \text{otherwie} \end{cases}$$

The first organism is unable to grow unless the qotient S_2/S_1 is small enough, say, $S_2 < L_2S_1$. Notice that μ_1 can be written

$$\mu_1(S_1, S_2) = \max\left(\frac{m_1(S_1 - S_2/L_2)}{K_1 + S_1 + K_3S_2}, 0\right)$$

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Syntrophic associations

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• El Hajji et al. 2011 : General functions satisfying

$$\frac{\partial \mu_1}{\partial S_1} > 0, \quad \frac{\partial \mu_1}{\partial S_2} < 0, \quad \frac{d \mu_2}{dS_2} > 0$$

 The system has not a cascade structure : the determination of steady states is more delicate.

$$\begin{cases} 0 = D(S_1^{in} - S_1) - k_3 \mu_1(S_1, S_2) X_1 \\ 0 = \mu_1(S_1, S_2) X_1 - D X_1 \\ 0 = k_1 \mu_1(S_1, S_2) X_1 - D S_2 - k_2 \mu_2(S_2) X_2 \\ 0 = \mu_2(S_2) X_2 - D X_2 \end{cases}$$

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Chemostat Modèle à deux étapes Commensalisme Syntrophie Anaerobic digestion

Anaerobic Digestion

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Inhibition of X_2 by S_1

$$\begin{cases} \dot{S}_1 &= D(S_1^{in} - S_1) - k_3 \mu_1(S_1, S_2) X_1 \\ \dot{X}_1 &= \mu_1(S_1, S_2) X_1 - D X_1 \\ \dot{S}_2 &= k_1 \mu_1(S_1, S_2) X_1 + D(S_2^{in} - S_2) - k_2 \mu_2(S_1, S_2) X_2 \\ \dot{X}_2 &= \mu_2(S_1, S_2) X_2 - D X_2 \end{cases}$$

- The first organism is inhibited by high concentrations of the product S_2
- The second organism is inhibited by high concentrations of the substrate S_1
- If $\frac{\partial \mu_1}{\partial S_1} > 0$ and $\frac{\partial \mu_1}{\partial S_2} < 0$ and $\frac{\partial \mu_2}{\partial S_1} < 0$ and $\frac{\partial \mu_2}{\partial S_2} > 0$ a stable coexistence steady state can occur. Also bistability can occur.

Kreikenbohm & Bohl 1988, Sari et al. 2012

Rescaling

$$s_1 = \frac{k_1}{k_3}S_1, \ x_1 = k_1X_1, \ s_2 = S_2, \ x_2 = k_2X_2, \ s_1^{in} = \frac{k_1}{k_3}S_1^{in}, \ s_2^{in} = S_2^{in}.$$

$$\begin{cases} \dot{s}_1 = D(s_1^{in} - s_1) - f_1(s_1, s_2)x_1 \\ \dot{x}_1 = f_1(s_1, s_2)x_1 - Dx_1 \\ \dot{s}_2 = D(s_2^{in} - s_2) - f_2(s_1, s_2)x_2 + f_1(s_1, s_2)x_1 \\ \dot{x}_2 = f_2(s_1, s_2)x_2 - Dx_2 \end{cases}$$

where

$$f_1(s_1, s_2) = \mu_1\left(\frac{k_3}{k_1}s_1, s_2\right) \quad f_2(s_1, s_2) = \mu_2\left(\frac{k_3}{k_1}s_1, s_2\right)$$

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Reduction to the plane

$$\begin{cases} \dot{s}_1 &= D(s_1^{in} - s_1) - f_1(s_1, s_2)x_1 \\ \dot{x}_1 &= f_1(s_1, s_2)x_1 - Dx_1 \\ \dot{s}_2 &= D(s_2^{in} - s_2) - f_2(s_1, s_2)x_2 + f_1(s_1, s_2)x_1 \\ \dot{x}_2 &= f_2(s_1, s_2)x_2 - Dx_2 \end{cases}$$

Notice that

$$\dot{z}_1 = D(s_1^{in} - z_1), \qquad z_1 = s_1 + x_1$$

 $\dot{z}_2 = D(s_2^{in} - z_2), \qquad z_2 = s_2 + x_2 - x_1$

Thus

$$s_1(t)+x_1(t) o s_1^{in}, \quad s_2(t)+x_2(t)-x_1(t) o s_2^{in}$$

We can restrict the study to the positive invariant attractor

$$\Omega = \left\{ (s_1, x_1, s_2, x_2) \in \mathbb{R}_+^4 : s_1 + x_1 = s_1^{in}, \quad s_2 + x_2 - x_1 = s_2^{in} \right\}$$

Reduction to the plane

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Let
$$s_1 = s_1^{in} - x_1$$
, $s_2 = s_2^{in} + x_1 - x_2$. We have

$$\begin{cases}
\dot{x}_1 = [\Phi_1(x_1, x_2) - D] x_1, \\
\dot{x}_2 = [\Phi_2(x_1, x_2) - D] x_2.
\end{cases}$$

where

$$\begin{split} \Phi_1(x_1, x_2) &= f_1\left(s_1^{in} - x_1, s_2^{in} + x_1 - x_2\right), \\ \Phi_2(x_1, x_2) &= f_2\left(s_1^{in} - x_1, s_2^{in} + x_1 - x_2\right). \end{split}$$

For s_1 and s_2 to be positive, the state-vector (x_1, x_2) belongs to the following subset of the plane :

$$\mathcal{S} = \left\{ \left(x_1, x_2
ight) \in \mathbb{R}_+^{-2} : 0 < x_1 \leq s_1^{\textit{in}}, 0 < x_2 \leq x_1 + s_2^{\textit{in}}
ight\}.$$

Isoclines and steady states



Multistability can occur in

$$\dot{x}_1 = [\Phi_1(x_1, x_2) - D] x_1,$$

$$\dot{x}_2 = [\Phi_2(x_1, x_2) - D] x_2.$$

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Bistability



 $f_1(s_1, s_2) = \frac{m_1 s_1}{K_1 + s_1} \frac{1}{1 + s_2/L_2}, \quad f_2(s_1, s_2) = \frac{m_2 s_2}{K_2 + s_2} \frac{1}{1 + s_1/L_1}$

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Bistability



 $f_1(s_1, s_2) = rac{m_1 s_1}{K_1 + s_1} rac{1}{1 + s_2/L_2}, \quad f_2(s_1, s_2) = rac{m_2 s_2}{K_2 + s_2} rac{1}{1 + s_1/L_1}$

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Chemostat Modèle à deux étapes Commensalisme Syntrophie Anaerobic digestion Maintenance

ADM1 : Propionate degradation

$$\frac{dS_{pro}}{dt} = D(S_{pro,in} - S_{pro}) - f_0(S_{pro}, S_{H2}) X_{pro}
\frac{dX_{pro}}{dt} = -DX_{pro} + Y_{pro} f_0(S_{pro}, S_{H2}) X_{pro} - k_{dec,pro} X_{pro}
\frac{dS_{H2}}{dt} = -DS_{H2} + 0.43 (1 - Y_{pro}) f_0(S_{pro}, S_{H2}) X_{pro} - f_1(S_{H2}) X_{H2}
\frac{dX_{H2}}{dt} = -DX_{H2} + Y_{H2} f_1(S_{H2}) X_{H2} - k_{dec,H2} X_{H2}$$

- S_{pro} and X_{pro} are propionate substrate and biomass concentrations, S_{H2} and X_{H2} are those for hydrogen
- Y_{pro} and Y_{H2} are the Yield coefficients and 0.43 $(1 Y_{pro})$ represents the part which goes to hydrogen substrate

$$f_{0}(S_{pro}, S_{H2}) = \frac{k_{m, pro}S_{pro}}{K_{s, pro} + S_{pro}} \frac{1}{1 + \frac{S_{H2}}{K_{I, H2}}}, \quad f_{1}(S_{H2}) = \frac{k_{m, H2}S_{H2}}{K_{s, H2} + S_{H2}}$$

Xu et al. 2011

Xu et al 2011

Journal of Theoretical Biology 276 (2011) 35-41



Maintenance affects the stability of a two-tiered microbial 'food chain'?

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maintenance on the stability of the food chain. In the absence of maintenance our two-tiered 'food chain' too is always stable, but when maintenance is included in its description our two-tiered generalised 'food chain' is not necessarily stable in theory. However, using the consensus parameters of ADM1 we have shown in numerical simulations that our model of the methanogenic two-tiered propionate-hydrogen food chain is always stable. Direct application of symbolic analysis programs, such as Maple or Mathematica, turned out fruitless. Stiefs et al. (2008) have proposed a more

Maintenance does not affect the stability

$$\frac{dS_{pro}}{dt} = D(S_{pro,in} - S_{pro}) - f_0(S_{pro}, S_{H2}) X_{pro}
\frac{dX_{pro}}{dt} = -DX_{pro} + Y_{pro} f_0(S_{pro}, S_{H2}) X_{pro} - k_{dec,pro} X_{pro}
\frac{dS_{H2}}{dt} = -DS_{H2} + 0.43 (1 - Y_{pro}) f_0(S_{pro}, S_{H2}) X_{pro} - f_1(S_{H2}) X_{H2}
\frac{dX_{H2}}{dt} = -DX_{H2} + Y_{H2} f_1(S_{H2}) X_{H2} - k_{dec,H2} X_{H2}$$

- Xu et al. 2011 : For ADM1 consensus parameter values, the positive steady state is stable as long as it exists (numerical verification)
- Sari & Harmand 2014 : for all values of the parameters the positive steady state is stable as long as it exists

Xu et al. 2011, Sari & Harmand 2014

Change of notation

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$$\begin{cases} \dot{S}_{0} = D(S_{0}^{in} - S_{0}) - f_{0}(S_{0}, S_{1})X_{0} \\ \dot{X}_{0} = Y_{0}f_{0}(S_{0}, S_{1})X_{0} - DX_{0} - a_{0}X_{0} \\ \dot{S}_{1} = Y_{2}f_{0}(S_{0}, S_{1})X_{0} - DS_{1} - f_{1}(S_{1})X_{1} \\ \dot{X}_{1} = Y_{1}f_{1}(S_{1})X_{1} - DX_{1} - a_{1}X_{1} \end{cases}$$

• Maintenance does not affect the stability of the food chain, for general growth function

$$\frac{\partial f_0}{\partial S_0} > 0, \quad \frac{\partial f_0}{\partial S_1} < 0, \quad \frac{d f_1}{dS_1} > 0$$

Sari & Harmand 2014

Rescaling

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$$s_0 = Y_2 S_0, \ x_0 = \frac{Y_2}{Y_0} X_0, \ s_1 = S_1, \ x_1 = \frac{1}{Y_1} X_1, \ s_0^{in} = Y_2 S_0^{in}$$

$$\begin{cases} \frac{ds_0}{dt} &= D(s_0^{in} - s_0) - \mu_0(s_0, s_1)x_0 \\ \frac{dx_0}{dt} &= -Dx_0 + \mu_0(s_0, s_1)x_0 - a_0x_0 \\ \frac{ds_1}{dt} &= -Ds_1 + \mu_0(s_0, s_1)x_0 - \mu_1(s_1)x_1 \\ \frac{dx_1}{dt} &= -Dx_1 + \mu_1(s_1)x_1 - a_1x_1 \end{cases}$$

where

$$\mu_0(s_0, s_1) = Y_0 f_0\left(\frac{1}{Y_2}s_0, s_1\right), \quad \mu_1(s_1) = Y_1 f_1(s_1)$$

Steady states

$$\begin{cases} \frac{ds_0}{dt} = D(s_0^{in} - s_0) - \mu_0(s_0, s_1)x_0 \\ \frac{dx_0}{dt} = -Dx_0 + \mu_0(s_0, s_1)x_0 - a_0x_0 \\ \frac{ds_1}{dt} = -Ds_1 + \mu_0(s_0, s_1)x_0 - \mu_1(s_1)x_1 \\ \frac{dx_1}{dt} = -Dx_1 + \mu_1(s_1)x_1 - a_1x_1 \end{cases}$$

- SS0 : $x_0 = 0$, $x_1 = 0$ where both species are washed out.
- SS1 : $x_0 > 0$, $x_1 = 0$, where species x_1 is washed out while x_0 survives.
- SS2 : $x_0 > 0$, $x_1 > 0$, where both species survives.

Xu et al. 2011, Sari & Harmand 2014

Operating diagram

$$\begin{cases} \frac{ds_0}{dt} = D(s_0^{in} - s_0) - \mu_0(s_0, s_1)x_0 \\ \frac{dx_0}{dt} = -Dx_0 + \mu_0(s_0, s_1)x_0 - a_0x_0 \\ \frac{ds_1}{dt} = -Ds_1 + \mu_0(s_0, s_1)x_0 - \mu_1(s_1)x_1 \\ \frac{dx_1}{dt} = -Dx_1 + \mu_1(s_1)x_1 - a_1x_1 \end{cases}$$

- Apart from the two operating (or control) parameters, which are D and s₀ⁱⁿ, that can vary, all others parameters in μ₀ and μ₁ have biological meaning and are fixed depending on the organisms and substrate considered.
- The operating diagram shows how the system behaves when we vary the two control parameters

Xu et al. 2011, Sari & Harmand 2014



Region	SS0	SS1	SS2
$(s_0^{in}, D) \in \mathcal{J}_0$	\mathbf{S}		
$(s_0^{in}, D) \in \mathcal{J}_1$	U	\mathbf{S}	
$(s_0^{in}, D) \in \mathcal{J}_2$	U	U	\mathbf{S}

Concluding remarks

- Commensalism : if growth functions are increasing, bistability cannot occur
- Commensalism : If μ_1 or μ_2 are of Haldane type, bistability can occur
- Syntrophy : If the growth rate of the second organism is of Haldane type then bistability can occur
- Syntrophy : If the growth rate of the second organism is increasing and not influenced by the first substrate, bistability cannot occur, even if maintenance terms are added
- Syntrophy : If the growth rate of the second organism is negatively influenced by the first substrate then bistability can occur

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Chemostat Modèle à deux étapes Commensalisme Syntrophie Anaerobic digestion Maintenance Modèle à 3 étapes

Chlorophenol degradation

$$\begin{aligned} \frac{dX_{ch}}{dt} &= -DX_{ch} + Y_{ch}f_0\left(S_{ch}, S_{H_2}\right)X_{ch} - k_{dec,ch}X_{ch} \\ \frac{dX_{ph}}{dt} &= -DX_{ph} + Y_{ph}f_1\left(S_{ph}, S_{H_2}\right)X_{ph} - k_{dec,ph}X_{ph} \\ \frac{dX_{H_2}}{dt} &= -DX_{H_2} + Y_{H_2}f_2\left(S_{H_2}\right)X_{H_2} - k_{dec,H_2}X_{H_2} \\ \frac{dS_{ch}}{dt} &= D\left(S_{ch,in} - S_{ch}\right) - f_0\left(S_{ch}, S_{H_2}\right)X_{ch} \\ \frac{dS_{ph}}{dt} &= D\left(S_{ph,in} - S_{ph}\right) + \frac{224}{208}\left(1 - Y_{ch}\right)f_0\left(S_{ch}, S_{H_2}\right)X_{ch} \\ &- f_1\left(S_{ph}, S_{H_2}\right)X_{ph} \\ \frac{dS_{H_2}}{dt} &= \left(S_{H_2,in} - S_{H_2}\right) + \frac{32}{224}\left(1 - Y_{ph}\right)f_1\left(S_{ph}, S_{H_2}\right)X_{ph} \\ &- \frac{16}{208}f_0\left(S_{ch}, S_{H_2}\right)X_{ch} - f_2\left(S_{H_2}\right)X_{H_2} \end{aligned}$$

Chlorophenol degradation

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- $S_{\rm ch}$ and $X_{\rm ch}$ are the chlorophenol substrate and biomass concentrations
- $S_{\rm ph}$ and $X_{\rm ph}$ those for phenol and $S_{\rm H_2}$ and $X_{\rm H_2}$ those for hydrogen
- $Y_{\rm ch},~Y_{\rm ph}$ and $Y_{\rm H2}$ are the yield coefficients,
- $224/208(1 Y_{ch})$ represents the part of chlorophenol degraded to phenol,
- + 32/224 (1 $Y_{\rm ph})$ represents the part of phenol that is transformed to hydrogen

Growth functions take Monod form with hydrogen inhibition acting on the phenol degrader.

$$\begin{split} f_0\left(S_{\rm ch}, S_{\rm H_2}\right) &= \frac{k_{m,{\rm ch}}S_{\rm ch}}{K_{S,ch}+S_{\rm ch}} \frac{S_{H_2}}{K_{S,{\rm H_2},{\rm c}}+S_{{\rm H_2}}} \\ f_1\left(S_{\rm ph}, S_{{\rm H_2}}\right) &= \frac{k_{m,{\rm ph}}S_{\rm ph}}{K_{S,{\rm ph}}+S_{\rm ph}} \frac{1}{1+\frac{S_{{\rm H_2}}}{K_{i,{\rm H_2}}}}, \quad f_2\left(S_{{\rm H_2}}\right) = \frac{k_{m,{\rm H_2}}S_{{\rm H_2}}}{K_{S,{\rm H_2}}+S_{{\rm H_2}}} \end{split}$$

Wade et al. 2015, Sari et Wade 2015



FIG. 2. Steady-state diagram for operational parameters D and $S_{ch,in}$ in the three-tier chlorophenol model ($S_{ph,in} = S_{H_2,in} = 0$).

The system has 3 steady states SS1, SS4 and SS6. The diagram indicates the stable steady states Wade et al. 2015

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Change of notations and resacling

$$\begin{split} \frac{\mathrm{d}X_{0}}{\mathrm{d}t} &= -DX_{0} + Y_{0}f_{0}\left(S_{0}, S_{2}\right)X_{0} - a_{0}X_{0} \\ \frac{\mathrm{d}X_{1}}{\mathrm{d}t} &= -DX_{1} + Y_{1}f_{1}\left(S_{1}, S_{2}\right)X_{1} - a_{1}X_{1} \\ \frac{\mathrm{d}X_{2}}{\mathrm{d}t} &= -DX_{2} + Y_{2}f_{2}\left(S_{2}\right)X_{2} - a_{2}X_{2} \\ \frac{\mathrm{d}S_{0}}{\mathrm{d}t} &= D\left(S_{0}^{\mathrm{in}} - S_{0}\right) - f_{0}\left(S_{0}, S_{2}\right)X_{0} \\ \frac{\mathrm{d}S_{1}}{\mathrm{d}t} &= D\left(S_{1}^{\mathrm{in}} - S_{1}\right) + Y_{3}f_{0}\left(S_{0}, S_{2}\right)X_{0} - f_{1}\left(S_{1}, S_{2}\right)X_{1} \\ \frac{\mathrm{d}S_{2}}{\mathrm{d}t} &= D\left(S_{2}^{\mathrm{in}} - S_{2}\right) + Y_{4}f_{1}\left(S_{1}, S_{2}\right)X_{1} - Y_{5}f_{0}\left(S_{0}, S_{2}\right)X_{0} - f_{2}\left(S_{2}\right)X_{2} \end{split}$$

Rescaling

Rescaling

$$\begin{aligned} \frac{\mathrm{d}x_0}{\mathrm{d}t} &= -Dx_0 + \mu_0 \left(s_0, s_2\right) x_0 - a_0 x_0 \\ \frac{\mathrm{d}x_1}{\mathrm{d}t} &= -Dx_1 + \mu_1 \left(s_1, s_2\right) x_1 - a_1 x_1 \\ \frac{\mathrm{d}x_2}{\mathrm{d}t} &= -Dx_2 + \mu_2 \left(s_2\right) x_2 - a_2 x_2 \\ \frac{\mathrm{d}s_0}{\mathrm{d}t} &= D \left(s_0^{\mathrm{in}} - s_0\right) - \mu_0 \left(s_0, s_2\right) x_0 \\ \frac{\mathrm{d}s_1}{\mathrm{d}t} &= D \left(s_1^{\mathrm{in}} - s_1\right) + \mu_0 \left(s_0, s_2\right) x_0 - \mu_1 \left(s_1, s_2\right) x_1 \\ \frac{\mathrm{d}s_2}{\mathrm{d}t} &= D \left(s_2^{\mathrm{in}} - s_2\right) + \mu_1 \left(s_1, s_2\right) x_1 - \omega \mu_0 \left(s_0, s_2\right) x_0 - \mu_2 \left(s_2\right) x_2 \end{aligned}$$

$$\begin{aligned} \mu_0 \left(s_0, s_2\right) &= \frac{m_0 s_0}{K_0 + s_0} \frac{s_2}{L_0 + s_2}, \quad \mu_1 \left(s_1, s_2\right) &= \frac{m_1 s_1}{K_1 + s_1} \frac{1}{1 + s_2/K_i}, \\ \mu_2 \left(s_2\right) &= \frac{m_2 s_2}{K_2 + s_2}, \quad \omega &= \frac{Y_5}{Y_3 Y_4} = \frac{1}{2(1 - Y_0)(1 - Y_1)} \end{aligned}$$

General growth functions

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We assume only that the growth functions are positive and satisfy

H1
$$\mu_0(s_0, s_2) < +\infty, \ \mu_0(0, s_2) = 0, \ \mu_0(s_0, 0) = 0.$$

H2 $\mu_1(s_1, s_2) < +\infty, \ \mu_1(0, s_2) = 0.$
H3 $0 < \mu_2(s_2) < +\infty, \ \mu_2(0) = 0.$
H4 $\frac{\partial \mu_0}{\partial s_0}(s_0, s_2) > 0, \ \frac{\partial \mu_0}{\partial s_2}(s_0, s_2) > 0.$
H5 $\frac{\partial \mu_1}{\partial s_1}(s_1, s_2) > 0,, \ \frac{\partial \mu_1}{\partial s_2}(s_1, s_2) < 0.$
H6 $\frac{d \mu_2}{d s_2}(s_2) > 0.$
H7 $s_2 \mapsto \mu_0(+\infty, s_2)$ is monotonically increasing
H8 $s_2 \mapsto \mu_1(+\infty, s_2)$ is monotonically decreasing.

These properties are satisfied by

$$\mu_0(s_0, s_2) = \frac{m_0 s_0}{K_0 + s_0} \frac{s_2}{L_0 + s_2} \\ \mu_1(s_1, s_2) = \frac{m_1 s_1}{K_1 + s_1} \frac{1}{1 + s_2/K_i} \\ \mu_2(s_2) = \frac{m_2 s_2}{K_2 + s_2}$$

Steady-states when
$$s_1^{\text{in}} = s_2^{\text{in}} = 0$$

$$[\mu_0(s_0, s_2) - D - a_0] x_0 = 0 \tag{1}$$

$$[\mu_1(s_1, s_2) - D - a_1] x_1 = 0$$
(2)

$$[\mu_2(s_2) - D - a_2] x_2 = 0$$
 (3)

$$D(s_{0}^{in}-s_{0})-\mu_{0}(s_{0},s_{2})x_{0}=0$$

$$-Ds_{1} + \mu_{0}(s_{0}, s_{2})x_{0} - \mu_{1}(s_{1}, s_{2})x_{1} = 0$$

$$-Ds_{2} + \mu_{1}(s_{1}, s_{2}) x_{1} - \omega \mu_{0}(s_{0}, s_{2}) x_{0} - \mu_{2}(s_{2}) x_{2} = 0$$

(4) (5) (6)

• $x_0 = 0 \Longrightarrow x_1 = 0$ and $x_2 = 0$, $x_1 = 0 \Longrightarrow x_0 = 0$ and $x_2 = 0$

- If $x_0 = 0$, then (4) $\implies s_0 = s_0^{\text{in}}$ and (5) $\implies Ds_1 + \mu_1(s_1, s_2)x_1 = 0$, Thus $s_1 = 0$ and $\mu_1(s_1, s_2)x_1 = 0$. Therefore (2) $\implies x_1 = 0$ and (6) $\implies Ds_2 + \mu_2(s_2)x_2 = 0$ Thus $s_2 = 0$ and $\mu_2(s_2)x_2 = 0$. Therefore, (3) $\implies x_2 = 0$.
- If $x_1 = 0$, then (6) $\implies Ds_2 + \omega \mu_0(s_0, s_2)x_0 + \mu_2(s_2)x_2 = 0$. Thus $s_2 = 0$, $\mu_0(s_0, s_2)x_0 = 0$ and $\mu_2(s_2)x_2 = 0$. Therefore, (1) $\implies x_0 = 0$.

Steady-state SS1

• **Proposition 1**. The only steady-state, for which $x_0 = 0$ or $x_1 = 0$, is the steady-state

$$SS1 = (x_0 = 0, x_1 = 0, x_2 = 0, s_0 = s_0^{in}, s_1 = 0, s_2 = 0)$$

where all species are washed out. This steady-state always exists. It is always stable.

Besides the steady-state SS1, the system can have at most two other steady-states.

- SS2 : $x_0 > 0$, $x_1 > 0$ and $x_2 = 0$, where species x_2 is washed out while species x_0 and and x_1 exist.
- SS3 : $x_0 > 0$, $x_1 > 0$, and $x_2 > 0$, where all populations are maintained.

SS2 : $x_0 > 0$, $x_1 > 0$ and $x_2 = 0$

$$\begin{aligned} \left[\mu_0 \left(s_0, s_2 \right) - D - a_0 \right] x_0 &= 0 & (7) \\ \left[\mu_1 \left(s_1, s_2 \right) - D - a_1 \right] x_1 &= 0 & (8) \\ \left[\mu_2 \left(s_2 \right) - D - a_2 \right] x_2 &= 0 & (9) \\ D \left(s_0^{\text{in}} - s_0 \right) - \mu_0 \left(s_0, s_2 \right) x_0 &= 0 & (10) \\ -Ds_1 + \mu_0 \left(s_0, s_2 \right) x_0 - \mu_1 \left(s_1, s_2 \right) x_1 &= 0 & (11) \\ -Ds_2 + \mu_1 \left(s_1, s_2 \right) x_1 - \omega \mu_0 \left(s_0, s_2 \right) x_0 - \mu_2 \left(s_2 \right) x_2 &= 0 & (12) \end{aligned}$$

• If
$$x_0 > 0$$
 and $x_1 > 0$, then, (7) and (8) imply $\mu_0(s_0, s_2) = D + a_0$ and
 $\mu_1(s_1, s_2) = D + a_1$. Hence, $s_0 = M_0(D + a_0, s_2)$ and $s_1 = M_1(D + a_1, s_2)$

- (10) and (11) imply $x_0 = \frac{D}{D+a_0}(s_0^{\text{in}} s_0)$ and $x_1 = \frac{D}{D+a_1}(s_0^{\text{in}} s_0 s_1)$
- Therefore

$$(12) \Longrightarrow -s_2 + (s_0^{\rm in} - s_0 - s_1) - \omega(s_0^{\rm in} - s_0) = 0$$

If $\omega \geq 1$ this equation has no solution. If $\omega < 1$ this equation is equivalent to

$$s_0^{\text{in}} = s_0 + \frac{s_1 + s_2}{1 - \omega}.$$

Steady-state SS2

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Proposition 2. If $\omega \ge 1$ then SS2 does not exist. If $\omega < 1$ then SS2 exists if, and only if, $s_0^{\text{in}} \ge F_1(D)$. If $s_0^{\text{in}} \ge F_1(D)$ then each solution s_2 of equation $\psi(s_2) = s_0^{\text{in}}$ gives a steady-state $SS2 = (x_0, x_1, x_2 = 0, s_0, s_1, s_2)$ where

$$s_{0} = M_{0}(D + a_{0}, s_{2}), \quad s_{1} = M_{1}(D + a_{1}, s_{2})$$

$$x_{0} = \frac{D}{D + a_{0}}(s_{0}^{in} - s_{0}), \quad x_{1} = \frac{D}{D + a_{1}}(s_{0}^{in} - s_{0} - s_{1})$$

$$s_{0} = M_{0}(D + a_{0}, s_{2}) \Longleftrightarrow D + a_{0} = \mu_{0}(s_{0}, s_{2})$$

$$s_{1} = M_{1}(D + a_{1}, s_{2}) \Longleftrightarrow D + a_{1} = \mu_{1}(s_{1}, s_{2})$$

$$\psi(s_{2}) = M_{0}(D + a_{0}, s_{2}) + \frac{M_{1}(D + a_{1}, s_{2}) + s_{2}}{1 - \omega},$$

$$F_{1}(D) = \inf_{s_{2}} \psi(s_{2})$$

The function $\psi(s_2)$ and $F_1(D)$

• The function $\psi(s_2) = M_0(D + a_0, s_2) + \frac{M_1(D+a_1, s_2)+s_2}{1-\omega}$ is defined for $s_2^1 < s < s_2^1$ where s_2^1 and s_2^2 are given by

$$\mu_0(+\infty, s_2^0) = D + a_0, \quad \mu_1(+\infty, s_2^1) = D + a_1$$

•
$$\psi(s_2) > 0$$
 for $s_2^0 < s_2 < s_2^1$ and

$$\lim_{s_2 \to s_2^0} \psi(s_2) = \lim_{s_2 \to s_2^1} \psi(s_2) = +\infty$$

- We define $F_1(D) = \inf_{s_2 \in (s_2^0, s_2^1)} \psi(s_2)$
- If s₀ⁱⁿ > F₁(D) then equation ψ(s₂) = s₀ⁱⁿ has exactly two solutions denoted by s₂^b and s₂[‡]. To these solutions, s₂^b and s₂[‡], correspond two steady-states of SS2, which are denoted by SS2^b and SS2[‡].

SS3 : $x_0 > 0$, $x_1 > 0$ and $x_2 > 0$

$$\begin{aligned} \left[\mu_0 \left(s_0, s_2 \right) - D - a_0 \right] x_0 &= 0 & (13) \\ \left[\mu_1 \left(s_1, s_2 \right) - D - a_1 \right] x_1 &= 0 & (14) \\ \left[\mu_2 \left(s_2 \right) - D - a_2 \right] x_2 &= 0 & (15) \\ D \left(s_0^{\text{in}} - s_0 \right) - \mu_0 \left(s_0, s_2 \right) x_0 &= 0 & (16) \\ \mu_0 \left(s_0, s_2 \right) x_0 - \mu_1 \left(s_1, s_2 \right) x_1 &= 0 & (17) \end{aligned}$$

$$-Ds_{1}+\mu_{0}(s_{0},s_{2})x_{0}-\mu_{1}(s_{1},s_{2})x_{1}=0$$

$$-Ds_{2} + \mu_{1}(s_{1}, s_{2}) x_{1} - \omega \mu_{0}(s_{0}, s_{2}) x_{0} - \mu_{2}(s_{2}) x_{2} = 0$$

• If
$$x_0 > 0$$
, $x_1 > 0$ and $x_2 > 0$, then, (13), (14) and (15) imply
 $\mu_0(s_0, s_2) = D + a_0$, $\mu_1(s_1, s_2) = D + a_1$ and $\mu_2(s_2) = D + a_2$. Hence,
 $s_2 = M_2(D + a_2)$, $s_0 = M_0(D + a_0, s_2)$ and $s_1 = M_1(D + a_1, s_2)$.

• (16), (17) and (18) imply
$$x_0 = \frac{D}{D+a_0}(s_0^{\text{in}} - s_0), x_1 = \frac{D}{D+a_1}(s_0^{\text{in}} - s_0 - s_1)$$
 and
 $x_2 = \frac{D}{D+a_2}\left((1-\omega)(s_0^{\text{in}} - s_0) - s_1 - s_2\right)$
• $x_i > 0$ iff $s_0^{\text{in}} > \psi(s_2)$

(18)

Steady-state SS3

Proposition 3. If $\omega \ge 1$ then SS3 does not exist. If $\omega < 1$ then SS3 exists if, and only if, $s_0^{\text{in}} > F_2(D)$. If $s_0^{\text{in}} > F_2(D)$ then the steady-state $SS3 = (x_0, x_1, x_2, s_0, s_1, s_2)$ is given by

$$s_0 = M_0(D + a_0, M_2(D + a_2))$$

$$s_1 = M_1(D + a_1, M_2(D + a_2))$$

$$s_2 = M_2(D + a_2)$$

and

$$\begin{aligned} x_0 &= \frac{D}{D + a_0} (s_0^{\text{in}} - s_0), \quad x_1 &= \frac{D}{D + a_1} (s_0^{\text{in}} - s_0 - s_1) \\ x_2 &= \frac{D}{D + a_2} \left((1 - \omega) (s_0^{\text{in}} - s_0) - s_1 - s_2 \right) \end{aligned}$$

$$s_2 = M_2(D + a_2) \iff D + a_2 = \mu_2(s_2)$$
$$F_2(D) = \psi \left(M_2(D + a_2) \right)$$

Notations

$$s_{0} = M_{0}(D + a_{0}, s_{2}) \iff D + a_{0} = \mu_{0}(s_{0}, s_{2})$$

$$s_{1} = M_{1}(D + a_{0}, s_{2}) \iff D + a_{1} = \mu_{1}(s_{1}, s_{2})$$

$$s_{2} = M_{2}(D + a_{2}) \iff D + a_{2} = \mu_{2}(s_{2})$$

$$\psi(s_{2}) = M_{0}(D + a_{0}, s_{2}) + \frac{M_{1}(D + a_{1}, s_{2}) + s_{2}}{1 - \omega},$$

$$F_{1}(D) = \inf_{s_{2}} \psi(s_{2})$$

$$F_{2}(D) = \psi(M_{2}(D + a_{2}))$$

Since $F_1(D) \leq F_2(D)$, the condition $s_0^{\text{in}} > F_2(D)$ for the existence of SS3 implies that the condition $s_0^{\text{in}} > F_2(D)$ for the existence of SS2^b and SS2^{\sharp} is satisfied.



Region	Steady states		
\mathcal{J}_1	SS1		
$\mathcal{J}_2\cup \mathcal{J}_4$	SS1, SS2 [♭] , SS2 [♯]		
\mathcal{J}_3	SS1, $\mathrm{SS2}^{\flat}$, $\mathrm{SS2}^{\sharp}$, SS3		

Model without maintenance

The change of variables

$$z_0 = s_0 + x_0$$
, $z_1 = s_1 + x_1 - x_0$, $z_2 = s_2 + x_2 + \omega x_0 - x_1$

Therefore, the model with $a_0 = a_1 = a_2 = 0$, become

$$\begin{aligned} \frac{\mathrm{d}x_0}{\mathrm{d}t} &= -Dx_0 + \mu_0 \left(z_0 - x_0, z_2 - \omega x_0 + x_1 - x_2 \right) x_0 \\ \frac{\mathrm{d}x_1}{\mathrm{d}t} &= -Dx_1 + \mu_1 \left(z_1 + x_0 - x_1, z_2 - \omega x_0 + x_1 - x_2 \right) x_1 \\ \frac{\mathrm{d}x_2}{\mathrm{d}t} &= -Dx_2 + \mu_2 \left(z_2 - \omega x_0 + x_1 - x_2 \right) x_2 \\ \frac{\mathrm{d}z_0}{\mathrm{d}t} &= D \left(s_0^{\mathrm{in}} - z_0 \right) \\ \frac{\mathrm{d}z_1}{\mathrm{d}t} &= -Dz_1 \\ \frac{\mathrm{d}z_2}{\mathrm{d}t} &= -Dz_2 \end{aligned}$$

Stability without maintenance

Proposition 4.

- SS2 is stable if, and only if, $\mu_2(s_2) < D$ and $\frac{d\psi}{ds_2} > 0$.
- If $F_3(D) \ge 0$ then SS3 is stable as long as it exists.
- If $F_3(D) < 0$ then SS3 is stable if, and only if, $F_4(D, s_0^{in}) > 0$.

$$F_3(D) = \frac{d\psi}{ds_2}(M_2(D))$$

$$F_4(D, s_0^{in}) = (Elx_0x_2 + [E(G + H) - (1 - \omega)FG]x_0x_1)f_2 + (Ix_2 + (G + H)x_1 + \omega Fx_0)Glx_1x_2$$

where $f_2 = Ix_2 + (G + H)x_1 + (E + \omega F)x_0$ and

$$E = \frac{\partial \mu_0}{\partial s_0}, \quad F = \frac{\partial \mu_0}{\partial s_2}, \quad G = \frac{\partial \mu_1}{\partial s_1}, \quad H = -\frac{\partial \mu_1}{\partial s_2}, \quad I = \frac{d \mu_2}{ds_2}$$

evaluated at the steady-state SS3, that is to say, for

$$s_2 = M_2(D), \quad s_0 = M_0(D, s_2), \quad s_1 = M_1(D, s_2)$$



Region	SS1	$\mathrm{SS2}^{\flat}$	$\mathrm{SS2}^{\sharp}$	SS3
\mathcal{J}_1	S			
\mathcal{J}_2	S	U	S	
\mathcal{J}_3	S	U	U	S
\mathcal{J}_4	S	U	U	
\mathcal{J}_5	S	U	U	U













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Fro. 4. — Montage d'un appareil à croissance continue. N, nourrice; Srp, serpentin capillaire; C.G., compte-gouttes; R, ballon rotatif; T₁, tubulure d'arrivée; E, tubulure d'ensemencement: Pr, tubulure de prélèvement (en pointillé, fiole de prélèvement); T₂, tubulure de niveau; P, produit; M, moteur.