About the chemostat model with a lateral diffusive compartment

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Abstract

We consider the classical chemostat model with an additional compartment connected by pure diffusion, and analyze its asymptotic properties. We investigate conditions under which this spatial structure is beneficial for species survival and yield conversion, compared to single chemostat. Moreover we look for the best structure (volume repartition and diffusion rate) which minimizes the volume required to attain a desired yield conversion. The analysis reveals that configurations with a single tank connected by diffusion to the input stream can be the most efficient.

Key-words. chemostat model, compartments, diffusion, stability, yield conversion, optimal design.

1 Introduction

The model of the chemostat has been developed as a mathematical representation of the chemostat apparatus invented in the fifties simultaneously by Monod \cite{monod1958} and Novick & Szilard \cite{novick1957}, for studying the culture of micro-organisms, and is still today of primer importance (see for instance \cite{gould1970, ritchie1969, stenström1970}). Its mathematical analysis has led to the so-called “theory of the chemostat” \cite{odell1972, ritchie1971}. This model is widely used for industrial applications with continuously fed “bioreactors” for fermentations \cite{pouton1981, saito1980} or waste-water treatments \cite{biedermann1982, engasser1982, paterson1982}, but also in ecology for studying populations of micro-organisms (or plankton) in lakes, wetlands, rivers or aquaculture ecosystems \cite{ferson1986, jaffres1988, jaffres1995, jaffres1997, jaffres1998}. The word “chemostat” is often used to describe continuous cultures of micro-organisms, even though it can be quite far from the the original experimental setup. The classical model of the chemostat assumes a perfectly mixed media which is generally verified for small volumes. For industrial bioreactors or natural lakes with large volumes, the validity of this assumption becomes questionable. This is why several extensions of this model with spatial considerations have been proposed and studied in the literature.

The classical approaches for modeling non ideally mixed chemostats or bioreactors rely on a continuous representation of the spatial dimension (with systems of p.d.e. as in \cite{matsuno1985, matsuno1987}) or on a finite number of interconnected compartments with different flow conditions (with systems of o.d.e. as in the “general gradostat” \cite{richter1982, richter1984, richter1985}). Although there are many works in the literature on p.d.e. models for unmixed bioreactors (where nutrient diffuses on the media from the boundary of the domain, see for instance \cite{richter1982, richter1984}), there are comparatively few works for bioreactors with an advection term that represents an incoming nutrient which is pushed inward (as in the chemostat apparatus). Moreover, most of the mathematical analysis available in the literature consider a spatial heterogeneity only in the axial dimension of the bioreactors (leading to 1d p.d.e. or compartments connected in series) as in tubular or “plug-flow” bioreactors \cite{biedermann1982, engasser1982, paterson1982} and (simple) gradostats \cite{matsuno1985, matsuno1987, matsuno1989}. Surprisingly, configurations of tanks in parallel rather than in series have been much less investigated, apart simple considerations in chemical reaction engineering \cite{richter1982, richter1984}.

In many cases, the axial direction appears to be the one that generates the larger heterogeneity between the input and output (when the main current lines are along this axis), especially for height and relatively thin tanks under significant flow rate. The modeling with compartments has become quite popular in the
optimal design of bio-processes [59], as it allows to determine easily the optimal sizes of a given number of tanks in series for minimizing the residence time [34, 23, 4, 22, 21, 18, 39, 42]. Several studies have shown the huge benefit that can be obtained from one to two tanks in series (and even more but marginally less with more than two). Such considerations are similar to patches models or islands models, commonly used in theoretical ecology [35, 17] (or lattice differential equations [18]). For instance, a recent investigation studies the influence of these structures on a consumer/resource model [15]. However, ecological consumer/resource models are similar to chemostat models apart the source terms that are modeled as constant intakes of nutrient, instead of dilution rates (or Robin boundary conditions) that are rather met in liquid media.

Recent mathematical studies have revealed that considering heterogeneity in directions transverse to the axial one (with 2d or 3d p.d.e models or compartments models with non serial interconnections) could have a significant impacts on the performances of the bioreactor and the input-output behavior [3]. From an operational viewpoint, it is often reported that “dead zones” are observed in bioreactors and that the effective volumes of the tanks have to be corrected in the models to provide accurate predictions [21, 20, 13, 15, 44, 58, 17]. Segregated habitats are also considered in lakes, where the bottom can be modeled as a dead zone and nutrient mixing between the two zones is achieved by diffusion rate [38]. In a similar way, stagnant zones are well-known to occur in porous media such as soils, at various extents depending on soil structure. The effect of these dead zones on reactive and conservative mass transport, and thus in turn on the biogeochemical cycles of elements, can also be significant [57, 49]. However there have been relatively few analysis of models with explicit “dead-zones”. The wording “dead-zone” might be slightly miss-leading as it can make believe that a part of the tank where there is no advection stream from the input flow has no biological activity. But this does not necessarily mean that these “dead-zones” are entirely disconnected from other parts of the reactor. It is likely to be influenced by diffusion rather than convection. This is why we prefer to qualify these zones as “lateral-diffusive compartments”.

The aim of the present work is to analyze the chemostat model with two compartments (or two tanks), one of them being connected by “lateral-diffusion”, and to investigate conditions under which having this compartment could be beneficial for the yield conversion compared to the chemostat model with a single compartment of the same total volume. Although this structure falls into a particular case of the general gradostat, the existing results in the literature (see, e.g., [56, 53]) are too general to give accurate conditions for the existence of a positive equilibrium and its stability, and do not compare the performances of each configuration. The structure considered here can be also seen as a limiting case of the pattern “chemostats in parallel with diffusion connection” studied in [16], with only one vessel receiving an input flow rate. Nevertheless, this later reference imposes some restrictions such as linear reaction between species and removal rate large enough to avoid washout with a single tank. In the present work, we conduct a deeper model analysis and investigate the impact of lateral diffusion from two view points:

1. From an ecological perspective, we study the effect of the diffusion on a given volume repartition in terms of resource conversion. In particular, we aim at characterizing situations for which having a structure with lateral diffusion is better than having a single perfectly mixed volume.

2. From an engineering perspective, we look for the best volume repartition which, for a given diffusion rate, minimizes the total volume required to attain a desired resource conversion. This allows us to revisit the optimal design problem with such configurations, that was previously tackled but considering tanks connected in series (see, e.g., [4, 22, 18]). Additionally, we aim at determining the diffusion rate parameter that gives the best volume reduction.

The article is organized as follows: in Section 2 we introduce the model describing the dynamics in the chemostat composed of two compartments, one of them being connected by diffusion, and give results for the nonnegativity and boundedness of its solutions. In Section 3 we determine the steady states and analyze its asymptotic stability. Section 4 investigates the resource conversion rate and characterizes when this structure is better than the single chemostat (i.e. a single perfectly mixed volume). Section 5 is dedicated to optimal design questions, firstly when the diffusion rate is fixed and then when it can be tuned. Finally, Section 6 discusses and interprets the results.
2 Modeling and preliminaries results

We consider configurations of one tank of volume $V_1$ interconnected by Fickian diffusion with a tank of volume $V_2$, as depicted on Figure 1.

We denote by $s_i, x_i$ the concentrations of substrates and biomass in tank $i = 1, 2$ and write the equations of the chemostat model for such interconnections:

\[
\begin{align*}
\dot{s}_1 &= -\mu(s_1)x_1 + \frac{Q}{V_1}(s_{\text{in}} - s_1) + \frac{d}{V_1}(s_2 - s_1) \\
\dot{x}_1 &= \mu(s_1)x_1 - \frac{Q}{V_1}x_1 + \frac{d}{V_1}(x_2 - x_1) \\
\dot{s}_2 &= -\mu(s_2)x_2 + \frac{d}{V_2}(s_1 - s_2) \\
\dot{x}_2 &= \mu(s_2)x_2 + \frac{d}{V_2}(x_1 - x_2)
\end{align*}
\]

where we have assumed, without any loss of generality, that the yield conversion factor of substrate into biomass is equal to 1. The parameters $Q$ and $s_{\text{in}}$ denote the flow rate and substrate concentration of the input stream, while the parameter $d > 0$ is the diffusion coefficient between the two tanks (that we assume to be identical for the substrate and the micro-organisms). The specific growth rate function of the micro-organisms is denoted $\mu$ and fulfills the classical following assumption.

**Hypothesis 1.** The growth function $\mu(\cdot)$ is increasing concave function with $\mu(0) = 0$.

A typical such instance of function $\mu$ is given by the Monod law (see, e.g., [19, 53]):

\[\mu(s) = \mu_{\text{max}} \frac{s}{K + s},\]

where $\mu_{\text{max}}$ is the maximum specific growth rate and $K$ is the half-saturation constant.

**Lemma 1.** The non-negative orthant $\mathbb{R}^4_+$ is invariant by dynamics (1) and any solution in $\mathbb{R}^4_+$ is bounded.

**Proof.** Define $z_i = s_{\text{in}} - s_i - x_i$ for each tank $i = 1, 2$ and consider the dynamics (1) in $(z, s)$ coordinates:

\[
\begin{align*}
\dot{z}_1 &= -\frac{Q}{V_1}z_1 - \frac{d}{V_1}(z_1 - z_2), \\
\dot{s}_1 &= -\mu(s_1)(s_{\text{in}} - s_1 - z_1) + \frac{Q}{V_1}(s_{\text{in}} - s_1) + \frac{d}{V_1}(s_2 - s_1), \\
\dot{z}_2 &= -\frac{Q}{V_2}(z_2 - z_1), \\
\dot{s}_2 &= -\mu(s_2)(s_{\text{in}} - s_2 - z_2) + \frac{d}{V_2}(s_1 - s_2).
\end{align*}
\]
This system has a cascade structure with a first independent sub-system linear in $z$

$$
\dot{z} = \begin{bmatrix}
\frac{Q+d}{V_1} & \frac{d}{V_1} \\
\frac{d}{V_2} & -\frac{d}{V_2}
\end{bmatrix} z,
$$

where one has

$$
\text{tr}(A) = -\frac{Q+d}{V_1} - \frac{d}{V_2} < 0 \quad \text{and} \quad \det(A) = \frac{Qd}{V_1V_2} > 0.
$$

Therefore the matrix $A$ is Hurwitz and any solution $z$ of (4) converges exponentially to 0. Then, the solution $s$ can be written as the solution of the non-autonomous dynamics

$$
\dot{s} = F(t, s) = \begin{bmatrix}
\left(\frac{Q}{V_1} - \mu(s_1)\right)(s_{in} - s_1) + \frac{d}{V_1}(s_2 - s_1) + \mu(s_1)z_1(t) \\
-\mu(s_2)(s_{in} - s_2) + \frac{d}{V_2}(s_1 - s_2) + \mu(s_2)z_2(t)
\end{bmatrix}.
$$

Notice that, for any $(t, s)$, one has

$$
\frac{\partial F_1(t, s)}{\partial s_2} = \frac{d}{V_1} > 0 \quad \text{and} \quad \frac{\partial F_2(t, s)}{\partial s_1} = \frac{d}{V_2} > 0,
$$

and so the dynamics (4) is cooperative (see, e.g., [50]).

Define $\tilde{F}_1(t, s) := -\frac{d}{V_1} s_1 - \mu(s_1)(s_{in} - s_1) + \frac{d}{V_1}(s_2 - s_1) + \mu(s_1)z_1(t)$, for which it follows that $F_1(t, s) > \tilde{F}_1(t, s)$ for any $(t, s)$. Proposition 2.1 in [50] allows to state that any solution of (4) with $s_i(0) \geq 0$ $(i = 1, 2)$ satisfies $s_i(t) \geq \tilde{s}_i(t)$ $(i = 1, 2)$ for any $t > 0$, where $\tilde{s}$ is solution of the dynamics

$$
\dot{\tilde{s}} = \tilde{F}(t, \tilde{s}) = \begin{bmatrix}
\tilde{F}_1(t, \tilde{s}) \\
\tilde{F}_2(t, \tilde{s})
\end{bmatrix}, \quad \tilde{s}(0) = 0.
$$

As one has $\tilde{F}(t, 0) = 0$ for any $t$, the solution $\tilde{s}$ is identically null and one obtains that $s_i(t) (i = 1, 2)$ stays non-negative for any positive $t$.

Similarly, $x$ can be written as a solution of a non-autonomous cooperative dynamics

$$
\dot{x} = H(t, x) = \begin{bmatrix}
\left(\mu(s_1(t)) - \frac{Q+d}{V_1}\right)x_1 + \frac{d}{V_1}x_2 \\
\frac{d}{V_2}x_1 + \left(\mu(s_2(t)) - \frac{d}{V_2}\right)x_2
\end{bmatrix}
$$

with $H(t, 0) = 0$, which allows to conclude that $x_i(t) (i = 1, 2)$ stays non-negative for any positive $t$.

Finally, the convergence of $z$ to 0 provides the boundedness of the solutions $s(t), x(t)$.

Let us discuss the modeling of the two limiting cases that are not covered by system (1):

- $V_1 = 0$. Physically, this corresponds to a single tank (of volume $V_2$) connected by diffusion to the input pipe with flow rate $Q$ (see Figure 2). There is no biological activity in the pipe but simply a dilution given by the mass balance at the connection point:

$$
\begin{cases}
Q(s_{in} - s_{out}) = d(s_{out} - s_2) \\
-Qx_{out} = d(x_{out} - x_2)
\end{cases} \quad \Rightarrow \quad s_{out} = \frac{Qs_{in} + ds_2}{Q+d}, \quad x_{out} = \frac{dx_2}{Q+d}
$$

(5)
Figure 2: Limiting case when $V_1 = 0$.

Then the dynamics in the tank with $(s_{out}, x_{out})$ instead of $(s_1, x_1)$ is given by the equations

\[
\begin{align*}
\dot{s}_2 &= -\mu(s_2)x_2 + \frac{Qd}{(Q+d)V_2}(s_{in} - s_2) \\
\dot{x}_2 &= \mu(s_2)x_2 - \frac{Qd}{(Q+d)V_2}x_2
\end{align*}
\]

This is equivalent to have a single tank of volume $V_2$ with input flow rate $Qd/(Q + d)$ but with an output given by $s_{out} = (Qs_{in} + ds_2)/(Q + d)$. Equivalently, one can consider the system (1) as a slow-fast dynamics when the parameter $\epsilon = V_1$ is small. Then the fast dynamics is

\[
\begin{align*}
\epsilon \dot{s}_1 &= -\epsilon \mu(s_1)x_1 + Q(s_{in} - s_1) + d(s_2 - s_1) \\
\epsilon \dot{x}_1 &= \epsilon \mu(s_1)x_1 - Qx_1 + d(x_2 - x_1)
\end{align*}
\]

and the slow manifold is given exactly by the system of equations (5) with $(s_1, x_1) = (s_{out}, x_{out})$.

- $V_2 = 0$. The dynamics of $(s_1, x_1)$ is the one of the single chemostat model with volume $V_1$

\[
\begin{align*}
\dot{s}_1 &= -\mu(s_1)x_1 + \frac{Q}{V_1}(s_{in} - s_1) \\
\dot{x}_1 &= \mu(s_1)x_1 - \frac{Q}{V_1}x_1
\end{align*}
\]

This is also equivalent to having no diffusion ($d = 0$) between the tanks.

### 3 Study of the equilibria

For the analysis of the steady states, it is convenient to introduce the function

\[
\beta(s) = \mu(s)(s_{in} - s)
\]

that verifies the following property.

**Lemma 2.** Under Hypothesis 1 the function $\beta$ is strictly concave on $[0, s_{in}]$. Thus, one can define the unique value

\[
\hat{s} = \arg \max_{s \in [0, s_{in}]} \beta(s).
\]

**Proof.** One has $\beta'(s) = \mu'(s)(s_{in} - s) - \mu(s)$ and $\beta''(s) = \mu''(s)(s_{in} - s) - 2\mu'(s)$, which is negative for any $s \in [0, s_{in}]$. \hfill \square

One can check that the washout state $E^0 = (0, s_{in}, 0, s_{in})^T$ is always a steady-state of the dynamics (1). In the next Propositions, we characterize the existence of other equilibrium and their global stability.
Proposition 1. The washout equilibrium $E^0$ is the unique steady state of (11) exactly when $s_{in}$ satisfies the condition
\[ \mu(s_{in}) \leq \frac{Q}{V_1} \text{ and } P(\mu(s_{in})) \geq 0 \] (9)
where $P$ is defined as
\[ P(X) = V_1V_2X^2 - (dV_1 + (Q + d)V_2)X + dQ \]
When the condition (9) is not fulfilled, there exists an unique positive steady state $E^*$ of (11) distinct from $E^0$.

Proof. From the two last equations of (11), one has $s_1 + x_1 = s_2 + x_2$ at steady-state, and from the two first ones $s_1 + x_1 = s_{in}$. The values $s_1, s_2$ at steady state are solutions of the system of two equations
\[ 0 = \left( \frac{Q}{V_1} - \mu(s_1) \right) (s_{in} - s_1) + \frac{d}{V_1} (s_2 - s_1) \] (10)
\[ 0 = -\mu(s_2)(s_{in} - s_2) + \frac{d}{V_2} (s_1 - s_2) \] (11)
and $x_1, x_2$ at steady state are uniquely defined from each solution $(s_1, s_2)$ of (10)-(11).

Clearly $(s_{in}, s_{in})$ is a solution of (10)-(11). We look for (positive) solutions different to $(s_{in}, s_{in})$.

Posit
\[ \lambda_1(s_{in}) := \max \left\{ s_1 \in [0, s_{in}] \mid \mu(s_1) \leq \frac{Q}{V_1} \right\} \]

From equations (10)-(11), a solution different to $(s_{in}, s_{in})$ has to verify $s_1 > s_2 > 0$ and then from equation (10), one has also $s_1 < \lambda_1(s_{in})$. Define then the functions:
\[ \phi_1(s_1) := s_1 - \frac{Q - V_1\mu(s_1)}{d}(s_{in} - s_1) = s_1 - \frac{Q}{d}(s_{in} - s_1) + \frac{V_1}{d}\beta(s_1), \]
\[ \phi_2(s_2) := s_2 + \frac{V_2\mu(s_2)}{d}(s_{in} - s_2) = s_2 + \frac{V_2}{d}\beta(s_2). \]

It is straightforward to see that any solution of (10)-(11) fulfills $s_2 = \phi_1(s_1)$ and $s_1 = \phi_2(s_2)$. One has
\[ \phi_1'(s_1) = 1 + \frac{V_1}{d} \mu'(s_1)(s_{in} - s_1) + \frac{Q - V_1\mu(s_1)}{d}. \]

Therefore $\phi_1$ is increasing on $[0, \lambda_1(s_{in})]$, with $\phi_1(0) = -(Q/d)s_{in} < 0$ and $\phi_1(\lambda_1(s_{in})) = \lambda_1(s_{in}) > 0$. Thus, $\phi_1$ is invertible on $[-(Q/d)s_{in}, \lambda_1(s_{in})]$ with
\[ \phi_1^{-1}(0) \in (0, \lambda_1(s_{in})). \]

From Lemma 2, it follows that $\phi_1$ and $\phi_2$ are strictly concave functions on $[0, s_{in}]$. Consider then the function
\[ \gamma(s_2) = \phi_2(s_2) - \phi_1^{-1}(s_2) \quad s_2 \in [0, s_{in}], \]
which is also strictly concave on $[0, s_{in}]$. Then, a solution $(s_1, s_2)$ can be written as a solution of
\[ \gamma(s_2) = 0, \quad s_1 = \phi_2(s_2) \quad \text{with } s_2 \in [0, \lambda_1(s_{in})]. \]

Notice that one has $\gamma(s_{in}) = 0$, and as $\gamma$ is strictly concave, it cannot have more than two zeros. Therefore there is at most one solution $(s_1, s_2)$ different to $(s_{in}, s_{in})$. Furthermore, one has $\gamma(0) = -\phi_1^{-1}(0) < 0$. Now, distinguish two different cases:

- When $\lambda_1(s_{in}) < s_{in}$ (or equivalently $\mu(s_{in}) > Q/V_1$), one has
  \[ \gamma(\lambda_1(s_{in})) = \frac{QV_2}{dV_1}(s_{in} - \lambda_1(s_{in})) > 0. \]
By using the Mean Value Theorem, one concludes that there exists \( s_2 \in (0, \lambda_1(s_{in})) \) such that \( \gamma(s_2) = 0 \).

- When \( \lambda_1(s_{in}) = s_{in} \) (that is when \( \mu(s_{in}) \leq Q/V_1 \)), the function \( \gamma \) takes positive value on the interval \([0, s_{in}]\) if and only if \( \gamma'(s_{in}) < 0 \) (\( \gamma \) being strictly concave on \([0, s_{in}]\)), or equivalently when the condition

\[
\phi_2'(s_{in}) < \frac{1}{\phi_1'(s_{in})}
\]

is fulfilled. Notice that one has \( \phi_1'(s_{in}) > 0 \) because \( \lambda_1(s_{in}) = s_{in} \). So the condition can be also written as

\[
\phi_1(s_{in})\phi_2'(s_{in}) < 1.
\]

From the expressions of \( \phi_1 \) and \( \phi_2 \), one can write this condition as

\[
\frac{(d + Q - V_1\mu(s_{in}))(d - V_2\mu(s_{in}))}{d^2} < 1,
\]

and easily check that this amounts to require \( s_{in} \) to satisfy \( P(\mu(s_{in})) < 0 \).

We conclude that there exists a positive steady state if and only if \( \mu(s_{in}) > Q/V_1 \) or \( P(\mu(s_{in})) < 0 \) and that this steady state (when it exists) is unique.

**Proposition 2.** When the washout equilibrium \( E^0 \) is the unique steady state, it is globally asymptotically stable on \( \mathbb{R}^4_+ \).

When the positive steady state \( E^* \) exists, for any initial condition except on a set of null measure, the solution of (11) converges asymptotically to \( E^* \), which is moreover locally exponentially stable.

**Proof.** As shown in the proof of Lemma 1 the dynamics (11) has a cascade structure in \((z, s)\) coordinates, where \( z \) converges exponentially to 0. Then \( s \) converges to the set \( S = [0, s_{in}] \times [0, s_{in}] \) and is solution of the non-autonomous system (11) in the plane, which is asymptotically autonomous with limiting dynamics

\[
\dot{s} = F_a(s) = \begin{bmatrix}
\left(\frac{Q}{V_1} - \mu(s_1)\right)(s_{in} - s_1) + \frac{d}{V_1}(s_2 - s_1) \\
-\mu(s_2)(s_{in} - s_2) + \frac{d}{V_2}(s_1 - s_2)
\end{bmatrix}
\]

(12)

We study now the asymptotic behavior of dynamics (12) in the domain \( S \). Denote by \( B = \{s_1 = s_{in}\} \cup \{s_2 = s_{in}\} \) the subset of its boundary. Accordingly to Proposition 1 this dynamics has \( s^0 = (s_{in}, s_{in}) \) (which is the projection of \( E^0 \) on the s-plane) as an equilibrium, and at most another equilibrium \( s^* \) (which is the projection of \( E^* \) on the s-plane) that has to belong to \( S \setminus B \). On this last subset, we consider the variables \( \sigma_i = \log(s_{in} - s_i) \), whose dynamics are given by

\[
\dot{\sigma} = \tilde{F}_a(\sigma) = \begin{bmatrix}
-\frac{Q}{V_1} + \mu(s_{in} - e^{\sigma_1}) - \frac{d}{V_1}(1 - e^{\sigma_2 - \sigma_1}) \\
\mu(s_{in} - e^{\sigma_2}) - \frac{d}{V_2}(1 - e^{\sigma_1 - \sigma_2})
\end{bmatrix}
\]

(13)

One obtains

\[
\text{div}(\tilde{F}_a) = -\mu'(s_{in} - e^{\sigma_1})e^{\sigma_1} - \mu'(s_{in} - e^{\sigma_2})e^{\sigma_2} - \frac{d}{V_1}e^{\sigma_2 - \sigma_1} - \frac{d}{V_2}e^{\sigma_1 - \sigma_2} < 0
\]

From Dulac criteria and Poincaré-Bendixon theorem (see for instance [41]), we conclude that bounded trajectories of (13) cannot have limit cycle or closed path and necessarily converge to an equilibrium point. Consequently, any trajectory of (12) in \( S \) either converges to the equilibrium \( s^* \) (if it exists) or approaches the boundary \( B \). But

if there exists \( t \) such that \( s_i(t) = s_{in} \) and \( s_j(t) < s_{in} \), then \( \dot{s}_i(t) < 0 \quad (i \neq j) \).
and so the only possibility for approaching $B$ is to converge to $s^0$. This shows that the only non-empty closed connected invariant chain recurrent subsets of $S$ are the isolated points $s^0$ and $s^*$. 

We use the theory of asymptotically autonomous systems (see Theorem 1.8 in [36]) to deduce that any trajectory of system (11) in $\mathbb{R}^4$ converges asymptotically to $E^0$ or $E^*$.  

Due to the cascade structure of the dynamics (11) that is made explicit in the proof of Lemma 11, the Jacobian matrix in the $(z, s)$ coordinates is  

$$J(s) = \begin{bmatrix} A & 0 \\ * & J_0(s) \end{bmatrix} \quad \text{with} \quad J_0(s) = \begin{bmatrix} \frac{d}{V_1} \phi'_1(s_1) & \frac{d}{V_2} \\ \frac{d}{V_1} & -\frac{d}{V_2} \phi'_2(s_2) \end{bmatrix}$$

where the matrix $A$ defined in (9) is Hurwitz. Thus, the eigenvalues of $J(s)$ are the ones of the matrix $A$ plus the ones of $J_0(s)$. One has  

$$\text{tr}(J_0(s)) = -d \left( \frac{\phi'_1(s_1)}{V_1} + \frac{\phi'_2(s_2)}{V_2} \right) \quad \text{and} \quad \det(J_0(s)) = \frac{d^2}{V_1 V_2} \left( \phi'_1(s_1) \phi'_2(s_2) - 1 \right).$$

Accordingly to Proposition 11, the equilibrium $E^* \neq E^0$ exists when $P(\mu(s_{in})) > 0$ or $\mu(s_{in}) > Q/V_1$. 

- When $P(\mu(s_{in})) > 0$, one has $\phi'_1(s_{in})\phi'_2(s_{in}) < 1$ or equivalently $\det(JF_a(s^0)) < 0$. Then $E^0$ is a saddle point (with a stable manifold of dimension one) and we deduce that almost any trajectory of (11) converges to $E^*$. 

- When $\mu(s_{in}) > Q/V_1$, notice that the equilibrium $E^0$ is not necessarily hyperbolic (as one can have $P(\mu(s_{in})) = 0$ which implies then $\det(JF_a(s^0)) = 0$) and we cannot conclude its stability properties directly. We setup a proof by contradiction, inspired by [10]. Consider a solution of (12) with initial condition different to $E^0$ that converges asymptotically to $E^0$, and define the function  

$$v(t) = \min(\bar{x}(t), x_1(t)) \quad \text{with} \quad \bar{x} = \frac{V_1 x_1 + V_2 x_2}{V_1 + V_2},$$

which verifies $v(t) > 0$ for any $t > 0$ and has to converge to 0 when $t$ tends to $+\infty$. The condition $\mu(s_{in}) > Q/V_1$ implies the existence of positive numbers $T$ and $\eta$ such that $\mu(s_1(t)) - Q/V_1 > \eta$ for any $t > T$. If $x_1(t) \leq x_2(t)$ with $t > T$, one has $v = x_1$ and  

$$\dot{x}_1 \geq \left( \mu(s_1(t)) - \frac{Q}{V_1} \right) x_1 \geq \eta x_1 \geq 0$$

If $x_1(t) \geq x_2(t)$ with $t > T$, one has $v = \dot{x}$ and  

$$\dot{x} = \frac{V_1}{V_1 + V_2} \left( \mu(s_1(t)) - \frac{Q}{V_1} \right) x_1 + \frac{V_2}{V_1 + V_2} \mu(s_2(t)) x_2 \geq \frac{V_1}{V_1 + V_2} \eta x_1 \geq 0$$

The positive function $v$ is thus non decreasing for $t > T$, in contradiction with its convergence to 0. We conclude that any solution of (11) with initial condition different to $E^0$ converges to $E^*$.

Finally, when the equilibrium $E^*$ exists, the analysis conducted in the proof of Proposition 11 allows us to deduce the inequalities $\phi'_1(s_1^*) > 0$ and $\gamma'(s_2^*) > 0$, which in turn imply $\phi'_1(s_1^*) \phi'_2(s_2^*) > 1$ and so $\phi'_2(s_2^*) > 0$. Then, one has $\text{tr}(J_a(s^*)) < 0$ and $\det(J_a(s^*)) > 0$ i.e. $J(s^*)$ is Hurwitz, which proves that the attractive equilibrium $E^*$ is also locally exponentially stable. \qed
4 Influence of lateral diffusion on the performances

Here, we investigate conditions under which having a second compartment (as proposed in Section 2) is beneficial for the yield conversion compared to the chemostat model with a single compartment of the same total volume. To this aim, we fix the hydric volumes $V_1$ and $V_2$, the input flow $Q$, and analyze the output map at steady state, as function of the diffusion parameter $d$. The benefits of the structured chemostat in terms of resource conversion are discussed in Section 6.

Proposition 3 defines properly the map $d \rightarrow s^*_1(d)$ for the unique non-trivial steady-state of system (1), that we study here as a function of $d$. We start by deducing the range of existence of this steady-state.

**Proposition 3.** Let $V = V_1 + V_2$ and $\bar{d} = V_2\mu(s_{in})/Q - V_1\mu(s_{in})/V_1 \mu(s_{in})$. It follows that:

(i) If $\mu(s_{in}) < Q/V$, then the non-trivial equilibrium $s^*_1(d) < s_{in}$ exists when $d \in (0, \bar{d})$.

(ii) If $Q/V \leq \mu(s_{in}) \leq Q/V_1$, then the non-trivial equilibrium $s^*_1(d) < s_{in}$ exists when $d > 0$.

(iii) If $\mu(s_{in}) > Q/V_1$, then the non-trivial equilibrium $s^*_1(d) < s_{in}$ exists when $d \geq 0$.

**Proof.** When $d = 0$ (that is, when the volume $V_2$ is detached) the classical equilibria analysis of the single chemostat model with volume $V_1$ (see, e.g., [53]) assures that the positive equilibrium $s^*_1$ exists when $\mu(s_{in}) > Q/V_1$, which corresponds to the case (iii) on the proposition statement.

When $d > 0$, we prove cases (i)-(iii) by taking into account that they correspond to three different scenarios where condition (19) is not fulfilled. For ease of reasoning, we rewrite $P(\mu(s_{in}))$ as

$$P(\mu(s_{in})) = V_2\mu(s_{in}) \bigg\{ V_1\mu(s_{in}) - Q \bigg\} + d \bigg\{ Q - (V_1 + V_2)\mu(s_{in}) \bigg\}.$$

(i). In this case, the non-trivial equilibrium exists when $P(\mu(s_{in})) < 0$. It is straightforward to see that $A < 0$, $B > 0$ and so $s^*_1(d) < s_{in}$ exists when $0 < d < \bar{d} = -V_2\mu(s_{in})A/B$.

(ii). In this case, the non-trivial equilibrium exists when $P(\mu(s_{in})) < 0$. It is straightforward to see that $A < 0$, $B < 0$ and so $s^*_1(d) < s_{in}$ exists for all $d > 0$.

(iii). In this case, the non-trivial equilibrium exists for all values of $P(\mu(s_{in}))$, and so $s^*_1(d) < s_{in}$ exists for all $d \geq 0$.

We now study the two extreme situations: no diffusion and infinite diffusion.

**Lemma 3.** It follows that

(i) When $\mu(s_{in}) > Q/V_1$, the non trivial equilibrium of system (1) fulfills

$$s^*_1(0) = s^*_{1,0},$$

where $s^*_1 = \mu^{-1} \left( \frac{Q}{V_1} \right)$ is the non-trivial steady state of the single chemostat model with volume $V_1$. In other case $\lim_{d \to +0} s^*_1(d) = s_{in}$.

(ii) When $\mu(s_{in}) \geq Q/V$, the non trivial equilibrium of system (1) fulfills

$$\lim_{d \to +\infty} s^*_1(d) = s^*_{1,\infty},$$

where $s^*_{1,\infty} = \mu^{-1} \left( \frac{Q}{V} \right)$, is the non-trivial steady state of the single chemostat model with volume $V = V_1 + V_2$. 

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Consequently, one has

\[ \mu^*(s_1^*) \] where the classical equilibria analysis of the single chemostat model with volume \( V_1 \) (see, e.g., [53]), which assures that \( s_1^* = 0 \) exists when \( \mu(s_m) > Q/V_1 \).

(ii). For any \( d > 0 \), Proposition 3 guarantees the existence of a unique non trivial equilibrium \( s^* = (s_1^*, s_2^*) \in (0, s_m) \times (0, s_m) \) that is solution of

\[
\begin{align*}
    d(s_2^* - s_1^*) &= (V_1 \mu(s_1^*) - Q)(s_m - s_1^*), \\
    d(s_1^* - s_2^*) &= V_2 \mu(s_2^*)(s_m - s_2^*).
\end{align*}
\]

(15)

When \( d \) is arbitrary large, one obtains

\[
\lim_{d \to +\infty} s_1^* - s_2^* = 0.
\]

From equations (15), one can also deduce the following equality (valid for any \( d \))

\[
(V_1 \mu(s_1^*) - Q)(s_m^* - s_1^*) = -V_2 \mu(s_2^*)(s_m^* - s_2^*).
\]

(16)

Consequently, one has

\[
\lim_{d \to +\infty} s_1^*(d) = \lim_{d \to +\infty} s_2^*(d) = s_m \quad \text{or} \quad \lim_{d \to +\infty} s_1^*(d) = \lim_{d \to +\infty} s_2^*(d) = s_1^{*\infty} \quad \text{as} \quad V = V_1 + V_2,
\]

where the classical equilibria analysis of the single chemostat model with volume \( V \) assures that \( s_1^{*\infty} \exists \) exists when \( \mu(s_m) > Q/V \). But Proposition 3 shows that, under the assumptions of the lemma, \( s_1^*(d) \) cannot converge to \( s_m \).

We now present our main result concerning properties of the map \( d \to s_1^*(d) \), defined at the non-trivial steady state.

**Proposition 4.** Let \( \hat{s} \) be defined in (8) and \( V = V_1 + V_2 \). It follows that:

(i) If \( \mu(s_m) < Q/V \), then the map \( d \to s_1^*(d) \) admits a minimum in \( d^* < \hat{d} \) that is strictly less than \( s_m \).

(ii) If \( \mu(s_m) \geq Q/V \) and \( s_1^{*\infty} \leq \hat{s} \), then the map \( d \to s_1^*(d) \) admits a minimum in \( d^* < +\infty \), that is strictly less than \( s_1^{*\infty} \).

(iii) If \( \mu(s_m) \geq Q/V \) and \( s_1^{*\infty} \geq \hat{s} \), then the map \( d \to s_1^*(d) \) is decreasing and \( s_1^*(d) > s_1^{*\infty} \) for any \( d > 0 \).

**Proof.** If one differentiates system (15) with respect to \( d \), it follows that

\[
\begin{align*}
    (s_2^* - s_1^*) + d(\partial_d s_2^* - \partial_d s_1^*) &= \partial_d s_1^* (Q + V_1 \mu(s_1^*)(s_m - s_1^*) - V_1 \mu(s_1^*)), \\
    (s_1^* - s_2^*) + d(\partial_d s_1^* - \partial_d s_2^*) &= \partial_d s_2^* (V_2 \mu(s_2^*)(s_m - s_2^*) - V_2 \mu(s_2^*)).
\end{align*}
\]

which can be rewritten as

\[
\begin{bmatrix}
    A + d & -d \\
    d & -B - d
\end{bmatrix}
\begin{bmatrix}
    \partial_d s_1^* \\
    \partial_d s_2^*
\end{bmatrix}
= (s_2^* - s_1^*) \begin{bmatrix} 1 \\ 1 \end{bmatrix}.
\]

Remark that

\[
\begin{align*}
    A + d &= d \phi'(s_1^*), \\
    B + d &= d \phi'(s_2^*), \\
    \det(\Gamma) &= d^2 (1 - \phi'(s_1^*)\phi'(s_2^*)).
\end{align*}
\]
As seen in the proof of Proposition 2, one has that $\det(\Gamma) < 0$ and so the derivatives $\partial_d s_1^*$ and $\partial_d s_2^*$ can be defined as

$$
\partial_d s_1^* = (s_2^* - s_1^*) \frac{-B}{\det(\Gamma)},
$$

$$
\partial_d s_2^* = (s_2^* - s_1^*) \frac{A}{\det(\Gamma)}.
$$

(17)

Firstly, we prove that $A > 0$ by showing that $\phi_1'(s_1^*(d)) > 1$.

From Proposition 1, one has that the positive steady-state fulfills

$$0 < s_1^*(d) < \lambda_1(s_{in}) = \min(s_{in}, s_1^{*,0}).$$

Since $\phi_1$ is concave (equivalently, $\phi_1'$ is decreasing) on $[0, \lambda_1(s_{in})]$, one has that $\phi_1'(s_1^*(d)) > \phi_1'(\lambda_1(s_{in}))$. Thus, we prove that $A > 0$ by showing $\phi_1'(\lambda_1(s_{in})) > 1$:

- If $\mu(s_{in}) \leq Q/V_1$, then $\lambda_1(s_{in}) = s_{in}$ and $\phi_1'(s_{in}) = 1 + \frac{Q-V_1\mu(s_{in})}{d} > 1$,

- If $\mu(s_{in}) > Q/V_1$, then $\lambda_1(s_{in}) = s_1^{*,0}$ and $\phi_1'(s_1^{*,0}) = 1 + \frac{Q}{d} \lambda_1'(s_1^{*,0})(s_{in} - s_1^{*,0}) > 1$.

Therefore one has $\partial_d s_1^* > 0$ i.e. $s_2^*(\cdot)$ is an increasing map.

Now, notice that $B = V_2 \beta'(s_2^*(d))$ and its sign depends on the relative position of $s_2^*(d)$ with respect to parameter $\hat{s}$. The cases considered on the proposition statement are treated separately.

(i) Since $s_2^*(\cdot)$ is increasing, $\lim_{d \to 0} s_2^*(d) = 0$, $\lim_{d \to d^*} s_2^*(d) = s_{in}$ and $\hat{s} \in (0, s_{in})$, by using the Mean Value Theorem it follows that there exists a unique value $d \in (0, d^*)$ such that $s_2^*(d^*) = \hat{s}$, with $\beta'(s_2^*(d)) > 0$ for $d < d^*$ and $< 0$ for $d > d^*$. Consequently, $\partial_d s_1^*$ admits a unique minimum in $d^*$, as $\sgn(\partial_d s_1^*(d)) = -\sgn(B)$.

(ii) Since $s_2^*(\cdot)$ is increasing, $\lim_{d \to 0} s_2^*(d) = 0$, $\lim_{d \to +\infty} s_2^*(d) = s_1^{*,\infty}$ and $\hat{s} \in (0, s_1^{*,\infty})$, by using the Mean Value Theorem it follows that there exists a unique value $d > 0$ (denoted by $d^*$) such that $s_2^*(d^*) = \hat{s}$. Consequently, $\partial_d s_1^*$ admits a unique minimum in $d^*$, with $s_1^*(\cdot)$ decreasing on $[0, d^*)$ and increasing on $(d^*, +\infty)$. As $s_1^*(\cdot)$ is increasing on $(d^*, +\infty)$ and $\lim_{d \to +\infty} s_1^*(d) = s_1^{*,\infty}$ (from Lemma 3), one necessarily has $s_1^*(d^*) < s_1^{*,\infty}$.

(iii) Since $s_2^*(\cdot)$ is increasing, $\lim_{d \to +\infty} s_2^*(d) = s_1^{*,\infty}$ and $\hat{s} > s_1^{*,\infty}$, one has that $\beta'(s_2^*(d)) < 0$, i.e., $s_1^*(d)$ is decreasing for any $d > 0$. As $\lim_{d \to +\infty} s_1^*(d) = s_1^{*,\infty}$, it follows that $s_1^*(d) > s_1^{*,\infty}$.

A schematic representation of the three situations depicted in Proposition 4 can be observed in Figures 3(a), 3(b) and 3(c), respectively.

Figure 3: Graphical plot of the function $d \to s_1^*(d)$. 

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5 Optimal configurations

In this section, we optimize the main design parameters of the structured chemostat depicted on Figure 4 (reactor volumes and diffusion rate) for minimizing the total volume, the output concentration being prescribed at steady state. One can easily check that minimizing the total volume is equivalent to maximizing the mean residence time of the system, i.e., the mean time that a molecule spends in the chemostat (which affects its probability of reacting). A more detailed definition of the mean residence time, its measurement and interpretation can be found in Chapter 15 of [62].

This section is organized as follows: in Section 5.1, we solve the problem when the diffusion parameter is fixed. Then, in Section 5.2 we solve the full optimization problem in which the diffusion parameter is also considered as an optimization variable. Interpretations of the optimal results are presented in Section 6.

5.1 Parameter d is fixed

Given a nominal desired value $s_{\text{ref}} < s_{\text{in}}$ as output of the process, we look for solutions of the optimization problem

$$\min_{(V_1, V_2) \in \mathbb{R}_+^2} \{ V_1 + V_2 : \text{such that } s_1 = s_{\text{ref}} \text{ at steady state} \},$$

(18)

that we denote by $(V_1^{\text{opt}}, V_2^{\text{opt}})$.

For the analysis of the solution of problem (18), it is convenient to introduce the functions

$$g(s) = \frac{1}{\beta(s)} \text{ and } G(s) = (g(s_{\text{ref}}) - g(s))(s - s_{\text{ref}}),$$

(19)

defined on $(0, s_{\text{in}})$, where $\beta$ is defined in [17]. Notice that function $g$ admits an unique minimum at $\hat{s}$, by Lemma 2, and satisfies $\lim_{s \to 0} g(s) = \lim_{s \to +\infty} g(s) = +\infty$.

The solution to optimization problem (18) is given by the following proposition.

**Proposition 5.** Define $\alpha = \max(0, s_{\text{ref}} - \frac{Q}{\mu}(s_{\text{in}} - s_{\text{ref}}))$. The solution of problem (18) satisfies:

(i) If $\hat{s} \leq \alpha$, then $V_1^{\text{opt}} = 0$ and $V_2^{\text{opt}} = d\alpha(s_{\text{ref}} - \alpha)$.

(ii) If $\hat{s} \in (\alpha, s_{\text{ref}})$, then $V_1^{\text{opt}} = Q/\mu(s_{\text{ref}}) + dg(s_{\text{ref}})(s_2^{\text{opt}} - s_{\text{ref}})$ and $V_2^{\text{opt}} = dg(s_2^{\text{opt}})(s_{\text{ref}} - s_2^{\text{opt}})$, where

$$s_2^{\text{opt}} = \begin{cases} s_{\text{G}} & \text{if } \alpha \in [0, s_{\text{G}}], \\ \alpha & \text{if } \alpha \in (s_{\text{G}}, \hat{s}), \end{cases}$$

$s_{\text{G}}$ being the unique minimum of the function $G$ on the interval $[\alpha, s_{\text{ref}}]$. Moreover, $G'(s_2^{\text{opt}}) > 0$ when $s_2^{\text{opt}} = \alpha$.

(iii) If $\hat{s} \geq s_{\text{ref}}$, then $V_1^{\text{opt}} = Q/\mu(s_{\text{ref}})$ and $V_2^{\text{opt}} = 0$.

**Remark 1.** From Proposition 5, one concludes that the particular configuration with $V_1 = 0$ (as the one depicted in Figure 3) is optimal if $\hat{s} \leq \alpha$ or if $s_{\text{G}} < \alpha < \hat{s} < s_{\text{ref}}$.

**Proof of Proposition 5.** We replace the value of $s_1$ in system (10)-(11) by $s_{\text{ref}}$

$$\begin{cases} 0 = \frac{Q}{V_1}(s_{\text{in}} - s_{\text{ref}}) + \frac{d}{V_1}(s_2 - s_{\text{ref}}) - \mu(s_{\text{ref}})(s_{\text{in}} - s_{\text{ref}}), \\ 0 = \frac{d}{V_2}(s_{\text{ref}} - s_2) - \mu(s_2)(s_{\text{in}} - s_2). \end{cases}$$

(20)

Considering function $g$, system (20) can be written as

$$\begin{cases} V_1 = Qg(s_{\text{ref}})(s_{\text{in}} - s_{\text{ref}}) + dg(s_{\text{ref}})(s_2 - s_{\text{ref}}) := v_1(s_2), \\ V_2 = dg(s_2)(s_{\text{ref}} - s_2) := v_2(s_2). \end{cases}$$

(21)
Thus, given model parameters \(d, Q, s_{\text{in}}\) and \(s_{\text{ref}}\), the volumes are completely characterized by variable \(s_2\) and solving the optimization problem \([18]\) is equivalent to look for solutions of the problem

\[
\min_{s_2 \in \mathcal{S}_2} v_1(s_2) + v_2(s_2),
\]

where \(\mathcal{S}_2\) is the set of admissible values of \(s_2\). That is, the solution of problem \([18]\) is given by \((v_1(s_2^{\text{opt}}), v_2(s_2^{\text{opt}}))\), where \(s_2^{\text{opt}}\) is solution of problem \([22]\).

In order to determine the admissible set \(\mathcal{S}_2\), we take into account that both volumes must be nonnegative and proceed as follows:

\[\begin{align*}
&v_1(s_2) \geq 0 \iff Qg(s_{\text{ref}})(s_{\text{in}} - s_{\text{ref}}) + dg(s_{\text{ref}})(s_2 - s_{\text{ref}}) \geq 0 \iff s_2 \geq s_{\text{ref}} - \frac{Q}{d}(s_{\text{in}} - s_{\text{ref}}). \\
&v_2(s_2) \geq 0 \iff dg(s_2)(s_{\text{ref}} - 2) \geq 0 \iff s_2 \leq s_{\text{ref}}.
\end{align*}\]

Moreover, we impose variable \(s_2\) to be nonnegative, since it describes a (substrate) concentration. One concludes that \(\mathcal{S}_2 = [\alpha, s_{\text{ref}}]\).

For analytical purposes, we rewrite problem \([22]\) as

\[
\min_{s_2 \in [\alpha, s_{\text{ref}}]} Qg(s_{\text{ref}})(s_{\text{in}} - s_{\text{ref}}) + dG(s_2).
\]

The term \(QA\) corresponds to the optimal volume obtained with a single tank, and with a view to reduce this value, we aim to characterize solutions of problem \([23]\) with function \(G\) being negative.

The cases considered on the proposition statement are treated separately.

(i) \(\hat{s} \leq \alpha\): Since function \(g(\cdot)\) is increasing on the right of \(\hat{s}\), then \(g(s_{\text{ref}}) \geq g(s_2)\) for all \(s_2 \in [\alpha, s_{\text{ref}}]\). Consequently, function \(G\) is negative on \([\alpha, s_{\text{ref}}]\) and is minimized for \(s_2^{\text{opt}} = \alpha\).

(ii) \(\hat{s} \in (\alpha, s_{\text{ref}})\): In order to find \(s_2^{\text{opt}}\) on \([\alpha, s_{\text{ref}}]\) such that \(G(s_2^{\text{opt}})\) is minimum, we look for critical points of \(G\), which satisfy

\[
g'(s) = \frac{g(s_{\text{ref}}) - g(s)}{s - s_{\text{ref}}} := H(s).
\]

By construction, function \(g'\) is increasing on \((0, s_{\text{in}})\), \(g'(\hat{s}) = 0\) (since \(g\) is strictly convex, being equal to \(1/\beta\) and \(\beta\) strictly concave by Lemma \([2]\)) \(g'(\cdot) < 0\) on \((0, \hat{s})\) and \(g'(\cdot) > 0\) on \((\hat{s}, s_{\text{in}})\). Moreover, it is easy to see that the equation \(H(s) = 0\) has two solutions (and not more, as \(g\) is strictly convex): \(s_{\text{ref}}\) and \(\bar{s}_{\text{ref}} := \{s \in (0, \hat{s}) : g(s_{\text{ref}}) = g(s)\}\). In addition, it follows that \(H(\cdot) > 0\) on \([0, s_{\text{ref}}]\) and \(H(\cdot) < 0\) on \((s_{\text{ref}}, \bar{s}_{\text{ref}})\). As a result, we can state that any critical point of function \(G\) belongs to the interval \((\bar{s}_{\text{ref}}, \hat{s})\).

We show that there exists a unique critical point \(s_G \in (\bar{s}_{\text{ref}}, \hat{s})\) of \(G\) by proving that function \(H\) is decreasing on this interval

\[
H'(s) = -\frac{g'(s)(s - s_{\text{ref}}) - (g(s_{\text{ref}}) - g(s))}{(s - s_{\text{ref}})^2} = -\frac{g'(s) + H(s)}{s - s_{\text{ref}}} < 0.
\]

Graphically, the critical point \(s_G\) is the abscissa of the intersection of the graphs \(g'\) and \(H\) (see Figure \([4]\)). Since we look for the minimum value of function \(G\) on the interval \([\alpha, s_{\text{ref}}]\), one has that \(s_2^{\text{opt}}\) depends on the value of \(\alpha\). A direct conclusion is that \(G'(s_2^{\text{opt}}) = 0\) when \(s_2^{\text{opt}} = s_G\), while \(G'(s_2^{\text{opt}}) > 0\) when \(s_2^{\text{opt}} = \alpha\).

(iii) \(s_{\text{ref}} \leq \hat{s}\): One has that \(s_2 \leq s_{\text{ref}} \leq \hat{s}\) for all \(s_2 \in [\alpha, s_{\text{ref}}]\). Since function \(g(\cdot)\) is decreasing on the left of \(\hat{s}\), then \(g(s_{\text{ref}}) \leq g(s_2)\). Consequently, function \(G\) is nonnegative on \([\alpha, s_{\text{ref}}]\) and the optimal value which makes it equal to zero is \(s_2^{\text{opt}} = s_{\text{ref}}\). \(\square\)
Characterization of the best value of the parameter $d$

Given a nominal desired value $s_{\text{ref}} < s_{\text{in}}$ as output of the process, we look for solutions of the optimization problem

$$\min_{(V_1, V_2, d) \in \mathbb{R}_+^3} \{ V_1 + V_2 : \text{such that } s_1 = s_{\text{ref}} \text{ at steady state} \},$$

that we denote by $(V_1^*, V_2^*, d^*)$.

**Proposition 6.** The solution of problem (24) satisfies:

(i) If $\hat{s} < s_{\text{ref}}$, then $V_1^* = 0$, $V_2^* = Q(s_{\text{in}} - s_{\text{ref}})g(\hat{s})$ and $d^* = \frac{\mu \hat{s}}{s_{\text{ref}} - \hat{s}}$.

(ii) If $\hat{s} \geq s_{\text{ref}}$, then $V_1^* = \frac{Q}{\mu(s_{\text{ref}})}$, $V_2^* = 0$ and $d^*$ can take any value on the interval $[0, +\infty)$.

**Proof.** In order to solve problem (24), we rely on the optimization results obtained in Section 5.1. Thus, $(V_1^*, V_2^*, d^*) = (V_{\text{opt}}^1(d^*), V_{\text{opt}}^2(d^*), d^*)$, where $d^*$ minimizes $V_{\text{opt}}^1(d) + V_{\text{opt}}^2(d)$ and $V_{\text{opt}}^1, V_{\text{opt}}^2$ are given by Proposition 5.

(i) From Proposition 5, one easily deduces that the total volume $V_{\text{opt}}(d) = V_{\text{opt}}^1(d) + V_{\text{opt}}^2(d)$ fulfills

$$V_{\text{opt}}(d) = \left\{ \begin{array}{ll} \frac{Q}{\mu(s_{\text{ref}})} + dG(s_{\text{opt}}(d)) & \text{if } 0 \leq d < d^* \text{ (case (ii) in Prop.5),} \\ Q(s_{\text{in}} - s_{\text{ref}})g(s_{\text{ref}} - \frac{Q}{d}(s_{\text{in}} - s_{\text{ref}})) & \text{if } d \geq d^* \text{ (case (i) in Prop.5).} \end{array} \right.$$  

where $s_{\text{opt}}$ must be now seen as a function of parameter $d$.

We analyze the monotonicity of function $V_{\text{opt}}$.

- When $0 \leq d < d^*$, one has that

$$\frac{\partial V_{\text{opt}}}{\partial d} = G(s_{\text{opt}}(d)) - d\frac{\partial G}{\partial s}\bigg|_{s=s_{\text{opt}}(d)} \frac{\partial s_{\text{opt}}(d)}{\partial d}.$$

From Proposition 5, it follows that $G(s_{\text{opt}}(d)) < 0$ and $s_{\text{opt}}(d)$ corresponds either to $s^G$ (with $G'(s^G) = 0$) or to $\alpha$ (with $G'(\alpha) > 0$). In both cases one has $\frac{\partial V_{\text{opt}}}{\partial d} < 0$, that is, $V_{\text{opt}}$ is decreasing on $[0, d^*)$.

- When $d \geq d^*$, one has that

$$\frac{\partial V_{\text{opt}}}{\partial d} = \frac{Q^2}{2d^2}(s_{\text{in}} - s_{\text{ref}})^2g'(s_{\text{ref}} - \frac{Q}{d}(s_{\text{in}} - s_{\text{ref}})).$$
By definition, \( \hat{s} \) is the only value satisfying \( g'(\hat{s}) = 0 \) and so \( d^* \) is the only critical point of function \( V_{\text{opt}}(\cdot) \).

It remains to prove that \( d^* \) is a minimum of function \( V_{\text{opt}}(d) \). But

\[
\frac{\partial^2 V_{\text{opt}}}{\partial d^2}(d^*) = \frac{Q^3}{4(d^*)^4} (s_{\text{in}} - s_{\text{ref}})^3 g''(\hat{s}),
\]

which is positive as \( g \) is strictly convex. Therefore \( V_{\text{opt}} \) is increasing on \([d^*, \infty)\).

From these two points we conclude that the optimal value of \( d \) is \( d^* \).

(ii) This is a direct consequence of the statement (iii) in Proposition 5, since in this case the optimal volumes solution of problem (18) do not depend on parameter \( d \).

6 Discussion and interpretation of the results

Here, we discuss the impact of the lateral diffusion from ecological and engineering points of view. Sections 6.1 and 6.2 give a general interpretation of the results, while Section 6.3 aims to quantify the benefits of the lateral diffusion in a particular numerical case.

6.1 From an ecological viewpoint

In Section 4, we have investigated the yield conversion of the proposed structured chemostat and compared it with the one of a single-tank chemostat. Our main result, presented in Proposition 4, can be interpreted depending on the global removal rate \( D = Q/V \) and a threshold \( \hat{s} \) (that is defined as the maximizer of the function \( \beta \) defined in (7)) as follows:

1. If \( D > \mu(s_{\text{in}}) \), a spatial distribution of the total volume \( V \) could avoid the extinction of the microorganisms while it happens when the volume \( V \) is perfectly mixed. Therefore, the lateral-diffusive compartment plays the role of a “refuge” for the microorganisms in case of large removal rate.

2. If \( D \in [\mu(\hat{s}), \mu(s_{\text{in}})] \), a spatial distribution of the total volume \( V \) makes systematically increasing the output substrate concentration obtained when the volume \( V \) is perfectly mixed.

3. If \( D < \mu(\hat{s}) \), a spatial distribution of the total volume \( V \) could reduce the output substrate concentration obtained when the volume \( V \) is perfectly mixed, but this is not systematic. This means that for small removal rates \( D \) (as often met in soil ecosystems) one cannot know if a perfectly mixed model is under- or over-estimating the expected output level of the resource.

We have also analyzed the influence of the diffusion parameter \( d \) on the yield conversion in cases 1 and 3 and shown the existence of a most efficient value \( d^* \). The fact that a lateral-diffusive compartment is beneficial for “extreme” cases (i.e. large or small removal rates) does not appear to be an intuitive result for us.

6.2 From an engineering viewpoint

In Section 5, we studied optimal choices of the main design parameters (reactor volume and diffusion rate) that minimize the required volume for a given conversion rate. Our main results, presented in Propositions 5 and 6, state that, when the desired substrate output concentration is above certain threshold (more precisely, when \( s_{\text{ref}} > \hat{s} \)), the volume of a single-tank chemostat can be reduced by using the structure with lateral diffusion. This result complements the work in [34, 4, 18, 39, 61], where the authors propose a methodology to diminish the volume of a single-tank chemostat when \( s_{\text{ref}} \leq \hat{s} \), by using either \( N \) CSTR (continuous stirred tank reactor) in series or a CSTR connected in series to a PFR (plug flow reactor). We distinguish between the following cases:
Diffusion coefficient is fixed. Depending on model parameters \( s_{in}, s_{ref}, Q, d \) and \( \mu(\cdot) \), the optimal structure may be composed of two tanks (of non null volumes \( V_1^{opt} \) and \( V_2^{opt} \)) or a a single lateral tank (of volume \( V_2^{opt} \)) connected by diffusion to the main stream.

Diffusion coefficient can be optimized as well. The optimal structure is necessarily a single lateral tank (of volume \( V_2^{opt} \)) connected by diffusion (with optimal diffusion rate \( d^o = \frac{Q(s_{in} - s_{ref})}{s_{ref} - s_{opt}} \)) to the main stream.

So an important message of this study is that the particular structure of a single tank connected by diffusion to a pipe that conducts the input stream, as depicted on Figure 2, can be an efficient configuration, better than a single tank directly under the main stream. To our knowledge, this result is new in the literature.

The mathematical analysis has also revealed that the function \( g \), i.e. the inverse of the function \( \beta \) defined in (7), is playing an important role in determining if the best configuration is composed of one or two tanks (more precisely the relative position of the output reference value \( s_{ref} \) with respect to the minimizer \( \hat{s} \) of \( g \)). This is the same function than the one used for the optimal design of tanks in series (with also a discussion on the relative position of \( s_{ref} \) with respect to \( \hat{s} \), see, e.g., [4, 22]), but with two main differences:

1. Due to the particular considered structure, there is a trichotomy (one single mixed tank, two tanks, or one single lateral tank) instead of the dichotomy (one or more tanks) found for the problem with tanks in series. This trichotomy is discussed below with the help of the additional parameter \( \alpha = \max(0, s_{ref} - \frac{Q}{\mu}(s_{in} - s_{ref})) \).

2. For small values of \( s_{ref} \) (compared to \( \hat{s} \)), a lateral-diffusion compartment does not bring any improvement compared to a single perfectly mixed tank, while this is the opposite for tanks in series (i.e. several tanks are better than a single one when \( s_{ref} < \hat{s} \)).

These points can be grasped by the following graphical interpretation. Consider the total volume \( V \) required to obtain the output concentration \( s_{ref} \) at steady state. In our case, it can be written in terms of the function \( g \) as follows

\[
V = Q g(s_{ref})(s_{in} - s_{ref}) + d(g(s_{ref}) - g(s_{2}^*)(s_{2}^* - s_{ref}))
\]

where \( s_{2}^* \) is the steady state in the second compartment. One can notice that the number \( A \) is proportional to the volume necessary for a single chemostat to have \( s_{ref} \) as resource concentration at steady state (remind that this volume is equal to \( Q/\mu(s_{ref}) \equiv QA \)). Therefore, a configuration with a lateral-diffusive compartment would require a smaller volume than that of the single chemostat exactly when the number \( B \) is negative. Figure 5 illustrates that this is possible only when \( s_{ref} \) is above the minimizer \( \hat{s} \) of the function \( g \) (remind that the function \( g \) is strictly convex, since it is equal to \( 1/\beta \) and \( \beta \) is strictly concave by Lemma 4).

Furthermore, the quantity \( B \) is equal to \( G(s_{2}^*) \), where the function \( G \) defined in (19) admits an unique minimum at \( s_{2}^* \in [0, s_{ref}] \). Proposition 6 states that, when \( s_{ref} > \hat{s} \), the optimal value of \( s_{2}^* \) (that is, the value of \( s_{2}^* \) which minimizes the total volume) is \( s_{G} \) when \( \alpha \leq s_{G} \) and \( \alpha \) in other case, corresponding to the particular configuration with \( V_1 = 0 \) (since \( V_1 = Qg(s_{ref})(s_{in} - s_{ref}) + d(g(s_{ref})/(s_{2}^* - s_{ref})) \)). A graphical interpretation of the optimized structures obtained when parameter \( d \) is fixed is given in Figure 6. When the diffusion rate can be tuned, the optimized configuration is as depicted in Figure 6(c).

Finally, let us recall from the theory of optimal design of chemostats in series that the first tank (when it is optimal to have more than one tank) has systematically a resource concentration \( s_1^* \) above \( \hat{s} \) at steady state (see, e.g., [3, 22]). Thus, for an industrial perspective, we can state that a lateral-diffusive compartment for the first tank of an optimal series of chemostat could systematically improve the performance of the overall process.
6.3 A numerical example

One may wonder how much could be gained (in terms of residence time) by using the proposed structure. Nevertheless, it is difficult to quantify the overall profit since the optimal design depends on parameters \( s_{\text{in}}, s_{\text{ref}}, Q, \mu(\cdot) \) and \( d \) (when it is not fixed beforehand). As an illustrative example, we compare the total optimal volumes \( V^{\text{opt}}(0) \), \( V^{\text{opt}}(Q) \) and \( V^{\text{opt}}(d^*) \), obtained by solving problem (18) when \( Q = 1 \), \( s_{\text{in}} = 10 \), \( \mu(\cdot) \) is the Monod function with \( \mu_{\text{max}} = 1 \) and \( K = 0.5 \) (in this case, \( \hat{s} \approx 1.79 \)) and diffusion coefficients \( d = 0 \), \( Q \) and \( d^* \), respectively. More precisely, Figure 7-(a) compares the three diffusion coefficients (seen as functions of parameter \( s_{\text{ref}} \)) while the associated optimal volumes are depicted in Figure 7-(b). Notice that \( V^{\text{opt}}(0) \) corresponds to the volume of the single-tank chemostat.

From Figure 7-(b) we remark that, when \( d = Q \), there exists a certain value of parameter \( s_{\text{ref}} \) in which the optimal design transits from having two to one tank. Proposition 6 infers that this transition occurs when \( s_{\text{ref}} = \frac{2s_{\text{in}} + K}{2} \). In this case, when \( s_{\text{ref}} \approx 5.9 \). One can observe that, for this particular value of \( s_{\text{ref}} \), the single-tank volume is reduced approximately to its half and, in general, the volume reduction becomes more significant as the value \( s_{\text{ref}} \) increases. In those cases the gains are quite significant.

7 Conclusion

In this work, we have identified situations for which a compartment connected by “lateral diffusion” is beneficial for ecological or engineering outcomes.

The analysis has first revealed two thresholds on the input resource concentration which allow to distinguish three kinds of situations for guaranteeing the existence of a positive equilibrium depending on the diffusion rate \( d \): 1. \( d \) has to be positive but below a maximal value \( d \), 2. \( d \) has simply to be positive, 3. \( d \)
Considered diffusion parameters (seen as functions of $s_{\text{ref}}$).

Optimal volumes associated to the diffusion parameters in (a).

Figure 7: Comparison between the volumes $V_{\text{opt}}^0$, $V_{\text{opt}}^Q$ and $V_{\text{opt}}^{d^*}$, obtained by solving problem (18) when $Q = 1$, $s_{\text{in}} = 10$ and $\mu(\cdot)$ is the Monod function with $\mu_{\text{max}} = 1$ and $K = 0.5$ and diffusion coefficients $d = 0$, $Q$ and $d^*$ ($d^*$ being the solution of problem (24)), respectively. The solid, dashed and dotted lines in (b) represent, respectively, the values of $s_{\text{ref}}$ for which the optimal design is composed of two tanks (of volumes $V_{\text{opt}}^1$ and $V_{\text{opt}}^2$), a single tank of volume $V_{\text{opt}}^2$ or a single tank of volume $V_{\text{opt}}^1$.

can take any nonnegative value. When the positive equilibrium exists, we have proved that it is necessary asymptotically stable (although not always hyperbolic).

We have also studied the impact of the diffusion rate $d$ on the yield conversion and concluded that there exists an optimal value of $d$ that maximizes the yield conversion (which is then necessarily better than for a single tank) for "extreme" cases of the removal rate (i.e. either small or large), which did not appear to be an intuitive result to us. This property implies that in natural habitats (such as in soil ecosystems) the type of feeding (by convection or diffusion) from a given flow rate could have a significant impact on the resource conversion.

In terms of total volume required for achieving a given yield conversion, we have provided conditions that discriminate which configurations between one or two tanks are the best. Our conclusion is that a lateral compartment is beneficial compared to a single chemostat when the yield conversion is not too important (i.e. when the output resource concentration is not too small compared to the input one). Surprisingly, we have also found that the limiting case of a single tank purely connected by diffusion to the main stream (as depicted on Figure 2), and not crossed by the stream as in the classical chemostat, can provide the minimal volume. For an industrial perspective, we can state that a lateral diffusive compartment for the first tank of an optimal series of chemostat could systematically improve the performance of the overall process. Therefore, the analysis of combinations of series and lateral diffusive compartments (which is out of the scope of the present study) would most probably exhibit non-intuitive configurations that have not yet been considered in the literature. This would be the matter of a future work.

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