

COMPETITIVE EXCLUSION PRINCIPLE IN A MODEL OF CHEMOSTAT WITH DELAYS*

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Abstract. This paper is devoted to the study of the global asymptotic behavior of a model of chemostat with an arbitrary number of competitors following a Monod law on their specific growth rate functions. The model incorporates discrete time delays in order to take into account the delay in the conversion of nutrient consumed to the viable biomass. In this context, we state sufficient conditions ensuring that the presence of these time delays do not alter the prediction of the competitive exclusion principle. Our analysis and proofs rely on the construction of a Lyapunov-Krasovskii functional.

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AMS (MOS) subject classification: 34D05, 34D20, 34D23, 37B25.

1 Introduction

The chemostat is a laboratory apparatus used for the continuous culture of microorganisms. It is a benchmark model in microbial ecology, used for experimentally reproducing a wide variety of systems ranging from lakes, waste-water treatment plants, to reactors for commercial production of substances by genetically altered organisms.

Roughly speaking, it is basically a culture vessel having an input aperture for the influx of sterile nutrient medium from a reservoir and an overflow aperture for the efflux of exhausted medium, living cells, and cellular debris. The device (and the term "chemostat") was invented by Novick and Szilard [15]; the "bactogene" is a virtually identical device developed independently and simultaneously by Monod [14]. See, for instance, [6], [16], [4] for more details on this apparatus.

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Despite its nonlinear character, the mathematical theory of the chemostat in the absence of delay is well-known. It was first achieved by Spicer [17] and can be found in many textbooks (e.g. Smith and Waltman [16]).

A central result of this theory is the Competitive Exclusion Principle. It states that, when the growth rates of the micro-organisms are increasing, at most one competitor can survive on a single resource. This principle is valid when no delay is present in the model of the system. However, as pointed out in [3] (see also Caperon [5] and Smith and Waltman [16]), delays occur naturally in biological systems. For instance, there are two obvious sources of delays: delays due to the possibility that the organism stores the nutrient and delays due to the cell cycle. Moreover, it has been proved that the presence of a sufficiently large discrete time delay generates oscillations of the variables in a model with several species. See for instance Freedman et al. [7], where 2 species with increasing growth rate functions are considered. Therefore a question naturally arises: in which cases the presence of delays does not change the prediction of the Competitive Exclusion Principle?

One cannot expect to give a complete answer to this very general question. However, important partial answers are already available in the literature. Let us briefly summarize some of them:

Wang and Wolkowicz [18] have shown that the Competitive Exclusion Principle holds for a chemostat model where the nutrient conversion process involves time delays simultaneously in variables of nutrient (or substrate) and of species concentrations. This model describes the case where there are n species, with monotone growth functions, competing for a single resource. Recently, Wolkowicz and Xia [19] have extended this result, proving that the Competitive Exclusion Principle holds true for the same model but with general non-monotone growth functions. In both papers, global stability is demonstrated through approaches which do not rely on a Lyapunov technique.

In the present work, we give a new answer to this question for a well-known delayed chemostat model with n species, which is related to the model studied in Freedman et al. [7]. Indeed, our study is concerned with a model of chemostat with growth rates of Monod type, where only delays of time τ_i in converting substrate (or nutrient) into concentrations x_i of the species i are considered. A justification of the way that the delay is introduced in the one-species chemostat model can be found in Bush and Cook [3]. For this model, we determine a positive constant, expressed as a function of the growth rates of the species, the substrate input concentration and the dilution rate, such that, if the delays are smaller than this constant, the stability property of the system is not modified by the presence of the delay, that is the Competitive Exclusion Principle holds. Our technique of proof consists in determining first an attractive invariant domain and next in constructing a Lyapunov-Krasovskii functional whose derivative along the solutions is smaller than a definite negative function when the solutions are in the invariant domain.

The potential advantages of the knowledge of such a functional are mul-

tiple and appealing. In particular observe that strict Lyapunov functionals are known to be very efficient tools for robustness analysis, but this issue is beyond the scope of this paper.

Our main result complements the global stability results given in Beretta and Kuang [2] for the same delayed chemostat model but with only one species.

This paper is organized as follows. In Section 2 we introduce the mentioned chemostat model in the absence of delays as well as the assumptions of our work. In Section 3 a Lyapunov function for this model is constructed. In Section 4 our chemostat model with time delays is introduced, and then we prove our main result: the Competitive Exclusion Principle holds for sufficiently small time delays. Some numerical simulations are given in Section 5, and we conclude in Section 6 with a discussion.

2 The Model and Basic Assumptions

Throughout the paper, the arguments of the functions will be simplified or omitted whenever no confusion can arise from the context. The chemostat model with n species is given by (see [16])

$$\begin{cases} \dot{s} &= D(s_{in} - s) - \sum_{i=1}^n \frac{\mu_i(s)}{Y_i} x_i, \\ \dot{x}_1 &= [\mu_1(s) - D]x_1, \\ &\vdots \\ \dot{x}_n &= [\mu_n(s) - D]x_n, \end{cases}$$

evolving on the state space $\mathcal{D} = \mathbb{R}_{++}^{n+1} = (0, +\infty) \times (0, +\infty) \times \dots \times (0, +\infty)$ where

1) $s(t)$ is the concentration of the nutrient (or substrate) in the chemostat at time t (usually measured in hours), and s_{in} is the concentration of the input nutrient from the reservoir. They are measured in units of micrograms per millimeter,

2) $x_i(t)$ is the concentration of the species i of micro-organisms at time t . It is measured in units of cells per millimeter,

3) D is the dilution rate of the chemostat, that is the fraction of the chemostat volume replaced per hour by inflow from the reservoir,

4) Each function $\mu_i(\cdot)$ is an uptake function. It represents the growth rate of species i . Units of $\mu_i(\cdot)$ are hours⁻¹,

5) Y_i is the yield constant of species i . Units of Y_i are cells per microgram of nutrient,

In the above model we have supposed that the removal rates of the species are all equal to dilution rate D .

Since we are taking s_{in} and the Y_i to be fixed positive constants, using the change of variables:

$$\bar{s} = \frac{s}{s_{in}}, \quad \bar{x}_i = \frac{x_i}{s_{in}Y_i}, \quad \bar{\mu}_i(\bar{s}) = \mu_i(s_{in}\bar{s}),$$

and dropping bars, we eliminate parameters s_{in} and Y_i obtaining the new dynamics

$$\begin{cases} \dot{s} &= D(1-s) - \sum_{i=1}^n \mu_i(s)x_i, \\ \dot{x}_1 &= [\mu_1(s) - D]x_1, \\ &\vdots \\ \dot{x}_n &= [\mu_n(s) - D]x_n, \end{cases} \quad (1)$$

evolving on the state space \mathcal{D} .

Throughout this paper we use the following assumptions:

Assumption H1. The uptake functions μ_i follow a Monod law [14]: that is, they are given by the expressions

$$\mu_i(s) = \frac{m_i s}{a_i + s},$$

where the constants m_i, a_i are strictly positive. These constants represent, respectively, the theoretical maximum of the function $\mu_i(\cdot)$ and its saturation constant or “assimilation parameter” corresponding to the substrate concentration giving a half-maximal specific growth rate. The Monod law is based on the assumption that the specific growth rate (μ_i) relative to its theoretical maximum (m_i) is described by a conventional Michaelis saturation equation involving the nutrient concentration, which yields to the equation stated above.

Assumption H2. The constants m_i, a_i, D satisfy

$$\frac{m_i}{a_i + 1} > D. \quad (2)$$

From Assumption H2, it follows that there are n positive constants λ_i , called *break-even concentrations*, such that

$$\mu_i(\lambda_i) = D.$$

Moreover, Assumption H2 also implies that $\lambda_i < 1$ for all $i = 1, \dots, n$. These constants play an important role in determining competitive ability. For instance, the inequalities (2) (which imply $\lambda_i < 1$ for all i) are enough to ensure competitive exclusion when no delay is presented in the model (1) (see Theorem 1 below).

Assumption H3. The inequalities

$$0 < \lambda_1 < \lambda_2 \leq \dots \leq \lambda_n$$

are satisfied.

This assumption is made in order to fix the first species as the most performant one. We shall prove that, in the presence of sufficiently small delay, the species whose concentration is x_1 is the only survivor (see Theorem 3 below).

Let us define the constants s_*, x_{1*} by

$$s_* = \lambda_1, \quad x_{1*} = 1 - s_*, \quad (3)$$

and, for $i = 2, \dots, n$, the constants c_i by

$$c_i = D - \mu_i(s_*) = \mu_1(s_*) - \mu_i(s_*). \quad (4)$$

and introduce the notation

$$E_* = (s_*, x_{1*}, 0, \dots, 0). \quad (5)$$

The values s_* and x_{1*} given in (3) determine the equilibrium reached asymptotically when the competitive exclusion principle holds. The constants c_i play an important role in the computation of the theoretical upper bound for the time delays τ_i , under which the competitive exclusion principle is guaranteed to hold.

Remarks.

- It is well-known, and easy to check, that \mathcal{D} is a positively invariant domain of the system (1).
- Observe that Assumptions H1 and H3 imply that $s_* > 0$, $x_{1*} > 0$ and E_* is an equilibrium point of the system (1).
- The assumptions that the uptake functions are Monod is a technical assumption which enables to construct a Lyapunov function. This construction given for the first time in [9] can be also found in [16, Chapter 2] which is devoted to classical cases where the Competitive Exclusion Principle can be proved.
- Assumption H3 and the fact that the functions μ_i are increasing imply that, for $i = 2, \dots, n$, the constants c_i are positive.

3 Strict Lyapunov Function in the Absence of Delay

In this section, we revisit the Lyapunov construction proposed in [9] (see also [16]) for a chemostat model with species-specific removal rates. This construction is carried out for a chemostat model with Monod functions for the growth rates. The Lyapunov function obtained in [9] is a so-called weak Lyapunov function i.e. its derivative along the trajectories is non-positive but not definite negative. In contrast with strict Lyapunov functions i.e. Lyapunov functions whose derivative along the trajectories is definite

negative, weak Lyapunov functions cannot be used in general to analyze the effect of the presence of delays. With a view to such an analysis for the system (1), we determine a strict Lyapunov function for this system by modifying the Lyapunov function established in [9].

Theorem 1. *Assume that the functions μ_i of the system (1) satisfy Assumptions H1,H2, and H3. Then, the point E_* defined in (5) is a globally asymptotically and locally exponentially stable equilibrium point of (1) on the domain \mathcal{D} . Moreover, the derivative of the function*

$$U(\tilde{s}, \tilde{x}_1, \xi) := V(\tilde{s}, \tilde{x}_1, \xi) + \frac{1}{2} \left(\tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right)^2, \tag{6}$$

where $\tilde{s} = s - s_*$, $\tilde{x}_1 = x_1 - x_{1*}$, $\xi = (x_2, \dots, x_n)$, and

$$V(\tilde{s}, \tilde{x}_1, \xi) := \tilde{s} - s_* \ln \left(1 + \frac{\tilde{s}}{s_*} \right) + \frac{a_1 + s_*}{a_1} \left[\tilde{x}_1 - x_{1*} \ln \left(1 + \frac{\tilde{x}_1}{x_{1*}} \right) \right] + \sum_{i=2}^n \frac{a_i + s_*}{a_i} x_i \tag{7}$$

along the trajectories of the system (1) is

$$\dot{U} = -W(\tilde{s}, \tilde{x}_1, \xi) \tag{8}$$

where

$$W(\tilde{s}, \tilde{x}_1, \xi) := \frac{D\tilde{s}^2 + [\mu_1(s) - \mu_1(s_*)]\tilde{s}x_{1*}}{s} + \sum_{i=2}^n \frac{c_i(a_i + s_*)}{a_i} x_i + D \left(\tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right)^2 \tag{9}$$

is a positive definite function.

Proof. In the variables \tilde{s}, \tilde{x}_1 , the system (1) rewrites

$$\begin{cases} \dot{\tilde{s}} &= -D\tilde{s} - \mu_1(s)x_1 + \mu_1(s_*)x_{1*} - \sum_{i=2}^n \mu_i(s)x_i, \\ \dot{\tilde{x}}_1 &= [\mu_1(s) - D]x_1, \\ \dot{x}_2 &= [\mu_2(s) - D]x_2, \\ &\vdots \\ \dot{x}_n &= [\mu_n(s) - D]x_n. \end{cases} \tag{10}$$

Next observe that the system (10) is equivalent to the system

$$\begin{cases} \dot{\tilde{s}} &= -D\tilde{s} - [\mu_1(s) - \mu_1(s_*)]x_{1*} - \mu_1(s)\tilde{x}_1 - \sum_{i=2}^n \mu_i(s)x_i, \\ \dot{\tilde{x}}_1 &= [\mu_1(s) - \mu_1(s_*)]x_1, \\ \dot{x}_2 &= -c_2x_2 + [\mu_2(s) - \mu_2(s_*)]x_2, \\ &\vdots \\ \dot{x}_n &= -c_nx_n + [\mu_n(s) - \mu_n(s_*)]x_n. \end{cases} \quad (11)$$

One can easily check that for $i = 1, \dots, n$

$$\mu_i(s) - \mu_i(s_*) = \frac{a_i}{a_i + s_*} \frac{\mu_i(s)}{s} \tilde{s}.$$

These equalities imply the derivative of the function V defined in (7) along the trajectories of (11) satisfies

$$\dot{V} = \frac{-D\tilde{s}^2 - [\mu_1(s) - \mu_1(s_*)]\tilde{s}x_{1*}}{s} - \sum_{i=2}^n \frac{c_i(a_i + s_*)}{a_i} x_i \leq 0. \quad (12)$$

The right hand side of (12) is not a negative definite function of $(\tilde{s}, \tilde{x}_1, x_2, \dots, x_n)$ because it is independent of \tilde{x}_1 . But since the derivative of the variable

$$\zeta = \tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i$$

satisfies

$$\dot{\zeta} = D[1 - s_* - x_{1*} - \zeta] = -D\zeta,$$

it follows that the derivative of the function U , defined in (6), along the trajectories of (11) satisfies (8), which ensures that U is a strict Lyapunov function because W is positive definite. \square

4 Stability in the Presence of Delays

In this section we prove the main result of the paper, namely that the presence of small delays does not modify the prediction of the Competitive Exclusion Principle under Monod hypothesis on the uptake functions. For this purpose, we construct a Lyapunov-Krasovskii functional [12] for the chemostat model. As far as we know, this is the first time that such a type of functionals has been used in this context.

Consider the delayed chemostat model

$$\begin{cases} \dot{s} &= D(1-s) - \sum_{i=1}^n \mu_i(s)x_i, \\ \dot{x}_1 &= [\mu_1(s(t-\tau_1)) - D]x_1, \\ &\vdots \\ \dot{x}_n &= [\mu_n(s(t-\tau_n)) - D]x_n, \end{cases} \quad (13)$$

where τ_i are constants such that

$$0 \leq \tau_i \leq \tau_M, \quad (14)$$

and τ_M is a known positive real number.

For the sake of simplicity of notation, we introduce the constants

$$M = \max_{i=2,\dots,n} \{m_i\}, \quad c = \min_{i=2,\dots,n} \{c_i\}. \quad (15)$$

For the initial conditions of the model above, we consider $n + 1$ continuous functions $\phi_i : [-\tau_M, 0] \rightarrow \mathbb{R}_+$, $i = 0, \dots, n$. By the method of steps (see for instance [1]), it can be shown that there is a unique solution $(s(t), x_1(t), \dots, x_n(t))$ of (13), defined over $[0, +\infty)$ and such that $s(t) = \phi_0(t)$ and $x_i(t) = \phi_i(t)$ for all $i = 1, \dots, n$ and for all $t \in [-\tau_M, 0]$.

In order to prove our main result which is based on the construction of a Lyapunov Krasovskii functional [12], we give the following technical lemma.

Lemma 2. *Assume that the functions μ_i of the system (13) satisfy Assumptions H1,H2,H3, and that*

$$\tau_M \leq \min \left\{ \frac{1}{M-D} \ln \left(\frac{4M}{4M-D} \right), \frac{1}{D} \ln \left(\frac{6}{5} \right) \right\}. \quad (16)$$

Then, for any trajectory $(s(t), x_1(t), \dots, x_n(t))$ of (13) with initial condition in \mathcal{D} there exists a finite instant T_f such that, for all $t \geq T_f$ one has $(s(t), x_1(t), \dots, x_n(t)) \in D_1$ where

$$D_1 = \left\{ (s, x_1, x_2, \dots, x_n) \in \mathcal{D} : s < 1, \sum_{i=1}^n x_i \leq 2 \right\}. \quad (17)$$

Proof. Since the domain \mathcal{D} is positively invariant, for all $t \geq 0$, the inequality

$$\sum_{i=1}^n \mu_i(s(t))x_i(t) \geq 0$$

is satisfied. This sign property implies that there exists $T_1 \geq 0$ such that, for all $t \geq T_1$,

$$s(t) \leq 2.$$

By integrating each x_i equation in (13), we deduce that

$$\begin{aligned} x_i(t + \tau_i) &= x_i(t) \exp \left[\int_t^{t+\tau_i} [\mu_i(s(l - \tau_i)) - D] dl \right] \\ &= x_i(t) \exp \left[\int_{t-\tau_i}^t [\mu_i(s(l)) - D] dl \right]. \end{aligned} \quad (18)$$

On the other hand

$$\dot{x}_i(t + \tau_i) = [\mu_i(s(t)) - D] x_i(t + \tau_i).$$

It follows that the derivative of

$$Z(t) = s(t) + \sum_{i=1}^n x_i(t + \tau_i)$$

satisfies

$$\begin{aligned} \dot{Z}(t) &= D(1 - s(t)) - \sum_{i=1}^n \mu_i(s(t)) x_i(t) + \sum_{i=1}^n [\mu_i(s(t)) - D] x_i(t + \tau_i) \\ &= D(1 - Z(t)) \\ &\quad + \sum_{i=1}^n \mu_i(s(t)) x_i(t + \tau_i) \left(1 - \exp \left[- \int_{t-\tau_i}^t [\mu_i(s(l)) - D] dl \right] \right). \end{aligned}$$

Since each function μ_i is upper bounded by the constant $m_i \leq M$, we deduce that

$$\dot{Z}(t) \leq D(1 - Z(t)) + M \sum_{i=1}^n x_i(t + \tau_i) \left(1 - \exp \left[\int_{t-\tau_i}^t [D - M] dl \right] \right).$$

On the other hand, from (14), we deduce that

$$\begin{aligned} \dot{Z}(t) &\leq D(1 - Z(t)) + M(1 - \exp[\tau_M(D - M)]) \sum_{i=1}^n x_i(t + \tau_i) \\ &\leq D(1 - Z(t)) + M(1 - \exp[\tau_M(D - M)]) Z(t). \end{aligned}$$

The inequality (16) ensures that

$$\dot{Z}(t) \leq D \left(1 - \frac{3}{4} Z(t) \right).$$

Thus, we deduce easily that there exists $T_2 \geq T_1$ such that,

$$Z(t) \leq \frac{5}{3}, \quad \forall t \geq T_2. \quad (19)$$

First, we will prove that there exists $T_3 \geq T_2$ such that $s(t) < 1$ for all $t \geq T_3$. Let us proceed by contradiction. Assume that there is a trajectory such that $s(t) \geq 1$ for all $t \geq T_2$. It follows that, for all $t \geq T_2 + \tau_1$,

$$\dot{x}_1(t) \geq [\mu_1(1) - D]x_1.$$

Assumption H2 in particular says that $\mu_1(1) - D > 0$, obtaining that $x_1(t)$ is unbounded. This yields a contradiction. Hence there exists $T_3 \geq T_2 + \tau_1$ such that $s(T_3) < 1$. We easily deduce that $s(t) < 1$ for all $t \geq T_3$.

Inequality (19) implies that

$$\sum_{i=1}^n x_i(t + \tau_i) \leq \frac{5}{3}, \forall t \geq T_3,$$

and from (18), it follows that

$$\sum_{i=1}^n x_i(t) \exp \left[\int_{t-\tau_M}^t [\mu_i(s(l)) - D] dl \right] \leq \frac{5}{3}, \forall t \geq T_3,$$

which implies

$$\sum_{i=1}^n x_i(t) \leq \frac{5}{3} \exp [\tau_M D], \forall t \geq T_3.$$

Finally, from (16), we obtain

$$\sum_{i=1}^n x_i(t) \leq 2, \forall t \geq T_3,$$

which proves the desired result. □

Theorem 3. *Assume that the functions μ_i of the system (13) satisfy Assumptions H1,H2,H3 and that*

$$\tau_M \leq \min_{j=0,\dots,4} \{A_j\} \tag{20}$$

with

$$\begin{aligned} A_0 &= \frac{1}{D} \ln \left(\frac{6}{5} \right), \\ A_1 &= \frac{1}{M-D} \ln \left(\frac{4M}{4M-D} \right), \\ A_2 &= \frac{a_1^2 c}{8(a_1+1)m_1 M}, \\ A_3 &= \frac{c}{8M \max_{i=2,\dots,n} \left\{ \left(\frac{1}{a_i} + 3 \right) \frac{m_i}{a_i} \right\}}, \\ A_4 &= \frac{a_1^2 D}{2\sqrt{2}m_1(3a_1+1) \max \left\{ 1, \frac{1}{a_1}, \frac{\sqrt{D}}{\sqrt{c}} \right\}}. \end{aligned}$$

Then, the point $(s_*, x_{1*}, 0, \dots, 0)$ is a globally asymptotically and a locally exponentially stable equilibrium point of (13) on the domain \mathcal{D} .

Proof. We construct a Lyapunov functional by taking advantage of the function U , defined in (6). We rewrite the system (13) as

$$\begin{cases} \dot{\tilde{s}} &= D(1-s) - \sum_{i=1}^n \mu_i(s)x_i, \\ \dot{\tilde{x}}_1 &= [\mu_1(s) - D]x_1 + r_1(s(t - \tau_1), s(t), x_1(t)), \\ &\vdots \\ \dot{\tilde{x}}_n &= [\mu_n(s) - D]x_n + r_n(s(t - \tau_n), s(t), x_n(t)), \end{cases} \quad (21)$$

with

$$r_i(s(t - \tau_i), s(t), x_i(t)) = [\mu_i(s(t - \tau_i)) - \mu_i(s(t))]x_i(t).$$

We deduce from Theorem 1 that

$$\begin{aligned} \dot{U} &= -W(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) + \frac{\partial U}{\partial \tilde{x}_1}(\tilde{s}(t), \tilde{x}_1(t), \xi(t))r_1(s(t - \tau_1), s(t), x_1(t)) \\ &\quad + \sum_{i=2}^n \frac{\partial U}{\partial x_i}(\tilde{s}(t), \tilde{x}_1(t), \xi(t))r_i(s(t - \tau_i), s(t), x_i(t)), \end{aligned}$$

where the function W is defined in (9). From the definition of c in (15), the fact that μ_1 is increasing, and $s < 1$ for all $t \geq T_f$ (see Lemma 2), the derivative of the function U satisfies for all $t \geq T_f$

$$\begin{aligned} \dot{U} &\leq -W_2(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) + \frac{\partial U}{\partial \tilde{x}_1}(\tilde{s}(t), \tilde{x}_1(t), \xi(t))r_1(s(t - \tau_1), s(t), x_1(t)) \\ &\quad + \sum_{i=2}^n \frac{\partial U}{\partial x_i}(\tilde{s}(t), \tilde{x}_1(t), \xi(t))r_i(s(t - \tau_i), s(t), x_i(t)) \end{aligned} \quad (22)$$

where

$$W_2(\tilde{s}, \tilde{x}_1, \xi) := D\tilde{s}^2 + c \sum_{i=2}^n x_i + D \left(\tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right)^2 \leq W(\tilde{s}, \tilde{x}_1, \xi).$$

Immediate calculations give

$$\begin{aligned}
 \left| \frac{\partial U}{\partial \tilde{x}_1} r_1 \right| &= \\
 &= \left| \frac{a_1 + s_*}{a_1} \frac{\tilde{x}_1(t)}{x_1(t)} + \tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right| |\mu_1(s(t - \tau_1)) - \mu_1(s(t))| x_1(t) \\
 &= \left| \frac{a_1 + s_*}{a_1} \tilde{x}_1(t) + \left(\tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right) x_1(t) \right| |\mu_1(s(t - \tau_1)) - \mu_1(s(t))| \\
 &= \left| \frac{a_1 + s_*}{a_1} [\tilde{s}(t) + \sum_{j=2}^n x_j(t)] - \left(\tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right) \left(x_1(t) + \frac{a_1 + s_*}{a_1} \right) \right| \\
 &\times |\mu_1(s(t - \tau_1)) - \mu_1(s(t))|. \tag{23}
 \end{aligned}$$

Observe that the function μ_1 satisfies $|\mu_1(a) - \mu_1(b)| \leq \frac{m_1}{a_1} |a - b|$ for all $a, b \geq 0$. Thus, the inequality

$$\begin{aligned}
 \left| \frac{\partial U}{\partial \tilde{x}_1} r_1 \right| &\leq \frac{(a_1 + s_*)m_1}{a_1^2} \left| \tilde{s}(t) + \sum_{j=2}^n x_j(t) \right| |s(t - \tau_1) - s(t)| \\
 &\quad + \frac{m_1}{a_1} \left| \tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right| \left| x_1(t) + \frac{a_1 + s_*}{a_1} \right| |s(t - \tau_1) - s(t)|
 \end{aligned}$$

holds.

On the other hand, since $\mu_i \leq M$, $D \leq 2M$ (see (2)), and for all $t \geq T_f$ one has $D(1 - s) < D$ and $\sum_{i=2}^n \mu_i(s)x_i \leq 2M$. We observe that

$$|\dot{s}| = \left| D(1 - s) - \sum_{i=1}^n \mu_i(s)x_i \right| \leq 2M \quad \forall t \geq T_f.$$

So, the state s satisfies

$$|s(t_1) - s(t_2)| \leq 2M|t_1 - t_2| \quad \forall t_1, t_2 \geq T_f.$$

Hence, for all $t \geq T_f + \tau_M$, we obtain

$$\begin{aligned}
 \left| \frac{\partial U}{\partial \tilde{x}_1} r_1 \right| &\leq \frac{(a_1 + s_*)m_1}{a_1^2} |\tilde{s}(t)| |s(t - \tau_1) - s(t)| + 2\tau_1 M \frac{(a_1 + s_*)m_1}{a_1^2} \sum_{j=2}^n x_j(t) \\
 &\quad + \frac{m_1}{a_1} \left(3 + \frac{s_*}{a_1} \right) \left| \tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right| |s(t - \tau_1) - s(t)|.
 \end{aligned}$$

Using the triangular inequality we deduce

$$\begin{aligned} \left| \frac{\partial U}{\partial \tilde{x}_1} r_1 \right| &\leq \frac{D}{4} \tilde{s}(t)^2 + \frac{1}{D} \frac{(a_1 + s_*)^2 m_1^2}{a_1^4} |s(t - \tau_1) - s(t)|^2 \\ &\quad + 2\tau_1 M \frac{(a_1 + s_*) m_1}{a_1^2} \sum_{j=2}^n x_j(t) + \frac{D}{4} \left(\tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right)^2 \\ &\quad + \frac{1}{D} \left[\frac{m_1}{a_1} \left(3 + \frac{s_*}{a_1} \right) |s(t - \tau_1) - s(t)| \right]^2 . \end{aligned}$$

From (20) we know that $\tau_M \leq \frac{a_1^2 c}{8(a_1 + s_*) m_1 M}$, and since $\frac{(a_1 + s_*)^2}{a_1^2} \leq \left(3 + \frac{s_*}{a_1} \right)^2$ we have

$$\left| \frac{\partial U}{\partial \tilde{x}_1} r_1 \right| \leq \frac{1}{4} W_2(\tilde{s}, \tilde{x}_1, \xi) + \frac{2m_1^2}{a_1^2 D} \left(3 + \frac{s_*}{a_1} \right)^2 |s(t - \tau_1) - s(t)|^2 . \quad (24)$$

Next, it is straightforward to check

$$\left| \frac{\partial U}{\partial x_i} r_i \right| = \left| \frac{a_i + s_*}{a_i} + \tilde{s}(t) + \tilde{x}_1(t) + \sum_{j=2}^n x_j(t) \right| |\mu_i(s(t - \tau_i)) - \mu_i(s(t))| x_i(t) ,$$

for all $i = 2, \dots, n$. Using again the fact that for all $t \geq T_f$ one has $0 \leq s(t) < 1$, $\sum_{i=1}^n x_i(t) \leq 2$ and recalling that $1 - s_* = x_{1*}$ together with the inequalities $|\mu_i(a) - \mu_i(b)| \leq \frac{m_i}{a_i} |a - b|$ for all $a, b \geq 0$, we deduce for all $i = 2, \dots, n$, that

$$\begin{aligned} \left| \frac{\partial U}{\partial x_i} r_i \right| &\leq \left(\frac{s_*}{a_i} + s(t) + x_1(t) + \sum_{j=2}^n x_j(t) \right) \frac{m_i}{a_i} |s(t - \tau_i) - s(t)| x_i(t) \\ &\leq \left(\frac{s_*}{a_i} + 3 \right) \frac{m_i}{a_i} |s(t - \tau_i) - s(t)| x_i(t) . \end{aligned}$$

Using again the inequality $|\dot{s}(t)| \leq 2M$, which holds for all $t \geq T_f$, we deduce, for all $t \geq T_f + \tau_M$, that

$$\left| \frac{\partial U}{\partial x_i} r_i \right| \leq 2M\tau_M \left(\frac{s_*}{a_i} + 3 \right) \frac{m_i}{a_i} x_i(t) .$$

Consequently,

$$\sum_{i=2}^n \frac{\partial U}{\partial x_i} r_i \leq 2M\tau_M \sum_{i=2}^n \left(\frac{s_*}{a_i} + 3 \right) \frac{m_i}{a_i} x_i(t) .$$

Inequality (20) ensures that

$$\tau_M \leq \frac{c}{8M \max_{i=2, \dots, n} \left\{ \left(\frac{s_*}{a_i} + 3 \right) \frac{m_i}{a_i} \right\}} ,$$

and hence

$$\sum_{i=2}^n \frac{\partial U}{\partial x_i} r_i \leq \frac{c}{4} \sum_{i=2}^n x_i(t) \leq \frac{1}{4} W_2(\tilde{s}, \tilde{x}_1, \xi). \tag{25}$$

Combining (22), (24), and (25), we obtain that, for all $t \geq T_f + \tau_M$,

$$\dot{U} \leq -\frac{1}{2} W_2 + \frac{2m_1^2}{a_1^2 D} \left(3 + \frac{s_*}{a_1}\right)^2 |s(t - \tau_1) - s(t)|^2. \tag{26}$$

Recalling the Cauchy-Schwarz's inequality

$$\left(\int_a^b f(l)g(l)dl\right)^2 \leq \left(\int_a^b f(l)^2 dl\right) \left(\int_a^b g(l)^2 dl\right), \tag{27}$$

for all a, b such that $b \geq a$ and for all continuous functions f, g , we deduce

$$|s(t - \tau_1) - s(t)|^2 = \left|\int_{t-\tau_1}^t \dot{s}(l)dl\right|^2 \leq \tau_1 \int_{t-\tau_1}^t \dot{s}(l)^2 dl. \tag{28}$$

On the other hand, observe that, for all $t \geq T_f + \tau_M$,

$$|\dot{\tilde{s}}| = \left| D\tilde{s} + (\mu_1(s) - \mu_1(s_*))x_{1*} + \mu_1(s)\tilde{x}_1 + \sum_{i=2}^n \mu_i(s)x_i \right|.$$

Using the equalities $\tilde{x}_1 = \tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i - \tilde{s} - \sum_{i=2}^n x_i$, $\mu_1(s_*) = D$, and the triangular inequality, we obtain, for all $t \geq T_f + \tau_M$,

$$\begin{aligned} |\dot{\tilde{s}}| &\leq \left| \delta(s)(\tilde{s} - x_{1*}) + \mu_1(s) \left(\tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right) + \sum_{i=2}^n (\mu_i(s) - \mu_1(s))x_i \right| \\ &\leq |\delta(s)| |\tilde{s} - x_{1*}| + \mu_1(s) \left| \tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right| + \sum_{i=2}^n |\mu_i(s) - \mu_1(s)| x_i, \end{aligned}$$

with $\delta(s) = \mu_1(s_*) - \mu_1(s)$. Using again the fact that for all $t \geq T_f$ one has $0 \leq s(t) < 1$, and $\sum_{i=1}^n x_i(t) \leq 2$, which in particular implies that $|\tilde{s} - x_{1*}| = |s - 1| \leq 1$, and recalling that the inequality $|\mu_1(a) - \mu_1(b)| \leq \frac{M}{a_1} |a - b|$ is satisfied for all $a, b \geq 0$, one obtains

$$|\dot{\tilde{s}}| \leq M \left(\frac{1}{a_1} |\tilde{s}| + \left| \tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right| + 2\sqrt{2} \sqrt{\sum_{i=2}^n x_i} \right) \quad \forall t \geq T_f.$$

It follows that, for all $t \geq T_f$,

$$\begin{aligned} \dot{\tilde{s}}^2 &\leq 16M^2 \left(\frac{1}{a_1^2} \tilde{s}^2 + \left(\tilde{s} + \tilde{x}_1 + \sum_{i=2}^n x_i \right)^2 + \left(\sum_{i=2}^n x_i \right) \right) \\ &\leq C_1 W_2(\tilde{s}, \tilde{x}_1, \xi) \end{aligned} \tag{29}$$

where

$$C_1 = 16M^2 \max \left\{ \frac{1}{Da_1^2}, \frac{1}{c}, \frac{1}{D} \right\} .$$

From (26), (28), (29), we deduce that, for all $t \geq T_f + \tau_M$, we have

$$\dot{U} \leq -\frac{1}{2}W_2(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) + \tau_M C_2 \int_{t-\tau_1}^t W_2(\tilde{s}(l), \tilde{x}_1(l), \xi(l))dl$$

with

$$C_2 = \frac{2m_1^2}{a_1^2 D} \left(3 + \frac{s_*}{a_1} \right)^2 C_1 .$$

This leads us to consider the functional

$$U_f(\tilde{s}_t, \tilde{x}_{1t}, \xi_t) = U(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) + \tau_M C_2 \int_{t-\tau_M}^t \left(\int_r^t W_2(\tilde{s}(l), \tilde{x}_1(l), \xi(l))dl \right) dr .$$

Its derivative along the trajectories of (21) satisfies, for all $t \geq T_f + \tau_M$,

$$\begin{aligned} \dot{U}_f &\leq -\frac{1}{2}W_2(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) + \tau_M C_2 \int_{t-\tau_1}^t W_2(\tilde{s}(l), \tilde{x}_1(l), \xi(l))dl \\ &\quad + \tau_M^2 C_2 W_2(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) - \tau_M C_2 \int_{t-\tau_1}^t W_2(\tilde{s}(l), \tilde{x}_1(l), \xi(l))dl \\ &\leq \left(-\frac{1}{2} + \tau_M^2 C_2 \right) W_2(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) . \end{aligned}$$

One can easily check that (20) implies $\tau_M \leq \frac{1}{2\sqrt{C_2}}$ and therefore, for all $t \geq T_f + \tau_M$,

$$\dot{U}_f \leq -\frac{1}{4}W_2(\tilde{s}(t), \tilde{x}_1(t), \xi(t)) .$$

This inequality and the boundedness of the trajectories ensure that $(\tilde{s}(t), \tilde{x}_1(t), \xi(t))$ goes to the origin. The local exponential stability is obtained by analyzing the linear approximation at the equilibrium point $E_* = (s_*, x_{1*}, 0, \dots, 0)$ of (21). \square

5 Numerical Simulations

In this section we present some numerical simulations. We consider two species with Monod uptake functions $\mu_i(s) = \frac{m_i s}{a_i + s}$. For each figure, concentrations of substrate (s), species 1 (x_1), and species 2 (x_2) are drawn with solid or continuous lines (-), dashed lines (--), and crosses (xx), respectively.

Example 1. Letting $D = 1$, $m_1 = 2$, $a_1 = 3$, $m_2 = 3$, $a_2 = 7$, $\tau_1 = 0.001$, $\tau_2 = 0.002$, we obtain $A_0 = 0.1823$, $A_1 = 0.0435$, $A_2 = 0.0047$, $A_3 = 0.0031$, $A_4 = 0.0503$, and consequently $\tau_M = \max_i \tau_i = 0.002$ and $\min_i A_i = 0.0031$. These values satisfy inequality (20) of Theorem 3, but we have that $\lambda_1 = 3$ and $\lambda_2 = 3.5$ because Assumption H2 does not hold (indeed $\mu_1(D) =$

0.5 and $\mu_2(D) = 0.375$). This configuration of parameters leads to a *wash-out* equilibrium $(s_*, x_{1*}, x_{2*}) = (1, 0, 0)$ as we see in this first simulation (see Fig. 1).

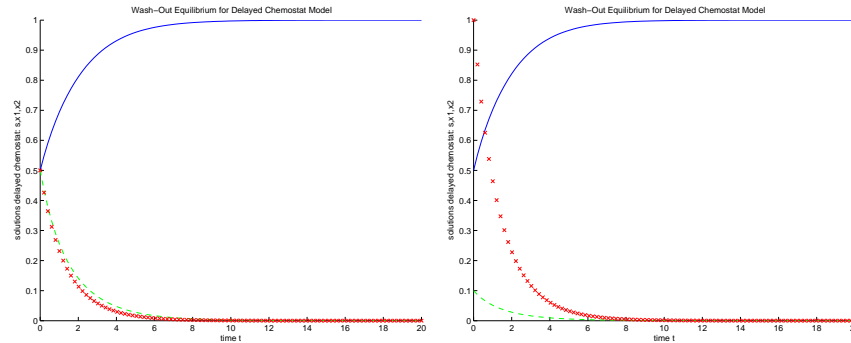


Figure 1: Numerical simulations of Example 1; Wash-out equilibrium. Initial data: (Left) $s(t) = x_1(t) = x_2(t) = 0.5$; (Right) $s(t) = 0.2$, $x_1(t) = 1$, $x_2(t) = 0.1$, for all $t \in [-\tau_M, 0]$.

Example 2. Letting $D = 1$, $m_1 = 3.8$, $a_1 = 1.2$, $m_2 = 7$, $a_2 = 5.5$, $\tau_1 = 0.001$, $\tau_2 = 0.0002$, we obtain $A_0 = 0.1823$, $A_1 = 0.0061$, $A_2 = 0.0015$, $A_3 = 0.0022$, $A_4 = 0.0205$, and consequently $\tau_M = \max_i \tau_i = 0.001$ and $\min_i A_i = 0.0015$. These values satisfy inequality (20) of Theorem 3. Since $\lambda_1 = 0.4286$ and $\lambda_2 = 0.9167$, Assumptions H2 and H3 also hold. Then the Competitive Exclusion Principle implies that the equilibrium $(s_*, x_{1*}, x_{2*}) = (0.4286, 0.5714, 0)$ is globally asymptotically stable as we see in our second simulation (see Fig. 2)

Example 3. We use the same parameters as in Example 2 except we choose $\tau_1 = 10$ and $\tau_2 = 20$. Hence $\tau_M = \max_i \tau_i = 20$ and inequality (20) of Theorem 3 is no longer satisfied. We can see in our simulations that the solution of delayed chemostat model (13) does not converge to the equilibrium (s_*, x_{1*}, x_{2*}) given in Example 2 (see Fig. 3). In this case, concentration of species 1 (x_1) and of substrate (s) oscillate, while the species 2 (x_2) disappears.

Example 4. In this example we use the parameters of the example given in Freedman et al. [7], that is, $D = 1$, $m_1 = 3.1$, $a_1 = 1$, $m_2 = 3.09$, $a_2 = 1$. For these values we obtain $\lambda_1 = 0.4762$ and $\lambda_2 = 0.4785$, thus Assumptions H2 and H3 hold. We also obtain $A_0 = 0.1823$, $A_1 = 0.0404$, $A_2 = 2.1047 \cdot 10^{-5}$, $A_3 = 1.0558 \cdot 10^{-5}$, $A_4 = 0.0016$, and consequently $\min_i A_i = 1.0558 \cdot 10^{-5}$. Even when this last value is very small, (then inequality (20)

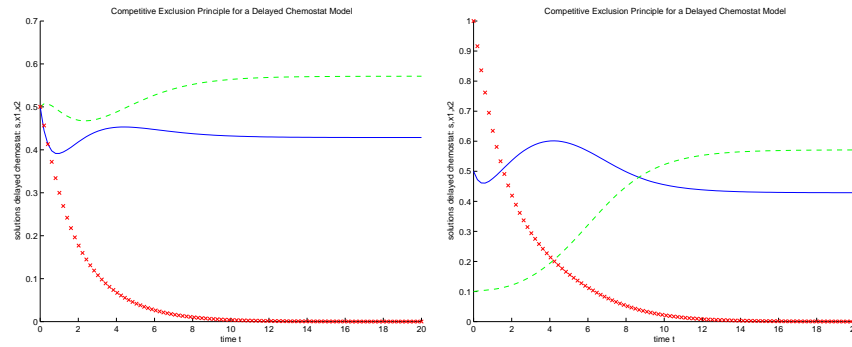


Figure 2: Numerical simulations of Example 2; Competitive Exclusion Principle. Initial data: (Left) $s(t) = x_1(t) = x_2(t) = 0.5$. (Right) $s(t) = 0.2, x_1(t) = 1, x_2(t) = 0.1$, for all $t \in [-\tau_M, 0]$.

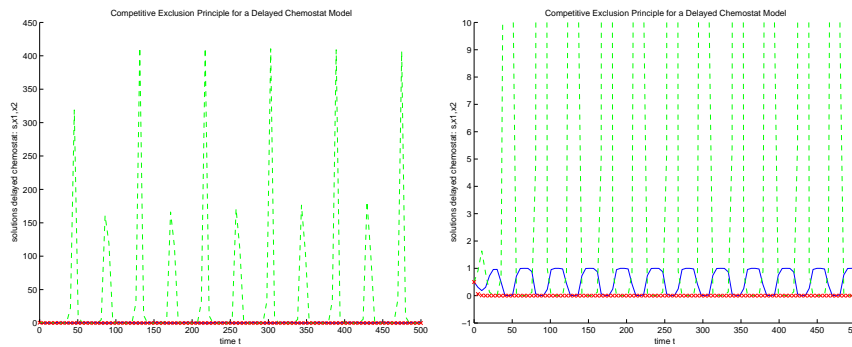


Figure 3: Numerical simulations of Example 3; Conclusions of Theorem 3 are no longer true. Initial data: $s(t) = x_1(t) = x_2(t) = 0.5$, for all $t \in [-\tau_M, 0]$. (Left) axis $Y \in [0, 450]$; (Right) Zoom: axis $Y \in [-1, 10]$.

of Theorem 3 only allows for small values of the time delays τ_1 and τ_2), our simulations (see Fig. 4(Left)) show that the Competitive Exclusion Principle hold for larger time delays, such as $\tau_1 = 0.1$ and $\tau_2 = 0.2$. In this case the equilibrium $(s_*, x_{1*}, x_{2*}) = (0.4762, 0.5238, 0)$ is globally asymptotically stable. However, when the time delays are $\tau_1 = 3$ and $\tau_2 = 4$, we recover the example of [7] showing that the coexistence between the two species is possible (see Fig. 4(Right)).

6 Discussion

In this paper, for a chemostat model under the Monod hypothesis on the uptake functions, we have determined an explicit expression of a constant

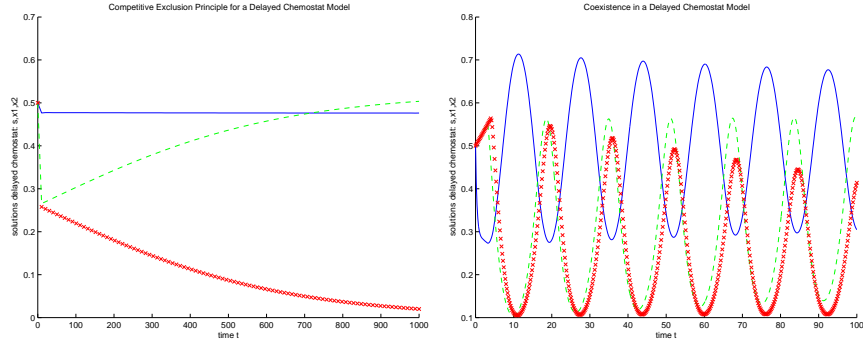


Figure 4: Numerical simulations of Example 4; Competitive Exclusion Principle and coexistence. Initial data: $s(t) = x_1(t) = x_2(t) = 0.5$, for all $t \in [-\tau_M, 0]$. (Left) $\tau_1 = 0.1$ and $\tau_2 = 0.2$; (Right) $\tau_1 = 3$ and $\tau_2 = 4$.

ensuring that the prediction of the Competitive Exclusion Principle is valid when the delays are smaller than it. To establish this result, we have constructed a Lyapunov-Krasovskii functional.

Through intricate calculations, one can obtain a better estimate of the largest size the delays can have without changing the stability properties of the system. Indeed, some of our simulations (see for instance Example 4) suggest that the global asymptotic stability result of Theorem 3 holds even for time delays τ_i that do not satisfy inequality (20). However, for the sake of clarity, we have chosen to establish our result with an upper bound for the delays which leads to reasonably simple proofs. Observe that the result of [7] guarantees that there exists of a critical value $\tau_0 > 0$ such that for delays larger then this value, the system is neither globally nor locally asymptotically stable (see Example 4).

We summarize our main result for the general delayed chemostat model where no change of variables is made. Recall that in this case, the model is given by

$$\begin{cases} \dot{s} &= D(s_{in} - s) - \sum_{i=1}^n \frac{\mu_i(s)}{Y_i} x_i, \\ \dot{x}_1 &= [\mu_1(s(t - \tau_1)) - D]x_1, \\ &\vdots \\ \dot{x}_n &= [\mu_n(s(t - \tau_n)) - D]x_n, \end{cases} \quad (30)$$

where the uptake functions μ_i follow a Monod law (see Assumption H1). Hence, we have proven that if the maximal delay $\tau_M = \max_{i=1, \dots, n} \tau_i$ satisfies

$$\tau_M \leq \min_{j=0,1,2,3,4} A_j \text{ with}$$

$$\begin{aligned}
A_0 &= \frac{1}{D} \ln \left(\frac{6}{5} \right), \\
A_1 &= \frac{1}{M-D} \ln \left(\frac{4M}{4M-D} \right), \\
A_2 &= \frac{a_1^2 c}{8s_{in}(a_1+s_{in})m_1 M}, \\
A_3 &= \frac{c}{8M \max_{i=2,\dots,n} \left\{ \left(\frac{s_{in}}{a_i} + 3 \right) \frac{s_{in} m_i}{a_i} \right\}}, \\
A_4 &= \frac{a_1^2 D}{2\sqrt{2}m_1 s_{in}(3a_1+s_{in}) \max \left\{ 1, \frac{s_{in}}{a_1}, \frac{\sqrt{D}}{\sqrt{c}} \right\}},
\end{aligned}$$

then the point $(s_*, x_{1*}, 0, \dots, 0)$ is a globally asymptotically and a locally exponentially stable equilibrium point of (30). Here $s^* \in (0, s_{in})$ is such that $\mu_1(s^*) = D$, and $x_{1*} = s_{in} - s^*$. Constants c and M are redefined to be

$$c := \min_{i=2,\dots,n} D - \mu_i(s_*), \quad M := \max_{i=2,\dots,n} m_i.$$

Notice that $c > 0$ provided that Assumptions H1-H3 hold.

In future works, we expect to exploit the construction of our Lyapunov-Krasovskii functional for investigating other issues on delayed chemostat model with several species, such as robustness with respect to the uptake functions or other parameters of the model (such as s_{in} , D), and robustness with respect to distributed delays.

References

- [1] R. BELLMAN AND K. L. COOKE. *Differential-Difference Equations*. Academic Press, New York, 1963.
- [2] E. BERETTA AND Y. KUANG. *Global stability in a well known delayed chemostat model*, Communications in Applied Analysis, 4, 147–155, 2000.
- [3] A. W. BUSH AND A. E. COOK. *The effect of time delay and growth rate inhibition in the bacterial treatment of wastewater*, J. Theoret. Biol. 63, 385–395, 1975.
- [4] G.J. BUTLER, S.B. HSU AND P. WALTMAN. *A mathematical model of the chemostat with periodic washout rate*. SIAM Journal on Applied Mathematics, vol. 45, pp 435–449, 1985.
- [5] J. CAPERON. *Time lag in population growth response of dsochryis galana to a variable nitrate environment*, Ecology, 50, pp. 188–192, 1969.
- [6] P. DE LEENHEER AND H.L. SMITH. *Feedback control for chemostat models*. Journal of Mathematical Biology, vol. 46, pp. 48–70, 2003.
- [7] H.I. FREEDMAN, J. SO, P. WALTMAN *Coexistence in a model of competition in the chemostat incorporating discrete delays*. SIAM J. Appl. Math., Vol. 49, No.3, pp. 859–870, June 1989.

- [8] J.K. HALE AND S.M.V. LUNEL. Introduction to Functional Differential Equations. *New York: Springer-Verlag, vol. 99, Applied Math. Sciences*, 1993.
- [9] S.B. HSU. *Limiting behavior for competing species*. SIAM Journal on Applied Mathematics, 34: 760-763, 1978.
- [10] I. KARAFYLLIS. *Lyapunov Theorems for Systems Described by Retarded Functional Differential Equations*. Nonlinear Analysis: Theory, Methods and Applications, 64(3), 590-617, 2006.
- [11] V.L. KHARITONOV, S.I. NICULESCU. *On the Stability of Linear Systems With Uncertain Delay*. IEEE Trans. on Automatic Control, Vol.48, No.1, pp.127-132, January 2003.
- [12] N.N. KRASOVSKII. Stability of Motion. *Stanford, CA: Stanford Univ. Press*, 1963.
- [13] F. MAZENC, P.A. BLIMAN. *Backstepping Design for Time-Delay Nonlinear Systems*. IEEE Trans. on Automatic Control, Vol.51, No.1, pp.149-154, January 2006.
- [14] J. MONOD. *La technique de culture continue. Théorie et applications*. Ann. Inst. Pasteur Paris 79, pp. 390-410, 1950.
- [15] A. NOVICK, L. SZILARD. *Description of the chemostat*. Science 112, pp. 715-716, 1950.
- [16] H.L. SMITH AND P. WALTMAN. The Theory of the Chemostat. *Cambridge University Press*, 1995.
- [17] C.C. SPICER. The Theory of bacterial constant growth apparatus. *Biometrics*, 1955.
- [18] L. WANG AND G. S. K. WOLKOWICZ. *A delayed chemostat model with general non-monotone response functions and differential removal rates*, J. Math. Anal. Appl. 321, no. 1, 452-468, 2006.
- [19] G. S. K. WOLKOWICZ AND H. XIA. *Global asymptotic behavior of a chemostat model with discrete delays*, SIAM J. Appl. Math. 57, no. 4, 1019-1043, 1997.
- [20] Y. HE, M. WU, J.-H. SHE, AND G.-P. LIU. *Parameter-Dependent Lyapunov Functional for Stability of Time-Delay Systems With Polytopic-Type Uncertainties*. IEEE Trans. on Automatic Control, Vol.49, No.5, pp.828-832, May 2004.

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