Generalization of the Concept for Biological Control in the Chemostat*

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Abstract: The present paper is devoted to the concept of the so called biological control of the chemostat, recently proposed by A. Rappaport and J. Harmand (2008). This concept is based on the competitive exclusion principle for a dynamic model describing competition between species with general (nonmonotone) response functions and distinct removal rates. Here we present a generalization of this concept, aimed to extend the applicability of the biological control. This is demonstrated numerically on particular examples.

Key-Words: chemostat model, competitive exclusion principle, global stability, biological control

1 Introduction

The coexistence of species in competition on a single resource is a subject of investigation by specialists in different fields – molecular biology, microbial ecology, biotechnology, as well as biomathematics, see e. g. [20], [24], [25] and the references therein. The interest in this topic is due to the observation that if two or more species in some environment compete for a single resource, only one species eventually survives – this is the species that possesses the best affinity to the substrate. This observation has been conceptualized by Gause [10] and formalized by Hardin [13] as the Competitive Exclusion Principle (CEP). CEP was experimentally confirmed in laboratory conditions (in a chemostat) by Hansen and Hubbell [12]. Recently there is a large number of papers devoted to modeling and investigating competition problems in the chemostat. The objective is to establish conditions for global stability of the dynamics. Some recent results in this topic are presented below.

A. Rapaport and J. Harmand proposed in [21] a new way of controlling an unstable biosystem model through adding new species in the chemostat with particular characteristics to globally stabilize the system towards the desired outcome. In section 2 we propose more general assumptions under which the concept of the biological control remains valid. Numerical examples demonstrating the advantages of our result are reported in section 3.

The competition dynamics in a chemostat is described by the following model

$$\begin{aligned} \dot{s} &= (s_0 - s)D - \sum_{i=1}^{n} \mu_i(s)x_i \\ \dot{x}_i &= (\mu_i(s) - D_i)x_i, \quad i = 1, 2, \ldots, n; \\ & \quad s(0) \geq 0, \quad x_i(0) > 0, \end{aligned} \tag{1}$$

where s_0 and s are the input and the substrate concentrations respectively, D is the dilution rate of the chemostat, x_i are the concentrations of the microorganisms with response (growth rate) functions $\mu_i(s)$ and removal rates D_i, $i = 1, 2, \ldots, n$.

Let the following assumptions be fulfilled.

Assumption A1. For $i = 1, 2, \ldots, n$, the functions $\mu_i(s)$ are nonnegative with $\mu_i(0) = 0$, and Lipschitz continuous.

Assumption A2. There exist unique, positive real numbers α_i and β_i with $\alpha_i < \beta_i$ (β_i possibly equal to $+\infty$) such that

$$\mu_i(s) \begin{cases} < D_i, & \text{if } s \notin [\alpha_i, \beta_i] \\ > D_i & \text{if } s \in (\alpha_i, \beta_i) \end{cases}, \quad i = 1, 2, \ldots, n.$$

The numbers α_i and β_i are the solutions of $\mu_i(s) = D_i$, called also break-even concentrations [24]. If $\mu_i(s)$ is a monotone increasing function (like the Monod law), then we set $\beta_i = +\infty$.

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The equilibrium solutions $(s, x_1, x_2, \dots, x_n)$ of the model are of the form

$$\begin{aligned} E_0 &= (s_0, 0, 0, \dots, 0) \\ E_i &= \left(\alpha_i, 0, \dots, 0, \frac{D(s_0-\alpha_i)}{D_i}, 0, \dots, 0\right) \\ F_i &= \left(\beta_i, 0, \dots, 0, \frac{D(s_0-\beta_i)}{D_i}, 0, \dots, 0\right), \\ i &= 1, 2, \dots, n; \end{aligned}$$

all components of E_i (F_i) are equal to zero except for the first and the $(i+1)$-st, which are $s = \alpha_i$ ($s = \beta_i$) and $x_i = \dfrac{D(s_0-\alpha_i)}{D_i}$ $\left(x_i = \dfrac{D(s_0-\beta_i)}{D_i}\right)$. The equilibrium E_i (F_i) exists for all $i = 1, 2, \dots, n$, such that $\alpha_i < s_0$ ($\beta_i < s_0$). If $\mu_i(s)$ is monotone increasing then the equilibrium F_i does not exist. Moreover, the equilibrium F_i is not stable if it exists (see [24]).

There are lot of papers devoted to stability analysis of the model (1). The main objective is to give sufficient conditions for global asymptotic stability of the equilibrium points. A survey of results is presented in [24], see also [3], [15], [17], [27], [28] and the references therein. It is shown that under certain conditions every solution converges to one of the above equilibrium points. In particular, since at most one population has a nonzero component at equilibrium, no more than one population can survive. If $s_0 < \alpha_1$, then E_0 is the global attractor.

The most general result (to our knowledge) in the case of different removal rates $D_i \neq D_j$, $i \neq j$ and $D \neq D_i$ is given by B. Li in [17]. Different removal rates typically appear in chemostats with output membranes that remove the biomass selectively, depending on the size of the microorganisms. The usual assumption is $D_i < D$. When however the mortality of a species is predominant, one may consider $D_i > D$.

Theorem 1 (cf. [17]). Assume that

$$\alpha_1 < \alpha_2 \le \alpha_3 \le \dots \le \alpha_n.$$

If $\alpha_1 < s_0 < \beta_1$ and

$$\frac{Ds^0}{\min(D, D_1, \dots, D_n)} - \frac{Ds^0}{\max(D, D_1, \dots, D_n)} < \alpha_2 - \alpha_1$$

are fulfilled then all solutions of (1) satisfy $\lim_{t\to+\infty}(s(t), x_1(t), \dots, x_n(t)) = E_1$. □

Biological control of the chemostat. Based on CEP, the original concept of the so called biological control of the chemostat has been recently developed by A. Rapaport and J. Harmand in [21]. More precisely, consider (1) for $n = 1$:

$$\begin{aligned} \dot{s} &= (s_0 - s)D - \mu_1(s)x_1 \\ \dot{x}_1 &= (\mu_1(s) - D_1)x_1 \\ & \quad s(0) \ge 0, \;\; x_1(0) > 0. \end{aligned} \tag{2}$$

Assume that the response function $\mu_1(s)$ is not monotone (such as the Haldane law). Let α_1 and β_1 be defined as in Assumption A2 with $\beta_1 < s_0$. Then it is well known that the dynamics (2) possesses two locally stable equilibrium points, the wash-out steady state $E_0 = (s_0, 0)$ and the positive steady state $E_1 = \left(\alpha_1, \dfrac{D(s_0-\alpha_1)}{D_1}\right)$ (see e. g. [3], [24], [28]): from some initial conditions the dilution rate can lead to wash-out (extinction) of the biomass and breaking-down of the process.

Different control strategies are known in the literature, cf. [1], [4]–[9], [16], [18], [19], [22], [23], [26], aimed to globally stabilize a given system to a desired state. The new approach in [21] is the so called biological control; it is based on the idea of introducing additional species x_2 in the chemostat to globally asymptotically stabilize (2) to the equilibrium E_1. Below we present the main result of [21] (see also [14]).

Consider the model (1) with two populations

$$\begin{aligned} \dot{s} &= (s_0 - s)D - \mu_1(s)x_1 - \mu_2(s)x_2 \\ \dot{x}_1 &= (\mu_1(s) - D_1)x_1 \\ \dot{x}_2 &= (\mu_2(s) - D_2)x_2 \\ & \quad s(0) \ge 0, \;\; x_1(0) > 0, \;\; x_2(0) > 0 \end{aligned} \tag{3}$$

and nonmonotone response functions $\mu_1(s)$ and $\mu_2(s)$. With $d \in \{D, D_1, D_2\}$ define the sets

$$(\alpha_i(d), \beta_i(d)) = \{s \ge 0 : \; \mu_i(s) > d\};$$

in particular, denote $\alpha_i = \alpha_i(D_i)$, $\beta_i = \beta_i(D_i)$, $i = 1, 2$.

Assumption A3. The sets $(\alpha_i, \; \beta_i)$, $(\alpha_i(D), \beta_i(D))$, $i = 1, 2$, are intervals, where β_i and/or $\beta_i(D)$ is possibly equal to $+\infty$.

Denote for convenience

$$\begin{aligned} & D_{\max} = \max\{D, D_1, D_2\}, \\ & D_{\min} = \min\{D, D_1, D_2\}, \\ & s_0^{\min} = \frac{s_0 D}{D_{\max}}, \;\; s_0^{\max} = \frac{s_0 D}{D_{\min}}. \end{aligned} \tag{4}$$

Let $\overline{D}_i = \max(D, D_i)$, $i = 1, 2$.

Assumption A4. Let the following inequalities be fulfilled: $\beta_1 \le s_0^{\min}$, $\alpha_1(\overline{D}_1) < \alpha_2(\overline{D}_2) < \beta_1(\overline{D}_1)$ and $s_0 < \beta_2(\overline{D}_2)$.

Define the point

$$\bar{s} \;=\; \min\left\{s \in \left(\alpha_2(\overline{D}_2), \beta_1(\overline{D}_1)\right) : \mu_1(s) - \overline{D}_1 = \mu_2(s) - \overline{D}_2\right\}.$$

Assumption A5. Let the following inequality be fulfilled:

$$\mu_1(\bar{s}) - \overline{D}_1 = \mu_2(\bar{s}) - \overline{D}_2 > \frac{s_0 - s_0^{\min}}{s_0^{\min} - \bar{s}} \cdot D.$$

Theorem 2 (cf. [21]). Let the assumptions A1 (with $n = 2$) to A5 be fulfilled. If

$$s_0^{\max} - s_0^{\min} < \alpha_2 - \alpha_1,$$

then any solution of (3) converges asymptotically towards $E^* = (\alpha_1, x_1^*, 0)$ with $x_1^* = \dfrac{D(s_0 - \alpha_1)}{D_1}$. □

In the next section 2 we propose a generalization of Theorem 2.

2 Generalization of the Biological Control Concept

Consider the model (3) including two populations with concentrations x_1 and x_2, which compete for a single substrate s. For better readability we rewrite Assumption A1 for the case $n = 2$ as Assumption B1:

Assumption B1. The functions $\mu_i(s)$, $i = 1, 2$, are nonnegative with $\mu_i(0) = 0$, and Lipschitz continuous.

Assumption B2. There exist unique positive real numbers α_i, β_i, $i = 1, 2$, with

$$\alpha_1 < \alpha_2 < \beta_1 < s_0 < \beta_2$$

(β_2 possibly equal to $+\infty$) such that

$$\mu_i(s) \begin{cases} < D_i, & \text{if } s \notin [\alpha_i, \beta_i] \\ > D_i & \text{if } s \in (\alpha_i, \beta_i) \end{cases} \quad i = 1, 2.$$

Define the function

$$H(s) = (s_0 - s)D - \min\{\mu_1(s),\, \mu_2(s)\} \cdot (s_0^{\min} - s). \tag{5}$$

Assumption B3. There exists points s_1, s_2 with $s_1 < s_2$ and $[s_1, s_2] \subset (\alpha_2, \beta_1]$ such that $H(s) < 0$ for all $s \in (s_1, s_2)$.

In the proof of our main result we shall use the following Lemmata.

Barbălat's Lemma (cf. [11]). If $f : (0, \infty) \to R$ is Riemann integrable and uniformly continuous, then $\lim\limits_{t\to\infty} f(t) = 0$. □

Lemma 1 (cf. [27]). Let the Assumptions B1 and B2 be satisfied. Then $s(t) < s_0$ for all sufficiently large $t > 0$. □

Lemma 2 (cf. [28]). Let the Assumption B1 be satisfied. Then for any $\varepsilon > 0$, the solutions $s(t)$, $x_1(t)$, $x_2(t)$ of (3) satisfy $s_0^{\min} - \varepsilon < s(t) + x_1(t) + x_2(t) < s_0^{\max} + \varepsilon$ for all sufficiently large $t > 0$. □

The next Theorem 3 presents the main result of the paper.

Theorem 3. Let Assumptions B1, B2 and B3 be fulfilled. Then any solution of (3) converges asymptotically towards $E^* = (\alpha_1, x_1^*, 0)$, with $x_1^* = \dfrac{D(s_0 - \alpha_1)}{D_1}$.

Proof. Let $(s(\cdot), x_1(\cdot), x_2(\cdot))$ be a trajectory of the system (3) starting from the point $(s(0), x_1(0), x_2(0)) \geq 0$. Then Lemma 1 and Lemma 2 imply that there exists a sufficiently large time $T_1 > 0$, so that for each $t \geq T_1$ the inequalities $s(t) < s_0$ and $s_0^{\min} - s(t) - \sum_{i=1}^{2} x_i(t) < \varepsilon$ hold true.

Assume that $s(t) \geq \alpha_2$ for all $t \geq T_1$. The derivative $\dot{x}_2(t)$ of $x_2(t)$ is uniformly continuous (because $\mu_2(\cdot)$ and $x_2(\cdot)$ are bounded and Lipschitz continuous) and Riemann integrable. Clearly, $\dot{x}_2(\cdot) \geq 0$ whenever $s \in [\alpha_2, s_0)$, and so $x_2(t) \geq x_2(T_1) > 0$ for $t \geq T_1$. Applying Barbălat's Lemma, we obtain $\lim_{t\to\infty} \mu_2(s(t)) = D_2$. According to Assumption B2, α_2 is the unique point from the interval $[\alpha_2, s_0)$ such that $\mu_2(s) = D_2$; therefore $\lim_{t\to\infty} s(t) = \alpha_2$. This means that for each positive integer n there exists $T_n > 0$ such that $s(t) \in [\alpha_2, \alpha_2 + 1/n]$ for each $t \geq T_n$. Since $\mu_1(\alpha_2) - D_1 = \eta > 0$ there exists a positive integer n such that $\mu_1(s) - D_1 \geq \eta/2$ for each $s \in [\alpha_2, \alpha_2 + 1/n]$. Therefore, for each $t \geq T_n$ we have

$$\frac{d}{dt} x_1(t) \geq \frac{\eta}{2} x_1(t),$$

and hence

$$x_1(t) \geq x_1(T_n)\, \exp\left(\frac{\eta}{2} t\right) \to +\infty \text{ as } t \to +\infty.$$

But this is impossible because $x_1(\cdot)$ is bounded. Hence, there exists time $T_2 > T_1$ such that $s(T_2) < \alpha_2$.

Consider the function $H(s)$ from (5). Let us fix a sufficiently small $\varepsilon > 0$ and choose a point $\hat{s} \in (s_1, s_2)$, such that

$$(s_0 - \hat{s})D < (s_0^{\min} - \hat{s} - \varepsilon) \min\{\mu_1(\hat{s}), \mu_2(\hat{s})\}. \tag{6}$$

Assume that there exists $\hat{t} \ge T_2$ with $s(\hat{t}) = \hat{s}$; set $\hat{x}_1 = x_1(\hat{t})$ and $\hat{x}_2 = x_2(\hat{t})$. Then using Lemma 2 and (6) we obtain

$$\begin{aligned}
\dot{s}(\hat{t}) &= D(s_0 - s(\hat{t})) - \mu_1(s(\hat{t}))x_1(\hat{t}) - \mu_2(s(\hat{t}))x_2(\hat{t}) \\
&= D(s_0^{\min} - \hat{s} - \hat{x}_1 - \hat{x}_2) + D(s_0 - s_0^{\min}) \\
&\quad - (\mu_1(\hat{s}) - D)\hat{x}_1 - (\mu_2(\hat{s}) - D)\hat{x}_2 \\
&< D\varepsilon + D(s_0 - s_0^{\min}) - (\hat{x}_1 + \hat{x}_2) \\
&\quad \times \left(\frac{\hat{x}_1}{\hat{x}_1 + \hat{x}_2}(\mu_1(\hat{s}) - D) + \frac{\hat{x}_2}{\hat{x}_1 + \hat{x}_2}(\mu_2(\hat{s}) - D) \right) \\
&\le D\varepsilon + D(s_0 - s_0^{\min}) \\
&\quad - (\hat{x}_1 + \hat{x}_2) \min\{(\mu_1(\hat{s}) - D), (\mu_2(\hat{s}) - D)\} \\
&< (s_0 - \hat{s})D - (s_0^{\min} - \hat{s} - \varepsilon) \min\{\mu_1(\hat{s}), \mu_2(\hat{s})\} < 0.
\end{aligned}$$

The last inequality implies that $s(t) \le \hat{s}$ for all $t \ge T_2$.

Further we shall show that $\lim_{t\to\infty} x_2(t) = 0$. Since $\dot{x}_2(t)$ is uniformly continuous and Riemann integrable, Barbălat's Lemma implies

$$\lim_{t\to\infty} [x_2(t)(\mu_2(s(t)) - D_2)] = 0,$$

which is fulfilled if $\lim_{t\to\infty} x_2(t) = 0$ or $\lim_{t\to\infty}(\mu_2(s(t)) - D_2) = 0$. According to Assumption B2, the equality $\mu_2(s) - D_2 = 0$ is satisfied when $s = \alpha_2$; this means $\lim_{t\to\infty} s(t) = \alpha_2$. Then for any positive integer m there exists time T_m such that $s(t) \in (\alpha_2 - 1/m, \alpha_2 + 1/m)$ for each $t \ge T_m$. But we have $\mu_1(\alpha_2) - D_1 = \eta_1 > 0$, thus there exists $m > 0$ such that $\mu_1(s) - D_1 \ge \eta_1/2$ for all $s \in (\alpha_2 - 1/m, \alpha_2 + 1/m)$. This means that for all $t \ge T_m$, $\dot{x}_1(t) \ge (\eta_1/2)x_1(t)$ and therefore $\lim_{t\to\infty} x_1(t) = +\infty$, a contradiction with the boundedness of $x_1(t)$. Therefore

$$\lim_{t\to\infty} x_2(t) = 0.$$

Then the trajectory $(s(\cdot), x_1(\cdot), x_2(\cdot))$ of (3) starting from the point $(s(0), x_1(0), x_2(0))$ approaches the set

$$\mathcal{L}_\infty = \{(s, x_1, x_2) :\ s \ge 0,\ x_1 \ge 0,\ x_2 = 0\}.$$

The dynamics of (3) on the set $\mathcal{L}_\infty$ is described by the system

$$\begin{aligned}
\dot{s} &= (s_0 - s)D - \mu_1(s)x_1, \quad s(0) \ge 0, \\
\dot{x}_1 &= (\mu_1(s) - D_1)x_i, \quad x_1(0) > 0, \qquad (7) \\
\dot{x}_2 &= 0, \quad x_2(0) = 0.
\end{aligned}$$

Following [15], we define the function

$$V(s, x_1, x_2) = \int_{\alpha_1}^{s} Q(\xi)\, d\xi + \int_{x_1^*}^{x_1} \frac{\zeta - x_1^*}{\zeta}\, d\zeta,$$

where

$$Q(s) := \frac{(\mu_1(s) - D_1)(s_0 - \alpha_1)}{D_1(s_0 - s)} = \frac{(\mu_1(s) - D_1)x_1^*}{D(s_0 - s)}.$$

The Lie derivative of V with respect to the trajectories of the system (7) is

$$\begin{aligned}
\dot{V}(s, x_1, x_2) = &\ Q(s)[D(s_0 - s) - \mu_1(s)x_1] \\
+ &\ \frac{x_1 - x_1^*}{x_1}(\mu_1(s) - D_1)x_1 \\
= &\ [Q(s)D(s_0 - s) - (\mu_1(s) - D_1)x_1^*] \\
+ &\ (\mu_1(s) - D_1)x_1 \left[1 - \frac{Q(s)\mu_1(s)}{\mu_1(s) - D_1}\right].
\end{aligned}$$

The first term is zero according to the choice of $Q(s)$. Since

$$\begin{aligned}
&\frac{Q(s)\mu_1(s)}{\mu_1(s) - D_1} \\
&\quad = \frac{\mu_1(s)(s_0 - \alpha_1)}{D_1(s_0 - s)} \begin{cases} \le 1, & \text{if } 0 < s \le \alpha_1 \\ > 1, & \text{if } \alpha_1 < s < \beta_1, \end{cases}
\end{aligned}$$

we obtain that the second term is nonpositive and is equal to zero when $\mu_1(s) = D_1$ or $x_1 = 0$. Therefore, $\dot{V}(s, x_1, x_2) \le 0$ for all $s \in (0, \hat{s}]$. According to the LaSalle invariance principle, the trajectory $(s(t), x_1(t), x_2(t))$, $t \ge T_2$, approaches the largest invariant set $\mathcal{L}_\infty^*$ contained in the set

$$\begin{aligned}
\hat{\mathcal{L}}_\infty &= \{(s, x_1, x_2) : \dot{V}(s, x_1, x_2) = 0, \\
&\qquad s \in [0,\ \hat{s}],\ x_1 \ge 0, x_2 = 0\} \\
&= \{(s, x_1, x_2) : (\mu_1(s) - D_1)x_1 = 0, \\
&\qquad x_2 = 0,\ s \in [0,\ \hat{s}],\ x_1 \ge 0\}.
\end{aligned}$$

If $x_1 = 0$, then (because $x_2 = 0$) we have $\dot{s}(t) \ge D(s_0 - \hat{s}) > 0$, and so $\lim\limits_{t\to\infty} s(t) = +\infty$, which is impossible. Hence $x_1 > 0$ and $\mu_1(s) = D_1$. Further, since $s(t) \le \hat{s} < s_2 \le \beta_1$ for sufficiently large $t > 0$, it follows that $\mu_1(s) - D_1$ cannot vanish at $s = \beta_1$. This implies $\mathcal{L}_\infty^* = \{(\alpha_1, x_1^*, 0)\} = \{E^*\}$. Using a refinement of the LaSalle invariance principle (see Theorem 6 in [2]) we obtain that the trajectory $(s(t), x_1(t), x_2(t))$, $t \ge T_2$, tends to the set $\mathcal{L}_\infty^*$, which completes the proof. ☐

3 Numerical Examples

We demonstrate the result from Theorem 3 on three numerical examples including nonmonotone response functions of the form

$$\begin{aligned}
\mu_1(s) &= \frac{m_1 s}{a_1 + s + \gamma_1 s^2}, \\
\mu_2(s) &= \frac{m_2 s}{a_2 + s + \gamma_2 s^2}.
\end{aligned} \qquad (8)$$

It is worth to mention that the numerical examples are not based on experimental results; they are presented here for illustration of the theoretical studies.

Example 1. Consider the following coefficient values in the expressions of $\mu_1(s)$ and $\mu_2(s)$:

$$m_1 = 0.9, \quad a_1 = 0.05, \quad \gamma_1 = 1.5,$$
$$m_2 = 1, \quad a_2 = 0.05, \quad \gamma_2 = 0.001;$$

let

$$s_0 = 1, \quad D = 0.5, \quad D_1 = 0.41, \quad D_2 = 0.55.$$

Simple computations deliver

$$\alpha_1 = 0.0443, \quad \alpha_2 = 0.0611,$$
$$\beta_1 = 0.752, \quad \beta_2 = 818; \quad s_0 < \beta_2,$$

hence Assumption B2 is satisfied. The response functions $\mu_1(s)$ and $\mu_2(s)$ are visualized on Figure 1. Figure 2 visualizes the graph of the function $H(s) = (s_0 - s)D - \min\{\mu_1(s), \mu_2(s)\}(s_0^{\min} - s)$; obviously, there exist the points $s_1 = 0.111$ and $s_2 = 0.257$, such that $H(s) < 0$ for all $s \in (s_1, s_2)$ and $(s_1, s_2) \subset (\alpha_2, \beta_1) = (0.0611, 0.752)$ (the solid boxes on the horizontal axis mark the points α_2 and β_1); therefore Assumption B3 is also satisfied. According to Theorem 3, the equilibrium point $E^* = (\alpha_1, x_1^*, 0) = (0.0443,\ 1.165,\ 0)$ is globally asymptotically stable.

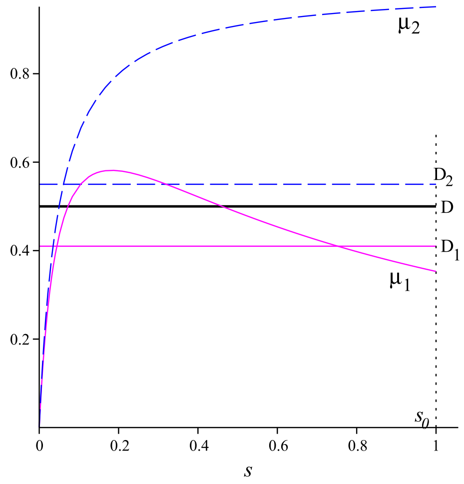

Figure 1. Example 1: The graphs of $\mu_1(s)$ and $\mu_2(s)$

To demonstrate the concept of the biological control, we first consider the model (3) starting from a point with $x_2(0) = 0$; obviously, $x_2(t) = 0$ for all $t \geq 0$. As mentioned above, the model (2) possesses two locally stable equilibrium points, the wash-out steady state E_0 and E_1. Consider the following initial point $(s(0), x_1(0), x_2(0)) = (0.5,\ 0.1,\ 0)$.

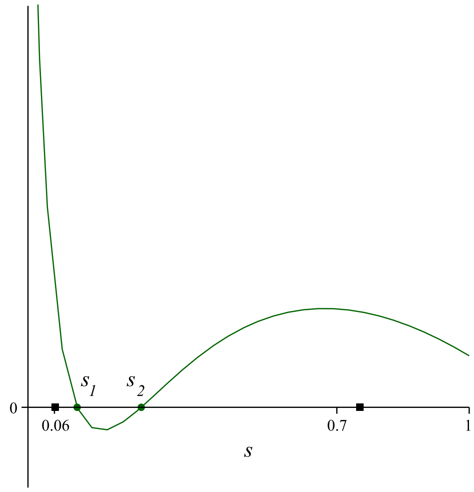

Figure 2. Example 1: The graph of $H(s)$; the solid boxes on the horizontal axis correspond to the points α_2 and β_1

Figure 3 presents the solutions $x_1(t)$ and $s(t)$ of (3) for this initial point; in this case $x_1(t)$ tends to zero, and $s(t)$ approaches s_0, marked by the horizontal dash line on the second plot.

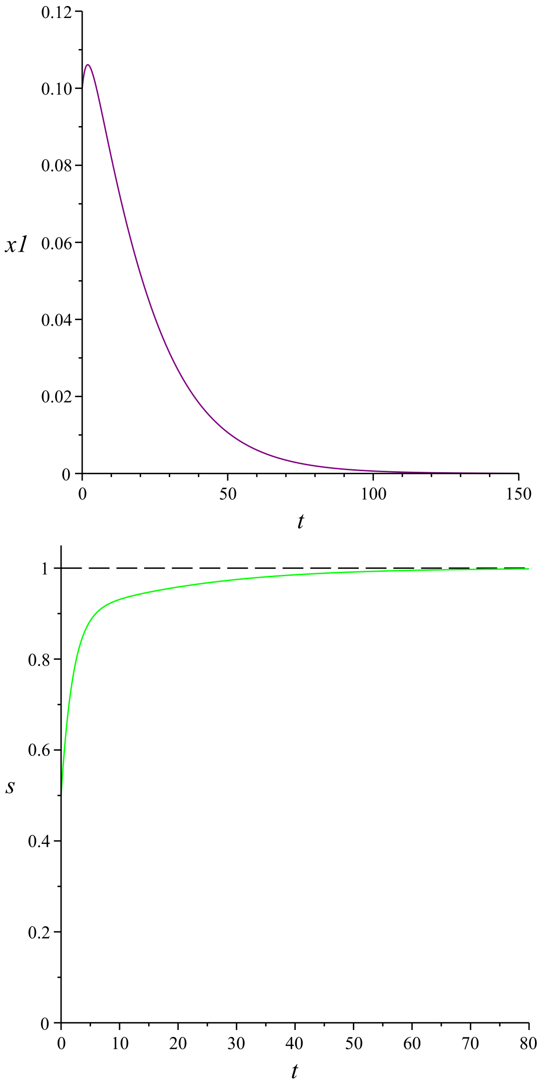

Figure 3. Example 1: The solution $x_1(t)$ and $s(t)$ with $x_2(0) = 0$

In the same example we take now a small positive value for $x_2(0)$, i. e. $(s(0), x_1(0), x_2(0)) = (0.5, 0.1, 0.01)$. The solutions $x_1(t)$, $x_2(t)$ and $s(t)$ are presented in the next Figure 4. We see that $x_1(t)$ tends to the positive equilibrium component $x_1^* = 1.165$, $s(t)$ approaches α_1, and $x_2(t)$ tends to zero.

To compare our result with that one of Theorem 2, we note that in this example we have

$$D_{\max} = D_2, \quad s_0^{\max} = 1.219, \quad s_0^{\min} = 0.909.$$

Since $s_0^{\max} - s_0^{\min} - (\alpha_2 - \alpha_1) \approx 0.294 > 0$, the assumption in Theorem 2 is not fulfilled.

Moreover, Assumption A5 is also not satisfied due to the following values:

$$\bar{s} = 0.0358,$$
$$\mu_1(\bar{s}) - \bar{D}_1 - \frac{s_0 - s_0^{\min}}{s_0^{\min} - \bar{s}} D = -0.185 < 0.$$

Assumption A4 is also not fulfilled because

$$\alpha_1(\bar{D}_1) = 0.0723, \quad \alpha_2(\bar{D}_2) = 0.0611,$$
$$\beta_1(\bar{D}_1) = 0.461, \quad \beta_2(\bar{D}_2) = 819;$$

obviously, $\beta_1 < s_0^{\min}$, but $\alpha_1(\bar{D}_1) > \alpha_2(\bar{D}_2)$.

Example 2. Consider the following coefficient values for the response functions (8):

$$m_1 = 0.5, \quad a_1 = 0.05, \quad \gamma_1 = 0.8,$$
$$m_2 = 1, \quad a_2 = 0.6, \quad \gamma_2 = 0.5;$$

let $s_0 = 1$, $D = 0.32$, $D_1 = 0.3$, $D_2 = 0.26$. Here, $D_{\max} = D$; we have further

$$\alpha_1 = 0.0833, \quad \alpha_2 = 0.219,$$
$$\beta_1 = 0.75, \quad \beta_2 = 5.473; \quad s_0 < \beta_2;$$

hence Assumption B2 is satisfied. The response functions are visualized on Figure 5. Figure 6 shows the graph of the function $H(s)$ from (5); there exist the points $s_1 = 0.304$ and $s_2 = 0.599$, such that $H(s) < 0$ for all $s \in (s_1, s_2)$ and $(s_1, s_2) \subset (\alpha_2, \beta_1)$ (the latter two points are denoted by solid boxes); therefore Assumption B3 is also satisfied. According to Theorem 3, the equilibrium point E^* is globally asymptotically stable.

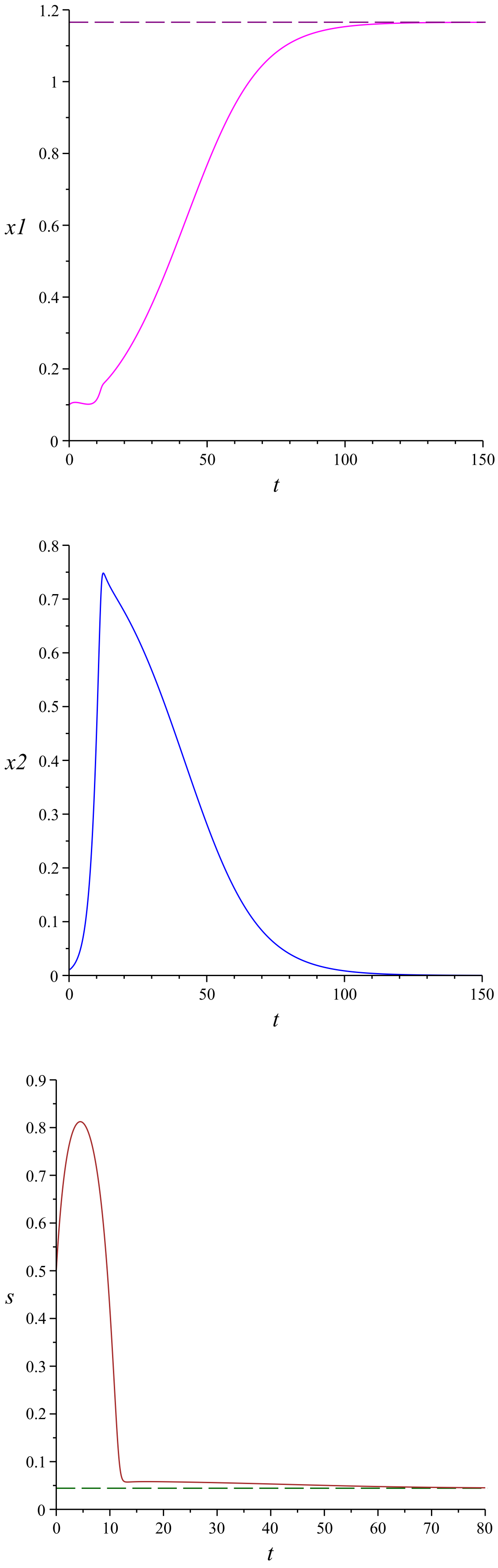

Figure 4. Example 1: The solutions $x_1(t)$, $x_2(t)$ and $s(t)$ with $(s(0), x_1(0), x_2(0)) > 0$. The horizontal dash-lines pass through x_1^* (in the first plot) and α_1 (in the third plot)

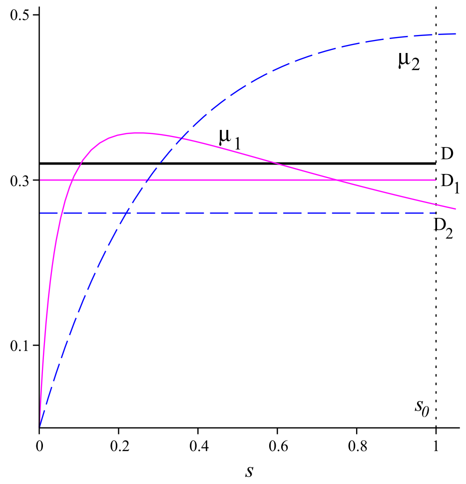

Figure 5. Example 2: The graphs of $\mu_1(s)$ and $\mu_2(s)$

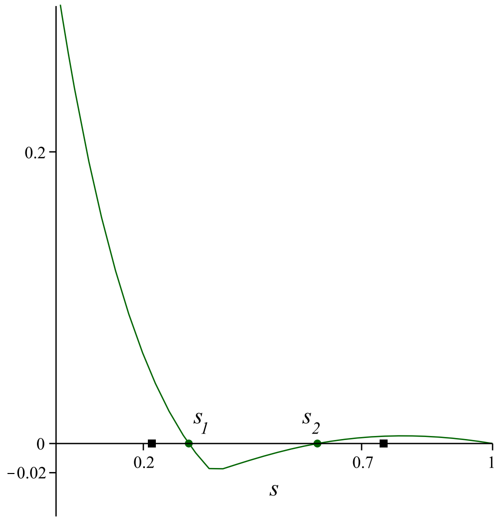

Figure 6. Example 2: The graph of $H(s)$; the solid boxes on the horizontal axis correspond to the points α_2 and β_1

Figure 7 presents the solutions $x_1(t)$, $x_2(t)$ and $s(t)$ of the model with initial point $(s(0), x_1(0), x_2(0)) = (0.1,\, 0.005,\, 0.0001)$. The horizontal dash line in the first plot passes through the equilibrium point $x_1^* = 0.978$, in the third plot – through the point $\alpha_1 = 0.0833$.

In this example we have $s_0^{\max} = 1.231$, $s_0^{\min} = 1$, and $s_0^{\max} - s_0^{\min} - (\alpha_2 - \alpha_1) \approx 0.0948 > 0$, thus the assumption in Theorem 2 is not fulfilled. Assumption A4 is however satisfied; we have: $\beta_1 < s_0^{\min}$; $\alpha_1(\bar{D}_1) = 0.104$, $\alpha_2(\bar{D}_2) = 0.304$, $\beta_1(\bar{D}_1) = 0.599$, $\beta_2(\bar{D}_2) = 3.95$. Assumption A5 is also satisfied, because

$$\bar{s} = 0.359,$$

$$\mu_1(\bar{s}) - \bar{D}_1 - \frac{s_0 - s_0^{\min}}{s_0^{\min} - \bar{s}} D = 0.03056 > 0.$$

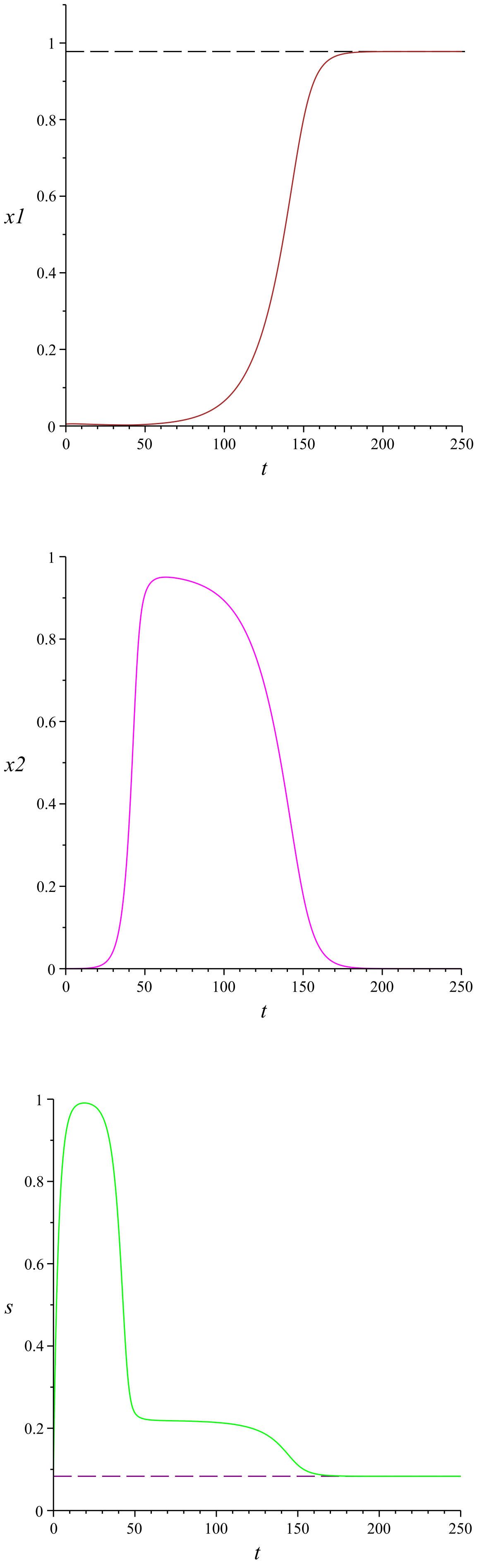

Figure 7. Example 2: The solutions $x_1(t)$, $x_2(t)$ and $s(t)$

Example 3. Consider the following coefficient values in the expressions of the response functions $\mu_1(s)$ and $\mu_2(s)$ from (8)

$$m_1 = 1, \;\; a_1 = 1, \;\; \gamma_1 = 0.18,$$
$$m_2 = 0.53, \;\; a_2 = 0.2, \;\; \gamma_2 = 0.026,$$

and let $s_0 = 11$, $D = 0.33$, $D_1 = 0.35$, $D_2 = 0.4$. Simple computations produce the values $\alpha_1 = 0.57$, $\alpha_2 = 0.65$, $\beta_1 = 9.75$, $\beta_2 = 11.85$; obviously, $s_0 < \beta_2$ holds, thus Assumption B2 is satisfied.

The response functions are visualized in Figure 8. The graph of the function $H(s)$ from (5) is shown in Figure 9, together with the points $s_1 = 0.755$ and $s_2 = 4.13$ (marked by solid circles on the horizontal axis) meaning that Assumption B3 is also satisfied. According to Theorem 3, the equilibrium point E^* is globally asymptotically stable.

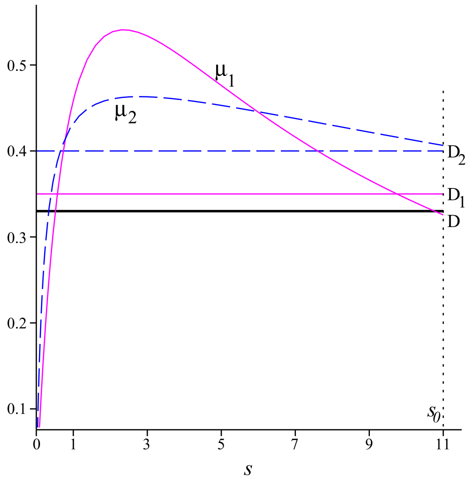

Figure 8. Example 3: The graphs of $\mu_1(s)$ and $\mu_2(s)$

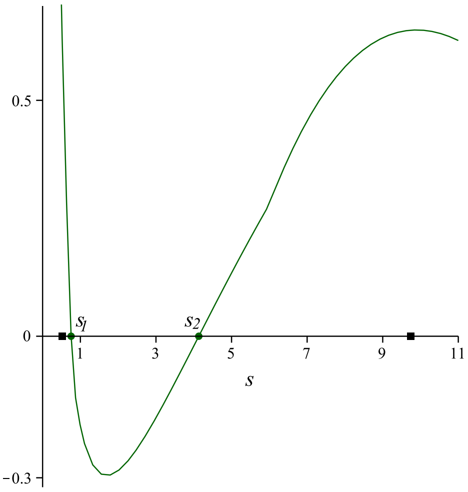

Figure 9. Example 3: The graph of $H(s)$; the solid boxes on the horizontal axis correspond to the points α_2 and β_1

Figure 10 presents the solutions $x_1(t)$, $x_2(t)$ and $s(t)$ of the model with different initial points $(s(0), x_1(0), x_2(0)) > 0$. The horizontal dash line on the first plot passes through $x_1^* = 9.83$, on the third plot – through $\alpha_1 = 0.57$.

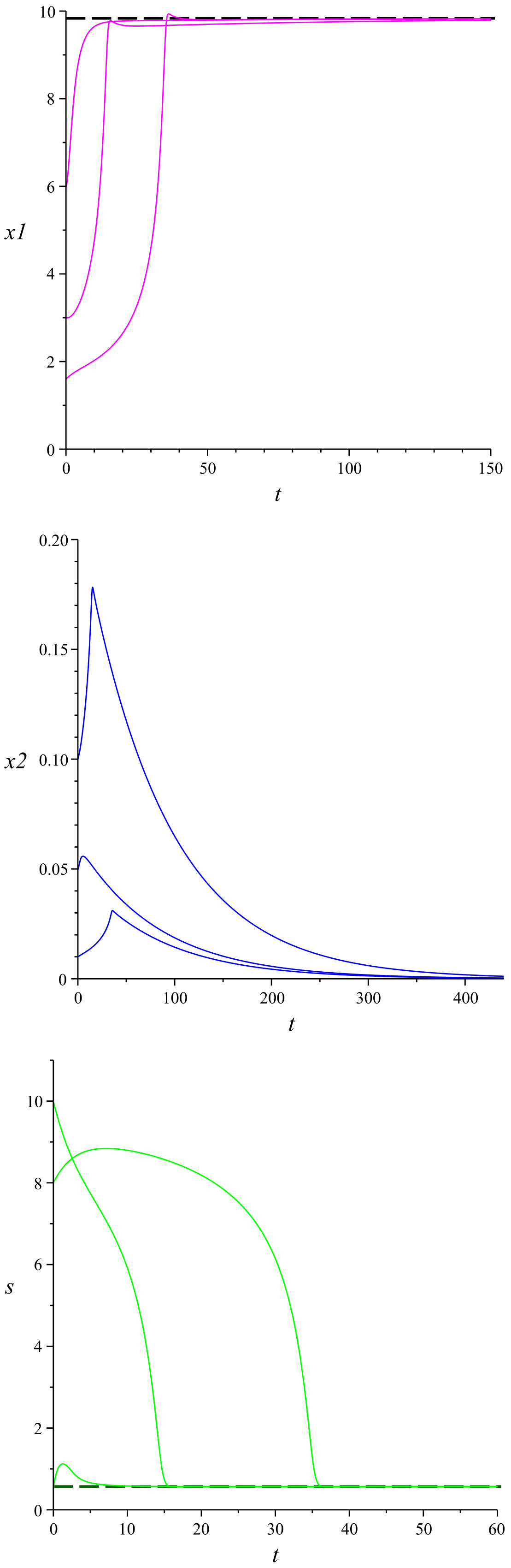

Figure 10. Example 3: The solutions $x_1(t)$, $x_2(t)$ and $s(t)$

In this example we have $s_0^{\max} = 11$, $s_0^{\min} = 9.075$. Since $s_0^{\max} - s_0^{\min} - (\alpha_2 - \alpha_1) \approx 1.846 > 0$, the assumption in Theorem 2 is not fulfilled. Assumption A5 is also not satisfied, because

$$\bar{s} = 0.0411,$$

$$\mu_1(\bar{s}) - \bar{D}_1 - \frac{s_0 - s_0^{\min}}{s_0^{\min} - \bar{s}} D = -0.382 < 0.$$

To check Assumption A4 we note that $\alpha_1 = \alpha_1(\bar{D}_1)$, $\alpha_2 = \alpha_2(\bar{D}_2)$, $\beta_1 = \beta_1(\bar{D}_1)$, $\beta_2 = \beta_2(\bar{D}_2)$; the inequality $\beta_1 < s_0^{\min}$ is however not fulfilled because $\beta_1 - s_0^{\min} = 0.672 > 0$.

4 Conclusion

The present paper extends the applicability of the model-based biological control of the chemostat model (3), recently developed by A. Rapaport and J. Harmand in [21] (and formulated here in Theorem 2). More precisely, we require the following ordering $\alpha_1 < \alpha_2 < \beta_1 < s_0 < \beta_2$ of the break-even concentrations, which seems to be more natural than the inequalities in Assumption A4. The restrictive assumption $s_0^{\max} - s_0^{\min} < \alpha_2 - \alpha_1$ from Li's Theorem 1 is also avoided in our new Theorem 3. Illustrative numerical examples show the applicability of our main result.

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