Further Results on Stabilization of Periodic Trajectories for a Chemostat with Two Species

Frédéric Mazenc, Michael Malisoff, and Jérôme Harmand^{*}

November 20, 2008

Abstract

We discuss an important class of problems involving the tracking of prescribed trajectories in the chemostat model. We provide new tracking results for chemostats with two species and one limiting substrate, based on Lyapunov function methods. In particular, we use a linear feedback control of the dilution rate and an appropriate time-varying substrate input concentration to produce a locally exponentially stable oscillatory behavior. This means that all trajectories for the nutrient and corresponding species concentrations in the closed loop chemostat that stay near the oscillatory reference trajectory are attracted to the reference trajectory exponentially fast. We also obtain a globally stable oscillatory reference trajectory for the species concentrations, using a nonlinear feedback control depending on the dilution rate and the substrate input concentration. This guarantees that all trajectories for the closed loop chemostat dynamics are attracted to the reference trajectory. Finally, we construct an explicit Lyapunov function for the corresponding global error dynamics. We demonstrate the efficacy of our method in a simulation.

bf keywords: chemostats, tracking, stabilization, Lyapunov functions, systems biology

1 INTRODUCTION

Since the pioneering research of Monod [27] and Novick & Szilard [28], continuous cultures of micro-organisms in chemostats (also known as continuously stirred tank

^{*}Manuscript submitted December 7, 2006 and in revised form November 20, 2008. The second author was supported by NSF/DMS Grant 0424011.

[†]F. Mazenc is with Projet MERE INRIA-INRA, UMR Analyse des Systèmes et Biométrie, INRA 2, pl. Viala, 34060 Montpellier, France Frederic.Mazenc@supagro.inra.fr.

[‡]M. Malisoff is with the Department of Mathematics, Louisiana State University, Baton Rouge, LA 70803-4918 malisoff@lsu.edu.

[§]J. Harmand is with Institut National de la Recherche Agronomique (INRA), UR050, Laboratoire de Biotechnologie de l'Environnement, Narbonne, F-11100, France harmand@supagro.inra.fr.

reactors) have been a very popular way to study the growth of populations of microorganisms. The usual assumption about the chemostat is that it is perfectly stirred, so each individual has equal access to the nutrients. Under this assumption, the basic mathematical model for a chemostat containing n species with concentrations x_i for $i = 1, \ldots, n$ and one limiting nutrient with concentration s has the form

$$\begin{cases} \dot{s} = D(s_{in} - s) - \sum_{i=1}^{n} \mu_i(s) x_i / \gamma_i \\ \dot{x}_i = x_i (\mu_i(s) - D), \quad i = 1, \dots, n \end{cases}$$
(1.1)

where s_{in} is the input nutrient concentration, D > 0 is the dilution rate, μ_i is the per capita growth rate of species i, and \dot{s} and \dot{x}_i indicate time derivatives. The conversion of nutrient into new biomass for species i happens with constant yield $\gamma_i > 0$. We specify the μ_i 's, s_{in} , and D below.

The natural control variables for (1.1) are the input substrate concentration s_{in} and the dilution rate D. The dilution rate is the ratio of the volumetric flow rate (with units of volume over time) to the constant reactor volume. Equations (1.1) easily follow from writing the mass-balance equations for the total amounts of the nutrient and each of the species, assuming the reactor content is well-mixed.

The model (1.1) plays an essential role in current research in bio-engineering, ecology, and population biology [1, 4, 12, 17, 34]. Much of the chemostat literature is based on experiments and data analysis or intensive calculations that use mathematical models only to generate data. However, a number of ecological concepts such as resilience or resistance of an ecosystem are closely related to the notions of stability and robustness from dynamical systems theory. Moreover, rigorous control theory is clearly needed to characterize systems which naturally evolve far from the equilibrium. This has motivated a great deal of significant research at the interface of control theory and chemostat biology [4, 6, 7, 8, 9].

One important issue related to chemostats that lends itself to rigorous control theoretic analysis is the stability of coexistence behaviors. In fact, the relationship between diversity and stability has fascinated ecologists for more than five decades [26]. It is well-known that in a classical chemostat model with N substrates, at most N microorganism species can coexist. This concept is usually attributed to Hardin [15] and is called the "competitive exclusion principle". However, a number of natural observations seem to contradict this principle, e.g. the literature originating with the famous "paradox of the plankton" discussed in [16].

There is a large literature aimed at trying to resolve this paradox. During the last 40 years, a number of explanations have been proposed. Among important studies, McGehee and Armstrong noted that "coexistence at equilibrium" is not equivalent to "coexistence in a dynamical environment" and that non-equilibrium conditions may favor coexistence [2, 3]; see also Section 2.1 below for related results. Recent advances in molecular biology make it possible to investigate such ecological concepts in microbial ecosystems. Another approach to explaining coexistence, which we will not pursue

here, involves relaxing the assumption that the reactor is perfectly stirred, i.e., allowing spatial heterogeneity and crowding effects [29, 33, 34, 35].

In the present paper, we use feedback control (with the dilution rate and the input substrate concentration as control variables) to force two independent species in competition for one substrate to oscillate around predefined trajectories while the output substrate concentration remains constant; see e.g. [18, 31] for the necessary control theory background. This reproduces observations reported in the ecology literature (i.e. oscillating levels of coexisting species). It also suggests a possible strategy to preserve bio-diversity and thus improve robustness while the output substrate concentration is kept constant under normative constraints, in the presence of fluctuating inputs.

Our work is a continuation of [22] where a prescribed oscillatory behavior for a chemostat with *one species* is generated by an appropriate choice of a time-varying dilution rate, and the global uniform asymptotic stability of the behavior is proved by a Lyapunov approach; see Section 2.2 for details. In the present work, we generate a periodic oscillating trajectory for the *two species* case. However, this trajectory has no a priori stability. To stabilize the trajectory, we design specific time-varying functions for the dilution rate and the input concentration, called feedbacks. We use two control theoretic approaches. First, we provide *linear* stabilizing control laws whose utility lies in their simple expressions that are independent of the nutrient concentration. However, these control laws only exponentially stabilize the reference trajectory in a *neighborhood*.

To achieve global asymptotic stability of the reference trajectory, we design nonlinear control laws using a Lyapunov approach. Our control laws depend only on the concentrations of the species. They possess the required properties of positiveness and boundedness of the dilution rate. See also [7, 8] for related results where feedbacks are used to generate coexistence. While it is known that oscillatory inputs can give oscillatory coexistence [5], our work differs from the earlier results because we use Lyapunov function methods to globally feedback stabilize a predefined oscillating behavior.

2 REVIEW OF LITERATURE

2.1 Competitive Exclusion versus Coexistence

The chemostat dynamics is well understood for cases where there are two species and one of the chemostat controllers (i.e., the dilution rate or the input concentration) is constant while the other is periodic in time, as well as for cases were these controllers are both constant [5, 14, 32, 34]. When the controllers are constant and there is one limiting nutrient, the so-called "competitive exclusion principle" holds, which implies that at most one species survives. This provides an attractive steady state for the chemostat that attracts almost all solutions of the dynamics [34]. However, the competitive exclusion principle is at odds with the observation that many species can coexist in real ecological systems, even if there is only one limiting nutrient. See [11, 15] for related papers.

The existing results on periodically-varying chemostats attempt to explain this paradox. They use periodic forcing of the dilution rate or input concentration controllers to give coexistence in the form of a periodic solution. See also [30] which produces an arbitrary number of coexisting periodically varying species using a periodic input concentration and a fixed dilution rate. However, this earlier work does not address the stability of the species oscillation. See also [6, 7, 8] which use state-dependent time-invariant dilution rates to generate coexistence in two and three species chemostats with monotone growth rates. The effects of more complicated growth rates were studied in [12, 21, 23], including non-monotone growth rates that may depend on both the substrate level and the species concentrations. See also [19] where coexistence is studied via a bifurcation with the dilution rate as the control. The main purpose of these papers is to investigate environmental conditions under which the competitive exclusion principle fails and several species can coexist.

2.2 Tracking Prescribed Trajectories

The preceding results leave open the complementary problem of designing dilution rates and input concentrations that stabilize *prescribed* chemostat trajectories e.g. so that all of the chemostat trajectories asymptotically track a prescribed stable oscillation. Solving this problem is important since it would reproduce and explain complex stability behaviors that are commonly observed in microbial systems.

For one species chemostats, this problem was first addressed by [22]. The main model in [22] is therefore (1.1) with n = 1 (so we omit the subscripts) and the growth rate was assumed to have the standard Monod form $\mu(s) = ms/(a + s)$ for suitable constants m, a > 0 such that m > 4a + 1. The state space is then $\mathcal{X} := (0, \infty)^2$. The input concentration s_{in} in [22] is taken to be a positive constant, so a simple rescaling gives the dynamics

$$\begin{cases} \dot{s} = D(1-s) - \mu(s)x \\ \dot{x} = x(\mu(s) - D). \end{cases}$$
(2.2)

The main result in [22] is that if we choose

$$D(t) = \frac{\sin(t)}{2 + \cos(t)} + \frac{m(2 - \cos(t))}{4a + 2 - \cos(t)},$$
(2.3)

then all trajectories $t \mapsto (s, x)(t)$ of (2.2) asymptotically converge to the reference trajectory $(s_r(t), x_r(t)) := (0.5 - 0.25 \cos(t), 0.5 + 0.25 \cos(t))$ of (2.2) for all initial conditions, i.e., $(s(t) - s_r(t), x(t) - x_r(t)) \to 0$; see [24] for analogs for more general reference trajectories.

Unlike the earlier results on periodically forced chemostat models, the proofs in [22, 24] use a Lyapunov-type analysis to show the *stability* of the prescribed periodic behaviors. The advantage of having a Lyapunov function is that it can be used to investigate the robustness of the stability of the periodic solution with respect to perturbations [24]. However, Lyapunov functions have only rarely been used to prove stability in the chemostat. An exception is Theorem 4.1 on [34, p.35], and more recently [13]. See also [20, 36] where *weak* Lyapunov functions are used in conjunction with suitable variants of the LaSalle Invariance Principle. See also [10]. Closely related to [22] is [9] where a single-species chemostat with a continuous and bounded (but otherwise arbitrary) function $s_{in}(t)$ and constant dilution rate is investigated; there it is shown that two positive solutions converge to each other. However, the proof is not based on a Lyapunov function.

The results of [22, 24] reproduce and explain oscillating chemostat behaviors of the type commonly observed in biotechnology applications. However, the methods of [22, 24] are limited to cases where there is only *one* species competing for the nutrient. This suggests the important and more complicated problem of explicitly designing the controllers D and s_{in} for two species chemostats in such a way that the corresponding trajectories of the closed loop chemostats track a prescribed oscillating vector of concentrations. In the present paper, we show that this design problem can indeed be solved, provided D and s_{in} are also allowed to depend on the current state as well as time i.e. using time-varying *feedbacks* instead of simply time varying stabilizers such as (2.3).

3 CHEMOSTAT MODEL WITH TWO SPECIES

3.1 The Model and the Basic Assumptions

Consider the chemostat model (1.1) for the two species case (i.e., n = 2). Scaling via $x_i \mapsto x_i/\gamma_i$ gives the dynamics

$$\begin{cases} \dot{s} = D[s_{in} - s] - \sum_{j=1}^{2} \mu_j(s) x_j , \\ \dot{x}_i = [\mu_i(s) - D] x_i , \quad i = 1, 2 \end{cases}$$
(3.4)

evolving on $[0, \infty) \times (0, \infty) \times (0, \infty)$. We specify our choices of D and s_{in} below. We assume the functions μ_i satisfy:

The functions μ_1 and μ_2 are zero at zero, continuously differentiable (C^1) , and have positive bounded first derivatives. Also, there exists a positive constant s_c such that the function $\chi(s) = \mu_2(s) - \mu_1(s)$ satisfies

$$\chi(s_c) = 0 \; ; \; \chi(s) < 0 \; \text{ when } 0 < s < s_c \; ;$$

and $\chi(s) > 0 \; \text{ when } s > s_c$ (3.5)

and χ is such that $\chi'(s_c) > 0$.

To simplify formulas, we set $\Gamma = \mu_1(s_c)$. Also, we understand all inequalities and equalities to hold globally unless indicated otherwise. Assumption 3.1 is frequently satisfied e.g. by pairs of Monod functions; see e.g. Section 7 below. An immediate consequence of (3.5) is that $\Gamma = \mu_1(s_c) = \mu_2(s_c)$.

3.2 New Coordinates

The change of coordinates

$$\xi_1 = \ln(x_1) , \ \xi_2 = \ln(x_2) , \ \psi = \xi_2 - \xi_1$$
 (3.6)

and the definition of χ transform the system (3.4) into

$$\begin{cases} \dot{s} = D[s_{in} - s] - \mu_1(s)e^{\xi_1} - \mu_2(s)e^{\psi + \xi_1}, \\ \dot{\xi}_1 = \mu_1(s) - D, \quad \dot{\psi} = \chi(s). \end{cases}$$
(3.7)

We denote the right-hand side of (3.7) by $\mathcal{F}(D, s_{in}, (s, \xi_1, \psi))$, with the understanding that D is to be evaluated at the third argument (s, ξ_1, ψ) of \mathcal{F} when D depends on the state.

4 REFERENCE TRAJECTORY

We next determine a family of trajectories for (3.7) which can be generated by appropriate choices for the dilution rate D and the substrate input concentration s_{in} . We refer to these trajectories as *reference trajectories*. Later we specialize to a periodic oscillatory reference trajectory, the choice of which is motivated by the importance of oscillating trajectories in ecology. The following general result is easily checked:

Lemma 1 Let Assumption 3.1 hold. Let s_r , ξ_{1r} , and ψ_r be C^2 functions for which the functions

$$D_r(t) := -\xi_{1r}(t) + \mu_1(s_r(t))$$

and

$$s_{inr}(t) := \frac{\dot{s}_r(t) + \mu_1(s_r(t))e^{\xi_{1r}(t)} + \mu_2(s_r(t))e^{\xi_{1r}(t) + \psi_r(t)}}{-\dot{\xi}_{1r}(t) + \mu_1(s_r(t))} + s_r(t)$$

are positive everywhere and $\dot{\psi}_r(t) = \chi(s_r(t))$ everywhere. Then $(s_r(t), \xi_{1r}(t), \psi_r(t))$ is a solution to:

$$\dot{s}_{r}(t) = D_{r}(t)[s_{inr}(t) - s_{r}(t)]
-\mu_{1}(s_{r}(t))e^{\xi_{1r}(t)}
-\mu_{2}(s_{r}(t))e^{\xi_{1r}(t) + \psi_{r}(t)},$$

$$\dot{\xi}_{1r}(t) = \mu_{1}(s_{r}(t)) - D_{r}(t),
\dot{\psi}_{r}(t) = \chi(s_{r}(t)).$$
(4.8)

In particular, if $s_c > 0$ and $\alpha \in [0, \Gamma)$ are both constants and

$$(s_r(t), \xi_{1r}(t), \psi_r(t)) := (s_c, \cos(\alpha t), 0), \tag{4.9}$$

then (4.8) is satisfied with the choices

$$D_r(t) = \Gamma + \alpha \sin(\alpha t) \tag{4.10}$$

and

$$s_{inr}(t) = s_c + \frac{2\Gamma e^{\cos(\alpha t)}}{\Gamma + \alpha \sin(\alpha t)}$$
(4.11)

in which case $D_r(t)$ and $s_{inr}(t)$ are periodic and positive.

5 LOCAL STABILIZATION OF A TRAJECTORY

We next show how to locally track some of the trajectories $(s_r(t), \xi_{1r}(t), \psi_r(t))$ from Lemma 1, using linear feedback. Consider the two-species chemostat error dynamics

$$\dot{z}(t) = \mathcal{F}(D, s_{in}, z(t) + (s_r, \xi_{1r}, \psi_r)(t)) -\mathcal{F}(D, s_{in}, (s_r, \xi_{1r}, \psi_r)(t))$$
(5.12)

where \mathcal{F} is the right-hand side of (3.7) as before, $(s_r, \xi_{1r}, \psi_r)(t)$ is from (4.9), and the control laws D and s_{in} are to be specified in such a way that (5.12) is the dynamics of the error

$$(\tilde{s}, \tilde{\xi}_1, \tilde{\psi}) := (s - s_r, \xi_1 - \xi_{1r}, \psi - \psi_r)$$
 (5.13)

between any trajectory (s, ξ_1, ψ) of (3.7) and the reference signal (4.9). We will choose D and s_{in} so that (5.12) is also locally uniformly exponentially stable to the origin; i.e. such that (4.9) is locally uniformly exponentially stable. This means that (5.13) exponentially converges to zero when (s, ξ_1, ψ) stays in a neighborhood of (4.9), hence all chemostat trajectories of (3.7) that stay in a neighborhood of (4.9) are actually attracted to (4.9) exponentially fast. See [18] for the standard definitions.

Let Assumption 3.1 hold and $\alpha \in [0, \Gamma)$ be constant. Consider the reference trajectory (4.9). Then

$$D(t,\xi_1) := \Gamma + \alpha \sin(\alpha t) + \frac{(\Gamma - \alpha)^2}{\Gamma} (\xi_1 - \cos(\alpha t))$$
(5.14)

$$s_{in}(t) := s_c + \frac{2\Gamma e^{\cos(\alpha t)}}{\Gamma + \alpha \sin(\alpha t)}$$
 (5.15)

render the error dynamics (5.12) locally exponentially stable to the origin. Hence (5.14)-(5.15) render the reference trajectory $(s_r(t), \xi_{1r}(t), \psi_r(t))$ locally exponentially stable.

With the choices (5.14)-(5.15) of D and s_{in} , the linearization of (5.12) around the origin [18] is

$$\begin{cases} \dot{s}_{a} = [s_{inr}(t) - s_{r}(t)]U_{1} \\ - [D_{r}(t) + \mu'_{1}(s_{r}(t))e^{\xi_{1r}(t)} \\ + \mu'_{2}(s_{r}(t))e^{\xi_{1r}(t) + \psi_{r}(t)}]s_{a} \\ - \mu_{1}(s_{r}(t))e^{\xi_{1r}(t) + \xi_{1a}} \\ - \mu_{2}(s_{r}(t))e^{\xi_{1r}(t) + \psi_{r}(t)}(\xi_{1a} + \psi_{a}) , \\ \dot{\xi}_{1a} = \mu'_{1}(s_{r}(t))s_{a} - U_{1} , \\ \dot{\psi}_{a} = \chi'(s_{r}(t))s_{a} \end{cases}$$
(5.16)

where D_r and s_{inr} are defined in (4.10)-(4.11) and

$$U_1 := (\Gamma - \alpha)^2 \xi_{1a} / \Gamma.$$
(5.17)

Formula (4.9) for the reference trajectory simplifies (5.16) to

$$\dot{s}_{a} = \frac{2\Gamma e^{\cos(\alpha t)}}{\Gamma + \alpha \sin(\alpha t)} U_{1} -\Gamma e^{\cos(\alpha t)} [2\xi_{1a} + \psi_{a}] - B_{r}(t, s_{c}, \alpha) s_{a}, \qquad (5.18)$$

$$\dot{\xi}_{1a} = \mu_{1}'(s_{c}) s_{a} - U_{1}, \quad \dot{\psi}_{a} = \chi'(s_{c}) s_{a},$$

where

$$B_r(t, s_c, \alpha) := \Gamma + \alpha \sin(\alpha t) + e^{\cos(\alpha t)} \sum_{j=1}^2 \mu'_j(s_c).$$

By Assumption 3.1, $\chi'(s_c) > 0$ and $\mu'_1(s_c) > 0$. Therefore,

$$V(t, s_a, \xi_{1a}, \psi_a) := \frac{1}{2} e^{-\cos(\alpha t)} s_a^2 + \frac{\Gamma}{\mu_1'(s_c)} \xi_{1a}^2 + \frac{\Gamma}{2\chi'(s_c)} \psi_a^2$$
(5.19)

is well-defined and upper and lower bounded by positive definite quadratic functions of (s_a, ξ_{1a}, ψ_a) . Its derivative along the trajectories of (5.18) satisfies

$$\dot{V} = s_a \left(\frac{2\Gamma}{\Gamma + \alpha \sin(\alpha t)} U_1 - e^{-\cos(\alpha t)} B_r(t, s_c, \alpha) s_a - \Gamma[2\xi_{1a} + \psi_a] \right) + \frac{2\Gamma}{\mu_1'(s_c)} \xi_{1a} [\mu_1'(s_c) s_a - U_1]$$
$$+ \frac{1}{2} e^{-\cos(\alpha t)} \alpha \sin(\alpha t) s_a^2 + \frac{\Gamma}{\chi'(s_c)} \psi_a \chi'(s_c) s_a$$
$$= - \left[e^{-\cos(\alpha t)} \left(\Gamma + \frac{1}{2} \alpha \sin(\alpha t) \right) + \sum_{j=1}^2 \mu_j'(s_c) \right] s_a^2$$
$$+ \frac{2\Gamma}{\Gamma + \alpha \sin(\alpha t)} s_a U_1 - \frac{2\Gamma}{\mu_1'(s_c)} \xi_{1a} U_1 .$$

Therefore, our choice of U_1 yields

$$\dot{V} = -\left[e^{-\cos(\alpha t)}\left(\Gamma + \frac{1}{2}\alpha\sin(\alpha t)\right) + \sum_{j=1}^{2}\mu'_{j}(s_{c})\right]s_{a}^{2}$$
$$+ \frac{2(\Gamma - \alpha)^{2}}{\Gamma + \alpha\sin(\alpha t)}s_{a}\xi_{1a} - \frac{2(\Gamma - \alpha)^{2}}{\mu'_{1}(s_{c})}\xi_{1a}^{2}.$$

The relation $2|pq| \leq \varepsilon p^2 + \frac{1}{\varepsilon}q^2$ for $p, q \geq 0$ and $\varepsilon > 0$ gives

$$\left| \frac{2(\Gamma - \alpha)^2}{\Gamma + \alpha \sin(\alpha t)} s_a \xi_{1a} \right| \leq \frac{(\Gamma - \alpha)^2}{\Gamma + \alpha \sin(\alpha t)} \left[\frac{\mu'_1(s_c)}{\Gamma + \alpha \sin(\alpha t)} s_a^2 + \frac{\Gamma + \alpha \sin(\alpha t)}{\mu'_1(s_c)} \xi_{1a}^2 \right] ,$$

where we chose $p = s_a$ and $q = \xi_{1a}$. It follows that

$$\dot{V} \leq -\left[e^{-\cos(\alpha t)}\left(\Gamma + \frac{1}{2}\alpha\sin(\alpha t)\right) + \sum_{j=1}^{2}\mu'_{j}(s_{c})\right]s_{a}^{2} + \frac{(\Gamma - \alpha)^{2}}{(\Gamma + \alpha\sin(\alpha t))^{2}}\mu'_{1}(s_{c})s_{a}^{2} - \frac{(\Gamma - \alpha)^{2}}{\mu'_{1}(s_{c})}\xi_{1a}^{2}.$$

Since $\Gamma + \alpha \sin(\alpha t) \ge \Gamma - \alpha > 0$ everywhere, we obtain

$$\dot{V} \leq -\left[e^{-\cos(\alpha t)}\left(\Gamma + \frac{1}{2}\alpha\sin(\alpha t)\right) + \mu_2'(s_c)\right]s_a^2$$
$$-\frac{(\Gamma - \alpha)^2}{\mu_1'(s_c)}\xi_{1a}^2 \leq 0.$$

Since (5.18) in closed loop with U_1 from (5.17) is linear and periodic, we deduce from the LaSalle Invariance Principle [31, Theorem 5.26, p. 204] (which is a generalization of a standard differential equations result for periodic systems) that (5.18) is uniformly globally asymptotically stable, hence exponentially stable [18, Section 4.6]. This allows us to conclude by a standard linearization principle e.g. [18, Theorem 4.13, p.161].

Note that the Lyapunov function (5.19) is time periodic. The feedback $D(t, \xi_1)$ in (5.14) does not depend on the substrate concentration or the concentration of the second species. The feedback $s_{in}(t)$ is a periodic time-varying function, and D and s_{in} are positive in a neighborhood of the trajectory. Our proof of Theorem 5 relies on the LaSalle invariance principle. However, one can explicitly construct a strict Lyapunov function for (5.12) with the choices (5.14)-(5.15).

6 GLOBAL STABILIZATION OF A TRAJECTORY

As noted above, the utility of our local feedbacks (5.14)-(5.15) lies in their simple form (i.e., affineness in the transformed state variable ξ_1) and their applicability to local stability analysis. While local analysis suffices for many applications, it is often important to have *global* convergence for all initial conditions. Therefore, we next choose D and s_{in} so that the error dynamics

$$\begin{cases} \dot{\tilde{s}} = D[s_{in} - s_c - \tilde{s}] - \mu_1(s_c + \tilde{s})e^{\xi_1} \\ -\mu_2(s_c + \tilde{s})e^{\psi + \xi_1} , \\ \dot{\tilde{\xi}}_1 = \mu_1(s_c + \tilde{s}) - D - \dot{\xi}_{1r}(t) , \\ \dot{\tilde{\psi}} = \chi(s_c + \tilde{s}) , \end{cases}$$
(6.20)

for the deviations (5.13) from (4.9) is globally asymptotically stable to the origin. This means that *all* trajectories (s, ξ_1, ψ) of the chemostat dynamics (3.7) are attracted to the reference trajectory in the sense that the errors (5.13) converge to zero. For given choices of D and s_{in} , to say that the reference trajectory (4.9) is globally asymptotically stable means [18] that (6.20) is globally asymptotically stable to the origin. We assume:

The functions μ_1 and μ_2 are C^2 and there are two constants $\theta_1 > 0, \theta_2 > 0$ such that

$$\sup_{l} |\mu_1''(l)| \le \theta_1 , \ \sup_{l} |\mu_2''(l)| \le \theta_2 .$$
(6.21)

Under Assumption 3.1, $\chi'(s_c) > 0$ and $\mu'_1(s_c) > 0$, so we can define

$$c_{1} := \frac{\Gamma}{16} \min\left\{\frac{s_{c}}{\mu_{1}'(s_{c})}, \frac{1}{\theta_{1}}\right\},$$

$$c_{2} := \frac{\Gamma}{16} \min\left\{\frac{s_{c}}{\mu_{2}'(s_{c}) - \mu_{1}'(s_{c})}, \frac{1}{\theta_{1} + \theta_{2}}\right\}.$$
(6.22)

We set $\langle a \rangle = a/\sqrt{1+a^2}$ for all real valued functions a. Let Assumptions 3.1 and 6 hold and consider the functions $(s_r(t), \xi_{1r}(t), \psi_r(t))$ defined in (4.9) and the error defined in (5.13). If $\alpha \in [0, \frac{1}{2}\Gamma)$, then the control laws

$$D(t, \tilde{\xi}_1) = \Gamma + \alpha \sin(\alpha t) + \frac{\Gamma}{4} \langle \tilde{\xi}_1 \rangle , \qquad (6.23)$$

$$s_{in}(t, \tilde{\xi}_{1}, \tilde{\psi}) = s_{c} + \frac{1}{D(t, \tilde{\xi}_{1})} \left\{ \Gamma e^{\cos(\alpha t)} \left(e^{\tilde{\xi}_{1}} + e^{\tilde{\psi} + \tilde{\xi}_{1}} \right) - c_{1} \mu_{1}'(s_{c}) \langle \tilde{\xi}_{1} \rangle - c_{2} [\mu_{2}'(s_{c}) - \mu_{1}'(s_{c})] \langle \tilde{\psi} \rangle \right\} , \qquad (6.24)$$

with c_1 and c_2 defined in (6.22), render (6.20) globally asymptotically stable to the origin and locally exponentially stable. Hence (4.9) is a globally asymptotically stable trajectory.

Since $s \ge 0$, the stability in Theorem 6 must be understood to be relative to the set where $s \ge 0$. We will prove that $D(t, \tilde{\xi}_1)$ and $s_{in}(t, \tilde{\xi}_1, \tilde{\psi})$ defined in (6.23) and (6.24) are positive. Our proof of Theorem 6 relies on the LaSalle Invariance Principle. However, one can explicitly construct a strict Lyapunov function for the error dynamics (6.20) which leads to the uniform global asymptotic stability of (6.20). We discuss two approaches to building the Lyapunov function in the appendix below.

To prove Theorem 6, we construct the control laws (6.23)-(6.24) step by step in the next subsections.

6.1 Changes of Feedbacks and Coordinates

To simplify our analysis, we first introduce the functions λ_i and χ_n defined by

$$\lambda_{i}(\tilde{s})\tilde{s} = \mu_{i}(s_{c} + \tilde{s}) - \mu_{i}(s_{c}), \quad \tilde{s} \neq 0,$$

$$\chi_{n}(\tilde{s})\tilde{s} = \chi(s_{c} + \tilde{s}), \quad \tilde{s} \neq 0,$$

$$\lambda_{i}(0) = \mu_{i}'(s_{c}), \quad \chi_{n}(0) = \chi'(s_{c}),$$

$$\Omega(t, \tilde{s}, \tilde{\xi}_{1}, \tilde{\psi}) = D + \lambda_{1}(\tilde{s})e^{\xi_{1}} + \lambda_{2}(\tilde{s})e^{\psi + \xi_{1}}.$$
(6.25)

In terms of (6.25), the system (6.20) becomes

$$\begin{cases} \dot{\tilde{s}} = -\Omega(t, \tilde{s}, \tilde{\xi}_{1}, \tilde{\psi})\tilde{s} + D[s_{in} - s_{c}] \\ -\Gamma e^{\xi_{1r}(t)} \left(e^{\tilde{\xi}_{1}} + e^{\tilde{\psi} + \tilde{\xi}_{1}} \right) , \\ \dot{\tilde{\xi}}_{1} = \mu_{1}(s_{c} + \tilde{s}) - D - \dot{\xi}_{1r}(t) , \\ \dot{\tilde{\psi}} = \chi_{n}(\tilde{s})\tilde{s} . \end{cases}$$

$$(6.26)$$

By performing the changes of feedback

$$v = D[s_{in} - s_c] - \Gamma e^{\xi_{1r}(t)} \left(e^{\tilde{\xi}_1} + e^{\tilde{\psi} + \tilde{\xi}_1} \right)$$

$$D = \mu_1(s_c) - \dot{\xi}_{1r}(t) + \mu$$
(6.27)

with μ and v to be specified, we obtain the system

$$\begin{cases} \dot{\tilde{s}} = -\Omega(t, \tilde{s}, \tilde{\xi}_1, \tilde{\psi})\tilde{s} + v ,\\ \dot{\tilde{\xi}}_1 = \lambda_1(\tilde{s})\tilde{s} - \mu , \quad \dot{\tilde{\psi}} = \chi_n(\tilde{s})\tilde{s} . \end{cases}$$
(6.28)

Consider the function defined (for $s \ge 0$) by

$$V(\tilde{s}, \tilde{\xi}_{1}, \tilde{\psi}) := \frac{1}{2}\tilde{s}^{2} + c_{1}\left(\sqrt{1 + \tilde{\xi}_{1}^{2}} - 1\right) + c_{2}\left(\sqrt{1 + \tilde{\psi}^{2}} - 1\right)$$
(6.29)

where c_1 and c_2 are defined in (6.22). In terms of the function $\langle a \rangle = a/\sqrt{1+a^2}$, we deduce from (6.28) that its derivative along the trajectories of (6.28) is

$$\dot{V} = -\Omega(t, \tilde{s}, \tilde{\xi}_1, \tilde{\psi})\tilde{s}^2 + \left[v + c_1 \langle \tilde{\xi}_1 \rangle \lambda_1(\tilde{s}) + c_2 \langle \tilde{\psi} \rangle \chi_n(\tilde{s}) \right] \tilde{s} - c_1 \langle \tilde{\xi}_1 \rangle \mu.$$

6.2 Globally Asymptotically Stabilizing Control Laws

Substituting the feedbacks

$$\mu(\tilde{\xi}_1) = \frac{\Gamma}{4} \langle \tilde{\xi}_1 \rangle
v(\tilde{\xi}_1, \tilde{\psi}) = -c_1 \langle \tilde{\xi}_1 \rangle \lambda_1(0) - c_2 \langle \tilde{\psi} \rangle \chi_n(0)$$
(6.30)

into (6.27) produces the corresponding feedback functions s_{in} and D in (6.23)-(6.24). Since $\alpha \in [0, \Gamma/2)$, we get $D(t, \tilde{\xi}_1) \geq \Gamma/4$ for all $(t, \tilde{\xi}_1)$. The constants c_1 and c_2 from (6.22) satisfy

$$c_1 \le \frac{s_c \Gamma}{16\mu_1'(s_c)}$$
 and $c_2 \le \frac{s_c \Gamma}{16\chi'(s_c)}$

so $s_{in}(t, \tilde{\xi}_1, \tilde{\psi}) \geq \frac{s_c}{4}$ for all $(t, \tilde{\xi}_1, \tilde{\psi})$. On the other hand,

$$\dot{V} = -\Omega(t, \tilde{s}, \tilde{\xi}_1, \tilde{\psi})\tilde{s}^2 + \left[c_1\langle \tilde{\xi}_1 \rangle [\lambda_1(\tilde{s}) - \lambda_1(0)] + c_2 \langle \tilde{\psi} \rangle [\chi_n(\tilde{s}) - \chi_n(0)]\right] \tilde{s} - \frac{\Gamma}{4} c_1 \langle \tilde{\xi}_1 \rangle^2 .$$
(6.31)

Using Assumption 6 and the Mean Value Theorem, it follows that for each \tilde{s} , we have $|\lambda_1(\tilde{s}) - \lambda_1(0)| \leq |\mu'_1(\hat{\xi}) - \mu'_1(s_c)| \leq |\tilde{s}|\theta_1$ for some $\hat{\xi} \in [\min\{s_c, \tilde{s} + s_c\}, \max\{s_c, \tilde{s} + s_c\}]$, and similarly $|\chi_n(\tilde{s}) - \chi_n(0)| \leq |\tilde{s}|(\theta_1 + \theta_2)$. Hence, (6.31) gives

$$\dot{V} \leq -\Omega(t,\tilde{s},\tilde{\xi}_1,\tilde{\psi})\tilde{s}^2 + c_1\theta_1\tilde{s}^2 + c_2(\theta_1 + \theta_2)\tilde{s}^2 -\frac{\Gamma}{4}c_1\langle\tilde{\xi}_1\rangle^2 .$$
(6.32)

Since the μ_i 's are strictly increasing, both λ_1 and λ_2 are positive. We deduce that $\Omega \ge D \ge \Gamma/4$ everywhere, so

$$\dot{V} \leq \left[-\frac{\Gamma}{4} + c_1 \theta_1 + c_2 (\theta_1 + \theta_2) \right] \tilde{s}^2 - \frac{\Gamma}{4} c_1 \langle \tilde{\xi}_1 \rangle^2 .$$
(6.33)

The constants c_1 and c_2 we defined in (6.22) also satisfy

$$c_1 \leq \frac{\Gamma}{16\theta_1}$$
 and $c_2 \leq \frac{\Gamma}{16(\theta_1 + \theta_2)}$

We deduce that

$$\dot{V} \leq -\frac{\Gamma}{8}\tilde{s}^2 - \frac{\Gamma}{4}c_1\langle\tilde{\xi}_1\rangle^2 \leq 0 , \qquad (6.34)$$

and the closed-loop system given by (6.28) and (6.30) is

$$\dot{\tilde{s}} = -\Omega \tilde{s} - c_1 \langle \tilde{\xi}_1 \rangle \lambda_1(0) - c_2 \langle \tilde{\psi} \rangle \chi_n(0),
\dot{\tilde{\xi}}_1 = \lambda_1(\tilde{s}) \tilde{s} - \frac{\Gamma}{4} \langle \tilde{\xi}_1 \rangle, \quad \dot{\tilde{\psi}} = \chi_n(\tilde{s}) \tilde{s}.$$
(6.35)

The asymptotic stability property therefore follows as before from the LaSalle Invariance Principle. Moreover the linearization of (6.35) around the origin is uniformly globally asymptotically stable. This follows from the LaSalle Invariance Principle as well, since the time derivative of $\omega(s_a, \xi_{1a}, \psi_a) := As_a^2 + B\xi_{1a}^2 + C\psi_a^2$ along the trajectories of the linearization of (6.35) satisfies $\dot{\omega} \leq -\frac{\Gamma}{4} \min\{A, B\}[s_a^2 + \xi_{1a}^2]$ when the constants A, B, C > 0 are chosen so that $Ac_1 = B$ and $Ac_2 = C$. The local exponential stability asserted in the theorem now follows from the linearization principle as in the proof of Theorem 5. This concludes the proof of Theorem 6.

7 ILLUSTRATION

7.1 Control Synthesis

We illustrate the globally stabilizing control laws from Theorem 6 using the system

$$\dot{s} = D[s_{in} - s] - \frac{10s}{1+20s} x_1 - \frac{s}{1+s} x_2 ,$$

$$\dot{x}_1 = \left[\frac{10s}{1+20s} - D\right] x_1 , \quad \dot{x}_2 = \left[\frac{s}{1+s} - D\right] x_2 .$$
(7.36)

In terms of our earlier notation, we have

$$\mu_1(s) = \frac{10s}{1+20s}, \ \mu_2(s) = \frac{s}{1+s}, \ s_c = \frac{9}{10}, \ \Gamma = \frac{9}{19}$$

and the function $\chi = \mu_2 - \mu_1$ is

$$\chi(s) = \frac{s(-9+10s)}{(1+s)(1+20s)} . \tag{7.37}$$

One can prove that Assumption 3.1 is satisfied with this χ . Moreover, Assumption 6 is satisfied with $\theta_1 = 400$ and $\theta_2 = 2$. Hence, Theorem 6 applies as long as $0 < \alpha < \Gamma/2 = 9/38$.

In terms our new coordinates ξ_1 , ξ_2 , and ψ from (5.13), the chemostat dynamics become

$$\begin{cases} \dot{s} = D[s_{in} - s] - \frac{10s}{1+20s}e^{\xi_1} - \frac{s}{1+s}e^{\psi + \xi_1} ,\\ \dot{\xi}_1 = \frac{10s}{1+20s} - D , \quad \dot{\psi} = \frac{s(-9+10s)}{(1+s)(1+20s)}. \end{cases}$$
(7.38)

Let us consider this reference trajectory for (7.38):

$$(s_r(t), \xi_{1r}(t), \psi_r(t)) := (0.9, \cos(0.075t), 0).$$
(7.39)

In terms of the constants (6.22) and the error variables $\tilde{\xi}_1$, $\tilde{\xi}_2$, and $\tilde{\psi}$ from (5.13),

Theorem 6 provides us with the control laws

$$D(t,\tilde{\xi}_{1}) = \frac{9}{19} + 0.075\sin(0.075t) + \frac{9}{76}\frac{\xi_{1}}{\sqrt{1+\tilde{\xi}_{1}^{2}}}$$

$$s_{in}(t,\tilde{\xi}_{1},\tilde{\psi}) = \frac{1}{D(t,\tilde{\xi}_{1})} \left\{ \frac{9}{19}e^{\cos(0.075t)} \left(e^{\tilde{\xi}_{1}} + e^{\tilde{\psi}+\tilde{\xi}_{1}} \right) - c_{1}\frac{10}{19^{2}}\frac{\tilde{\xi}_{1}}{\sqrt{1+\tilde{\xi}_{1}^{2}}} - c_{2}\frac{90}{19^{2}}\frac{\tilde{\psi}}{\sqrt{1+\tilde{\psi}^{2}}} \right\} + \frac{9}{10}$$

$$(7.40)$$

which globally asymptotically stabilize and locally exponentially stabilize the trajectory of (7.38) defined in (7.39).

7.2 Numerical Simulation

To validate our results, we simulated (7.36) with the control laws (7.40) over 1000 time units for the initial value $(s, x_1, x_2)(0) = (1, 0.9, 0.8)$. The corresponding plots for x_1 , x_2 , D, and s_{in} are in Figures 1-2 below.



Figure 1: Species Levels x_1 and x_2 for Chemostat Model (7.36)



Figure 2: Controllers D and s_{in} for Chemostat Model (7.36)

They illustrate how the global controls (7.40) cause the trajectories of (7.36) to track $(9/10, e^{\cos(.075t)}, e^{\cos(.075t)})$. Moreover, while the feedback controllers D and s_{in} from (7.40) are more complicated than the local controllers from Theorem 5, they are guaranteed to remain positive for all initial conditions.

8 CONCLUSION

The chemostat forms the basis for much current research in systems biology. Two important problems in the area are (a) the search for and analysis of mechanisms that yield coexistence and (b) the design of feedback controllers that force the chemostat trajectories to track prescribed behaviors such as oscillations. To address these problems, we used a Lyapunov-type analysis to find explicit dilution rates and substrate input concentrations ensuring that the species concentrations in a two species chemostat with one limiting substrate track a prescribed stable periodic coexistence behavior.

While other methods exist for analyzing the stability of the chemostat error dynamics (e.g., Floquet theory for (5.18)), we believe that our approach is better suited for control theoretic analysis. For example, we conjecture that our explicit Lyapunov function constructions (from the appendix below) can be used to prove that the stability is robust to small perturbations of the dilution rates and input concentrations. See [24] where the analogous robustness analysis was done for a single species chemostat using input-to-state stability.

APPENDIX

We provide two constructions for a global strict Lyapunov function for the error dynamics (6.35). The first is based on the generalized Matrosov theorem results from [25], using the weak Lyapunov function (6.29) and the auxiliary function

$$V_3(\tilde{s}, \tilde{\xi}_1, \tilde{\psi}) := \tilde{s} \langle \tilde{\psi} \rangle, \tag{A.1}$$

where $\langle a \rangle := a/\sqrt{1+a^2}$ for all real numbers a. The second method constructs a positive increasing function κ so that

$$V_a(\tilde{s}, \tilde{\xi}_1, \tilde{\psi}) := \tilde{s} \langle \tilde{\psi} \rangle + \int_0^{V(\tilde{s}, \tilde{\xi}_1, \tilde{\psi})} \kappa(r) dr$$
(A.2)

is a strict Lyapunov function for (6.35). Our Lyapunov function constructions are significant because Lyapunov functions are useful for proving robustness of stability [24].

A.1 First Method

Choose V_3 as in (A.1). Set $V_2 := V$ as defined in (6.29) and $N_2 := \frac{\Gamma}{8}\tilde{s}^2 + \frac{\Gamma}{4}c_1\langle \tilde{\xi}_1 \rangle^2$. By (6.34), $\dot{V}_2 \leq -N_2 =: Y_2$. Also, when $\alpha \in C^1$ is real valued,

$$\frac{d}{dt}\langle\alpha\rangle = \dot{\alpha}/(1+\alpha^2)^{3/2}.$$

The time derivative of V_3 along the trajectories of (6.35) satisfies

$$\dot{V}_{3} = -\Omega(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi})\tilde{s}\langle\tilde{\psi}\rangle - c_{1}\lambda_{1}(0)\langle\tilde{\xi}_{1}\rangle\langle\tilde{\psi}\rangle -c_{2}\chi_{n}(0)\langle\tilde{\psi}\rangle^{2} + \frac{\tilde{s}^{2}\chi_{n}(\tilde{s})}{(1+\tilde{\psi}^{2})^{3/2}}.$$
(A.3)

Since the μ'_i s are bounded, so is χ' . Also, $\chi_n(0) = \chi'(s_c) > 0$. It follows from the Mean Value Theorem and the definition of χ_n in (6.25) that χ_n is bounded. Hence, $ab \leq c_2\chi_n(0)a^2/4 + b^2/\{c_2\chi_n(0)\}$ with $a = \langle \tilde{\psi} \rangle$, applied to the first two terms on the right side of (A.3), first with $b = -\Omega(t, \tilde{s}, \tilde{\xi}_1, \tilde{\psi})\tilde{s}$ and then with $-c_1\lambda_1(0)\langle \tilde{\xi}_1\rangle$, provides constants $\underline{c}, \overline{c} > 0$ such that

$$\dot{V}_{3} \leq -\frac{c_{2}}{2}\chi_{n}(0)\langle\tilde{\psi}\rangle^{2} + \frac{\left(\Omega(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi})\tilde{s}\right)^{2}}{c_{2}\chi_{n}(0)} \\
+ \frac{\left(c_{1}\lambda_{1}(0)\langle\tilde{\xi}_{1}\rangle\right)^{2}}{c_{2}\chi_{n}(0)} + \frac{\tilde{s}^{2}\chi_{n}(\tilde{s})}{\left(1+\tilde{\psi}^{2}\right)^{3/2}} \\
\leq -\underline{c}\langle\tilde{\psi}\rangle^{2} + \bar{c}N_{2}[1+\Omega^{2}(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi})]$$

Note that $\chi_3(t, (\tilde{s}, \tilde{\xi}_1, \tilde{\psi}), Y_2) := \bar{c}N_2[1 + \Omega^2(t, \tilde{s}, \tilde{\xi}_1, \tilde{\psi})]$ is bounded uniformly in t in the usual sense of [25] and is zero when $Y_2 = 0$. Moreover, $(\tilde{s}, \tilde{\xi}_1, \tilde{\psi}) \mapsto N_2 + \underline{c}\langle \tilde{\psi} \rangle^2$ is positive definite. Hence, [25, Corollary 3.4] with $V_1 = V_2$, $N_3 = \underline{c}\langle \tilde{\psi} \rangle^2$, and j = 3 constructs nonnegative functions p_1 and p_2 for which $V^{\sharp} := p_1(V)V + p_2(V)V_3$ is the desired Lyapunov function.

A.2 Second Method

To construct κ so that (A.2) is a Lyapunov function for (6.35), first note that the inequality $-ab \leq \frac{1}{2}a^2 + \frac{1}{2}b^2$ and (A.3) give

$$\dot{V}_{3} = -\left\{ \frac{\Omega(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi})\tilde{s}+c_{1}\lambda_{1}(0)\langle\tilde{\xi}_{1}\rangle}{\sqrt{c_{2}\chi_{n}(0)}} \right\} \left\{ \langle \tilde{\psi} \rangle \sqrt{c_{2}\chi_{n}(0)} \right\} -c_{2}\chi_{n}(0)\langle \tilde{\psi} \rangle^{2} + \frac{\tilde{s}^{2}\chi_{n}(\tilde{s})}{(1+\tilde{\psi}^{2})^{3/2}} \leq \frac{1}{2c_{2}\chi_{n}(0)} \left[\Omega(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi})\tilde{s}+c_{1}\lambda_{1}(0)\langle\tilde{\xi}_{1}\rangle \right]^{2} -\frac{c_{2}\chi_{n}(0)}{2} \langle \tilde{\psi} \rangle^{2} + \frac{\tilde{s}^{2}\chi_{n}(\tilde{s})}{(1+\tilde{\psi}^{2})^{3/2}} .$$

The relation $(a+b)^2 \leq 2a^2 + 2b^2$ therefore gives

$$\dot{V}_{3} \leq \frac{1}{c_{2}\chi_{n}(0)} \left[\Omega^{2}(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi})\tilde{s}^{2} + c_{1}^{2}\lambda_{1}^{2}(0)\langle\tilde{\xi}_{1}\rangle^{2} \right]
- \frac{c_{2}\chi_{n}(0)}{2}\langle\tilde{\psi}\rangle^{2} + \frac{\chi_{n}(\tilde{s})\tilde{s}^{2}}{(1+\tilde{\psi}^{2})^{3/2}}
\leq \left[\frac{1}{c_{2}\chi_{n}(0)} \Omega^{2}(t,\tilde{s},\tilde{\xi}_{1},\tilde{\psi}) + \chi_{n}(\tilde{s}) \right] \tilde{s}^{2}
- \frac{c_{2}\chi_{n}(0)}{2}\langle\tilde{\psi}\rangle^{2} + \frac{c_{1}^{2}\lambda_{1}^{2}(0)}{c_{2}\chi_{n}(0)}\langle\tilde{\xi}_{1}\rangle^{2}.$$
(A.4)

By enlarging θ_1 in (6.21) without relabeling, we can assume c_2 satisfies $c_2 < 16$. Since V is proper and positive definite and the λ_i 's are bounded (because the μ'_i 's are bounded), we can find a positive strictly increasing function κ such that

$$\kappa(V(\tilde{s}, \tilde{\xi}_1, \tilde{\psi})) \geq \frac{4}{\sqrt{c_2}} + \frac{4}{\Gamma} \frac{c_1 \lambda_1^2(0)}{c_2 \chi_n(0)} \\ + \frac{8}{\Gamma} \left[\frac{1}{c_2 \chi_n(0)} \Omega^2(t, \tilde{s}, \tilde{\xi}_1, \tilde{\psi}) + \chi_n(\tilde{s}) \right]$$

everywhere. Therefore, since $1 < 4/\sqrt{c_2}$ (because we assumed $c_2 < 16$) and χ_n as defined in (6.25) is nonnegative (by Assumption 3.1), (6.34) and (A.4) give

$$\dot{V}_{3} \leq -\frac{c_{2}\chi_{n}(0)}{2} \langle \tilde{\psi} \rangle^{2} \\
+ \left[\frac{\Gamma}{8} \tilde{s}^{2} + \frac{\Gamma}{4} c_{1} \langle \tilde{\xi}_{1} \rangle^{2} \right] \left[\kappa(V(\tilde{s}, \tilde{\xi}_{1}, \tilde{\psi})) - 1 \right] \\
\leq -\frac{c_{2}\chi_{n}(0)}{2} \langle \tilde{\psi} \rangle^{2} - \dot{V} \left[\kappa(V(\tilde{s}, \tilde{\xi}_{1}, \tilde{\psi})) - 1 \right].$$
(A.5)

Let us now make the preceding choice of κ in the formula (A.2) of V_a . It then follows from (6.34) and (A.5) that the time derivative of (A.2) along the trajectories of (6.35) satisfies

$$\dot{V}_a \le -\frac{c_2 \chi_n(0)}{2} \langle \tilde{\psi} \rangle^2 - \frac{\Gamma}{8} \tilde{s}^2 - \frac{\Gamma}{4} c_1 \langle \tilde{\xi}_1 \rangle^2, \tag{A.6}$$

which is negative definite. Set $K = 4/\sqrt{c_2}$. Then $\kappa \ge K$ everywhere. It follows from the relations

$$\tilde{s}\langle\tilde{\psi}\rangle \geq -\frac{K}{4}\tilde{s}^2 - \frac{1}{K}\langle\tilde{\psi}\rangle^2, \qquad \sqrt{1+\tilde{\psi}^2} - 1 = \frac{\tilde{\psi}^2}{\sqrt{1+\tilde{\psi}^2}+1}$$

and the formula (6.29) for V that we also have

$$\begin{split} V_{a}(\tilde{s}, \tilde{\xi}_{1}, \tilde{\psi}) &\geq KV(\tilde{s}, \tilde{\xi}_{1}, \tilde{\psi}) + \tilde{s} \langle \tilde{\psi} \rangle \\ &\geq K \left[\frac{1}{4} \tilde{s}^{2} + c_{1} \left(\sqrt{1 + \tilde{\xi}_{1}^{2}} - 1 \right) \right. \\ &+ c_{2} \frac{\tilde{\psi}^{2}}{\sqrt{1 + \tilde{\psi}^{2} + 1}} \right] - \frac{1}{K} \langle \tilde{\psi} \rangle^{2} \\ &\geq \frac{K}{4} \tilde{s}^{2} + K c_{1} \left(\sqrt{1 + \tilde{\xi}_{1}^{2}} - 1 \right) \\ &+ \frac{K c_{2} \tilde{\psi}^{2}}{2 \left(\sqrt{1 + \tilde{\psi}^{2} + 1} \right)} + K c_{2} \frac{\tilde{\psi}^{2}}{4 (1 + \tilde{\psi}^{2})} - \frac{1}{K} \frac{\tilde{\psi}^{2}}{1 + \tilde{\psi}^{2}}. \end{split}$$

Recalling our choice of K therefore gives

$$V_{a}(\tilde{s}, \tilde{\xi}_{1}, \tilde{\psi}) \geq \frac{K}{4}\tilde{s}^{2} + Kc_{1}\left(\sqrt{1 + \tilde{\xi}_{1}^{2}} - 1\right) + \frac{Kc_{2}\tilde{\psi}^{2}}{2\left(\sqrt{1 + \tilde{\psi}^{2} + 1}\right)}.$$
(A.7)

Also, $V_a \leq \frac{1}{2}\tilde{s}^2 + \frac{1}{2}\langle \tilde{\psi} \rangle^2 + \kappa(V)V$. It follows that V_a is proper and positive definite. By (A.6) and (A.7), V_a is a Lyapunov function for (6.35), as claimed.

Acknowledgments

The authors thank Patrick De Leenheer for illuminating discussions. They also thank the two referees for their extensive comments.

References

- J. Arino, J-L. Gouzé, and A. Sciandra, "A discrete, size-structured model of phytoplankton growth in the chemostat. Introduction of non constant cell division," *J. Math. Biol.*, vol. 45, pp. 313-333, 2002.
- [2] R.A. Armstrong and R. McGehee, "Competitive exclusion," Amer. Naturalist, vol. 115, pp. 151-170, 1980
- [3] R.A. Armstrong and R. McGehee, "Coexistence of species competing for shared resources," *Theoretical Population Biology*, vol. 9, pp. 317-328, 1989.
- [4] O. Bernard and J-L. Gouzé, "Nonlinear qualitative signal processing for biological systems: Application to the algal growth in bioreactors," *Mathematical Biosciences*, vol. 157, pp. 357–372, 1999.
- [5] G.J. Butler, S.B. Hsu, and P. Waltman, "A mathematical model of the chemostat with periodic washout rate," *SIAM J. Appl. Math.*, vol. 45, pp. 435–449, 1985.
- [6] P. De Leenheer, B. Li, and H.L. Smith, "Competition in the chemostat: some remarks," *Canadian Applied Mathematics Quarterly*, vol. 11, pp. 229–248, 2003.
- [7] P. De Leenheer and S.S. Pilyugin, "Feedback-mediated oscillatory coexistence in the chemostat," in *Positive Systems. Proceedings of the Second Multidisciplinary International Symposium on Positive Systems: Theory and Applications (POSTA* 06), Grenoble, France, C. Commault and N. Marchand, Eds. Heidelberg: Springer-Verlag, 2006, pp. 97-104.
- [8] P. De Leenheer and H.L. Smith, "Feedback control for chemostat models," J. Math. Biol., vol. 46, pp. 48-70, 2003.
- [9] S.F. Ellermeyer, S.S. Pilyugin, and R. Redheffer, "Persistence criteria for a chemostat with variable nutrient input," *Journal of Differential Equations*, vol. 171, pp. 132-147, 2001.
- [10] T.C. Gard, "A new Liapunov function for the simple chemostat," Nonlinear Analysis: Real World Applications, vol. 3, pp. 211–216, 2002.
- [11] G.F. Gause and A.A. Witt "Behavior of mixed populations and the problem of natural selection" Am. Naturalist, vol. 69, pp. 596-609, 1935.
- [12] J-L. Gouzé and G. Robledo, "Feedback control for nonmonotone competition models in the chemostat," *Nonlinear Analysis: Real World Applications*, vol. 6, pp. 671-690, 2005.

- [13] F. Grognard, F. Mazenc, and A. Rapaport, "Polytopic Lyapunov functions for the stability analysis of persistence of competing species," in *Proceedings of the* 44th IEEE Conference on Decision and Control and European Control Conference ECC 2005, Seville, Spain, 2005, pp. 3699-3704.
- [14] J.K. Hale and A.S. Somolinos, "Competition for fluctuating nutrient," J. Math. Biol., vol. 18, pp. 255–280, 1983.
- [15] G. Hardin, "The competitive exclusion principle," Science, vol. 131, pp. 1292-1298, 1960.
- [16] G.E. Hutchinson, "The paradox of the plankton," American Naturalist, vol. 95, pp. 137-145, 1961.
- [17] A. Karama, O. Bernard, J-L. Gouzé, A. Benhammou, and D. Dochain, "Hybrid neural modelling of an anaerobic digester with respect to biological constraints," *Wat. Sci. Technol.*, vol. 43, pp. 1-8, 2001.
- [18] H. Khalil, Nonlinear Systems, Third Edition. Upper Saddle River, NJ: Prentice Hall, 2002.
- [19] P. Lenas and S. Pavlou, "Coexistence of three competing microbial populations in a chemostat with periodically varying dilution rate," *Mathematical Biosciences*, vol. 129, pp. 111-142, 1995.
- [20] B. Li, "Asymptotic behavior of the chemostat: General responses and different removal rates," SIAM J. Appl. Math., vol. 59, pp. 411-422, 1998.
- [21] C. Lobry, F. Mazenc, and A. Rapaport, "Persistence in ecological models of competition for a single resource," *Comptes Rendus Mathématique. Académie des Sciences*, vol. 340, pp. 199–204, 2005.
- [22] F. Mazenc, P. De Leenheer, and M. Malisoff, "Stabilizing a periodic solution in the chemostat: A case study in tracking," in *Proceedings of the 45th IEEE Conference* on Decision and Control, San Diego, CA, 2006, pp. 1794–1799.
- [23] F. Mazenc, C. Lobry, and A. Rapaport, "Persistence in ratio-dependent models for consumer-resource dynamics," *Electronic Journal of Differential Equations*, vol. 15, pp. 211–220, 2007.
- [24] F. Mazenc, M. Malisoff, and P. De Leenheer, "On the stability of periodic solutions in the perturbed chemostat," *Mathematical Biosciences and Engineering*, vol. 4, pp. 319–338, 2007.
- [25] F. Mazenc and D. Nesic, "Lyapunov functions for time varying systems satisfying generalized conditions of Matrosov theorem," in *Proceedings of the 44th IEEE Conference on Decision and Control and European Control Conference*, Seville, Spain, 2005, pp. 2432-2437.

- [26] K.S. McCann, "The diversity-stability debate," Nature, vol. 405, pp. 228-233, 2000.
- [27] J. Monod, *Recherches sur la Croissance des Cultures Bactériennes*. Paris: Eds. Hermann et cie, 1942.
- [28] A. Novick and L. Szilard, "Experiments with the chemostat on spontaneous mutations of bacteria," Proc. Nat. Acad. Sci., vol. 36, pp. 708–719, 1950.
- [29] S. Pilyugin and P. Waltman, "Competition in the unstirred chemostat with periodic input and washout," SIAM J. Appl. Math., vol. 59, pp. 1157–1177, 1999.
- [30] N.S. Rao and E.O. Roxin, "Controlled growth of competing species," SIAM J. Appl. Math., vol. 50, pp. 853–864, 1990.
- [31] S. Sastry, Nonlinear Systems, Analysis, Stability and Control. New York: Springer Verlag, 1999.
- [32] H.L. Smith, "Competitive coexistence in an oscillating chemostat," SIAM J. Appl. Math., vol. 40, pp. 498–522, 1981.
- [33] H.L. Smith, "Microbial growth in periodic gradostats," Rocky Mountain J. Math., vol. 20, pp. 1173–1194, 1990.
- [34] H.L. Smith and P. Waltman, *The Theory of the Chemostat.* Cambridge: Cambridge University Press, 1995.
- [35] H.L. Smith and P. Waltman, "Competition in the periodic gradostat," Nonlinear Analysis: Real World Applications, vol. 1, pp. 177-188, 2000.
- [36] G. Wolkowicz and Z. Lu, "Global dynamics of a mathematical model of competition in the chemostat: general response functions and differential death rates," *SIAM J. Appl. Math.*, vol. 52, pp. 222-233, 1992.