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Stabilization in a Chemostat with Sampled and Delayed Measurements

Frédéric Mazenc Jérome Harmand Michael Malisoff

***Abstract*— We study control problems for chemostat models with one species, one limiting substrate, and a constant substrate input concentration. We allow Haldane growth functions and other growth functions that are not necessarily monotone. The measurement is assumed to be the substrate concentration, which is piecewise constant with a constant delay. Under conditions on the size of the delay and on the largest sampling interval, we solve the problem of asymptotically stabilizing a componentwise positive equilibrium point with the dilution rate as control. We use a new type of Lyapunov approach.**

***Key Words*: output-feedback, stabilization, delay, sampling**

I. Introduction

The chemostat is a laboratory device used for the continuous culture of microorganisms. It was proposed simultaneously by Monod and Novick and Szilard in the 1950s; see [11], [12]. Today, it is often viewed in biotechnology, ecology, and microbiology as an ideal representation for modeling microorganisms or cells growth rates, wastewater treatment processes, or any natural environment such as a lake [4], [5], [7], [15]. The dynamics of the main variables evolving in the chemostat (which are basically the microorganisms and substrates concentrations) are usually based on mass-balance equations described by various mathematical models [1], [2], [16]. The problem of controlling such models is often difficult, notably because of the nonlinearity of the equations. Also, these systems like many other biological systems suffer from a lack of online sensors and actuators.

Even more crucial is the fact that online devices, such as those used for measuring substrate or biomass concentrations, deliver discrete variables with delays when they are available. In practice, the control laws are usually designed using continuous models and are discretized before being applied on the real system. Practitioners then rely on the robustness of control laws with respect to measurement delays in order for the control to realize its objectives. Measurement delays and their discrete nature are not the only disturbances the user has to deal with and it is expected that control performances could be improved if these characteristics are taken into account at the control design step. To the best of the authors' knowledge, no rigorous theoretical study addresses this problem, except for [8]. The paper [14] assumes that the measurements are continuous.

These remarks motivated [8] and the present work, which complements [8]. In this paper, we consider the classical model of the chemostat described in [16] with one substrate and one species. The growth rate is assumed to be of Haldane type (i.e., having a limitation of the growth for low substrate concentrations and inhibition at high concentrations) and the input substrate concentration is assumed to be constant. The dilution rate is used as a control. Controlling this system is a challenging problem, for two main reasons. First, results such as [10] that establish global asymptotic stability under suitable bounds on the delay and sampling intervals are based on state feedbacks and certain strict Lyapunov function constructions. The work in this paper entails output feedbacks, and so is beyond the scope of [10].

Second, the model generally admits two equilibria when the dilution rate is constant. One is locally exponentially stable and the other is unstable. In [8], the problem of stabilizing points of the first type was addressed, while here we stabilize points of the second type, i.e., under inhibition at high substrate concentration as modeled in the Haldane function. For this latter case, we construct a stabilizing control law that only requires measurements of the substrate concentration, which are assumed to be piecewise constant and with constant delay. The control law ensures asymptotic convergence to the equilibrium point, when suitable bounds on the size of the delay and on the largest sampling interval are satisfied. This contrasts with [8], where no constraint of this type was imposed. The reason why this extra constraint is needed is that we stabilize points which can be exponentially unstable when a constant dilution rate is chosen.

In this work, we design a new feedback, and perform a stability analysis for the system in closed loop with the feedback. It is reminiscent of the theoretical contribution of [10]. However, the main result of [10] does not apply directly, so an ad hoc proof has to be proposed. Our proof is also very different from the one in [9], which is based on the assumptions that the growth rates are given by a known analytic expression of Haldane or Monod type and that measurements for the species levels are available in the control design, making it possible to design Lyapunov functionals.

II. The model

We consider the following model of chemostat:

$$\left\{ \begin{array}{rcl} \dot{s}(t) & = & D[s_{in} - s(t)] - \mu(s(t))x(t) \\ \dot{x}(t) & = & [\mu(s(t)) - D]x(t) \end{array} \right. \tag{1}$$

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where $s_{in} > 0$ is a constant, and where the states x and s are positive and real valued, and where D is a positive valued control. In what follows, C^1 means continuously differentiable.

Assumption 1: The function μ is of class C^1 and $\mu(0) = 0$. There is a constant $s_M > 0$ such that $\mu'(s) > 0$ for all $s \in [0, s_M)$ and $\mu'(s) \leq 0$ for all $s \in (s_M, +\infty)$. Finally, $\mu(s) > 0$ for all $s > 0$.

Assumption 1 is satisfied by all functions of the form

$$\mu(s) = \frac{k_1 s}{1 + k_2 s + k_3 s^2}, \tag{2}$$

where $k_i > 0$ for $i = 1$ to 3 are arbitrary constants. Functions of the form (2) are called Haldane functions. Moreover, we can prove:

Lemma 1: If Assumption 1 holds, then we can find a C^1 class $\mathcal{K}_\infty$ function μ_1 and a nondecreasing C^1 function $\gamma : \mathbb{R} \to [0, +\infty)$ such that $\gamma(m) = 0$ for all $m \leq 0$ and such that

$$\mu(s) = \frac{\mu_1(s)}{1 + \gamma(s)} \tag{3}$$

holds for all $s \geq 0$.

For the proof of Lemma 1, see Appendix VI.

Remark 1: When $s_{in} > s_M$ and D is constant such that $D \in (\mu(s_{in}), \mu(s_M))$, then one can easily check that the system (1) admits a locally stable equilibrium $(s_{in}, 0)$ and a locally unstable positive equilibrium point of the form $(s_*, s_{in} - s_*)$. Here $s_* > 0$ is such that $D = \mu(s_*)$ and $s_* \in (s_M, s_{in})$. In [8], we solved the problem of globally stabilizing an equilibrium point that can be locally exponentially stabilized through a constant dilution rate.

To make our sampling control objective precise, fix any two constants $\epsilon_1 > 0$ and $\epsilon_2 > 0$ such that $\epsilon_2 > \epsilon_1$, and let t_i be a sequence of real numbers such that $t_0 = 0$ and such that

$$0 < \epsilon_1 \leq t_{i+1} - t_i \leq \epsilon_2 \tag{4}$$

for all $i \in \mathbb{N}$, where $\mathbb{N} = \{1, 2, \ldots\}$. We let $\tau_f \geq 0$ be a constant, and we define the function τ by

$$\tau(t) = \begin{cases} \tau_f, & t \in [0, \tau_f) \\ \tau_f + t - t_j, & t \in [t_j + \tau_f, t_{j+1} + \tau_f) \text{ and } j \geq 0 \end{cases} \tag{5}$$

which is reminiscent of the representation of sampling used for instance in [3]. From this definition, it follows that when $t \in [t_j + \tau_f, t_{j+1} + \tau_f)$, then $t - \tau(t) = t - (\tau_f + t - t_j) = t_j - \tau_f$. Thus, the function $t - \tau(t)$ is piecewise constant. For instance, when $\tau_f = 0$ and $t_j = j$ for all $j \geq 0$, then $t - \tau(t) = j$ for all $t \in [j, j + 1)$ and $j \geq 0$.

Notice for later use that for all $t \geq 0$, we have

$$0 \leq \tau(t) \leq \tau_M, \tag{6}$$

where

$$\tau_M = \tau_f + \epsilon_2. \tag{7}$$

We assume that the only measurement available is $s(t-\tau(t))$. Our control objective is the asymptotic stabilization of the point $E_* = (s_*, s_{in} - s_*)$ for any constant $s_* \in (0, s_{in})$, with a nonnegative feedback of the form $D(s(t - \tau(t)))$. Notice that E_* is positive and is an equilibrium point of (1) if and only if $D(s_*) = \mu(s_*)$.

III. Main Result

Under our Assumption 1, we fix any functions μ_1 and γ that satisfy the requirements from Lemma 1 and any constants $s_{in} > 0$ and $s_* \in (0, s_{in})$. We use the constants

$$\mu_a = \mu_1(s_*) s_{in} \ , \tag{8}$$

$$\begin{aligned} &\varpi_s = \inf_{s \in [0, s_{in}]} \mu_1'(s) \ , \ \varpi_l = \sup_{s \in [0, s_{in}]} \mu_1'(s) \ , \\ &\rho_l = \sup_{s \in [0, s_{in}]} \gamma'(s), \end{aligned} \tag{9}$$

and

$$\rho_m = \frac{\rho_l^2}{2\varpi_s} \sup_{l \in [0, s_{in}]} \frac{\mu_1 \left(l + 1.1 \mu_a \tau_M\right)^2}{1 + \gamma(l)} \tag{10}$$

where τ_M is from (7). The properties of μ_1 and γ ensure that they are well-defined and positive. Finally, we assume:

Assumption 2: The constant τ_M from (7) is such that

$$\frac{\mu_1(s_{in})}{1 + \gamma(s_{in})} - \frac{\mu_1(s_*)}{1 + \gamma\left(s_{in} - \mu_a \tau_M\right)} > 0 \ , \tag{11}$$

$$\tau_M < \frac{1}{2\sqrt{2\rho_m \varpi_l} s_{in}}, \ \text{ and } \ \tau_M \leq \frac{1}{2\rho_l s_{in} \mu(s_M)} \tag{12}$$

are all satisfied.

Since $s_* < s_{in}$ and μ_1 is increasing, it is usually easy to determine a constant $\overline{\tau} > 0$ such that (11) is satisfied for all $\tau_M \in (0, \overline{\tau})$. See the example below where we check our assumptions. Our main result is then:

Theorem 1: If Assumptions 1-2 hold, then for each constant $s_* \in (0, s_{in})$, all solutions of (1) in closed loop with

$$D(t) = \tfrac{\mu_1(s_*)}{1 + \gamma(s(t - \tau(t)))} \tag{13}$$

asymptotically converge to $(s_*, s_{in} - s_*)$.

IV. Proof of Theorem 1

Fix any continuous initial function $(\phi_s, \phi_x) : [-\tau_M, 0] \to (0, \infty)^2$ for the corresponding closed loop system

$$\begin{cases} \dot{s}(t) &= \frac{\mu_1(s_*)}{1 + \gamma(s(t - \tau(t)))} [s_{in} - s(t)] - \mu(s(t)) x(t) \\ \dot{x}(t) &= \left[\mu(s(t)) - \frac{\mu_1(s_*)}{1 + \gamma(s(t - \tau(t)))}\right] x(t). \end{cases} \tag{14}$$

We must prove that this initial condition generates a positive valued solution $(x(t), s(t))$ of the system (14) that defined over $[0, +\infty)$, positive and such that

$$\lim_{t \to +\infty} (s(t), x(t)) = (s_*, s_{in} - s_*). \tag{15}$$

First Step. One can easily prove that the solution $(s(t), x(t))$ is defined over $[-\tau_M, +\infty)$ and positive valued, since $D(t) s_{\text{in}} > 0$ would give $\dot{s}(t) > 0$ at any time t when $s(t) = 0$. We next prove that the solution is bounded. Set

$$z(t) = s_{in} - s(t) - x(t) \ . \tag{16}$$

An elementary calculation gives

$$\dot{z}(t) = -\tfrac{\mu_1(s_*)}{1 + \gamma(s(t - \tau(t)))} z(t). \tag{17}$$

Here and in the sequel, all equalities and inequalities should be understood to hold for all $t \geq 0$ unless otherwise noted. Consequently, $|z(t)| \leq |z(0)|$ for all $t \geq 0$. It follows that for all $t \geq 0$, we have

$$\begin{array}{rcl} |(x(t), s(t))| & \leq & s(t) + x(t) \ = \ -z(t) + s_{in} \\ & \leq & |z(0)| + s_{in} \ \leq \ c_a, \end{array} \tag{18}$$

where $c_a = s_{in} + |s_{in} - s(0) - x(0)|$. Also, (17)-(18) give

$$|z(t)| \leq |z(\tau_M)| e^{\frac{\mu_1(s_*)}{1+\gamma(c_a)}(\tau_M - t)} \tag{19}$$

for all $t \geq \tau_M$.

Second step. We prove by contradiction that there is a $t_a > 2\tau_M$ such that $s(t_a) \in (0, s_{in})$. Assume that for all $t > 2\tau_M$, we have $s(t) \geq s_{in}$. Then for all $t > 2\tau_M$, we get

$$\begin{array}{l} -\mu(s(t))x(t) < 0 \ \text{ and} \\ \frac{\mu_1(s_*)}{1+\gamma(s(t-\tau(t)))}[s_{in} - s(t)] \leq 0 \ . \end{array} \tag{20}$$

Hence, $\dot{s}(t) < 0$ for all $t > 2\tau_M$. Since $s(t)$ is lower bounded by s_{in}, it follows that $s(t)$ converges to some limit s_l such that $s_l \geq s_{in}$. Since $s(t) = s_{in} - x(t) - z(t) < s_{in} - z(t)$ and $z(t)$ converges to zero, we get $s_l = s_{in}$. Therefore,

$$\begin{array}{l} \lim\limits_{t \to +\infty} \mu(s(t)) = \dfrac{\mu_1(s_{in})}{1 + \gamma(s_{in})} \ \text{ and} \\ \lim\limits_{t \to +\infty} \dfrac{\mu_1(s_*)}{1 + \gamma(s(t - \tau(t)))} = \dfrac{\mu_1(s_*)}{1 + \gamma(s_{in})} \ . \end{array} \tag{21}$$

Since μ_1 is increasing and $s_{in} > s_*$, we deduce from the two equalities in (21) that there is $t_b > t_a$ such that for all $t \geq t_b$, $\mu(s(t)) - \frac{\mu_1(s_*)}{1+\gamma(s(t-\tau(t)))} \geq c_b$, where

$$c_b = \frac{\mu_1\left(\frac{s_{in}+s_*}{2}\right)}{1 + \gamma(s_{in})} - \frac{\mu_1(s_*)}{1 + \gamma(s_{in})} > 0. \tag{22}$$

It follows from (14) that $\dot{x}(t) \geq c_b x(t)$ holds for all $t \geq t_b$, so $\lim_{t \to +\infty} x(t) = +\infty$. This contradicts the fact that $x(t)$ is bounded. Since D is positive valued, we conclude that there is $t_a > 2\tau_M$ such that $s(t) \in (0, s_{in})$ for all $t \geq t_a$, since the structure of the dynamics ensure that we would have $\dot{s}(t) < 0$ at any time t when $s(t) \geq s_{in}$.

Third step. We prove that there are constants $t_c \geq t_a$ and $s_\triangle \in (0, s_{in})$ such that for all $t \geq t_c$, we have $s(t) < s_\triangle$.

With z defined in (16), we can use the fact that $s(t) = s_{in} - z(t) - x(t)$ to get

$$\begin{array}{rcl} \dot{x}(t) & = & \Big[\frac{\mu_1(s_{in}-x(t)-z(t))}{1+\gamma(s_{in}-x(t)-z(t))} \\ & & - \frac{\mu_1(s_*)}{1+\gamma(s_{in}-x(t)-z(t)+s(t-\tau(t)-s(t)))} \Big] \, x(t) \ . \end{array} \tag{23}$$

Also, for all $t \geq 2\tau_M$, we get

$$s(t - \tau(t)) - s(t) = -\int_{t-\tau(t)}^{t} \dot{s}(m) dm \tag{24}$$

and

$$\begin{array}{l} \int_{t-\tau(t)}^{t} \dot{s}(m) dm \\ = \int_{t-\tau(t)}^{t} \left(\frac{\mu_1(s_*)}{1+\gamma(s(t-\tau(t)))} - \frac{\mu_1(s(m))}{1+\gamma(s(m))} \right) [s_{in} - s(m)] dm \\ + \int_{t-\tau(t)}^{t} \frac{\mu_1(s(m))}{1+\gamma(s(m))} z(m) dm. \end{array}$$

Since $s_{in} - s(t) \geq 0$ holds for all $t \geq t_a$, it follows that for all $t \geq t_a + 2\tau_M$ we get

$$\begin{array}{l} \int_{t-\tau(t)}^{t} \dot{s}(m) dm \leq \\ \mu_a \tau_M + \mu_1(s_{in}) \int_{t-\tau(t)}^{t} |z(m)| dm, \end{array} \tag{25}$$

where μ_a was defined in (8) and τ_M is from (7).

Let q denote the left side of (11) from Assumption 2. Since γ is nondecreasing, we deduce from (23), (24) and (25) and the fact that $x(t) \leq c_a$ for all $t \geq 0$ that

$$\dot{x}(t) \geq [q + \kappa(x(t)) + \lambda(x_t, z_t)] \, x(t) \tag{26}$$

holds for all $t \geq t_a + 2\tau_M$, where

$$\begin{array}{l} \lambda(x(t), z_t) = \frac{\mu_1(s_{in}-x(t)-z(t))}{1+\gamma(s_{in}-x(t)-z(t))} - \frac{\mu_1(s_{in}-x(t))}{1+\gamma(s_{in}-x(t))} \\ + \frac{\mu_1(s_*)}{1+\gamma(s_{in}-x(t)-\mu_a\tau_M)} \\ - \dfrac{\mu_1(s_*)}{1+\gamma\left(s_{in}-x(t)-\mu_a\tau_M-z(t)-\mu_1(s_{in})\int_{t-\tau(t)}^{t}|z(m)|dm\right)} \end{array} \tag{27}$$

and

$$\begin{array}{rcl} \kappa(x) & = & \frac{\mu_1(s_{in}-x)}{1+\gamma(s_{in}-x)} - \frac{\mu_1(s_{in})}{1+\gamma(s_{in})} \\ & & + \frac{\mu_1(s_*)}{1+\gamma(s_{in}-\mu_a\tau_M)} - \frac{\mu_1(s_*)}{1+\gamma(s_{in}-x-\mu_a\tau_M)}. \end{array} \tag{28}$$

Since $\lim_{t \to +\infty} z(t) = 0$, we get $\lim_{t \to \infty} \lambda(x(t), z_t) = 0$ so we deduce from Assumption 2 that there is a $t_c > 2\tau_M$ such that for all $t \geq t_c$, we have

$$\dot{x}(t) \geq \left[\tfrac{q}{2} + \kappa(x(t)) \right] x(t) \ . \tag{29}$$

Since the function κ is continuous and $\kappa(0) = 0$, there exists $x_p \in (0, s_{in})$ such that for all $x \in [0, x_p]$, we have $\kappa(x) \geq -\frac{q}{4}$. One can then prove that there is a $t_e \geq t_d$ such that for all $t \geq t_e$, we have

$$x(t) \geq x_p. \tag{30}$$

This follows because $\dot{x}(t) \geq qx(t)/4$ at all times t when $x(t) \in (0, x_p]$. Also, (19) implies that there is a $t_f \geq t_e$ such that for all $t \geq t_f$, the inequality

$$|z(t)| \leq \tfrac{x_p}{4} \tag{31}$$

holds. By using the definition of z, (31) and (30), we deduce that for all $t \geq t_f$, we have

$$s(t) \leq -x(t) + \tfrac{x_p}{4} + s_{in} \leq -x_p + \tfrac{x_p}{4} + s_{in} = s_\triangle, \tag{32}$$

where $s_\triangle = s_{in} - \frac{3x_p}{4}$. Since $x_p \in (0, s_{in})$, it follows that $s_\triangle \in (0, s_{in})$.

Fourth step. We build a functional $\mathcal{U}_1$ that is reminiscent of barrier Lyapunov functions that are used in adaptive control and parameter identification. Later, we add double integral term to $\mathcal{U}_1$ to prove our stability property. Using z defined in (16) gives the following for all $t \geq t_M$:

$$\begin{array}{rcl} \dot{s}(t) & = & \left[\frac{\mu_1(s_*)}{1+\gamma(s(t-\tau(t)))} - \frac{\mu_1(s(t))}{1+\gamma(s(t))} \right] [s_{in} - s(t)] \\ & & + \mu(s(t)) z(t) \ . \end{array} \tag{33}$$

Since $\gamma(s(t)) - \gamma(s(t-\tau)) = \int_{t-\tau(t)}^{t} \gamma'(s(m)) \dot{s}(m) dm$ holds for all $t \geq 2\tau_M$, we can use (33) to get

$$\begin{array}{l} \dot{s}(t) = \mu(s(t)) z(t) + \\ \frac{[\mu_1(s_*) - \mu_1(s(t))][1+\gamma(s(t))] + \mu_1(s(t))\mathcal{I}(t)}{[1+\gamma(s(t-\tau(t)))][1+\gamma(s(t))]} [s_{in} - s(t)] \end{array} \tag{34}$$

for all $t \geq 2\tau_M$, where $\mathcal{I}(t) = \int_{t-\tau(t)}^{t} \gamma'(s(m))\dot{s}(m)dm$.

We use

$$\mathcal{U}_1(s) = \int_0^{s-s_*} \frac{m}{s_{in}-s_*-m} dm, \tag{35}$$

which is of class C^1 over $[0, s_{in})$ and nonnegative valued. It follows from (34) that its derivative along all trajectories of the closed loop system for all $t \geq t_a + 2\tau_M$ satisfies

$$\begin{aligned} \dot{\mathcal{U}}_1(t) = \tfrac{s(t)-s_*}{s_{in}-s(t)}\mu(s(t))z(t) + \\ \tfrac{[\mu_1(s_*)-\mu_1(s(t))][1+\gamma(s(t)) + \mu_1(s(t))\mathcal{I}(t)}{[1+\gamma(s(t-\tau(t)))][1+\gamma(s(t))]}[s(t)-s_*] \ . \end{aligned} \tag{36}$$

From the third step, we deduce that when $t \geq t_c + 2\tau_M$, the inequality

$$\begin{aligned} &\dot{\mathcal{U}}_1(t) \leq \\ &\tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{1+\gamma(s(t-\tau(t)))} + \tfrac{|s(t)-s_*|\mu(s_{in})}{s_{in}-s_\triangle}|z(t)| \\ &+|s(t)-s_*|\tfrac{\mu_1(s(t))\int_{t-\tau(t)}^{t}\gamma'(s(m))|\dot{s}(m)|dm}{1+\gamma(s(t-\tau(t)))} \end{aligned} \tag{37}$$

is satisfied. From the definition ρ_l in (9) and the fact that $s(t) < s_\delta$ holds for all $t \geq t_c + 2\tau_M$, we deduce that

$$\begin{aligned} \dot{\mathcal{U}}_1(t) \leq & \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{1+\gamma(s(t-\tau(t)))} \\ & + \rho_l|s(t)-s_*|\tfrac{\mu_1(s(t))\int_{t-\tau(t)}^{t}|\dot{s}(m)|dm}{1+\gamma(s(t-\tau(t)))} \\ & + \tfrac{|s(t)-s_*|\mu(s_{in})}{s_{in}-s_\triangle}|z(t)| \\ \leq & \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ & - \varpi_s\tfrac{(s(t)-s_*)^2}{2[1+\gamma(s(t-\tau(t)))]} \\ & + \rho_l|s(t)-s_*|\tfrac{\mu_1(s(t-\tau(t))+2.2\mu_a\tau_M)}{1+\gamma(s(t-\tau(t)))} \\ & \times\int_{t-\tau(t)}^{t}|\dot{s}(m)|dm \\ & + \tfrac{|s(t)-s_*|\mu(s_{in})}{s_{in}-s_\triangle}|z(t)| \end{aligned} \tag{38}$$

when t is large enough. The last inequality in (38) is a consequence of the definition of ϖ_s in (9), which implies that $(\mu_1(s_*) - \mu(s(t))(s_* - s(t)) \geq \varpi_s|s_* - s(t)|^2$ when we use the Mean Value Theorem, combined with (17) and (25).

Consequently,

$$\begin{aligned} \dot{\mathcal{U}}_1(t) \leq & \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ & + \tfrac{\rho_l^2}{2\varpi_s}\tfrac{\mu_1(s(t-\tau(t))+1.1\mu_a\tau_M)^2}{1+\gamma(s(t-\tau(t)))}\tau_M \\ & \times\int_{t-\tau(t)}^{t}|\dot{s}(m)|^2dm \\ & + \tfrac{|s(t)-s_*|\mu(s_{in})}{s_{in}-s_\triangle}|z(t)| \\ \leq & \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ & + \rho_m\tau_M\int_{t-\tau(t)}^{t}|\dot{s}(m)|^2dm \\ & + \tfrac{|s(t)-s_*|\mu(s_{in})}{s_{in}-s_\triangle}|z(t)|, \end{aligned} \tag{39}$$

where ρ_m is defined in (10), where we used the triangle and Jensen inequalities and the third step of the proof.

Fifth step. We next transform our function $\mathcal{U}_1$ to obtain a new function $\mathcal{U}_2$ that is reminiscent of Lyapunov-Krasovskii functionals, but which does not satisfy the classical Lyapunov-Krasovskii conditions. However, we will use it to derive stability properties. We prove that its derivative is nonpositive when t is above a certain constant. We introduce the functional $\mathcal{U}_2$, whose expression along the trajectories is

$$\mathcal{U}_2(s_t) = \mathcal{U}_1(s(t)) + 2\rho_m\tau_M\int_{t-\tau_M}^{t}\int_{\ell}^{t}\dot{s}(m)^2dmd\ell \ . \tag{40}$$

Then elementary calculations give, for all $t \geq t_c$,

$$\begin{aligned} \dot{\mathcal{U}}_2(t) \leq & \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ & -\rho_m\tau_M\int_{t-\tau(t)}^{t}|\dot{s}(m)|^2dm \\ & + 2\rho_m\tau_M^2\dot{s}(t)^2 + \tfrac{|s(t)-s_*|\mu(s_{in})}{s_{in}-s_\triangle}|z(t)| \end{aligned} \tag{41}$$

From (34), and from the general relation $(a+b)^2 \leq 2a^2+2b^2$ for suitable values $a \geq 0$ and $b \geq 0$, we can find a constant $c_d > 0$ such that

$$\begin{aligned} &\dot{\mathcal{U}}_2(t) \leq \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ &-\rho_m\tau_M\int_{t-\tau(t)}^{t}|\dot{s}(m)|^2dm \\ &+\left[\tfrac{[\mu_1(s_*)-\mu_1(s(t))][1+\gamma(s(t))]+\mu_1(s(t))\rho_l\int_{t-\tau(t)}^{t}|\dot{s}(m)|dm}{[1+\gamma(s(t-\tau(t)))][1+\gamma(s(t))]}\right]^2 \\ &\times 2\rho_m\tau_M^2[s_{in}-s(t)]^2 + c_d|z(t)|. \end{aligned}$$

Using our definition of ϖ_l in (9), it follows that

$$\begin{aligned} &\dot{\mathcal{U}}_2(t) \leq \\ &\tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} - \rho_m\tau_M\int_{t-\tau(t)}^{t}|\dot{s}(m)|^2dm \\ &+4\rho_m\tau_M^2\left[\tfrac{(\mu_1(s_*)-\mu_1(s(t)))^2}{[1+\gamma(s(t-\tau(t)))]^2}\right. \\ &\left.+\tfrac{\mu_1(s(t))^2\rho_l^2\tau_M\int_{t-\tau(t)}^{t}|\dot{s}(m)|^2dm}{[1+\gamma(s(t-\tau(t)))]^2[1+\gamma(s(t))]^2}\right][s_{in}-s(t)]^2 + c_d|z(t)| \\ &\leq \tfrac{(s(t)-s_*)(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ &+4\rho_m\tau_M^2\varpi_l\tfrac{(s_*-s(t))(\mu_1(s_*)-\mu_1(s(t)))}{[1+\gamma(s(t-\tau(t)))]^2}[s_{in}-s(t)]^2 \\ &+\left(4\rho_m\tau_M^2\tfrac{\mu_1(s(t))^2\rho_l^2}{[1+\gamma(s(t-\tau(t)))]^2[1+\gamma(s(t))]^2}[s_{in}-s(t)]^2-\rho_m\right) \\ &\times\tau_M\int_{t-\tau(t)}^{t}\dot{s}(m)^2dm + c_d|z(t)|. \end{aligned}$$

This gives

$$\begin{aligned} \dot{\mathcal{U}}_2(t) \leq & \left[-1+8\rho_m\tau_M^2\varpi_l\tfrac{[s_{in}-s(t)]^2}{[1+\gamma(s(t-\tau(t)))]}\right] \\ & \times\tfrac{(s_*-s(t))(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ & +\left(4\tau_M^2\rho_l^2\tfrac{\mu(s(t))^2}{[1+\gamma(s(t-\tau(t)))]^2}[s_{in}-s(t)]^2-1\right) \\ & \times\rho_m\tau_M\int_{t-\tau(t)}^{t}\dot{s}(m)^2dm + c_d|z(t)| \\ \leq & \left(8\rho_m\varpi_l s_{in}^2\tau_M^2-1\right)\tfrac{(s_*-s(t))(\mu_1(s_*)-\mu_1(s(t)))}{2[1+\gamma(s(t-\tau(t)))]} \\ & +\left(4\rho_l^2\mu(s(t))^2s_{in}^2\tau_M^2-1\right) \\ & \times\rho_m\tau_M\int_{t-\tau(t)}^{t}\dot{s}(m)^2dm + c_d|z(t)| \end{aligned} \tag{42}$$

We therefore conclude from our bounds (12) on τ_M from Assumption 2 that that there is a constant $c_e > 0$ such that for all $t \geq t_c$, we have

$$\dot{\mathcal{U}}_2(t) \leq -c_e(s(t)-s_*)^2 + c_d|z(t)| \ . \tag{43}$$

Last step. Integrating (43) over $[t_c, t]$ with $t \geq t_c$ gives

$$\begin{aligned} \mathcal{U}_2(t) - \mathcal{U}_2(t_c) \leq & -c_e\int_{t_c}^{t}(s(m)-s_*)^2dm \\ & +c_d\int_{t_c}^{t}|z(m)|dm \ . \end{aligned} \tag{44}$$

Since $\mathcal{U}_2$ is nonnegative valued, it follows that

$$c_e\int_{t_c}^{t}(s(m)-s_*)^2dm \leq \mathcal{U}_2(t_c) + c_d\int_{t_h}^{t}|z(m)|dm \ . \tag{45}$$

Since the function $(s(t), x(t))$ is bounded, it follows that $\dot{s}(t)$ is bounded. Also, $z(m)$ is integrable, since (19) ensures that $|z(m)|$ exponentially decays to 0. We deduce that $s(t)$ is uniformly continuous. It follows from Barbalat's lemma and the inequality (45) that $\lim_{t\to+\infty}(s(t) - s_*) = 0$. This implies that $\lim_{t\to+\infty} s(t) = s_*$ and $\lim_{t\to+\infty} x(t) = s_{in} - s_*$. This concludes the proof.

V. Example

We use the growth rate and constant

$$\mu(s) = \frac{0.5s}{1+s^2} \quad \text{and} \quad s_{in} = 1\,. \tag{46}$$

Since

$$\mu'(s) = 0.5\frac{1-s^2}{(1+s^2)^2}, \tag{47}$$

Assumption 1 holds with $s_M = 1$. Also, the requirements of Lemma 1 are met using $\mu_1(s) = 0.5s$ and $\gamma(s) = s^2$.

We take $s_* = 0.25$. Then the constants from Section III above are $\varpi_s = \varpi_l = 0.5$, $\rho_l = 2$, $\mu_a = 0.2$, and

$$\rho_m = \max_{\ell\in[0,1]} \frac{(\ell + 0.1375\tau_M)^2}{1+\ell^2}. \tag{48}$$

If $\tau_M < 1$, then the maximum in (48) occurs at $\ell = 1$, so $\rho_m \le 0.5(1+0.1375)^2 = 0.6469$. Also our condition (11) from Assumption 2 reads

$$\frac{0.5}{2} - \frac{0.5(0.25)}{1+(1-0.2\tau_M)^2} \;>\; 0, \tag{49}$$

which holds for all $\tau_M \in [0,1]$. Finally, the requirements (12) from Assumption 2 hold if

$$\tau_M \;<\; \min\left\{\frac{1}{2\sqrt{2(0.6469)(0.5)}}, \frac{1}{4(0.5)}\right\} \;=\; 0.5 \tag{50}$$

so all of our assumptions hold if $\tau_M < 0.5$.

To illustrate our findings, we ran Mathematica simulations with $\tau_M = 0.5$ and $\tau_f = 0$, which produces the closed loop dynamics

$$\begin{cases} \dot{s}(t) &= \frac{0.125}{1+(s(0.5\lfloor 2t\rfloor))^2}[1-s(t)] - \frac{0.5s(t)}{1+s^2(t)}x(t) \\ \dot{x}(t) &= \left[\frac{0.5s(t)}{1+s^2(t)} - \frac{0.125}{1+(s(0.5\lfloor 2t\rfloor))^2}\right]x(t). \end{cases} \tag{51}$$

where

$$\lfloor a \rfloor = \max\{j \in \{0,1,2,\ldots\} : j \le a\}$$

is the floor function. In Figures 1-3 below, we plot the components of the state and the control values for three different initial conditions. The control values $D(t)$ appear as jagged lines in the plots because of the 0.5 sampling time in the control. In each case, the state vector converges to $(s_*, s_{\text{in}} - s_*) = (0.25, 0.75)$, so our simulations help validate our theoretical findings.

VI. Conclusions

We provided a new feedback analysis for two state chemostats whose uptake functions are not necessarily monotone, including cases where the uptake functions are of Haldane type. Our new feedback only requires piecewise constant delayed measurements of the substrate level, and it ensures global asymptotic stability to an equilibrium point. Our convergence proof was based on a novel Lyapunov-Krasovskii functional method. In future work, we hope to exploit our Lyapunov-Kraovskii functional decay conditions to generalize our analysis to chemostats with several competing species with uncertainties [6] acting on the system.

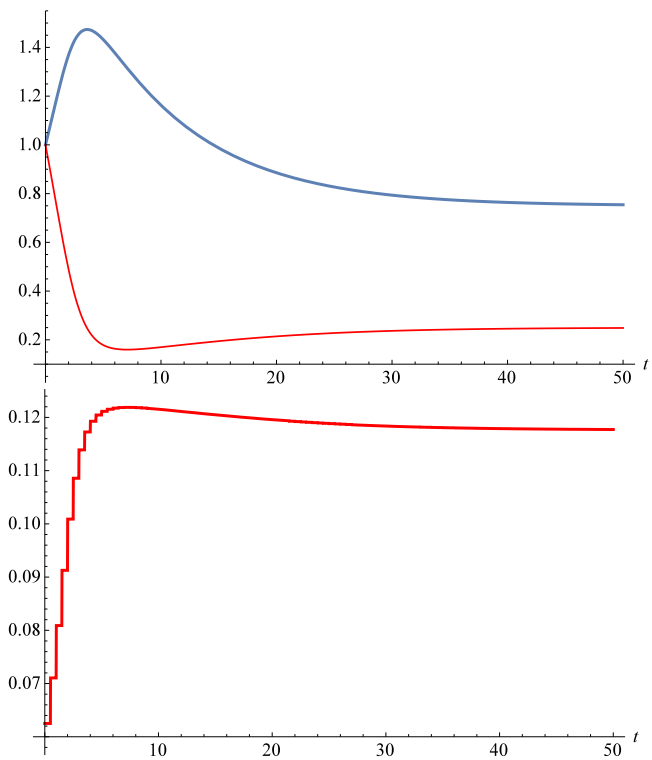

Fig. 1. Top: Solution $(s(t), x(t))$ of (51) for Initial State $(1,1)$ Converging to $(0.25, 0.75)$ with $\tau_M = 0.5$ with Substrate $s(t)$ in Red and Species $x(t)$ in Blue. Bottom: Control Values $D(t)$.

Appendix: Proof of Lemma 1

We construct functions μ_1 and γ that satisfy the requirements of Lemma 1. Let $\varepsilon \in (0, s_M/2)$ be a constant such that $\varepsilon \max\{\mu'(\ell) : 0 \le \ell \le s_M\} < 2\mu(s_M/2)$ and set

$$\begin{aligned} \mu_1(s) \;&=\; (\max\{0, s - s_M + \varepsilon\})^2 \\ &\quad + \begin{cases} \mu(s), & 0 \le s \le s_M \\ 2\mu(s_M) - \mu(s), & s > s_M \end{cases} \end{aligned} \tag{A.1}$$

and

$$\gamma(s) = \frac{\mu_1(\max\{0,s\})}{\mu(\max\{0,s\})} - 1 \tag{A.2}$$

for all $s > 0$ and $\gamma(s) = 0$ for all $s \le 0$. If $s \le s_M - \varepsilon$, then $\gamma(s) = 0$. If $s \in (s_M - \varepsilon, s_M]$, then

$$\begin{aligned} \gamma'(s) \;&=\; \tfrac{1}{\mu^2(s)}[\mu(s)(2(s - s_M + \varepsilon) + \mu'(s)) \\ &\quad - ((s - s_M + \varepsilon)^2 + \mu(s))\mu'(s)] \\ &\ge\; \tfrac{1}{\mu^2(s)}(s - s_M + \varepsilon)[2\mu(s) \\ &\quad - (s - s_M + \varepsilon)\mu'(s)] \\ &\ge\; \tfrac{1}{\mu^2(s)}(s - s_M + \varepsilon)[2\mu(s_M/2) \\ &\quad - \varepsilon \max\{\mu'(\ell) : 0 \le \ell \le s_M\}] \;>\; 0\,. \end{aligned} \tag{A.3}$$

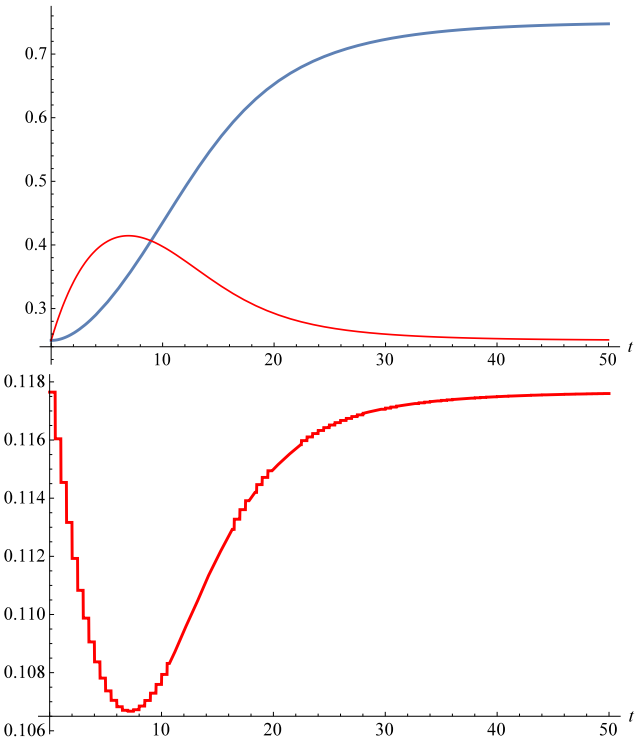

Fig. 2. Top: Solution $(s(t), x(t))$ of (51) for Initial State $(0.25, 0.25)$ Converging to $(0.25, 0.75)$ with $\tau_M = 0.5$ with Substrate $s(t)$ in Red and Species $x(t)$ in Blue. Bottom: Control Values $D(t)$.

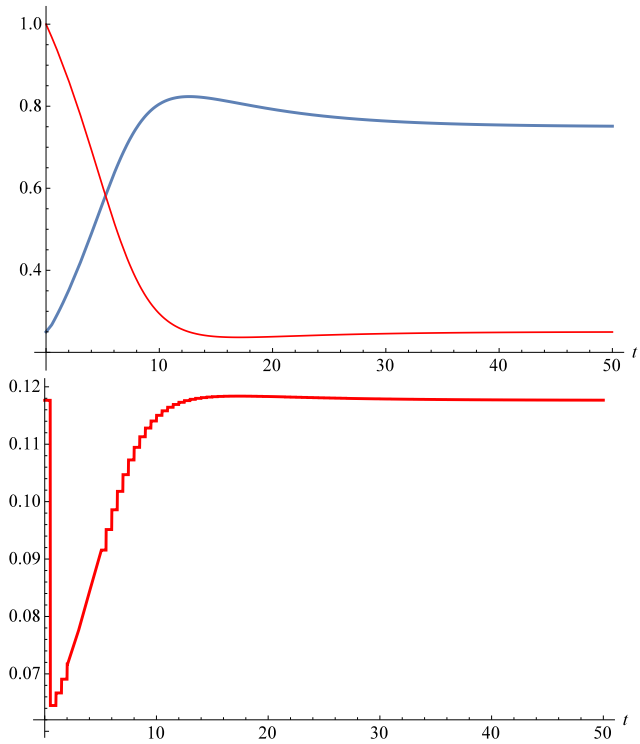

Fig. 3. Top: Solution $(s(t), x(t))$ of (51) for Initial State $(1, 0.25)$ Converging to $(0.25, 0.75)$ with $\tau_M = 0.5$ with Substrate $s(t)$ in Red and Species $x(t)$ in Blue. Bottom: Control Values $D(t)$.

If $s > s_M$, then $\mu'(s) \leq 0$, so

$$\begin{aligned} \gamma'(s) &= \tfrac{1}{\mu^2(s)}[\mu(s)[2(s - s_M + \varepsilon) - \mu'(s)] \\ &\quad - [2\mu(s_M) - \mu(s) + (s - s_M + \varepsilon)^2]\mu'(s)] \qquad \text{(A.4)} \\ &> 0\,, \end{aligned}$$

since $\mu(s_M) > 0$. Hence, γ is nondecreasing, and μ_1 and γ satisfy our requirements.

References

[1] G. Butler, S. Hsu, and P. Waltman. A mathematical model of the chemostat with periodic washout rate. *SIAM Journal on Applied Mathematics* 45(3):435-449, 1985. DOI:10.1137/0145025.

[2] A. Drame, M. Kothari and P. Wolenski. Almost periodic solutions of distributed parameter biochemical systems with time delay and time varying input. *Electronic Journal of Differential Equations* (2013)161:1-11, 2013

[3] E. Fridman, A. Seuret and J-P. Richard. Robust sampled-data stabilization of linear systems: an input delay approach. *Automatica* 40(8):1441-1446, 2004. DOI: 10.1016/j.automatica.2004.03.003.

[4] C. Fritsch, J. Harmand, and F. Campillo. A modeling approach of the chemostat. *Ecological Modelling* 299:1-13, 2015. DOI: 10.1016/j.ecolmodel.2014.11.021.

[5] J.-L. Gouzé and G. Robledo. Feedback control for nonmonotone competition models in the chemostat. *Nonlinear Analysis: Real World Applications* 6(4):671-690, 2005. DOI: 10.1016/j.nonrwa.2004.12.003.

[6] J.-L. Gouze and G. Robledo. Robust control for an uncertain chemostat model. *Internat. Journal of Robust and Nonlinear Control* 16(3):133–155, 2006. DOI: 10.1002/rnc.1047.

[7] V. Lemesle and J.-L. Gouze. A simple unforced oscillatory growth model in the chemostat. *Bulletin of Mathematical Biology* 70(2):344–357, 2008. DOI: 10.1007/s11538-007-9254-5.

[8] F. Mazenc, J. Harmand, and H. Mounier. Global stabilization of the chemostat with delayed and sampled measurements and control. In *Proceedings of the 9th IFAC Symposium on Nonlinear Control Systems*, Toulouse, France, pp. 170-174, 2013. DOI: 10.3182/20130904-3-FR-2041.00049.

[9] F. Mazenc and M. Malisoff. Stabilization of a chemostat model with Haldane growth functions and a delay in the measurement. *Automatica* 46(9):1428-1436, 2010. DOI: 10.1016/j.automatica.2010.06.012.

[10] F. Mazenc, M. Malisoff, and T. Dinh. Robustness of nonlinear systems with respect to delay and sampling of the controls. *Automatica* 49(6):1925-1931, 2013. DOI: 10.1016/j.automatica.2013.02.064.

[11] J. Monod. La technique de culture continue théorie et applications. *Annales de l'Institut Pasteur* 79:390-410, 1950. DOI: 10.1016/B978-0-12-460482-7.50023-3.

[12] A. Novick and L. Szilard. Description of the chemostat. *Science* 112(2920):715-716, 1950. DOI: 10.1126/science.112.2920.715/.

[13] S. Pilyugin and P. Waltman. Competition in the unstirred chemostat with periodic input and washout. *SIAM Journal on Applied Mathematics* 59(4):1157-1177, 1999. DOI: 10.1137/S0036139997323954.

[14] G. Robledo. Feedback stabilization for a chemostat with delayed output. *Mathematical Biosciences and Engineering* 6(3):629-647, 2009. DOI: 10.3934/mbe.2009.6.629.

[15] G. Robledo, F. Grognard, J.-L. Gouze. Global stability for a model of competition in the chemostat with microbial inputs. *Nonlinear Analysis: Real World Applications* 13(2):582-598. DOI: 10.1016/j.nonrwa.2011.07.049.

[16] H. Smith and P. Waltman. *The Theory of the Chemostat*. Cambridge University Press, Cambridge, UK, 1995.

[17] H. Xia, G. Wolkowicz, and L. Wang. Transient osciallations induced by delayed growth response in the chemostat. *Journal of Mathematical Biology* 50(5):489-530, 2005. DOI: 10.1007/s00285-004-0311-5.