



## Brief paper

# Stabilization in a chemostat with sampled and delayed measurements and uncertain growth functions<sup>☆</sup>

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## ABSTRACT

We provide a new control design for chemostats, under constant substrate input concentrations, using piecewise constant delayed measurements of the substrate concentration. Our growth functions can be uncertain and are not necessarily monotone. The dilution rate is the control. We use a new Lyapunov approach to derive conditions on the largest sampling interval and on the delay length to ensure asymptotic stabilization properties of a componentwise positive equilibrium point.

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## 1. Introduction

This work continues our search for controls that stabilize componentwise positive equilibria in chemostat models, under the incomplete state measurements and model uncertainties that usually occur in biotechnology laboratories, and so is strongly motivated by the ubiquity of the chemostat in a plethora of biological and engineering settings that are of compelling interdisciplinary interest, in which stabilization of componentwise positive equilibria is needed to ensure persistence of species. The chemostat is used for the continuous culture of microorganisms. It was first studied in [Monod \(1950\)](#) and [Novick and Szilard \(1950\)](#). It is regarded in biotechnology, ecology, and microbiology as an ideal way to represent cell or microorganism growth, wastewater treatment, or natural environments like lakes; see [Beauthier, Winkin, and Dochain \(2015\)](#), [Bernard, Hadj-Sadok, Dochain, Genovesi, and Steyer \(2001\)](#), [Fritsch, Harmand, and Campillo \(2015\)](#), [Gouzé and Robledo \(2005\)](#), [Lemesle and Gouzé \(2008\)](#), and [Robledo,](#)

[Grogard, and Gouzé \(2012\)](#). The variables are the microorganism and substrate concentrations, whose dynamics are based on mathematical models, e.g., mass-balance equations; see [Mazenc, Malisoff, and Harmand \(2008\)](#) and [Smith and Waltman \(1995\)](#). Two challenges in designing controls for chemostats are their nonlinearity and their lack of online actuators and sensors; see [Cougnon, Dochain, Guay, and Perrier \(2011\)](#).

Moreover, when online devices are available to measure biomass and substrate concentrations, they usually only provide delayed discrete measurements. It is common to design controls using continuous time models, which are then discretized before being applied. However, to prove that continuous time controllers ensure that the desired stability objectives are met, one must show robustness with respect to discretization. Chemostats are also subjected to uncertainty in the growth functions, which should also be taken into account in the control design. To the best of our knowledge, no rigorous theoretical analysis in the literature has addressed the delay, robustness, and sampling problems that we consider here. The work [Robledo \(2009\)](#) assumes that the measurements are continuous.

The preceding remarks motivated ([Mazenc, Harmand, & Mounier, 2013](#)) and this work, which solves a complementary problem to the ones in [Mazenc et al. \(2013\)](#). Here we consider the classical chemostat model in [Smith and Waltman \(1995\)](#) that contains one substrate and one species, except here we also include delays, sampling, and uncertainties, which are three features that are not contained in the classical chemostat model.

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We assume that the input substrate concentration is constant, and that the growth rate is of Haldane type (which has a growth limitation for low substrate concentrations, and inhibition at high concentrations). The dilution rate is the control, and uses delayed and sampled observations. Controlling this system is difficult, for two reasons. First, works such as Mazenc, Malisoff, and Dinh (2013) that prove global asymptotic stability under delay and sampling use state feedbacks. Since our work has output feedbacks, it is outside the scope of Mazenc et al. (2013).

Second, chemostats with non-monotonic growth rates generally have multiple equilibria, under constant dilution rates. One is unstable, while another is locally exponentially stable. The work Mazenc et al. (2013) stabilized points of the second type, but here we stabilize points of the first type in cases where the growth rate is uncertain and not necessarily monotone. Our stabilizing controller only requires measurements of the substrate, which are piecewise constant and delayed. Under suitable bounds on the delay size and on the sampling interval, our control provides global asymptotic stability to a componentwise positive equilibrium when the growth function is known, and input-to-state stability (or ISS) (as defined in Khalil, 2002) with respect to uncertainties in the growth functions. This differs from Mazenc et al. (2013), where no constraints on the delay and sampling intervals were used. We believe that these extra constraints are needed because under constant dilution rates, the equilibrium that we stabilize in this paper would have been unstable.

While reminiscent of Mazenc et al. (2013), the barrier functions that we use here allow us to certify ISS, which was not considered in Mazenc et al. (2013). The main result of Mazenc et al. (2013) does not apply here, even in the special case where the growth functions are known. Our proof also differs from Mazenc and Malisoff (2010), which assumes that species measurements are available. When there are no perturbations, our results contrast with Gouzé and Robledo (2006) and other works that do not include delays or sampling or ISS. Our new work also improves on our conference version (i.e., Mazenc, Harmand, & Malisoff, 2016), which did not allow uncertainties in the growth functions, because here, we prove ISS with respect to the uncertainties in the growth functions under arbitrarily large uncertainty bounds and positivity constraints on the states. See Section 3 for our main result, Section 4 for its proof, and Section 5 for an illustration including simulations.

## 2. Model and notation

Our basic chemostat model is

$$\begin{cases} \dot{s}(t) = D[s_{\text{in}} - s(t)] - \mu(s(t))x(t) \\ \dot{x}(t) = [\mu(s(t)) - D]x(t) \end{cases} \quad (1)$$

(where we used the standard technique of scaling the species level  $x(t)$  in order to eliminate the constant yield) but see below for generalizations where the growth function  $\mu$  can be uncertain. The states  $x$  and  $s$  are positive valued (and represent the species and substrate levels, respectively), the substrate input concentration  $s_{\text{in}} > 0$  is a constant, the dilution rate  $D$  is a positive valued control that we will specify, and the growth function  $\mu$  satisfies:

**Assumption 1.** The function  $\mu$  is of class  $C^1$  and  $\mu(0) = 0$ . Also, 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  $s > 0$ .  $\square$

By  $C^1$ , we mean continuously differentiable. Assumption 1 holds for all functions of the form

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

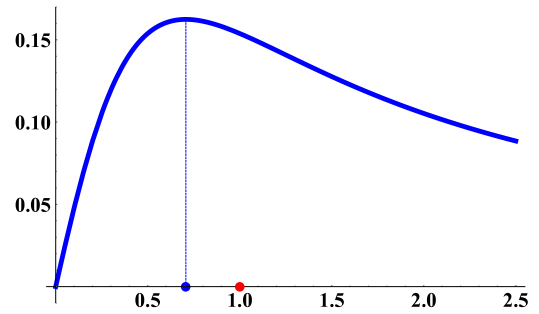


Fig. 1. Uptake function from (3), showing maximizer  $s_M = 1/\sqrt{2}$  as Blue Dot and  $s_{\text{in}} = 1$  as Red Dot. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

for any constants  $k_i > 0$  for  $i = 1$  to 3, with  $s_M = 1/\sqrt{k_3}$ . Functions of the form (2) are called Haldane functions. In Fig. 1, we plot the special case of (2) and  $s_{\text{in}}$  where

$$\mu(s) = \frac{0.5s}{1 + 0.25s + 2s^2} \quad \text{and} \quad s_{\text{in}} = 1 \quad (3)$$

including the maximizer  $s_M = 1/\sqrt{2}$ . In Appendix A, we prove the next lemma, where a function  $\alpha : [0, \infty) \rightarrow [0, \infty)$  is defined to be of class  $\mathcal{K}_\infty$  provided  $\alpha(0) = 0$  and  $\alpha$  is continuous, strictly increasing, and unbounded; and  $\mu'_1(0)$  is the derivative from the right.

**Lemma 1.** If Assumption 1 holds, then we can construct a function  $\mu_1 \in C^1 \cap \mathcal{K}_\infty$  and a nondecreasing  $C^1$  function  $\gamma : \mathbb{R} \rightarrow [0, \infty)$  such that  $\gamma(m) = 0$  for all  $m \leq 0$ ,

$$\mu(s) = \frac{\mu_1(s)}{1 + \gamma(s)} \quad \text{for all } s \geq 0, \quad (4)$$

$\mu'_1(s) > 0$  for all  $s \geq 0$ , and  $\gamma'(s) > 0$  for all  $s \geq s_M$ .  $\square$

**Remark 1.** If  $\mu'(s) < 0$  for all  $s > s_M$  (which holds for (2)), and  $s_{\text{in}} > s_M$ , and the dilution rate  $D$  is a constant  $D \in (\mu(s_{\text{in}}), \mu(s_M)) \subseteq (0, \infty)$ , then the system (1) has a locally unstable positive equilibrium point of the form  $(s_*, s_{\text{in}} - s_*)$  and the locally stable equilibrium  $(s_{\text{in}}, 0)$ , where  $s_* \in (s_M, s_{\text{in}})$  and  $D = \mu(s_*)$ . Our work (Mazenc et al., 2013) globally stabilized an equilibrium that can be locally exponentially stabilized by a constant dilution rate.  $\square$

To explain our sampling control goals, 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  $0 < \epsilon_1 \leq t_{i+1} - t_i \leq \epsilon_2$  for all  $i \in \mathbb{N} \cup \{0\}$ , where  $t_0 = 0$  and  $\mathbb{N} = \{1, 2, \dots\}$ . Given any constant  $\tau_f \geq 0$ , we define the function  $\tau$  as follows:

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

This is reminiscent of the representation of sampling in Fridman, Seuret, and Richard (2004). For all  $j \geq 0$  and  $t \in [t_j + \tau_f, t_{j+1} + \tau_f)$ , we have  $t - \tau(t) = t - (\tau_f + t - t_j) = t_j - \tau_f$ , so  $t - \tau(t)$  is piecewise constant. In the special case where  $\tau_f = 0$ , we also have  $t - \tau(t) = t_j$  for all  $t \in [t_j, t_{j+1})$  and  $j \geq 0$ .

Moreover, for all  $t \geq 0$ , we have

$$0 \leq \tau(t) \leq \tau_M, \quad \text{where } \tau_M = 2\tau_f + \epsilon_2. \quad (5)$$

We assume that  $s(t - \tau(t))$  is the only available measurement. Our control  $D$  will be computed in terms of the delayed sampled values  $s(t - \tau(t))$  of the substrate, so when  $\tau_f = 0$ , the control values will be computed from the sequence of observations  $\{s(t_j)\}$  at the sample times; see (12). When  $\mu$  is known, our goal is asymptotic stabilization of  $E_* = (s_*, s_{\text{in}} - s_*)$  for any constant  $s_* \in (0, s_{\text{in}})$ , using our positive valued dilution rate feedback. Then the components of  $E_*$  are positive, and  $E_*$  is an equilibrium of (1) if and only if  $D$  takes the value  $\mu(s_*)$  when  $s = s_*$ .

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