ABOUT FEEDBACK STABILIZATION OF CONTINUOUS BIOPROCESSES THROUGH RECIRCULATION[1]

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Abstract: In this paper, we propose to regulate the output of an autocatalytic bioprocess by means of a recirculation loop. We show that controlling the recirculation flow rate allows the stabilization of a particular output under a constant or even an unknown input flow. Furthermore, we obtain a convergence in finite time with a smooth feedback law

Keywords: bioprocess, recirculation loop, output regulation, nonlinear control.

1. INTRODUCTION

For about thirty years, the control of bioprocesses has attracted lots of attention. Motivated by important application domains (in particular agro-food, pharmaceutical and wastewater treatment industries), a number of control techniques have been proposed. Because the most common process used in the above cited industries can be assimilated to the well-known chemostat (also known as the Continuous Stirred Tank Reactor or CSTR), most of the available approaches have been developed for this popular process and consider the control of the output substrate concentration S using the input flow rate as the control variable such that S remains smaller than a upper limit $S^\star$ as synthetically shown in Figure 1. Note that closer S and $S^\star$ are, greater is the mean value of Qin. In other terms, in this context controlling S around the setpoint $S^\star$ is a common control objective when dealing with these systems.

Among all available nonlinear approaches to do so, no doubt that the linearizing control first proposed in (Bastin and Dochain, 1990) is the most popular one. It is based on the following general mass balance model of a biological reactor

$$\begin{cases} \dot{X} = \dfrac{Q}{V}(X_{in} - X) + \mu(S)X \ , \\ \dot{S} = \dfrac{Q}{V}(S_{in} - S) - \dfrac{\mu(S)}{Y}X \ , \end{cases} \tag{1}$$

where S and X stand for the biomass and the substrate concentrations (in mg/l) in the reactor, Q is the input flow rate (in l/h), S_{in} and X_{in} are the input substrate and input biomass concentrations (in mg/l), Y is the conversion yield (in mg of substrate consumed by mg of biomass formed), $\mu(S)$ is the reaction rate (in t^{-1}) and V is the volume of the reactor (in l).

One can check readily that the feedback $Q(X,S) = V\frac{\lambda(S^\star - S) + \mu(S)X}{Y(S_{in} - S)}$, with $\lambda > 0$, globally exponentially stabilizes the variable S of the model (1) about $S^\star$ with a linear dynamics. A number of advantages and drawbacks of this control can be

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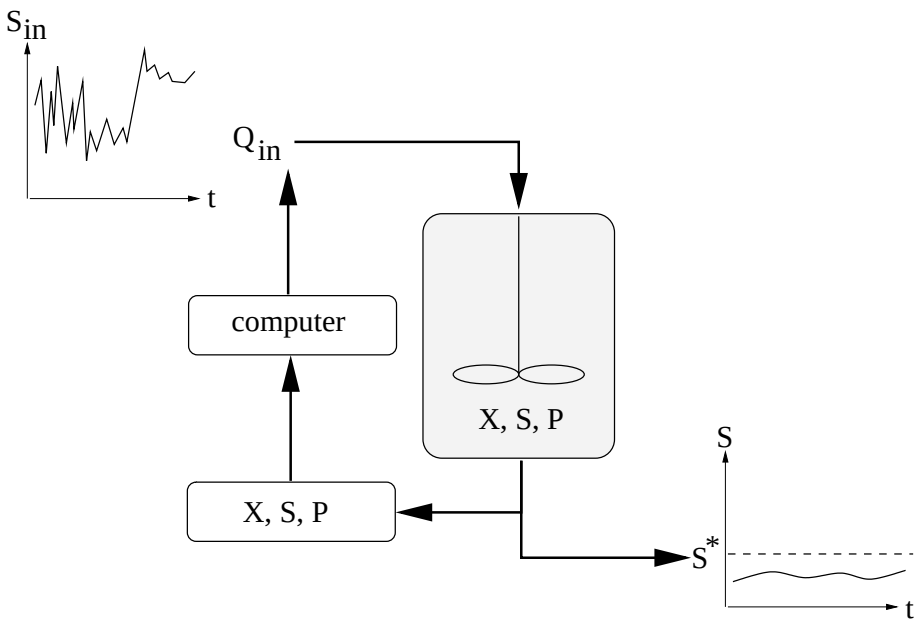

Fig. 1. General view of a CSTR controlled by means of input flow rate.

advanced. On the one hand, in particular, the knowledge of both the kinetics and the biomass concentration are necessary. That is why an adaptive version has been suggested. On the other hand, the stabilization of the process is global, which means that the output substrate concentration can be controlled in the unstable range of a non-monotonic kinetics such as an Haldane growth function. Following this study, a number of alternative control feedback laws have been proposed, in particular to take into account uncertainty on the measurements of either the input or output substrate concentration and/or on the kinetics. For example, PI based controllers (Cf. (Alvarez-Ramirez and Femat, 1999)) or adaptive gain techniques (Cf. (Allgower *et al.*, 1997)) can be used to stabilize bioreactors without using any knowledge about the kinetics. However, in these cases no guarantee on the speed of convergence is provided. Sliding mode techniques allow a convergence in finite time but yield discontinuous feedback laws, which are robust only against matched disturbances (Cf. (Zlateva, 1997) and (Tham *et al.*, 2003)). Another approach is based on guaranteed dynamical intervals on the uncertainty (Cf (Rapaport and Harmand, 2002)). In particular, this control strategy allows an exponential convergence towards an arbitrarily small interval about the setpoint. Finally, other approaches only need a limited knowledge of the process and guarantee asymptotic convergence, Cf. for instance (Antonelli *et al.*, 2003) for monotonic kinetics or (Mailleret *et al.*, 2004) in which an additional measurement (the gaseous flow rate) is needed.

However, to the best of our knowledge, all the above cited approaches use the input flow rate as the control variable. As a consequence, a storage tank is needed before the process. In this paper, we consider the particular process configuration represented in Figure 2 where $0 \leq \alpha \leq 1$ and $\beta \geq 0$. This configuration was recently proposed within the framework of studies devoted to the optimal steady state design of bioprocesses (cf. (Harmand *et al.*, 2003)). In bioprocess engineering, an usual objective is to regulate a particular output about a nominal value or a reference trajectory. Typically, in biological wastewater treatment plants, the aim is to regulate the output substrate concentration under some prescribed value. Here the use of the α and β parameters is investigated for the control of the output substrate concentration.

Thus, under some conditions that will be highlighted hereafter, the output of the process can be tracked along a desired reference trajectory, while the input flow rate Q, possibly unknown, can vary with time.

This paper is organized as follows. First (Section 2), the model of the process is presented. Then, in Section 3, the control design is exposed. In Section 4, simulations are performed and discussed while conclusions and perspectives are drawn in Section 5.

2. PROBLEM STATEMENT

Consider the device configuration pictured in Figure 2 where the function $D(t) = Q(t)/V$ is given,

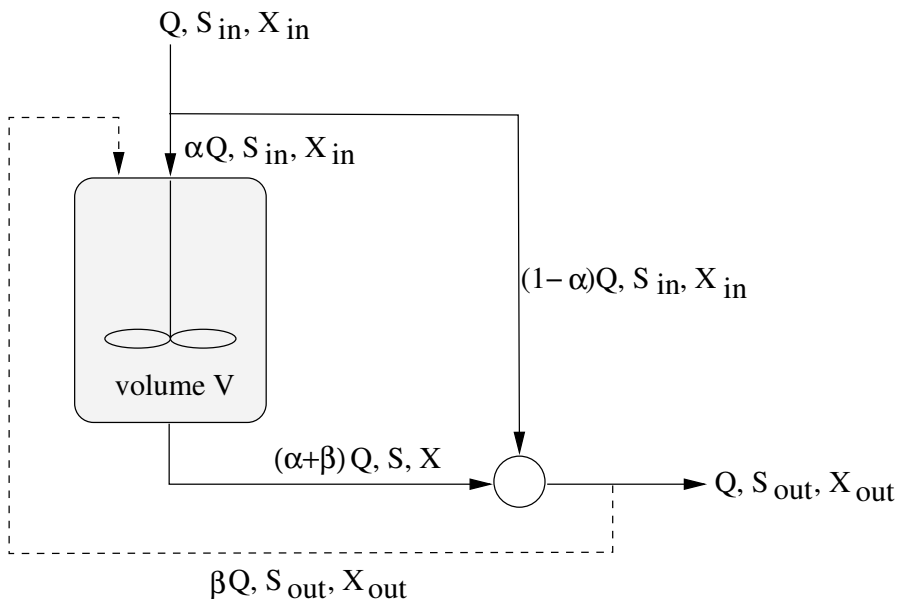

Fig. 2. General view of the bioprocess configuration under interest in the present study.

possibly constant. The model of this second system can be written as

$$\begin{cases} \dot{X} \;=\; D(t)(\beta X_{out} + \alpha X_{in} - (\alpha+\beta)X) + \mu(S)X \;, \\ \dot{S} \;=\; D(t)(\beta S_{out} + \alpha S_{in} - (\alpha+\beta)S) - \dfrac{\mu(S)}{Y}X \;, \end{cases}$$

where

$$\begin{cases} X_{out} \;=\; \dfrac{(1-\alpha)X_{in} + (\alpha+\beta)X}{1+\beta} \;, \\ S_{out} \;=\; \dfrac{(1-\alpha)S_{in} + (\alpha+\beta)S}{1+\beta} \;, \end{cases}$$

with $0 \leq \alpha \leq 1$ and $\beta \geq 0$.

Introducing these expressions of X_{out} and S_{out} in the dynamics given above, and posing $u = (\alpha + \beta)/(1+\beta)$ $(0 \leq u \leq 1)$ simplify the system as follows

$$\begin{cases} \dot{X} \;=\; uD(t)\,(X_{in} - X) + \mu(S)X \;, \\ \dot{S} \;=\; uD(t)\,(S_{in} - S) - \dfrac{\mu(S)}{Y}X \;. \end{cases} \tag{2}$$

We recall that Y is a positive constant.

The problem investigated in the remaining part of the paper is the regulation of the output

$$S_{out} = uS + (1-u)S_{in} \;. \tag{3}$$

To summarize, instead of regulating the variable S of the system (1) by means of D, one intends to control the output S_{out} of the system (2) about $S^\star_{out}$ by means of u.

We solve this problem under the realistic assumption that the input concentrations are time-varying but bounded

$$(X_{in}(t), S_{in}(t)) \in [\underline{X}_{in}, \overline{X}_{in}] \times [\underline{S}_{in}, \overline{S}_{in}], \quad \forall t \geq 0,$$

where $\overline{X}_{in} \geq \underline{X}_{in} \geq 0$ and $\overline{S}_{in} \geq \underline{S}_{in} > 0$ are known numbers.

We consider also $S^\star_{out}$ as a time-varying reference trajectory to be tracked, with the following hypothesis.

Hypothesis H0. There exist numbers $\overline{S}^\star_{out} \geq \underline{S}^\star_{out} > 0$ such that $S^\star_{out}(t) \in [\underline{S}^\star_{out}, \overline{S}^\star_{out}]$ for all $t \geq 0$, with

$$\overline{S}^\star_{out} < \underline{S}_{in} \;.$$

3. CONTROL DESIGN

We first introduce usual assumptions on the growth function $\mu(\cdot)$.

Hypothesis H1. The function $\mu(\cdot)$ is a non-decreasing Lipschitz continuous function with $\mu(0) = 0$.

In this approach, the input flow rate $D(\cdot)$ is not chosen and could even be unknown. Nevertheless, we require it to be bounded, with known bounds.

Hypothesis H2. There exist numbers $\underline{D} \leq \overline{D}$ and $T \geq 0$ such that $D(t) \in [\underline{D}, \overline{D}]$ for all $t \geq T$, with $\underline{D} > 0$ and

$$\overline{D} < \mu(\underline{S}^\star_{out}) \frac{\underline{X}_{in} + Y(\underline{S}_{in} - \underline{S}^\star_{out})}{Y(\overline{S}_{in} - \underline{S}^\star_{out})} \;. \tag{4}$$

Proposition 1. Assume H0-H1-H2 are satisfied by the system (2). Then for any initial condition such that $X(0) > 0$ and $0 \leq S(0) < \overline{S}_{in}$, the feedback

$$u^\star(t,S) = \left| \begin{array}{cc} \dfrac{S_{in}(t) - S^\star_{out}(t)}{S_{in}(t) - S} & \text{if } S \leq S^\star_{out}(t) \\ 1 & \text{if } S > S^\star_{out}(t) \end{array} \right. \quad (5)$$

tracks the output $S_{out}(\cdot)$, defined in (3), at $S^\star_{out}(\cdot)$ in finite time.

Proof. From H1 and $0 \leq S(0) < \overline{S}_{in}$, we straightforwardly deduce that the solution of (2) is such that $0 \leq S(t) < \overline{S}_{in}$, $\forall t \geq 0$ for any non-negative control law. Furthermore, from H0, the feedback law (5) is well defined and the inequality $u^\star(t,S) > 1 - \overline{S}^\star_{out}/\underline{S}_{in} > 0$ is satisfied for any $S \in [0, \overline{S}_{in}[$. From (2) and $X(0) > 0$, we deduce also that $X(t) > 0$ for all $t \geq 0$.

Consider the function

$$Z(t) = X(t) + YS(t) \quad (6)$$

along with $Z_{in}(t) = X_{in}(t) + YS_{in}(t) \in [\underline{Z}_{in}, \overline{Z}_{in}]$, where $\underline{Z}_{in} = \underline{X}_{in} + Y\underline{S}_{in}$ and $\overline{Z}_{in} = \overline{X}_{in} + Y\overline{S}_{in}$. A simple calculation yields

$$\dot{Z} = -u^*(t,S(t))D(t)(Z - Z_{in}(t)) \ .$$

Thus, from H2, we infer that $Z(t)$ converges exponentially towards $[\underline{Z}_{in}, \overline{Z}_{in}]$. The dynamics of the variable S can also be written as follows

$$\begin{aligned} \dot{S} &= F(t,S,Z) \\ &= u^*(t,S)D(t)(S_{in}(t) - S) - \frac{\mu(S)}{Y}(Z - YS) \end{aligned}$$

from which we derive the following inequality

$$\begin{aligned} F(t,S,Z) \leq\ & u^*(t,S)D(t)(\overline{S}_{in} - S) \\ & -\frac{\mu(S)}{Y}(\underline{Z}_{in} - YS) + \frac{\mu(S)}{Y}(\underline{Z}_{in} - Z) \ . \end{aligned} \quad (7)$$

Before analyzing the behavior of the solutions of the S subsystem, we give some remarks, which are instrumental in establishing the output regulation result.

Posit $\delta = \mu(\underline{S}^\star_{out})(\underline{Z}_{in} - Y\underline{S}^\star_{out})/Y - \overline{D}(\overline{S}_{in} - \underline{S}^\star_{out})$. The condition (4) ensures that $\delta > 0$ and, for all $t \geq T$,

$$F(t, \underline{S}^\star_{out}, Z) \leq -\delta + \frac{\mu(\underline{S}^\star_{out})}{Y}(\underline{Z}_{in} - Z) \ .$$

The convergence of $Z(t)$ towards $[\underline{Z}_{in}, \overline{Z}_{in}]$ implies then the existence of $T_1 \geq T$ such that

$$F(t, \underline{S}^\star_{out}, Z(t)) \leq -\frac{\delta}{2} < 0, \quad t \geq T_1 \ . \quad (8)$$

Let us consider now $S \in [\underline{S}^\star_{out}, \overline{S}_{in}[$ that we regard as a constant. Let $t \geq T$. One can check readily that

$$\begin{aligned} F(t,S,Z) \leq\ & (\overline{D} - \mu(\underline{S}^\star_{out}))(\overline{S}_{in} - S) \\ & -\frac{\mu(S)}{Y}(\underline{Z}_{in} - Y\overline{S}_{in}) + \frac{\mu(S)}{Y}(\underline{Z}_{in} - Z) \ . \end{aligned} \quad (9)$$

We are ready now to prove the announced result. We distinguish between two cases.

Case 1: $S(T_1) \leq \underline{S}^\star_{out}$. The property (8) implies then that for all $t > T_1$, one has $S(t) < \underline{S}^\star_{out}$. It follows that $u^*(t,S(t)) = (S_{in}(t) - S^\star_{out}(t))/(S_{in}(t) - S(t))$. Consequently, $S_{out}(t) = S^\star_{out}(t)$.

Case 2: $S(T_1) > \underline{S}^\star_{out}$. We will show that necessarily $S(t)$ reaches $S^\star_{out}$ in finite time, which will bring us back to Case 1.We proceed by contradiction: assume that $S(t) > \underline{S}^\star_{out}$ for all $t \geq T_1$.

If $\underline{Z}_{in} > Y\overline{S}_{in}$ and $\overline{D} \leq \mu(\underline{S}^\star_{out})$ (note that condition (4) is necessarily fulfilled), then from (9) and the convergence of $Z(\cdot)$ towards $[\underline{Z}_{in}, \overline{Z}_{in}]$, we deduce the existence of $T_2 \geq T_1$ such that

$$F(t,S,Z(t)) \leq -\tfrac{1}{2}\frac{\mu(\underline{S}^\star_{out})}{Y}(\underline{Z}_{in} - Y\overline{S}_{in}) < 0$$

for all $t \geq T_2$. We conclude that $S(\cdot)$ reaches $\underline{S}^\star_{out}$ in finite time, thus a contradiction.

If $\underline{Z}_{in} > Y\overline{S}_{in}$ and $\overline{D} > \mu(\underline{S}^\star_{out})$, we obtain the following inequality from (9) and (4)

$$F(t,S,Z) \leq -\delta + \frac{\mu(S)}{Y}(\underline{Z}_{in} - Z) \ .$$

The asymptotic properties of $Z(\cdot)$ allow then to write

$$F(t,S,Z(t)) \leq -\frac{\delta}{2} < 0, \quad t \geq T_2'$$

for a certain $T_2' \geq T_1$. Thus we obtain again a contradiction.

Finally, if $\underline{Z}_{in} \leq Y\overline{S}_{in}$, then condition (4) ensures $\overline{D} < \mu(\underline{S}^\star_{out})$. One can then write, from (2) and (6) the following inequalities for all $t \geq T_1$

$$\begin{aligned} \dot{X} &\geq (\mu(\underline{S}^\star_{out}) - \overline{D})X \ , \\ \dot{S} &\leq -(\mu(\underline{S}^\star_{out}) - \overline{D})\frac{X}{Y} \\ &\quad + \frac{\overline{D}}{Y}(Y\overline{S}_{in} - \underline{Z}_{in}) + \frac{\overline{D}}{Y}(\underline{Z}_{in} - Z(t)) \ . \end{aligned}$$

As $X(T_1)$ is positive, $X(\cdot)$ is increasing, and there exist $\gamma > 0$, $T_1' \geq T_1$ such that $(\mu(\underline{S}^\star_{out}) - \overline{D})X(t) > \overline{D}(Y\overline{S}_{in} - \underline{Z}_{in}) + \gamma$ for all $t \geq T_1'$. From the convergence of $Z(\cdot)$, we deduce that there exists $T_2'' \geq T_1'$ such that

$$\dot{S}(t) \leq -\frac{\gamma}{2Y} < 0, \quad t \geq T_2''$$

that leads again to a contradiction.

Remark 2. Neither D (which can be time-varying), nor the biomass concentration or the kinetics need to be known for the synthesis of this law: only the online values of $S(t)$ and the knowledge of $S_{in}(t)$ are necessary. However, since we use a specific configuration including a recirculation loop, two valves (or at least one controllable valve and one pump) are necessary to independently control α and β instead of only one, as in the case of a simple chemostat.

4. NUMERICAL SIMULATIONS AND DISCUSSION

Numerical simulations were performed using the control law presented hereabove, with a Monod growth function: $\mu(S) = \mu_{\max} S/(K_S + S)$. In other words, only S and S_{in} were measured online. The following model parameters were used : $\mu_{max} = 0.045$, $K_S = 10$, $Y = 0.05$, $V = 40$, Q is the sum of a constant ($\bar{Q} = 0.8\ l/h$) and of three other signals

i) a sinusoide of magnitude 0.1 and of frequency 0.02,
ii) a signal of magnitude 0.04 and of frequency 0.0002,
iii) a random signal of maximum magnitude 0.06.

Thus, at $t = 500$, a setpoint step was simulated. The input substrate concentration is measured and is built as follows. It consists in the sum of

i) a constant equal to 475 mg/l
ii) a sinusoide of magnitude 25 and of frequency 0.01
iii) a square signal of magnitude 15 and of frequency 0.005
iv) a random signal of maximum magnitude 5.

The objective is to regulate the output substrate concentration S_{out} about $S^\star_{out} = 20\ mg/l$. First, it was verified that condition (4) holds given the extreme expected values of D, S_{in} and $S^\star_{out}$. The simulations were performed over a period of 300 hours. The results are shown in Figures 3 to 6.

From these numerical simulations, a number of general advantages and drawbacks of this control algorithm can be pointed out :

(1) First, since D is disturbed, the performances of the control can be affected during transient periods if the state if far from its equilibrium setpoint. In particular, if $X(0)$ is very small, it can take some time for S_{out} to converge towards $S^\star_{out}$. However, after the controlled variable has converged towards that setpoint - in finite time - the performances are obviously excellent. The price to pay when choosing this configuration is that, in most cases, the volume of the reactor of the configuration (2) is greater than that one obtained when optimally designing a single chemostat. It is due to the fact that using our control leads to an equilibrium value $\bar{S}$ in the reactor which is smaller than the equilibrium value $S^\star_{out}$ (and

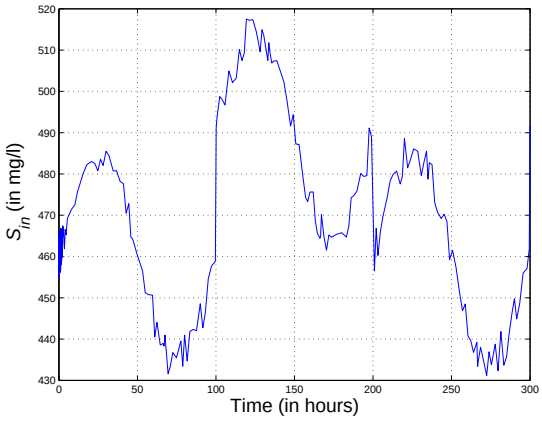

Fig. 3. The input substrate concentration $S_{in}(t)$

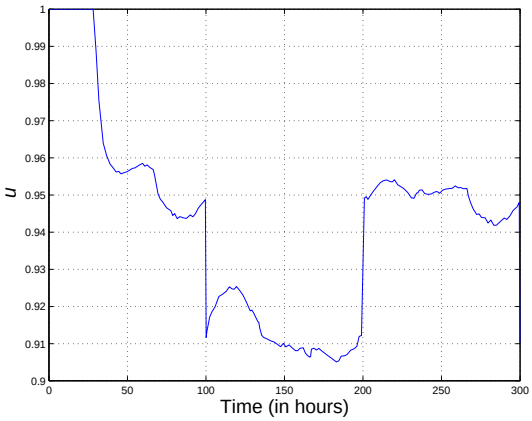

Fig. 4. The control signal u

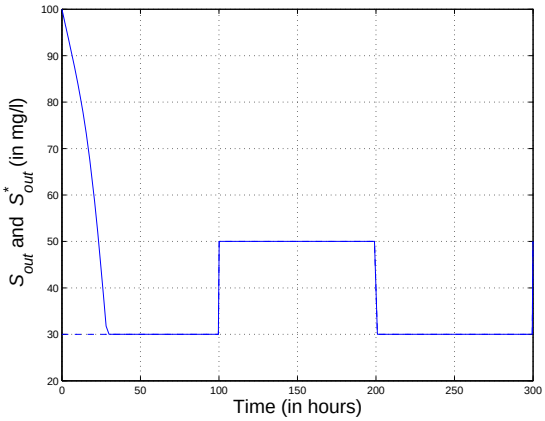

Fig. 5. The controlled variable (S_{out}, dotted line) and the setpoint ($S^\star_{out}$)

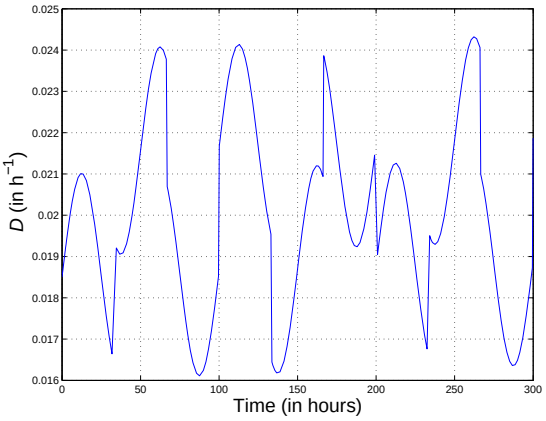

Fig. 6. The unknown time-varying dilution rate (D)

that is precisely what condition (4) guarantees).

(2) Second, it should be noticed that S_{in}, D and $S^{\star}_{out}$ can be time-varying. The only need is to measure S and S_{in} continuously.

(3) Finally, it should also be noted that this control law seems to be particularly appropriate when a clogging can arise in the pump used to feed in the reactor (in particular because the control does not use D). It seems also particularly well suited for wastewater treatment control where the input flow rate is really a disturbance.

Of course, the above results have been obtained in assuming that no noise were corrupting measurements. In order to show the robustness of the control law (however we do not investigate the theoretical robustness of the control here) and investigate its practical implementation, we have added some noise in the measurements of S and S_{in}. The result of the regulated variable is plotted in figure 7.

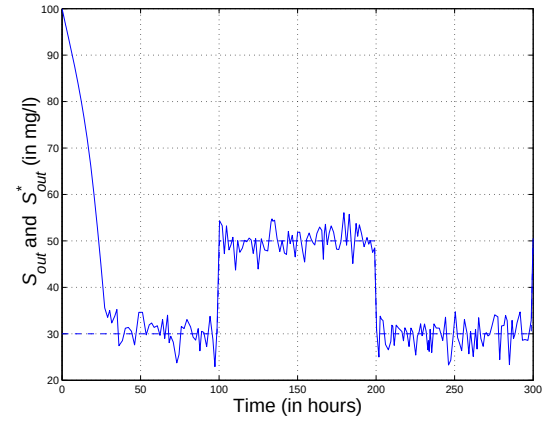

Fig. 7. The controlled variable (S_{out}, dotted line) and the setpoint ($S^{\star}_{out}$) when the measurements are noisy

5. CONCLUSIONS

In this paper, the control of a bioprocess by means of a recirculation loop was investigated. The control law proposed needs more actuators than when controlling a single chemostat. However, the required knowledge is very limited: only the on line measures of S_{in} and S are necessary. Furthermore, the satisfactory simulation results obtained make this control law really attractive. The case where S_{in} is unknown will be the matter of a forthcoming work, leading to an adaptive feedback law.

REFERENCES

Allgower, F., J. Asman and A. Ilchman (1997). High-gain adaptive λ-tracking for nonlinear systems. *Automatica* **33**, 881–888.

Alvarez-Ramirez, J. and R. Femat (1999). Pi stabilization of a class of chemical reactors. *systems and control Letters* **38**, 219–225.

Antonelli, R., J. Harmand, J. P. Steyer and A. Astolfi (2003). Set point regulation of an anaerobic digestion process with bounded output feedback. *IEEE transactions on Control systems Technology* **11**, 495–504.

Bastin, G. and D. Dochain (1990). *On-Line Estimation and Adaptive Control of Bioreactors*. Elsevier.

Harmand, J., A. Rapaport and A. trofino (2003). Optimal design of two interconnected bioreactors : new results. *AIChE J.* **49**, 1349–1612.

Mailleret, L., O. Bernard and J. P. Steyer (2004). Nonlinear adaptive control for bioreactors with unknown kinetics. *Automatica* **40**, 1379–1385.

Rapaport, A. and J. Harmand (2002). Robust regulation of partially observed nonlinear continuous bioreactors. *Journal of Process Control* **12**, 291–302.

Tham, H. J., K. B. Ramachandran and M. A. Hussain (2003). Sliding mode control for a continuous bioreactor. *Chem. Biochem. Eng.* **17**, 267–275.

Zlateva, P. (1997). Sliding-mode control of fermentation processes. *Bioprocess Engineering* **16**, 383–387.