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On-line optimization of fedbatch bioreactors by adaptive extremum seeking control

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Abstract: In this paper, we present an adaptive extremum seeking control scheme for fed-batch bioreactors with Haldane kinetics. The proposed adaptive extremum seeking approach utilizes the structure information of the process kinetics to derive a seeking algorithm that drives the system states to the desired set-points that maximize the biomass production. It assumes that only the substrate concentration is available for on-line measurement. Lyapunov stability is used in the design of the extremum seeking controller structure and the development of the parameter learning laws. The performance of the approach is illustrated via numerical simulations.

Keywords: Fedbatch reactors, on-line optimization, adaptive extremum seeking.

1. INTRODUCTION

Fed-batch bioreactors represent an important class of bioprocesses, mainly in the food industry (e.g. yeast production) and in the pharmaceutical industry (like the production of the vaccine against the Hepatitis B) but also e.g. for biopolymer applications (PHB). It is also very much involved in the field of enzyme production which has been developed over the past decade due to the recombinant ADN technology and via the use of filamentous microorganisms.

One of the key issues in the operation of fed-batch reactors is to optimize the production of synthesis product (e.g. penicillin, enzymes, etc) or biomass (e.g. baker's yeast). They are therefore a priori ideal candidates for optimal control strategies. An intensive research activity has been devoted to optimal control of (fed-batch) bioreactors mainly in the seventies and in the eighties (see e.g. [2][11][13][14]). Yet in practice, because of the large uncertainty related to the modelling of the process dynamics [1], poor performance may be expected from such control strategies, and , although a priori attractive, optimal control has not been largely applied to industrial bioprocesses. Alternative approaches have been proposed that are aimed at handling the process uncertainties with an adaptive control scheme [3].

The task of extremum seeking is to find the operating set-points that maximize or minimize an objective function. Since the early research work on extremum control in the 1920's [10], several applications of extremum control approaches have been reported, e.g. [4][18][15]. Krstic et al [7][8] presented several extremum control schemes and stability analysis for extremum-seeking of linear unknown systems and a class of general nonlinear systems [7][8][9]. The implications for the chemical and biochemical industries are clear. In these sectors, it is recognized that even small performance improvements in key process control variables may result in substantial economic benefits.

In this paper, we investigate an alternative extremum seeking scheme for fed-batch bioreactors. The proposed scheme utilizes explicit structure information of the objective function that depends on system states and unknown plant parameters. The scheme presented in this paper is based on Lyapunov's stability theorem. As a result, the global stability is ensured during the seeking of the extremum of the nonlinear continuous stirred tank bioreactors. It is also shown that once a certain level of persistence of excitation (PE) condition is satisfied, the convergence of the extremum seeking mechanism can be guaranteed.

A similar approach has been considered for a simple microbial growth model with Monod kinetics in continuous stirred tank reactors [19]. In the present paper, we consider a fed-batch reactor and the Haldane model as the process kinetics model. The present approach results in a structure of the extremum seeking algorithm which is rather different. The innovative aspects of the present extremum seeking controller are basically threefold. First, the optimization problem to be handled is different : in [19], the problem is to optimize the gas production rate while in the present paper, the objective is to maximize the production of biomass at the end of the fed-batch operation. Secondly, the use of the Haldane kinetics model

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(typical of the kinetics in fed-batch bioreactors) induces an increased complexity in the design and analysis of the extremum seeking (although the complexity of the extremum seeking controller remains similar).

The adaptive extremum seeking ontrol of fedbatch bioreactors has also been addressed in [16][17] under the assumption that both the susbstrate concentration and the gaseous outflow rates are accessible for on-line measurements. The third innovative aspect of this paper is that it is shown here how to design the real-time optimizer when only the substrate concentration is measured on-line. This is performed by considering the on-line estimation of the biomass concentration via an asymptotic observer.

The paper is organized as follows. Section 2 presents the problem. In Section 3 the adaptive extremum seeking controller is developed, and its stability and convergence properties are analyzed. Numerical simulations are presented in Section 4 in order to illustrate the adaptive extremum seeking performance.

2. PROBLEM FORMULATION

Consider the following dynamical model of a simple microbial growth process with one gaseous product in a fed-batch reactor :

$$\dot{X} = \mu X - uX \tag{1}$$

$$\dot{S} = -k_1 \mu X + u(S_0 - S) \tag{2}$$

$$\dot{V} = uv \tag{3}$$

where states X (g/l) and S (g/l) hold for biomass and substrate concentrations, respectively. μ (h^{-1}) is the specific growth rate, u (h^{-1}) is the dilution rate, S_0 (g/l) denotes the concentration of the substrate in the feed, k_1 is a yield coefficient, and v (l) is the volume of liquid medium in the tank. A typical situation in bioprocess applications is when the biomass concentration is not available for on-line measurement. That's why we consider here that only S is measurable while the biomass concentration X is not available for feedback control.

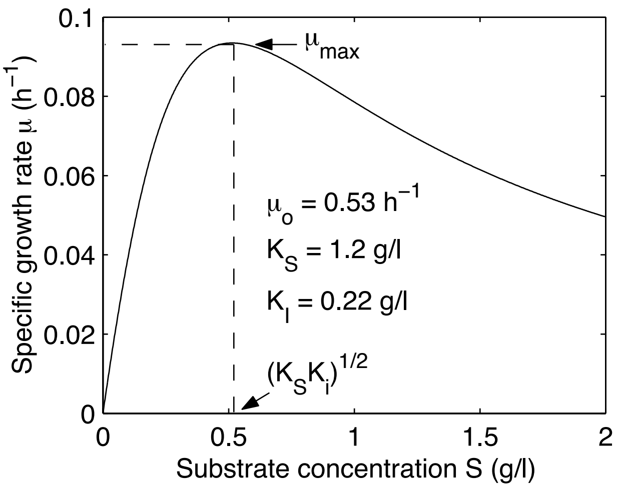

Fig. 1. Haldane Model

In this work, we consider the extremum seeking problem for the bioprocess model (1)-(3) with a specific growth rate μ expressed by the Haldane model. This model (see Figure 1) is given by the following equations :

$$\mu = \frac{\mu_0 S}{K_S + S + \frac{S^2}{K_I}} \tag{4}$$

where μ_0 is a parameter related to the maximum value of the specific growth rate as follows : $\mu_0 = \mu_{max}(1 + 2\sqrt{\frac{K_S}{K_I}})$.The coefficients K_S and K_I denote the saturation constant and the inhibition constant, respectively. The Haldane model is a growth model commonly used in situations where substrate inhibition is important. This situation is typical of fed-batch bioprocesses. The control objective is to design a controller, u, such that the biomass production X achieves its maximum at the end of the fed-batch operation. It is well-known (e.g. [1]) that the maximization will be completed if the specific growth rate is kept at its maximum value :

$$S^* = \sqrt{K_S K_I} \tag{5}$$

From the above considerations, we know that if the substrate concentration S can be stabilized at the set-point S^* then the production of biomass is maximized. However, since the exact values of the Haldane model parameters K_S, μ_0 and K_I, are usually unknown, the desired set-point S^* is not available. In this work, an adaptive extremum seeking algorithm is developed to search this unknown set-point such that the biomass production at the end of the reactor operation, i.e. $v(t_f)X(t_f)$ (with v the reactor volume and t_f the final time of the fed-batch operation) is maximized.

In the technical developments here below, we shall consider the following assumption for the parameters K_S and K_I of the Haldane model.

Assumption : K_S and K_I are known to be bounded as follows : $K_{S,min} \leq K_S \leq K_{S,max}$, $K_I \leq K_{I,max}$.

This assumption is only important for the technical developments in order to avoid singularities in the extremum seeking controller.

3. ESTIMATION AND CONTROLLER DESIGN

The design of the adaptive extremum seeking controller will proceed in different steps. First of all, we shall start with the estimation equation for S, then include the controller equations and the estimation equations for the unknown parameters in a Lyapunov based derivation framework, and end up with the stability and convergence analysis that includes the selection of appropriate design parameters in order to guarantee the convergence to the optimum.

3.1 Estimation equation for the subtstrate concentration S

Let us first consider the state transformation [1] :

$$Z = k_1 X + S \tag{6}$$

Let $\theta = [\theta_S \ \theta_\mu \ \theta_I]^T$ with $\theta_\mu = \frac{\mu_0}{K_S}$, $\theta_S = \frac{1}{K_S}$, $\theta_I = \frac{1}{K_I K_S}$. Then equations (1)(2) can be reformulated as follows :

$$\dot{Z} = u(S_0 - Z) \quad (7)$$

$$\dot{S} = -\frac{\theta_\mu S}{1+\theta_S S+\theta_I S^2}(Z-S) + u(S_0 - S) \quad (8)$$

Let $\hat{\theta}$ denote the estimate of the true parameter θ, and $\hat{S}$ be the prediction of S by using the estimated parameter $\hat{\theta}$. The predicted state $\hat{S}$ is generated by :

$$\dot{\hat{S}} = -\frac{\hat{\theta}_\mu S}{1+\hat{\theta}_S S+\hat{\theta}_I S^2}(Z-S) + u(S_0 - S) + k_S e_S \quad (9)$$

with $k_S > 0$ and the prediction error $e_S = S - \hat{S}$. This equation will the driving term for the estimation of the three unknown parameters θ_μ, θ_S and θ_I in an observer-based estimator framework [1].

It follows from (8)(9) that the estimation error on S follows the following dynamics :

$$\dot{e}_S = -k_S e_S - \frac{\theta_\mu S}{1+\theta_S S+\theta_I S^2}(Z-S) + \frac{\hat{\theta}_\mu S}{1+\hat{\theta}_S S+\hat{\theta}_I S^2}(Z-S) \quad (10)$$

3.2 Design of the adaptive extremum seeking controller

The desired setpoint (5) can be re-expressed as follows :

$$S^* = \frac{1}{\sqrt{\theta_I}}$$

Since the parameter θ_I is unknown, we design a controller to drive the substrate concentration S to

$$\frac{1}{\sqrt{\hat{\theta}_I}}$$

that is an estimate of the unknown optimum S^*. An excitation signal is then designed and injected into the adaptive system such that the estimated parameter $\hat{\theta}_I$ converge to its true value. The extremum seeking control objective can be achieved when the substrate concentration S is stabilized at the optimal operating point S^*.

Define

$$w_s = \hat{S} - \frac{1}{\sqrt{\hat{\theta}_I}} - d(t) \quad (11)$$

where $d(t) \in C^1$ is a dither signal that will be assigned later. Note that w_s corresponds of the sum of an image of the control error (the second term would be exactly the desired point if $\hat{\theta}_I = \theta_I$) and of the dither signal.

The time derivative of w_s is given by :

$$\dot{w}_s = -\frac{\hat{\theta}_\mu S}{1+\hat{\theta}_S S+\hat{\theta}_I S^2}(Z-S) + u(S_0 - S) + k_S e_S + \frac{1}{2}\hat{\theta}_I^{-\frac{3}{2}}\frac{d\hat{\theta}_I}{dt} - \dot{d}(t) \quad (12)$$

We consider a Lyapunov function candidate :

$$V = \frac{w_s^2}{2} + \frac{1}{2}\left(\frac{\tilde{\theta}_\mu^2}{\gamma_\mu} + \frac{\tilde{\theta}_S^2}{\gamma_S} + \frac{\tilde{\theta}_I^2}{\gamma_I}\right) + (1+\theta_S S+\theta_I S^2)\frac{e_S^2}{2}$$

with constants $\gamma_\mu, \gamma_S, \gamma_I > 0$.

Let us consider the following dynamic state feedback :

$$\dot{d}(t) = a(t) + \frac{1}{2}\hat{\theta}_I^{-\frac{3}{2}}\frac{d\hat{\theta}_I}{dt} - k_d d(t) \quad (13)$$

$$u(t) = \frac{1}{S_0 - S}\left[-k_w w_s + \frac{\hat{\theta}_\mu S(Z-S)}{1+\hat{\theta}_S S+\hat{\theta}_I S^2} + a(t) - k_d d(t)\right] \quad (14)$$

with $a(t)$ a dither signal and k_d and k_w strictly positive constants, and the following parameter update law :

$$\dot{\hat{\theta}}_i = \begin{cases} \gamma_I \Psi_I, & \text{if } \hat{\theta}_I > \epsilon_I \text{ or } \hat{\theta}_I = \epsilon_I \text{ and } \Psi_I > 0 \\ 0 & \text{otherwise} \end{cases} \quad (15)$$

$$\dot{\hat{\theta}}_s = \begin{cases} \gamma_S \Psi_S, & \text{if } \hat{\theta}_S > \epsilon_S \text{ or } \hat{\theta}_S = \epsilon_S \text{ and } \Psi_S > 0 \\ 0 & \text{otherwise} \end{cases} \quad (16)$$

$$\dot{\hat{\theta}}_\mu = \gamma_\mu \Psi_\mu \quad (17)$$

with the initial conditions $\hat{\theta}_S(0) \geq \epsilon_S = \frac{1}{K_{S,max}} > 0$, and $\hat{\theta}_I(0) \geq \epsilon_I = \frac{1}{K_{s,max}K_{I,max}} > 0$, and :

$$\Psi_I = e_S\frac{\hat{\theta}_\mu S^3(Z-S)}{1+\hat{\theta}_S S+\hat{\theta}_I S^2} - \frac{e_S^2}{2}(2k_S S^2 - 2uS(S_0 - S))$$

$$\Psi_S = e_S\frac{\hat{\theta}_\mu S^2(Z-S)}{1+\hat{\theta}_S S+\hat{\theta}_I S^2} - \frac{e_S^2}{2}(2k_S S - u(S_0 - S))$$

$$\Psi_\mu = -e_S S(Z-S)$$

The update laws (15)(16) are projection algorithms that ensure that $\hat{\theta}_S(t) \geq \epsilon_S > 0$ and $\hat{\theta}_I(t) \geq \epsilon_I > 0$. They also ensure that :

$$(\Psi_I - \frac{\dot{\hat{\theta}}_I}{\gamma_I})\tilde{\theta}_I + (\Psi_S - \frac{\dot{\hat{\theta}}_S}{\gamma_S})\tilde{\theta}_S + (\Psi_\mu - \frac{\dot{\hat{\theta}}_\mu}{\gamma_\mu})\tilde{\theta}_\mu \leq 0 \quad (18)$$

It is also worth noting that the structure of the controller (14) is that of an adaptive linearizing controller (the first two terms divided by the denominator) [1] to which terms related to the dither signal have been added.

3.3 Stability and convergence analysis

The stability and convergence analysis of the fedbatch reactor coupled to the adaptive extremum seeking controller follows arguments to those considered in [17].

By considering (13)-(17), it is routine to check that the time derivative of the Lyapunov function candidate is bounded as follows :

$$\dot{V} \leq -k_w w_s^2 + \Gamma + k_S e_S w_S \quad (19)$$

with :

$$\Gamma = -\frac{e_S^2}{2}\left(2k_S(1+\hat{\theta}_S S+\hat{\theta}_I S^2) - (\hat{\theta}_S + 2\hat{\theta}_I S)u(S_0 - S)\right) - \frac{e_S^2}{2}\left(\frac{\theta_\mu S(\theta_S + 2\theta_I S)}{1+\hat{\theta}_S S+\hat{\theta}_I S^2}(Z-S)\right) \quad (20)$$

By completing the squares, we have :

$$k_S e_S w_S = \frac{\alpha}{2}k_S^2 e_S^2 + \frac{1}{2\alpha}w_S^2 - \left(\sqrt{\frac{\alpha}{2}}k_S e_S - \frac{1}{\sqrt{2\alpha}}w_S\right)^2 \quad (21)$$

with $\alpha > 0$. Therefore an upper bound on $k_S e_S w_S$ is given by :

$$k_S e_S w_S \leq \frac{\alpha}{2} k_S^2 e_S^2 + \frac{1}{2\alpha} w_S^2 \tag{22}$$

Therefore the time derivative of V can be bounded as follows :

$$\begin{aligned} \dot{V} \leq & -w_s^2 \left(k_w - \frac{1}{2\alpha} \right) - \frac{e_S^2}{2} \left(\frac{\theta_\mu S(\theta_S + 2\theta_I S)}{1 + \hat{\theta}_S S + \hat{\theta}_I S^2} (Z - S) \right) \\ & - \frac{e_S^2}{2} \Big(-\alpha k_S^2 + 2k_S (1 + \hat{\theta}_S S + \hat{\theta}_I S^2) \\ & - (\hat{\theta}_S + 2\hat{\theta}_I S) u (S_0 - S) \Big) \end{aligned} \tag{23}$$

In order to have the time derivative of V to be negative, we must have $k_w > \frac{1}{2\alpha}$ and α such that the expression between brackets in the third term of the right hand side of the above inequality (23) is positive. The latter condition is fulfilled if :

$$\rho = (1 + \hat{\theta}_S S + \hat{\theta}_I S^2)^2 - \alpha(\hat{\theta}_S + 2\hat{\theta}_I S) u (S_0 - S) > 0$$

i.e. if :

$$\alpha < \frac{(1 + \hat{\theta}_S S + \hat{\theta}_I S^2)^2}{(\hat{\theta}_S + 2\hat{\theta}_I S) u (S_0 - S)} \tag{24}$$

Then the roots of the expression between brackets in the third term of the right hand side of the inequality (23) are equal to :

$$k_S^{'} = \frac{(1 + \hat{\theta}_S S + \hat{\theta}_I S^2) \pm \sqrt{\rho}}{\alpha} \tag{25}$$

Since $\sqrt{\rho} < (1 + \hat{\theta}_S S + \hat{\theta}_I S^2)$, we have two positive roots. Therefore any value of k_S between these two values guarantees that the expression between brackets in the third term of the right hand side of the above inequality (23) is positive. We finally have :

$$\dot{V} \leq -\lambda_1 w_s^2 - \lambda_2 e_S^2, \ \ \lambda_1 > 0, \ \lambda_2 > 0 \tag{26}$$

Following LaSalle-Yoshizawa's Theorem, it can be concluded that $\hat{\theta}$, w_s and e_S are bounded, and

$$\lim_{t\to\infty} w_s = 0, \qquad \lim_{t\to\infty} e_S = 0 \tag{27}$$

This implies that :

$$\lim_{t\to\infty} \dot{\hat{\theta}}_I(t) = 0, \qquad \lim_{t\to\infty} \dot{\hat{\theta}}_S(t) = 0, \qquad \lim_{t\to\infty} \dot{\hat{\theta}}_\mu(t) = 0$$

Hence, the auxiliary variable $d(t)$ is bounded if $a(t)$ is bounded and $d(t)$ tends to zero if $a(t)$ does. Thus all signals of the closed-loop system are bounded. It should be noted that the convergence of the state error e_S does not mean that the estimated parameters converge to their true values as $t \to \infty$. In the following, we investigate the condition that guarantees the parameter convergence.

By LaSalle's Invariance Principle, the error vector $(w_s, e_S, \tilde{\theta})$ converges to the largest invariant set M of the dynamic system (10) and (15)-(17) contained in the set $E = \{(w_s, e_S, \tilde{\theta}) \in R^5 | w_s = e_S = 0\}$. Since e_S converges to zero, we know that $\int_0^\infty \dot{e}_S dt = e_S(\infty) - e_S(0) = -e_S(0)$. This implies that $\dot{e}_S$ is integrable. It follows from the error equation (10) that $\ddot{e}_S$ is a function of Z, S, $\hat{S}$, $\hat{\theta}$, d and its time derivatives. Since $\hat{\theta}, e_S \in L_\infty$, and the excitation signal d and $\dot{d}$ are bounded, we know that $\ddot{e}_S$ is bounded. This implies the uniform continuity of $\dot{e}_S$. By Barbalat's Lemma [5], we conclude that $\dot{e}_S \to 0$ as $t \to \infty$.

On the invariant set M, we have $e_S \equiv 0$ and $\dot{e}_S \equiv 0$. By setting $e_S = \dot{e}_S = 0$, equation (10) leads to

$$\tilde{\theta}^T \Phi(S, Z, \hat{\theta}, u) = 0, \qquad (w_s, e_S, \tilde{\theta}) \in M \tag{28}$$

where

$$\tilde{\theta} = [\tilde{\theta}_I \ \tilde{\theta}_S \ \tilde{\theta}_\mu]^T \tag{29}$$

$$\Phi(S, Z, \hat{\theta}, u) = \begin{bmatrix} -(1 + \hat{\theta}_S S + \hat{\theta}_I S^2) \\ \hat{\theta}_\mu S \\ \hat{\theta}_\mu S^2 \end{bmatrix} \tag{30}$$

It follows from (28) that $\forall (w_s, e_S, \tilde{\theta}) \in M$

$$\tilde{\theta}^T \Psi(t) \tilde{\theta} = \tilde{\theta}^T \Phi(S, Z, \hat{\theta}, u) \Phi^T(S, Z, \hat{\theta}, u) \tilde{\theta} = 0 \tag{31}$$

As a result, if the dither signal $d(t)$ is designed such that the following condition holds

$$\lim_{t\to\infty} \frac{1}{T_0} \int_t^{t+T_0} \Psi(\tau) d\tau \geq c_0 I \tag{32}$$

for some $c_0 > 0$, then, the parameter error $\tilde{\theta}$ converges to zero asymptotically.

3.4 The asymptotic observer

In the above developments and analysis, we have assumed that Z is perfectly known. However, since the biomass concentration X is assumed to be unknown, an asymptotic observer [1] is used to provide an on-line estimate of Z :

$$\dot{\hat{Z}} = u(S_0 - \hat{Z}) \tag{33}$$

Considering the definition of Z (6) we readily obtain an on-line estimate of the biomass concentration X :

$$\hat{X} = \frac{Z - S}{k_1} \tag{34}$$

The estimation error $e_Z (= Z - \hat{Z})$ dynamics is therefore given by the following expression :

$$\dot{e}_Z = -u e_Z \tag{35}$$

which shows that e_Z tends asymptotically to zero. One potential drawback of the asymptotic observer is that there is no tuning parameter for the convergence rate. Yet it is worth noting that in fedbatch processes, the biomass concentration typically follows large variations (ideally, an "exponential" growth). Therefore apparently large initial error on the (usually small) initial value of the biomass is more likely to result in negligible error by the end of the fedbatch operation even in presence of apparently low convergence rate.

The stability and convergence properties of the asymptotic observer (33) coupled to those of the adaptive extremum seeking controller presented above guarantee that the substrate concentration will converge to its optimal value in the fedbatch bioreactor.

4. SIMULATION RESULTS

The performance of the adaptive extremum seeking controller have been tested in a number of numerical simulations, performed using a realistic example of a fed-batch process. The kinetic model parameters, yield coefficients and initial states used during numerical simulations are:

$$\mu_0 = 0.53\,h^{-1},\ K_S = 1.2\,g/l,\ K_I = 0.22\,g/l,\ k_1 = 0.4$$
$$X(0) = 7.2\,g/l,\ S(0) = 2.5\,g/l,\ S_0 = 20\,g/l \qquad (36)$$

For the Haldane model, from Figure 1, the maximum on the growth specific rate occurs at $S^* = \dfrac{1}{\sqrt{\theta_i}} = 0.52$ g/l. The control objective is to design a controller for the dilution rate, u, to regulate the substrate S at S^*. The controller requires on-line measurements of the variable S as well as the knowledge of the kinetic parameters, determining the S^*. These values are obtained using the estimation algorithm previously presented, through the measurements of S.

For the simulation study, we consider the following initial estimates of the kinetic parameters : $\hat{\theta}_\mu = 1$, $\hat{\theta}_S = 0.1$, $\hat{\theta}_I = 1.5$ ($\hat{\mu}_0 = 10$, $\hat{K}_S = 10$, $\hat{K}_I = 0.0067$). The design parameters for the extremum-seeking controller are set to : $\gamma_\mu =$, $\gamma_S = 10$, $\gamma_i = 50$, $k_w = 1$, $k_d = 1$, $\alpha = 0.1$. The dither signal $a(t)$ is chosen as follows :

$$a(t) = \sum_{i=1}^{5} A_{1i} sin\Big((0.001 + (5 - 0.001)i/4)t\Big) + \sum_{i=1}^{5} A_{2i} cos\Big((0.01 + (5 - 0.01)i/4)t\Big) \qquad (37)$$

where A_{1i} and A_{2i} are normally distributed random numbers in the interval [-0.1,0.1].

The performance of the extremum seeking control scheme is illustrated in Figures 2-6. We consider the initial conditions, $\hat{X}(0) = 7.2$ and $\hat{S}(0) = 2.0$. It is shown from Figure 5 that the extremum seeking scheme converges to the intended growth rate value. The substrate concentration (Figure 2) converges to the unknown optimum as well. The dilution rate manipulation resulting from the extremum-seeking control is also shown in Figure 3. Convergence of the kinetic parameters to their true values is shown in Figure 6. Note that after a fast convergence close to the true parameter values, the subsequent convergence is slower without any major negative effect on the convergence of the substrate concentration S to its optimal value. Overall, the extremum-seeking is shown to perform satisfactorily for this case.

5. CONCLUSIONS

We have solved a class of extremum seeking control problems for fed-batch bioreactors with Haldane kinetics. The proposed extremum seeking controller drives the substrate concentrations to unknown desired set-points that optimize the biomass production rate. A persistence of excitation condition is derived to ensure the convergence of the production rate of the bioreactor to a neighborhood of its maximum. The performance of the adaptive extremum

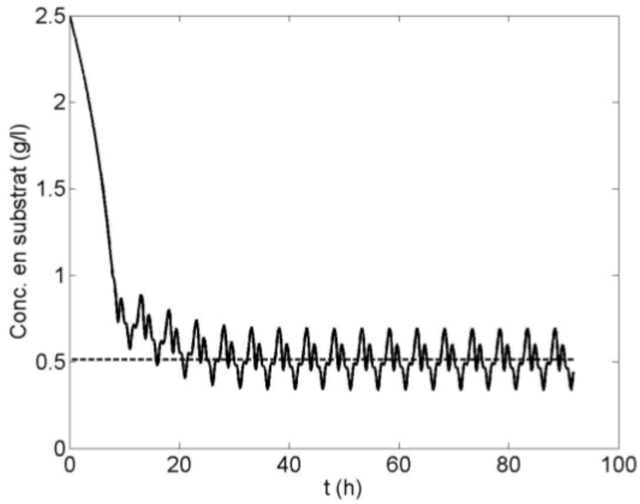

Fig. 2. Simulation results : the substrate concentration S

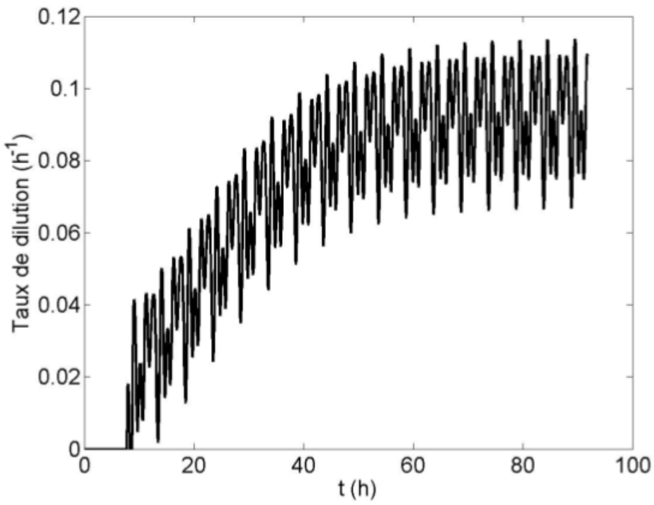

Fig. 3. Simulation results : the dilution rate u

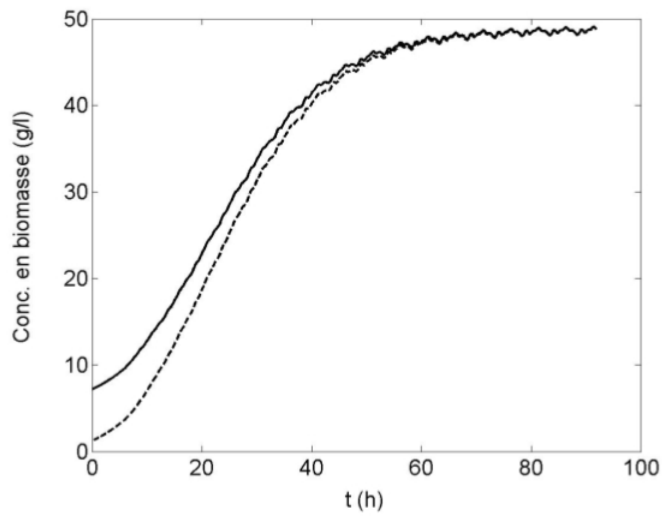

Fig. 4. Simulation results : the biomass concentration X and its on-line estimate $\hat{X}$ (dotted line)

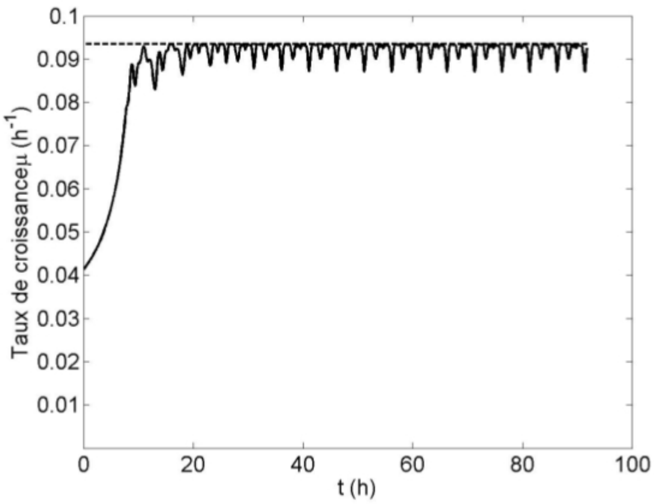

Fig. 5. Simulation results : the on-line estimate of the specific growth rate $\hat{\mu}$ (dotted line)

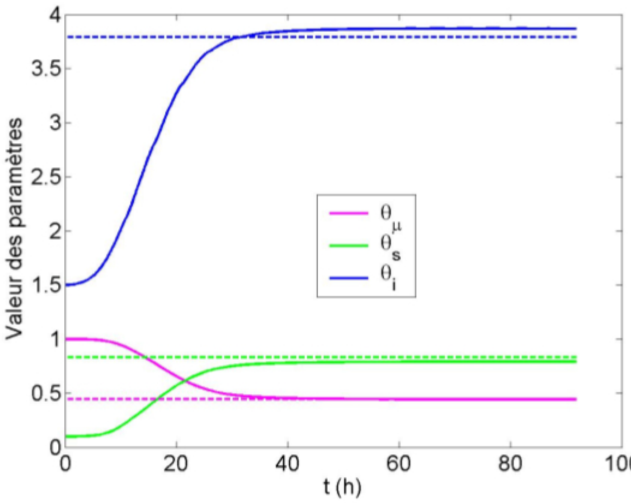

Fig. 6. Simulation results : $\hat{\theta}_I$, $\hat{\theta}_S$, $\hat{\theta}_\mu$ (true values in dotted lines)

seeking algorithm has been illustrated on a fed-batch process model.

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