# **On Adaptive Control of a Biochemical Process**

EMIL PETRE and DAN SELIŞTEANU Department of Automatic Control University of Craiova A.I. Cuza Str. No. 13, RO-200585 Craiova ROMANIA http://www.automation.ucv.ro

*Abstract:* - This paper deals with the design and the analysis of some nonlinear and adaptive control strategies capable to deal with the model uncertainties in an adaptive way for a complex and time varying bioprocess resulting from the association of a recycling bioreactor with an electrochemical reactor. The nonlinear controller design is based on the input-output linearizing technique. Computer simulations are included to demonstrate the performances of the proposed controllers.

Key-Words: - Nonlinear systems, Bioprocesses, Nonlinear control, On-line estimation, Adaptive control.

### **1** Introduction

During the last years, the control of biotechnological processes has been an important problem attracting wide attention. The main engineering motivation in applying control methods to such living processes is to improve operational stability and production efficiency. But the use of modern control for these bioprocesses is still low. Two known factors make biotechnological processes control particularly difficult. First, these processes exhibit large nonlinearities, strongly coupled variables and often poorly understood dynamics. Second, the real-time monitoring and on-line measurements of biological process variables, for example, biomass and/or product concentrations, which are essential for control design, is hampered by the lack of cheap and reliable on-line sensors. Due to the two above characteristic factors, bioprocesses constitute a natural field of application for adaptive techniques [1], [5]. So, the difficulties encountered in the measurement of the state variables of the bioprocesses impose the use of the so-called "software sensors" [1]. Note that these software sensors are used not only for the estimation of the concentrations but also for the estimation of the kinetic parameters [1], [5].

This paper presents the design and the analysis of some nonlinear and adaptive control strategies capable to deal with the model uncertainties in an adaptive way for a complex bioprocess resulting from the association of a recycling bioreactor with a time delay electrochemical reactor [4]. More exactly, the process consists of a completely stirred tank reactor for bacteria growth coupled with an electrochemical reactor for substrate regeneration. The controller is obtained via the input-output linearization technique [3]. The only information required about the process are the measurements of the state variables and its relative degree. It must be noted that if for the analyzed process there are no accessible state variables, these will be estimated by using an appropriately state observer. Since in practice the continuous processes are much more efficient, for this bioelectrochemical process it is proposed and analysed a continuous-flow control strategy. Computer simulations performed under identical circumstances are included to demonstrate the performances of the designed controllers.

The rest of this paper is organized as follows. Section 2 is devoted to description and modelling of a recycled biochemical process. Some nonlinear and adaptive control strategies are proposed in Section 3. Simulations results presented in Section 4 illustrate the performances of the proposed control algorithms and, finally, Section 5 concludes the paper.

# 2 Process description and modelling

The bioprocess under consideration deals with the production of *Thiobacillus ferrooxidans* bacteria (biomass) interesting for its uptake properties of heavy and toxic metals in waste water. These bacteria derive their growth energy through oxidation of ferrous iron according to [2]:

$$4Fe^{2+} + O_2 + 4H^+ \to 4Fe^{3+} + 2H_2O \tag{1}$$

A schematic view of this continuous bioprocess is presented in Fig. 1. The bacterial growth is carried out in a completely stirred tank reactor that contains a culture medium in which  $Fe^{2+}$  is considered as the single limited substrate, denoted *S*. By bacterial growth process through oxidation of ferrous iron,



Fig. 1. A schematic view of bioprocess

the substrate  $Fe^{2+}$  is transformed in  $Fe^{3+}$ , denoted by *P*. For the substrate regeneration is used an electrochemical reactor connected with the reactor as in Fig. 1. Note that, at the bioreactor output, the culture medium is filtered in order to retain biomass *X*, which is recirculated in the bioreactor.

Based on the mass balance, for the bioreactor, the mathematical model is given by the following set of differential equations [4], [6]:

$$\dot{X}(t) = \mu(S)X(t) \tag{2}$$

$$\dot{S}(t) = -\frac{1}{Y_{SX}} \mu(S)X(t) + D(t)(S_{in}(t) - S(t))$$
(3)

$$\dot{P}(t) = \frac{1}{Y_{SX}} \mu(S) X(t) + D(t) (P_{in}(t) - P(t))$$
(4)

where X, S and P are the concentrations of biomass, the substrate  $Fe^{2+}$  and the product  $Fe^{3+}$ , respectively,  $D(t) = F(t)/V_{br}(t)$  is the dilution rate, F is the circulating flow rate,  $V_{br}$  is the bioreactor volume,  $Y_{SX}$  is the yield coefficient considered constant and  $\mu(S)$  is the specific growth rate. For the modelling of the specific growth rate was adopted a Haldane model [4], given by

$$\mu(S) = \mu_{\max} \frac{S}{K_{S} + S + S^{3} / K_{I}}$$
(5)

where  $\mu_{max}$ ,  $K_s$  and  $K_I$  are kinetic parameters. Note that the total iron concentration in the system denoted  $Fe_{tot}$  remains constant and is given by

$$Fe_{tot} = S(t) + P(t) = S_{in}(t) + P_{in}(t)$$
 (6)

The electrochemical reactor is represented by a fixed bed reactor with plug flow that here is modelled by the following two delay time equations [4], [6]:

$$P_{in}(t) = (1 - r)P(t - \tau)$$
(7)

$$S_{in}(t) = S(t-\tau) + rP(t-\tau)$$
(8)

where

$$r = \frac{P(t-\tau) - P_{in}(t)}{P(t-\tau)}$$
(9)

represents the product conversion rate or, in other words, the substrate regeneration rate and  $\tau = V_r / F$  represents the delay time corresponding to the stay time of the culture medium in the electrochemical reactor for a flow rate *F* and a reactor volume  $V_r$ .

In this process the variables S(t) and P(t) are not directly measurable, but the iron oxidation rates P(t)/S(t) and  $P_{in}(t)/S_{in}(t)$  are on-line measured through the redox potential probes defined as [4]:

$$R_{p}(t) = R_{p0} + k \ln \frac{P(t)}{S(t)}$$
(10)

where k is a constant parameter and  $R_{p0}$  is an initial value of  $R_p$  determined by probe calibration. It must be noted that the redox potential measurements allow to obtain indirect measurements of the model variables (substrate, biomass, product) if the model parameters are assumed known.

## **3** Control Strategies

#### **3.1 Problem statement**

For the presented bioprocess, the control objective is to get a large production of biomass in a desired physiological state. From the above considerations, it follows that the biomass production process requires regulation of the substrate concentration Sinside the bioreactor at a set point  $S^*$  corresponding to a desired biomass specific growth rate by acting on the feeding substrate concentration  $S_{in}(t)$ . Since the substrate S is not on-line measurable, in practice, this is achieved by regulation of the redox potential  $R_p$  in the bioreactor at a set point  $R_p^*$ corresponding to  $S^*$  such that the total iron concentration in the system is constant.

To solve this problem, one can observe that there are two possible control variables: (i) the substrate regeneration rate r controlled by the current intensity I applied to the electrochemical reactor; (ii) the circulating flow rate F in the system.

In the paper both mentioned control variables are used. As the second possibility is more difficult since the flow rate variations induce a varying delay time in the system, in this section, will be analysed the behaviour of the controlled system when the control variable is the substrate regeneration rate r.

Using (6), (7) and (8) the process model (2)-(4) takes the form:

$$X(t) = \mu(S)X(t) - k_d X(t)$$
(11)

$$\dot{S}(t) = -\frac{1}{Y_{SX}} \mu(S)X(t) + D(t)(P(t) - (1 - r)P(t - \tau))$$
(12)

$$\dot{P}(t) = \frac{1}{Y_{SX}} \mu(S)X(t) + D(t)((1-r)P(t-\tau) - P(t))$$
(13)

where  $k_d$  is the death rate of biomass.

Thus, we are dealing with a control problem of a nonlinear single input – single output system with state delay time, given by the equations (11)-(13) where r is the control variable and the controlled variable is given by (10). Note that the control variable r is bounded as,  $r \in [0, 1]$ .

#### 3.2 Exactly linearizing feedback controller

Controller design is made by the input-output linearizing technique [3] that consists of the calculus of a nonlinear control law such that the behaviour of closed loop system (controller + process) is the same to the behaviour of a linear stable system.

Firstly, we consider an ideal case, where maximum prior knowledge concerning the process is available, that is the kinetics  $\mu(\cdot)$ , the yield coefficient  $Y_{SX}$  and the delay time  $\tau$  in process model (11)-(13) are assumed completely known and all the state variables are available for on-line measurement. Assume now that for the closed loop system we wish to have the following first-order linear stable dynamics:

$$\frac{d}{dt}\left(R_{p}^{*}-R_{p}\right)+\lambda\left(R_{p}^{*}-R_{p}\right)=0, \quad \lambda\in\mathfrak{R}, \ \lambda>0 \quad (14)$$

It can be seen that equations (12) and (13) in the model (11)-(13) have the relative degree equal to 1 [3]. Then, from (10) with (12) and (13), the above closed-loop dynamics will be achieved by implementing the following *nonlinear linearizing control law*:

$$r(t) = -\frac{\mu(S)X(t)}{Y_{SX}DP(t-\tau)} + 1 - \frac{P(t)}{P(t-\tau)} - \frac{P(t)S(t)}{Fe_{tot}DP(t-\tau)}\lambda\left(R_p^*(t) - R_p(t)\right)$$
(15)

where  $R_p^*$  is the desired value of  $R_p$ .

The control law (15) leads to the following linear error model:

$$\dot{e} = -\lambda e \tag{16}$$

with  $e = R_p^* - R_p$ . It is clear that for  $\lambda > 0$ , the error model (16) has an asymptotic stable point at e = 0.

### **3.3** Adaptive linearizing feedback controller

The practical implementation of the above control law requires the knowledge of the states  $S(\cdot), P(\cdot)$ and  $X(\cdot)$ , and of the specific reaction rate  $\mu(S)$ . Since the variables  $S(\cdot)$  and  $P(\cdot)$  are not directly measurable, these are substituted by their values obtained using the redox potential  $R_p$ . So, the value of  $S(\cdot)$  is given by:

$$S_{c}(\cdot) = \frac{Fe_{tot}}{1 + \exp\left(\left(R_{p}(\cdot) - R_{p0}\right)/k\right)}$$
(17)

and the value of  $P(\cdot)$  is given by:

$$P_{c}(\cdot) = Fe_{tot} \frac{\exp\left(\left(R_{p}(\cdot) - R_{p0}\right)/k\right)}{1 + \exp\left(\left(R_{p}(\cdot) - R_{p0}\right)/k\right)}$$
(18)

where  $S_c(\cdot)$  and  $P_c(\cdot)$  stand for the calculated values of *S* and *P* respectively.

For the estimation of unmeasured variable X, independent of the specific reaction rate  $\mu(\cdot)$ , we use an *asymptotic state observer* [5], which can be derived as follows. Considering that the yield coefficient  $Y_{SX}$  is known and constant, let us define the auxiliary state z as:

$$z = (1/Y_{SX})X + S$$
(19)

The dynamic of z deduced from model (11)-(13), in which  $k_d$  is considered zero, is expressed by the following linear stable equation:

$$\hat{z}(t) = D(t)(S_{inc}(t) - S_{c}(t))$$
(20)

where  $S_{inc}(t)$  and  $S_{c}(t)$  are calculated through (17). Then, the on-line estimation of X is given by:

$$\hat{X} = Y_{SX} \left( \hat{z} - S_c \right) \tag{21}$$

Regarding the specific reaction rate  $\mu(S)$  there are two possibilities: (i) if the functional form of the nonlinearity  $\mu$  as well as the kinetic parameters are known, the values of  $\mu(S)$  are calculated through (5) in which the value of *S* is substituted by  $S_c$  from (17); (ii) the specific reaction rate  $\mu(S)$  may be considered as an unknown parameter denoted also  $\mu$  that will be substituted by this on-line estimate  $\hat{\mu}$ calculated by using an observer-based parameter estimator [1], [5] applied only the dynamics of *S* and *P*. Then, the algorithm for on-line computation of  $\hat{\mu}$  is given by the following equations:

$$\hat{S}(t) = -(1/Y_{SX})\mu\hat{X} + D(S_{inc} - S_c) + \omega_1(S_c - \hat{S})$$
(22)

$$\hat{P}(t) = (1/Y_{SX})\mu\hat{X} + D(P_{inc} - P_c) + \omega_2(P_c - \hat{P}) \quad (23)$$

$$\dot{\hat{\mu}}(t) = -\frac{\gamma_1}{Y_{SX}} \hat{X}(S_c - \hat{S}) + \frac{\gamma_2}{Y_{SX}} \hat{X}(P_c - \hat{P})$$
(24)

where  $\gamma_1, \gamma_2 > 0$  and  $\omega_1, \omega_2 > 0$  are design parameters at the user's disposal to control the stability and the tracking properties of the estimator (see [5], for stability and convergence properties).

Finally, an *adaptive linearizing controller* is obtained by combination of (17), (18), (20), (21), (22)-(24) and (15) rewritten as follows:

$$r(t) = -\frac{\hat{\mu}(t) X(t)}{Y_{SX} DP_c(t-\tau)} + 1 - \frac{P_c(t)}{P_c(t-\tau)} - \frac{P_c(t)S_c(t)}{Fe_{tot} DP_c(t-\tau)} \lambda \left( R_p^*(t) - R_p(t) \right)$$
(25)

### 3.4 A continuous-flow process strategy

Consider now that at the bioreactor output the culture medium is not filtered and the biomass X is not recirculated in bioreactor. Consequently, the bioreactor and the whole system become a continuous depollution system with a feed rate F. In this case the equation (2) takes the form:

$$X(t) = \mu(S)X(t) - DX(t)$$
(26)

Now, for controlling this process is more efficient to be used the flow rate F, respectively the dilution rate D, as the control variables, the controlled variable being the substrate (pollutant) concentration S. In the ideal case when the process model is completely known, the *exactly feedback linearizing control law* (15) takes the form:

$$D(t) = \frac{1}{S_{in}(t) - S(t)} \left[ \lambda \left( S^* - S(t) \right) + \frac{1}{Y_{SX}} \mu(S) X(t) \right]$$
(27)

where  $S^*$  is the desired value of *S*. Of course, the values  $S^*$  and *S* correspond to some values of  $R_p^*$  and  $R_p$  respectively. Since the control law (27) contains the variables *S* and *S<sub>in</sub>* that are not directly measurable, the variable *X* that is not measured and the specific reaction rate  $\mu(S)$  that is incompletely known and time varying, the law (27) becomes an adaptive control law by substituting of the unknown variable *X* and parameter  $\mu$  with their on-line estimations. So, for the estimation of unmeasured variable *X*, the asymptotic state observer (20), (21) takes the form:

$$\hat{z}(t) = -D(t)\hat{z}(t) + D(t)S_{inc}(t)$$
(28)

$$\hat{X} = Y_{SX} \left( \hat{z} - S_c \right) \tag{29}$$

where the auxiliary variable z is given by (19). The on-line estimate  $\hat{\mu}$  of the parameter  $\mu$  is obtained with the same parameter estimator (22)-(24).

The *adaptive linearizing controller* is obtained by combination of (17), (28), (29), (22)-(24) and (27) rewritten as:

$$D_{a}(t) = \frac{1}{S_{inc} - S_{c}} \left[ \lambda \left( S^{*} - S_{c}(t) \right) + \frac{1}{Y_{SX}} \hat{\mu}(t) \hat{X}(t) \right]$$
(30)

### **4** Simulation Results

The performances of the above nonlinear and adaptive controllers have been tested through extensive simulation experiments by using the process model (11)-(13) under realistic conditions. The nominal values of the kinetic parameters and the yield coefficient are [4]:  $\mu_{\text{max}}^N = 0.276 \ h^{-1}$ ,  $K_s^N = 4.85 \ g/l$ ,  $K_I^N = 4.5 \ g/l$ ,  $Y_{sx} = 0.93 \ mgX/gS$ ,  $F^N = 4 \ l/h$ ,  $Fe_{tot} = 6.64 \ g/l$ ,  $V_{br} = 4 \ l$ ,  $V_r = 0.8 \ l$ ,  $k_d = 0.01 \ h^{-1}$ , k = 7.5.

The system's behaviour is analyzed considering the kinetic parameters varying with time as:

$$\mu_{\max}(t) = \mu_{\max}^{N} (1 - 0.1 \sin(\pi t / 3))$$

$$K_{S}(t) = K_{S}^{N} (1 + 0.1 \cos(\pi t / 3))$$

$$K_{I}(t) = K_{I}^{N} (1 + 0.1 \sin(\pi t / 4))$$
(31)

Fig. 2 shows the open-loop behaviour of the system. The initial values of variables used in the simulations are: X = 1.0 mg/l, S = 6.1 g/l, P = 0.54 g/l,  $S_{in} = 6.1 g/l$ ,  $P_{in} = 0.54 g/l$ ,  $E_0 = 450 mV$ .

The graphics marked by 1, 2 and 3 correspond to three delay time values of culture medium in the electrochemical reactor:  $1 : \tau = 6 \text{ min}, 2 : \tau = 12 \text{ min}$ and  $3 : \tau = 24 \text{ min}$ , respectively. These delay time values are obtained considering the following three values for flow rate  $F^N$  respectively 8, 4 and 2 *l/h*. Much more, we consider that the flow rate is time varying as:

$$F(t) = F^{N} (1 + 0.1 \sin(\pi t / 2))$$
(32)

Note that the smooth curves in Fig. 2 correspond to the situation in which the process parameters are constants and equal to their nominal values.

From Fig. 2 it can be seen that a large amount of biomass is obtained after 200 hours. From this time the reaction in bioreactor is strongly limited and the process must be interrupted.

The behaviour of closed-loop system using the adaptive algorithm (25) by comparison to the exactly linearizing law (15) is presented in Fig. 3. Remember that the only measured variable is the redox potential that is also the controlled variable and the control input is the conversion rate r which variation is bounded as:  $0 \le r(t) \le 1$ . The simulation



conditions are the same as in the above open-loop situation. The initial value of the estimated auxiliary variable  $\hat{z}$  is  $\hat{z}(0) = 7.5 \ g/l$ . For the parameter estimator (22)-(24), the values of the design parameters are  $\omega_1 = \omega_2 = 50$  and  $\gamma_1 = \gamma_2 = 0.305$ , and the initial value of estimated parameter  $\hat{\mu}(0) = 0.1 \ h^{-1}$ . The gain of control laws (15), respectively (25) is  $\lambda = 0.5$ .

The graphics marked by 1, 2 and 3 correspond



also to the three above mentioned delay time values.

Note that for biomass variation in Fig. 3, for clarity, the presented curves correspond to the case 2:  $\tau = 12$  min. But it must be also noted that the other two cases are very closely to these. The graphics in Fig. 3 show a good behaviour of closed-loop adaptive system by comparison to behaviour of closed-loop system when the control law is one exactly.



Fig. 4. Closed-loop behaviour in the continuous case: the time delay  $\tau = 60$  min

The goal of the control is achieved, that means that, in this case, a large amount of biomass is obtained in a time interval much shorter that in the open-loop case.

The graphics in Fig. 4 present the behaviour of closed-loop system using the adaptive algorithm (30) by comparison to the exactly linearizing law (27) in the case of a continuous-flow process control strategy. In this situation the controlled variable is the substrate concentration *S* and the control input is the dilution rate *D*. The simulation conditions are the same as in the above closed-loop situation. One exception is the delay time considered in this simulation whose value is  $\tau = 60$  min. The smooth curves correspond to the nominal values of the process parameters. Other curves are obtained when the process parameters are varying in time such as (31). From these graphics it can be seen that the

behaviour of adaptive system is very good, being very close to the closed-loop system in the ideal case, when the control law is given by (27) even if the time delay varies in large limits. In our simulations, the conversion rate r was maintained at a constant value, for example, r = 0.85. One can observe also a good behaviour both of state observer and parameter estimator.

In this case the biomass concentration inside the bioreactor does not achieve the large values as in the above case because the biomass does not recirculate in bioreactor. Since the efficiency of a continuous biosystem that contains inhibitory reactions, as in our bioprocess, is superior to other process types, a realistic case that must be analysed in the future is the case when the bioreactor is continuously fed with a pollutant that must be cleaned of heavy metal.

### 5 Conclusions

Some nonlinear and adaptive control strategies have been designed for a complex and time varying bioelectrochemical process in order to produce biomass in a desired physiological state. Since, in most situations, the kinetic parameters are uncertain and time varying and the process nonlinearities are not exactly known and, much more, not all the state variables are on-line measurable, it can be concluded that adaptive controllers are the only viable alternative. The resulting performances of the proposed adaptive controllers, especially for the continuous case, are very good.

References:

- [1] G. Bastin, D. Dochain, *On-line Estimation and Adaptive Control of Bioreactors*, Elsevier, Amsterdam, 1990.
- [2] D. Dochain, J.P. Babary, N. Tali-Maamar, Modelling and adaptive control of nonlinear distributed parameter bioreactors via orthogonal collocation, *Automatica*, Vol.28, No.5, 1992, pp. 873-883.
- [3] A. Isidori, *Nonlinear Control Systems The Third Edition*, Springer Verlag, 1995.
- [4] M. Luca, F. Baillet, J.P. Magnin, A. Chéruy, P. Ozil, Nonlinear control of a bioelectrochemical process, 4-th IFAC Conference "System Structure and Control" - SSC'97, Oct. 23-25, 1997, Bucharest, Romania, Pergamon Press, London (IFAC Series), pp. 484-488.
- [5] E. Petre, *Nonlinear Systems Applications in Biotechnology* (in Romanian), Universitaria, Craiova, 2002.
- [6] E. Petre, Adaptive Control Strategies for a Class of Time Delay Nonlinear Bioprocesses, *Rev. Roum. Sci. Techn. - Électrotechn. et Énerg.* Vol.48, No.4, 2003, pp. 567-582.