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Nonlinear Control Strategies for Bioprocesses: Sliding Mode Control versus Vibrational Control

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1. Introduction

Nowadays, the domain of biotechnology is characterized by rapid changes in terms of novelty and by highly complex processes that require advanced procedures for design, operation and control. From the engineering point of view, the control of bioprocesses poses a number of challenging problems. These problems arise from the presence of living organisms, the high complexity of the interactions between the micro-organisms, as well as the high complexity of the metabolic reactions. Moreover, for monitoring and control applications, only a few measurements are available, either because the measuring devices do not exist or are too expensive, or because the available devices do not give reliable measurements. Therefore, we can deduce that the main difficulties arising in the control of bioprocesses arrive from two main sources: the process complexity and the difficulty to have reliable measurements of bioprocess variables (Bastin & Dochain, 1990; Selişteanu et al., 2007a).

In order to overcome these difficulties several strategies for the control of bioprocesses were developed, such as adaptive approach (Bastin & Dochain, 1990; Mailleret et al., 2004), vibrational control (Selişteanu & Petre, 2001; Selişteanu et al., 2007a), sliding mode control (Selişteanu et al., 2007a; Selişteanu et al., 2007b), fuzzy and neural strategies etc.

Sliding mode control (SMC) has been widely accepted as an efficient method for control of uncertain nonlinear systems (Utkin, 1992; Slotine & Li, 1991; Edwards & Spurgeon, 1998). The classical applications of SMC (such as robotics, electrical machines etc.) were extended to SMC of chemical processes (Sira-Ramirez & Llanes-Santiago, 1994) and to SMC of bioprocesses (Selişteanu et al., 2007a; Selişteanu et al., 2007b). The well-known advantages of the SMC are the robustness, controller order reduction, disturbance rejection, and insensitivity to parameter variations. The main disadvantage of the SMC strategies used in real applications remains the chattering phenomenon, even if some techniques of chattering reduction were developed (Slotine & Li, 1991; Edwards & Spurgeon, 1998).

Vibrational control (VC) is a non-classical open-loop control method proposed by Bellman, Bentsman and Meerkov (Meerkov, 1980; Bellman et al., 1986a; Bellman et al., 1986b). Applications of the vibrational control theory can be found for: stabilization of plasma, lasers, chemical reactors, biotechnological processes (Selişteanu et al., 2007a) etc. The VC technique is applied by oscillating an accessible system component at low amplitude and high frequency. Therefore, this technique can be considered, like the SMC, a form of high-frequency control (obviously high-frequency relative to the natural frequency of the system).

But, unlike the SMC, the amplitude and the frequency of the control input are constants and independent of the state of the system, so this technique is a form of open-loop control.

In this chapter, which is an extended work of (Selişteanu et al., 2007a), two nonlinear control strategies for bioprocesses are designed: a feedback SMC law and a vibrational control strategy. First, a class of bioprocesses is briefly analysed and a nonlinear prototype model is presented in detail. Then, the design of a feedback control law for a prototype bioprocess is developed. The design is based on a combination between exactly linearization, sliding mode control, and generalized observability canonical forms. In order to implement this SMC law, asymptotic observers (Bastin & Dochain, 1990) will be used for the reconstruction of unmeasured states. The next paragraph deals with the presentation of most important results of vibrational control theory. Also, a VC strategy for a continuous bioprocess is developed. The existence and the choice of stabilizing vibrations, which ensure the desired behaviour of the bioprocess are analysed. Some simulations results, comparisons of the proposed nonlinear control strategies, and final remarks are also presented.

2. Nonlinear dynamical models of the bioprocesses

2.1 The dynamical model of a class of bioprocesses

In bioindustry, the bioprocesses take place in biological reactors, also called bioreactors. A bioreactor is a tank in which several biological reactions occur simultaneously in a liquid medium (Bastin & Dochain, 1990). These reactions can be classified into two classes: microbial growth reactions and enzyme-catalysed reactions. The bioreactors can operate in three modes: the continuous mode, the fed-batch mode and the batch mode. For example, a Fed-Batch Bioreactor (FBB) initially contains a small amount of substrates and micro-organisms and is progressively filled with the influent substrates. When the FBB is full the content is harvested. By contrast, in a Continuous Stirred Tank Bioreactor (CSTB) the substrates are fed to the bioreactor continuously and an effluent stream is continuously withdrawn from the reactor such that the culture volume is constant.

In practice, the bioprocess control is often limited to regulation of the temperature and pH at some constant values favourable to the microbial growth.

There is however no doubt that the control of the biological state variables (biomass, substrates, products) can help to increase the bioprocess performance. In order to develop and apply advanced control strategies for these biological variables, obviously is necessary to obtain a useful dynamical model. The modelling of bioprocesses is a difficult task; however, using the mass balance of the components inside the bioreactor and obeying some modelling rules, a dynamical state-space model can be obtained (Bastin & Dochain, 1990; Bastin, 1991).

A process carried out in a bioreactor can be defined as a set of m biochemical reactions involving n components (with $n \geq m$). The reaction scheme of a bioprocess (the reaction network) contains n components and m reactions. The concentrations of the physical components will be denoted with the notations $\xi_i, i = \overline{1, n}$. The reaction rates will be denoted as $\varphi_j, j = \overline{1, m}$. The evolution of each component is described by the differential equation (Bastin & Dochain, 1990):

$$\dot{\xi}_i = \sum_{j=1}^m (\pm) k_{ij} \varphi_j - D \xi_i + F_i - Q_i \quad (1)$$

where $\dot{\xi}_i$ is the time derivative of the concentration ξ_i (g/l) and the notation $j \sim i$ indicates that the sum is done in accordance with the reactions j that involve the component i . The positive and dimensionless constants k_{ij} are yield coefficients. The sign of the first term of (1) is given by the type of the component ξ_i : plus (+) when the component is a reaction product and minus (-) otherwise. D is the specific volumetric rate (h^{-1}), usually called dilution rate. F_i represents the rate of supply of the component ξ_i (external substrate) to the bioreactor per unit of volume (g/lh). When this component is not an external substrate, then $F_i \equiv 0$. Q_i represents the rate of removal of the component ξ_i from the bioreactor in gaseous form per unit of volume (g/lh).

In order to obtain a dynamical state-space model of the entire bioprocess, we denote $\xi = [\xi_1 \ \xi_2 \ \dots \ \xi_n]^T$, where ξ is the n -dimensional vector of the instantaneous concentrations, also is the state of the model. The vector of the reaction rates (the reaction kinetics) is denoted $\varphi = [\varphi_1 \ \varphi_2 \ \dots \ \varphi_m]^T$. The reaction rate vector is m -dimensional. Usually, a reaction rate is represented by a non-negative rational function of the state ξ . The yield coefficients can be written as the $(n \times m)$ - dimensional yield matrix $K = [K_{ij}]$, $i = \overline{1, n}; j = \overline{1, m}$, where $K_{ij} = (\pm)k_{ij}$ if $j \sim i$ and 0 otherwise. Next, we introduce the notations $F = [F_1 \ F_2 \ \dots \ F_n]^T$, $Q = [Q_1 \ Q_2 \ \dots \ Q_n]^T$, where F is the vector of rates of supply and Q is the vector of rates of removal of the components in gaseous form.

From (1), with the above notations, the global dynamics can be represented by the dynamical state-space model (Bastin & Dochain, 1990):

$$\dot{\xi} = K \cdot \varphi(\xi) - D\xi + F - Q \quad (2)$$

This model describes in fact the behaviour of an entire class of biotechnological processes and is referred to as the general dynamical state-space model of this class of bioprocesses (Bastin & Dochain, 1990; Bastin, 1991). In (2), the term $K \cdot \varphi(\xi)$ is in fact the rate of consumption and/or production of the components in the reactor, i.e. the reaction kinetics. The term $-D\xi + F - Q$ represents the exchange with the environment, i.e. the dynamics of the component transportation through the bioreactor. The strongly nonlinear character of the model (2) is given by the reaction kinetics. In many situations, the yield coefficients, the structure and the parameters of the reaction rates are partially known or unknown.

Remark 1. In a FBB, the term $D\xi_i$ represents the dilution of a component due to the increase in volume. In this case D is the specific rate of volume increase ($\dot{V} = D \cdot V$, with V the liquid volume in the FBB and \dot{V} its time derivative). In a CSTB, $D\xi_i$ represents the rate of removal of a component in liquid form (in a CSTB, $\dot{V} = 0$).

Often in practice, the bioprocess control goal is to regulate a scalar output y , which can be defined as a linear combination of the state variables. Usually, this control objective is reached using as a control input one of the components of F , i.e. a rate of supply of an external substrate: $u = F_i$. Consequently, the vector F can be written as $F = b \cdot u + \tilde{F}$, with

$b = [b_1 \ b_2 \ \dots \ b_n]^T$; $b_i = 1$, $b_j = 0$, $i \neq j$; and $\tilde{F} = [\tilde{F}_1 \ \tilde{F}_2 \ \dots \ \tilde{F}_n]^T$; $\tilde{F}_i = 0$, $\tilde{F}_j = F_j$, $j \neq i$. Then, the model (2) can be rewritten as

$$\begin{aligned}\dot{\xi} &= K \cdot \varphi(\xi) - D\xi + \tilde{F} - Q + b \cdot u = f(\xi) + b \cdot u \\ y &= h(\xi)\end{aligned}\quad (3)$$

2.2 The model prototype of a continuous bioprocess

A model prototype of a continuous bioprocess that takes place inside a CSTB is described by the following nonlinear system (Bastin & Dochain, 1990; Dochain & Vanrolleghem, 2001):

$$\frac{d\xi_1}{dt} = \mu(\xi_1, \xi_2) \cdot \xi_1 - D \cdot \xi_1 \quad (4)$$

$$\frac{d\xi_2}{dt} = -k_1 \mu(\xi_1, \xi_2) \cdot \xi_1 - D \cdot \xi_2 + D \cdot S_{in} \quad (5)$$

where ξ_1 , ξ_2 represent the biomass and the limiting substrate concentrations (g/l). S_{in} is the influent substrate concentration, and D is the dilution rate (h^{-1}). In (4), (5) μ is the specific growth rate and $k_1 > 0$ the yield coefficient.

The bioprocess (4), (5) is in fact a fermentation process, which usually occurs in a bioreactor. A compact representation of (4), (5) is:

$$\dot{\xi} = f(\xi) \quad (6)$$

with $f(\xi) = [f_1(\xi_1, \xi_2), f_2(\xi_1, \xi_2)]^T$ and $\xi = [\xi_1 \ \xi_2]^T$ the state vector.

The equilibrium states of (4), (5) are of two types:

E1. Wash-out state, defined by:

$$\xi_s = [\xi_{s1} \ \xi_{s2}]^T = [0 \ S_{in}]^T \quad (7)$$

This equilibrium is a state when the bacterial life has disappeared; therefore, the wash-out state has not practical interest.

E2. Operational equilibrium states, implicitly defined by:

$$\begin{cases} \mu(\xi_{s1}, \xi_{s2}) = D \\ k_1 \mu(\xi_{s1}, \xi_{s2}) \xi_{s1} + D \xi_{s2} = D S_{in} \end{cases} \quad (8)$$

These equilibria can be attractive or repulsive depending on the particular form of $\mu(\xi_1, \xi_2)$. Only these equilibria have a practical interest. Let's assume that the specific growth rate is of the form:

$$\mu(\xi_1, \xi_2) = \mu(\xi_2) = \mu_0 \frac{\xi_2}{K_M + \xi_2 + \xi_2^2 / K_i} \quad (9)$$

This is the Haldane kinetic model of the specific growth rate (Bastin & Dochain, 1990), where K_M is the Michaelis-Menten constant, K_i the inhibition constant and μ_0 the maximum specific growth rate.

Let's analyse the stability of the equilibria (E2) for given constant inputs D and S_{in} . The linear approximation of the system (4), (5) around the equilibrium point (E2) is:

$$\frac{d}{dt}(\xi - \xi_s) = A(\xi_s)(\xi - \xi_s) \tag{10}$$

where $A(\xi_s)$ is the matrix of the linearized system, which takes for the specific rate (6) the form:

$$A(\xi_s) = A(\xi_{s1}, \xi_{s2}) \overset{\Delta}{=} J(\xi_{s1}, \xi_{s2}) = \begin{bmatrix} \frac{\partial f_1}{\partial \xi_1} & \frac{\partial f_1}{\partial \xi_2} \\ \frac{\partial f_2}{\partial \xi_1} & \frac{\partial f_2}{\partial \xi_2} \end{bmatrix}_{\xi=\xi_s} = \begin{bmatrix} 0 & \rho \\ -k_1\mu(\xi_{s2}) & -k_1\rho - D \end{bmatrix} \tag{11}$$

where $\rho = \xi_{s1}^N \left[\frac{d\mu(\xi_2)}{d\xi_2} \right]_{\xi_2=\xi_{s2}} = \xi_{s1}\mu_0 \frac{K_M - \xi_{s2}^2 / K_i}{(K_M + \xi_{s2} + \xi_{s2}^2 / K_i)^2}$.

The eigenvalues of the matrix (11) are $\lambda_1 = -D < 0$ (D is positive) and $\lambda_2 = -k_1\rho$. The equilibrium state is stable only if $\rho > 0$, i.e.:

$$0 \leq \xi_{s2} < \sqrt{K_M K_i} = \max_{\xi_2} \{ \mu(\xi_2) \} \tag{12}$$

Two possibilities appear for the equilibria (E2):

a) - if the condition (12) is achieved:

$$\xi_{s1} = \frac{S_{in} - \xi_{s2}^N}{k_1} = \xi_{s1,1} = \frac{S_{in} - \xi_{s2,1}^N}{k_1}; \tag{13}$$

$$\xi_{s2} = \xi_{s2,1}$$

b) - or contrarily:

$$\xi_{s1} = \frac{S_{in} - \xi_{s2}^N}{k_1} = \xi_{s1,2} = \frac{S_{in} - \xi_{s2,2}^N}{k_1}; \tag{14}$$

$$\xi_{s2} = \xi_{s2,2}$$

The case a) corresponds to a stable equilibrium point (stable node) with $\lambda_1 < 0, \lambda_2 < 0$. The case b) leads to a saddle type for the equilibria (E2): $\lambda_1 < 0, \lambda_2 > 0$. The phase plane of the system (4), (5) for the values of the parameters: $\mu_0 = 6h^{-1}$, $K_M = 10g/l$, $K_i = 100g/l$, $D = 3.6h^{-1}$, $k_1 = 1$, $S_{in} = 100g/l$ and for different initial conditions is represented in Fig. 1. From this picture it can be seen that when the substrate inhibition appears, the process can exhibit unstable or, maybe worse, the evolution leads to wash-out steady-state, for which the microbial life has disappeared and the reactor is stopped. In these situations, the

bioprocess requires control to stabilize the CSTB. Moreover, in many cases, the stable equilibrium point corresponding to a) is not technological operable (requires a big initial amount of biomass).

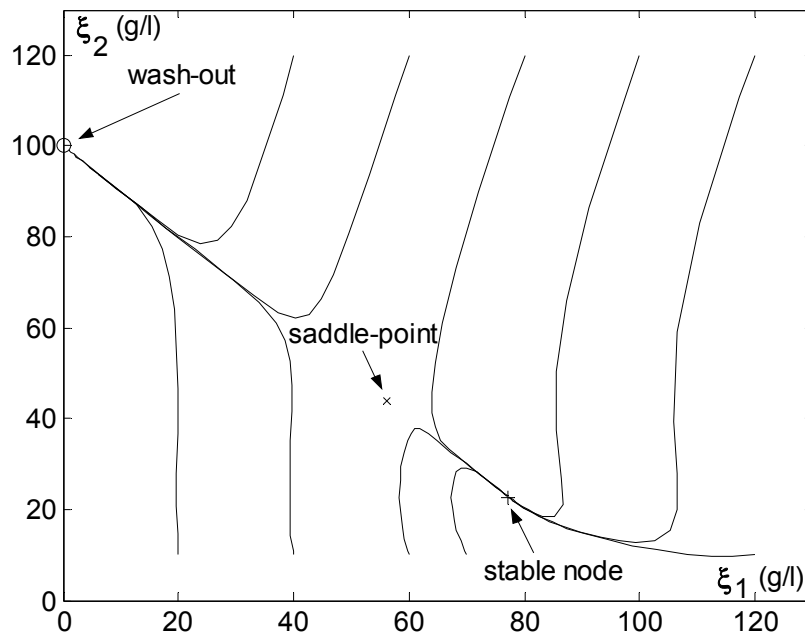


Fig. 1. Phase portrait of the continuous bioprocess – state trajectories and equilibrium points

The model (4), (5) is a prototype model for some bioprocesses, as the activated sludge bioprocess, anaerobic digestion process for wastewater treatment etc. (Dochain & Vanrolleghem, 2001) and for other biotechnological applications. For instance, the control objective for the waste treatment processes is to control the concentration of some pollutants at a constant (low) level. Various control strategies were developed for this prototype bioprocess: exact linearizing strategy (Bastin & Dochain, 1990), adaptive control (Bastin & Dochain, 1990; Bastin, 1991; Dochain & Vanrolleghem, 2001) and so on. The exact linearizing control does not work when the kinetics are imprecisely known because the exact cancellation of the nonlinearities would not be possible. The performance of adaptive control decreases when large and abrupt changes occur in bioprocess parameters.

Viable alternatives are the sliding mode control (Fossas et al., 2001; Stanchev, 2003; Tham et al., 2003) and adaptive sliding mode control strategies (Selișteanu & Petre, 2005; Selișteanu et al., 2007b) with good performance in the presence of parameter uncertainties and external disturbances. Another possible strategy is the open-loop vibrational control (Selișteanu et al., 2007a); in this situation, on-line measurements of the state variables are no more needed.

3. Sliding mode control design

3.1 Linearizing sliding mode control law design

In order to implement a viable SMC strategy for the continuous bioprocess, the control goal is to design a discontinuous feedback law by using the exactly linearization of the system (Isidori, 1995) and by imposing a SMC action that stabilize the output. The control strategy is obtained by repeated output differentiation and by imposing a discontinuous feedback controller, which drives the output of the system to satisfy a stable linearized dynamics; for

details see (Sira-Ramirez, 1992; Sira-Ramirez & Llanes-Santiago, 1994; Selişteanu et al., 2007b). Let's define the output of the system (4), (5) as

$$y = h(\xi) = \xi_1 - C \tag{15}$$

The control variable is the rate of supply of substrate to the reactor per unit of volume, i.e. $u = D \cdot S_{in}$ (g/lh). The control goal for the biological process (4), (5), (15) is to regulate the concentration error y towards zero so that the biomass concentration value ξ_1 converges to a prescribed setpoint value specified by the constant C . It is assumed that the control variable u is naturally bounded in the interval $[0, U_{max}]$. This SMC strategy can be applied for the nonlinear bioprocess (4), (5), (15) if the so-called observability matrix

$$O = \begin{bmatrix} \frac{\partial h(\xi)}{\partial \xi} & \frac{\partial h^{(1)}(\xi)}{\partial \xi} \end{bmatrix}^T \tag{16}$$

is full rank (Fliess, 1990; Sira-Ramirez, 1992; Sira-Ramirez & Llanes-Santiago, 1994). It is easy to verify, after some straightforward calculations, that the rank of the observability matrix is equal to 2 (full rank), except on line $\xi_1 = 0$, which is devoid of practical significance (ξ_1 represents the biomass concentration; so $\xi_1 = 0$ means no micro-organisms and the life in the bioreactor is stopped).

Assume that $u = u_s$, $\xi = \xi_s(u_s)$ expresses a constant equilibrium point for the system (4), (5), (15) such that $h(\xi_s(u_s))$ is zero. The stability nature of an equilibrium point $u = u_s$ of the zero dynamics (Sira-Ramirez, 1992; Sira-Ramirez & Llanes-Santiago, 1994) determines the minimum or non-minimum phase character of the system (4), (5), (15). Next, the constant equilibrium point of this system is represented as $(\xi_s(u_s), u_s, y_s = 0) = (\xi_s(u_s), u_s, 0)$. A stable constant equilibrium point for (4), (5), (15) is given by (13), if the condition (12) is achieved. In this case, the system is locally minimum phase around this equilibrium point (i.e. the zero dynamics is locally asymptotically stable to the equilibrium point).

The following input-dependent state coordinate transformation:

$$\begin{aligned} z_1 &= y = \xi_1 - C \\ z_2 &= \dot{y} = \dot{\xi}_1 = \mu(\xi_2)\xi_1 - D\xi_1 \end{aligned} \tag{17}$$

allows one to obtain an observability canonical form for the system (4), (5), (15) (for details about the generalized observability canonical forms see (Fliess, 1990)). The inverse of this transformation is obtained by solving (17) with respect to ξ_1 and ξ_2 . One can obtain also the transformed system equations, which are of the form:

$$\begin{aligned} \dot{z}_1 &= z_2 \\ \dot{z}_2 &= \psi(z_1, z_2, u) \\ y &= z_1 \end{aligned} \tag{18}$$

where ψ is a nonlinear function of state variables and of the input.

For the design of SMC, consider now the auxiliary output function (the sliding surface):

$$\sigma = z_2 + \gamma_1 z_1 = \dot{y} + \gamma_1 y = \mu(\xi_2)\xi_1 - D\xi_1 + \gamma_1(\xi_1 - C) \quad (19)$$

If (19) is zeroed by means of a discontinuous control strategy, then it follows that the time response of the controlled output y is ideally governed by an asymptotically stable linear time-invariant dynamics $\dot{z}_1 = -\gamma_1 z_1$ (for the design parameter $\gamma_1 > 0$).

Proposition 1. The following discontinuous feedback control law (sliding mode control law):

$$u(t) = k_1 \mu(\xi_2)\xi_1 + D\xi_2 - \frac{(\mu(\xi_2) - D)^2}{\mu'(\xi_2)} - \frac{1}{\mu'(\xi_2)\xi_1} \cdot [\gamma_1(\mu(\xi_2) - D)\xi_1 + k \cdot \text{sgn}(\sigma)] \quad (20)$$

imposes to the output of the system (18), in finite time, a linearized dynamics of the form $\dot{y} + \gamma_1 y = 0$. In (20), k is a strictly positive scalar, “sgn” stand for the signum function,

$$\gamma_1 > 0, \text{ and } \mu'(\xi_2) \triangleq \frac{d\mu(\xi_2)}{d\xi_2}.$$

Proof. The proof is immediate considering the auxiliary output function (19) and imposing on this auxiliary output the discontinuous dynamics $\dot{\sigma} = -k \cdot \text{sgn}(\sigma)$, which leads to the implicit discontinuous equation $\psi(z_1, z_2, u) = -\gamma_1 z_2 - k \text{sgn}(\sigma)$. Then the control law (20) is easily obtained using the original state coordinates. This discontinuous system globally exhibits a sliding regime on $\sigma = 0$. Any trajectory starting on the value $\sigma = \sigma(0)$ at time 0 reaches the condition in finite time T given by $T = k^{-1}|\sigma(0)|$ (see (Utkin, 1978; Sira-Ramirez & Llanes-Santiago, 1994)).

The basic idea for the design of the SMC law (20) is to use the auxiliary output $\sigma = 0$ as a sliding surface, and so to force the system trajectories to remain on this surface.

Remark 2. In the case of a static SMC law, the inherent chattering can be reduced using various continuous approximations of the SMC (Slotine & Li, 1991; Edwards & Spurgeon, 1998; Bartoszewicz, 2000), which are designed to make a boundary layer attractive such that the trajectories started off the boundary layer will be attracted to this region in a finite time. A possibility is to use the so-called sampled SMC (Sira-Ramirez & Llanes-Santiago, 1994). To reach a good compromise between small chattering and tracking precision a range of other compensation strategies have been proposed, such as integral sliding mode control, sliding mode control with time-varying boundary layers (Slotine & Li, 1991), fuzzy sliding mode control (Palm et al., 1997) and complementary SMC (Su & Wang, 2002).

3.2 Design of state observers for bioprocesses

The SMC law presented in the previous paragraph can be implemented only if the measurements of state variables are available on-line. However, in many practical applications, only a part of the concentrations of the components involved are measurable on-line. In such cases, an alternative is the use of state observers. An important difficulty when applying state observers to bioprocesses is related to the uncertainty of models describing their dynamics. Presently two classes of state observers for bioprocesses can be found in the literature (Bastin & Dochain, 1990; Bastin, 1991; Dochain & Vanrolleghem, 2001).

The first class of observers (including classical observers like Luenberger and Kalman observers, nonlinear observers) are based on a perfect knowledge of the model structure. A

disadvantage of this class is that the uncertainty in the model parameters can generate possibly large bias in the estimation of the unmeasured states. A second class of observers, called asymptotic observers, is based on the idea that the uncertainty in process models lies in the process kinetics models. The design of these observers is based on the mass and energy balances without the knowledge of the process kinetics being necessary. The potential drawback of the asymptotic observers is that the rate of estimation convergence depends on the operating conditions (Selişteanu et al., 2007b).

A general class of observers for bioprocesses of the form (2) is (Bastin & Dochain, 1990):

$$\dot{\hat{\xi}} = K\varphi(\hat{\xi}) - D \cdot \hat{\xi} + F - Q + \Omega(\hat{\xi}) \cdot (\zeta_1 - \hat{\zeta}_1) \tag{21}$$

where $\hat{\xi}$ is the estimated state vector, $\Omega(\hat{\xi})$ is a gain matrix, and ζ_1 is the vector of measurable state variables: $\zeta_1 = L \cdot \xi$, L being a selection matrix. The design of observer lies in the choice of the gain matrix.

If in the model (2) the reaction rate $\varphi(\xi)$ is completely known, it is possible to design the so-called exponential observers, such as extended Luenberger or Kalman observers based on the general form (21). But the reaction rates are usually incompletely known (uncertainties of parametric or structural nature); therefore it is not possible to design and to use such observers. A possibility is to use an asymptotic observer (Bastin & Dochain, 1990; Bastin, 1991; Dochain & Vanrolleghem, 2001), which can be designed even without knowledge of kinetic reaction. The design of an asymptotic observer is based on some useful changes of coordinates, which lead to a submodel of (2) which is independent of the kinetics. In order to achieve the change of coordinates, a partition of the state vector ξ in two parts is considered. This partition denoted (ξ_a, ξ_b) induces partitions of the yield matrix K : (K_a, K_b) , also of the rate vectors F and Q : (F_a, F_b) , (Q_a, Q_b) accordingly. We suppose that a state partition is chosen such that the submatrix K_a is full rank and $\dim(\xi_a) = \text{rank}(K_a) = \text{rank}(K)$. Then a linear change of coordinates can be defined as follows: $z = G \cdot \xi_a + \xi_b$, with z an auxiliary state vector and G the solution of the matrix equation $G \cdot K_a + K_b = 0$. In the new coordinates, model (2) can be rewritten as

$$\begin{aligned} \dot{\xi}_a &= K_a \varphi(\xi_a, z - G\xi_a) - D \cdot \xi_a + F_a - Q_a \\ \dot{z} &= -D \cdot z + G \cdot (F_a - Q_a) + F_b - Q_b \end{aligned} \tag{22}$$

The main achievement of the change of coordinates is that the dynamics of the auxiliary state variables z is independent of the reaction kinetics. Now z can be rewritten as a linear combination of the vectors of measured states ζ_1 and unmeasured states ζ_2 :

$$z = G_1 \cdot \zeta_1 + G_2 \cdot \zeta_2 \tag{23}$$

with G_1 and G_2 well defined matrices. If the matrix G_2 is left invertible, the asymptotic observer equations for (2) derive from the structure of equations (22) and (23):

$$\begin{aligned} \dot{\hat{z}} &= -D \cdot \hat{z} + G \cdot (F_a - Q_a) + F_b - Q_b \\ \hat{\zeta}_2 &= G_2^+ \cdot (\hat{z} - G_1 \zeta_1) \end{aligned} \tag{24}$$

where $G_2^+ = (G_2^T G_2)^{-1} G_2^T$. The asymptotic observer is indeed independent of the kinetics. The asymptotic observer (24) has good convergence and stability performance (Bastin & Dochain, 1990; Bastin, 1991; Dochain & Vanrolleghem, 2001).

Concerning the continuous bioprocess (4), (5), (15), a possible practical situation, which can appear when the sliding mode control law (20) is implemented, is that the only measurement on-line available is the biomass concentration inside of CSTB. In this case, the unmeasured variable ξ_2 (the substrate concentration) can be estimated by using an asymptotic state observer. For that, let us define the auxiliary variable ζ as follows:

$$\zeta = k_1 \xi_1 + \xi_2$$

In the new coordinates, the model (4), (5), (15) can be rewritten

$$\begin{aligned}\dot{\xi}_1 &= \mu(\zeta - k_1 \xi_1) \xi_1 - D \xi_1 \\ \dot{\zeta} &= -D \zeta + u \\ y &= \xi_1 - C\end{aligned}$$

The asymptotic observer equations derive from the above model:

$$\begin{aligned}\frac{d\hat{\zeta}}{dt} &= -D \cdot \hat{\zeta} + u \\ \hat{\xi}_2 &= \hat{\zeta} - k_1 \xi_1\end{aligned}\quad (25)$$

The dynamics of the auxiliary variable ζ is independent of the reaction kinetics. The estimations of ξ_2 obtained using this asymptotic observer can be used in the sliding mode control law (20), which takes the form:

$$u(t) = k_1 \mu(\hat{\xi}_2) \xi_1 + D \hat{\xi}_2 - \frac{(\mu(\hat{\xi}_2) - D)^2}{\mu'(\hat{\xi}_2)} - \frac{1}{\mu'(\hat{\xi}_2) \xi_1} \cdot [\gamma_1 (\mu(\hat{\xi}_2) - D) \xi_1 + k \cdot \text{sgn}(\sigma)] \quad (26)$$

4. Vibrational control design

4.1 Vibrational control theory fundamentals

The general theory of vibrational control was developed by Bellman, Bentsman and Meerkov (Meerkov, 1980; Bellman et al., 1986a; Bellman et al., 1986b), who presented the criteria for vibrational stabilizability and vibrational controllability of linear and nonlinear systems. Consider a nonlinear system given by the equation:

$$\dot{x} = f(x, \alpha) \quad (27)$$

with $f: \mathcal{R}^n \times \mathcal{R}^m \rightarrow \mathcal{R}^n$, $x \in \mathcal{R}^n$ is a state and $\alpha \in \mathcal{R}^m$ is a parameter, in fact a vector that contains the system parameters. Suppose that for a fixed $\alpha = \alpha_0$ the system (27) has the equilibrium $x_s = x_s(\alpha)$. Let introduce now in (27) parametric vibrations according to the law:

$$\alpha(t) = \alpha_0 + g(t) \quad (28)$$

where α_0 is a constant vector and $g(t)$ is an almost periodic vector function with average equal to zero (APAZ vector). Then (27) becomes:

$$\dot{x} = f(x, \alpha_0 + g(t)) \tag{29}$$

Definition 1 (Bellman et al., 1986a). An equilibrium point $x_s(\alpha_0)$ of (27) is vibrationally stabilizable if for any $\delta > 0$ there exists an APAZ vector $g(t)$ such that (29) has an asymptotically stable almost periodic solution $x^s(t)$ characterized by $\|\bar{x}^s - x_s(\alpha_0)\| < \delta$, $\bar{x}^s = \overline{x^s(t)} \stackrel{\Delta}{=} \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T x^s(\tau) d\tau$.

Definition 2 (Bellman et al., 1986a). An equilibrium point $x_s(\alpha_0)$ of (27) is totally vibrationally stabilizable if it is vibrationally stabilizable and in addition we have $x^s(t) = \text{const} = x_s(\alpha_0), \forall t \in \mathfrak{R}$.

The vibrational stabilizability problem consists of finding conditions for existence of stabilizable vibrations. Meerkov has demonstrated since 1980 (Meerkov, 1980) that for linear systems, vibrational stabilizability implies total stabilizability. If the matrix A of the linear system $\dot{x} = Ax$ is a nonderogatory matrix, i.e. the minimal and characteristic polynomials coincide, a sufficient condition of v -stabilizability is $\text{tr}(A) < 0$.

Considered now a class of nonlinear systems such that (29) is represented as:

$$\dot{x}(t) = f(x, \alpha_0) + f_v(g(t), x) \tag{30}$$

with $f_v(\cdot, \cdot)$ a vector function linear with respect to its first argument and $f(x) \stackrel{N}{=} f(x, \alpha_0)$ (α_0 fixed).

For this large class of nonlinear systems with parametric oscillations, a classification can be done with respect to the form of $f_v(\cdot, \cdot)$:

- i) $f_v(g(t), x) = L(t)$, where $L(t)$ is an APAZ vector and the vibrations are called *vector additive*. If $L(t) = [0 \ 0 \ \dots \ 1(t)]^T$, i.e. all but the last components of $L(t)$ are zero, the vibrations are *AP - forcing*;
- ii) $f_v(g(t), x) = B(t)x$, with $B(t)$ an APAZ matrix. These vibrations are *linear multiplicative*;
- iii) $f_v(g(t), x) = B(t)\Gamma(x)$ - vibrations are *nonlinear multiplicative*. $B(t)$ is an APAZ matrix.

In (Bellman et al., 1986a; Bellman et al., 1986b) the existence of stabilizing vibrations for the class of the nonlinear system (30) is analyzed and it is shown in what sense and under which conditions an equilibrium of (30) can be stabilized. The general conclusion of (Bellman et al., 1986a; Bellman et al., 1986b) is that the VC with vibrations of the form i) and ii) is not feasible if the Jacobian matrix has a positive trace. The case of nonlinear multiplicative vibrations iii) was studied for a subclass of nonlinear systems in (Bentsman, 1987). Once the conditions for existence of vibrational stabilizability are settled for a system, it is necessary to solve another important problem: finding the specific form of stabilizing vibrations. This problem is referred as vibrational controllability (Bellman et al., 1986b).

Consider the general solution of

$$\dot{x}(t) = f_v(g(t), x) \tag{31}$$

denoted as $x(t) = \vartheta(t, c)$, where $c \in \mathfrak{R}^n$ is a constant uniquely defined for every initial condition (x_0, t_0) and assume that this general solution is almost periodic. The substitution

$x(t) = \vartheta(t, \tilde{x}(t))$ transforms the nonlinear system (30) into $\dot{\tilde{x}} = \left[\frac{\partial \vartheta}{\partial \tilde{x}} \right]^{-1} \cdot f(\vartheta(t, \tilde{x})) = X(t, \tilde{x})$. Then, the averaging of this system is:

$$\dot{x}_a = \bar{X}(x_a) = \overline{X(t, \tilde{x})} = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T X(t, \tilde{x}) dt \quad (32)$$

Consider $x_{a,s}$ an equilibrium of (32), and the linearization of (32) around $x_{a,s}$:

$$\dot{x}_a = \left[\frac{\partial \bar{X}(x_a)}{\partial x_a} \right]_{x_a = x_{a,s}} \cdot x_a \quad (33)$$

The goal is to find an APAZ vector $g(t)$ that induces a dynamic equivalence between systems (30) and (32). Assume that the equilibrium x_s of (30) satisfies the equality $x_s = \overline{\vartheta(t, x_{a,s})}$. Then, for the equilibrium $x_{a,s}$ corresponding to x_s , the linearization (33) can be represented as:

$$\dot{x}_a = (J + H) \cdot x_a \quad (34)$$

where J is the Jacobian matrix of (30) for the equilibrium x_s and H is a constant $n \times n$ matrix.

Definition 3 (Bellman et al., 1986b). An element j_{ij} of matrix J is vibrationally controllable if there exists an APAZ vector $g(t)$ such the corresponding element h_{ij} of H is nonzero.

The type of vibrations and their parameters depend of the particular nonlinear system that is analysed. Calculation formulas have been obtained in (Bellman et al., 1986b). Assume that the Jacobian matrix J of the nonlinear system (30) has negative trace. Then the calculation formula for *linear multiplicative vibrations* applied to the nonlinear system is:

$$H = R - J, \quad R = \overline{\Phi^{-1}(t, 0) \cdot J \cdot \Phi(t, 0)} \quad (35)$$

where $\Phi(t, 0)$ is the state transition matrix of the system (30), in the particular case of the linear multiplicative vibrations ii): $f_v(g(t), x) = B(t)x$.

4.2 The vibrational control strategy for the continuous bioprocess

The basic idea of vibrational controlled CSTB is to vibrate the flow rates and in this way to operate the bioreactor at *average conversion rates* which were previously unstable. By using this technique is possible to eliminate significant expenses associated with feedback. Since the vibrations depend only on time and not on the value of states, there no longer was a need to take measurements of concentrations.

In order to apply the vibrational control we have three possibilities: additive vibrations, linear multiplicative vibrations or nonlinear multiplicative vibrations. The general

conclusion of (Selişteanu & Petre, 2001) is that the additive vibrations and AP-forcing VC are not applicable to the bioprocess described in Section 2. A study about the linear multiplicative VC of the CSTB is achieved next.

Consider the bioprocess (4), (5) with the equilibria (E1) or (E2). From operational point of view, only the equilibrium (E2) is interesting. With the Haldane kinetic model of the specific rate (9), we have two possibilities for the equilibrium (E2): stable equilibrium point (13) - a stable nod - if $\rho > 0$ and saddle type of equilibrium point (14), i.e. instability, if $\rho < 0$ (see also Fig. 1). In those situations when the substrate inhibition appears, the bioprocess can exhibit unstable or can go to the wash-out; in these cases the system requires control in order to stabilize the CSTB.

The trace condition for the Jacobian matrix (11) of the bioprocess (4), (5) is achieved if:

$$\text{tr}(J) = -k_1\rho - D < 0 \tag{36}$$

Assume that (36) is respected. The vibrational controlled bioprocess is of the form:

$$\dot{\xi} = f(\xi) + B(t) \cdot \xi \tag{37}$$

where $B(t)$ is an APAZ matrix.

There exists positive $\varepsilon_0 = \text{const.}$ such that vibrations $(1/\varepsilon) \cdot B(t/\varepsilon)$, $0 < \varepsilon \leq \varepsilon_0$, induce a dynamic equivalence between the linearized averaged system of the form (32), denoted here $\dot{\bar{\xi}} = \Xi(\bar{\xi})$, and the vibrationally controlled process $\dot{\xi} = f(\xi) + (1/\varepsilon) \cdot B(t/\varepsilon) \cdot \xi$. In order to apply the VC, it is important to find the particular form of $B(t)$ such that this dynamical equivalence is achieved. Consider $B(t)$ of the form:

$$B(t) = \begin{bmatrix} 0 & 0 \\ b(t) & 0 \end{bmatrix} \tag{38}$$

Then the state transition matrix of $\dot{\xi} = B(t)\xi$ is: $\Phi(t) = \begin{bmatrix} 1 & 0 \\ \varphi(t) & 1 \end{bmatrix}$, with $\varphi(t) = \int_0^t b(\tau) d\tau$.

Assuming that $\overline{\varphi(t)} = 0$ we obtain from (35):

$$R = \begin{bmatrix} 0 & \rho \\ -k_1\mu(\xi_{s2}) - \rho\overline{\varphi^2(t)} & -k_1\rho - D \end{bmatrix} \tag{39}$$

For $b(t)$ - an APAZ function - we consider the cosinusoidal form: $b(t) = \beta \cos(t)$.

Consequently we have $\overline{\varphi^2(t)} = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T \varphi^2(\tau) d\tau = \beta^2 / 2$, and finally R and then H using the calculation formula (35) are obtained:

$$R = \begin{bmatrix} 0 & \rho \\ -k_1\mu(\xi_{s2}) - \rho \cdot \beta^2 / 2 & -k_1\rho - D \end{bmatrix} \tag{40}$$

$$H = R - J = \begin{bmatrix} 0 & 0 \\ -\rho \cdot \beta^2 / 2 & 0 \end{bmatrix} \quad (41)$$

For β chosen such that R is Hurwitz, and for ε sufficiently small, the vibrations (38) stabilize the equilibrium (14) of (4), (5). A theoretical value for ε_0 is complicated to obtain, but a practical value can be obtained via simulation.

Remark 3. Because the equilibrium (14) is nonzero (nontrivial), in fact it is stabilizable by a combination of linear multiplicative and vector additive vibrations $B(t) \cdot (\xi - \xi_s)$.

5. Simulation results

Sliding mode control. Simulation were performed for a continuous stirred tank bioreactor (CSTB) described by the model (4), (5), (15) with the parameters from paragraph 2. Two simulation cases are considered:

i) The simulated control task considered the problem of stabilizing the output y to $y^* = 0$, using the SMC law (20). In fact, the closed loop system was tested for a step profile of the external substrate reference C . The final reference value is achieved in two steps: first the reference is set to 70 g/l; the next reference is set to the value $\xi_1^* = C = 80$ g/l. The SMC law parameters are $\gamma_1 = 1$ and $k = 3$.

Figure 2 presents the time evolution of the concentrations, and Fig. 3 depicts the output and the control input.

The behaviour of the concentrations is good, but it can be seen that the control action exhibits a chattering, which can be unacceptable in practice. The profile of the auxiliary output function (the "sliding surface") and a magnification of this auxiliary output are depicted in Fig. 4. In order to obtain a smoothed control input, a saturation function is used and the results are presented in Fig. 5.

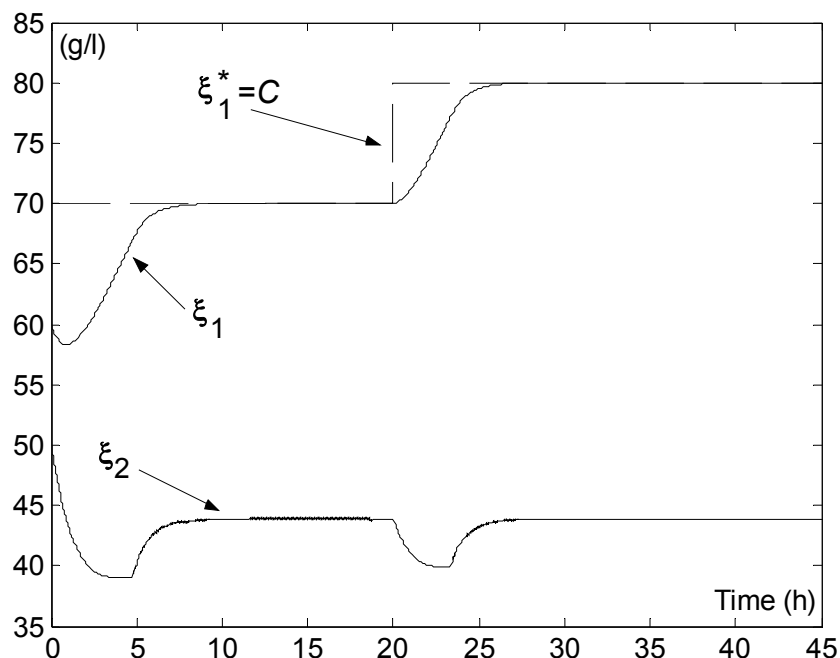


Fig. 2. Time evolution of the substrate and biomass concentrations – SMC case

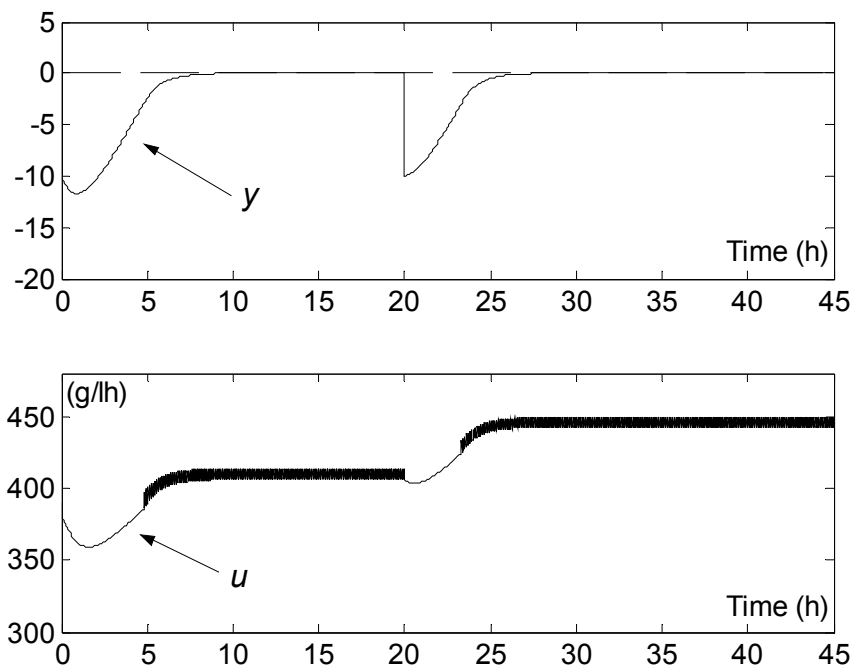


Fig. 3. Profiles of output and control input (rate of supply of substrate per unit of volume)

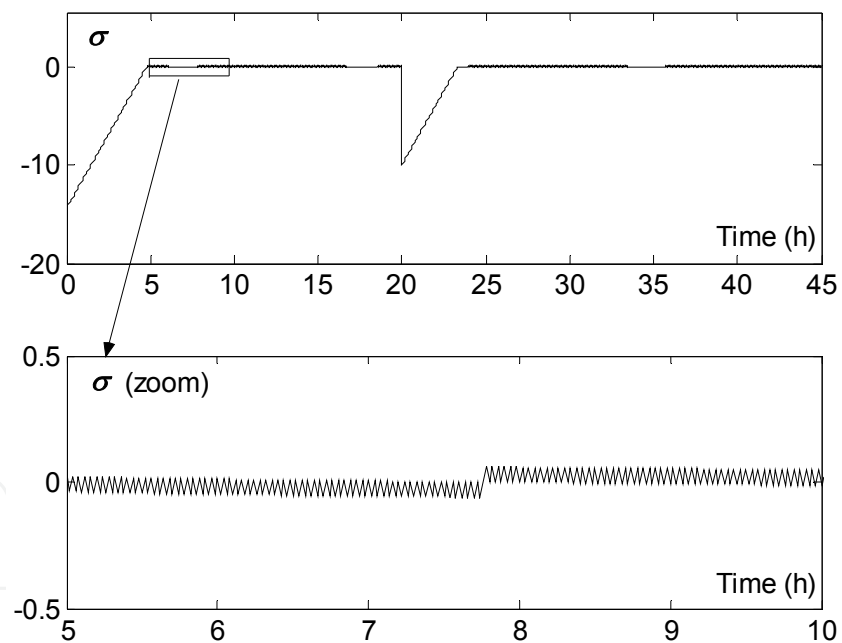


Fig. 4. The evolution of the auxiliary output (the sliding surface), including a zoom area

ii) In order to test the robustness properties of the controlled bioprocess and to add realism to the simulation, a parametric disturbance in the yield coefficient k_1 was considered (a 50% variation from the nominal value); this coefficient is uncertain in practice. The disturbance occurs once in the simulation time interval, about 1 h in duration (time interval 30h - 31h). Also, in this simulation case, only the biomass concentration is considered on-line measurable.

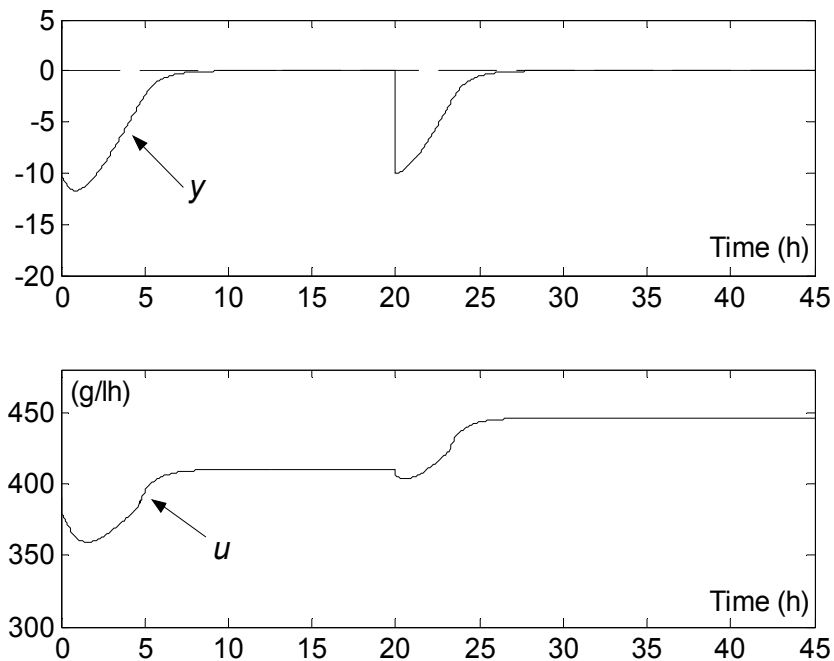


Fig. 5. Time evolution of the output and the control input – the chattering reduction case

Therefore, the SMC law (26) was implemented, using the estimations $\hat{\xi}_2$ provided by the asymptotic observer (25). The profile of the reference is the same as in the first simulation case. The performance of the asymptotic observer can be noticed in Fig. 6, where the substrate concentration and its estimate are depicted. Fig. 7 shows that in this simulation case, the controlled process exhibits a good behaviour and the SMC law can cope with the parametric disturbance.

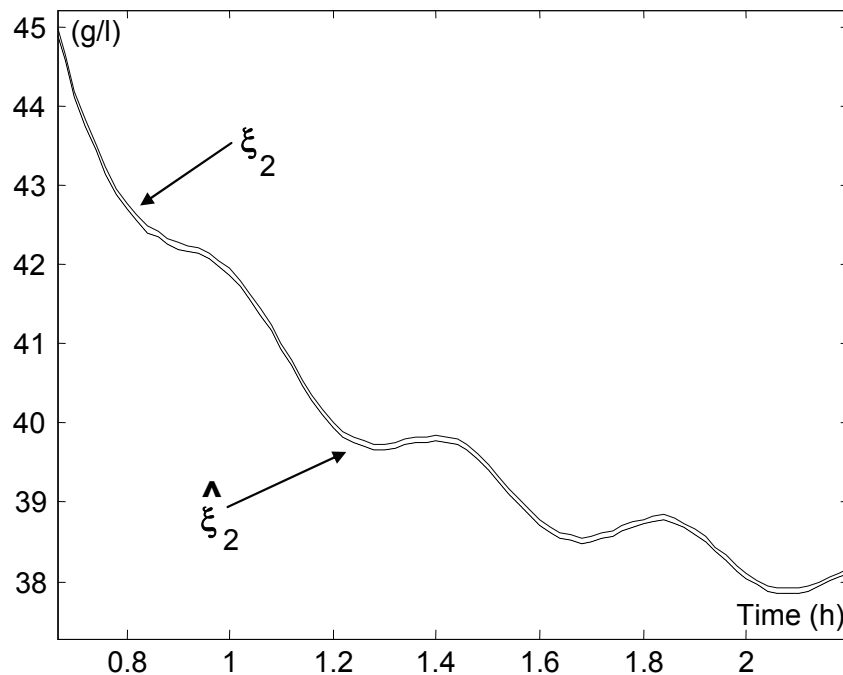


Fig. 6. Profiles of the substrate concentration and its estimate (magnification of a small area)

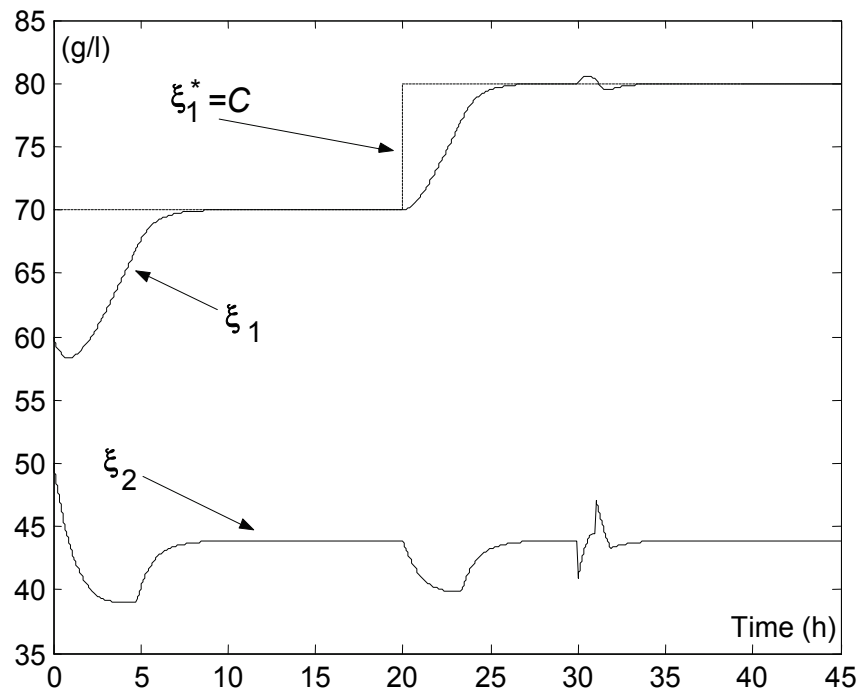


Fig. 7. Time evolution of the concentrations – the SMC parametric disturbance case

Remark 4. In practice, there exist the so-called parasitic or unmodelled dynamics, along with the principal dynamics of the plant (Boiko, 2005; Boiko & Fridman, 2006). The principal dynamics are used for the SMC design. On the other hand, to implement the designed algorithms, some equipment such as actuators, sensors etc. are needed. Hence it is required to take into consideration the parasitic dynamics, introduced mainly by the actuators. Often, a first-order (plus time lag) model of the actuator is used, with the transfer function $H_a(s) = K_a e^{-\tau s} / (T_a s + 1)$, where K_a, T_a are the parameters of the actuator, and τ is the time lag. However, for our CSTB, the dynamics of the actuator are faster than the principal dynamics and the time lag is negligible, hence their contribution to the overall system dynamics is small. Nevertheless, some supplementary simulation results show that the performance of the sliding mode controlled process is deteriorated in this case (in comparison with the ideal sliding mode controlled bioprocess) – for example the chattering of the control input is increasing and the setpoint regulation performance is deteriorated.

Remark 5. A problem in the case of SMC is that the robustness of the sliding surface (used in the SMC design procedure) with respect to the parametric uncertainties is valid only for small variations of the parameters. If the parameters are imprecisely known, then the switchings cannot take place with precision on the switching manifold and furthermore the stability of the closed loop system can be affected. In that case, an adaptive dynamical SMC law can be used in order to improve the performance of the controlled bioprocess (Selișteanu et al., 2007b).

Vibrational control. The simulation is given for the same bioprocess parameters. The value of the control parameter $\beta = 5$ is chosen such that the matrix R is Hurwitz. In Figure 8, the averaged phase portrait of the vibrationally controlled bioprocess (the averaged state trajectories) is presented. It can be seen that the previously unstable equilibrium (see Fig. 1) is stabilized into a stable node.

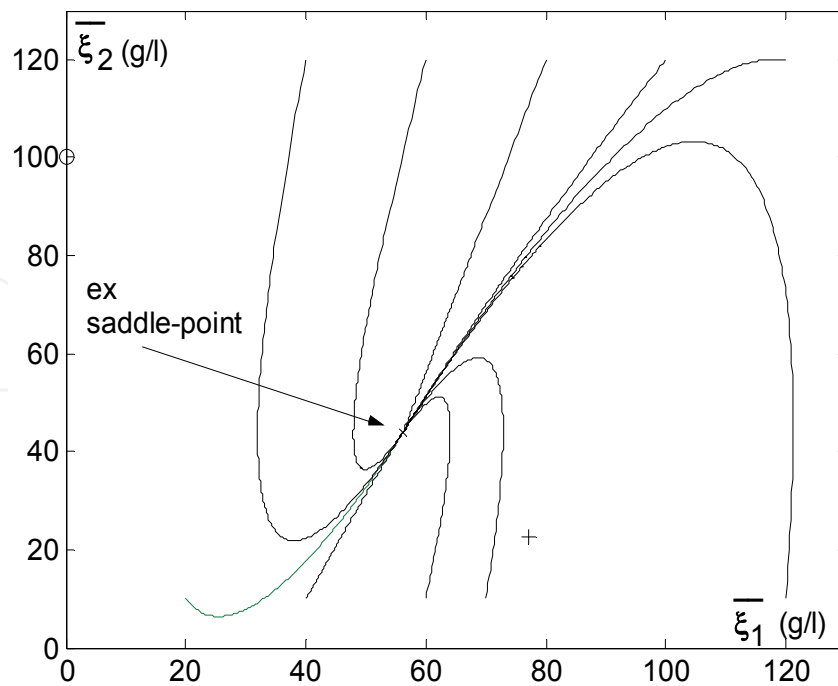


Fig. 8. The averaged phase portrait of the vibrationally controlled continuous bioprocess

The time evolution of concentrations and the averaged time trajectories are provided in Fig. 9. This picture gives a comparison of $\xi(t)$ (solid curves) and the averaged state variables $\bar{\xi}(t)$ (dashed curves) for $\varepsilon = 0.066$. To test the robustness of the vibrationally controlled bioprocess, the same parametric disturbance in the yield coefficient like in the SMC case was considered (in the time interval 10h - 11h). The simulation results are presented in Fig. 10.

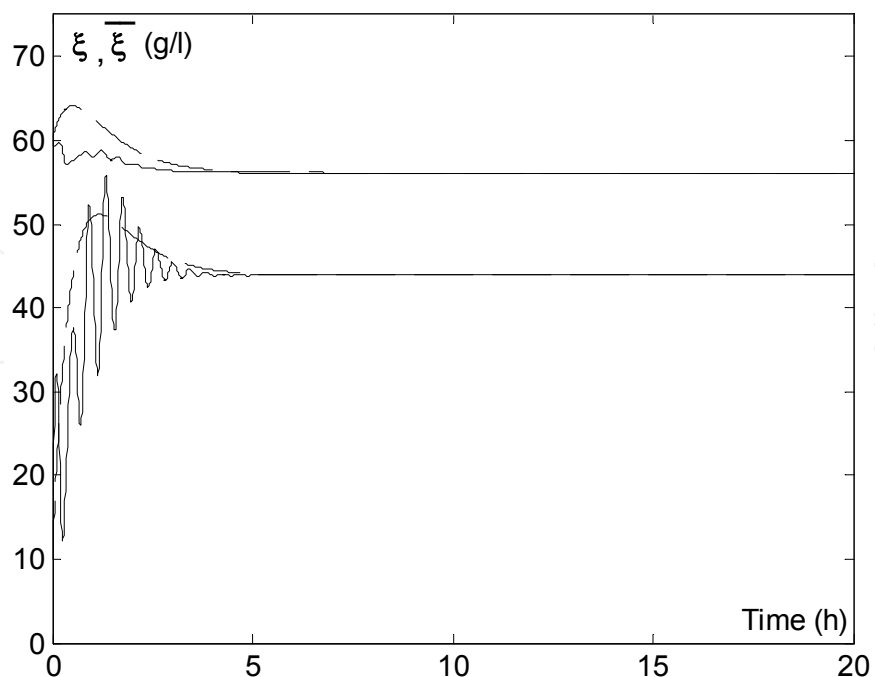


Fig. 9. Time evolution of the biomass and substrate concentrations - VC strategy

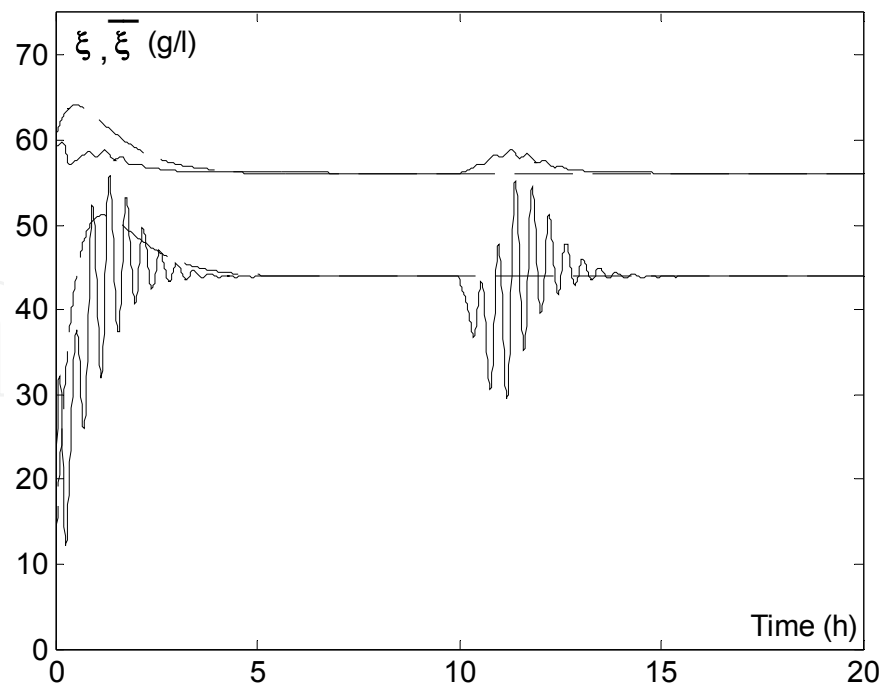


Fig. 10. Time profiles of the concentrations – VC parametric disturbance case

6. Conclusion

In this work, two nonlinear high-frequency control strategies for bioprocesses are proposed: a feedback sliding mode control law and a vibrational control strategy. In order to implement these strategies, a prototype bioprocess that is carried out in a Continuous Stirred Tank Bioreactor was considered. First, a discontinuous feedback law was designed using the exact linearization and by imposing a SMC that stabilizes the output of the bioprocess. When some state variables used in the control law are not measurable on-line, an asymptotic state observer was used in order to reconstruct these states. Second, using the vibrational control theory, a VC strategy for the continuous bioprocess was developed. The existence and the choice of stabilizing vibrations, which ensure the desired behaviour of the bioprocess are widely analysed.

Some discussions and comparisons regarding the application of the sliding mode control and vibrational control techniques to bioprocesses can be done. Both the SMC and VC strategies are high-frequency methods, obviously high frequency relative to the natural frequency of the bioprocess. A main difference between VC and SMC is that in vibrational case, no measurements of state variables are required.

The idea of vibrational stabilization is to determine vibrations such the unstable equilibrium point of a bioprocess bifurcates into a stable almost periodic solution. The practical engineering VC problem can be described as a three steps technique: first it is necessary to find the conditions for existence of stabilizing vibrations, second to find which parameter or component is physically possible to vibrate and finally to find the parameters of vibrations that ensure the desired response.

From the simulations, the conclusion is that both methods can deal with some parametric disturbances. However, from this point of view, the behaviour of the feedback SMC is better. For the vibrational technique to be effective, one needs to have an accurate

description of system dynamics. This fact together with physical limitation on the magnitude and the frequency of vibrations in some cases are the disadvantages of the vibrational technique. A drawback of the SMC strategy is the chattering phenomenon. This chattering can be reduced using various techniques, but it cannot be eliminated, due to the inherent presence of the so-called parasitic dynamics, which are introduced principally by the actuator.

The proposed high-frequency techniques were tested using a prototype of a continuous bioprocess. For that reason, the presented results cannot be extended without intensive studies to other bioprocesses.

However, there exist some studies and implementations of the SMC strategy for fed-batch bioprocesses (Selișteanu & Petre, 2005). On another hand, using the results obtained by (Lehman & Bentsman, 1992; Lehman et al., 1994), the vibrational control theory can be extended for time lag systems with bounded delay. Such systems are the bioprocesses that take place inside the CSTB with delay in the recycle stream (Selișteanu et al., 2006).

The obtained results are quite encouraging from a simulation viewpoint and show the robustness of the controllers and good setpoint regulation performance. These results must to be verified in the laboratory using some real bioreactors. Further research will be focused on this real implementation. Also, some theoretical approaches will be the development of the high-frequency control strategies for multivariable bioprocesses and of some hybrid control strategies for these bioprocesses, like the closed-loop vibrational control (see for example (Kabamba et al., 1998)) and the adaptive sliding mode techniques.

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