Modelling and Adaptive Control of a Yeast Fermentation Process inside a Fed-batch Bioreactor

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Abstract: This work presents several issues concerning the modelling, kinetic estimation and nonlinear control of a baker’s yeast process that takes place inside a fed-batch bioreactor (FBB). First, a nonlinear model of the bioprocess is presented taking into consideration two approaches: the classical modelling scheme and the bond graph method. Second, to reconstruct the missing on-line kinetic information, estimation strategies are proposed. Finally, by using the process dynamical model and the on-line estimation strategies, an adaptive control scheme is designed in order to maintain a certain level of ethanol concentration, regardless of uncertainties and disturbances. This objective is attained by designing an adaptive controller as a combination between a linearizing control law and a high-gain observer. Numerical simulations are provided to illustrate the behaviour of the proposed estimation and control techniques.

Keywords: Adaptive control, Biotechnology, Fermentation processes, Modelling.

I. Introduction

The design of efficient control strategies is a significant and at the same time a difficult key issue in biotechnology industrial applications. In most cases, the biochemical reactions involved in such biotechnological processes are very complex, and consequently the kinetic models are typically achieved using simplified approaches. Other problematical issues, crucial for control design and implementation, are the identification of some kinetic parameters and the absence of suitable instrumentation for biological variables, such as concentrations of substrates, biomass and products [1, 2].

The baker’s yeast process is a well-known biotechnological process, which is extensively used in bakery, beer and wine industries. Typically, the baker’s yeast production takes place inside Fed-batch Bioreactors (FBBs). This process is characterized by strong nonlinearities and its reaction rates are complicated. Yet, a lot of models were elaborated in the last decades to depict this process. One of the largely utilized kinetic models, based on the bottleneck hypothesis, was initially obtained by Sonnleitner and Käppeli [3], and since then it has been used in several works [4 - 8]. The dynamical nonlinear model of the baker’s yeast process can be obtained by using the mass balance of the components inside the process and obeying some modelling rules [1, 2]. A different option to the classical modelling is the pseudo bond graph method [9, 10], with certain advantages such as model achievement in terms of dynamical state space equations in an easier way than using classical methods, the availability of information about the system structural properties, etc. Pseudo bond graphs are appropriate for biochemical systems due to the physical meaning of the effort and flow variables [11].

Concerning the estimation of parameters, particularly of the kinetic rates, often reported as software sensors design, various approaches have been proposed: Kalman filter theory based techniques, the adaptive approach developed by Bastin and Dochain [1], etc. This last approach resides in the estimation of unavailable state variables with asymptotic observers, and after that the available measurements and the state estimates are utilized for on-line kinetics estimation [4, 8]. A drawback is that it needs the calibration of many design parameters. A good alternative is to design high-gain observers [12 - 14], which involve a single tuning parameter whatever the number of components and reactions.

In order to design control laws, these techniques were applied by several authors for the estimation of uncertain reaction rates and/or specific growth rates of the baker’s yeast bioprocess: extended Kalman estimators, adaptive approach with observer-based estimators [8, 15 - 17], etc. An exhaustive study about the estimation methods in baker’s yeast processes is given in [18]. In the present work, the high-gain observers developed for the uncertain kinetic rates in [8, 19] will be used for the control design.

Several control strategies were developed for baker’s yeast processes. Most of these strategies take into account the metabolic pathways of the process and the two main regimes: respirative and respiro-fermentative [3, 4]. The main idea is that a substantial ethanol production should be avoided, because this accumulation reduces the yield and the biomass productivity. The control algorithms designed to this end are mono-variable (control of ethanol concentration) or multi-variable (control of ethanol and dissolved oxygen concentrations), and various techniques were developed: classical PID control with its inherent limitations, adaptive approaches such as linearizing control plus classical parameter adaptation techniques [5, 20], robust and robust-adaptive control [21], fuzzy control [7], etc. Most of the nonlinear techniques, including the classical adaptive approach, lead to complicated control laws, with numerous tuning parameters.

In the present work, the kinetic model of the baker’s yeast fermentation introduced by Sonnleitner and Käppeli [3] is used to develop an adaptive control strategy for a bioprocess that takes
place inside a FBB. More exactly, the nonlinear model derived from the reaction scheme by using either bond graph method or classical approach is transformed into a structure with two partial models which takes into account the two main regimes of the bioprocess [4, 7, 17]. In the first step of the control design, an exact linearizing controller is obtained. Then, the nonlinear controller thus obtained is combined with a high-gain observer for the unknown kinetic rates [8, 19]. If the high-gain observer and the adaptive controller require on-line state estimates, these will be provided by an asymptotic observer. The proposed adaptive controller requires a small number of design and tuning parameters. Several simulations were performed to illustrate the behaviour of the adaptive control scheme.

2. Dynamical Model of Baker’s Yeast Process

_Saccharomyces cerevisiae_ is a species of yeast, perhaps one of the most useful in industry, having been instrumental to brewing, winemaking and baking since a long time ago. In recent days, due to the modern gene technology, _S. cerevisiae_ are also used as host organisms for producing recombinant proteins (insulin for diabetics, vaccines, etc.) [21]. Baker’s yeast production takes place inside fed-batch fermenters (but also in continuous cultures) with inoculums of _S. cerevisiae_ culture and a glucose solution as substrate feed. Three main metabolic pathways can be identified: respiratory growth on glucose, respiratory growth on ethanol, and fermentative growth on glucose. Respirative pathways take place in presence of oxygen and the fermentative one in its absence, associated with ethanol production [3].

A reaction scheme of this fermentation process was established by Sonnleitner and Käppeli [3] as follows:

\[
\begin{align*}
S + C \rightarrow X + G, & \quad S \rightarrow X + E + G, \\
E + C \rightarrow X + G.
\end{align*}
\]

(1)

In these schemes, _S_ is the glucose, _X_ the biomass, _E_ the ethanol, _C_ the dissolved oxygen, and _G_ the dissolved carbon dioxide. The first reaction scheme corresponds to the respiratory growth on glucose; the second one is the fermentative growth on glucose; the third reaction gives the respiratory growth on ethanol. _μ_1, _μ_2 and _μ_3 are the so-called specific growth rates.

In the following, we will consider the fed-batch operation of this bioprocess. In the beginning, a fed-batch reactor has a small amount of substrates and micro-organisms and it is increasingly filled with the influent substrates. When the reactor is full, the content is harvested. From the reaction scheme (1), by taking into account the mass transfer through the reactor and using the classical modelling procedure (see, for example, the Bastin and Dochain approach [1]) or the pseudo bond graph method for fed-batch processes [11], the dynamical model of the baker’s yeast process can be obtained.

This model is quite complicated, and it consists of nonlinear differential equations describing the time evolution of concentrations inside the bioreactor. The bond graph model was obtained in [11] and is presented in Fig. 1. The directions of the halfl arrows in the bond graph match to the reactions progress, from the components _S_ and _C_ towards _X_ and _G_ for the first reaction, from _S_ towards _X_, _E_ and _G_ for the second reaction, and from _E_ and _C_ towards _X_ and _G_ for the third reaction. In bond graph terms, the mass balances of the components involved in the reactor are represented by five 0-junctions: _0_{1,2,3,4,33} (mass balance for _C_), _0_{6,7,9,20} (mass balance for _S_), _0_{13,14,15,24,37} (mass balance for _X_), _0_{17,18,19,26,30} (mass balance for _G_), and _0_{28,29,30,31} (mass balance for _E_) [11]. The accumulations of components _C_, _S_, _X_, _G_ and _E_ in the reactor are represented by bonds 2, 7, 14, 18 and 29, and are modelled using capacitive elements _C_. Mass flows of the components entering the reaction are modelled using two flow sources elements, and the transformer elements were used for the modelling of yield coefficients. To model the reaction rates, three modulated _R_-elements were used. By using this model and appropriate bond graph techniques, the dynamical nonlinear model of the bioprocess can be obtained.

This model is equivalent with that achieved via classical approach [8], and consists of the following system:

\[
\begin{align*}
\dot{X} &= (\mu_1 + \mu_2 + \mu_3)X - DX \\
\dot{S} &= (-k_1\mu_1 - k_2\mu_2)X + D(S_{in} - S) \\
\dot{E} &= (k_3\mu_2 - k_4\mu_3)X - DE \\
\dot{C} &= (-k_5\mu_1 - k_6\mu_3)X - DC + OTR \\
\dot{G} &= (k_7\mu_1 + k_8\mu_2 + k_9\mu_3)X - DG - CTR \\
\dot{V} &= F_{in} = DV
\end{align*}
\]

(2)

(3)

Figure 1. Baker’s yeast fermentation process – the pseudo bond graph model.
The model (2), (3) is a set of differential equations, in terms of the components concentrations, and with the supplementary equation (3) that expresses the dynamics of the culture volume in the bioreactor. For simplicity, the same symbols were used for the components and for their concentrations: $X$ is the biomass concentration; $S$, $E$, $C$ and $G$ are the glucose, ethanol, dissolved oxygen and dissolved carbon dioxide concentrations (all in g/L). $F_{in}$ is the input feed rate (L/h), $k_{ij}$, $i,j = 1, 2, 3, 4$ are the yield coefficients, $S_{in}$ represents the glucose concentration on the feed (g/L), $V$ is the culture volume in the reactor (L), and the dilution rate is $D = F_{in}/V$ (h$^{-1}$).

The oxygen transfer rate is given as $OTR = K_{V}a(C^* - C)$ (h$^{-1}$g/L), where $C^*$ is the equilibrium concentration of the dissolved oxygen (g/L) and $K_{V}$ is the mass transfer coefficient (h$^{-1}$). The carbon dioxide transfer is defined as $CTR = K_{V}aG$ (h$^{-1}$g/L), where $K_{V}$ is a transfer coefficient.

Thus the nonlinear model (2) can be expressed as [8]:

$$
\begin{bmatrix}
\dot{X} \\
\dot{S} \\
\dot{E} \\
\dot{C} \\
\dot{G}
\end{bmatrix} =
\begin{bmatrix}
1 & 1 & 1 & 0 & 0 \\
-k_1 & -k_2 & 0 & \mu_i & 0 \\
-k_3 & -k_4 & 0 & \mu_2 & 0 \\
-k_5 & 0 & 0 & 0 & 0 \\
k_7 & k_8 & k_9 & 0 & 0
\end{bmatrix}
\begin{bmatrix}
X \\
S \\
E \\
C \\
G
\end{bmatrix} +
\begin{bmatrix}
F_{in} \\
O_{in} \\
V_{in} \\
T_{in} \\
Q_{in}
\end{bmatrix}
+ \begin{bmatrix}
0 \\
0 \\
0 \\
0 \\
0
\end{bmatrix}$

The following notations are used: $\xi = [X \ S \ E \ C \ G]^T$ - the state vector, $F = [0 \ DS_{in} \ 0 \ OTR \ 0]^T$ - the vector of feeding rates, $Q = [0 \ 0 \ 0 \ CTR \ 0]^T$ - vector of rates of removal of components in gaseous form, $\phi(\xi) = \mu(X)$ - the vector of reaction rates (reaction kinetics), and $K$ the matrix of yield coefficients. Then the model (4) can be compactly expressed as:

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

(5)

The state-space model (5) describes not only the dynamics of the baker’s yeast fermentation, but also the behaviour of an entire class of bioprocesses [1]. $K \cdot \phi(\xi)$ represents the reaction kinetics, and the term $-D \xi + F - Q$ the exchange with the environment. The nonlinear character of the model (5) is due to the reaction kinetics, the modelling of this part being a challenging task. The kinetics structure is complex and in many situations unknown.

The reaction rates can be written as

$$
\phi(\xi,t) = H(\xi) \cdot \mu(\xi,t)
$$

(6)

where $H(\xi)$ is a diagonal matrix. In the following, the specific growth rates will be expressed as a vector of time varying parameters. In the case of yeast process (4), $H(\xi)$ is:

$$
H(\xi) =
\begin{bmatrix}
X & 0 & 0 \\
0 & X & 0 \\
0 & 0 & X
\end{bmatrix}
$$

(7)

Then the dynamical model (5) is written as:

$$
\dot{\xi} = K \cdot H(\xi) \cdot \mu(\xi,t) - D \cdot \xi + F - Q
$$

(8)

This model will be used in order to design estimation and control strategies for the baker’s yeast bioprocess. The first critical problem is to find kinetic rates models or to estimate on-line the reaction kinetics.

3. Modelling and Estimation of the Kinetic Rates

3.1. Models of the Kinetic Rates

The yeast growth on glucose with ethanol production can be described by three main metabolic reactions. First, the reaction rate of the respiratory growth on glucose, and the associated specific growth rate are [8, 21]:

$$
\mu_g(\xi) = \mu_g(X) \cdot \xi
$$

(9)

$$
\mu(\xi) = \min(\mu_g, \mu_{max}/k_{S})
$$

(10)

where $\mu_g$ and $\mu_{max}$ are modelled by Monod-type laws: $\mu_g = q_{max}S/(S + K_s)$, $\mu_{max} = q_{max}C/(C + K_c)$. $q_{max}$ is the maximal glucose specific growth rate (g glucose/(g biomass-h)), $q_{max}$ is the maximal oxygen specific growth rate (g O$_2$/(g biomass-h)), and $K_s$, $K_c$ are saturation parameters for glucose and oxygen uptake, respectively (g/L).

Second, the reaction rate of fermentative growth on glucose, and the associated specific rate are [8, 21]:

$$
\mu_f(\xi) = \mu_f(X) \cdot \xi
$$

(11)

$$
\mu_f(\xi) = \max(0, \mu_g - \mu_{max}/k_{S})
$$

(12)

Third, the reaction rate of the respiratory growth on ethanol, and the specific growth rate are [8, 21]:

$$
\mu(\xi) = \max(0, \min(\mu_g, \mu_f - k_{S} \mu_e)/k_{S})
$$

(13)

$$
\mu_f(\xi) = \max(0, \mu_{max}/k_{S})
$$

(14)

with $\mu_e$ modelled by: $\mu_e = q_{max}E/(E + K_e)$, where $q_{max}$ is the maximal ethanol growth rate (g ethanol/(g biomass-h)), and $K_e$ is a saturation parameter for growth on ethanol (g/L).

The kinetic model (9)-(14) supposes a limited capacity of yeast, which lead to the production of ethanol under conditions of oxygen limitation and/or high glucose concentration. Two operating regimes can be observed. For glucose concentration lower than its critical value, the process is in the so-called respirative regime (R), while at glucose concentration higher than its critical value, the process is in the respiro-fermentative regime (RF) [3, 8, 21].

In industrial practice, the analytical models of reaction rates $\phi(t)$ or of specific growth rates $\mu(t)$ are hard or even impossible to obtain. As consequence, because the kinetic rates are necessary for control design, they need to be on-line estimated. Next, the vector of unknown parameters will be denoted $\theta(t)$ (with $\theta(t) = \phi(t)$ or $\theta(t) = \mu(t)$). Thus, the model (8) of the bioprocess can be written as:

$$
\dot{\xi} = K \cdot H(\xi) \cdot \mu(\xi,t) - D \cdot \xi + F - Q
$$

(15)

where $H(\xi)$ is given by (7) if $\mu(t)$ is unknown, and $H(\xi)$ is the identity matrix if $\phi(t)$ is unknown.

The dynamical model (14) is based on three imprecisely known rates, which are unknown variables. One of the design problems is that the on-line kinetics estimation algorithms require the knowledge of minimum three states. From technological point of view, $E$, $C$ and $G$ are the on-line available states, but these variables are linearly dependent and consequently the corresponding yield matrix is ill-conditioned [16, 21], which lead to algorithms vulnerable to numerical errors. In order to solve this...
problem Pomerleau and Perrier [15] proposed a reformulation of model (4), based on the division of the bioprocess model into two partial models: the respiro-fermentative partial model (RF) for the ethanol production state, and the respirative partial model (R), for the ethanol consumption state of the bioprocess [8, 15]:

\[
\begin{align*}
\dot{X} &= \begin{bmatrix} 1 & 0 \\ -k_1 & -k_2 \\ -k_3 \\ k_7 \\ k_8 \\ k_9 \\ k_{10} \end{bmatrix} X - D \cdot E + X \cdot D \cdot S_{in} + OTR \\
\dot{S} &= \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \cdot X + D \cdot E \\
\dot{E} &= \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \cdot X + D \cdot S_{in} + OTR \\
\dot{G} &= \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \cdot X + D \cdot CTR \\
\end{align*}
\]

RF and R partial models possess identical structures; the dissimilarity is given by the different yield matrices and by the specific growth rates vector:

\[
K_{RF} = \begin{bmatrix} 1 & 1 & 0 & 0 & k_7 \\ 1 - k_1 & 0 & k_3 & 0 & k_8 \\ 0 & k_9 & k_{10} \end{bmatrix} \cdot \mu_{RF} = \begin{bmatrix} \mu_1 \\ \mu_2 \\ \mu_3 \end{bmatrix}
\]

\[
K_R = \begin{bmatrix} 1 & 1 & 0 & 0 & k_7 \\ 1 - k_1 & 0 & k_3 & 0 & k_8 \\ 0 & k_9 & k_{10} \end{bmatrix} \cdot \mu_R = \begin{bmatrix} \mu_1 \\ \mu_2 \\ \mu_3 \end{bmatrix}
\]

It results the compact partial models RF and R [8]:

\[
\begin{align*}
\dot{\xi} &= K_{RF} \cdot H(\xi) \cdot \mu_{RF} (\xi, t) - D \cdot \xi + F - Q \\
\dot{\xi} &= K_R \cdot H(\xi) \cdot \mu_R (\xi, t) - D \cdot \xi + F - Q
\end{align*}
\]

3.2. High-gain Observers for the Uncertain Kinetic Rates

In the following the vectors of uncertain parameters will be denoted \( \rho_{RF}(t) \) (with \( \rho_{RF}(t) = [\rho_1, \rho_2, \rho_3] \)) and \( \rho_{R}(t) \) (with \( \rho_{R}(t) = [\rho_1, \rho_2, \rho_3] \)) respectively. Subsequently the model (14) is rewritten as two partial models:

\[
\begin{align*}
\dot{\xi} &= K_{RF} \cdot H(\xi) \cdot \rho_{RF}(t) - D \cdot \xi + F - Q \\
\dot{\xi} &= K_R \cdot H(\xi) \cdot \rho_{R}(t) - D \cdot \xi + F - Q
\end{align*}
\]

where \( H(\xi) \) is given by (7) if \( \mu(t) \) is unknown, and \( H(\xi) \) is the identity matrix if \( \phi(t) \) is unknown.

Because for the given process only some concentrations of the involved components are on-line available, it may be required to use state observers. For instance, asymptotic observers can be designed without the knowledge of the kinetics being necessary. Next, we will presume that the states of the bioprocess are on-line measured or are provided by state estimators. In the process of observer design, a factorization of model (15) is necessary [8, 19]. Under the assumption that the yield matrix \( K \) is of full rank (which is true for our particular model), the partition \((K_a, K_b)\) can be chosen such that \( K_a \) has full rank. Then a partition \((\xi_a, \xi_b)\) of the state vector and related partitions for \( F \) and \( Q \) are obtained: \((F_a, F_b)\), \((Q_a, Q_b)\). Thus, the system (15) can be written as follows [8]:

\[
\begin{align*}
\dot{\xi}_a &= K_a : H(\xi_a, \xi_b) \cdot \rho(t) - D \cdot \xi_a + F - Q_a \\
\dot{\xi}_b &= K_b : H(\xi_a, \xi_b) \cdot \rho(t) - D \cdot \xi_b + F + Q_b
\end{align*}
\]

The design of nonlinear high-gain observers for a class of nonlinear systems is given in [12, 13]. To obtain feasible high-gain observers for the baker’s yeast bioprocess, in [8] the partial models RF and R (19), (20) were used. \( C, G, OTR, CTR \) and \( F_{in} \) are considered on-line available [4, 17]. The other state variables \((X, S, E)\) may be provided by using state observers if it is necessary. The high gain observer is of the form [8]:

\[
\dot{\rho} = -\theta^2 \cdot [K_a : H(\xi_a, \xi_b)]^{-1} (\hat{\xi}_a - \hat{\xi}_a)
\]

The high gain observer (24), which gives on-line kinetics estimates \( \hat{\rho} \), is a copy of the process model, but with \( \xi_a \) replaced by its estimate \( \hat{\xi}_a \), plus a corrective term. The tuning is very simple due to the fact that only the parameter \( \theta \) is used. \( \hat{\xi}_a \) is an “estimate” of \( \xi_a \) given by the algorithm to be compared with the real state, and the resulting error \( \hat{\xi}_a - \xi_a \) to be used in the estimator (24). The high gain estimator will be used for estimation of reaction rates, for both RF and R partial models. To this end, the partition \( \xi_a = [C \ G F] \), \( \xi_b = [X \ S \ E] \) is considered and we obtain:

\[
\begin{align*}
F_a &= [OTR \ 0 \ 0 \ 0], \\
F_b &= [0 \ DS_{in} \ 0 \ 0], \\
Q_a &= [0 \ CTR \ 0 \ 0], \\
Q_b &= [0 \ 0 \ 0 \ 0], (K_{a}, K_{b}).
\end{align*}
\]

Taking into consideration that \( \phi_1(\xi) = \mu_1(\xi)X, i = 1 \), it results the high gain observer [8]:

\[
\begin{align*}
\dot{\hat{\rho}} &= K_a \begin{bmatrix} \hat{\rho}_1 \\ \hat{\rho}_2 \end{bmatrix} - D \cdot \hat{\rho} + OTR \cdot CTR - 2\theta \cdot \hat{\rho} + C \\
\hat{\rho} &= \begin{bmatrix} \hat{\rho}_1 \\ \hat{\rho}_2 \end{bmatrix} - \theta^2 \cdot [K_a]^{-1} \begin{bmatrix} \hat{\rho} - C \\ \hat{\rho} - G \end{bmatrix}
\end{align*}
\]

The high-gain estimator (26), (27) will be implemented for both RF and R models. Two partial algorithms are resulting and these must be alternatively used depending on the actual process state (ethanol production or consumption). The two algorithms have the same equations, but different yield matrices \( K_{a, RF} \) and \( K_{a, R} \) respectively) and different rates: \( \rho(t) = \rho_{RF}(t) = [\rho_1(\xi) \ \phi(t)] \) (RF model) and \( \rho(t) = \rho_{R}(t) = [\rho_1(\xi) \ \phi(t)] \) (R model) are used (see [8]). For the partial model (RF) we have \( H(\xi_a, \xi_b) \) the identity matrix and

\[
\begin{align*}
\hat{\rho}_1 &= \hat{\rho}_{RF} = \hat{\phi}_1, \\
\hat{\rho}_2 &= \hat{\rho}_{2RF} = \hat{\phi}_2.
\end{align*}
\]

For the model (R) we have \( H(\xi_a, \sigma) \) the identity matrix and

\[
\begin{align*}
\hat{\rho}_1 &= \hat{\rho}_{RF} = \hat{\phi}_1, \\
\hat{\rho}_2 &= \hat{\rho}_{2RF} = \hat{\phi}_2.
\end{align*}
\]
4. Adaptive Control Design

A typical strategy used in fed-batch bioprocess control consists in the generation of a substrate feed rate profile utilized to optimize a performance criterion [1], but this technique is inadequate when the kinetics is imprecisely known. In the case of the baker’s yeast bioprocess it is required to maintain a certain low level of ethanol production to keep a good yield and biomass productivity [5, 21]. This objective can be achieved by designing an adaptive control scheme, which ensures a good behaviour with respect to disturbances and kinetic uncertainties. It should be mentioned that usually the controlled output is the ethanol concentration or the dissolved oxygen concentration (in multi-variable approaches), and the control action is either the dilution rate or the input feed rate.

The adaptive controller will be designed in two steps. First, a so-called exact linearizing control law is obtained. Second, an adaptive version of this controller is designed, by using the high-gain observers for reconstruction of uncertain kinetic rates needed by the controller.

The control objective is that the ethanol concentration \( y(t) = \bar{y}(t) = E(t) \) to track the desired trajectory \( \bar{y}'(t) = E'(t) \), with the dilution rate as control action: \( u(t) = D(t) \).

The exact linearizing control law for the model (5) is obtained in a classical manner [1, 22]. First, from the system (5) a process input-output model is obtained

\[
\dot{y} = \dot{E} = \dot{\bar{y}} = k_3\phi_2(\bar{x}) - k_4\phi_3(\bar{x}) - u \cdot y = k_3\mu_2(\bar{x})X - k_4\mu_3(\bar{x})X - u \cdot y.
\]

Next, a stable and linear reference model for the tracking error \( y' - y \) is chosen:

\[
(y' - y) + \lambda(y' - y) = 0, \quad \lambda > 0.
\]

Finally, the control law is achieved by calculating the control action such that (30) has the same behaviour as (31):

\[
u(t) = (1/y')\cdot[k_3\phi_3(\bar{x}) - k_4\phi_3(\bar{x}) - \lambda(y' - y)]

= (1/y')\cdot[k_3\mu_2(\bar{x})X - k_4\mu_3(\bar{x})X - \lambda(y' - y)],
\]

where \( y' = \text{const} \).

The exact linearizing control law (32) can achieve the control objective only if the concentration \( \bar{x} = X \) is on-line available and if the specific growth rates are known (or the reaction rates are known). Because in practice these requirements cannot be fulfilled, it is necessary to replace the uncertain variables with their estimations provided by appropriate observers. Consequently, an adaptive version of the exact linearizing control law can be achieved. For instance, if the estimations \( \hat{\phi}(t) = \hat{\phi}(t) \) given by (26)-(29) are used in the controller (32), the adaptive controller is designed as:

\[
u(t) = (1/y(t))\cdot[k_3\hat{\phi}_2(t) - k_4\hat{\phi}_3(t) - \lambda(y' - y(t))].
\]

Similar to previous section, the adaptive control law given in equation (33) is associated with a switching mechanism that depends on the transition between positive and negative values of the reaction rate estimate that are related to the ethanol production (\( \hat{\phi}_2 \)) or consumption (\( \hat{\phi}_3 \)). The adaptive control scheme is given in Fig. 2.

5. Simulation Results

To analyse the performance of the proposed control strategy for the baker’s yeast process, several simulations were performed. The bioprocess model (4) was used in order to provide the data for simulation. The reaction kinetics form is that given by relations (9)-(14), but these equations are for simulation and are not used for observer and control law design. The kinetic parameters and coefficients values are as follows [3, 4, 8]:

\[
k_1 = 2.04 \text{ g glucose/g biomass}, k_2 = 20 \text{ g glucose/g biomass},
\]

\( k_{biomass} = 1.38 \text{ g ethanol/g biomass}, k_4 = 0.83 \text{ g O}_2 / \text{g biomass}, k_5 = 1.56 \text{ g O}_2 / \text{g biomass}, k_6 = 1.23 \text{ g CO}_2 / \text{g biomass}, k_7 = 9.09 \text{ g CO}_2 / \text{g biomass}, k_8 = 0.90 \text{ g CO}_2 / \text{ g biomass}, K_s = 0.2 \text{ g/L}, K_c = 0.000 \text{ g/L}, q_{c_{max}} = 0.256 \text{ gO}_2 / (\text{gbiomass-h})/\text{L}, K_{a_{max}} = 0.1 \text{ g/L} S_{in} = 100 \text{ g/L}, q_{a_{max}} = 3.5 \text{ gglucose/g biomass-h}, K_{a_{max}} = 100 \text{ g/L}, C_{y_{max}} = 0.2, q_{a_{max}} = 0.236 \text{ g ethanol/(gbiomass-h)}, C^* = 0.007 \text{ g/L}.

To examine the behaviour of the proposed control strategy, two simulation cases were designed:

(i) The adaptive control law (33) was implemented by considering that the on-line available measurements are \( C \) and \( G \) (directly or indirectly), the oxygen transfer rate is computed as \( OTR = K_{a_{max}}(C - C^*) \), and the carbon dioxide transfer as \( CTR = K_{a_{max}}(C - C^*) \). Also, we suppose that all the measurements are noise-free.

The adaptive control scheme consists of the control law (33), the high-gain observer (26)-(29) that provides the kinetic rates estimates, and the switching mechanism. The tuning parameter of the high-gain observer was set to \( \theta = 25 \), and the controller parameter to \( \lambda = 2 \). The setpoint profile (\( E' \)) was chosen such that to avoid the inhibition of biomass growth, but it also allows a small ethanol production to induce the enzymatic system of the fermentative pathway [5, 21].

The simulation results were presented in Fig. 3 (evolution of the ethanol concentration versus the setpoint). The behaviour of the adaptive control law is compared with that of the exact linearizing control law (32) (ideal case – all the states and kinetics are known).
(ii) The second simulation case is performed in the same conditions as the first one, but considering that the on-line measurements of \( C \) and \( G \) are corrupted by an additive Gaussian noise (zero mean and amplitude 5% of free noise values), and some systematic measurement errors were also considered, as it can be seen in Fig. 4. The simulation results are given in Fig. 5 (ethanol concentration for both exact and adaptive controllers) and Fig. 6 (control action). Also, the time evolution of one of the estimated reaction rates (\( \phi_2 \)) was plotted in Fig. 7 (free-noise or noisy measurements). It should be mentioned that the high gain observer provides also the estimation of \( \phi_3 \), but this is not used for the control design. Also, due to the setpoint profile, the respire-fermentative regime is kept and the third reaction rate is zero.

It can be seen that the overall performance is affected; however, the effect of noise and systematic errors is quite limited. The control goal was achieved, i.e. the ethanol concentration was kept to a low level such that to obtain a good production of biomass (Fig. 8), despite the kinetic uncertainties and disturbances occurring on the bioprocess.

6. Conclusion

An adaptive controller for a baker’s yeast fed-batch process was designed by combining an exact linear controller with a high-gain observer for the uncertain kinetics of the bioprocess. The tuning of the control algorithm is quite simple because only two tuning parameters are used. The control goal was to maintain a low ethanol concentration level in order to increase the biomass production. The simulation results show that the adaptive controller ensures a good behaviour with respect to noisy measurements and disturbances.
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