ON EXPONENTIAL AND ASYMPTOTIC ESTIMATION OF STATE VARIABLES IN BIOPROCESSES

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Abstract: The paper presents on-line estimation strategies for bioprocesses, which are characterized by strongly nonlinear dynamics. A general form for the state observers is analysed and the exponential observability of bioprocesses is discussed. For those biotechnological processes that possess the property of exponential observability, an extended Luenberger observer is implemented. If exponential observers cannot be used, a solution is the design of asymptotic observers. The proposed observers are implemented for a microbial growth process coupled with an enzyme-catalysed reaction, which is a usual bioprocess that takes place in a fed-batch bioreactor. Illustrative computer simulations and conclusions are included.

Keywords: Biotechnology, Nonlinear Systems, Exponential Observability, Asymptotic Observers

1. INTRODUCTION

The absence of reliable and cheap sensors in bioindustry is a characteristic of most applications. This problem leads to the incapacity of the control system to provide on-line measurements of the biological state variables. Therefore, the design and the implementation of state observers (so-called software sensors: Bastin and Dochain, 1990) for those state variables which are not measurable in real-time is very important for numerous practical bioprocess control applications.

The paper is organized as follows. In Section 2, the general dynamical model of the bioprocesses is presented. Based on this model, a general form of state observer is analysed and the property of exponential observability is discussed. For those cases when the bioprocess is exponentially observable, an extended Luenberger observer is designed. Section 3 deals with the design and implementation of asymptotic observers. In Section 4, the proposed exponential and asymptotic observers

are analysed and implemented for a microbial growth process coupled with an enzyme-catalysed reaction. Finally, Section 5 collects the conclusions.

2. EXPONENTIAL OBSERVERS

The dynamical state-space model of a biotechnological process in a bioreactor expresses the mass balance of the components in the bioreactor, and a general dynamical model can be obtained (Bastin and Dochain, 1990; Bastin, 1991):

$$\frac{d\boldsymbol{x}}{dt} = K\boldsymbol{j}(\boldsymbol{x}) - D \cdot \boldsymbol{x} + F - Q \qquad (1)$$

where $\boldsymbol{x}$ represent the state vector, i.e. the vector of the concentrations of the n components inside the bioreactor. K is the matrix of yield coefficients, φ is the vector of reaction rates; D is the dilution rate, F the vector of the rates of supply and Q the vector of the rates of removal (for the components in gazeous form).

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If there are some state variables x_i, which are not measurable in real-time, a state observer must be designed in order to obtain a good control strategy. A general class of observers for bioprocesses of form (1) is proposed by Bastin and Dochain, 1990:

$$\frac{d\hat{x}}{dt} = K\boldsymbol{j}(\hat{x}) - D\cdot\hat{x} + F - Q + W(\hat{x})\cdot(x_m - \hat{x}_m) \quad (2)$$

where $\hat{x}$ is the estimated state vector, $W(\hat{x})$ is a gain matrix and x_m is the vector of measurable state variables: $x_m = L\cdot x$, with L a selection matrix. The design of the observer consists in the choice of gain matrix. The dynamic of the estimation error $e = x - \hat{x}$ is

$$\frac{de}{dt} = K\big[\boldsymbol{j}(\hat{x}+e) - \boldsymbol{j}(\hat{x})\big] - D\cdot e - W(\hat{x})\cdot L\cdot e \quad (3)$$

It is clear that $e = 0$ is an equilibrium point of (3). The linear approximation around $e = 0$ can be easily obtained:

$$\frac{de}{dt} = \big[A(\hat{x}) - W(\hat{x})\cdot L\big]\cdot e \quad (4)$$

where $A(\hat{x}) = K\left[\dfrac{\partial \boldsymbol{j}(x)}{\partial x}\right]_{x=\hat{x}} - D\cdot I_n$.

If it is possible to impose desired values for the eigenvalues of matrix $\big[A(\hat{x}) - W(\hat{x})\cdot L\big]$ by choosing the gain matrix, then the system (1) is exponentially observable and the observer (2) is an exponential observer (Bastin and Dochain, 1990; Deza, *et al.*, 1993). A necessary condition of exponential observability is that the observability matrix

$$O = \big[L \;\; L\cdot A(x) \;\; L\cdot A(x)^2 \; \dots \; L\cdot A(x)^{n-1}\big]^T \quad (5)$$

is a full rank matrix: rank(O) = n along the state trajectories, with n the dimension of state vector.

When the bioprocess is exponentially observable, is possible to try the implementation of an extended observer, for example an extended Luenberger observer. The design of this exponential observer consists in the choice of gain matrix $W(\hat{x})$ such that the equilibrium point e = 0 of (4) is asymptotically stable. Therefore, the gain matrix must to obey two conditions (Bastin and Dochain, 1990):

(i) the matrix $\big[A(\hat{x}) - W(\hat{x})\cdot L\big]$ and his derivative are bounded;

(ii) the real parts of eigenvalues of $\big[A(\hat{x}) - W(\hat{x})\cdot L\big]$ are strictly negative:

$$Re\big[\boldsymbol{l}_i\big\{A(\hat{x}) - W(\hat{x})\cdot L\big\}\big] \le \boldsymbol{d} < 0, \; \boldsymbol{d} > 0, \forall \hat{x} \quad (6)$$

Finally, the state estimator consists in the system (2) where the gain matrix is obtained using the conditions (i) and (ii), with the design parameters $\boldsymbol{l}_i$.

3. ASYMPTOTIC OBSERVERS

When the system is not exponentially observable, a possibility is to design and to implement an asymptotic observer for the state variables (Petre, 1997). The asymptotic observer can be designed even without knowledge of kinetic reaction, which is a great advantage because the kinetic modelling is a difficult task (Charbonnier and Cheruy, 1994; Selisteanu and Petre, 1999).

The design of an asymptotic observer is based on some useful changes of coordinates, which lead to a submodel of (1) independent of the kinetics. In order to achieve the change of coordinates, a partition of the state vector x in two parts is considered. This partition denoted (x_a, x_b) induces correspondingly partitions of the yield matrix K: (K_a , K_b) and the rate vectors F and Q: (F_a ,F_b), (Q_a, Q_b). We suppose that the state partition is chosen such that submatrix K_a is full rank and $dim(x_a) = rank(K_a) = rank(K)$. Then a linear change of coordinates (a diffeomorphism) can be defined:

$$z = C\cdot x_a + x_b \quad (7)$$

with z the auxiliary state vector and C the solution of the matrix equation $C\cdot K_a + K_b = 0$.

In the new coordinates, the model (1) can be rewritten

$$\frac{dx_a}{dt} = K_a \boldsymbol{j}(x_a, z - Cx_a) - D\cdot x_a + F_a - Q_a$$
$$\frac{dz}{dt} = -D\cdot z + C\cdot(F_a - Q_a) + F_b - Q_b \quad (8)$$

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

$$z = C_1 \cdot x_m + C_2 \cdot x_{nm} \quad (9)$$

with C_1 and C_2 well defined matrices.

Remark: The asymptotic observers can be designed only if the dimension of measurable sate vector is bigger than the rank of matrix K.

If the matrix C_2 is left invertible, the asymptotic observer equations for (1) derive from the structure of equations (8) and (9):

$$\frac{d\hat{z}}{dt} = -D \cdot \hat{z} + C \cdot (F_a - Q_a) + F_b - Q_b$$

$$\hat{x}_{nm} = C_2^+ \cdot (\hat{z} - C_1 x_m) \tag{10}$$

where $C_2^+ = (C_2^T C_2)^{-1} C_2^T$.

The asymptotic observer is indeed independent of the kinetics. The asymptotic observer (10) has good convergence and stability performances (Bastin and Dochain, 1990; Petre, 1997).

4. ESTIMATION OF STATE VARIABLES IN A COMBINED GROWTH PLUS ENZYME-CATALYSED BIOPROCESS

The above described state observers are designed and implemented for a microbial growth process coupled with an enzyme-catalysed reaction, which is a usual bioprocess that takes place in a fed-batch bioreactor. The reaction scheme and the dynamical model are (Bastin, 1991; Selisteanu and Petre, 1996)

$$S + O \xrightarrow{j_1} X$$

$$S + X \xrightarrow{j_2} P + X \tag{11}$$
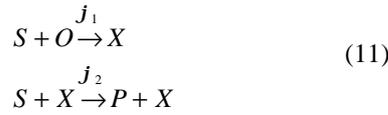
In the reaction scheme (11) S is the substrate, O is the dissolved oxygen, X represents the biomass and P is the synthesis product.

$$\frac{d}{dt}\begin{bmatrix} S \\ X \\ P \\ O \end{bmatrix} = \begin{bmatrix} -k_1 & -k_2 \\ 1 & 0 \\ 0 & 1 \\ -k_3 & 10 \end{bmatrix} \cdot \begin{bmatrix} j_1 \\ j_2 \end{bmatrix} - D \cdot \begin{bmatrix} S \\ X \\ P \\ O \end{bmatrix} + \begin{bmatrix} F_1 \\ 0 \\ 0 \\ F_2 \end{bmatrix} \tag{12}$$

In the dynamical model (12), S, X, O, and P are the concentrations of the components from the reaction scheme, j_1 and j_2 are the reaction rates. The state vector and the yield matrix are

$$x = [S\ X\ P\ O]^T; \quad K = \begin{bmatrix} -k_1 & -k_2 \\ 1 & 0 \\ 0 & 1 \\ -k_3 & 10 \end{bmatrix}$$

Then the model (12) can be compactly written

$$\frac{dx}{dt} = Kj(x) - Dx + F \tag{13}$$

where $j = [j_1(x)\ j_2(x)]^T$, $F = [F_1\ 0\ 0\ F_2]^T$, F_1 represents the substrate rate supply and F_2 the oxygen rate supply.

If the dissolved oxygen is not limited and the synthesis product P has not an inhibitory action, then the reaction rates can be modelled as follows

$$j_1(S,X,P,O) = m(S) \cdot X$$

$$j_2(S,X,P,O) = n(S) \cdot X \tag{14}$$

with $m(S)$ the specific growth rate, considered of Monod type, and $n(S)$ the specific accumulation product rate, considered of Haldane type:

$$m(S) = m^* \frac{S}{K_{M_1} + S} \tag{15}$$

$$n(S) = n_0 \frac{S}{K_{M_2} + S + S^2 / K_i} \tag{16}$$

In relations (15), (16), K_{M_1}, K_{M_2} are the Michaelis-Menten coefficients, K_i is the inhibition coefficient and m^*, n_0 are the maximum specific rates.

The influent substrate rate can be defined as

$$F_1 = D \cdot S_{in} \tag{17}$$

where D is the dilution rate and S_{in} the influent substrate concentration.

4.1 The exponential observability property

For the bioprocess described by the model (13)-(17), the design of an exponential observer can be tried. In most practical applications, the biomass cannot be measured. It can be considered that the measured states are P and O, and the unmeasured states are X and S.

$$x_m = [P\ O]^T, \quad x_{nm} = [S\ X]^T, \quad L = \begin{bmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Under the hypothesis that D, S_{in} and F_2 can be on-line measurable, that the structure and the coefficients of kinetics are known and furthermore that the yield coefficients are also known, the equations of the state observer of type (2) for the bioprocess (13)-(17) are

$$\frac{d}{dt}\begin{bmatrix} \hat{S} \\ \hat{X} \\ \hat{P} \\ \hat{O} \end{bmatrix} = \begin{bmatrix} -k_1 & -k_2 \\ 1 & 0 \\ 0 & 1 \\ -k_3 & 10 \end{bmatrix}\begin{bmatrix} m(\hat{S})\hat{X} \\ n(\hat{S})\hat{X} \end{bmatrix} - D\begin{bmatrix} \hat{S} \\ \hat{X} \\ \hat{P} \\ \hat{O} \end{bmatrix} + \begin{bmatrix} DS_{in} \\ 0 \\ 0 \\ F_2 \end{bmatrix} +$$

$$+ W(\hat{S},\hat{X},\hat{P},\hat{O})\left(\begin{bmatrix} P \\ O \end{bmatrix} - \begin{bmatrix} \hat{P} \\ \hat{O} \end{bmatrix}\right) \tag{18}$$

The form of gain matrix $W(\hat{x})$ is

$$W(\hat{x}) = \begin{bmatrix} w_{11}(\hat{S},\hat{X},\hat{P},\hat{O}) & w_{12}(\hat{S},\hat{X},\hat{P},\hat{O}) \\ w_{21}(\hat{S},\hat{X},\hat{P},\hat{O}) & w_{22}(\hat{S},\hat{X},\hat{P},\hat{O}) \\ w_{31}(\hat{S},\hat{X},\hat{P},\hat{O}) & w_{32}(\hat{S},\hat{X},\hat{P},\hat{O}) \\ w_{41}(\hat{S},\hat{X},\hat{P},\hat{O}) & w_{42}(\hat{S},\hat{X},\hat{P},\hat{O}) \end{bmatrix} \quad (19)$$

The estimation error $e = x - \hat{x}$ verifies the equation (3) and the linear approximation around $e = 0$ is given by (4), where

$$A(\hat{x}) = K\left[\frac{\partial j(x)}{\partial x}\right]_{x=\hat{x}} - D \cdot I_4 .$$

The calculation of the matrix $A(\hat{x})$ implies the calculation of the derivatives of the reaction rates:

$$\left[\frac{\partial j(x)}{\partial x}\right]_{\hat{x}} = \begin{bmatrix} \left[\frac{\partial j_1}{\partial S}\right]_{\hat{x}} & \left[\frac{\partial j_1}{\partial X}\right]_{\hat{x}} & \left[\frac{\partial j_1}{\partial P}\right]_{\hat{x}} & \left[\frac{\partial j_1}{\partial O}\right]_{\hat{x}} \\ \left[\frac{\partial j_2}{\partial S}\right]_{\hat{x}} & \left[\frac{\partial j_2}{\partial X}\right]_{\hat{x}} & \left[\frac{\partial j_2}{\partial P}\right]_{\hat{x}} & \left[\frac{\partial j_2}{\partial O}\right]_{\hat{x}} \end{bmatrix}$$

If the form (14) is taken into account, after straightforward calculation the vector of derivatives is obtained:

$$\left[\frac{\partial j(x)}{\partial x}\right]_{\hat{x}} = \begin{bmatrix} m'(\hat{S}) \cdot \hat{X} & m(\hat{S}) & 0 & 0 \\ n'(\hat{S}) \cdot \hat{X} & n(\hat{S}) & 0 & 0 \end{bmatrix}$$

where $\left[\frac{dm(S)}{dS}\right]_{\hat{S}}^N = m'(\hat{S}),\ \left[\frac{dn(S)}{dS}\right]_{\hat{S}}^N = n'(\hat{S})$.

The final form of the matrix $A(\hat{x})$ is

$$A(\hat{x}) = \begin{bmatrix} a_{11} & a_{12} & 0 & 0 \\ m'(\hat{S})\hat{X} & m(\hat{S})-D & 0 & 0 \\ n'(\hat{S})\hat{X} & n(S) & -D & 0 \\ -k_3 m'(\hat{S})\hat{X} & -k_3 m(\hat{S}) & 0 & -D \end{bmatrix} \quad (20)$$

with $\qquad a_{11} = -k_1 m'(\hat{S})\hat{X} - k_2 n'(\hat{S})\hat{X} - D,$

$\qquad\qquad a_{12} = -k_1 m(\hat{S}) - k_2 n(\hat{S})$.

The observability matrix O can be obtained easily from (5):

$$O = \begin{bmatrix} L \\ L \cdot A(x) \\ L \cdot A^2(x) \\ L \cdot A^3(x) \end{bmatrix} \quad (21)$$

After some calculations, by analysing the observability matrix (21), it can be concluded that the rank of O is maximum (i.e. n = 4) if it is achieved the condition $k_3 m(S)n'(S) \cdot X - k_3 n(S)m'(S)X \neq 0$ or equivalent (k_3 and X are positive values)

$$m(S)n'(S) - n(S)m'(S) \neq 0 \quad (22)$$

along the trajectories of the system. If the specific rates have the particular form (15), (16) then the condition (22) becomes

$$S^2 + 2K_{M_1} \cdot S + K_i \cdot (K_{M_1} - K_{M_2}) \neq 0 \quad (23)$$

Because the variables S and X are concentrations (positive values), the analysis of the relations (22) and (23) shows that the rank condition rank(O) = 4 is achieved only if $K_{M_1} > K_{M_2}$. While the conditions $S \neq 0,\ X \neq 0$ are in general accomplished, the condition $K_{M_1} > K_{M_2}$ is not universally valid.

Concluding, an exponential observer of the form (18) cannot be always designed for our bioprocess. In such situations is preferable the design of an asymptotic state observer. However, if the particular values for the Michaelis-Menten coefficients K_{M_1}, K_{M_2} allow the construction of the exponential observer, another problem is the design of the gain matrix (19). For instance, if an extended Luenberger observer is designed, it is quite difficult to obtain the components of the gain matrix. The conditions (i) and (ii) must be accomplished by imposing 4 eigenvalues with negative real part for the matrix of the linearized estimation error system.

4.2 The asymptotic observer design

The design of an asymptotic observer for the bioprocess has two advantages: first the problem of the exponential observability checking is avoided and second the state observer can be obtained without the knowledge of the reaction kinetics.

For the bioprocess described by the model (13)-(17), the design of an asymptotic observer will be achieved by considering that the measured states are S and O, and the unmeasured states are X and P. In order to achieve the change of coordinates described in Section 3, a partition of the state vector x in two parts (x_a, x_b) is considered:

$$x_a = [S\ X]^T, \quad x_b = [P\ O]^T \quad (24)$$

The partition (24) induces correspondingly partitions of the yield matrix K and the rate vector F:

$$K_a = \begin{bmatrix} -k_1 & -k_2 \\ 1 & 0 \end{bmatrix}, \quad K_b = \begin{bmatrix} 0 & 1 \\ -k_3 & 0 \end{bmatrix}$$

$$F_a = \begin{bmatrix} D \cdot S_{in} \\ 0 \end{bmatrix}, \quad F_b = \begin{bmatrix} 0 \\ F_2 \end{bmatrix} \quad (25)$$

The submatrix K_a is full rank, so the linear change of coordinates (7) can be defined. The new coordinates are

$$\boldsymbol{x}_a = \begin{bmatrix} S & X \end{bmatrix}^T$$
$$z = C \cdot \boldsymbol{x}_a + \boldsymbol{x}_b \tag{26}$$

with z the auxiliary state vector and C the solution of the matrix equation $C \cdot K_a + K_b = 0$. The matrix C can be easily obtained:

$$C = -K_b \cdot K_a^{-1} = \begin{bmatrix} \dfrac{1}{k_2} & \dfrac{k_1}{k_2} \\ 0 & k_3 \end{bmatrix}$$

Therefore, the auxiliary coordinates are

$$z_1 = \frac{1}{k_2} S + \frac{k_1}{k_2} X + P$$
$$z_2 = k_3 X + O \tag{27}$$

In the new coordinates (26), (27) the bioprocess model can be rewritten as

$$\frac{dS}{dt} = -k_1 \boldsymbol{m}(S)X - k_2 \boldsymbol{n}(S)X - D \cdot S + D \cdot S_{in}$$
$$\frac{dX}{dt} = \boldsymbol{m}(S)X$$
$$\frac{dz_1}{dt} = -D \cdot z_1 + \frac{1}{k_2} D \cdot S_{in} \tag{28}$$
$$\frac{dz_2}{dt} = -Dz_2 + F_2$$

The auxiliary state vector z can be written as a linear combination of the measured and unmeasured state vectors $\boldsymbol{x}_m = \begin{bmatrix} S & O \end{bmatrix}^T$, $\boldsymbol{x}_{nm} = \begin{bmatrix} X & P \end{bmatrix}^T$:

$$z = C_1 \cdot \boldsymbol{x}_m + C_2 \cdot \boldsymbol{x}_{nm} \tag{29}$$

The matrices C_1 and C_2 are obtained by calculation from (27) and (29):

$$C_1 = \begin{bmatrix} \dfrac{1}{k_1} & 0 \\ 0 & k_3 \end{bmatrix}, \quad C_2 = \begin{bmatrix} \dfrac{k_1}{k_2} & 1 \\ k_3 & 0 \end{bmatrix} \tag{30}$$

Now the equations of the asymptotic observer (10) for the bioprocess (13)-(17) can be written

$$\frac{d}{dt}\begin{bmatrix} \hat{z}_1 \\ \hat{z}_2 \end{bmatrix} = -D\begin{bmatrix} \hat{z}_1 \\ \hat{z}_2 \end{bmatrix} + \begin{bmatrix} \dfrac{1}{k_2} DS_{in} \\ F_2 \end{bmatrix} \tag{31}$$
$$\hat{\boldsymbol{x}}_{nm} = C_2^+(\hat{z} - C_1 \boldsymbol{x}_m)$$

where $\hat{z}$ and $\hat{\boldsymbol{x}}_{nm}$ are the estimations of z and respectively $\boldsymbol{x}_{nm}$, and $C_2^+ = C_2^{-1} = \begin{bmatrix} 0 & \dfrac{1}{k_3} \\ 1 & -\dfrac{k_1}{k_2 k_3} \end{bmatrix}$.

Then the detailed equations of the asymptotic observer (31) are

$$\frac{d\hat{z}_1}{dt} = -D \cdot \hat{z}_1 + \frac{1}{k_2} D \cdot S_{in}$$
$$\frac{d\hat{z}_2}{dt} = -D \cdot \hat{z}_2 + F_2$$
$$\hat{X} = \frac{1}{k_3}(\hat{z}_2 - O) \tag{32}$$
$$\hat{P} = \hat{z}_1 - \frac{1}{k_1} S - \frac{k_1}{k_2 k_3}(\hat{z}_2 - O)$$

The inspection of the equations (32) shows that indeed the knowledge of the reaction kinetics is not necessary for the estimation of state variables X and P. For the implementation of the asymptotic observer the knowledge of the yield matrix K is required.

Simulation results. The asymptotic observer (32) was implemented for the bioprocess of microbial growth coupled with enzyme-catalysed reaction (13)-(17). The data used in simulation are

$$\boldsymbol{m}^* = 1h^{-1}, K_{M_1} = 1g/l, K_{M_2} = 20g/l,$$
$$\boldsymbol{n}_0 = 6h^{-1}, K_i = 10g/l, k_1 = k_3 = 1, k_2 = 2,$$
$$D = 0.2h^{-1}, S_{in} = 15g/l, F_2 = 2g/lh.$$

First, in Fig. 1 the time evolutions of the concentrations (S), biomass (X), synthesis product (P) and dissolved oxygen (O) are presented (for a constant value of the rate dilution $D = 0.2h^{-1}$). For the implementation of the asymptotic observer (32), the dilution rate is considered of the rectangular form depicted in Fig. 2. This evolution of the dilution rate assures the achievement of the well-known persistence excitation condition.

In Fig. 3 the concentrations of X and P (solid line) and the estimates of these concentrations (dashed line) are represented. It can be seen that the evolution of the estimated concentrations is good, even if there are different initial conditions for X, $\hat{X}$, and P, $\hat{P}$.
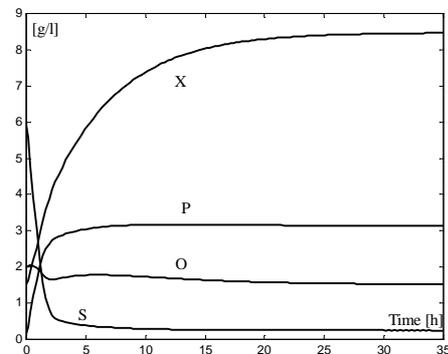

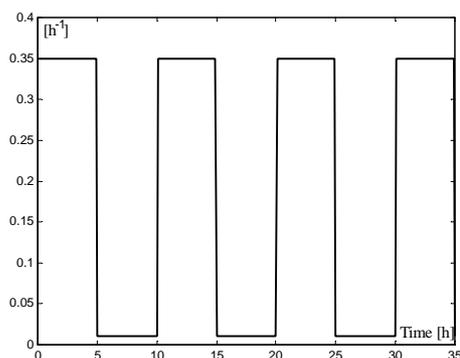Fig. 1. Evolution of concentrations (for D constant)

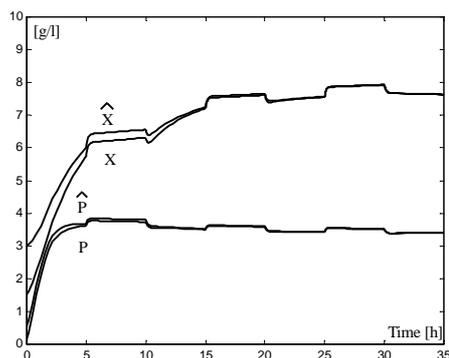Fig. 2. The rectangular profile of the dilution rate *D*

Fig. 3. The evolution of concentrations *X*, *P* and of
the estimated concentrations

5. CONCLUSIONS

In this paper on-line estimation strategies for bioprocesses were presented. The property of exponential observability of bioprocesses was analysed. If the bioprocess is exponentially observable, an exponential observer such as the extended Luenberger observer can be designed and the on-line estimates of the unmeasured states are obtained. Another possible solution in this case is the extended Kalman observer. For those bioprocesses, which are not exponentially observable, a solution is the design of the asymptotic observers. These observers possess another advantage: the complete knowledge of the reaction kinetics is not needed.

The estimation strategies are analysed and implemented for a microbial growth process coupled with an enzyme-catalysed reaction, which is a usual bioprocess that takes place in a fed-batch bioreactor. The appropriate solution for the estimation of state variables in the particular case of this bioprocess is the design of the asymptotic observer. The obtained results were tested by computer simulations and are optimistic from simulation point of view.

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