Pseudo Bond Graph Modelling of Some Prototype Bioprocesses

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Abstract: The paper presents a novel modelling method for biotechnological processes, based on pseudo Bond Graph approach. The stages for the design of pseudo Bond Graph models of bioprocesses are obtained using the reaction schemes and the analysis of biochemical phenomena. These stages are applied in order to design the Bond Graph models of some prototype bioprocesses: the simple micro-organisms growth process, followed by the aerobic micro-organisms growth process, combined with an enzyme-catalysed reaction. These models provide information on the time variation of the reaction products and reactants concentrations. It is assumed that the bioprocesses considered take place into bioreactors functioning in the following three modes: the batch mode, the continuous mode, and the fed-batch mode. Several simulations are conducted using 20sim modelling and simulation environment. This modelling procedure represents a valuable illustration of the power of Bond Graph technique, and can be used as a base for the development of the models of bioprocesses with high level of complexity.

Keywords: Biotechnology, Nonlinear models, Bond Graphs.

1. INTRODUCTION

In industry, the bioprocess control is often limited to regulation of the temperature and pH at constant values favourable to the microbial growth - see Bastin and Dochain (1990), Dochain (2008), Schugerl (2001). There is, however, no doubt that the control of biological state variables such as biomass, substrates, products, can help to increase the process performances. In order to develop and apply advanced control strategies for these biological variables, it is necessary to obtain a useful dynamical model. The bioprocess modelling is a difficult task; however, using the mass balance of the components inside the process and obeying some modelling rules, a dynamical state-space model can be obtained - see Bastin and Dochain (1990), Schugerl (2001).

A viable alternative to the classical modelling is the Bond Graph method. Bond Graph method was first introduced by Paynter in 1961, and further developed by Karnopp and Rosenberg (1974), and by Thoma (1975). Over the last four decades there have been a lot of publications regarding the theory and application of Bond Graphs in different engineering domains: Gawthrop and Smith (1996), Thoma and Ould Bouamama (2000), Păstrăvanu and Ibănescu (2001), Pirvu et al. (2007). The Bond Graph approach is a powerful tool for modelling, analysis and design of different kind of systems, such as electrical, mechanical (Păstrăvanu and Ibănescu (2001), Roman et al. (2008)), hydraulic (Dauphin-Tanguy (2000)), thermal, chemical (Heny et al. (2000), Thoma et al. (2000), Couenne et al. (2006)) etc. This method provides a uniform manner to describe the dynamical behaviour for all types of physical systems and illustrates the exchange power in a system, which is normally the product between the effort and flow variables in the true Bond Graph. Besides this representation there is another one, in which the product effort-flow does not have the physical dimension of power, called pseudo Bond Graph (Thoma and Ould Bouamama (2000), Heny et al. (2000)). Pseudo Bond Graphs are more suitable for chemical systems due to the physical meaning of the effort and flow variables. The advantages of Bond Graph modelling are the following: offers a unified approach for all types of systems; allows to display the exchange of power in a system by its graphical representation; due to causality assignment it gives the possibility of localization of the state variables and achieving the mathematical model in terms of state space equations in an easier way than using classical methods; provides information regarding the structural properties of the system, in terms of controllability and observability (Dauphin-Tanguy (2000), Roman and Bobasu (2006)); offers the possibility of building some observers (for example proportional-integer observers as an extension of Luenberger observers – see Pichardo-Almarza et al. (2005)), which can be used in the control design.

The Bond Graph modelling of some biological systems was reported in some works, such as Schnakenberg (1981), Linkens (1990). However, the Bond Graph modelling of biotechnological processes is not exploited yet. The present work addresses the pseudo Bond Graph modelling of nonlinear bioprocesses. The model of a prototype bioprocess is obtained using the reaction scheme. This bioprocess modelling approach will allow the exploit of the above mentioned advantages of Bond Graph technique, especially the analysis of structural properties and the observers design.

The organization of the paper is as follows. In Section 2, the Bond Graph technique and some issues regarding the bioprocess modelling are presented. Section 3 deals with the design of pseudo Bond Graph model of the simple micro-organisms growth process taking place in the batch and

continuous bioreactors. In Section 4, pseudo Bond Graph technique is applied to the aerobic micro-organisms growth process combined with an enzyme-catalysed process, which takes place into a fed-batch bioreactor. The behaviour of the model is simulated using the modelling and simulation environment 20sim (registered trademark of Controllab Products B.V. Enschede, Netherlands). The Bond Graph of the studied bioprocess and the time evolution of some state variables are presented and analysed. Finally, concluding remarks are collected in Section 5.

2. BOND GRAPH METHODOLOGY AND BIOPROCESSES MODELLING ISSUES

Bond Graph method uses the effort-flow analogy to describe physical processes. A Bond Graph consists of subsystems linked together by lines representing power bonds. Each process is described by a pair of variables, effort *e* and flow *f*, and their product is the power. The direction of power is depicted by a half arrow. In a dynamic system the effort and the flow variables, and hence the power fluctuate in time.

One of the advantages of Bond Graph method is that models of various systems belonging to different engineering domains can be expressed using a set of only nine elements. A classification of Bond Graph elements can be made up by the number of ports; ports are places where interactions with other processes take place. There are one port elements represented by inertial elements (I), capacitive elements (C), resistive elements (R), effort sources (Se) and flow sources (Sf), two ports elements represented by transformer elements (TF) and gyrator elements (GY), and multi ports elements - effort junctions (J0) and flow junctions (J1). I, C, and R elements are passive elements because they convert the supplied energy into stored or dissipated energy. Se and Sf elements are active elements because they supply power to the system and TF, GY, 0 and 1-junctions are junction elements that serve to connect I, C, R, Se and Sf, and constitute the junction structure of the Bond Graph model.

The concept of causality is an important concept embedded in Bond Graph theory. This refers to cause and effect relationship. Thus, as part of the Bond Graph modelling process, a causality assignment is implicitly introduced - see Karnopp and Rosenberg (1974), Thoma (1975). Causality is graphically represented by a short stroke, called causal stroke, placed perpendicular to the bond at one of its ends indicating the direction of the effort variable. Causal stroke assignment is independent of the power flow direction. This leads to the description of Bond Graphs in the form of state – space equation. The sources (Se and Sf) have fixed causality, the dissipative element (R) has free causality depending on the causality of the other elements of Bond Graph, and the storage elements (I, C) have preferential causality, that is integral causality or derivative causality, but it is always desirable that C and I elements to be in integral causality. Transformers, gyrators and junction elements have constrainedly causality.

Besides the power variables, two other types of variables are very important in describing dynamic systems and these variables, sometimes called energy variables, are the generalized momentum *p* as time integral of effort and the generalized displacement *q* as time integral of flow (Karnopp and Rosenberg (1974), Thoma (1975)).

In industry, the bioprocesses take place inside biological reactors, also called bioreactors, in which several biological reactions occur simultaneously in a liquid medium (Bastin and Dochain (1990), Dochain (2008)). The bioreactors can operate in three modes: the continuous mode, the fed-batch mode, and the batch mode. For example, in a Continuous Stirred Tank Bioreactor (CSTB), the substrates are fed to the bioreactor continuously and the effluent stream is continuously withdrawn from the CSTB, such that the culture volume is constant. By contrast, a Fed-Batch Bioreactor (FBB) initially contains a small amount of substrate and microorganisms, and is progressively filled with the influent stream.

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

$$\dot{\xi}_i = \sum_{j\sim i}(\pm)k_{ij}\varphi_j - D\xi_i + F_i - Q_i \,, \tag{1}$$

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

In order to obtain a dynamical state-space model of the entire bioprocess, we denote with $\xi = [\xi_1 \;\; \xi_2 \;\; \cdots \;\; \xi_n]'$ the n-dimensional vector of concentrations (the state of the model), where the apostrophe denote the transpose operator. The vector of the reaction rates (the reaction kinetics) is denoted $\varphi = [\varphi_1 \;\; \varphi_2 \;\; \cdots \;\; \varphi_m]'$. Usually, a reaction rate is represented by a non-negative rational function of the state ξ. The yield coefficients can be written as the $n \times m$ yield matrix $K = [K_{ij}]$, $i = \overline{1,n}$, $j = \overline{1,m}$, with $K_{ij} = (\pm)k_{ij}$ if $j \sim i$ and 0 otherwise.

$F = [F_1 \;\; F_2 \;\; \cdots \;\; F_n]'$ and $Q = [Q_1 \;\; Q_2 \;\; \cdots \;\; Q_n]'$ are the vector of rates of supply and the vector of rates of removal of the components in gaseous form, respectively.

From (1), using these notations, the global dynamics of the bioprocess can be represented by the following dynamical state-space model:

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

This model describes the behaviour of an entire class of bioprocesses and is referred to as the general dynamical state-space model of this class - see Bastin and Dochain (1990), Dochain (2008)).

In (2), the term $K \cdot \varphi(\xi)$ represents the reaction kinetics, and the term $-D\xi + F - Q$ represents the exchange with the environment.

3. BOND GRAPH MODELS OF THE SIMPLE MICRO-ORGANISMS GROWTH PROCESS

One of the simplest biological reactions is the micro-organisms growth process, with the reaction scheme (Bastin and Dochain (1990), Dochain (2008)) given by:

$$S \xrightarrow{\varphi} X \,, \tag{3}$$

where S is the substrate, X is the biomass and φ is the reaction rate.

This simple growth reaction represents in fact a prototype reaction, which can be found in almost every bioprocess. The dynamic of the concentrations of the components from reaction scheme (3) can be modelled considering the mass balance of the components; accordingly, a dynamical model of the form (2) can be obtained.

The dynamical model of the bioprocess (3) is quite simple, but if the reaction scheme is more complicated, the achievement of the dynamical model is difficult. In such cases, the Bond Graph method can be a suitable approach. In order to model bioprocesses, pseudo Bond Graph method is more appropriate because of the meaning of variables involved – effort (concentration) and flow (mass flow). Next, pseudo Bond Graph models for two prototype bioprocesses are obtained: the first one for a bioprocess taking place into a batch bioreactor and the second one for a CSTB case.

3.1 Batch bioreactor case

In the case of the batch bioreactor, there is no influent into or effluent stream from the bioreactor and the biomass X is periodically collected. From the reaction scheme (3) and taking into account the mass transfer through the batch bioreactor, using the modelling procedure described above, the pseudo Bond Graph model of the batch bioprocess is achieved and is depicted in Fig. 1. The directions of half arrows correspond to the run of the reaction, going out from the substrate S towards biomass X.

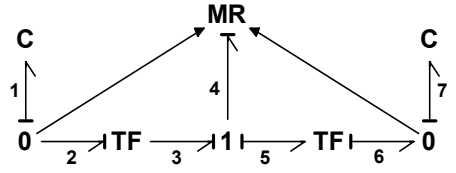

Fig. 1. Bond Graph model of the batch prototype bioprocess.

In the Bond Graph model, the mass balances of the species involved in the bioreactor are represented by two 0-junctions: $0_{1,2}$ (mass balance for substrate), $0_{6,7}$ (mass balance for biomass).

The constitutive relations of these junctions are characterized by the equality to zero of the sum of flow variables corresponding to the junction bonds. In order to model the rate of reaction φ, because of the dependency of substrate and biomass concentrations, we have used a modulated R element, denoted MR_4.

Thus, the accumulations of species S and X in the bioreactor are represented by bonds 1 and 7 and are modelled using capacitive elements C. The constitutive equations of C-elements are as follows:

$$e_1 = \frac{1}{C_1} q_1 = \frac{1}{C_1} \int_t (-f_2)dt \,,\; e_7 = \frac{1}{C_7} q_7 = \frac{1}{C_7} \int_t (f_6)dt \,. \tag{4}$$

From the constitutive relations of 1-junction, we obtain:

$$f_3 = f_4 = f_5 \,. \tag{5}$$

Using the constitutive relations of transformer elements $TF_{2,3}$ and $TF_{5,6}$ we obtain the relations for the flows f_2 and f_6:

$$f_2 = k_{2,3} f_4 \,,\; f_6 = \frac{1}{k_{5,6}} f_4 \,, \tag{6}$$

with $k_{2,3}$ and $k_{5,6}$ the transformers modulus, which are in fact yield coefficients of the bioprocess (their values equal one for this batch bioprocess).

In fact, e_1 is the substrate concentration, which will be denoted with S (g/l), e_7 is the biomass concentration X (g/l), f_4 is φ, and $C_1 = C_7 = V$ (l) is the volume of the bioreactor. Therefore, from (4)-(6) we will obtain the dynamical model of the batch bioproces:

$$\begin{aligned} V \frac{dS}{dt} &= V \cdot \dot{S}(t) = -\varphi V, \\ V \frac{dX}{dt} &= V \cdot \dot{X}(t) = \varphi V. \end{aligned} \tag{7}$$

The model (7) expresses the equations of mass balance for the reaction scheme (3). The dynamical behaviour of the concentrations can be easily obtained from (7):

$$\begin{aligned} \dot{S}(t) &= -\varphi, \\ \dot{X}(t) &= \varphi. \end{aligned} \tag{8}$$

A difficult task for the complete construction of the dynamical model (8) is the modelling of the reaction kinetics. The form of kinetics is complex, nonlinear and in many cases unknown. A general assumption (Dochain (2008)) is that a reaction can take place only if all reactants are presented in the bioreactor. Therefore, the reaction rates are necessarily zero whenever the concentration of one of the reactants is zero.

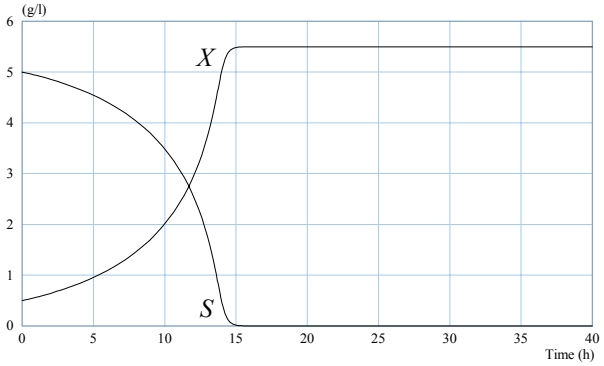

Fig. 2. Time profile of concentrations – batch bioprocess.

Thus, the reaction rate can be expressed as (see Bastin and Dochain (1990)):

$$\varphi(S,X) = \mu(S,X)\cdot X\,, \tag{9}$$

where μ is the specific growth rate. For the specific growth rate it exist many possible models, like Monod's law or Haldane kinetics.

We will consider that the specific growth rate is modelled as a Haldane law that takes into account the substrate inhibition on the growth:

$$\mu(S) = \mu^* \frac{S}{K_M + S + S^2/K_i}, \tag{10}$$

where K_M is the Michaelis-Menten constant, μ^* is the maxim specific growth rate, and K_i is the inhibition constant.

Using 20sim environment, the Bond Graph model from Fig. 1 is implemented. The time evolution of concentrations is also obtained, for different values of initial conditions. The simulation results for the time profile of S and X, using the reaction rate (9), (10), and the following bioreactor parameters: $\mu^* = 0.6\,h^{-1}$, $K_M = 10\,g/l$, $K_i = 0.1\,g/l$, are depicted in Fig. 2.

It can be observed that after the consumption of the substrate, the biomass growth is limited, which is a typical behaviour for the batch bioprocess with Haldane kinetics.

3.2 Continuous bioreactor case

In the second case - the continuous bioprocess, the substrate (the nutrient) is fed to the bioreactor continuously and an effluent stream is continuously withdrawn such that the culture volume is constant.

From the reaction scheme (3) and taking into account the mass transfer through the CSTB, using the Bond Graph modelling procedure, the pseudo Bond Graph model of the continuous bioprocess is achieved and is given in Fig. 3. The directions of half arrows correspond to the run of the reaction, going out from S to X.

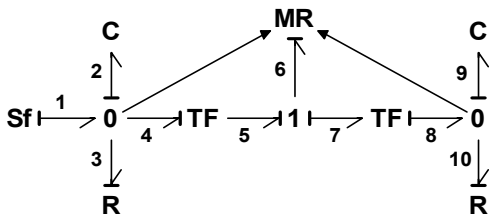

Fig. 3. Bond Graph model of the continuous bioprocess.

For the model presented in Fig. 3, the mass balances of the species involved in the bioreactor are represented by two 0-junctions: $0_{1,2,3,4}$ (mass balance for S), $0_{8,9,10}$ (mass balance for biomass X). A modulated resistive element MR_6 was used to model the reaction rate φ. Mass flow of the component entering the reaction is modelled using a source flow element Sf and quantities exiting from the reaction are modelled using resistive elements R represented by bonds 3 and 10. From the constitutive equations of R-elements we obtain:

$$f_3 = e_3 / R_3\,,\ f_{10} = e_{10} / R_{10}\,. \tag{11}$$

The accumulations of substrate and biomass in the CSTB are represented by bonds 2 and 9, and are modelled using capacitive elements C, with the constitutive equations:

$$e_2 = \frac{1}{C_2} q_2 = \frac{1}{C_2}\int_t (f_1 - f_3 - f_4)dt\,, \tag{12}$$

$$e_9 = \frac{1}{C_9} q_9 = \frac{1}{C_9}\int_t (f_8 - f_{10})dt\,. \tag{13}$$

The signification of Bond Graph elements is as follows: e_2 is the substrate concentration S (g/l), e_9 is the biomass concentration X (g/l), f_6 is the reaction rate φ, $C_2 = C_9 = V$ (l) is the volume of the bioreactor, and $R_3 = R_{10} = 1/F_0$, where F_0 is the output flow (l/h).

Therefore, from (11)-(13) and taking into account the constitutive relations of junction elements, we will obtain the dynamical model of the continuous bioprocess:

$$\begin{aligned} V\cdot\dot{S}(t) &= F_{in}S_{in} - F_0 S - \varphi V,\\ V\cdot\dot{X}(t) &= -F_0 X + \varphi V, \end{aligned} \tag{14}$$

where F_{in} is the influent substrate flow (l/h), S_{in} is the influent substrate concentration (g/l).

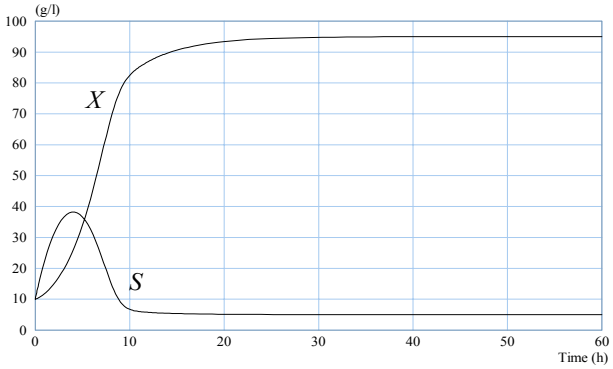

Fig. 4. Time evolution of concentrations- continuous process.

From the equation of continuity $F_{in} = F_0$ and using the so-called dilution rate $D = F_{in} / V = 1/t_r$, with t_r - medium residence time, the equations (14) become:

$$\begin{aligned} \dot{S}(t) &= DS_{in} - DS - \varphi, \\ \dot{X}(t) &= -DX + \varphi. \end{aligned} \tag{15}$$

The reaction rate can be expressed like in (9); here for the specific growth rate we will consider the Monod's law:

$$\mu(S) = \mu^* \frac{S}{K_M + S}, \tag{16}$$

where μ^* represents the maxim specific growth rate and K_M the Michaelis-Menten constant.

Using 20sim environment, the Bond Graph model from Fig. 3 is implemented. The simulation results for the time evolution of substrate and biomass concentrations are depicted in Fig. 4, using the reaction rate (9), (16), and the parameters:

$$\mu^* = 0.6h^{-1},\ K_M = 10g/l,\ D = 0.2h^{-1},\ S_{in} = 100g/l.$$

Again, the typical consumption of substrate and the growth of the biomass can be observed in Fig. 4.

4. BOND GRAPH MODEL OF AEROBIC MICRO-ORGANISMS GROWTH PLUS ENZYME – CATALYZED REACTION

In this section the micro-organisms growth process, combined with an enzyme-catalysed reaction will be modelled using pseudo Bond Graphs. The reaction scheme (see Bastin and Dochain (1990), Dochain (2008)) is:

$$\begin{cases} S + O \xrightarrow{\varphi_1 \leftarrow} X + P_1 \\ S + X \xrightarrow{\varphi_2 \leftarrow} P_2 + X \end{cases} \tag{17}$$

In the reaction scheme (17), S is the substrate, O is the dissolved oxygen, X is the biomass, P_1, P_2 are the products, and φ_1, φ_2 are the reaction rates.

Using the Bond Graph method, we will derive a model of the bioprocess (17). In order to model this kind of processes, pseudo Bond Graph method is more appropriate because of the meaning of variables involved – effort (concentration) and flow (mass flow). This offers a flexible way to manage the material balances in terms of differential equations without losing the advantages of true Bond Graphs.

From the reaction scheme (17), and considering the mass transfer through the fed-batch bioreactor, using the modelling procedure described in Section 2, the pseudo Bond Graph model of the bioprocess is achieved. This model is presented in Fig. 5.

The directions of the half arrows in the Bond Graph correspond to the progress of the reactions, going out from the components S and O towards X and P_1 for the first reaction, and from S and X towards X and P_2 for the second reaction. In Bond Graph terms, the mass balances of the species involved in the bioreactor are represented by five 0-junctions: $0_{1,2,3,4,20}$ (mass balance for S), $0_{6,7,8,9}$ (mass balance for O), $0_{13,14,15,28,29}$ (mass balance for X), $0_{17,18,19}$ (mass balance for P_1), and $0_{24,25,26}$ (mass balance for P_2).

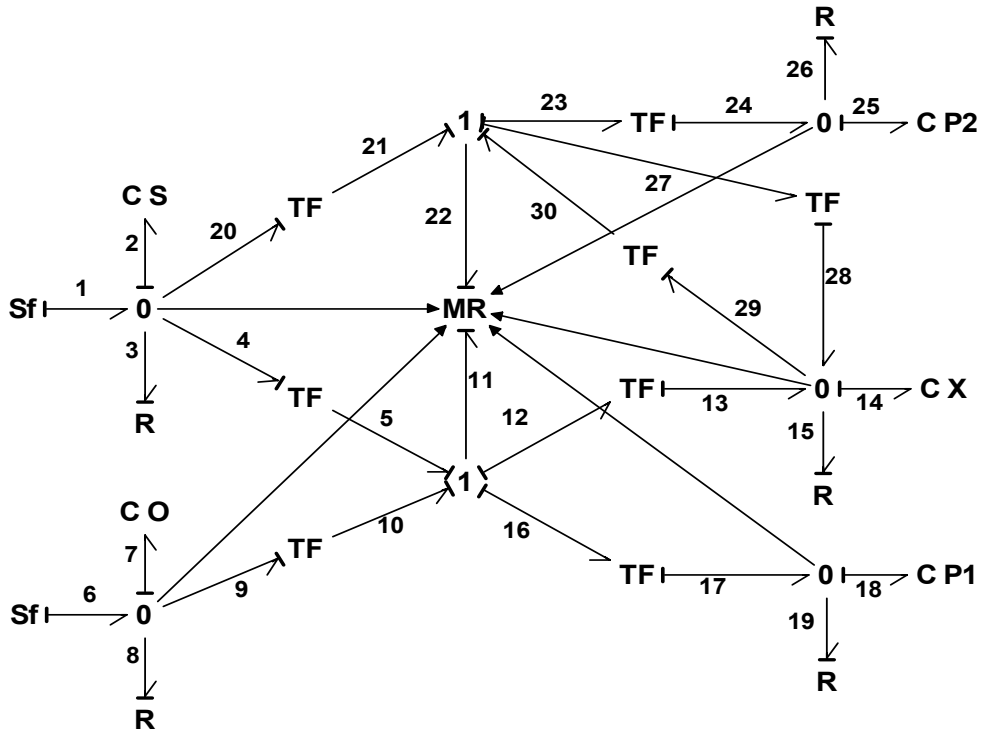

Fig. 5. Pseudo Bond Graph model of the aerobic micro-organism growth bioprocess.

The constitutive relations of these junctions are characterized by the equality to zero of the sum of flow variables corresponding to the junction bonds; therefore, the next relations are obtained:

$$f_1 - f_2 - f_3 - f_4 - f_{20} = 0,\ f_6 - f_7 - f_8 - f_9 = 0,$$
$$f_{13} - f_{14} - f_{15} + f_{28} - f_{29} = 0,$$
$$f_{17} - f_{18} - f_{19} = 0,\ f_{24} - f_{25} - f_{26} = 0.$$

Thus, the accumulations of species *S*, *O*, *X*, P_1 and P_2 in the bioreactor are represented by bonds 2, 7, 14, 18 and 25, respectively, and are modelled using capacitive elements C. The constitutive equations of C-elements are as follows:

$$e_2 = \frac{1}{C_2} q_2 = \frac{1}{C_2} \int_t (f_1 - f_3 - f_4 - f_{20}) dt,$$
$$e_7 = \frac{1}{C_7} q_7 = \frac{1}{C_7} \int_t (f_6 - f_8 - f_9) dt,$$
$$e_{14} = \frac{1}{C_{14}} q_{14} = \frac{1}{C_{14}} \int_t (f_{13} - f_{15} + f_{28} - f_{29}) dt, \quad (18)$$
$$e_{18} = \frac{1}{C_{18}} q_{18} = \frac{1}{C_{18}} \int_t (f_{17} - f_{19}) dt,$$
$$e_{25} = \frac{1}{C_{25}} q_{25} = \frac{1}{C_{25}} \int_t (f_{24} - f_{26}) dt,$$

where C_2, C_7, C_{14}, C_{18} and C_{25} are the parameters of C-elements:

$$C_2 = C_7 = C_{14} = C_{18} = C_{25} = V,$$

with *V* being the bioreactor volume (l).

The unreacted masses exiting from the reaction are modelled using resistive elements R represented by bonds 3, 8, 15, 19 and 26; the constitutive equations of these elements are:

$$f_3 = e_3 / R_3,\ f_8 = e_8 / R_8,\ f_{15} = e_{15} / R_{15}, \quad (19)$$
$$f_{19} = e_{19} / R_{19},\ f_{26} = e_{26} / R_{26}, \quad (20)$$

where R_3, R_8, R_{15}, R_{19} and R_{26} are parameters of R-elements: $R_3 = R_8 = R_{15} = R_{19} = R_{22} = 1/F_0$ and F_0 is the output flow (*l*/*h*).

Mass flows of the components entering the reaction are modelled using two flow sources elements Sf_1 and Sf_6, and the transformer elements $TF_{4,5}$, $TF_{9,10}$, $TF_{12,13}$, $TF_{16,17}$, $TF_{20,21}$, $TF_{23,24}$, $TF_{27,28}$, $TF_{29,30}$ were introduced to model the yield coefficients. For the modelling of the reaction rates we used a modulated two-port R-element, $MR_{11,22}$.

The first port of this element represents the reaction rate φ_1, and the second one gives the reaction rate φ_2. From the constitutive relations of the two 1-junction elements, $1_{5,10,11,12,16}$ and $1_{21,22,23,27,30}$ we obtain:

$$f_5 = f_{10} = f_{11} = f_{12} = f_{16},$$
$$f_{21} = f_{22} = f_{23} = f_{27} = f_{30},$$

where f_{11} is the reaction rate φ_1 and f_{22} the reaction rate φ_2.

From the constitutive relations of transformer elements we obtain the relations for the flows:

$$f_4 = k_{4,5} f_5,\ f_9 = k_{9,10} f_{10},\ f_{13} = f_{12} / k_{12,13},$$
$$f_{17} = f_{16} / k_{16,17},\ f_{20} = k_{20,21} f_{21},\ f_{23} = f_{24} / k_{23,24}, \quad (21)$$
$$f_{29} = k_{29,30} f_{30},\ f_{28} = f_{27} / k_{27,28},$$

with $k_{4,5}$, $k_{9,10}$, $k_{12,13}$, $k_{16,17}$, $k_{20,21}$, $k_{23,24}$, $k_{29,30}$, $k_{27,28}$ being the transformers modulus, which are in fact yield coefficients of the bioprocess.

The signification of Bond Graph elements is as follows: e_2 is the substrate concentration *S* (*g*/*l*), e_7 - the oxygen concentration *O* (*g*/*l*), e_{14} - the biomass concentration *X* (*g*/*l*), e_{18} is the product concentration P_1 (*g*/*l*), e_{25} is the product concentration P_2 (*g*/*l*), $f_1 = F_{inS} S_{in}$, $f_6 = F_{inO} O_{in}$ where F_{inS} is the influent substrate flow (*l*/*h*), F_{inO} is the influent oxygen flow (*l*/*h*), S_{in} is the influent substrate concentration (*g*/*l*), O_{in} is the influent oxygen concentration (*g*/*l*). Using these notations, from (18) we will obtain the dynamical model of the microorganism growth bioprocess:

$$V \cdot \dot{S}(t) = F_{inS} S_{in} - F_0 S - k_{4,5} \varphi_1 V - k_{20,21} \varphi_2 V,$$
$$V \cdot \dot{O}(t) = F_{1inO} O_{in} - F_0 O - k_{9,10} \varphi_1 V,$$
$$V \cdot \dot{X}(t) = -F_0 X + 1/k_{12,13} \cdot \varphi_1 V - k_{29,30} \varphi_2 V + 1/k_{27,28} \cdot \varphi_2 V \quad (22)$$
$$V \cdot \dot{P}_1 = -F_0 P_1 + 1/k_{16,17} \cdot \varphi_1 V,$$
$$V \cdot \dot{P}_2 = -F_0 P_2 + 1/k_{23,24} \cdot \varphi_2 V.$$

From the equation of continuity $F_{in} = F_0$, using the dilution rate $D = F_{in} / V = 1/t_r$, with t_r - medium residence time, and taking into account that $k_{12,13} = k_{23,24} = 1$ and $k_{28,29} = k_{27,28}$, the above equations become:

$$\dot{S}(t) = DS_{in} - DS - k_{4,5} \varphi_1 - k_{20,21} \varphi_2,$$
$$\dot{O}(t) = DO_{in} - DO - k_{9,10} \varphi_1,$$
$$\dot{X}(t) = -DX + \varphi_1, \quad (23)$$
$$\dot{P}_1(t) = -DP + 1/k_{16,17} \cdot \varphi_1,$$
$$\dot{P}_2(t) = -DP_2 + 1/k_{23,24} \cdot \varphi_2.$$

The kinetics for this bioprocess can take the form:

$$\varphi_1 = X \cdot \mu_1(S) = X \cdot \frac{\mu_1^* S}{K_{M1} + S}, \quad (24)$$

$$\varphi_2 = X \cdot \mu_2(S) = X \cdot \frac{\mu_2^* S}{K_{M_2} + S + S^2 / K_{i_2}}, \quad (25)$$

where $K_{M_1}, \mu_1^*, K_{M_2}, \mu_2^*, K_{i_2}$ are the kinetic parameters.

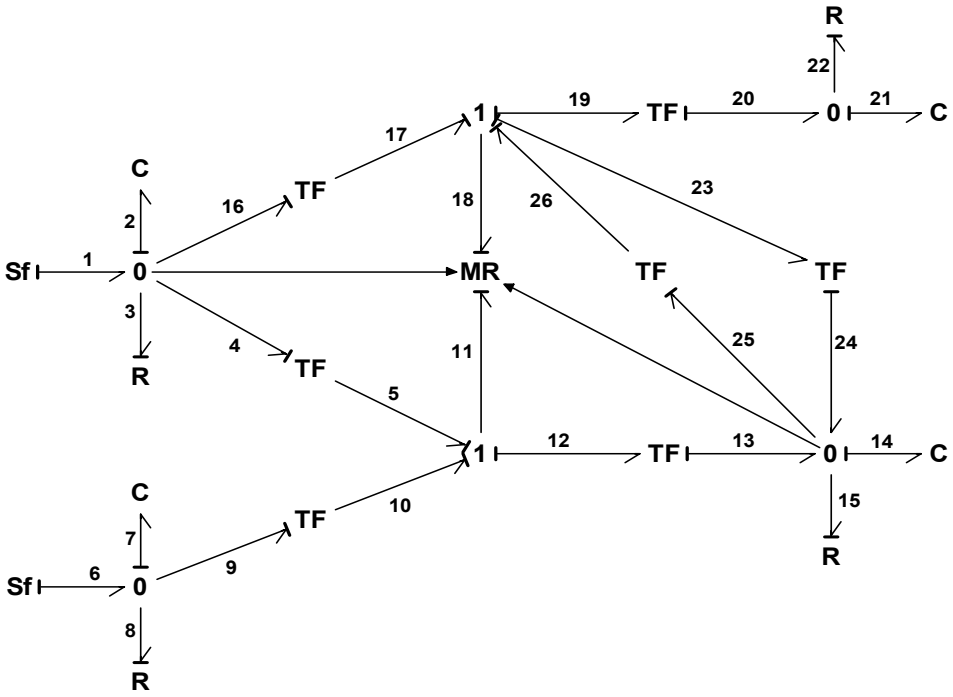

Fig. 6. Pseudo Bond Graph model of the simplified aerobic micro-organism growth plus enzyme-catalyzed bioprocess.

The dynamical model (22) (or (23)), obtained using the Bond Graph approach, is equivalent with the dynamical state-space model obtained using classical methods in Bastin and Dochain (1990), Dochain (2008).

The reaction scheme (17) and the dynamic model thus obtained are very complex and the design of useful control strategies is hampered because of the large dimension of the model. So, it is necessary to use a simplified model for control purposes, taking into consideration some particular aspects. For example, a simplified reaction scheme is:

$$\begin{cases} S + O \xrightarrow{\varphi_1} X \\ S + X \xrightarrow{\varphi_2} P + X \end{cases} \tag{26}$$

Using the same procedure as before, the pseudo Bond Graph model (Fig. 6) of the bioprocess is achieved starting from the reaction scheme (26), and considering the mass transfer through the fed-batch bioreactor.

Following the above steps it is obtained the dynamical model of the aerobic micro-organism growth plus enzyme-catalyzed reaction:

$$\begin{aligned} \dot{S}(t) &= DS_{in} - DS - k_{4,5}\varphi_1 - k_{16,17}\varphi_2 \\ \dot{O}(t) &= DO_{in} - DO - k_{9,10}\varphi_2 \\ \dot{X}(t) &= -DX + \varphi_1 \\ \dot{P}(t) &= -DP + \varphi_2 \end{aligned} \tag{27}$$

Several simulations were achieved in 20sim environment, using the Bond Graph from Fig. 6, for different initial conditions and values of the bioprocess parameters. The results of one of these simulations are depicted in Fig. 7, where the time evolution of concentrations is depicted.

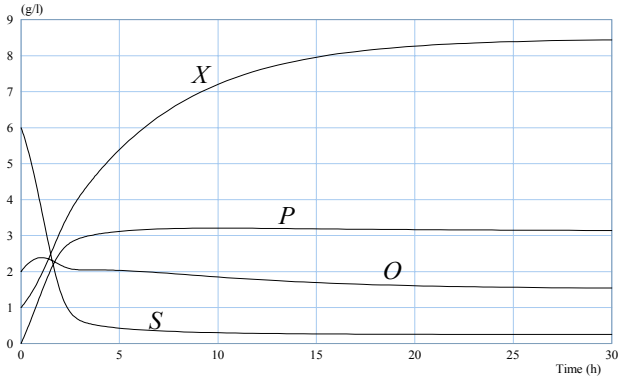

Fig. 7. Time evolution of concentrations – fed-batch process.

From Fig. 7, it can be seen that the consumption of the substrate and of dissolved oxygen is associated with the formation of the product and biomass growth.

The simulation was performed using the following CSTB parameters (Petre and Selişteanu (2005)):

$k_{4,5} = k_{9,10} = 1$, $k_{16,17} = 2$, $D = 0.2h^{-1}$, $S_{in} = 32g/l$, $F_2 = 2g/lh$, $\mu^* = 1h^{-1}$, $K_i = 10g/l$, $K_{M_1} = 20g/l$, $K_{M_2} = 1g/l$.

5. CONCLUSIONS

This paper deals with a novel modelling method for biotechnological processes based on pseudo Bond Graph technique. The rules for the design of pseudo Bond Graph models are applied on some prototype bioprocesses using the reaction schemes and the analysis of biochemical phenomena inside the bioreactor. The bioprocesses are considered taking place into bioreactors functioning in the batch, fed-batch and continuous modes. The dynamic models were achieved from

the pseudo Bond Graph model. The simulations using the 20sim environment show a good accuracy of the proposed method.

The models obtained, using the Bond Graph approach, are equivalent to bioprocess' models obtained using classical methods (see, for example, Bastin and Dochain, (1990), Dochain (2008)). The use of this technique for bioprocesses will allow the analysis of structural properties, and also the design of observers for control purposes.

ACKNOWLEDGEMENTS

This work was created in the frame of the research projects CNCSIS (National University Research Council), ID 686/ 2007 and ID 548/2009, Romania.

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