

ADAPTIVE CONTROL FOR MAXIMUM PRODUCTIVITY OF CONTINUOUS BIOPROCESSES

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Abstract

*A new adaptive linearizing control algorithm that stabilizes the target product concentration in the culture medium in such value that guarantees maximum production rate is presented. This algorithm is applied on gluconic acid production by *Aspergillus Niger*. A model for control of the investigated process is derived. The model identification is made on the basis of experimental data and a reduced biotechnological model of batch phase of the process. The switching from batch to continuous mode of cultivation was realized automatically in time when the gluconic acid production rate reaches one maximal value. This information was received by software sensor of gluconic acid production rate. The proposed control algorithm stabilizes the concentration of gluconic acid in the culture medium at value corresponding to the maximal gluconic acid production rate. The simulation results are promising and could be verified in laboratory conditions.*

Keywords: continuous fermentation, adaptive control, gluconic acid

1. INTRODUCTION

Biotechnological processes as highly nonlinear and non-stationary require special methods for their monitoring and control. One widely used approach is adaptive linearizing control, which solves the problems mentioned above. This approach is proposed in [1].

Gluconic acid finds extensive uses in the food, pharmaceutical, and other industrial fields. In the textile industries gluconic acid is used as acid catalysts. Now a day, the industrial production of gluconic acid is by the microorganisms *Aspergillus* and *Pseudomonas* genera. The main substrate is glucose. The conversion of glucose to gluconic acid is a simple oxidation of the aldehyde group of the sugar to a carboxyl group. In the case of *Aspergillus niger*, the basic process is well known and has been the subject of ongoing studies for some time [3,4,5]. The investigations are focused on areas such as the factors that regulate production [4], the selection of productive strains in moderate concentrations of glucose, the mechanisms of expression linked to overproduction, etc. There is much less information, regarding the kinetic aspects of the culture and its formal modeling, in spite of it being a case that presents aspects of special interest especially models like GDM.

In [4], the kinetics of fermentation of glucose to gluconic acid by *Pseudomonas* strain is investigated. A model for cell growth, gluconolactone, and gluconic acid formation and glucose consumed is proposed. The model parameters dependence on the temperature and pH is used to determine the optimal values of temperature (34.2°C) and pH (7.0) that maximize gluconic acid production. That optimal values are applied as set values of temperature and pH during the gluconic acid fermentation by *A. niger* with automatic control of that physical process variables. Another mathematical model of gluconic acid fermentation by *A. niger* is proposed in [5]. The model has been deduced from cell population balance and it is applied only for dynamics description of both batch and continuous cultures. In [8] and [9], the fermentation kinetics of gluconic acid by *Aspergillus niger* are studied in batch systems. Simple models as: logistic equation for biomass growth [8]; Contois model for specific growth rate on carbon and oxygen substrates [9] and the Luedeking-Piret equation for gluconic acid production ([8] and [9]). are proposed. Estimated parameters of these models indicate that the production of gluconic acid is mostly growth-associated.

On studying the production of glucose oxidase by the *A. niger* [3], it is found that both growth of microorganism and gluconic acid production are diauxic processes, with logistic and linear phases. Once

the glucose is exhausted, the microorganism begins to use the gluconic acid that had accumulated during the logistic stage as an alternative carbon source with basically linear kinetics. The gluconic acid is the target product in the process under consideration, so the linear phase have to be avoided during the investigations of batch cultivation.

The general requirement for process control design is to have available on-line information about all main process variables. The control task is to maintain a previously set value of gluconic acid concentration in the reactor.

The main purpose of this study is to design a linearizing control for continuous gluconic acid fermentation by *A. niger* according to the method proposed in [1]. For this purpose, a General Dynamical Model (GDM) of the process has to be derived using the process reaction scheme. The observers of unmeasured variables biomass and gluconic acid have to be designed using this GDM and on-line measured variables glucose and dissolved oxygen. Control algorithms have to be verified by simulation investigations.

2. PROCESS MODEL

2.1. Biotechnological model

The fermentation mechanism can be presented by the following reaction scheme:



The first four reactions describe the logistic phase of the fermentation [3]. The last reaction represents the consumption of gluconic acid as an alternative carbon source for biomass growth. That reaction has to be avoided as the gluconic acid is the target process product and its consumption is undesired. The reaction rates of glucosylolactone (*GOT*) production, R_{GOT} , and its consumption for gluconic acid (*GA*) production, R_{GA} , are equal. The dynamics of *GOT* could be neglected and because the dynamics of hydrogen peroxide (H_2O_2) is very fast, the fourth reaction can also be neglected. Following this the reaction scheme can be reduced to only two reactions:



The biotechnological model (BM) describes the process dynamics as follows:

$$\frac{dX}{dt} = R_X; \tag{3}$$

$$\frac{dG}{dt} = -k_1 R_X - k_2 \tag{4}$$

$$\frac{dGA}{dt} = R_{GA} \tag{5}$$

$$\frac{dO}{dt} = -k_3 R_{GA} + K_L a (O_2^* - O_2) \quad (6)$$

where

$$R_X = \mu_{max} X \frac{k-X}{k}; \quad (7)$$

$$R_{GA} = \mu_{GA} GA \frac{(k_{GA}-GA)}{k_{GA}}; \quad (8)$$

The biotechnological model (3 till 8) parameters are estimated using the experimental data of the logistic phase of a batch fermentation [6].

Coefficients	k_1	k_2	k_3	k	k_{GA}	μ_{max}	μ_{GA}
Values	1.0240	1.1647	0.4710	3.1114	146.0696	0.1986	0.2394

Table 1. Best parameter's values

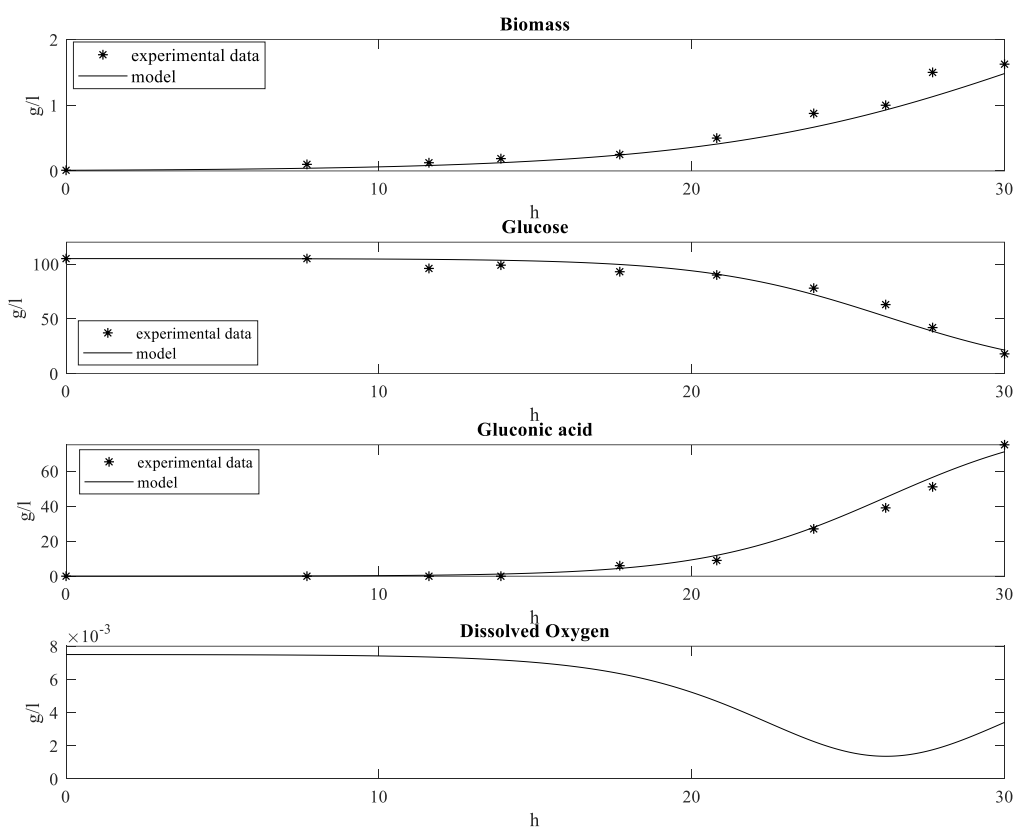


Fig. 1. Biochemical model validation

In Fig. 1, simulations of BM (3 till 8) are cross-validated on experimental data.

An algorithm for optimization that was proposed in [2] is applied for model parameter identification. The optimization criterion is chosen to obtain the minimal error between experimental data and the simulations of the system (3)-(8). The results of this parameter identification are shown in Table 1. The simulations show that the BM (lines) fits well with experimental points (stars) and a model with such a structure could be used instead the real object for future studies of the fermentation process.

2.2. Model for control

According to [1], the General Dynamical Model (GDM) of a continuous biotechnological process can be presented in matrix form as follows:

$$\dot{\xi} = \mathbf{K}\varphi - D\xi + \mathbf{F} \quad (9)$$

where

ξ is a vector-column of process variables;

$\mathbf{K}$ is a matrix of yield coefficients;

φ is a vector-column of reaction rates;

D is the dilution rate;

$\mathbf{F}$ is mass feed rate in the reactor.

It is considered the reaction rates, φ as unknown and the reaction scheme (2) is replaced with a new one:



Following the rules proposed in [1], the model of control is derived fully automatically on the basis of (10). For the continuous fermentation of gluconic acid, the operational model (9) is presented as follows:

$$\begin{bmatrix} \dot{X} \\ \dot{G} \\ \dot{O}_2 \\ \dot{GA} \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ -k_1 & -k_2 \\ 0 & -k_3 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} \varphi_1 \\ \varphi_2 \end{bmatrix} - D \begin{bmatrix} X \\ G \\ O_2 \\ GA \end{bmatrix} + \begin{bmatrix} 0 \\ DG_{in} \\ K_L a(O_2^* - O_2) \\ 0 \end{bmatrix} \quad (11)$$

The main role of GDM is to translate the available process information into appropriate inputs for process control design. For this purpose, a transformed version of the model has to be derived that uses the available process information only – on-line measured variables glucose (G), dissolved oxygen (O_2) and the known transport dynamics of oxygen ($K_L a(O_2^* - O_2)$) and of glucose DG_{in} , where G_{in} is the glucose concentration in the feed.

2.3 Observers design

The model transformation is made applying the basic property of GDM [1]. According to that property, there exists a state transformation

$$\mathbf{Z} = \mathbf{A}_0 \xi_a + \xi_b \quad (12)$$

where $\mathbf{A}_0$, is the unique solution to the matrix equation,

$$\mathbf{A}_0 \mathbf{K}_a + \mathbf{K}_b = 0 \quad (13)$$

such that the state-space model (9) is equivalent to

$$\dot{\xi}_a = \mathbf{K}_a \varphi(\xi_a, \xi_b) \quad (14a)$$

$$\dot{\mathbf{Z}} = \mathbf{A}_0 \mathbf{F}_a + \mathbf{F}_b \quad (14b)$$

State variables of model (9 till 11) are divided into unmeasured variables, ξ_a , and measured ones, ξ_b and appropriated matrix of yield coefficients are defined:

$$\begin{aligned} \xi_a &= \begin{bmatrix} X \\ GA \end{bmatrix}, \xi_b = \begin{bmatrix} G \\ O_2 \end{bmatrix}; \mathbf{K}_a = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}; \mathbf{K}_b = \begin{bmatrix} -k_1 & -k_2 \\ 0 & -k_3 \end{bmatrix}; \\ \mathbf{F}_a &= 0 \text{ and } \mathbf{F}_b = \begin{bmatrix} DG_{in} \\ K_L a(O_2^* - O_2) \end{bmatrix} \end{aligned} \quad (15)$$

$$\text{According to (13)} \quad \mathbf{A}_0 = \frac{-\mathbf{K}_b}{\mathbf{K}_a} = \begin{bmatrix} k_1 & k_2 \\ 0 & k_3 \end{bmatrix} \quad (16)$$

and according to (14b)

$$\mathbf{Z} = \mathbf{A}_0 \boldsymbol{\xi}_a + \boldsymbol{\xi}_b = \begin{bmatrix} Z_1 \\ Z_2 \end{bmatrix} = \begin{bmatrix} k_1 & k_2 \\ 0 & k_3 \end{bmatrix} \begin{bmatrix} X \\ GA \end{bmatrix} + \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} G \\ O_2 \end{bmatrix}$$

The expressions of the auxiliary variables ($\mathbf{Z}$) are as follows:

$$Z_1 = k_1 X + k_2 GA + G \quad (17a)$$

$$Z_2 = k_3 GA + O_2 \quad (17b)$$

As the values of kinetic parameters k_1 , k_2 and k_3 are known, the estimated values of X and GA could be obtained from (17) using the expressions

$$X_e = \frac{1}{k_1} Z_1 - \frac{k_2}{k_1 k_3} (Z_2 - O_2) - \frac{1}{k_1} G \quad (18a)$$

$$GA_e = \frac{1}{k_3} (Z_2 - O_2) \quad (18b)$$

where the values of auxiliary variables can be obtained on the basis of known process transport dynamics by the system

$$\dot{Z}_1 = -DZ_1 + DG_{in}; \quad (19a)$$

$$\dot{Z}_2 = -DZ_2 + K_L a(O_2^* - O_2); \quad (19b)$$

3. ADAPTIVE LINEARIZING CONTROL DESIGN

3.1. Transformation of the model for control

The adaptive linearizing control algorithm is designed under following conditions:

- all process variables are considered measured (glucose and dissolved oxygen) or observed (biomass and gluconic acid by (17 and 18));
- process transport dynamics is known;
- the yield coefficients are known;
- the initial conditions of process variables are known;
- the glucose concentration in the feed, G_{in} , is known;
- the reaction rates are unknown;
- the dilution rate, D , is the control system input;
- the gluconic acid concentration in the reactor is the control system output.

The main idea of control model transformation is to summarize all known process information in separated terms. At the same time, the unknown process kinetic has to be presented with unknown time varying parameters. For this purpose the model (9) can be rewritten:

$$\dot{\boldsymbol{\xi}} = \mathbf{K}\mathbf{H}\boldsymbol{\alpha} - D\boldsymbol{\xi} + \mathbf{F} \quad (20)$$

where $\boldsymbol{\xi}$, $\mathbf{K}$ and $\mathbf{F}$ are taken from (10) and the reaction rates. φ_1 and φ_2 , are presented as follows:

$$\varphi_1 = X_e G \alpha_1 \quad (21)$$

$$\varphi_2 = G O_2 \alpha_2 \quad (22)$$

$$\mathbf{H} = \begin{bmatrix} XG & 0 \\ 0 & GO_2 \end{bmatrix} \text{ is the matrix of known process variables (measured or observed);} \quad (23)$$

$$\alpha = \begin{bmatrix} \alpha_1 \\ \alpha_2 \end{bmatrix} \text{ is a vector-column of unknown time varying parameters;} \quad (24)$$

The unknown term $\mathbf{KH}\alpha$ on the right hand-side of the equation (20) can be presented in a linear regression form, $(\Phi\theta)$, as follows

$$\mathbf{KH}\alpha = \begin{bmatrix} 1 & 0 \\ -k_1 & -k_2 \\ 0 & -k_3 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} X_e G & 0 \\ 0 & G O_2 \end{bmatrix} \begin{bmatrix} \alpha_1 \\ \alpha_2 \end{bmatrix} \quad (25)$$

$$\mathbf{KH}\alpha = \Phi\theta = \begin{bmatrix} X_e G & 0 & 0 & 0 & 0 \\ 0 & -X_e G & -G O_2 & 0 & 0 \\ 0 & 0 & 0 & -G O_2 & 0 \\ 0 & 0 & 0 & 0 & G O_2 \end{bmatrix} \begin{bmatrix} \theta_1 \\ \theta_2 \\ \theta_3 \\ \theta_4 \\ \theta_5 \end{bmatrix} \quad (26)$$

$$\text{where } \theta_1 = \alpha_1; \theta_2 = k_1 \alpha_1; \theta_3 = k_2 \alpha_2; \theta_4 = k_3 \alpha_2; \theta_5 = \alpha_2. \quad (27)$$

are new unknown kinetic parameters. They are defined as polynomial combinations of yield coefficients and unknown time-varying parameters α_1 and α_2 .

Taking in to account (26) the model (20) can be rewritten in linear regression form

$$\dot{X}_e = X_e G \theta_1 - D X_e \quad (28)$$

$$\dot{G} = -X_e G \theta_2 - G O_2 \theta_3 - D(G - G_{in}) \quad (29)$$

$$\dot{O}_2 = -G O_2 \theta_4 - D O_2 + K_L \alpha (O_2^* - O_2) \quad (30)$$

$$\dot{G A}_e = G O_2 \theta_5 - D G A \quad (31)$$

3.2. Observer-based estimator of unknown kinetic parameters

The new unknown kinetic parameters (27) can be estimated by an observer-based estimator

$$\widehat{X}_e = X_e G \theta_1 - D X_e + \omega_1 (X_e - \widehat{X}_e) \quad (32)$$

$$\widehat{G} = -X_e G \theta_2 - G O_2 \theta_3 - D(G - G_{in}) + \omega_2 (G - \widehat{G}) \quad (33)$$

$$\widehat{O}_2 = -G O_2 \theta_4 - D O_2 + K_L \alpha (O_2^* - O_2) + \omega_3 (O_2 - \widehat{O}_2) \quad (34)$$

$$\widehat{G A}_e = G O_2 \theta_5 - D G A + \omega_4 (G A_e - \widehat{G A}_e) \quad (35)$$

$$\widehat{\theta}_1 = \widehat{X}_e G \gamma_1 (X_e - \widehat{X}_e) \quad (36)$$

$$\widehat{\theta}_2 = -\widehat{X}_e G \gamma_2 (G - \widehat{G}) \quad (37)$$

$$\widehat{\theta}_3 = -G O_2 \gamma_2 (G - \widehat{G}) \quad (38)$$

$$\widehat{\theta}_4 = -G O_2 \gamma_3 (O_2 - \widehat{O}_2) \quad (39)$$

$$\widehat{\theta}_5 = G O_2 \gamma_4 (G A_e - \widehat{G A}) \quad (40)$$

where $\omega_1, \omega_2, \omega_3, \omega_4$ and $\gamma_1, \gamma_2, \gamma_3, \gamma_4$ are the estimator design parameters. The observer-based estimator (32&40) design parameters $\omega_1, \omega_2, \omega_3, \omega_4$ are estimated using the batch data of process variables (experimental points for biomass, glucose and gluconic acid and model values of dissolved oxygen) by optimization procedure proposed in [2]. The estimated values are shown in Table 2.

Parameter	ω_1	ω_2	ω_3	ω_4
Value	0.615	3.115	329.832	4.771

Table 2. Best parameter's values

Values of design parameters $\gamma_1, \gamma_2, \gamma_3, \gamma_4$ are calculated as follows:

$$\gamma_1 = \omega_1^2 / 4(X_e G)^2; \quad (41)$$

$$\gamma_2 = \omega_2^2 / 4[(X_e G)^2 + (GO_2)^2]; \quad (42)$$

$$\gamma_3 = \omega_3^2 / 4(GO_2)^2; \quad (43)$$

$$\gamma_4 = \omega_4^2 / 4(GO_2)^2; \quad (44)$$

The relationships (41 till 44) are derived taking into account the requirements of suability analysis of observation and tracking error dynamics [1].

3.3. Adaptive linearizing control design

The linearizing control design consists of three main steps. The first one is a choice of the input/output model of the closed-loop system. In the case under consideration, the control system input is the dilution rate, D , and the system output is the glucose concentration, G . Hence, the input/output model is presented with equation (29).

$$dGA_e/dt = GO_2\theta_5 - DGA_e \quad (45)$$

In consequence of the specific structure of the GDM (28 till 31) the input/output model is linear with respect to the control input (D). Hence, the second step is to select a stable reference model of the tracking error, $(GA^*(t) - GA(t))$. A first order reference model is selected. In the case of stabilisation, $dGA^*/dt = 0$ because GA^* is a constant value, and the reference model can be presented as follows:

$$\lambda(GA^* - GA_e) = dGA_e/dt \quad (46)$$

where λ is the controller coefficient. Its value has obviously be chosen so that the equation $\lambda d(GA^* - GA_e)/dt = 0$ is stable.

The third step is a substitution of the input/output model (45) in the reference one (46):

$$\lambda(GA^* - GA_e) = GO_2\theta_5 - DGA_e \quad (47)$$

The control algorithm is derived solving the equation (46) with respect of control input D .

$$D = \frac{-\lambda(GA^* - GA_e) + GO_2\theta_5}{GA_e} \quad (48)$$

The algorithm (48) is adaptive one because the values of unknown kinetic parameters θ_2 and θ_3 as well as value of biomass concentration, X_e , are estimated on each iteration according (37), (38) and (18) respectively

4. RESULTS AND DISCUSSION

The control scheme including nonlinear bioreactor presented by biotechnological model (2&8); observer of unmeasured biomass and gluconic acid (18), estimator of unknown kinetic parameters (36&40) and adaptive controller (48) are investigated by simulations. That control system is given in figure 2.

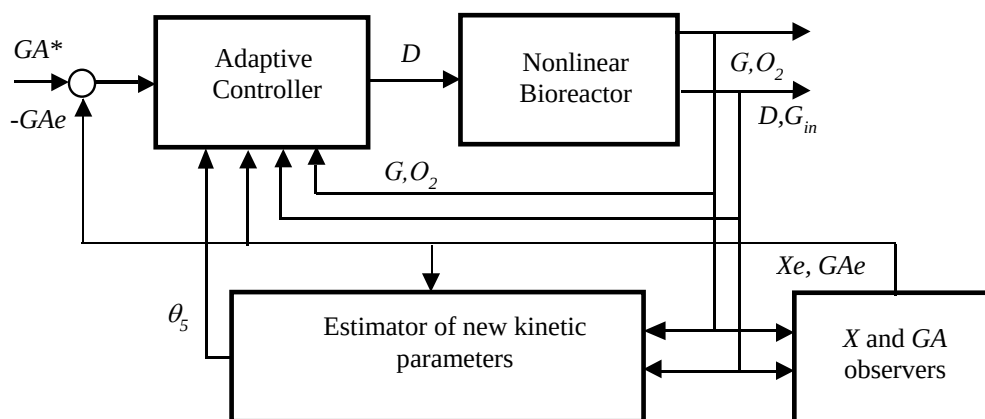


Fig. 2. Control scheme

The simulations are realized under following conditions:

The fermentation is started as batch one. The initial values of process variables are: $X_e(0) = 0.1$ [g/l]; $G(0) = 0.01$ [g/l]; $O_2(0) = 0.0075$ [g/l]; $GA_e(0) = 0.01$ [g/l]. The values of model (2 till 8) parameters are given in Table 1. The value of glucose concentration in the feed, G_{in} , is equal to 200 [g/l]. This value is chosen from expert's point of view. For initial values of biomass and gluconic acid estimators (18) are taken as the initial values of model equations (2) and (5) because these values are known at the begging of the fermentation.

One of the main problems that have to be solved is the appropriate moment of control turn on. In the case under gluconic acid production rate reaches at 33 h one maximal value of 8.5 g/lh corresponding to $GA = 93$ g/l in the culture brouth. This values is accepted as the set value, GA^* , in the control algorithm (48).

The simulation investigation of the control scheme is shown in figure 3. Model simulations are given with lines. Estimations of biomass and gluconic acid are shown with dashed lines. Experimental points of batch phase are given with circles. In figure 3a the curves of glucose and gluconic acid are shown. In figure 3b the biomass is given. In figure 3c, the dissolved oxygen is shown and in figure 3d the control input – dilution rate is given.

As can be seen in the sub-figure 3a (dashed line) during the control, gluconic acid keeps a high value closed to $GA^* = 93$ g/l. In the batch process its concentration decreases as it is used as a substrate for the biomass growth (see Fig. 3b (circles)). During the continuous process, the growth of biomass decreases (Fig. 3b (dashed line)) due to lack of substrate.

These results could be accepted as good because the estimates of biomass and gluconic acid obtained be same algorithms during the batch phase fit well with experimental points.

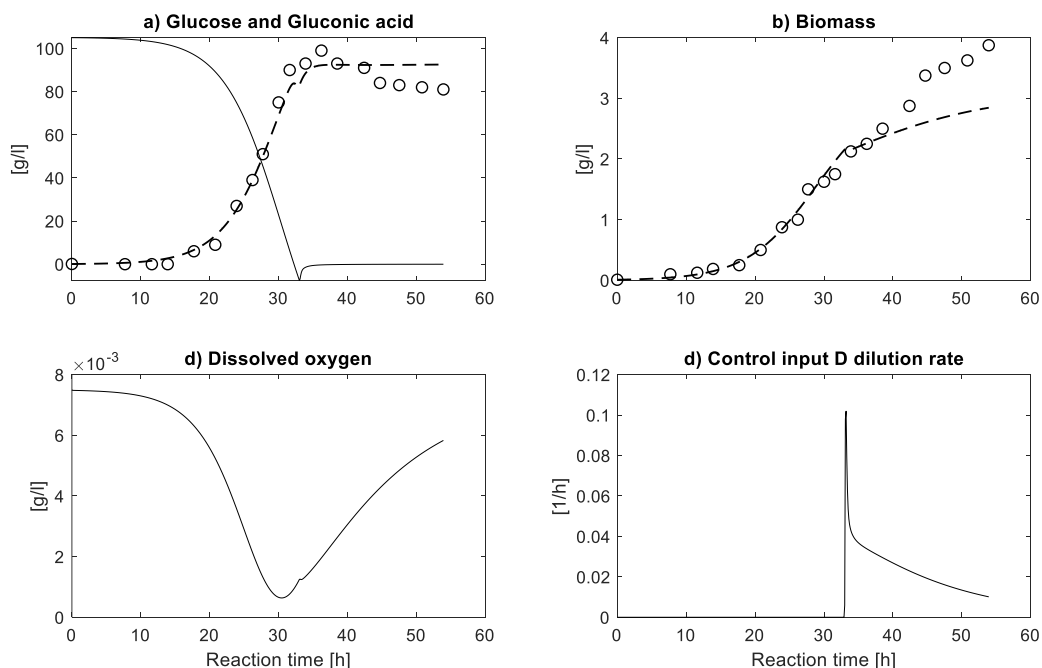


Fig. 3. Linearizing control algorithm investigation. Model values are shown with lines; batch experimental data – with circles; biomass and gluconic acid estimates – with dashed lines.

The simulation investigation shows that the proposed linearizing control algorithm could be used for real application.

5. CONCLUSIONS

A linearizing control of gluconic acid continuous fermentation by *Aspergillus Niger* is proposed. The biotechnological model is identified using the experimental data of batch fermentation. That model is extended for description of continuous mode of cultivation. A General Dynamical Model of that process is derived using the reduced process reaction scheme. The GDM is used for design of observers of unmeasured biomass and gluconic acid concentration in the reactor as well as the linearising adaptive control design.

Simulations demonstrate the applicability of the proposed control scheme.

The result could be used as basis for future investigation and some practical implementations of process control in laboratory conditions.

ACKNOWLEDGMENTS

This research has been supported by the National Scientific Fund of Bulgaria under the Grant KII-06-H3/23 “Interactive System for Education in Modelling and Control of Bioprocesses (InSEMCBio)”.

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