BATCH FERMENTATION PROCESS: MODELING AND DIRECT SENSITIVITY ANALYSIS

A. SIPOS[a*], P. S. AGACHI[b], X. M. MEYER[c] and P. STREHAIANO[c]

[a] „Lucian Blaga" University of Sibiu, Faculty of Food Industry, 7-9 Dr. Ion Ratiu Street, 550024 Sibiu, Romania

[b] "Babes-Bolyai" University of Cluj-Napoca, Faculty of Chemistry and Chemical Engneering, 11 Arany Janos Street, 400028 Cluj-Napoca, Romania

[c] INP Toulouse, ENSIACET, 118 Route de Narbonne, 31077 Toulouse, Cedex 4, France

Based on a nonlinear model, this article realizes an investigation of dynamic behavior of a batch fermentation process using direct sensitivity analysis (DSA). The used nonlinear mathematical model has a good qualitative and quantitative description of the alcoholic fermentation process. This model has been discussed and validated by authors in other studies. The DSA of dynamic model has been permitted to calculate the matrix of the sensitivity functions in order to determine the influence of the small deviations of initial state, control inputs, and parameters from the ideal nominal values on the state trajectory and system output in time. Process optimization and advanced control strategies can be developed based on this work.

Keywords: batch fermentation, nonlinear mathematical model, process simulation, direct sensitivity analysis

Alcoholic batch fermentation of white wine is a complex dynamic system involving must variety, microbiota, and winemaking technology (MARTINEZ et al., 1999). Moreover, this process is characterized for its complex dynamic response; for example, dead time, time delay in the instrument measurements, presence of parameters that vary with time, and high nonlinearities involving the variables (MELEIRO & MACIEL FILHO, 2000). For these reasons, modeling, simulation, and control of this system is still not a totally resolved problem.

The investigation of a dynamic system, based on its mathematical model, having optimal operation, optimal control, or design as objectives, should be accompanied by the sensitivity analysis of the model (UNGUREANU, 1988).

In general, the procedure of a dynamic system process control is as follows (HUANG et al., 2001):

- Sampling is performed in terms of the requirements of dynamic system process

* To whom correspondence should be addressed.

Phone: +40-269-211338; e-mail: anca.sipos@ulbsibiu.ro

control. It needs to design experiments which produce enough data samples in different conditions with certain statistical significance. For effective process control, the collected samples need to be able to produce the measured data to cover the designated frequency range to represent the process dynamics sufficiently.

- Data acquisition—with the prepared samples, the values of the dynamic system indication variables are measured by sensors and transducers, and the corresponding data for process operating conditions are recorded.

- Data processing and dynamic analysis—the data are processed, usually scaled or normalized, to produce a consistent magnitude between variables. The dynamic relationships between variables are tested. The autocorrelations and cross-correlations between variables are determined. This step helps to make the decision about the process modeling strategy.

- Modeling—linear or nonlinear dynamic mathematical models are built between the (input) manipulated variables at the levels of actuators and the (output) variables. The models determine quantitative, dynamic relationships between the input and output variables.

- Sensitivity analysis of the model is aimed at determining the influence of the small deviations of initial state, control inputs, and parameters from the ideal nominal values on the state trajectory and the system output in time, also allowing to appreciate the relative order regarding the significance of these influences.

- Prediction—based on the models, the quantities of dynamic system indications can be predicted in one-step-ahead or multiple-step-ahead modes. The accuracy of the predictions reflects the capability of the prediction models in control loops.

- Controller design—the built process models are used to design the controllers based on certain algorithms. The controllers are tuned to perform well in the regulation of the process operating conditions to ensure the consistent quality of the final products.

The authors passed the first four steps of the procedure as shown in SIPOS and co-workers.

The present article investigates the dynamic behavior of a batch fermentation process using the direct sensitivity analysis (DSA). For this analysis, the white-box method has been involved in the nonlinear dynamic model of white wine alcoholic fermentation process (SIPOS et al., 2007). This work allows the authors to develop, in parallel, a black-box model using a significant database and– to compare the behavior of the two models (using simulation mediums) and develop alternatives of fermentation advanced control process.

1. Material and methods

Strain and culture medium, culture apparatus and experimental conditions and fermentation parameters measurements have been presented by SIPOS and co-workers.

Based on the data obtained from these experiments, the following mathematical model has been proposed:

1.1. Mathematical model

As a distinct modeling principle of each phase, the evolution curve of biomass in time, for the viable cells, has been used. The $X_v(t)$ curve has been divided in correlation with phenomenological aspects of the development of microorganisms (Fig. 1); thus:

– latent phase, denoted by 1;

- growing phase, denoted by 2; and

– decline phase, denoted by 3.

Fig. 1.

The equations of this model are presented in Table 1 and have been validated by SIPOS and co-workers.

Table 1.

The variables and parameters of the model are presented in Tables 2 and 3.

Table 2.

Table 3.

The model has been implemented as a Matlab S-function and the numerical simultaneous integration of the model equations has been done using a fourth-order Runge-Kutta method.

1.2. Direct sensitivity analysis

The investigation of the dynamic system, based on the aforementioned mathematical model, has been realized using the DSA.

The system-state variables consider the substrate concentration (S), the biomass concentration (X), and the temperature in the bioreactor (T^0). The state variables' vector is

$$x = \begin{pmatrix} S \\ X \\ T^0 \end{pmatrix} = \begin{pmatrix} x_1 \\ x_3 \\ x_4 \end{pmatrix} \quad (1)$$

The flow of cooling agent (F_{ag}) is the manipulated variable: $u_1 = F_{ag}$. The parameters have

been taken as the pre-exponential factor in Arrhenius' equation (A), the ratio between activation energy and universal gas constant (E_a/R) as kinetics characteristics, and the heat transfer area (A_T) as a design characteristic. The parameters' vector is

$$p = \begin{pmatrix} A \\ \frac{E_a}{R} \\ A_T \end{pmatrix} = \begin{pmatrix} p_1 \\ p_2 \\ p_3 \end{pmatrix} \quad (2)$$

With the denotations from Eqs 1 and 2, the mathematical model from Table 1 has been transformed in the standard matrix equation, as shown in Table 4.

Table 4.

The aforementioned mathematical model had the following initial condition:

$$x = \begin{pmatrix} x_1 \\ x_3 \\ x_4 \end{pmatrix} = \begin{pmatrix} S_0 \\ X_0 \\ T_i^0 \end{pmatrix} \quad (3)$$

Following the algorithm of the DSA method for a nonlinear model, the Jacobean matrix based on equations from Table 4, and the matrix sensitivity functions of the state considering the influences of the initial state and the parameters (parameters' sensitivity) have been made. Using the Matlab simulation environment, the numerical simultaneous integration of the model equations from Table 1 and the sensitivity matrix equations with Jacobean's elements has been realized.

2. Results and discussions

2.1. Results for mathematical model simulation

Batch fermentation nonlinear mathematical model used in this investigation has the following aspects: an equation for latent phase of fermentation that describes the phase period of the dependence with temperature; the Bovée-Strehaiano model (BOVÉE et al., 1984) for growing and decline phases with two equations: one for substrate consumption and the other for alcohol formation; an equation that describes the biomass behavior along the fermentation, different for the Phase 2 and for the Phase 3, respectively; and an energy balance model in which the rate of change of medium's temperature (dT^0/dt) is a result of the balance between the rate of heat generation due to fermentation and the rate of heat transfer to the cooling medium from the bioreactor jacket. The Bovée-Strehaiano nonphysiological model has been chosen because it correctly describes the substrate consumption and evolution of alcohol in growing and decline phases. The equations for

biomass have in their structure the Monod microorganism's growth rate and a logarithmic term, for growing phase, and a linear equation for decline phase. The model offers a good qualitative and quantitative description of the alcoholic fermentation process behavior.

The simulation results considering this model are presented in Fig. 2 and 3, for 180 gl^{-1} substrate initial concentration and 28 ^{o}C fermentation temperature.

Fig. 2.

The latent phase equation is valid for a period between 0 and 100 h and the model has been tested for a must with an initial concentration in substrate varying between 180 and 210 gl^{-1}, a fermentation temperature between 26 and 30 ^{o}C, and without aeration.

Fig. 3.

2.2. Results for DSA

The graphics of sensitivity functions that have been obtained by numerical integration of sensitivity matrix equations are presented in Figs 4–9. Based on these graphics the following observations can be made:

1. The substrate consumption, biomass production, and fermentation temperature (fig. 4) present the same sensitivity for the substrate initial concentration variation. The influence of this variation touches a maximum (negative) after the growing phase. So, the initial value of substrate concentration will affect the durations of latent and growing phases, the beginning and producing of biomass processes. This can represent a modification of the total length of fermentation (the latent phase can be longer or shorter than normally and the biomass growing curve can presents a gentle or steep slope).

2. The change of biomass initial concentration upon the evaluation of three variables (substrate, biomass, and fermentation temperature) (fig. 5) drops very fast and ends before the growing phase is finished. This influence exists only in this phase, the yeast adaptation phase with the medium that is characterized by a minimal speed of yeast working (the sugar consumption is$\cong$0) and by a null multiplication yeast speed.

3. The change of initial temperature of fermentation upon the substrate, biomass, and temperature from bioreactor (fig. 6) presents a positive maximum at the beginning of decline phase and after that, disappears in time. This maximum confirms that the initial value of temperature will affect the hole multiplication process of yeast (beginning and growing phases), but because of

kinetic's reaction can disappear in time. The possibility that the fermentation duration may be changed is once again confirmed.

Fig. 4.

Fig. 5.

Fig. 6.

4. The parameters' sensitivity (Figs 7–9) highlights that the process kinetics (substrate consumption, biomass production, and fermentation temperature) is strongly influenced by the modification of the two kinetics parameters (A and E_a), whose values are frequently determined with uncertain precision. The alcoholic batch fermentation of white wine, being a process controlled by temperature, and heat transfer area modification lead to changes in the fermentation conditions, and these can affect the process duration and the wine quality and characteristics.

Fig. 7.

Fig. 8.

Fig. 9.

3. Conclusions

The matrix sensitivity functions calculated with DSA has been permitted:

- to estimate the singular or in group influences of input variables – substrate and biomass – on the fermentation process and the initial temperature on the progress of process stages;
- to establish the AAS (Automate Adjustment System) structure, the possibility to develop observers for substrate, biomass and product by temperature measuring;
- to develop the suitable control technique.

References

BOVÉE, J.P., STREHAIANO, P., GOMA, G. & SEVELY, Y. (1984): Alcoholic fermentation: modelling based on sole substrate and product measurement. *Biotechnol. Bioeng.*, *26*, 328–334.

COSTA, A.C., ATALA, D.I.P., MAUGERI, F. & MACIEL R. (2001): Factorial design and simulation for the optimization and determination of control structures for an extractive alcoholic fermentation. *Process Biochem.*, *37*, 125-137.

HUANG, Y., WHITTAKER, A.D. & LACEY, R.E. (2001): *Automation for food engineering: food quality quantization and process control*. CRC Press, Boca Raton, pp. 1–8.

KROTHAPALLY, M. & PALANKI S. (1999): A neural network strategy for end-point optimiation of batch processes. *ISA Transactions*, *38*, 383-396.

LEI, F., ROTBOLL, M. & JORGENSEN, S.B. (2001): A biochemically structured model for *Saccharomyces cerevisiae*. *J. Biotechnol.*, *88*, 205-221.

MARTINEZ, G., LOPEZ, A., ESNOZ, A., VIRSEDA, P. & IBARROLA, J. (1999): A new fuzzy control system for wine fermentation. *Fd Control*, *10*, 175–180.

MELEIRO, L.A.C. & MACIEL FILHO, R. (2000): A self-tuning adaptive control applied to an industrial large-scale ethanol production. *Comp. Chem. Eng.*, *24*, 925–930.

SIPOS, A., MEYER, X.M. & STREHAIANO, P. (2007): Development of a nonlinear, dynamic mathematical model for alcoholic fermentation. *Acta Alimentaria*, *36*, 429-438.

TORIJA, MA.J., ROZÈS, N., POBLET, M., GUILLAMÓN, J.M. & MAS, A.(2003): Effects of fermentation temperature on the strain population of *Saccharomyces cerevisiae*: *Int. J. Fd Microbiol.*, *80*, 47-53.

UNGUREANU, S. (1988): *Sensibilitatea sistemelor dinamice (cu aplicaţii în industria şi ingineria chimică).* (The dynamic systems sensitivity (with applications in industry and chemical engineering)), Editura Tehnică, Bucarest, chapter III, pp. 105-200.

VALENTINOTTI, S., SRINIVASAN, B., HOLMBERG, U., BONVIN, D., CANNIZZARO, C., RHIEL, M. & VON STOCKAR, U. (2003): Optimal operation of fed-batch fermentation via adaptive control of overflow metabolite. *Control Eng. Practice*, *11*, 665-674.

Table 1. Equations of author's model (SIPOS et al., 2007)

Phase	Equations
Kinetic model	
Latent phase	$t_{lat} = \frac{a}{T^0} + b$
Exponential growing phase	- biomass: $\frac{dX}{dt} = d \cdot X \cdot k \cdot \frac{S}{K_s + S} \cdot \ln\left(k \cdot \frac{S}{K_s + S} \cdot t\right)$; $k = A \cdot e^{-\frac{Ea}{R \cdot T^0}}$ - substrate: $\frac{dS}{dt} = -k \cdot S^{\alpha} \cdot P^{\beta}$ - alcohol: $P = P_0 + \eta \cdot (S_0 - S)$
Decline phase	- biomass: $\frac{dX}{dt} = f \cdot X \cdot k$; $k = A \cdot e^{-\frac{Ea}{R \cdot T^0}}$ - substrate: $\frac{dS}{dt} = -k \cdot S^{\alpha} \cdot P^{\beta}$ - alcohol: $P = P_0 + \eta \cdot (S_0 - S)$
Energetic model	
All phases	- for bioreactor: $\frac{\Delta Hr \cdot \frac{dS}{dt}}{\rho \cdot c_p} - \frac{K_T \cdot A_T}{V \cdot \rho \cdot c_p}(T^0 - T^0_{ag}) = \frac{dT^0}{dt}$ - for bioreactor's jacket: $\frac{F_{ag}}{V_{ag}}(T^0_{agi} - T^0_{ag}) + \frac{K_T A_T}{V_{ag} \cdot \rho_{ag} \cdot c_{pag}}(T^0 - T^0_{ag}) = \frac{dT^0_{ag}}{dt}$

*Table 2.*Variables and parameters of the kinetic model

X	Biomass concentration		g l^{-1}
S	Substrate concentration		g l^{-1}
P	Alcohol concentration		g l^{-1}
k	Kinetic constant		h^{-1}
A	Pre-exponential factor in Arrhenius' equation	148 (calculated using experimental data)	
E_a	Activation energy	21424 (calculated using experimental data)	J mol^{-1}
R	Universal gas constant	8.31	J/(mol.K)
T^0	Temperature in bioreactor	18 and 28	^{0}C
K_s	Substrate limitation constant	0.2[a]	g l^{-1}
d	Pseudo-constant of the biomass	1.67 (calculated using experimental data)	
f	Pseudo-constant of the biomass	0.34	
α	Pseudo-order of the substrate	0.69[b]	
β	Pseudo-order of the alcohol	0.32[b]	
η	Efficiency in alcohol of fermentation reaction	48[b]	%
S_0	Steady-state operation point of substrate	180	g l^{-1}
P_0	Steady-state operation point of alcohol	0	g l^{-1}
t	Time		h

[a] KROTHAPALLY & PALANKI, 1999; VALENTINOTTI et al., 2002; LEI et al., 2001;

[b] BOVEE et al., 1984.

Table 3. Parameters of the process model

K_T	Heat transfer coefficient	$3.6.10^{5}$ [a]	$W/(m^2.K)$
A_T	Heat transfer area	1 [b]	m^2
F_{ag}	Flow of cooling agent	1 [b]	$m^3\ h^{-1}$
V_{ag}	Volume of the jacket	2 [b]	l
V	Volume of the mass of reaction	10 [b]	l
T^0_{agi}	Temperature of cooling agent entering to the jacket	5 [b]	^0C
ΔH_r	Reaction heat of fermentation	98465 [c]	$J\ mol^{-1}$
ρ	Density of the mass of reaction	1100 [b]	kg/m^3
ρ_{ag}	Density of cooling agent	999.8 [a]	kg/m^3
c_p	Heat capacity of mass of reaction	3391 [b]	J/(kg.K)
c_{pag}	Heat capacity of cooling agent	4217 [a]	J/(kg.K)
T^0_{ag}	Temperature of cooling agent in the jacket		^0C

[a] TORIJA et al., 2002.

[b] experimental data.

[c] COSTA et al., 2001.

Table 4. Standard matrix equation of the mathematical model

Phase	Equations
Kinetic model	
Latent phase	$t = \frac{a}{x_4} + b$
Exponential growing phase	- biomass: $\frac{dx_3}{dt} = d \cdot x_3 \cdot p_1 \cdot \exp\left(-\frac{p_2}{x_4}\right) \cdot \frac{x_1}{K_s + x_1} \cdot \left[\ln\left(\frac{p_1 \cdot x_1 \cdot t}{K_s + x_1}\right) - \frac{p_2}{x_4}\right]$ - substrate: $\frac{dx_1}{dt} = -p_1 \cdot \exp\left(-\frac{p_2}{x_4}\right) \cdot x_1^{\alpha} \cdot x_2^{\beta}$ - alcohol: $\frac{dx_2}{dt} = -\eta \cdot \frac{dx_1}{dt}$
Decline phase	- biomass: $\frac{dx_3}{dt} = f \cdot x_3 \cdot p_1 \cdot \exp\left(-\frac{p_2}{x_4}\right)$ - substrate: $\frac{dx_1}{dt} = -p_1 \cdot \exp\left(-\frac{p_2}{x_4}\right) \cdot x_1^{\alpha} \cdot x_2^{\beta}$ - alcohol: $\frac{dx_2}{dt} = -\eta \cdot \frac{dx_1}{dt}$
Energetic model	
All phases	- for bioreactor: $\frac{dx_4}{dt} = \frac{\Delta H_r \cdot \frac{dx_1}{dt}}{\rho \cdot c_p} - \frac{K_T \cdot p_3}{V \cdot \rho \cdot c_p} \cdot (x_4 - x_5)$ - for bioreactor's jacket: $\frac{dx_5}{dt} = \frac{u_1}{V_{ag}} \cdot (T^0_{agi} - x_5) + \frac{K_T \cdot A_T}{V_{ag} \cdot \rho_{ag} \cdot c_{pag}} \cdot (x_4 - x_5)$

Fig. 1. Evolution of viable biomass X_v

Fig. 2. Authors' model: **A.** The evolution of glucose and alcohol versus time, confrontation of simulation results (lines) to experimental ones: (o) glucose, (+) alcohol **B.** Comparison of biomass simulation results (line) with experimental ones (o)

Fig. 3. The temperatures of fermentation medium and cooling agent simulation.

Fig. 4. Sensitivity functions' graphics

$$S_{x_{1,0}}^{x_1}\left[\frac{g\cdot l^{-1}biomass}{g\cdot l^{-1}biomass}\right],\qquad S_{x_{3,0}}^{x_1}\left[\frac{g\cdot l^{-1}biomass}{g\cdot l^{-1}alcohol}\right]\text{ and }\ S_{x_{4,0}}^{x_1}\left[\frac{g\cdot l^{-1}biomass}{K}\right]$$

Fig. 5. Sensitivity functions' graphics

$$S_{x_{1,0}}^{x_3}\left[\frac{g\cdot l^{-1}alcohol}{g\cdot l^{-1}biomass}\right],\qquad S_{x_{3,0}}^{x_3}\left[\frac{g\cdot l^{-1}alcohol}{g\cdot l^{-1}alcohol}\right]\text{ and }\ S_{x_{4,0}}^{x_3}\left[\frac{g\cdot l^{-1}alcohol}{K}\right]$$

Fig. 6. Sensitivity functions' graphics

$$S_{x_{1,0}}^{x_4}\left[\frac{K}{g\cdot l^{-1}biomass}\right],\qquad S_{x_{3,0}}^{x_4}\left[\frac{K}{g\cdot l^{-1}alcohol}\right]\text{ and }\ S_{x_{4,0}}^{x_4}\left[\frac{K}{K}\right]$$

Fig. 7. Parameter sensitivity functions' graphics

$$S_{p_1}^{x_1}\left[g\cdot l^{-1}biomass\right],\qquad S_{p_2}^{x_1}\left[\frac{g\cdot l^{-1}biomass}{K}\right]\text{ and }\qquad S_{p_3}^{x_1}\left[\frac{g\cdot l^{-1}biomass}{m^2}\right]$$

Fig. 8. Parameter sensitivity functions' graphics

$$S_{p_1}^{x_2}\left[g\cdot l^{-1}alcohol\right],\qquad S_{p_2}^{x_2}\left[\frac{g\cdot l^{-1}alcohol}{K}\right]\text{ and }\qquad S_{p_3}^{x_2}\left[\frac{g\cdot l^{-1}alcohol}{m^2}\right]$$

Fig. 9. Parameter sensitivity functions' graphics

$$S_{p_1}^{x_3}\left[K\right],\qquad S_{p_2}^{x_3}\left[\frac{K}{K}\right]\text{ and }\qquad S_{p_3}^{x_3}\left[\frac{K}{m^2}\right]$$

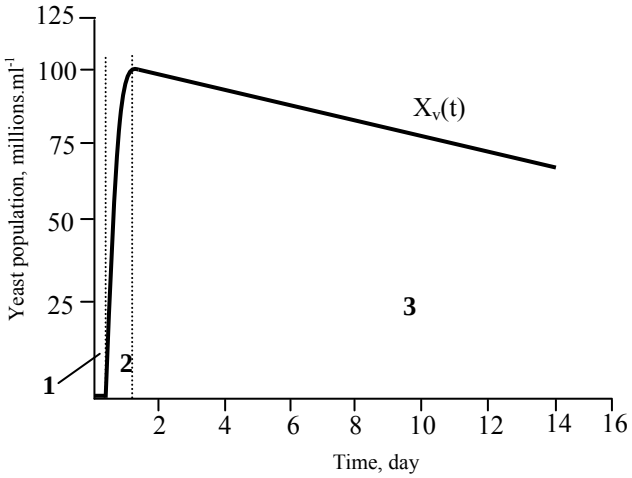
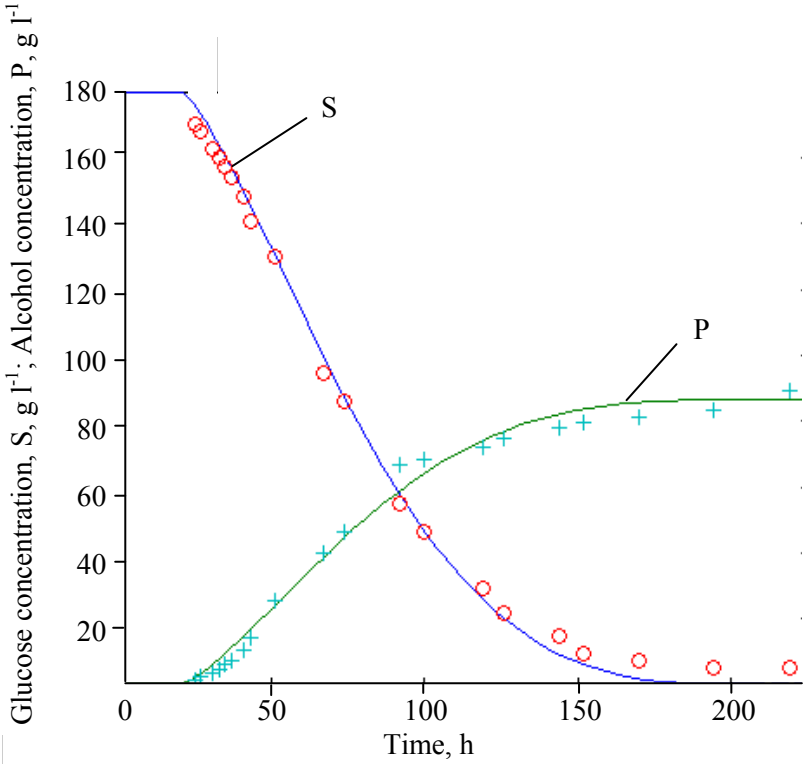

125
100
75
50
25
1
2
3
$X_v(t)$
Yeast population, millions.ml^{-1}
2
4
6
8
10
12
14
16
Time, day

Fig. 1.


180
160
140
120
100
80
60
40
20
S
P
0
50
100
150
200
Time, h
Glucose concentration, S, g l^{-1}; Alcohol concentration, P, g l^{-1}

A.

Fig. 2.

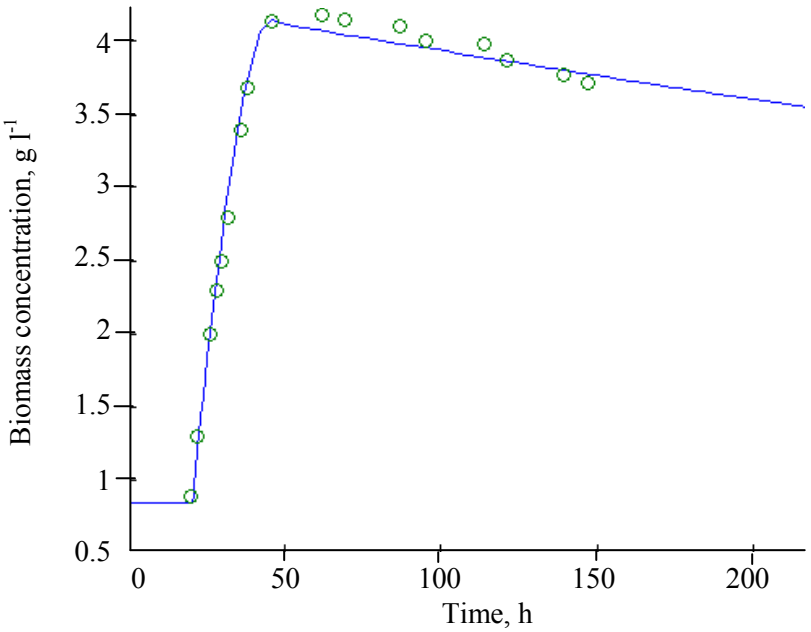

Biomass concentration, g l-1
4
3.5
3
2.5
2
1.5
1
0.5
0
50
100
150
200
Time, h

Fig. 2.

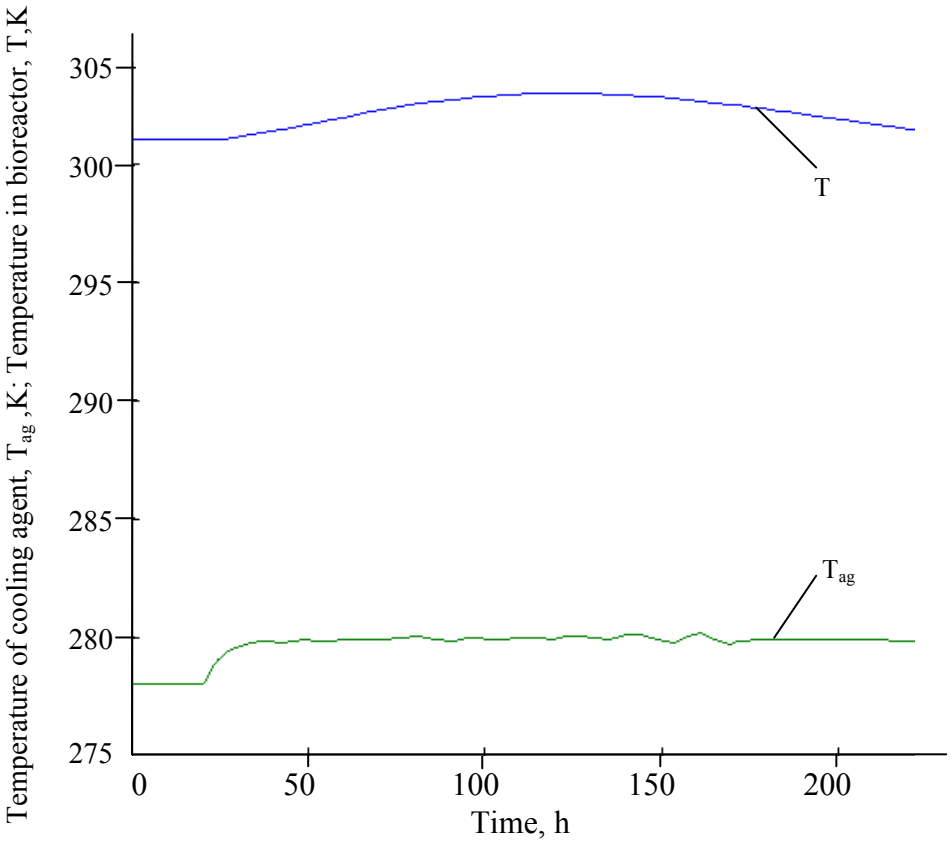

Temperature of cooling agent, Tag ,K; Temperature in bioreactor, T,K
305
300
295
290
285
280
275
T
Tag
0
50
100
150
200
Time, h

Fig. 3.

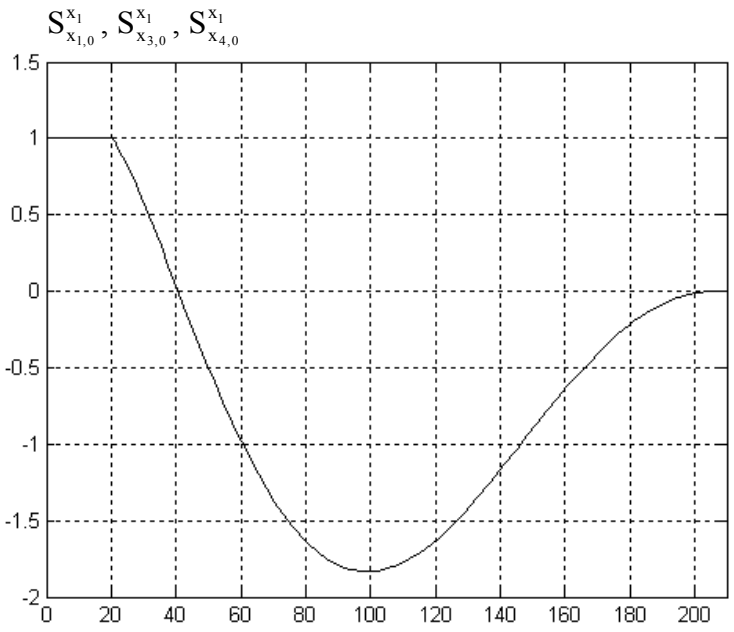

$S^{x_1}_{x_{1,0}}$, $S^{x_1}_{x_{3,0}}$, $S^{x_1}_{x_{4,0}}$
1.5
1
0.5
0
-0.5
-1
-1.5
-2
0
20
40
60
80
100
120
140
160
180
200
Time, [h]

Fig. 4.

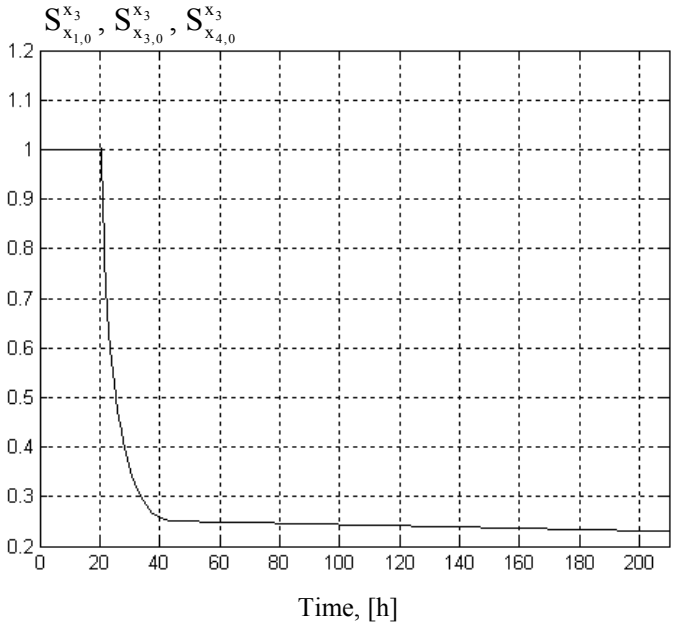

$S^{x_3}_{x_{1,0}}$, $S^{x_3}_{x_{3,0}}$, $S^{x_3}_{x_{4,0}}$
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0
20
40
60
80
100
120
140
160
180
200
Time, [h]

Fig. 5.

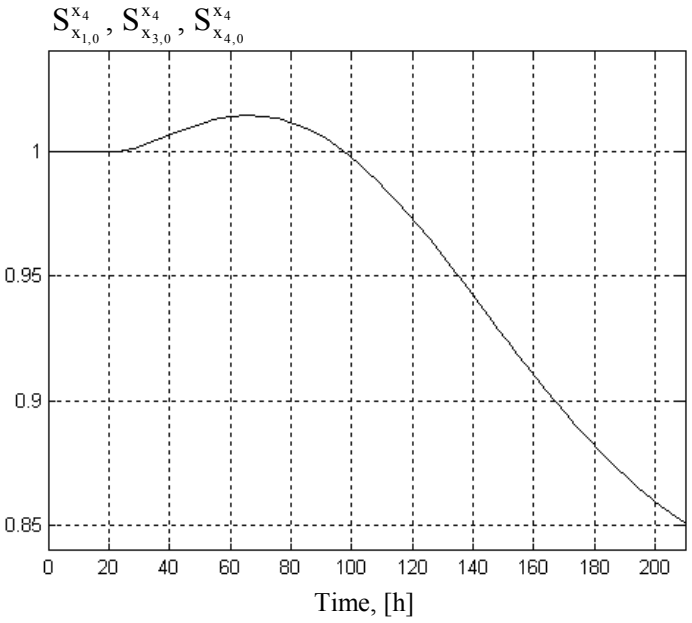

$S^{x_4}_{x_{1,0}}$, $S^{x_4}_{x_{3,0}}$, $S^{x_4}_{x_{4,0}}$
1
0.95
0.9
0.85
0
20
40
60
80
100
120
140
160
180
200
Time, [h]

Fig. 6.

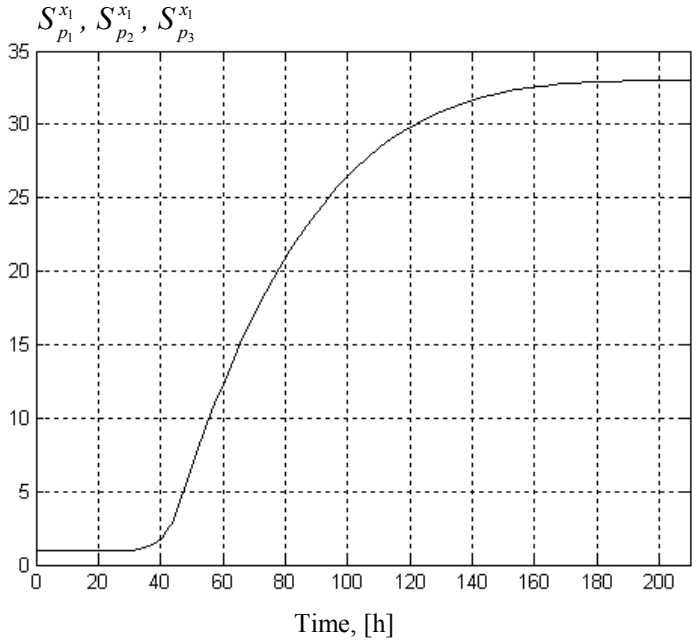

$S^{x_1}_{p_1}$, $S^{x_1}_{p_2}$, $S^{x_1}_{p_3}$
35
30
25
20
15
10
5
0
0
20
40
60
80
100
120
140
160
180
200
Time, [h]

Fig. 7.

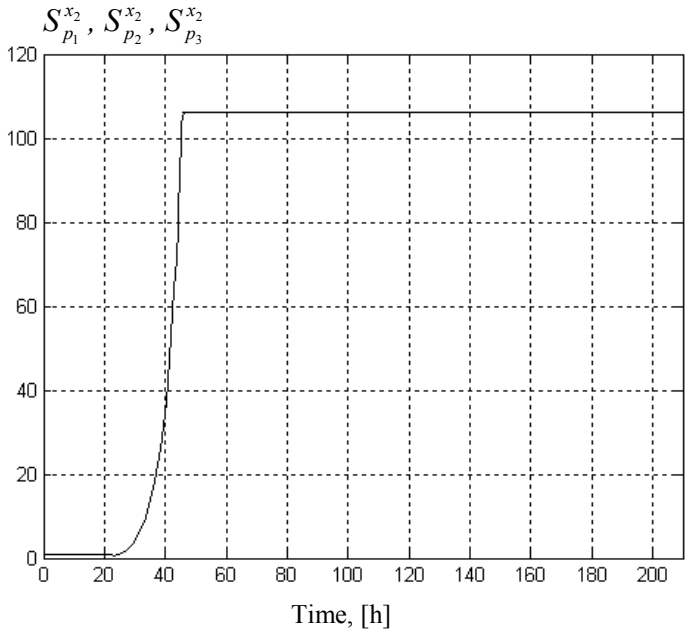

$S_{p_1}^{x_2}, S_{p_2}^{x_2}, S_{p_3}^{x_2}$
120
100
80
60
40
20
0
0 20 40 60 80 100 120 140 160 180 200
Time, [h]

Fig. 8.

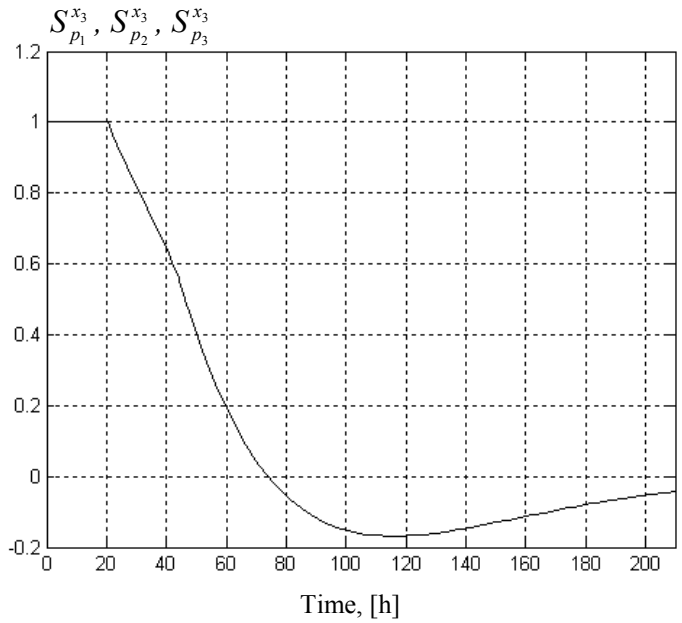

$S_{p_1}^{x_3}, S_{p_2}^{x_3}, S_{p_3}^{x_3}$
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
0 20 40 60 80 100 120 140 160 180 200
Time, [h]

Fig. 9.