A Combined Algorithm for Multi-objective Fuzzy Optimization of Whey Fermentation

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In this paper, multi-objective fuzzy optimization is applied to finding an optimal policy of a fed-batch fermentation process for lactose oxidation from a natural substratum by a strain *Kluyveromyces marxianus var. lactis* MC 5. The optimal policy consisted of feed flow rate, feed concentration of the substrate and initial concentration of the substrate. The multi-objective problem corresponds to the process productiveness, and the cost of the substrate. A simple combined algorithm guidelines the finding of a satisfactory solution to the general multi-objective optimization problem. The combined algorithm includes a method for random search for finding an initial point and a method based on fuzzy sets theory, combined in order to find the best solution of the optimization problem. The obtained optimal control results have shown an increase of process productiveness and a decrease of the remaining objective functions.

Key words:
Multi-objective fuzzy optimization, fuzzy sets theory, random search with back step, combined algorithm, whey fermentation

Introduction

Multi-objective optimization is a natural extension of the traditional optimization of a single-objective function. If the multi-objective functions are commensurate, minimizing single objective function, it is possible to minimize all criteria and the problem can be solved using traditional optimization techniques. On the other hand, if the objective functions are incommensurate, or competing, then the minimization of one objective function requires a compromise in another objective function. The competition between multi-objective functions is a key distinction between multi-objective optimization and traditional single-objective optimization.[1–5]

The fuzzy sets theory (FST) is widely used for modelling and optimization of biotechnological processes (BTP), for fuzzy-decision-making and optimal control of BTP.[6–11]

A method based on FST has been used for optimization of fed and fed-batch fermentation processes, and for optimization of gas-liquid mass-transfer in stirred tank bioreactors.[12–14] The main disadvantage of this method, namely decreases the number of discrete values of the control variables. A combined algorithm (CA) has been developed for elimination of this defect. The CA includes a method for random search with back step (RSBS) for finding an initial point and a method based on FST. CA has been used for optimization of the passage gas – liquid for stirred tank bioreactor also for single-objective optimization of fermentation processes.[15,16]

In this study, multi-objective fuzzy optimization for fed-batch processes of whey fermentation by a strain *Kluyveromyces marxianus var. lactis* MC 5 has been developed. The single-objective functions reflect process productiveness and cost of substrate. CA has been used for the determination of the optimization problem.

Materials and methods

Model of the batch process

The specific features of the process, cultivation condition and modelling of the batch processes of lactose oxidation from natural substratum in fermentation of *Kluyveromyces marxianus var. lactis* MC 5 have been shown in the paper of Petrov *et al.*[17] The batch model is used for identification of the parameters of the model on the basis of real experimental data. The batch model is based on the mass balance equations on the perfect mixing in the bioreactor:[17]

$$\frac{\mathrm{d}\gamma_X}{\mathrm{d}t} = \mu(\gamma_S, \gamma_{O_2})\gamma_X$$

$$\frac{\mathrm{d}\gamma_S}{\mathrm{d}t} = -\frac{1}{Y_1}\mu(\gamma_S, \gamma_{O_2})\gamma_X \qquad (1)$$

$$\frac{\mathrm{d}\gamma_{O_2}}{\mathrm{d}t} = \frac{k_L a}{(1-\varepsilon_G)}(\gamma^*_{O_2} - \gamma_{O_2}) - \frac{1}{Y_2}\mu(\gamma_S, \gamma_{O_2})\gamma_X$$

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where:[17,18]

$$\mu = \mu_m \frac{\gamma_S^2}{(K_S + \gamma_S^2)} \frac{\gamma_{O_2}}{(K_C + \gamma_{O_2} + \gamma_{O_2}^2 / K_i)},$$

$$k_L a = 52 \left(\frac{P}{V}\right)^{0.38} v_G^{0.23}, \qquad v_G = \frac{4 q_{v,G}}{\pi D^2},$$

$$P = 60.9 \rho n^3 d^5 \mathrm{Re}^{-0.4}, \qquad \mathrm{Re} = \frac{\rho n d^2}{\nu},$$

$$\varepsilon_G = 0.53 \left(\frac{q_{v,G}}{n d^3}\right)^{-0.014}.$$

The initial conditions of the model (1) are:

$$\gamma_{X(0)} = \gamma_{X_0} = 0.20 \text{ g L}^{-1};$$

$$\gamma_{S(0)} = \gamma_{S_0} = 44.0 \text{ g L}^{-1};$$

$$\gamma_{O_2(0)} = \gamma_{O_{2\,0}} = \gamma_{O_2}^* = 6.5 \cdot 10^{-3} \text{ g L}^{-1}.$$

The model parameters are identified with the non-linear regression technique with the assistance of a computer program which minimizes the deviation between the model prediction and the actual batch experimental data.

The kinetics model coefficients values, the basic indexes of mass transfer and the mixing of the process have the following values (mean values):[17]

$\mu_m = 0.89 \text{ h}^{-1}$; $k_S = 1.62 \text{ g L}^{-1}$;

$k_C = 3.37 \cdot 10^{-3} \text{ g L}^{-1}$; $k_i = 0.47$;

$Y_1 = 2.24$; $Y_2 = 3.24 \cdot 10^{-3} \text{ g g}^{-1}$;

$\varepsilon_G = 0.0123$; $q_{v,G} = 120 \text{ L h}^{-1}$;

$n = 800 \text{ min}^{-1}$, and $k_L a = 157 \text{ h}^{-1}$.

The validation of the batch model[17] is made on the basis of the experimental correlation quotients R^2 and experimental Fisher quotients F_E for each variable of model (1), and statistic λ.[19] The statistic λ has $F_{m,N-m}$ distribution.[19] Their values are:[17] $R^2 \gamma_X = 0.993$, $R^2 \gamma_S = 0.995$, and $R^2 \gamma_{O_2} = 0.994$; $F_E \gamma_X = 54.783$; $F_E \gamma_S = 47.373$, and $F_E \gamma_{O_2} = 50.043$; $\lambda = 66.837$. Their theoretical values are: $R_T^2 = 0.576$; $F_{T(10,3)} = 3.71$ and $F'_{T(3,10)} = 8.79$. The results after simulation are shown in Fig. 1.

The obtained results (correlation quotients, Fisher quotients, Statistics λ and Fig. 1) show that the model is adequate and can be used for the multi-objective optimization of the fed-batch fermentation process:

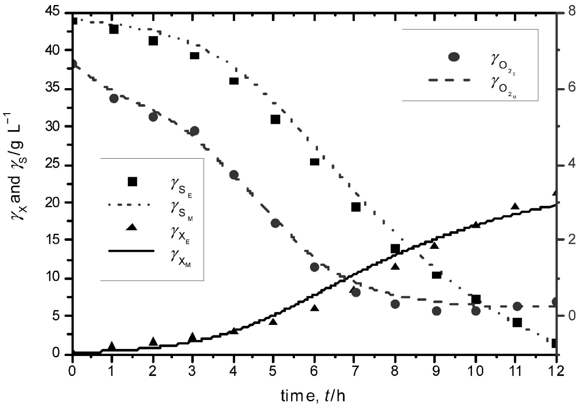


Fig. 1 – *Experimental and model results of the batch process*

$$\frac{d\gamma_X}{dt} = \mu(\gamma_S, \gamma_{O_2})\gamma_X - \frac{q_{v,F}}{V}\gamma_X$$

$$\frac{d\gamma_S}{dt} = \frac{q_{v,F}}{V}(\gamma_{S_{in}} - \gamma_S) - \frac{1}{Y_1}\mu(\gamma_S, \gamma_{O_2})\gamma_x \qquad (2)$$

$$\frac{d\gamma_{O_2}}{dt} = \frac{k_L a}{(1-\varepsilon_G)} \cdot (\gamma_{O_2}^* - \gamma_{O_2}) - \frac{1}{Y_2}\mu(\gamma_S, \gamma_{O_2})\gamma_x - \frac{q_{v,F}}{V}\gamma_{O_2}$$

$$\frac{dV}{dt} = q_{v,F}$$

where: $\gamma_{S_{in}} = \gamma_{S_0} = 44 \text{ g L}^{-1}$; $q_{v,F}(0) = 0.01 \text{ L h}^{-1}$; $V(0) = V_0 = 1$ L.

Systems variables constrains

Physical constraints have to be applied for most bioengineering processes. The bioreactor volume constraint can be described as follows:

$$g_1 = V(t) - V_f \le 0 \qquad (3)$$

The substrate and oxygen concentrations have to be positive over process time. We therefore have:

$$g_2 = -\gamma_{S(t)} \le 0 \qquad (4)$$

$$g_3 = -\gamma_{O_2(t)} \le 0 \qquad (5)$$

In addition, the stoichiometry of the biomass formation from substrate and oxygen must be obeyed, posing two constraints as follows:

$$g_4 = \frac{\gamma_{X(t)} V(t) - \gamma_{X_0} V_0}{\gamma_{S_{in}}[V(t) - V_0] + \gamma_{S_0} V_0 - \gamma_{S(t)} V(t)} - \frac{1}{Y_1} \le 0 \qquad (6)$$

$$g_5 = \frac{\gamma_{X(t)} V(t) - \gamma_{X_0} V_0}{\frac{k_L a}{(1-\varepsilon_G)} V(t)(\gamma_{O_2}^* - \gamma_{O_2}) + \gamma_{O_{20}} V_0 - \gamma_{O_2(t)} V(t)} - \frac{1}{Y_2} \le 0 \qquad (7)$$

If the constraints in eqs. (6) and (7) are not included in the optimization problem, an unrealistic predicted value may be found.

Control variable constrains

The control variables in this work are: feed flow rate – $q_{v,F}(t)$, feed concentration of the substrate and initial substrate concentration – γ_{S_m}, and γ_{S_0}. Here, the decision variables are bound in the solution space as follows:

$$0 \le q_{v,F}(t) \le q_{v,F_{max}} = 30.0 \cdot 10^{-3}\ L\ h^{-1};$$

$$40.0\ g\ L^{-1} = \gamma_{S_{in_{min}}} \le \gamma_{S_{in}} \le \gamma_{S_{in_{max}}} = 80.0\ g\ L^{-1}$$

$$\text{and } 40.0\ g\ L^{-1} = \gamma_{S_{0_{min}}} \le \gamma_{S_0} \le \gamma_{S_{0_{max}}} = 80.0\ g\ L^{-1}$$

Because the feed flow rate $q_{v,F}(t)$ is a time dependent variable, the optimal control problem can be considered such as an infinite dimensional problem. To solve this problem efficiently, the feed flow rate was represented by a finite set of control parameters in the time interval $t_{j-1} < t < t_j$ as follows: $q_{v,F}(t) = q_{v,F}(t)(j)$ for $j = 1, \ldots, K$ – number of time partitions.

Formulation of the optimization problem

The optimization task has been formulated as a multi-objective decision-making problem. Two requirements have to be satisfied in such a decision-making (DM) problem. The first requirement was to find the optimal values of the feed flow rate, feed concentration of the substrate and initial concentration of the substrate and the corresponding optimal objective function value. Such an optimal solution can be obtained by using multi-objective optimization techniques. On the other hand, the second requirement was to check whether the optimal solution should have satisfied the pre-assigned threshold values. If the optimal solution does not satisfy the threshold values, the DM has to trade-off some threshold values. The search efforts should be repeated to find another local optimal solution.

This problem is simply called the multi-objective optimization problem and is expressed as:

$$\max Q_1(\boldsymbol{u}) = \frac{1}{t_f}[\gamma_{X(t_f)} V(t_f) - \gamma_{X_0} V_0],\ g\ h^{-1} \quad (8)$$

$$\max Q_2(\boldsymbol{u}) = \frac{\gamma_{S_0} - \gamma_{S(t_f)}}{\gamma_{S_0}},\ - \quad (9)$$

$$\min Q_3(u) = \gamma_{S_{in}}[V(t_f) - V_0] + \gamma_{S_0} V_0,\ g \quad (10)$$

The first objective function corresponds to the processes productiveness, the second and third objective functions correspond to the cost of substrate.

The multi-objective optimization problem (8)–(10) was transformed to a problem with a single-objective function by general utility function with weight coefficients for each single utility coefficients criterion. The single-objective functions $Q_j(\boldsymbol{u})$ are transformed in utility coefficients $\eta_j(\boldsymbol{u})$ by the formula:[20]

$$\eta_j(\boldsymbol{u}) = k\frac{Q_1(\boldsymbol{u}) - Q_{c,j}}{Q_{max,j} - Q_{min,j}},$$
$$\kappa = \begin{cases} +1 \text{ for } Q_j(\boldsymbol{u}) \to \max \\ -1 \text{ for } Q_j(\boldsymbol{u}) \to \min \end{cases}, \quad j = 1,2,\ldots,N \quad (11)$$

After transforming the physical parameters into dimensionless, the generalized utility function is composed from the type:

$$Q_a(\boldsymbol{u}) = \frac{1}{N}\sum_{j=1}^{N} w_j \eta_j(\boldsymbol{u}) - \sum_{k=1}^{p} r_k \int_0^{t_f} \langle g_\kappa \rangle_+^2 dt \quad (12)$$

where: $\sum_{j=1}^{N} w_j = 1$; $\langle g_\kappa \rangle_+ = \max[0, g_k(t)]$; $N = 3$ and $p = 5$.

The optimal decision $\boldsymbol{u}^0$, maximizing the general utility function (12) was found by using CA for optimization.

A combined algorithm for optimization

Random search with back step algorithm

The random search algorithm is well-known from the literature.[20] Its rate of congruence, which is also valid for other algorithms, depends on the choice of a starting point. For augmentation of the congruence rate, a preliminary choice of a random set is used on the following scheme:[20]

A starting point in the admissible space is generated in an accidental method:

$$\boldsymbol{u}_{0,i} = \boldsymbol{u}_{min,i} + \xi_i(\boldsymbol{u}_{max,i} - \boldsymbol{u}_{min,i}),$$
$$i = 1,2,\ldots,M; \qquad M = \begin{cases} 2^m + 4 \text{ at } m \le 3 \\ 2m + 4 \text{ at } m > 3 \end{cases}$$

where: ξ_i = *URAND*(*IY*). *URAND*(*IY*) is a random generator of random numbers [0÷1].

The point with the best result concerning some criterion $Q_a(\boldsymbol{u})$, is chosen as a starting point. After that, random search with back step algorithm is applied.

Fuzzy algorithm

Fuzzy sets theory allows the possibility to develop a "*flexible*" model that reflects in more details all possible values of the criterion and control variables under the developed model.[8–11] The model of the fed-batch process (2) is considered as the most appropriate but deviations are admissible with small degree of acceptance. It is represented by fuzzy set of the following type γ_X, γ_S and γ_{O_2} is come into view approximately by the following relations:[8]

$$\beta_i(t,\boldsymbol{u}) = \frac{1}{1+\varepsilon_i^2} \quad (13)$$

where:

$$i = 1, \ldots, 3; \quad \varepsilon_1 = \gamma_{\dot{X}} - (\mu\gamma_X - D\gamma_X);$$

$$\varepsilon_2 = \gamma_{\dot{S}} - (D(\gamma_{S_0} - \gamma_S) - Y_1\mu\gamma_X);$$

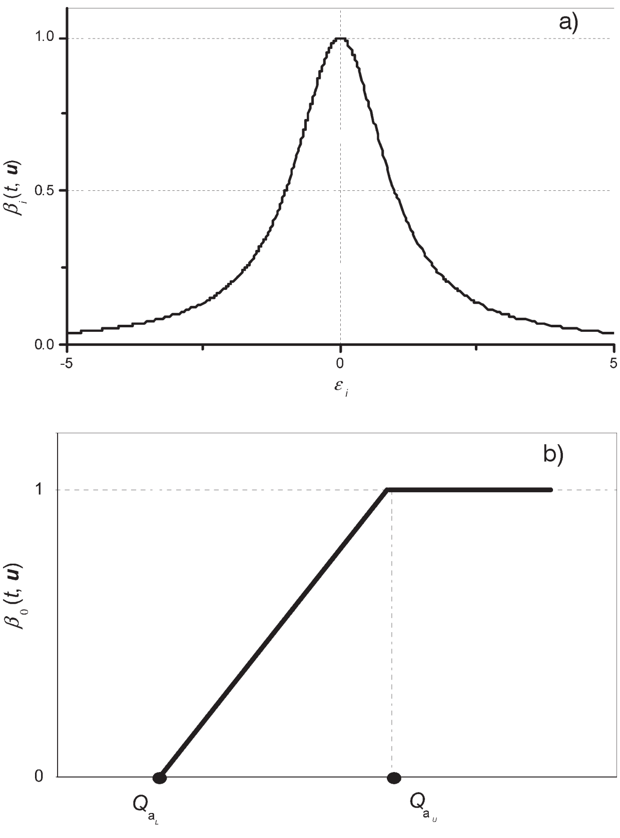
$$\varepsilon_3 = \gamma_{\dot{O}_2} - \left(\frac{k_L a}{(1-\varepsilon_G)}\left(\frac{\gamma^*_{O_2}}{m_L} - \gamma_{O_2}\right) - Y_2\mu\gamma_X - D\gamma_{O_2}\right).$$

The prepositional "*flexible*" model of process reflects the better influence of all well values of the kinetics variables.

Fuzzy criteria from the following type: "$Q_a(\boldsymbol{u})$ *to be in possibility higher*", is formulated and presented with the subsequent membership function:

$$\beta_0(t,\boldsymbol{u}) = \begin{cases} 0; & Q_a(\boldsymbol{u}) < Q_{a_L} \\ \dfrac{Q_a(\boldsymbol{u}) - Q_{a_L}}{Q_{a_U} - Q_{a_L}} & Q_{a_L} \le Q_a(\boldsymbol{u}) \le Q_{a_U} \\ 1; & Q_a(\boldsymbol{u}) > Q_{a_U} \end{cases} \quad (14)$$

The membership function of the model and criterion are shown in Fig. 2.



F i g . 2 – *Membership functions: a) Membership function for the model; b) Membership function for the general criteria*

The fuzzy set of the solution is presented with membership function of the criteria β_0 and model β_i:

$$\beta_D(t,\boldsymbol{u}) = (1-\gamma)\prod_{i=0}^{3}\beta_i^{\theta_i}(t,\boldsymbol{u}) + \gamma\left\{1 - \prod_{i=0}^{3}(1-\beta_i(t,\boldsymbol{u}))^{\theta_i}\right\} \quad (15)$$

The solution was obtained by using the common *defuzzification* method BADD:[9]

$$\boldsymbol{u}^0 = \sum_{i=1}^{q}\frac{\beta_{D_i}^{\theta_i}(t,\boldsymbol{u})\,\boldsymbol{u}_i}{\sum_{j=1}^{p}\beta_{D_j}^{\theta_i}(t,\boldsymbol{u})}, \quad (16)$$

$$i = 1,\ldots,q; \qquad j = 1,\ldots,p; \qquad p = q^m$$

An effective combined algorithm for process optimization is synthesized by using the fuzzy sets. The generalized combined algorithm scheme is:

START

1. **Input:** number of the control variables m, and single-objective function N; integer constant IY; minimal, maximal and initial values of vector of control variable: $\boldsymbol{u}_{\min}$, $\boldsymbol{u}_{\max}$ and $\boldsymbol{u}^0$ respectively; parameter for step HStep and initial variables for fuzzy method θ_i and γ; number of discrete values q of vector $\boldsymbol{u}$.

2. Computing step $\boldsymbol{h}$ for each control variable: $h = (u_{\max} - u_{\min})$/HStep.

3. Computing criterion $Q_{a_B}(\boldsymbol{u}^0)$ before optimization from (12)

4. CALL **RSBS** (m, IY, $\boldsymbol{u}_{\min}$, $\boldsymbol{u}_{\max}$, $\boldsymbol{h}$, $\boldsymbol{u}^0$, Q_a).

5. Optimal value of the vector of control variables $\boldsymbol{u}^0$ and criterion $Q_a(\boldsymbol{u}^0)$ received from **RSBS**.

6. Possible area for each control variable $\boldsymbol{U}_{\min}$ and $\boldsymbol{U}_{\max}$, are determined in the vicinity of ±20 % the received with **RSBS** point: $\boldsymbol{U}_{\min} = 0.8 \cdot \boldsymbol{u}^0$ and $\boldsymbol{U}_{\max} = 1.2 \cdot \boldsymbol{u}^0$. If $\boldsymbol{U}_{\min}$ or $\boldsymbol{U}_{\max}$ exceeds the admissible values $\boldsymbol{u}_{\min}$ or $\boldsymbol{u}_{\max}$, then $\boldsymbol{U}_{\min} = \boldsymbol{u}_{\min}$ and $\boldsymbol{U}_{\max} = \boldsymbol{u}_{\max}$.

7. Computing *low* and *upper* values for fuzzy criterion received from **RSBS**: $Q_{a_L} = 0.08 \cdot Q_a(\boldsymbol{u}^0)$ and $Q_{a_U} = 1.2 \cdot Q_a(\boldsymbol{u}^0)$.

8. CALL **FUZZY** (m, q, $\boldsymbol{U}_{\min}$, $\boldsymbol{U}_{\max}$, Q_{a_L}, Q_{a_U}, γ, θ, $\boldsymbol{u}^0$, Q_a)

9. Optimal value of the vector of control variables $\boldsymbol{u}^0$ and criterion $Q_a(\boldsymbol{u}^0)$ received from **FUZZY**.

10. Computing model *after* optimization.

11. **Print results:** constructive and regime parameters: d, D, L, n, $q_{v,G}$; parameters of mass-transfer: (P/V), ε_G, and $k_L a$, model *before* and *after* optimization; optimal values of control variables $\boldsymbol{u}^0$ and criterion $Q_a(\boldsymbol{u})$.

12. **END**

The generalized FUZZY Algorithm scheme is:

START

1. Computing discrete values of each control variable: $\boldsymbol{u}_i = \dfrac{(\boldsymbol{U}_{\min} + k(\boldsymbol{U}_{\max} - \boldsymbol{U}_{\min}))}{(q-1)}$, $(i = 1, \ldots, m)$, $(k = 0, \ldots, q)$.

2. Computing of deviations ε_i from the basic model (2);

3. Computing membership function $\beta_i(t, \boldsymbol{u})$ for model from (13).

4. Computing membership function $\beta_0(t, \boldsymbol{u})$ for criterion from (14).

5. Computing the membership function of the decision $\beta_D(t, \boldsymbol{u})$ from (15).

6. Obtaining of solution $\boldsymbol{u}^0$ using *defuzzification* operator from (16)

7. Returns optimal values of control variables $\boldsymbol{u}^0$ and criterion $Q_a(\boldsymbol{u})$.

END

All programs were written using a FORTRAN 77 programming language version 5.0. All computations were performed on a Pentium IV 1.8 GHz computer using a Windows XP operating system.

The obtained results after optimization were: $\gamma_{S_{in}} = 50.8$ g L^{-1} and $\gamma_{S_0} = 51.4$ g L^{-1}. It should be noticed that the values of $\gamma_{S_{in}}$ and γ_{S_0} are obtained with the dynamic process optimization. The results of the general kinetic variables before and after optimization with CA are shown in Fig. 3.

The optimal values of process productiveness – criteria $Q_1(\boldsymbol{u})$ and feed flow rate are shown in Fig. 4.

Results and discussion

The obtained results after optimization for the feed concentration and initial concentration of the substrate $\gamma_{S_{in}} = 50.8$ g L^{-1} and $\gamma_{S_0} = 51.4$ g L^{-1} show that the difference between them is insignificant, and the mean value between them can be chosen $\gamma_{S_0} = \gamma_{S_{in}} = 51.1$ g L^{-1}.

The obtained results (Fig. 3a) show increase of the biomass concentration by more than 16 % (19.69 g L^{-1} – before optimization and 23.0 g L^{-1} after optimization).

The residual substrate concentration (Fig. 3a) decreases by more than 69 % (0.146 g L^{-1} – before optimization and 0.044 g L^{-1} after optimization).

Fig. 3b shows good oxygen consumption from the microorganisms – at the end of the process it decreases by more than 7 %, from 6.05 mg L^{-1} to 5.63 mg L^{-1}.

Process productiveness increases by more than 19 % (Fig. 4a).

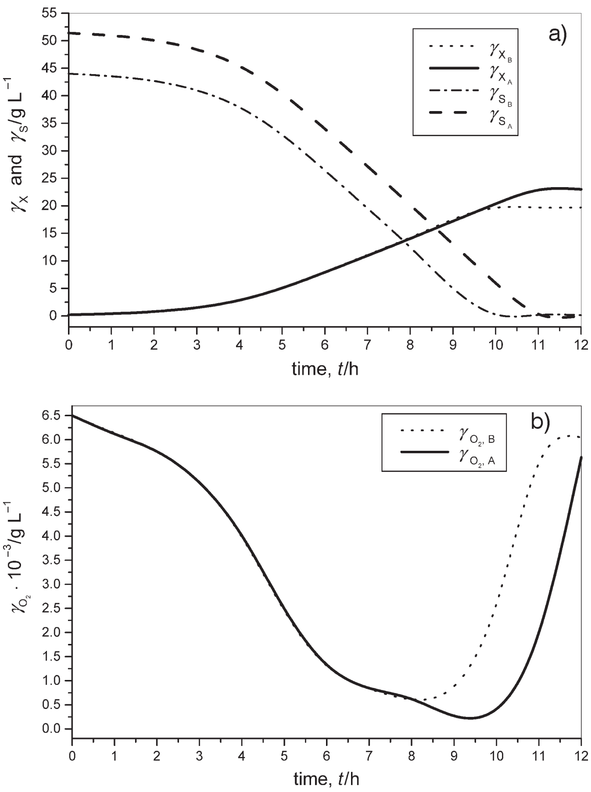


Fig. 3 – *The kinetics variables of the process, before and after optimization: a) Profiles of the biomass and substrate concentration, before and after optimization; b) Profile of the oxygen concentration, before and after optimization*

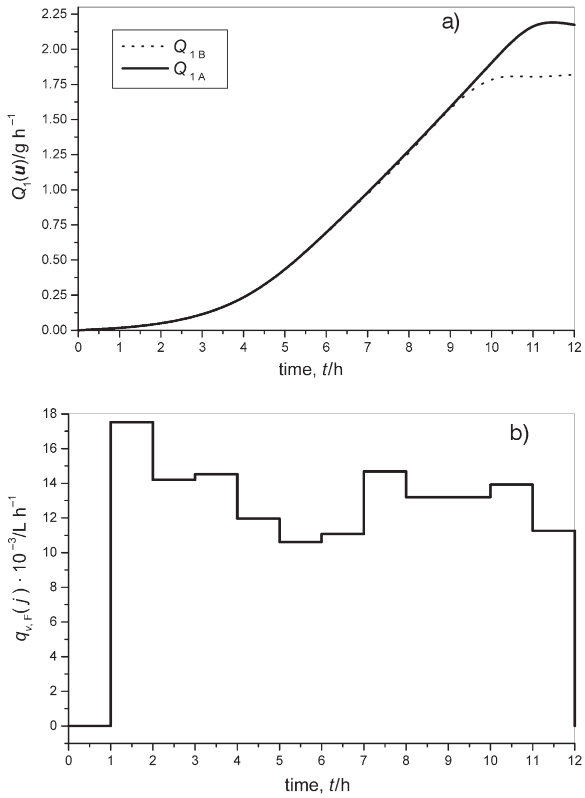


Fig. 4 – *The profile of the feed flow rate and the criteria $Q_1(\boldsymbol{u})$, before and after optimization: a) Criteria $Q_1(\boldsymbol{u})$, before and after optimization; b) Optimal profile of the feed flow rate*

Conclusions

1. Proposed combined algorithm for optimization, based of random search method with back step and fuzzy sets theory decreases vastly the time for the solution of the optimization problem. The application of the combined algorithm eliminates the main disadvantage of the used fuzzy optimization method, namely decreases number of discrete values of the control variables. Thus, the algorithm allows problems with larger scale to be solved. The combined algorithm can be used for decision of other optimization problems in the area of bioprocess systems.

2. The obtained optimal profile of the feed flow rate and obtained results after the theoretical optimization have shown clearly practical applicability of the used techniques, in particular, for maximization of process productivity.

3. The obtained results from the study have shown that multi-objective optimization is a more complex approach to minimizing the risk in the decision-making procedure and maximizing the formulated objective.

List of symbols

D – bioreactor diameter, m
d – impeller diameter, m
F'_T – theoretical values of the Fisher quotients for statistics λ
F_E – experimental values of the Fisher quotients
F_T – theoretical values of the Fisher quotients
IY – integer constant
K_i – inhibition constant, –
k_La – volumetric mass-transfer coefficient, h^{-1}
K_S, K_C – Monod saturation constants, g L^{-1}
L – height of the liquid in the bioreactor, m
m – number of the control variables
M – number of the generated point's
n – agitation speed, min^{-1}
N – number of single-objective functions, $N = 3$
p – number of constraints, $p = 5$
P – power input, W
q – number of discrete values for $\boldsymbol{u}$
$Q_1(\boldsymbol{u})$ – process productiveness, g h^{-1}
$Q_2(\boldsymbol{u})$ and $Q_3(\boldsymbol{u})$ – the cost of the substrate, – and g
Q_{a_L} – low values of general criteria
Q_a – general criteria
Q_{a_U} – upper values of general criteria
$Q_{c,j}$ – most superfluous result for $Q_j(\boldsymbol{u})$
$Q_{max,j}$ – maximal values of $Q_j(\boldsymbol{u})$, (i =1, …, 3)
$Q_{min,j}$ – minimal values of $Q_j(\boldsymbol{u})$, (i = 1, …, 3)
$q_{v,F}$ – feed flow rate, L h^{-1}
$q_{v,G}$ – gas flow rate, m^3 s^{-1}
R^2 – experimental values of the correlation quotients
R^2_T – theoretical values of the correlation quotients
Re – Reynolds number, –
r_k – penalty parameters, (k = 1, 2, …, p)
t – process time, h
$\boldsymbol{u}$ – vector of control variables,

$$\boldsymbol{u} = \boldsymbol{u}\left\lfloor \gamma_{q_{v,F(t)}},\ \gamma_{S_{in}}, \gamma_{S_0} \right\rfloor$$

$\boldsymbol{u}_{min}$ and $\boldsymbol{u}_{max}$ – possible limits for vector of control variable
V – working volume, L
v_G – gas velocity, m s^{-1}
w_j – weight coefficients
Y_1 and Y_2 – yield coefficients, g g^{-1}

Greek Letters

ε_G – gas hold-up, –
$\gamma_{O_{2B,A}}$ – oxygen concentration *before* and *after* the optimization
γ_{O_2} – dissolved oxygen concentration in liquid phase, g L^{-1}
$\gamma^*_{O_2}$ – equilibrium dissolved oxygen mass concentration, g L^{-1}
γ_S – concentration of substrate, g L^{-1}
$\gamma_{S_{in}}$ – feed concentration of substrate, g L^{-1}
γ_{S_0} – initial concentration of substrate, g L^{-1}
$\gamma_{S_{B,A}}$ – substrate concentration of the *before* and *after* the optimization, g L^{-1}
γ_X – biomass concentration, g L^{-1}
$\gamma_{X_{B,A}}$ – biomass concentration *before* and *after* the optimization, g L^{-1}
ρ – liquid density, kg m^{-3}
ν – liquid dynamic velocity, Pa s
γ – parameter, characterized the compensation degree
λ – parameter, characterized the compensation degree
μ – specific grown rate of biomass, h^{-1}
λ – statistic λ
β_i – membership functions, (i = 0, …, 3)
θ_i – parameters, given of weights of $\beta_i(\boldsymbol{u})$
ξ_i – uniformly distributed random numbers, (i = 1, 2, …, M)
μ_m – maximal grown rate of biomass, h^{-1}

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