2017 21st International Conference on Process Control (PC)
June 6–9, 2017, Štrbské Pleso, Slovakia

Control of a Biochemical Process Using Fuzzy Approach

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***Abstract*—The work deals with design and application of fuzzy controllers for a biochemical process. Fuzzy logic control based on the Takagi–Sugeno inference method has been applied for control of the baker's yeast fermentation. The advantage of the fuzzy control design is that it can be used very successfully for control of strongly non-linear processes and processes that are difficult to model because of complicated reaction kinetics. Obtained simulation results confirm this fact. The disadvantage of the fuzzy control design lies in the time-consuming tuning of controllers.**

Keywords—fermentation process; fuzzy control; Takagi–Sugeno inference method.

I. Introduction

Biochemical processes are very difficult to control from various aspects and the strong nonlinear dynamics, complicated reaction kinetics and time varying parameters belong to them. Fermentation process, wherein the cultivation medium consists of living microorganisms, is important in many biotechnological applications, and it is necessary to eliminate various negative effects as e.g. substrate inhibition, catabolite repression, product inhibition, glucose effect. Furthermore, many variables are difficult to measure and usually demand laboratory analyses.

Applications of artificial intelligence techniques have been used intensively to convert human experience into a form understandable by computers in last decades. A few applications of intelligent controllers have been discussed in [1] to show the effective and versatile use of these controllers in various bioprocesses. An effective biochemical network modelling framework for building dynamic cell-free metabolic models is presented in [2]. The key innovation of this approach is the seamless integration of simple effective rules encoding complex regulation with traditional kinetic pathway modelling. A new strategy to augment the pH process control is offered in [3]. The intelligent controller proposed herein is based on an inverse neural plant model. An integration term is introduced to improve the pure inverse neural controller performance. This element, adjusted by a fuzzy system with respect to the control error, operates in parallel with the neural controller to ensure offset-free performance in case of system uncertainties or modelling mismatch. The paper [4] deals with the control of uncertain highly nonlinear biological processes. An adaptive fuzzy control scheme represented by a Takagi-Sugeno fuzzy model is developed for the pre-treatment of wastewater. The proposed approach uses a fuzzy system to approximate the unknown substrate consumption rate in designing an adaptive controller, and then an observer is developed to estimate the substrate concentration at the bioreactor outlet. Numerous methods have been developed and presented to analyse and design a variety of fuzzy control systems [5]. Analytical structure for a fuzzy PID controller is introduced in [6]. In [7], a new method is proposed for automatic extracting all fuzzy parameters of a Fuzzy Logic Controller in order to control nonlinear industrial processes. A major contribution of fuzzy logic is its capability to represent vague data [8]. The paper [9] presents a general framework for dealing with uncertainties in each stage of consequence modelling. The aim of the paper [10] is to present the application of type-2 fuzzy logic controllers to the control of a fed-batch fermentation reactor in which penicillin production is carried out. In [11], a fuzzy logic control system has been developed for online feeding control in fed-batch enzymatic hydrolysis of dilute acid-pretreated corn stover. The work [12] addresses the fuzzy optimization of biochemical systems expressed with the S-system form under uncertainty. The paper [13] proposes a fuzzy logic inference system to model the yogurt fermentation process.

This paper is devoted to design and application of fuzzy controllers for a biochemical process. Fuzzy logic control based on the Takagi–Sugeno inference method has been applied for control of the baker's yeast fermentation. The generation of fuzzy rule base by subtractive clustering technique is used. This approach can reduce number of rules maintaining almost the same level of performance. The advantage of the fuzzy control design is that it can be used very successfully for control of strongly non-linear processes and processes that are difficult to model because of complicated reaction kinetics.

The paper is organized as follows. Section II introduces the model describing the response of Saccharomyces cerevisiae represented by dissolved oxygen concentration. Fuzzy logic control based on the Takagi–Sugeno inference method is described in Section III and obtained simulation results are presented in Section IV. Section V summarizes conclusions.

II. BAKER'S YEAST FERMENTATION PROCESS

Fermentation of Saccharomyces cerevisiae (baker's yeast) and using fuzzy control for this process have been studied. The non-linear model of the fermentation process has been used for fuzzy control design and simulation [14], [15]. The mathematical model is based on limited oxidation capacity of yeast leading to a switch-over from oxidative to oxide-reductive metabolism. Regarding the law of the mass conservation, the model for continuous fermentation process of baker's yeast can be expressed by the following set of ordinary differential equations [16], [17]:

cell mass concentration:

$$\frac{dc_x}{dt} = \frac{q}{V_l}\left(c_{xin} - c_x\right) + \mu c_x \tag{1}$$

substrate concentration:

$$\frac{dc_s}{dt} = \frac{q}{V_l}\left(c_{\sin} - c_s\right) - Q_s c_x \tag{2}$$

ethanol (product) concentration:

$$\frac{dc_e}{dt} = \frac{q}{V_l}\left(c_{ein} - c_e\right) + \left(Q_{epr} - Q_e\right)c_x \tag{3}$$

carbon dioxide concentration:

$$\frac{dc_c}{dt} = D_g\left(c_{cin} - c_c\right) + Q_c c_x \tag{4}$$

dissolved oxygen concentration:

$$\frac{dc_o}{dt} = \frac{q}{V_l}\left(c_{oin} - c_o\right) + Na - Q_o c_x \tag{5}$$

gas phase oxygen concentration:

$$\frac{dc_g}{dt} = D_g\left(c_{gin} - c_g\right) - Na\frac{V_l}{V_g} \tag{6}$$

where c_x is the biomass concentration, μ is the specific biomass growth rate, q is the flow rate of liquid phase, V_l is the liquid phase volume, c_s is the substrate concentration, c_{sin} is the input substrate concentration, Q_s is the substrate specific consumption, c_e is the ethanol concentration, c_{ein} is the input ethanol concentration, Q_e is the ethanol specific consumption, c_c is the carbon dioxide concentration, c_{cin} is the input carbon dioxide concentration, D_g is the gas phase dilution rate, Q_c is the carbon dioxide specific consumption, c_o is the dissolved oxygen concentration, c_{oin} is the input dissolved oxygen concentration, Na is the oxygen transfer, and Q_o is the oxygen specific consumption, c_g is the gas phase oxygen concentration, c_{gin} is the input gas phase oxygen concentration, V_g is the gas phase volume.

The mathematical description of the kinetic model mechanisms is shown in Table 1, the process parameters are given in Table 2.

Here, k is the saturation constant, Y_{ij} is the yield of the component j on i, k_{La} is the volumetric mass transfer coefficient based on the liquid volume, τ is the time constant for the induction of the production of consumption capacity, m is the gas liquid distribution coefficient, f is the induction or the repression factor, and the subscript and the superscript c is carbon dioxide, e is ethanol, g is the gas phase, i is the component, in is the input, I is inhibition, l is the liquid phase, lim is limited capacity, max is maximum, o is oxygen, ox is oxidative, and red is reductive.

TABLE I. KINETIC MODEL MECHANISMS OF THE BIOPROCESS.

Mechanism	Description
Glucose uptake	$Q_s = Q_{s\max}\dfrac{c_s}{k_s + c_s}$
Oxidation capacity	$Q_{o\lim} = Q_{o\max}\dfrac{c_o}{k_o + c_o}$
Oxidative glucose metabolism	$Q_{sox} = \min\begin{cases} Q_s \\ Y_{so}Q_{o\lim}\end{cases}$
Reductive glucose metabolism	$Q_{sred} = Q_s - Q_{sox}$
Ethanol uptake	$Q_e = Q_{e\max}\dfrac{c_e}{k_e + c_e}\dfrac{k_I}{k_I + c_s}$
Oxidative ethanol metabolism	$Q_{eox} = \min\begin{cases} Q_e \\ Y_{eo}\left(Q_{o\lim} - Q_{sox}Y_{so}\right)\end{cases}$
Ethanol production	$Q_{epr} = Y_{se}Q_{sred}$
Growth	$\mu = Y_{sx}^{ox}Q_{sox} + Y_{sx}^{red}Q_{sred} + Y_{ex}Q_e$
Carbon dioxide production	$Q_c = Y_{sc}^{ox}Q_{sox} + Y_{sc}^{red}Q_{sred} + Y_{ec}Q_e$
Oxygen consumption	$Q_o = Y_{so}Q_{sox} + Y_{eo}Q_{sox}$
Oxygen transfer	$Na = k_{La}\left(\dfrac{c_g}{m} - c_o\right)$
Maximum consumption rates	$\dfrac{dQ_{i\max}}{dt} = \dfrac{1}{\tau_i}\left(Q_{i\max}^{p} f_{ic} - Q_{i\max}\right)$, $i = e, s, o$
Induction or repression factors	$f_{oc} = \dfrac{c_o}{k_o + c_o}\dfrac{2c_s + c_e}{k_m + 2c_s + c_e}$ $f_{sc} = \dfrac{c_s}{k_n + c_s}$ $f_{ec} = \dfrac{c_e}{k_e + c_e}\dfrac{k_I}{k_I + c_s}\dfrac{c_o}{k_o + c_o}$

The main goal is to maintain a desired profile of dissolved oxygen concentration c_O in the fermenter by manipulating the gas phase dilution rate D_g that is the ratio between the gas phase volumetric flow rate and the gas phase volume.

III. FUZZY CONTROL

Fuzzy system has been known to provide a framework for handling uncertainties and imprecision by taking linguistic information from human experts. L. A. Zadeh described his view on the evolution of fuzzy logic and its current status in [18].

TABLE II. PROCESS PARAMETERS AND INPUTS

Variable	Unit	Value
k_e	mol l^{-1}	2.2×10^{-3}
k_I	mol l^{-1}	5.6×10^{-4}
k_m	mol l^{-1}	1.7×10^{-4}
k_n	mol l^{-1}	3.6×10^{-4}
k_o	mol l^{-1}	3.0×10^{-6}
k_s	mol l^{-1}	5.6×10^{-4}
k_{La}	h^{-1}	592
m	mol mol^{-1}	35
V_l	l	0.7
V_g	l	0.3
Y_{sx}^{ox}	C-mol mol^{-1}	3.65
Y_{sc}^{ox}	mol mol^{-1}	2.35
Y_{sx}^{red}	C-mol mol^{-1}	0.36
Y_{sc}^{red}	mol mol^{-1}	1.89
Y_{ec}	mol mol^{-1}	0.68
Y_{eo}	mol mol^{-1}	1.28
Y_{ex}	C-mol mol^{-1}	1.32
Y_{se}	mol mol^{-1}	1.88
Y_{so}	mol mol^{-1}	2.17
$Q_{e\max}^{p}$	mol (C-mol h)$^{-1}$	0.13
$Q_{s\max}^{p}$	mol (C-mol h)$^{-1}$	0.5
$Q_{o\max}^{p}$	mol (C-mol h)$^{-1}$	0.2
τ_e	h	2.8
τ_o	h	1.6
τ_s	h	2.5
$c_{sin}= c_{gin}$	mol l^{-1}	1×10^{-3}
c_{xin}	C-mol l^{-1}	0
$c_{ein}= c_{cin} = c_{oin}$	mol l^{-1}	0
$c_x(0)$	C-mol l^{-1}	3.2138×10^{-3}
$c_s(0)$	mol l^{-1}	1.1951×10^{-4}
$c_e(0)$	mol l^{-1}	1.2594×10^{-9}
$c_c(0)$	mol l^{-1}	1.7914×10^{-3}
$c_o(0)$	mol l^{-1}	2.6112×10^{-6}
$c_g(0)$	mol l^{-1}	9.3515×10^{-5}

Fuzzy controllers have found popularity in many practical situations. Design of a simple fuzzy controller [19] can be based on a three-step design procedure that is built on PID control. The algorithm is as follows: start with a PID controller, insert an equivalent, linear fuzzy controller and make it gradually nonlinear. A fuzzy controller (Figure 1) can include empirical rules that are called a rule base. The computer is able to execute the rules and compute a control signal depending on the measured input error and the change in error. The inputs are most often hard or crisp measurements from some measuring equipment.

A dynamic controller would have additional inputs, for example derivatives, integrals, or previous values of measurements backwards in time. The block fuzzification converts each piece of input data to degrees of membership by a lookup in one or several membership functions. The rules may use several variables, both in the condition and the conclusion of the rules. Basically, a linguistic controller contains rules in the if-then format, but they can be presented in different formats. The resulting fuzzy set must be converted to a number that can be sent to the process as a control signal. This operation is called defuzzification.

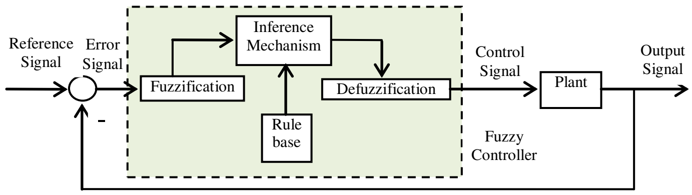

Fig. 1. Control system with a fuzzy controller [19].

The fuzzy controller based on the structure of the standard PID controller has following (absolute) form:

$$u = F\left(e(t), \frac{d}{dt} e(t), \int e(\tau) \right) \tag{7}$$

The output sets can often be linear combinations of the inputs, or even a function of the inputs.

The developed Fuzzy Logic Toolbox for the software package MATLAB implements one of the hybrid schemes known as the adaptive network based fuzzy inference system (ANFIS) [20]. In the ANFIS architecture, FIS is described in a layered, feedforward network structure (Figure 3). The parameters in layer 1 are called premise parameters and they are adjustable. The second layer represents the T-norm operators that combine the possible input membership grades in order to compute the firing strength of the rule. In the basic ANFIS method these parameters are not adjustable. The third layer implements a normalisation function to the firing strengths producing normalised firing strengths. The fourth layer represents the consequent parameters that are adjustable. The fifth layer represents the aggregation of the outputs performed by weighted summation. This is not adjustable [20]. The *subclust* function finds the clusters by using the subtractive clustering method. The *genfis2* function builds upon the *subclust* function to provide a fast method to generate a Sugeno-type fuzzy inference system.

A. Subtractive clustering

The fuzzy model suggested by Takagi and Sugeno in [21] and Sugeno and Kang in [22] also known as the Takagi-Sugeno-Kang (TSK) model, has gained increasing interest in theoretical analysis and applications of fuzzy modelling and control. The TSK model is associated with fuzzy rules that have a special format with a functional-type consequent instead of the fuzzy consequent that normally appears in the Mamdani model [23]. The idea of fuzzy clustering is to divide the data space into fuzzy clusters, each representing one specific part of the system behaviour [24]. After projecting the clusters onto the input space, the antecedent parts of the fuzzy rules can be found. The consequent parts of the rules can then be simple functions. In this way, one cluster corresponds to one rule of the TSK model [25]. An advantage of using a clustering method to find rules is that the resultant rules are more tailored to the input data than they are in an FIS generated without clustering.

Consider a collection of n data points $\{x_1, x_2, ..., x_n\}$ in a M dimensional space. Each data point is a candidate for cluster centres. Based on the density of surrounding data points, the potential value for each data point is calculated as follows

$$P_k = \sum_{j=1}^{N} exp\left(-\alpha\left\|x_k - x_j\right\|^2\right) \tag{8}$$

where $\alpha = \frac{\gamma}{(r_a)^2}$, $\|.\|$ denotes the Euclidean distance, P_k is the new potential-value of each examined point, α is the weight between k-data to j-data, x is the data point, γ is a variable (commonly set to 4), r_a is a cluster radius, it is a positive constant that represents the radius of data neighbourhood.

A data point will have a high density value if it has many neighbouring data points. The first cluster centre x_{c1} is chosen as the point having the largest density value P_{c1}. Next, the density measure of each data point x_k is revised as follows:

$$P_k^s = P_k - P_{c1}\exp\left(-\beta\left\|x_k - x_{c1}\right\|^2\right) \tag{9}$$

where $\beta = \gamma/(r_b)^2$, $r_b = r_a\eta$, r_b is a positive constant which defines a neighbourhood that has measurable reductions in density measure. Therefore, the data points near the first cluster centre x_{c1} will have significantly reduced density measure. P_{c1} is the potential-value data as cluster centre, β is the weight of k-data to cluster centre, η is the quash factor, usually set to 1.5.

When the potential of all data points have been revised according to (9), the data point with highest remaining potential is selected as the second cluster centre. This process continues until a sufficient number of clusters are attainted or all remained density values less than the threshold.

IV. Simulation Results

A. PI control of the fermentation process

PI controllers described by the transfer function

$$C = k_p\left(1 + \frac{1}{t_i s}\right) \tag{10}$$

with k_p the proportional gain, t_i the integral time, were tuned using Cohen-Coon and Chien-Hrones-Reswick methods [26]. The model was identified from the step response of the fermenter in the form of the first order plus time delay transfer function

$$S = \frac{K}{(\tau s + 1)} e^{-Ds} \tag{11}$$

The transfer function parameters are: the time constant $\tau = 0.4$ h, the gain $K = 6.9\times10^{-6}$ mol h l^{-1}, and the time delay $D = 0.01$ h. The PI controller parameters obtained using the Cohen-Coon formulas are $k_p = 5.2\times10^6$ mol^{-1} h^{-1} l, $t_i = 0.032$ h and those obtained using the Chien-Hrones-Reswick formulas are $k_p = 2.02\times10^6$ mol^{-1} h^{-1} l, $t_i = 0.47$ h.

B. Control of the fermentation process using Takagi-Sugeno fuzzy PI controller

Sugeno-type fuzzy inference system was generated using subtractive clustering in the form (12) for the fuzzy PI controller design.

$$\text{If } e \text{ is } A_i \text{ and } \int e \text{ is } B_i$$
$$\text{Then } f_i = p_i\, e + q_i \int e + r_i,\ i = 1, 2, 3 \tag{12}$$

where e is the control error, p_i, q_i, r_i are the consequent parameters. The symmetric Gaussian function was used for the fuzzification of inputs and it depends on two parameters σ and c as it is seen in (13):

$$\mu(x) = e^{-\frac{(x-c)^2}{2\sigma^2}} \tag{13}$$

The parameters σ and c for the Gaussian membership functions are listed in the Table 3. The consequent parameters in the control input rule (12) are listed in Table 4.

TABLE III. Parameters of the Gaussian membership functions.

e		$\int e$	
σ_i	c_i	σ_i	c_i
1.03×10^{-6}	-6.14×10^{-9}	3.27×10^{-6}	3.75×10^{-7}
1.03×10^{-6}	1.40×10^{-7}	3.27×10^{-6}	-5.50×10^{-6}
1.03×10^{-6}	6.05×10^{-10}	3.27×10^{-6}	-1.01×10^{-7}

TABLE IV. Consequent parameters.

p_i	q_i	r_i
-35853	2642452	-0.58
52151	87325	0.63
335853	-1677420	0.39

Rule viewer that simulates the entire fuzzy inference process is shown in Figure 2. Figure 3 shows the structure of ANFIS and Figure 4 shows the corresponding input-output surface of this fuzzy system.

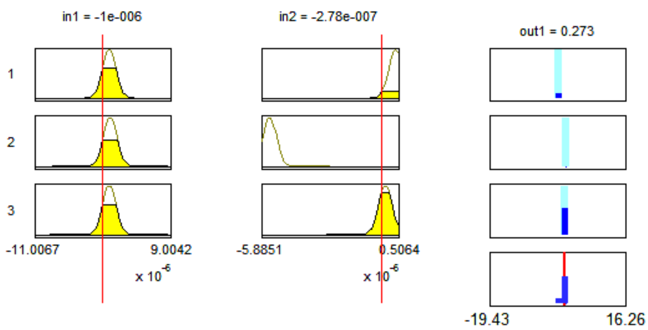

Fig. 2. Fuzzy inference system.

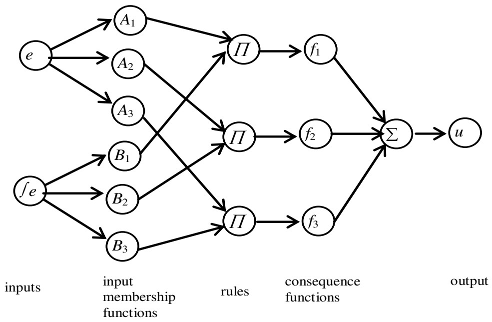

Fig. 3. Structure of ANFIS.

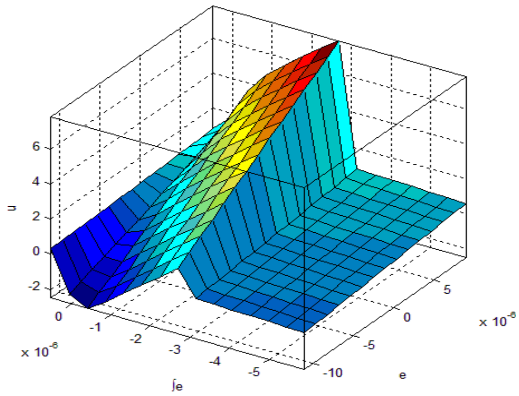

Fig. 4. Input-output surface.

To demonstrate the robustness of the designed fuzzy controller, parameter perturbations were applied. They represented changes of ±20% in the liquid phase dilution rate D_l and changes of ±20% in the substrate saturation constant k_s.

Simulation results obtained using designed PI and fuzzy PI controllers in the set-point tracking are shown in Figure 5 for the controlled output of the nominal system. The control inputs are presented in Figure 6. Figures 7 and 8 show controlled outputs and control inputs for the -20% parameter changes. Figures 9 and 10 show controlled outputs and control inputs for the +20% parameter changes.

PI and fuzzy PI controllers were compared using IAE criteria. The IAE values are given in Table 5. According to IAE, the fuzzy PI controller assured the best set-point tracking.

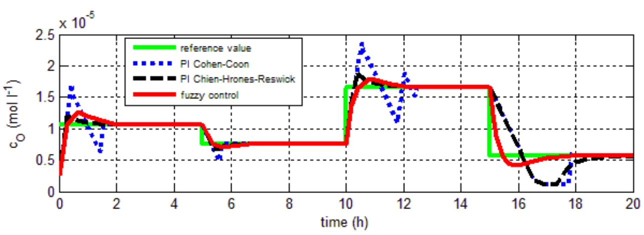

Fig. 5. Control of the dissolved oxygen concentration in the fermenter: nominal system.

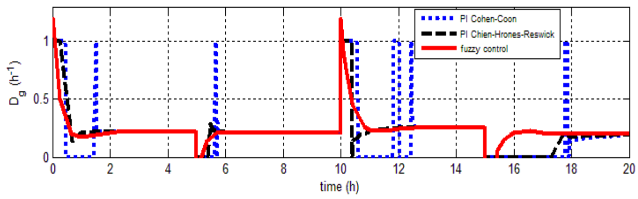

Fig. 6. Control inputs: nominal system.

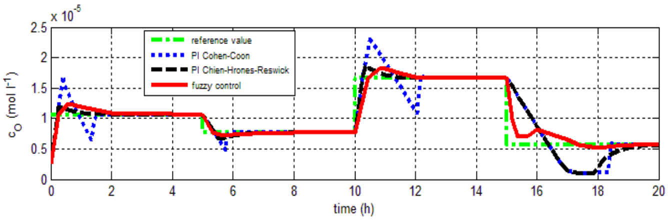

Fig. 7. Control of the dissolved oxygen concentration in the fermenter: -20% parameter changes.

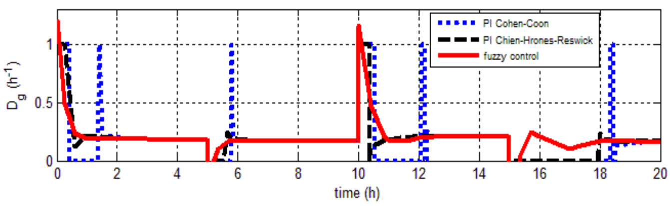

Fig. 8. Control inputs: -20% parameter changes.

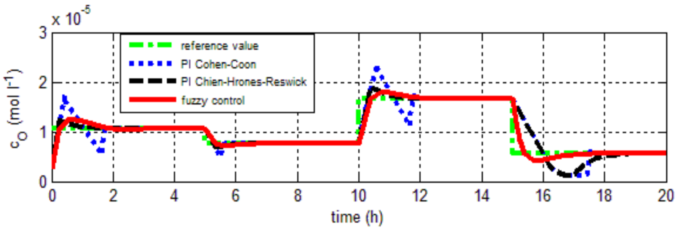

Fig. 9. Control of the dissolved oxygen concentration in the fermenter: +20% parameter changes.

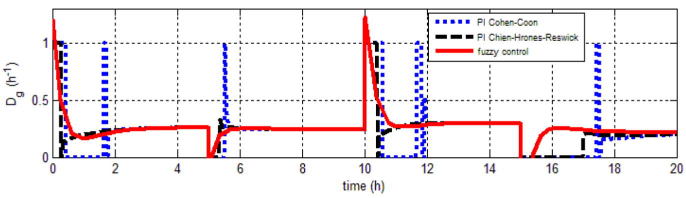

Fig. 10. Control inputs: +20% parameter changes.

TABLE V. COMPARISON OF THE SIMULATION RESULTS IN THE SET-POINT TRACKING BY INTEGRATED ABSOLUTE ERROR IAE .

controller	**IAE**		
	nominal system	-20 % changes	+20 % changes
PI Cohen-Coon	2.44×10^{-5}	2.71×10^{-5}	2.25×10^{-5}
PI Chien-Hrones-Reswick	1.78×10^{-5}	2.04×10^{-5}	1.60×10^{-5}
Fuzzy PI	0.95×10^{-5}	1.26×10^{-5}	1.02×10^{-5}

The designed controllers were tested also in the disturbance rejection in the nominal system. The disturbance was represented by ±50% changes of the gas liquid distribution coefficient *m*. Figures 11, 12 present the simulation results for the controlled output - the dissolved oxygen concentration c_O and the control input - the gas phase dilution rate D_g.

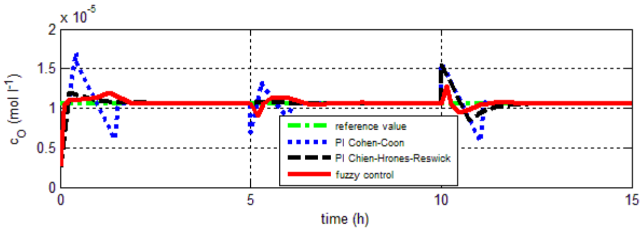

Fig. 11. Disturbance rejection in the nominal system: dissolved oxygen concentration.

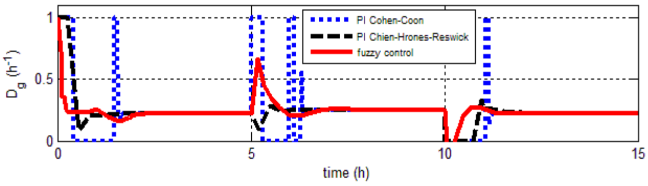

Fig. 12. Disturbance rejection in the nominal system: control inputs.

PI and fuzzy PI controllers in disturbance rejection were compared also using IAE criteria as it is seen in Table 6. Fuzzy PI controller assured the best results also in the disturbance rejection.

TABLE VI. COMPARISON OF THE SIMULATION RESULTS FOR DISTURBANCE REJECTION BY INTEGRATED ABSOLUTE ERROR IAE .

controller	IAE
	disturbance rejection – nominal system
PI Cohen-Coon	0.42×10^{-5}
PI Chien-Hrones-Reswick	0.82×10^{-5}
Fuzzy PI	0.40×10^{-5}

CONCLUSIONS

Fuzzy logic control based on the Takagi–Sugeno inference method has been applied for control of the baker's yeast fermentation. Simulation results confirm that fuzzy PI controllers are able to assure better performance in the set-point tracking as well as in the disturbance rejection than conventional PI controllers. Subtractive clustering method was used to identify the rule base needed to realize fuzzy PI controller. This approach was chosen to minimize the number of rules of designed fuzzy logic controller.

ACKNOWLEDGMENT

The authors gratefully acknowledge the contribution of the Scientific Grant Agency of the Slovak Republic under the grant 1/0112/16.

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