Modelling and Control of Milk Fermentation Process in Biochemical Reactor

Jožef Ritonja

Abstract—The biochemical industry is one of the most important modern industries. Biochemical reactors are crucial devices of the biochemical industry. The essential bioprocess carried out in bioreactors is the fermentation process. A thorough insight into the fermentation process and the knowledge how to control it are essential for effective use of bioreactors to produce high quality and quantitatively enough products. The development of the control system starts with the determination of a mathematical model that describes the steady state and dynamic properties of the controlled plant satisfactorily, and is suitable for the development of the control system. The paper analyses the fermentation process in bioreactors thoroughly, using existing mathematical models. Most existing mathematical models do not allow the design of a control system for controlling the fermentation process in batch bioreactors. Due to this, a mathematical model was developed and presented that allows the development of a control system for batch bioreactors. Based on the developed mathematical model, a control system was designed to ensure optimal response of the biochemical quantities in the fermentation process. Due to the time-varying and non-linear nature of the controlled plant, the conventional control system with a proportional-integral-differential controller with constant parameters does not provide the desired transient response. The improved adaptive control system was proposed to improve the dynamics of the fermentation. The use of the adaptive control is suggested because the parameters' variations of the fermentation process are very slow. The developed control system was tested to produce dairy products in the laboratory bioreactor. A carbon dioxide concentration was chosen as the controlled variable. The carbon dioxide concentration correlates well with the other, for the quality of the fermentation process in significant quantities. The level of the carbon dioxide concentration gives important information about the fermentation process. The obtained results showed that the designed control system provides minimum error between reference and actual values of carbon dioxide concentration during a transient response and in a steady state. The recommended control system makes reference signal tracking much more efficient than the currently used conventional control systems which are based on linear control theory. The proposed control system represents a very effective solution for the improvement of the milk fermentation process.

Keywords—Bioprocess engineering, biochemical reactor, fermentation process, modeling, adaptive control.

I. INTRODUCTION

BIOCHEMICAL, or Bioprocess Engineering, deals with the processes that involve biological organisms for production. The Biochemical Engineering industry is one of the most important modern industries. Its impact on the modern economy is enormous. This is the reason for the very intensive development in the field of Bioprocess Theory and Applications. The main motivation for such development is the requirement for large production of high-quality biologically manufactured products, such as pharmaceuticals, foods, and beverages. The most important devices in the Bioprocess Engineering industry are bioreactors, which must be properly designed and, what is even more important, applied. The great effort of research institutions in the field of Bioprocess Engineering is also intended for the discovery of better mathematical models of the fermentation process, and for the development of new algorithms for the control of the bioreactors' processes [1].

The fermentation process is the most important biological process which is being implemented in bioreactors. During the fermentation process a variety of products is generated by means of various micro-organisms. One of the oldest fermentation products is kefir, which is usually produced by fermentation of milk with kefir grains. Milk is an excellent growing media for microorganisms, which means that fermentation can be carried out with different starter cultures, producing a range of dairy products. One of the basic parameters for describing the starter culture is its ability to produce aromatic products [2]. Thus, yoghurt and similar products have a distinctive odour and taste, which is attributed to the volatile/non-volatile acids and carbonyl products produced during fermentation [3]. Among the milk beverages, kefir is widely known for its unique aroma and taste. During the fermentation process, the biophysical quantities must be controlled precisely to obtain a high-quality product. The biophysical quantities and an adequate control system must be developed and realised to assure the proper time response.

The basic step in the design of control systems is always the identification of a mathematical model that describes the steady state and dynamic properties of the controlled process satisfactorily, and is suitable for the development of the control system. The growth of the microbial community in the fermentation medium is described by a growth curve [4]. The main goal of mathematical modelling of the microorganisms' growth is to evaluate the biological parameters under different fermentation conditions and to develop predictive growth models [4]. These are mathematical expressions describing the growth, survival, inactivation or biochemical process of microorganisms. In addition, they can be defined as an effective technological tool for studying the growth of a wide variety of bio-populations. Growth curves have the shape of a stretched letter "S" [3]. Mathematically, they are classified in a group of sigmoid curves. Sigmoid functions contain functional parameters without biological significance. The

Jožef Ritonja is with the University of Maribor, Faculty of Electrical Engineering and Computer Science, Koroška cesta 46, 2000 Maribor, Slovenia (phone: 00386 2 220 7074; e-mail: jozef.ritonja@um.si).

World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:14, No:2, 2020

effective integration of sigmoid functions into the development of primary growth models requires bio-parameterization of these functions.

A thorough analysis was carried out of the fermentation process in bioreactors during the study for this paper. Existing mathematical models were examined. The conclusion was that the majority of known mathematical models of the fermentation process in bioreactors are suitable for fermentation process analysis, but they are not convenient for control system design, synthesis and realization [5]. This was the reason that we have undertaken extensive work for the derivation of a fermentation process mathematical model which will be adequate for the design and realisation of the bioreactor's control system.

We focused our study on modelling of the milk fermentation process in a batch bioreactor. The batch bioreactors have two input quantities which influence the fermentation process dynamics: The rotation speed of the mixer system and the temperature of the heating systems. There are many output quantities, but most of them are difficult to measure. An output quantity which has good correlation with bioreactors` dynamics and is relatively simple to measure is carbon dioxide (CO_2) [6]. CO_2 is one of the growth and metabolism products of microorganisms. For understanding and applying the effects of this gas on the microbiological metabolism, it is necessary to monitor the level of dissolved CO_2 in the fermentation medium. The fluctuations in CO_2 concentration can occur as a result of technological errors, or because of the unpredictable behaviour of microorganisms. The parametrical mathematical model which connects mixer speed and heater`s temperature as input quantities with CO_2 concentration as the output quantity is identified and presented in the paper.

The obtained mathematical model of the fermentation process was used for the design and synthesis of a control system which will assure the desired response of biochemical quantities in the fermentation process. Most of the commercial bioreactors are still equipped with an open loop control system or linear closed loop control system, with the Proportional-Integral-Differential (PID) controllers with constant parameters. Due to the non-linear characteristics and time-varying parameters of the controlled plant, the conventional control system with PID controllers does not contribute the optimal time response [7]. The advanced model reference adaptive control system was proposed to improve the dynamics of the fermentation process in a bioreactor. The use of the adaptive control is suggested because the parameters' variations of the studied biochemical process are, in most cases, very slow, which gives the possibility to adapt the controller's parameters [8].

The proposed control system was tested to produce the dairy products in a laboratory bioreactor. CO_2 concentration was chosen as the controlled variable. This correlates well with the others, for the quality of the fermentation process in significant quantities. The level of the CO_2 concentration gives important information about the fermentation process. Low levels of CO_2 cause an unpleasant flavour, but, on the other hand, high concentrations of CO_2 cause an inhibitory effect on the growth of microorganisms, leading to a slower fermentation process.

The modelling of the milk fermentation process is presented in Section II, the control system design in Section III and some results are shown in Section IV.

II. Modelling of the Milk Fermentation Process in a Batch Bioreactor

A. Description of a Batch Bioreactor

A batch bioreactor is a vessel filled with a liquid medium where several biological reactions occur [1]. A bioreactor consists of a tank with an integrated heating/cooling- and mixer system. The tank is made mainly of stainless steel. The volume of batch bioreactors varies from 0,7 L to 15,000 L [3]. Batch bioreactors allow more efficient media utilisation and avert sterility problems caused by continuous liquid removal. At the beginning of an operation, the batch bioreactors are initially charged with cells and a medium containing essential substrates for growth. The bioreactors then evolve to a predetermined final time with no media feed or liquid withdrawal. During the operation one fresh media feed is supplied into the batch bioreactors [1].

The control of the fermentation process was studied in an RC1e bioreactor from Mettler Toledo. The RC1e is a computer-controlled laboratory batch reactor with working volume 0.7 L, designed primarily for determination of the thermal characteristics of chemical reactions. The used batch bioreactor was equipped with additional actuators and sensors which enable identification and control of basic biochemical and physical quantities during the fermentation process.

In our case, dissolved CO_2 was chosen as an output and a controlled variable. The SevenMulti Apparatus (Mettler Toledo) equipped with an ISE51B ion selective electrode was used for monitoring the dynamics of CO_2 in liquid media. It was connected to a personal computer, which records measurements in a selected time period with Lab X direct pH 2.3 software. The electrode has a selective permeable membrane, which separates the medium from the electrolyte in the electrode. Dissolved CO_2 from the medium diffuses through the membrane until equilibrium between the partial pressure of CO_2 in the electrolyte and the partial pressure of CO_2 in the medium is reached. Since partial pressure is proportional to concentration, the concentration of CO_2 in the medium can be determined from a calibration curve.

B. Mathematical Model of Batch Bioreactors

Mathematical modelling of bioreactors is a demanding problem due to the complexity of cellular metabolism. The appropriate degree of model complexity is determined by factors such as the amount of fundamental knowledge, data requirements for model construction and validation, computational requirements, and the intended use of the model [4]. There are numerous models of fermentation processes based on different kinetic assumptions [2]. Most of them focus only on the process kinetics, some are more complicated, and involve equations for heat transfer, the temperature

World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:14, No:2, 2020

dependence of kinetic parameters, oxygen mass transfer... The conventional mathematical models are built mainly of the mass balances of the main components involved in the culture (biomass, substrates, metabolites and products). They describe the global behaviour of a given component, or an effect of some biochemical reactions involving the component. The concept of a specific growth rate is often used. It consists of modelling various influences of the growth kinetics.

Conventional mathematical models of the fermentation process in bioreactors use representation with Differential Equations. Variables used in the mathematical models are concentration or volume of the biomass, growth limiting substrate and desired product. The modern batch bioreactors are equipped with mixers and heaters which enable control of the biochemical processes in the bioreactors. In this way, additional mechanical energy or heat is added to the bioreactor. Because conventional mathematical models of bioreactors do not include these variables, an augmented mathematical model was developed which describes the influence of the input variables on the progress of the fermentation process [8].

The CO_2 production in the fermentation system could be described with 2-inputs and a 1-output mathematical model. Inputs are mixer speed and heater temperature. Mixer speed is the control variable, and heater temperature is considered as a disturbance. The output of the mathematical model is the CO_2 concentration.

In [8] the necessary simplified mathematical model of the bioreactor which enables the control system design and synthesis was developed by an intuitive approach. The mathematical model consists of two parts:
1) Exponential functions, which describe CO_2 release behaviour in response to initial conditions by different constant process inputs,
2) Transfer functions, which describe the influence of mixer speed and heater temperature on the CO_2 release.

The exponential functions are described by the equation:

$$\gamma(t) = K_s (1 - e^{\frac{t}{T_s}}) \qquad (1)$$

where t is a time variable, $\gamma(t)$ denotes the CO_2 concentration, and K_s and T_s are parameters describing the static and dynamic characteristics of initial conditions response by the constant (unchangeable) process input.

The transfer functions, which connect the input variables (mixer speed and heater temperature) with the output variable (CO_2), are shown in Fig. 1.

The transfer function $G_1(s)$ describes the influence of mixer speed, and transfer function $G_2(s)$ the influence of heater temperature on CO_2 release. They are described by:

$$G_1(s) = \frac{k_1}{sT_1 + 1} \qquad (2)$$

$$G_2(s) = \frac{k_2}{sT_2 + 1} \qquad (3)$$

where k_1 and k_2 denote gains, and T_1 and T_2 denote time constants of the transfer functions, respectively.
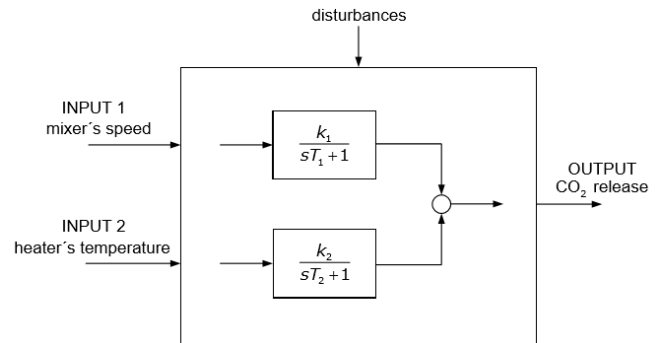

Fig. 1 Mathematical model of the influence of mixer speed and heater temperature on the CO_2 release of the fermentation process in the bioreactor

III. Control of the Milk Fermentation Process in a Batch Bioreactor

Conventional control systems based on the linear control theory are equipped mainly with PID controllers with constant parameters. Due to the nonlinear dynamic characteristic of the fermentation process, such control systems are inappropriate for fermentation process control. Considering the nature of the fermentation process, the use of adaptive control theory or robust control theory is most applicable [9]. In our study, we investigated the use of adaptive systems for bioreactor control. The advantage of the adaptive control system against the conventional control system with constant controller's parameters is the ability of the adaptive controllers to adapt to the changeable dynamics of the controlled plant. In this way, optimal operation is ensured in the entire operating range. There are numerous adaptive concepts, which can, in general, be divided into two groups [10]:
- Self Tuning Control (STC) systems, where identification of the controlled plant characteristics, the controller tuning and the controller implementation are separate. A very common combination is the recursive least square identification method, combined with the linear quadratic regulator. The parameters' identification and the controller's synthesis are executed on-line,
- Model Reference Adaptive Control (MRAC) systems, where identification of the controlled plant and controller tuning and implementation are connected in one module and the desired dynamics of the controlled plant are defined by the reference model.

Each of the two groups has its advantages and disadvantages. The advantage of the STC is that it is possible to design and realise the identification and regulation separately, which gives a more transparent structure to the control system. The advantage of MRAC is simpler implementation of the control system. There are very few

World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:14, No:2, 2020

publications describing the use of the STC for the fermentation process control. One of these is presented in [11] and [12]. However, there are no references which show the use of MRAC for fermentation process control. Therefore, in our work, we have focused on demonstrating the use of MRAC.

A detailed analysis of the fermentation process was performed. It was found out that only a single input of a fermentation process is sufficient to control the release of CO_2. The mixer's speed was selected as the control variable and heater's temperature is considered as a disturbance. An accurate synthesis of the conventional PID controller is not possible, because the parameters of the mathematical model are unknown and time varying.

The MRAC system consists of a reference model, adaptation mechanism and adjustable controller. The reference model describes the desirable nature of the fermentation system. The adaptation mechanism changes the parameters of the adjustable controller to assure the desirable dynamics. The block diagram of the MRAC system for the control of the fermentation process in a batch bioreactor is shown in Fig. 2.
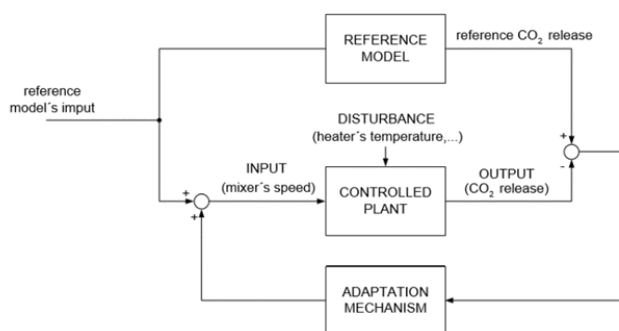

Fig. 2 The block diagram of the MRAC system for the control of the fermentation process in a batch bioreactor
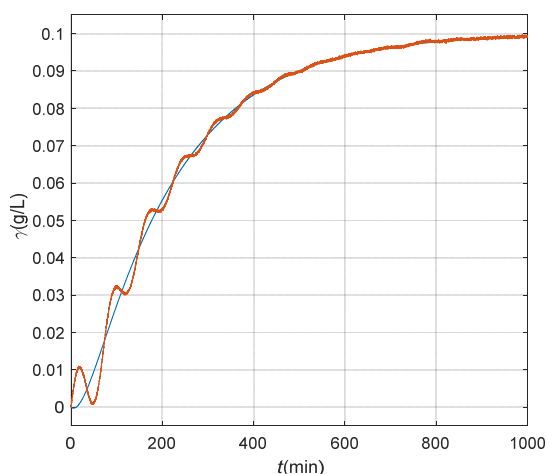

Fig. 3 The time response of the reference model and the actual CO_2 release response of the bioreactor when MRAC was used

IV. RESULTS

The applicability of the developed control system was tested for the control of a milk fermentation process in a batch

bioreactor. The bioreactor's mixer drive as input (control) variable and CO_2 release as output (controlled) variable were used for the biophysical quantities control.

Fig. 3 shows the output signal of the reference model and the CO_2 release response of the bioreactor in the case when a MRAC system was used. The tracking of the prescribed dynamic trajectory is evident.

From the obtained results, it is obvious that the proposed MRAC system assures much better following of the reference signal than a conventional linear control system with fixed control parameters.

V. CONCLUSION

The presented paper discusses the improvement of the control for a batch bioreactor`s fermentation process. Two phases of the development of the control system are described in detail: Identification of the mathematical model of the fermentation process, and control system design and synthesis. A description is presented of the fermentation process with the mathematical model with identified transfer function. The MRAC theory was used for the control system design.

Test results showed that the developed MRAC system provides minimum error between the reference and actual values of CO_2 concentration during a transient response and in a steady state.

The recommended control system makes reference signal tracking much more efficient than the currently used conventional control systems based on linear control theory. The proposed control system represents a very effective solution for the improvement of the milk fermentation process. The developed control system could be realised simply with a programmable logic controller.

REFERENCES

[1] M. A. Henson, "Biochemical reactor modeling and control," IEEE Control Systems Magazine, vol. 26, no. 4, pp. 54–62, Aug. 2006.
[2] M. Aghababaie, M. Khanahmadi, M. Beheshti, "Developing a kinetic model for co-culture of yogurt starter bacteria growth in pH controlled batch fermentation," *Journal of Food Engineering,* Vol. 166, pp. 72-90, Dec. 2015.
[3] G. Bylund, Dairy processing handbook. Lund, Sweden: Tetra Pak Processing Systems AB, 1995.
[4] P. Bogaerts, Castillo and R. Hanus, "A general mathematical modelling technique for bioprocesses in engineering applications", Systems Analysis Modelling Simulation, vol. 35, no. 2, pp. 87-113, Jan. 1999.
[5] D. Dochain and M. Perrier, "Dynamical modelling, analysis, monitoring and control design for nonlinear bioprocesses," in Biotreatment, Downstream Processing and Modelling, Berlin, Heidelberg: Springer Berlin Heidelberg, 1997, pp. 147–197.
[6] N. M. Dixon, D. B. Kell, "The control and measurement of CO2 during fermentations," *Journal of Microbiological Methods,* Vol. 10, pp. 155-176, Nov. 1989.
[7] Bastin G. and Dochain D., On-line Estimation and Adaptive Control of Bioreactors. Elsevier, 1990.
[8] A. Goršek, J. Ritonja, and D. Pečar, "Mathematical model of CO2 release during milk fermentation using natural kefir grains," J. Sci. Food Agric., vol. 98, no. 12, pp. 4680–4684, Sep. 2018.
[9] L. Mailleret, O. Bernard, and J.-P. Steyer, "Nonlinear adaptive control for bioreactors with unknown kinetics," Automatica, vol. 40, no. 8, pp. 1379–1385, Aug. 2004.
[10] Y. D. Landau, Adaptive Control: The Model Reference Approach. New York, NY, USA: Marcel Dekker, Inc., 1979.
[11] D. Williams, P. Yousefpour, and B. H. Swanick, "Online adaptive

World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:14, No:2, 2020

control of a fermentation process," IEE Proceedings D - Control Theory and Applications, vol. 131, no. 4, pp. 117–124, Jul. 1984.

[12] J. Ritonja, "Design of Identification Based Adaptive Control for Fermentation Process in Bioreactor", ICEET, 2019.