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Implementation of Stir-Speed Adopted Controllers Onto a Batch Bioreactor for Improved Fermentation

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ABSTRACT Quality, quantity, and economy of the fermentation product depend on the transient response and the steady-state of the fermentation process. Due to its simple construction, an industrial batch bioreactor cannot be equipped with a closed-loop control system that applies adding or removing substances during fermentation. This theoretical and practical study displays how fermentation can be controlled, in this case by altering the rotational speed of a stirrer system of such a bioreactor. A numerical analysis was employed to set up a mathematical model that describes the impact of the stirrer speed on the fermentation. The model consists of linear and non-linear parts. To determine their parameters, a least square identification and a particle swarm optimization method were utilized. The model was fitted and tested experimentally in a laboratory on the operating batch bioreactor. The design and synthesis of a conventional linear control system and an advanced model reference adaptive control system, which is also convenient for control of non-linear controlled plants, were carried out based on the determined mathematical model. Both control concepts were first implemented into the dSpace 1103 control system, convenient for faster development and prototyping. Finally, they were realized with the Siemens SIMATIC S7 programmable logic controller, which was ideal for industrial environment operation. During the operation of the bioreactor, the control systems were tested along with the acquisition of measured data involving CO_2 concentration of a fermentation product. The findings of successfully applying linear and adaptive controllers of the milk fermentation in the batch bioreactor are analyzed and presented.

INDEX TERMS Bioreactor, fermentation, modeling, particle swarm optimization, least-square identification, linear/adaptive control, control system implementation.

I. INTRODUCTION

A. CURRENT STATE AND MOTIVATION

Bioprocesses are phenomena where living microorganisms (bacteria, yeasts, molds, algae) or cells are used to obtain desired products. The bioprocesses are applied in the production of biopharmaceuticals, food, fuels, and chemicals. They also enable the decomposition of waste and its conversion into useful products. Due to the growing demand for bioprocess products and an appeal to lower dependence on fossil fuels and reduce greenhouse gas emissions, Bioprocess Engineering is becoming a discipline with extreme importance and enormous potential. The impact of Bioprocess Engineering on the global economy is substantial [1].

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The primary biological process used for an application in Bioprocess Engineering is industrial fermentation. During the fermentation, an agent causes an organic source substance to break down into a simpler final substance. The agents are mainly the microorganisms, the source substance is called a substrate, and the final substance is called a product [2]. In short, the microorganisms consume the substrate, and during their growth generate the product.

The most crucial industrial production units in Bioprocess Engineering are bioreactors. There are many ways to classify them. One of the basic divisions is the classification according to the feeding strategy. There are three basic bioprocess procedures: batch, fed-batch, and continuous. Many bioreactors enable only one type of the procedure, while others enable the operation of more types of bioprocessing. Depending on the type of bioprocess being enabled by a

bioreactor, industrial bioreactors can be divided into corresponding groups. They differ in the possibility of supplying or removing the microorganisms and the substances during the fermentation. The batch bioreactors have the simplest structure. This type does not allow the supply or removal of the microorganisms, the substrate, or the product during the working biological process. Thus, throughout the fermentation process, the content in the batch bioreactor has no contact with external organisms or substances, i.e., the bioreactor is closed during its operation. In the fed-batch bioreactors, it is possible to add the microorganisms, the substrate, or the product during the fermentation in order to cultivate one or more nutrients in the operating bioreactors. All the substances remain in the bioreactor till the end of the fermentation. The continuous bioreactors (also named flow bioreactors) enable inflow and outflow of the microorganisms, the substrate, or the product into/from the reactor as a flowing stream. The microorganisms in such the bioreactors are fed continuously. From the described modes of operation, it follows that the batch bioreactors have uncomplicated construction, which is reflected in low production and installation costs as well as low maintenance. Therefore, the batch bioreactors are the most widespread and the most used ones among the bioreactors.

Although a fundamental operating principle of the bioreactors is elementary, thorough knowledge of bioprocesses in the bioreactors is required to ensure quality, quantity, and economy of the products. Intense research and development, considering the bioprocesses in the bioreactors of various forms, can be witnessed in the last decades. Fields of Mathematical Modeling and Control are becoming more important in Bioprocess Engineering largely due to comprehensive investigation of the challenging complexity of biological cellular metabolisms. The accuracy of a mathematical model and its elaborate determination are crucial for the design of a control system. Proper control of the bioprocesses is essential for the efficiency of the bioreactors. The control's main objective is to maximize the total production of the desired product with high and constant quality in the shortest possible time. An appropriate strategy for achieving the control objective depends on the bioreactor's operating mode and geometry, the source substance for the bioprocess, availability of online measurement, pertaining equipment for realization and accuracy of the bioreactor's mathematical model.

The global market associated with Bioprocess Engineering is growing at about 10 % per year. It is projected that it will reach USD 727.1 billion by 2025 [4]. Investments in the development of new bioprocess technologies are extremely large. There is a growing increase in the involvement of other scientific and engineering disciplines with the field of Bioprocess Engineering. The bioprocess industry's importance for the quality of the modern world, rapid development, and interdisciplinarity of this field was the primary motivation for the presented study. In it, knowledges of Systems Theory, Mathematical Modeling, and Control Design are used to improve the efficiency of the milk fermentation process in the batch bioreactors.

B. EXISTING SOLUTIONS WITH LITERATURE REVIEW

The primary methods to control the fermentation process use adding or removing microorganisms and substances during the fermentation [5]. This is the most natural way to control fermentation. These control methods are possible with the both fed-batch and continuous bioreactors. Unfortunately, due to their simple construction, the batch bioreactors do not allow adding or removing the organisms and the substance during operation. And consequently, these bioreactors do not accommodate the implementation of such control. The secondary methods to control the fermentation process are based on changing physical or chemical attributes of the bioreactors' content. These control methods are possible for all the three types of bioreactors. The implementation of these methods depends on the equipment of the bioreactors. For example: by using a stirrer system, dissolved oxygen in the media in the bioreactor can be changed; with a heating/cooling system, the temperature in the bioreactor can be changed, and with an inlet of acid/base, a pH value of the content of the bioreactor can be changed.

Bioreactors equipped with an impeller for homogenizing culture media and a sparger for delivering oxygen to the cells are called stirred tank reactors and are the most widely used bioreactors. These range in sizes from 15 mL to 2000 L for single-use and are available in sizes larger than 2000 L for stainless-steel. The stirrer tank reactors are frequently used to scale-up the bioprocess from a research and development scale to a manufacturing scale. Due to the frequent equipment of existing and new bioreactors with the stirrer system, the stirrer system is a highly suitable final control element to control the fermentation process.

The problem of controlling the fermentation process is still ongoing. This is evident by a multitude of academic publications in recent years. A thorough review of relevant journal publications is carried out for the period 2000-2020. The purpose of the review was to determine research directions in this area and analyze existing solutions to this problem.

A tutorial review before the period under consideration is seen in [6], [7]. Reference [6] presents progress in Bioprocess System Engineering. Particular attention is focused on the control of the bioprocesses. The [7] presents the basics of bioreactor technology, mathematical models of all types of bioreactors, industrial reactors available on the market, control concepts for different reactors, and ''future'' trends.

Control concepts majorly differ in regards to a type of bioreactors. Therefore, the types of most present bioreactors in the industry and their prospects are reviewed hereafter. It is observed and predicted for years that batch bioreactors will be replaced by continuous bioreactors. However, based on data from manufactures and traders, industrial bioreactors are still primarily made for the batch processing (some reports even 90% presence in certain areas). In [8], a detail quantitative comparison of batch, fed-batch and continuous

bioreactors on E-coli fermentation benchmark is presented. Maximum biomass concentration, volumetric biomass productivity, biomass yield, and cost analysis for different operating modes are presented. The advantages and weaknesses of the bioreactors are highlighted therein. The article points out that the advantage of batch bioreactors is mainly their undemanding use, the advantage of fed-batch bioreactors is cost-effective operation (but they require complex handling and poses more challenges for operators), and continuous bioreactors enable operation in a state where the growth rate is purely controlled feeding rate, which is very useful for control in both academic rate and industrial production. In [9], a review of an economic analysis of batch and continuous biopharmaceutical production is carried out. The analysis particularly brought up that lack of automation still exists. In [10], the effort of making an assumption of anticipated bioreactors in the future is documented. Based on the assumption, it can be summarized that the integrated continuous bioprocessing will not shut down existing batch facilities any time soon.

There are quite a few new works in the field of Mathematical Modeling of the fermentation process in the bioreactors. They try to replace a fundamental kinetic model with a simpler or more accurate one [2], [7]. However, in control studies over the last decade, the fundamental mathematical model of the fermentation is still the most commonly used for a theoretical analysis or for quantitative simulation.

It can be seen that the fermentation process in the bioreactors has represented an attractive problem for testing different concepts of conventional and advanced control theories. As expected, most of the work in this field is intended for the control of the continuous bioreactors, which are the most suitable for the control of the fermentation process. Some of the works that confirm the topicality of the discussed issues are [11]–[16]. Feedback linearization and various versions of robust control have proven to be particularly effective methods for controlling continuous bioreactors. In [11], the control of multistage continuous bioreactors for wine fermentation with limiters on inlet flow rates of each tank is designed on the basis of the feedback linearization with an integrated anti-windup. Reference [12] shows the use of the feedback linearization for control of turbidostats; these are the continuous bioreactors, which are gaining interest due to the recent availability of micro- and small-scale devices. In [13], a cascaded-loop strategy was used for control of a perfusion/chemostat bioreactor. The inner loop of the strategy was linearized with a feedback controller, and the outer loop was designed based on an internal model principle. In [14], a robust decoupling method based on an artificial bee colony is shown for a marine fermentation process. Implementation of a sliding mode control for tubular bioreactors is presented in [15]. The use of a fuzzy neural network for marine fermentation is described in [16].

There are not so many publications in the field of the Fed-batch Bioreactor Control, as it is more difficult to implement the primary control methods. Again, the applicability of the robust control was investigated in [17]. The use of a simulation-based approximate dynamic programming method for optimal feedback control is extended and used in [18]. The fed-batch bioreactor control based on a linear algebra is shown in [19], and implementation of fractional-order iterative learning controller in [20].

However, there are very few publications dealing with the control of the fermentation in the batch bioreactors. Namely, due to their non-expensive and straightforward construction, they do not enable the primary control methods. Most contributions in the field of control of batch bioreactors deal with gas concentration- or transfer regulation. In [21], the use of the stirrer system is described for gain scheduling oxygen control. In [22], the oxygen transfer rate control is realized by utilizing a PI-controller that controls the input oxygen flow. Reference [23] presents the control of CO_2 production based on a linear controller, which generates a control input for the heating/cooling system. In [24] the dissolved CO_2 concentration is controlled by using the elementary model reference adaptive controller. All four references (21-24) show the use of linear or nonlinear controllers, which are basically intended for controlling linear processes. Nevertheless, the obtained simulation and experimental results prove that the regulators control the considered nonlinear fermentation process satisfactorily. It is necessary to point out that most commercial versions of the batch bioreactors are equipped with control systems that allow regulation of the temperature or the stirrer speed but do not have control systems that would control the dynamics of the entire fermentation process. Existing control systems, namely, do not ensure that transient responses of concentrations of substances will follow reference trajectories (except in [23], [24]).

An another interesting conclusion drawn from the literature review is that Adaptive Control Theory was used relatively rarely for the control of the fermentation.

C. CONTRIBUTION AND PAPER STRUCTURE

In the presented study, a focus is put on the fermentation process in the batch bioreactors equipped with stirrer systems. An uncomplicated structure of this type of bioreactor was preserved while upgraded with an efficient control system. The control system based on a conventional linear theory is established first. Following a goal of simplest implementation, a conventional control system was upgraded based on Adaptive Control Theory. Such implementation does not require knowledge of a mathematical model for tuning a controller for fermentation.

When designing a control system, it was assumed that standard measurement-, actuator- and final control equipment were available, such as for the batch bioreactors. In this way, the control system suitable for batch and for fed-batch bioreactors will be built. Although fed-batch bioreactors prevail in sales, a great portion of bioreactors with only batch bioprocessing is still presented in the industry. The only additional component needed for the implementation of the proposed

control system was a controller for the calculation of a control algorithm.

The presented work consists of two parts. The first part introduces a mathematical model of the fermentation process in the batch bioreactor. The second part shows the design and synthesis of a whole control system.

A preliminary hypothesis, which was confirmed in the study, was the idea that a stirrer system can be implemented to realize the control system for the fermentation process. In this way, a second chapter describes experiments and results, with which the impact of stirrer speed on transient response of the fermentation product can be evaluated. The enhanced mathematical model of the fermentation process in the batch bioreactors is introduced in the third chapter. The originality of this model is its ability to additionally evaluate the impact of the stirrer speed on the generation of the fermentation product. The obtained findings confirmed that it is possible to design a closed-loop system that controls the fermentation process as preferred. The control objective is specified in the fourth chapter. The linear controller developed on the basis of the enhanced model is designed, and test results are presented in the fifth chapter. The linear controller controls the fermentation process well if the parameters of the controller are determined precisely in advance. Therefore, a mathematical model of the fermentation process is needed. Its identification is demanding and time-consuming, so it makes sense to use an adaptive control technique to develop a control system that will be capable of autotuning and adapting to new operating conditions during the fermentation. The adaptive control system, also suitable for non-linear controlled plants, and the theory needed for this control system, are described in the sixth chapter. Concluding remarks are written in chapter seven. A detailed description of the laboratory batch bioreactor, proof of stability of the adaptive control system, procedure for estimation of the coefficients of the adaptation mechanism and essential definitions, lemma and theorems for proving the control system stability are presented in the Appendix.

II. EXPERIMENTAL ANALYSIS OF IMPACT OF STIRRER SPEED ON FERMENTATION PROCESS

To confirm the hypothesis, that the fermentation process could be controlled properly by changing the stirrer speed, a thorough experimental analysis of the effect of speed changes is carried out first. A well-equipped laboratory batch bioreactor was used for experiments. A multitude of static and dynamic measurements with constant or variable inputs of the fermentation process of probiotic beverage was conducted. The input quantity of the analyzed fermentation in the bioreactor was the stirrer speed, and the output quantity was the product of fermentation. In the considered case, the dissolved CO_2 was the observed fermentation product.

A. LABORATORY EQUIPMENT

Control of the fermentation process was studied in computer-controlled reaction calorimeter RC1e from Mettler Toledo, described in Appendix A [23]. During our study, the RC1e worked as a batch bioreactor. For the purposes of the study, it was equipped with sensors and an actuators.

The stirrer system was used to control the fermentation process. The stirrer system is an integral part of the batch bioreactor and allows continuous change of stirrer speed in a range from 0 min^{-1} to 400 min^{-1}. The stirrer speed drive consists of a DC motor with closed-loop speed control. The time constant of the controlled stirrer system is very short compared to the fermentation process. It can be assumed that the time needed for changing the stirrer speed is negligible compared to the time constant of the fermentation.

The controlled heating/cooling system was used to maintain a constant temperature of the mixture in the laboratory bioreactor during the entire fermentation process. The thermal system is an integral part of the bioreactor, and allows maintenance of or changing the internal temperatures in the range from 5 °C to 200 °C. An external thermostat controls the temperature of the bioreactor's content. Silicon oil is used as the heat transfer agent. It is pumped through the double jacket of the bioreactor in a closed circulation system. This keeps the temperature of the mixture in the bioreactor at the desired constant temperature. In all experiments with the laboratory bioreactor (i.e. measurements for the identification of the mathematical model of the fermentation process and tests for approval of the developed control systems), the heating/cooling system was maintained in the bioreactor at a constant temperature of 22 °C.

In the considered fermentation process, the dissolved CO_2 was the fermentation product. The multi-parameter measuring device SevenMulti (Mettler Toledo) with modular expansion possibilities was used as a basic unit. For the monitoring of dynamics of CO_2 in liquid media, the SevenMulti basic device was connected to the ISE51B ion-selective electrode [23]. Electrode potential response to CO_2 concentration is in a semilogarithmic scale a straight line over two decades of the concentration ($5{\cdot}10^{-4}$ g/L to $2{\cdot}10^{-2}$ g/L). A change in temperature causes the electrode response to shift and change a slope (temperature variation for a 5°C change, the slope for approx. 1.7 %). To eliminate this influence, the experiment was carried out in a constant temperature environment. For the connection of the SevenMulti basic unit and the ion-selective electrode sensor, an expansion module was added to the basic unit. The analog 1st order low pass filter for the elimination of sensor noise is integrated in the expansion module. For the transfer of measured signals from the SevenMulti basic device to PC, the basic unit was equipped with a USB communication module. For extensive measurement of several quantities over a long period of time and for their processing, software LabX direct pH 2.3 was installed on PC. This is professional equipment intended for a data logger and a data analysis. The sampling time of 10 min was selected. This time was sufficient due to the slow dynamics of the fermentation process. During the executing of the experiments, the sampling time was adjusted to the dynamics of the measured signal. Obtained data was saved into Microsoft Office 365 Excel documents, transferred

into MathWorks MATLAB, and processed using MATLAB with its Optimization toolbox functions. A block diagram of the batch bioreactor with a measurement system is displayed in Fig. 1.

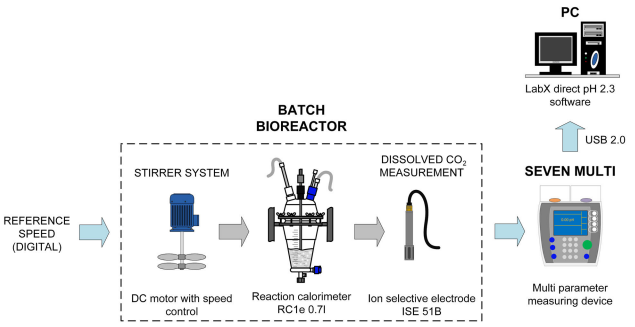

FIGURE 1. Block diagram of laboratory system for measurement of transient response of CO_2 concentration in tests with constant- and changeable stirrer speed.

Kefir grains for the fermentation process were obtained from a local dairy (Kele & Kele d.o.o., Logatec, Slovenia). They were maintained at room temperature in whole fresh full fat (3.5%) cow milk. For activation, the grains were washed with cold water and transferred into the fresh milk for five successive days. Milk from the same producer was used as fermentation medium.

B. TESTS WITH CONSTANT STIRRER SPEED

First, an analysis, how different values of constant stirrer speed during the entire fermentation process affects a transient response of dissolved CO_2, was carried out. Same initial values in all cases - the same initial concentrations of microorganisms, substrate and product were adopted. The outside temperature was kept constant in all tests, and the bioreactor stirrer system operated with constant speed. The obtained results were expected, meaning - by higher constant stirrer speed, the faster response of the fermentation process and the higher final value of the fermentation product were obtained. Same conclusions were obtained in tests with other initial values and other quality of substances. Fig. 2 presents the measured transient response of the dissolved CO_2 concentration for the different constant stirrer speed values of the studied bioreactor, all at a constant temperature of 22 °C.

C. TESTS WITH CHANGEABLE STIRRER SPEED

In the second stage, the effect of changing the stirrer speed during the fermentation process on the transient response of the fermentation was evaluated experimentally. All tests were performed at the constant bioreactor's content temperature 22 °C. Also, in this stage, various tests with different changes of stirrer speed (different magnitudes, up or down) in various phases of the fermentation process (in the starting induction phase, in the followed exponential growth phase, in the stationary phase, and in the end dying phase [5]) were carried out. In all the cases, increasing the speed accelerated the fermentation process, and reducing the speed slowed down

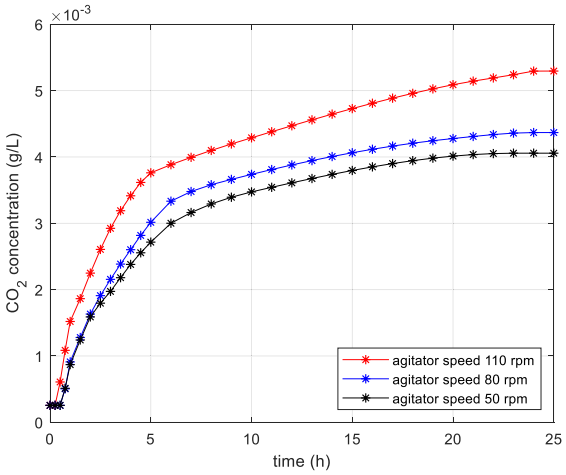

FIGURE 2. Measured transient response of dissolved CO_2 concentration (i.e., fermentation product) for different values of stirrer speed for studied bioreactor.

its development. The impact of a step change of the stirrer speed on a response of the fermentation process is presented in Figs. 3, 4 and 5.

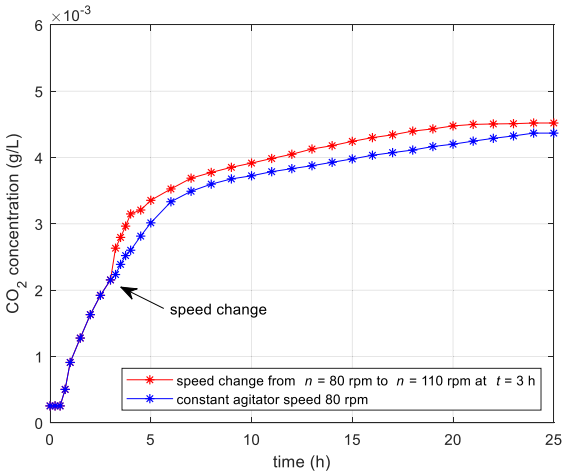

FIGURE 3. Measured transient response of dissolved CO_2 concentration by step change of stirrer speed from $n = 80$ min^{-1} to $n = 110$ min^{-1} in $t = 3$ h, compared with CO_2 transient response by constant stirrer speed $n = 80$ min^{-1} (also presented in Fig. 2).

Fig. 3 shows the transient response of the CO_2 concentration on the step change of the stirrer speed from $n = 80$ min^{-1} to $n = 110$ min^{-1}. The step change occurred at time $t = 3$ h. For comparison, the transient response of CO_2 concentration in a case of constant stirrer speed ($n = 80$ min^{-1}) during the operation is also added to this graph.

The results of the experiments where the step changes of the constant amplitude (from $n = 80$ min^{-1} to $n = 110$ min^{-1}) appears in different phases of the fermentation process ($t = 0$ h, $t = 3$ h, $t = 6$ h and $t = 12$ h) are presented in Fig. 4. The Figure presents deviations of the measured trajectories from the trajectory at constant speed $n = 80$ min^{-1}. It can be seen that the same amplitude changes in stirrer speed have different impacts on the course of the fermentation process if they appear in different phases of the fermentation process.

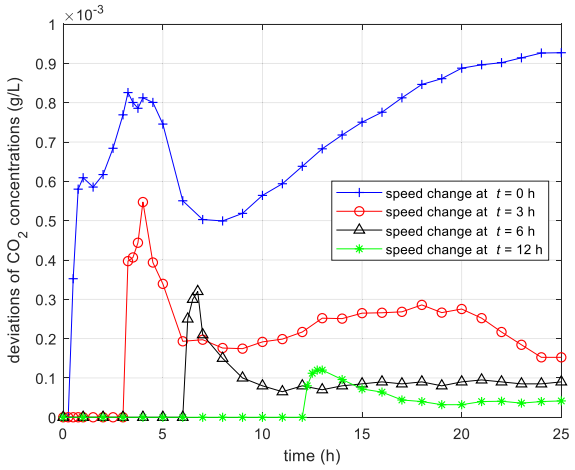

FIGURE 4. Time courses of deviations of CO_2 transient responses conducted with step changes of stirrer speed from $n = 80$ min^{-1} to $n = 110$ min^{-1} at different times ($t = 0$ h, $t = 3$ h, $t = 6$ h and $t = 12$ h) from CO_2 transient response of fermentation with constant stirrer speed $n = 80$ min^{-1}.

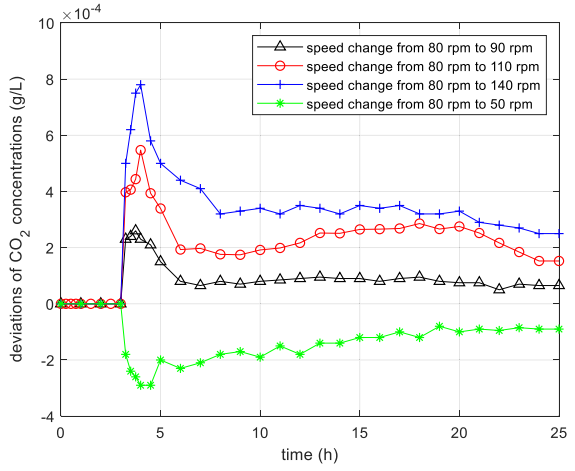

FIGURE 5. Time courses of deviations of CO_2 transient responses conducted with different amplitude stirrer speed step changes (from $n = 80$ min^{-1} to $n = 90$ min^{-1}, 110 min^{-1}, 140 min^{-1} and 50 min^{-1}) in time $t = 3$ h from CO_2 transient response of fermentation with constant stirrer speed $n = 80$ min^{-1}.

The presumption was confirmed that the influence of the stirrer speed change on the fermentation course is the biggest in the starting induction phase, smaller in the following exponential growth phase, and the smallest in the stationary- and end dying phase.

Fig. 5 presents the outcomes of the investigation of how different amplitudes of the stirrer speed changes, which happen at the same time of the fermentation process, affect the dynamics of the CO_2 production. Tests confirmed that an increase in stirrer speed accelerated, and that a decrease in stirrer speed, reduced CO_2 production. As expected, it was found that the dependence of the overshoot and stationary deviation on the amplitude of the stirrer speed change is not linear. Fig. 5 shows the results of the experiments where step changes with different amplitudes (from $n = 80$ min^{-1} to: $n = 90$ min^{-1}, $n = 110$ min^{-1}, $n = 140$ min^{-1} and $n = 50$ min^{-1}) occur in the same moment $t = 3$ h. The Figure presents deviations of the measured trajectories from the trajectory at constant speed $n = 80$ min^{-1} during the entire fermentation process.

Based on a multitude of the performed laboratory tests of the various fermentation processes, the hypothesis was confirmed that by changing the stirrer speed, the transient and the steady-states of the fermentation process could be influenced significantly. This finding led this study to the contemplation of the idea that the stirrer system alone could be successfully adopted to automatically control the fermentation process.

III. MATHEMATICAL MODEL OF FERMENTATION PROCESS

The first step in the development of a control system is the determination of an appropriate mathematical model. The fermentation is a non-linear, time-dependent, highly complex system with a poorly known structure and unknown and time-varying parameters. In the fermentation process, there are more than a thousand complex sets of different biochemical reactions representing enzyme kinetics inside a microorganism in addition to physical transfer rates [5]. It is impossible to assure unchangeable quality of the microorganisms and the substrate between different batches or during continuous flow. An additional challenge represents the adaptation of the microorganisms to an environment through their mutations. These are some of the reasons constituting complexity in forming such theoretical models.

The lack of mathematical models that would be suitable for the development of the control systems for the batch bioreactors' fermentation is particularly evident. This control can be performed only by changing the physical or chemical properties of the medium in the bioreactor. Therefore, for the design of the control system and its synthesis, a dynamic model that considers the influence of external variables (e. g., stirrer speed, temperature) on the growth of the microorganisms and execution of the fermentation process is needed.

In this article, development of a mathematical model for the fermentation in the bioreactor, which is primarily suitable for control engineers is considered. The required mathematical model describes the transient response of the fermentation process to initial concentrations of the substance. At the same time, the model describes the impact of the stirrer speed on the dynamics of the fermentation. Such a mathematical model has not been found in the current literature. Work in this field started with [23], [25] showing models that consider the influence of temperature on a response of a fermentation process.

A procedure of the modeling was divided into two phases. In the first phase, a mathematical model was determined, which describes a transient response of the fermentation only to concentrations of the microorganisms, the substrate and the product in the bioreactor at the beginning of the fermentation. This model was called a "constant stirrer speed model" because, in this case, external conditions are assumed constant. In a second phase, a mathematical model that describes

the impact of speed changes on the fermentation was established. This model was called a ''changeable stirrer speed model.'' A ''complete model'' consists of the both above mentioned submodels. It enables the calculation of an output of the bioreactor as a result of the initial conditions and the changeable input variable.

A. MODEL FOR CONSTANT STIRRER SPEED

There are many mathematical models of different grades of complexity that describe the fermentation process in the batch bioreactors [3], [5], [26]. Almost all the models are based on a mass balances of all the three components of the fermentation process and do not consider the mechanical or thermal impact on the fermentation process (changes in either the stirrer speed or the temperature in the bioreactor).

Choosing an appropriate degree of complexity of the model is of crucial importance. It is necessary to be aware of a purpose of the model and realistic possibilities when determining parameters of the model. Dynamic bioreactor models are classified according to a level of details used to describe an individual cell. Due to their mathematical simplicity, the dynamic models, which are based on unstructured description of a cellular metabolism and unsegregated representation of cell population are best suited for design of a model-based controller. Rather than individual enzyme-catalyzed reactions, lumped description of the cellular metabolism is employed. Cellular heterogeneity is ignored, and equations of the model describes pertaining phenomenological dynamics of an ''average cell'' [7], [27].

Such simple and the most frequently used mathematical model of the fermentation process is made up of a set of three non-linear differential equations, which define the concentration of the microorganisms, the substrate, and the product during the transient of the fermentation:

$$\dot{x}_1(t) = \frac{\mu_m x_2(t)}{S_m + x_2(t)} x_1(t) \tag{1}$$

$$\dot{x}_2(t) = -\frac{\mu_m x_2(t)}{S_m + x_2(t)} x_1(t), \tag{2}$$

$$\dot{x}_3(t) = \left[\alpha \frac{\mu_m x_2(t)}{S_m + x_2(t)} + \beta\right] x_1(t) \tag{3}$$

where variables of the mathematical model denote the following biological quantities:

$x_1(t)$ – the concentration of the microorganisms (g/L),

$x_2(t)$ - the concentration of the substrate (g/L),

$x_3(t)$ - the concentration of the product (g/L)

and parameters of the mathematical model are:

μ_m - the maximum microorganisms' growth rate (h^{-1}),

S_m - the substrate saturation constant (g/L),

α - the parameter that describes the relation between product yield and microorganism growth, and

β - the parameter that describes the product yield that is independent of the microorganism growth (h^{-1}).

In this model, a simplified expression called a Monod's law was used to describe a growth function [5].

TABLE 1. Measured initial values and identified parameters of constant stirrer speed model for studied fermentation process.

parameter	Value
initial concentration of microorganisms	$x_1(0) = 0.55 \cdot 10^{-3}$ g/L
initial concentration of the substrate	$x_2(0) = 3.70 \cdot 10^{-3}$ g/L
initial concentration of the product	$x_3(0) = 0.26 \cdot 10^{-3}$ g/L
maximum microorganisms' growth rate	$\mu_m = 9.462$ h^{-1}
substrate saturation constant	$S_m = 0.049$ g/L
parameter of product yield related to growth of microorganisms	$\alpha = 0.843 \frac{g/L}{g/L}$
parameter of product yield independent of growth of microorganisms	$\beta = 0.012$ h^{-1}
constant temperature	$T = 22$ °C
constant stirrer speed	$n = 80$ min^{-1}

In most cases, the model above is found to be suitable for modeling the batch bioreactor's fermentation process in a case of constant external variables. This model is found appropriate for and therefore used in this study as well.

For the determination of the model's parameters μ_m, S_m, α, and β of the studied fermentation process in the laboratory batch bioreactor a bound constrained optimization based on the Particle Swarm algorithm was used. Particle Swarm is a population-based algorithm that is similar to the Genetic Algorithms [28]. During the optimization procedure the set of particles varies throughout the selected region. The algorithm calculates the objective function at each step. After the evaluation of the objective function the algorithm sets the new particles' velocities. The algorithm moves each particle to the best-found location. A library of programs from MathWorks MATLAB / Optimization Toolbox was used for calculation of the model's parameters.

The optimization was carried out based on the measured response of the dissolved CO_2 concentration during the fermentation process. The error between the measured response from the laboratory bioreactor (i.e., measured CO_2) and the output of the non-linear mathematical model (i.e., $x_3(t)$, calculated from (1-3)), was computed for acquiring the objective function,. The integral absolute error (IAE) objective function was used to evaluate the matching of the mathematical model.

As the approximately range of values of the model's parameters was known, a constraint was made on the region in which the algorithm searches for optimal solutions. The bounds are shown in Appendix B. The optimization algorithm changed the parameters μ_m, S_m, α, and β for long enough to reach the minimum of the objective function. Optimization was ended when the relative change in the value of the objective function reached the default defined value. For this, in studied case, 1760 objective function calculations were necessary.

The measured initial values and the determined parameters of the mathematical model of the studied fermentation process for the constant stirrer speed $n = 80$ min^{-1} and constant temperature $T = 22°C$ are presented in Table 1.

Fitting of the measured CO_2 response with the result of simulation obtained with identified constant stirrer speed model is displayed in Fig. 6.

B. MODEL FOR CHANGEABLE STIRRER SPEED

A literature review shows that there are no theoretically derived models that would describe the influence of stirrer speed changes on the dynamics of the fermentation process. Therefore, the model for the changeable stirrer speed was determined through experimental identification.

Tests with changes in stirrer speed during the fermentation were carried out. From the analysis of the tests (as shown in Fig. 3), it was assumed that the effect of the speed changes on the transient responses of the produced CO_2 could be satisfactorily described by a linear model of an appropriate order.

In order to determine the parameters of the mathematical model, the fermentation process was for all analyzed speed changes conducted twice: at first with the constant stirrer speed; and secondly in a way that the speed was step changed during the fermentation. After that, the difference between the both measured responses was calculated, and the parameters were identified. The least-square identification method was used to identify such a model. A library of existing programs from MATLAB / System Identification Toolbox was used for the identification. The identification was repeated several times with the transfer functions of different orders and with the measured results of the dissolved CO_2 concentration from the various tests. It was found that a good match of simulation and measurement was in general obtained with a linear model of a 3rd order, described with:

$$X_{3\Delta}(s) = \frac{b_3 s^3 + b_2 s^2 + b_1 s^1 + b_0 s^0}{a_3 s^3 + a_2 s^2 + a_1 s^1 + a_0 s^0} N_\Delta(s) \qquad (4)$$

where symbols have the following meaning:

$N_\Delta(s)$ – the Laplace transform of the speed change signal (= input of changeable stirrer speed model),

$X_{3\Delta}(s)$ – the Laplace transform of the difference of CO_2 concentration (= output of changeable stirrer speed model),

$b_0, \ldots, b_3, a_0, \ldots, a_3$ - the parameters of the transfer function, and

s - the complex variable.

The results of the identification of the changeable stirrer speed model for the experiments shown in Fig. 4 are presented in the paper. In these experiments the step change of the stirrer speed was executed in different phases of the fermentation process. The deviation of the speed affected CO_2 response from the CO_2 response by constant stirrer speed $n = 80\ \text{min}^{-1}$ was calculated and the linear model was identified for each experiment. Tables 2-5 present the parameters, poles and zeros of the transfer functions, identified from the measured CO_2 responses, which follows the step changes of stirrer speed which occurred at $t = 0$ h, $t = 3$ h, $t = 6$ h and $t = 12$ h, respectively.

The impact of the step changes of the stirrer speed on the deviation of the measured CO_2 concentration is depicted together with the corresponding responses of the identified model $x_{3\Delta}(t)$ in Fig. 7-10.

TABLE 2. Parameters, poles and zeros of transfer function of changeable stirrer speed model identified from step response from $n = 80\ \text{min}^{-1}$ to $n = 110\ \text{min}^{-1}$ at $t = 0$ h.

Numerator	Denumerator
$b_3 = 0$	$a_3 = 1$
$b_2 = 1.985 \cdot 10^{-5}$	$a_2 = 0.597$
$b_1 = 0.324 \cdot 10^{-5}$	$a_1 = 0.282$
$b_0 = 0.065 \cdot 10^{-5}$	$a_0 = 0.0175$
$z_{1,2} = -0.0816 \pm i\ 0.1614$	$p_1 = -0.0719$
	$p_{2,3} = -0.2624 \pm i\ 0.4184$

TABLE 3. Parameters, poles and zeros of transfer function of changeable stirrer speed model identified from step response from $n = 80\ \text{min}^{-1}$ to $n = 110\ \text{min}^{-1}$ at $t = 3$ h.

Numerator	Denumerator
$b_3 = 0$	$a_3 = 1$
$b_2 = 8.56 \cdot 10^{-5}$	$a_2 = 5.108$
$b_1 = 2.16 \cdot 10^{-5}$	$a_1 = 2.436$
$b_0 = 0.92 \cdot 10^{-5}$	$a_0 = 1.160$
$z_{1,2} = -0.1264 \pm i\ 0.3037$	$p_1 = -4.6365$
	$p_{2,3} = -0.2357 \pm i\ 0.4413$

TABLE 4. Parameters, poles and zeros of transfer function of changeable stirrer speed model identified from step response from $n = 80\ \text{min}^{-1}$ to $n = 110\ \text{min}^{-1}$ at $t = 6$ h.

Numerator	Denumerator
$b_3 = 0$	$a_3 = 1$
$b_2 = 6.582 \cdot 10^{-5}$	$a_2 = 5.9162$
$b_1 = 2.382 \cdot 10^{-5}$	$a_1 = 5.1505$
$b_0 = 0.365 \cdot 10^{-5}$	$a_0 = 1.2261$
$z_{1,2} = -0.1810 \pm i\ 0.1506$	$p_1 = -4.9200$
	$p_{2,3} = -0.4981 \pm i\ 0.0332$

TABLE 5. Parameters, poles and zeros of transfer function of changeable stirrer speed model identified from step response from $n = 80\ \text{min}^{-1}$ to $n = 110\ \text{min}^{-1}$ at $t = 12$ h.

Numerator	Denumerator
$b_3 = 0$	$a_3 = 1$
$b_2 = 1.715 \cdot 10^{-5}$	$a_2 = 4.2843$
$b_1 = 0.724 \cdot 10^{-5}$	$a_1 = 2.3468$
$b_0 = 0.107 \cdot 10^{-5}$	$a_0 = 0.7463$
$z_{1,2} = -0.2112 \pm i\ 0.1333$	$p_1 = -3.7053$
	$p_{2,3} = -0.2895 \pm i\ 0.3429$

The most important conclusions of the performed identifications for different input signals in different stages of fermentation are that:

- the 3rd order transfer function enables the identification of a model that well describes the dynamics of the measured process,
- the relative degree of the identified transfer function is 1 and
- the identified transfer function is minimum-phase in all cases (not only in the presented ones).

C. COMPLETE MODEL

From the obtained results presented in Figs. 6-10, it can be seen that the proposed two-part structure of the mathematical model of the fermentation process allows matching of the simulations and the measurements on the laboratory

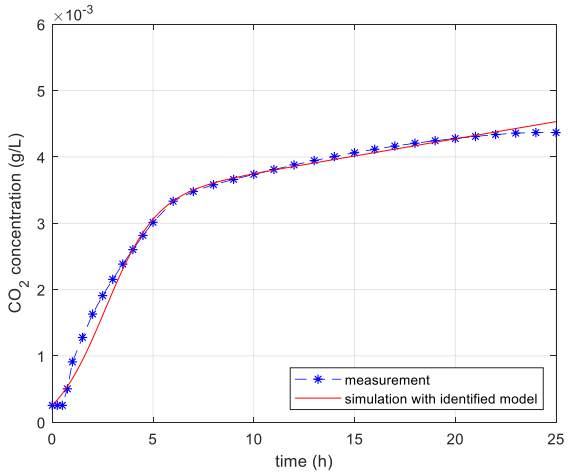

FIGURE 6. Transient responses of dissolved CO_2 concentration at constant stirrer speed $n = 80$ min^{-1} obtained with measurement and simulation (parameters in Table 1).

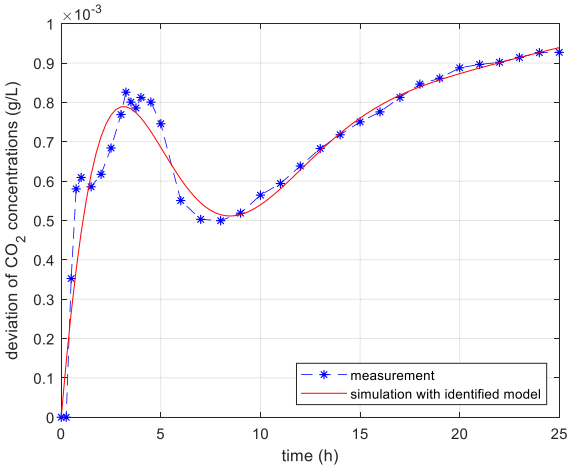

FIGURE 7. Time courses of deviations between CO_2 transient response conducted with step change of stirrer speed from $n = 80$ min^{-1} to $n = 110$ min^{-1} in $t = 0$ h and CO_2 transient response of fermentation with constant stirrer speed $n = 80$ min^{-1}, obtained with measurement and simulation using identified changeable stirrer speed model.

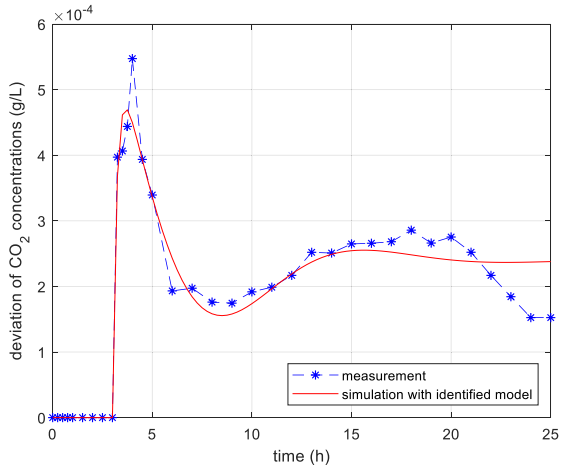

FIGURE 8. Time courses of deviations between CO_2 transient response conducted with step change of stirrer speed from $n = 80$ min^{-1} to $n = 110$ min^{-1} in $t = 3$ h and CO_2 transient response of fermentation with constant stirrer speed $n = 80$ min^{-1}, obtained with measurement and simulation using identified changeable stirrer speed model.

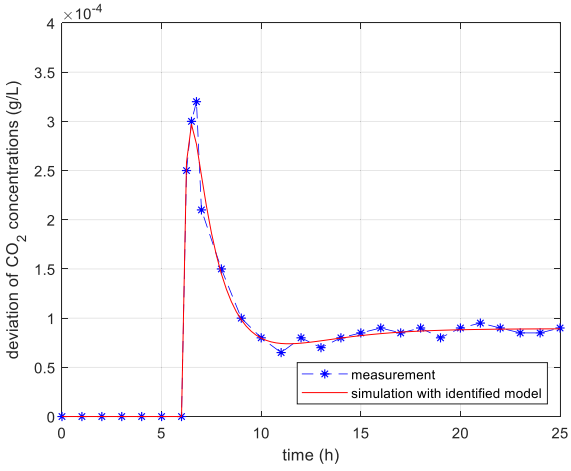

FIGURE 9. Time courses of deviations between CO_2 transient response conducted with step change of stirrer speed from $n = 80$ min^{-1} to $n = 110$ min^{-1} in $t = 6$ h and CO_2 transient response of fermentation with constant stirrer speed $n = 80$ min^{-1}, obtained with measurement and simulation using identified changeable stirrer speed model.

batch bioreactor very well. The particle swarm optimization method for the non-linear model, together with the least square identification method for the linear model, proved easy to use and efficient. A block diagram of the complete model is shown in Fig. 11, where $n_\Delta(t)$ denotes stirrer speed changes. The fitting of the response of the measured CO_2 with the response obtained with complete mathematical model $y(t)$ is displayed in Fig. 12. Note, the model involves the step change in the stirrer speed in $t = 3$ h and the temperature in the bioreactor was a constant $T = 22$ °C.

Simulation results of the complete mathematical model show that this model can be justifiably used to analyze the fermentation process and control system design. Numerical procedures for determining the model parameters are known and easy to use; however, the determination is time-consuming. Namely, in both cases, such as constant and changeable stirrer speed, the fermentation product's transient responses are necessary to be measured first.

IV. CONTROL OBJECTIVE

The conclusions presented in chapters 2 and 3 indicate that it is possible to control the fermentation process in the batch bioreactor by changing the stirrer speed and that the complete mathematical model represents a reasonable basis for the design and synthesis of the closed-loop control system.

The objective of the control system of the batch bioreactor is determined with a specific requirement. It requires to achieve the control of the fermentation process in a way that its end product tastes the best possible (quality) and that as much product as possible (productivity) is produced in the shortest time possible (economy). In order to achieve these goals, it is necessary to reshape the transient response of CO_2

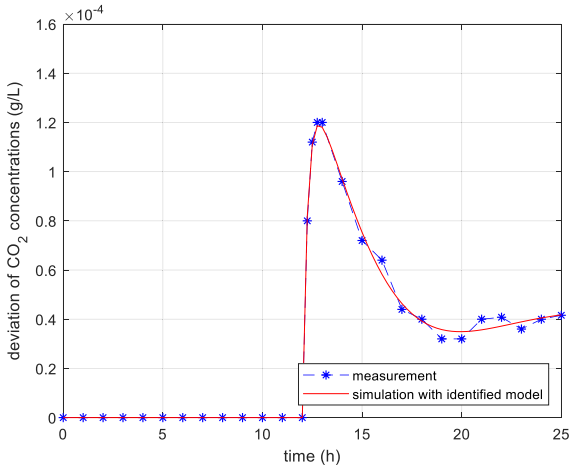

FIGURE 10. Time courses of deviations between CO_2 transient response conducted with step change of stirrer speed from n = 80 min^{-1} to $n = 110$ min^{-1} in $t = 12$ h and CO_2 transient response of fermentation with constant stirrer speed $n = 80$ min^{-1}, obtained with measurement and simulation using identified changeable stirrer speed model.

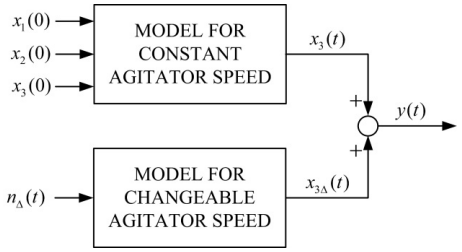

FIGURE 11. Block diagram of complete mathematical model of fermentation process in batch bioreactor with regards to changeable stirrer speed $n(t)$.

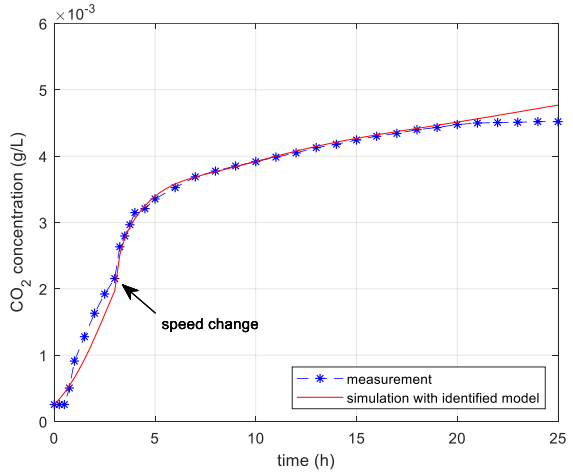

FIGURE 12. Measured transient response of dissolved CO_2 concentration with initial stirrer speed $n = 80$ min^{-1} following by step change of speed from $n = 80$ min^{-1} to $n = 110$ min^{-1} in $t = 3$ h compared with simulated transient response $y(t)$ of complete model for same initial conditions and input agitation.

production (shown in Fig. 2). The reshape should ensure the CO_2 product reaches its final stage with its higher value of CO_2 concentration in a shorter time. Besides, it is desired the increase in CO_2 concentration during the transition is continuous without quick rough changes in its gradient, which could reduce the quality [5]. All the mentioned above is possible only to the extent allowed by the available microorganisms and substrate. For the studied fermentation process, the ideal transient response of the CO_2 concentration was appraised on the systematic laboratory tests. On this basis it is possible to determine empirically what is the maximum possible achieved product concentration and what can be the shortest duration of fermentation at the desired fermentation product quality.

To find the "ideal" trajectory, the fermentation was executed without the control system many times, with the same mixture but with different stirrer speeds. Because too high a gradient affects the fermentation process negatively, we tried to estimate the maximum allowable gradient that led to the reference final yield. Such gradient will ensure fast fermentation with a reference value of the final product. Based on the open-loop tests, an ideal response was discovered, which can be described as a step response of the second-order term with the gain $k_r = 4.5{\cdot}10^{-3}$, the time constant $T_r = 2.5$ h and the damping $z_r = 1$. Compared to the CO_2 concentration transient response of the non-controlled original fermentation process, the proposed ideal response has a smaller gradient in the beginning phase of the fermentation (t < 1.5 h) and quicker progression to the final state value (t ≈ 12 h) along with little increase of the final state value (≈ 5 %). The appraised ideal response is described with:

$$y_r(t) = 4.50 \cdot 10^{-3} \cdot \left(1 - e^{-0.4t} - 0.4{\cdot}te^{-0.4t}\right) \qquad (5)$$

where $y_r(t)$ denotes the ideal (i.e., reference) transient response of the CO_2 concentration. It will be presented graphically later in figures with control results.

The goal of the control system is to assure that the fermentation process dynamics will be the same as the dynamics of the ideal trajectory. Therefore, the reference model was derived from the ideal CO_2 trajectory (5) in such a way that the step output of the reference model would be the same as the ideal trajectory.

V. CONTROL OF FERMENTATION PROCESS WITH LINEAR CONTROLLER

From the modeling and analysis of the fermentation process, it was evident that fermentation is a nonlinear process and, as such, is not suitable for control with a linear PI-controller. However, a more detailed analysis showed that the dynamics of the fermentation process can be represented very well by a linearized model of the small deviations from the nominal non-linear trajectory. When the reference transient response does not deviate excessively from the uncontrolled transient response, the dynamics of the fermentation process in this zone can be represented by a linearized model.

The basic problem when using a PI-controller to control the fermentation process is that the linearized deviation model is time-dependent. In different phases of the fermentation process the linearized model has different parameters. Therefore, several linearized models of the fermentation process should

be determined - different models for different fermentation phases, and also for different values of the input variable. For each identified linearized model it would be necessary to determine the parameters of the controller. Thus, a gain scheduling control system should be used, which would choose between different controller's parameters during the fermentation process. Of course, such a gain scheduled controller would only be suitable for a modeled fermentation process. Repeated fermentation with slightly altered properties and initial concentrations of microorganisms, substrate and product. would require re-modeling and repeated tuning of the controller's paramaters.

It should be noted, however, that the purpose of the paper was not a detailed study of the implementation of the PI-controller for the fermentation process. The development and capabilities of the control system with the PI regulator presented in the article are intended primarily to show the time-consuming and complex synthesis of this control system, and to discover its deteriorated performance in the case of changes in the fermentation parameters. For these reasons, a linear controller with constant parameters was determined on the basis of the identified linearized mathematical model of the fermentation process. The determined controller was used in the laboratory experiments for the control of the identified fermentation process, and for the control of the fermentation process with the modified type of microorganisms and changed initial concentrations of microorganisms, substrate and product.

A. CONTROL SYSTEM DESIGN

The batch bioreactor in the laboratory enables implementation of a conventional feedback control structure. Bioreactor is already equipped with the stirrer- and measuring systems. The stirrer system enables changing of the rotational speed, the measuring system measures the dissolved CO_2 concentration. An additional external controller calculates the reference speed of the stirrer system from the deviation between the reference- and measured values of CO_2 concentrations. A block diagram of the proposed linear control system is shown in Fig. 13.

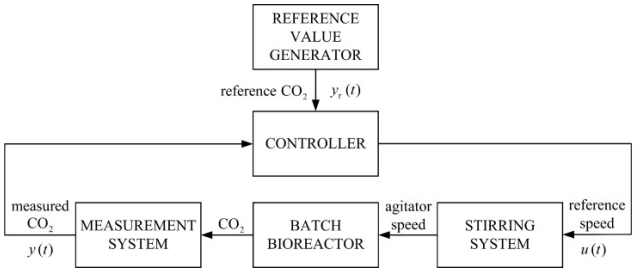

FIGURE 13. Block diagram of linear control system for fermentation control in batch bioreactor.

The identified mathematical model (Fig. 11, equations (1)-(4), Tables 1, 2) was used for synthesis of the proposed closed-loop control. Conventional Proportional-Integral (PI) controller was chosen in order to make the control system as uncomplicated as possible [29]. The PI-controller is described with the transfer function:

$$G_{\mathrm{PI}}(s) = k\frac{sT_i + 1}{sT_i}, \tag{6}$$

where parameter k denotes proportional gain and T_i is an integral time constant.

By using the identified linear changeable stirrer speed mathematical models of the fermentation process, the root locus analysis (and the simulations) show that the linear control system of the studied batch bioreactor with the PI- controller is stable for all identified transfer functions.

B. SYNTHESIS OF CONTROLLER

The optimization technique was used for the tuning of the controller parameters k and T_i. The objective function was selected to include:

- the error between the reference CO_2 transient response $y_\mathrm{r}(t)$ and the simulated CO_2 transient response $y(t)$ of the identified complete model, and
- the required stirrer speed $n_\Delta(t)$.

The objective function is presented with the integral equation:

$$J = \int \left[qe^2(t) + ru^2(t)\right] \mathrm{d}t, \tag{7}$$

where the used symbols have the following meanings:

J – the objective function (i.e., a cost function),

$e(t)$ – the deviation between reference and the actual values of CO_2 concentration (i.e., a control error),

$u(t)$ – the calculated required stirrer speed (i.e., a controller output), and

q, r – the weighting parameters.

The weighting parameters q and r can be used as design parameters. The scalar $q \geq 0$ penalizes the error $e(t)$ between the reference signal and controlled plant output signal. The scalar $r > 0$ penalizes the controlled plant input signal $u(t)$. The larger these values are, the more different signals are penalized. A large value of q results in control system behavior with the least possible changes in the output error. On the contrary, a large value of r means control of the system with less energy.

In the tuning procedure for the batch bioreactor PI-controller's parameters, it was assumed that the output error should be as small as possible. However, since the activator's limits and the saturation of the controlled plant were known, the restriction of the amplitude of the controlled plant inputs was set as a secondary requirement. In this way, we kept parameter q at value $q = 1$ and only altered parameter r.

For the determination of the controller parameters k and T_i the Particle Swarm Optimizing procedure was used again. For every chosen pair q, r the controller parameters k, T_i were optimized, and the control system was simulated based on these parameters.

Seeking such a value q, for which the optimized PI- controller will not require excessive amplitude values of the

controlled plant input, the parameters $q = 1$ and $r = 0.2$ were selected as appropriate values. For these weighting parameters, the controller parameters $k = 140.3 \cdot 10^3$ and $T_i = 50.8$ h were optimized with the particle swarm optimization method. A good response of an output value (the CO_2 concentration) with the required speed within the limits of availability of the stirrer system ($n = 0$ - 400 min^{-1}) was achieved in this way.

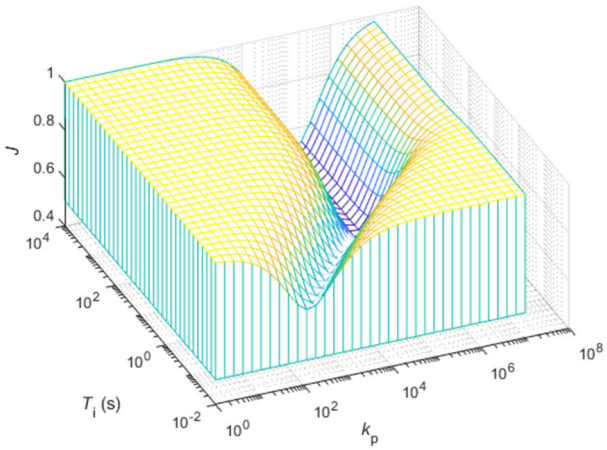

FIGURE 14. 3-d plot of objective function dependence on parameters k and T_i of controller in a logarithmic scale.

In Fig. 14, the objective function with parameters $q = 1$ and $r = 0.2$ was plotted as a function of the controller parameters k and T_i. The Figure shows the position of the globally optimal values of the controller parameters k and T_i, which coincide with the values obtained with the Particle Swarm Optimization.

C. RESULTS WITH LINEAR CONTROLLER

The developed control system was used to control the fermentation process in the laboratory batch bioreactor. Before carrying out laboratory tests, the control algorithm was tested with simulations with Matlab / Simulink. Simulation results are not presented in the manuscript due to more than otherwise condensed presentation, and because the focus of the paper was the practical solution of the control problem. For development and prototyping of the proposed control algorithms, a dSpace 1103 PPC controller board was utilized. The controller is equipped with 16 bit A / D and D / A converters as well as serial and CAN interfaces. An analog output module of basic device SevenMulti was used for transfer of measured signal of the CO_2 concentration from the bioreactor system to the controller's analog input. The additional analog 1st order low pass filter was used at the dSpace analog input to eliminate the noise signal. The analog output signal from the controller is sent to the reference input of the stirrer system. To enable this connection the stirrer system was equipped with an additional electronic interface. The control algorithm was graphically imported into MATLAB / Simulink, compiled and exported to the controller. In this way, fast adjustment and improvement of the control algorithm was possible.

After the proposed control concept was tested on the dSpace system, the program was migrated and tested also on programmable logic controller (PLC) Siemens SIMATIC S7 CPU 314 IFM. This PLC has on-board analog inputs and outputs on its disposal. The PLC presents very cost and performance suitable hardware for commercial realization of the proposed control system.

A block diagram of the laboratory control systems is presented on Fig. 15.

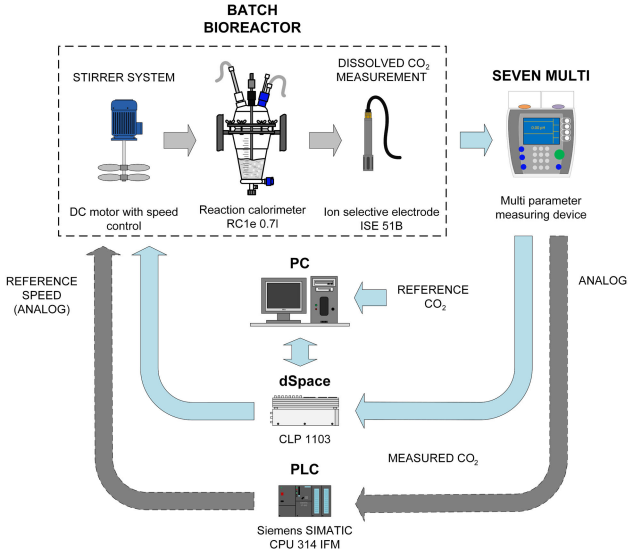

FIGURE 15. Block diagram of laboratory systems for stir-speed adopted control of transient response of dissolved CO_2 concentration of batch bioreactor.

The measured transient response of produced CO_2 in the non-controlled bioreactor with the constant stirrer speed $n = 80$ min^{-1} is shown in Fig. 2. The task of the closed-loop control system is to ensure that the transient response of the measured CO_2 concentration would be as close as possible to the reference transient response described with (5). The reference CO_2 concentration response and the obtained measured CO_2 response from the controlled batch bioreactor are shown in Fig. 16.

Fig. 16 clearly shows that the developed controller provides very good tracking of the actual CO_2 concentration to the reference concentration. In this way, the significantly more economical fermentation process with reproducible quality was able to make. The desired growth of the CO_2 concentration is guaranteed. The obtained transient response is more continuous and with significantly shortened fermentation time. Duration of the non-controlled fermentation was about 25 h (Fig. 2) and duration of the controlled fermentation was reduced to approximately 15 h (Fig. 16). Small increase in the CO_2 concentration of the final product in regard to the defined reference is also achieved (≈ 5 %).

The improvement shown was achieved by controlling the stirrer speed. The transient response of the speed is shown in Fig. 17. From this response, it is seen that significant improvement of the fermentation process is possible with relatively small changes in the speed.

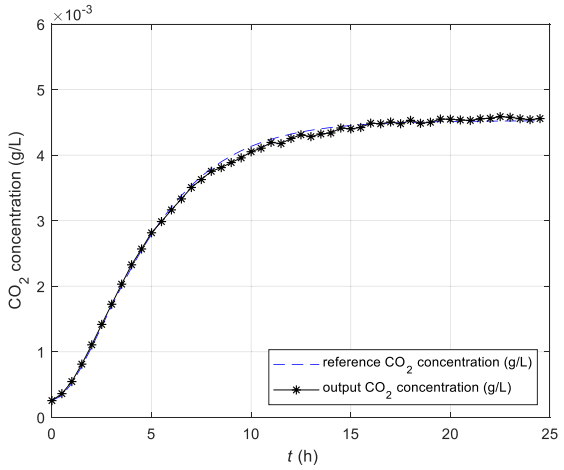

FIGURE 16. Transient response of reference- and output CO_2 concentration (both are almost identical) of studied fermentation processes with linear controller. Tuning of the controller's parameters was made on identified mathematical model of fermentation process.

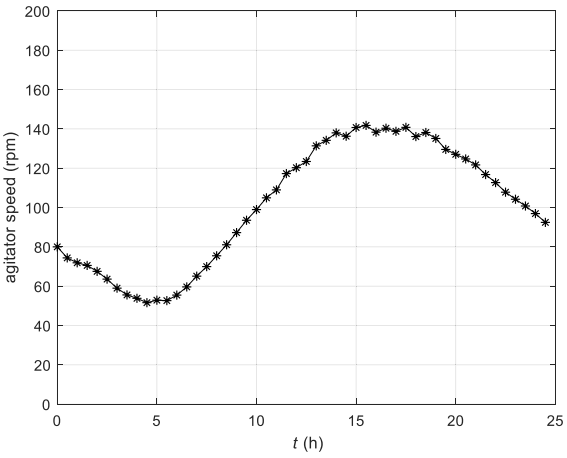

FIGURE 17. Transient response of bioreactor's stirrer speed from experiment in Fig. 16.

Results show that even though the controlled plant is non-linear, it is possible to use the linear controller with the fixed parameters. The controller chosen in this way ensures good tracking of the reference signal in the whole operation range. By selecting the weighting coefficients of the objective function and using the optimization method, it is ensured that the controller provides optimum performance in a broadest possible operating range and different operating modes.

Such the synthesis of the control system ensures optimal operation only in a case when the mathematical model of the fermentation process is well known. Namely, even a small change in the initial concentrations or in quality of the fermentation substance when using unchanged controller parameters impairs the tracking of the reference value and optimal behavior. Fig. 18 and 19 show a transient response of CO_2 release in a case when the fermentation process is only slightly modified and a controller from the previous case was used. In the test, other quality substances were used in the same batch bioreactor with the same initial concentrations of the microorganisms, the substrate, and the product.

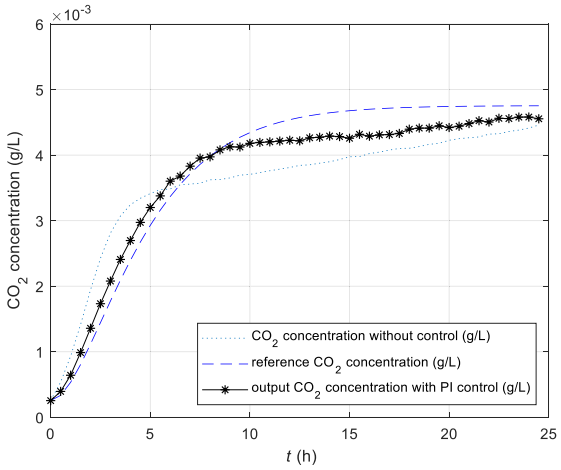

FIGURE 18. Transient response of reference- and output CO_2 concentration of modified fermentation process with linear controller with non-tuned parameters (controller parameters for previous case were used).

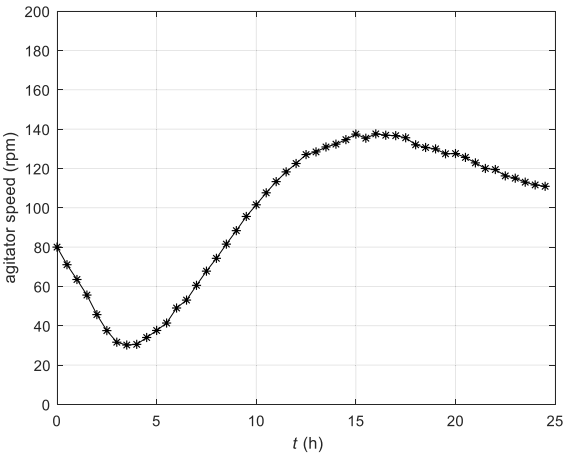

FIGURE 19. Transient response of bioreactor's stirrer speed from experiment in Fig. 13.

TABLE 6. Identified parameters of constant stirrer speed model for modified fermentation process.

parameter	value and unit
maximum microorganisms' growth rate	$\mu_m = 10.598\ h^{-1}$
substrate saturation constant	$S_m = 0.036$ g/L
parameter of product yield related to microorganisms' growth	$\alpha = 0.842\ \frac{g/L}{g/L}$
parameter of product yield independent of microorganisms' growth	$\beta = 0.012\ h^{-1}$
constant temperature	$T = 22$ °C
constant stirrer speed	$n = 80\ min^{-1}$

The parameters of the complete mathematical model of the modified fermentation process obtained by the described modeling are presented in Tables 6 and 7.

It can be seen from the results presented in Fig. 18 that even the small change in the quality or the initial quantity of the substances, even within the same bioreactor causes the controller with the unadjusted parameters to no longer provide perfect tracking of the reference signal.

TABLE 7. Parameters, poles and zeros of transfer function of changeable stirrer speed model for modified fermentation process identified from step response from $n = 80$ min^{-1} to $n = 110$ min^{-1} at $t = 3$ h.

numerator	denumerator
$b_3 = 0$	$a_3 = 1$
$b_2 = 11.56 \cdot 10^{-5}$	$a_2 = 4.342 \cdot 10^{-3}$
$b_1 = 3.57 \cdot 10^{-5}$	$a_1 = 2.801 \cdot 10^{-3}$
$b_0 = 1.18 \cdot 10^{-5}$	$a_0 = 1.392 \cdot 10^{-3}$
$z_{1,2} = -0.1544 \pm \mathrm{i}\ 0.2797$	$p_1 = -3.6843$
	$p_{2,3} = -0.3289 \pm \mathrm{i}\ 0.5193$

The main disadvantage of this approach is the request for knowledge of the most accurate mathematical model of the fermentation process. A structure and parameters of the mathematical model must be known to check a range of controller's parameters that assure global stability of the control system, and to enable optimization of the control system. Determining an appropriate mathematical model of a batch bioreactor is highly time-consuming. It is necessary to execute the whole fermentation process with a constant stirrer speed, measure transient responses of the fermentation product, and determine all parameters of the non-linear model (μ_m, S_m, α, β) from the measured transient response by means of the optimization method. After that, the fermentation process with the equal charge must be repeated, this time with a step change of the stirrer speed during execution. The parameters of the transfer function must be identified from the obtained transient response. Finally, synthesis of the linear control system must be made by optimizing the objective function calculated from the simulation results with the complete model. Due to the time-consuming and challenging identification procedure for determining the mathematical model, use of the linear control system proved to be inappropriate for industrial applications. It makes sense to use a more effective control approach that do not require accurate knowledge of the mathematical model of the batch bioreactor.

VI. CONTROL OF FERMENTATION PROCESS WITH ADAPTIVE CONTROLLER

An adaptive theory represents an ideal tool for developing a control system for the batch bioreactors. Adaptive control systems do not require accurate knowledge of the mathematical model of a controlled plant and the adaptive systems can adapt their parameters to changing dynamics of the controlled plant during its operation. An additional reason that simplifies use of the adaptive systems for control of the batch bioreactors is that the fermentation processes are carried out very slowly (time constants are in a hourly range), which allows very unproblematic implementation of even computationally complex control algorithms.

A. ADAPTIVE THEORY

Adaptive control emerged in late 1950s in Flight and Process Control. There are many publications in where systematic reviews of the adaptive control systems for dynamic processes are carried out [30]. Most adaptive control systems can be classified into two groups: Model Reference Adaptive Control (MRAC) and Self Tuning Control (STC). The MRAC proved to be very suitable for the control of the fermentation process since in this case a desired transient response of the fermentation process can be represented by a reference model. In MRAC, an adaptation mechanism changes adaptive law parameters thus generating a control signal ensuring a bioreactor's response close to that given by a reference model [31].

There are several different MRAC approaches. For control of industrial processes, modified Model Reference Adaptive Control which is based on a concept of almost strictly positive real systems (MRAC-ASPR) proved to be a very suitable [32]. The main advantage of this adaptive control concept compared to the other MRAC concepts is that the MRAC-ASPR theory is also applicable for non-linear controlled plants. The MRAC-ASPR approach was firstly developed for linear time-invariant processes [32]. The extension of the MRAC-ASPR theory to minimum-phase nonstationary and non-linear systems was made in 2009 [33]. Reference [34] shows a thorough and complete description of this theory, with added new results in the field of non-linear system stability analysis. The MRAC-ASPR concept has been used to control some non-linear controlled plants (robotics, electrical drives) [35], [36]. There is no reference showing the use of this adaptive concept to control the fermentation process in bioreactors. Additional advantages of this adaptive control theory are easy implementation, proven global stability and an undemanding choice of coefficients of the adaptation mechanism. Theoretical foundations of MRAC-ASPR are presented in detail in [32], [33]. Below is brief description of equations needed to determine the reference model, the adaptation mechanism, and the adaptive law for the studied fermentation process.

Selected MRAC-ASPR was used primarily to control the continuous linear systems subject to uncertainty in their parameters. The MRAC-ASPR is coherent with the studied fermentation process in the bioreactor. Namely, during the operation, the process quantities stay in zones limited to small proximity of the transient responses in non-perturbed operation. In this case, the non-linear model can be linearized around a trajectory and thus the dynamics of the fermentation process can be described by a linearized model with variable parameters.

A controlled plant subject to MRAC-ASPR is described by the non-linear state-space mathematical model:

$$\dot{\boldsymbol{x}}(t) = \boldsymbol{A}(\boldsymbol{x}, t)\boldsymbol{x}(t) + \boldsymbol{b}(\boldsymbol{x}, t)u(t), \tag{8}$$

$$y(t) = \boldsymbol{c}^{\mathrm{T}}(\boldsymbol{x}, t)\,\boldsymbol{x}(t), \tag{9}$$

where the symbols are:

$\boldsymbol{x}(t)$, $u(t)$, $y(t)$ - a state-space vector signal, an input scalar signal and an output scalar signal of the controlled plant's mathematical model, and

$\boldsymbol{A}(\boldsymbol{x}, t)$, $\boldsymbol{b}(\mathbf{x}, t)$, $\boldsymbol{c}^{\mathrm{T}}(\mathbf{x}, t)$ - are a non-linear functions.

The reference model is described as

$$\dot{\boldsymbol{x}}_{\mathrm{m}}(t) = \boldsymbol{A}_{\mathrm{m}}\boldsymbol{x}_{\mathrm{m}}(t) + \boldsymbol{b}_{\mathrm{m}}u_{\mathrm{m}}(t), \tag{10}$$

$$y_{\mathrm{m}}(t) = \boldsymbol{c}_{\mathrm{m}}^{\mathrm{T}}\boldsymbol{x}_{\mathrm{m}}(t), \tag{11}$$

with the following symbols are:

$\boldsymbol{x}_{\mathrm{m}}(t)$, $u_{\mathrm{m}}(t)$, $y_{\mathrm{m}}(t)$ - a state-space vector signal, input scalar signal and output scalar signal of the reference model, and

$\boldsymbol{A}_{\mathrm{m}}(t)$, $\boldsymbol{b}_{\mathrm{m}}(t)$, $\boldsymbol{c}_{\mathrm{m}}^{\mathrm{T}}(t)$ - a system matrix, an input vector and an output vector of the reference model.

It is important to mention that the reference model is only used to represent desired input-output behavior of the controlled plant. This means that a dimension of the reference model state could be much smaller than the dimension of a controlled plant state, such as

$$\dim\left[\boldsymbol{x}_{\mathrm{m}}(t)\right] \ll \dim\left[\boldsymbol{x}(t)\right]. \tag{12}$$

In general, this adaptive control method can also be used in situations where it is not realistic to assume that one can model or identify all parameters of the controlled plant.

Since the reference model may be of a very low order compared to the controlled plant, it cannot be assumed that the state of the plant follows the state of the model. Therefore, it is only possible to demand that output $y(t)$ of the controlled plant asymptotically tracks output $y_{\mathrm{m}}(t)$ of the reference model. An output tracking error is defined as

$$e_y(t) = y_{\mathrm{m}}(t) - y(t). \tag{13}$$

Techniques of a Lyapunov stability analysis and their extensions to non-linear nonautonomous systems were used for development of the adaptive control algorithm [34], [35]. The derived adaptive control algorithm is described with the equation:

$$u(t) = K_e(t)\,e_y(t) + \boldsymbol{K}_x(t)\,\boldsymbol{x}_{\mathrm{m}}(t) + K_u(t)\,u_{\mathrm{m}}(t), \tag{14}$$

where $K_{\mathrm{e}}(t)$ is an unknown stabilizing output feedback parameter, and $\boldsymbol{K}_{\mathrm{x}}(t)$ and $K_{\mathrm{u}}(t)$ are unknown control gains. Parameters $K_{\mathrm{e}}(t)$, $\boldsymbol{K}_{\mathrm{x}}(t)$ and $\mathrm{K_u}(t)$ and variables $e_y(t)$, $\boldsymbol{x}_{\mathrm{m}}(t)$ and $u_{\mathrm{m}}(t)$ can be concatenated in a vector of (unknown) adaptive gains $\boldsymbol{K}(t)$ and a vector of (known) control variables $\boldsymbol{r}(t)$:

$$\boldsymbol{K}(t) = \left[K_e(t)\ \boldsymbol{K}_x(t)\ K_u(t)\right], \tag{15}$$

$$\boldsymbol{r}^{\mathrm{T}}(t) = \left[e_y(t)\ \boldsymbol{x}_{\mathrm{m}}(t)\ u_{\mathrm{m}}(t)\right]. \tag{16}$$

The adaptive gains of $\boldsymbol{K}(t)$ are obtained as a combination of proportional term $\boldsymbol{K}_{\mathrm{p}}(t)$ and integral term $\boldsymbol{K}_{\mathrm{i}}(t)$, such as

$$\boldsymbol{K}(t) = \boldsymbol{K}_{\mathrm{p}}(t) + \boldsymbol{K}_{\mathrm{i}}(t). \tag{17}$$

While integral term $\boldsymbol{K}_{\mathrm{i}}(t)$ is used to guarantee convergence, proportional term $\boldsymbol{K}_{\mathrm{p}}(t)$ generates an immediate response for large errors and leads the system very quickly toward a small tracking error. It is worth mentioning that there is no longer an optimal gain value that the adaptive controller wants to achieve (as by linear model following control [31]). On the contrary, the gains increase only if high gains are needed (if the error attempts to increase), and decrease if they are not needed anymore. In [32], it is shown that the proportional- and integral terms can be calculated with the following non-linear expressions:

$$\boldsymbol{K}_{\mathrm{p}}(t) = e_y(t)\,\boldsymbol{r}^{\mathrm{T}}(t)\,\boldsymbol{T}', \tag{18}$$

$$\dot{\boldsymbol{K}}_{\mathrm{i}}(t) = e_y(t)\,\boldsymbol{r}^{\mathrm{T}}(t)\,\boldsymbol{T} - \sigma\boldsymbol{K}_{\mathrm{i}}(t), \tag{19}$$

where $\boldsymbol{T}'$ and $\boldsymbol{T}$ are positive semi-definite and positive definite adaptation coefficient matrices, respectively, and the σ-term is introduced to avoid divergence of the integral gains in presence of a disturbance.

A complete theory of development of the MRAC-ASPR control systems is described in detail in [32]–[34]. The stability analysis and the proof of stability for a non-linear model and linearized model are shown in Appendix C.

B. ADAPTIVE STRUCTURE AND PARAMETERS

A block diagram of the control system based on the used adaptive theory is shown in Fig. 20.

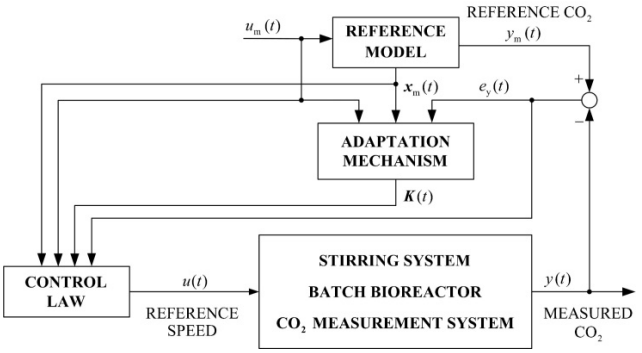

FIGURE 20. Block diagram of adaptive control system for fermentation control in batch bioreactor.

A dynamic model for block "Reference model" was derived from the reference transient response described with equation (5). A second-order state-space model was utilized to generate the defined reference trajectory. The following parameters were calculated for the reference model being of the same form as (10), (11) above:

$$\boldsymbol{A}_{\mathrm{m}} = \begin{bmatrix} 0 & 1 \\ -\dfrac{1}{T_{\mathrm{r}}^2} & -\dfrac{2z_{\mathrm{r}}}{T_r} \end{bmatrix} = \begin{bmatrix} 0 & 1 \\ -0.16 & -0.8 \end{bmatrix},$$

$$\boldsymbol{b}_{\boldsymbol{m}} = \begin{bmatrix} 0 \\ 1 \end{bmatrix}, \tag{20}$$

$$\boldsymbol{c}_{\mathrm{m}}^{\mathrm{T}} = \begin{bmatrix} k_{\mathrm{r}} & 0 \end{bmatrix} = \begin{bmatrix} 4.5 \cdot 10^{-3} & 0 \end{bmatrix}. \tag{21}$$

This reference model produces a step response equal to the reference signal in (5).

In block "Adaptation mechanism", adaptive gain $\boldsymbol{K}(t)$ is calculated by (15)-(19). The adaptation coefficient matrices were estimated by means of numerical simulation with the complete model. The estimation of the adaptation coefficients, together with the simulation results, are presented in Appendix D. No optimization technique was used to find optimal values for coefficients of the adaptation mechanism.

Numerical simulations were used only to determine approximate values of the coefficients. The obtained values are robust and suitable for different batch bioreactors and different fermentation processes tested with simulation. Adaptive system does not require an accurate setting of the parameters. The following adaptation coefficient matrices:

$$\boldsymbol{T}' = 1 \cdot 10^8 \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \end{bmatrix}, \tag{22}$$

$$\boldsymbol{T} = \boldsymbol{T}'. \tag{23}$$

and the σ-term to avoid divergence of the integral gains in presence of disturbance:

$$\sigma = 0.95 \tag{24}$$

were obtained through the simulations, and were used to carry out the adaptive control.

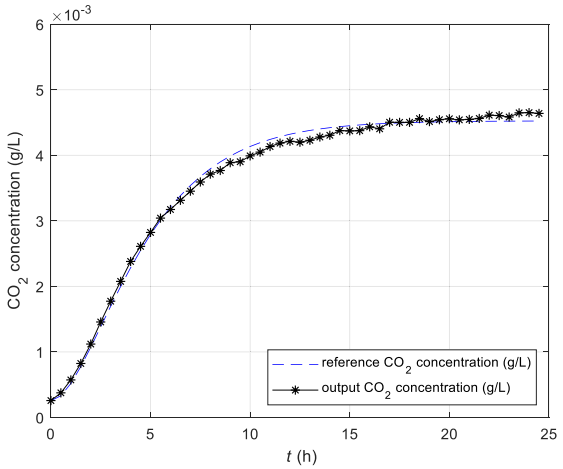

FIGURE 21. Transient responses of reference- and output CO_2 concentration of studied fermentation process with adaptive control system.

C. RESULTS WITH ADAPTIVE CONTROLLER

Equal control system (equal HW and SW) as with implementation of the linear controller were used for implementation of the adaptive controller. The reference model, the adaptation mechanism and the control law were programmed and compiled in the MATLAB / Simulink environment, and transferred onto the dSpace controller board and Siemens SIMATIC programmable logic controller. Transient response of the dissolved CO_2 concentration from the proposed adaptive control experiment for the studied fermentation process in the batch bioreactor are displayed in Fig. 21 and 22. Fig. 21 shows the corresponding reference- and measured transient responses of the concentration. The transient response of a generated product of the fermentation follows the reference transient response despite the parameters of the controlled plant's mathematical model are unknown and despite uncertainties of its structure. A transient response of the stirrer speed, which was necessary to assure that the actual dissolved CO_2 concentration follows the reference transient response, is plotted in Fig. 22. The controller's output stays in a feasible range and it does not exceed the maximum or minimum limits.

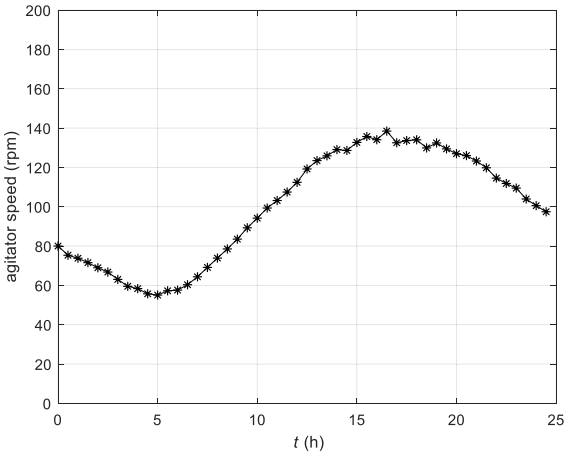

FIGURE 22. Transient response of bioreactor's stirrer speed from experiment in Fig. 21.

The presented adaptive control system assures that the measured dissolved CO_2 concentration follows the output of the reference model also in the case of unknown bioreactor's kinetics. In such a way, the adaptive controller enables that the carried-out fermentation will preserve equal dynamics in difference charges also when fermentation compounds will not be the same.

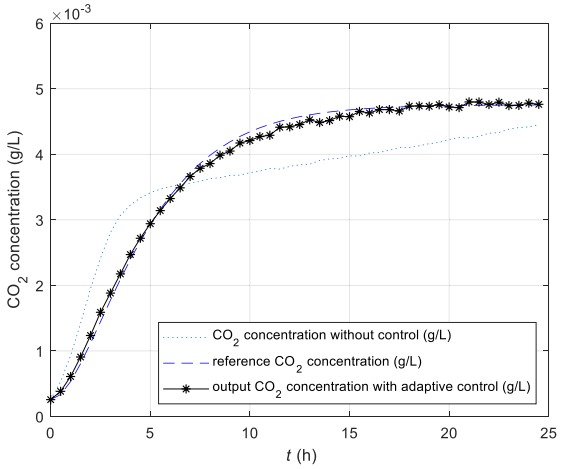

FIGURE 23. Transient responses of the reference- and output CO_2 concentration of modified fermentation process with adaptive control system.

Fig. 23 and 24 show a transient response of CO_2 release in a case of the modified fermentation process with the adaptive controller. The parameters of the complete mathematical model corresponding to the modified fermentation process are presented in Tables 6 and 7. It can be seen that the same adaptive controller also assures very good tracking by varying the parameters of the fermentation process.

For more objective assessment of the capabilities of the both control systems, the evaluation based on different

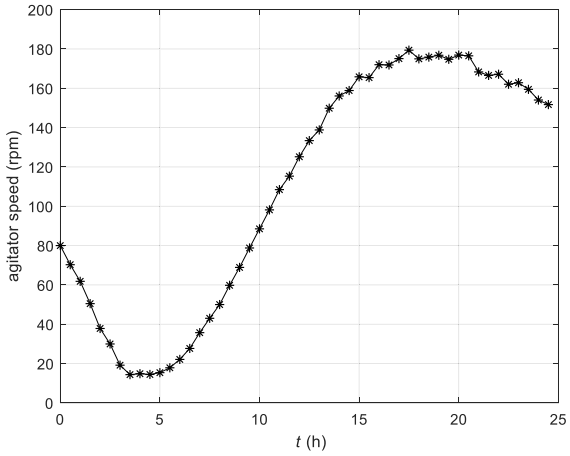

FIGURE 24. Transient response of the bioreactor's stirrer speed from experiment in Fig. 23.

TABLE 8. Performance index of control systems, fermentation process with data in tables 1 and 2 (original fermentation process).

criterion	PI controller	adaptive controller
IAE	$1.1 \cdot 10^{-3}$	$1.9 \cdot 10^{-3}$
ISA	$6.5 \cdot 10^{-8}$	$18.7 \cdot 10^{-8}$
ITAE	$12.9 \cdot 10^{-3}$	$23.4 \cdot 10^{-3}$

TABLE 9. Performance index of control systems fermentation process with data in tables 6 and 7 (modified fermentation process).

criterion	PI controller	adaptive controller
IAE	$6.2 \cdot 10^{-3}$	$1.7 \cdot 10^{-3}$
ISA	$183.5 \cdot 10^{-8}$	$17.4 \cdot 10^{-8}$
ITAE	$82.7 \cdot 10^{-3}$	$18.6 \cdot 10^{-3}$

performance indexes is advantageous. Integral absolute error (IAE), integral square error (ISE) and integral time absolute error (ITAE) indexes were used for the analysis of the control systems. Values of the performance indexes for linear and adaptive control systems for the first fermentations process (model data in Tables 1, 2) are shown in Table 8 and the results for the second fermentation process (modified model with data in Tables 6, 7) are shown in Table 9.

Both the control systems give satisfactory results for the original fermentation process. The differences between the calculated performance indexes are expectedly not significant. The PI-controller gives better results than the adaptive due to its optimized parameters. It is quite surprising that the adaptive controller gives only slightly worser results than the PI-controller, although the initial parameters of the adaptation mechanism were zero, and those weighting coefficients were chosen without any optimization.

The advantage of the adaptive controller is especially visible in the control of the modified fermentation process (data in Table 9). The results obtained with the PI- controller, whose parameters were not tuned for this process, are significantly worse than the results of the adaptive controller, which itself adapted to the changing dynamics of the modified fermentation process.

The proposed adaptive control approach presents a much better choice for the batch bioreactor's control system. Its main advantage is that the detailed knowledge of the batch bioreactor and the fermentation substances is unnecessary. The results showed that the proposed adaptive controller successfully adapts its operation automatically to the different dynamics of the fermentation processes. The pre-operation tuning is minimal. The disadvantage of the PI-controller is that it requests the preliminary time-consuming determination of the mathematical model of the fermentation process.

VII. SUMMARY WITH CONCLUSION

Following the initial hypothesis, the study has shown that a fermentation's transient response in batch bioreactors can be controlled by the rotational speed of the stirrer system. The reference transient response of the fermentation product (dissolved CO_2 concentration) captures a technological objective of maximum production with the best taste in the shortest time. The developed control systems thus ensure the fermentation with the measured dissolved CO_2 concentration as close as possible to its reference transient response.

The derived mathematical model enabled the design, realization, and utilization of the linear- and advanced adaptive controller.

In the case the mathematical model with its structure and parameters was known exactly in advance, the linear controller was adopted. The parameters of the conventional linear controller were tuned by means of the particle swarm optimization, allowing the optimal performance of the device in a wide range. The controller displayed stable operation and good tracking performance of the reference signal. The controller guaranteed continuous operation with the desired CO_2 concentration growth. The fermentation time was shortened significantly (from 25 h to 15 h), and the amount of the probiotic beverage was increased by approximately 5 % with respect to the uncontrolled fermentation. The results of other experiments showed that even the small change in the quality and in the initial concentration of the source substances significantly affects the performance of the linear control system.

In the case the mathematical model of the bioreactor is not known exactly in advance, the adaptive controller was used for improved operation. It enabled adaptation of the controller's parameters to the dynamics of the bioreactor during its operation even when parameters of a controlled plant cannot be identified and modeled. Used Model Reference Adaptive Control (MRAC) proved to be suitable for such the fermentation. It generates the signal forcing the bioreactor to operate asymptotically close to the response of the reference model. To ensure stability, easy realization and an undemanding choice of adaptation coefficients, the less known, modified MRAC approach based on the theory of Almost Strictly Positive Real (ASPR) systems was used. The results of the experiments showed that the transient responses of the dissolved CO_2 concentration of the fermentation product follow the reference transient response also when the same controller is used for significantly different fermentation processes. This aspect adds to the significance of the proposed

control application and thus, improvement of bioprocess with its product(s).

It is necessary to point out that the essence of the manuscript is not the usage of a known control method for solving a known problem. A primary and original contribution of the manuscript is to develop a new control concept that uses stirrer speed changes for the improvement of transient response of the fermentation process. Currently operating industrial batch bioreactors do not have a closed-loop control system to ensure that the transient response of the fermentation product follows the reference trajectory. One of the few solutions for this control is presented for laboratory batch bioreactor in [23]. The feature of the newly submitted control system is an unassuming implementation. The stirrer system is used, with which most batch bioreactors are equipped, but on the contrary, very few of them have the cooling system needed to implement the control presented in [23].

Increased performance of batch bioreactors owing to their control with such closed-loop linear and adaptive systems should encourage their wide industrial utilization also due to their simple realization and optimal performance even in suboptimal operation.

APPENDIX

A. LABORATORY BATCH BIOREACTOR

Reaction calorimeter RC1e from Mettler Toledo was used in this study [23]. The RC1e is a computer-controlled laboratory reactor with a working volume of 0.7 L. It was equipped with additional sensors and actuators, which enabled the measurement and control of necessary biochemical and physical quantities during the fermentation process. In this way, the laboratory reactor was able to operate as a batch bioreactor. The analyzed reactor is presented in Fig. 25.

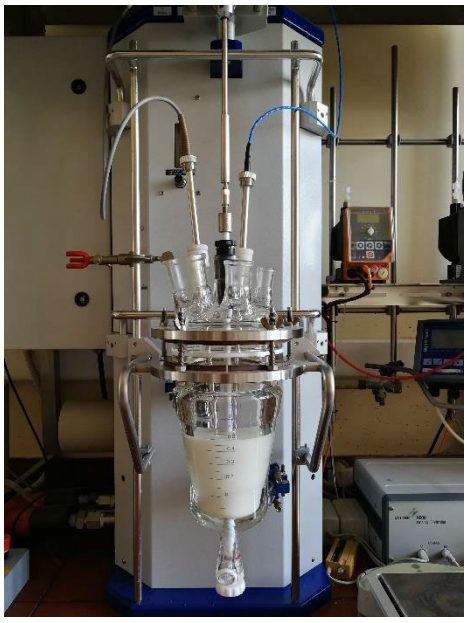

FIGURE 25. Laboratory batch bioreactor used for tests, analyses, and control implementation.

TABLE 10. Minimum and maximum values of the non-linear model parameters for the particle swarm optimization.

$\mu_{min} = 2\ h^{-1}$	$\mu_{max} = 30\ h^{-1}$
$S_{m,min} = 0.01$ g/L	$S_{m,max} = 0.1$ g/L
$\alpha_{min} = 0.5\ \frac{g/L}{g/L}$	$\alpha_{max} = 1.0\ \frac{g/L}{g/L}$
$\beta_{min} = 0.001\ h^{-1}$	$\beta_{min} = 0.1\ h^{-1}$

B. CONSTRAINED REGION FOR THE PARTICLE SWARM OPTIMIZATION OF THE PARAMETERS OF THE NON-LINEAR CONSTANT STIRRER SPEED MODEL

The bounds of the constrained region for the Particle Swarm Optimization of the parameters of the non-linear constant stirrer speed model are shown in Table 10.

C. STABILITY ANALYSIS

1) STABILITY ANALYSIS FOR NON-LINEAR MODEL OF THE FERMENTATION PROCESS

The paper derived a complete mathematical model of the batch bioreactor's fermentation process, consisting of a parallel-connected non-linear model and a time-varying linearized model. The advantage of this model is the very straightforward identification of the model's parameters. This model is suitable for analyzing the fermentation process, and allows simulations to test the effectiveness of the different control concepts. For the proof of stability, an augmented non-linear model was developed, which describes the influence of changes in the stirrer speed on the nonlinear model's parameters.

In the case of a constant stirrer speed, the maximum microorganisms' growth rate μ_m was constant. However, changing the stirrer speed affected growth - a higher speed accelerated growth, and a lower speed slowed growth. In [25], it was shown that the effect of speed variations on the growth rate can be described by a simple equation:

$$\mu_{m,n_\Delta}(t) = \mu_m\left(1 + k_{\mu_m} n_\Delta(t)\right) = \mu_m\left(1 + k_{\mu_m} u(t)\right) \quad (25)$$

where variables have the following meanings:

μ_m – the maximum microorganisms' growth rate at the constant nominal stirrer speed n_n (h^{-1}),

$\mu_{m,n\Delta}(t)$ – the maximum microorganisms' growth rate at the changed stirrer speed $n(t) = n_n + n_\Delta(t)$ (h^{-1}),

$n_\Delta(t) = u(t)$ – the deviation of the stirrer speed from the nominal stirrer speed (min^{-1}), and

$k_{\mu m}(t)$ – the parameter that describes the impact of the stirrer speed deviation on the maximum microorganisms' growth rate (h^{-1}/min^{-1}).

By including (25) in the non-linear model (1-3), we obtained the enhanced non-linear model:

$$\dot{x}_1(t) = \frac{\mu_m(1 + k_{\mu_m} u(t)) x_2(t)}{S_m + x_2(t)} x_1(t) \quad (26)$$

$$\dot{x}_2(t) = -\frac{\mu_m(1 + k_{\mu_m} u(t)) x_2(t)}{S_m + x_2(t)} x_1(t) \quad (27)$$

$$\dot{x}_3(t) = \left[\alpha \frac{\mu_m(1 + k_{\mu_m} u(t)) x_2(t)}{S_m + x_2(t)} + \beta\right] x_1(t) \quad (28)$$

$$y(t) = x_3(t) \quad (29)$$

The resulting equations (26-27) can be rearranged into a model realization (30-33).

$$\dot{x}_1(t) = \frac{\mu_{\mathrm{m}} x_1(t)\, x_2(t)}{S_{\mathrm{m}} + x_2(t)} + \frac{\mu_{\mathrm{m}} k_{\mu_{\mathrm{m}}} x_1(t)\, x_2(t)}{S_{\mathrm{m}} + x_2(t)} u(t) \tag{30}$$

$$\dot{x}_2(t) = -\frac{\mu_{\mathrm{m}} x_1(t)\, x_2(t)}{S_{\mathrm{m}} + x_2(t)} - \frac{\mu_{\mathrm{m}} k_{\mu_{\mathrm{m}}} x_1(t)\, x_2(t)}{S_{\mathrm{m}} + x_2(t)} u(t) \tag{31}$$

$$\dot{x}_3(t) = \alpha \frac{\mu_m x_1(t)\, x_2(t)}{S_{\mathrm{m}} + x_2(t)} + \beta x_1(t) + \alpha \frac{\mu_m k_{\mu_{\mathrm{m}}} x_1(t) x_2(t)}{S_{\mathrm{m}} + x_2(t)} u(t) \tag{32}$$

$$y(t) = x_3(t) \tag{33}$$

The obtained model coincides with the standard representation of a nonstationary (nonlinear and/or time-varying) system (33) for which Theorem 2 of Appendix D considers the stability of the studied adaptive control system.

$$\dot{\boldsymbol{x}}(t) = \boldsymbol{A}(\boldsymbol{x}, t) x(t) + \boldsymbol{b}(\boldsymbol{x}, t) u(t) \tag{34}$$

$$y(t) = \boldsymbol{c}^{\mathrm{T}}(\boldsymbol{x}, t) x(t) \tag{35}$$

Based on the comparison of the equations (30-33) and (34, 35), $\boldsymbol{b}(\boldsymbol{x}, t)$ and $\boldsymbol{c}^{\mathrm{T}}(\boldsymbol{x}, t)$ are evident. The product $\boldsymbol{b}(\boldsymbol{x}, t)\boldsymbol{c}^{\mathrm{T}}(\boldsymbol{x}, t)$ is a positive-definite symetric, which, taking into account Theorem 2, proves the stability of the adaptive control system described by the controlled plant mathematical model (26-29) and control law and adaptation mechanisms (13-19).

2) STABILITY ANALYSIS FOR THE LINEARIZED MODEL OF THE FERMENTATION PROCESS

Detailed analysis of the fermentation process showed that the response of the product concentration on the changes in stirrer speed can be described satisfactory with a linearized model of the small deviations from the nominal non-linear trajectory:

$$\dot{\boldsymbol{x}}_{\Delta}(t) = \boldsymbol{A}\boldsymbol{x}_{\boldsymbol{\Delta}}(t) + \boldsymbol{b} u_{\Delta}(t) \tag{36}$$

$$y(t) = \boldsymbol{c}^{\mathrm{T}} \boldsymbol{x}(t) \tag{37}$$

where $\boldsymbol{A}(t)$, $\boldsymbol{b}(t)$ and $\boldsymbol{c}^{\mathrm{T}}(t)$ are a system matrix, an input vector and an output vector of the controlled plant's linearized model.

A linearized model (36, 37) was obtained by linearizing the nonlinear model of the fermentation process (26-29) along trajectory $u*$, $\boldsymbol{x}*$. $\boldsymbol{A}(t)$, $\boldsymbol{b}(t)$ and $\boldsymbol{c}^{\mathrm{T}}(t)$ are presented by (38)–(40), as shown at the bottom of the page. The eigenvalues of the linearized model are (41), as shown at the bottom of the next page. and the transfer function is, after pole-zero cancelation, described with (42),

$$G_{n_{\Delta}-CO_2}(s) = \frac{b_1 s + b_0}{a_2 s^2 + a_1 s + a_0}, \tag{42}$$

where transfer function parameters are defined with (43).

$$\begin{aligned}
b_1 &= \alpha \mathrm{k}_{\mu_{\mathrm{m}}} \mu_{\mathrm{m}} x_1^* x_2^* \left(\mathrm{S}_{\mathrm{m}} + x_2^*\right) \\
b_0 &= \beta \mathrm{k}_{\mu_{\mathrm{m}}} \mu_{\mathrm{m}} x_1^* x_2^* \left(\mathrm{S}_{\mathrm{m}} + x_2^*\right) \\
a_2 &= S_m^2 + \left(x_2^*\right)^2 + 2 S_m x_2^* \\
a_1 &= -\mu_{\mathrm{m}} \left(x_2^*\right)^2 + S_m \mu_{\mathrm{m}} x_1^* - S_m \mu_{\mathrm{m}} x_2^* - \mathrm{k}_{\mu_{\mathrm{m}}} \mu_m u^* \left(x_2^*\right)^2 \\
&\quad + S_m \mathrm{k}_{\mu_{\mathrm{m}}} \mu_m u^* x_1^* - S_m \mathrm{k}_{\mu_{\mathrm{m}}} \mu_m u^* x_2^* \\
a_0 &= 0
\end{aligned} \tag{43}$$

From the calculated transfer function it is evident that the transfer function is minimum-phase with relative degree 1. According to the Lemma 1 the transfer function is ASPR, and according to Theorem 1, the control system with linearized model (36, 37) and control law and adaptation mechanism (13-19) is asymptotically stable.

D. DETERMINATION OF THE COEFICIENTS OF THE ADAPTATION MECHANISM

In the synthesis of conventional non-adaptive control systems, it is necessary to perform tuning of the controller parameters. The main advantage of the adaptive systems is that they perform tuning of the controller parameters themselves. However, even in the case of adaptive control systems, it is necessary to determine the coefficients of the adaptation mechanism that influence the course of adaptation. There are no analytical procedures that would allow rapid determination of the adaptation coefficients.

$$\boldsymbol{A} = \begin{bmatrix}
\dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_2^*}{S_m + x_2^*} & \dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_1^*}{S_m + x_2^*} - \dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_1^* x_2^*}{\left(S_m + x_2^*\right)^2} & 0 \\
-\dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_2^*}{S_m + x_2^*} & -\dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_1^*}{S_m + x_2^*} + \dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_1^* x_2^*}{\left(S_m + x_2^*\right)^2} & 0 \\
\alpha \dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_2^*}{S_m + x_2^*} + \beta & \alpha \dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_1^*}{S_m + x_2^*} - \alpha \dfrac{\mu_m \left(1 + k_{\mu_m} u^*\right) x_2^*}{\left(S_m + x_2^*\right)^2} & 0
\end{bmatrix} \tag{38}$$

$$\boldsymbol{b} = \begin{bmatrix}
\dfrac{k_{\mu_m} \mu_m x_1^* x_2^*}{S_m + x_2^*} \\
-\dfrac{k_{\mu_m} \mu_m x_1^* x_2^*}{S_m + x_2^*} \\
\alpha \dfrac{\mu_m k_{\mu_m} x_1^* x_2^*}{S_m + x_2^*}
\end{bmatrix} \tag{39}$$

$$c^{\mathrm{T}} = \begin{bmatrix} 0 & 0 & 1 \end{bmatrix} \tag{40}$$

The essential difference between the tuning of the regulator parameters and the tuning of the coefficients of the adaptation mechanism is that variations of the coefficients of the adaptation mechanism have a relatively small impact on the course of adaptation. Therefore, in most cases, it is sufficient to determine the appropriate values of the adaptation coefficients by simulations, and then these values ensure good control performance, even in the case of major changes in the parameters of the controlled plant.

For the presented adaptation mechanism it is necessary to determine the values of the adaptation coefficient matrices $\boldsymbol{T}'$ and $\boldsymbol{T}$, and the value of the σ-term for avoiding the divergence of the integral gains.

1) DETERMINATION OF THE COEFFICIENTS OF THE MATRICES T ′AND T

The matrices $\boldsymbol{T}'$ and $\boldsymbol{T}$ must be positive semi-definite and positive definite (4×4) square matrices, respectively. The tuning of the appropriate weighting matrices usually begins by selecting diagonal matrices with the corresponding high values of diagonal elements.

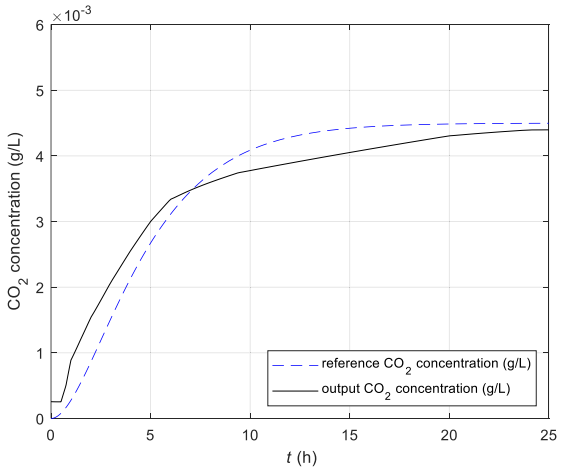

FIGURE 26. Simulation results of the transient responses of reference- and output CO_2 concentration of the studied fermentation process with adaptive control system with coefficients in (44).

Figs. 26-36 present the simulation results obtained with the complete mathematical model, consisting of the non-linear model (1-3) with parameters in Table 1 and the linearized model (4) with parameters in Table 3. In all simulations, the same reference signal was used (5), defined with the reference model (20, 21). The adaptive controller (13-19) was used to ensure that the controlled plant output signal was

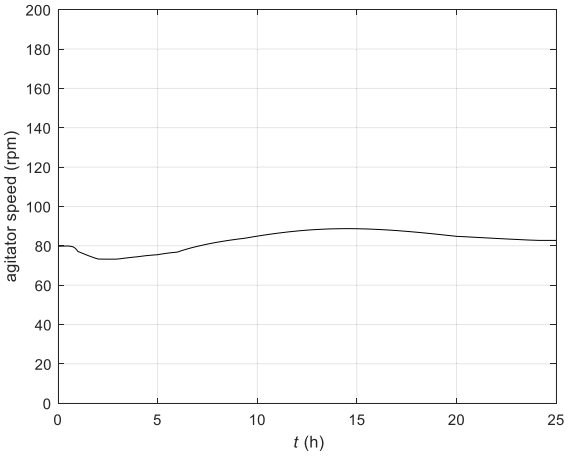

FIGURE 27. Simulation results of the stirrer speed as calculated with an adaptive controller corresponding to the coefficients (44) and results in Fig. 26.

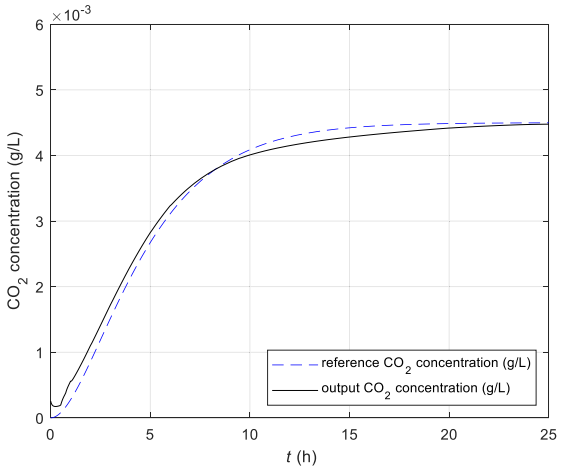

FIGURE 28. Simulation results of the transient responses of reference- and output CO_2 concentration of the studied fermentation process with an adaptive control system with the coefficients in (45).

traced to the output of the reference model. Different values were evaluated of coefficients of the adaptation mechanism $\boldsymbol{T}'$, $\boldsymbol{T}$ and σ.

Figs. 26 and 27 show the behavior of the control system when the following coefficients were selected of the adaptation mechanism:

$$\begin{aligned} \boldsymbol{T}' &= \boldsymbol{T} = 1 \cdot 10^4 \boldsymbol{I}_4 \\ \sigma &= 0 \end{aligned} \tag{44}$$

where $\boldsymbol{I}_4$ denotes a (4×4) identity matrix. It can be seen from Fig. 26 that such selected values of the coefficients of the adaptation mechanism do not ensure good tracking of the

$$\begin{aligned} \lambda_{1,2} &= 0, \\ \lambda_3 &= \frac{\mu_m \left[\left(x_2^*\right)^2 - S_m x_1^* + S_m x_2^* + k_{\mu_m} u^* \left(x_2^*\right)^2 - S_m k_{\mu_m} u^* x_1^* + S_m k_{\mu_m} u^* x_2^* \right]}{\left(S_m + x_2^*\right)^2} \\ &= \frac{\mu_m \left(1 + k_{\mu_m} u^*\right) \left[\left(x_2^*\right)^2 - S_m x_1^* + S_m x_2^* \right]}{\left(S_m + x_2^*\right)^2}, \end{aligned} \tag{41}$$

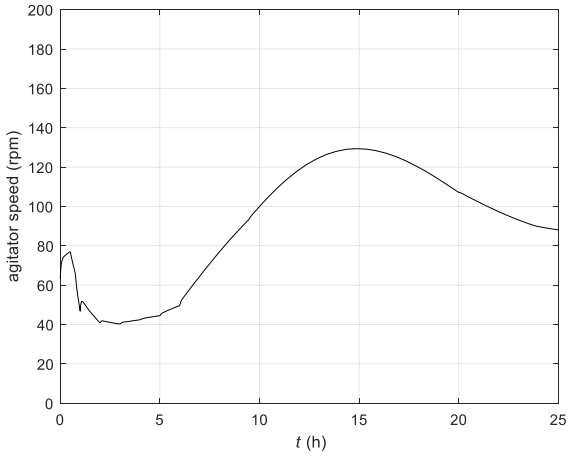

FIGURE 29. Simulation results of the stirrer speed as calculated with an adaptive controller corresponding to the coefficients (45) and results in Fig. 28.

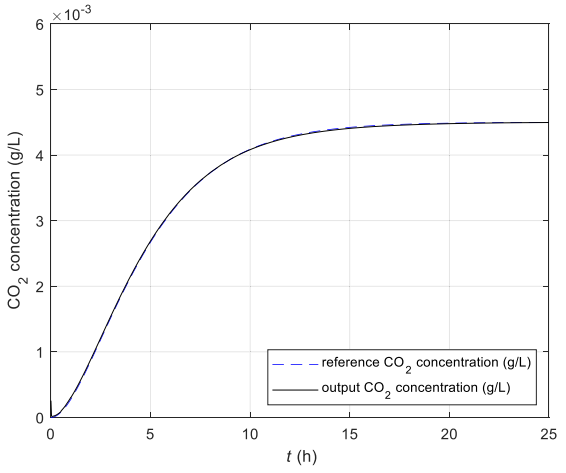

FIGURE 30. Simulation results of the transient responses of reference- and output CO_2 concentration of the studied fermentation process with an adaptive control system with coefficients in (46).

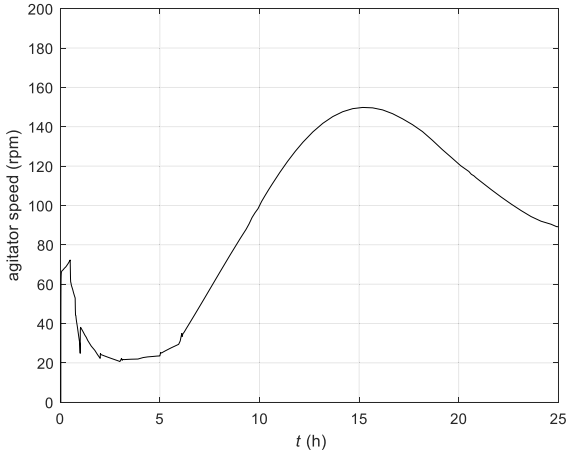

FIGURE 31. Simulation results of the stirrer speed as calculated with an adaptive controller corresponding to the coefficients (46) and results in Fig. 30.

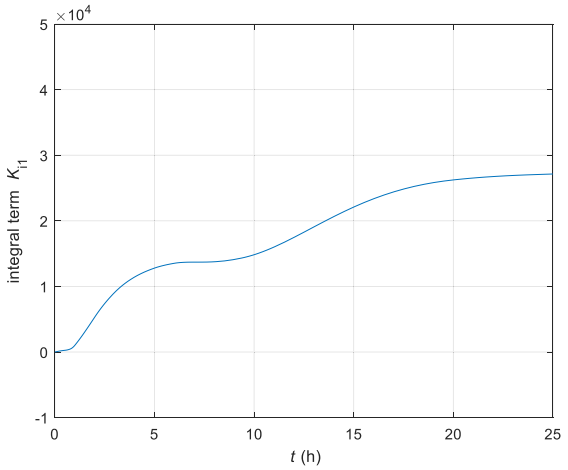

FIGURE 32. Response of the first element of the integral gain $K_i(t)$ in case of simulations with coefficients (44) with results presented in Fig. 26 and 27 ($\sigma = 0$).

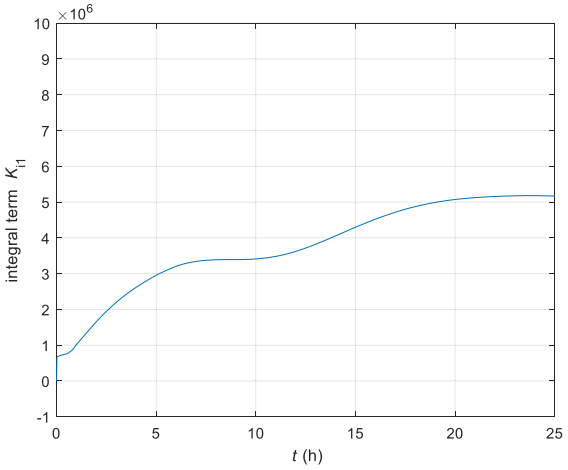

FIGURE 33. Response of the first element of the integral gain $K_i(t)$ in case of simulations with coefficients (46) with results presented in Fig. 30 and 31 ($\sigma = 0$).

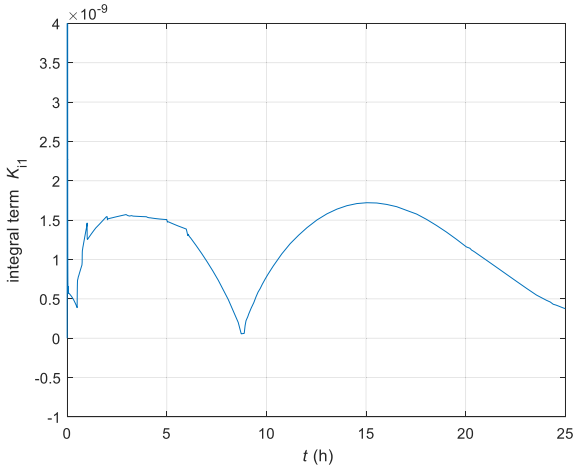

FIGURE 34. Response of the first element of the integral gain $K_i(t)$ in case of simulations with coefficients (47) with results presented in Fig. 35 and 36 ($\sigma = 0.95$).

output of the controlled plant to the output of the reference model (i.e.the reference signal). Fig. 27 shows the change in stirrer speed due to the operation of the controller. It is clear that the selected coefficients of the adaptation mechanism do not allow a sufficient output signal of the controller, so it makes sense to choose higher values of weight matrices.

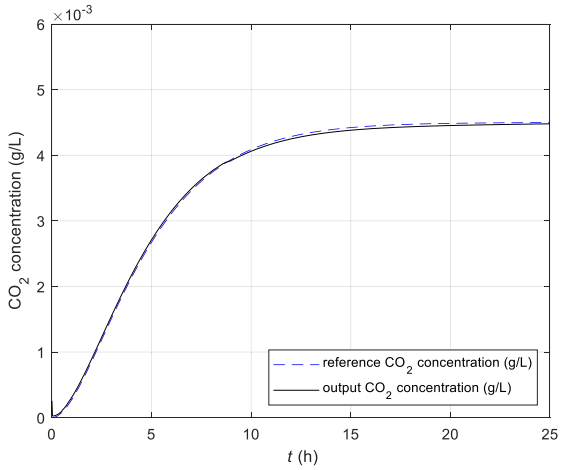

FIGURE 35. Simulation results of the transient responses of reference- and output CO_2 concentration of the studied fermentation process with an adaptive control system with coefficients in (47).

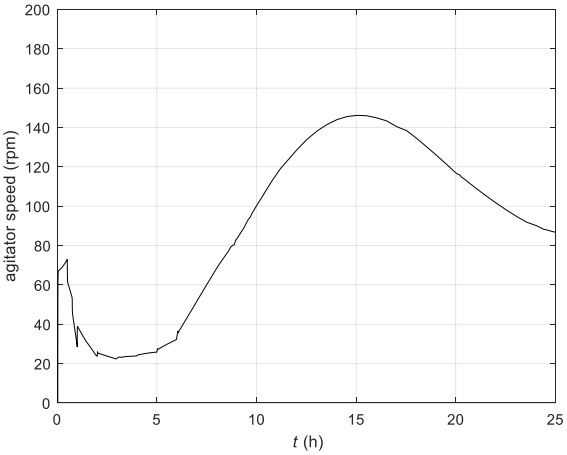

FIGURE 36. Simulation results of the stirrer speed as calculated with an adaptive controller corresponding to the coefficients (47) and results in Fig. 35.

To improve the tracking of the reference signal it makes sense to increase the values of the weighting matrices. Figs. 28 and 29 show the behavior of the control system when the following coefficients of the adaptation mechanism were selected:

$$\begin{aligned} \boldsymbol{T}' &= \boldsymbol{T} = 1 \cdot 10^6 \boldsymbol{I}_4 \\ \sigma &= 0 \end{aligned} \tag{45}$$

It can be seen from Fig. 28 that the increased values of the coefficients improve tracking of the output of the controlled plant to the output of the reference model. Fig. 29 shows the variation in the stirrer speed.

The increase of the values of the coefficients additionally improves the following to the reference signal. Figs. 30 and 31 show the behavior of the control system when the following coefficients of the adaptation mechanism were selected:

$$\begin{aligned} \boldsymbol{T}' &= \boldsymbol{T} = 1 \cdot 10^8 \boldsymbol{I}_4 \\ \sigma &= 0 \end{aligned} \tag{46}$$

Very good tracking of the reference signal is seen from Fig. 30. No excessive increase in stirrer speed occurred, as shown in Fig. 31.

2) DETERMINATION OF THE σ-TERM

It is worth mentioning that in the case when the σ-term of the adaptation mechanism is $\sigma = 0$, the integral term $\boldsymbol{K}_\mathrm{i}(t)$ (17, 19) increases whenever the error $e(t)$ is not zero, and may ultimately diverge. The σ-term was introduced in order to avoid divergence of the integral gains in the presence of the disturbances. Without the σ-term, the $\boldsymbol{K}_\mathrm{i}(t)$ is a perfect integrator and may increase steadily whenever perfect following ($e_\mathrm{y}(t) = 0$) is not possible, and may thus reach unnecessarily large values, or may even diverge. With the σ-term, the $\boldsymbol{K}_\mathrm{i}(t)$ is obtained from a first order filtering of $e_\mathrm{y}(t)\,\boldsymbol{r}^\mathrm{T}(t)\,\boldsymbol{T}$ (19), and therefore cannot diverge unless $e_\mathrm{y}(t)$ diverges.

Fig. 32 shows the response of the first element of the integral part $\boldsymbol{K}_{\mathrm{i}1}(t)$ for the simulations presented in Figs. 26 and 27. For these simulations the adaptation coefficients (44) were used. Fig. 33 shows the $\boldsymbol{K}_{\mathrm{i}1}(t)$ response for the simulation presented in Figs. 30 and 31, when the adaptation coefficients (46) were chosen. The divergence of $\boldsymbol{K}_\mathrm{i}(t)$ is well visible. Increasing the coefficients $\boldsymbol{T}'$ and $\boldsymbol{T}$ affects the speed of divergence. The $\sigma > 0$ was selected to assure stable $\boldsymbol{K}_\mathrm{i}(t)$ behavior. Fig. 34 shows the response of the integral gain $\boldsymbol{K}_{\mathrm{i}1}(t)$ when $\sigma = 0.95$ was selected. The stable and constrained $\boldsymbol{K}_\mathrm{i}(t)$ response is visible.

3) SIMULATION RESULTS OF THE FINAL TUNED ADAPTATION MECHANISM

The following coefficients of the adaptation mechanism were chosen based on the analysis of the results of many simulations:

$$\begin{aligned} \boldsymbol{T}' &= \boldsymbol{T} = 1 \cdot 10^8 \boldsymbol{I}_4 \\ \sigma &= 0.95 \end{aligned} \tag{47}$$

These values were used in the implemented practical realization of the adaptive controller. The simulation results for these values are shown in Figs. 35 and 36.

E. ALMOST STRICTLY POSITIVE REAL SYSTEMS

Strictly positive realness (SPR) is very strong property, not necessarily satisfied in the real world. This is the reason that the concept of the "Almost" SPR (ASPR) was introduced. The most important basic definitions and theorems are presented here.

Definition 1 (for the Time Domain) [32]: Let the linear system be described as:

$$\dot{\boldsymbol{x}}(t) = \boldsymbol{A}\boldsymbol{x}(t) + \boldsymbol{b}u(t), \tag{48}$$

$$y(t) = \boldsymbol{c}^\mathrm{T}\boldsymbol{x}(t). \tag{49}$$

If there exists a gain K_e such that the closed-loop system:

$$\dot{\boldsymbol{x}}(t) = \left(\boldsymbol{A} - \boldsymbol{b}K_\mathrm{e}\boldsymbol{c}^\mathrm{T}\right)\boldsymbol{x}(t) + \boldsymbol{b}u(t), \tag{50}$$

$$y(t) = \boldsymbol{c}^\mathrm{T}\boldsymbol{x}(t) \tag{51}$$

is SPR, the original open-loop system (48,49) is called ASPR. Note that the gain K_e is not needed for the implementation of the adaptive control algorithm.

Definition 2 (for the Frequency Domain) [32]: Let the linear system be described with a transfer function $G(s)$. If there exists a constant gain K_e such that the closed-loop transfer function:

$$G_{cl}(s) = \frac{G(s)}{1 + K_e G(s)} \tag{52}$$

is SPR, then $G(s)$ is called ASPR.

Lemma 1 [32]: Let G(s) be a minimum phase transfer function of relative degree 1. Then G(s) is ASPR.

The asymptotic stability of the output error for the controlled plant described with the linear time-invariant (LTI) model and studied adaptive control algorithm is shown by using a Lyapunov approach which involves (i) Finding a Lyapunov candidate $\dot{V}$ positive in the state variables, and (ii) Evaluating the closed-loop stability by analyzing the sign of derivative $\dot{V}$. This stability result is summarized in Theorem 1.

Theorem 1 (Stability for Linear Plants) [32]: The control system, consisting of the linear controlled plant described with mathematical model (36, 37) and control law and adaptation mechanism described with (13-19), has all states and gains bounded, and the output is asymptotically stable if the controlled plant model is ASPR.

Reference [33] extends the strict passivity results of LTI systems to nonstationary systems. The extensions to the minimum-phase nonstationary and nonlinear systems are quite straightforward in the case where the nonstationary product $\boldsymbol{b}(\boldsymbol{x}, t)\boldsymbol{c}^T(\boldsymbol{x}, t)$ is positive-definite symmetric. Stability conditions are recapitulated in Theorem 2.

Theorem 2 (Stability for Nonlinear Plants) [33]: The control system consisting of the non-linear controlled plant described with the mathematical model (34, 35) and control law and adaptation mechanism described with (13-19) has all states and gains bounded, and the output is asymptotically stable if the product $\boldsymbol{b}(\boldsymbol{x}, t)\boldsymbol{c}^T(\boldsymbol{x}, t)$ is positive-definite symmetric and the controlled plant model is ASPR.

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