Dissolved Oxygen Control of Batch Bioreactor using Model Reference Adaptive Control scheme

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Abstract: Bioreactor imparts a significant role in the manufacture of pharmaceuticals, enzymes, food products, etc. as these processes depend on the biotransformation catalyzed by microorganisms**.** Dissolved Oxygen(DO) is one of the significant parameter in an aerobic fermentation process. DO control is difficult to achieve due to the variations in process dynamics during batch/fed-batch processes and the complex nonlinear behavior of the Bioreactor. In this paper, design and implementation of Model Reference Adaptive Control(MRAC) scheme based on MIT rule is applied to DO control of the bioreactor using the stirrer speed as control signal. A PC-supported, fully automated, multi-task control system has been designed and built by the authors using LabVIEW .A comparative study is carried out for the experimental bioreactor with conventional PI controller and proposed MRAC scheme for DO control. Results show that MRAC controller provides good tracking performance in comparison to PI controller.

Keywords: Adaptive Control, Dissolved oxygen, MIT rule, MRAC, LabVIEW

1. INTRODUCTION

Most of the microorganisms employed industrially require oxygen for respiration. For bacteria and yeast cultures, the critical oxygen concentration is usually 10–50% of air saturation. Maintaining the appropriate concentration of dissolved oxygen is essential for the survival of microorganism thereby ensuring efficient operation of the fermenter. Measurements of $K_L a$ provide important information about a bioprocess or bioreactor. These determinations ensure that processing conditions are such that an adequate supply of oxygen is available for the rapid increase of cells [Schugerl, 2001].The rate of oxygen transfer from air bubble to the liquid phase may be described by the equation:

$$\frac{dC_L}{dt} = K_L a\left(C^* - C_L\right)$$

where , C_L is the concentration of DO in the fermentation broth (mmoles dm^{-3}), t is time (hours), $\frac{dC_L}{dt}$ is the change in oxygen concentration over a time period, (mmoles in O_2 dm^{-3} h^{-1}), K_L is the mass transfer coefficient (cm h^{-1}),*a* is the gas/liquid interface area per liquid volume (cm^2 cm^{-3}), C^* is the saturated dissolved oxygen concentration (mmoles dm^{-3}). Due to the limited aqueous solubility of oxygen, the overall volumetric mass transfer coefficient ($K_L a$) is a critical parameter in bioprocesses. Because of low solubility of oxygen, transfer from gas phase to the bulk liquid is relatively small in growth medium. As with all other transfer coefficients, the absolute value of is highly equipment and process specific. In general, its magnitude is a function of bioreactor geometry, agitation, aeration and pressure conditions. $K_L a$ also depends on medium composition (e.g. osmolarity, antifoam agent, etc.) and broth rheology. $K_L a$ can be determined experimentally by means of a dissolved oxygen probe using dynamic gassing-out technique[Clementschitsch et al., 2006].

When the reactor is run in batch or fed-batch mode, the process characteristics vary significantly with important process variables like cell mass, substrate concentration, and oxygen uptake rate. Many authors have reported tuning difficulties when PI controllers with fixed parameters are used [Lee et al., 1991] for DO control. To account for the process variations, a control strategy based on PID control and gain scheduling from the stirrer speed is suggested by Akesson et al., 1998. The drawback is that the process variations due to foaming and surface active components are not captured. The DO control in the Bacillus thuringiensis (Bt) process has been solved by using a Lyapunov-based controller [Amicarelli et al.,2010]. However, relatively poor performances were detected in several simulated cases for changes in the DO set point. In fed-batch cultivation for vaccine production, the control performance from sliding mode control [Dagci et.al., 2001] was not satisfactory. Wen-Tao Fu et al., 2015 verified that the control effort of DO concentration based on T-S fuzzy neural network was better compared to BPNN and PID.

DO concentration control is a difficult task, especially in batch fermentation because of time varying conditions, time

delays and the probe dynamics. Also, the system operating temperature, media composition, agitation speed, cell growth, headspace pressure, and aeration rate are the other important operational difficulties in controlling the DO in an aerobic fermentation [Kazemi et al., 2013]. For these reasons automatic control is necessary to operate a microbial process efficiently since the activity of microorganisms is readily affected by fluctuations in environmental conditions. In addition the control of DO concentration is very important for improving the productivity and for reducing the operating cost of a bioprocess. For control of complex industrial processes model-based control approaches have been proven the most effective among the different types of adaptive controllers. As the organism grows DO is consumed and to accommodate this varying disturbance Model Reference Adaptive control is implemented. The purpose of this study is to control the DO of the broth medium at a level that ensures maximum concentration of the microorganism. In general, the MRAC-based adaptive controllers are designed using a reference model which describes the desired characteristics of the plant to be controlled [Schügerl, 2001]. The use of a reference model facilitates the analysis of the adaptive system and provides a stability framework, since the controller design and stability analysis was performed in two steps. The MRAC scheme was analyzed in the presence of unmodelled dynamics, where the results showed improvement in DO control.

2. SYSTEM DESCRIPTION

The bioreactor set up available in the laboratory along with NI cards interfacing is shown in Fig. 1.The process and instrumentation diagram of experimental setup is shown in Fig. 2. The reactor is equipped with acid, base, antifoam and feed pumps. Air is supplied via compressor, Mass Flow Controller (MFC) to the reactor vessel. The bioreactors are equipped with four standard baffles and mechanically sealed stirrer shafts entering from the bottom. A pair of standard 6-bladed Rushton turbines is mounted on the shaft. The agitation rate is controlled by a motor driven from the bottom of the vessel. The vessel is equipped with probes for temperature, pH, dissolved oxygen, and foam level. Samples are taken via a sample valve for offline analysis of substrate and product concentrations.

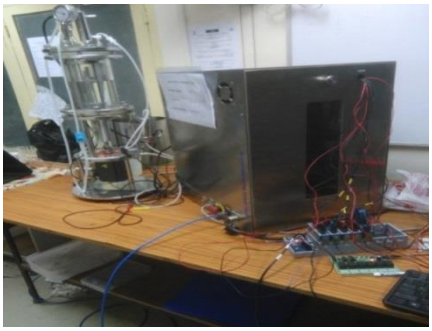

Fig. 1. Bioreactor lab set-up interfaced with NI-DAQ cards

The bioreactor can be operated in batch, fed-batch and continuous mode [Laiden et al., 2002]. In this work the bioreactor is operated in batch mode. The objective is to control the DO using adaptive controller. The operation of the bioreactor is performed via LabVIEW graphical user interface. It is preferred because of its data flow and parallel programming nature [Rudolf et al., 2005]. The human machine interface panel developed using this platform enhances accessibility to the reactor and also it ensures safety. The bioreactor includes measurement system for inlet gas flow rates, agitation rate, tank head pressure, temperature, pH, dissolved oxygen [Kumar et al., 2001]. RTD temperature probe is used to acquire the temperature inside the reactor. The current given to Solid State Relay[SSR] unit and the voltage given to the cooler can be used as manipulating variables. pH inside the reactor can be measured using the specially designed gel filled probe. Acid and base pump of fixed speed can be used as manipulating variables. DO probe is used for the online measurement of oxygen in the reactor. Variable speed pump is used to feed the substrate inside the reactor in case of fed batch process. To reduce the foam produced during the process, antifoam pump of fixed speed can be operated to inject silicone oil. Among the secondary variables, DO which is needed for most aerobic process is difficult to control. For enhancing research and to implement advanced control scheme, it is interfaced with PC using LabVIEW.

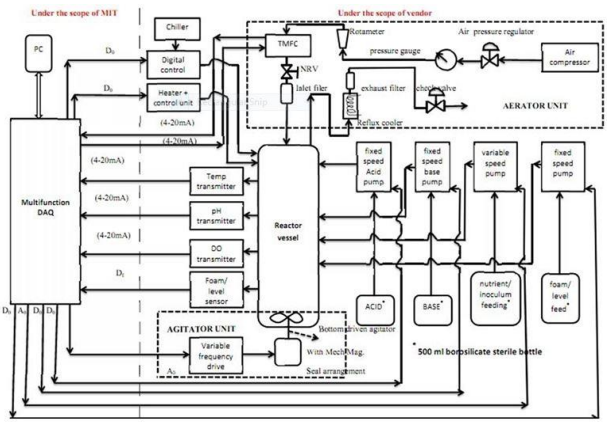

Fig. 2. P&ID of Bioreactor laboratory set-up

The signal from DO probe is taken as input via NI-DAQ 9203 to PC. The control signal is given by the PI controller implemented in LabVIEW to NI-DAQ 9263 which manipulates the stirrer speed in the range 0-1500 rpm. The stirrer speed is kept initially at 350 rpm and is varied to a maximum of 1200 rpm during the experiment. The block diagram of DO control is shown in Fig. 3.

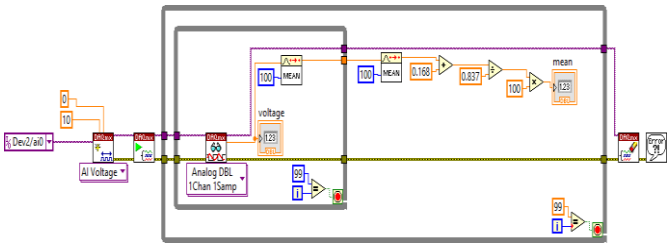

Fig. 3. Programming module for DO control

3. MODELING THE DO LOOP DYNAMICS

The process considered here is a bioreactor system shown in Fig. 4. For aerobic process such as cultivation of E.coli, the

supply of oxygen is crucial and has to be supplied continuously. The concentration of DO depends on three factors - oxygen transfer rate from gas phase to liquid phase, from liquid phase into the cells and oxygen uptake rate by the microbe[Garcia-Ochoa et al., 2009]. Mass transfer and mixing are mostly influenced by stirrer speed, type and number of stirrers and gas flow rate used [Linek V et al., 2005]. DO probe (4-20 mA) is used for inline measurement of oxygen in the reactor. If DO level is kept constant, the control input can be used as an indicator of the biological activity. Variations in oxygen dynamics are due to changes in $K_L a$. To have a tight control of dissolved oxygen $K_L a$ must be changed. The stirrer has direct relation with $K_L a$ hence it is manipulated.

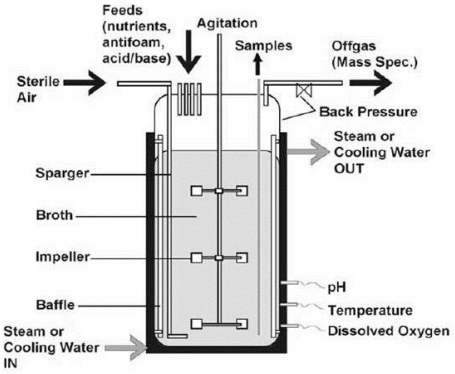

Fig. 4. Schematic diagram of a Bioreactor

The dissolved oxygen dynamics is represented in Eq. (1) as

$$\frac{dDO}{dt} = -q_{02}X + K_L a\,(DO^\circ - DO) - \frac{F}{V}(S_{in} - S) \qquad (1)$$

Here ,

- q_{02} - represents specific oxygen uptake rate,
- $K_L a$ - volumetric mass transfer coefficient , [1/h]
- DO° - Saturated concentration of dissolved oxygen[%]
- X - concentration of biomass, [g/l]
- S - concentration of substrate (glucose), [g/l]
- DO - concentration of dissolved oxygen, [%]
- F - feeding rate, [l/h]
- V - bioreactor volume , [l]
- S_{in} - concentration of the feeding solution, [g/l]

For a fixed air flow rate, the $K_L a$ can be modelled as a function of the stirrer speed, N [Akesson., 1998]. From estimation and correlation of $K_L a$ value with stirrer speed using the relation given in Eq. (2), control action can be implemented.

$$K_L a\,(N) = \alpha.(N - N_0) \qquad (2)$$

Where, α is an exponent ranging between 0.4 and 1. N_0 is the minimum stirrer speed for a particular operating range. For the laboratory bioreactor having total volume of 3 litres, the values of α and N_0 are 0.92h^{-1} rpm^{-1} and 323rpm respectively. The linearization parameters are carefully picked from the past experiment experience on a specific bioreactor, which means that they will not be valid for experiments performed on bioreactors with different scales.

4. DATA DRIVEN MODELING

The system model is obtained by designing an experiment in which the system input, agitator speed is varied to yield a measurable system output, DO level. The pertinent data are then used to create transfer function model corresponding to log phase of the fermentation cycle using system identification toolbox in Matlab

The experiment is started with the initial work which is done for a regular reactor run. This includes inoculation of E.coli strain to attain a minimum growth level and sterilization to avoid contamination. After sterilization, the organism inoculated is transferred to the bioreactor. It is assumed that well-mixed conditions apply and that any mechanical or electrical dynamics from control signal to stirrer speed are negligible. Using the HMI developed, temperature, pH and DO are maintained in their respective initial values. The organism is allowed to grow by maintaining DO above the critical value. Every one hour, sample is collected and once the organism reaches log phase the experiment to model the DO kinetics is started.

In this part of experiment the agitation speed is set at 350 rpm and the air sparge rate is maintained at 2 lpm for 30 seconds and then the agitator speed is stepped to 400 rpm. This step input is applied to agitator through NI card and response is recorded. The chance in DO concentration is sampled for every 4 second and it is used to find the required transfer function model. When the DO level has reached nearly steady state, the agitation speed is reduced back to the original set point. The above mentioned experiment is carried out in all the three stages of E.coli growth. The Model in log phase alone is taken into consideration due to increased oxygen starvation. Obtained model is validated by comparison of its output data with real time observed data and the model response is shown in Fig. 5.

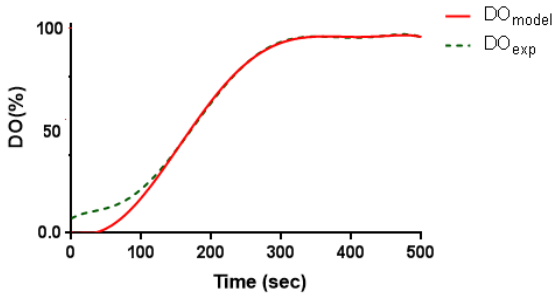

Fig. 5. Step response of model and real time system for change in stirrer speed

The experimental data are approximated to be a FOPDT model using system identification toolbox as in Eq. 3.

$$G(s) = \frac{1.2305}{(168s + 1)} \times e^{-35.8s} \qquad (3)$$

5. CONTROLLER IMPLEMENTATIONS

5.1 PID Controller design

The conventional PI controller is implemented initially for DO control. The PI controller design structure given in Eq. (4) is used in this study.

$$u(t) = K_p e(t) + K_i \int_0^t e(t)d\tau \quad (4)$$

where K_p , K_i are proportional gain and integral gain respectively[Åström., 1995].

The bioreactor is supplied with Programmable Logic Controller (PLC) based automation. The manufacturer's PI controller settings are used for this experiment as it yields better response than other tuning methods**.** The manufacturer's controller parameters *Kp* and K_i are 1.00 and 0.01 respectively. The criteria for selecting the PI gains was Integral Squared Error (ISE) ie; the controller setting which gives less ISE was selected as the gains of the controller. The block diagram is shown in Fig. 6.

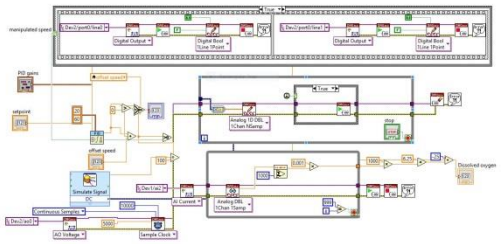

Fig. 6. PI controller implementation for DO Control

5.2 MRAC Control Scheme

MRAC strategy is used to design the adaptive controller that works on the principle of adjusting the controller parameters so that the output of the actual plant tracks the output of a reference model having the same reference input [Jain P.,2013]. The reference model is used to give an idyllic response of the adaptive control system to the reference input. The controller is usually described by a set of adjustable parameters. In this paper only one parameter θ is used to describe the control law. The value of θ is primarily dependent on adaptation gain. The adjustment mechanism is used to alter the parameters of the controller so that actual plant could track the reference model [Anuj et.al., 2016]. Mathematical approaches like MIT rule, Lyapunov theory and theory of augmented error can be used to develop the adjusting mechanism [Sun. J.,2015]. In this paper, MIT rule is adopted. The basic block diagram of MRAC system is shown in the Fig.7.The reference model chosen for this experiment is given in Eq. 5. As shown in the figure, $y_m(t)$ is the output of the reference model and y (t) is the output of the actual plant and difference between them is denoted by e(t).

$$G_r(s) = \frac{1}{(100s+1)} \quad (5)$$

The reference model $G_r(s)$ is an ideal model and its output $y_m(t)$ directly denotes the required dynamic response. The adaptive regulation process of the controller parameters is described as follows: when the input value *r*(*t*) is set to the controller, it is also simultaneously added to the reference model input; at the initial stage, since the origin parameters of controlled object are unknown, the controlled parameters are not determined causing the output response *y*(*t*) not in accordance with $y_m(t)$ and *e*(*t*) is produced. When *e*(*t*) is introduced into the adaptive regulation loop, through the calculation by adaptive laws and then proper dynamic signal of changing the controller parameters is derived to make the *y*(*t*) get approaching to $y_m(t)$.

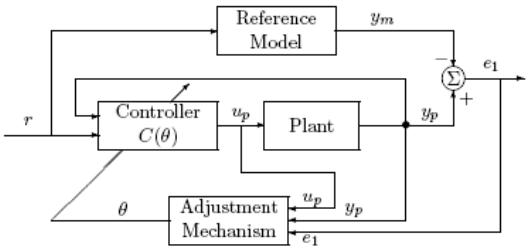

Fig. 7. Block diagram of MRAC scheme

The adjustment mechanism of MRAC system constructed from MIT rule which performs as follows,

Tracking error: $e = y_{plant} - y_{model}$ (6)

Where e is the error between the outputs of plant and the model, and θ is the adjustable parameter

Cost function: $J(\theta) = 0.5\, e^2(\theta)$ (7)

Parameter θ is adjusted in such a fashion so that the cost function can be minimized to zero.

Controller law: $u = \theta u_c$ (8)

Update rule: $\frac{d\theta}{dt} = -\gamma \frac{\partial J}{\partial \theta} = -\gamma e \frac{\partial e}{\partial \theta}$ (9)

where, γ is the tuning parameter and adjustable parameter is θ .

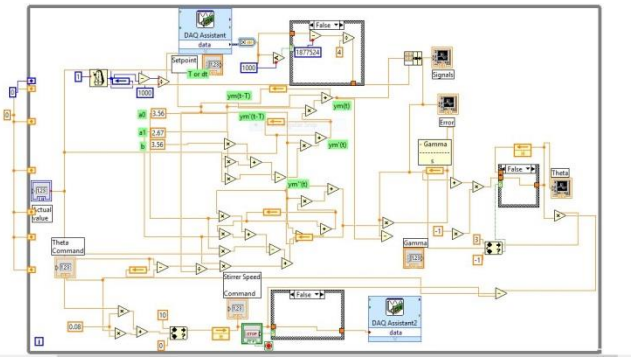

Fig.8 MRAC controller implentation for DO Control

The partial derivative term $\partial e / \partial \theta$ is called as the sensitivity derivative of the system. This term indicates how the error is changing with respect to the parameter θ . And eq. (9) describes the change in the parameter θ with respect to time so that the cost function J (θ) can be reduced to zero. Here γ is a positive quantity which indicates the adaptation gain of the controller. In the present work, adaptation gain is chosen as 0.7. The MIT rule is a gradient scheme that aims to minimize the cost function.

6. COMPARATIVE RESULTS

The summary of performance of MRAC and PI controller is given in Table.1.The desired closed loop performance

specifications are given in terms of reference model in MRAC.

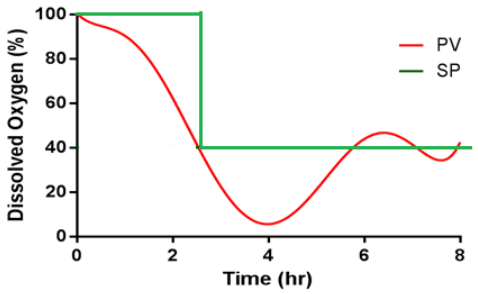

Fig. 9(a). DO Concentration profile of E.Coli cultivation for the batch of 8h with PI Controller

The real time implementation results for DO control with PI controller is shown in Fig. 9(a) .It is observed from the graph that DO concentration is not maintained at desired level throughout the batch.

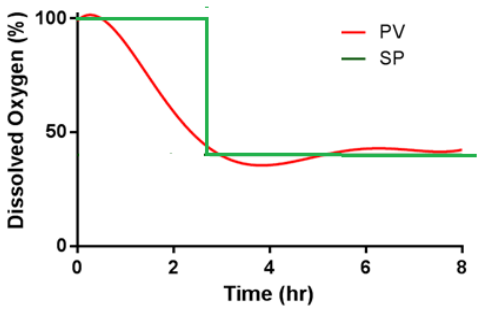

Fig. 9(b). DO Concentration profile of E.Coli cultivation for the batch of 8h with MRAC Controller

The servo response of the system with PI controller is shown in Fig.9(a) with a change in the stirrer speed of 50 rpm at 120 sec. Fig.9(b) shows the servo response of the system with MRAC controller with same change in the stirrer speed input at the same time (120 sec).

Table 1: Process performance parameters

Process Performance Parameters	**PI**	**MRAC**
Rise time(sec)	75	60
Peak overshoot (%)	30	8

It is observed that the proposed MRAC controller gives the satisfactory response. Rise time is calculated as the time taken for change in response from 10% to 90% with respect to set point (40%).Peak overshoot is the maximum peak value of the response curve measured from the desired set point(40%) of the system. The rise time and peak overshoot are significantly decreased with MRAC controller when compared to PI controller and are listed in Table 1.

The designed MRAC controller is implemented using LabVIEW as in Fig.8 .The input command via change in stirrer speed and the corresponding results are represented in Fig.9(b) .The purpose of DO control is to improve the biomass concentration. The graph representing increase in biomass during control of DO using MRAC scheme is shown in Fig.10.

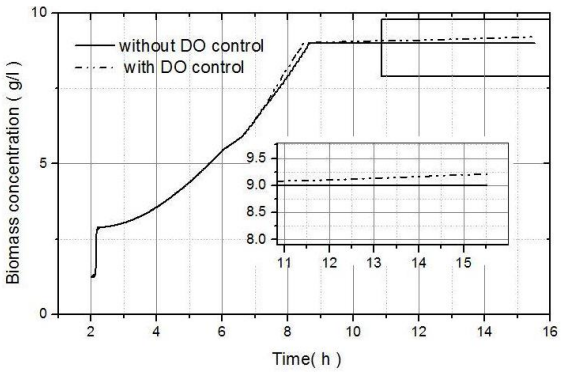

Fig. 10. Variation in biomass concentration with and without DO control

7. CONCLUSIONS

The secondary state variable DO is monitored continuously and is controlled using PI and MRAC schemes. The performance evaluation is carried out through LabVIEW platform. The developed user interface, gives the flexibility to observe the variation of input and output of the process in real-time mode. The conventional PI controller did not produce desired results during DO control. The adaptive control methodology designed using MRAC scheme found to give improved results.

ACKNOWLEDGEMENT

The authors gratefully acknowledge Anna University, Chennai for providing financial support to carry out this research work under Anna Centenary Research Fellowship (ACRF) scheme.

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