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Research article

An event triggered control scheme for enhanced production of Escherichia coli and biomass concentration during fed-batch cultivation

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A R T I C L E I N F O

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A B S T R A C T

Control of a bioprocess is a challenging task mainly due to the nonlinearity of the process, the complex nature of microorganisms, and variations in critical parameters such as temperature, pH, and agitator speed. Generally, the optimum values chosen for critical parameters during Escherichia coli (E.coli) K-12fed-batch fermentation are37 $^{\circ}$C for temperature, 7 for pH, and 35 % for Dissolved Oxygen (DO). The objective of this research is to enhance biomass concentration while minimizing energy consumption. To achieve this, an Event-Triggered Control (ETC) scheme based on feedback-feed forward control is proposed. The ETC system dynamically adjusts the substrate feed rate in response to variations in critical parameters. We compare the performance of classical Proportional Integral (PI) controllers and advanced Model Predictive Control (MPC) controllers in terms of bioprocess yield. Initially, the data are collected from a laboratory-scaled 3L bioreactor setup under fed-batch operating conditions, and data-driven models are developed using system identification techniques. Then, classical Proportional Integral (PI) and advanced Model Predictive Control (MPC) based feedback controllers are developed for controlling the yield of bioprocess by manipulating substrate flow rate, and their performances are compared. PI and MPC-based Event Triggered Feed Forward Controllers are designed to increase the yield and

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to suppress the effect of known disturbances due to critical parameters. Whenever there is a variation in the value of a critical parameter, it is considered an event, and ETC initiates a control action by manipulating the substrate feed rate. PI and MPC-based ETC controllers are developed in simulation, and their closed-loop performances are compared. It is observed that the Integral Square Error (ISE) is notably minimized to 4.668 for MPC with disturbance and 4.742 for MPC with Feed Forward Control. Similarly, the Integral Absolute Error (IAE) reduces to 2.453 for MPC with disturbance and 0.8124 for MPC with Feed Forward Control. The simulation results reveal that the MPC-based ETC control scheme enhances the biomass yield by 7 %, and this result is verified experimentally. This system dynamically adjusts the substrate feed rate in response to variations in critical parameters, which is a novel approach in the field of bioprocess control. Also, the proposed control schemes help reduce the frequency of communication between controller and actuator, which reduces power consumption.

1. Introduction

Fed-batch fermentation is widely used in bioprocess industries due to its good productivity. Improving biomass yield is still challenging for bioprocessing engineers [1,2]. E.coli is gram-negative bacteria which serves as a popular production host for industrial fermentation. E.coli fermentation is harnessed to produce organic acids, biofuels, antibiotics and in addition E.coli assists synthesizing enzymes.

E.coli fed-batch fermentation has been helpful in food and pharmaceutical industries for producing vitamin B_{12} and riboflavin (vitamin B_2) and for manufacturing medicines like antibiotics [3]. Optimizing critical parameters such as pH, agitation rate, and temperature of a bioreactor using advanced control technologies aids in achieving higher cell growth [4,5].

Fermentation is normally classified based on the mode of operation as continuous, batch, and fed-batch. The fed-batch mode is highly utilized in industries. In fermentation, microorganisms generate the product by providing them with the necessary substrate [6]. Critical parameters such as dissolved oxygen, pH, and temperature greatly influence the growth of microorganisms. The sufficient inflow of substrates and proper environmental conditions ensures a good yield. During batch/fed-batch fermentation, the critical parameters fluctuate due to the non-linearity in the growth of microorganisms. There exist several challenges in bioreactor control, including control of dissolved oxygen by manipulating stirrer speed/airflow rate [7], control of temperature by manipulating the cooler system [8], and control of pH by manipulating acids/bases [9]. The conventional controllers used to maintain critical parameters within a desired range exhibit poor performance due to the nonlinearity of the process. Process Analytical Technology (PAT) tools implement advanced control techniques that ensure product quality and enhance yield [10,11].

Bioprocesses are sensitive to parameter variations. The significance of temperature during fermentation and maturation was verified experimentally during yeast fermentation [12]. Temperature regulation in a fermenter using fuzzy logic-based split range control was proposed by Fonseca et al., 2013 [13]. Wang et al., 2010 [14] presented an optimized smooth profile for temperature using an ant colony system during beer fermentation. pH is another critical parameter that exhibits significant changes in productivity during bacterial growth [15].Chidambaram2020 [16]developed a PID controller scheme based on Haalman's tuning rules and have demonstrated improvement in MIMO processes. Optimization strategies for pH control during succinic acid production have also been discussed [17]. Dissolved Oxygen (DO) is another important parameter that decreases nonlinearly during bacterial growth. The volumetric productivity of β-carotene was explored by carrying out DO-stat fed-batch fermentation in the Yarrowiali polytica C11 strain [18]. Chitra et al., 2018 [19] achieved DO control during fed-batch fermentation using Model Reference Adaptive Control (MRAC) to improve biomass yield is achieved. Although recent studies reveal that the continuous monitoring and control of critical parameters is essential for the fermentation process, controlling all three parameters (temperature, pH, and DO) simultaneously throughout the fed-batch, using appropriate control techniques, is limited.

Nowadays, fermentation is modernized with remote monitoring and control at desired operating conditions, and integrating sensors and actuators helps improve process efficiency [20]. Various monitoring tools used to control E. coli fermentation and the effect of various factors on E. coli membrane integrity was discussed [21]. A feedback control system is chosen based on whether the bioreactor is maintained at some critical parameters and experimentation is performed on substrate composition to improve product efficiency and on monitoring and maintaining critical parameters (temperature, pH, agitation speed, etc.) within acceptable ranges [22]. A model based adaptive tuning method for the PI controller was implemented for a pH neutralization process [23]. However, implementing the adapted PI controller was only a simple process model. Rose et al., 2020 [24]implemented Afuzzy optimal controller for temperature and pH using the ANFIS algorithm for penicillin production. However, the accuracy of the ANFIS algorithm depends on the effective training of membership functions, and the interpretation of ANFIS to the developed model is difficult.

One of the approaches for integrating sensors and actuators to decrease communications in a network management system is the implementation of ETC [25]. The ET-PID controller has been developed to control the position of a mini quadrotor helicopter. The controller was reported to perform well and to decrease communication effort [26] compared to a PID controller. An event-triggered robust adaptive controller has been designed to reduce the communication burden, and the results were applied to a robot manipulator [27]. Cao et al., 2019 [28] proposed an event-triggered control for multi-agent systems with unknown disturbances to save network transmission resources and minimize the number of controller updates. In Event triggered PI controller design, the event is generated based on the performance degradation of the Linear Quadratic (LQ) objective function [29]. The Event triggered based Sliding Mode Control (ET-SMC) finds its use for both nonlinear systems affected by external disturbances and linear systems under uncertainties [30, 31].

Some research has been reported on using ETC in bioprocesses. Event-based control strategies have been developed to control the feed profile of the E.coli cultivation process for different values of pH and Dissolved Oxygen (DO) [32]. However, the development of ETC for control of critical parameters to enhance the biomass concentration has not been performed; this novel work is the focus of this research paper. Also, the possibility of oxygen and temperature control during bacterial cultivation via substrate feeding was proved [33]. The fed-batch fermentation process is carried out in this research work with conventional and MPC controllers [34]. ETC is developed to control the critical parameters with feed substrate as the manipulating variable.

Numerous contributions are expected from this research. The first one is to develop process and disturbance models based on the data collected from an experimental setup. Data analysis is done to derive the relationship between critical variables and biomass concentration. Next, the Event Triggered Control is designed to maintain critical parameters at a constant value throughout the fed-batch. The last step involves integrating a feedback (PI and MPC) and a feed-forward control scheme (ETC) using an event detection mechanism, so as to compare their performances. This comparative study is unique as it not only develops these controllers but also designs PI and MPC-based Event Triggered Feed Forward Controllers to increase the yield and suppress the effect of known disturbances due to critical parameters.

2. Materials and methods

2.1. Laboratory set-up

The laboratory bioreactor used for data collection and E.coli cultivation by maintaining several process parameters is shown in Fig. 1.

Before starting the experiment, the bioreactor, substrate, and sensors are sterilized. Also, the inoculum is prepared in a sterilized medium. The steady-state operating conditions used in this fed-batch fermentation are as follows. The temperature is maintained at 37°C. The airflow rate and agitator speed are maintained at 1.5 l/min and 150–750 rpm, respectively. The volume of the bioreactor is maintained at 1.2litres. The pH variation during E.coli growth is maintained at7. The laboratory scale bioreactor experimental setup along with the PC interface used for E.coli fed batch cultivation is presented in Fig. 2. Agitator speed, air flow rate, coolant flow rate, and substrate flow rate are the process manipulating variables. The controlled variables are reactor temperature, pH, dissolved oxygen concentration, and biomass concentration.

2.2. Strain and media

The process described involves the preparation of a specific type of media for the growth of E.coli, following the guidelines set by Sohoniet al. 2015 [35]. The feed media is enriched with glucose at a concentration of 40 g/L. For the growth of E.coli, Luria Broth (LB) is utilized. LB is a nutrient-rich media that contains tryptone (9.8 g), yeast extract (4.7 g), and NaCl (10 g) per liter of distilled water. These components provide the necessary nutrients for the bacteria to be alive.In addition to the LB, a trace solution is prepared in 5 N HCl. This solution contains various compounds including $FeSO_4{\cdot}7H_2O$, $MnSO_4{\cdot}H_2O$, $AlCl_3{\cdot}6H_2O$, $CoCl_2$, $ZnSO_4{\cdot}7H_2O$, $Na_2MoO_2{\cdot}2H_2O$, $CuCl_2{\cdot}2H_2O$, and H_3BO_3. These trace elements are essential for various biochemical reactions within the bacterial cells.

The inoculation process involves the introduction of the E.coli strain into a 1000 mL shake flask containing 200 mL of the prepared media. This flask is then placed in an orbital shaker, which provides the necessary agitation for the bacteria to grow. The shaker is set at 180 rpm and the temperature is maintained at 37 °C overnight. This environment mimics the optimal conditions for E.coli growth, allowing for a successful cultivation process.

Fig. 1. Laboratory scale bioreactor.

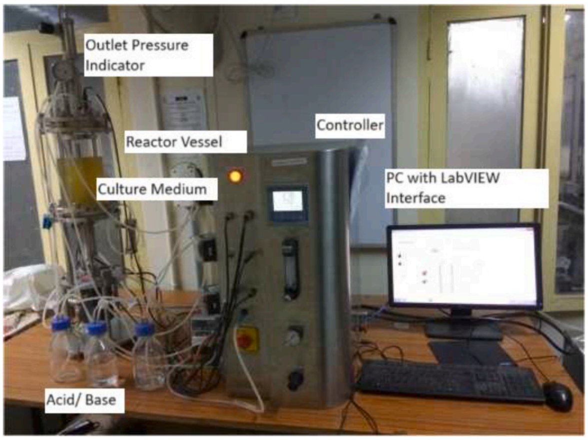


Fig. 2. Bioreactor experimental setup with Lab VIEW Interface.

3. Modeling of E.coli fermentation

3.1. Data driven model development

For nonlinear systems, data-driven models are useful [36]. Data are collected by conducting fed-batch experiments on an experimental bioreactor setup under the operating conditions discussed in the previous section. As given in equation (1), the process model developed using MATLAB(18a) with the substrate feeding rate as the manipulated variable and biomass concentration as a controlled variable as follows:

$$Gp(s) = \frac{X(s)}{F(s)} = \frac{200}{1.5s + 1} \tag{1}$$

Disturbances in the plant are unavoidable; hence to take prior action before the impact of disturbances, the measurable critical parameter disturbances are considered. From the data analysis, variations in pH, temperature, and DO significantly affect the biomass product concentration (pc). As given in equations (2)–(4), their respective Transfer Functions are identified using MATLAB (18a) as follows:

$$Gd(pH) = \frac{X(s)}{T(s)} = \frac{35.5s + 3.5}{1.72s^2 + s} \tag{2}$$

$$Gd(temp) = \frac{X(s)}{T(s)} = \frac{40s + 4}{2s^2 + s} \tag{3}$$

$$d(DO) = \frac{X(s)}{T(s)} = \frac{27s + 2}{2.5s^2 + s} \tag{4}$$

The process model (1) is used for designing PI-based FB controllers, and (2)–(4) are used for the design of Feed Forward controllers. From equations (5) and (6), state space models developed for use in the development of MPC controllers are as follows:

$$\dot{X} = AX + BU \tag{5}$$

$$Y = CX \tag{6}$$

For the laboratory bioreactor, the data-driven state space model obtained from the following equation (7) as follows:

$$\dot{X} = \begin{bmatrix} \dot{x} \\ \dot{s} \\ \dot{v} \\ \dot{ph} \end{bmatrix}; \ A = \begin{bmatrix} -0.13 & -6.67e-05 & -6.14e-16 & 2.97e-16 \\ 0 & -2 & 0 & 0 \\ 0 & 1 & -2 & 0 \\ 0 & 0 & 1 & -2 \end{bmatrix}; X = \begin{bmatrix} x \\ s \\ v \\ ph \end{bmatrix}$$

$$B = \begin{bmatrix} 4.11 \\ 2494 \\ -9.085e-08 \\ 3.8.3e-08 \end{bmatrix}; \ U = F \tag{7}$$

$$C = [6.43 \quad -0.0002 \quad 1.14e-14 \quad -5.53e-15] \text{ and } D = [0]$$

where the state vectors are product concentration (pc), substrate concentration (s), biomass concentration (x), and volume of the reactor (v), and the input vector is the substrate feed rate (F).

3.2. Development of event-triggered control scheme

ETC schemes are becoming notable nowadays as they improve control efficiency. In ETC, acquiring output data at fixed time intervals is unnecessary. The error due to pH, temperature, and DO disturbances are calculated and compared with their threshold values. Whenever the error value reaches the threshold value, an event is triggered to acquire the output data, a new control command is generated, and the manipulating variables are updated accordingly. This control command is in action until another new event is triggered, and then this process repeats [37]. Therefore, the sampling frequency is decreased without any compromise in bioreactor performance.

Event-based sampling and transmission systems are significant components of event-triggered mechanisms [38]. The temperature, pH, and DO variations from optimal operating conditions directly affect the biomass inside the bioreactor and hence are considered disturbance variables. The change in bioreactor critical parameters is continuously measured, and when the parameter variation exceeds its threshold, the feed-forward controller triggers. Event-triggered FF reduces the effect of the disturbance on biomass concentration by manipulating substrate feed rate. The event-triggered mechanism with threshold policy is considered in this work. Initially, the ETC scheme is developed and tested for a single disturbance [39]. The block diagram of the proposed controller based on an Event triggered scheme is provided in Fig. 3. It consists of a feedback controller, Event generator, and feed forward controller.

In this work, as disturbances of small magnitude d are considered, there is a trade-off between the threshold of the event T_e and the controller performance. The control problem is realizable for all $d(k) \in D, k \geq 0$ and maintained $e(k) \in E, k \geq 0$ [37]. If the event condition is satisfied, process data are transmitted over the feedback path. Those discrete time instants are represented by k_i where $i \in N$, the event counter. An event is generated whenever the error exceeds a threshold, as represented by equation (8)

$$\|x(k) - \hat{x}(k / k_i)\| \geq T_e \tag{8}$$

3.2.1. PI-based event-triggered control

One of the challenges during E.coli cultivation is maintaining the critical parameters constant throughout the fed-batch. In order to achieve this, initially, an Event Triggered scheme-based PIcontroller is developed, as shown in Fig. 4, and its capabilities of minimizing slight variations in critical parameters are examined.

The direct synthesis method to design the PI controller and its parameters is presented in Table 1.

The influence of temperature, pH, and dissolved oxygen (DO) on the biomass concentration is analyzed. These three parameters are considered measurable disturbancesto the plant; hence the Feedforward Control parameter (K_{FFC}) is obtained (see Table 2).

During the operation of the given E.coli bio fermentation process, temperature, pH, and DO variations occur many times at different time instants. Initially, for simulation, these disturbances are generated once at a separate time instant to determine the controller's performance. The dynamic gain of the Feed-forward controller for these three disturbances is generated as per the disturbances transfer function (G_d's) together with the plant transfer function (G_p) as described in Table 2. It is observed that temperature, pH, and DO disturbances occur on the 4th, 8th, and 14th hour with variations of $+1$ °C, pH of $+1$, and -5% DO from the operating point of the process, respectively. The disturbances are rejected by an event-triggered Feed-forward control having separate FFC for the disturbances temperature, pH, and DO. In this case, the Feedback controller manages biomass concentration by manipulating the substrate feed flow rate.

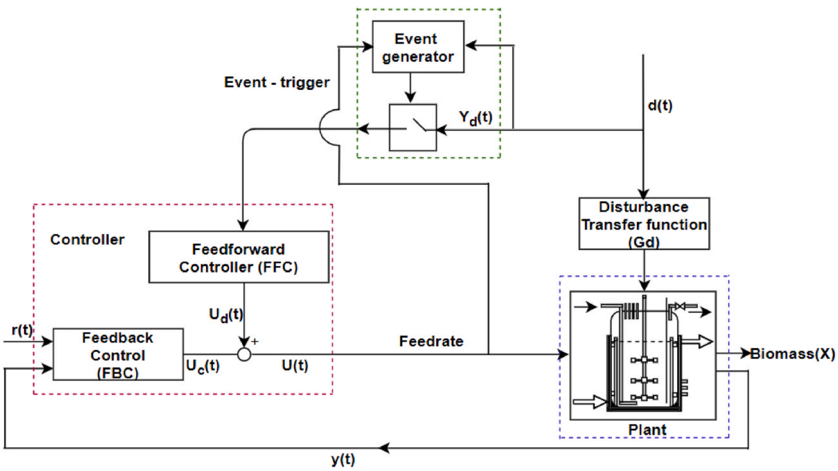


Fig. 3. Block diagram of Event-Triggered control scheme.

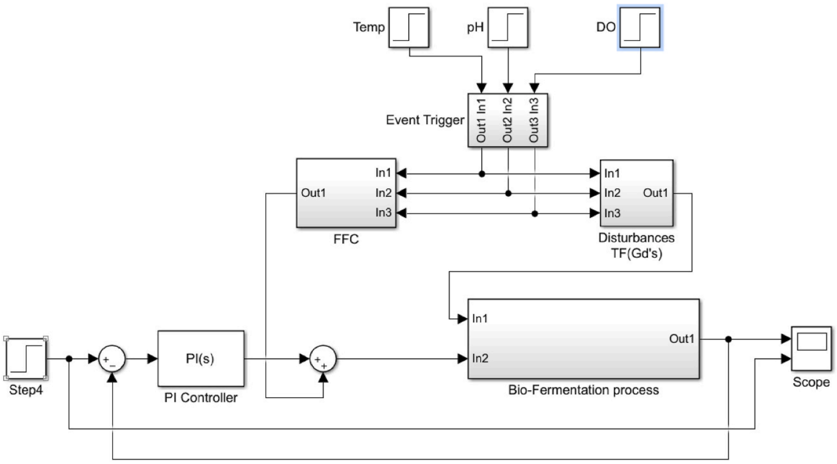


Fig. 4. Block diagram of Closed loop Event Triggered based PI controller.

Table 1
Controller parameters of Event-Triggered based PI.

Controller parameter	Value
K_p	1.508
K_i	0.912

Table 2
Feed-forward Control parameters for disturbances.

Parameter	Value
K_{FFC}(temp)	$\frac{Gd}{Gp(Temp)} = -\frac{53.25s^2+40.75s+3.5}{344s^2+200s}$
K_{FFC}(pH)	$\frac{Gd}{Gp(pH)} = -\frac{60s^2+46s+4}{400s^2+200s}$
K_{FFC}(DO)	$\frac{Gd}{Gp(DO)} = -\frac{40.5s^2+30s+2}{500s^2+200s}$

The plant responses to multiple disturbances are shown in Fig. 5. It is inferred from Fig. 5 that the Set Point is constant around 80 g/l.The response when using a PI controller with feedback and disturbance compensation fluctuates due to disturbances and response when using a PI controller with feedback and feed forward compensation remains stable despite disturbances. It is seen that, ataround 2 h, there is a disturbance related to temperature. For PI-FB-D, the biomass concentration decreases, while for PI-FB-FFC, it remains unaffected. At around 12 h, there is another disturbance related to DO. Again, PI-FB-D shows a drop in biomass concentration, whereas PI-FB-FFC maintains stability.

It is seen that the output of PI-FB + D is affected while the response for PI-FB + FFC is unaffected by the disturbances. However, FFC suppresses disturbances with higher control effort, as shown in Fig. 6.It is inferred from Fig. 6 that, the feed rate changes at the4thhr, 8th hr and 14thhr during fermentation.Fig. 5 shows that biomass concentration decreases as temperature increases beyond the operating point. Similarly, an increase in pH increases biomass concentration. Meanwhile a decrease in dissolved oxygen content in the

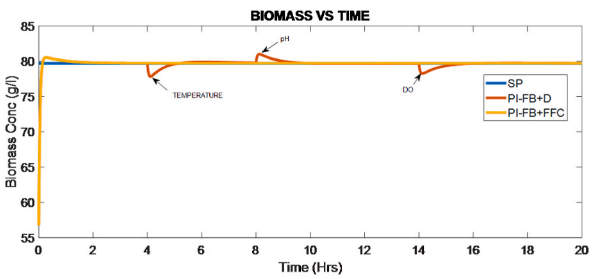


Fig. 5. Plant response with PI with disturbance and with Feed Forward control.

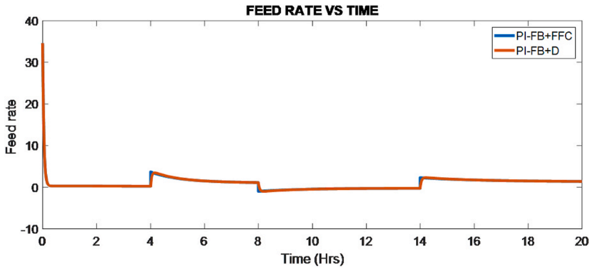


Fig. 6. Control effort of PI controller with disturbance and with Feed Forward control.

broth inside the bioreactor decreases the biomass concentration.

3.2.2. MPC based event triggered control (ETC)

Model-based control strategies are widely applicable nowadays due to improved product efficiency [40]. Model Predictive Control (MPC) is widely used in bioprocess industries due to its ability to manage constraints, so as to minimize time delay [41]. The MPC updates the states of the system and the constraints at each time step [34]. Thus, overall closed-loop performance is improved. Fig. 7 shows the Event Triggered based MPC controller. This configuration minimizes communication in networked control systems by optimizing the data transmission only if the event conditions are satisfied. This characteristic of ETC is found to be helpful when combining with feedback control systems. The MPC must satisfy input constraints and external disturbances to critical parameters in this work.

The following quadratic objective function is considered here for this work, as given in equation (9)

$$J = \sum_{k=1}^{n} \vec{e}_{k+1}^{\,T} Q \vec{e}_{k+1} + \left(\triangle \vec{\bar{u}}_k\right)^T R \left(\triangle \vec{\bar{u}}_k\right) \tag{9}$$

where $\vec{e}_{k+1} = r_{k+1} - y_{k+1}$ represents the error equation and $\triangle \vec{\bar{u}}_k$ is the change in future control inputs that is assumed between 0.0 and 0.1 to keep the microbes alive (Chitra et al., 2021). The current measurements and future predictions are used for control calculations. The objective function J is minimized by the manipulated variable, u_k, calculated at the kth sampling instant. The state and output prediction equations are given in equations (10) and (11), respectively.

$$\vec{x}_{k+1} = P_x x_K + H_x \vec{u}_k \tag{10}$$

where P_x depends on past values, and H_x depends on u_k.

$$\vec{y}_{k+1} = P_x x_k + H \vec{u}_k + Ld_k \tag{11}$$

The objective function is obtained by substituting $\vec{x}_k$ and $\vec{y}_{k+1}$, as follows:

$$\min_{u_k} \vec{u}_k^{\,T} \left(H^T H + R\right) \vec{u}_k - 2 \vec{u}_k \left(H^T [r_{k+1} - P_x x_k - Ld_k]\right) \tag{12}$$

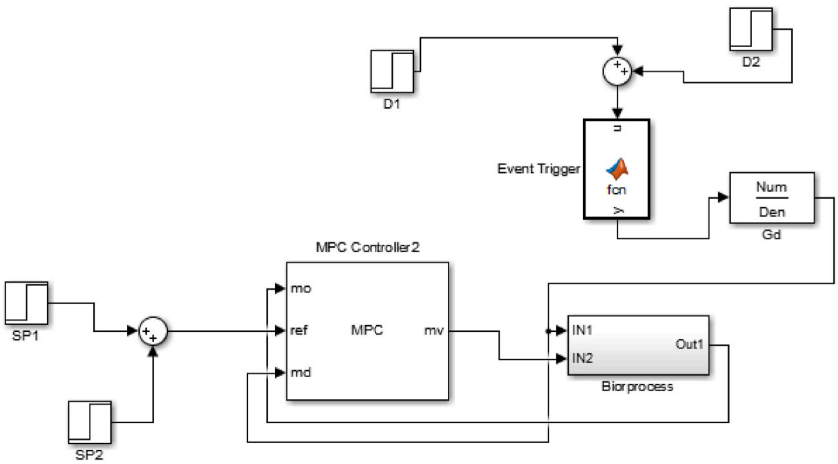


Fig. 7. Block diagram of Closed loop Event Triggered based MP Controller.

The main aim is to find $\vec{u}_k$ such that the objective function is minimum. To obtain $\vec{u}_k$, we differentiate equation (12) with respect to $\vec{u}_k$ and equate it to zero. The $\vec{u}_k$ thus obtained as follows is given in equation (13):

$$\vec{u}_k = \left(H^T H + R\right)^{-1} \left(H^T [r_{k+1} - P_x x_k - L d_k]\right) \tag{13}$$

$\vec{u}_k$ is obtained by solving (13) will satisfy the objective function described. The first value of $\vec{u}_k$ alone is considered and given to the process, and the remaining values are discarded. Again, $\vec{u}_k$ is determined for next instant. The closed-loop response can be obtained when the determined $\vec{u}_k$ is applied to the data-driven model.

MPC depends on real-time models. The improvement in optimal control performance is achieved through control horizon and predicted horizon selection. In this work, values for control and prediction horizon are chosen as 2 h and 13 h, respectively. The weight matrix R and Q are chosen as 10 and 0.001, respectively. The real-time implementation of MPC is based on an optimization procedure at every sampling instant and is chosen as 10 ms.

Table 3 lists the control settings for Event-Triggered MPC. The sampling rate is determined by the system's time constant. The Q matrix is given more weight to increase the performance of the bioprocess. In this case, the temperature, pH, and DO disturbances are generated at the same time instants as in PI-based Control. Therefore, in the 4th hour, 8th hour, and 14th hour, disturbances due to temperature variation, pH variation, and DO variation occur in the process. A FFC loop is developed to minimize the effect of disturbances, as shown in Fig. 8(a).

Fig. 8(b) shows the effort made by the MPC with Disturbance and with Feed Forward control to suppress multiple disturbances, temperature, pH, and Dissolved oxygen (DO) that occur in the plant at the 4th,8th, and 14th hours, respectively. Table 4 depicts the inferences of Fig. 8(a) and (b).

For qualitative comparison, the closed-loop response of the event-triggered control scheme based on PI and MPC is shown in Fig. 9 (a), and the associated manipulated variable is shown in Fig. 10. It is inferred from Fig. 9(a) that MPC based on ETC quickly settled with a small peak overshoot as compared to PI-based ETC. Fig. 9(b) above shows the effort made by PI and MPC-based FB + FFC to suppress multiple disturbances, temperature, pH, and Dissolved oxygen (DO) in the plant at the 4th,8th, and 14th hours, respectively, by manipulating substrate feed rate to the bioreactor.

The real-time plant response with PI-based and MPC-based ETC schemes are compared and are shown in Fig. 9(b). There, it is inferred that the performance of MPC –FB + FFC is better than PI-FB + FFC since it has a smooth system response without overshoot; hence it has less settling time compared to Event triggered based PI control schemes.

4. Discussion

From the closed loop responses of PI and MPC-based feedback controllers with and without disturbances, it is found that the PI controller provides better performances for regulatory operation, and MPC provides better performances for servo operation. In the presence of measured disturbance, the feed-forward controller takes appropriate actions to reject the disturbance before it affects biomass concentration.

4.1. *Performance metric comparison*

The PI and MPC controllers based on Event-triggered control are developed, and their responses are compared qualitatively. The performance measures such as the control effort (CE), Integral Square Error (ISE), and the Integral Absolute Error (IAE) are calculated for four controlschemes: PI with Disturbance and with Feed Forward control, MPC with Disturbance and with Feed Forward control (see Table 5 and Table 6).

It can be inferred from Tables 5 and 6 that the Event Triggered MPC performs better than other control schemes listed as it has a lower Integral Square Error (ISE) and Integral Absolute Error (IAE). After designing the PI-based and MPC-based control schemes, our main interest is implementing the Event Triggered control scheme in real-time.

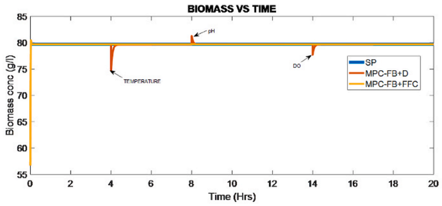
Fig. 10 illustrates the variation in biomass concentration with MPC FB controller and MPC-based ETC in real-time. The biomass concentration is plotted with respect to time fora range of 0–100 g/L. The MPC FB controller modifies the environmental parameters based on the variation between the actual and expected biomass. This indicates that the controller adjusts the environmental settings in response to variations in the biomass concentration. When the MPC FB controller is employed, the biomass concentration exhibits a gradual rise over time, peaking at 76.4 g/L atthe end of fermentation. But, the MPC ET-FFC scheme employs a feed-forward control approach. This implies that rather than waiting for an error to happen, it modifies the environmental parameters depending on the expected future behaviour of the biomass concentration. This may result in a more aggressive approach to control, which may raise the concentration of biomass. The biomass concentration in the MPC ET-FFC system increases steadily over time, but it exceeds the MPC FB controller and reaches about 83.7 g/L. This shows that the MPC ET-FFC scheme can optimize the feed substrate and capable of achieving a greater biomass concentration.

5. Conclusion

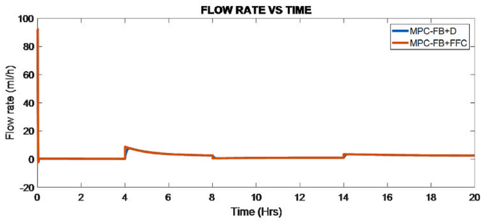
In this study, fed-batch data are collected from the laboratory bioreactor set up during E.coli cultivation and with that real-time data an empirical process model and a disturbance model are developed using the system identification technique. Four control

Table 3
Controller parameters of Event-Triggered MPC.

Controller Parameter	Value
Control Horizon	2
Prediction Horizon	13
Weight matrix R	10
Weight matrix Q	0.001
Sampling Instant	0.1



(a) Plant response with MPC with Disturbance and with Feed Forward control



(b) Control effort (CE) of MPC with Disturbance and with Feed Forward control

Fig. 8(a). Plant response with MPC with Disturbance and with Feed Forward control. Fig. 8(b) Control effort (CE) of MPC with Disturbance and with Feed Forward control.

Table 4
Disturbance occurrence during Fermentation and Control Effort.

Hour	Disturbance	Control Effort
4	Temperature Variation	MPC with Disturbance and Feed Forward Control
8	pH Variation	
14	Dissolved Oxygen (DO) Variation	

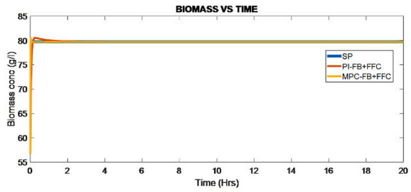
schemes were developed and examined, namely PI with Disturbance and Feed Forward control, and MPC with Disturbance and Feed Forward control. The investigation focused on the influences of critical parameters such as temperature, pH, and agitation speed on biomass concentration. An Event-triggered Feed Forward controller was activated in response to disturbance events exceeding critical parameter thresholds. The performances of the four control schemes were then analyzed both quantitatively and qualitatively. The findings presented indicate that the Event-Triggered MPC outperforms other proposed control schemes, exhibiting lower CE and ISE. Consequently, it has been demonstrated that this approach leads to reduced production costs through effective control. The real-time implementation of MPC-based Event-Triggered Control (ETC) was validated experimentally, highlighting its effectiveness in managing critical parameter disturbances during E.coli fed-batch fermentation and significantly enhancing biomass concentration.

6. Future work

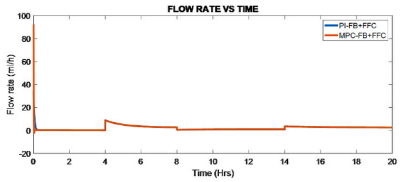
The proposed controller will be extended for fermentation of T.reesei, a microorganism capable of producing recombinant proteins and enzymes. This research used data from a 3L laboratory bioreactor, future work could scale up the application of these control schemes in large industrial bioreactors. Also, while implementing the proposed control schemes in industrial bioreactors other ways to improve energy efficiency can be analyzed.

Consent to participate

I have been informed of the risks and benefits involved, and all my questions have been answered to my satisfaction. Furthermore, I have been assured that any future questions I may have will also be answered by a member of the research team. I voluntarily agree to



(a) Plant response for PI & MPC based FB+FFC with multiple disturbances (temperature, pH and DO)



(b) Control effort for PI & MPC based FB+FFC with multiple disturbances (temperature, pH and DO)

Fig. 9(a). Plant response for PI & MPC based FB + FFC with multiple disturbances (temperature, pH and DO). Fig. 9**(b)** Control effort for PI & MPC based FB + FFC with multiple disturbances (temperature, pH and DO).

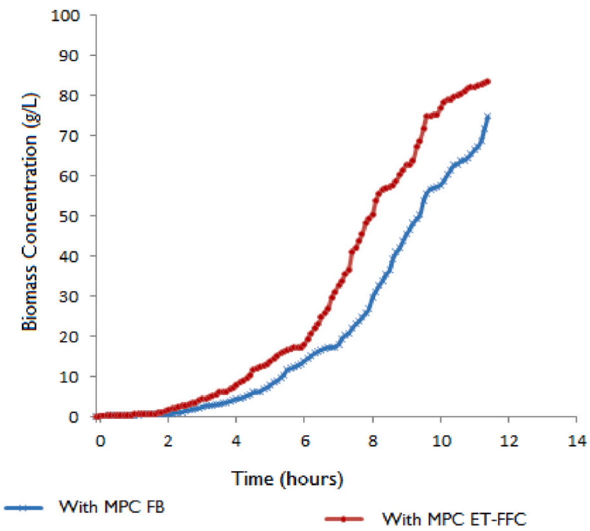


Fig. 10. Yield of biomass concentration from experimental bioreactor with MPC FB and with MPC ETC.

Table 5
Performance metric comparison for PI.

Parameter	PI with Disturbance	PI with Feed Forward Control
ISE	384.1	353.6
IAE	38.64	22.42
CE	1.432	1.514

Table 6
Performance metric comparison for MPC.

Parameter	MPC with Disturbance	MPC with Feed Forward Control
IAE	2.453	0.8124
CE	6.542	6.567
ISE	4.668	4.742

take part in this study.

Consent to publish

All authors gave consent to publish.

Data availability

The data will be available on reasonable request from the corresponding author.

CRediT authorship contribution statement

Chitra Murugan: Data curation. **Sutha Subbian:** Formal analysis. **Saravanan Kaliyaperumal:** Investigation. **Kishor Kumar Sadasivuni:** Conceptualization. **Md Irfanul Haque Siddiqui:** Supervision. **Suresh Muthusamy:** Methodology. **Marc A. Rosen:** Writing – original draft. **Chander Prakash:** Validation. **Choon Kit Chan:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Nomenclature

Dissolved Oxygen (DO)
Escherichia coli (E.coli)
Event-Triggered Control (ETC)
Event Triggered based Sliding Mode Control (ET-SMC)
Feed Forward FF
Feed Back FB
Linear Quadratic (LQ)
Model Predictive Control (MPC)
Model Reference Adaptive Control (MRAC)
Process Analytical Technology (PAT)
Proportional Integral (PI)
Product concentration (pc)
Substrate concentration (s)
Biomass concentration (x)
Volume of reactor (v)
Substrate feed rate (F)
Control effort (CE)
Integral Square Error (ISE)
Integral Absolute Error (IAE)
Trichoderma reesei (T. reesei)

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