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Implementation Bioreactor of Fed-Batch Operating Mode using Biomass Growth Adaptive Control System

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Abstract— ***This paper work describes the glycerol control system. The operation of the glycerol control system has been analyzed and actual showing intervals determined.The research part describes the research methods: First order time delay models, second order polynomial model, PID control algorithm, Cohen and Coon tuning rules. The goal of present work develop and investigate biomass growth control system in fed-batch operating mode bioreactor. This paper provides the develop and investigate a model for simulation of adaptive control system performance for tracking of specific growth rate at specific set point time trajectories and compare the result with ordinary control system performance indices. In the investigation part of the study, the calculation was made according to three different methods. The mathematical model parameters are obtained using an open loop test. The calculated reaction curve results are compared with experimental results using a second order polynomial method. The experimental results were carried out using an adaptive system and non-adaptive system methods. The results of the two methods were compared and the problem was solved. The tables of calculation with the results and the optimized results graphs are presented. Experimental calculations, programming and modelling performed using MATLAB/SIMULINK software.***

Index Terms— ***glycerol,PID, fed-batch, bioreactor.***

I. INTRODUCTION

Initially, some universal characteristics of bioreactors are highlighted with reference to control applications. Two main features, it is important to know before designing a control system for bioreactors, are:

- The multivariable system, and
- Non-linear dynamics.

The control of a bioreactor comprises many variables. Device measurement and control technologies applied to a standard bioreactor are well known in classical process engineering [1].

1.1. Control system

In recent years, control systems have played a central role in improving and advancing current technology and civilization. Practically each one of the subjects of our daily life is affected with the help of some system of manipulation. A bathroom, a tank, a refrigerator, an air conditioner, an ironing machine, a computerized iron, a vehicle, everything is a control system [2][1].

1.1.1. Open loop control systems

Any physical system without any automatic correction of variation towards the output change which is called an open loop control system. This type of systems is simple to construct, stable and cheap but it will not maintain its accuracy and reliability. These systems do not have external disturbance to affect the output and it will not initiate correction action automatically [2].

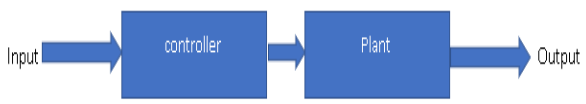

Fig.1. Block diagram of the open-loop control system [2]

1.1.2. Closed loop control systems

A closed loop control system is a system will maintain desired output values in accordance with input quantity in a closed loop manner, as shown in Figure 2. This type of systems is complicated to construct as compared to an open loop system [2].

1.1.3. Biomass Growth Control System

In collaboration with NASA under the SBIR (Small Business Innovation Research) program, it is established by orbital technologies corporation to meet the growing needs of commercial, biotechnology and science plants in the era of the Space Station. The BPS was developed based on interactions with NASA engineers and scientists and on the "lessons learned" from already flown plant growth systems, including the ASTROCULTURETM unit, Plant Growth Plant and Bio-processing Apparatus of plants [3].

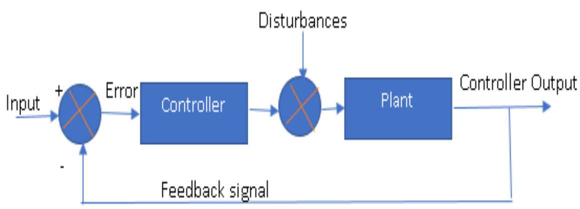

Fig.2. Block diagram of closed loop control systems [2]

1.2. Types of bioreactors or fermenters

A biological reaction carried out into a vessel and culture aerobic cells are used for conducting enzymatic immobilization [4]. Different types of bio-reactor or fermenters: *Continuous Stirred Tank Bioreactor:* In a vessel, the time will no longer vary the contents to hold up of micro-organisms and the components will contain some concentration in the fermenter. To achieve steady-state conditions by chemo static principles. These types of

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bioreactor are commonly used in a continuous process to activate in wastewater sludge industry. *Airlift Bioreactor:* The capacity, kinetic data, the specific growth rate is determined from rector volume of the organism used. The airlift pump works on a principle of fermenter are internal loop type and external loop type respectively. The uniform cylindrical cross type and has a configuration of the internal and external loop.*Fluidized Bed Bioreactor:* The regular particles contain some characteristics that are suspended in a flowing liquid stream with some additional gas phase is involved in this bioreactor, the tendency of particles which are involved in the bed that is less evenly distributed.Photo-Bioreactor: Phototrophic microorganism is used with some light source to cultivate. The photosynthesis is used by organisms to trigger biomass from the light source and carbon dioxide. The respective species are controlled for the artificial environment of a photobioreactor. In the photobioreactor, growth rate and level of purity in nature will be higher other than anywhere. *Membrane Bioreactor:* The various microbial bioconversions are applied successfully by membrane bioreactor. The alcoholic fermentation, solvents, organic acid production, wastewater treatment used in microbial conversions. The soluble enzyme and substrate are used in membrane bioreactor on one side of the ultrafilter membrane [5].

1.3. The operating modes of bioreactor

In a bioreactor, all the bioprocesses are carried out, where a microorganism like bacteria, fungi, yeast is cultivated under product formation conditions. For this reason, nutrients are compulsorily required to grow and under some conditions like temperature, pressure, PH and oxygen concentration are required to control the microorganism and these are the basic requirements to control bioprocess in a bioreactor [6].Batch mode, in this mode no substrate is added to the initial charge and no product is taken until it finishes the process. In batch operation have a major advantage for low investment cost, it does not require much control and without skilled labor, it can be accomplished operation. It has greater flexibility can be accomplished by using a bioreactor in various fields of product [6]. Fed-batch mode, in this mode during operation substrates are fed into the bioreactor. The combination of the batch and continuous operation are very popular in the ethanol industry. It has the main advantage is that inhibition and catabolite repression are avoided and additionally improves the productivity of the broth by holding at a low substrate concentration [6]. The continuous mode in this mode the substrate is added continuously until it finishes the process and product removal. In this process, the product is taken from the top of the bioreactor such as ethanol, cells and residual sugar as shown in Figure 3. Here operation is classified into two types, single stage continuous fermentation and multi-stage continuous fermentation [6]. The research part describes the research methods, first order time delay models, second order polynomial model, PID control algorithm, Cohen and Coon tuning rules Experimental calculations, programming and modelling performed using MATLAB/SIMULINK software.

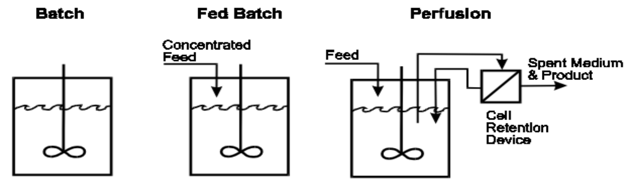

Fig.3. Alternate stirred bioreactor processes [7]

II. LITERATURE SURVEY

In microbiology, researchers often faced problems in describing the growth-rate of microorganisms growing on sub-strategy or in the study of competition through depletion resource. Improved growth rate and growth function from a mathematical model of flocs and microbial using negative feedback density-dependent process Compared growth rate and cell size in homeostasis at the metabolic signal in the cell division according to animal cell [8][9].Obtained biofilm growth from purple non-sulfur bacteria using a mathematical model of photo-bioreactor. The synthesis, design, and decision making related to the wastewater treatment process modelling Measured leaf chlorophyll from biomass production under various heat stress treatments during climate change occur in critical wheat production [10] [11]. Developed leaf elongation and leaf appearance derived from maize production during crop modelling and climate change condition [13].

Identified heat stress and grain filling in leaf chlorophyll of photosynthesis during leaf area index dynamics are carried in climate change for wheat production. The Wheat Grow model is a process-based wheat model, which can predict wheat phenology, photosynthesis and biomass production, biomass partitioning and organ establishment, and grain yield and quality formation under various environmental factors and management practices [10]. Compared to large cells and small cells are achieved multiple signaling pathways in cell division of growth rate and cell cycle progression helps to find in homeostasis [8]. Indicated unidentified extracellular components from bacteria will increase biomass and lipid productivities in a co-cultivation of algae and will reduce the expenditure in mass algae cultivation process in microorganisms [12].

2.1. Mathematical modelling of Fed-batch fermentation

Maximized enzyme activity by reducing metabolic heat and feeding inlet air in solid-state fermentation of a fixed bed reactor [14]. Developed excessive lovastatin 3.5-fold by microparticles of the preculture during bioreactor process [15]. Improved simultaneously high solids of saccharification and fermentation by recycle membrane from paper production of lactic acid [16]. The developed dynamic model for metabolic pathway in a sequential identification method [17]. Modified ethanol production at different temperature in the production of wine using yeast hinder [18]. Removed aerobic oxide of biomass segmentation with ammonium-oxidizing and nitrite-oxidizing impact on microbial [19]. Developed growth and decline phase of specific growth rate and biomass estimation in penicillin production of microorganisms [20]. Integrated model computation and biomass model of

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NIR data applied control overflow metabolism using partial least square and control a cholera-toxin in the monitor of batch cultivation [21]. Obtained numerical simulation of substrate feed rate in batch-to-batch process and leads to a robust process from measured problems in protein production [22]. Showed that heat capacity calorimeter of growth behavior will help to find validity and accuracy in a fermentation process used in many applications by this simple strategy [23]. Evidenced that glycan fractions with a heavy chain and the protein abundance enzyme to measure the time evolution of heterogeneities in pharmaceutical production as shown in Figure 4 [24][25]. Solved multi-objective optimization in a significant way the feed recipe helps to create productivity from dynamic optimization problems [26]. Showed the strain stability in ABE concentrations carried from oxygen tolerant process enforced by a butanol and acetate production [27]. Introduced multi-objective optimization in a distinct objective is computed to optimum algorithms for the productivity of dynamic optimization problems [26]. Observed enzyme activity of monoclonal antibodies in a bioreactor scale to improve intracellular clustering of micro-heterogeneities mining method for an absolute measure of scale in a pharmaceutical production [25]. Compared heat capacity calorimetry to compensation mode in a validity and accuracy, since mainly deal with PAT solution [23]. Analyzed the NIR data and EN data in partial least square with high correlation biomass, glucose, and acetate during monitoring and control of spectral identification [21]. Estimated the growth and decline phase for the development of control strategy in specific growth rate via online estimation method for specific production in penicillin production of bioprocess filamentous microorganisms to control quantitative and qualitative process [20].

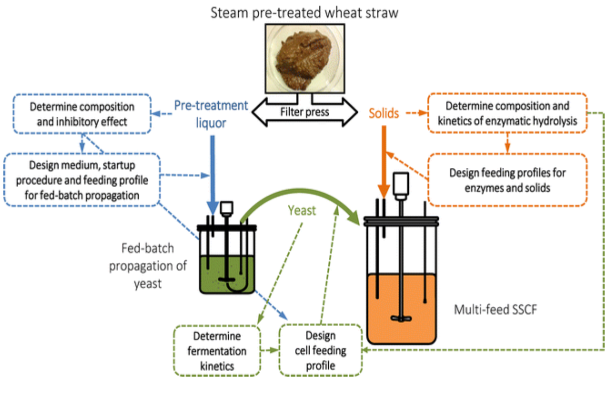

Fig.4. Process optimization [24]

2.2. Adaptive control system applied for biomass growth control in fed-batch cultivation processes

The oxygen concentration in the exhaust gas and the air supply rate no need of a mathematical model for the culture of microorganisms under control using fed-batch cultivation process having inferential control algorithm [28]. The recombinant production systems for collecting the data straight forward by controlling experiments for optimization predefined specific growth rate of the green fluorescent protein for keeping a microbial cultivation process in a generic control model [29].In simulation experiment fast adaptation, robust behavior significant changes in control performance for controlling dissolved oxygen concentration into control algorithm of steady-state action for adaptation controller to process on-linearity and time-varying operating conditions of microbial process [30].The transient response and robustness sliding observer an estimation growth rate it is implemented to control law using Lyapunov functions feed-back proportional output error for nonlinear integral action of the biomass specific growth rate based on the minimal model paradigm. The yeast Saccharomyces cerevisiae in glucose-limited chemostat culture indeed the affinity of the enzyme its transport on the specific growth rate for its growth-limiting substrate [31].The recombinant proteins are produced more in the robust process which is reliable, fast for various monitoring techniques of the specific growth rate in the microbial fed-batch mode for real-time estimation and other measurable variables to grow the microorganisms essential in product quality [32]. The fermentation of glucose and acetate developed observer, estimator and controller in E.coli fed-batch fermentation desired recombinant protein for a specific growth rate it often related simulations by characterizing microorganisms [33]. Online regulation is usually limited to maintaining a small number of environmental conditions such as broth temperature, pH and dissolved oxygen level.

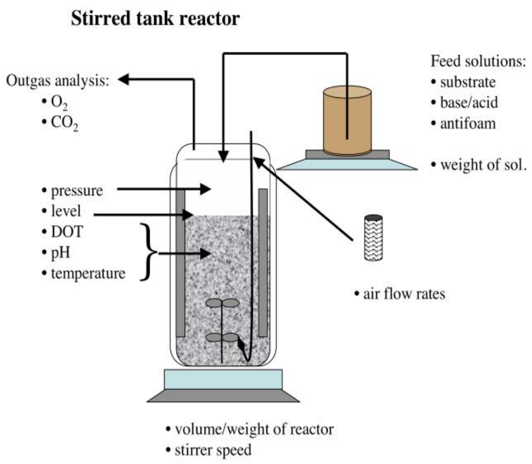

Fig.5. Instrumentation and monitoring of bioreactor [34]

Fermentation processes can also have a classical problem associated with interactions between multiple variable systems, which help complicate regulator regulation. The controller is usually tuned by loop loops, ignoring the effects of any process interactions. A trajectory of the benchmark that optimizes fermentation is difficult to specify and a more in-depth approach to specifications should be developed as shown in Figure 5 [34].

III. PROPOSED SYSTEM

3.1.Development Of Adaptive Control Systems

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The modelling of the modelled data management system structure is shown in Figure 6 an experimental research idea and experimental design of the subject was created. Based on polynomial results of gain coefficient(k), a time constant(T) and time delay (Tau) were evaluated, next moving to experimental results using the least square method. For example, the polynomial model of the process parameter was created, and the ACS model was created using the MATLAB/SIMULINK software tool. By modifying the control law adaptive system works slowly the time changes of any parameters of a specific system. ACS motivated to improve the performance of the fixed gain control system. The adaptive control can have less dependent to the accuracy of the mathematical models of the system, but fixed gain controller mainly relies on it, since there will be no variation in the system dynamics [35](appendix Number 14).

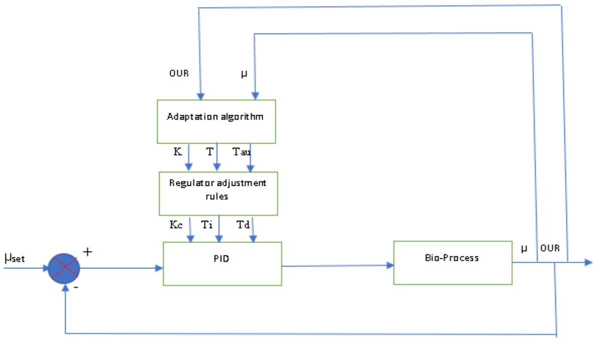

Fig.6. Block scheme of ACS [35]

The dynamic parameters of the system consist of the oxygen uptake rate(OUR) and the growing of specific growth rate(μ) for glycerol. In this parameter, the gain coefficient(k), time constant(T) and time delay(τ) is determined. The Cohen and Coon method (Smith method) is provided for tuning of the controller parameters. In both cases, the PID regulator's parameter remains the same as the algorithm for the regulatory variation. The differential parameter is integrated into the DEE block at the control object.

Development of controller gain scheduling algorithm

a) Design of ACS:

The model of the control system, which compensates for the effect of the two major parts to develop the adaptive system, shown in Figure 32. The model system consists of(appendix Number 11, Number 12, Number 14, Number 15 and Number 16):

- Controller adaptation subsystem
- PID controller subsystem
- DEE block (Differential Equation Editor)
- Process dynamic parameter subsystem
- Measurement noise modelling subsystem

Table 1. process model input

Variable	Description	Inputs
U	Feeding rate	U (1)

Table 2. process model outputs

Variable	Description	Output
X	Biomass concentration	X (1)
S	Substrate concentration	X (2)
μ(SGR)	Specific growth rate	X (3)
V	Volume broth	X (4)
OUR	Oxygen uptake rate	OUR

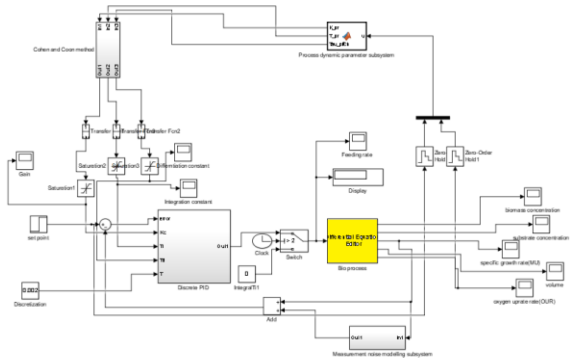

Fig.7. Block scheme of adaptative control system realized in MATLAB /SIMULINK environment

b) On-line estimation of control process dynamic parameters

The set algorithm parameter consists of the second order polynomial rules that calculate the gain coefficient(K), time constant(T) and time delay(τ) respectively. After the model is built in MATLAB/SIMULINK tool, the second order of the polynomial rules is entered the subsystem block containing the one variable, oxygen uptake rate at specific values of the specific growth rate [38]. The gain coefficient is calculated by function.

$$K=a_0+a_1(OUR)+a_2(OUR)^2$$

The time constant is calculated by function:

$$T=a_0+a_1(OUR)+a_2(OUR)^2$$

The time delay is calculated by function:

$$\tau=a_0+a_1(OUR)+a_2(OUR)^2$$

Note: I have analyzed the data and found the reason for the 2 variable model identification problem. The problem is that the ranges of the OUR variation at various levels of mu are very different and the data obtained is not suitable for identification of the 2 variable relationships, covering full observed ranges of the mu and the OUR variations. So, for the μ controller adaptation, the algorithm based on the expert "IF-THEN" rules and the single variable OUR relationships can be used.

c) PID controller gain scheduling algorithm

The tuning method was selected to tune discrete PID control is calculated by using Cohen and Coon tuning rules [39]. They consist of a regulator gain factor, calculated according to the formula in the book, the integration time constant, calculated according to the formula in the book and the differentiation time constant, calculated according to the formula in the book. The formulas assume that the process is characterized by the first series of suffixes. the duration of the charge and the range of the constant ratio of time are in the rules of adjustment.

$$0.1<\tau_{pr}/T_{pr}<1.0$$

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A model MATLAB / SIMULINK developed for the tuning parameter compensation, calculated using subsystems block. Tuning parameters the regulator gain coefficient is calculated according to the formula [39]:

$$K_r(t_k) = \frac{T_{pr}(t_k)}{K_{pr}(t_k)\tau_{pr}(t_k)}\left(1.33 + \frac{\tau_{pr}(t_k)}{4T_{pr}(t_k)}\right) \qquad (3.11)$$

Integration time constant is calculated according to the formula [39]

$$T_i(t_k) = \frac{32+6\frac{\tau_{pr}(t_k)}{T_{pr}(t_k)}}{13+8\frac{\tau_{pr}(t_k)}{T_{pr}(t_k)}}\tau_{pr}(t_k) \qquad (3.12)$$

The differentiation time constant is calculated according to the formula [39]

$$T_d(t_k) = \frac{4}{11+2\frac{\tau_{pr}(t_k)}{T_{pr}(t_k)}}\tau_{pr}(t_k) \qquad (3.13)$$

d) The control algorithm of discrete PID controller

The control system PID controller model consists of the input parameters that are entered in the formula (3.15). The obtained by rotating the engine of the modelled air water cooler according to the given data parameters available(appendix Number 15).

- Present error signal - e_n
- Previous error signal - e_{n-1}
- Last two previous error signal - e_{n-2}
- Proportional gain - K_r
- Integration time constant - T_i
- Differentiation time constant - T_d
- Discretization step – T

Frequently used algorithms used by the regulator are reflected in the change of the controlling effect [39]:

$$U_n = U_{n-1} + \Delta U_n \qquad (3.14)$$

All data is entered in a formula prepared by the PID editor, which calculates the engine brush N. The discrete change in the control effect of the PID controller is calculated according to the formula [39]:

$$\Delta U_n = k_r\left[\left(1+\frac{T_d}{T}+\frac{T}{T_i}\right)e_n - \left(1+\frac{2T_d}{T}\right)e_{n-1} + \frac{T_d}{T}e_{n-2}\right.$$

IV. RESULTS

Experiment 1: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.0501 h^{-1} to μ_{set} = 0.3 h^{-1} and simulation time 6 (h) as shown in Figure 33. The overshoot and settling time of the adaptive system is decreased 42 %, 34% compared to non-adaptive system respectively.

Table 3. PID controller tuning parameters

Model parameters (Initial 0.0501; Final 0.3)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	6.854	10
Integration time constant (Ti)	0.02669	0.0347
Differentiation time constant (Td)	0.004103	0.00524

Experiment 2: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.5 h^{-1} to μ_{set} = 0.6 h^{-1} and simulation time 8 (h) as shown in Figure 34. The overshoot and settling time of an adaptive system is increased 73% and decreased 25% compared to non-adaptive system.

Table 4. PID controller model parameters

Model parameters (Initial 0.5; Final 0.6)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	34.75	10
Integration time constant (Ti)	0.0219	0.0313
Differentiation time constant (Td)	0.0034	0.0048

Experiment 3: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.2 h^{-1} to μ_{set} = 0.6 h^{-1} and simulation time 8 (h) as shown in Figure 35. The overshoot and settling time of the adaptive system is decreased 11 %, decreased 50% compared to non-adaptive system respectively.

Table 5. PID controller model parameters

Model parameters (Initial 0.2; Final 0.6)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	17.05	30.5
Integration time constant (Ti)	0.02946	0.0288
Differentiation time constant (Td)	0.0045	0.0044

Experiment 4:The set-point of specific growth rate(μ) was changed from μ_{set} = 0.4 h^{-1} to μ_{set} = 0.5 $h^{-1}$and simulation time 6 (h) as shown in the Figure 36. The overshoot and settling time of the adaptive system is decreased 19%, decreased 67% compared to non-adaptive system respectively.

Table 6. PID controller model parameters

Model parameters (Initial 0.4; Final 0.5)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	21.75	20
Integration time constant (Ti)	0.022	0.027
Differentiation time constant (Td)	0.0035	0.0041

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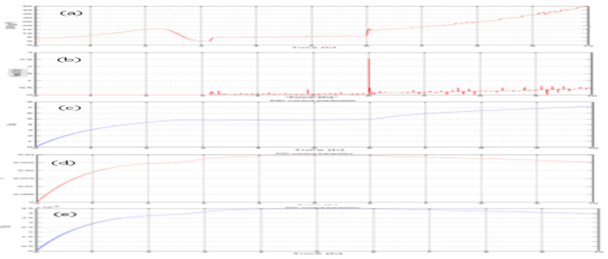

Fig.8. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.0501 h^{-1} to μ_{set}=0.3 h^{-1}) by automatic control system and simulation time is 6 (h)

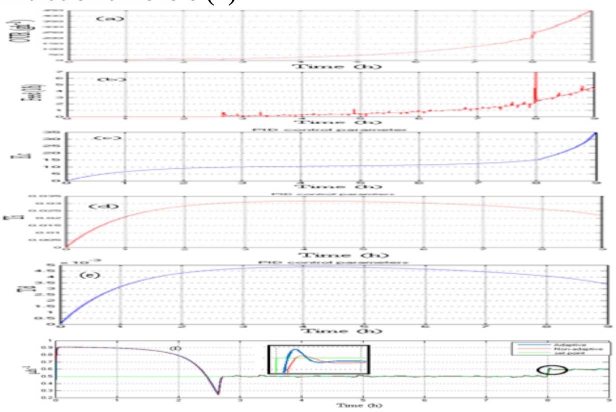

Fig.9. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.5 h^{-1} to μ_{set}=0.6 h^{-1}) by automatic control system and simulation time is 8 (h)

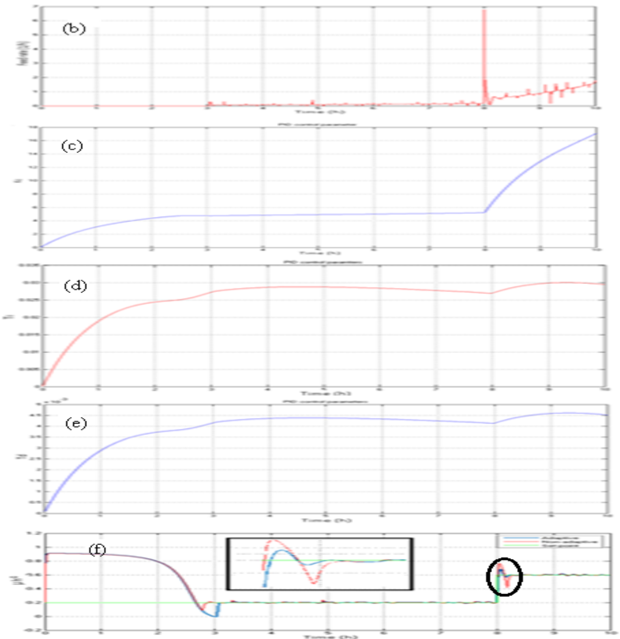

Fig.10. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.2 h^{-1} to μ_{set}=0.6 h^{-1}) by automatic control system and simulation time is 8 (h)

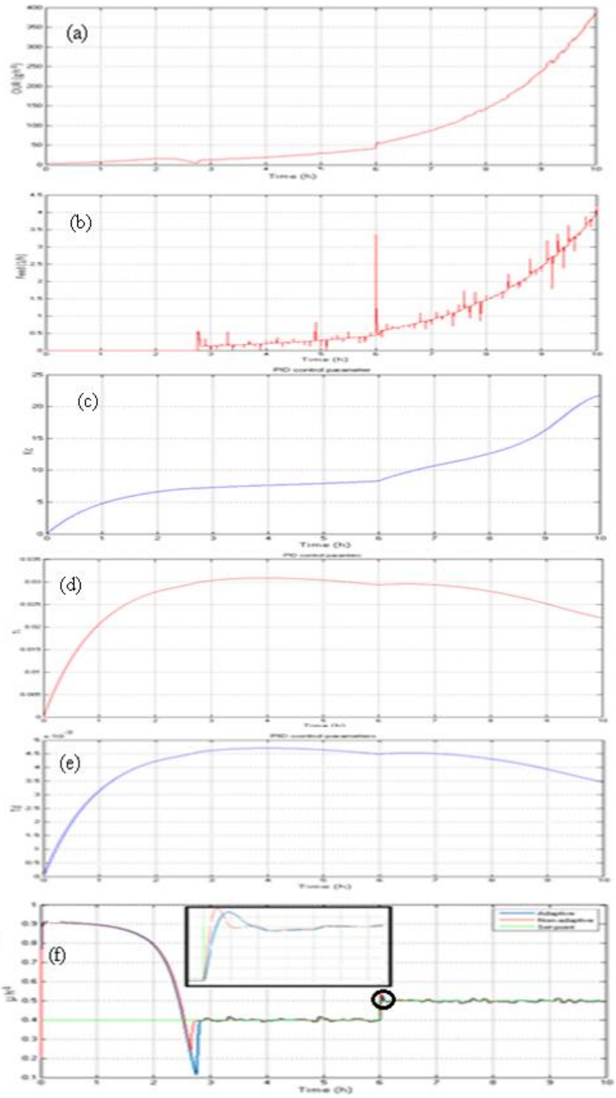

Fig.11. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.4 h^{-1} to μ_{set}=0.5 h^{-1}) by automatic control system and simulation time is 6(h)

Experiment 5: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.0501 h^{-1} to μ_{set} = 0.1 h^{-1} and simulation time 6 (h) as shown in Figure 37. The overshoot and settling time of the adaptive system is decreased 37 %, decreased 28.75% compared to non-adaptive system respectively.

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Table7. PID controller model parameters

Model parameters (Initial 0.0501; Final 0.1)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	5.545	8
Integration time constant (Ti)	0.023	0.035
Differentiation time constant (Td)	0.0035	0.0052

Experiment 6: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.2 h^{-1} to μ_{set} = 0.5 h^{-1} and simulation time 6 (h) as shown in Figure 38. The overshoot and settling time of the adaptive system is decreased 17%, decreased 22.22% compared to non-adaptive system respectively.

Table 8. PID controller model parameters

Model parameters (Initial 0.2; Final 0.5)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	14.49	20
Integration time constant (Ti)	0.02643	0.0288
Differentiation time constant (Td)	0.004115	0.00438

Experiment 7: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.2 h^{-1} to μ_{set} = 0.3 h^{-1} and simulation time 6 (h) as shown in Figure 39. The overshoot and settling time of the adaptive system is decreased 75%, decreased 57.14% compared to non-adaptive system respectively.

Table 9. PID controller model parameters

Model parameters (Initial 0.2; Final 0.3)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	7.613	15
Integration time constant (Ti)	0.0244	0.0281
Differentiation time constant (Td)	0.0038	0.0043

Experiment 8: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.3 h^{-1} to μ_{set} = 0.6 h^{-1} and simulation time 8 (h) as shown in Figure 40. The overshoot and settling time of the adaptive system is decreased 31 %, decreased 50% compared to non-adaptive system respectively.

Table 10. PID controller model parameters

Model parameters (Initial 0.3; Final 0.6)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	20.93	25
Integration time constant (Ti)	0.0264	0.0281
Differentiation time constant (Td)	0.0041	0.0043

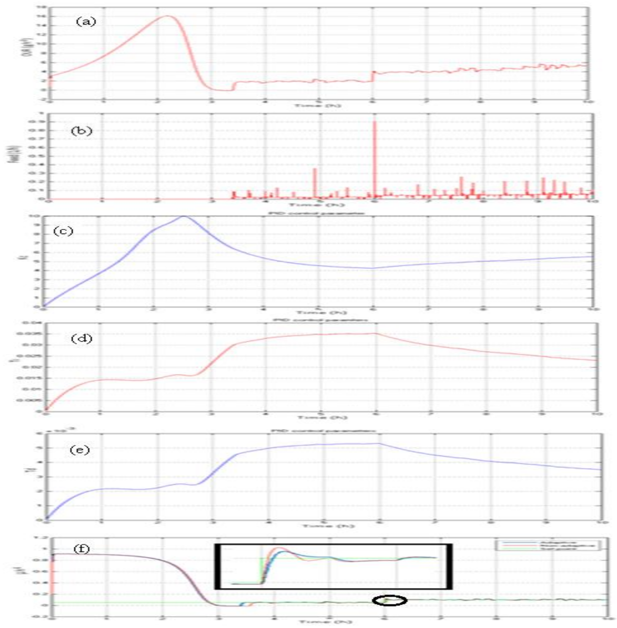

Fig.12. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.0501 h^{-1} to μ_{set}=0.1 h^{-1}) by automatic control system and simulation time is 6(h)

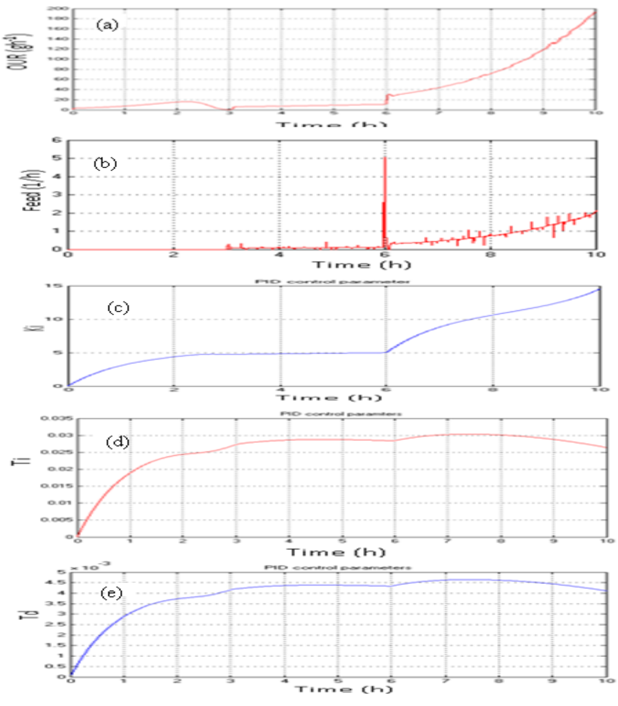

Fig.13. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant

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(Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.2 h^{-1} to μ_{set}=0.5 h^{-1}) by automatic control system and simulation time is 6(h)

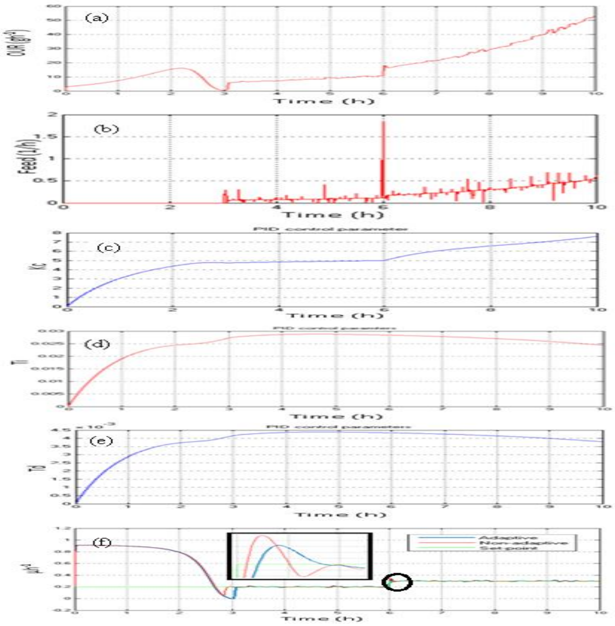

Fig.14. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.2 h^{-1} to μ_{set}=0.3 h^{-1}) by automatic control system and simulation time is 6(h)

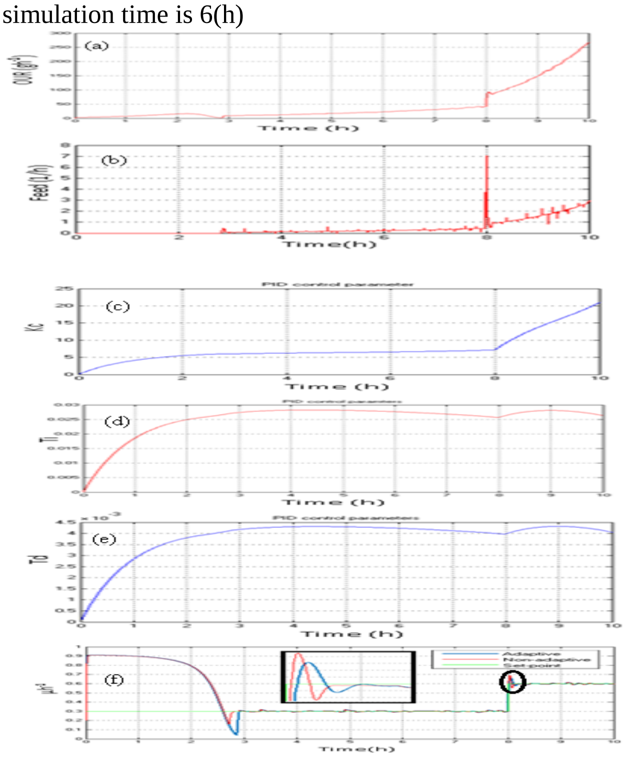

Fig.15. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.3 h^{-1} to μ_{set}=0.6 h^{-1}) by automatic control system and simulation time is 8(h)

Experiment 9: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.3 h^{-1} to μ_{set} = 0.1 h^{-1} and simulation time 7 (h) as shown in Figure 41. The overshoot and settling time of the adaptive system is decreased 20 %, decreased 60% compared to non-adaptive system respectively.

Table 11. PID controller model parameters

Model parameters (Initial 0.3; Final 0.1)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	12.5	10
Integration time constant (Ti)	0.0167	0.0282
Differentiation time constant (Td)	0.0025	0.0043

Experiment 10: The set-point of specific growth rate(μ) was changed from μ_{set} = 0.4 h^{-1} to μ_{set} = 0.1 h^{-1} and simulation time 7 (h) as shown in Figure 42. The overshoot and settling time of the adaptive system is decreased 45%, decreased 18.18 compared to non-adaptive system respectively.

Table 12. PID controller model parameters

Model parameters (Initial 0.4; Final 0.1)	Adaptive system	Non-adaptive system
Gain proportional (Kc)	6	15
Integration time constant (Ti)	0.0465	0.0304
Differentiation time constant (Td)	0.0070	0.0064

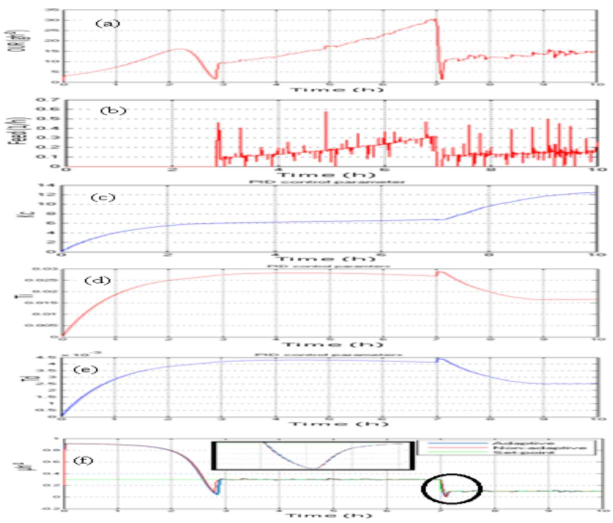

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Fig.16. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.3 h^{-1} to μ_{set}=0.1 h^{-1}) by automatic control system and simulation time is 7(h)

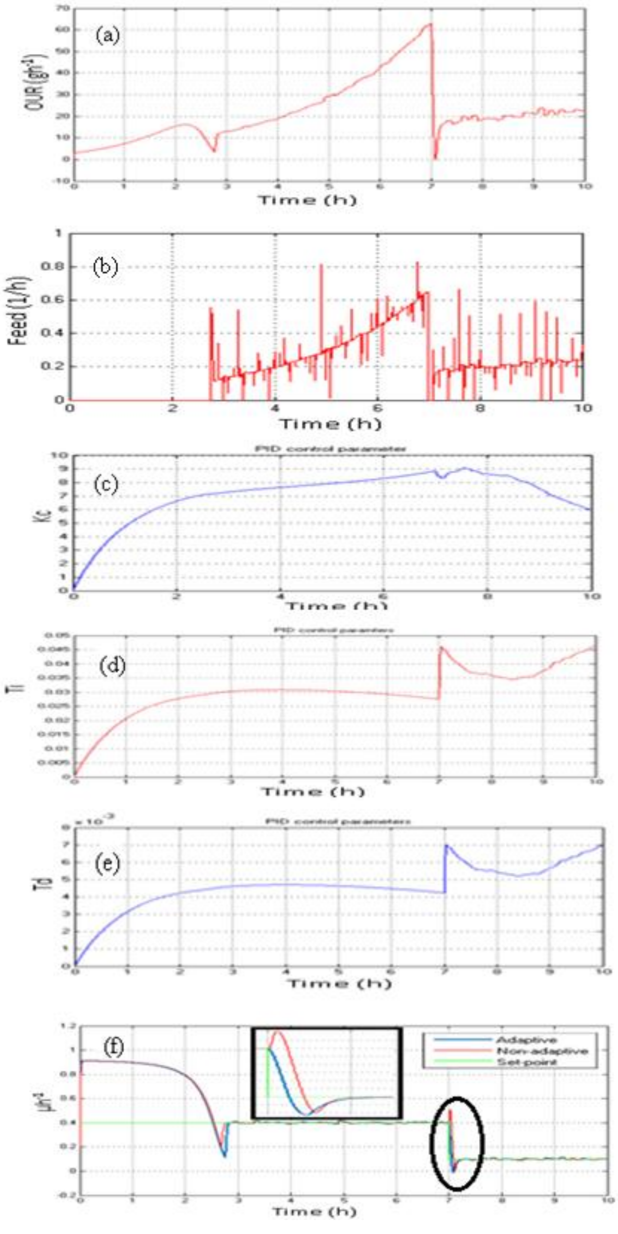

Fig.17. The simulation results show the dynamics of the process a)oxygen uptake rate (OUR), b) feeding rate (U_F), c) gain proportional (Kc), d) integration time constant (Ti), e) differentiation time constant (Td), f) specific growth rate (μ) with setpoint control change from (μ_{set} = 0.4 h^{-1} to μ_{set}=0.1 h^{-1}) by automatic control system and simulation time is 7(h)

IV. CONCLUSION

Analysis of Fed-batch cultivation process an object of monitoring and control and analysis of mathematical models applied for modelling of fed-batch cultivation processes are presented.MATLAB/SIMULINK model for simulation of E. coli fed-batch cultivation is developed and applied for investigation of the controlled process dynamics at various cultivation conditions.

3. PID controller gain scheduling algorithm is developed for controller adaptation to time-varying cultivation conditions. In the adaptation algorithm, the biomass specific growth rate and the oxygen uptake rate are used as gain scheduling variables. MATLAB/SIMULINK models are developed for modelling of ordinary and the adaptive control systems. Simulation results of the investigated control systems performance under various cultivation conditions show that the adaptive control system outperforms the ordinary system. An overshoot of specific growth rate step response decreases in (11%-75%) and settling time decrease in (18.18%-67.63%).The presented specific growth rate controller adaptation approach can be applied for the development of biomass growth control systems of various fed-batch cultivation processes.

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