Simulation of Continuously Operated Fermenter

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I. Introduction

Fermentation process control has become a vibrant area of research in recent times[5]. People are looking for new control methodologies to control fermentation processes on account of productivity conditions imposed on the operation[6]. Fermentation processes show nonlinear dynamical behaviours such as input multiplicity (i.e. identical outputs for multiple inputs) and asymmetric dynamic response in desired operating region[1, 3]. The singular optimum operating point of a fermentation system is obtained where the gain is reduced to zero and the sign of the gain gets changed across the optimum[1]. The nonlinear behaviour of fermentation process makes it difficult to operate the fermenter at the operating point [1, 3]. Fermentation processes can be operated in three modes, they are as follows [2]:

- **Continuous Mode:** Here substrate is continuously added into the system and products are removed simultaneously from the system.
- **Batch Mode:**In this case, all of the substrate is added at the beginning of the batch but no product is withdrawn until the end of the batch.
- **Fed-batch mode:** In fed-batch mode, the substrate is added at, or over, particular intervals of time during the course of the batch, and, as in batch reactors, the product is withdrawn only at the end of the batch.

Among the different modes of operation of a fermenter, continuous mode of operation offer advantages such as higher productivity and ease of operation compared to the other two operations, as batch operations have certain disadvantages associated with them such as equipment failures, infection by other microorganisms, and spontaneous mutations in the strain [2].Moreover, when there is a requirement of biomass or product optimization, continuous operation has better efficacy [5]. In this study we are trying to develop a simulation model of a continuously operated fermenter in order to generate input-output data for the application in system identification technique.

II. Modeling of Continuously Operated Fermenter

A model of a physical process is a mathematical representation of a physical system which attempts to capture the relationship between the inputs and outputs [2]. Models of a system may be derived using first principle method or empirical method using input-output data [2]. Various modeling frameworks for fermenter processes are as follows:

- **Unstructured Models:** : Unstructured models are the simplest of all modeling philosophies used to describe the biological model. They consider the cell mass as a single chemical species and do not consider any intracellular reactions occuring within the cell. Unstructured models typically describe the growth phenomena based on a single limiting substrate and consider only substrate uptake, biomass growth, and product formation in the modeling framework. Thus the biological component of the system depends directly on the macroscopic reactor variables. These models give an adequate representation of the biological growth phenomena in relatively simple cases, when the cell response time to environmental changes is either negligibly small or much longer than the batch time[4].

- **Structured Models:** In contrast to the unstructured models, structured models include a greater level of detail about the biochemical phenomena occuring within the cell. The biological detail is no longer lumped into a single biomass variable. In structured models, the biomass is structured into several components or functional groups that are interconnected with each other and with the macroscopic reactor environment by material balances [4].
- **Segregated Models:** Segregated models take into account the fact that a culture can have cells in different stages of growth, and they account for these stages using population balances. These models can be broadly grouped into two main types, age structured or mass structured. If the intra- cellular chemical structure is described in terms of a mass conservation then the population balance is mass-structured, whereas if age is used to dierentiate cells in a population, then the model is referred to as an age structured model [2].
- **Material Balance Models:** This model treats the biomass as a compound with a fixed elemental composition consisting of Carbon, Hydrogen, Oxygen, and Nitrogen. Based on a stoichiometric balance of these elements and the uptake and evolution of Oxygen and Carbon Dioxide gases, the state of the fermenter is obtained. This state information is somehow related to the physiological state of the growing cells and this relationship is usually determined empirically [2]. Material balance models, (also known as stoichiometric models) were very popular in the 1970's and 1980's when computational resources were expensive and sensor technology was not well developed. However, these models do not account for the biomass as an actual living species and are thus only a chemical approximation to the biology [2].
- **Cybernetic Models:** The main principle of the cybernetic modeling approach can be summarized as [2] : *"The metabolic processes within cells are regulated in an optimal manner by the cell (developed through evolution), and an accurate description of the overall system can be formed if the net outcome of the process is captured, without knowing the full reaction mechanism ".* Therefore, in cybernetic modeling, no mechanistic framework for the utilization of substrates is assumed, but it is believed that whatever the underlying framework may be, it leads to optimal regulation of the cells[2].

In this study we are trying to model a continuously operated fermenter using unstructured model structure and then we try to simulate it in MATLAB.

I. Unstructured Model of Continuous Fermenter

As per [1, 5], the unstructured model of a continuously operated fermenter can be described using the following set of equations,

$$\frac{dX}{dt} = -DX + \mu X \tag{1}$$

$$\frac{dS}{dt} = D(S_f - S) - \frac{1}{Y_{X/S}}\mu X \tag{2}$$

$$\frac{dP}{dt} = -DP + (\alpha\mu + \beta)X \tag{3}$$

Where,
X = effluent cell mass or bio-mass concentration (i.e. yeast concentration)
S = substrate concentration (i.e. glucose concentration)
P = product concentration (i.e. ethanol concentration)
D = dilution rate
S_f = feed substrate concentration
μ = specific growth rate
$Y_{X/S}$ = cell-mass yield
α, β are kinetic parameters

It has been assumed that the fermenter has a constant volume, its contents are well-mixed and the feed is sterile [5]. The specific growth rate (μ) can be modelled as [1],

$$\mu = \frac{\mu_m(1 - \frac{P}{P_m})S}{K_m + S + S^2/K_i} \tag{4}$$

Where,
μ_m = maximum specific growth rate
K_m = product saturation constant
K_i = substrate inhibition constant

II. Control Relevant Modeling

From control perspective,we assume that product concentration (S) and the cell-mass concentration (X) are measured process outputs, while dilution rate (D) and the feed substrate concentration S_f are manipulated process inputs. The nominal values of fermenter parameters and operating conditions are listed in Table 1.

Variable	Nominal Value
$Y_{X/S}$	0.4 g/g
α	2.2 g/g
β	0.2 h^{-1}
μ_m	0.48 h^{-1}
P_m	50 g/l
K_m	1.2 g/l
K_i	22 g/l
D	0.15 h^{-1}
S_f	20 g/l
X	7.038 g/l
S	7 2.404 g/l
P	24.87

Table 1: Nominal Paraemters and Operating Conditions of Fermenter

Control objective of most of the continuous fermentation processes is to the maximize the productivity (Q) [5].

The productivity (Q) of a continuous fermenter can be defined as [1, 5],

$$Q \cong DP \tag{5}$$

Now, let us consider a state vector with X, S, P being the states of the fermentation process as, $x \cong [\text{X S P}]^T$

Therefore, from equations 1, 2 and 3,we can write [5],

$$\dot{x} = F(x, D, S_f) \tag{6}$$

In order to get the optimum operating conditions, the following problem need to be optimized, maximize,

$$Q = DP \tag{7}$$

with D, S_f,
subject to,

$$F(x, D, S_f) = 0 \tag{8}$$

The optimum steady-state operating conditions obtained for the fermenter, using the paramters listed in Table 1 are [1, 5],

$$S^* = \sqrt{K_m K_i} = 5.138 g/l \tag{9}$$

$$P^* = 25.0 g.l \tag{10}$$

The optimum can be obtained by setting the values, $D = D^* = 0.1636 h^{-1}$ and $S_f = S_f^* = 23.39 g/l$ [1].

One problem associated with the control of a continuous fermenter is the change in process optimum over time due to a variety of disturbances. The growth rate microorganism is affected by some biological factors such as change in metabolic path, enzymatic deactivation, culture aging, and spontaneous mutations [1].In terms of model parameters, this implies that the cell-mass yield coefficient ($Y_{X/S}$) and the maximum specific growth rate (μ_m) tend to be especially sensitive to changes in the operating conditions. From the control perspective, these changes can be regarded as unmeasured disturbances because these variations may exhibit significant time-varying behavior [1].

The schematic of a continuously operated fermenter has been shown in figure 1.

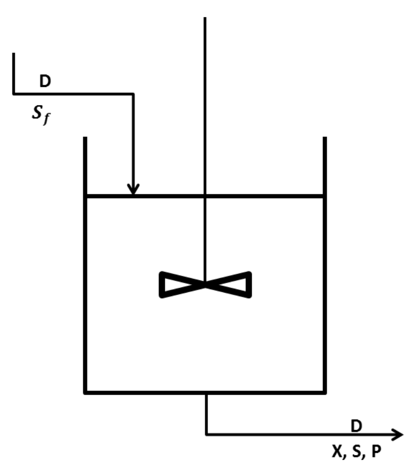

Figure 1: Schematic of A Continuously Operated Fermenter [5]

III. Simulation Study

To develop a suitable methodology for system identification and control of a continuously operated fermenter, simulation is needed in order to generate the necessary input-output data. Here the fermenter model, as described by equations 1, 2 and 3 along with the specific growth rate (μ) model as described by equation 4, is constructed in block diagram using SIMULINK environment of MATLAB. The nominal parameters and operating conditions used in simulation are same as in Table 1. The ordinary differential equation solver 45 (ode45) of MATLAB is used to solve the model equation in order to generate the necessary input-output data.

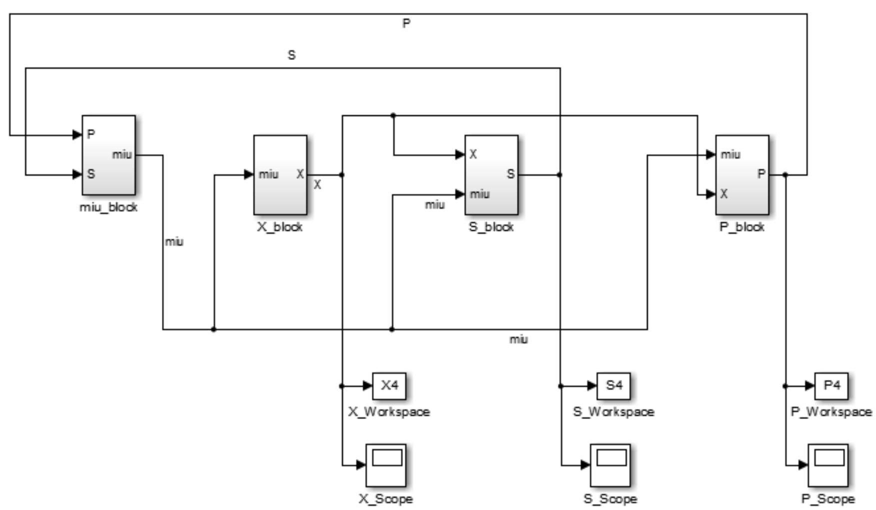

Figure 2: SIMULINK Block Diagram for The Simulation of Continuous Fermnter

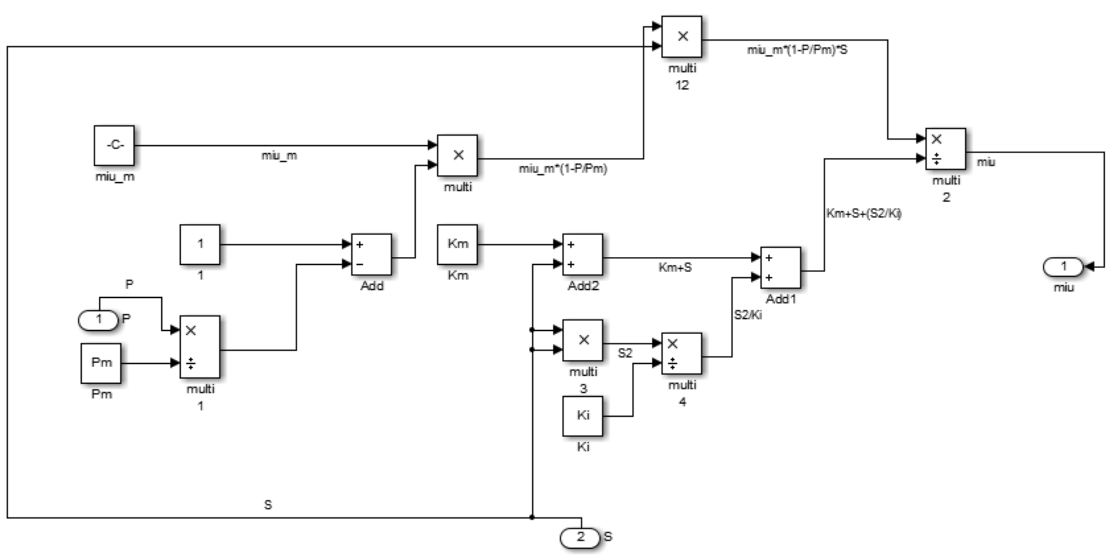

Figure 3: SIMULINK Sub-Block 1 (miu_block) for The Simulation of Continuous Fermnter

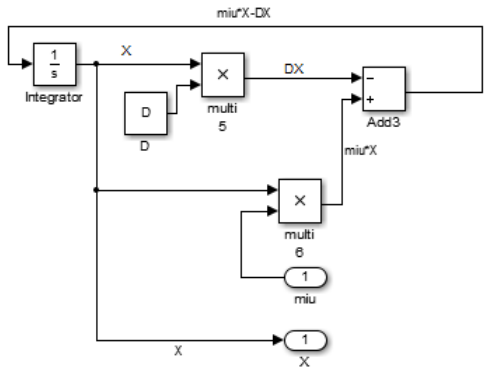

Figure 4: SIMULINK Sub-Block 2 (X_block) for The Simulation of Continuous Fermnter

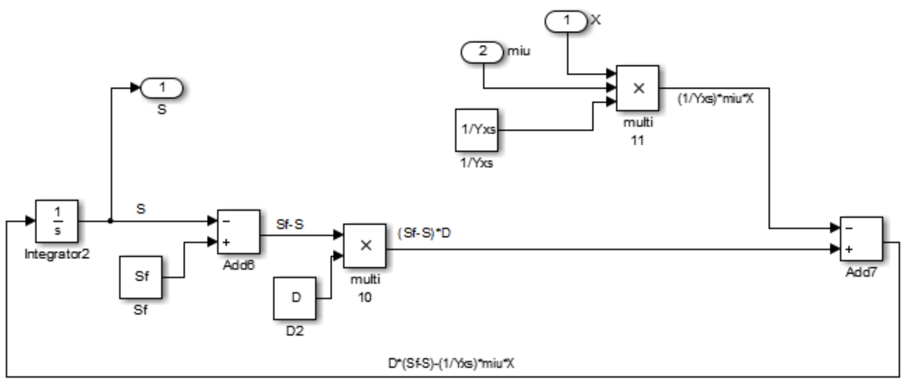

Figure 5: SIMULINK Sub-Block 3 (S_block) for The Simulation of Continuous Fermnter

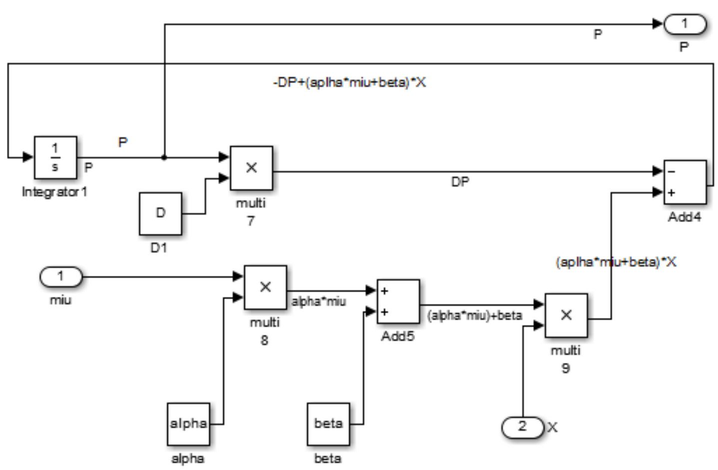

Figure 6: SIMULINK Sub-Block 4 (P_block) for The Simulation of Continuous Fermnter

I. Simulation Results and Open-Loop Behaviour

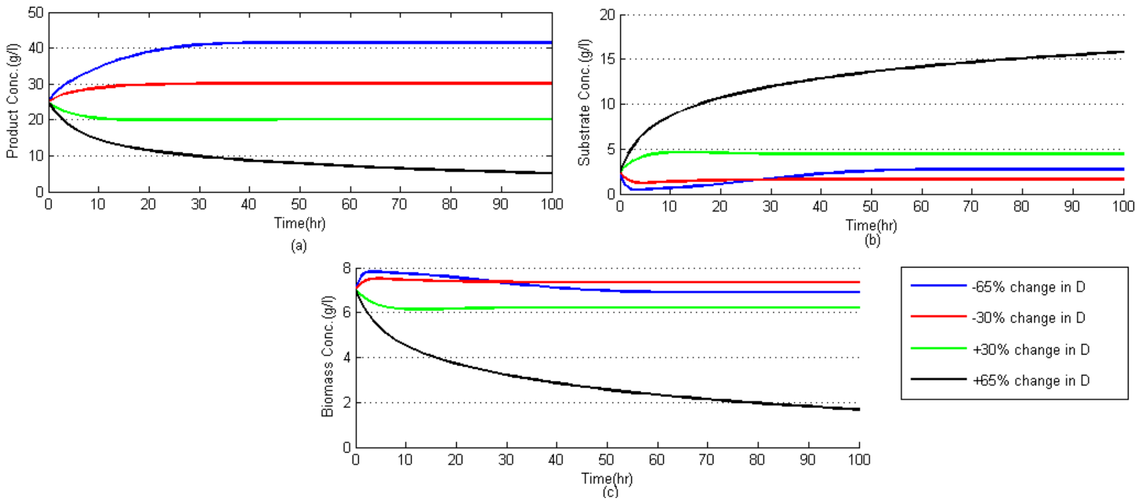

Figure 7: Response of the Fermenter for Various % Step Changes of D with S_f = 20 g/l

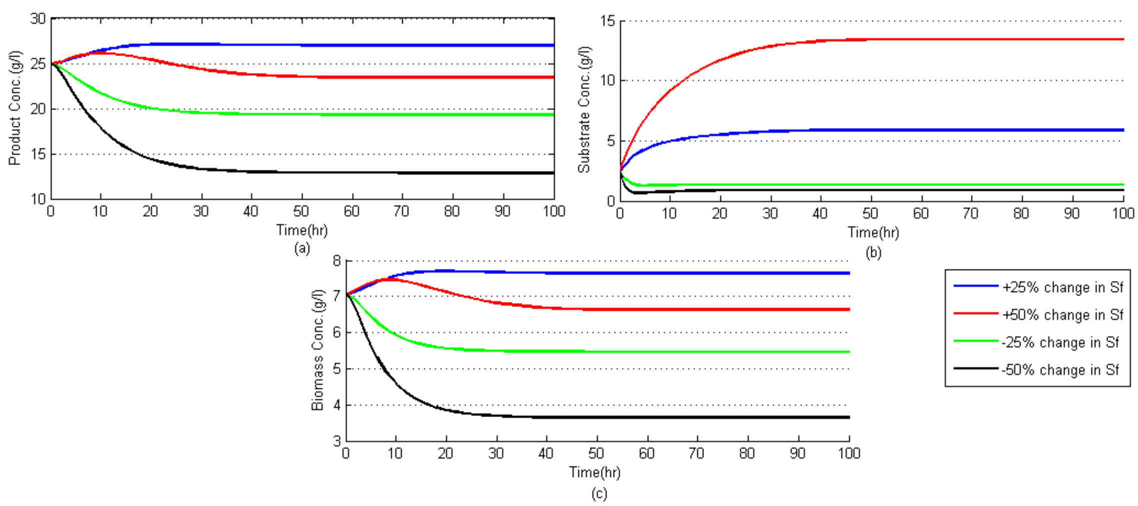

Figure 8: Response of the Fermenter for Various % Step Changes of S_f with D = 0.15 h^{-1}

The following two strategies are taken for simulation study of the SIMULINK model,

- D is changed in steps from the nominal value keeping the value of S_f as the same as the nominal value. Then the plots for product concentration (P), bio-mass concentration (X) and the substrate concentration (S) are obtained as shown in Figure 7.
- S_f is changed in steps from the nominal value keeping the value of D as the same as the nominal value. Then the plots for product concentration (P), bio-mass concentration (X) and the substrate concentration (S) are obtained as shown in Figure 8

I.1 Open-Loop Behaviour

We can see, from Figure 7 that the response of the process to large dilution rate (D) changes from nominal value are almost symmetrical. that means that the input-output behaviour is nearly linear.

However, for changes in feed substrate concentration (S_f), as in Figure 8, the behaviour of the process is severly non-linear. Even the step responses for similar +/- changes in S_f from nominal value are not symmetrical. Also there are some inverse response of the process for +50% increase in S_f from nominal value.

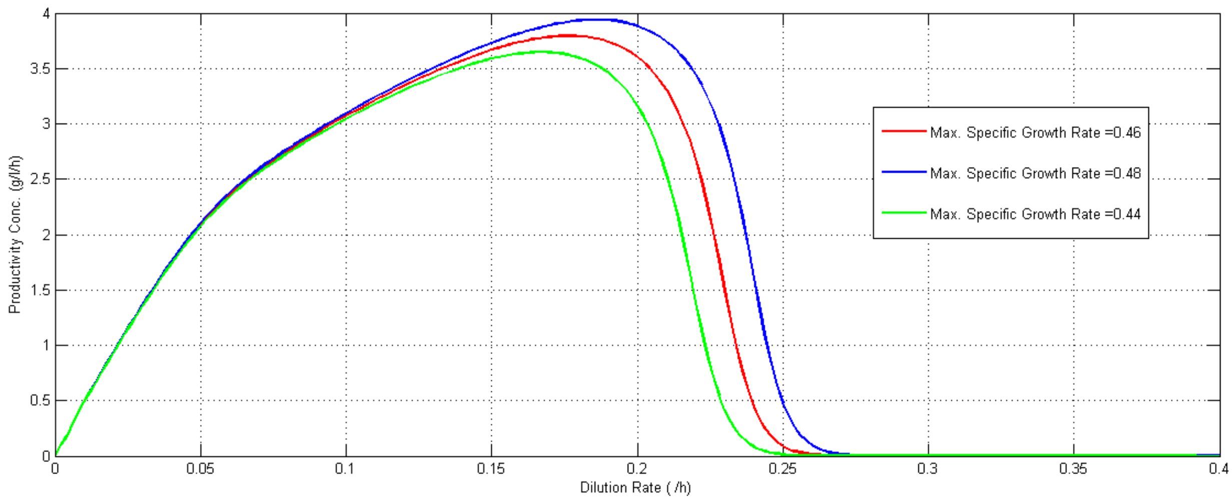

Figure 9: Effect of D on Productivity

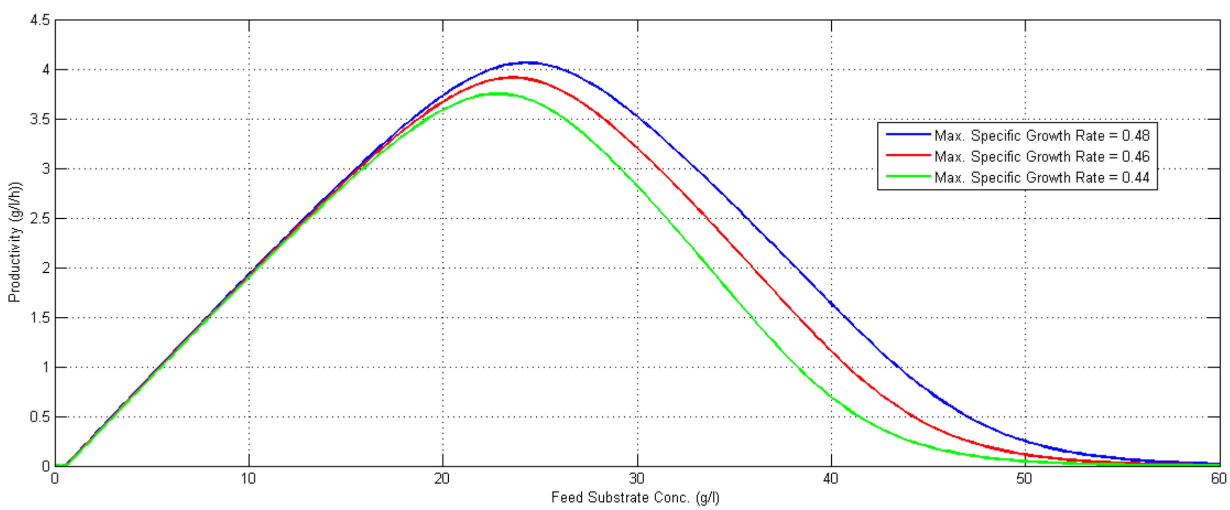

Figure 10: Effect of S_f on Productivity

Figure 9 and 10, shows the effect of dilution rate (D) and feed substrate concentration (S_f) on the productivity (Q) of the process for 3 different values of maximum growth rate (μ_m). It has been clear that even small change in μ_m can have significant effects on the optimum productivity. Also the nominal operating conditions for the fermenter are found to be satisfactory.

IV. Conclusions

We have succesfully done a simulation study of a open-loop continuous fermenter in SIMULINK environment of MATLAB. The result found has been in agreement with both [1] & [5].

V. Future Scopes

- To implement few suitable system identification techniques on the input-output data generated from the simulation in order to develop models for control of continuous fermenter. Comparison between the various identified models and selection of the best fit model based on various information criteria.
- To implement suitable linear and/or nonlinear control startegy for the continuous fermenter based on the selected identified model.

References

[1] Saha, P., Krishnan, S.H., Rao, V.S.R. and PATWARDHAN, S.C., 2004. Modeling and predictive control of MIMO nonlinear systems using Wiener-Laguerre models. *Chemical Engineering Communications, 191(8), pp. 1083-1119*.

[2] Soni A. (2002). *A multi-scale approach to fed-batch bioreactor control* (Doctoral dissertation, University of Pittsburgh).

[3] Parker, R.S. and Doyle, F.J., 2001. Optimal control of a continuous bioreactor using an empirical nonlinear model. *Industrial engineering chemistry research, 40(8), pp.1939-1951*.

[4] Bellgardt, K.H., 2000. Bioprocess models. In *Bioreaction Engineering* (pp. 44-105). Springer Berlin Heidelberg.

[5] Henson, M.A. and Seborg, D.E., 1992. Nonlinear control strategies for continuous fermenters.*Chemical Engineering Science, 47(4), pp.821-835.*.

[6] Alvarez, G.J. and Alvarez, G.J., 1988, June. Analysis and control of fermentation processes by optimal and geometric methods. In *American Control Conference, 1988 (pp. 1112-1117). IEEE.*