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System of Nonlinear Reaction Diffusion Processes at Cyclodextrin Glucanotransferase Based on Batch Cultivation

S. Kalaiselvi*, K. M. Dharmalingam

Department of Mathematics, The Madurai College, Madurai, Tamilnadu, India

Abstract A mathematical model of cyclodextrin-glucanotransferase based on batch cultivation has been discussed. This paper presents an approximate analytical method (He's Homotopy perturbation method) to solve the non-linear differential equations that describe the microbial growth, the substrate inhibition, and the microbial decay with time. Analytical expressions pertaining to biomass concentration, substrate concentration and product concentration for all values of relevant parameters are presented. All the analytical results are compared with experimental data and with numerical results.

Keywords Cyclodextrin-glucanotransferase, Enzyme production, Modeling, Non-linear reaction diffusion equations, Homotopy perturbation method

1. Introduction

Non-linear phenomena play a very important role in physics [1], chemistry [2] and biology [3]. In biology, cyclodextrin-glucanotransferase is an important enzyme of cyclodextrin synthesis and it is produced by different bacterial species. The enzyme cyclodextrin-glucanotransferase (CGTase) is produced by different bacteria. Cyclodextrin-glucanotransferase (CGTase) plays a role in the starch utilization pathway of some bacteria and catalyzes various glucan transfer reactions with starch. Cyclodextrins are cyclic, non-reducing malto oligosaccharides composed of 6-60 glucose units linked with α-1, 4-glucosidic bounds [4]. Cyclodextrin products are very clean and useful environmental protection products [5]. It has numerous applications in the pharmaceutical, cosmetics, food and textile industry, etc., cyclodextrin glyscosyl transferase is a multifunctional enzyme which catalyses the formation of cyclodextrins from starches.

All of the CGTases can catalyze up to four reactions: cyclization, coupling, disproportionation and hydrolysis. All these activities share the same catalytic mechanism which is common to all glycosyl-hydrolases. Cyclization is the process through which a linear polysaccharidic chain is cleaved and the two ends of the cleaved fragment are joined to produce a circular dextrin (cyclodextrin or CD): on the basis of the number of sugar residues this circular product is made of three main type of cyclodextrins can be distinguished, α-CD with six residues, β-CD with seven residues and γ-CD with eight residues. The coupling reaction can be easily described as the reverse process of cyclization: the enzyme cleaves a cyclodextrin to produce a linear dextrin which is subsequently joined to a linear oligosaccharide. Disproportionation is very similar to coupling, but the cleaved dextrin is not a cyclodextrin, but a linear oligosaccharide that is then joined to a second oligosaccharide. CGTase also has a weak hydrolyzing activity which consists in cleaving the longer polysaccharidic chains into shorter fragments. Glycerol is transglycosylated by cyclodextrin-glucanotransferases using starch as a donor substrate [6]. Starch is the main carbon substrate used for the CGTase production by microorganisms [7].

Cyclodextrins and their derivatives enhance the solubility of complexed substrates in aqueous media, but do not damage the microbial cells or the enzymes [8]. Sri Rezeki Muria et. al., developed a mathematical model for simultaneously studying the effect of substrate concentration and temperature on β–cyclodextrin production by cyclodextrin glycosyltransferase (CGTase) [9]. Fatma Ellouze et. al., developed a mathematical mass balance model based on the sieving effect [10]. The purpose of this communication is to propose a mathematical model based on experimental data and to derive approximate analytical expressions for the biomass concentration, substrate concentration and product concentration presented as CGTase activity.

* Corresponding author:
kalaiguruprasath@gmail.com (S. Kalaiselvi)
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2. Mathematical Formulation of the Problem

The proposed mathematical model consists of a set of ordinary differential equations taking into account the microbial growth, the substrate inhibition, and the microbial decay with time.

$$\frac{dX}{dt} = (\mu - \gamma) X \tag{1}$$

$$\frac{dS}{dt} = -\mu \frac{X}{Y_{X/S}} \tag{2}$$

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

Different assumptions for the kinetic models well known from the literature are applied in our case. First, it is assumed that microbial growth is based on monod equation, and the substrate inhibition is taken into account by the Andrews model [11].

$$\mu = \mu_{\max} \frac{S}{K_S + S + K_1 S^2} \tag{4}$$

Substituting (4) in (1-3), the following equations are obtained.

$$\frac{dX}{dt} + \gamma X = \frac{\mu_{\max} SX}{K_S + S + K_1 S^2} \tag{5}$$

$$\frac{dS}{dt} = -\frac{\mu_{\max} SX}{\left(Y_{X/S}\right) K_S + S + K_1 S^2} \tag{6}$$

$$\frac{dP}{dt} - \beta X = \frac{\alpha\mu_{\max} SX}{K_S + S + K_1 S^2} \tag{7}$$

X is the biomass concentration, S is the substrate concentration, P is the product concentration, $\mu_{\max}$ is the maximum specific growth rate, K_s is the saturation constant in monod equation, α is the rate constant for CGTase production in the growth phase, β is the rate constant for CGTase production in the stationary phase of microbial growth, γ is the coefficient of microbial decay for the microbial growth, $Y_{X/S} = \Delta X/\Delta S$ is the yield coefficient of biomass growth, K_1 is the inhibition constant according to the Andrews model.

The above equations are solved for the following initial conditions

$$\text{At } t = 0,\ X = X_0,\ S = S_0,\ P = 0 \tag{8}$$

3. Solution of the Problem Using Homotopy Perturbation Method

Recently, many authors have applied the Homotopy perturbation method (HPM) to solve the non-linear problem in physics and engineering sciences [16-19]. This method is also used to solve some of the non-linear problem in physical sciences [20-22]. This method is a combination of Homotopy in topology and classic perturbation techniques. Ji-Huan He used to solve the Lighthill equation [20], the Duffing equation [21] and the Blasius equation [22-23]. The HPM is unique in its applicability, accuracy and efficiency. The HPM uses the imbedding parameter p as a small parameter, and only a few iterations are needed to search for an asymptotic solution. Using this method [24-28], we can obtain solution of the eqns. (5) - (7) are as follows:

$$X(t) = \frac{X_0 S_0 \mu_{\max} t e^{-\gamma t}}{K_s} + X_0 e^{-\gamma t} \tag{9}$$

$$S(t) = S_0 + \frac{X_0 S_0 \mu_{\max} \left(e^{-\gamma t} - 1\right)}{\gamma Y_{X/S} K_s} \tag{10}$$

$$P(t) = A + Be^{-\gamma t} + Ce^{-2\gamma t} + Dte^{-\gamma t} + Et^2 e^{-\gamma t} + F\left(\frac{te^{-\gamma t}}{\gamma} - \frac{e^{-\gamma t}}{\gamma^2}\right) \tag{11}$$

Where,

$$A = \frac{X_0 S_0 \mu_{\max}}{K_s \gamma}\left[\alpha + \alpha S_0 - \alpha S_0^2 K_1 + \frac{\beta}{\gamma} + \frac{K_s \beta}{S_0 \mu_{\max}} - \frac{S_0^2 \beta K_1}{\gamma} + \frac{S_0^2 \beta K_1}{\gamma^2} - \frac{\beta \mu_{\max} X_0}{\gamma^2 Y_{X/S}} - \frac{\beta S_0}{\gamma} + \frac{\alpha S_0}{\gamma} - \frac{\alpha \mu_{\max} S_0}{\gamma Y_{X/S}}\right]$$

$$B = \frac{X_0 S_0}{\gamma K_s}\left[-\alpha\mu_{\max} - \alpha\mu_{\max} S_0 + \alpha\mu_{\max} S_0^2 K_1 - \frac{K_s \beta}{S_0} - \frac{\beta\mu_{\max}}{\gamma} + \frac{\alpha\mu_{\max}^2 X_0}{\gamma Y_{X/S}} - \frac{\beta\mu_{\max}^2 S_0}{\gamma^2}\right]$$

$$C = \frac{X_0^2 S_0 \mu_{\max}^2}{2K_s \gamma^3 Y_{X/S}} [\beta - \alpha\gamma];$$

$$D = -\frac{X_0 S_0 \beta \mu_{\max}}{\gamma K_s}\left[1 - \frac{\mu_{\max} S_0}{2\gamma}\right]; E = -\frac{X_0 S_0^2 \beta \mu_{\max}^2}{2\gamma K_s}$$

$$F = \frac{\beta \mu_{\max} X_0 S_0^3 K_1}{K_s} + \frac{\alpha \mu_{\max} X_0 S_0^2}{K_s} - \frac{\beta \mu_{\max} X_0 S_0^2}{K_s} + \frac{\beta \mu_{\max} X_0 S_0^2}{K_s \gamma Y_{X/S}}$$

When $\gamma = 0$, the following relationship can be obtained

$$X(t) = Y_{X/S}\, S(t) - Y_{X/S} S_0 + X_0$$

Table 1. The values of model parameters as estimated by the optimization procedure using the data from [12] Ks = 0.8 gl-1; YX/S = 26.3 OD660/(g/l)

S_0 (gl^{-1})	μ_{max} (h^{-1})	α ((U/ml) /(OD))	β (U/ml) /(OD)h^{-1}	γ (h^{-1})	K_1 ($g^{-1}l$)	A (U/ml) (g/l)	B (U/ml) (g/l)	C (U/ml) (g/l)	D (U/ml)h	E (U/ml) (g/l)$(h^{-1})^2$	F (U/ml) (g/l)h^{-1}
0.4	1.9	1.48	0.11	0.06	0.149	13.929	1.4887	11.3797	0.0264	0.1645	0.0967
0.8	1.9	4.41	0.13	0.06	0.1	80.6462	12.5303	0.0066	0.0864	0.2681	0.3233
1.0	1.7	2.20	0.25	0.06	0.1	70.9001	4.3107	0.8420	0.0167	0.5672	0.2747
2.0	2.0	1.11	0.07	0.06	0.168	12.4851	0.4005	0.7481	0.0046	0.6333	0.0400
10.0	2.4	0.048	0.06	0.35	0.06	78.5698	15.4766	0.3447	10.485	30.8571	4.5777

Table 2. Values of the parameters estimated in [12] K_S = 0.8 gl^{-1}; K_1=0.06 $g^{-1}l$; $Y_{X/S}$ = 26.3 OD_{650}/(g/l)

Strain; substrate concentration	Data source	μ_{max} (h^{-1})	α (U/ml) /oD	β (U/ml) /ODh^{-1}	γ (h^{-1})	A (U/ml) (g/l)	B (U/ml) (g/l)	C (U/ml) (g/l)	D (U/ml)h	E (U/ml) (g/l)$(h^{-1})^2$	F (U/ml) (g/l)h^{-1}
B.circulans ATCC 21783;soluble starch (10 gl^{-1})	Cf. [4]	2.4	0.048	0.06	0.35	3.9077	0.6044	1.9995	1.9682	0.2678	0.0056
Bacillus sp.BE101; starch (no data)	Cf. [35]	2.4	0.036	0.02	0.71	5.9288	1.2604	0.1371	0.6002	0.0288	0.0197
B.cereus (RJ-30); starch and glucose (no data)	Cf. [34]	2.0	0.044	0.06	0.29	2.9971	0.9983	2.9460	0.9255	0.2786	0.0099
B.circulans DF 9R; cassava starch (15 gl^{-1})	Cf. [25]	1.0	0.164	0.06	0.6	1.9069	1.0341	10.912	0.0672	0.0002	0.0051

4. Comparison of Analytical Work with Experimental Data

To show the efficiency of the present method, the obtained analytical results (9-11) are compared with experimental data [12]. Experimental data are given in Table.1 and Table.2 Graphical results are presented and discussed quantitatively to illustrate the solution in Figs. (1-2). An agreement between analytical and experimental results is noted.

5. Numerical Simulation

The non-linear differential equations (5-6) are also solved by numerical methods using MATLAB software. Its numerical solution is compared with HPM as shown in figures (3–4) and it gives satisfactory result for all small values parameters.

6. Results and Discussion

Equations (9-11) are the new and simple approximate analytical expressions of biomass, substrate and product concentrations respectively calculated using HPM. The product concentration represents equation (11) is compared to the experimental values given in [12].

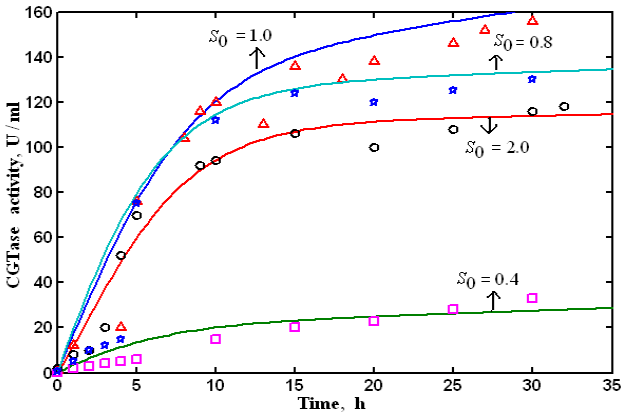

Figure 1. Plot of Product Concentration $P(t)$ (CGTase activity) for various values of S_0. Values of $P(t)$ are calculated using (11). Line represents analytical results from (11). Symbols ○, Δ, □, * indicates the experimental results for various values of S_0

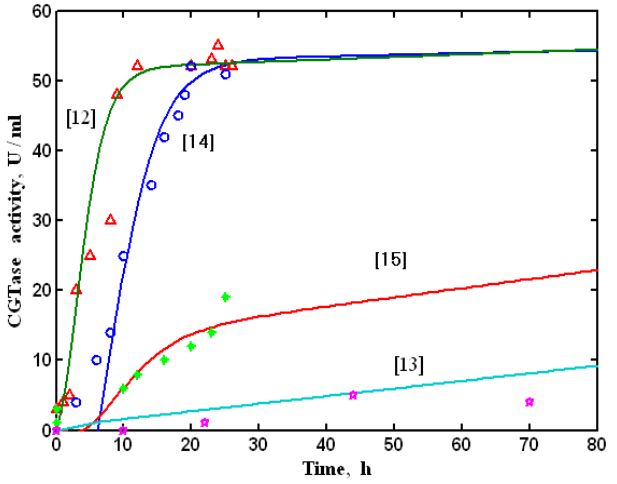

Figure 2. Shows the data presented by [13-15]. A comparison of parameters is given in Table 2

Fig.1. shows the model curves for product concentration. The maximum growth rate increases moderately with S_0. The main variable of interest in this paper is the concentration of product $P(t)$. The exponential growth phase lasted for 9h as shown in figure.1. This result is same as reported in [12]. CGTase synthesis began in the early exponential phase and intensive enzyme production is established after the end of exponential growth (9h). Maximal CGTase yield is determined from the 14th h to 30th h in figure 1. The review of data as in Table 2 for the estimated constants and the analytical result as per (11) shows reasonable agreement. Our analytical results represented in (9-11) are compared with experimental results as shown in Tables 1, 2. At higher starch concentrations, strong substrate inhibition of microbial growth may occur.

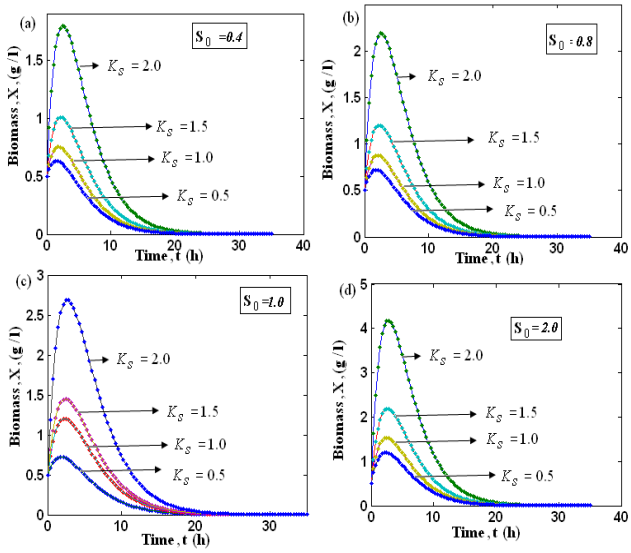

Figure 3. Plot of Biomass Concentration X versus time t for various values of K_S and S_0 using Eq. (9). Here, $\mu_{max} = 1.9$, $\gamma = 0.35$, $X_0 = 0.5$

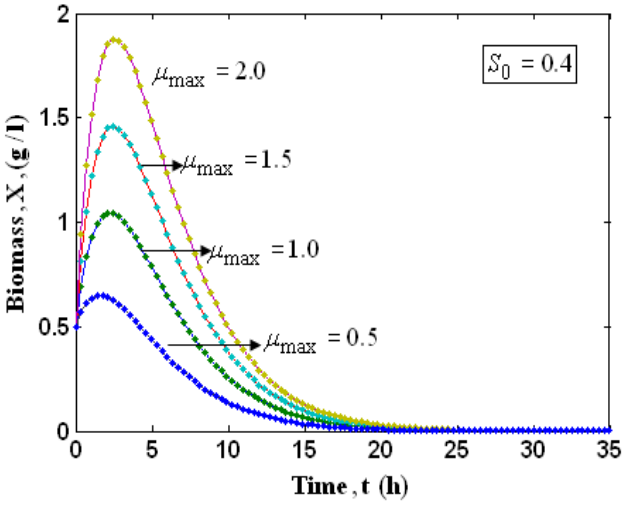

Figure 4. Plot of Biomass Concentration X versus time t for various values of μ_{max} using Eq. (9)

In figure 3, the biomass concentration is maximum when $t = \frac{1}{\gamma} - \frac{K_s}{S_0 \mu_{max}}$ for all values of parameters K_S, S_0, μmax and γ. The maximum value of the biomass is

$$X_{max}(t) = \frac{X_0 S_0 \mu_{max} t_{max} e^{-\gamma t_{max}}}{K_s} + X_0 e^{-\gamma t_{max}} ,$$

where, $t_{max} = \frac{1}{\gamma} - \frac{K_s}{S_0 \mu_{max}}$. After reaches the maximum value the biomass concentration gradually decreases and attain the steady state when t = 20.

Figures (4-6) shows the biomass concentration profile varies according to the parameters. These figures are

particular case when $S_0 = 0.4$.

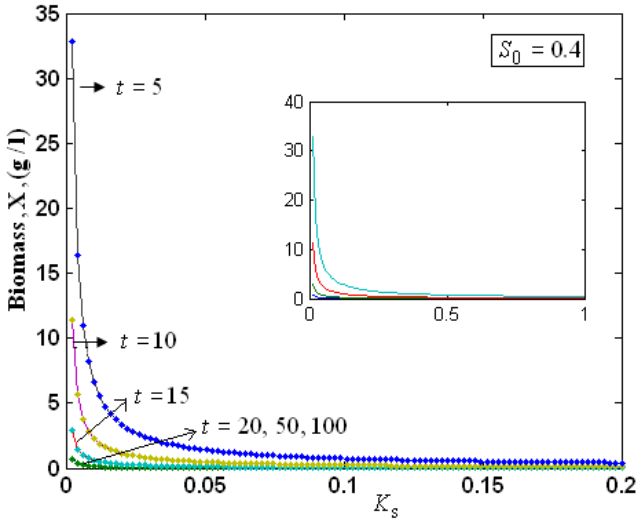

Figure 5. Biomass concentration versus K_S for various values of time t using Eq. (9)

In figure 7, the substrate concentration profile is presented as a function of various values of S_0, $Y_{X/S}$ and for some fixed values of X_0, γ, μ_{max}, K_S. From this figure it is confirmed that the value of the substrate concentration increases when the value of S_0 increases for all values of parameters.

7. Conclusions

A system of time dependent nonlinear differential equations in cyclodextrin-glucanotransferase production model has been solved analytically. The analytical expressions of the concentrations of cyclodextrin-glucanotransferase have been derived using Homotopy perturbation method for all experimental values. This method can be easily extended to find out the solution of all other non-linear equations. The theoretical analysis of our analytical result will be useful for the better understanding of the system and as well as to predict the behavior of the system.

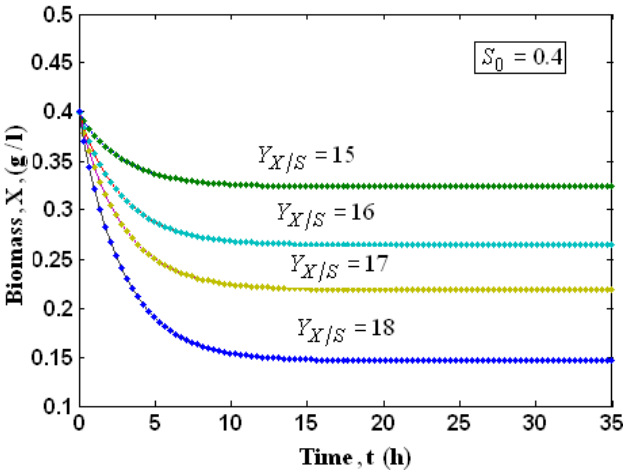

Figure 6. Biomass concentration X with respect to time t for various values of $Y_{X/S}$ using Eq. (9)

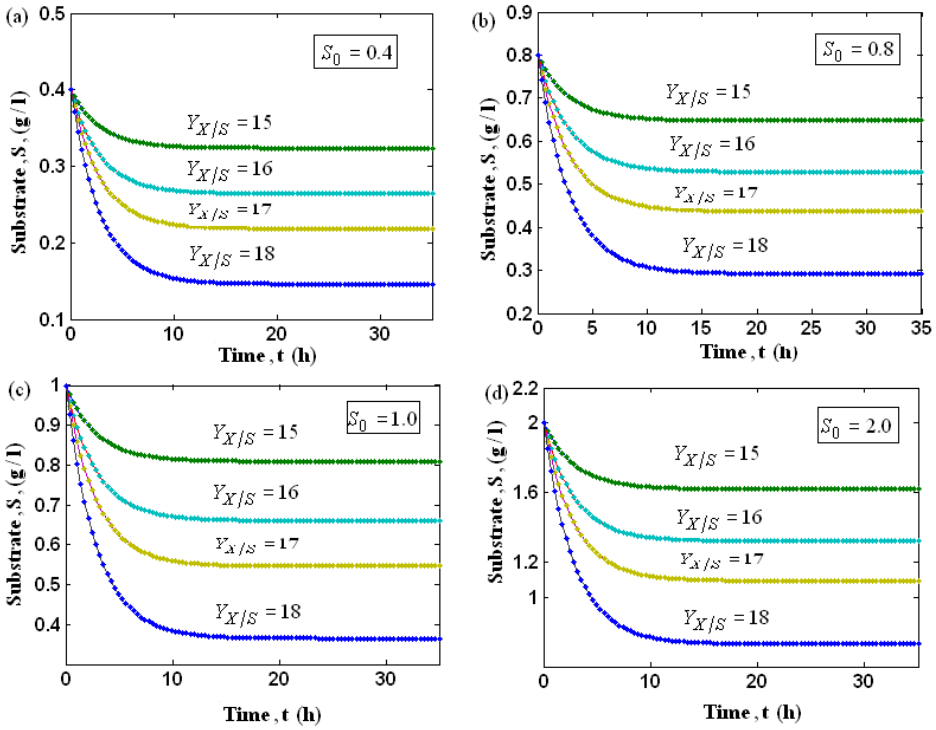

Figure 7. The substrate concentration S versus time t for various values of $Y_{X/S}$ and S_0 using Eq. (10). $\mu_{max} = 1.9$, $K_S = 0.8$, $X_0 = 0.5$, $\gamma = 0.35$

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