



An Approach to Estimate the Parameters of Monod and Teissier Models Using the Growth of *Escherichia Coli*

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ABSTRACT:

Monod and Teissier models are the two most elegant mathematical models widely used to study the kinetic growth of microbial. Five new methods have been introduced to estimate the model parameters using the growth data of *Escherichia Coli*. The performance of the new methods has been analyzed by following a standard selection criterion. It is found from this study, that all newly introduced methods provide satisfactory results for both the candidate models. It is also observed that, the Monod model is provided a comparatively better fit than the Teissier model with the newly introduced method of estimations.

Keywords: Kinetic models, Microbial growth, Parameter estimation.

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1. Introduction

Microorganisms are microscopic or submicroscopic organisms with undifferentiated unicells [9] such as bacteria, archaea, and fungus [12]. Microorganisms have a huge impact on environment around us as well as on animal and human health. They can produce both beneficial and harmful effects depending on the type and nature of microorganisms. The most significant beneficial effects of these microbial on human and environmental health is that, they can degrade and detoxify pollutants. The contamination of the environment with hazardous and poisonous material is a severe problem faced by today's world. Microbes, mostly bacteria, degrade the organic chemicals to harmless compounds and this process is known as biodegradation. The growth of the microbial is an area with great potential for much

scientific researches and has many impacts on our lives. The collaboration of mathematical modeling and experimental work provides a comprehensive description of experimental results and opens new dimensions into microbial study. Blackman in 1905 [4] derived an equation to describe a biological process, which is considered as the earliest growth model introduced to study microbial growth. Blackman assumed that the growth is proportional to the concentration of the substrate. Leonor Michaelis and Maud Menten in 1913 [16] studied the growth of enzyme and derived a mathematical model for enzyme growth kinetics. In 1940 Monod [17] observed the existence of non-linear relation between the growth rate and the substrate concentration while studying *Escherichia Coli* bacteria. In 1942 Teissier [21] derived an exponential model. This model involves specific growth as a continuous function of substrate. The Teissier model is more reliable than the Blackman model but lesser reliable than the Monod model [13]. Teissier model does not consider the inhibition effect and fails to describe the initial and the last phases of microbial growth. Microbial growth kinetics deals with the study of a microbial population using specific growth rate μ and the substrate concentration. The Teissier model is mathematically represented as

$$\mu = \mu_{\max} \left(1 - e^{-\frac{S}{k_T}} \right). \quad (1)$$

Where μ represents specific growth rate, μ_{\max} is called the maximum growth rate, k_T is the proportional constant and S is the substrate present at time t .

The mathematical representation of the Monod model is

$$\mu = \frac{\mu_{\max} S}{k_s + S}. \quad (2)$$

Here μ represents specific growth rate and S represents the substrate concentration at time t . μ_{\max} represents the maximum growth rate. The constant k_s is called the half saturation constant. When $\mu = \frac{\mu_{\max}}{2}$, $S = k_s$. The parameter μ_{\max} varies with the species and k_s value depends on substrate [6]. Since μ_{\max} is the maximum specific growth rate, $\frac{S}{k_s + S}$ must be less than one and this is only possible if k_s is positive value. Therefore, growth starts after S reached a critical value [10]. According to Contois [7], the accuracy of Monod model is very high. and suitable for homogeneous culture but the accuracy is low for heterogeneous culture with complex substrate [19]. Pfeffer [18] studied the Monod model and observed that this model is incapable of describing the degradation of municipal waste. Kong in 2017 [13] pointed out five limitations regarding the Monod model. Kong reported that at high substrate concentration, the maximum specific growth does not depend of substrate concentration while at low substrate concentration growth rate depends on substrate concentration. The Monod model cannot be applied when a substrate exhibit inhibition [11].

The objectives of this study are:

1. To introduce some new methods of estimation for estimating the parameters of the candidate models.
2. To fit the candidate models for some bacterial growth data to test the validity of the newly introduced methods.
3. To select the best fit model and the best performing method.

2. Methods

In this study five new methods have been introduced for parameter estimation of the candidate models based on the idea given by Borah and Mahanta [5]. The performances of the candidate models have been analyzed by using the selection criterion given in a section below. A growth data of *Escherichia coli* has been used to fit the models in this paper [20]. The required data set are presented in table-1.

Table 1. Growth rate data of *Escherichia Coli*.

S(1/h)	5.1	8.3	13.3	20.3	30.4	37	43.1	58	74.5	96.5	112	161	195	266	386
μ(mg/L)	.059	.091	.124	.177	.241	.302	.358	.425	.485	.546	.61	.662	.725	.792	.852

Method of Estimations

Method I:

Monod Model: Let the total number of observations be n . Let S₁ and S₂ be two substrate concentration and μ₁ and μ₂ the corresponding specific growth rate.

From the Monod Model using these two data points we have

$$\mu_1 = \frac{\mu_{max}S_1}{k_s + S_1} \tag{3}$$

$$\mu_2 = \frac{\mu_{max}S_2}{k_s + S_2} \tag{4}$$

From (3) and (4) we can estimate the parameter k_s as

$$k_s = \frac{S_1S_2(\mu_2 - \mu_1)}{\mu_1S_2 - \mu_2S_1} \tag{5}$$

Using k_s in (3) or (4) we can estimate the parameter μ_{max}.

Teissier model: The Teissier model we can be reduced to the form

$$\lambda S = \log \left(1 - \frac{\mu}{\mu_{max}} \right) \tag{6}$$

where $\lambda = -\frac{1}{k_T}$. Since μ_{max} > μ, expanding the right-hand side using logarithm series and neglecting the third and higher order terms for two arbitrary substrate concentrations S₁ and S₂ we have

$$\lambda \mu_{max} S_1 = -(\mu_1 \mu_{max} + \mu_1^2) \tag{7}$$

$$\lambda \mu_{max} S_2 = -(\mu_2 \mu_{max} + \mu_2^2) \tag{8}$$

From these two equations we can estimate the parameters as

$$\mu_{max} = \frac{\mu_1^2 S_2 - \mu_2^2 S_1}{\mu_2 S_1 - \mu_1 S_2} \tag{9}$$

$$k_T = -\frac{S_1}{\log \left(1 - \frac{\mu_1}{\mu_{max}} \right)} \tag{10}$$

Method II:

Monod model: Consider any substrate concentration S₁ from the observed data set. Assuming λ_{max} as known parameter, the parameter k_s of the Monod model can be estimated as

$$k_s = \frac{\mu_{max}S_1}{\mu_1} - S_1 \tag{11}$$

Teissier model: Consider any substrate concentration S₁ from the observed data set. The parameter k_T can be evaluated by assuming μ_{max} as known parameter. The largest value of μ of the used data set is considered as the known value of μ_{max}. The parameter k_T can be estimated as,

$$k_T = -\frac{S_1}{\log \left(1 - \frac{\mu_1}{\mu_{max}} \right)} \tag{12}$$

Method III:

Monod model: Let the n be the number of observations. Let us divide the data set into two equal parts. Let $r = \left\lfloor \frac{n}{2} \right\rfloor$. The first partial sums contain first r observations and the second partial sums contains (r + 1)th to nth observations. Then we have from Monod model the following two equations.

$$\mu_{\max} \sum_{i=1}^r S_i - k_s \sum_{i=1}^r \mu_i = \sum_{i=1}^r \mu_i S_i \tag{13}$$

$$\mu_{\max} \sum_{i=r+1}^n S_i - k_s \sum_{i=r+1}^n \mu_i = \sum_{i=r+1}^n \mu_i S_i \tag{14}$$

Solving the equations (13) and (14) the parameters can be estimated as

$$k_s = \frac{C_1 A_2 - C_2 A_1}{B_2 A_1 - B_1 A_2} \tag{15}$$

$$\mu_{\max} = \frac{k_s B_1 + C_1}{A_1} \tag{16}$$

Where $\sum_{i=1}^r S_i = A_1$, $\sum_{i=r+1}^n S_i = A_2$, $\sum_{i=1}^r \mu_i = B_1$, $\sum_{i=r+1}^n \mu_i = B_2$
 $\sum_{i=1}^r \mu_i S_i = C_1$, $\sum_{i=r+1}^n \mu_i S_i = C_2$.

Teissier model: Let the n be the number of observations. Let us divide the data set into two equal parts. Let $r = \lfloor \frac{n}{2} \rfloor$. The first partial sums contain first r observations and the second partial sums contains (r + 1)th to nth observations. Let $r = \lfloor \frac{n}{2} \rfloor$. The first partial sums contain first r observations and the second partial sums contains (r + 1)th to nth observations. Then we have for Teissier model

$$\lambda \mu_{\max} \sum_{i=1}^r S_i = -(\mu_{\max} \sum_{i=1}^r \mu_i + \sum_{i=1}^r \mu_i^2) \tag{17}$$

$$\lambda \mu_{\max} \sum_{i=r+1}^n S_i = -(\mu_{\max} \sum_{i=r+1}^n \mu_i + \sum_{i=r+1}^n \mu_i^2) \tag{18}$$

Solving these equations, the parameters can be estimated as

$$\mu_{\max} = \frac{A_2 C_1 - A_1 C_2}{A_1 B_2 - A_2 B_1} \tag{19}$$

$$k_T = \frac{\mu_{\max} A_1}{\mu_{\max} B_1 + C_1} \tag{20}$$

where $A_1 = \sum_{i=1}^r S_i$, $A_2 = \sum_{i=r+1}^n S_i$, $B_1 = \sum_{i=1}^r \mu_i$, $B_2 = \sum_{i=r+1}^n \mu_i$
 and $C_1 = \sum_{i=1}^r \mu_i^2$, $C_2 = \sum_{i=r+1}^n \mu_i^2$

Method IV:

Monod model: The equation of Monod model is

$$\mu = \frac{\mu_{\max} S}{k_s + S} \text{ which can be reduced to the form}$$

$$\mu k_s + \mu S = \mu_{\max} S \tag{21}$$

Taking the summations over the entire n observations of the used data set we have

$$\sum_{i=1}^n \mu_i k_s + \sum_{i=1}^n \mu_i S_i = \sum_{i=1}^n \mu_{\max} S_i \tag{22}$$

Assuming k_s as known parameter from method 1 we can estimate μ_{\max} as

$$\mu_{\max} = \frac{k_s B + C}{A}$$

Where $\sum_{i=1}^n S_i = A$, $\sum_{i=1}^n \mu_i = B$, $\sum_{i=1}^n S_i \mu_i = C$

Similarly considering μ_{\max} as known parameter, from **method 1** we can estimate k_s as

$$k_s = \frac{\mu_{\max} A - C}{B} \tag{23}$$

Teissier model: The Teissier model can be rewritten as

$$\frac{S}{k_T} = -\log\left(1 - \frac{\mu}{\mu_{\max}}\right) \tag{24}$$

Assuming μ_{\max} as known parameter and taking the summations over the n observations we can evaluate the parameter k_T as

$$k_T = -\frac{\sum_{i=1}^n S_i}{\sum_{i=1}^n \log\left(1 - \frac{\mu_i}{\mu_{\max}}\right)} \tag{25}$$

Method V:

Monod model: The Monod model can be linearized in the form

$$y = (ax + b) \quad (26)$$

$$\text{where } y = \frac{1}{\mu}, \quad x = \frac{1}{S}, \quad a = \frac{K_s}{\mu_{\max}}, \quad b = \frac{1}{\mu_{\max}}$$

Teissier model: The Teissier model can be linearized in the form $y = (ax + b)$

$$\text{where } y = \mu, \quad x = e^{-\frac{S}{k_T}}, \quad a = -\mu_{\max}, \quad b = \mu_{\max}$$

3. Steps for Selection of the best fit model

The candidate models are fitted using the five new methods of estimation and the best fitted model method are selected using our election procedure adopted for this study. The steps are explained below.

Criteria I: Logical and biological consistency

The estimation methods which can provide logically consistent and biologically meaningful estimation of the parameters are taken into consideration. The methods giving inconsistent estimation of parameters and unrealistic values are excluded.

Criteria II: Chi Square goodness-of-fit test (χ^2)

The methods of estimation giving results with 95% level of signification with their associated degrees of freedom are considered.

Criteria III: The root mean square error (RMSE)

The RMSE for different estimation methods applied to the models are compared to select the best performed methods and model.

Criteria IV: Coefficient of determination R^2 and adjusted coefficient of determination R_a^2

We evaluate the coefficient of determination R^2 . The value of R^2 generally lies between 0 and 1

($0 \leq R^2 \leq 1$). The values above 0.9 are considered as efficient estimation methods.

In our study, we considered the results which have R_a^2 value not less than 0.99.

Criteria V: Approximation R^2 for prediction

In this step, the approximate R^2 for prediction is calculated and then the selection criterion of the best estimation method is completed.

4. Results

The estimated values of the model parameters and the associated values of the statistical parameters χ^2 , RMSE, R^2 , R_a^2 and $R_{\text{prediction}}^2$ are given in the table-2. In the case of Monod model, the Chi-Square (χ^2) for 99.5% level of significance is found to be higher than our calculated Chi-Square (χ^2) for all the methods. We also observed that the values estimated for μ_{\max} in all the five methods for Monod model is slightly greater than the maximum value of μ which is 0.852 in the considered empirical data set. Hence the estimation of the parameter μ_{\max} are logically consistent and biologically realistic. The estimated values of the half saturation constant k_s are also found to be logical and biologically consistent, since k_s is defined as the value of the substrate concentration when $\mu = \frac{\mu_{\max}}{2}$. For the methods I, II, III and IV the RMSE is 0.013 (up to three digits after the decimal sign). The coefficient of determination R^2 is greater than 99, the adjusted coefficient of determination R_a^2 is greater than .99 and the approximation R^2 for prediction $R_{\text{prediction}}^2$ is also greater than 99. The adjusted coefficient of determination R_a^2 and the approximation R^2 for prediction $R_{\text{prediction}}^2$ are 0.97558 and 96.97080 respectively for Monod model in method I, which are less than the other methods. The performance of this method on Monod model is rejected in our study. In case of the Teissier model the method III is rejected due to inconsistent value of μ_{\max} which should be around

0.852. The method I is rejected due to low value of μ_{max} and coefficient of determination R^2 is less than 99. For the methods II, IV and V the values of the estimated parameters μ_{max} and proportionality constant k_T are found consistent both logically and biologically for Teissier model. The Chi-Square (χ^2) for 99.5% level of significance is found to be higher than our calculated Chi-Square (χ^2) for the methods II, IV and V. The RMSE is 0.02 (up to two digits after the decimal sign) for the methods II, IV and V. The coefficient of determination R^2 is greater than 99, the adjusted coefficient of determination R_a^2 is greater than .99 and the approximation R^2 for prediction $R_{prediction}^2$ is also greater than 99. Dabes, Finn and Wilke (Shuler et al. 1979) compared the ability of the Monod and Blackman model using an *Escherichia Coli* bacteria data set and found that the Blackman model performed better than the Monod model. Mahanta and Saikia [15] applied four growth models including the Monod model to analysis the *Escherichia Coli* bacteria growth and estimated the RMSE value are almost similar with our study. The parameters of the Monod model were estimated using a data set on biodegradation kinetics of Azo dye Mixture by Krishnan in 2017 [14]. Annuar in 2008 estimated the model parameters while fitting the Monod model on growth of the bacteria *Pseudomonas putida* [2]. Ardestani and Shafiei in 2014 [2] in their study to fit the Monod model on the cell growth of a species of yeast *Saccharomyces cerevisiae* in a batch culture and estimated the model parameters. On the other hand, Dey and Mukherjee [8] estimated the parameters while fitting the Teissier model on phenol bio degradation by mixed microbial culture in a batch reactor. Annuar estimated the parameters to fit the Teissier model on the growth of the bacteria *Pseudomonas putida*, [2]. While fitting the Teissier model on fungus *Aspergillus oryzae* [1] estimated the model parameters.

Table 2: Estimated values of the model’s parameters and statistical parameters.

Models	Methods	Parameters			χ^2	RMSE	R^2	R_a^2	R_{pre}^2
		k_s	μ_{max}	k_T					
Monod	I	86.9095	1.0438		0.00907	0.01317	99.7306	0.99710	99.70215
	II	85.8363	1.0438		0.01016	0.01371	99.70827	0.99687	99.68004
	III	96.3646	1.0826		0.00792	0.01386	99.7018	0.99679	99.65228
	IV	87.2947	1.0438		0.00879	0.01310	99.7338	0.99713	99.70433
	V	77.2263	0.9322		0.03781	0.03822	99.7322	0.97558	96.97080
Teissier	I		0.7435	63.5739	0.04062	0.03859	97.6884	0.97511	96.83916
	II		0.8520	91.4314	0.02013	0.02023	99.3645	0.99316	99.24295
	III		0.0811	28.6753	37.4016	0.13679	-196.132	2.18912	-----
	IV		0.8520	95.2566	0.03107	0.02314	99.1686	0.99105	99.05368
	V		0.8485	95.2566	0.03283	0.02369	99.1287	0.99062	99.01107

5. Discussion

The primary objective of this paper is the mathematical deduction of the five different methods and to estimate the parameters of Monod and Teissier models by applying these methods as

described above and to select the best performed methods and the model. The parameters are estimated and the statistical parameters Chi-Square (χ^2), RMSE, R^2 , R_a^2 and R_{pre}^2 are calculated and given in the table-2. It is observed that the table value of Chi-Square (χ^2) for 99.5% level of significance is found to be higher than our calculated Chi-Square (χ^2) for all methods as well as for both the models except for method III in Teissier model. Teissier model provides unrealistic parameter estimation and poor statistical values of Chi-Square (χ^2), RMSE, R^2 , R_a^2 and R_{pre}^2 with respect to methods I and III. In case of Monod model, methods I, II, III and IV provided the best satisfactory result while methods II, IV and V performed well in Teissier model.

In our study we have observed that both the candidate models Monod and Teissier producing satisfactory results while using the five new methods of parameter estimation on *Escherichia Coli* bacterial growth. Based on our results we can conclude that both the Monod and the Teissier models as well as these methods can be used to study any microbial growth phenomenon in a simple way.

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