Communications in Mathematics and Applications
Vol. 14, No. 4, pp. 1367–1374, 2023
ISSN 0975-8607 (online); 0976-5905 (print)
Published by RGN Publications
DOI: 10.26713/cma.v14i4.2573

http://www.rgnpublications.com

***Special Issue*: Recent Trends in Applied and Computational Mathematics**
Proceedings of the Third International Conference on Recent Trends in Applied and Computational Mathematics (ICRTACM-2022)
School of Applied Sciences, Department of Mathematics, Reva University, Bangaluru, India, 10th & 11th October, 2022
***Editors*: M. Vishu Kumar, A. Salma, B. N. Hanumagowda and U. Vijaya Chandra Kumar**

Research Article

An Approach to Estimate the Parameters of Aiba-Edward Growth Model Using the Growth of *Escherichia Coli*

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Received: March 4, 2023 **Accepted:** June 8, 2023

Abstract. In microbial growth kinetics mathematical models are used to correlate the growth rate to the concentration of the limiting substrate with the parameters. Aiba-Edward model is one of the widely used models to describe microbial growth kinetics. In this study, four new methods are introduced to estimate the model's parameter using a standard bacterial growth data of *Escherichia Coli*. The performance of the introduced methods are analyzed by using a standard selection criterion. In this study, it has been observed that the newly introduced methods are performed well and estimated parameters are biologically significant.

Keywords. Microbial growth, Parameter estimation, Growth model, Inhibition

Mathematics Subject Classification (2020). Primary 93A30, Secondary 92B15

1. Introduction

Microorganisms are microscopic or sub microscopic organisms with undifferentiated unicells such as bacteria, archaea, and fungus (Edmonds [6], and Kirchman [9]. Microorganisms have a huge impact on environmental and human health. They can produce huge beneficial effects as well as harmful and mixed effects depending on the type and nature of microorganisms. The growth kinetics of the microbial has been an area of vast potentiality for scientific researches and it has many impact in the society and environment. Experimental works relating to any biological growth process when collaborated with mathematical models always can generate more quantitative and meaningful results and helps unfolding many new dimensions of the biological process. F. F. Blackman [2] was one of the pioneers in the field of mathematical modeling and he derived an equation to describe a biological process in the year 1905. Michaelis and Menten [13] studied the growth of enzyme and initiated the application of mathematical modeling of the microbial growth process in 1913. In the year 1940, Monod [14] introduced a mathematical model in his study of the growth process of *Escherichia Coli* bacteria based on the non-linear relationship between the growth rate and substrate concentration. In 1942, Teissier [18] introduced an exponential model to study microbial growth process. Later, Aiba *et al*. [1] (1968) introduced a growth model for microbial growth study, and Edward (Muloiwa *et al*. [15]) (1970) modified the model and later it was named as Aiba-Edward model. This model is an unstructured, inhibitory model and can be considered as an extension of the Monod model [14]. The Aiba-Edward model introduced the concept of inhibitory constant (Sadhukhan *et al*. [16]). The inhibitory constant introduced in this model is responsible to deal with the effect of toxic material in substrate concentration. This model can take care the presence of toxic substrate, and can explain the lag and death phase of the growth process (Michaelis *et al*. [10]). The Aiba-Edward model is defined by

$$\mu = \mu_{\max}\frac{S}{k_S - S}(e^{-\frac{S}{k_i}}), \tag{1.1}$$

where μ represents the specific growth rate, S represents the substrate concentration, $\mu_{\max}$ represents the maximum growth rate, k_S represents the half saturation constant, and k_i represents the inhibition constant.

2. Material and Methods

In this study, four new estimation methods are introduced to estimate the Aiba-Edward model's parameters $\mu_{\max}$, k_S and k_i. The methods are extensively explained and parameters are evaluated using a standard data set given in Table 1 of *Escherichia Coli* (Schulze and Lipse [17]). The idea of the methods are based on work of Borah and Mahanta [3]. MATLAB software has been applied for calculation of the model's parameters and required statistical parameters. Performance of the introduced methods are examined by analyzing the evaluated statistical parameters and best fitting method is selected. The selection criterion is explained in Section 4.

Table 1. *Escherichia Coli* growth rate data

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

3. Method of Estimations

3.1 Method I

Estimation of the parameters based on three arbitrary points:
The Aiba-Edward model can be written as

$$\frac{\mu_{\max} S}{\mu}\left(e^{-\lambda S}\right) = k_S + S, \tag{3.1}$$

where $\lambda = \frac{1}{k_i}$.
Expanding $(e^{-\lambda S})$ and neglecting third and higher order terms the equation (3.1) can be written as

$$\frac{\mu_{\max} S}{\mu}\left(1 - \lambda S + \lambda^2 \frac{S^2}{2}\right) = k_S + S. \tag{3.2}$$

Let S_1, S_2 and S_3 be three arbitrary substrate concentration, from equation we can write

$$\frac{\mu_{\max} S_1}{\mu_1}\left(1 - \lambda S_1 + \lambda^2 \frac{S_1^2}{2}\right) = k_S + S_1, \tag{3.3}$$

$$\frac{\mu_{\max} S_2}{\mu_2}\left(1 - \lambda S_2 + \lambda^2 \frac{S_2^2}{2}\right) = k_S + S_2, \tag{3.4}$$

$$\frac{\mu_{\max} S_3}{\mu_3}\left(1 - \lambda S_3 + \lambda^2 \frac{S_3^2}{2}\right) = k_S + S_3. \tag{3.5}$$

Equation (3.4)–(3.3) and (3.5)–(3.4) implies

$$\frac{\mu_{\max} S_2}{\mu_2}\left(1 - \lambda S_2 + \lambda^2 \frac{S_2^2}{2}\right) - \frac{\mu_{\max} S_1}{\mu_1}\left(1 - \lambda S_1 + \lambda^2 \frac{S_1^2}{2}\right) = S_2 - S_1, \tag{3.6}$$

$$\frac{\mu_{\max} S_3}{\mu_3}\left(1 - \lambda S_3 + \lambda^2 \frac{S_3^2}{2}\right) - \frac{\mu_{\max} S_2}{\mu_2}\left(1 - \lambda S_2 + \lambda^2 \frac{S_2^2}{2}\right) = S_3 - S_2. \tag{3.7}$$

Assuming $\frac{S_1}{\mu_1} = a_1$, $\frac{S_2}{\mu_2} = a_2$, $\frac{S_3}{\mu_3} = a_3$, $S_2 - S_1 = d_1$, and $S_3 - S_2 = d_2$.
From equations (3.6) and (3.7) we can have a quadratic equation

$$A\lambda^2 + B\lambda + C = 0 \tag{3.8}$$

which is a quadratic equation in $\lambda = \frac{1}{k_i}$. Considering the real positive root of λ from equation (3.8) we can estimate the parameter $\mu_{\max}$ from equation (3.6) or (3.7) as

$$\mu_{\max} = \frac{d_1}{a_2\left(1 - \lambda S_3 + \lambda^2 \frac{S_3^2}{2}\right) - a_1\left(1 - \lambda S_1 + \lambda^2 \frac{S_1^2}{2}\right)}.$$

Substituting the values of k_i and $\mu_{\max}$ in equation (3.3) the parameter k_S can be estimated as

$$k_S = \frac{\left(\mu_{\max} S_1 e^{\frac{-S_1}{k_i}}\right)}{\mu_1} S_1.$$

3.2 Method II

Estimation of the parameters based on three equidistant points:
Taking natural logarithm on both sides of the Aiba-Edward model given by equation (1.1) we

can write

$$\log(\mu) = \log(\mu_{\max}) + \log(S) - \lambda S - \log(k_S + S), \tag{3.9}$$

where $\lambda = \frac{1}{k_i}$.
Let S_1, S_2 and S_3 be three equidistant substrate concentration such that $S_2 - S_1 = S_3 - S_2$.
From equation (3.9) we have the equations

$$\log(\mu_1) = \log(\mu_{\max}) + \log(S_1) - \lambda S_1 - \log(k_S + S_1), \tag{3.10}$$

$$\log(\mu_2) = \log(\mu_{\max}) + \log(S_2) - \lambda S_2 - \log(k_S + S_2), \tag{3.11}$$

$$\log(\mu_3) = \log(\mu_{\max}) + \log(S_3) - \lambda S_3 - \log(k_S + S_3). \tag{3.12}$$

Now (3.10)–(3.11) implies

$$\log\left(\frac{\mu_1}{\mu_2}\right) = \log\left(\frac{S_1}{S_2}\right) - \lambda(S_2 - S_1) - \log\left(\frac{k_S + S_2}{k_S + S_1}\right). \tag{3.13}$$

Now (3.11)–(3.12) implies

$$\log\left(\frac{\mu_2}{\mu_3}\right) = \log\left(\frac{S_2}{S_3}\right) - \lambda(S_3 - S_2) - \log\left(\frac{k_S + S_3}{k_S + S_2}\right). \tag{3.14}$$

Now (3.13)–(3.14) implies

$$\log\left(\frac{\mu_1 S_2(k_S + S_1)}{\mu_2 S_1(k_S + S_2)}\right) = \lambda(S_2 - S_1), \tag{3.15}$$

$$\log\left(\frac{\mu_2 S_3(k_S + S_2)}{\mu_3 S_2(k_S + S_3)}\right) = \lambda(S_3 - S_2). \tag{3.16}$$

Equations (3.15) and (3.16) implies

$$\left(\frac{\mu_1 S_2(k_S + S_1)}{\mu_2 S_1(k_S + S_2)}\right) = \left(\frac{\mu_2 S_3(k_S + S_2)}{\mu_3 S_2(k_S + S_3)}\right). \tag{3.17}$$

Simplifying equation (3.17) we get

$$A k_S^2 + B k_S + C = 0, \tag{3.18}$$

where $A = (\mu_1\mu_2 S_2^2 - \mu_2^2 S_1 S_3)$, $B = (\mu_1\mu_3 S_2^2(S_1 + S - 3) - 2\mu_2^2 S_1 S_2 S_3)$, $C = (\mu_1\mu_3 S - 2^2 S_1 S - 3 - \mu_2^2 S_1 S_2^2 S_3)$ which is a quadratic equation in k_S. Considering the real positive root of k_S from equation (3.18) we can estimated $\lambda = \frac{1}{k_i}$ as

$$k_i = \frac{(S_2 - S_1)}{\log\left(\frac{\mu_1 S_2(k_S + S_1)}{\mu_2 S_1(k_S + S_2)}\right)}.$$

Substituting the values of k_S and k_i in equation (3.10) the parameter $\mu_{\max}$ can be estimated as

$$\mu_{\max} = \frac{\mu_1(k_S + S_1)}{S_1 e^{-\frac{S_1}{k_i}}}. \tag{3.19}$$

3.3 Method III

Estimation of parameters based on two substrate concentrations:
Let S_a and S_b be any two arbitrary substrate concentration and μ_a and μ_b the respective growth rate. Then, form the Aiba-Edward model we can write two equations as

$$\log(\mu_a) = \log(\mu_{\max}) + \log(S_a) - \lambda S_a - \log(k_S + S_a), \tag{3.20}$$

$$\log(\mu_b) = \log(\mu_{\max}) + \log(S_b) - \lambda S_b - \log(k_S + S_b). \tag{3.21}$$

From the equations (3.19) and (3.20) we have

$$k_i = \frac{1}{\lambda} = \frac{(S_a - S_b)}{\log\left(\frac{\mu_b S_a (k_S + S_b)}{\mu_a S_b (k_S + S_a)}\right)}.$$

Assuming the parameter k_S as as the known parameter the parameter k_i can be estimated from the equation (3.21). The parameter $\mu_{\max}$ can be estimated form the Aiba-Edward model as

$$\mu_{\max} = \frac{\mu_a (k_S + S_a)}{S_a e^{-\frac{S_a}{k_i}}}. \tag{3.22}$$

3.4 Method IV

Estimation of the parameters based on two partial sums:

Let us divide the observed data points n into two equal sets of data points each containing r points where $r = \left[\frac{n}{2}\right]$.

For the first partial sum we can write from the Aiba-Edward equation

$$\sum_{i=1}^{r} \log(\mu_i) = r\log(\mu_{\max}) + \sum_{i=1}^{r} \log(S_i) - \lambda \sum_{i=1}^{r} S_i + \sum_{i=1}^{r} \log(k_S + S_i). \tag{3.23}$$

For the second partial sum we can write from the Aiba-Edward equation

$$\sum_{i=r+1}^{n} \log(\mu_i) = r\log(\mu_{\max}) + \sum_{i=r+1}^{n} \log(S_i) - \lambda \sum_{i=r+1}^{n} S_i + \sum_{i=r+1}^{n} \log(k_S + S_i). \tag{3.24}$$

From equations (3.23) and (3.24) we have

$$\log\left(\prod_{i=1}^{r} \mu_i\right) = r\log(\mu_{\max}) + \log\left(\prod_{i=1}^{r} S_i\right) - \lambda \sum_{i=1}^{r} - \log\left(\prod_{i=1}^{r} (k_S + S_i)\right), \tag{3.25}$$

$$\log\left(\prod_{i=r+1}^{n} \mu_i\right) = r\log(\mu_{\max}) + \log\left(\prod_{i=r+1}^{n} S_i\right) - \lambda \sum_{i=1+r}^{n} - \log\left(\prod_{i=1+r}^{n} (k_S + S_i)\right). \tag{3.26}$$

Equation (3.25)-(3.26) implies

$$\lambda\left(\sum_{i=1+r}^{n} S_i - \sum_{i=1}^{r} S_i\right) = \log\left(\frac{\prod_{i=1}^{r} \mu_i}{\prod_{i=r+1}^{n} \mu_i}\right) + \log\left(\frac{\prod_{i=r+1}^{n} S_i}{\prod_{i=1}^{r} S_i}\right) + \log\left(\frac{\prod_{i=1+r}^{n} (k_S + S_i)}{\prod_{i=1}^{r} (k_S + S_i)}\right). \tag{3.27}$$

Assuming the parameter k_S as known parameter the parameter $\lambda = \frac{1}{k_i}$ can be estimated from the equation (3.27)

$$k_i = \frac{\left(\sum_{i=1+r}^{n} S_i - \sum_{i=1}^{r} S_i\right)}{\log\left(\frac{\prod_{i=1}^{r} \mu_i}{\prod_{i=r+1}^{n} \mu_i}\right) + \log\left(\frac{\prod_{i=r+1}^{n} S_i}{\prod_{i=1}^{r} S_i}\right) + \log\left(\frac{\prod_{i=1+r}^{n} (k_S + S_i)}{\prod_{i=1}^{r} (k_S + S_i)}\right)}.$$

Using equation (3.25) the parameter $\mu_{\max}$ can be estimated as

$$\mu_{\max} = e^{\frac{1}{r}\log\left(\frac{\prod_{i=1}^{r} \mu_i \prod_{i=1}^{r} (k_S + S_i)}{\prod_{i=1}^{r} S_i}\right) + \lambda \sum_{i=1}^{r} S_i}. \tag{3.28}$$

4. Selection Criteria for Best Fit Model

After fitting the growth models using the introduced methods of estimation, the best fit model is selected based on the standard selection criteria. The selection criteria are adopted from the paper of Mahanta *et al*. [12] which consists of five distinct steps.

5. Results and Discussion

The estimated parameters of the model along with the values of the statistical parameters χ^2, $RMSE$, R^2, R_a^2 and R_{pre}^2 with respect to the four introduced methods are given in Table 2. The performances of the methods are checked in five steps.

In Step 1, we have observed that the model parameters k_S, $\mu_{\max}$ and k_i are logically and biologically consistent for all the methods.

In Step 2, we have observed that the estimated significance level for chi-square (χ^2) is above 99.5% for all the methods with respect to the associated degrees of freedom.

In Step 3, the $RMSE$ of the surviving methods in Step 1 and Step 2 are observed and rejected the methods having $RMSE$ higher than 0.06 (considering up to two digits after decimal sign). In this step, Method IV is rejected in our study.

In Step 4, the value of R_a^2 is observed for the surviving methods. The methods having value of R_a^2 lower than 0.90 are rejected in our study.

Finally, in Step 5, observing the surviving methods having the values of R^2 and R_{pre}^2 higher than 95%, the best fit method is selected. In our study, the Method III is selected as the best method. All the eliminated results in each step are highlighted in every step.

The Aiba-Edward model successfully applied by various researchers in different microbial growth studies using existing estimated methods. Some of the existing works are compared with our study. Aiba-Edward model was used by Krishan *et al*. [11] (2017) on the study of biodegradation of Azo dye and found R^2 of 99.9%.

Ibrahim *et al*. [8] fitted the Aiba-Edward model on a data of caffeine degradation and calculated R^2 of 92.3%

Study by Gharibzahedi *et al*. [7] of *Dietzia natronolimnaea* using Aiba-Edward model, calculated R^2 of 90%

Dey and Mukherjee [4] (2010) calculated R^2 of 91% and $RMSE$ of 0.0078 in Aiba-Edward model during the study of biodegradation of phenol.

Table 2. Estimated parameters along with statistical analysis

Model	Method	Parameters			χ^2	$RMSE$	R_a^2	R^2 (in %)	R_p^2 (in %)
		k_S	$\mu_{\max}$	k_i					
Aiba-Edward	I	301.1182	3.0326	391.8572	.08956	.06052	.9336	94.314	91.6612
	II	604.6052	5.5484	312.5135	.10381	.06260	.9290	93.917	91.1183
	III	301.0000	2.6481	590.9083	.04256	.03159	.9819	98.454	98.0258
	IV	301.0000	3.0820	612.3163	.12637	.08096	.8813	89.827	86.6546

6. Conclusion

The basic aim of this study was to estimate the model's parameters of the Aiba-Edward growth model using the newly introduced methods of estimation and to select the best fit method. The newly introduced methods are easy to use and require fewer amounts of calculations. In our study, the Method III shown the best performance in comparison to other three methods.

The introduced methods can be used for parameter estimation of any growth model using any growth data.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All the authors contributed significantly in writing this article. The authors read and approved the final manuscript.

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