A New Logistic Model for Bacterial Growth
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A new logistic model for bacterial growth was developed in this study. The model is based on a logistic model, which is often applied for biological and ecological population kinetics. The new model is described by a differential equation and contains an additional term for suppression of the growth rate during the lag phase, compared with the original logistic equation. The new model successfully described sigmoidal growth curves of Escherichia coli and Salmonella under various initial conditions. Data for E. coli were obtained from our experiments and data for Salmonella from the literature. When the new model was compared with a modified Gompertz model, which is widely used by many predictive microbiology researchers, it proved to be superior to the Gompertz model. Further, Salmonella growth at varying temperature could be well simulated by the new model. These results indicate that the new model will be a useful tool to predict bacterial growth under various temperature profiles.

Key words: growth; mathematical model; logistic model; Gompertz model; predictive microbiology; Escherichia coli; Salmonella

Introduction

A number of mathematical models to describe microbial growth in food and culture media have been developed. They include some basic models such as the logistic model and Gompertz model. It is well known that the growth curves of organisms are well described using the logistic model. The growth rate according to the model is given by a differential equation as follows:

\[ \frac{dN}{dt} = rN(1 - N/N_{\text{max}}) \]  

where \( N \) is the population of the organism at time \( t \) and \( r \) is the rate constant, or the maximum specific growth rate. \( N_{\text{max}} \) is the maximum population (at the stationary phase), which is often called the carrying capacity of the environment. The logistic model contains the term, \( 1 - N/N_{\text{max}} \), which suppresses the growth rate at a high population. When \( N \) is small during the lag phase, the value of this term is almost one, which does not affect the growth rate. As \( N \) increases to approach \( N_{\text{max}} \), the value approaches zero, thus making the growth rate almost zero during the stationary phase. A growth curve described with this model is sigmoid on an ordinary Cartesian plane.

The growth curve of bacteria, however, is generally sigmoid on a semi-logarithmic plot. The logistic model cannot be applied to bacterial growth curves. It can easily be shown by using numerical calculation that a curve described with the model does not have a lag phase on a semi-logarithmic plot. Some efforts have been made to overcome this shortcoming of the original logistic model. Hutchinson introduced a time delay term in the logistic equation (1), but there are objections to using the delay model. Gibson et al. modified the logistic model to fit bacterial growth data as follows:

\[ \log N = A + C/(1 + \exp(-B(t-M))) \]  

where \( A, C, B, \) and \( M \) are parameters and \( \exp \) is an exponential function. The modified model fits real bacterial growth curves. Similarly, they also proposed a modified Gompertz model for bacterial growth as follows:

\[ \log N = A + C/\exp(-B(t-M)) \]  

where \( A, C, B, \) and \( M \) are also parameters. Among the modified models, the modified Gompertz model has been used in predictive microbiology software programs such as Pathogen Modeling Programs (http://www.arserc.gov/mfs/) and the Food Micromodel, which are internationally well known.

Baranyi et al. reported a new mathematical model for bacterial growth. This model is a combination of the logistic model and the Michaelis–Menten model. While the Baranyi model fits real bacterial growth, it is complex and built on several hypotheses.

On the other hand, one of the most important environmental factors that affect microbial growth is temperature. The real temperatures of food products change with time between production and consumption of the products. Prediction of microbial growth at varying temperatures, therefore, is very important for practical food safety management. Several investigators have proposed models, but they have not always
been successful in predicting the influence of varying temperatures\(^{9-12}\). Growth models that can do this are urgently required for practical use.

Under these circumstances we have developed a new mathematical model for bacterial growth, based on the logistic model. In this study, we examined its utility for \textit{Escherichia coli} and \textit{Salmonella}. \textit{Salmonella} growth data were obtained from the literature\(^{5,7-10}\). We predicted \textit{Salmonella} growth at varying temperature using the new model.

**Materials and Methods**

**Cell preparation**

Bacterial strain 1952 was isolated from a food source in our laboratory and identified as \textit{Escherichia coli}\(^{14}\). Bacterial cells were activated on a freshly prepared nutrient agar plate (Nissui Pharmaceuticals, Tokyo, Japan) at 35°C for 24 hr. Cells of several well-grown colonies on the plate were inoculated in a 5-mL portion of nutrient broth (Nissui Pharmaceuticals) with shaking at 35°C and 160 strokes per min for 24 hr. Cultured cells were washed twice with 0.1 mol/L phosphate buffer, pH 7.0, with 0.005% Tween 80 by centrifugation at 6,200 \textit{g} for 10 min. Cells were finally suspended in a 5-mL portion of the buffer. This gave a cell suspension of 10\(^{10}\) CFU/mL.

**Incubation**

The cell suspension prepared above was diluted with the nutrient broth to make 104 CFU/mL. A 3.5-mL portion of the cell suspension was inoculated carefully into Pyrex test tubes, 10 mm in inner diameter 100 mm long with a screw cap, using a capillary\(^{15}\). Tubes were then allowed to stand in a test tube rack. The rack was placed in a water bath unit (DH-12, Taitec Corporation, Koshigaya, Japan) that was set at 33 or 36°C. The surface of the suspension in each test tube was 4 cm below that of the circulating water in the bath\(^{15}\). At each given interval of incubation, three test tubes were taken and cooled in ice water. The temperature of the cell suspension in test tubes was monitored using a digital thermometer (AM-7002, Anritsu Meter, Tokyo). The come-up time of the suspension temperature to a designated temperature was measured, and was about 30 sec. Immediately after the come-up time at each temperature, the initial time samples were taken.

**Cell counts**

The cell counts in the cell suspensions tested were measured with the standard plate count agar method\(^{14}\). Namely, the sample suspension was diluted with saline and incubated with the standard plate count agar (Eiken Chemicals, Tokyo) at 35°C for 48 hr. The measured cell counts of the samples were transformed to the common logarithm with base 10. Averages and standard deviations of the transformed values were then calculated.

**Growth data**

Growth data for \textit{Salmonella} were taken from the literature\(^{7,13}\). Growth data for \textit{Salmonella} under various initial conditions of pH and temperature (code 25-40) were kindly provided by Dr. Baranyi (http://www.ifr.bbsrc.ac.uk/Safety/DMFit/default.html), having being derived from Gibson et al.\(^{16}\).

**Modeling**

The new logistic model is based on the logistic model described in equation (1). It is suggested that bacterial cells during the initial period of incubation make a physiological adaptation to a new environment\(^7\) and consequently the growth rate during this period is low. To represent this, we assumed that the growth rate of bacterial cells is controlled by a factor related to the minimum cell concentration, \(N_{\min}\). Here \(N_{\min}\) is almost equal to the initial cell concentration observed (the inoculum size), \(N_0\), of the sample. That is, we assumed that the growth rate would be proportional to a term, \(1 - \frac{N_{\min}}{N}\), which is an “inverse” analog of the term \(1 - \frac{N}{N_{\max}}\) in the original logistic model (1). The growth rate of the new logistic model, therefore, is expressed as follows:

\[
\frac{dN}{dt} = rN \left(1 - \frac{N}{N_{\max}}\right) \left(\frac{1 - N_{\min}}{N}\right) \quad (4)
\]

\(c(\geq 0)\) is an adjustment factor. To keep the value of the new term positive and to avoid \(dN/dt < 0\), \(N_{\min}\) needs to be slightly smaller than \(N_0\). When \(N\) is near \(N_{\min}\) during the lag phase, the value of this new term is rather small, thus making the growth rate very low. As \(N\) increases to approach \(N_{\max}\), the value approaches zero. Consequently, the growth rate of the new model is strongly suppressed by the term \(1 - \frac{N_{\min}}{N}\) during the lag phase and by the term \(1 - \frac{N}{N_{\max}}\) during the stationary phase. In this model, thus, \(N\) increases between the two asymptotes, \(N_{\max}\) and \(N_{\min}\), with time \(t\).

**Numerical solution of the model**

Equation (4) was solved numerically with the 4-order Runge–Kutta method in this study\(^{17}\). The programming was done using spread-sheet software, Microsoft Excel '97. Parameter \(r\) was set to be a measured rate constant of growth during the exponential phase, \(k\), in an experimental curve. The value of \(k\) was calculated to be \((\ln 10) \times \text{(the slope at the exponential phase)}\). Here \(\ln\) is the natural logarithm. The slope was estimated using linear regression analysis with Excel '97. \(N_{\max}\) and \(N_0\) were the observed values of an experimental curve.

When numerically solving equation (3), the difference between \(N_{\min}\) and \(N_0\) should be very small. When the difference is great, a correlation between \(c\) and \(N_{\min}\) is observed. In this study, thus, \(N_{\min}\) was set to be \(N_{\min} = (1 - 10^{-c}) \times N_0\) for each growth curve. That is, \(N_{\min}\) was one ppm smaller than \(N_0\). Parameter \(c\) was determined as the value that minimizes the sum of the absolute
difference, SAD, between cell concentrations predicted with the new model and those observed (log unit) at the observation points.

For varying temperature, an imaginary temperature history of the test sample was input into the program for prediction. The time interval was one minute.

*Generation of the modified Gompertz curve*
Curve fitting to the modified Gompertz model (3) for experimental growth curves were done by a least-squares method. Values of parameters \( A, C, B, \) and \( M \) obtained were used to generate Gompertz curves.

*Estimation of the rate constant and the lag period*
The rate constant at the exponential phase of a curve generated with the new logistic was estimated from the slope of a linear portion of the curve using linear regression analysis with Excel '97. For a Gompertz curve, the rate constant was estimated from the slope of the linear portion (2 log units around the inflection point at time \( M \)) of the curve. For both models, the correlation coefficient of the measured linear portion was over 0.999.

The lag period of the predicted curve was estimated as the period between the initial point and the point where the regression line for the exponential phase intersects the horizontal line penetrating the initial point on the semi-logarithmic plot.

**Results and Discussion**

**Growth prediction under various initial conditions**
The new logistic model was studied for *E. coli* growth curves at different temperatures. The curves were well described using the model (Fig. 1). The modified Gompertz model also well described the growth curves (Fig. 1). The new model gave a better straight line in the exponential period than the Gompertz model; the Gompertz curves were more variable over this period. Also, the Gompertz model predicted a slightly higher maximum population at the stationary period. The values of the rate constant and the lag period estimated from the new model were closer to the observed values than those from the Gompertz model (Table 1). The value of SAD for the new model was lower than that of the modified Gompertz model (Table 1). These results demonstrate that the new model is superior to the Gompertz model for *E. coli* growth.

Similar results were found for growth data of *Salmonella* taken from the literature (Fig. 2 and Table 2).

Further we studied the new model using *Salmonella* growth data under 16 initial conditions of pH, temperature, and NaCl concentration in Tryptone soya broth that were reported by Gibson et al. All the curves were well described using the model. Two examples are shown in Fig. 3. The new model also gave better predictions for the growth curves than the Gompertz model (Fig. 3 and Table 3).

The real mechanism of the physiological adaptation of cells to a new environment during the lag period of growth is too complex to express with mathematical models at present. Therefore, a mathematical substitution (or simplification) for this period is needed in a growth model. A simpler substitution is better for numerical calculation and practical use. In the new model, the term \( 1 - N_{\text{min}}/N \), was used for mathematical substitution. In this sense, the model is not a mechanistic one. On the other hand, the growth suppression by \( N_{\text{max}} \) in the original and new logistic models is a substitute for the stationary phase. The reason for occurrence of this phase is also not fully understood, but is considered to be due to lack of nutrients and/or the accumulation of harmful wastes from cells.

Parameter \( c \) in the new logistic model was introduced...
as an adjustment factor. The parameter shifts a sigmoidal curve parallel to the time axis; as the value of the parameter is smaller, the curve shifts to the more left side, and vice versa. Thus, with a smaller value of \(c\), the model can describe a growth curve with a shorter lag period. When \(c/c_0\), the new model (equation (4)) is mathematically equivalent to the original logistic model and the Gompertz model, respectively. Values of \(c\) of the new model were (A) 0.63 and (B) 0.73.

**Table 2.** Parameter Values of the New Logistic and the Modified Gompertz Models for Growth Curves in Fig. 2

<table>
<thead>
<tr>
<th>Curve</th>
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<th>Gompertz</th>
<th>Observed</th>
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<tbody>
<tr>
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<td>0.73</td>
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<tr>
<td></td>
<td>Lag (hr)</td>
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<td></td>
<td>SAD (log)</td>
<td>2.1</td>
<td>3.1</td>
<td>—</td>
</tr>
<tr>
<td>B</td>
<td>(k) (1/hr)</td>
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<td>1.2</td>
<td>1.2</td>
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**Table 3.** Parameter Values of the New Logistic and the Modified Gompertz Models for Growth Curves in Fig. 3

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**Growth prediction at varying temperature**

Bacterial growth at varying temperature was simulated with the new logistic and the modified Gompertz models. The organism was grown in Tryptone soya broth at 20°C and pH 6.48, with 0.77% (w/v) NaCl\(^{14}\). (B) The organism was grown in egg yolk at 30°C\(^{13}\). Closed circles are experimental data. Thick and thin lines are predicted with the new logistic model and the Gompertz model, respectively. Values of \(c\) of the new model were (A) 0.63 and (B) 0.73.

**Fig. 2.** Growth curves of *Salmonella* predicted with the new logistic and the modified Gompertz models

(A) The organism was grown in Tryptone soya broth at 20°C and pH 6.48, with 0.77% (w/v) NaCl\(^{14}\). (B) The organism was grown in egg yolk at 30°C\(^{13}\). Closed circles are experimental data. Thick and thin lines are predicted with the new logistic model and the Gompertz model, respectively. Values of \(c\) of the new model were (A) 0.63 and (B) 0.73.

**Fig. 3.** Growth curves of *Salmonella* predicted with the new logistic and the modified Gompertz models

The organism was grown in Tryptone soya broth at pH 5.63, and 1.30% (w/v) NaCl\(^{14}\). The temperatures were (A) 20°C and (B) 25°C. Closed circles are experimental data. Thick and thin lines are predicted with the new logistic model and the Gompertz model, respectively. Values of \(c\) of the new model were (A) 0.64 and (B) 0.73.

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Here we assumed that \( N_0 = 4 \times 10^8 \) (CFU/mL) and \( N_{\text{max}} = 1 \times 10^9 \) (CFU/mL). Using an imaginary temperature history, a growth curve was predicted using the model, as shown in Fig. 5.

![Fig. 4. Square root analysis of the rate constant in *Salmonella* growth curves in Tryptone soya broth at pH 5.63 and 1.30% (w/v) NaCl. The temperature range was 10–30°C. Closed circles are experimental data. The straight line is a linear regression line.](image)

![Fig. 5. Prediction of *Salmonella* growth at varying temperature in Tryptone soya broth at pH 5.63 and 1.30% (w/v) NaCl. The thin line is an imaginary temperature pattern of a sample. The thick line is the growth curve predicted from the temperature pattern using the new logistic model.](image)

From these results, a growth curve in the temperature range of 15–30°C, where \( c \) was almost constant \( (0.74) \), was simulated using the model in this study. Here we assumed that \( N_0 = 4 \times 10^8 \) (CFU/mL) and \( N_{\text{max}} = 1 \times 10^9 \) (CFU/mL). Using an imaginary temperature history, a growth curve was predicted using the model, as shown in Fig. 5.

There were no experimental data on *Salmonella* growth at varying temperatures in the work of Gibson et al.\(^\text{10}\) We are now studying *E. coli* growth curves in liquid media at varying temperatures with the new logistic model. The procedures of prediction are the same as those described above. A good concordance between predicted and measured cell concentrations has been found so far. Various types of temperature pattern should be examined to validate the model. The results will be reported soon. If the new model is validated for predicting bacterial growth at varying temperature, it could be embedded into a device such as a time-temperature integrator, which predicts bacterial growth from the temperature history of a tested food.

Another type of the new model could be also derived from the original logistic model. This is described as follows:

\[
dN/dt = r N(1 - N/N_{\text{max}})(1 - (N_{\text{min}}/N))
\]

In this model, an adjusting parameter \( c \) is introduced for the fraction \( N_{\text{min}}/N \). This model shows a slightly better straight line at the beginning of the exponential period than the model in equation (4) studied here. The model in equation (5) well described *E. coli* and *Salmonella* growth curves, being similar to the new model in equation (4). Thus, both models may have the potential to accurately predict bacterial growth.

**References**


