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An Extension of a Logistic Model for Microbial Kinetics

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Abstract
In contrast to the traditional logistic model, a series of asymmetrical models have been proposed for modeling bacterial growth. These models are similar to the logistic model for the lag-phase and exponential phase of the population growth, but quite different in the stationary phase − the growth becomes remarkably slower after the inflection point. At this point, limiting factors within the population such as competition or environmental stress inhibit further exponential growth. Moreover, models as variations of the traditional exponential model are also proposed. The models presented demonstrate more general patterns and representative properties, from which relevant algorithms can be developed for calculating the population specific growth rate occurring in the exponential phase.
Keywords Maclaurin series, logistic growth, exponential growth, point of inflection, carrying capacity, specific growth rate

1 Introduction

The study of microbial kinetics is of particular significance to research in the fields of microbiology and biotechnology [1]. Although existing models and methods have been developed, an issue arises over the precision of potentially subjective, traditional methods of culture analysis. Calculating population growth rate is essential to microbial kinetic studies of substrate-culture interactions, and the introduction of a new model for population growth increases the precision of the method. Pinpointing this microbial specific growth rate, represented as μ or r, with accuracy and precision is at the heart of consistency in understanding laboratory results. Furthermore, extending calculations to model the data uses growth patterns to provide insight into characteristics of the microbe. An exploration of four models incorporates a review and extension of the traditional exponential and logistic growth function, and introduces the potential for exponential-like and logistic-like functions using a modified form of the exponential Maclaurin series.

Several models have been fit for microbial growth curves, modifications of the idealized exponential (Malthusian) and logistic (limited) growth to fit the reality of microbial patterns. Among growth models, competition models, and nutrient uptake models are included theta logistic functions, trans-theta logistic functions, time-delay logistic functions, general logistic functions. Michaelis-Menten kinetics, Gompertz, von Bertalanffy and General von Bertalanffy, Verhlust, and

Lotka-Volterra are specific cases of these models [2-11].

Exponential growth, or unlimited and ever-increasing growth, is represented by the general differential form $\frac{dP}{dt} = rP$, and its solution $P(t) = P_0e^{rt}$[8]. Logistic growth is sigmoidal and limited. It is represented by the general differential form $\frac{dP}{dt} = rP(1 - \frac{P}{M})$, and its solution $P(t) = \frac{MP_0e^{rt}}{M+P_0(e^{rt}-1)}$[8]. Previous extensions to the logistic model involve the general logistic model and the time-sensitive carrying capacity logistic model [8-11]. The general logistic model takes the differential form $\frac{dP}{dt} = rP^{\alpha}[1 - (\frac{P}{M})^{\nu}]^{\gamma}$, which is simplified to $P(t) = \frac{M}{[1+[(\gamma-1)\beta rM^{(\alpha-1)}t+[(\frac{M}{P_0})^{\beta}-1]^{(1-\gamma)}]^{1/(1-\gamma)}]^{1/\beta}}$ or $P(t) = A + \frac{M-A}{(1+Qe^{-r(t-t_1)})^{1/\nu}}$, ($t_1$ is defined as time of maximum growth, A is the value of the lower asymptote, Q is an initial condition constant, ν is a constant determining the point of inflection, and α and γ represent constant inflection value parameters) [8]. This introduces new parameters so that the curve can idealize scenarios previously considered "less ideal" by existing models. The time-varying model introduces the upper bound itself as a function of time, and it therefore cannot be definitely determined as an analytical solution. This model further complicates the function with the introduction of a variable parameter. It is represented as $\frac{dP}{dt} = rP(1 - \frac{P}{M(t)})$[11].

The introduction of a series incorporates the concept of a traditional model modified through extension. This new function is explored as a differential, and characterized by its non-integrable form. The exponential and logistic models represent the first two terms of a Maclaurin series. Previously, the remaining terms were not considered significant, and the use of a series was disregarded [8]. However, discovering and incorporating the terms as an expanded series removes inconsistencies between methods of calculation for parameters, such as rate of increase. The convergence of the series represents an ideal model, that can be characterized by the properties of several functions, and to which these functions converge. The first terms reflect its most basic exponential and logistic properties. As it continues to expand and the series converges, truncation produces a series of polynomial functions with exponential and logistic-like (sigmoidal) growth patterns. The final closed model itself appears to grow infinitely, like an exponential function, but at a slower rate, like a hyperbolic pattern. Indeed, elements of the series resemble the Taylor series expansions for the hyperbolic sine (sinh) and cosine (cosh) functions, and the geometric series hyperbolic expansion, in addition to the inherently exponential elements. The potentially hyperbolic properties connect this model to the Monod and Michaelis-Menten models [2], while they provide a basis for parametric data analysis through the function. However, it is not a distinct hyperbola because the values of $\frac{dP}{dt}$ approach infinity as P approaches infinity, without any distinct limit or asymptote.

This new series relies on the parameters of growth limit, rate of increase, and population size related through time. It is unique in that it does not introduce new factors or parameters with each additional term, but builds upon known parameters. Manipulation of the series model over its interval of convergence opens applications in both symmetrical and asymmetrical (semi-logistic) growth patterns. Analysis of the curve to the upper bound of its convergence (below and including the inflection point) produces a precise estimate for the initial takeoff of the microbe; the rotation of the existing curve and intersection of another curve are two approaches for determining the upper bound. Evaluating the series as a whole, or as an individual polynomial function at any point of truncation, allows for the ability to fit both limited and unlimited growth patterns.

The models, likewise, are consistent with numerical (nonparametric) methods for determining microbial specific growth rate [12-13]. Numerical methods analyze the data without assumption, whereas the models provide a framework for the data. Each introduces a degree of precision and understanding of the data.

2 Procedure

To determine the value of the specific growth rate numerically, an algorithm was developed to analyze the data through elimination. It removes all subjectivity and assumptions found in previous methods. The new algorithm focuses on eliminating non-significant data points. Initially, all points past the point of inflection are eliminated. This is defined as the point at which the concavity of the data changes from up to down, or the second derivative changes from positive to negative. Thus, the deceleration phase is disregarded in analyzing growth. The next step is to isolate the growth phase from the lag and acceleration phases. Further elimination is accomplished through regression. The natural logarithm of the function is taken, and the slope of the linearized function is determined from the line of best fit. Points from the left that lower the slope are eliminated, and another regression line is fitted to the remaining points. The process is repeated as the slope increases and iterations continue until either the change in slope (indicative of growth rate) is not statistically significant, or until the number of remaining points becomes too small. The slope of the regression line for the final remaining points is the specific growth rate.

3 Cases of the Series - Discussion

There are four notable models that serve appropriate data set fit. Fitting an appropriate model to the data set is critical for the most accurate approximations of data parameters and descriptions of the populations.

The most basic is the exponential model [8, 14-15]. Also known as the Malthusian model, it depicts unlimited growth. Biologically, there is no carrying capacity of the population, and it therefore multiplies infinitely. Mathematically, there is no asymptote to describe limiting factors. These may include competition, lack of nutrients, or density-dependent inhibition in the microbial population [16]. The model is represented as a direct proportion between the rate of population change and population size (Equation 1, Fig.1).

$$\frac{dP}{dt} = rP \tag{1}$$

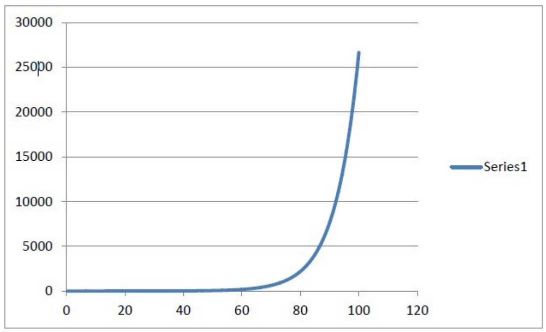

Fig.1 Graphical representation of the exponential model for microbial population growth

Of course, the simplest model given above does not reflect most biological growth systems. More appropriate models were thus explored by researcher, as stated below.

Microbial growth may be logistic [17]. This model is a special case of limited growth in which rate of population decrease mirrors rate of increase. The population grows exponentially but encounters one or more obstacles that prohibit it from increasing indefinitely. As the definite limit M approaches infinity, growth patterns approach the exponential model. Logistic growth, often used as a standard in population studies, is represented by the differential Equation 2 (see also Fig.2).

$$\frac{dP}{dt} = rP(1 - \frac{P}{M}) \tag{2}$$

The logistic growth model introduces the first two terms of a Maclaurin series that can be used to model microbial growth. Limiting the series to two terms introduces truncation error [14-15]. This error can be reduced with the introduction of additional terms. Successive terms alternate in sign, and each is smaller in value than the term it follows [14-15]. Extending the series another step produces a differential function to the fourth power of P. This function is similar to logistic growth in the lower portion of the curve, up to the point of

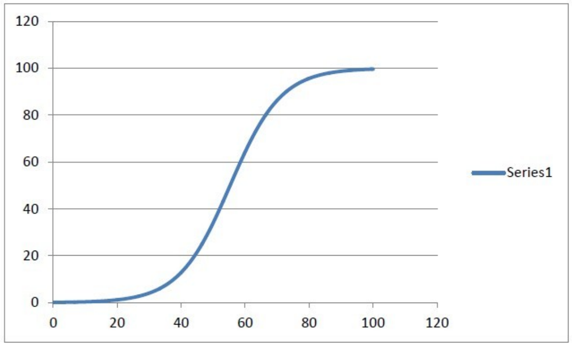

Fig.2 Graphical representation of the logistic growth model

inflection. However, the point of inflection is no longer the midpoint between the upper and lower limits of growth. Beyond the point of inflection, growth reduces rapidly and tapers until it reaches its actual limit. The population may have been subjected to extreme pressure over a short period of time, so realized growth does not reach the theoretical, ideal estimate of M. This reduced upper bound is characteristic of higher even degrees of P in the extension of the formula due to factorial growth in the denominator. The end behavior of odd degrees of P mimics exponential-like growth. The fourth-degree formula is represented as Equation 3, and its graphical interpretation as Fig.3.

$$\frac{dP}{dt} = rP - \frac{2rP^2}{M(2!)} + \frac{8rP^3}{M^2(3!)} - \frac{48rP^4}{M^3(4!)} \tag{3}$$

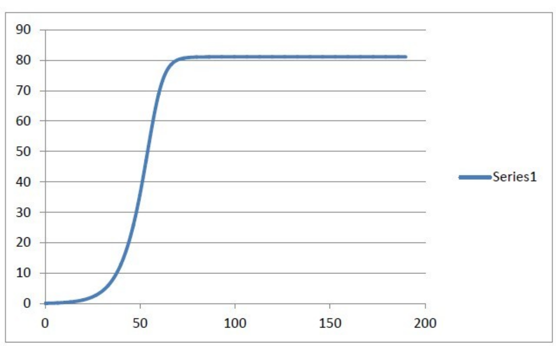

Fig.3 Graphical representation of the fourth-degree model

The most idealized model is the use of the full infinite series, represented in its closed form for precision. It states that the rate of change of the population and a function of the population size are directly proportional. The function of population size is the Maclaurin series. The function, or the series, incorporates the exponential model when M (the upper limit) approaches infinity. It incorporates the logistic model as the ideal symmetrical case in which the point of inflection is the midpoint between the upper and lower limits of growth. If the lower limit is 0, P represents population size at the point of inflection, and M represents the upper growth limit, then this is represented as $2P = M$. All of the previous models converge, as a series of overestimates and underestimates, to the model presented by the complete series. It is an exponential-like function, but its predictions for population ($P(t)$) lie between the exponential and logistic predictions. The Modified Alternating Maclaurin series is convergent for all points up to and including the point of inflection. It satisfies the conditions of the Ratio Test and Leibniz's Theorem for this domain and range [14-15]. Past the point of inflection, divergence becomes more extreme with additional terms. As a model, therefore, it accurately produces the lower portion of the curve. If the growth pattern is symmetrical, a 180^o rotation about the point of inflection projects the upper portion. If the growth is semi-logistic, it appears as portions of intersecting logistic curves, and the point of intersection is the point of inflection. In this scenario, the bottom portion of the curve is accurately described by the model (Equation 4, Fig.4).

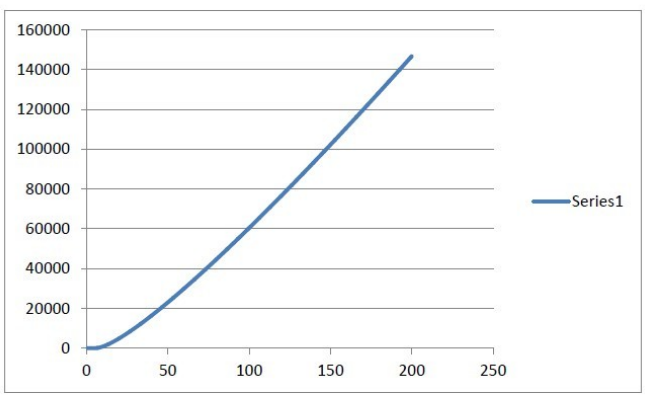

Fig.4 Graphical depiction of the Modified Alternating Maclaurin Series Model

$$\frac{dP}{dt} = \sum_{n=0}^{\infty} \frac{(-1)^n (2^n n!) r P^{n+1}}{M^n (n+1)!} \tag{4}$$

Its expanded form appears as Equation 5.

$$\begin{aligned}\frac{dP}{dt} =& rP - \frac{2rP^2}{M(2!)} + \frac{8rP^3}{M^2(3!)} - \frac{48rP^4}{M^3(4!)} + \frac{384rP^5}{M^4(5!)} - \frac{3840rP^6}{M^5(6!)} \\ &+ ... + \frac{(-1)^n(2^n n!)rP^{n+1}}{M^n(n+1)!}\end{aligned} \tag{5}$$

Its simplified form appears as Equation 6.

$$\frac{dP}{dt} = rP\sum_{n=0}^{\infty}\frac{(-1)^n}{(n+1)} \times (\frac{2P}{M})^n \tag{6}$$

Its closed form appears as Equation 7.

$$\frac{dP}{dt} = rln(1 + \frac{P}{\frac{M}{2}})^{\frac{M}{2}} \tag{7}$$

The similarities of the function to the exponential function are evident in the simplified form of the model. The factor rP represents exponential growth. In addition, the behavior of the series is similar to that of exponential growth for sufficiently small values of P ($P << 1$).

$$\frac{dP}{dt} = rln(1 + \frac{P}{\frac{M}{2}})^{\frac{M}{2}}$$

$$\frac{dP}{dt} = r \times \frac{M}{2} \times ln(1 + \frac{2P}{M})$$

$$ln(1 + \frac{2P}{M}) \approx \frac{2P}{M}$$

$$\frac{dP}{dt} = r \times \frac{M}{2} \times \frac{2P}{M} = rP$$

This property does not apply when $\frac{2P}{M}$ is greater than 1, because $ln(1+x) = x - \frac{1}{2}x^2 + \frac{1}{3}x^3 - \frac{1}{4}x^4 + ...$ holds only for $-1 < x \leq 1$.

Also like an exponential function, the graph of the population P over time is concave up, as justified by the always positive second derivative:

$$\frac{d^2P}{dt^2} = r\frac{M}{2}\frac{1}{1+\frac{P}{\frac{M}{2}}}(1 + \frac{P}{\frac{M}{2}})'_t = r\frac{M}{2}\frac{1}{1+\frac{P}{\frac{M}{2}}}\frac{1}{\frac{M}{2}}\frac{dP}{dt} = r^2\frac{M}{2}\frac{1}{1+\frac{P}{\frac{M}{2}}}ln(1 + \frac{P}{\frac{M}{2}}) > 0$$

However, the rate of growth as P approaches infinity is much slower than that of an exponential function since by limit comparison:

$$\lim_{P\to\infty}\frac{rP}{r \times \frac{M}{2} \times ln(1 + \frac{P}{M})} = \lim_{P\to\infty}\frac{2P}{M \times ln(1 + \frac{P}{M})} = \infty$$

It is known that the numerator becomes infinitely large at a faster rate than the denominator. $L'H\hat{o}pital's$ rule confirms this assertion by removing the infinite term from the function, to arrive at the definite conclusion:

$$\begin{aligned}\lim_{P\to\infty}\frac{rP}{r\times\frac{M}{2}\times ln(1+\frac{P}{M})} &= \frac{\lim\limits_{P\to\infty}(rP)'}{\lim\limits_{P\to\infty}(r\times\frac{M}{2}\times ln(1+\frac{P}{M}))'} \\ &= \frac{r}{\lim\limits_{P\to\infty}(r\times\frac{M}{2}\times\frac{\frac{1}{M}}{1+\frac{P}{M}})} = \infty\end{aligned}$$

This property is the result of the alternating series succession of positive and negative terms.

The positive and negative terms indicate the properties of the series at any point of truncation. If truncated up to an even degree of P (say up to P^{N+1} where N is odd), then the solution P has an upper bound, and an inflection point (see Theorem 2). The inflection point will always occur when $P=\frac{M}{2}$ as justified by the second derivative of $P(t)$ as follows.

$$\frac{dP}{dt}=\sum_{n=0}^{N}\frac{(-1)^n 2^n rP^{n+1}}{M^n(n+1)} \tag{8}$$

$$\frac{d^2P}{dt^2}=\sum_{n=0}^{N}\frac{(-1)^n 2^n r(n+1)P^n}{M^n(n+1)}(\frac{dP}{dt})=r(\frac{dP}{dt})\sum_{n=0}^{N}(-1)^n(\frac{2P}{M})^n \tag{9}$$

In the case $2P=M$, we have

$$\frac{d^2P}{dt^2}=r(\frac{dP}{dt})\sum_{n=0}^{N}(-1)^n$$

Hence, when N is odd, it holds that

$$\frac{d^2P}{dt^2}|_{P=\frac{M}{2}}=0$$

It follows from the Chain Rule of derivatives [14-15]:

$$\frac{d}{dt}(\frac{dP}{dt})=\frac{d}{dP}(\frac{dP}{dt})\times\frac{dP}{dt}$$

that the derivative of $\frac{dP}{dt}$ with respect to t is equal to the derivative of $\frac{dP}{dt}$ with respect to P.

The value for $\frac{dP}{dt}$ decreases at it nears its upper bound but never becomes 0. It is always positive (Theorem 3). Continued simplification of the Modified Alternating Maclaurin series and its truncations, as shown below, reveals its properties and its relationship to the form of a transcritical bifurcation.

4 Simplified Series

$$\begin{aligned}\frac{dP}{dt} &= rP\sum_{n=0}^{\infty}\frac{(-1)^n}{n+1}(\frac{2P}{M})^n \\ &= rP[1-\frac{1}{2}(\frac{2P}{M})+\frac{1}{3}(\frac{2P}{M})^2-\frac{1}{4}(\frac{2P}{M})^3+\frac{1}{5}(\frac{2P}{M})^4-\frac{1}{6}(\frac{2P}{M})^5+...]\end{aligned} \tag{10}$$

Theorem 1 For Equation (10),

(i) the closed form of the series on the right-hand side is $\frac{dP}{dt} = rln(1+\frac{P}{\frac{M}{2}})^{\frac{M}{2}}$;

(ii) it holds that $\frac{dP}{dt} > 0$ at any time t.

Proof

(i) Equation (10) is simplified to $\frac{dP}{dt} = r\sum_{n=0}^{\infty}\frac{(-1)^n 2^n P^{n+1}}{M^n(n+1)}$ (by cancelling n!). Then we have

$$\begin{aligned}\frac{dP}{dt} &= r\sum_{n=0}^{\infty}\frac{(-1)^n 2^n P^{n+1}}{M^{n+1}(n+1)} = rP\sum_{n=0}^{\infty}(-1)^n\frac{(\frac{2P}{M})^n}{n+1} = rP\sum_{n=0}^{\infty}\frac{(\frac{-2P}{M})^n}{n+1} \\ &= rP[1+\frac{x}{2}+\frac{x^2}{3}+\frac{x^3}{4}+...+\frac{x^n}{n+1}+...](\text{for } x=-\frac{2P}{M}) \\ &= \frac{rP}{x}[x+\frac{x^2}{2}+\frac{x^3}{3}+\frac{x^4}{4}+...+\frac{x^{n+1}}{n+1}+...] \\ &= \frac{rP}{x}(-1)ln(1-x) = r\frac{M}{2}ln(1+\frac{2P}{M})\end{aligned}$$

by the Taylor expansion of natural logarithm: $ln(1-x) = \sum_{n=0}^{\infty}\frac{x^n}{n}$ for $-1 \leq x < 1$. Hence, we have $r = \frac{\frac{dP}{dt}}{ln(1+\frac{P}{\frac{M}{2}})^{\frac{M}{2}}}$, and this holds whenever $-1 \leq -\frac{2P}{M} < 1$, i.e., $P \leq \frac{M}{2}$.

Thus, the closed form of the series is given by

$$\frac{dP}{dt} = rln(1+\frac{P}{\frac{M}{2}})^{\frac{M}{2}}. \tag{11}$$

(ii) This is implied by the closed form given in (i).

Theorem 2: For the following tail-truncated equation

$$\frac{dP}{dt} = rP\sum_{n=0}^{N}\frac{(-1)^n}{n+1}(\frac{2P}{M})^n \tag{12}$$

(i) If N is odd (so the highest power of P is even), then $\frac{d^2P}{dt^2}$ is positive when $P < \frac{M}{2}$, is zero when $P = \frac{M}{2}$, and is negative when $P > \frac{M}{2}$. This is an asymmetrical model.

(ii) If N is even (so the highest power of P is odd), then $\frac{d^2P}{dt^2}$ is always positive.

Since the second derivative is always positive, the first derivative is always increasing. Therefore, if the first derivative is positive initially, the first derivative is never zero or negative. (The least upper bound of P is finite and determined as described in Theorem 3.)

Proof

It has been established above that in the case $2P = M$

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\sum_{n=0}^{\infty}(-1)^n = r(\frac{dP}{dt})[1 - 1 + 1 - 1 + ...]$$

For an even number of terms, or odd N:

Case $2P = M$.

The truncation of the above equation results in an even pairing of terms that cancel out, and the derivative is equal to 0.

Case $2P < M$.

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\sum_{n=0}^{\infty}(-1)^n = r(\frac{dP}{dt})[1-(\frac{2P}{M})+(\frac{2P}{M})^2-(\frac{2P}{M})^3+(\frac{2P}{M})^4-(\frac{2P}{M})^5+...]$$

A grouping of the first 6 terms of the second derivative results in

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\Big[[1 - (\frac{2P}{M})] + [(\frac{2P}{M})^2 - (\frac{2P}{M})^3] + [(\frac{2P}{M})^4 - (\frac{2P}{M})^5]\Big] > 0.$$

Case $2P > M$.

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\sum_{n=0}^{\infty}(-1)^n = r(\frac{dP}{dt})\Big[1-(\frac{2P}{M})+(\frac{2P}{M})^2-(\frac{2P}{M})^3+(\frac{2P}{M})^4-(\frac{2P}{M})^5+...\Big]$$

A grouping of the first 6 terms results in

$$\Big[[1-(\frac{2P}{M})]+[(\frac{2P}{M})^2-(\frac{2P}{M})^3]+[(\frac{2P}{M})^4-(\frac{2P}{M})^5]\Big] < 0. \text{(each bracket is negative.)}$$

For an odd number of terms, or even N:

The truncation of

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\sum_{n=0}^{\infty}(-1)^n = r(\frac{dP}{dt})[1 - 1 + 1 - 1 + 1 - 1 + ...]$$

results in a pairing with an additional positive term that is not cancelled. So this second derivative is positive.

Case $2P < M$.

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\sum_{n=0}^{\infty}(-1)^n = r(\frac{dP}{dt})\Big[1-(\frac{2P}{M})+(\frac{2P}{M})^2-(\frac{2P}{M})^3+(\frac{2P}{M})^4-(\frac{2P}{M})^5+...\Big]$$

A grouping of the first 5 terms of the second derivative results in

$$\Big[[1-(\frac{2P}{M})]+[(\frac{2P}{M})^2-(\frac{2P}{M})^3]+(\frac{2P}{M})^4\Big] > 0.$$

Case $2P > M$.

$$\frac{d^2P}{dt^2} = r(\frac{dP}{dt})\sum_{n=0}^{\infty}(-1)^n = r(\frac{dP}{dt})\Big[1-(\frac{2P}{M})+(\frac{2P}{M})^2-(\frac{2P}{M})^3+(\frac{2P}{M})^4-(\frac{2P}{M})^5+...\Big]$$

A grouping of the first 5 terms results in

$$\Big[1+[-(\frac{2P}{M})+(\frac{2P}{M})^2]+[-(\frac{2P}{M})^3+(\frac{2P}{M})^4]\Big] > 0.$$

Theorem 3: For the above tail-truncated Equation (12),

(i) $\frac{dP}{dt}$ is always positive (i.e., the right-hand side is always positive).

(ii) When N is odd (i.e., including up to an even power of P in the partial sum), the equation $rP\sum_{n=0}^{N}\frac{(-1)^n}{n+1}(\frac{2P}{M})^n = 0$ has a unique positive solution and the supremum value of P is determined by this positive zero of the equation. Moreover, it holds that $rP\sum_{n=0}^{N}\frac{(-1)^n}{n+1}(\frac{2P}{M})^n = \frac{rM}{2}\int_0^{\frac{2P}{M}}\frac{1-x^{N+1}}{1+x}dx$. These models are all asymmetrical.

Proof

(i) If N is even, this is clearly true.

$$\text{Let} \quad g_N(x) = \sum_{n=0}^{N}\frac{(-1)^n}{n+1}x^n. \text{ Then} \frac{dP}{dt} = rP\sum_{n=0}^{N}\frac{(-1)^n}{n+1}(\frac{2P}{M})^n = rPg_N(\frac{2P}{M}).$$

Since $xg_N(x) = \sum_{n=0}^{N}\frac{(-1)^n}{n+1}x^{n+1}$, we have $(xg_N(x))' = \sum_{n=0}^{N}(-x)^n = \frac{1-(-x)^{N+1}}{1+x}$, and hence it holds that

$$\Big[xg_N(x)\Big]\Big|_0^{\frac{2P}{M}} = \int_0^{\frac{2P}{M}}\Big(xg_N(x)\Big)'dx = \int_0^{\frac{2P}{M}}\frac{1-(-x)^{N+1}}{1+x}dx,$$

implying

$$\frac{2P}{M}g_{_N}\Big(\frac{2P}{M}\Big)-0=\begin{cases}\int_0^{\frac{2P}{M}}\frac{1-x^{N+1}}{1+x}dx, \text{if } N+1 \text{ even,}\\ \int_0^{\frac{2P}{M}}\frac{1+x^{N+1}}{1+x}dx, \text{if } N+1 \text{ odd.}\end{cases}$$

Therefore,

$$\frac{dP}{dt}=rPg_{_N}\Big(\frac{2P}{M}\Big)=rP\times\frac{M}{2P}\times\frac{2P}{M}g_{_N}\Big(\frac{2P}{M}\Big)=\frac{rM}{2}\begin{cases}\int_0^{\frac{2P}{M}}\frac{1-x^{N+1}}{1+x}dx, \text{if } N+1 \text{ even,}\\ \int_0^{\frac{2P}{M}}\frac{1+x^{N+1}}{1+x}dx, \text{if } N+1 \text{ odd.}\end{cases}$$

It is obvious that $\frac{dP}{dt}=\frac{rM}{2}\int_0^{\frac{2P}{M}}\frac{1+x^{N+1}}{1+x}dx>0$ when N is even ($N+1$ is odd).

Next we consider the case that N is odd (or $N+1$ is even). It follows from the above proof that $\frac{dP}{dt}=\frac{rM}{2}\int_0^{\frac{2P}{M}}\frac{1-x^{N+1}}{1+x}dx$. When $P\le\frac{M}{2}$ ($\frac{2P}{M}\le 1$), $\frac{dP}{dt}$ is positive because $1-x^{N+1}$ is always positive except at the single point $x=\frac{2P}{M}$, at which $1-x^{N+1}$ is zero. We claim that $\frac{dP}{dt}$ never becomes 0. In fact, if $\frac{dP}{dt}$ becomes 0 at some infimum time t_0, it must strictly be after the time at which the inflection point occurs. (At this point, $\frac{dP}{dt}$ changes from positive with upward concavity and begins to decrease. The value of the integral, likewise, begins to decrease after the shift in $\frac{dP}{dt}$ at this point, corresponding to the concavity, but the value still must be positive. It follows that $\frac{dP}{dt}$ cannot be 0 at the inflection point.) Since $\frac{d^2P}{dt^2}$ is still negative at t_0, $P(t)$ by definition would have attained its local maximum $P(t_0)$ (at a specific $P(t_0)>\frac{M}{2}$). Now, let t_1 be a nearby point of t_0, on the right of t_0 such that $\frac{M}{2}<P(t_1)<P(t_0)$. (Since $\frac{dP}{dt}|_{t=t_0}=0$ and $\frac{d^2P}{dt^2}<0$ after $t=t_0$, $\frac{dP}{dt}$ is negative after $t=t_0$). Then the result would become $0=\frac{dP}{dt}|_{t=t_0}=\frac{rM}{2}\int_0^{\frac{2P(t_0)}{M}}\frac{1-x^{N+1}}{1+x}dx<\frac{rM}{2}\int_0^{\frac{2P(t_1)}{M}}\frac{1-x^{N+1}}{1+x}dx=\frac{dP}{dt}|_{t=t_1}$, a contradiction. Because the value of $P(t_1)$ is less than the value of $P(t_0)$, the inequality is inconsistent with the fact that $\frac{dP}{dt}$ at t_1 must be negative. Hence, $\frac{dP}{dt}$ never reaches 0, and it follows from the continuity of $\frac{dP}{dt}$ that $\frac{dP}{dt}$ can never be negative. Therefore, $\frac{dP}{dt}$ is always positive.

Proof of (ii) - Method for determining the supremum of P: Let us illustrate the method using two (logistic), four, or six terms.

If $N=1$, $N+1=2$ (the traditional logistic model), then $\frac{dP}{dt}=...=rP(1-\frac{P}{M})$. Hence, $\frac{dP}{dt}>0$ if and only if $P<M$. Observe that if P could exceed M, then $\frac{dP}{dt}$ would become negative and consequently P would be immediately lowered making $\frac{dP}{dt}$ positive. Therefore, $\frac{dP}{dt}$ is always positive. Again, continuity indicates that $\frac{dP}{dt}$ must reach and cross through a point of 0 slope to become negative, which is impossible.

If $N = 3$, $N+1 = 4$ (four terms), then $\frac{dP}{dt} = \frac{rM}{2}\int_0^{\frac{2P}{M}} \frac{1-x^4}{1+x}dx = rP(1 - \frac{1}{2}\frac{2P}{M} + \frac{1}{3}(\frac{2P}{M})^2 - \frac{1}{4}(\frac{2P}{M})^3)$. The equation $1 - \frac{1}{2}x + \frac{1}{3}x^2 - \frac{1}{4}x^3 = 0$ has a real solution 1.621. For example, this gives the maximum of P as 81.05, assuming $M = 100$.

If $N = 5$, $N+1 = 6$ (six terms), then $\frac{dP}{dt} = \frac{rM}{2}\int_0^{\frac{2P}{M}} \frac{1-x^6}{1+x}dx = rP(1 - \frac{1}{2}\frac{2P}{M} + \frac{1}{3}(\frac{2P}{M})^2 - \frac{1}{4}(\frac{2P}{M})^3 + \frac{1}{5}(\frac{2P}{M})^4 - \frac{1}{6}(\frac{2P}{M})^5)$. The equation $1 - \frac{1}{2}x + \frac{1}{3}x^2 - \frac{1}{4}x^3 + \frac{1}{5}x^4 - \frac{1}{6}x^5 = 0$ has a real solution 1.462. This gives the maximum of P as 73.1, assuming $M = 100$.

Generally, for any odd N, $\frac{dP}{dt}$ is always positive, and the supremum value of P is determined by a positive real solution (that exists uniquely) of the equation $\frac{dP}{dt} = \frac{rM}{2}\int_0^{\frac{2P}{M}} \frac{1-x^{N+1}}{1+x}dx = rP\sum_{n=0}^{N} \frac{(-1)^n}{n+1}(\frac{2P}{M})^n$. The supremum values decrease as N is increased. $rP\sum_{n=0}^{N} \frac{(-1)^n}{n+1}(\frac{2P}{M})^n = \frac{rM}{2}\int_0^{\frac{2P}{M}} \frac{1-x^{N+1}}{1+x}dx$ cannot be zero when $P \leq \frac{M}{2}$; the equation $\sum_{n=0}^{N} \frac{(-1)^n}{n+1}x^n = 0$ does not have a solution less than 1 (hence divergence as the partial series extends to infinite form). $\int_0^{\alpha} \frac{1-x^{N+1}}{1+x}dx > 0$ if $\alpha \leq 1$ and $\int_0^{\beta} \frac{1-x^{N+1}}{1+x}dx < 0$ if β is (sufficiently) large. There exists γ between α and β such that $\int_0^{\gamma} \frac{1-x^{N+1}}{1+x}dx = 0$; $\int_0^{\alpha} \frac{1-x^{N+1}}{1+x}dx > \int_0^{\beta} \frac{1-x^{N+1}}{1+x}dx$ for $\alpha \leq 1 < \beta$. More precisely, an arbitrary α beyond the point of inflection presents a scenario that is consistent with the definition of a maximum point and downward concavity in this domain.

Hence, the equation

$$\sum_{n=0}^{N} \frac{(-1)^n}{n+1}x^n = 0 \tag{13}$$

has a unique positive solution x_0. The formula for calculating the supremum of P is $P_{sup} = x_0 P = x_0 \frac{M}{2}$.

In summary, each term is smaller than the term preceding it until P is equal to the least upper bound. At $P = \frac{M}{2}$, $\frac{dP}{dt}$ has reached its maximum value and will decrease but will still be positive, so the negative terms cannot be larger than the positive terms before them. The slopes remain positive and decrease as $\frac{dP}{dt}$ approaches 0 at the least upper bound without ever reaching it. Therefore, $\frac{dP}{dt}$ will always be positive despite negative concavity (reduction in value) past the point of inflection, and the limit of $\frac{dP}{dt}$ as P approaches a set of arbitrary values reveals an approximation of the least upper bound of the function. If the limit reveals that $\frac{dP}{dt}$ is less than 0 at a particular value of P, then the least upper bound is below that value; the value can never be reached. At the upper limit, a horizontal asymptote, $\frac{dP}{dt}$ is 0. Therefore, $\frac{dP}{dt}$ approaches this value at the transition from a small positive value to a small negative value. When limit comparison reveals that one value results in a positive $\frac{dP}{dt}$ and the next value for P results in a negative $\frac{dP}{dt}$, the bound must lie between these two points. In the logistic case, this limit is M.

By contrast, a function with an odd degree of P resembles the properties of an exponential function. It is concave up as well as always increasing; the sum of the alternating terms is positive, plus the addition of a positive term. It has neither a point of inflection nor an upper bound. In terms of the second derivative defined above, the incomplete pairings ensure positive concavity (Theorem 2).

The series and its truncations can be analyzed as a transcritical bifurcation [18]. The concept of "harvesting", initially applied to logistic growth, remains. For even degrees of P, the model exhibits logistic-like properties and therefore the potential for two positive zeros. In logistic growth (power of P is 2), zeros are found as the solutions to a simplified, basic quadratic form of the equation. In the general situation (power of P is even and larger than or equal to 4), by the integral representation given in Theorem 3 (ii), $\frac{dP}{dt} = 0$ has two positive zeros, one positive zero, or no positive (real) zeros. Such zeros in the forms of the series can be determined by utilizing numerical methods. As the degree increases, the amount of symmetry as found in logistic models decreases. As the number of terms in the polynomial increases, and approaches the closed form of the series, the equation becomes increasingly complex to solve.

In this parametric approach, fixed points are determined as the variable values that set the equation at equilibrium. A harvesting term introduces a parameter that affects the location of such points, and their position for approaching or separating from one another as the differential increases or decreases.

The equation for transcritical bifurcation is as follows (Equation 14):

$$\frac{dP}{dt} = rP\sum_{n=0}^{\infty} \frac{(-1)^n}{n+1} \times (\frac{2P}{M})^n - H \tag{14}$$

Because the model is idealized, it can be used as a method to solve for rate of growth. Such calculations are consistent with the numerical estimates. Like theta logistic models, this model introduces precision through specific terms added to the traditional logistic model. It is unique in that it achieves this precision without the introduction of new parameters and accounts for lack of symmetry (semi-logistic scenarios) through the model itself rather than a term in the formula. This form of the series is appropriate to solve for growth rate of any indicator (Equation 15):

$$\mu = r = \frac{\frac{dP}{dt}}{\sum_{n=0}^{\infty} \frac{(-1)^n (n!2^n) P^{n+1}}{M^n (n+1)!}} \tag{15}$$

Closed form of the series (Equation 16):

$$r = \frac{\frac{dP}{dt}}{\frac{M}{2}ln(1+\frac{2P}{M})}. \tag{16}$$

Consider that: $ln(1+\frac{2P}{M}) = ln(2)$ when $M = 2P$.

The Modified Alternating Maclaurin Series accurately models the data as it converges, over the domain of initial data collection to the point of inflection P. The model converges with the condition that $P \leq \frac{M}{2}$. The applicability of the Maclaurin series as a method for determining growth rate is categorized as one of three cases, based on the relationship between P and M.

The following procedure applies for the first case of the Modified Alternating Maclaurin Series: if data is symmetrical (ideally logistic) and $P = \frac{M}{2}$.

1) The y-coordinate of the point of inflection (value substituted for P) is the midpoint between the upper and lower limits of growth (asymptotes). It is calculated as lower limit + (1/2) (upper limit - lower limit).

2) $\frac{dP}{dt}$ represents change in population (growth) over time. It should reach its maximum value at the point of inflection. $\frac{dP}{dt}$ should therefore reflect the change at the point of inflection as a tangent line. It is determined more precisely as the mean value of the rates of change surrounding the point of inflection. For even greater precision, arbitrary ranges chosen to include the point of inflection can be averaged and compared; the greatest value among these is taken as $\frac{dP}{dt}$.

3) M is the upper limit of growth. It is identified as a horizontal asymptote.

4) Values for P, $\frac{dP}{dt}$ and M are substituted into the series to solve for r (μ).

Example of the First Case :

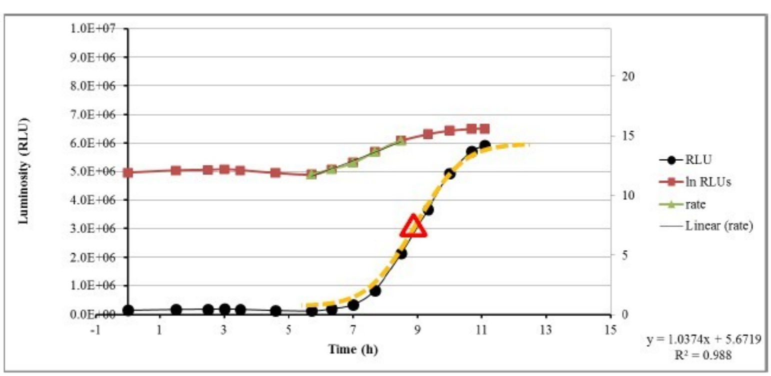

Fig.5 Graphical traditional method: μ=1.0374

Graphical Traditional Method: μ=1.0374
Maclaurin Series Method:
$P = 3; \frac{dP}{dt} = 2.2; M = 6$
$\mu = 1.0580$
Error (disparity between the methods): 1.99 %

The following procedure applies for the second case of the Modified Alternating Maclaurin Series: if the point of inflection is less than half of the carrying capacity, or $P < \frac{M}{2}$.

1) The y-coordinate of the point of inflection (value substituted for P) is less than the midpoint between the upper and lower limits of growth (asymptotes). It is calculated as the point in the center of the range of maximum change in population over time (largest values of $\frac{dP}{dt}$). When averages are taken for $\frac{dP}{dt}$, P should be at or near the center of the range.

2) $\frac{dP}{dt}$ represents change in population (growth) over time. It should reach its maximum value at the point of inflection. $\frac{dP}{dt}$ should therefore reflect the change at the point of inflection as a tangent line. It is determined more precisely as the mean value of the rates of change surrounding the point of inflection. For even greater precision, arbitrary ranges chosen to include the point of inflection can be averaged and compared; the greatest value among these is taken as $\frac{dP}{dt}$.

3) M is the upper limit of growth. It is identified as a horizontal asymptote.

4) Values for P, $\frac{dP}{dt}$, and M are substituted into the series to solve for r (μ).

5) Because P is low with respect to M, convergence of the series occurs more rapidly than in the symmetrical first case. The result is more precise at a smaller number of terms.

Example of the Second Case :

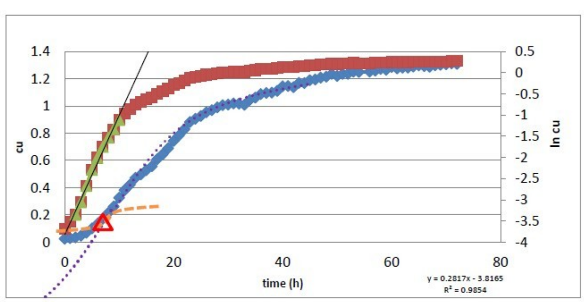

Fig.6 Graphical traditional method: μ=0.2817

Graphical Traditional Method: μ=0.2817

Maclaurin Series Method:
$P = 0.15; \frac{dP}{dt} = 0.04; M = 1.3$
$\mu = 0.2964$
Error (disparity between the methods): 5.22 %

The following procedure applies for the third case of the Modified Alternating Maclaurin Series: if the point of inflection is greater than half of the carrying capacity, or $P > \frac{M}{2}$.

1) The y-coordinate of the point of inflection (value substituted for P) is greater than the midpoint between the upper and lower limits of growth (asymptotes). It is calculated as the point in the center of the range of maximum change in population over time (largest values of $\frac{dP}{dt}$). When averages are taken for $\frac{dP}{dt}$, P should be at or near the center of the range.

2) $\frac{dP}{dt}$ represents change in population (growth) over time. It should reach its maximum value at the point of inflection. $\frac{dP}{dt}$ should therefore reflect the change at the point of inflection as a tangent line. It is determined more precisely as the mean value of the rates of change surrounding the point of inflection. For even greater precision, arbitrary ranges chosen to include the point of inflection can be averaged and compared; the greatest value among these is taken as $\frac{dP}{dt}$. Furthermore, the use of means contributes to the robustness and applicability of the symmetrical case.

3) M is the upper limit of growth. It is identified as a horizontal asymptote. In this case, use of the horizontal asymptote results in divergence of the series. Therefore, ratios are implemented to calculate r or μ. Let the horizontal asymptote be denoted as M_0. Set M_1, an alternate limit, as equal to $2P$.

4) Values for P, $\frac{dP}{dt}$, and M_1 are substituted into the series to solve for r (μ). The series converges as in the symmetrical first case.

5) The use of M_1 results in an inflated value for r (μ). To account for the substitution of M_1, the result of the series is divided by the value of $\frac{M_1}{M_0}$.

Example of the Third Case :
Graphical Traditional Method: μ=0.1704
Maclaurin Series Method:
$P = 0.38; \frac{dP}{dt} = 0.05; M_0 = 0.61; M_1 = 0.76$
$\mu = 0.1523$
Error (disparity between the methods): 10.62 %

5 Limitations

Irregular data is the greatest limitation to any method of determining microbial kinetics. Environmental factors such as pH inconsistency, culture contamination,

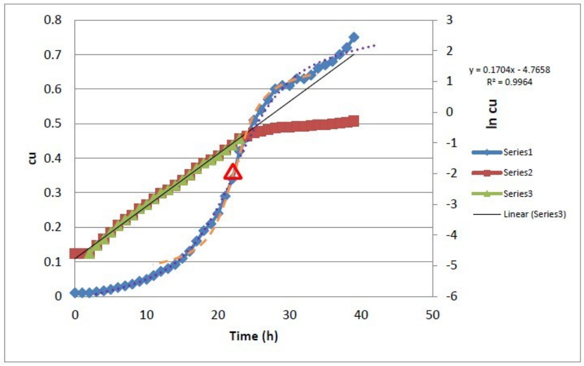

Fig.7 Graphical traditional method: μ=0.1704

or other laboratory error introduce complications to the data [16]. Furthermore, microbial cultures are inherently not ideal. The use of an ideal model provides a basis of comparison by which inconsistencies may be determined. A numerical method strictly relies upon the data. However, irregular data will produce an irregular result. Neither method will produce an accurate or precise estimate. The expansion of the Maclaurin series is currently under investigation to extend the model beyond the point of inflection. Successful extension would eliminate divergence as a limitation to the microbial growth model and its applications.

6 Conclusion

Microbial growth kinetics is the numerical analysis of a complex living system. A data-based approach is significant as it determines microbial growth rate through a procedure designed to fit the data exactly. The use of models is essential to understanding the population structure through the relationship of population, population growth rate, carrying capacity, and time. Population, and the population growth rate, change as a function of time. The models relate this through direct variation and a more complex function. The explored models are built upon exponential and logistic growth, and related through the transcritical bifurcation. Each model is unique in its ability to predict and determine the growth of a particular microbe. Culturing technique is also a factor in that it imposes or prevents natural limiting factors. Batch cultures, and secondary metabolite fed batch, for example, display a pattern that may fall into the logistic, the symmetrical series, or the fourth-degree model. Primary metabolite and continuous cultures tend towards exponential-like growth patterns, as modeled by exponential growth or the closed form of the Modified Alternating Maclaurin Series. For calculations using these models, the point of manipulation of culture conditions represents the point of environmental change, indicated graphically as the point of inflection. In full expansion, the discussed models converge to the curve of the Modified Alternating Maclaurin Series, up to the point of inflection. The partial curve is precise for this domain and range, and presents a scenario of semi-logistic analysis - viewing the growth curve as the intersection of separate curves. In all cases, the models can be solved for the microbial specific growth rate, and yield precise results consistent with traditional methods of analysis.

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