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International Journal of Food Microbiology 57 (2000) 183–192

INTERNATIONAL JOURNAL OF
Food Microbiology

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# Predictive microbiology and food safety

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Received 11 October 1999; received in revised form 24 January 2000; accepted 8 February 2000

**Abstract**

The evaluation of risk in food safety requires knowledge of the probability that microbial population sizes will not exceed defined levels. This probability is evaluated assuming that the growth of the microbial population can be described by the Gompertz equation with the variance of growth depending on the population size. It is shown that the probability density associated with this phenomenon is skewed, so that the risk of a high microbial population is greater than that which would be estimated using a symmetrical probability distribution such as the Gaussian. Maximum likelihood estimates of the parameters of the Gompertz equation based on the derived probability density are calculated using data published by Zwietering et al. [23] for the growth of *Lactobacillus plantarum* under different temperatures. The probability that a microbial population of a given size will exceed an unacceptable level within a given time is calculated for growth at two temperatures, 10 and 25°C. The implication of these theoretical results for the management of risk in food safety and in the design of hazard analysis critical control point procedures is discussed. 

*Keywords:* Modelling; Population size; Probability distributions

## 1. Introduction

Models that describe the growth of a population of micro-organisms form the basis for adopting strategies for food safety. The goal of a model is to predict when, and under what circumstances, microbial numbers might grow to a level that may threaten human health. A recent review of these issues has been published by Skinner et al. (1994). A good model of microbial growth is also an advantage for the construction of hazard analysis critical control point (HACCP) procedures for food safety.

Various workers (e.g. Ratkowsky et al., 1983; Zwietering et al., 1994a,b; Rosso et al., 1995; Wijtzes et al., 1995; Henk et al., 1997 and Ganzle et al., 1998) have proposed a variety of deterministic models, in the form of algebraic curves, describing microbial growth in response to environmental factors (temperature, pH, salinity etc.). Generally these models are based on variations of the Gompertz, Logistic or Richards models, with the different environmental effects being expressed through changes in the equation parameters. In this paper we have chosen to work with the Gompertz growth law

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0168-1605/00/$ – see front matter 
PII: S0168-1605(00)00265-8

recommended by Zwietering et al. (1990) on the basis of their experience.

An alternative approach is to formulate the interactions driving the growth of the population of interest into a differential equation (Van Impe et al., 1992). The solution of this equation with given initial conditions gives the growth curve of the population. In most cases the models referred to above can be formulated in dynamical form as differential equations (the differential equation describes the growth rate as a function of the current state). These models are generally more interpretable biologically. It also provides the scope to naturally include additional factors driving the growth at each time point that cannot be done using algebraic equations, which are integrated forms of the underlying differential equations.

All the above models are deterministic (ignore random effects), and aim to estimate the average growth rate of the microbial population, but this average is insufficient to judge the risk related to variation in the growth curves. This variation in growth requires random elements to be included in the model. Then quantitative risk is calculated from the probability density function associated with each point on the growth curve of interest (Vose, 1998). For example, if the consequences of unacceptable levels of micro-organisms in a food are grave, then knowledge only of the mean population growth of the microbes is unlikely to be a sufficient basis for management decisions. A better approach might be to base food safety strategies on the 99% or higher quantiles of the probability frequency distribution of the microbial population size. That is, when the consequences of something happening are grave, one would wish to find a strategy to reduce the probability of occurrence to an acceptable level. If the acceptable level of probability is 0.01, then the 99% quantile of the probability density describing the process must be calculated. To do this the probability density of the process must be known.

Uncertainty issues have been raised in predictive microbiology by several authors (Schaffner, 1994; Ross and McMeekin, 1999). However, invariably the approach has been to assume that deviations about the mean function follow a given form of probability distribution. For example, Ratkowsky et al. (1996) considered gamma and inverse Gaussian probability densities to be suitable models for deviations of aspects of microbial growth based on inferences about the mean variance relationships observed. Baranyi (1998) assumed that the individual cell lag times followed an exponential distribution, and from this calculated the lag time of the microbial population. The accuracy of this method will depend on how well the assumed probability distribution models the deviations of the microbial population from the mean value.

The approach in this paper is different. We consider how various perturbations, due to fluctuations in temperature, pH, water activity etc., effect the growth of a microbial population and the frequency with which different population sizes are achieved. It is natural to introduce this uncertainty by assuming that the coefficients of the differential equations are subject to variation, reflecting the variation experienced by the microbial population. This formulation is a more natural description of the biology than assuming a form for the probability distribution a priori. Furthermore, in this method the form of the probability density is not constrained to be of the same type (e.g. Gaussian) throughout the growth of the microbial population. Such an assumption may conflict with the nonlinear interactions driving the population growth process.

This paper describes the evolution of the probability density function for the growth of a microbial population using the Gompertz equation as the basis of growth. A similar approach could be taken for any of the other equations used to describe microbial population growth.

## 2. The model

Zwietering et al. (1990) modified the Gompertz equation so the parameters had a biological interpretation. Let the size of the microbial population at time $t$ be $y$. Then

$$y = y^* \exp\left\{ -\exp\left[ \frac{\mu_m \exp(1)}{y^*}(\lambda - t) + 1 \right] \right\} \qquad (1)$$

The parameters are the asymptotic value, $y^*$, the maximum specific growth rate, $\mu_m$, and the lag period, $\lambda$. The maximum specific growth rate is defined as the slope of the growth curve at the point of inflexion. The lag period is defined as the intersec-

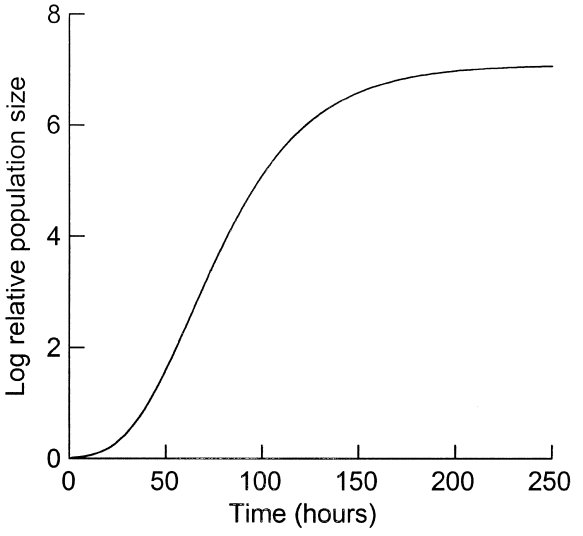


Fig. 1. Deterministic Gompertz curve of the log relative population size over time for *Lactobacillus plantarum* growing at 10°C.

tion of the line defining the maximum specific growth rate with the time axis. Eq. (1) is plotted in Fig. 1.

The Gompertz Eq. (1) describing population growth is the solution of the following differential equation

$$\frac{dy}{dt} = ay(\ln y^* - \ln y) \tag{2}$$

where $a = \mu_m \exp(1)/y^*$. Eq. (1) has one more parameter than Eq. (2), and it might appear that there is more information in Eq. (1) than in Eq. (2), in particular it might seem that information about the lag period, $\lambda$, does not appear in Eq. (2). However, the solution of Eq. (2) depends on the initial conditions of microbial population, which restores the necessary information. The lag phase, $\lambda$, is related to the initial condition $y_0$ of Eq. (2) by

$$\lambda = \frac{1}{a}\left[\ln\ln\left(\frac{y^*}{y_0}\right) - 1\right]$$

This relationship is found by equating the solution of Eq. (2) with initial condition $y_0$ to Eq. (1).

The parameter $y_0$ is the log of the initial relative population size $y_0 = y(t=0) = \ln[N(t=0)/N_0]$. It is convenient when modelling the growth of microbial populations to express the size of the population ($N$) relative to some reference population ($N_0$). This variable is dimensionless, so the logarithm is defined. The logarithm of this ratio is used to avoid dealing with a large range of numbers, i.e. in Eqs. (1) and (2) $y = \ln(N/N_0)$.

The reference population, $N_0$, cannot be taken as the initial size of the population because then the initial log of the relative population size would be equal to zero, and no growth could occur. This problem has been discussed by Van Impe et al. (1992) who noted the inconsistency of using $y_0 = 0$ in Eq. (1). Thus, $N_0$ (or equivalently $y_0$) must be treated as another parameter of the differential Eq. (2). The lag time, which depends on the initial physiological state of the population, is naturally incorporated into the description of the population growth by Eq. (2) through the initial conditions. In this sense, $N_0$ confounds the size of the initial population with the activity of this population.

A microbial population may evolve along an infinite number of pathways due to various perturbations disturbing population growth. We consider the situation where fluctuations are rapid compared with the macroscopic time scale of the model (Eq. (2)) defined by $1/a$. These perturbations may arise due, e.g. to fluctuations in an external factor such as temperature or relative humidity operating at a faster scale than the time scale of the model abstraction. Other influences would be changes in pH, which is an intrinsic factor, associated with microbial growth itself. The interaction of these fluctuations with the nonlinear dynamics of population growth gives rise to a number of possible growth paths. That is, we assume that such fluctuations have an influence on the growth of the population, and that the effect of these fluctuations does depend on the state of the system.

Therefore, the growth of a microbial population should be described by a stochastic process $Y_t$ which obeys the stochastic differential equation

$$dY_t = aY_t(\ln y^* - \ln Y_t)dt + B(Y_t,t)dW \tag{3}$$

The function $B(Y_t,t)$ describes the instantaneous random variation in the growth of the log of the relative population size, and $dW$ is a Wiener process, i.e. a Gaussian distributed random process with zero mean, independent increments and variance proportional to time. For further explanation Arnold and Lefever (1981) and Horsthemke and Lefever (1984)

discuss stochastic differential equations in biology and interpret the Wiener process in a biological context.

We assume that the fluctuations affect the system through the growth rate of the population. In general, the appropriate function for the amplitude of the population growth rate noise can be determined statistically by testing various alternatives using measurements on changes of the population through time. In this case $B(Y_t,t)$ is a linear function of $Y_t$, and Eq. (3) becomes

$$dY_t = aY_t \ln\left(\frac{y^*}{Y_t}\right)dt + \sigma Y_t dW \tag{4}$$

The $\sigma$ in Eq. (4) refers to the amplitude of the noise in the change of the population. It does not describe the variance of the population size at any time of the population evolution. The population coefficient of variation for the stochastic Gompertz equation actually decreases as the population evolves as shown in Soboleva and Pleasants (1999).

Eq. (4) is the basis for our calculation of the probability distribution of microbial growth. Since the increase in a microbial population through cell division is an intrinsically discrete process in time, we follow the Ito interpretation (Arnold and Lefever, 1981) of the stochastic differential Eq. (3).

It is important to understand the phenomenology of Eq. (4). The equation describes an average drift in population growth, given by the deterministic part, which is the usual Gompertz equation. However, this drift is perturbed by random elements, and the size of these perturbations depends on the current size of the microbial population. Each sequence of random events incorporated into Eq. (4) describes one path or realisation of population growth. The ensemble of such paths forms the multivariate probability density of the population size at any time. The main feature of this approach using stochastic differential equations is that the uncertainty inherent in population growth is incorporated into the dynamics rather than being added after integration of the differential equation, i.e. the deviations are intrinsic to, rather than independent of the modelled growth.

An expression for the probability density for the process defined by Eq. (4) can be found explicitly if the initial population size is known. Let the probability that the log of the relative microbial population size is $y$ at time $t$ be $P(y,t)$, and the log of the relative population size at time $t = 0$ be $y_0$. Then the probability density given in Appendix A is

$$P(y,t) = \frac{1}{y\sigma\sqrt{\pi/a(1-e^{-2at})}} \cdot \exp\left(-\frac{a(\ln y - \ln y^* + (\sigma^2/2a) - e^{-at}\ln y_0)^2}{\sigma^2(1-e^{-2at})}\right) \tag{5}$$

The evolution of this probability density through time is illustrated in Fig. 2. The probability density for the relative population size $x = N_t/N_0$ follows:

$$P(x,t) = \frac{1}{x\sigma\ln x\sqrt{\pi/a(1-e^{-2at})}} \times \exp\left[-\frac{a\left(\ln\ln x - \ln y^* + \frac{\sigma^2}{2a} - e^{-at}\ln y_0\right)^2}{\sigma^2(1-e^{-2at})}\right] \tag{6}$$

where $y_0 = \ln N(t=0)/N_0$.

The situation is different if only the probability density of the initial condition (which includes knowledge of both population size and previous history, see above) is known. In this case the solution

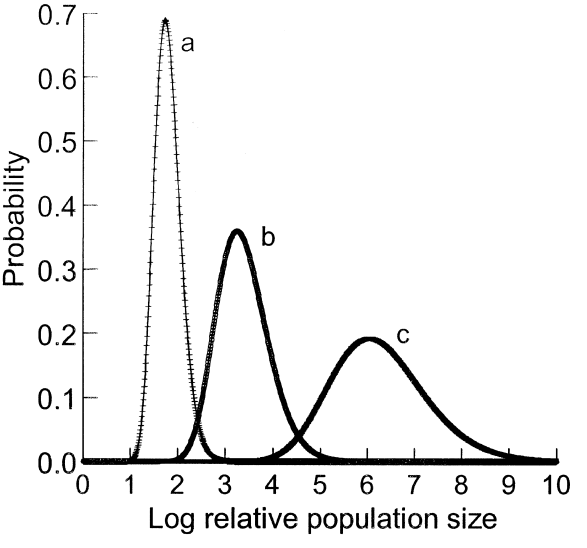


Fig. 2. Evolution of the probability density through time for the log relative population size of *Lactobacillus plantarum* at 10°C calculated at 20 h (a), 100 h (b) and 200 h (c) after inoculation.

takes a more complex form involving an infinite series of Hermite polynomials. Nevertheless, the steady state solution when the population size reaches an asymptote is the same in both cases (Appendix A).

Because population growth is a random process, a dangerous population size may be reached with a given probability in a given time. In terms of calculating the food safety risk, the relevant problem is to determine the probability that an initial small population of microbes will reach the exponential phase of growth, and then grow to dangerous numbers. The average time it takes a population of given size to grow to another particular population size is called the mean first passage time. The calculation of the first passage time for a population growing according to the Gompertz law is given in Appendix B.

## 3. Materials and methods

The probability density (5) related to the stochastic differential Eq. (4) given a log initial relative population size can be used to derive maximum likelihood estimates of the parameters. The parameters to be estimated are the rate, $a$, the degree of the random perturbations, $\sigma$, the log maximum population size, $y^*$, and the log initial population size, $y_0$.

The data set published by Zwietering et al. (1994b) for the growth of the bacteria *Lactobacillus plantarunum* over four different temperatures was used to obtain estimates for the parameters of Eq. (4) by maximum likelihood based on the probability density (Eq. (5)). These data were combined from ten growth curve realisations at each temperature.

The form of the function *B(Y,t),* describing the instantaneous fluctuations, is chosen to be proportional to the size of the population, i.e. $\sigma Y$ in Eq. (4). Other forms of this function shown in Table 1 were tested by fitting the stochastic differential equation directly using a numerical solution (Kloeden and Platen, 1992) and comparing the residual sum of squares. The numerical solution of stochastic differential equations must deal with issues involved with the definition of the stochastic differential. This introduces complications not present in the numerical solution of deterministic differential equations. Kloeden and Platen (1992) explain these issues.

Table 1
Residual standard deviations for each growth curve for different choices of the variance function in Eq. (4)

| Temperature (°C) | Residual standard deviations | | |
|---|---|---|---|
| Variance function | $\sigma Y_t^2$ | $\sigma Y_t$ | $\sigma\sqrt{Y_t}$ |
| 10 | 1.49 | 1.13 | 1.49 |
| 15 | 0.82 | 0.81 | 0.82 |
| 20 | 0.43 | 0.42 | 0.75 |
| 25 | 0.53 | 0.44 | 0.74 |

To justify the proportional form adopted for the variance function in Eq. (4) function forms ranging from $Y^2$ to $Y^{-1}$ were fitted to the data of Zwietering et al. (1994b), and the likelihoods compared.

## 4. Results and discussion

The form of the variance function $\sigma Y_t$ fitted each of the data sets of Zwietering et al. (1994b) better than the other function forms. The residual standard deviations are given in Table 1. The estimates of the parameters using Eq. (4) as the stochastic model of population growth are given in Table 2. This estimation shows that the parameters $a$ and $y^*$ responded to changes in the temperature.

The estimate of the parameter $y_0$ is confounded by the actual initial population size of the microbes ($N$) and the nature of the reference population $N_0$. This estimate is also affected by the previous history of the microbial population, i.e. whether the initial population was derived from the exponential phase of growth or from the asymptotic (stationary) phase of growth.

The plots in Fig. 3 illustrate the difference between a model based on the usual deterministic

Table 2
Maximum likelihood estimates of the parameters of the stochastic Gompertz Eq. (3) from probability density (4) for the growth of *Lactobacillus plantarum* at 10, 15, 20 and 25°C

| Temperature (°C) | $a$ ($h^{-1}$) | $y^*$ | $\sigma$ | $y_0$ | $\mu_m$ ($h^{-1}$) | $\lambda$ (h) |
|---|---|---|---|---|---|---|
| 10 | 0.031 | 7.06 | 0.041 | 0.009 | 0.081 | 28.31 |
| 15 | 0.055 | 9.50 | 0.052 | 0.014 | 0.214 | 15.91 |
| 20 | 0.141 | 9.21 | 0.030 | 0.001 | 0.475 | 8.59 |
| 25 | 0.151 | 9.90 | 0.046 | 0.006 | 0.548 | 6.64 |

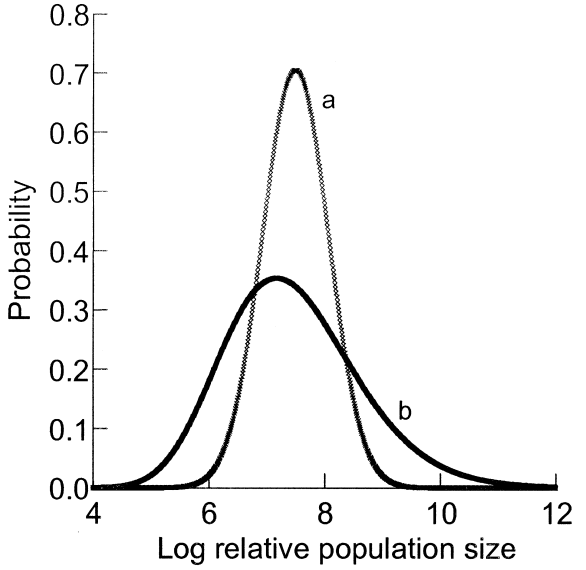


Fig. 3. Probability density at the maximum population size for *Lactobacillus plantarum* growing at 10°C. Fitting data to the Gompertz Eq. (1) by non-linear regression and assuming Gaussian distributed residuals. (b) Fitting Eq. (5), developed from stochastic differential Eq. (4). Note the difference in the modes and the tails of the probability distributions.

approach and the stochastic approach adopted here using estimates of the probability density at the steady state. One probability density is given by a deterministic Gompertz equation which is fitted by least squares regression to the data on the bacterial growth at 10°C assuming a Gaussian error distribution. The second probability density is the steady state probability density associated with the stochastic differential Eq. (4). This is derived by letting $t \to \infty$ in Eq. (5). The distribution (5) based on the stochastic Gompertz equation is asymmetric, with the positive tail of the density being longer. The comparison shows that this asymmetry has implications for the determination of the risk, since the long positive tail indicates that the probability that a population will become large may be higher than would be assumed from naive calculations based on an assumed Gaussian distribution. The error in calculating the higher quantiles using the deterministic model with independent additive errors can be seen.

Also the mode (the value which has the greatest probability) in the stochastic model is always less than the mode in the deterministic model, as illustrated in Fig. 3.

Fig. 4 shows an example of the probability that the population size starting at a particular value will exceed some critical value (for illustration a log relative population size of 4 is chosen) in a given time. This example involves the probability that a bacterial population with a log relative population

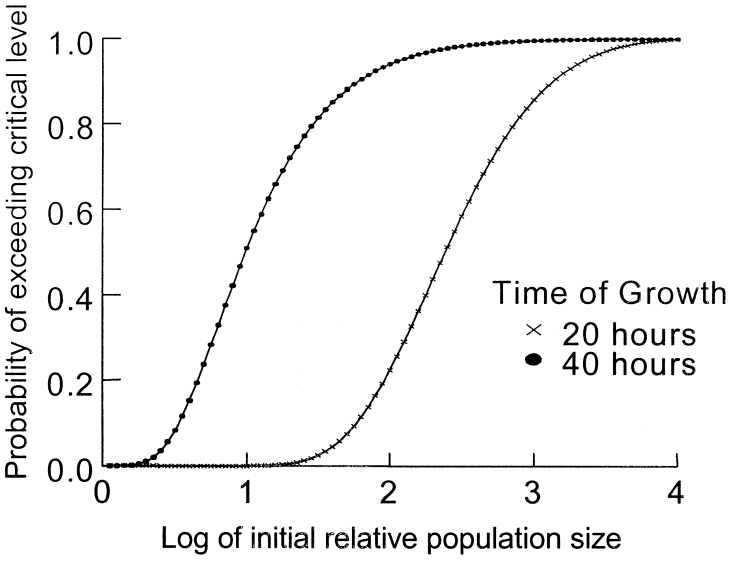


Fig. 4. Probability of *Lactobacillus plantarum* exceeding a log of the relative population size of 4 in either 20 or 40 h given the log of the initial relative population size.

size of between 0 and 4 will grow to reach this critical value in either 20 or 40 h at a temperature of 10°C. The result is shown in Fig. 4. For example, a population starting from a log relative size of 1 would grow to the level $\ln(N/N_0) = 4$ with a probability close to 0.0 in 20 h (meaning that the probability of remaining less than size 4 is close to 1, i.e. effectively certain). However, if the time allowed is increased to 40 h then the probability of exceeding level $\ln(N/N_0) = 4$ is 0.55.

Fig. 5 shows the mean first passage time for *L. planatarum* with an initial log relative population size of less than 4 and growing at either 10 or 25°C, to reach a level $\ln(N/N_0) = 4$. For example, microbes with an initial log relative population size of 1 would take an average of 7.6 h at 25°C, or an average of 40 h at 10°C, to reach a $\ln(N/N_0) = 4$. This can be compared with the estimate from the deterministic curve in Fig. 1, which gives 42 h at 10°C. But note that at this time the stochastic calculation shows that the probability of exceeding the critical level will be about 0.6.

## 5. Conclusions

Models used in predictive microbiology generally assume that the growth law driving the evolution of the microbial population is deterministic. Any stochastic aspects of population growth are considered in terms of the deviations about the deterministic growth law. Two assumptions are made in this approach. First the form of the probability distribution of the data is taken a priori, e.g. it is assumed to be Gaussian. Second, the form of the probability distribution is assumed to remain the same throughout the growth of the microbial population (identically distributed). While such assumptions are probably robust for estimating the mean population growth curve, they are much less satisfactory for estimating the risks associated with the growth of a microbe of interest. This is because the calculation of risk generally requires evaluation of the quantiles of a probability distribution. To do this accurately, the form of the probability density needs to be known.

A model based on the stochastic version of the

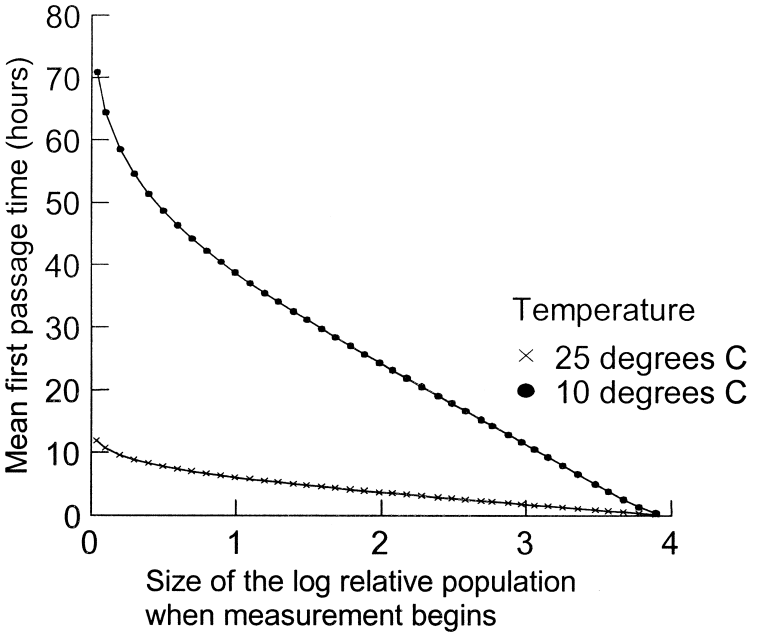


Fig. 5. Mean first passage time for *Lactobacillus plantarum* growing at 10°C to reach a log relative population size of 4 for a range of log initial relative population sizes less than 4.

differential equation used to describe the interactions governing the growth of a microbial population provides an estimate of the form of the probability density at any time arising directly from these interactions. Thus, this model should be a more accurate representation than methods assuming that the deviations in growth are independent of the growth process. When the interactions are nonlinear, as they are for the Gompertz law of growth, it is unlikely that this probability density will be Gaussian. This approach deals with the need to model variation in microbial growth, which Whiting (1997) identified as a necessary step to estimating the risk of food contamination. It also fits smoothly into the HACCP framework for managing food safety discussed by Hathaway and Cook (1997).

The difference in the tails of the probability density between a model based on stochastic Gompertz growth, and a model based on deterministic Gompertz growth, assuming that the deviations follow a Gaussian density, is shown in Fig. 3 for *Lactobacillus plantarum* grown at 10°C. If, for example, it was undesirable for the microbes to reach a log relative population size of 9, the model based on deterministic Gompertz growth indicates the risk would be insignificant, whereas the stochastic Gompertz model indicates the risk is substantial.

Two calculations are useful for strategies designed to manage food safety. The first is the probability that a microbial population of given size will reach a dangerous size within a given time. The second is the average time that a microbial population of given size will take to reach a dangerous size (the average first passage time). These solutions will depend on effects like temperature. Therefore, a management goal might be to find a suitable combination of storage conditions that will keep the probability low that the microbial populations will reach dangerous levels within the period of interest. The average time for the population to grow from a log relative size of 1–4 is slightly less for the stochastic model (40 h at 10°C) than the deterministic model (42 h at 10°C). When the temperature increases the average time for the population growth decreases. For example at 25°C the average time for the population to grow from a log relative size of 1 to 4 is 7.2 h.

Alternatively, the probability that the microbial population will exceed a given amount at any given time can be calculated. For example, the probability that a microbial population beginning at a log relative size of 1 will exceed a log relative size of 4 in 40 h is 0.55 at 10°C.

A similar problem, important for designing HACCP protocols, is to determine the maximum number of microbes which can be present at a given time without causing an unacceptable risk at some defined future time.

This paper introduces the methods of stochastic calculus to the problems of microbial growth in order to formulate a basis for the calculation of risk, particularly in food safety. The nonlinear nature of microbial growth results in probability densities of population size peculiar to the type of growth encountered. The calculation of these probability densities from the principles of growth, and the associated calculations to derive figures for first passage times will be an important tool in the design and management of schemes to ensure food safety.

## Appendix A

Given the stochastic differential equation with drift $A(X_t,t)$ and variance $B(X_t,t)$

$$dX_t = A(X_t,t)dt + B(X_t,t)dW$$

then the evolution of the probability density $P(x,t)$ of the stochastic process $X_t$ through time is given by the related partial differential equation (Fokker–Planck equation)

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial x}A(x,t)P + \frac{\sigma^2}{2}\frac{\partial}{\partial x^2}B(x,t)P$$

For the Gompertz stochastic differential equation

$$dY_t = aY_t \ln\left(\frac{y^*}{Y_t}\right)dt + \sigma Y_t dW \qquad (1A)$$

the Fokker–Planck equation for the probability density $P(y,t)$ is

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial y}a(\ln y^* - \ln y)P + \frac{\sigma^2}{2}\frac{\partial}{\partial y^2}y^2P \qquad (2A)$$

Providing that the initial state is known exactly, $P(y,0) = \delta(y - y_0)$, then the solution of Eq. (2A) can be found in explicit analytical form:

$$P(y,t) = \frac{1}{\sigma y\sqrt{\pi(1-\mathrm{e}^{-2at})/a}} \times \exp\left[ -\frac{a\left(\ln y - \ln y^* + \frac{\sigma^2}{2a} - \mathrm{e}^{-at}\ln y_0\right)^2}{\sigma^2(1-\mathrm{e}^{-2at})} \right]$$

Then if the initial condition *P(y,0)* is some distributed function, the probability density *P(y,t)* takes the form of an infinite series over Hermitian polynomials of variable $z = \ln y$ with time-dependent coefficients. Alternatively a numerical solution of Eq. (2A) can be used.

The steady state probability density $P_s$, when the population has reached equilibrium (i.e. when $\partial P/\partial t = 0$), does not depend on initial conditions. Letting $t \to \infty$ in *P(y,t)*

$$P_s = \frac{1}{\sigma y\sqrt{\pi/a}}\exp\left[ -\frac{a}{\sigma^2}\left(\ln y - \ln y^* + \frac{\sigma^2}{2a}\right)^2 \right]$$

The probability density $P_s(y)$ is a unimodal asymmetrical distribution with the positive tail of the density being higher and the maximum at the point

$$y_m = y^*\mathrm{e}^{-\sigma^2/a}$$

Applying the Ito formula for transforming stochastic variables (Gardiner, 1985) we can obtain expression for the probability density *P(x,t)* of the stochastic process $X_t = N_t/N_0$, which is connected to the process $Y_t$ by $X_t = \exp(Y_t)$. The mode $x_m$ of steady-state distribution of this process is implicitly determined by the solution of algebraic equation

$$a\ln y^* - \sigma^2 - \frac{\sigma^2}{2}\ln x_m - a\ln\ln x_m = 0$$

and is always less than values which can be expected from the naive estimation $x_m = \mathrm{e}^{y_m}$.

## Appendix B

Suppose that the value of the log of the relative population size at time $t = 0$was $y$. Then the probability *φ(y,t)* that the random process $Y_t$ will exceed some critical level $b$, $(b < y)$ obeys the differential equation

$$\frac{\partial\varphi}{\partial t} = ay(\ln y^* - \ln y)\frac{\partial\varphi}{\partial y} + \frac{\sigma^2y^2}{2}\frac{\partial^2\varphi}{\partial t^2} \qquad (1B)$$

with the conditions

$$\varphi(y,0) = 0$$
$$\varphi(b,t) = 1$$

It is obvious that the probability $\varphi(y,t)$ (that the value of the log of the relative population size will exceed the critical level $b$) increases with time at any given value of initial point $y$.

The results of the numerical solution of the Eq. (1B) for times $t_1$ equal to 20 h and $t_2$ equal to 40 h are shown in Fig. 3.

The first passage time is the time that the stochastic process takes to reach a given level. The mean first passage time *T(y)* required for a population of log relative size $y$ to exceed log relative population size $b$ $(0 < y < b)$ is given by

$$T = \int_0^\infty t\frac{\partial\varphi}{\partial t}\mathrm{d}t \qquad (2B)$$

From Eqs. (1B) and (2B) a differential equation for *T(y)* follows

$$\frac{\sigma^2y^2}{2}\frac{d^2T}{dy^2} + ay(\ln y^* - \ln y)\frac{\mathrm{d}T}{\mathrm{d}y} = -1$$

The solution of this equation can be represented in the form

$$T_b(y) = \frac{2}{a}\int_{\beta\ln y}^{\beta\ln b} V(z)\mathrm{d}z \qquad (3B)$$

with the following notation

$$V(z) = \mathrm{e}^{(z-\mu)^2}\int_{-\infty}^{z}\mathrm{e}^{-(x-\mu)^2}\mathrm{d}x$$

with

$$\mu = \beta(\ln y^* - \beta^2);\ \beta = \sqrt{a}/\sigma^2$$

The first passage time for the process $X_t = N_t/N_0$ can be obtained from expression (3B) by the direct substitution $y = \ln x$. The probability that the stochastic process $X_t$ initially situated at the point $x$ will exceed its critical level $B$ at time $t$ is equal to the probability that the process $Y_t$, initially situated at the point $y = \ln x$ will exceed the level $b = \ln B$ at the same time $t$. The latter means that the curves presented in Fig. 3 characterise the probability for

microbial cell concentration to exceed the critical level as well.

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