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ON STOCHASTIC GROWTH PROCESSES WITH APPLICATION TO STOCHASTIC LOGISTIC GROWTH

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Abstract: In this paper we develop a general theory for some non-homogeneous density-dependent birth-death processes with special applications to stochastic logistic growth. Approximations to the mean and variance of the logistic process are derived. It is shown that these processes can be closely approximated by diffusion processes. Using this method, new results are developed for approximating the absorption probabilities and the moments of first absorption times for the logistic process.

Key words and phrases: Absorption probability, diffusion process, moments of first absorption time, nonhomogeneous density-dependent birth-death process, stochastic logistic growth.

1. Introduction

In biomedical and ecological research, scientists are frequently confronted with the problem of modeling the growth of cell populations (Eisen (1979), Chapter 2; Pielou (1977), Chapter 1). Because of the limitations of space and food, the logistic growth model is often more realistic than the simple exponential. Examples of the successful use of the logistic model include the growth of human breast cancer cells (Moolgavkar (1986)) and the growth of Chinese hamster ovary cells in the CHO/HGPRT bioassay for testing mutagenicity of chemicals (Tan (1983)).

In the modeling of the growth of cell populations by the logistic function (Eisen (1979)), to date, only deterministic logistic growth has been used. However, in the real world, stochastic fluctuations in growth appear to be prevalent. Pielou (1977) has attempted to construct a stochastic version of logistic growth, however a general theory is still nonexistent. In this paper, we develop a theory for some very general density-dependent non-homogeneous birth-death processes. The general theory of stochastic logistic growth is developed as a special case. This theory is useful for developing stochastic models in many areas of biomedical research such as stochastic models of carcinogenesis.

In Section 2 we consider the general theory for a non-homogeneous density-dependent birth-death process. By using results from Tan (1984) in Section 3 we give some general formulas for the absorption probabilities and the means and variances of the first absorption time for stochastic logistic growth. As an alternative approach in Section 4 we develop a diffusion approximation for the general process and develop approximation for the ultimate absorption probabilities and the moments of first absorption times. Finally in Section 5 we provide some numerical illustrations.

2. Stochastic Growth Models

Consider a population of individuals with M as the maximum population size. Let $X(t)$, $t \geq 0$, be the size of the population at time t. For describing probabilistically the growth in this population, we make the following assumptions.

(i) $\{X(t), t \geq 0\}$ is a Markov process. For many biological and cell populations, this assumption is expected to hold since the population size $X(t)$ usually depends only on most recent events, independent of past history.

(ii) Given j individuals at time t, the probabilities that there are $j+1$, $j-1$, or j individuals at time $t + \Delta t$ are given respectively by

$$\Pr\{X(t+\Delta t) = j+1 | X(t) = j\} = b_j(t)\Delta t + o(\Delta t),$$
$$\Pr\{X(t+\Delta t) = j-1 | X(t) = j\} = d_j(t)\Delta t + o(\Delta t), \quad \text{and}$$
$$\Pr\{X(t+\Delta t) = j | X(t) = j\} = 1 - [b_j(t) + d_j(t)]\Delta t + o(\Delta t),$$

where $b_j(t) \geq 0$, $d_j(t) \geq 0$ and $\lim_{\Delta t \to \infty} o(\Delta t)/\Delta t = 0$ for all $j = 0, 1, \ldots, M$, with $d_0(t) = 0$ and $b_M(t) = 0$.

Given the above specifications, it is easy to see that the state space of $X(t)$ is $S = \{0, 1, 2, \ldots, M\}$. If $b_j(t) > 0$ and $d_j(t) > 0$ for $j = 1, \ldots, M-1$ and if $d_M(t) = 0$ and $b_0(t) = 0$, then the states 0 and M are absorbing states while $j = 1, \ldots, M-1$ are transient states. If $b_j(t) = jb(t)[1 - (j/M)]$ and $d_j(t) = jd(t)[1 - (j/M)]$ for $j = 0, 1, 2, \ldots, M$ and $b(t) > 0$ and $d(t) > 0$, the above model is called a stochastic logistic birth-death process with birth rate $b(t)$, death rate $d(t)$ and maximum population size M. We shall use the notation $X(t) \sim \mathrm{SL}(b(t), d(t); M)$. If $b(t) = b$ and $d(t) = d$, then $X(t) \sim \mathrm{SL}(b, d; M)$ is a stochastic version of a two parameter logistic growth law considered by Jensen (1975).

Let $P_{uv}(s,t) = \Pr\{X(t) = v \mid X(s) = u\}$, $t \geq s$, and let $Q(u, z; s, t) = \sum_{v=0}^{M} z^v P_{uv}(s,t)$ be the probability generating function of $X(t)$ given $X(s) = u$. By using Kolmogorov forward equation, it is straightforward to show that

$Q(u,z;s,t)$ satisfies

$$\frac{\partial}{\partial t}Q(u,z;s,t) = (z-1)\sum_{v=0}^{M} z^v b_v(t)P_{uv}(s,t)+(z^{-1}-1)\sum_{v=0}^{M} z^v d_v(t)P_{uv}(s,t). \quad (2.1)$$

In the case of $X(t) \sim \mathrm{SL}(b(t),d(t);M)$, Equation (2.1) reduces to

$$\frac{\partial}{\partial t}Q(u,z;s,t) = (z-1)[zb(t)-d(t)]\left\{\left(1-\frac{z}{M}\right)\frac{\partial}{\partial z} - \frac{z}{M}\frac{\partial^2}{\partial z^2}\right\}Q(u,z;s,t). \quad (2.2)$$

For $0 < M < \infty$, obtaining the solution of (2.2) is very difficult if not impossible. Instead of solving (2.2) directly, we use (2.2) to obtain the cumulants $\kappa_j(t)$ of $X(t)$ given $X(t_0) = m_0$ and derive a diffusion approximation for $Y(t) = X(t)/M$. Given below are the differential equations for the first two cumulants of $X(t) \sim \mathrm{SL}(b(t),d(t);M)$. The differential equations for the third and fourth cumulants of $X(t) \sim \mathrm{SL}(b(t),d(t);M)$ are available from Tan and Piantadosi (1988).

$$\frac{d}{dt}\kappa_1(t) = \epsilon(t)\{\kappa_1(t) - (1/M)[(\kappa_1(t))^2 + \kappa_2(t)]\},$$

where $\kappa_1(t_0) = m_0$ and $\epsilon(t) = b(t) - d(t)$;

$$\begin{aligned}\frac{d}{dt}\kappa_2(t) &= \kappa_2(t)\{2\epsilon(t)[1-(2\kappa_1(t)/M)] - [\omega(t)/M]\} \\ &\quad + \kappa_1(t)\omega(t)\{1-[\kappa_1(t)/M]\} - 2\epsilon(t)[\kappa_3(t)/M],\end{aligned}$$

where $\kappa_2(t_0) = 0$ and $\omega(t) = b(t) + d(t)$. If $\kappa_i(t) = O(M)$ for $i = 1,2$, then

$$\begin{aligned}\frac{d}{dt}\kappa_1(t) &= \epsilon(t)\{\kappa_1(t) - (1/M)[(\kappa_1(t))^2 + \kappa_2(t)]\} \\ &\cong \epsilon(t)\kappa_1(t)[1-(1/M)\kappa_1(t)], \quad \kappa_1(t_0) = m_0.\end{aligned}$$

It follows that if $\kappa_i(t) = O(M)$ for $i = 1,2$, a close approximation to $\kappa_i(t)$ is given by

$$\kappa_1(t) \cong m_0 \exp\left\{\int_{t_0}^{t} \epsilon(x)dx\right\} \cdot \left\{1-(m_0/M) + (m_0/M)\exp\left[\int_{t_0}^{t}\epsilon(x)dx\right]\right\}^{-1}. \quad (2.3)$$

Equation (2.3) refers to the non-homogeneous logistic growth function. When $b(t) = b$ and $d(t) = d$, (2.3) provides a very close approximation for most of the situations which correspond to doubling time of bacteria and cell populations (Section 5). Similarly, if $\kappa_i(t) = O(M)$, $i = 1,2$, and if $\epsilon(t)\kappa_3(t) = O(M)$, then

$$\frac{d}{dt}\kappa_2(t) \cong \kappa_2(t)\{2h_1(t) + [\omega(t)/M]\} + \kappa_1(t)\omega(t)\{1 - [\kappa_1(t)/M]\}$$
$$= \kappa_2(t)f_1(t) + f_2(t), \tag{2.4}$$

where $\kappa_2(t_0) = 0$, $f_1(t) = 2h_1(t)+[\omega(t)/M]$ and $f_2(t) = \kappa_1(t)\omega(t)\{1-[\kappa_1(t)/M]\}$. From (2.4),

$$\kappa_2(t) \cong \exp\left\{\int_{t_0}^{t} f_1(x)dx\right\}\int_{t_0}^{t} f_2(x)\exp\left[-\int_{t_0}^{x} f_1(s)ds\right]dx$$
$$= m_0\left(1 - \frac{m_0}{M}\right)g_1(t)\int_{t_0}^{t}\omega(x)g_2(x)dx, \tag{2.5}$$

where

$$g_1(t) = \exp\left\{\int_{t_0}^{t}[2\epsilon(x)-\frac{1}{M}\omega(x)]dx\right\}\cdot\left\{1-(m_0/M)+(m_0/M)\exp\left[\int_{t_0}^{t}\epsilon(x)dx\right]\right\}^{-4}$$

and

$$g_2(t) = \exp\left\{-\int_{t_0}^{t}[\epsilon(x)-\frac{1}{M}\omega(x)]dx\right\}\cdot\left\{1-(m_0/M)+(m_0/M)\exp\left[\int_{t_0}^{t}\epsilon(x)dx\right]\right\}^{2}.$$

When $b(t) = b$ and $d(t) = d$, (2.5) provides a very close approximation for many plausible values of the doubling time of bacteria and cell populations (Section 5).

3. Absorption Probabilities, Mean Absorption Time and the Variance of First Absorption Time

Consider the stochastic growth model in Section 2 with $b_j(t)>0$ and $d_j(t)>0$ for $1 \le j \le M-1$ and with $b_0(t) = d_M(t) = 0$. Then starting with any stage j $(0 < j < M)$, with probability one the process will eventually be absorbed into either 0 or M. In cancer prevention studies, it is often of interest to obtain these absorption probabilities and the first absorption time.

Let $F_{j,0}(t)$, $F_{j,D}(t)$ and $F_j(t)$ denote respectively the probabilities of absorption into 0, M and the set $C = (0, M)$ at or before time t starting with the state j $(0 < j < M)$ at time t_0 $(t < t_0)$. Let U_j be the mean absorption time into 0 or M starting with the state j $(0 < j < M)$ at time t_0 and V_j the variance of first absorption time into 0 or M starting with the state j $(0 < j < M)$ at time t_0.

Let $r = M - 1$ and put

$$\underset{\sim}{F}(t) = (F_1(t), F_2(t), \ldots, F_r(t))',$$
$$\underset{\sim}{F}_0(t) = (F_{1,0}(t), F_{2,0}(t), \ldots, F_{r,0}(t))',$$
$$\underset{\sim}{F}_D(t) = (F_{1,D}(t), F_{2,D}(t), \ldots, F_{r,D}(t))',$$
$$\underset{\sim}{U} = (u_1, u_2, \ldots, u_r)' \quad \text{and} \quad \underset{\sim}{V} = (V_1, V_2, \ldots, V_r)'.$$

To obtain $\underset{\sim}{F}(t)$, $\underset{\sim}{F}_0(t)$, $\underset{\sim}{F}_D(t)$, $\underset{\sim}{U}$ and $\underset{\sim}{V}$ for stochastic logistic growth, we let $B_1 = \left(b_{uv}^{(1)}\right)$ and $B_2 = \left(b_{uv}^{(2)}\right)$ be $r \times r$ matrices defined by

$$\begin{aligned}
b_{uv}^{(1)} &= -u[1-(u/M)] && \text{if } v = u+1\ (u = 1, \ldots, r-1),\\
&= u[1-(u/M)] && \text{if } v = u\ (u = 1, \ldots, r),\\
&= 0 && \text{if } v = u \text{ and } v = u+1;\\
b_{uv}^{(2)} &= -u[1-(u/M)] && \text{if } v = u-1\ (u = 2, \ldots, r),\\
&= u[1-(u/M)] && \text{if } v = u\ (u = 1, \ldots, r),\\
&= 0 && \text{if } v = u \text{ and } v = u-1.
\end{aligned}$$

Let $\underset{\sim}{1}_r$ be the $r \times 1$ column of 1's and define the matrix function

$$\exp[H(t)] = \sum_{j=0}^{\infty} \frac{1}{j!} H^j(t).$$

By results given in Tan (1984) we have for stochastic logistic growth

$$\underset{\sim}{F}(t) = \{I_r - \exp[-B_1\Theta_1(t) - B_2\Theta_2(t)]\}\, \underset{\sim}{1}_r$$

where $\Theta_1(t) = \int_{t_0}^{t} b(x)dx$ and $\Theta_2(t) = \int_{t_0}^{t} d(x)dx$,

$$\underset{\sim}{F}_0(t) = [B_1 b(t) + B_2 d(t)]^{-1}\{I_r - \exp[-B_1\Theta_1(t) - B_2\Theta_2(t)]\}[B_2 d(t)]\, \underset{\sim}{1}_r,$$
$$\underset{\sim}{F}_D(t) = [B_1 b(t) + B_2 d(t)]^{-1}\{I_r - \exp[-B_1\Theta_1(t) - B_2\Theta_2(t)]\}[B_1 b(t)]\, \underset{\sim}{1}_r,$$
$$\underset{\sim}{U} = \int_{t_0}^{\infty} t\,d\underset{\sim}{F}(t) = t_0\, \underset{\sim}{1}_r + \underset{\sim}{a}$$

where $\underset{\sim}{a} = \int_{t_0}^{\infty}\{\exp[-B_1\Theta_1(t) - B_2\Theta_2(t)]\, \underset{\sim}{1}_r\}dt = (a_1, a_2, \ldots, a_r)'$, and

$$\underset{\sim}{V} = \int_{t_0}^{\infty} t^2 d\underset{\sim}{F}(t) - \underset{\sim}{u}_s = 2\int_{t_0}^{\infty} (t - t_0)\{\exp[-B_1\Theta_1(t) - B_2\Theta_2(t)]\, \underset{\sim}{1}_r\}dt - \underset{\sim}{a}_s,$$

where $\underset{\sim}{u}_s = (u_1^2, u_2^2, \ldots, u_r^2)$ and $\underset{\sim}{a}_s = (a_1^2, a_2^2, \ldots, a_r^2)'$. Note that

$$\lim_{t\to\infty} \underset{\sim}{F}(t) = \underset{\sim}{1}_r,$$
$$\underset{\sim}{P}_0 = \lim_{t\to\infty} \underset{\sim}{F}_0(t) = [B_1 b(\infty) + B_2 d(\infty)]^{-1}[B_2 d(\infty)]\, \underset{\sim}{1}_r \quad \text{and}$$
$$\underset{\sim}{P}_D = \lim_{t\to\infty} \underset{\sim}{F}_D(t) = [B_1 b(\infty) + B_2 d(\infty)]^{-1}[B_1 b(\infty)]\, \underset{\sim}{1}_r,$$

where $b(\infty) = \lim_{t\to\infty} b(t)$ and $d(\infty) = \lim_{t\to\infty} d(t)$. $\underset{\sim}{P}_0$ and $\underset{\sim}{P}_D$ are the ultimate absorption probability vectors into 0 and M respectively. If $b(t) = b$ and $d(t) = d$, then, one may take $t_0 = 0$ so that

$$\underset{\sim}{U} = (B_1 b + B_2 d)^{-1}\, \underset{\sim}{1}_r \quad \text{and} \quad \underset{\sim}{V} = 2(B_1 b + B_2 d)^{-1}\, \underset{\sim}{U} - \underset{\sim}{u}_s.$$

These are the results first obtained by Tan (1976).

If M is very large, computing $\underset{\sim}{U}$, $\underset{\sim}{V}$ and the absorption probabilities requires the inversion of large matrices. In the next section we will show that to order $O(M^{-2})$, the stochastic logistic growth processes can be approximated by diffusion processes. Using the diffusion approximation, computations of the absorption probabilities and $\underset{\sim}{U}$ are considerably simplified. Furthermore, the diffusion approximation also makes it possible to obtain absorption probabilities and moments of first absorption time for the very general density-dependent birth-death processes considered in Section 2.

4. Diffusion Approximation

Let $Y(t) = X(t)/M$, $x = u/M$, $y = v/M$ and $dt = M^{-1}$. Since M is usually very large, one may approximate the transition probabilities by $\Pr\{X(t) = v \mid X(s) = u\} = \Pr\{Y(t) = y \mid Y(s) = x\} \cong f(x, y; s, t)dt$, where $f(x, y; s, t)$ is a continuous function of x and y. In fact, we have

Theorem 4.1. *If $b_v(t) = M\sum_{j=0}^{n_1} \beta_j(t)(v/M)^j$ and $d_v(t) = M\sum_{j=0}^{n_2} \mu_j(t)(v/M)^j$, then, to order $O(M^{-2})$, $\Pr\{X(t) = v|X(s) = u\}$ is approximated by $f(x, y; s, t)dt$ which satisfies the partial differential equation*

$$\begin{aligned} \frac{\partial}{\partial t} f(x, y; s, t) &= -\frac{\partial}{\partial y}\{m(y, t) f(x, y; s, t)\} + \frac{1}{2M}\frac{\partial^2}{\partial y^2}\{V(y, t) f(x, y; s, t)\}, \\ f(x, y; s, s) &= \delta(y - x) \end{aligned} \tag{4.1}$$

where $\delta(x)$ is Dirac's δ-function,

$$m(y, t) = \sum_{j=0}^{n_1} \beta_j(t) y^j - \sum_{j=0}^{n_2} \mu_j(t) y^j \quad \text{and} \quad V(y, t) = \sum_{j=0}^{n_1} \beta_j(t) y^j + \sum_{j=0}^{n_2} \mu_j(t) y^j.$$

Remarks. If $\beta_0(t) = \mu_0(t) = 0$, $\beta_1(t) = b(t)$, $\beta_2(t) = -b(t)$, $\mu_1(t) = d(t)$ and $\mu_2(t) = -d(t)$, the results of Theorem 4.1 reduce to the results for stochastic logistic birth-death process.

Proof. A proof of Theorem 4.1 is given in Tan and Piantadosi (1988).

Using the Kolmogorov backward equation, one may similarly prove

Theorem 4.2. *Given the conditions of Theorem* 4.1, *to order* $O(M^{-2})$, $f(x,y;s,t)$ *also satisfies the partial differential equation*

$$\frac{\partial}{\partial s} f(x,y;s,t) = m(x,s)\frac{\partial}{\partial x} f(x,y;s,t) + \frac{1}{2M} V(x,s)\frac{\partial^2}{\partial x^2} f(x,y;s,t), \qquad (4.2)$$
$$f(x,y;s,s) = \delta(y-x).$$

Equations (4.1) and (4.2) imply that to order $O(M^{-2})$, $Y(t) = X(t)/M$ is approximated by a non-homogeneous diffusion process with coefficients $m(y,t)$ and $V(y,t)$. In the case of $X(t) \sim \mathrm{SL}(b,d;M)$, $f(x,y;s,t) = f(x,y;t-s)$ and (4.1) and (4.2) reduce to

$$\frac{\partial}{\partial t} f(x,y;t) = -\epsilon\frac{\partial}{\partial y}\{y(1-y)f(x,y;t)\} + \frac{\omega}{2M}\frac{\partial^2}{\partial y^2}\{y(1-y)f(x,y;t)\}, \qquad (4.3)$$
$$\frac{\partial}{\partial t} f(x,y;t) = \epsilon x(1-x)\frac{\partial}{\partial x} f(x,y;t) + \frac{\omega}{2M} x(1-x)\frac{\partial^2}{\partial x^2} f(x,y;t), \qquad (4.4)$$

with $f(x,u;0) = \delta(y-x)$, $\epsilon = b-d$ and $\omega = b+d$.

The solution of (4.4) is available from Crow and Kimura (1970, pp. 396–398) in infinite series involving Gegenbauer polynomials. Unfortunately, the solution is too complicated to be of practical use. However, using (4.2) and (4.4), we can obtain absorption probabilities and the moments of first absorption times.

4.1. Absorption probabilities

Let $U_1(s,x)$ $(x = u/M)$ be the ultimate absorption probability into M given $X(s) = u$ $(0 < u < M)$ and $U_0(s,x)$ the ultimate absorption probability into 0 given $X(s) = u$ $(0 < u < M)$. Then, to order $O(M^{-2})$,

$$U_1(s,x) = \frac{1}{2M}\lim_{t\to\infty} f(x,1;s,t) \quad \text{and} \quad U_0(s,x) = \frac{1}{M}\lim_{t\to\infty} f(x,0;s,t).$$

In the backward Equation (4.2), putting $y = 0$ or 1 and letting $t \to \infty$, we obtain

Theorem 4.3. *To order $O(M^{-2})$, $U_i(s,x)$ $(i=0,1)$ satisfies*

$$m(x,s)\frac{\partial}{\partial x}U_i(s,x)+\frac{1}{2M}V(x,s)\frac{\partial^2}{\partial x^2}U_i(s,x)=-\frac{\partial}{\partial s}U_i(s,x)\quad (i=0,1)\tag{4.5}$$

with $U_1(s,1)=1=U_0(s,0)$ *and* $U_1(s,0)=0=U_0(s,1)$.

If $\beta_j(t)=\beta_j$ and $\mu_j(t)=\mu_j$, then $m(x,s)=m(x)$, $V(x,s)=V(x)$ and $U_i(s,x)=U_i(x)$ are independent of s. In this case, (4.5) reduces to

$$m(x)\frac{d}{dx}U_i(x)+\frac{1}{2M}V(x)\frac{d^2}{dx^2}U_i(x)=0,\quad i=0,1,\tag{4.6}$$

with $U_1(1)=1=U_0(0)$ and $U_1(0)=0=U_0(1)$. On solving (4.6) we obtain $U_1(x)=\eta(x)/\eta(1)$ and $U_0(x)=1-U_1(x)$, where $\eta(x)=\int_0^x \exp[-\int_0^y \phi(z)dz]dy$ with $\phi(y)=2Mm(y)/V(y)$.

In the special case of homogeneous logistic growth SL$(b,d;M)$, $U_1(x)=[1-\exp(-N_0x)]/[1-\exp(-N_0)]$ and $U_0(x)=1-U_1(x)$ where $N_0=2M\epsilon/\omega$.

4.2. The moments of first absorption times

Let $\beta_j(t)=\beta_j$ and $\mu_j(t)=\mu_j$ so that $m(x,s)=m(x)$ and $V(x,s)=V(x)$ and let $f_q(x;t)$ be the probability density function of the first absorption time T_q given $Y(0)=u/M=x$. Then, to order $O(M^{-2})$, $f_q(x;t)$ satisfies

$$\frac{\partial}{\partial t}f_q(x;t)=m(x)\frac{\partial}{\partial x}f_q(x;t)+\frac{1}{2M}V(x)\frac{\partial^2}{\partial x^2}f_q(x;t),\quad f_q(x;0)=0\tag{4.7}$$

(For proof, see Ewens (1969, p. 53)).

Let $T_j(x)=\int_0^\infty t^j f_q(x;t)dt$, $j=1,2,\ldots$, be the jth moment of T_q around the origin. For computing $T_j(x)$ we prove

Theorem 4.4. *Let $T_0(x)=1$. Then, to order $O(M^{-2})$, $T_j(x)$ satisfies*

$$m(x)\frac{d}{dx}T_j(x)+\frac{1}{2M}V(x)\frac{d^2}{dx^2}T_j(x)=-jT_{j-1}(x),\tag{4.8}$$

$j=1,2,3,\ldots$, *with* $T_{j-1}(0)=T_{j-1}(1)=0$.

Proof. Integrating by parts,

$$\int_0^\infty t^j\frac{\partial}{\partial t}f_q(x;t)dt=t^jf_q(x;t)\Big]_0^\infty-j\int_0^\infty t^{j-1}f_q(x;t)dt=-jT_{j-1}(x).$$

By multiplying both sides of Equation (4.7) by t^j and integrating t from 0 to ∞ we obtain

$$\begin{aligned} -jT_{j-1}(x) &= \int_0^\infty t^j \frac{\partial}{\partial t} f_q(x;t)dt \\ &= m(x)\frac{\partial}{\partial x}\int_0^\infty t^j f_q(x;t)dt + \frac{1}{2M}V(x)\frac{\partial^2}{\partial x^2}\int_0^\infty t^j f_q(x;t)dt \\ &= m(x)\frac{d}{dx}T_j(x) + \frac{1}{2M}V(x)\frac{d^2}{dx^2}T_j(x). \end{aligned}$$

Let $\Psi(x) = \exp\{-\int_0^x [2Mm(y)/V(y)]dy\}$. By the method of variation of parameters, it can be shown that with $T_0(x) = 1$ the solution of (4.8) is given by

$$\begin{aligned} T_j(x) &= (2j)U_0(x)\int_0^x [\Psi(y)V(y)]^{-1}T_{j-1}(y)\Big[\int_0^y \Psi(z)dz\Big]dy \\ &\quad + (2j)U_1(x)\int_x^1 [\Psi(y)V(y)]^{-1}T_{j-1}(y)\Big[\int_y^1 \Psi(z)dz\Big]dy \quad \text{for} \quad j = 1,2,\ldots. \end{aligned}$$

In the special case of $X(t) \sim \mathrm{SL}(b,d;M)$, we have

$$\begin{aligned} T_1(x) = \mu(x) &= [U_0(x)/M\epsilon]\int_0^x (\exp(N_0 y) - 1)[y(1-y)]^{-1}dy \\ &\quad + [U_1(x)/M\epsilon]\int_0^1 \{1 - \exp[-N_0(q-y)]\}[y(1-y)]^{-1}dy \end{aligned} \tag{4.9}$$

and

$$\begin{aligned} T_2(x) &= [2U_0(x)/M\epsilon]\int_0^x T_1(y)[\exp(N_0 y) - 1][y(1-y)]^{-1}dy \\ &\quad + [2U_1(x)/N\epsilon]\int_x^1 T_1(y)[1 - \exp(-N_0 q + N_0 y)][y(1-y)]^{-1}dy. \end{aligned} \tag{4.10}$$

5. Some Numerical Illustrations

To illustrate some basic results of this paper, we examined computer simulations of a homogeneous stochastic logistic birth-death process. For given time t, we chose $\Delta t = .01$ so that the interval $[0,t]$ was divided into $t/0.01$ increments. The values chosen for b and d were $(b,d) = (0.05, 0.01)$ and (0.03, 0.005). Note that $(b,d) = (0.05, 0.01)$ corresponds to the doubling time of 16–18 days for bacteria or cell growth (Tan (1982, 1983)) while $(b,d) = (0.03, 0.005)$ corresponds to the doubling time of approximately 27–29 days for human tumor cells (see Coldman and Goldie (1983)). We examined the behavior of the model for other values of (b,d) as well and found the results similar to those given here. The initial and final population sizes were $m_0 = 100$ and $M = 1,000$. M was intentionally chosen to be modest in size because otherwise m_0/M is very small and the process reduces to exponential growth. For each set of parameter values chosen, 100 replications of the simulation were performed. Mean values and variances for the population size and absorption times were calculated.

A comparison of the mean simulated population size with the approximation given by (2.3) shows excellent agreement at all time points for a variety of parameter values (Figures 1–2). Similarly, Figures 3 and 4 show that the variance of the simulated values agrees very well at all time points with the approximation given by (2.5).

The ultimate absorption probabilities $U_1(x)$, as a function of x, are shown in Figure 5. Note that if $b = d$, then $U_1(x) = x$ and $U_0(x) = 1 - x$. The approximated mean absorption times using (4.9) agree very well with the mean simulated absorption time (Table 1).

Table 1. Simulated and approximated mean absorption times $\mu(x)$ for $x = m_0/M$

b	d	m_0	M	Simulated mean absorption time	Approximate mean absorption time ($\mu(x)$)
0.05	0.01	100	1000	55.2	54.9
0.03	0.005	100	1000	86.4	87.8
0.01	0.001	1000	10000	90.3	90.0
0.01	0.001	4000	10000	197.7	200.0

6. Conclusions

We have developed a general theory for certain non-homogeneous density-dependent birth-death processes. The stochastic logistic growth process is a special case of our general theory. In addition, approximations to the first two moments of the stochastic logistic process have been derived. Using computer simulation of the logistic process, we have demonstrated that the approximations are quite accurate. Also, we have developed approximations for the absorption probabilities and the moments of the first absorption times using a diffusion approximation. The theory outlined in this paper should be useful for building stochastic models in many areas of biomedical research.

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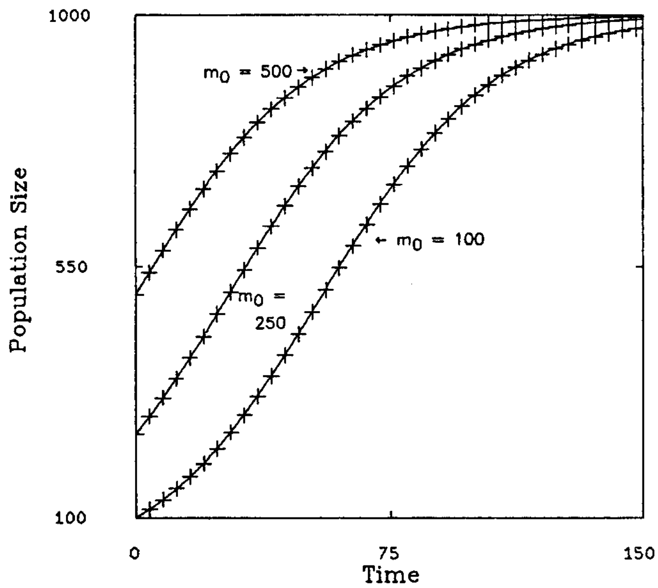

Figure 1. Average of simulated (+) and approximated (solid line) mean population sizes for stochastic logistic growth with $b = 0.05$, $d = 0.01$, $M = 1,000$, and various values for m_0.

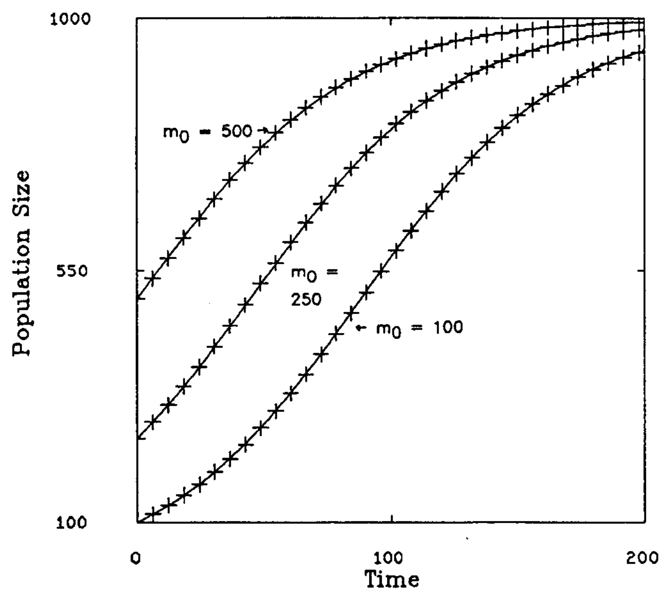

Figure 2. Average of simulated (+) and approximated (solid line) mean population sizes for stochastic logistic growth with $b = 0.03$, $d = 0.005$, $M = 1,000$, and various values for m_0.

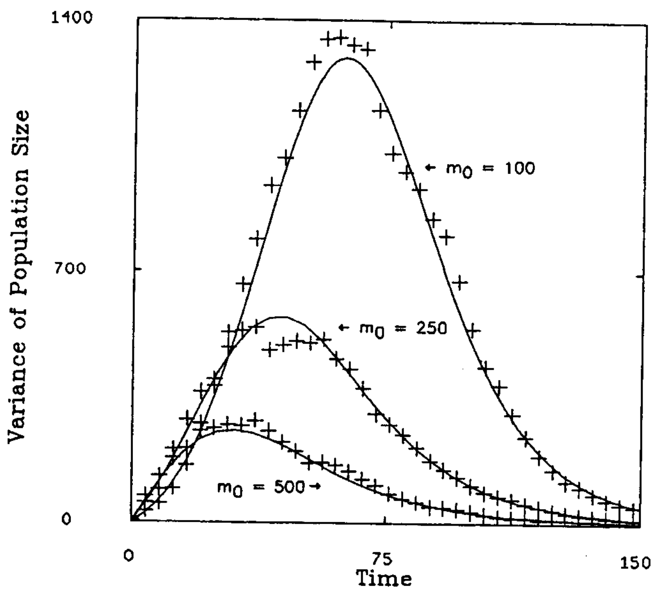

Figure 3. Average of simulated (+) and approximated (solid line) variance of population sizes for stochastic logistic growth with $b = 0.05$, $d = 0.01$, $M = 1,000$, and various values for m_0.

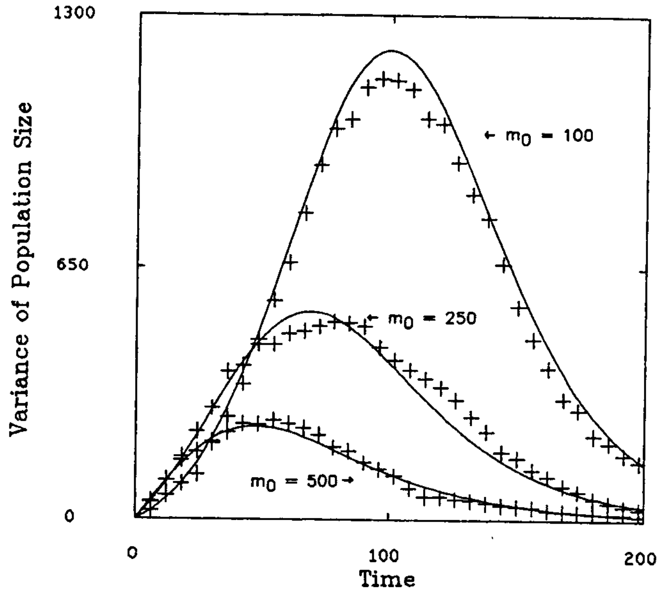

Figure 4. Average of simulated (+) and approximated (solid line) variance of population sizes for stochastic logistic growth with $b = 0.03$, $d = 0.005$, $M = 1,000$, and various values for m_0.

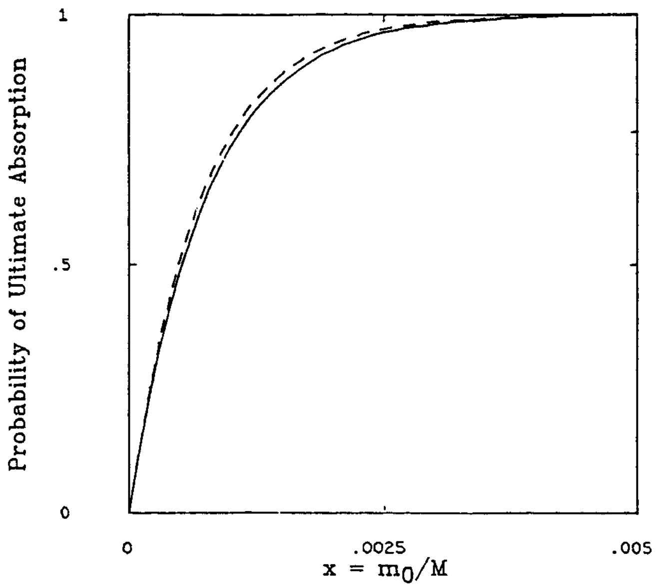

Figure 5. Ultimate absorption probabilities into $M = 1000$ for $b = 0.05$, $d = 0.01$ (solid line) and for $b = 0.03$, $d = 0.005$ (dashed line).

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