Stochastic Processes and their Applications 10 (1980) 105–113

A LINEAR CELL-SIZE DEPENDENT BRANCHING PROCESS

G.R. GRIMMETT

School of Mathematics, University of Bristol, Bristol, United Kingdom

Received 19 October 1979
Revised 22 January 1980

We consider a cell-size dependent branching process in which each cell grows at a linear rate and divides into a pair of daughter cells, preserving total size, at a rate proportional to its size. Such processes expand exponentially fast. If, on division, each possible combination of daughter sizes occurs with equal probability, then conventional analysis provides explicit values for the limiting distribution of the size of a typical cell, together with the distributions of its size just after its birth and just before its division.

Branching processes
cell-size dependent processes
multitype processes

1. Introduction

Many phenomena in the natural and social sciences are suitably modelled by branching processes, the members of which divide at rates which depend upon their sizes rather than their ages. The evolution of such processes has been discussed recently by Clifford and Sudbury [2, 5], who have studied a general formulation of such Markov chains. They were concerned with populations of replicating cells which grow in size until they split into pairs of daughter cells whose combined sizes equal those of their parents. The analysis of such processes is generally very hard because of the dependence between the number of members of the population and their sizes. Clifford and Sudbury were able to make some progress towards knowledge of the asymptotic distribution of the size of a typical cell, and the correlation between the life spans of the two daughter cells of a shared parent; the latter quantity is of interest in certain applications in biology. Also, they studied a specific example in which each cell grows at a constant rate and divides at a rate which is directly proportional to its size. In this paper I consider a particular cell-size-dependent branching process which differs only trivially from that of [2], and which is related to an existing model of Morgan and Leventhal [4] for the behaviour of algae and gorillas. I make two observations about this process. Firstly, it may be thought of as a two-dimensional version $A(t) = (X(t), Y(t))$ of an ordinary branching process, in which X and Y take integer values with X growing at a rate proportional to Y, and Y growing at a rate proportional to X. By constructing a related multitype branching process, I show that $A(t) \exp(-\kappa t)$ approaches a constant vector as $t \to \infty$ for some $\kappa > 0$. This answers a conjecture of Clifford. Secondly, the process is unusual in that the size of a typical cell may be observed as it evolves in time, and it is possible to calculate explicitly the asymptotic distribution of its size after a long length of time. This follows from conventional methods of analysis, which have sufficient power to describe other characteristics of typical cells as $t \to \infty$.

This process is not only of interest in that it allows solution. Also, it may be used to model processes describing the aggregation of cells in biology and the growth and division of polymers in physical chemistry (see [3] for details of the latter). Morgan and Leventhal's process differs from that considered here, but some of the methods of this paper may be applied to their model to gain information about its asymptotic behaviour.

More specifically, consider a population which comprises *particles*; at time $t = 0$ there is exactly one particle present. At any subsequent time t, the collection of particles present are aggregated into clumps called *cells*; if there are $X(t)$ cells and N_i is the number of particles in the ith, then there are $Z(t) = \sum_{i=1}^{X} N_i$ particles in all. The *size* of a cell is the number of particles it contains. As time passes, cells grow and divide. A unit of growth is represented by the creation of a new particle which is added to the growing cell; on division a cell splits into two daughter cells, the union of whose particle sets is the content of their mother. The rates at which growth and division occur are as follows.

Let $N(t)$ be the size of a particular cell at time t. Then

$$\mathbf{P}(N(t+h) = j \mid N(t) = i) = \begin{cases} 1 - \alpha h + o(h), & \text{if } j = i, \\ \alpha h + o(h), & \text{if } j = i + 1. \end{cases}$$

Thus, prior to division each cell grows like a Poisson process parameter α. The probability that the cell divides in $(t, t+h)$ is prescribed as $\beta(N(t) - 1)h + o(h)$; thus, large cells divide faster than small cells. When a cell divides, it is replaced by a pair of daughter cells whose sizes are one of the $(N-1)$ possible combinations $(1, N-1)$, $(2, N-2), \ldots, (N-1, 1)$; note here that we are assuming that the individual particles are distinguishable, so that the outcomes $(i, N-i)$ and $(N-i, i)$ are different for $i \neq \frac{1}{2}N$. One of these combinations is chosen at random according to some prescribed probability law. Possible distributions include cases when the daughter cells are as close in size as possible, or when each possible outcome occurs with equal probability. The evolutions of distinct cells are independent, as are events occurring in specified disjoint time intervals.

Let $Y(t) = Z(t) - X(t)$. The pair $A(t) = (X(t), Y(t))$ is a Markov chain, with possible transitions

$$A \to \begin{cases} A + (0, 1) & \text{for a growth,} \\ A + (1, -1) & \text{for a division.} \end{cases}$$

The infinitesimal transition probabilities

$$[\mathbf{P}((i,j)\,|\,(k,l)) = \mathbf{P}(A(t+h)=(i,j)\,|\,A(t)=(k,l))]$$

are given by

$$\begin{aligned} &\mathbf{P}((i,j+1)\,|\,(i,j)) = \alpha i h + o(h),\\ &\mathbf{P}((i+1,j-1)\,|\,(i,j)) = \beta j h + o(h),\\ &\mathbf{P}((i,j)\,|\,(i,j)) = 1-\alpha i h - \beta j h + o(h), \end{aligned} \tag{1}$$

with the boundary condition $A(0)=(1,0)$.

In Section 3 I shall show that there exist constants κ, λ and a random variable V such that $(X(t), Y(t))\exp(-\kappa t)\to V(1,\lambda)$ almost surely as $t\to\infty$.

When the probability distribution for the sizes of the daughters of a dividing cell is specified, it may be possible to trace the evolution in time of the size of a typical cell. This is certainly so in the case when each pair $(1, k-1), (2, k-2), \dots, (k-1, 1)$ of sizes of offspring from a mother of size k occurs with equal probability; this is done in Section 4. Results there include the asymptotic distribution of the size of a cell chosen at random as t approaches infinity, and the distributions of cell sizes immediately after their birth and before their death. In this case it is convenient to think of each cell as a configuration of particles drawn in a straight line, each pair of neighbouring particles being connected by a *link*. When a cell grows, a new particle together with a new link is added at an end of the chain. In any time interval $(t, t+h)$ each link breaks with probability $\beta h + o(h)$, breaking the cell into two corresponding constituent members. The number of links in the whole population at time t is $Y(t)=Z(t)-X(t)$.

2. The probability generating function and moments

Consider the cell-size-dependent branching process defined in the last section, with any specified probability distribution for the sizes of the daughter cells formed by a division. Let $p_{ij}(t)=\mathbf{P}(X(t)=i,\ Y(t)=j)$. The forward system of Kolmogorov equations is

$$p'_{ij}(t) = i\alpha p_{i,j-1}(t) - (i\alpha + j\beta)p_{ij}(t) + (j+1)\beta p_{i-1,j+1}(t), \quad \text{if} \quad i,j\geq 1$$

$$p'_{i0}(t) = -i\alpha p_{i0}(t) + \beta p_{i-1,1}(t), \quad \text{if} \quad i\geq 1;$$

the generating function

$$G(u,v;t) = \sum_{i\geq 1}\sum_{j\geq 0} u^i v^j p_{ij}(t)$$

satisfies the partial differential equation

$$G_t = \alpha u(v-1)G_u + \beta(u-v)G_v \tag{2}$$

subject to the boundary conditions

$$G(1, 1; t) = 1, \qquad G(u, v; 0) = u.$$

Through the characteristics of this equation, we may draw certain inferences about the evolution of the pair (X, Y), but it seems to be very hard to deduce rigorously the asymptotic behaviour of the chain. In the next section I use an alternative approach which is available for this particular cell-size-dependent chain.

We may at least calculate all moments of the chain by appropriate differentiation of (2).

Let $x(t) = \mathbf{E}(X(t))$ and $y(t) = \mathbf{E}(Y(t))$, and denote by κ and ν ($\kappa > \nu$) the two roots of the quadratic $z^2 + \beta z - \alpha\beta = 0$: $2\kappa = -\beta + (\beta^2 + 4\alpha\beta)^{1/2}$, $2\nu = -\beta - (\beta^2 + 4\alpha\beta)^{1/2}$.

Lemma 1.

$$x(t) = \beta(\gamma^2 + 4\gamma)^{-1/2}(\kappa^{-1}\,\mathrm{e}^{\kappa t} - \nu^{-1}\,\mathrm{e}^{\nu t}), \qquad y(t) = (\gamma^2 + 4\gamma)^{-1/2}(\mathrm{e}^{\kappa t} - \mathrm{e}^{\nu t}),$$

where $\gamma = \beta/\alpha$.

Hence,

$$x(t)\,\mathrm{e}^{-\kappa t} \to \beta(\kappa(\gamma^2 + 4\gamma)^{1/2})^{-1}, \qquad y(t)\,\mathrm{e}^{-\kappa t} \to (\gamma^2 + 4\gamma)^{-1/2}$$

and we have that

$$y(t)/x(t) \to \kappa/\beta. \tag{3}$$

Proof of Lemma 1. Differentiate (2) to obtain

$$x' = \beta y, \qquad y' = \alpha x - \beta y$$

with boundary conditions $x(0) = 1$, $y(0) = 0$.

A similar argument will, in theory at least, yield any moment $\mathbf{E}(X^m Y^n)$ of the process.

3. The limiting distribution as $t \to \infty$

Consider a two type branching process in which each particle is labelled either C or L ($C \sim$ cell, $L \sim$ link). Each C-particle divides into a C-particle together with a L-particle with intensity α, and each L-particle dies, leaving behind it a single C-particle, with intensity β; at time $t = 0$ there is a single C-particle. This branching process has the same infinitesimal transition probabilities (1) as the cell-size dependent process studied here, and this construction enables us to apply standard theorems of multitype branching processes (see, for example [1, p. 181]). That is, although the cell-size dependent process is not a multitype branching process, there exists such a process with the same transition probabilities.

The next theorem is an immediate consequence of this observation.

Theorem 2. *There exists a random variable V with absolutely continuous distribution such that*

$$X(t)\exp(-\kappa t)\to V, \qquad Y(t)\exp(-\kappa t)\to \kappa\beta^{-1}V$$

almost surely as $t\to\infty$.

A similar argument may be applied to certain other growth processes, including models obtainable by slight variations of the rules which govern the transition rates of the process studied by Morgan and Leventhal [4].

4. Cell size in equilibrium

Henceforth, suppose that when a cell of size k divides, the sizes of its daughters are equally likely to be any of the possible combinations $(1, k-1), (2, k-2), \ldots, (k-1, 1)$; think about the process as a 'linear' branching process in which each cell is a linear configuration of particles joined by links, as described in the introduction. At any instant in time, the lengths of the cells are random variables which are highly dependent upon each other. So far, I have been concerned with the global problem of watching the evolution of the whole population. Now I propose to restrict myself to the local formulation of the model, observing as time passes the development of one particular cell, chosen randomly to represent the cells which are present contemporaneously in the population. That is to say, define the Markov chain $W(t)$ as follows. Let c_1 denote the cell which exists alone from time $t=0$ to the time $t=T_1$ of the first cell division of the process. Immediately after T_1, pick, at random with equal probability, one of the two daughter cells of c_1; call this cell c_2. At the time T_2 of the division of cell c_2, pick again one of the two daughter cells with equal probability; call this cell c_3. Continue in this manner to obtain a sequence $c_1, c_2, \ldots$ of cells and $T_1, T_2, \ldots$ of times such that T_k is the instant of birth of cell c_{k+1}. Let $W(t)$ be the *length*, or number of links, in the cell c_k which is present in the population at time t. That is

$$W(t)=|c_K|, \quad \text{where } T_K\le t<T_{K+1}.$$

Clearly W is a Markov chain with state space $\{0, 1, 2, \ldots\}$. Its infinitesimal generator is $Q=(q_{ij})$, where

$$q_{i,i+1}=\alpha, \qquad i\ge 0,$$

$$q_{i,j}=\beta, \qquad i\ge 1, 0\le j<i,$$

$$q_{i,i}=-\alpha-\beta i.$$

Let $\pi = (\pi_0, \pi_1, \pi_2, \dots)$ be the limiting distribution of W and let $F(v) = \sum v^k \pi_k$ be its generating function.

Lemma 3. *$F(v) = \Gamma(\rho)A'(v)$, where*

$$A(v) = \exp(v\rho)v^{-\rho}(\Gamma(\rho))^{-1}\int_0^v t^{\rho-1}\, \mathrm{e}^{-t\rho}\mathrm{d}t \quad \textit{and} \quad \rho = \gamma^{-1} = \alpha/\beta.$$

Also

$$\pi_n = \rho^n(n+1)\Gamma(\rho+1)/\Gamma(\rho+n+2), \quad n \geq 0.$$

Proof. π is specified by the equation $\pi Q = 0$, which is the system

$$\alpha\pi_{n-1} - (\alpha + n\beta)\pi_n + \beta\sum_{n+1}^{\infty}\pi_k = 0, \quad n \geq 0 \tag{4}$$

together with the convention $\pi_{-1} = 0$ and the fact that

$$\sum_0^{\infty}\pi_k = 1, \quad \pi_k \geq 0. \tag{5}$$

It is easy to check that the sequence

$$\pi'_n = \rho^n(n+1)\Gamma(\rho+1)/\Gamma(\rho+n+2)$$

satisfies (4). To check that (5) holds, observe that

$$\pi'_n = \Gamma(\rho+1)(a_n - a_{n+1}),$$

where

$$a_n = \rho^n/\Gamma(\rho+n+1).$$

Thus

$$\sum_n^{\infty}\pi'_k = a_n\Gamma(\rho+1)$$

and in particular (5) holds. Hence $\pi' = \pi$.

Let $A(v)$ be the generating function of the sequence $(a_0, a_1, a_2, \dots)$. Then

$$A(v) = \sum_0^{\infty}(\rho v)^n/\Gamma(\rho+n+1)$$

and differentiation yields $F(v) = \Gamma(\rho)A'(v)$. Furthermore,

$$\begin{aligned} A'(v) &= \sum_0^{\infty}(\rho v)^{n-1}\frac{((n+\rho)-\rho)\rho}{\Gamma(\rho+n+1)} \\ &= \sum_0^{\infty}\frac{\rho(\rho v)^{n-1}}{\Gamma(\rho+n)} - (\rho/v)\sum_1^{\infty}\frac{\rho(\rho v)^n}{\Gamma(\rho+n+1)} \\ &= \rho A(v) - (\rho/v)(A(v) - (\Gamma(\rho+1))^{-1}). \end{aligned}$$

Hence,

$$A'(v)+\rho A(v)(v^{-1}-1)=\rho/(v\Gamma(\rho+1)) \tag{6}$$

which, subject to the condition $A(0)<\infty$, has solution given by Lemma 3.

Corollary 4. *The mean equilibrium number of links in a cell is given by*

$$\sum_0^\infty k\pi_k=-1+\rho\,\mathrm{e}^{\rho}\int_0^1 t^{\rho-1}\,\mathrm{e}^{-t\rho}\,\mathrm{d}t.$$

Proof. The mean cell length is

$$F'(1)=\Gamma(\rho)A''(1)$$

and the result follows from (6).

Other interesting distributions are the probability distribution of the number of links in a cell just after its birth and just before it divides. Let b_i and d_i be the number of links in cell c_i as it is born and as it divides respectively. Certainly the sequences $\{b_1, b_2, \ldots\}$ and $\{d_1, d_2, \ldots\}$ are Markov chains; $\boldsymbol{\mu}=(\mu_0, \mu_1, \ldots)$ and $\boldsymbol{\delta}=(\delta_0, \delta_1, \ldots)$ denote their limiting distributions respectively and call these vectors the *birth* and *death* distributions. $M(v)$ and $D(v)$ denote their generating functions.

Lemma 5. *Let* $H(v)=\int_0^1 t^{\rho-1}F(tv)\,\mathrm{d}t$. *Then*

$$M(v)=\frac{H(1)-H(v)}{(1-v)(1-\rho H(1))}$$

$$D(v)=\frac{F(v)-\rho H(v)}{1-\rho H(1)}.$$

Also

$$\mu_n=S^{-1}\sum_{n+1}^{\infty}\frac{\pi_k}{k+\rho}, \qquad \delta_n=S^{-1}\frac{n}{n+\rho}\pi_n,$$

where $S=\sum_1^\infty \pi_k k/(k+\rho)$.

Proof. In equilibrium

$$\begin{aligned}\delta_n&=\mathbf{P}(\text{cell is of length } n\,|\,\text{cell divides})\\&=\mathbf{P}(\text{cell divides}\,|\,\text{cell is of length } n)\pi_n/\mathbf{P}(\text{cell divides})\\&=S^{-1}n\beta/(\alpha+n\beta),\end{aligned}$$

where

$$S=\mathbf{P}(\text{cell divides})=\sum_1^\infty\frac{\pi_n n\beta}{\alpha+n\beta}.$$

Similarly, in equilibrium, if A_n denotes the event that a cell is born with n links and B_k denotes the event that its immediate ancestor had k links then

$$\mathbf{P}(A_n)=\sum_{k>n}\mathbf{P}(A_n\,|\,B_k)\mathbf{P}(B_k)=\sum_{k>n}\frac{\delta_k}{k}.$$

Hence,

$$D(v)=\sum v^n\delta_n=S^{-1}\sum_0^\infty v^n\pi_n\frac{(n+\rho)-\rho}{n+\rho}=S^{-1}(F(v)-\rho H(v)),$$

where $H(v)=\sum_0^\infty v^n\pi_n/(n+\rho)$.

An argument similar to that of the proof of Lemma 3 for $A(v)$ shows that H is given by

$$H(v)=\int_0^1 t^{\rho-1}F(tv)\,\mathrm{d}t$$

as required. The proof is easily completed.

Corollary 6. *The mean birth and death cell lengths are*

$$M'(1)=\sum n\mu_n=\frac{H''(1)}{2H'(1)},\qquad D'(1)=\sum n\delta_n=\frac{F'(1)-\rho H'(1)}{H'(1)}.$$

Proof. From Lemma 5.

Note that $D'(1)=1+2M'(1)$, as we would expect from the simple argument by symmetry that, on division, the parent cell passes all its links to its daughters save for that link which breaks in the act.

Finally, consider the pair (B_1, B_2) of birth lengths of the two daughter cells of a single parent, assuming that the process is in equilibrium.

Lemma 7. *The covariance of B_1 and B_2 is*

$$\operatorname{cov}(B_1,B_2)=\tfrac{1}{6}(D''(1)-2D'(1)+2)-D'(1)^2.$$

Proof. Let J be the length of the parent cell on division. Then

$$\begin{aligned}\mathbf{E}(B_1B_2)&=\sum_n\mathbf{E}(B_1B_2\,|\,J=n+1)\delta_{n+1}=\sum_n\delta_{n+1}\sum_{k=0}^{n}\frac{k(n-k)}{n+1}\\&=\sum_n\tfrac{1}{6}\delta_{n+1}n(n-1)=\frac{\mathrm{d}^2}{\mathrm{d}v^2}\frac{D(v)}{6v}\bigg|_{v=1}\end{aligned}$$

as required.

It is easy to deduce a formula for the correlation of B_1 and B_2 from Lemmas 5 and 7. Similarly, expressions for quantities such as the correlation between the life spans of sister cells (see [5]) may be found. Numerical calculations may in general be quite involved.

Examples. (a) *The case* $\rho = 1$. Easy calculations give

$$A(v) = v^{-1}(\mathrm{e}^{v} - 1), \qquad F(v) = v^{-2}(1 - \mathrm{e}^{v} + v\,\mathrm{e}^{v}),$$

$$H(v) = v^{-2}(\mathrm{e}^{v} - 1 - v), \qquad D(v) = \frac{2 + v + v\,\mathrm{e}^{v} - 2\mathrm{e}^{v}}{v^2(3 - \mathrm{e})}.$$

Hence the mean birth and death lengths are 0.275 . . . and 1.55 . . . respectively, and the mean cell length is $F'(1) = 0.718\ldots$. Approximating the number of links per cell by expectations (3) gives

$$y(t)/x(t) \to -\tfrac{1}{2} + \tfrac{1}{2}\sqrt{5} = 0.618\ldots.$$

The correlation between the birth sizes of the daughter cells of a shared parent in equilibrium is −0.053. . . . .

(b) *The case* $\rho = 2$. Similar calculations give

$$A(v) = \frac{\mathrm{e}^{2v} - 1 - 2v}{4v^2}, \qquad F(v) = \frac{v\,\mathrm{e}^{2v} + 1 + v - \mathrm{e}^{2v}}{2v^2}.$$

Other functions may be expressed in terms of integrals with no closed form solution. An easy numerical calculation shows that the mean cell length is $F'(1) = 1.19\ldots$; approximating by expectations (3) gives

$$y(t)/x(t) \to 1.$$

References

[1] K.B. Athreya and P.E. Ney, Branching Processes (Springer, Berlin, 1972).

[2] P. Clifford and A. Sudbury, The linear cell-size-dependent branching process, J. Appl. Probability 9 (1972) 687–696.

[3] N. Grassie, The Chemistry of High Polymer Degradation Processes (Butterworths, London, 1956).

[4] B.J.T. Morgan and B. Leventhal, A model for blue-green algae and gorillas, J. Appl. Probability 14 (1977) 675–688.

[5] A. Sudbury and P. Clifford, Some results for general cell-size-dependent branching processes, J. Appl. Probability 10 (1973) 289–298.