Interconnected Birth and Death Processes

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Summary

Two general cases of multiple linearly interconnected linear birth and death processes are considered. It is found that in general the solution of the Kolmogorov differential equations for the probability generating function (p.g.f) g of the random variables involved is not obtainable when subjected to standard methods; although one can obtain moments of the random variables from these equations. A method is considered for obtaining an approximate solution for g. This is based on the introduction of a sequence of stochastic processes such that the sequence $\{f^{(n)}\}$ of their p.g.f.'s tends to g as $n \rightarrow \infty$ in an appropriate manner. The method is applied to the simple case of two birth and death processes with birth and death rates λ_i and μ_i , i=1,2, interconnected linearly with transition rates ν and δ (see Figure 3). For this case some limit theorems are established and the probability of ultimate extinction of both the processes is considered. In particular, for the special cases (i) $\lambda_1 = \delta = 0$, with the remaining rates \cdot : time dependent and (ii) $\lambda_0 = \delta = 0$, with the remaining rates constant, explicit solutions for g have been obtained and studied.

This paper was prepared with the partial support first of the N.I.H Grant I-SO1-FR-05441, to the School of Public Health and subsequent ly of the N.I.H. Grant GM-10525 at the Statistical Laboratory, University of California, Berkeley.

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1. Introduction

Two or more interconnected birth and death processes (B-D processes, for short) arise so often in practical situationsparticularly in the field of biology -that they deserve special attention leading towards their theoretical investigation. The interconnections of B-D processes may arise, in biology for instance, due to mutations occurring in self-reproducing entities such as bacteria, viruses, etc. It is well known (refer Mitchison (1954))that when susceptible bacteria are exposed (in vitro or in vivo) to antibiotics, resistant strains of bacteria develop possibly due to mutation. A similar phenomenon appears to occur when populations of insects are exposed to insecticides, such as D.D.T. The development of so-called resistant strains of bacteria, or of insects which can multiply freely in the presence of antibiotic or insecticide is a well known phenomenon of great importance in medicine and public health. The development of such strains is a very undesirable phenomenon in the chemotherapy of infectious diseases, particularly because such resistant strains can spread and infect other persons, who then cannot be treated effectively with the antibiotics.

More recently, the studies concerning the production of blood cells indicate several stages in the cell-differentiation process. Here, the interconnection between any two consecutive stages of the cell appears to be due to some inner changes in the cell; although at each stage it is free to undergo a growth process. Readers interested in this application may refer to a series of papers by Till, et. al (1964), Siminovitch et al (1963), Fowler et al (1967).

The work concerning the mathematical aspects of interconnected birth and death processes which has been done in the past, although small in amount, needs a brief mention. Armitage (1952) has considered the case of two interconnected growth processes in a probabilistic manner but under a rather restrictive assumption; namely that the population growth at each of the two interconnected stages is deterministic. Wiggins (1957) has studied a case of two interconnected processes where mutation is assumed to occur only from normal cells to mutants. Furthermore, the normal cells may die but do not multiply and the birth and death rates involved are assumed to be independent of time.

One of the reasons that not much attention has been devoted to interconnected B-D processes in the past, even though they arise so often in practical situations, is the mathematical intractability to solution of the differential equations concerning these ... processes. Because of this, there has recently been a trend towards considering -not the original model of interconnected B-D processes- but a much more simplified one where the B-D processes are in effect left disconnected. Nissen Meyer (1966) has considered a simplified model concerning the effect of antibiotics on bacteria where the two B-D processes are left disconnected for obvious reasons. Here the number of mutants appearing during time interval (0,t) is assumed to be a Poisson process with Poisson parameter $v \int_0^t E[X(\tau)]d\tau$, where E[X(t)] is the expected number of susceptible bacteria at time t. Also, the susceptible bacteria are assumed to grow with no direct connection with the growth process of the

mutant bacteria. Gani and Yeo (1965) considered the case of two one-way connected B-D processes in connection with phage-reproduction where mutation may change a normal phage into a mutant one. Having found the equations of these processes intractable to solution, they consider a rather simplified model where the instantaneous risk of birth of a phage at any moment t is assumed to depend on the expectation of the number of phages of that type at time t rather than on the number itself.

In view of the growing importance of the interconnected B-D processes it is intended to consider such processes in this paper and to indicate in the simplest case of two interconnected B-D processes, a method which yields an approximate solution to the problem of obtaining the distribution of the random variables involved. The method, however, is also applicable to the multiple interconnected B-D processes in an analogous manner.

Throughout this paper, we shall restrict ourselves to the case of linear B-D processes. In section 2, we introduce the simple case of s interconnected B-D processes, while in section 3 we consider briefly a more general case which appears to arise in the blood cells growth and differentiation process. In section 4 we restrict ourselves to the case of two interconnected B-D processes, although the methods used there are equally applicable to more general cases.

2. Linearly Interconnected B-D processes.

Let the system have s states denoted by S_i , $i=1,2,\cdots,s$ as shown in Figure 1. Let $X_i(t)$ denote the number of particles

$$\begin{bmatrix} \lambda_1, \mu_1 & & & \lambda_2, \mu_2 & & & & \lambda_1, \mu_1 & & & \lambda_s, \mu_s \\ S_1 & & \delta_2 & & S_2 & & & & & & & & & & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & \lambda_s, \mu_s & & & & & \\ \delta_i & & & & & & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & & \lambda_s, \mu_s & & & \\ \delta_i & & & & & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & & \lambda_s, \mu_s & & \\ \delta_s & & & & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & & & \\ \delta_s & & & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & & \\ \delta_s & & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \delta_s & & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu_2 & & & \\ \end{bmatrix} \underbrace{ \begin{bmatrix} \lambda_1, \mu_1 & & & \\ \lambda_1, \mu$$

Figure 1 Linearly Interconnected B-D Processes

in state S_i at time t, with $X_i(0) = m_i$. It is assumed that for $i=1,2,\cdots,s$,

Pr[an
$$S_i$$
-particle multiplies to two in $(t,t+\tau)$] = $\lambda_i \tau$ + $o(\tau)$

Pr[" " dies in $(t,t+\tau)$] = $\mu_i \tau$ + $o(\tau)$

Pr[" " transfers to state S_{i+1} in $(t,t+\tau)$] = $\nu_i \tau$ + $o(\tau)$

Pr[" " " " S_{i-1} " "] = $\delta_i \tau$ + $o(\tau)$

Pr[" " undergoes no transition in $(t,t+\tau)$]=1- $(\lambda_i + \mu_i + \nu_i + \delta_i) \tau$ + $o(\tau)$

Pr[" " more than one transition in $(t,t+\tau)$] = $o(\tau)$.

Furthermore, it is assumed that all the events that might occur to a particle in $(t,t+\tau]$ are independent of the events occurring to other particles and of the events that occurred to this particle in the past. With these assumptions the vector process $\{X_1(t),\cdots,X_s(t)\}$ is a Markov process. Here the transition rates λ_1,μ_1,ν_1 and δ_1 are nonnegative and are assumed to be dependent on t unless otherwise specified. Let for $x_1=0,1,2,\cdots,$; $i=1,2,\cdots,s$; ${}^px_1,\cdots,x_s(t)=\Pr[X_1(t)=x_1;i=1,2,\cdots,s|X_1(0)=m_1;i=1,2,\cdots,s]$

and $G(u_1, \dots, u_s; t)$, or G for short, be their generating function (p.g.f., for short); with $|u_i| \le 1$, i=1,2,...,s. Following the standard argument, the Kolmogorov forward differential equation for G is given by

$$G_{t} + \sum_{i=1}^{s} [(1-u_{i})(\lambda_{i}u_{i}-\mu_{i})+\nu_{i}(u_{i}-u_{i+1})+\delta_{i}(u_{i}-u_{i-1})]G_{u_{i}} = 0$$
 (1)

with

$$G(u_1, \dots, u_s; 0) = \prod_{i=1}^{s} u_i^{m_i},$$
 (2)

where G_t and G_{u_i} denote the respective partial derivatives of G. We use here the convention that $\delta_1 = v_s = u_{s+1} = u_0 = 0$. Let g_j denote the p.g.f. of the probabilities $P_{x_1, \dots, x_s}(t)$ given that $m_i = 0$ for $i \neq j$ and that $m_j = 1$. Because of the assumption of independent growth of the particles, it is clear that

$$G(u_1, \dots, u_s; t) = \prod_{j=1}^{n} [g_j(u_1, \dots, u_s; t)]^{m_j},$$
 (3)

so that without loss of generality we assume that for some 1 < j < s, $m_j = 1$ and $m_i = 0$ for $i \neq j$. The equation for g_j accordingly is given by (1) with G replaced by g_j . It is this equation which has been found untractable to solution. One way however is to use it in a well known manner to obtain moments of the process $\{X_1(t), \cdots, X_s(t)\}$. For instance, if $\xi_i(t) = EX_i(t)$, then the vector $\xi_i'(t) = (\xi_1(t), \cdots, \xi_s(t))$ satisfies the following differential equation

$$\frac{\mathrm{d}}{\mathrm{d}t}\,\xi(t) = A\,\xi(t) \tag{4}$$

subject to the initial condition $\xi_{i}(0) = \delta_{ij}, i=1,2,\dots,s$, where

$$\frac{\mathrm{d}}{\mathrm{d}t}\,\xi^{'}(t)\,=\,(\frac{\mathrm{d}}{\mathrm{d}t}\,\xi_{1}(t)\,,\cdots,\frac{\mathrm{d}}{\mathrm{d}t}\,\xi_{s}(t))\,,$$

 $\overset{A}{\sim}$ is the s \times s matrix

and A is the s × s matrix
$$\begin{bmatrix}
(\lambda_1 - \mu_1 - \nu_1) & \delta_2 & 0 & 0 \cdots 0 & 0 & 0 \\
\nu_1 & (\lambda_2 - \mu_2 - \nu_2 - \delta_2) & \delta_3 & 0 \cdots 0 & 0 & 0 \\
0 & 0 & 0 & 0 \cdots \nu_{s-2} & (\lambda_{s-1} - \mu_{s-1} - \nu_{s-1} - \delta_{s-1}) & \delta_s \\
0 & 0 & 0 & 0 \cdots 0 & \nu_{s-1} & (\lambda_s \mu_s - \delta_s)
\end{bmatrix}$$
(5)

In principle, if all the rates are assumed to be constant, the equation (4) can be solved by standard methods. The solution will of course depend upon the characteristic roots of the matrix $\frac{A}{\sim}$. Similarly one can obtain higher moments such as variance-covariances of $X_{i}(t)$; the expressions for these , however, get rather involved. On the other hand, if the rates are time dependent, there does not appear to be any simple way of solving the equation (4). In the special case when $\delta_{i}=0$, $i=1,2,\dots,s$, (or instead if $v_{i}=0,i=1,2,\dots,s$) and the remaining rates are time dependent, one can again solve the equation (3) without andy real difficulty and can also find the higher moments. For instance, when $\delta_i = 0$, $i=1,2,\dots,s$, $m_1=1$ and

 $m_{j}=0$ for $j \geq 2$, we have

$$\xi_{1}(t) = \exp\{\int_{0}^{t} \psi_{1}(\tau) d\tau\}$$

$$\xi_{1}(t) = \int_{0}^{t} v_{i-1}(\tau) \exp\{\int_{\tau}^{t} \psi_{i}(s) ds\} \xi_{i-1}(\tau) d\tau; 2 \le i \le s,$$

$$(6)$$

where $\psi_{\bf i}(\tau) = \lambda_{\bf i}(\tau) - \mu_{\bf i}(\tau) - \nu_{\bf i}(\tau)$. For the case with s=2, these have been given by Gani and Yeo (1965). When all $\psi_{\bf i}$'s and $v_{\bf i}$'s are constant with all the $\psi_{\bf i}$'s being distinct, (6) reduces to the simpler form

$$\xi_{1}(t) = e^{\psi_{1}t}$$

$$\xi_{1}(t) = (\prod_{j=1}^{i-1} v_{j}) \sum_{j=1}^{i} \prod_{\substack{k=1\\k \neq j}}^{i} (\psi_{j} - \psi_{k})^{-1} e^{\psi_{j}t}; 2 \leq i \leq s.$$
(7)

In particular, if the $\psi_{\mathbf{i}}$'s are all equal to ψ say, then (6) simplifies to

$$\xi_{i}(t) = \frac{\int_{j=1}^{\pi} \int_{j-1}^{\nu_{i}} t^{i-1} e^{\psi t}}{(i-1)!} t^{i-1} e^{\psi t}; i=1,2,\dots,s; \nu_{0} = 1.$$
 (8)

If a particle is known to undergo a certain unknown number s of stages with a B-D process at each stage and if it is possible to observe the random variable $X_s(t)$ for various time points, then the fitting of the expression (7) or (8) to these will easily yeild an estimate of the number s. Determination of the number of stages

involved in the formation of cancer tumor (see Neyman and Scott(1966) is still an unsolved problem and a modified form of the expression (7) may help answer this question. The question as to how many stages are involved in the cell differentiation process for the production of certain blood cells starting from a stem cell (see Fowler et al(1967) may again partly be answered by fitting expressions such as (7) to the appropriate data. The process here is more general than the one considered above and is presented briefly in the next section.

3. A more general model with linearly interconnected B-D processes.

A discussion with Dr. J.E. Till of the Ontario Cancer Institute, Canada, led to the following possible model for the process concerned with the blood cells' formation and their differentiation starting with a stem cell. Hypothetically, stem cells are the progenitor cells with the capacity to produce differentiated blood cells and Siminovitch et al(1963)). new stem cells—(see Fowler et al(1967), Normally, when the body does not need red blood cells or some other forms of blood cells such as erythroblasts, the stem cells are in the resting state S_0 (see Figure 2). Anytime that some of the blood cells are killed and the body needs their replacement with fresh blood cells, the resting stem cells go into action and go through various stages — possibly more than one, say S_1, S_2, \cdots, S_k — where at each stage they undergo a B-D process with birth and death rates λ_i and $\mu_i, i=1,2,\cdots,k$. While the cell is in stage S_k and is undergoing a B-D process, its transition to one of the ℓ chains of stages (starting with

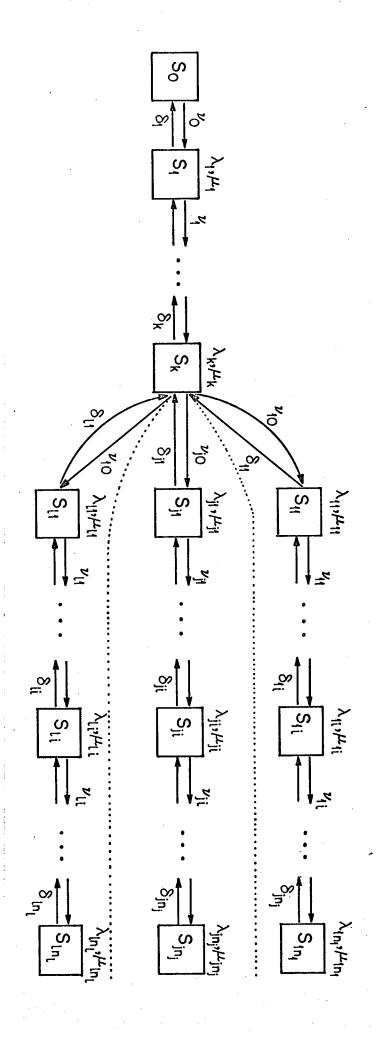


Figure 2 A System of Linearly Interconnected B-D Processes

stage S_{i1} for the jth chain, with j=1,2,..., ℓ ; see Figure 2)may take place with rates v_{j0} , $j=1,2,\dots,\ell$. The transition of a cell at kth stage to one of the ℓ chains is a step towards its differentition and eventually ending up with a particular type of blood cell specific to that chain. Typically, in the jth chain the cell goes through n_i interconnected stages starting with S_{i1} where at each stage the cell may undergo a B-D process, except possibly the last stage where λ_{j,n_i} may be zero since the cell is already in the state of the needed blood cell of jth type. This description is well exhibited in Figure 2, where for every two consecutive stages the transitions are shown both ways with rates v's and Each box represents a stage with the corresponding birth and death rates λ 's and μ 's indicated on the top with appropriate subscripts corresponding to that box. For the cell-differentiation problem it is not unreasonable to assume that the transitions between any two consecutive stages are only one-way so that all the δ 's are zero except possibly the first one, the δ_1 .

While the above model and its application to the relevant data will be discussed elsewhere, our aim here is merely to point out the fact that the models based on interconnected B-D processes and as complicated looking as in Figure 2, do arise in practical situations. Unfortunately , however, the corresponding differential equations for the p.g.f. of the random variables involved remain as untractable to solution as ever. In the present case, for instance, if $X_s(t)$ denotes the number of cells at time t in the sth stage of the first k stages with $s=1,2,\cdots,k$; $X_{ii}(t)$ denotes the number

in the ith stage of the jth chain, with i=1,2,...,n; j=1,2,..., ℓ ; and $G(u_0,u_1,...,u_k,u_{11},...,u_{\ell,n_{\ell}};t)$, or G for short, denotes the p.g.f. of the usual probabilities

$$P_{x_0,x_1,\dots,x_{\ell},n_{\ell}}(t),$$

then the Kolmogorov forward differential equation for G is given by

$$G_{t} = \sum_{s=0}^{k-1} [v_{s}(u_{s+1} - u_{s}) + \delta_{s}(u_{s-1} - u_{s}) - (1 - u_{s})(\lambda_{s}u_{s} - \mu_{s})]G_{u_{s}}$$

$$+ [\sum_{j=1}^{k} v_{j0}(u_{j1} - u_{k}) + \delta_{k}(u_{k-1} - u_{k}) - (1 - u_{k})(\lambda_{k}u_{k} - \mu_{k})]G_{u_{k}}$$

$$+ \sum_{j=1}^{k} [v_{j1}(u_{j2} - u_{j1}) + \delta_{j1}(u_{k} - u_{j1}) - (1 - u_{j1})(\lambda_{j1}u_{j1} - \mu_{j1})]G_{u_{j1}}$$

$$+ \sum_{j=1}^{k} \sum_{i=2}^{n_{j}} [v_{ji}(u_{ji+1} - u_{ji}) + \delta_{ji}(u_{ji-1} - u_{ji}) - (1 - u_{ji})(\lambda_{ji}u_{ji} - \mu_{ji})]G_{u_{ji}}.$$

$$(9)$$

One needs to solve (9) with the appropriate side condition, for example: G evaluated at t=0 is equal to u_0 . As before, the standard methods fail to yield a solution for this equation, although one can obtain expressions for moments from (9) when all the rates are constant. No way appears to work even for obtaining moments if the rates are time dependent. However, if all the δ 's are zero and the remaining rates are time dependent, one can easily obtain moments. For instance, if $\xi(t)$ with appropriate subscripts denotes the expected value of the corresponding X(t), then we have

$$\xi_{0}(t) = \exp[\int_{0}^{t} \psi_{0}(\tau) d\tau]$$

$$\xi_{s}(t) = \exp[\int_{0}^{t} \psi_{s}(\tau) d\tau] \{\int_{0}^{t} v_{s-1}(\tau) \xi_{s-1}(\tau) \exp[-\int_{0}^{\tau} \psi_{s}(u) du] d\tau\}; 1 \le s \le k,$$

$$\xi_{j1}(t) = \exp[\int_{0}^{t} \psi_{j1}(\tau) d\tau] \{\int_{0}^{t} v_{j0}(\tau) \xi_{k}(\tau) \exp[-\int_{0}^{\tau} \psi_{j1}(u) du] d\tau\}; j = 1, 2, , \ell$$

$$\xi_{j1}(t) = \exp[\int_{0}^{t} \psi_{j1}(\tau) d\tau] \{\int_{0}^{t} v_{j1-1}(\tau) \xi_{j1-1}(\tau) \exp[-\int_{0}^{\tau} \psi_{j1}(u) du] d\tau\};$$

$$for i = 1, 2, \dots, n_{j}; j = 1, 2, \dots, \ell, where$$

$$\begin{cases}
\psi_{0} = -\nu_{0}; \ \psi_{s} = \lambda_{s} - \mu_{s} - \nu_{s} & \text{for } 1 \leq s \leq k-1; \\
\psi_{k} = \lambda_{k} - \mu_{k} - \sum_{j=1}^{\Sigma} \nu_{j0}; \ \psi_{ji} = \lambda_{ji} - \mu_{ji} - \nu_{ji}.
\end{cases}$$
(11)

If all the ψ 's and v's are constant with all the ψ 's distinct, we have

$$\xi_{s}(t) = (\prod_{r=0}^{s-1} v_{r}) \sum_{r=0}^{s} A_{r} e^{\psi_{r}t}; \quad 0 \leq s \leq k,$$

$$\xi_{ji}(t) = (\prod_{r=0}^{k-1} v_{r}) (\prod_{r=0}^{i-1} v_{jr}) [\sum_{r=1}^{s} B_{jr} e^{\psi_{jr}t} + \sum_{r=0}^{k} C_{r} e^{\psi_{r}t}],$$

$$(12)$$

 $i = 1, 2, \dots, n_{j}; j=1, 2, \dots, \ell$, where

$$A_{\mathbf{r}} = \prod_{\substack{p=1\\p\neq\mathbf{r}}}^{\mathbf{s}} (\psi_{\mathbf{r}} - \psi_{\mathbf{p}})^{-1}$$
(13)

$$B_{jr} = \begin{bmatrix} i \\ \pi \\ p=1 \\ p \neq r \end{bmatrix} (\psi_{jr} - \psi_{jp})^{-1} \begin{bmatrix} k \\ \pi \\ p=0 \end{bmatrix} (\psi_{jr} - \psi_{p})^{-1}$$
(14)

$$C_{r} = \begin{bmatrix} i \\ \prod_{p=1}^{I} (\psi_{r} - \psi_{jp})^{-1} \end{bmatrix} \begin{bmatrix} k \\ \prod_{p=0}^{I} (\psi_{r} - \psi_{p})^{-1} \end{bmatrix}.$$
 (15)

While we shall discuss elsewhere the fitting of these expressions to the data on the cell differentiation, we wish to emphasize here that the mathematical problem of obtaining the distribution of the X(t) process at any time t still remains. Even in the simplest case of two interconnected B-D processes, one fails to find a way out for obtaining an explicit expression for p.g.f. G. In the next section, while restricting ourselves only to this simple case, we shall demonstrate (subsections 4.3 and 4.4) an approximating recursive approach for obtaining G, while using the Kolmogorov backward equation for G instead. The method, however, appears to be fairly general in its applicability to more complicated cases of interconnected B-D processes.

4.0 Two linearly interconnected B-D processes.

In this section we restrict ourselves to the case of two B-D processes as exhibited in Figure 3. The Kolmogorov forward differential equation for the p.g.f. $G(u_1,u_2;t)$ of probabilities $P_{x_1,x_2}(t)$ is given from (1) by

$$G_{t}^{+}[(1-u_{1})(\lambda_{1}u_{1}^{-\mu_{1}})+\nu(u_{1}^{-u_{2}})]G_{u_{1}}^{+}[(1-u_{2})(\lambda_{2}u_{2}^{-\mu_{2}})+\delta(u_{2}^{-u_{1}})]G_{u_{2}}^{-\mu_{2}}=0 \quad (16)$$

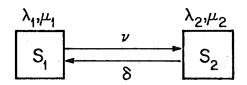


Figure 3 Two Linearly Interconnected B-D Processes

Let $m_1=1$ and $m_2=0$, so that $G(u_1,u_2;0)=u_1$. In its present generality equation (16) is not tractable to solution when subjected to standard methods. However, in the special cases,(i) $\lambda_1=\delta=0$, where all the remaining rates may be time dependent and (ii) $\lambda_2=\delta=0$, where all the other rates are constant, the author was successful in solving (16) for $G(u_1,u_2;t)$ explicitly. These cases are presented respectively in subsections 4.1 and 4.2. Before proceeding to these we consider briefly the case when all the rates are positive constants. Besides $X_1(t)$ and $X_2(t)$ we consider also the random variables $Y_1(t)$ and $Y_2(t)$ which denote the numbers of transitions during (0,t) from state S_1 to S_2 and from state S_2 to S_1 respectively. Let for i,j=1,2,

$$g_{i}(u_{1}, u_{2}, v_{1}, v_{2}; t)$$

$$= E\{u_{1}^{X_{1}(t)}, u_{2}^{X_{2}(t)}, v_{1}^{Y_{1}(t)}, v_{2}^{Y_{2}(t)}, v_{1}^{Y_{2}(t)}, v_{2}^{Y_{2}(t)}, v_{1}^{Y_{2}(t)}, v_{2}^{Y_{2}(t)}, v_{1}^{Y_{2}(t)}, v_{2}^{Y_{2}(t)}, v_{$$

Then it is easy to establish that the p.g.f.'s g_1 and g_2 satisfy the integral equations

$$g_{1}(u_{1}, u_{2}, v_{1}, v_{2}; t)$$

$$= u_{1}e^{-\theta_{1}t} + \int_{0}^{t} e^{-\theta_{1}\tau} (u_{2} + \lambda_{1}g_{1}^{2}(u_{1}, u_{2}, v_{1}, v_{2}; t - \tau)) d\tau$$

$$+ vv_{1}g_{2}(u_{1}, u_{2}, v_{1}, v_{2}; t - \tau) d\tau \qquad (18)$$

$$g_{2}(u_{1},u_{2},v_{1},v_{2};t)$$

$$= u_{2}e^{-\theta_{2}t} + \int_{0}^{t} e^{-\theta_{2}\tau} (\mu_{2}+\lambda_{2}g_{2}^{2}(u_{1},u_{2},v_{1},v_{2};t-\tau))$$

$$+ \delta v_{2}g_{1}(u_{1},u_{2},v_{1},v_{2};t-\tau) d\tau, \qquad (19)$$

where $\theta_1=\mu_1+\lambda_1+\nu$ and $\theta_2=\mu_2+\lambda_2+\delta$. These equations can be easily transformed into Kolmogorov backward equations for g_1 and g_2 given by

$$\frac{dg_1}{dt} = \lambda_1 g_1^2 - \theta_1 g_1 + v_1 g_2 + \mu_1 \tag{20}$$

$$\frac{dg_2}{dt} = \lambda_2 g_2^2 - \theta_2 g_2 + \delta v_2 g_1 + \mu_2, \tag{21}$$

with the side condition $g_i(u_1,u_2,v_1,v_2;0) = u_i;i=1,2$.

Equations (20) and (21) again are not tractable to solution. One may use these for obtaining moments; the first moments are given under $X_1(0)=1, X_2(0)=0$, by

$$EX_{1}(t) = \frac{1}{\alpha_{1} - \alpha_{2}} [(\alpha_{1} - \lambda_{2} + \mu_{2} + \delta) e^{\alpha_{1}t} - (\alpha_{2} - \lambda_{2} + \mu_{2} + \delta) e^{\alpha_{2}t}]$$

$$EX_{2}(t) = \frac{\nu}{\alpha_{1} - \alpha_{2}} [e^{\alpha_{1}t} - e^{\alpha_{2}t}]$$

$$EY_{1}(t) = \frac{\nu}{\alpha_{1} - \alpha_{2}} [\frac{1}{\alpha_{1}} (\alpha_{1} - \lambda_{2} + \mu_{2} + \delta) (e^{\alpha_{1}t} - 1) - \frac{1}{\alpha_{2}} (\alpha_{2} - \lambda_{2} + \mu_{2} + \delta) (e^{\alpha_{2}t} - 1)]$$

$$EY_{2}(t) = \frac{\delta \nu}{\alpha_{1} - \alpha_{2}} [\frac{1}{\alpha_{1}} (e^{\alpha_{1}t} - 1) - \frac{1}{\alpha_{2}} (e^{\alpha_{2}t} - 1)]$$

$$(22)$$

where

$$\alpha_{1}, \alpha_{2} = \frac{1}{2} [(\lambda_{2}^{-\mu_{2}} - \delta + \lambda_{1}^{-\mu_{1}} - \nu) + [(\lambda_{2}^{-\mu_{2}} - \delta - \lambda_{1}^{+\mu_{1}} + \nu)^{2} + 4\nu\delta]^{\frac{1}{2}}]$$
(23)

4.1 Case with $\lambda_1 = \delta = 0$. Here we allow all the remaining rates to be time dependent, so that Wiggins' case (1957) is only a special case of this. The equation (16) can be easily solved by standard methods when $\lambda_1 = \delta = 0$. Thus, omitting the details we find that

$$G(u_1, u_2; t) = P_{00}(t) + u_1 P_{10}(t) + \sum_{k=1}^{\infty} u_2^k P_{0k}(t)$$
 (24)

where

$$P_{00}(t) = 1 - \exp[-\int_{0}^{t} (\mu_{1} + \nu) d\tau]$$

$$- \int_{0}^{t} \nu(\tau) \exp[-\int_{0}^{\tau} (\lambda_{2} - \mu_{2} + \mu_{1} + \nu) ds]$$

$$\cdot \{\exp[-\int_{0}^{t} (\lambda_{2} - \mu_{2}) ds] - \frac{1}{2}$$

$$+ \int_{\tau}^{t} \exp[-\int_{0}^{s} (\lambda_{2} - \mu_{2}) dt] \lambda_{2}(s) ds\}^{-1} d\tau, \quad (25)$$

$$P_{10}(t) = \exp[-\int_{0}^{t} (\mu_1 + \nu) d\tau],$$
 (26)

$$P_{0k}(t) = \exp[-\int_{0}^{t} (\lambda_{2} - \mu_{2}) d\tau] \int_{0}^{t} \nu(\tau) \exp[-\int_{0}^{\tau} (\lambda_{2} - \mu_{2} + \mu_{1} + \nu) ds]$$

$$\cdot \{\int_{\tau}^{t} \lambda_{2}(s) \exp[-\int_{0}^{s} (\lambda_{2} - \mu_{2}) dt] ds\}^{k-1}$$

$$\cdot \{\exp[-\int_{0}^{t} (\lambda_{2} - \mu_{2}) ds]$$

$$+ \int_{\tau}^{t} \exp[-\int_{0}^{s} (\lambda_{2} - \mu_{2}) dt] \lambda_{2}(s) ds\}^{-(k+1)} d\tau, \quad (27)$$

for $k = 1, 2, \dots,$

When all the rates are constant, it is well known that $X_1(t) \to 0$ a.s., whereas $X_2(t) \to 0$ a.s. as $t \to \infty$ if $\mu_2 \geq \lambda_2$. On the other hand if $\mu_2 < \lambda_2$, $X_2(t) \to 0$ with probability p_{00} and to ∞ with probability $1 - p_{00} = p_{0,\infty}$ where

$$p_{00} = \lim_{t\to\infty} P_{00}(t) = \frac{\mu_1 + \nu(\mu_2/\lambda_2)}{\mu_1 + \nu}$$
 (28)

4.2 Case with $\lambda_2 = \delta = 0$ Assuming that all the remaining rates are constant we shall attempt here to solve the backward equations (20) and (21) instead, although one could treat the forward equation (16) in a similar manner. Since $\delta = 0$, $Y_2(t) = 0$. Again with $\lambda_2 = 0$, (21) easily yields solution for g_2 which now is only a function of u_2 and t, and is given by

$$g_2(u_2;t) = [1 - (1-u_2)e^{-\mu_2 t}].$$
 (29)

Rewriting (20) we have

$$\frac{dg_1}{dt} = \lambda_1 g_1^2 - \theta_1 g_1 + (\mu_1 + \nu v_1) - \nu v_1 (1 - u_2) e^{-\mu_2 t}.$$
 (30)

The problem here is to solve this subject to the side condition

$$g_1(u_1, u_2, v_1; 0) = u_1.$$
 (31)

Substituting $z = g_1 - (\theta_1/2\lambda_1)$ in (30) we have

$$\frac{dz}{dt} = \lambda_1 z^2 - \frac{1}{4\lambda_1} \{ (\mu_1 + \nu - \lambda_1)^2 + 4\lambda_1 \nu (1 - \nu_1) \} - \nu \nu_1 (1 - \nu_2) e^{-\mu_2 t}$$

$$= \frac{\phi'(t)}{h(t)} z^2 - \frac{h'(t)}{\phi(t)}$$
(32)

say, where the functions ϕ and h satisfy the relations

$$\begin{cases} \frac{\phi'(t)}{h(t)} = \lambda_1, \\ \frac{h'(t)}{\phi(t)} = \frac{1}{4\lambda_1} \{ (\mu_1 + \nu - \lambda_1)^2 + 4\lambda_1 \nu (1 - \nu_1) \} + \nu \nu_1 (1 - \nu_2) e^{-\mu_2 t}. \end{cases}$$
(33)

Once (33) is solved for ϕ and h, (32) immediately yields

$$z(t) = -\frac{h(t)}{\phi(t)} + \frac{1}{\phi^{2}(t)} \left(D - \int_{0}^{t} \frac{\phi'(\tau)}{\phi^{2}(\tau)h(\tau)} d\tau\right)^{-1}, \tag{34}$$

where D is the constant of integration to be evaluated from the side condition (31). Eliminating h from equations (33) we have

$$\phi''(t) = \{ (\frac{\mu_1 + \nu - \lambda_1}{2})^2 + \lambda_1 \nu (1 - \nu_1) + \nu \lambda_1 \nu_1 (1 - \nu_2) e^{-\mu_2 t} \} \phi(t).$$
 (35)

With change of variable from t to s where

$$s = \frac{2}{\mu_2} \left(v \lambda_1 v_1 (1 - u_2) \right)^{1/2} e^{-(\mu_2/2)t}, \tag{36}$$

(35) yields

$$s^{2} \frac{d^{2} \phi}{ds^{2}} + s \frac{d \phi}{ds} - \left[\left(\frac{\mu_{1} + \nu - \lambda_{1}}{\mu_{2}} \right)^{2} + \frac{\mu_{\lambda_{1}} \nu (1 - \nu_{1})}{\mu_{2}^{2}} + s^{2} \right] \phi = 0.$$
 (37)

Referring to Kamke (pages 437-42 (1945)), its solution is immediately given by

$$Z_a(i \ s) = C_1 J_a(i \ s) + C_2 Y_a(i \ s)$$
 (38)

where

$$a = \left\{ \left(\frac{\mu_1 + \nu - \lambda_1}{\mu_2} \right)^2 + \frac{\mu_{\lambda_1} \nu (1 - \nu_1)}{\mu_2^2} \right\}^{1/2}$$
(39)

and $J_a(y)$ and $Y_a(y)$ are Bessel functions as defined in Kamke(1945). In our case the appropriate values of the constants C_1 and C_2 turn out to be $C_2 = 0$, $C_1 = i^{-a}$, so that the relevant solution of (37) is given by

$$\phi(s) = \frac{1}{i^a} J_a(i \ s) = \sum_{r=0}^{\infty} \frac{(s/2)^{a+2r}}{r! \sqrt{(a+r+1)}} = \psi_a(s), say. \tag{40}$$

Thus we have

$$\phi(t) = \psi_a(x e^{-(\mu_2/2)t}) \tag{41}$$

and

$$h(t) = \psi_a(x e^{-(\mu_2/2)t})(-\frac{\mu_2}{2\lambda_1} x) e^{-(\mu_2/2)t}$$
 (42)

where

$$x = \frac{2}{\mu_2} \left\{ v \lambda_1 v_1 (1 - u_2) \right\}^{1/2}$$
 (43)

Finally substituting these in (34) and using the side condition (31) we obtain the desired solution for g_1 as

$$g_{1}(u_{1},u_{2}v_{1};t) = \frac{\theta_{1}}{2\lambda_{1}} + \frac{\psi_{a}^{'}(x e^{-(\mu_{2}/2)t})}{\psi_{a}(x e^{-(\mu_{2}/2)t})} \frac{\mu_{2}}{2\lambda_{1}} x e^{-(\mu_{2}/2)t}$$

$$+ \psi_{a}^{-2}(x e^{-(\mu_{2}/2)t})[\{(u_{1} - \frac{\theta_{1}}{2\lambda_{1}})\psi_{a}^{2}(x) - \psi_{a}^{'}(x)\psi_{a}(x)\frac{\mu_{2}}{2\lambda_{1}}x\}^{-1}$$

$$- \lambda_{1} \int_{0}^{t} \frac{d\tau}{\psi_{a}^{2}(x e^{-(\mu_{2}/2)\tau})} \int_{0}^{1} .$$
(44)

This solution is rather involved although it is expressed in terms of the function $\psi_a(y)$ whose properties are well known. Furthermore, it is suggestive as to how the solution in the more general case with $\lambda_2 > 0$ and $\delta > 0$ may be complicated. Again, it also appears difficult to express (44) in terms of probabilties $P_{x_1,x_2,y_1}(t)$. On the other hand, letting $t \to \infty$ in (44) we have for $|u_2| < 1$,

$$\lim_{t \to \infty} g_{1}(u_{1}, u_{2}, v_{1}; t) = \frac{\theta_{1}^{-\mu} 2^{a}}{2\lambda_{1}}$$

$$= \frac{1}{2\lambda_{1}} [\theta_{1}^{-\{\theta_{1}^{2} - \mu\lambda_{1}(\mu_{1} + \nu v_{1})\}^{\frac{1}{2}}] = p(v_{1}), \text{ say.}$$
(45)

Since $Y_1(t)$ is a nondecreasing function of t, $Y_1(t)^{\dagger}$ Y a.s. as $t \to \infty$ where the p.g.f. of Y turns out to be equal to $p(v_1)$. Notice that p(1) = 1 if and only if $\lambda_1 \le \nu + \mu_1$, in which case Y is an honest random variable. On the other hand if $\lambda_1 > \nu + \mu_1$, $\Pr(Y = \infty) = 1 - p(1)$; here $p(1) = (\nu + \mu_1)/\lambda_1$ is also the probability p_{00} of ultimate extinction of both $X_1(t)$ and $X_2(t)$.

4.3 Case where $\delta = 0$ and the remaining rates are positive constants.

This is a case more general than the ones considered in the last two subsections. Here it was found difficult to obtain an exact expression for the p.g.f. $g_1(u_1,u_2,v_1;t)$ from (20). The expression for g_2 of (21) is known for the present case (see Bartlett (1955)) and is given by

$$g_{2}(u_{2};t) = \frac{(\lambda_{2}u_{2}-\mu_{2})-\mu_{2}(1-u_{2})e^{(\lambda_{2}-\mu_{2})t}}{(\lambda_{2}u_{2}-\mu_{2})-\lambda_{2}(1-u_{2})e^{(\lambda_{2}-\mu_{2})t}}.$$
(46)

The method that will yield an approximate solution for gains based of

The method that will yield an approximate solution for g_1 is based on the introduction of a sequence of stochastic processes $\{X_1^{(n)}(t), X_2^{(n)}(t), Y_1^{(n)}(t)\}$ with the initial condition $X_1^{(n)}(0) = 1, X_2^{(n)}(0) = Y_1^{(n)}(0) = 0, n=0,1,2,\cdots$, such that

sequence $\{f^{(n)}(u_1,u_2,v_1;t)\}$ of their p.g.f.'s tends to $g_1(u_1u_2,v_1;t)$ as $n\to\infty$. Here since $\delta=0$, $Y_2(t)\equiv0$. For convenience we define for n = 0, $f^{(0)}(u_1, u_2, v_1; t) = 1$, for t > 0. This would imply that starting with $X_1^{(0)}(0) = 1$, the particle is considered as dead right from the start. For n = 1, we defined the process $\{X_1^{(1)}(t), X_2^{(1)}(t), Y_1^{(1)}(t)\}$ as follows: The starting particle in state $\, S_{1} \,$ may either die with rate $\, \mu_{1} \,$ or may undergo a transition to state S_2 with rate $\,
u\,$ where it undergoes a simple homogeneous B-D process with rates $~\lambda_2^{}~$ and $~\mu_2^{}~$ respectively, or finally it may give a birth with rate λ_1 with the property that as soon as the event of birth takes place it follows from then on the process corresponding to n = 0; whereas its progeny follows the process with n = 1. In general the nth process is defined in a similar manner except that here the particle after giving a birth follows the (n-1)th process whereas its progeny follows the nth process. Similar to (18) we have the integral equation for $f^{(n)}$, $n=1,2,\cdots$, as

$$f^{(n)}(t) = u_1 e^{-\theta_1 t} + \int_0^t e^{-\theta_1 (t-\tau)} \{\mu_1 + \lambda_1 f^{(n-1)}(\tau) f^{(n)}(\tau) + \nu v_1 g_2(\tau) \} d\tau$$
 (47)

which yields the differential equation

$$\frac{df^{(n)}}{dt} = \lambda_1 f^{(n-1)} f^{(n)} - \theta_1 f^{(n)} + \mu_1 + \nu v_1 g_2$$
 (48)

with

$$f^{(n)}(u_1,u_2,v_1;0) = u_1.$$
 (49)

Here the arguments u_1, u_2 and v_1 of f's and g_2 are suppressed for convenience. In the following, we shall use this convention without reservation. Because of the recursive character of the equation (48), it can be solved for $f^{(n)}$ recursively yielding for $n=1,2,\cdots$

$$f^{(n)} = u_1 e^{-\theta_1 t + \lambda_1 \int_0^t f^{(n-1)}(\tau) d\tau} + \int_0^t e^{-\theta_1 (t - \tau) + \lambda_1 \int_\tau^t f^{(n-1)}(s) ds} \{\mu_1 + \nu v_1 g_2(\tau)\} d\tau.$$
(50)

Remark Notice that the process corresponding to n= 1 is equivalent to the original process with $\lambda_1=0$, the case which was studied by Wiggins (1957). Also, one of the essential features of the nth process is that the particle starting at t = 0, is allowed to yield at most n births after which it is considered as dead. It may however die with rate μ_1 or undergo transition to state S_2 with rate ν before even touching the limit of n births. Taking $0 \le u_1 \le 1$, $0 \le u_2 \le 1$, $0 \le v_1 \le 1$, we have the following theorem.

 $\frac{\text{Theorem 1}}{\text{sequence for every fixed}} \; \text{(i)} \; \left\{f^{(n)}(u_1,u_2,v_1;t)\right\} \; \underline{\text{is a monotone nonincreasing}} \\ \underline{\text{sequence for every fixed}} \; \left(u_1,u_2,v_1;t\right) \; \underline{\text{and is uniformly bounded}}.$

(ii) $\{f^{(n)}(u_1,u_2,v_1;t)\}$ converges to $g_1(u_1,u_2,v_1;t)$ uniformly for $t \in [0,T]$, $0 \le u_1 \le 1$, $0 \le u_2 \le 1$, $0 \le v_1 \le 1$; where T is finite but arbitrary.

 $\underline{\underline{Proof}}$ (i) $\{f^{(n)}\}$ is a sequence of p.g.f.'s and hence $|f^{(n)}| \le 1$ for all n. That it is a monotone nonincreasing sequence can be easily proved by an induction argument while using (50).

(ii) $\{f^{(n)}(u_1,u_2,v_1;t)\}$ being a bounded monotone sequence, must converge as $n\to\infty$ pointwise for every point $(u_1,u_2,v_1;t)$. Let

$$f(u_1, u_2, v_1; t) = \lim_{n \to \infty} f^{(n)}(u_1, u_2, v_1; t).$$
 (51)

Again since $0 \le (1-f^{(n)}) \dagger (1-f)$, by monotone convergence theorem, $\int_0^t f^{(n)}(\tau) d\tau \downarrow \int_0^t f(\tau) d\tau$ for every finite t, where the other arguments u_1, u_2 and v_1 of f.'s are suppressed for convenience. From this it follows that $\int_0^t f^{(n-1)}(\tau) f^{(n)}(\tau) d\tau \downarrow \int_0^t f^2(\tau) d\tau$, and hence as $0 \to \infty$

$$\int_{0}^{t} e^{-\theta_{1}(t-\tau)} f^{(n-1)}(\tau) f^{(n-1)}(\tau) d\tau + \int_{0}^{t} e^{-\theta_{1}(t-\tau)} f^{2}(\tau) d\tau$$
 (52)

for every finite t. Using this while taking limit of (47) as $n\to\infty$, we have

$$f(t) = u_1 e^{-\theta_1 t} + \int_0^t e^{-\theta_1 (t-\tau)} \{\mu_1 + \lambda_1 f^2(\tau) + \nu v_1 g_2(\tau)\} d\tau.$$
 (53)

Comparing this with (18) and using the fact that such equations have unique solutions, we have

$$f(u_1, u_2, v_1; t) = g_1(u_1, u_2, v_1; t).$$
 (54)

Thus as $n\to\infty$ the sequence $\{f^{(n)}\}$ converges pointwise to g_1 . That this convergence is uniform as stated in the theorem follows easily now from **Dini**'s theorem(see page 425 Apostol(1957)), keeping in mind that all the f's are continuous functions of their arguments.

Theorem 2. For every fixed (u_1, u_2, v_1) with $0 \le u_1 < 1$, $0 \le u_2 < 1$ and $0 \le v_1 \le 1$, the limits $q = \lim_{t \to \infty} g_2(u_2; t)$, $p_n = \lim_{t \to \infty} f^{(n)}(u_1, u_2, v_1; t)$ for $n = 0, 1, 2, \cdots$, and $p = \lim_{t \to \infty} g_1(u_1, u_2, v_1; t)$ all exist and the following relations hold.

(i)
$$p_n = \frac{\mu_1 + \nu v_1 q}{\theta_1 - \lambda p_{n-1}}, \quad n = 1, 2, \dots,$$

(ii)
$$p = \lim_{n \to \infty} p_n$$

(iii)
$$f^{(n)}(t) \downarrow g_1(t)$$
 as $n \to \infty$, uniformly for $t \in [0,\infty)$.

We need the following lemma for the proof of this theorem.

$$h^{(n)}(t) = u_1 e^{-(\theta_1 - \lambda_1 p_{n-1})t} + \int_0^t e^{-(\theta_1 - \lambda_1 p_{n-1})} (t - \tau)$$

$$(v v_1 q + \mu_1) d\tau \qquad (55)$$

where $q = \lim_{t \to \infty} g_2(u_2;t) = \min(1, \mu_2/\lambda_2)$, then $\lim_{t \to \infty} f^{(n)}(t)$ exists and for $n = 1, 2, \dots, \underline{\text{we have}}$

$$p_n = \lim_{t \to \infty} f^{(n)}(t) = \lim_{t \to \infty} h^{(n)}(t) = \frac{v v_1 q + \mu_1}{\theta_1 - \lambda_1 p_{n-1}}$$
 (56)

Proof. Since $\lim_{t\to\infty} \exp\{-\theta_1 t + \lambda_1 \int_0^t f^{(n-1)}(\tau) d\tau\} = 0$, and for every finite b > 0,

$$\lim_{t \to \infty} \int_{0}^{b} \exp[-\theta_{1}(t-\tau) + \lambda_{1} \int_{\tau}^{t} f^{(n-1)}(s) ds]$$

$$(v \ v_{1} \ g_{2}(\tau) + \mu_{1}) d\tau = 0, \tag{57}$$

we have from (50)

$$\lim_{t\to\infty} f^{(n)}(t) = \lim_{t\to\infty} \int_{b}^{t} \exp[-\theta_1(t-\tau) + \lambda_1 \int_{\tau}^{t} f^{(n-1)}(s) ds]$$

$$(v \ v_1 \ g_2(\tau) + \mu_1)d\tau$$
 (58)

Similarly from (55), we have for every finite b > 0,

$$\lim_{t \to \infty} h^{(n)}(t) = \lim_{t \to \infty} \int_{b}^{t} \exp[-\theta_{1} - \lambda_{1} P_{n-1}](t-\tau)]$$

$$(v \ v_{1} \ q + \mu_{1}) d\tau \tag{59}$$

In order to prove (56), it is sufficient to show that for a given arbitrary $\epsilon > 0$, it is possible to choose $b(\epsilon) > 0$ such that for any $t > b(\epsilon)$

$$D = \int_{b}^{t} \exp[-\theta_{1}(t-\tau) + \lambda_{1} \int_{\tau}^{t} f^{(n-1)}(s) ds] (v v_{1}g_{2} + \mu_{1}) d\tau$$

$$- \int_{b}^{t} \exp[-(\theta_{1} - \lambda_{1} p_{n-1})(t-\tau)] (v v_{1} q + \mu_{1}) d\tau | < \epsilon.$$
 (60)

Chose a positive constant η less than $\min[\epsilon] \frac{\mu_1 + \nu}{2 \lambda_1 + \nu}$, $\frac{\nu + \mu_1}{2 \lambda_1}$. Having chosen η , choose $b(\epsilon)$ large enough such that for $\tau > b(\epsilon)$

$$|f^{(n-1)}(\tau) - p_{n-1}| \le \eta ; |g_2(\tau) - q| \le \eta .$$
 (61)

Rewritting the left hand side of (60), we have

$$D = |(v \ v_1 \ q + \mu_1)| \int_{b}^{t} \exp[(-\theta_1 + \lambda_1 \ p_{n-1})(t-\tau)] \exp[\lambda_1 \int_{\tau}^{t} f^{(n-1)}(s) ds]$$

$$-\lambda_1 \ p_{n-1}(t-\tau) \int_{b}^{\tau} d\tau + v \ v_1 \int_{b}^{t} \exp[-\theta_1(t-\tau) + \lambda_1 \int_{\tau}^{t} f^{(n-1)}(s) ds]$$

$$(g_2(\tau) - q) d\tau | (62)$$

Again, by virtue of (61), for $b(\epsilon) < \tau < t$,

$$\left| \int_{\tau}^{t} f^{(n-1)}(s) ds - (t-\tau) p_{n-1} \right| \leq \int_{\tau}^{t} |f^{(n-1)}(s) - p_{n-1}| ds \leq (t-\tau) \eta,$$
(63)

and hence

$$|1-\exp[\lambda_1 \int_{\tau}^{t} f^{(n-1)}(s) ds - \lambda_1(t-\tau) p_{n-1}]| \le \exp[\lambda_1 \eta(t-\tau)] -1$$
 (64)

From this it follows that for any $t > b(\epsilon)$

$$D \leq (\nu v_{1}q + \mu_{1}) \int_{0}^{t-b} \exp[(-\theta_{1} + \lambda_{1}p_{n-1})\tau] \{\exp[\lambda_{1}\eta\tau] - 1\} d\tau$$

$$+ \nu v_{1}\eta \int_{0}^{t-b} \exp[(-\theta_{1} + \lambda_{1})\tau] d\tau$$

$$\leq \frac{\nu_{1}v_{1}q + \mu_{1}}{\theta_{1} - \lambda_{1}(p_{n-1} + \eta)} - \frac{\nu v_{1}q + \mu_{1}}{\theta_{1} - \lambda_{1}p_{n-1}} + \frac{\nu v_{1}\eta}{\theta_{1} - \lambda_{1}}$$

$$\leq \left[\frac{2\lambda_{1} + \nu}{\mu_{1} + \nu}\right] \eta \leq \epsilon,$$
(65)

where in the end we have used the facts that $0 \le p_{n-1} \le 1$, $0 \le q \le 1$ and $\eta < \frac{\nu + \mu_1}{2\lambda_1}$. Thus $\lim_{t \to \infty} f^{(n)}(t) = \lim_{t \to \infty} h^{(n)}(t)$. From this and (59) the lemma follows.

Remark Since $p_0 = 1 = f^{(0)}(t)$, from the above lemma it follows by induction argument that for n=0,1,2,..., $f^{(n)}(t) \rightarrow p_n$ as $t \rightarrow \infty$; and p_n 's satisfy the relation

$$p_n = \frac{vv_1^{q+\mu_1}}{\theta_1^{-\lambda_1}p_{n-1}}, n = 1, 2, \cdots.$$
 (66)

Proof of Theorem 2. The beginning part of the theorem 2 and
part (i) follow in part from the above lemma. For (ii) let

$$h(t) = u_1 e^{-(\theta_1 - \lambda_1)t} + (\nu v_1 q + \mu_1) \int_0^t e^{-(\theta_1 - \lambda_1 p)(t - \tau)} d\tau, 0 \le v_1 \le 1.$$
 (67)

Then following the lines of argument used in proving the above lemma it can be shown that

$$p = \lim_{t \to \infty} g_1(t) = \lim_{t \to \infty} h(t).$$
 (68)

However on simplifying right side of (67) and taking its limit as $t \rightarrow \infty$, we obtain

$$p = \frac{v v_1 q + \mu_1}{\theta_1 - \lambda_1 p} . \tag{69}$$

On the other hand $\lim_{n\to\infty} p_n$ also satisfies the relation (69). This is clear from (66). This proves (ii). Thus we have shown so far that

$$p = \lim_{n \to \infty} \lim_{t \to \infty} f^{(n)}(t) = \lim_{t \to \infty} \lim_{n \to \infty} f^{(n)}(t) = \lim_{t \to \infty} g_{\underline{1}}(t).$$
 (70)

From this and the assertion (ii) of theorem 1, assertion (iii) of Theorem 2 easily follows. This completes the proof of theorem 2.

Solving (69) for p we have

$$\lim_{t\to\infty} g_1(u_1, u_2, v_1; t) = p(v_1, q) = \frac{1}{2\lambda_1} [\theta_1 - \{\theta_1^2 - 4\lambda_1(\mu_1 + v_1 q)\}^{\frac{1}{2}}].$$
 (71)

If $p_{00} = \lim_{t\to\infty} \Pr(X_1(t) = X_2(t) = 0)$ which is also the probability of ultimate extinction of both $X_1(t)$ and $X_2(t)$, then we have

$$p_{00} = p(1,q) = \begin{cases} \frac{1}{2\lambda_{1}} [\theta_{1}^{-1} {\theta_{1}^{2} - \mu_{\lambda_{1}}} (\mu_{1} + \nu q)]^{\frac{1}{2}}] & (\mu_{2} < \lambda_{2}) \\ (\mu_{1} + \nu) / \lambda_{1} & (\mu_{2} \ge \lambda_{2}; \mu_{1} + \nu < \lambda_{1}) & (72) \\ 1 & (\mu_{2} \ge \lambda_{2}; \mu_{1} + \nu \ge \lambda_{1}) \end{cases}$$

When $p_{00} < 1$, with probability $1-p_{00}$, $(X_1(t), X_2(t)) \rightarrow (0, \infty)$ or (∞, ∞) as $t \rightarrow \infty$ according as $\mu_1 + \nu \geq \lambda_1$ and $\mu_2 < \lambda_2$ or $\mu_1 + \nu < \lambda_1$ and $\mu_2 < \lambda_2$ respectively.

If we ignore the random variable $X_2(t)$, one can obtain explicitly the expression for the p.g.f. $g_1(u_1,v_1;t)$ of $X_1(t)$ and $Y_1(t)$ as follows: Replacing g_2 by unity in (20) we observe that our new $g_1(u_1,v_1;t)$ satisfies the equation

$$\frac{dg_1}{dt} = \lambda_1 g_1^2 - \theta_1 g_1 + \nu v_1 + \mu_1, \tag{73}$$

which can be solved easily subject to the side condition $g_1(u_1,v_1;0) = u_1$, yielding

$$= \underbrace{\begin{bmatrix} \mathbf{r}_{1}(\mathbf{v}_{1}, \mathbf{v}_{1}; t) \\ \mathbf{r}_{2}(\mathbf{v}_{1}) + & \frac{\mathbf{r}_{1}(\mathbf{v}_{1}) - \mathbf{r}_{2}(\mathbf{v}_{1})}{1 - \left(\frac{\mathbf{u}_{1} - \mathbf{r}_{1}(\mathbf{v}_{1})}{\mathbf{u}_{1} - \mathbf{r}_{2}(\mathbf{v}_{1})}\right)} e^{\lambda_{1}(\mathbf{r}_{1}(\mathbf{v}_{1}) - \mathbf{r}_{2}(\mathbf{v}_{1}))t}$$
(74)

where $\mathbf{r}_1(\mathbf{v}_1)$ and $\mathbf{v}_2(\mathbf{v}_1)$ are with positive and negative signs respectively,

$$\frac{1}{2\lambda_{1}}[\theta_{1} \pm \{\theta_{1}^{2} - 4\lambda_{1}(\nu v_{1} + \mu_{1})\}^{\frac{1}{2}}]. \tag{75}$$

Now being a nondecreasing function of t, $Y_1(t)^{\dagger}$ Y a.s. as $t \to \infty$, where the p.g.f. of Y is given by

$$\lim_{t\to\infty} g_1(1,v_1;t) = r_2(v_1) = \frac{1}{2\lambda_1} [\theta_1 - \{\theta_1^2 - \mu_{\lambda_1}(v_1 + \mu_1)\}^{\frac{1}{2}}] = p(v_1,1). \quad (76)$$

From this we easily obtain

$$Pr(Y=0) = \frac{1}{2\lambda_1} \left[\theta_1 - \{ \theta_1^2 - \mu_1 \lambda_1 \}^{\frac{1}{2}} \right]$$
 (77)

and for $r=1,2,\cdots$,

$$P(Y=r) = \frac{1}{\lambda_1} \left\{ \frac{(2r-2)!}{r!(r-1)!} \cdot \frac{(\lambda_1 v)^r}{\{\theta_1^2 - 4\mu_1 \lambda_1\}} \right\}$$
 (78)

These probabilities add up to one only when $\mu_1 + \nu \ge \lambda_1$. When $\mu_1 + \nu < \lambda_1$, $\mu_2(1) < 1$, so that $P(Y=\infty) = 1 - r_2(1)$.

4.4 Case where all the rates are positive constants

This is the case where we allow transitions from both ways between states S_1 and S_2 . Let us denote random variables of section 4.0 by $\{X_{11}(t), X_{12}(t), Y_{11}(t), Y_{12}(t)\}$ if $X_1(0) = 1$ and $X_1(0) = 0$ and by $\{X_{21}(t), X_{22}(t), Y_{21}(t), Y_{22}(t)\}$ if $X_1(0) = 0$ and $X_2(0) = 1$, with their p.g.f.'s $g_1(u_1, u_2, v_1, v_2; t)$ and $g_2(u_1, u_2, v_1, v_2; t)$ respectively. We introduce two sequences of stochastic processes namely; $\{X_{11}^{(n)}(t), X_{12}^{(n)}(t), Y_{11}^{(n)}(t), Y_{12}^{(n)}(t)\}$ with $X_{11}^{(n)}(0) = 1$, $X_{12}^{(n)}(0) = Y_{11}^{(n)}(0) = Y_{12}^{(n)}(0) = 0$, and $\{X_{21}^{(n)}(t), X_{22}^{(n)}(t), Y_{21}^{(n)}(t), Y_{22}^{(n)}(t)\}$ with $X_{22}^{(n)}(0) = 1$,

 $X_{21}^{(n)}(0) = Y_{21}^{(n)}(0) = Y_{22}^{(n)}(0) = 0$, for n=0,1,2,... Let the sequences $\{f_1^{(n)}(u_1,u_2,v_1,v_2;t)\}$ and $\{f_2^{(n)}(u_1,u_2,v_1,v_2;t)\}$ denote their respective p.g.f.'s. For convenience, define for t > 0, $f_1^{(0)}(u_1,u_2,v_1,v_2;t) = 1$; i=1,2. As before in a recursive manner we define the nth process of the two sequences as follows: The starting particle in state $S_1^{(i=1,2)}$ either dies with rate $\mu_1^{(i)}$,

or undergoes a transition to state S_j ($j \neq i, j=1,2$) and there it follows the growth according to the (n-1)th process of the jth sequence, or gives a birth with rate λ_i with the feature that after this event it follows the (n-1)th process of the ith sequence whereas its progeny follows the nth process of the same sequence. With this definition, the analogues of (48) are given by

$$\frac{df_{1}^{(n)}}{dt} = \lambda_{1}f_{1}^{(n-1)}f_{1}^{(n)}-\theta_{1}f_{1}^{(n)}+\mu_{1}+\nu v_{1}f_{2}^{(n-1)}$$

$$\frac{df_{2}^{(n)}}{dt} = \lambda_{2}f_{2}^{(n-1)}f_{2}^{(n)}-\theta_{2}f_{2}^{(n)}+\mu_{2}+\delta v_{2}f_{1}^{(n-1)}.$$
(79)

These can be solved recursively yielding

$$f_{1}^{(n)} = u_{1} e^{-\theta_{1}t + \lambda_{1} \int_{0}^{t} f_{1}^{(n-1)}(\tau) d\tau}$$

$$+ \int_{0}^{t} e^{-\theta_{1}(t-\tau) + \lambda_{1} \int_{\tau}^{t} f_{1}^{(n-1)}(s) ds} \{\mu_{1} + \nu v_{1} f_{2}^{(n-1)}(\tau) \} d\tau.$$

$$f_{2}^{(n)} = u_{2} e^{-\theta_{2}t + \lambda_{2} \int_{0}^{t} f_{2}^{(n-1)}(\tau) d\tau}$$

$$+ \int_{0}^{t} e^{-\theta_{2}(t-\tau) + \lambda_{2} \int_{\tau}^{t} f_{2}^{(n-1)}(s) ds} \{\mu_{2} + \delta v_{2} f_{1}^{(n-1)}(\tau) \} d\tau.$$

$$(81)$$

The following theorem is the analogue of results given in theorems 1 and 2, and is given without proof as it follows along similar lines.

Theorem 3 (i) $\{f_1^{(n)}, f_2^{(n)}\}$ is a monotone nonincreasing double sequence for every fixed (u_1, u_2, v_1, v_2, t) and $\{f_i^{(n)}\}$ is uniformly bounded for all n, and i=1,2.

(ii) For every fixed point (u_1, u_2, v_1, v_2) with $0 \le u_i < 1$, $0 \le v_i \le 1$, i=1,2, the limits $q_i = \lim_{t \to \infty} g_i(u_1, u_2, v_1, v_2; t)$; $p_{in} = \lim_{t \to \infty} f_i^{(n)}(u_1, u_2, v_1, v_2; t)$ for n=1,2,..., all exist and the following relations hold.

(a)
$$p_{1n} = \frac{\mu_1 + \nu \nu_1 p_{2,n-1}}{\theta_1 + \lambda_1 p_{1,n-1}}$$
; $p_{2n} = \frac{\mu_2 + \delta \nu_2 p_{1,n-1}}{\theta_2 - \lambda_2 p_{2,n-1}}$, $n=1,2,\cdots$,

(b)
$$q_i = \lim_{n\to\infty} p_{in}$$
; i=1,2,

(c)
$$(f_1^{(n)}(t), f_2^{(n)}(t))$$
 ($g_1(t), g_2(t)$) as $n \rightarrow \infty$, uniformly for $t \in [0, \infty)$.

Letting $n\to\infty,$ in theorem 3, [(ii)a], we observe that q_1 and q_2 satisfy the equations

$$\lambda_1 q_1^2 - \theta_1 q_1 + \mu_1 + \nu v_1 q_2 = 0$$

$$\lambda_2 q_2^2 - \theta_2 q_2 + \mu_2 + \delta v_2 q_1 = 0.$$
(82)

With $v_1=v_2=1$, the solution of these equations for q_1 and q_2 are the probabilities of ultimate extinction of $(X_1(t),X_2(t))$ when $X_1(0)=1$, $X_2(0)=0$ and $X_1(0)=0$, $X_2(0)=1$ respectively. One may study (82) as two parabolas in (q_1,q_2) plane, and the problem is to find the solution for (q_1,q_2) which lie in the unit square with points (0,0) and (1,1) as its diagonal vertices. Explicit solution in terms of v_1 and v_2 appears rather involved. Thus,

from now on we restrict ourselves to the case with $v_1=v_2=1$. Clearly (1,1) is a solution of (82). Also, from the geometry of two parabolas, one can easily establish that the necessary condition for (1,1) to be the only admissible solution of (82) is

$$\nu + \mu_1 > \lambda_1; \delta + \mu_2 > \lambda_2.$$
 (83)

Writing (82) differently with $v_1 = v_2 = 1$, we have

$$q_2 = \frac{1}{\nu} [\theta_1 q_1 - \lambda_1 q_1^2 - \mu_1] \tag{84}$$

$$q_1 = \frac{1}{\delta} [\theta_2 q_2 - \lambda_2 q_2^2 - \mu_2]. \tag{85}$$

Now given that the conditions (83) are satisfied, in order that the two parabolas (84) and (85) do not intersect each other again in the unit square after once intersecting at point (1,1), the necessary and sufficient condition is that the slope of the parabola (85) at point (1,1) be less than or equal to that of (84) at the same point. The slope S_1 of (84) at (1,1) is given by

$$S_1 = \frac{dq_2}{dq_1} \bigg|_{q_1 = q_2 = 1} = \frac{\mu_1 + \nu - \lambda_1}{\nu} , \qquad (86)$$

and that of (85) is given by

$$S_2 = \frac{dq_2}{dq_1}\Big|_{q_1 = q_2 = 1} = \frac{\delta}{\mu_2 + \delta - \lambda_2}$$
 (87)

Thus given (83) , the necessary and sufficient condition that (1,1) be the only admissible solution of (82) is $S_2 \leq S_1$ or

$$(\mu_1 + \nu - \lambda_1) (\mu_2 + \delta - \lambda_2) \ge \nu \delta . \tag{88}$$

Combining (83) and (88), we observe that in order that (1,1) be the only admissible solution of (82) with $v_1=v_2=1$, it is necessary and sufficient that

$$A + B \ge C, \tag{89}$$

where

$$A = v + \mu_1 - \lambda_1, B = \delta + \mu_2 - \lambda_2 \text{ and } C = \{(A-B)^2 + 4v\delta\}^{\frac{1}{2}}$$
.

ACKNOWLEDGEMENTS

The author is greatly indebted to Professors J. Neyman and L. LeCam for their encouragement and inspiration during the course of these investigations. He is also grateful to Dr. Bucy and to Dr. Till for some very helpful discussions.

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