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Part 3. Biological applications

APPROXIMATIONS: REPLACING RANDOM VARIABLES WITH THEIR MEANS

JOE GANI, *Australian National University*
Mathematical Sciences Institute, The Australian National University, Bldg 26B, Canberra ACT 0200, Australia.

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APPROXIMATIONS: REPLACING RANDOM VARIABLES WITH THEIR MEANS

BY JOE GANI

Abstract

One of the standard methods for approximating a bivariate continuous-time Markov chain $\{X(t), Y(t) : t \geq 0\}$, which proves too difficult to solve in its original form, is to replace one of its variables by its mean, This leads to a simplified stochastic process for the remaining variable which can usually be solved, although the technique is not always optimal. In this note we consider two cases where the method is successful for carrier infections and mutating bacteria, and one case where it is somewhat less so for the SIS epidemics.

Keywords: Markov chain; random variable; mean; approximation

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1. Introduction

2014 marks the fiftieth anniversary of the founding of the Applied Probability Trust (APT) in 1964. The APT is currently the publisher of four journals (*Journal of Applied Probability*, *Advances in Applied Probability*, *Mathematical Spectrum*, and *The Mathematical Scientist*) as well as several occasional Festschrifts and other volumes. The present volume celebrates this anniversary, and the efforts of the APT Trustees, the editors of these journals, the numerous authors of their articles, and not least the members of the editorial office in Sheffield. I can only wish the APT continuing success in the future; as one of the APT's founding fathers, it has been a singular privilege to witness its growth and its contributions to the development of the field of applied probability.

The study of models in applied probability is riven with approximations. This note illustrates both 'success' and 'failure' of a common technique of approximating the behaviour of a stochastic process by replacing a component by a suitably defined first moment so as, hopefully, to elicit more information about other aspects of the process.

2. The case of carrier infectives

In the basic model for an epidemic spread via carriers, the probability distribution of the number of susceptibles $X(t)$ at time t after the onset of disease spread, with n susceptibles initially, is known to be

$$p_r(t) = \mathbb{P}\{X(t) = r\} = \binom{n}{r} \sum_{j=r}^{n} (-1)^{j-r} \binom{n-r}{j-r} \left[\frac{\rho + j\mathrm{e}^{-(\rho+j)t}}{\rho + j} \right]^b$$

with probability generating function (PGF)

$$\mathbb{E}[u^{X(t)}] = \sum_{j=0}^{n} \binom{n}{j} (u-1)^j \left[\frac{\rho + j\mathrm{e}^{-(\rho+j)t}}{\rho + j} \right]^b, \qquad 0 < u \leq 1,$$

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where b is the initial numbers of carriers, $X(0) = n$, and $\rho = a/\beta$ with a the death rate of carriers and β the infection rate. (For further details, see Bailey (1975, p. 194) and Daley and Gani (1999, p. 97)).

A possible approximation to the stochastic model is obtained by replacing $Y(t)$, the number of carriers at time t, by its mean $b\mathrm{e}^{-at}$. In this case, the probability $p_r(t) = \mathbb{P}\{X(t) = r \mid X(0) = n\}$ satisfies the forward Kolmogorov equation

$$\frac{\mathrm{d}p_r(t)}{\mathrm{d}t} = (-\beta r b\mathrm{e}^{-at})p_r(t) + \beta(r+1)b\mathrm{e}^{-at}p_{r+1}(t)$$

for $r = 0, 1, \ldots, n$. The PGF $f(u,t) = \sum_{r=0}^{n} p_r u^r$, $0 < u \leq 1$, satisfies the partial differential equation

$$\frac{\partial f}{\partial t} = -\beta b\,\mathrm{e}^{-at}(1-u)\,\frac{\partial f}{\partial u}\,.$$

This equation is readily solved by the method of characteristics, yielding

$$(u-1)\mathrm{e}^{(\beta b/a)\mathrm{e}^{-at}} = C, \qquad f = K,$$

where C and K are constants. It follows that

$$f(u,t) = g((u-1)\mathrm{e}^{(\beta b/a)\mathrm{e}^{-at}}),$$

where g is an unknown function, such that, for $t = 0$,

$$f(u,0) = u^n = g((u-1)\mathrm{e}^{\beta b/a}).$$

Writing $w = (u-1)\mathrm{e}^{\beta b/a}$, or $u = 1 + w\mathrm{e}^{-\beta b/a}$, we obtain

$$f(u,t) = [(u-1)\mathrm{e}^{\beta b/a}(\mathrm{e}^{-at} - 1) + 1]^n,$$

a binomial with

$$\mathbb{E}[X(t)] = n\,\mathrm{e}^{(-\beta b/a)(1-\mathrm{e}^{-at})} = n\,\mathrm{e}^{-(b/\rho)(1-\mathrm{e}^{-at})}.$$

The exact mean is known to be

$$n\left[\frac{\rho + \mathrm{e}^{-(\rho+1)t}}{\rho+1}\right]^b,$$

although both are asymptotically the same for small t. Here the exact and approximate models are similar, but as we shall see in Section 4, the replacement of a random variable by its mean does not always work so well.

3. Mutating bacteria

Consider now a pool of bacteria $X(t)$ which reproduce at rate k, some of which mutate to $Y(t)$ at rate β and may then become unresponsive to antibiotics. The mutants reproduce at rate a, and die at rate m. See Figure 1.

For the bivariate probability p_{xy} at time $t \geq 0$, defined by

$$p_{xy} = \mathbb{P}\{(X,Y)(t) = (x,y) \mid (X,Y)(0) = (x_0, 0)\},$$

we derive the forward Kolmogorov equations

$$\frac{\mathrm{d}p_{xy}}{\mathrm{d}t} = -[(k+\beta)x + (a+m)y]p_{xy} + k(x-1)\,p_{x-1,y} + \beta(x+1)\,p_{x+1,y-1}.$$

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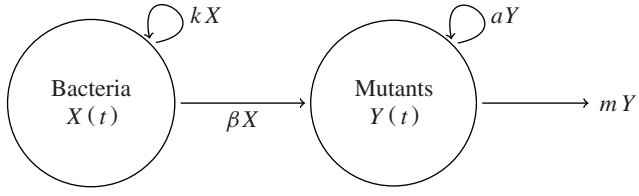

FIGURE 1: Mutating bacteria.

The PGF $f(u,v,t)=\sum_{x,y=0}^{\infty}p_{xy}(t)u^x v^y$, $0<u,v\le 1$, satisfies the partial differential equation

$$\frac{\partial f}{\partial t}=(ku^2-(k+\beta)u+\beta v)\frac{\partial f}{\partial u}+(av^2-(a+m)v+m)\frac{\partial f}{\partial v},$$

whose auxiliary equations are

$$\frac{\mathrm{d}t}{-1}=\frac{\mathrm{d}u}{ku^2-(k+\beta)u+\beta v}=\frac{\mathrm{d}v}{av^2-(a+m)v+m}=\frac{\mathrm{d}f}{0}.$$

These equations are difficult to solve, so we fall back on the replacement of $X(t)$ by its deterministic mean $x_0\mathrm{e}^{(k-\beta)t}$. The Kolmogorov equations for the probabilities $p_y=\mathbb{P}\{Y(t)=y\mid Y(0)=0\}$ are then

$$\begin{aligned}\frac{\mathrm{d}p_y(t)}{\mathrm{d}t}&=-((k+\beta)x_0\,\mathrm{e}^{(k-\beta)t+(a+m)y})p_{xy}+kx_0\mathrm{e}^{(k-\beta)t}p_y+\beta x_0\mathrm{e}^{(k-\beta)t}p_{y-1}\\&\quad+a(y-1)p_{y-1}+m(y+1)p_{y+1}\end{aligned}$$

for which the PGF $f(v,t)=\sum_{y=0}^{\infty}p_y(t)v^y$, $0<v\le 1$, satisfies the partial differential equation

$$\frac{\partial f}{\partial t}=(av^2-(a+m)v+m)\frac{\partial f}{\partial v}-\beta x_0(v-1)\,f\,\mathrm{e}^{(k-\beta)t}.$$

The auxiliary equations here are

$$\frac{\mathrm{d}t}{1}=\frac{\mathrm{d}v}{(v-1)(m-av)}=\frac{\mathrm{d}f}{\beta x_0(v-1)f\mathrm{e}^{(k-\beta)t}},$$

yielding

$$\frac{av-m}{v-1}\mathrm{e}^{-(a-m)t}=C\quad\text{or}\quad v=\frac{m\,\mathrm{e}^{(m-a)t}-C}{a\,\mathrm{e}^{(m-a)t}-C},$$

where C is a constant. Hence,

$$\frac{\mathrm{d}f}{f}=\beta(v-1)x_0\,\mathrm{e}^{(k-\beta)t}=\frac{\beta x_0\mathrm{e}^{(k-\beta)t}(m-a)\mathrm{e}^{(m-a)t}}{a\mathrm{e}^{(m-a)t}-C},$$

so that

$$\ln f=\int\frac{(m-a)\beta x_0\mathrm{e}^{(k-\beta+m-a)t}}{a\mathrm{e}^{(m-a)t}-C}\,\mathrm{d}t.$$

This is not easy to integrate unless $k=\beta$, when we see that

$$\frac{\mathrm{d}f}{\beta x_0(v-1)f}=\frac{\mathrm{d}v}{(m-av)(v-1)}\quad\text{or}\quad\frac{\mathrm{d}f}{\beta x_0 f}=\frac{\mathrm{d}v}{m-av},$$

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so that

$$\ln f = -\frac{\beta x_0}{a}\ln(av - m).$$

Hence, when $k = \beta$, $f(av - m)^{\beta x_0/a} = f((av - m)\mathrm{e}^{-(a-m)t}/(v - 1))$.

When $t = 0$,

$$(av - m)^{\beta x_0/a} = f\left(\frac{av - m}{v - 1}\right).$$

Writing $z = (av - m)/(v - 1)$, we find that

$$f(z) = \left[\frac{(a - m)z}{z - a}\right]^{\beta x_0/a},$$

so that

$$f(v, t) = \left[\frac{a - m}{av(1 - \mathrm{e}^{(a-m)t} + a\mathrm{e}^{(a-m)t} - m)}\right]^{\beta x_0/a}.$$

From this, we can obtain an approximation to the mean of $Y(t)$ as

$$\mathbb{E}[Y(t)] \approx \frac{\beta x_0}{a - m}(\mathrm{e}^{(a-m)t} - 1).$$

4. The case of the SIS epidemic

We now consider the standard deterministic SIS epidemic, with x susceptibles and y infectives governed by the equations

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -\beta xy + ay, \qquad \frac{\mathrm{d}y}{\mathrm{d}t} = \beta xy - ay = -\frac{\mathrm{d}x}{\mathrm{d}t},$$

where β is the infection parameter and a is the rate of recovery of the infectives; see Figure 2. This is a case where the replacement of the infectives by their mean in the stochastic version leads to a model somewhat different from the original.

If $x(0) = N$ and $y(0) = 1$, where $x + y = N + 1$ for all $t \geq 0$, solving the differential equations shows that

$$x(t) = \frac{(N + 1)(a - \beta N) - a\,\mathrm{e}^{(\beta(N+1)-a)t}}{a - \beta N - \beta\,\mathrm{e}^{(\beta(N+1)-a)t}}$$

and

$$y(t) = N + 1 - x(t) = \frac{K}{\beta + (\beta N - a)\mathrm{e}^{-Kt}},$$

where $K = \beta(N + 1) - a$.

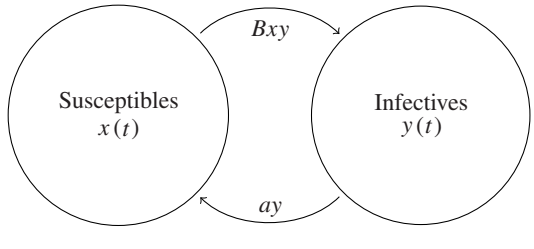

FIGURE 2: SIS epidemic.

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We proceed to replace $Y(t)$ in the stochastic version of this model by its deterministic mean $y(t)$. Writing

$$p_i(t) = \mathbb{P}\{X(t) = i \mid X(0) = N\},$$

we obtain the forward Kolmogorov equations as

$$\frac{\mathrm{d}p_i}{\mathrm{d}t} = \frac{\beta(N+1)-a}{\beta+(\beta N-a)\mathrm{e}^{-Kt}}\big[-(\beta i+a)p_i+\beta(i+1)p_{i+1}+ap_{i-1}\big].$$

Define now

$$T = \frac{1}{\beta}\ln\left(1+\frac{\beta(\mathrm{e}^{Kt}-1)}{K}\right),$$

where $\mathrm{d}T/\mathrm{d}t = y(t)$, with $T = 0$ when $t = 0$. Hence,

$$\frac{\mathrm{d}p_i}{\mathrm{d}T} = -(\beta i+a)p_i+\beta(i+1)p_{i+1}+ap_{i-1},$$

whose PGF $f(u,T) = \sum_{i=0}^{N+1} p_i(t)u^i$ satisfies the partial differential equation

$$\frac{\partial f}{\partial T} = -\beta(u-1)\frac{\partial f}{\partial u}+a(u-1)f.$$

Its auxiliary equations are

$$\frac{\mathrm{d}T}{1} = \frac{\mathrm{d}u}{\beta(u-1)} = \frac{\mathrm{d}f}{a(u-1)f},$$

leading to $\ln f = (a/\beta)u + C$ and $\ln(u-1) = \beta T + D$, where C and D are constants. Thus,

$$f\,\mathrm{e}^{-a/\beta} = g\big((u-1)\mathrm{e}^{-\beta T}\big)$$

with g an unknown function, where

$$u^N = (g(u-1))\mathrm{e}^{(a/\beta)u} \quad \text{when } T = 0.$$

Writing $w = (u-1)$, we find that $(w+1)^N = g(w)\mathrm{e}^{(a/\beta)(w+1)}$, so that

$$f(u,t) = [1+(u-1)\mathrm{e}^{-\beta T}]^N \exp\left(\frac{a}{\beta}(1-\mathrm{e}^{-\beta T})(u-1)\right),$$

with mean $\mathbb{E}[X(t)] = (N-a/\beta)\mathrm{e}^{-\beta T}+a/\beta$. This convolution of a death and immigration process appears to differ from the original stochastic model to some degree, but may still prove useful as an approximation.

5. Concluding remarks

Each of the three models discussed in this paper can be formally described as a continuous-time Markov process $\{(X(t), Y(t)) : t \geq 0\}$ on a countable state space, whose probability distribution we may not know easily but for which, when $Y(\cdot)$ is replaced by a suitable approximation to its expectation, the distribution of $X(t)$ may become more accessible. The extent to which this distribution resembles the marginal distribution in the original process can depend on the detailed relation of the structures of the original and approximation: the parameters of the particular model may be close to a critical point in the parameter space (e.g. $k = \beta$ and $a = m$ in Section 3) or the approximation may be better when interpreted conditionally (e.g. $Y(t) \neq 0$ in Section 4). These are matters left to another place.

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JOE GANI, *Australian National University*

Mathematical Sciences Institute, The Australian National University, Bldg 26B, Canberra ACT 0200, Australia..