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Stochastic effects in a model of nematode infection in ruminants

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Abstract

We illustrate the importance of stochastic effects in population models of biological systems and demonstrate a number of analytic and simulation-based approaches that can usefully be applied to such models. In so doing, we compare the stochastic approach to the more usual deterministic one. The model studied represents the gastro-intestinal infection of ruminants by nematodes when the hosts maintain a fixed density. The incorporation of a feed-back mechanism, which accounts for the immune response of the infected animals, results in a highly non-linear model; similar forms of non-linearity are a feature of many plausible models in population biology. In the absence of an analytic solution to the full stochastic model we explore a number of approximations and compare them to simulations of the full stochastic process. We explore three modes of behaviour of the system. In the *endemic regime* the stochastic system fluctuates widely around the non-zero fixed points of the deterministic model. In the *managed regime*, where the system is subject to external periodic perturbation, stochastic effects are negligible. Finally, we find that in a regime in which the deterministic model predicts the long-term persistence of oscillations the stochastic model shows that extinction can occur. Of the approximation procedures we consider, the Normal approximation to the full stochastic process is the most generally applicable, and also the most accurate in the light of simulation results. Local linearization provides reasonably accurate prediction of the variance-covariance structure, and a transfer function approach allows calculation of the time-lagged auto- and cross-correlations in the endemic regime. Linearization of the stochastic updates themselves results in poor prediction of the population variances.

Keywords: Stochastic Processes; Population Models; Birth-Death Processes; Normal Approximation; Simulation; Local Linearization.

1 Introduction

In this presentation we examine stochastic effects in a model of nematode infection of ruminants. Our aim is two-fold. First, we explore the importance of stochastic effects for the model in question. Our second goal is to compare various analytic approaches to the study of stochastic processes. As expounded in Renshaw (1991), we take the view that both deterministic and stochastic formulations of biological models are valuable. Further, we argue that the complexity of many biological systems forces one to adopt a fundamentally stochastic approach. Thus an initial stochastic analysis is essential, even if this simply leads to the conclusion that the deterministic analysis is adequate. Often it does not. The main reasons for the frequent avoidance of the stochastic route are the relative lack of familiarity with associated analytic methods and the computationally intense nature of stochastic simulation as compared with deterministic modelling. In this paper we demonstrate a range of analytic approaches and make use of simulation-based methods. These techniques are general in that they can be brought to bear on a wide range of problems, and the system we study is of sufficient complexity to demonstrate their practical utility.

The model describes a nematode population infecting a ruminant population of fixed density in which the hosts exhibit acquired immunity. Such a situation might arise in a commercial agricultural setting where fluctuations in the host density are negligible. The infection is directly transmitted to the hosts in grazing, and acquired immunity impedes the processes of parasite establishment, development and reproduction. Our model is a natural stochastic formulation of the deterministic model proposed by Roberts and Grenfell (1991) for nematode infections in ruminants. This system is particularly suitable for our purposes because, as these authors point out, it captures *the essence of previous more complicated formulations of the processes of parasite demography and herd immunity*, as expounded in Anderson and May (1985), Barnes and Dobson (1990), Berding *et al.,* (1987), Callinan *et al.,* (1982) and Grenfell *et al.,* (1987). Thus our results may well have relevance far beyond the specific model considered. Moreover, mirroring the study of Roberts and Grenfell (1991) facilitates direct comparison between the deterministic and stochastic methods. To this end we consider an autonomous stochastic system and focus on two regimes, the *endemic* and the *managed*. The endemic regime corresponds to the equilibrium state of the deterministic system and is analytically amenable to local linearization. We stress that whilst study of this regime is enlightening in comparing stochastic and deterministic approaches, more realistic models would need to represent features not dealt with in the basic model considered here. Such features include age structure and spatio-temporal heterogeneities. In the managed regime hosts are periodically removed and replaced with animals with no acquired immunity. This corresponds to a periodic forcing of the system which results in a marked transient response. The question of temporal variation in the development and transmission rates of the infection is tackled in the deterministic setting by Roberts and Grenfell (1992), and we hope to explore the issue of environmental variability in the stochastic context in a subsequent publication.

The remainder of this paper is organized as follows. In the next section we present our model and demonstrate that the deterministic model of Roberts and Grenfell (1991) results from consideration of the expected updates in our stochastic formulation; in Section 3 we review the results derived by these authors. Subsequently, we study the behaviour of the stochastic model both analytically and by using numerical simulations. In Section 4 we apply four approximations to the stochastic process, and in Section 5 the quantities thus calculated are compared to one another in the light of simulation results. Finally, we summarize our results comparing the deterministic and stochastic approaches, discussing the reliability of the approximations used and exploring the implications for the model studied.

2 Formulation of the model

The life cycle of nematode parasites of ruminants such as *Ostertagia ostertagi* consists of larval and adult stages. The larvae are *free-living* on the pasture, whilst the adults exist as parasites within the hosts, producing eggs which subsequently re-infect the pasture via the host's faeces. Transmission to the host occurs through the ingestion of infected material during grazing. In reality the parasites' life cycle includes a number of larval stages, but we consider only the final infective stage explicitly. Denote by $n_L(t)$ the number of these infective larval individuals, at time t, in the area associated with one host animal, and by $n_A(t)$ the number of adult parasites infecting a host. Transmission rates from larvae to host naturally reflect the stocking density of the host animals. In addition, we model the level of immunity to these parasites in the host population by some notional level $n_r(t)$, which we consider to be discrete and non-negative.

Let us now briefly consider how each of these quantities evolve. We write the population level, $n(t+\delta t)$, at time $t+\delta t$ in terms of the population, $n(t)$, at time t and some random change in population level δn. Thus

$$n_L(t+\delta t) = n_L(t) + \delta n_L, \;\; n_A(t+\delta t) = n_A(t) + \delta n_A, \;\; n_r(t+\delta t) = n_r(t) + \delta n_r. \tag{2.1}$$

If the time increment δt is sufficiently small then we can assume that no more than one birth or death event will occur: formally the probability of two or more such events is $O(\delta t^2)$.

Following Roberts and Grenfell (1991), in our model the larval population can increase only from the birth of a new individual. The birth rate depends on the rate of egg production, $\lambda(n_r)$, and also the probability, q, that any particular egg will develop into a larva. The rate of egg production is a monotonic non-increasing function of the immunity level, n_r, reflecting the assumption that increasing immunity is detrimental to fecundity. Therefore, we write the probability of a birth in the larval population as $Pr(\delta n_L = +1) = q\lambda(n_r)n_A\delta t$. Similarly, the number of larvae can decrease for two reasons only. The first, mortality, we model by assuming that any individual has a probability ρ of dying per unit of time. The second, encountering a host, we account for by a contact rate β per larva. Thus, an individual in the free-living larval stage can either die or attempt to parasitize a host animal with total probability given by $Pr(\delta n_L = -1) = (\beta + \rho)n_L\delta t$.

Turning to the adult population level, n_A, we note that this can increase due to the maturation of larvae or decrease due to adult mortality. The increase in the adult population depends on the number of larval individuals in contact with the host, namely βn_L. Once the larval parasites have been ingested they are assumed to develop into adults with probability, $p(n_r)$, which is a monotonic non-increasing function of the immunity level n_r. Thus we write $Pr(\delta n_A = +1) =$

$p(n_r)\beta n_L \delta t$. Similarly, the adult mortality rate, $\mu(n_r)$, is a monotonic non-decreasing function of n_r with $Pr(\delta n_A = -1) = \mu(n_r) n_A \delta t$. Finally, the level of acquired immunity is assumed to increase upon contact with the larval parasites, whilst fading in their absence at a rate σ per unit of immunity. So we have $Pr(\delta n_r = +1) = \beta n_L \delta t$ and $Pr(\delta n_r = -1) = \sigma n_r \delta t$. The approximation we consider in Section 4.4 effectively replaces this probabilistic model of the immune-response with one in which the immunity is expressed as a deterministically evolving number.

3 Deterministic treatment

The simplest approach is to consider the expected updates at time t, namely

$$\begin{aligned} E[\delta n_L] &= [q\lambda(n_r)n_A - (\beta+\rho)n_L]\delta t \ , \\ E[\delta n_A] &= [\beta p(n_r)n_L - \mu(n_r)n_A]\delta t \ , \\ E[\delta n_r] &= [\beta n_L - \sigma n_r]\delta t \ . \end{aligned} \tag{3.1}$$

In the limit of $\delta t \to 0$ the update equations (3.1) are equivalent to the deterministic system of Roberts and Grenfell (1991), i.e.

$$\begin{aligned} dL(t)/dt &= q\lambda(r)A - (\beta+\rho)L \ , \\ dA(t)/dt &= \beta p(r)L - \mu(r)A \ , \\ dr(t)/dt &= \beta L - \sigma r \ . \end{aligned} \tag{3.2}$$

Here we have introduced the notation L, A and r for deterministic population levels corresponding to n_L, n_A and n_r, respectively.

The stability of system (3.2) has been previously examined by Roberts and Grenfell (1991) who point out that a useful system parameter is

$$Q = \frac{\beta\lambda(0)p(0)q}{(\rho+\beta)\mu(0)} \ . \tag{3.3}$$

For the unperturbed system (3.2) this is equivalent to the basic reproduction rate of the infection. These authors show, by linearizing around the zero equilibrium ($L = 0, A = 0, r = 0$) and arguing that these linear trajectories bound the true solution, that if $Q < 1$ then this zero solution is globally asymptotically stable. However, for $Q > 1$ the zero solution is unstable, but in the case where $p'(r) = \mu'(r) = 0$ the non-zero (endemic) equilibrium (L_0, A_0, r_0) is locally stable; small perturbations from this endemic equilibrium result in damped oscillatory behaviour. Indeed, for the biologically plausible parameter settings shown in Table 1, weakly damped cycles with a period of ≈ 15 years develop. These parameter settings are based on the parameterization of the detailed simulation of the gastrointestinal infection of calves by the nematode parasite *Ostertagia ostertagi* (Grenfell *et al.,* 1987). Furthermore, Roberts and Grenfell (1991) also demonstrate the existence of small amplitude solutions of the system (3.2) which satisfy periodic boundary conditions of the form

$$L(0) = d_1 L(1), \qquad A(0) = d_2 A(1), \qquad r(0) = d_3 r(1) \ . \tag{3.4}$$

TABLE 1

Parameter values suggested by Roberts and Grenfell (1991): $p(0)$, q, r and λ_1 are dimensionless whilst the remaining quantities are in units of year^{-1}.

$p(0)$	$= 0.65$	q	$= 0.35$
β	$= 0.365$	ρ	$= 7$
$\mu(0)$	$= 25$	σ	$= 0.01$
$p'(r)$	$= \mu'(r) = 0$	$\lambda(r)$	$= \lambda_0 \exp(-\lambda_1 r)$
λ_1	$= 10^{-6}$	λ_0	$= 39420$

Numerical examination of the full non-linear system with the parameter values of Table 1 reveals a solution satisfying the boundary conditions (3.4) with $d_1 = 1$, and $d_2 = d_3 = 0$ (Figure 1). This boundary condition corresponds to the managed regime, that is the annual removal of hosts who have built up immunity to the parasites and their replacement by un-infected hosts with no acquired immunity. The subsequent infection of these individuals results from the free-living (larval) population which remains. A feature of Figure 1 is the strong peak in parasite numbers in the first half of the year. Since the model (3.2) is autonomous, this seasonal variation results from the dynamics of the interacting populations and the imposed management regime, rather than from environmental variation.

4 Stochastic analyses

In the previous section we investigated the deterministic evolution of population levels using expected updates at time t, and saw that the corresponding trajectory satisfied the system of ordinary differential equations (3.2) analysed by Roberts and Grenfell (1991). However, this deterministic treatment ignores the fundamentally stochastic nature of the system described in Section 2.

In general, although analytic solution of stochastic systems such as (2.1) is highly non-trivial, there are a number of ways in which progress can be made. Essentially, there are two approaches: one is based on stochastic differential equations, whilst the other focuses on the evolution of the joint probability distribution of the population variables and hence on the moments of the random process. In this section we explore the stochastic model using approximations based on both approaches. First, by formulating the model in terms of stochastic difference equations and linearizing around the endemic equilibrium of the deterministic system we examine the local variance-covariance structure of the stochastic model. We then consider the temporal variation in this structure using Fourier transform methods. Secondly employing the moment generating function of the process and following Whittle (1957) yields approximate update equations for the first- and second-order moments. An alternative to both these is to construct a process, in which the updates are linear in the stochastic variables, in the hope that the resulting system approximates the full model of equation (2.1). Our results are summarized in Section 5 where we compare each method in the light of direct numerical simulation.

4.1 Local variance-covariance structure

In order to consider stochastic effects we first express the update equations (2.1) in a stochastic difference form. We do this by writing the random updates in terms of their means plus a random variable with zero mean (see, for example, Renshaw 1991), that is

$$\begin{aligned} n_L(t+\delta t) - n_L(t) &= [q\lambda(n_r)n_A - (\beta+\rho)n_L]\delta t + \delta Z_L \\ n_A(t+\delta t) - n_A(t) &= [\beta p(n_r)n_L - \mu(n_r)n_A]\delta t + \delta Z_A \\ n_r(t+\delta t) - n_r(t) &= [\beta n_L - \sigma n_r]\delta t + \delta Z_r . \end{aligned} \tag{4.1}$$

The variances of these new random variables must equal that in the population updates δn_L, δn_A and δn_r. For small time increment δt, this condition reduces to $E[\delta Z_L^2] = E[\delta n_L^2]$ *etc.* where

$$\begin{aligned} E[(\delta n_L)^2] &= [q\lambda(n_r)n_A + (\beta+\rho)n_L]\delta t + O(\delta t^2) \ , \\ E[(\delta n_A)^2] &= [\beta p(n_r)n_L + \mu(n_r)n_A]\delta t + O(\delta t^2) \ , \\ E[(\delta n_r)^2] &= [\beta n_L + \sigma n_r]\delta t + O(\delta t^2) \ . \end{aligned}$$

In general, analytic solution of the stochastic equations (4.1) is difficult. However, we can make progress if we linearize around the endemic equilibrium point (L_0, A_0, r_0) of the deterministic system (3.2). We write the linearized trajectories $n_L(t) = L_0[1+u_L(t)]$, $n_A(t) = A_0[1+u_A(t)]$ and $n_r(t) = r_0[1+u_r(t)]$. Similarly, we rewrite the random variables $\delta Z_L = \eta_L\surd[Q_L\delta t]$, $\delta Z_A = \eta_A\surd[Q_A\delta t]$ and $\delta Z_r = \eta_r\surd[Q_r\delta t]$, where $Q_L \equiv q\lambda(r_0)A_0 + (\beta+\rho)L_0$, $Q_A \equiv \beta p(r_0)L_0 + \mu(r_0)A_0$ and $Q_r \equiv \beta L_0 + \sigma r_0$ and the time-dependent random variables η_L, η_A and η_r are uncorrelated and have zero mean and unit variance. Although this linearization procedure is rather crude it often seems to work remarkably well (see Renshaw 1991). In addition, it is the first in a systematic series of approximations (see Bartlett 1957 and 1960). The linearized stochastic updates can now be written in the form

$$\begin{aligned} u_L(t+\delta t) &= u_L(t) + \{[q\lambda(r_0)A_0u_A(t) + qA_0\lambda'(r_0)r_0u_r(t)) - (\beta+\rho)L_0u_L(t)]\delta t + \eta_L\surd[Q_L\delta t]\}/L_0 \ , \\ u_A(t+\delta t) &= u_A(t) + \{[\beta p(r_0)L_0u_L(t) + \beta p'(r_0)r_0u_r(t)L_0]\delta t \\ &\quad - [\mu(r_0)A_0u_A(t) + \mu'(r_0)u_r(t)r_0]\delta t + \eta_A\surd[Q_A\delta t]\}/A_0 \ , \\ u_r(t+\delta t) &= u_r(t) + \{[\beta L_0u_L(t) - \sigma r_0u_r(t)]\delta t + \eta_r\surd[Q_r\delta t]\}/r_0 \ . \end{aligned} \tag{4.2}$$

On squaring and cross-multiplying, equations (4.2) yield six equations, and taking expectations of these (assuming stationarity) leads to equations for the variances ($\sigma^2_{u_L}$, $\sigma^2_{u_A}$, $\sigma^2_{u_r}$) and covariances ($\sigma_{u_Lu_A}$, $\sigma_{u_Lu_r}$, $\sigma_{u_Au_r}$) of the variables u_L, u_A and u_r. For example, the expectation of the square of the equation for $u_r(t+\delta t)$ is

$$2\,\beta\,L_0\,\sigma_{u_Lu_r}/r_0 - 2\,\sigma\,\sigma^2_{u_r} + Q_r/r_0^2 = 0 \ . \tag{4.3}$$

For a more detailed description of this procedure in a simple case see Renshaw (1991, $p182-184$). The other five equations thus derived from (4.2) are

$$-2\ (\beta+\rho)\,\sigma^2_{u_L} + 2\,q\,A_0\ [\lambda(r_0)\sigma_{u_Lu_A} + \lambda'(r_0)\,r_0\sigma_{u_Lu_r}]\,/L_0 + Q_L/L_0^2 = 0 \tag{4.4}$$

$$2\,\beta\,L_0\,\left[p(r_0)\sigma_{u_L u_A} + p'(r_0)\,r_0\,\sigma_{u_A u_r}\right]/A_0 - 2\,\mu(r_0)\,\sigma^2_{u_A} - 2\,\mu'(r_0)\,r_0\,\sigma_{u_A u_r} + Q_A/A_0^2 = 0 \;\;,$$

$$-\mu(r_0)\sigma_{u_L u_A} - \mu'(r_0)\,r_0\,\sigma_{u_L u_r} + \beta\,L_0\,\left[p(r_0)\sigma^2_{u_L} + p'(r_0)r_0\,\sigma_{u_L u_r}\right]/A_0$$
$$- (\beta+\rho)\,\sigma_{u_L u_A} + q\,A_0\,\left[\lambda(r_0)\,\sigma^2_{u_A} + \lambda'(r_0)\,r_0\,\sigma_{u_A u_r}\right]/L_0 = 0 \;\;,$$

$$\beta\,L_0\,\sigma^2_{u_L}/r_0 - \sigma\,\sigma_{u_L u_r} - (\beta+\rho)\,\sigma_{u_L u_r} + q\,A_0\,\left[\lambda(r_0)\,\sigma_{u_A u_r} + \lambda'(r_0)\,r_0\,\sigma^2_{u_r}\right]/L_0 = 0 \;\;,$$

$$\beta\,L_0\,\sigma_{u_L u_A}/r_0 - \sigma\,\sigma_{u_A u_r} - \mu(r_0)\sigma_{u_A u_r} - \mu'(r_0)\,r_0\,\sigma^2_{u_r} + \beta\,L_0\,\left[p(r_0)\sigma_{u_L u_r} + p'(r_0)r_0\sigma^2_{u_r}\right]/A_0 = 0 \;\;.$$

It is straight-forward to solve equations (4.3) and (4.4) for the variances and covariances either using a symbolic mathematics package, such as *Maple* (see e.g. Heck, 1996), or numerically for particular parameter values. Appropriate rescaling results in the variances and covariances in n_L, n_A and n_r which we denote by σ_L^2, σ_A^2, σ_r^2, σ_{LA}, σ_{Lr} and σ_{Ar}. The resulting expressions are rather lengthy and hence omitted here, but using the parameter values of Table 1 we find, for example, that $\sigma_L \approx 31137$, $\sigma_A \approx 297$ and $\sigma_r \approx 28083$. In Table 2 we also show the cross-correlations (e.g. $\sigma_{LA}/(\sigma_L\sigma_A)$), and compare these estimates with those obtained by the Normal approximation (see Section 4.3) and by direct simulation (see Section 5).

4.2 Auto-covariances

We now describe an alternative approach, also based on the linearized stochastic process described in the previous section, which enables us to estimate the time-dependence of the local variance-covariance structure. Similar techniques have been employed by Roberts and Grenfell (1992) to analyse environmental variation in the deterministic model of section 3 (for a straight-forward introduction to the stochastic case see Nisbet and Gurney (1982, p 190)). We begin by taking the limit $\delta t \to 0$, and thus recasting equation (4.2) in the matrix form

$$d\mathsf{v}(t)/dt = \mathsf{H}\mathsf{v}(t) + \mathsf{Z}(t) \;\;. \tag{4.5}$$

Here we define $\mathsf{v}^T = (\nu_1, \nu_2, \nu_3) = (v_L, v_A, v_r)$, where $\mathsf{n} = \mathsf{n}_0 + \mathsf{v}$ with $\mathsf{n}^T = (n_1, n_2, n_3) = (n_L, n_A, n_r)$ and $(\mathsf{n}_0)^T = (L_0, A_0, r_0)$. The random updates $\mathsf{Z}^T = (\gamma_L(t)\sqrt{Q_L}, \gamma_A(t)\sqrt{Q_A}, \gamma_r(t)\sqrt{Q_r})$, where $\gamma_L(t)$, $\gamma_A(t)$ and $\gamma_r(t)$ are uncorrelated Gaussian white noise. Finally, the matrix

$$\mathsf{H} = \begin{pmatrix} -(\beta+\rho) & q\lambda(r_0) & q\lambda'(r_0) \\ \beta p(r_0) & -\mu(r_0) & \beta p'(r_0)L_0 - \mu'(r_0)A_0 \\ \beta & 0 & -\sigma \end{pmatrix} \;\;. \tag{4.6}$$

For a given function $g(t)$ define

$$\widetilde{g}(\omega, T) = \int_{-T/2}^{+T/2} g(t)e^{-i\omega t}dt \;\;, \tag{4.7}$$

whence the Fourier transformation of $g(t)$ is $\widetilde{g}(\omega) = \lim_{T\to\infty}\widetilde{g}(\omega, T)$. Since $\nu(t)$ and $Z(t)$ are undefined for $t < 0$, we define new variables $f(t) = \mathsf{v}(t)$ and $\mathsf{Y}(t) = \mathsf{Z}(t)$ for $t \geq 0$ with $f = (0,0,0)^T$ and $\mathsf{Y}(t) = (0,0,0)^T$ if $t < 0$. Equation (4.5) then takes the Fourier form

$$\widetilde{f}(\omega) = \mathsf{T}(\omega)\widetilde{\mathsf{Y}}(\omega) \;\;. \tag{4.8}$$

The transfer matrix $\mathsf{T}(\omega) = (i\omega\mathbf{I} - \mathsf{H})^{-1}$ and $\mathbf{I}$ is the identity matrix. We are now in a position to calculate the auto- and cross-covariances associated with the populations $\mathsf{n}(t)$. Assuming that the process is fully recurrent, it is straightforward to show (see Nisbet and Gurney 1982 p 349 & 350) that the time-lagged covariances are given by

$$\mathrm{Cov}[\mathsf{n}_k(t), \mathsf{n}_l(t+\tau)] = \int_0^\infty \mathbf{E}\left[v_k(t)v_l(t+\tau)\right] dt = \frac{1}{2\pi}\int_{-\infty}^{+\infty} \mathcal{S}_{f_k,f_l}(\omega)e^{i\omega\tau}d\omega \quad , \tag{4.9}$$

where the cross-spectral density

$$\mathcal{S}_{f_k,f_l}(\omega) \equiv \lim_{T\to\infty} \frac{\mathbf{E}\left[\widetilde{f_k}(\omega,T)(\tilde{f}_l(\omega,T))^*\right]}{T} \quad . \tag{4.10}$$

Here $(f)^*$ denotes the complex conjugate of f, the expectation, $\mathbf{E}$, is taken over the white noise processes and the subscripts $k, l = 1, 2, 3$. The second integral in (4.9) can be performed analytically in the limit $\tau \to 0$, in which case the problem reduces to the calculation of the variance-covariance characteristics of the previous section. For $\tau > 0$ we have performed the calculation numerically for the parameter values shown in Table 1. The time-lagged correlations $\mathcal{C}_{\mathsf{n}_k,\mathsf{n}_l}(\tau) \equiv \mathrm{Cov}[\mathsf{n}_k(t), \mathsf{n}_l(t+\tau)]/(\sigma_{\mathsf{n}_k}\sigma_{\mathsf{n}_l})$ are compared with values obtained by numerical simulation in Figure 3 and we defer further discussion of them until Section 5.

4.3 Normal approximation

As noted earlier, an alternative to dealing directly with the stochastic updates (2.1) is to deduce the joint probability distribution, $\{P(n_L, n_A, n_r, t)\}$, and from this the moments themselves. A step towards this goal is to consider how this joint density changes over time. Given the distribution at time t we can calculate the probability, $\{P(n_L, n_A, n_r, t+\delta t)\}$, of being in state (n_L, n_A, n_r) a short time, δt, later by considering the possible events that will lead to this from the *unknown* population at time t. Fortunately, the number of events is limited to a single birth or death in one of the populations, since the probability of two or more such events is $O(\delta t^2)$. Thus, the probabilities of the following occurrences in the interval $(t, t+\delta t)$ must be considered: a birth in the free-living population given $n_L - 1$ individuals at time t or a death given $n_L + 1$ members at t; the corresponding births and deaths in the adult population and the immunity level; and no change in any population given the state (n_L, n_A, n_r) at time t. Summing these probabilities leads to

$$\begin{aligned} P(n_L, n_A, n_r, t+\delta t) &= \delta t\,[P(n_L - 1, n_A, n_r, t)q\lambda(n_r)n_A \\ &+ P(n_L + 1, n_A, n_r, t)(\beta+\rho)(n_L+1) \\ &+ P(n_L, n_A - 1, n_r, t)p(n_r)\beta n_L + P(n_L, n_A + 1, n_r, t)\mu(n_r)(n_A+1) \\ &+ P(n_L, n_A, n_r - 1, t)\beta n_L + P(n_L, n_A, n_r + 1, t)\sigma(n_r+1)] \\ &+ P(n_L, n_A, n_r, t)\,[1 - \delta t(q\lambda(n_r)n_A + (\beta+\rho)n_L + P(n_r)\beta n_L \\ &+ \mu(n_r)n_A + \beta n_L + \sigma n_r)] \end{aligned} \tag{4.11}$$

In the limit $\delta t \to 0$, subtracting $P(n_L, n_A, n_r, t)$ from both sides and dividing by δt leads to the difference-differential *Chapman-Kolmogorov forward equation*

$$\partial P(n_L, n_A, n_r, t)/\partial t = -P(n_L, n_A, n_r, t)\,[q\lambda(n_r)n_A + (\beta+\rho)n_L + P(n_r)\beta n_L \tag{4.12}$$

$$
\begin{aligned}
&+ \quad \mu(n_r)n_A + \beta n_L + \sigma n_r] \\
&+ \quad P(n_L-1, n_A, n_r, t)q\lambda(n_r)n_A + P(n_L+1, n_A, n_r, t)(\beta+\rho)(n_L+1) \\
&+ \quad P(n_L, n_A-1, n_r, t)p(n_r)\beta n_L + P(n_L, n_A+1, n_r, t)\mu(n_r)(n_A+1) \\
&+ \quad P(n_L, n_A, n_r-1, t)\beta n_L + P(n_L, n_A, n_r+1, t)\sigma(n_r+1)
\end{aligned}
$$

For an introduction to the formulation of such equations see, for example Cox and Miller (1965, p 147 $-$ 151 & p 179). Equations of this type can be transformed into a partial differential form through the introduction of so called, generating functions. The *moment generating function* (m.g.f.) is the expected value, over the density $\{P(n_L, n_A, n_r, t)\}$, of the product of $\exp\{\theta n_L(t)\}$, $\exp\{\phi n_A(t)\}$ and $\exp\{\psi n_r(t)\}$, viz:

$$
\begin{aligned}
M(\theta,\phi,\psi,t) &\equiv \sum_{n_L,n_A,n_r=0}^{\infty} P(n_L,n_A,n_r,t)\exp\{\theta n_L(t)+\phi n_A(t)+\psi n_r(t)\} \qquad (4.13) \\
&= \mathbf{E}\left[\exp\{\theta n_L(t)+\phi n_A(t)+\psi n_r(t)\}\right] \quad .
\end{aligned}
$$

Henceforth we assume that $\lambda(n_r)$, $\mu(n_r)$ and $p(n_r)$ take the functional forms suggested in Table 1. Whence on multiplying expression (4.12) by $\exp\{\theta n_L(t)+\phi n_A(t)+\psi n_r(t)\}$ and summing over $n_L, n_A, n_r = 0, 1, ...\infty$ we obtain

$$
\begin{aligned}
\partial M(\theta,\phi,\psi,t)/\partial t &= q\lambda_0(e^{\theta}-1)\partial M(\theta,\phi,\psi-\lambda_1,t)/\partial\phi \qquad (4.14) \\
&+ \quad (\beta+\rho)(e^{-\theta}-1)\partial M(\theta,\phi,\psi,t)/\partial\theta \\
&+ \quad p(0)\beta(e^{\phi}-1)\partial M(\theta,\phi,\psi,t)/\partial\theta + \mu(0)(e^{-\phi}-1)\partial M(\theta,\phi,\psi,t)/\partial\phi \\
&+ \quad \beta(e^{\psi}-1)\partial M(\theta,\phi,\psi,t)/\partial\theta + \sigma(e^{-\psi}-1)\partial M(\theta,\phi,\psi,t)/\partial\psi \quad .
\end{aligned}
$$

Although solution of this equation is currently an open problem, if we expand in powers of θ, ϕ and ψ and equate coefficients, we obtain ordinary differential equations for the raw moments of the process. We write the means as $\mathbf{E}[n_L(t)]$, $\mathbf{E}[n_A(t)]$ and $\mathbf{E}[n_r(t)]$, and the second-order moments as $\mathbf{E}[n_L^2(t)]$, $\mathbf{E}[n_L n_A]$, *etc.* The resulting equations of motion for the first- and second-order moments of the stochastic process are

$$
\begin{aligned}
d\mathbf{E}[n_L(t)]/dt &= q\mathbf{E}[n_A(t)\lambda(n_r)] - (\beta+\rho)\mathbf{E}[n_L(t)] \quad , \qquad (4.15) \\
d\mathbf{E}[n_A(t)]/dt &= p(0)\beta\mathbf{E}[n_L(t)] - \mu(0)\mathbf{E}[n_A(t)] \quad , \\
d\mathbf{E}[n_r(t)]/dt &= \beta\mathbf{E}[n_L(t)] - \sigma\mathbf{E}[n_r(t)] \quad , \\
d\mathbf{E}\left[n_L^2(t)\right]/dt &= (\beta+\rho)(\mathbf{E}[n_L(t)] - 2\mathbf{E}\left[n_L^2(t)\right]) \\
&\quad +q(\mathbf{E}[n_A(t)\lambda(n_r)] + 2\mathbf{E}[n_A n_L\lambda(n_r)]) \quad , \\
d\mathbf{E}\left[n_A^2(t)\right]/dt &= \beta p(0)(\mathbf{E}[n_L(t)] + 2\mathbf{E}[n_L n_A]) + \mu(0)(\mathbf{E}[n_A(t)] - 2\mathbf{E}\left[n_A^2(t)\right]) \quad , \\
d\mathbf{E}\left[n_r^2(t)\right]/dt &= \beta(\mathbf{E}[n_L(t)] + 2\mathbf{E}[n_L n_r]) + \sigma(\mathbf{E}[n_r(t)] - 2\mathbf{E}\left[n_r^2(t)\right]) \quad , \\
d\mathbf{E}[n_L n_A]/dt &= -(\beta+\rho+\mu(0))\mathbf{E}[n_L n_A] + \beta p(0)\mathbf{E}\left[n_L^2(t)\right] + q\mathbf{E}\left[n_A^2(t)\lambda(n_r)\right] \quad , \\
d\mathbf{E}[n_L n_r]/dt &= \beta\mathbf{E}\left[n_L^2(t)\right] - (\beta+\rho+\sigma)\mathbf{E}[n_L n_r] + q\mathbf{E}[n_A n_r\lambda(n_r)] \quad , \\
d\mathbf{E}[n_r n_A]/dt &= \beta\mathbf{E}[n_L n_A] - (\sigma+\mu(0))\mathbf{E}[n_r n_A] + \beta p\mathbf{E}[n_L n_r] \quad .
\end{aligned}
$$

To illustrate the construction of these equations let us examine the derivation of a specific case in more detail. We expand the m.g.f. in powers of θ, ϕ and ψ as

$$
M(\theta,\phi,\psi,t) = 1 + \theta\mathbf{E}[n_L(t)] + \phi\mathbf{E}[n_A(t)] + \psi\mathbf{E}[n_r(t)] + \theta^2\mathbf{E}\left[n_A^2(t)\right]/2... \quad ,
$$

so that the partial derivative $w.r.t.$ ψ of the left-hand side of equation (4.14) reduces to $d\mathbf{E}\left[n_r(t)\right]/dt + O(\psi)$. A similar, although longer, calculation for this derivative of the right-hand side leads to $\beta\mathbf{E}\left[n_L(t)\right] - \sigma\mathbf{E}\left[n_r(t)\right] + O(\psi)$, and evaluation of both these expressions at $\theta = \phi = \psi = 0$ leads to the third equation of (4.15). Other terms are obtained in the same fashion; for example the last results from the derivative of equation (4.14) $w.r.t.$ both ψ and ϕ.

Note that since the transition probabilities are non-linear in the population variables, the deterministic trajectories $L(t)$, $A(t)$ and $r(t)$, defined by equation (3.2), do not correspond to the mean trajectories of the stochastic process. However, the most important point concerning the coupled set of non-linear ordinary differential equations (4.15) is that they are not closed. For example, the equation for the mean $\mathbf{E}\left[n_L(t)\right]$ reveals a dependence on the expression,

$$\mathbf{E}\left[n_A(t)\exp\left\{-\lambda_1 n_r(t)\right\}\right] \quad , \tag{4.16}$$

which can be expanded as an infinite series of higher-order moments. It is therefore not possible to solve these equations for the first- and second-order moments, even numerically.

However, at this point we can make use of an approximation based on the Normal distribution which was first suggested by Whittle (1957) and then used more recently by Isham (1991). In this approach we approximate the distribution of the populations n_L, n_A and n_r according to a joint Normal density. For such an approximation the population distribution is fully described by the first- and second-order moments. It would be interesting to examine other approximations, both in regard to the order of moments considered and the form of the distribution chosen. Indeed, since the Normal distribution has a non-zero probability density for negative values, perhaps a form based on, say, the multivariate gamma distribution would be structurally more suitable. If fully parameterized multivariate forms existed, discrete distributions would be even more appealing choices, especially in the light of empirical and theoretical results which suggest likely parasite distributions across hosts are negative binomial (see e.g. Anderson and May, 1978, Adler and Kretzschmar, 1992). However, for the parameters of Table 1, simulations in the endemic regime suggest that the Normal and negative binomial distributions fit the sampled marginal distributions equally well. Therefore, we focus on the Normal distribution since it is relatively easy to handle.

Let $\mathbf{x}^T = (n_L, n_A, n_r)$ with expectation $\bar{\mathbf{x}} = \mathbf{E}\left[\mathbf{x}\right]$ and variance-covariance matrix $\Sigma = \mathbf{E}\left[(\mathbf{x}-\bar{\mathbf{x}})^T(\mathbf{x}-\bar{\mathbf{x}})\right]$. We shall subsequently find the time-dependence of these moments from the equations (4.15). First, however, we must evaluate expectations such as (4.16) over this Normal$(\bar{\mathbf{x}}, \Sigma)$ distribution. Fortunately this is straightforward, since the associated moment generating function is

$$M_{\mathcal{N}}(\mathbf{w}) = \mathbf{E}\left[\exp\left\{w_1 n_L + w_2 n_A + w_3 n_r\right\}\right] = \exp\left(\mathbf{w}^T\bar{\mathbf{x}} + \frac{1}{2}\mathbf{w}^T\Sigma\mathbf{w}\right) \quad , \tag{4.17}$$

where $\mathbf{w}^T = (w_1, w_2, w_3)$. It is apparent that the relevant quantities can be obtained from appropriate derivatives of $M_{\mathcal{N}}(\mathbf{w})$. For example,

$$\left.\frac{\partial M_{\mathcal{N}}(\mathbf{w})}{\partial w_2}\right|_{\mathbf{w}^T=(0,0,-\lambda_1)} = \mathbf{E}\left[n_A(t)\exp\left\{-\lambda_1 n_r(t)\right\}\right] \quad . \tag{4.18}$$

Thus, the approximation of the full joint density, $\{P(n_L, n_A, n_r, t)\}$, by a Normal distribution allows all the components of equations (4.15) to be written solely in terms of the first- and second-order

TABLE 2

Local variance-covariance structure: comparison of calculations based on local linearization and the Normal approximation together with results from direct numerical simulation of the endemic regime, for standard deviations σ_L, σ_A and σ_r and normalized cross-correlations, $\mathcal{C}_{n_L,n_A}(0) = \mathrm{Cov}(n_L, n_A)/(\sigma_L \sigma_A)$ etc.

	σ_L	σ_A	σ_r	$\mathcal{C}_{n_L,n_A}(0)$	$\mathcal{C}_{n_L,n_r}(0)$	$\mathcal{C}_{n_A,n_r}(0)$
Local linearization	31137	297	28083	0.997	0.0246	0.0406
Normal approximation	38373	365	34613	0.999	0.0246	0.0407
Simulations	39300	374	33300	0.997	0.0208	0.0393

moments. We shall refer to the resulting set of non-linear equations as the *Normal approximation*. Since the dependence on raw moments higher than second-order has been eliminated, the Normal approximation can be solved by numerical integration. In Section 5 we will use this method to explore fully the properties of this approximation, but for the moment we consider analytic results only.

Suppose we linearize the Normal approximation to equation (4.15), assuming that both the expected population levels and their second-order moments are small. It is straightforward, if lengthy, to show that the eigenvalues of this linearized system are the roots of a ninth-order polynomial, which can be solved numerically. Exploration of this numerical solution suggests that the zero solution of this set of equations is stable if $Q \leq 1$, and unstable otherwise, in agreement with the deterministic analysis outlined earlier. Thus, in so far as this Normal approximation mirrors the full stochastic process the infection is liable to become established, i.e. persist, if $Q > 1$. However, in section 5 we will see that the Normal approximation does break down when the population is close to extinction. Two possible future improvements include direct truncation of the negative tail and its incorporation into the probability mass at zero. In both cases the new distributions may have to be rescaled to obtain the required mean and variance.

A linearization can also be obtained around the non-zero fixed point of the Normal approximation; this corresponds to the endemic equilibrium of the deterministic system (3.2). Once again the resulting characteristic equation has to be solved numerically. We find, for the parameter values suggested in Table 1, that the fixed points are locally stable and that initial conditions close to the fixed points will result in damped oscillatory solutions with a period of approximately 15 years, in close agreement with the deterministic analysis. Furthermore, we find that the fixed points for the means of the Normal approximation are in good agreement with those of the deterministic model (3.2). In addition, examination of the standard deviations of the population fluctuations around this fixed point reveals that $\sigma_L \approx 38373$, $\sigma_A \approx 365$ and $\sigma_r \approx 34613$, which are of similar magnitude to those values obtained from the local variance-covariance analysis of Section 4.1. Table 2 lists these values, along with the normalized cross-correlations of the population fluctuations in the endemic regime obtained from the Normal approximation.

4.4 Approximating stochastic process

Finally, we examine an approximation technique suggested by Tan and Hsu (1989) and brought to our attention by Isham (1991). The essence of this approach is the linearization of the *stochastic* updates. In the context of the parameterizations suggested in Table 1, the functional form of $\lambda(n_r)$ means that this can only be achieved by assuming that $n_r(t)$ is described by the deterministic process $r(t)$ which evolves according to

$$dr(t)/dt = \beta\mathbf{E}\left[n_L(t)\right] - \sigma r(t) \quad . \tag{4.19}$$

Effectively, we have replaced our stochastic sub-model of immune-response with a deterministic one. The resulting stochastic process is linear in n_L and n_A and it is straightforward to write down the following exact evolution equations for its first- and second-order moments:

$$\begin{aligned}
d\mathbf{E}\left[n_L(t)\right]/dt &= q\lambda(r)\mathbf{E}\left[n_A(t)\right] - (\beta+\rho)\mathbf{E}\left[n_L(t)\right] \\
d\mathbf{E}\left[n_A(t)\right]/dt &= p(0)\beta\mathbf{E}\left[n_L(t)\right] - \mu(0)\mathbf{E}\left[n_A(t)\right] \\
d\mathbf{E}\left[n_L^2(t)\right]/dt &= 2\left(q\lambda(r)\mathbf{E}\left[n_L n_A\right] - (\beta+\rho)\mathbf{E}\left[n_L^2(t)\right]\right) \\
&+ q\lambda(r)\mathbf{E}\left[n_A(t)\right] + (\beta+\rho)\mathbf{E}\left[n_L(t)\right] \\
d\mathbf{E}\left[n_A^2(t)\right]/dt &= 2\left(p(0)\beta\mathbf{E}\left[n_L n_A\right] - \mu(0)\mathbf{E}\left[n_A^2(t)\right]\right) \\
&+ p(0)\beta\mathbf{E}\left[n_L(t)\right] + \mu(0)\mathbf{E}\left[n_A(t)\right] \\
d\mathbf{E}\left[n_L n_A\right]/dt &= q\lambda(r)\mathbf{E}\left[n_A^2(t)\right] + p(0)\beta\mathbf{E}\left[n_L^2(t)\right] \\
&- (\beta+\rho+\mu(0))\mathbf{E}\left[n_L n_A\right] \quad .
\end{aligned} \tag{4.20}$$

Together with equation (4.19) these form a closed set of non-linear ordinary differential equations. Moreover, the equations for the means, $\mathbf{E}[n_L(t)]$ and $\mathbf{E}[n_A(t)]$, along with equation (4.19) for $r(t)$, are identical to the deterministic model of Roberts and Grenfell (1991) (see equation (3.2)). Thus for $Q < 1$, $\mathbf{E}[n_L(t)]$, $\mathbf{E}[n_A(t)]$ and $r(t)$, tend to zero as $t \to \infty$; whilst for $Q > 1$ the zero equilibrium is unstable. We now consider the evolution of the second-order moments. For large t and $Q < 1$ the means $\mathbf{E}[n_L(t)]$ and $\mathbf{E}[n_A(t)]$ are negligible, and equations (4.20) reduce to a three-dimensional linear system with eigenvalues $-(\beta+\rho+\mu(0))$ and $\lambda_{\pm} = -(\beta+\rho+\mu(0)) \pm \sqrt{\{(\beta+\rho+\mu(0))^2 + 4\mu(0)(\beta+\rho)(Q-1)\}}$, which are all negative. Thus for $Q < 1$ the first- and second-order moments of this linear stochastic process decay to zero. For both the deterministic and Normal approximations, we have seen that the infection will persist if $Q > 1$ and die or fail to establish if $Q < 1$. We have also shown, in the case of our approximating stochastic process, that the infection will die out if $Q < 1$. Similarly, at the start of the infection when expected population levels are negligible, the eigenvalue $\lambda_+ > 0$ if $Q > 1$, and the fluctuations increase. As we have already seen, in this case $\mathbf{E}[n_L(t)] = L(t)$, $\mathbf{E}[n_A(t)] = A(t)$ and $r(t)$ also grow with t.

Numerical investigation suggests that one failing of this approximating process is that no non-zero fixed point exists; as the system evolves the fluctuations around the endemic solution of the deterministic system diverge. We see in the next section that this is a poor reflection of the behaviour of the full process and indicates the need to consider the stochastic nature of the immune-response to the infection. Furthermore, we examine the approximating stochastic process (4.20) and (4.19) in the managed regime via numerical solution. We then compare each of the analytic approximations discussed so far, in the light of stochastic simulations.

5 Stochastic investigations

The analytic results derived in the previous section are limited in their applicability by the conditions it was necessary to impose in order to derive them. So numerical simulations of the system prove very useful not only in supporting the analytic results but also in exploring behavioural patterns not amenable to theoretical analysis.

In order to simulate the stochastic updates of equation (2.1) we make use of the result that the waiting times between random events are distributed exponentially (see Renshaw, 1991). Thus

$$Pr(\text{an event occurs in interval } (t, t+s)) = 1 - \exp\{-Rs\} \tag{5.1}$$

where $R = q\lambda(n_r)n_A + (\beta+\rho)n_L + p(n_r)n_L + \mu(n_r)n_A + \beta n_L + \sigma n_r$. To simulate the system one simply needs to generate inter-event times from the above distribution and then choose specific events, based on the relative magnitude of the corresponding probabilities, according to a uniform $(0, 1)$ distribution. So at each update we will have either a birth or a death in one of the three population variables, n_L, n_A or n_r.

Endemic regime. Figure 2 shows the results of such a simulation where the initial conditions are the endemic equilibrium (L_0, A_0, r_0) of the deterministic system, and the parameter values are those of Table 1. The graphs show strong evidence for the oscillatory behaviour predicted by the deterministic analysis, though to quantify the period of these oscillations it is best to consider the auto- and cross-correlations in the time series. Figure 3 shows the auto-correlation function $\mathcal{C}_{\mathsf{n}_L,\mathsf{n}_L}(\tau)$ and the cross-correlation $\mathcal{C}_{\mathsf{n}_A,\mathsf{n}_r}(\tau)$ for a range of values of the time lag τ. The corresponding analytic results derived using the transfer function approach (see Section 4.2) are shown along with the simulation results. Oscillatory behaviour is clearly evident, with the estimated wavelength ≈ 15 years. Both the simulation and analytic results are in good agreement with the deterministic prediction. Recall that the Normal approximation also gives a similar prediction. However, it is clear that whilst both theory and simulations are in close agreement for small lag times, τ (see equation (4.9)), this is not so for larger τ. As τ increases, the discrepancy, both in the phase and amplitude, between the analytic and simulation results increases.

Numerical solution of the Normal approximation provides variances and covariances along with the mean trajectories. For the free-living population n_L, in the endemic regime, ± 1 standard deviation intervals around the mean are shown in Figure 4, together with a realization of the stochastic process. This graph shows that the Normal approximation provides a reasonable indication of the fluctuations around the mean. Indeed, similar behaviour is found in the other populations, n_r and n_A. However, fluctuations do not appear to be symmetric around the mean value of the Normal approximation. This indicates a potential draw-back of the assumption of Normality, and suggests that a skewed distribution might be more appropriate.

In contrast, the approximating stochastic process of Section 4.4 exhibits fluctuations which diverge as t increases. Furthermore, as these fluctuations are much larger than those shown in Figure 4, the approximating stochastic process would seem to be somewhat misleading.

We can also use our simulations to check the variances and covariances calculated in the previous section. If the system is ergodic then we can obtain simulated moment estimates by considering a single, but long-lived realization (see, for example, Nisbet and Gurney 1982). This yields $\sigma_L \approx 39000$, $\sigma_A \approx 370$ and $\sigma_r \approx 33000$, which are similar in magnitude to our predictions based on the local variance-covariance calculations, and are even closer to those based on the Normal approximation (see Sections 4.1 and 4.3). The results of both approximations, along with values based on simulation of the endemic regime for $t = 0, ..., 3000$ years, are compared in Table 2. We find that the Normal approximation estimates the standard deviation in the population fluctuations more accurately than the local linearization procedure. In terms of the normalized cross-correlations of these fluctuations there is a remarkable similarity between the two methods and both agree well with simulation results. However, we note that neither set of covariance terms are in such good agreement with simulated estimates.

Our results show that stochastic effects play a considerable role in the endemic regime. This is understandable as the competing effects of the parasitic life-cycle and the immune-response of the hosts are roughly balanced in this case. There is therefore no strong deterministic reason for the system to move from equilibrium, and the fluctuations we observe around it are largely stochastic. Note that damped deterministic behaviour often leads to sustained stochastic cycles (Renshaw (1991)).

Managed regime. Here the adult population and host immunity are set to zero at the start of every year, but the infection persists due to the remaining larval population. In this case the immune-response is initially zero whilst the infective pressure of the larval population is large. The transition probabilities thus favour a rapid rise in the adult parasite burden and one might expect stochastic effects to be muted. Indeed stochastic simulations reveal a behaviour which is visually indistinguishable (on the scale of Figure 1) from the deterministic result. The fact that simulated trajectories differ so slightly from the deterministic path suggests a rather tight ± 1 standard deviation interval. In this case we find that the means and corresponding interval resulting from the Normal approximation are also indistinguishable (on this scale) from the simulated stochastic process. This contrasts with the approximating linearized process of Section 4.4 which, for this managed regime, is shown in Figure 5. As noted earlier, the mean of this approximation is the deterministic solution, which as we have seen approximates the stochastic trajectory well in this regime. However, Figure 5 reveals that the ± 1 standard deviation intervals around this mean are rather broader than those suggested by direct simulation.

Extinction. Finally, we consider the question of extinction. Recall that both the deterministic analysis and the approximations to the stochastic process indicate that the infection will continue unless $Q < 1$. In the cases so far examined in this section the condition $Q > 1$ has been satisfied and the infection does seem to persist. However, Figure 6 shows the case where $Q \approx 14.8$ and the parameters are as in Table 1 but with $\mu(0) = 30$. The solid line represents a typical stochastic trajectory and shows that the infection becomes extinct at around $t \approx 31$ years, despite Q being considerably greater than unity, and the indefinite oscillation of the deterministic trajectory. The approximating stochastic process once again exhibits large fluctuations about the mean suggesting that extinction may occur. Initially the Normal approximation follows the stochastic trajectory closely, with both the deterministic and the simulated trajectories (Figure 6) lying within ± 1 standard deviation intervals (i.e. $\mathbf{E}[n_L(t)] \pm \sigma_L$). However, at $t \approx 10$ years the lower level, $\mathbf{E}[n_L(t)] - \sigma_L$, is negative indicating that the probability of extinction may now be substantial. Whilst for $t \approx 16$ years the Normal approximation predicts large fluctuations around a negative $\mathbf{E}[n_L(t)]$, thus the approximation has clearly broken down. It is clear that care is needed in interpreting all stochastic analytic approximations and that direct stochastic simulation of the full process is an indispensable tool.

This phenomenon of extinction may be of interest in the case examined by Roberts (1994) who has applied the deterministic model (3.2) to the case of nematode infection of lambs by using parameterizations different to those of Table 1 (recall that these pertain to *Ostertagia ostertagi* infection of calves). In this case $Q = 7.746$ (i.e. $Q > 1$) but our stochastic formulation of the model reveals that typical trajectories in the endemic regime quickly become extinct, despite persistent oscillations predicted by the deterministic model. This difference remains even with temporal inhomogeneity in the probability of egg development (q), which is a further indication that deterministic modelling fails to capture the subtleties of the stochastic process.

6 Conclusions

We applied a number of approaches to the analysis of a stochastic population model and assessed these by comparing the analytic predictions with simulations of the full stochastic process. The approximations chosen are applicable to a broad range of stochastic systems. The test system is a natural stochastic formulation of a deterministic model of nematode infection in ruminants, and has features common to many host-parasite systems.

Although deterministic analysis reveals a range of interesting behaviour, consideration of the full stochastic process shows that although the deterministic treatment is highly accurate in the managed regime, significant departures from deterministic predictions occur in the endemic regime and for settings not considered by Roberts and Grenfell (1991). In the endemic regime there are large fluctuations around the deterministic steady state; evaluation of the time-lagged correlations reveals cyclic behaviour whose period is in close agreement with deterministic predictions. In a regime for which the deterministic model predicts persistent oscillations the full stochastic model produces extinction events. Thus there is significant discrepancy between the stochastic process and the deterministic model.

Both the Normal approximation and the calculation of the local variance-covariance structure are shown to be reliable indicators of the size of the fluctuations expected in the endemic regime, with those of the former being most accurate. In addition, for small lag times, calculations of the auto- and cross-correlations using transfer function methods are accurate. In the managed regime, where local linearization of the stochastic updates is not appropriate, the Normal approximation correctly predicts small fluctuations. The use of a linear approximating stochastic process is shown to be inferior to the Normal approximation, with the former suggesting very wide 'confidence' intervals in both regimes. Finally, in contrast to the deterministic treatment, both the Normal approximation and the approximating process indicate that extinction is a real possibility: in this regime simulation of the full stochastic process does indeed result in extinction.

In summary, much care is needed in interpreting these approximate analytical results and direct simulation is an indispensable tool. Nevertheless, the analytic methods explored seem remarkably accurate. In particular, the Normal approximation is seen to be both robust and flexible. Whilst it should be stressed that this relative efficiency of the Normal approximation may not hold universally, it does seem that it should become an important and widely used technique. However, the assumption of Normality is perhaps not the most appropriate in the context of population models, and it would be exciting if other more plausible, but tractable, distributional approximations could be made in its place.

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References

ADLER, R., & KRETZSCHMAR M. 1992. Aggregation and stability in parasite-host models. *Parasitology* **104**, 199-205.

ANDERSON, R. M., & MAY, R. M., 1978. Regulation and stability of host-parasite population interactions. I. regulatory processes. *J. Anim. Ecol.* **47**, 219-247.

ANDERSON, R. M., & MAY, R. M., 1985. Herd immunity to helminth infection and implications for parasite control. *Nature* **315**, 493-496.

BARNES, E. H., & DOBSON, R.J., 1990. Population dynamics of *Trichostrongylus colubriformis* in sheep: mathematical model of worm fecundity. *Int. J. Parasitol.* **20**, 375-380.

BARTLETT, M. S., 1957. On theoretical models for competitive and predatory biological systems. *Biometrika* **44**, 27-42.

BARTLETT, M. S., 1960. *Stochastic Population Models.* Spottiswoode-Ballantyne: London.

BERDING. C., KEYMER, A. E., MURRAY, J. D., & SLATER, A. F. G., 1987. The population dynamics of acquired immunity to helminth infection: experimental and natural transmission. *J. Theor. Biol.* **126**, 167-182.

CALLINAN, A. P. L., MORLEY, F. H. W., ARUNDEL, J. H. & WHITE, D. H. 1982. A model for the life cycle of sheep nematodes and the epidemiology of nematodiasis in sheep. *Agric. Syst.* **9**, 199-255.

COX, D.R. & MILLER, H.D. 1965. *The Theory of Stochastic Processes.* London: Chapman & Hall.

GRENFELL, B. T., SMITH, G., & ANDERSON, R. M., 1987. A mathematical model of the population biology of *Ostertagia ostertagi* in calves and yearlings. *Parasitology* **95**, 389-406.

HECK, A., 1996. *Introduction to Maple.* Springer: New York.

ISHAM, V., 1991. Assessing the variability of stochastic epidemics. *Math. Biosciences* **107**, 209-224.

NISBET, R. M., & GURNEY, W. S. C., 1982. *Modelling Fluctuating Populations.* Wiley: Chichester.

RENSHAW, E., 1991. *Modelling Biological Populations in Space and Time.* Cambridge University Press: Cambridge.

ROBERTS, M. G. 1994. The population dynamics of nematode infections of ruminants. In *Mathematical Population Dynamics: Analysis of Heterogeneity.* (ed. Arino O., Axelrod D., Kimmel M., & Langlais M.) Chp. **21** , 357-365. Wuerz: Winnipeg.

ROBERTS, M. G., & GRENFELL, B. T., 1991. The population dynamics of nematode infections of ruminants: periodic perturbations as a model for management. *IMA J. Math. Appl. Med. Biol.* **8**, 83-93.

ROBERTS, M. G., & GRENFELL, B. T., 1992. The population dynamics of nematode infections of ruminants: the effect of seasonality in the free living stages. *IMA J. Math. Appl. Med. Biol.* **9**, 29-41.

TAN, W. Y., & HSU, H., 1989. Some stochastic models of AIDS spread. *Stat. Med.* **8**, 121-136.

WHITTLE, P., 1957. On the use of the Normal approximation in the treatment of stochastic processes. *J. R. Statist. Soc.* **B 19**, 266-281.

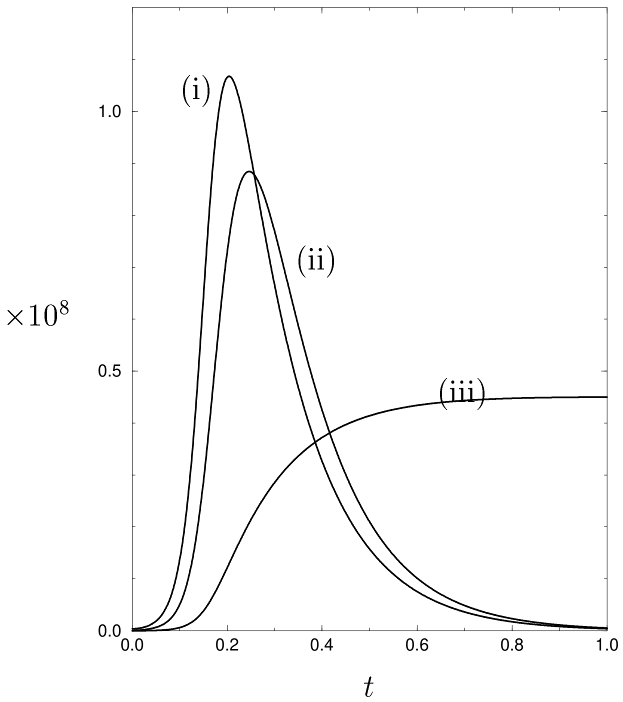

Figure 1: Deterministic trajectory; (i) $L(t)$, (ii) $A(t) \times 100$ and (iii) $r(t) \times 5$; the time t is measured in years. The initial condition for the system is $L(0) = 401500$, $A(0) = r(0) = 0$.

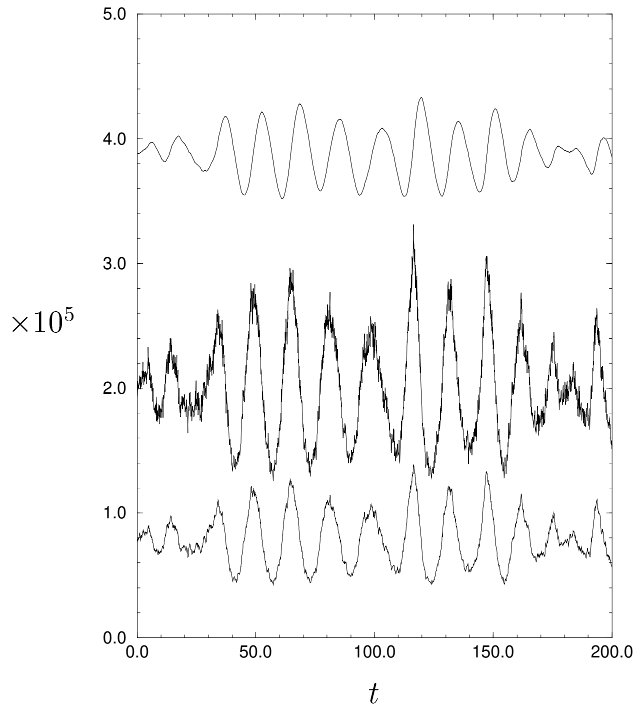

Figure 2: Stochastic time series: $n_L(t)$ (*lower curve*), $200n_A(t) + 5 \times 10^4$ (*middle curve*) and $n_r(t) - 2.54 \times 10^6$ (*upper curve*). The initial condition for the system is close to the endemic equilibrium (L_0, A_0, r_0) of the deterministic model. Oscillations with a period close to the deterministic prediction of $\tau \approx 15$ years are discernible.

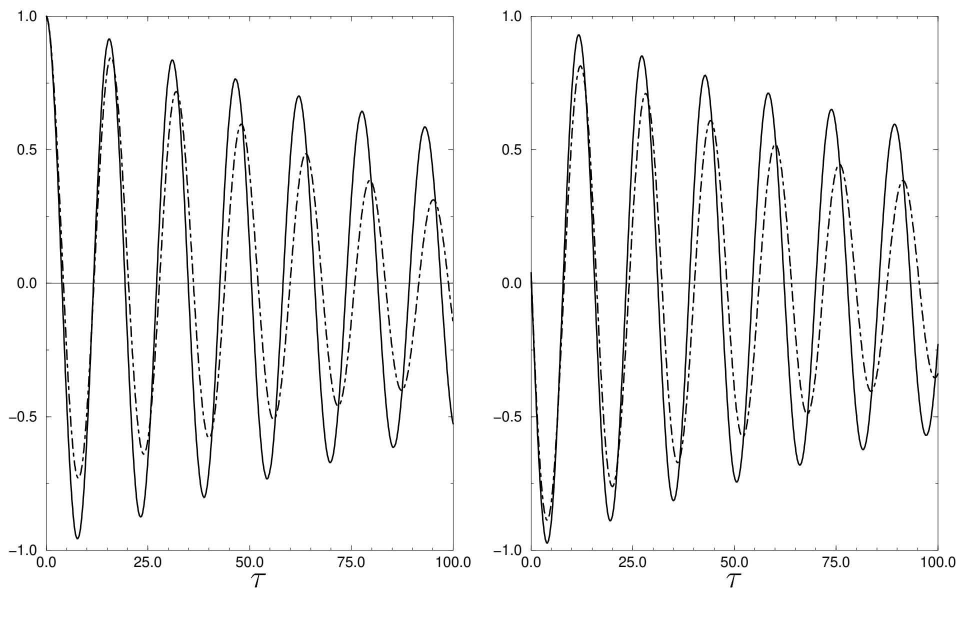

Figure 3: Correlation functions: (a) shows the time-lagged auto-correlation, $\mathcal{C}_{\mathsf{n}_L,\mathsf{n}_L}(\tau)$, of the fluctuations in the free-living population; (b) shows the time-lagged cross-correlation, $\mathcal{C}_{\mathsf{n}_A,\mathsf{n}_r}(\tau)$ (τ is measured in years). Solid curves shows the theoretical values obtained in Section 4.2, whilst the dot-dashed curves show the simulation results. The period of oscillation obtained from the calculated time-lagged correlations, ≈ 15.5 years, is in good agreement to the ≈ 15.8 years from the simulations.

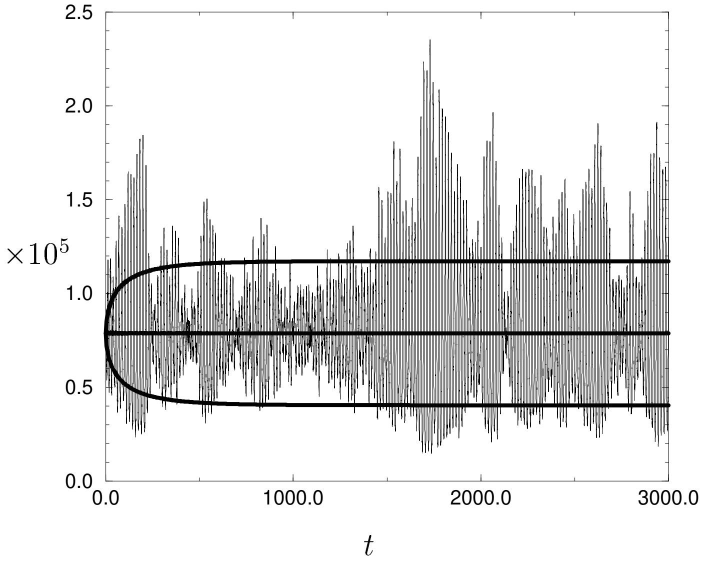

Figure 4: Normal approximation in the endemic regime, showing the Normal approximation to the mean, $\mathbf{E}\left[n_L(t)\right]$, and ± 1 standard deviation (pitchfork curve) along with one realization of the full stochastic dynamic. The time t is measured in years. Similar graphs are obtained for the other populations (n_A and n_r), showing that in this regime the Normal approximation gives a fair indication of the spread around the mean.

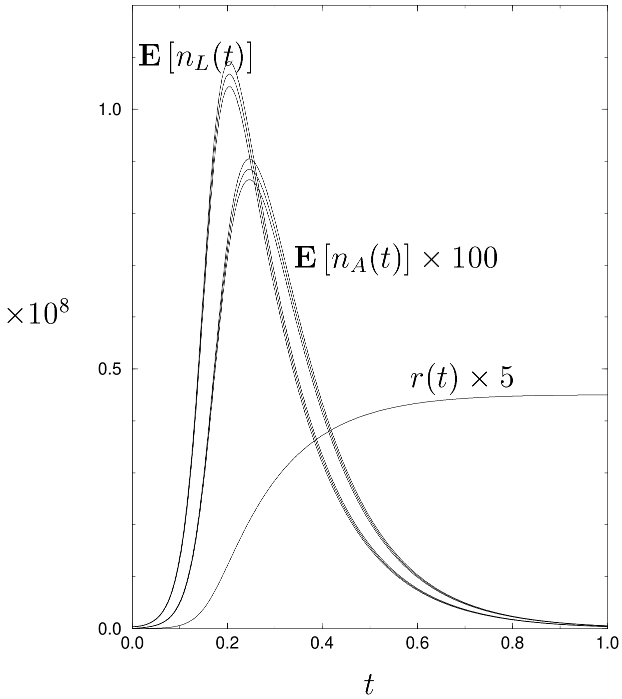

Figure 5: Approximating linearized stochastic process, showing the means ($\mathbf{E}\left[n_L(t)\right]$ and $\mathbf{E}\left[n_A(t)\right]$) and one standard deviation intervals, together with the deterministic value $r(t)$, against the time t in years. The quantities have been re-scaled as indicated.

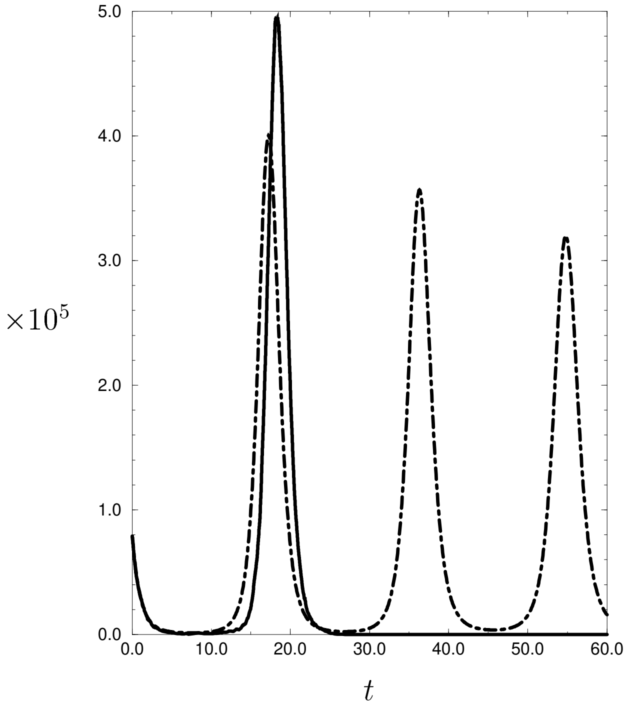

Figure 6: Extinction: The full curve shows a stochastic realization of the larval population $n_L(t)$ with initial condition $n_L = 78850, n_A = 748, n_r = 2870000$ and parameters as in Table 1 except that $\mu(0) = 30$ (i.e. $Q \approx 14.8$). The infection dies out at around $t \approx 31$ years. The dashed curve shows the associated deterministic model output $L(t)$.