# Novel Moment Closure Approximations in Stochastic Epidemics

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**Abstract**

Moment closure approximations are used to provide analytic approximations to nonlinear stochastic models. They often provide insights into model behaviour and help validate simulation results. However, existing closure schemes typically fail in situations where the population distribution is highly skewed or extinctions occur. In this study we address these problems by introducing novel second- and third-order moment closure approximations which we apply to the stochastic ***SI*** and ***SIS*** models. In the case of the *SI* model, which has a highly skewed distribution of infection, we develop a second-order approximation based on the **beta-binomial**. In addition, a novel closure approximation is developed in order to capture the behaviour of the stochastic *SIS* model at the critical point of persistence or extinction of the process. This **mixture** approximation, is a third-order approximation and comprises a probability distribution designed to capture the behaviour of the system conditioned on non-extinction (quasi-equilibrium) and a probability mass at 0 which represents the probability of extinction. Two versions of this mixture approximation are considered in which the **log-normal** and the **beta-binomial** are used to model the quasi-equilibrium distribution. Comparison with simulation results show: 1) the beta-binomial approximation is flexible in shape and matches the skewness predicted by simulation as shown by the stochastic *SI* model and 2) mixture approximations are able to predict transient and extinction behaviour as shown by the stochastic *SIS* model in marked contrast with existing approaches.

*Key words:* log-normal approximation, beta-binomial approximation, mixture approximation, moment-closure, epidemics, *SIS*, *SI*, *R. Solani*

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## 1 Introduction

In this study, we obtain analytic approximations to nonlinear stochastic processes based on the closure of second- and third-order moment evolution equations and compare the results obtained to those from stochastic simulations. The stochastic $SI$ (susceptible - infected) model is used as a case where the population exhibits a highly skewed distribution but totality of infection is guaranteed. In contrast, the stochastic $SIS$ (susceptible - infected - susceptible) model is used as an example that exhibits behaviours of persistence and extinction, common to many stochastic population models in ecology, epidemiology and biochemistry. Both skewness and the transition between persistence and extinction of a disease are often difficult to capture using existing analytic methods. Thus, novel closure approximations are developed to study the transition region between persistence and extinction of a disease.

Stochastic models are useful in epidemiology and ecology and are used widely (Isham, 1991; Allen and Cormier, 1996; Bolker and Pacala, 1997; Filipe and Gibson, 1998; Marion et al., 1998; Matis and Kiffe, 1999; Bauch and Rand, 2000; Keeling, 2000). Usually, the transition probabilities exhibit non-linear dependence on population size or number of infectives which makes the resultant stochastic processes analytically intractable. Hence, techniques of approximation are needed to capture the underlying behaviour of the stochastic processes. Linearisation is one such approximation, where, the behaviour of small stochastic fluctuations can be examined around a fixed point of the deterministic dynamics (Bailey, 1963). An alternative approach is to analyse the quasi-equilibrium probabilities which give a picture of the distribution independent of time and conditional on extinction not having occurred (Renshaw, 1991). Both linearisation and quasi-equilibrium probabilities are limited in their application to regions close to the fixed points or equilibrium. In contrast, closure methods are based on equations describing the temporal evolution of moments or cumulants and in principle apply to both transient and equilibrium dynamics. Moment closure approximation was introduced by Whittle (1957) and has been widely used in recent years (Isham, 1991; Bolker and Pacala, 1997; Marion et al., 1998; Keeling, 2000; Nåsell, 2003). Most commonly in these approximations, the population distribution is only described by the first- and second-order moments and these typically fail to describe the skewness or extinction. Thus, we extend the use of moment closure to a third moment developing a novel closure approach called the **mixture** approximation.

Two generic epidemic models are studied: the stochastic $SIS$, as an example which exhibits extinction and the stochastic $SI$, a simpler version of $SIS$,

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used in a case where recovery is impossible and therefore totality of infection is guaranteed. Depending on the disease transmission rate, the $SIS$ model exhibits meta-stable persistence of disease, rapid extinction and a critical region corresponding to the border between the two regions. Both $SI$ and $SIS$ models have been used before in other studies in either stochastic or deterministic form, for example (Jacquez and Simon, 1993; Allen and Cormier, 1996; Nåsell, 2002). In section 2, we introduce the $SIS$ model, present some simulation results and show how a system of moment equations is obtained from the stochastic model. The moment closure approximations are described in section 3 where various methods of closure are shown with a general formulation of moment equations. Here, we present the $SI$ model, as an ideal starting point for illustration of problems with existing second-order moment closure approximations. In section 4 we compare the various closure approximations used with the simulation results from the stochastic model. Finally in section 5, we lay out our conclusions based on the results discussed in section 4.

## 2 SIS model

An $SIS$ epidemic model with fixed population size, $N$, is considered where the individuals may be in one of two states, either susceptible ($S$) or infected ($I$). When a susceptible individual is infected, it moves to the $I$ class. After some exponentially distributed time, the infected individuals move back to the $S$ class. Hence the model assumes that the disease is non-fatal and induces no resistance in the recovered individuals. The number of infected individuals at time $t$ is denoted by $n(t)$ and since the population size, $N$, is fixed, the number of susceptibles at time $t$ is $N - n(t)$. Two parameters involved in the dynamics of the model are $\alpha$ and $\beta$, where $\alpha$ is the *contact rate* and $\beta$ is the individual *recovery rate*. Infection occurs at rate $\alpha n(t)(N - n(t))$ per unit of time and recovery occurs at rate $\beta n(t)$ per unit time.

Interpreting this model as a discrete state-space Markov process, gives the following probabilities of a change, $\delta n$, occuring in $(t, t + \Delta t)$

$$\text{Prob}[\delta n(t + \Delta t) = 1] = \alpha n(N - n)\Delta t \equiv \psi_\alpha(n)\Delta t \qquad (2.1)$$

$$\text{Prob}[\delta n(t + \Delta t) = -1] = \beta n \Delta t \equiv \psi_\beta(n)\Delta t \qquad (2.2)$$

where $\Delta t$ is sufficiently small that multiple events which occur with probability $O(\Delta t^2)$ may be ignored. The dependence on time is implicit, through $n(t)$.

The inter-event time is exponentially distributed with rate $R{=}\beta n + \alpha n(N - n)$ and the nature of the event will either be an infection with probability $\alpha n(N -$

$n)/R$ or a recovery with probability $\beta n/R$ (Renshaw, 1991). By repeating the procedure, until a given finite time is reached or the disease becomes extinct, single realizations of the stochastic model can be obtained for a given initial condition $n = n_0$. The results presented here are based on generating the initial infectives $n_0$ from a beta-binomial distribution: the beta-binomial being a discrete distribution where the parameter $p$ of a binomial distribution is itself a beta variate (Evans et al., 2000), hence $n_0 \sim bin(20, p)$, $p \sim beta(26.7, 80.0)$. Without loss of generality, we set $\beta = 1$ throughout so that time units are equal to the expected infectious period between infection and recovery (Filipe and Gibson, 1998).

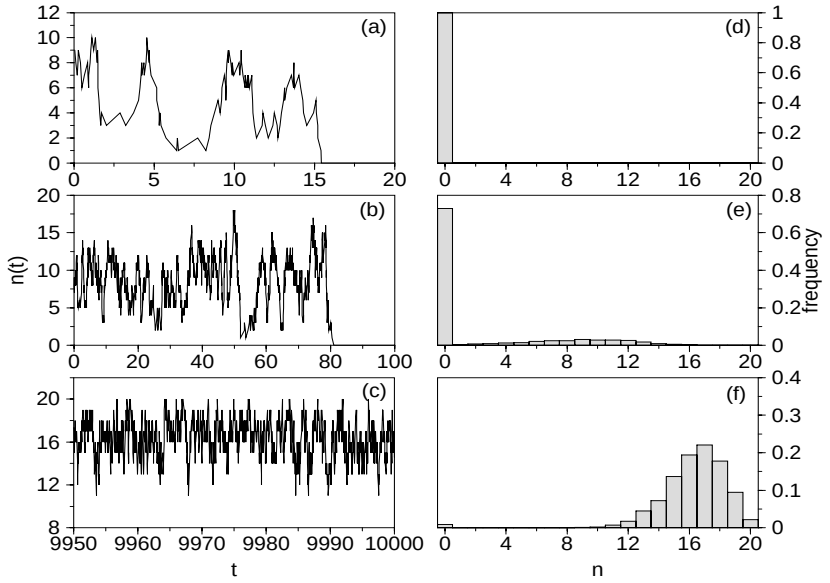


Fig. 1. **Single realisations of stochastic process *(a-c)* and Histogram representing number of infectives *(d-f)***: *(a,d)*: $\alpha = 0.06$; *(b,e)*: $\alpha = 0.10$ and *(c,f)*: $\alpha = 0.30$. Observed number of infectives from single realisations of the stochastic $SIS$ process exhibits $(a)$: Subcritical region where the epidemic quickly dies out, $(b)$: Critical region where the epidemic persist for a short period of time before it dies out and $(c)$: Meta-stable region where the epidemic has reached equilibrium. Histogram representing the number of infectives obtained from 10 000 simulations for $t = 80$ shows $(d)$: Subcritical region where there is a mode at 0 meaning all realisations have gone extinct, $(e)$: Critical region where some of the realisations persists longer and $(f)$: Meta-stable region where extinction is rare.

Graphs, *(a-c)*, of figure 1 show the simulation results of single realisations of the stochastic process for the parameter values representing three regions namely subcritical, critical and meta-stable corresponding to the three different qualitative behaviours which are disease extinction, the transition between disease extinction and meta-stable persistence and meta-stable equilibrium respectively. In the subcritical region ($\alpha = 0.06$), the epidemic dies out quickly (before $t$ reaches 20). When $\alpha = 0.10$ (critical region), the simulation result fluctuates around 10 for the number of infectives before it becomes extinct.

The process seems to have reached equilibrium when $\alpha = 0.30$ for the finite time considered ($t$=10 000) and the number of infectives fluctuates around 17. In this meta-stable region, the epidemic persists and extinction is rare at least for the finite time considered, $t$=10 000.

The histograms, *(d-f)*, of figure 1 were obtained from 10000 simulations by allowing the system to run until $t = 80$. For $\alpha = 0.06$, it can be seen that there is a probability mass only at $n = 0$, meaning all realisations become extinct quickly. In the critical region, $\alpha = 0.10$, the distribution is bimodal with a probability mass at $n = 0$ and a nonsymmetric unimodal contribution to $p(n)$ at $n > 0$. This indicates that some realisations become extinct and some do not, at least for the finite time considered. Finally, in the third parameter region, $\alpha = 0.30$, the histogram is clustered nearer $n = 20$ meaning that extinction is rare in the finite time considered. However, this state is only meta-stable because as $t \to \infty$, ultimate extinction is assured.

### *2.1* ***Analytic approximations***

The transition probabilities (2.1) depend non-linearly on the number of infectives and the resultant stochastic processes are analytically intractable to direct solutions. Thus, techniques of approximations are applied in order to capture the underlying behaviours of the stochastic processes. Linearisation is an example of such approximation, where, the behaviour of small stochastic fluctuations can be examined around a fixed point of the deterministic dynamics. An alternative approach is to analyse the quasi-equilibrium probabilities which give a picture of the distribution independent of time and conditional on extinction not having occurred (Renshaw, 1991). Both linearisation and quasi-equilibrium probabilities are applicable to processes in equilibrium. In contrast, closure methods are based on equations describing the evolution of moments or cumulants that can be applied to both transient and equilibrium dynamics. Since, our aim is to obtain analytic approximations to predict transient aspects of the stochastic process, we focus on applying the moment closure approximation.

### *2.2* ***Moment evolution equations***

Consider (2.1) and (2.2) as representing a Markov chain in discrete time $t$, the probability of an event being a recovery or infection at time $t + \Delta t$ is $\beta n(t)\Delta t$ and $\alpha n(t)(N - n(t))\Delta t$ respectively. The transition probability that there is no change in the state occupied is $1 - \alpha n(t)(N - n(t))\Delta t - \beta n(t)\Delta t$. This assumption is based on the Markov property, that the state at time $t + \Delta t$ is only dependent on the state at time $t$ and not on any previous time (Cox

and Miller, 1965). Let $p_t(n)$ be the conditional probability that there are $n$ infectives at time $t$ given that there are $n_0$ infectives at time $t = 0$. Taking the limit as $\Delta t \to 0$, the forward equation obtained is

$$\begin{aligned}\frac{\partial p_t(n)}{\partial t} =& p_t(n-1)\psi_\alpha(n-1) - p_t(n)\psi_\alpha(n) + \\ & p_t(n+1)\psi_\beta(n+1) - p_t(n)\psi_\beta(n). \end{aligned} \tag{2.3}$$

The evolution of the epidemic can also be described from the evolution of the moments. For example, the first moment describes the expectation of the number of infectives or susceptibles. We derive the evolution of moments of the process, $E[n^k]$, for $k$=1,2,3,.... , by using the moment generating function, $M_t(\theta) \equiv E[\exp(n\theta)] \equiv \sum_{n=0}^{\infty} \exp(n\theta)p_t(n)$.

When (2.3) is multiplied by $\exp(n\theta)$ and the sum taken over $n = 0, 1, 2, ..$, we obtain (Bailey, 1963):

$$\frac{\partial M_t(\theta)}{\partial t} = (e^{\theta} - 1)\widehat{\psi}_\alpha\left(\frac{\partial}{\partial\theta}\right) M_t(\theta) + (e^{-\theta} - 1)\widehat{\psi}_\beta\left(\frac{\partial}{\partial\theta}\right) M_t(\theta) \tag{2.4}$$

where, if $\psi_\alpha(n) = \alpha nN - \alpha n^2$ and $\psi_\beta(n) = \beta n$, then $\widehat{\psi}_\alpha(\frac{\partial}{\partial\theta})M_t(\theta) \equiv \alpha N\frac{\partial M_t(\theta)}{\partial\theta} - \alpha\frac{\partial^2 M_t(\theta)}{\partial\theta^2}$ and $\widehat{\psi}_\beta(\frac{\partial}{\partial\theta})M_t(\theta) \equiv \beta\frac{\partial M_t(\theta)}{\partial\theta}$ respectively. By taking the first, second and third derivatives of (2.4) w.r.t. $\theta$ and setting $\theta = 0$, we obtain ordinary differential equations describing how the first, second and third moment equations of the stochastic process evolve over time.

$$\frac{dE[n(t)]}{dt} = (\alpha N - \beta)E[n(t)] - \alpha E[n^2(t)] \tag{2.5}$$

$$\frac{dE[n^2(t)]}{dt} = (\alpha N + \beta)E[n(t)] + (2\alpha N - \alpha - 2\beta)E[n^2(t)] - 2\alpha E[n^3(t)] \tag{2.6}$$

$$\begin{aligned}\frac{dE[n^3(t)]}{dt} =& (\alpha N - \beta)E[n(t)] + (3\alpha N - \alpha + 3\beta)E[n^2(t)] \\ & +(3\alpha N - 3\alpha - 3\beta)E[n^3(t)] - 3\alpha E[n^4(t)] \end{aligned} \tag{2.7}$$

These equations are open, in the sense that the equation describing the rate of change of the $k^{th}$ moment depends on the $(k+1)^{th}$ moment. Therefore, these equations cannot be solved successively. This is true for all orders of $k$, not just the $k = 1, 2, 3$ shown here. In order to proceed, the system of equations for the first $k$ moments need to be closed and this is done by approximating the

$(k+1)^{th}$ moment in terms of the first $k$ moments. The resulting closed system is then solved numerically. Generally, this method is known as moment closure (Whittle, 1957; Isham, 1991; Marion et al., 1998). In the following section, we discuss problems with existing closure approximation and introduce two novel schemes.

## 3 Closure approximations

### *3.1* ***Second-order approximation***

First we consider second-order moment closure schemes where $E[n^3(t)]$ is approximated in terms of $E[n(t)]$ and $E[n^2(t)]$ by assuming that $n$ is governed by appropriate distribution function. The nonsymmetric bimodal shape and the mode at $n = 0$ shown by the histogram in figure 1 suggest that a symmetric distribution will not be a good approximation. Furthermore, the average number of infectives tends to zero in the subcritical region, $\alpha = 0.06$. Since the normal distribution has zero skewness and no lower bound, using a normal approximation seems inappropriate in this case. Instead, we employ a commonly used alternative, the log-normal distribution because its non-negative support makes it a more appropriate description of population variables. The primary interest in this study is the subcritical and critical regions, thus, the fact that the log-normal does not have an upper bound is ignored. Since the most commonly used distributions for moment closure, for example the normal (Whittle, 1957) and log-normal (Keeling, 2000), are continuous whereas the process we are looking at is discrete, we also consider a discrete distribution, namely the beta-binomial.

The log-normal is a continuous distribution in which the logarithm of the variable of interest is assumed to have a normal distribution. If the number of infectives, $n$, is log-normally distributed, then $y = \log(n)$ is normal with moment generating function

$$M_y(\theta) = E[\exp(\theta y)] = \exp\left(k_1\theta + \frac{k_2\theta^2}{2}\right)$$

where $k_1$ is the mean and $k_2$ the variance of $y$ (Kendall, 1994) . It is straightforward to obtain the moments of the log-normally distributed variable $n$ since $E[n^\theta]$=$E[\exp(\theta y)]$=$M_y(\theta)$.

Thus, the first, second and third moments for the log-normal distribution can be obtained by substituting $\theta = 1, 2, 3$, for example, the third moment is:

$$M_y(\theta = 3) = E[n^3] = \exp\left(3k_1 + \frac{9k_2}{2}\right)$$

The beta-binomial distribution has been in existence since Eggenberger and Pólya (1923) proposed their urn model, although it remained unnamed and under-used until Skellam (1948) gave it a thorough description. The beta-binomial distribution has more recently been used in plant epidemiology by Madden and Hughes (1995) to represent quadrat counts of disease incidence. The beta-binomial is a discrete distribution where the parameter $p$ of a binomial distribution is itself a beta variate (Evans et al., 2000). If the number of infectives, $n$ is from a beta-binomial distribution, then the moment generating function (Skellam, 1948) is

$$M_n(\theta) = \frac{1}{beta(a,b)} \int_0^1 p^{a-1}(1-p)^{b-1}(1-p+p\exp(\theta))^N dp$$

where $a$ and $b$ are the shape parameters and $N$ is the population size. By taking the first, second and third derivatives of the moment generating function and evaluating at $\theta = 0$ we obtain the moments which are

$$E[n] = \frac{Na}{a+b} \tag{3.1}$$

$$E[n^2] = \frac{Na(Na+N+b)}{(a+b)(a+b+1)} \tag{3.2}$$

$$E[n^3] = \frac{Na}{a+b}\left(1 + \frac{3(N-1)(a+1)}{a+b+1} + \frac{(N-1)(N-2)(a+1)(a+2)}{(a+b+1)(a+b+2)}\right). \tag{3.3}$$

Note that both the log-normal and beta-binomial are described by just two free parameters and thus only two moments, $E[n]$ and $E[n^2]$ are required, to solve for parameters in terms of moments. For example, solve (3.1) and (3.2) simultaneously for $a$ and $b$ of the beta-binomial. Thus the log-normal and beta-binomial distributions may be completely determined by the first- and second-order moments. This is precisely what is required for a second-order approximation. With these assumptions the third-order term, $E[n^3(t)]$ in the equation describing the evolution of the second-order moment is replaced by appropriate functions of $E[n]$ and $E[n^2]$ for the log-normal and beta-binomial distributions.

To illustrate second-order approximation and the application of the beta - binomial approximation to a set of observed data (Kleczkowski et al., 1996;

Gibson et al., 1999), we present the $SI$ model in the following subsection.

### *3.2* ***Case Study: fungal plant epidemic***

Kleczkowski et al. (1996) carried out experiments on radish seedlings by inoculating them with the pathogen *Rhizoctonia solani* Kühn, a fungus that attacks root vegetables and is responsible for what is known as damping-off disease (Green, 1943). They monitored 10 microcosms, each containing 50 seedlings and inoculated by means of 10 mycelial discs of *R. solani*, and recorded the number of infected seedlings daily. Five of the microcosms were also exposed to the antagonistic fungus *Trichoderma viride* Pers ex Gray, which has a controlling effect on the pathogenic fungus, *R. solani*. These data are reproduced in figure 2.

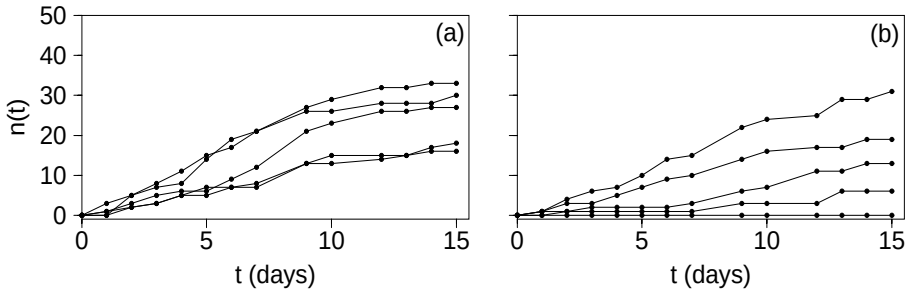


Fig. 2. Number of radishes infected by damping-off in five replicate microcosms in the absence *(a)* and presence *(b)* of the antagonistic fungus *T. viride*.

| **Parameter** | **T. viride absent** | **T. viride present** |
|---|---|---|
| $\alpha_p$ | 0.0265 | 0.0074 |
| $\alpha$ | 0.0118 | 0.0102 |
| $v$ | 0.167 | 0.127 |

Table 1
Maximum likelihood estimates for the three parameters, under the presence or absence of the antagonistic fungus *Trichoderma viride*, estimated by Gibson et al. (1999).

Kleczkowski et al. (1996) formulated and fitted a deterministic model to their data, which Gibson et al. (1999) recast in stochastic form, the stochastic model having the benefit of being able to capture the variability observed in the experiments. Both models contain terms accounting for infection of radishes by primary sources, that is, the initial inoculum, as well as by the secondary sources we have been considering so far, representing infection via an already-infected plant. In addition, both models include a time-varying susceptibility

of the plants to the disease. The probabilistic rule given by Gibson et al. (1999), re-written to our notation, is:

$$\text{Prob}[\delta n(t+\Delta t)=1] = (\alpha_p + \alpha n(t))(N - n(t))e^{-vt}\Delta t \tag{3.4}$$

with $\alpha_p$ being the new primary rate of infection, $\alpha$ the secondary, and $e^{-vt}$ the time-varying susceptibility of plants to the disease. This time varying susceptibility can be accomodated by rescaling time as $\tau = (1 - e^{-vt})/v$.

We derive the following equations for the rate of change of the first- and second-order moments of $n(\tau)$ with respect to $\tau$, which are analogous to equations (2.5) and (2.6):

$$\frac{\partial E(n(\tau))}{\partial \tau} = \alpha_p N + (\alpha N - \alpha_p)E(n(\tau)) - \alpha E(n^2(\tau)) \tag{3.5}$$

$$\begin{aligned}\frac{\partial E(n^2(\tau))}{\partial \tau} =& \alpha_p N + (\alpha N + (2N-1)\alpha_p)E(n(\tau)) \\ &+((2N-1)\alpha - 2\alpha_p)E(n^2(\tau)) - 2\alpha E(n^3(\tau))\end{aligned} \tag{3.6}$$

Assuming that $n(\tau) \sim$ *beta-bin*$(N, a(\tau), b(\tau))$, we can write $E(n^3(\tau))$ in terms of the first two moments of $n(\tau)$, as described in section (3.1), and substitute this value in equation (3.6). This means that we can use some numerical method to evaluate approximations to the first two moments over time, for a given parameter set $\{\alpha_p, \alpha, v\}$ and given the initial conditions in this case that no seedlings were infected at the start of the epidemic (i.e. $n(0) = 0$). Here we use Euler's scheme. We also apply normal and log-normal approximations, in the same way.

Gibson et al. (1999) used profile likelihoods to estimate these three parameters from the two data sets, corresponding to the presence or absence of the biological control agent *T. viride*; these values are reproduced in table 1. We perform $3 \times 10^6$ simulation runs of the model for both parameter sets. The simulations and approximations are plotted in figure 3.

As can be seen in figure 3, the beta-binomial approximation captures the dynamics of the evolution of the true probability mass function far better than either the normal or log-normal approximations. The normal approximation is only able to capture the shape of the observed distributions when their skewness is approximately 0. Furthermore, the normal approximation assigns probability to negative numbers of infectives; these probabilities may be substantial for particularly skewed observations. In contrast, the log-normal approximation does not support negative numbers of infectives, and matches the

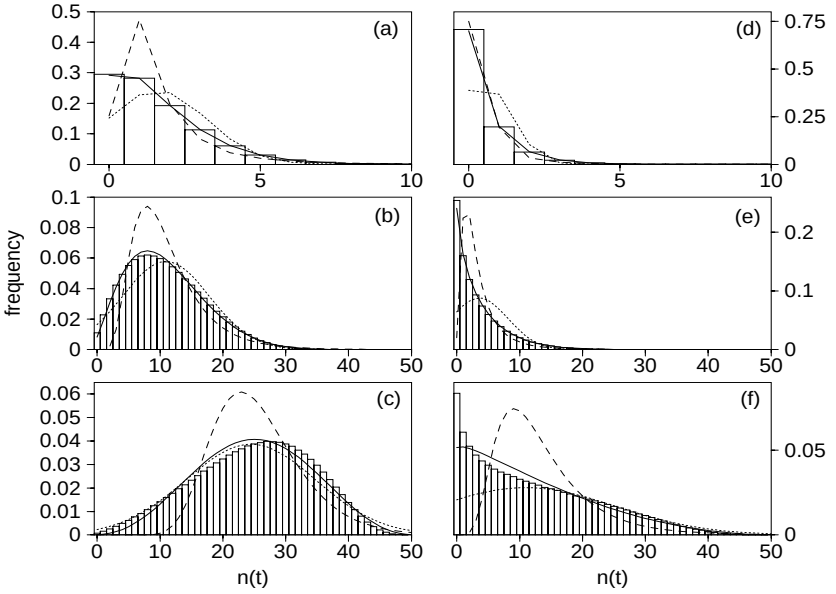


Fig. 3. **Distribution of the number of radishes infected by damping-off** in the absence (*a-c*) and presence (*d-f*) of the antagonistic fungus *T. viride*, at 1 *(a,d)*, 5 *(b,e)* and 15 *(c,f)* days after the first emergence of seedlings. The initial condition is that the plants are all disease free (i.e. $n(0) = 0$). The histograms represent the average frequencies from a series of $3 \times 10^6$ simulations, the unbroken curves our beta-binomial moment closure approximations, the dotted curves the Normal, and the dashed the log-normal. Continuity correction has been used for the continuous distributions; however, we represent all three approximations as continuous curves for clarity of comparison. Both simulations and moment closure approximations make use of the maximum likelihood parameter estimates found by Gibson et al. (1999), reproduced in table 1.

skewness present in the early stages of the epidemics better than the normal, although its shape is not as flexible as that of the beta-binomial.

### *3.3* ***Second-order approximation results for the SIS model***

Having seen the results in the case of the $SI$ model, we now consider approximating the more complex behaviours of the $SIS$ model as shown in figure 1 where we have the subcritical, critical and meta-stable regions. Results from numerical solution for the log-normal and beta-binomial approximation using the Runge-Kutta fourth-order scheme are shown in figure 4.

It is seen that the beta-binomial is the better approximation in the subcritical region where it is able to predict extinction as seen in stochastic simulation. In the critical region, both log-normal and beta-binomial approximations break down where they are unable to show the observed extinction as seen in stochastic simulation for large $t$. In the meta-stable region, both log-normal and beta-

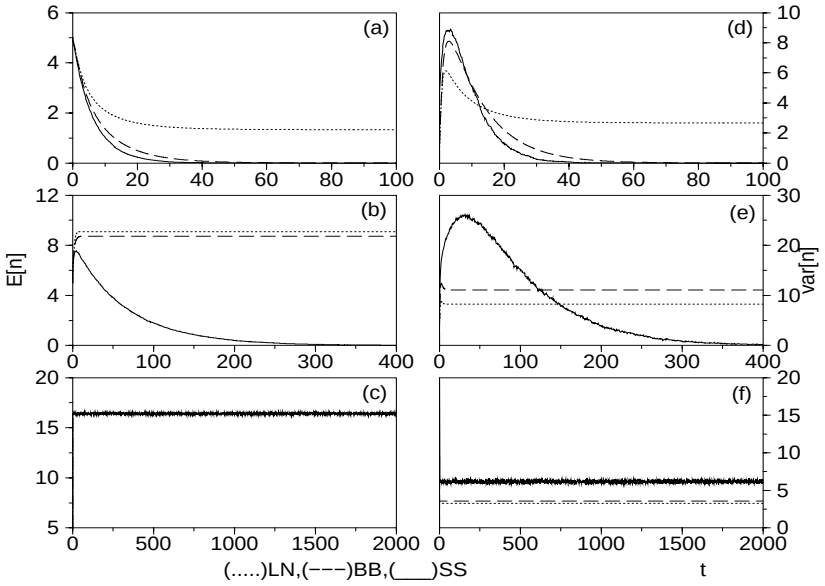


Fig. 4. **Second-order approximation and stochastic simulation**: Expected number of infectives, *(a-c)*, and variance, *(d-f)*, from closure approximations and stochastic simulations. Subcritical region: *(a,d)*: $\alpha = 0.06$; Critical region: *(b,e)*: $\alpha = 0.10$; Meta-stable region: *(c,f)*: $\alpha = 0.30$.

binomial approximations agree well with stochastic simulations where extinction is rare for the finite time considered. The beta-binomial approximation is able to estimate the variation in the process better than the log-normal in the subcritical region.

In summary, the beta-binomial gives reasonable estimates in the subcritical but not the critical region and the log-normal gives poor estimates in both the regions. Both approximations are good in the meta-stable region but predict indefinite persistence. Both the beta-binomial and log-normal are approximately same in the critical and meta-stable region. Overall, second-order approximations did not give good description of extinction in the subcritical and critical regions for the $SIS$ model. Thus, third-order closure approximation is developed and hoped to give an improved description of these regions.

### *3.4* ***Third-order approximation***

In the histogram in figure 1, it is seen that there is a shift in the shapes of the distribution shown when there is a change in the parameter value: In the subcritical region ($\alpha = 0.06$), it is simply a mass at $n = 0$; in the critical region ($\alpha = 0.10$), it becomes a bimodal with a mode at $n = 0$ corresponding to the proportion of realisations that become extinct and a nonsymmetric unimodal portion resulting from those remaining extant realisations; and in

the meta-stable region ($\alpha = 0.30$), the mode at $n = 0$ shrinks and there is a nonsymmetric unimodal shape clustered nearer to $n = 20$. In this region, extinction is rare on relatively large time scales though ultimate extinction is guaranteed. Thus, the persistent state is said to be meta-stable. This can be understood by noting that for $n$ infectives, the probability of the next $n$ events being recovery ($I \to S$) is finite. Here, a novel closure approximation is developed in which the population is assumed to be described by a distribution which is a mixture of mass at $n = 0$ and a probability distribution representing extant realisations in order to obtain an improved description of the transient aspects of the process. A major advantage of this third-order approximation is that it estimates probability of extinction in the critical and meta-stable regions which a second-order approximation cannot do, as seen in figure 4. Therefore, it allows prediction of extinction probability, the transient distribution and the quasi-equilibrium distribution. For this study, first we use a log-normal mixture and then a beta-binomial mixture.

In general, the probability function of this mixture distribution is represented by $p(n) = p\pi_1(n) + (1-p)\pi_2(n)$ where $\pi_1(0) = 1$ and $\pi_2(n)$ is a probability mass function for $n = 0, 1, 2, ..., N$. Thus, $E[n^k] = (1-p)E_{\pi_2}[n^k]$. If $\pi_2$ is from a two parameter, say $(\mu, \nu)$, family of distributions then the mixture defines third-order approximation since $p, \mu$ and $\nu$ are determined by solving three equations for $k$=1, 2 and 3 (for example, the first three moments). Thus, the mixture distribution is completely determined by the first-, second- and third-order moments, $E[n], E[n^2]$ and $E[n^3]$.

Since this is a third-order approximation, the fourth moment of the log-normal mixture and beta-binomial mixture are needed in order to close the system of differential equations (2.5)-(2.7). Thus, when $\pi_2$ is the log-normal, the fourth moment of the log-normal mixture is

$$E[n^4] = (1-p)\exp(4k_1 + 8k_2)$$

where $p$, $k_1$ and $k_2$ are determined as described above in terms of $E[n]$, $E[n^2]$ and $E[n^3]$ by solving the equations for the first three moments of log-normal mixture simultaneously.

If $\pi_2$ is the beta-binomial, the fourth moment of the beta-binomial mixture is

$$\begin{aligned} E[n^4] = {} & (1-p)\frac{Na}{a+b}\left(1 + \frac{7(N-1)(a+1)}{a+b+1}\right) + \\ & (1-p)\frac{Na}{a+b}\left(\frac{6(N-1)(N-2)(a+1)(a+2)}{(a+b+1)(a+b+2)}\right) + \\ & (1-p)\frac{Na}{a+b}\left(\frac{(N-1)(N-2)(N-3)(a+1)(a+2)(a+3)}{(a+b+1)(a+b+2)(a+b+3)}\right) \end{aligned}$$

where $p$, $a$ and $b$ are determined in terms of $E[n]$, $E[n^2]$ and $E[n^3]$ by solving the equations for the first three moments of beta-binomial mixture simultaneously with $N$ fixed by the population size.

Therefore, the fourth-order term, $E[n^4(t)]$ in the equation describing the evolution of the third-order moment, equation (2.7) is approximated by a function of $E[n]$, $E[n^2]$ and $E[n^3]$ for both the log-normal mixture and beta-binomial mixture. Results of these third-order approximations are shown in the following section.

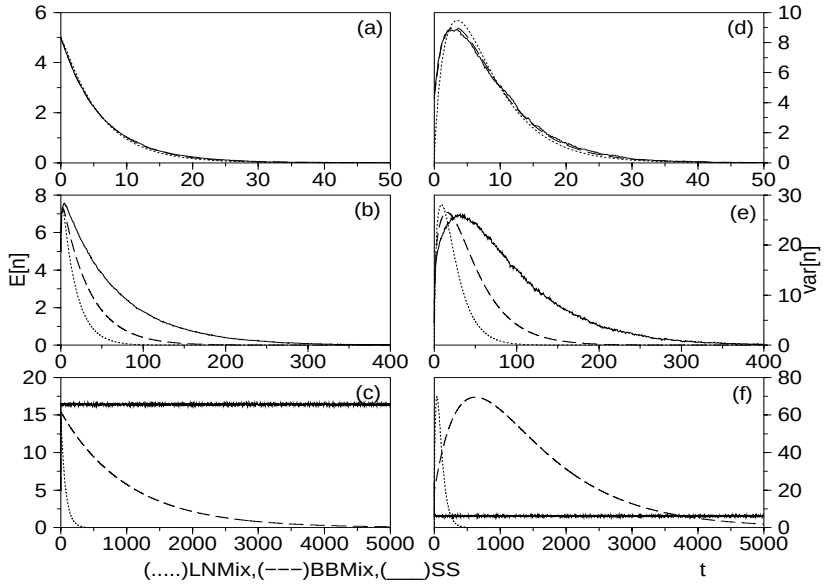


Fig. 5. **Mixture approximation and stochastic simulation**: Expected number of infectives, *(a-c)*, and variance, *(d-f)*, from mixture approximations and stochastic simulations. Subcritical region: *(a,d)*: $\alpha = 0.06$; Critical region: *(b,e)*: $\alpha = 0.10$; Meta-stable region: *(c,f)*: $\alpha = 0.30$.

## 4 Results and Comparison

Here we discuss the results of the third-order approximations for the $SIS$ model. Numerical solution for the log-normal mixture and beta-binomial mixture approximation using the Runge-Kutta fourth-order scheme are compared with stochastic simulation in figure 5.

There is improvement for both mixtures over second-order approximations in the subcritical region where the log-normal mixture is able to predict extinction and the beta-binomial mixture predicts extinction on a more accurate time scale than the corresponding second-order approximation. Furthermore, in this region, the estimated variances also agree with the stochastic simula-

tion. In the critical region, there is again a large improvement for both mixtures as they are able to capture the behaviour shown by stochastic simulation, which can be interpreted as a short-term outbreak which becomes extinct after a relatively short time. Unfortunately, the mixtures estimate this on a slightly shorter time scale than that observed in stochastic simulations. In the meta-stable region, the behavior shown by the mixtures is qualitatively correct but it is unable to mimic the observed meta-stability of the epidemic. Both log-normal and beta-binomial mixture tend to overestimate the probability of extinction and therefore underestimate the time to extinction. However, the beta-binomial mixture does slightly better in estimating its time scale. Since the mixtures predict extinction on a shorter time scale compared to stochastic simulation, we consider the expected number of infectives as a function of the probability of extinction and this is seen in figure 6.

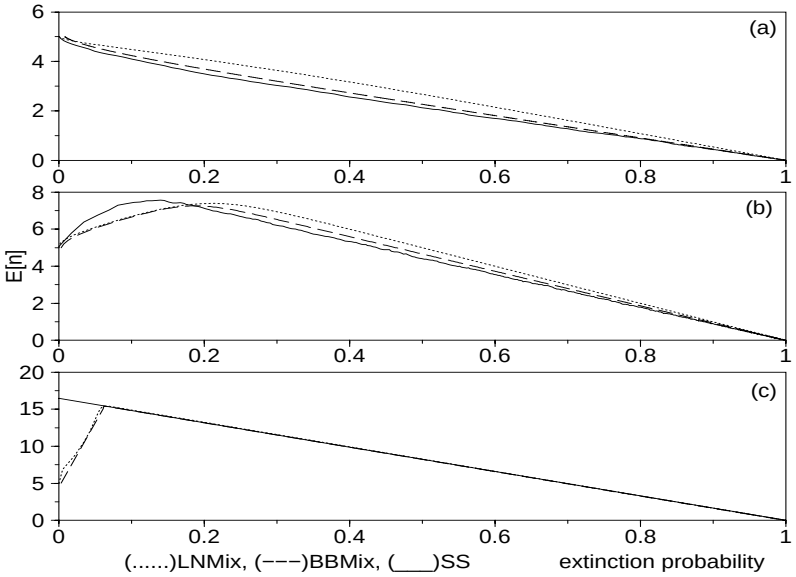


Fig. 6. A diagram of expected number of infectives vs extinction probability obtained from mixture approximations and stochastic simulations for ($a$): subcritical region ($\alpha = 0.06$), ($b$): critical region ($\alpha = 0.10$), ($c$): meta-stable region ($\alpha = 0.30$)

In both the subcritical and critical regions, it can be seen that the beta-binomial mixture is the better approximation. In the critical region ($\alpha = 0.10$), for an extinction probability of approximately 0.2, the expected number of infectives estimated by the mixtures is close to the result from the stochastic simulations. In the meta-stable region, both mixtures are able to match the simulation results for probability $> 0.05$. The result from stochastic simulation shows that the expected number of infectives is a linear function of the probability of extinction. This is due to the large rate of infection when $\alpha = 0.30$ which speeds the disease to reach epidemic level that persists over a long time ($t \approx 6 \times 10^7$). In the meta-stable region, the expected number of infectives is a linear function of probability of extinction because the mean is conditioned on

non-extinction. Although the expected time to extinction is poorly estimated by our mixture approximations in the meta-stable region, figure 6 shows that they are able to predict the relationship between probability of extinction and expected epidemic size seen in stochastic simulations.

## 5 Conclusion

In this paper we have introduced a new second-order moment closure approximation and applied this to the SI model. The approximation (which assumes that the distribution of the numbers of infections follows a beta-binomial distribution) agrees well with the true frequencies obtained by simulation, and offers a considerable improvement on approximations based on the normal or log-normal distributions. The beta-binomial approximation may be similarly applicable to approximate other stochastic models on fixed-size populations.

In the case of the SIS model, which exhibits a richer range of dynamics including extinction and meta-stability, the second-order beta-binomial approximation performs well in the subcritical region (where extinction occurs rapidly), but is unable to predict the extinction occuring in the critical region, whilst the log-normal approximation fails to capture extinction in both critical and subcritical regions. This led us to propose the three-parameter mixture distributions combining probability mass at 0 with log-normal and beta-binomial distributions, respectively.

These new approximations are able to predict the extinction exhibited by the SIS model, although both predict that extinction occurs over a shorter time scale than observed in simulations. The beta-binomial mixture gives a superior approximation to the log-normal mixture, predicting extinction on a longer times-scale that is closer to the simulation results, and agreeing extremely closely with the simulations in the subcritical region.

There are a number of areas where the work of this paper can potentially be extended. One such example is to apply the mixture approximation to other one dimensional models such as the Verhulst (Goel and Richter-Dyn, 1974) and $SIR$ (Nåsell, 2002) model. Alternatively, the mixture approximation could be extended to higher dimensional systems, for example, the predator-prey (Renshaw, 1991) and chemical-kinetics (Marion et al., 2002) processes. Finally, it would be interesting to consider moment closure schemes based on more general mixture distributions than those considered in this contribution.

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