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The quasi-deterministic limit of population dynamics

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ABSTRACT

We review, discuss and compare different, but related, approximations to the stochastic dynamics of populations, all of them having as limit the same deterministic dynamics. The diffusion approximation, linearized diffusion approximation and the Poisson approximation are briefly revisited and their quality as approximations for large, but given, populations is addressed analytically as well as with demonstrative examples. To this end we introduce the Integer-Gauss approximation to the Poisson approach and use it to discuss the relation among different techniques.

Keywords: Stochastic Population Dynamics, Feller Process, Poisson Approximation, Diffusion Approximation, Langevin approach, SDE.

1 Introduction

A standard, and to a large extent reasonable, assumption in theoretical ecology is that individuals in an ecosystem interact mostly through processes that are highly localized in space and time. Hence, individual based models, following each individual over time, can provide a quite realistic picture of the system in study. However, this approach is not cost-free. Inference about population dynamics must be obtained only through extensive numerical explorations and such simulations are restricted (in practice) to relatively small populations because of computational limits. Moreover, such detailed account for every single individual may be irrelevant as, in many cases, only some form of average behaviour is of interest for further decision making. Hence, dynamical models for populations have become the core of theoretical ecology. Such models retain the occurrence of individual processes as a fundamental part of the description, but describe *classes* of individuals instead. However, there is no systematic procedure to define a population model by grouping individual characteristics into classes (see for example (Brauer and Chavez, 2001; Volkov, Banavar, Hubbell and Maritan, 2003; Brauer, van der Driessche and Wu, 2008)). The success of a model rests on the researcher's skills and her/his knowledge of the system under study.

For a given situation, a variety of models may be constructed, potentially displaying dramatically different dynamics. For example (Natiello and Solari, 2007), a two-dimensional deterministic population model with a non-extinction focus stable fixed point predicts monotonic (unavoidable) approach to equilibrium for any initial condition close to the fixed point, while its stochastic counterpart has essentially zero probability to attain equilibrium. See also (Henson, Costantino, Cushing, Desharnais, Dennis and King, 2001) where the necessity of using discrete dynamical variables (beyond an ODE population description) is experimentally established.

In natural processes, regardless of the size of the system, it is impossible to predict or model when and where the "next" interaction will take place, nor which kind of interaction it will be. For this reason alone, an accurate description of natural processes involving groups of individuals demands for a stochastic treatment. Nevertheless, for very large populations where a lot of individual events take place in any

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sufficiently short interval of time, it is possible to approximate the dynamics via a deterministic model (Kurtz, 1971). Deterministic models lie at the origin of population dynamics since Malthus (Malthus, 1798) and Verhulst (Verhulst, 1838), while the stochastic description of population models arrived no more than 100 years later (McKendrick, 1914; Kermack and McKendrick, 1927). This historical reason, as much as the relative difficulty of the stochastic formulation as compared with the deterministic one, may account for the widespread use (and at times abuse) of deterministic approaches. Nevertheless, in some cases, deterministic solutions provide a template for stochastic dynamics (Coulson, Rohani and Pascual, 2004).

We call *environmental stochasticity* that which is independent of the population. Such type of stochasticity is also sorted under the label *external noise*. On the other hand, *demographic stochasticity* is associated to the inherent variability of individual behaviour and of individual responses to the actions of other individuals. Fundamental demographic stochasticity effects in homogeneous systems can be observed in epidemic systems with total populations below the *critical community number* (Bartlett, 1957) which can be as "small" as 250000 individuals. Since relative fluctuations with respect to mean values due to demographic stochasticity depend on the population sizes, demographic stochasticity is also called *internal noise* (we will use this name in the sequel). This choice of wording verbalizes the intention of being able to describe natural populations via some "deterministic mean-value" equation plus "fluctuations" (noise) around the mean. Let us further explore this idea.

We say that a population is *local* when spatial effects can be ignored. Whether a population is to be considered local or not, strongly depends on the case and the questions of interest. Individuals within the local population are grouped in different subpopulations and the sizes of the different subpopulations become the dynamical variables. Every individual becomes an average individual responding to the mean influence produced by the rest of the individuals in the subpopulations. The size of each subpopulation may vary due to the occurrence of several different types of events (we assume that the fundamental factors driving the dynamics of the population have been identified). A stochastic model is built assigning a probability of occurrence per unit of time, or *transition rate*, to each of these events. In general, these probabilities are functions of the population sizes. Such a model is the most detailed and realistic population model for the dynamics of a local population (Renshaw, 1991). When spatial effects play a significant role on the dynamics, the previous approach can be generalized to a network of linked local populations.

Let us further consider the stochastic local model described above. The sizes of each subpopulation (N_i) are discrete random variables. The probability that these variables have definite values (n_i) at time t is denoted by $P(N_1 = n_1, N_2 = n_2, ...; t)$. The main underlying assumption for the dynamics is that time-evolution is ruled by the successive occurrence of individual events in time. This is an example of a Markov Jump Process (Ethier and Kurtz, 1986). The evolution of this process is governed by the *Kolmogorov forward equation* (Feller, 1940; Bartlett, 1953; Durrett, 2001), KFE (sometimes called *master equation*, but this name is also used to denote a truncation of KFE, which is a differential equation for the probability P).

Solutions of the KFE for given initial conditions provide the maximum possible information about the system. Unfortunately, to solve such differential equation is a formidable task, even for the simple case of a birth-death process in a single subpopulation. The chances to obtain analytical solutions to the master equation when more than one population are in interaction is really feeble. One possibility is to solve the equation numerically or, what is equivalent, to perform numerical simulations of it with a Feller process (see below), sometimes mentioned in the physics literature as *Markov chain Monte Carlo simulation* (Metropolis and Ulam, 1949; Bartlett, 1953; Spigler, 1987). However, because analytical solutions provide more insight about the dynamical properties of the system, other approaches are usually considered.

The inherent difficulties in dealing with the KFE has reinforced the efforts in achieving success via " deterministic mean value + fluctuations" approaches. This idea has emerged in different contexts and, as such, it has several names associated to it. Indeed, a widely used procedure consists in giving up KFE and assuming that the involved probabilities can be described by a different equation, namely the *Fokker-Planck equation* (van Kampen, 1981a). Because this partial differential equation is of diffusive type, this approach is also known as the *diffusion approximation* (Ethier and Kurtz, 1986). Also, attempts to associate a system of stochastic differential equations with the realizations of the Fokker-Plank process is known as the *Langevin approach* (van Kampen, 1981b). This alternative approach should be weighed against implementing descriptions based on the KFE. We will later introduce the ideas of *Feller process* (Ethier and Kurtz, 1986, Ch. 2), *Poisson approximation* (Aparicio and Solari, 2001a; Solari and Natiello, 2003a) and *Integer-Gauss approximation* (introduced in this manuscript) as

different such attempts.
In this article we will attempt to deepen our understanding of the different treatments attempting to handle a population dynamics problem with stochastic methods. We show that standard approaches of the type "deterministic mean value + fluctuations" give in general a poor description of the underlying natural process, although in some cases (that cannot be fully specified beforehand) they may hit closer to the target. We discuss further the reasons why such procedures result in a poor approximation of the stochastic dynamics, as well as how to proceed to obtain good approximations preserving (and moreover taking advantage of) the stochastic nature of the underlying system.
To this end, we describe a simplified population problem in Section 2, to be addressed with different methods. In Section 2.2, we review the full stochastic realization of the problem. In Section 2.3 we review some standard approaches relating stochastic dynamics to its deterministic counterpart (diffusion and Langevin mentioned above, the standard SDE presentation (Arnold, 1974) and also Van Kampen's linear noise approximation (van Kampen, 1981b)). It should be noted that these procedures are not approximations to the original (KFE) problem but *substitutions* of this problem with another one (Fokker-Planck). The rest of this section is devoted to approximations in the proper meaning. Firstly, in Section 2.4 we review the Truncated Poisson Approximation to the full Feller process (Section 2.2), a method going back to Bartlett (Bartlett, 1960) and recently improved (Aparicio and Solari, 2001a; Solari and Natiello, 2003a; Solari and Natiello, 2003b)). Further, Section 2.5 introduces the Integer-Gauss approximation to the Poisson approach. This approximation is conceptually appealing for various reasons: (a) it provides a finer validity range for its use that just the limit $N \to \infty$ and (b) it has a sound foundation as an approximation to the Poisson distribution and helps to provide a clear validity limit to the indiscriminate use of substitution approaches.
In Section 3 we test the approaches discussed in Section 2 on our model problem. The Integer-Gauss approximation allows to bridge the gap between Sections 2.3 and 2.4. If the truncated Poisson distribution is replaced by a Gaussian *in the region where their difference is negligible*, then both approaches give very similar results (this is the method called "hybrid" in Section 3) while when the replacement is done also *outside* the validity range (i.e, where the correct quantity and the replacement quantity are *not* similar), then the improvement over the method described in Section 2.3 is only marginal. Finally, Section 4 is devoted to Conclusions.

2 Approximations

We will present our ideas using a simple model for measles epidemic dynamics. This real example exhibits different dynamics covering the cases of interest (Aparicio and Solari, 2001b; Aparicio and Solari, 2001a). Generalization is straightforward, but the presentation benefits by using a simple example. Before the measles vaccine was available, measles epidemics showed two qualitatively different regimes. In populations sized below the *critical community size*, the disease was unable to persist for long periods of time. Epidemic recurrence was due to the immigration of infective individuals, producing sharp outbreaks followed by fast extinction of the disease. The mean period between successive outbreaks diminishes as population increases. The critical community size for measles was estimated in around 250,000 individuals (Bartlett, 1957; Bartlett, 1960). In populations above this value, measles was able to persist for very long periods of time presenting small outbreaks along the year.

2.1 A Model for Measles Dynamics

It is possible to build a simple stochastic model whose solutions mimic the observed behaviour of measles epidemics.
The incubation period of infected individuals is of about one week. After this latent, non-infective, period, individuals become infective and capable to transmit the disease. Recovery occurs after about one week, and the acquired immunity is permanent. Newborns are susceptible. Therefore we can consider each individual belonging to one of the four epidemiological classes: susceptible, latent, infective, or recovered. The number of individuals in each class is denoted by $S(t)$, $E(t)$, $I(t)$, and $R(t)$ respectively, and the total population becomes $N(t) = S(t) + E(t) + I(t) + R(t)$. As a further simplification we disregard the latency period, i.e., we consider that infected individuals are infective without delay.
We will also consider a population with constant recruitment (Λ) and constant per capita mortality rate (μ). Therefore, for long enough time, the standard expectation is that the population will fluctuate around the value $N_{eq} \simeq \Lambda/\mu$ with amplitude $\sqrt{N_{eq}}$.

Event	Effect	Transition rate
Birth	$(S, I) \to (S+1, I)$	$w_{bs} \equiv \mu N$
Arrival of infective	$(S, I) \to (S, I+1)$	$w_\epsilon \equiv \epsilon\mu N$
Contagion	$(S, I) \to (S-1, I+1)$	$w_c \equiv \beta SI/N$
Death of a susceptible	$(S, I) \to (S-1, I)$	$w_{\mu s} \equiv \mu S$
Death of an infective	$(S, I) \to (S, I-1)$	$w_{\mu i} \equiv \mu I$
Recovery from infection	$(S, I) \to (S, I-1)$	$w_r \equiv \gamma I$

Table 1: Events and transition rates defining the stochastic epidemic model.

Because we will consider values of N_{eq} larger than 10000, relative fluctuations of the total population around the N_{eq} are negligible. For the sake of simplicity we will assume that the total population size remains constant with value $N = N_{eq}$. Therefore, recruitment and mortality compensate as $\Lambda = \mu N$. There are only two remaining independent variables which we choose as $S(t)$ and $I(t)$, while the (approximate) value of the recovered population is $R(t) = N - [S(t) + I(t)]$. These approximations are not mandatory. We introduce them in order to simplify the problem under reasonable conditions since, our goal is to discuss and illustrate different methods. Real-life applications usually demand the full treatment, which may be computationally more involved but it need not present additional theoretical challenges.
In Table 1 we list all the relevant events, transition rates and associated parameters defining the stochastic model. Each infected individual encounters (per unit time) susceptible individuals in a form proportional to the fraction of susceptibles present in the total population, S/N. A fraction β of the encounters results in new infections, thus the average total of new infected people associated to one infected individual during its average infective time ($1/\gamma$) is $\beta S/(N\gamma)$. Therefore, the expected number of infections occurred per unit of time becomes $\beta SI/N$. We assume that a small number of external infected individuals per unit time (ν) is entering the community. This external flux of infected individuals is assumed to be proportional to the population size N, that is, $\nu = \epsilon\Lambda = \epsilon\mu N$ with $\epsilon \ll 1$. We disregard the small contribution to population size of this small external flux of infective individuals.

The corresponding KFE reads,

$$\begin{aligned}\frac{d}{dt}P(S=s, I=i, t) &= w_{bs}P(s-1, i, t) + w_\epsilon P(s, i+1, t) + w_c P(s+1, i-1, t) \\ &\quad + w_{\mu s}P(s+1, i, t) + w_{\mu i}P(s, i+1, t) + w_r P(s, i+1, t) \\ &\quad - (w_{bs} + w_c + w_\epsilon + w_{\mu s} + w_{\mu i} + w_r)P(s, i, t), \end{aligned} \tag{2.1}$$

but even in this very simple case, explicit solutions are unknown. Therefore, the study of models like this one is usually performed seeking for alternatives to an explicit solution of the KFE. We will describe some standard and newer methods in the coming subsections.

2.2 The Feller Process

Given an initial condition, the probabilities in eq.(2.1) are known with certainty for $t = 0$. As long as no events occur, the system remains unchanged. Changes in the set of P's for $t > 0$ are driven by the occurrence of the different events. Therefore, stochastic simulations of the model are performed taking into account that the interval between successive events is a random variable exponentially distributed with mean $1/w$, where w is the sum of all of the transition rates (Renshaw, 1991)[1]. The probability of occurrence for the different events is proportional to the corresponding transition rate. The process just described is here called a *Feller process*, inspired in (Ethier and Kurtz, 1986, Ch.2 pp.163–). As numerical method, this idea goes back to Kendall (Kendall, 1950) and Bartlett (Bartlett, 1953; Bartlett, 1957) and is popularly known as Gillespie's method, after (Gillespie, 1977).
Realizations of the process described by eq.(2.1) are produced recording the evolution of $S(t), I(t)$ starting from the initial condition, by letting the different events occur randomly in time. Such stochastic realizations are in qualitative agreement with the experimental observations (Bartlett, 1957; Bartlett, 1960)

[1] A standard theoretical result, see (Durrett, 2001), states that the occurrence of the *next* event out of a set of exponentially distributed independent events is also exponentially distributed, with mean $1/w$ as above.

(see Figure 1, a population well below the estimated threshold presents illness bursts and extinction while a population well above the threshold presents endemicity).

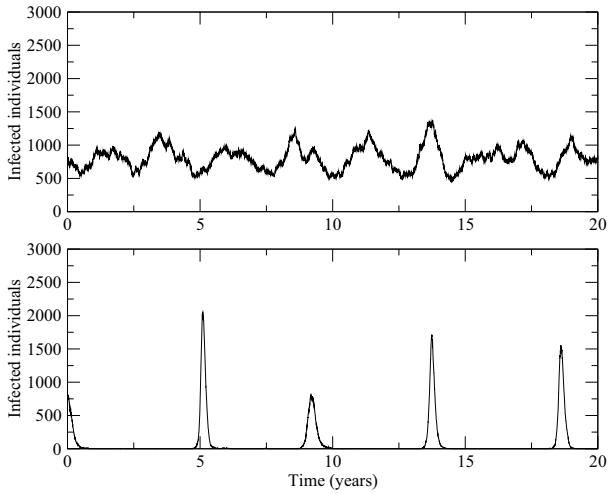

Figure 1: Realizations of the Feller process corresponding to eq.(2.1) for the evolution of infected populations for a total population of $N = 10^6$ (top) and $N = 10^5$ (bottom), including recovered individuals.

2.3 The Diffusion Approximation

The diffusion approximation recognizes two origins at least. The first one consists in considering the deterministic equation associated to the problem, an equation that describes how average fractions of large populations are expected to evolve in time in the limit of large N.
In our case, they read

$$\begin{aligned} \frac{d(S/N)}{dt} &= \mu - \beta(S/N)(I/N) - \mu(S/N) \\ \frac{d(I/N)}{dt} &= \epsilon\mu + \beta(S/N)(I/N) - (\mu+\gamma)(I/N) \end{aligned} \tag{2.2}$$

Then, the temptation is to restore the stochastic character of the original problem by adding up noise terms of zero average to the vector field. The usual choice, namely adding noise terms that have the same covariance matrix at the order $O(dt)$ than the original process, allows us to produce the following Stochastic Differential Equation (SDE):

$$\begin{aligned} \frac{d(S/N)}{dt} &= \mu - \beta(S/N)(I/N) - \mu(S/N) + \\ &\quad \sqrt{\frac{\mu}{N}}\,\sigma_1 - \frac{\sqrt{\beta SI}}{N^{3/2}}\,\sigma_2 - \frac{\sqrt{\mu S}}{N}\,\sigma_3 \\ \frac{d(I/N)}{dt} &= \epsilon\mu + \beta(S/N)(I/N) - (\mu+\gamma)(I/N) + \\ &\quad \sqrt{\frac{\epsilon\mu}{N}}\,\sigma_4 + \frac{\sqrt{\beta SI}}{N^{3/2}}\,\sigma_2 - \frac{\sqrt{(\mu+\gamma)I}}{N}\,\sigma_5 \end{aligned} \tag{2.3}$$

where $\langle \sigma(t)\sigma(t') \rangle = \delta(t-t')$, i.e., σ_i are δ-normalized Gaussian random variables.
The second origin corresponds to obtaining the equation for the generating function from eq.(2.1), subsequently producing a formal expansion in powers of $N^{-1/2}$ known as the Ω-expansion (van Kampen, 1981a). When only the lowest-order terms are kept, this procedure results in a partial differential equation of diffusive type (Ethier and Kurtz, 1986) which happens to be (Arnold, 1997) the equation associated to the process of eq.(2.3). This approach can be recasted as the Fokker-Planck equation for the probabilities. In all, eq.(2.3), the truncated Ω-expansion and the Fokker-Planck equation they all represent the same object, sharing also the names *Langevin approach* and *Diffusion approximation*. The next task is to find a solution to the problem.
Beyond the well-established mathematical apparatus behind SDE, its usefulness for the case of the internal noise in natural sciences depends on the quality of the formal procedure used for the derivation: van Kampen's Ω-expansion.
Unfortunately, although the Langevin approach may go in line with our hopes and expectations, it is not well defined. The difficulties inherent to this approach arise immediately when trying to solve eq.(2.3). Attempting to integrate eq.(2.3) via an expansion in dt, as e.g., in a numerical integration procedure, fails in the first attempt, since it is not clear where in the interval $[t, t+dt]$ the factors accompanying the σ's should be evaluated (the σ's are *not* slowly-varying smooth functions as it is assumed in conventional numerical integration schemes). This fact gave origin to the Itô and Stratonovich interpretation rules, among others.
An illuminating criticism was advanced by van Kampen almost thirty years ago. Three main points are raised in (van Kampen, 1981b), namely (quotes refer to van Kampen's wording):

(a) The Langevin approach "as it stands has no meaning" (unless some interpretation rule à la Itô or Stratonovich emerges naturally from the problem).

(b) The original problem arising in applications can be described by the "linear noise approximation" (see below) which may also be regarded as an approximation to the Langevin approach. Indeed, van Kampen concludes that the usefulness of the approach in eq.(2.3) is *exhausted* by the use of the linearized version around the deterministic solutions of eq.(2.2). In his words, "the physical contents of the Langevin equation is exhausted by its approximate solution".

(c) Itô and Stratonovich interpretations are attempts to "extend the meaning of [the Langevin approach] beyond its physical validity".

In the light of van Kampen's three criticisms the natural action to take in order to describe population dynamics problems with internal noise is to dispose of (a), since it bears no relevance to the problem in natural sciences, ignore (c) as a consequence, since it is unnecessary to provide interpretation to an equation which bears no relevance to the problem, and focus our interest in (b) to begin with, which is the only approach retaining biological content.
Approach (b) is *not* an approximation to the original KFE, but rather an *alternative* approach, with the advantage of satisfying some stochastic limit theorems. It can be described as (A) obtaining a trajectory by solving the resulting ODE once the fluctuations have been set equal to zero (the deterministic trajectory) and (B) integrating the linearized version of eq.(2.3) along this trajectory, restoring the fluctuations. We obtain:

$$\begin{aligned} \Delta S/N &= \int_t^{t+\delta t} (M_{ss}\Sigma_1(t) + M_{si}\Sigma_2(t))dt \\ \Delta I/N &= \int_t^{t+\delta t} (M_{is}\Sigma_1(t) + M_{ii}\Sigma_2(t))dt \end{aligned} \tag{2.4}$$

where the fluctuations are described by $\Sigma_1 = \sqrt{\frac{\mu}{N}}\ \sigma_1 - \frac{\sqrt{\beta SI}}{N^{3/2}}\ \sigma_2 - \frac{\sqrt{\mu S}}{N}\ \sigma_3$ and $\Sigma_2 = \sqrt{\frac{\epsilon\mu}{N}}\ \sigma_4 + \frac{\sqrt{\beta SI}}{N^{3/2}}\ \sigma_2 - \frac{\sqrt{(\mu+\gamma)I}}{N}\ \sigma_5$. The populations are evaluated along the deterministic solution and M_{xy} are the matrix elements of the monodromy matrix associated to the evolution of the infinitesimal deviations from the deterministic solution. Recall that the monodromy matrix M is the solution of the equation $\dot{M} = F(x)M$, $M(0) = I$, where $F(x)$ is in this case the Jacobian of the rhs of eq.(2.2) evaluated along a deterministic trajectory $x(t)$.
This approach represents what van Kampen calls an "approximate solution" to the Langevin problem (van Kampen, 1981b). The difference between eqs.(2.3) and (2.4) is subtle, the latter being a sort of

linearisation of the former (only linear contributions in the fluctuations –also called the noise terms– are considered).
The deterministic limit of the process given by eq.(2.1) was addressed by Kurtz (Kurtz, 1970; Kurtz, 1971; Kurtz, 1981; Ethier and Kurtz, 1986) who also considered the stochastic process for the deviations of the deterministic prescription in the scale $N^{-1/2}$. Kurtz shows that (i) this process, corresponding to eq.(2.4), approximates the original problem (2.1) in the limit of large N and (ii) this process and eq.(2.3) are more or less similar to each other. Indeed, Ethier and Kurtz conclude (Ethier and Kurtz, 1986) that the only justification for the "heuristic" approach represented by eq.(2.3) is that the formal solution (whatever this may be) of this approach ends up giving a description which differs very little in practice with eq.(2.4).

2.3.1 Additional Caveats for the Diffusion Approximation

The use of the diffusion approximation has at least two more problems:

1. State space (sample space). The original problem is naturally stated in Z_0^2, with Z_0 the non-negative integers, but the stochastic processes (2.3) and (2.4) are defined in R^2, with R the real numbers. A rule is needed to interpret the real numbers as integers and most likely than not a second rule is needed forbidding negative populations.

2. In mathematics "large" or "sufficiently large" means "as big as needed", in natural sciences there is at most "larger than" since populations are always finite. How can we know if the large N we have is *sufficiently large* for the approximations to hold? Computable error estimates are needed but seldom offered.

Before we address these issues, we will discuss a different approximation recently introduced.

2.4 The (Truncated) Poisson Approximation

An alternative (arguably better) approximation to the original description given by the KFE is based on the Poisson distribution (Aparicio and Solari, 2001a; Solari and Natiello, 2003a). The idea of using Poisson distributions to approximate the problem has a long history, going back at lest to (Bartlett, 1960). Features of this approximation, as well as the extent and validity range where the diffusion approximation can be regarded as an approximation to the KFE, have been discussed in (Solari and Natiello, 2003a). Further approximation to the Poisson approach using adequate Gaussian fluctuations as well as some ideas about how to recast the diffusion approximation in order to avoid absurdities have been recently advanced (Solari and Natiello, 2003b).
We discuss here the approximation scheme (Solari and Natiello, 2003a) for the stochastic simulations mentioned above[2]. The stochastic model is defined by the events and rates given in table 1. The probability that one of these events (event m) takes place in a small enough interval δt is approximately $w_m \delta t + \mathcal{O}(dt^2)$ where $\mathcal{O}(dt^2)$ collects all contributions of order dt^2 and higher.
On the other hand, for a discrete random variable with Poisson distribution and parameter $w_m \delta t$, the probability of occurrence of an event of type m in the time-interval δt can also be described via $w_m \delta t + \mathcal{O}(dt^2)$, provided that $\delta t \ll 1$ is small enough. The crucial question then is whether there exists a δt value such that a Poisson-type approximation for all event types yields an acceptable description of the original stochastic simulation. In such case, we can perform approximate realizations of the original stochastic process by means of the system of difference equations,

$$\begin{aligned} S(t+\delta t) &= S(t) + n_{bs} - n_{\mu s} - n_c \\ I(t+\delta t) &= I(t) + n_c + n_\epsilon - n_{\mu i} - n_r \end{aligned} \tag{2.5}$$

where n_{bs}, n_ϵ, n_c, $n_{\mu s}$, $n_{\mu i}$, and n_r are discrete random variables with Poisson distribution corresponding to each one of the events given in table 1. The mean of each of those random variables is $w_m \delta t$ for each event type m. The equations (2.5) are the intuitive basis for the *Poisson approximation*.
Clearly, if δt is small enough, at most one event will occur in the interval δt (regardless of event-type) and a numerical implementation of the Poisson approximation will not differ from the full stochastic simulation of the Feller process. Moreover, for too small δt the numeric implementation of the Poisson

[2] A less accurate version of this approximation (with larger error bounds and difficulties at the boundaries), named τ-leaping, was independently introduced in (Gillespie, 2001).

approximation can be slower than the corresponding implementation of the Feller process (see below). The added value of the approximation becomes clear when δt is small enough so that the approximation is valid but still large enough to hold a significant number of events.
This situation occurs in many cases when population numbers are large, in which case the number of events occurring in a small period δt may be also approximated by a Poisson process whenever the expected number of events becomes much smaller than the population size. In such a case, the transition rate remains approximately constant in δt and the Poisson process is a good approximation to the real process. For example, the expected number of deaths of susceptible individuals over a small enough interval δt is approximately $\mu S \delta t$. Then it is enough to set δt such that $\mu S \delta t \ll S$.
A *truncated* Poisson description is proposed, in order to properly handle "border" states, i.e., where transitions have special constraints not intrinsic to the Poisson distribution. In practice, the description should be adapted to the natural borders of the problem, so that e.g., no transition occurs to negative subpopulations. Moreover, the parameters of the Poisson distributions obey a differential equation in the limit of sufficiently large populations and sufficiently small times corresponding to the system (2.5). In fact, system (2.5) can be regarded as an integration scheme for the projection of the dynamical equation for the Poisson parameters from "event-space" onto the natural variables of the problem.
The general case for the Truncated Poisson Approximation has been treated in (Solari and Natiello, 2003a). We refer to the Appendix A for a short presentation of the details of the approximation.

2.4.1 Utility Range

The mean time T_c between epidemics can be regarded as a characteristic time for the macroscopic evolution. It is clear that in any scheme like (2.5) we must require $\delta t \ll T_c$. This is the validity range of the Poisson approximation.
On the other hand, there are characteristic times for the "microscopic" dynamics given by the expected interval between successive events of each type. We call $\tau_m \equiv 1/w_m$ the expected time between successive events of type m, where w_m is the corresponding transition rate. In the example, for the susceptible death events we have $\tau_{\mu s} = \frac{1}{\mu S}$, which decreases as the S-population increases. Therefore it is possible to set $\delta t \ll T_c$ and yet $\tau_m \ll \delta t$ for some events. In such a case the expected number of events (of type m) occurred in δt may become $w_m \delta t > 1$ but also $w_m \delta t \ll N_{mi}$, where N_{mi} are the sizes of the populations affected by the event m. Assuming this situation valid for all of the events, we have

$$\tau_m \ll \delta t \ll T_c, \qquad \forall m \tag{2.6}$$

which describes the *utility range* of the Poisson approximation. Note that the range actually depends on both the time-scale and the population size. We choose to stress the "utility" of the Poisson approximation in addition to its (wider) validity range, since for arbitrarily small values of δt the Poisson approximation is still valid, but may be computationally inefficient. Indeed, computations using the original Feller process require one simulation step per event. With the Poisson approximation we can describe many events in one simulation step for δt within the utility range, whereas for very small δt one may need many simulation steps to produce just one event.

2.5 The Integer-Gauss Approximation to the Poisson Probabilities

The moment generating function for the deviations from the mean value of the populations in the scale $\sqrt{N}$ converges, in the limit of large N and small time-intervals, to those of a Gaussian distribution (Solari and Natiello, 2003a). Hence, in this restricted sense, the Poisson distribution may be approximated by a Gaussian distribution with expected value and variance $\lambda = w_m \delta t$ in the form (see Appendix B):

$$p_n(\lambda) = \left(\frac{1}{\sqrt{2\pi}} \int_{\frac{n-\lambda}{\sqrt{\lambda}}}^{\frac{n-\lambda+1}{\sqrt{\lambda}}} \exp(-v^2/2) dv \right) \left(1 + O(\frac{|n-\lambda|^3}{\lambda^2}, \frac{1}{\lambda}) \right) \tag{2.7}$$

where $p_n(\lambda)$ represents the probability of $n \neq 0$, events according to a Poisson distribution of mean λ. The error of such an approximation is small whenever λ is large and n is also large, not very far away from λ.
Let us review the context in which this approximation is obtained, in order to understand how it can be used. The wording of this setup coincides with the traditional view, namely that the Feller process associated to the KFE (or rather its description via the Poisson approximation), *within a given specific*

validity range can be represented by a "mean value" + "Gaussian fluctuation" setup. There are however many differences in favour of this presentation:

1. **The order of the limits**. Equation (2.7) coincides with the Poisson description in the limit of large N and short time, *taken in the given order*: first $N \to \infty$, then $t \to 0$. In order to obtain stochastic differential equations or a Langevin description in this context, it would be necessary to erroneously invert the order of the limits.

2. **The discrete nature of the problem**. Equation (2.7) is ultimately an approximation to the original Feller process, which is discrete in nature, and **not** an implementation of an hypothetical stochastic differential equation (which is unjustified in this context, see the previous item). Hence, however large N is, the dynamical variable n/N only can attain discrete values (i.e., rational numbers between 0 and 1 with denominator N).

3. **The state-dependence of the fluctuations**. Again, the mean value and the fluctuation discussed above are not independent phenomena that can be added-up together in some formula, but rather, they are different features of one and the same phenomenon, i.e., the one described by the Feller process. Hence, the amplitude of the fluctuations depend on the parameters of the problem in a prescribed way (note the limits of the integral).

4. **The large-N validity**. In most applications the index n (or as in the present measles model the indices S and I) denote populations, and hence they can only take non-negative values. If the mean value of n is sufficiently small, Gaussian fluctuations used irreflexively will push n towards incorrect negative values (just think of $n = \langle n \rangle + \psi$, where ψ denotes a Gaussian fluctuation, for the case $\langle n \rangle = 0$). In particular, extinction phenomena cannot be described using equation (2.7), while they are properly handled with the Poisson approximation. Hence, the use of eq.(2.7) may shift from being roughly correct to fundamentally incorrect within a relatively small size-range.

Summarizing, the discrete random variables n_m can be approximated by *discrete* random variables with Gaussian distribution of mean and variance $w_m \delta t$. Letting ξ_m a random variable with Normal(0,1) distribution, we have: $n_m \simeq NearestInteger(w_m \delta t + \xi_m \sqrt{w_m \delta t})$. The term $w_m \delta t$ represents the 'deterministic' drift, while the term $\xi_m \sqrt{w_m \delta t}$ represents the 'stochastic' diffusion. Under this description, the system (2.5) becomes

$$\begin{aligned} S(t+\delta t) &= S(t) + g_{bs} - g_{\mu s} - g_c \\ I(t+\delta t) &= I(t) + g_c + g_\epsilon - g_{\mu i} - g_r, \end{aligned} \tag{2.8}$$

where the g's are discrete variables of the form $g = NearestInteger(\lambda + \sqrt{\lambda}\chi)$, (recall that $\lambda = w_m \delta t$) and χ a Normal(0,1) random variable. The *nearest integer* function corresponds to (2.7). We call system (2.8) the *Integer-Gauss approximation*.
Let us repeat once again that the Integer-Gauss approximation is nothing more than an approximation to an approximation. In fact, any other distribution having the same limit for large N could be used in eq.(2.7) to approximate the Poisson description, and corresponding validity limits could be computed.
It is worth mentioning that the approximation process leading to (2.4) as well as the convergence of (2.3) to (2.4) is also based in the approximation (2.7) of a Poisson-distributed variable by a Gaussian-distributed variable for large Poisson parameter (Ethier and Kurtz, 1986; Andersson and Britton, 2000).

3 Numerical Simulations

At this point one could perform stochastic simulations of the model defined in table 1 in many different manners: (i) An implementation of the Feller process, (we refer to it as Feller in the sequel), (ii) an implementation of the Poisson approximation (Poisson in the sequel), (iii) the standard diffusion or Fokker-Plank approximation of eq.(2.3) implemented following (Rümelin, 1982), corresponding to Itô's interpretation rule, recasting the outcome of the simulation as integers via the $NearestInteger$ function (SDE in the sequel), (iii)' van Kampen's linear noise approximation given by eq.(2.4), (iv) A wild extension of the Integer-Gauss approximation of eq.(2.8) so that it is used for all $n \geq 0$ and without regard to the value of λ (IG-Wild in the sequel), and (v) an ad-hoc hybrid between (ii) and (iv) where Poisson deviates are used instead of the Gaussian deviates of eq.(2.8) whenever the rate λ lies below a pre-defined threshold (hybrid in the sequel). If the threshold is taken to be zero, (v) reduces to (iv), while for infinite threshold (v) becomes (ii). Simulation (v) is an attempt to discriminate the contribution

to the error coming from the use of the Integer-Gauss approximation to the Poisson process outside its limits of validity.
The step taken to supplement the SDE with a cast onto integer numbers is critical in several aspects. One of them is that we do not have to deal with conceptual challenges such as 10^{-7} individuals. It is also a requirement to pass the statistical tests such as Kolmogorov-Smirnov's test. But, which is the correct form of casting real numbers into integers for SDE? In addition, we reset the infective population to zero whenever the SDE simulations jump to negative population values.
We did not simulate eq.(2.4) (label (iii)' above), despite the fact that van Kampen regards it as a sounder procedure within the context of the present study, since we cannot expect dramatic discrepancies with the present implementation of eq.(2.3) (label (iii) above), which in fact is the diffusion approach (Rümelin, 1982) that is usually adopted.
We illustrate the difficulties with the approximations using Gaussian deviates in Figure 2. We notice that during the initial period of the simulation, IG-wild as well as SDE closely follow the Feller process. However, once IG-Wild produces the extinction of the infected individuals, it cannot reproduce subsequent epidemic outbreaks, since the process representing the arrival of infected individuals is severely distorted by attempting a Gaussian approximation to a Poisson process with rates as small as 0.0011 and the fact that the sum of integer Gauss processes does not satisfy the conditions for convergence to a Poisson law (Renyi, 1976). The Feller and Poisson simulations cannot be discriminated but SDE and Wild-IG present substantial statistical differences.

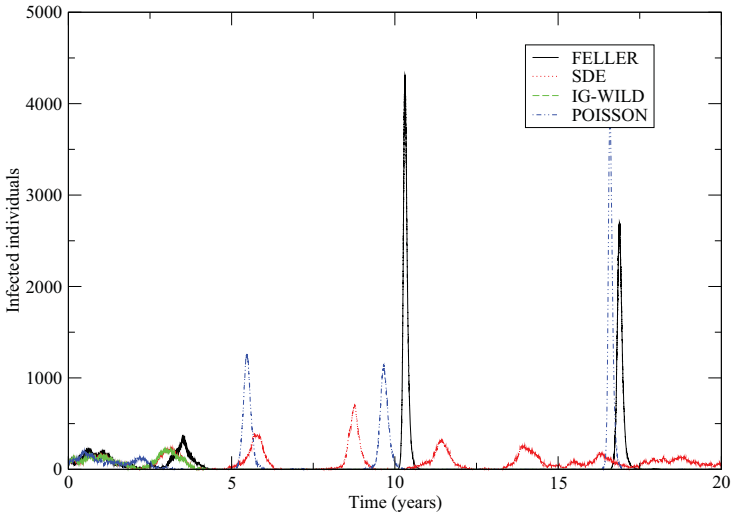

Figure 2: Number of infective individuals for $N = 10^5$, initial condition $(S, I) = (800, 70)$ as a function of time (in years) for the Feller process, the SDE process and the Wild-Integer-Gauss process. The time step is $\delta t = 10^{-3} years$ (see eq.(2.8)).

In the light of this presentation, it is clear that we cannot expect a good performance for the simulations performed solely with eq.(2.8) (case (iv), IG-Wild). In fact, in case (iv) one is using an approximation without checking its validity range. Whenever one is lucky enough to lie within that range, the results will look satisfactory, and conversely.
A typical situation where λ may be very small and case (iv) will fail occurs when the total population is below the critical size. In this case, we expect the infected population to be null for long periods of time. The epidemic dynamics is dictated by a low probability event: the arrival of infective individuals to an infection-free community. For such *rare* events, the condition (2.6) is not fulfilled, since τ_m is of the same order as T_c and therefore we expect the Integer-Gauss approximation not to be valid.
For populations well above the critical community size, the disease is present for all times with values much larger than one. In such cases, the arrival of external infected individuals, which increase the infected population by one unit and are very rare events, can be expected to be irrelevant, that is:

Process	d	Probability	Variable	N	equation
Poisson	0.0049	0.30	I	10^5	2.5
Hybrid	0.0038	0.62	I		2.8
SDE	0.0381	0.0	I		2.3
Poisson	0.0027	0.87	S		2.5
Hybrid	0.0041	0.37	S		2.7,2.8
SDE	0.0043	0.33	S		2.3
Poisson	0.0046	0.24	I	10^6	2.5
Hybrid	0.0027	0.86	I		2.8
SDE	0.0041	0.37	I		2.3
Poisson	0.0031	0.73	S		2.5
Hybrid	0.0042	0.35	S		2.7,2.8
SDE	0.0058	0.07	S		2.3

Table 2: Results of Kolmogorov-Smirnov tests for the approximations with respect to Feller process after 10^5 repetitions. The threshold for the application of the approximation 2.7 in the hybrid calculations was arbitrarily set to $\lambda = 5$. The label "SDE" corresponds to eq.(2.3) with the supplemental integer casts and consistency checks described in the text.

Condition (2.6) holds at least for the relevant events.
In Table 2 we show the results of Kolmogorov-Smirnov tests performed for two different populations values, one below and one above the critical community size. The parameter values are as follows: Total time $2\ years$, time step $\delta t = 1\ day$, $\mu = 0.0222/year$, $\epsilon = 0.0005$, $\beta = 360.0/year$, $\gamma = 25.71/year$. The Kolmogorov-Smirnov test (von Mises, 1964) is the standard tool to decide whether two distributions are "the same" or not. In our case, one of them is a reference distribution (corresponding to the outcome of a Feller run) and the test attempts to establish if the other distribution is statistically different to the Feller outcome or not. This test takes two distributions and produces two numbers: A measure d estimating the difference between the distributions and a probability value. The latter expresses the probability of discarding a true distribution if the tested one is discarded. Low probabilities (and large d-values) indicate that the distributions are different. Usually the value 0.1 for the probabilities is taken as decision threshold. The tests were performed comparing the number of infected individuals or the number of susceptible individuals after the 2-years period for populations of $N = 10^5$ and $N = 10^6$ individuals using 10^5 simulations, with the same initial conditions. Initial conditions were chosen close to the endemic equilibrium for the deterministic model. SDE falls below the acceptance threshold in both tests. We do not report in the table the results for IG-Wild, which fails as badly as SDE.
In Figure 3 we plot a typical input for the Kolmogorov-Smirnov tests, namely 10^5 repetitions for the statistics of the infective population after two years of evolution. Observe the departure of the SDE (main graph) and the IG-Wild (inset) simulations from the Feller process in contrast with the Poisson simulations which can hardly be distinguished from the Feller runs. We do not report case (v) (hybrid, with threshold at $\lambda = 5$) in the Figure, since it is almost indistinguishable from Feller and Poisson, as could be expected after the results in Table 2.

3.1 Comments on the Simulations

The Feller simulations (i) reproduce many of the main features of the observed recurrent measles epidemics. Realizations obtained by means of the Poisson approximation (ii) are very similar to the stochastic simulations of the Feller process (see Figure 3).
The standard diffusion approximation (iii) of eq.(2.3) with the ad-hoc rule of converting real numbers into nearest integer produces marginally acceptable results (p is within round-up error of the acceptance threshold) for populations above the critical community size but deteriorates gradually for small populations. We shall emphasize that without casting the real numbers produced by SDE onto integer numbers, the Kolmogorov-Smirnov test always indicates that SDE fails to produce the same statistics than the Feller process.
Simulations carried out using the hybrid process defined by eq.(2.8) replacing the Poisson probabilities by Gaussian probabilities (simulation (v)) according to eq.(2.7) for $\lambda > 5$, show no significant differences with (ii) and (i). The choice of threshold was rather arbitrary. The goal was to avoid using the Integer-

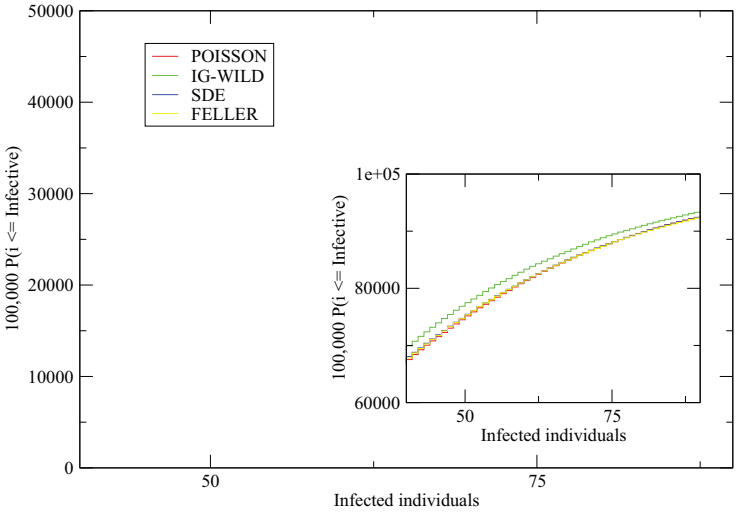

Figure 3: Statistics of the infective population after two years of evolution starting with the initial condition $(S, I) = (8000, 70)$ for a population size of $N = 10^5$. Observe the departure of the SDE (main graph) and IG-Wild (inset) simulations from the Feller process in contrast with the Poisson simulations which can hardly be distinguished from the Feller runs.

Gauss approximation far away from its limit of validity. In relation to the Poisson method, the hybrid simulations are more efficient in terms of computational speed.

4 Discussion and Conclusions

Individuals are the natural units of populations and their evolution in terms of a continuous time is marked by random events that are assumed to be instantaneous. The mean interval between events determines a natural unit of time. These "microscopic" intervals (τ_m) are given by the transition rates, $\tau_m = 1/w_m$. In general, the values of these intervals depend on the population numbers.
Let τ_M be the largest of such intervals. In the quasi-deterministic limit the frequent population variations are averaged on a time-scale δt with $\tau_M \ll \delta t$. However, quasi-determinism also requires $\delta t \ll T_c$ (we recall that T_c is the mean interval between epidemies, a macroscopic time). Microscopic and macroscopic time-scales must be of very different magnitudes. There is a general agreement as well as theoretical basis showing that when population sizes are large enough the dynamics is quasi-deterministic. But, what is large enough? At first, we can think that it is simply $N_i \gg 1$, because one individual is the natural unit of population size. In the first place, the relation $\tau_M \ll \delta t \ll T_c$ must be satisfied. This relation depends on the population values as well as on the parameters characterizing the interactions between the individuals. We can then conclude that for any fixed population size, N, the (integer casted) SDE is an approximation to the original process only when finite and sufficiently large time intervals between samples are considered and paths are constrained to regions of the phase space where the given inequalities between times hold. The use of SDE without a-priori consideration of the region of phase-space where it can be used makes the distinction between an approximation and the replacement of one stochastic process with another one.
Within its utility range, the Poisson approximation is a successful alternative to full simulations. Moreover, the Poisson description allows us to derive the Integer-Gauss approximation.
The purely deterministic behaviour provides a template where the stochastic evolution takes place, at the cost of resigning the discrete nature of the population problem. Yet, such template faces difficulties, for example when extinctions of populations are relevant. It is advisable to use the Poisson approximation in such circumstances.
In summary, we have discussed the hybrid approximation as a further approximation of the Poisson

method introduced in (Aparicio and Solari, 2001a; Solari and Natiello, 2003a) and discussed the relation between both approximations and the diffusion approximation. Poisson and hybrid approximations cannot be distinguished from the Feller simulations in a 10^5 set of runs (or even larger), for simulations above the critical community size.
The diffusion approximation produces real numbers in place of the integer numbers representing individuals. When complemented with the $Nearest\ Integer$ casting into integer numbers, it performs in a marginally acceptable way above the critical community size. Below the critical size, the diffusion approximation cannot be mistaken with the Feller process in statistics based on 10^5 simulations. On the contrary, the Integer-Gauss approximation when modified in order to take appropriate (Poisson) care of low-probability events, cannot be distinguished from the Feller process under such statistics.

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A Appendix: The (Truncated) Poisson Approximation

We shall briefly describe in this appendix the main ideas involved in the formulation of the Truncated Poisson Approximation (Solari and Natiello, 2003a) for density-dependent Markov process.
Let X be an integer vector having as entries the populations under consideration, and $e_\alpha, \alpha = 1 \dots \kappa$ the events at which the population change by a fixed amount Δ_α in a Poisson process with density-dependent rates. Then, a theorem by Kurtz (Ethier and Kurtz, 1986) allows us to rewrite the stochastic process as:

$$X(t) = X(0) + \sum_{\alpha=1}^{\kappa} \Delta_\alpha Y_\alpha(\int_0^t \omega_\alpha(X(s))ds) \tag{A.1}$$

where $\omega_\alpha(X(s)$ is the transition rate associated to the event α and $Y(x)$ is a random Poisson process of rate 1.
This expression is the starting point for several approximations (Kurtz, 1970), in particular, the deterministic limit is obtained for transition rates of the form $\omega_\alpha(X) = N\Omega_\alpha(X/N)$ (a relation known as the mass-action law) and considering the stochastic variable X/N in the limit $N \to \infty$ for fixed t (in this approximation only the mean values of the Poisson variables are relevant).
The deviations from the deterministic limit scaled by a factor $1/\sqrt{N}$ correspond in the same limit to a Brownian process (Kurtz, 1971; Andersson and Britton, 2000) (in this case, the Poisson variables are approximated by Gaussian variables).
The Poisson approximation to the stochastic process represented by equation (A.1) consists in introducing a self-consistent deterministic approximation for the arguments of the Poisson variables $Y(x)$ in equation (A.1) (Solari and Natiello, 2003a; Aparicio and Solari, 2001a). Also, a truncation procedure is introduced in order to constrain the system to stay within its natural borders (non-negative subpopulations). The rationale under such a proposal is that the transition rates change at a slower rate than the populations. The number of each type of events are then approximated as independent Poisson processes with deterministic arguments satisfying a differential equation.
The probability of n_α events of type α having occurred after a time dt is approximated by a Poisson distribution with parameter λ_α. Hence, the probability for the population to take the value

$$X = X_0 + \sum_{\alpha=1}^{\kappa} \Delta_\alpha n_\alpha \tag{A.2}$$

at a time interval dt after being in the state X_0 is approximated by a product of independent Poisson distributions of the form ($P_\alpha(\lambda_\alpha)$ denotes a Poisson distribution for n_α with mean λ_α)

$$\text{Probability}(n_1 \dots n_\kappa, dt/X_0) = \prod_{\alpha=1}^{\kappa} P_\alpha(\lambda_\alpha) \tag{A.3}$$

Finally,

$$d\lambda_\alpha/dt = \langle \omega_\alpha(X) \rangle \tag{A.4}$$

where the averages are taken (self-consistently) with the proposed distribution ($\lambda_\alpha(0) = 0$). Actually, there are some small ($O(dt^2)$) corrections to this presentation when one of the populations is one event

away from extinction (Solari and Natiello, 2003a). Such correction has not been implemented in the present case, being the extinction processes very slow.
From the Poisson approximation it is possible to recover the deterministic equation and the Brownian approximation of the fluctuations in the proper limit. The approximation is accurate not only in the $N \to \infty$ (with fixed t) limit, but also in the infinitesimal time limit when the average number of events is small. It is this latter property what makes it especially suitable for the study of process involving extinction.
The use of the Poisson approximation represents a substantial saving of computer time compared to direct (Monte Carlo) implementations of the stochastic process.

B Approximation of the Poisson Distribution by the Normal Distribution

We present here the naive form of the approximation of the Poisson distribution via integrals involving the Normal distribution.
The probability for a Poisson distributed variable with mean r to produce an outcome n is given by $P_n(r) = \exp(-r)r^n/n!$. When the factorial is replaced by Stirling's formula, the expression for this probability reads: $P_n(r) = \exp(-r)(er/n)^n \exp(-\theta_n/(12n))/\sqrt{2\pi n}$, where $0 \leq \theta_n \leq 1$. Constructing the auxiliary variable $x = (n-r)/\sqrt{r}$ and considering values of n such that $|x| \ll A$ (a fixed constant that determines the error of the approximation) we get ($\epsilon = 1/\sqrt{r}$)

$$P_n(r) = e^{-(x+\frac{\epsilon}{2})^2/2} \frac{\epsilon}{\sqrt{2\pi}} e^{O(x^3\epsilon,\epsilon^2)} \tag{B.1}$$

We finally notice that (B.1) is also an approximation to the integral

$$P_n(r) = \int_x^{x+\epsilon} \frac{e^{-y^2/2}}{\sqrt{2\pi}} dy (1 + O(x^3\epsilon, \epsilon^2)) \tag{B.2}$$

Actually, centering the integral in $x + \epsilon a$ for small a would not change the convergence statement as it would contribute only terms of order $O(|ax|\epsilon^2)$.
The approximation $p_n(\lambda)$ amounts then to disregarding the O-terms in eq.(B.2). The validity of this approximation is hence, small A, small ϵ, small θ_n and large n. In particular, Stirling's formula is undefined for $n = 0$ and $\theta_1 \sim 0.9727$. By defining $s_0 = (1-r)/\sqrt{r}$ and $p_0(r) = \int_{-\infty}^{s_0} \frac{e^{-y^2/2}}{\sqrt{2\pi}} dy$, the probability distribution p has the same domain as the Poisson distribution and their relative difference goes to zero for sufficiently large n. This distribution is implemented in eq.(2.8) via Gaussian deviates and the $NearestInteger$ function.

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