Modelling population processes with random initial conditions

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Abstract

Population dynamics are almost inevitably associated with two predominant sources of variation: the first, *demographic variability*, a consequence of chance in progenitive and deleterious events; the second, *initial state uncertainty*, a consequence of partial observability and reporting delays and errors. Here we outline a general method for incorporating random initial conditions in population models where a deterministic model is sufficient to describe the dynamics of the population. Additionally, we show that for a large class of stochastic models the overall variation is the sum of variation due to random initial conditions and variation due to random dynamics, and thus we are able to quantify the variation not accounted for when random dynamics are ignored. Our results are illustrated with reference to both simulated and real data.

Keywords: Population processes; Epidemic models; Stochastic models.

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1 Introduction

Often the initial state of population processes is not known with certainty. This can happen because of delays and inaccuracies in reporting, partial observability, and difficulties in assessing the actual population size. The initial state is often assumed to be known, or approximated and then treated as known, in which case mathematical models can give only partial information about dynamics and do not describe the full range of behaviour that may be exhibited. This may lead to inaccurate predictions and result in the implementation of non-optimal control actions.

Kegan and West [25] addressed this issue, in the context of the SI (*susceptible-infectious*) epidemic model, by investigating the effect of random initial conditions on the state of the deterministic SI model. Using the Beta distribution to model the initial proportion of infectives, they obtained explicit information about the distribution of the proportion of susceptibles at any time during the epidemic, as well as the distribution of the time until a given proportion of the population remains susceptible. We explain how their approach can be extended to allow initial state uncertainty to be incorporated in general population processes where a deterministic model is sufficient to describe the dynamics of the population, thus allowing one to model variability in dynamics, at any point in time, due solely to uncertainty in the initial state. For one-dimensional processes, such as those used for modelling sexually transmitted infections [2] and hospital-acquired infections [37], and a range of single-species population models, we demonstrate how this can be effected without the need to exhibit the trajectories explicitly. We illustrate our results with reference to several population models.

We also consider a wide class of stochastic models, called *density-dependent processes*, for which there are natural deterministic analogues, and summarise results that quantify variation not accounted for when demographic variability is ignored. Many models appearing in the ecology and epidemiology literature belong to this class. Our purpose here is simply to delineate and quantify variation due to initial state uncertainty and variation due to random dynamics, rather than to study the approximations in detail. The ability to delineate variability in this way has been shown to be of great importance in understanding both population and disease dynamics [13, 17, 20, 32]. We illustrate these results for several population models, including

a detailed study of simulated data from a model for disease spread in metapopulations, and real data on the prevalence of HIV antibodies in homosexual men [3, 25].

2 Initial state uncertainty in deterministic models

We outline how to account for initial state uncertainty in a general population modelling context. Let n_t be the state of our process at time t , and assume that n_t lies in some subset S of $\mathbb{Z}^D$ (the D -dimensional integer lattice). This would typically be a vector of numbers of individuals of various types (D in total). Suppose also that there is a parameter N , which would usually be related to the size of the system (for example N might be a population ceiling), such that $x_t = n_t/N$ can be interpreted as a vector of population *densities*, and that we have identified an appropriate deterministic model for x_t . We will suppose that $x_t = x_t(x_0)$ satisfies the ordinary differential equation

$$x'_s = F(x_s) \quad (x_s \in E, 0 \leq s \leq t), \quad (1)$$

where the function $F : E \rightarrow \mathbb{R}^D$ is specified and E is an appropriate subset of $\mathbb{R}^D$ (D -dimensional Euclidean space). For example, if the state x_t were a vector of proportions, such as the proportions of individuals of various types, then it would be natural to take $E = [0, 1]^D$.

We will exploit the standard change of variable technique to assess the effect of assuming that the initial state is random. Let $X = (X_1, \dots, X_D)$ be a D -dimensional random vector whose probability density function (pdf) f_X is specified, and let $g : \mathbb{R}^D \rightarrow \mathbb{R}^D$ be an injective (one-to-one) map with continuous first partial derivatives. Denote by $\partial g(x)$ the Jacobian matrix $(\partial g_i(x)/\partial x_j)$. Then, the pdf of $Y = (Y_1, \dots, Y_D)$, where $Y = g(X)$, is given by $f_Y(y) = |J(y)|f_X(g^{-1}(y))$, $y \in \mathbb{R}^D$, where $J(y)$ is the Jacobian of $g^{-1}(y)$ (the determinant of $\partial g^{-1}(y)$) and $|J(y)|$ is its absolute value (see for example [21, Section 4.7]). If the map is not injective, then it is usually possible to partition the domain into regions over which the map *is* injective.

Now think of the initial state as being a random variable X_0 with a specified pdf f_0 . In determining the action of the map $g_t(x_0) = x_t(x_0)$ (for simplicity, assumed to be injective) on f_0 , we obtain a pdf f_t that summarises the effect of random initial conditions in our

population: for any $t > 0$,

$$f_t(y) = |J_t(y)| f_0(g_t^{-1}(y)) \quad (y \in \mathcal{R}_t), \quad (2)$$

where $J_t(y)$ is the Jacobian of $g_t^{-1}(y)$ and $\mathcal{R}_t = g_t(E)$ is the image of E under g_t . We emphasise that f_t is the pdf of the state of our process at time t , assuming deterministic dynamics with an initial pdf f_0 .

Since our trajectory satisfies (1) with F specified, we can often take this a step further. In the one-dimensional case ($D = 1$) we can exhibit f_t explicitly. Let $L(u)$ be the primitive $L(u) = \int^u dw/F(w)$. Suppose L is injective, so that L^{-1} is well defined (it is sufficient that F be everywhere positive or everywhere negative). Then, the solution to (1) can be written $x_t(x_0) = L^{-1}(t + L(x_0))$. The Jacobian can also be evaluated. Since $g_t(x) = y$ if and only if $L(y) - t = L(x)$, we get $g_t^{-1}(y) = L^{-1}(L(y) - t)$ ($= g_{-t}(y)$), and so

$$J_t(y) = \frac{d}{dy} L^{-1}(L(y) - t) = (L^{-1})'(L(y) - t) L'(y) = \frac{L'(y)}{L'(L^{-1}(L(y) - t))} = \frac{F(L^{-1}(L(y) - t))}{F(y)},$$

where here we have used the inverse function theorem, $(L^{-1})'(y) = 1/(L'(L^{-1}(y)))$, together with $L' = 1/F$. Therefore, from (2),

$$f_t(y) = \left| \frac{F(L^{-1}(L(y) - t))}{F(y)} \right| f_0(L^{-1}(L(y) - t)). \quad (3)$$

We will illustrate these results in Section 5.

The corresponding expected value m_t and covariance matrix V_t of the state of the process at time t can be evaluated either directly from (2) or from (3), or via the trajectory $x_t(x_0)$:

$$m_t = \mathbb{E} x_t(X_0) = \int_E x_t(u) f_0(u) du \quad (4)$$

and, taking $x_t(u)$ and m_t to be row vectors,

$$V_t = \text{Cov}(x_t(X_0)) = \int_E x_t(u)^\top x_t(u) f_0(u) du - m_t^\top m_t, \quad (5)$$

where $^\top$ denotes transpose.

One might expect that in most instances f_t would be a poor model for the state of the population at time t , because randomness in the dynamics of the process (*demographic variability*) is not taken into account. The effect of ignoring random dynamics would be particularly pronounced when t becomes large, for it quickly becomes the *only* source of variation. Suppose

that the trajectory $x_t(x_0)$ approaches an equilibrium point x_{eq} of (1) (that is, $F(x_{\text{eq}}) = 0$ and x_{eq} is stable). Then, it is clear from (4) and (5) that, under mild conditions (for example, $x_t(u)$ monotonic in t , $\mathbb{E} x_t(X_0) < \infty$ or E finite), $m_t \rightarrow x_{\text{eq}}$ and $V_t \rightarrow 0$ as $t \rightarrow \infty$ (that is, the randomness induced by the initial distribution disappears). Thus, it would be useful to quantify demographic variation and to be able to delineate this and initial state uncertainty. This will be achieved for a wide class of stochastic population models, termed *density-dependent*, using properties of conditional expectation coupled with the idea of a diffusion approximation, whereby the process is approximated by a simpler one (a Gaussian diffusion) whose properties can be exhibited explicitly in terms of the parameters of the original model.

3 Density-dependent population models

Our population process $(n_t, t \geq 0)$ is now assumed to be a continuous-time Markov chain with state space $S \subseteq \mathbb{Z}^D$. We let $q(m, n)$ denote the rate at which the process moves from state m to state n for $n \neq m$ and set $q(m, m) = -q(m)$, where $q(m) = \sum_{n \neq m} q(m, n)$ ($< \infty$) is the total rate at which the process leaves state m .

We will suppose that population process is *density dependent* in the sense of Kurtz [26]: there is a parameter N with the property

$$q(n, n + l) = N f\left(\frac{n}{N}, l\right) \quad (n, n + l \in S), \quad (6)$$

for suitable functions $f(x, l)$, $x \in E$, where E is a subset of $\mathbb{R}^D$. As before, N will usually be related to the size of the system and n/N will usually be interpreted as a population density (or vector of population densities). Condition (6) stipulates that n_t changes at a rate that depends on n_t *only through* (the density) $X_t = n_t/N$, a property shared by a wide variety of models that arise in areas as diverse as ecology [40, 42, 43, 45], epidemiology [6, 12, 48], parasitology [38], chemical kinetics [4, 28, 35, 41], telecommunications [39, 46] and random graphs [14, 52]. Notice that the density *process* $(X_t, t \geq 0)$, being itself a Markov chain, takes values in the set E no matter what the value of N .

Before proceeding, we note that there is a larger class of models termed *asymptotically density dependent* [38], where more general dependence on N is permitted, but which disappears in the limit as N gets large. All of the results presented below carry over without change.

Now, a formal argument based on the forward equations (the master equation) for state probabilities, shows that $(d/dt) \mathbb{E} X_t = \mathbb{E} F(X_t)$, where

$$F(x) = \sum_{l \neq 0} l f(x, l) \quad (x \in E), \quad (7)$$

suggesting that (6) entails a law of motion of the kind (1) for the mean path $m_t = \mathbb{E} X_t$. However, it is not generally true that $m'_t = F(m_t)$. For example, the SI model has $F(x) = -\beta x(1-x)$, $x \in E$, where β is the transmission rate (see Section 5), and therefore $m'_t = F(m_t) + \beta \text{Var}(X_t)$. This was observed by Isham [23] and exploited in West and Thompson's study [51], where they argued that the variance is small when the initial number of susceptibles is large. In fact this is true in great generality, being a consequence of the basic limit theorems of Kurtz [26, 27], which we will now describe. These results allow us to identify the most appropriate approximating deterministic model and to quantify variation not accounted for when random dynamics are ignored. As N will vary, we need to make the dependence on N explicit in our notation; we write $X_t^{(N)} = n_t/N$.

Suppose that F , given by (7), is Lipschitz on E , that is, for some positive constant K_E , $|F(x) - F(y)| < K_E |x - y|$, $x, y \in E$ (true for example if F has a bounded first derivative on E). This guarantees a unique solution $x_t = x_t(x_0)$ to (1) for any given initial value x_0 .

Next we impose two technical conditions. They are: (i) $\sup_{x \in E} \sum_{l \neq 0} |l| f(x, l) < \infty$, and (ii) $\lim_{d \rightarrow \infty} \sup_{x \in E} \sum_{|l| > d} |l| f(x, l) = 0$, $x \in E$ (notice that if S is a finite set, which is typically the case for population processes, both will *automatically* be satisfied). Then (Theorem 3.1 Kurtz [26]), if $\lim_{N \rightarrow \infty} X_0^{(N)} = x_0$, the density process $(X_t^{(N)}, t \geq 0)$ converges *uniformly in probability* on $[0, t]$ to the deterministic trajectory starting at x_0 , that is, for every $\epsilon > 0$, $\Pr(\sup_{0 \leq s \leq t} |X_s^{(N)} - x_s(x_0)| > \epsilon) \rightarrow 0$ as $N \rightarrow \infty$. This *functional law of large numbers* establishes that the density process can be approximated by a limiting deterministic trajectory, provided that they start sufficiently close to one another. It is important to realize that for a given density-dependent population model the deterministic analogue is *identified* and convergence (on finite time intervals) to its trajectory is established.

However, for N moderately large there will usually be sizeable variation about the deterministic path. Kurtz [27] provides results which allow us to quantify this variation precisely. Theorem 3.5 of [27] is a *functional central limit law*, which establishes, under extra mild con-

ditions, that the fluctuations about the deterministic trajectory follow a *Gaussian diffusion*. Define a process $(Z_t^{(N)}, t \geq 0)$ by

$$Z_t^{(N)} = \sqrt{N} (X_t^{(N)} - x_t(x_0)). \quad (8)$$

In addition to the conditions stated earlier, suppose that (iii) $\lim_{d \rightarrow \infty} \sup_{x \in E} \sum_{|l| > d} |l|^2 f(x, l) = 0$. Suppose also that F has uniformly continuous first partial derivatives on E , and that the $D \times D$ matrix $G(x)$, defined by $G_{ij}(x) = \sum_{l \neq 0} l_i l_j f(x, l)$, $x \in E$, is uniformly continuous on E . Then, if $\lim_{N \rightarrow \infty} \sqrt{N} (X_0^{(N)} - x_0) = z$, the process $(Z_t^{(N)})$ converges weakly in $D[0, t]$ (the space of right continuous functions with left limits, defined on $[0, t]$) to a Gaussian diffusion $(Z_s, s \geq 0)$ with initial value $Z_0 = z$ and with mean $\mathbb{E} Z_s = M_s z$, where $M_s = \exp(\int_0^s B_u du)$ and $B_u = \partial F(x_u(x_0))$, and covariance

$$\Sigma_s(x_0) = \text{Cov}(Z_s) = M_s \int_0^s M_u^{-1} G(x_u(x_0)) (M_u^{-1})^\top du M_s^\top, \quad (9)$$

being the unique solution to

$$\frac{d}{ds} \Sigma_s(x_0) = B_s \Sigma_s(x_0) + \Sigma_s(x_0) B_s^\top + G(x_s(x_0)) \quad (10)$$

with $\Sigma_0(x_0) = 0$. The idea is to use the diffusion process, whose parameters can often be determined explicitly, to approximate quantities for the original process by way of (8)—hence the term *diffusion approximation*. In particular, for all $t > 0$, $X_t^{(N)}$ has an approximate (D -dimensional) normal distribution with $\text{Cov}(X_t^{(N)}) \simeq \Sigma_t(x_0)/N$, where $\Sigma_t(x_0)$ is given by (9). We would usually take $X_0^{(N)} = x_0$, giving $\mathbb{E} X_t^{(N)} \simeq x_t(x_0)$. The quality of these approximations improves as N gets large.

An important special case of the above is when x_0 is chosen as an equilibrium point (usually a stable equilibrium) of the deterministic model (so $x_t(x_0) = x_0$ for all t). Then, the approximating diffusion is an *Ornstein-Uhlenbeck process* (OU process), and more precise results are available [47]. In particular, if $F(x_{\text{eq}}) = 0$ and $B = \partial F(x_{\text{eq}})$, our approximating normal distribution has $\mathbb{E} X_t^{(N)} \simeq x_{\text{eq}}$ and $\text{Cov}(X_t^{(N)}) \simeq \Sigma_t/N$, where

$$\Sigma_t = \int_0^t e^{Bu} G(x_{\text{eq}}) e^{B^\top u} du = \Sigma_{\text{eq}} - e^{Bt} \Sigma_{\text{eq}} e^{B^\top t}, \quad (11)$$

and Σ_{eq} satisfies $B \Sigma_{\text{eq}} + \Sigma_{\text{eq}} B^\top + G(x_{\text{eq}}) = 0$, being the stationary solution to (10). For example, in the one-dimensional case ($D = 1$), one obtains the very simple expression $\Sigma_t =$

$(G(x_{\text{eq}})/(-2B))(1 - e^{2Bt})$. One would use (11) in place of (9) when t is large and N is not so large that random dynamics can be ignored. While important in general population modelling contexts, it is less important in epidemiological modelling, for there one is usually interested in assessing the progress of a disease at times well before equilibrium (endemicity) is reached.

We emphasise that $\Sigma_t(x_0)/N$ measures the *variation* at time t not accounted for when random dynamics only are ignored. It can thus be used to assess whether a deterministic model will suffice or whether the full stochastic model is needed. For further details and extensions of these methods, see Kurtz [29, 30], Barbour [5, 7, 8, 9] and, more recently, Darling and Norris [15].

We now have a straightforward means of quantifying demographic variation for density dependent models. Next we examine how to delineate demographic variation and initial state uncertainty.

4 Initial state uncertainty and random dynamics

We will use conditional expectation. Our functional law of large numbers permits us to approximate the expected state at any time t by the deterministic trajectory $x_t(x_0)$ starting at a fixed state x_0 : for large N , $\mathbb{E}(X_t|X_0 = x_0) \simeq x_t(x_0)$. If the initial state is now a random variable X_0 , we have $\mathbb{E} X_t = \mathbb{E} \mathbb{E}(X_t|X_0) \simeq \mathbb{E} x_t(X_0) = m_t$ (refer to (4)). For the covariance of the state at time t we use the identity $\text{Cov}(X_t) = \text{Cov}(\mathbb{E}(X_t|X_0)) + \mathbb{E} \text{Cov}(X_t|X_0)$, which follows from basic properties of conditional expectation. It shows, in effect, that if the diffusion approximation is employed the overall variation is the *sum* of variation due to deterministic dynamics under random initial conditions and the variation due to random dynamics, for the first term is approximately $\text{Cov}(x_t(X_0)) = V_t$ (refer to (5)), and, under the diffusion approximation, $\text{Cov}(X_t|X_0 = x_0) \simeq \Sigma_t(x_0)/N$, where $\Sigma_t(x_0)$ is given by (9). Therefore,

$$\text{Cov}(X_t) \simeq V_t + \frac{1}{N} \int_E \Sigma_t(u) f_0(u) du. \quad (12)$$

The second term on the right-hand side measures the variation not accounted for when using a deterministic model with initial state uncertainty. It is asymptotically negligible in the limit as $N \rightarrow \infty$. Thus evaluation of this term when the initial state is not known with certainty

helps us decide whether a deterministic model will suffice, or if the full stochastic model is needed.

5 Investigation

We first consider the SI (*susceptible-infectious*) model, used to study diseases for which there is no recovery following infection; examples of such are HIV/AIDS, Hepatitis C for the majority of carriers, and many plant diseases. The model is also often used to study the initial stages of emerging infectious disease growth in a single community (see for example [44]). We can assess the degree of uncertainty not accounted for when deterministic SI model is used in place of the stochastic model, and when there is uncertainty in the initial state of the disease process or demographic variability in the population at risk.

The SI model. Our state n_t is the number of susceptibles at time t . We may take $S = \{0, 1, \dots, N-1\}$, where N is the total number of individuals, for we will assume that there is at least one infective. The process has non-zero transition rates $q(n, n-1) = (\beta/N)n(N-n)$, where β is the transmission rate. The model is density dependent with $f(x, -1) = \beta x(1-x)$, $x \in E = [0, 1]$, and so the approximating deterministic model for the *proportion* $X_t^{(N)} = n_t/N$ of susceptibles is (1) with $F(x) = -\beta x(1-x)$. It has the unique solution

$$x_t(x_0) = x_0 / (x_0 + (1-x_0)e^{\beta t}) \quad (t \geq 0), \quad (13)$$

for any given initial proportion x_0 . Since S is finite and F' exists and is bounded on E , uniform convergence in probability (over finite time intervals) of the process $X_t^{(N)}$ to the deterministic trajectory x_t is guaranteed provided $X_0^{(N)} \rightarrow x_0$.

The primitive $L(u) = \int^u dw/F(w)$ can be evaluated as $L(u) = (1/\beta) \log(1-1/u)$ and its inverse is $L^{-1}(u) = 1/(1-e^{\beta u})$. Therefore, $L^{-1}(L(y)-t) = ye^{\beta t}/(1-y+ye^{\beta t})$, and so, from (3),

$$f_t(y) = \frac{e^{\beta t}}{(1-y+ye^{\beta t})^2} f_0 \left(\frac{ye^{\beta t}}{1-y+ye^{\beta t}} \right) \quad (y \in E), \quad (14)$$

the image of E under $x_0 \mapsto x_t(x_0)$ being E itself (for all t). Thus, if N is sufficiently large that random dynamics can be ignored, the pdf f_t can be used to model the proportion of susceptibles at time t given an initial pdf f_0 .

A commonly used distribution that captures uncertainty in the initial proportion of susceptible (or infectious) individuals is the Beta(a, b) distribution, because it has support $[0, 1]$ and because of its amenability in shape:

$$f_0(y) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} y^{a-1}(1-y)^{b-1} \quad (0 \leq y \leq 1).$$

If the Beta distribution is employed, (14) leads to Equation (3) of Kegan and West [25]:

$$f_t(y) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} e^{a\beta t} \frac{y^{a-1}(1-y)^{b-1}}{(1-y+ye^{\beta t})^{a+b}} \quad (0 \leq y \leq 1).$$

If random dynamics are significant, we may employ the diffusion approximation. The SI model is a case where we can solve (9) explicitly. We have that $G(x) = \beta x(1-x) = -F(x)$, and this leads to

$$\Sigma_t(x_0) = e^{\beta t} x_0(1-x_0) \frac{(1-x_0)^2 e^{2\beta t} - (1-2x_0-2\beta t x_0(1-x_0))e^{\beta t} - x_0^2}{(x_0 + (1-x_0)e^{\beta t})^4}.$$

For fixed x_0 , $X_t^{(N)}$ has an approximate normal distribution with mean $\mathbb{E} X_t^{(N)} \simeq x_t(x_0)$ and variance $\text{Var}(X_t^{(N)}) \simeq \Sigma_t(x_0)/N$, the quality of the approximation improving as N gets large.

If N is small then one is forced to use the full stochastic model. Since the SI model is a pure-birth process one can evaluate $p_n(t) = \Pr(n_t = n)$ explicitly. It is easy to show that

$$p_n(t) = \sum_{k=n}^{n_0} \frac{k(N-k)}{n(N-n)} e^{-(\beta/N)k(N-k)t} \prod_{l=n, l \neq k}^{n_0} \frac{l(N-l)}{(l-k)(N-l-k)} \quad (n = 1, \dots, n_0),$$

with $p_n(0)$ being the complementary probability (tweak Exercise 6.8.31 of Grimmett and Stirzaker [21]).

For the SI model with $\beta = 0.3$ and with the initial proportion of susceptibles following a Beta(8, 1.5) distribution, we evaluated the difference between exact variance (evaluated numerically) and the variance obtained from mapping the initial distribution using the trajectory (13). Figure 1 shows the variability ignored, at times $t \in [0, 15]$, along with the corresponding proportion of the total variation. Notice that the variation not accounted for decreases with increasing population size. It is also apparent that the unexplained variation can be a sizeable proportion of the total variation in the dynamics and that the proportion of variation unexplained increased over time; as the effect of the initial distribution dissipates, the variation predicted by the stochastic model predominates. One can thus make an informed

decision about the use of the deterministic or the stochastic model through demarcation and quantification of variability. In particular, they allow for this assessment to be made at any stage in the progress of the infection.

We now consider disease trajectories from the stochastic SI model with transmission rate parameter $\beta = 0.5$, a Beta(20, 1) initial distribution and $N = 50$ (Figure 2a). Here we can think of a metapopulation consisting of $N = 50$ patches, in which a disease is spreading between these patches. It can be seen that there is sizeable variability between individual trajectories (red dashed with crosses, nine realisations). Furthermore, we can see that the deterministic model incorporating an initial distribution (blue lines; circles – mean, dashed – two standard deviations) does not account for all of the variability in trajectories but does account for the majority of it. The corresponding stochastic model standard deviation bounds (black dashed) provide an improved estimate of the potential disease progression seen in reality; the standard deviation bounds arising from accounting for stochasticity only, that is, with no random initial conditions, also fail to account for all of the variability witnessed (green dashed). It is possible that the disease trajectory may be outside the bounds given by the deterministic model, as seen in four of the nine realisations shown, suggesting that the stochastic model incorporating an initial distribution might be used for pandemic and emerging infectious disease preparedness in this particular metapopulation scenario. Finally, we note that as time progresses the need to account for stochasticity, in concert with random initial conditions, increases.

An example used previously to illustrate incorporating an initial distribution for the SI model is early growth (1978–1984) of HIV prevalence in San Francisco [3, 25]. In Figure 2b we plot the available data (black filled circles) along with the corresponding mean (blue circles) and two standard error bounds (stochastic only – green dashed, deterministic with random initial conditions – blue dashed, stochastic with random initial conditions – black dashed). A Beta(3.4998, 0.2168) distribution was used for the initial proportion of susceptible individuals. It can be seen that since the population estimated to be at risk is large ($N = 100,000$), the additional variation due to random dynamics is small compared with the variability due to initial state uncertainty, as the deterministic and stochastic bounds almost coincide; this is reinforced by the bounds for the stochastic model with no initial uncertainty. In this scenario

it may thus be sufficient to adopt the deterministic model with initial uncertainty for prediction. However, note that while the mean disease trajectory fits the observed data extremely well, individual realisations from the fitted model (Figure 2b: red dashed with crosses, seven realisations) provide a poor representation of the shape of the observed data. This illustrates the importance of using a stochastic model for model calibration and verification, even if a deterministic model is sufficient to give bounds on disease behaviour (as is the case here).

It is not surprising that the SI model provides a poor representation of HIV prevalence, as ‘network’ properties for such diseases have been shown to be of importance [16]. Bailey (1988) modified the model by dividing the population into two classes: a fraction that were not at risk due to a ‘safe’ lifestyle, and the remainder at risk. Here we consider an alternate approach to explain the observed data. We modify the SI model so that the transmission parameter β decreases through time, following the identification of HIV in 1981—a modification to incorporate an element of rational/precautionary behaviour as awareness and perceived risk increases. This modified model provides realisations that give an accurate representation of the observed trajectory (Figure 2c: black filled circles – data; red dashed with red crosses – five realisations from initial data proportion) ($\beta \leftarrow 0.99988\beta$ following each new infection after 1981). Obviously, as already mentioned, specific network properties are important, along with demography (age structure); however, we also believe that this rational behavioural aspect of the model is an important and interesting component of the disease dynamics [11, 19].

Next we consider the SIS (*Susceptible-Infective-Susceptible*) model, which was one of the earliest stochastic models for the spread of infections that do not confer any long lasting immunity, and where individuals become susceptible again after infection [18, 50]. It has been applied, not only in epidemiology, but also in the propagation of rumours [10], in chemical reaction kinetics [34] and in metapopulation ecology [40].

The SIS model. Our state n_t is now the number of infectives at time t and $S = \{0, 1, \dots, N\}$, where N is the total number of individuals. The non-zero transition rates are $q(n, n+1) = (\beta/N)n(N-n)$ and $q(n, n-1) = \nu n$, where β is the transmission rate and ν is the recovery rate. The model is density dependent with $f(x, +1) = \beta x(1-x)$ and $f(x, -1) = \nu x$, $x \in E = [0, 1]$, and so the approximating deterministic model for the *proportion* $X_t^{(N)} = n_t/N$ of infectives is (1) with $F(x) = \beta x(1 - \rho - x)$, where $\rho = \nu/\beta$, being the classical Verhulst model [49] for

population growth (see also [36, 31]). It has the unique solution

$$x_t(x_0) = \frac{(1 - \rho)x_0}{x_0 + (1 - \rho - x_0)e^{-\kappa t}} \quad (t \geq 0),$$

where $\kappa = \beta(1 - \rho)$, if $\rho \neq 1$ and $x_t(x_0) = x_0/(1 + \beta x_0 t)$ ($t \geq 0$) if $\rho = 1$. Again uniform convergence in probability (over finite time intervals) of the process $X_t^{(N)}$ to the deterministic trajectory x_t is guaranteed provided $X_0^{(N)} \rightarrow x_0$. The primitive L and its inverse are given by

$$L(u) = \frac{1}{\kappa} \log \left(\frac{u}{1 - \rho - u} \right) \quad \text{and} \quad L^{-1}(u) = \frac{1 - \rho}{1 + e^{-\kappa u}} \quad \text{if } \rho \neq 1,$$

and $L(u) = L^{-1}(u) = 1/(\beta u)$ if $\rho = 1$, and this leads to

$$f_t(y) = \frac{(1 - \rho)^2 e^{-\kappa t}}{(1 - \rho - y + y e^{-\kappa t})^2} f_0 \left(\frac{(1 - \rho) y e^{-\kappa t}}{1 - \rho - y + y e^{-\kappa t}} \right) \quad (y \in \mathcal{R}_t) \quad \text{if } \rho \neq 1, \quad (15)$$

and

$$f_t(y) = \frac{1}{(1 - \beta t y)^2} f_0 \left(\frac{y}{1 - \beta t y} \right) \quad (y \in \mathcal{R}_t) \quad \text{if } \rho = 1, \quad (16)$$

where $\mathcal{R}_t$ is the interval $[0, x_t(1)]$. Note that, although $\mathcal{R}_t$ decreases to the point set $\{0\}$ as $t \rightarrow \infty$ if $\rho \geq 1$ and to the interval $[0, 1 - \rho]$ if $\rho < 1$, the argument of f_0 in (15) and in (16) always lies in $(0, 1)$. We might then take f_0 to be the Beta(a, b) pdf to obtain a model for the proportion of susceptibles at time t , assuming random dynamics can be ignored:

$$f_t(y) = \frac{\Gamma(a + b)}{\Gamma(a)\Gamma(b)} (1 - \rho)^{a+1} e^{-a\kappa t} \frac{y^{a-1} (1 - \rho - y + \rho y e^{-\kappa t})^{b-1}}{(1 - \rho - y + y e^{-\kappa t})^{a+b}} \quad (y \in \mathcal{R}_t) \quad \text{if } \rho \neq 1,$$

and

$$f_t(y) = \frac{\Gamma(a + b)}{\Gamma(a)\Gamma(b)} \frac{y^{a-1} (1 - y - \beta t y)^{b-1}}{(1 - \beta t y)^{a+b}} \quad (y \in \mathcal{R}_t) \quad \text{if } \rho = 1.$$

We can again solve (9) explicitly. We have that $G(x) = \beta x(1 - x) + \nu x = F(x) + 2\nu x$, and a lengthy calculation gives

$$\begin{aligned} \Sigma_t(x_0) = & \frac{x_0}{(x_0 + (1 - \rho - x_0)e^{-\kappa t})^4} \left(\rho x_0^3 (1 - e^{-2\kappa t}) + (1 + 5\rho) x_0^2 (1 - \rho - x_0) e^{-\kappa t} (1 - e^{-\kappa t}) \right. \\ & \left. + 2(1 + 2\rho) x_0 (1 - \rho - x_0)^2 \kappa t e^{-2\kappa t} + (1 + \rho) (1 - \rho - x_0)^3 e^{-2\kappa t} (1 - e^{-\kappa t}) \right) \quad \text{if } \rho \neq 1, \end{aligned}$$

and

$$\Sigma_t(x_0) = \frac{(3\beta^3 x_0^3 t^3 + 2\beta^2 x_0^2 t^2 (6 - x_0) + 6\beta x_0 t (3 - x_0) + 6(2 - x_0)) \beta x_0 t}{6(1 + \beta x_0 t)^4} \quad \text{if } \rho = 1.$$

If random dynamics are significant, we may approximate the distribution of $X_t^{(N)}$ using a normal distribution with mean $x_t(x_0)$ and variance $\Sigma_t(x_0)/N$.

If $\rho \geq 1$ the infection will die out quickly. However if $\rho < 1$ the process will move quickly towards the stable point $x_{\text{eq}} = 1 - \rho$, in which case if t is large and N is not so large that random dynamics can be ignored we may employ the OU approximation: $X_t^{(N)}$ has an approximate normal distribution with mean $1 - \rho$ and variance Σ_t/N , where $\Sigma_t = \rho(1 - e^{-2\kappa t})$ (which settles quickly to $\Sigma_{\text{eq}} = \rho$).

The SIS model has been used in the study of metapopulations [40] to model the number of occupied habitat patches in a population network, where the transmission and recovery events correspond to colonization of unoccupied patches through dispersal of individuals from occupied patches and local extinction of occupied patches. Within this context, we examine next an elaboration of the model which accounts for an external source of colonization [1, 43].

A mainland-island metapopulation model. Now n_t represents the number of occupied patches in a network consisting of N habitat patches (imagine a network of islands). Each occupied patch becomes empty at rate e (the per-patch local extinction rate), colonization of empty patches occurs at rate c/N for each suitable pair consisting of an empty patch and a non-empty patch (c is the colonization rate), and immigration from an external source (the “mainland”) occurs at rate α (the per-patch immigration rate). The non-zero transition rates are $q(n, n+1) = \alpha(N - n) + (c/N)n(N - n)$ and $q(n, n-1) = en$. Again we have density dependence, now with $f(x, +1) = (\alpha + cx)(1 - x)$ and $f(x, -1) = ex$, $x \in E = [0, 1]$, and so the approximating deterministic model for the proportion $X_t^{(N)} = n_t/N$ of occupied patches is (1) with $F(x) = \alpha + (c - e - \alpha)x - cx^2$, a model identified by Hanski [22]. It has the unique solution

$$x_t(x_0) = \phi + \theta \frac{x_0 - \phi + \theta \tanh(\theta ct)}{\theta + (x_0 - \phi) \tanh(\theta ct)} \quad (t \geq 0),$$

where $\phi = (c - e - \alpha)/(2c)$ and $\theta = \sqrt{\phi^2 + \alpha/c}$ (see [43]). Furthermore,

$$L(u) = \frac{1}{\theta c} \tanh^{-1} \left(\frac{u - \phi}{\theta} \right) \quad \text{and} \quad L^{-1}(u) = \phi + \theta \tanh(\theta cu),$$

leading to

$$f_t(y) = \frac{\theta^2 \text{sech}^2(\theta ct)}{(\theta - (y - \phi) \tanh(\theta ct))^2} f_0 \left(\phi + \theta \frac{y - \phi - \theta \tanh(\theta ct)}{\theta - (y - \phi) \tanh(\theta ct)} \right) \quad (y \in \mathcal{R}_t),$$

where $\mathcal{R}_t$ is the interval $[x_t(0), x_t(1)]$. As before, we might then take f_0 to be the $\text{Beta}(a, b)$ pdf to obtain a model for the proportion of occupied patches at time t , assuming random dynamics can be ignored.

If random dynamics are significant, we can again use a diffusion approximation, but, while it is feasible to evaluate $\Sigma_t(x_0)$ explicitly, the expression is too complicated to be of any practical use. However, for the present model the process moves quickly towards a region containing the stable point $x_{\text{eq}} = \theta + \phi$ (being the *unique* equilibrium point in E), in which case if t is large and N is not so large that random dynamics can be ignored we may employ the OU approximation: $X_t^{(N)}$ has an approximate normal distribution with mean $\theta + \phi$ and variance Σ_t/N , where

$$\Sigma_t = \frac{e(\theta + \phi)}{2\theta c}(1 - e^{-2\theta ct}),$$

which settles quickly to $\Sigma_{\text{eq}} = e(\theta + \phi)/(2\theta c)$.

A further elaboration of the basic metapopulation model accounts for dynamics in habitat by allowing the number of patches suitable for occupancy to vary stochastically [42, 43]. Here we examine the case $c = 0$ (not considered in detail by Ross), where colonization from within the network is insignificant compared with colonization from the mainland. This model is not only of interest in its own right, but also serves to illustrate how our results can be applied to a two-dimensional ($D = 2$) model.

A mainland-island metapopulation model incorporating habitat dynamics. The state at time t is (m_t, n_t) , where m_t is the number of patches suitable for occupancy and n_t is the number occupied. The network contains a total of N patches, and so the state space is $S = \{(m, n) : 0 \leq n \leq m \leq N\}$. The non-zero transition rates are

$$\begin{aligned} q((m, n); (m+1, n)) &= r(N-m), & q((m, n); (m-1, n)) &= d(m-n), \\ q((m, n); (m-1, n-1)) &= dn, & q((m, n); (m, n+1)) &= \alpha(m-n) \\ \text{and } q((m, n); (m, n-1)) &= en, \end{aligned}$$

where the two new parameters, d and r , represent the (per-patch) rate at which patches are disturbed (and thus rendered unsuitable for occupancy) and the (per-patch) rate at which patches recover. Notice that if an occupied patch is disturbed it becomes unoccupied. For

simplicity, we will assume that $r \neq \alpha + e$. The model is density dependent with

$$\begin{aligned} f((u, v); (+1, 0)) &= r(1 - u), & f((u, v); (-1, 0)) &= d(u - v), \\ f((u, v); (-1, -1)) &= dv, & f((u, v); (0, +1)) &= \alpha(u - v) \\ \text{and } f((u, v); (0, -1)) &= ev, \end{aligned}$$

taking $E = \{(u, v) : 0 \leq v \leq u \leq 1\}$, and so the approximating deterministic model for $X_t^{(N)} = (U_t^{(N)}, V_t^{(N)})^\top$, where $U_t^{(N)} = m_t/N$ and $V_t^{(N)} = n_t/N$ are the proportion of suitable and occupied patches, is (1) with $x = (u, v)^\top$ and

$$F(x) = F(u, v) = \begin{pmatrix} r - (r + d)u \\ \alpha u - \kappa v \end{pmatrix} = \begin{pmatrix} r \\ 0 \end{pmatrix} - Ax, \quad \text{where } A = \begin{pmatrix} r + d & 0 \\ -\alpha & \kappa \end{pmatrix},$$

and $\kappa = \alpha + e + d$. Its solution $x_t = (u_t, v_t)^\top$ has components

$$u_t(u_0, v_0) = u_{\text{eq}} + (u_0 - u_{\text{eq}})e^{-(r+d)t}$$

and

$$v_t(u_0, v_0) = v_{\text{eq}} + (v_0 - v_{\text{eq}})e^{-\kappa t} + \delta(u_0)(e^{-\kappa t} - e^{-(r+d)t}),$$

where $u_{\text{eq}} = r/(r + d)$ and $v_{\text{eq}} = \alpha u_{\text{eq}}/\kappa$ are the limiting ($t \rightarrow \infty$) values, and $\delta(y) = \alpha(y - u_{\text{eq}})/(r - e - \alpha)$. The trajectories are curves in E satisfying

$$v_t = v_{\text{eq}} + (v_0 - v_{\text{eq}}) \left(\frac{u_t - u_{\text{eq}}}{u_0 - u_{\text{eq}}} \right)^{\frac{\kappa}{r+d}} + \frac{\alpha(u_0 - u_{\text{eq}})}{r - e - \alpha} \left(\left(\frac{u_t - u_{\text{eq}}}{u_0 - u_{\text{eq}}} \right)^{\frac{\kappa}{r+d}} - \frac{u_t - u_{\text{eq}}}{u_0 - u_{\text{eq}}} \right).$$

We will now determine the action of the map $g_t(u_0, v_0) = x_t(u_0, v_0)$ on f_0 , the joint pdf of the initial proportions (U_0, V_0) of suitable and occupied patches, to obtain a pdf f_t that summarises the effect of random initial conditions in our metapopulation. A simple calculation shows that the map is injective with

$$g_t^{-1}(y) = g_{-t}(y) = \begin{pmatrix} u_{\text{eq}} + (y_1 - u_{\text{eq}})e^{(r+d)t} \\ v_{\text{eq}} + (y_2 - v_{\text{eq}})e^{\kappa t} + \delta(y_1)(e^{\kappa t} - e^{(r+d)t}) \end{pmatrix} \quad (y = (y_1, y_2)^\top \in \mathcal{R}_t),$$

where $\mathcal{R}_t = g_t(E)$, the image of E under g_t , is the triangle with vertices $g_t(0, 0)$, $g_t(1, 0)$ and $g_t(1, 1)$. (Note that $\mathcal{R}_t$ decreases to $\{(u_{\text{eq}}, v_{\text{eq}})\}$ as $t \rightarrow \infty$.) Clearly

$$\partial g_t^{-1}(y) = \begin{pmatrix} e^{(r+d)t} & 0 \\ \frac{\alpha}{r-e-\alpha}(e^{\kappa t} - e^{(r+d)t}) & e^{\kappa t} \end{pmatrix},$$

and so $J_t(y) = |\partial g_t^{-1}(y)| = e^{(r+d+\kappa)t} (> 0)$. Therefore, from (2),

$$f_t(y) = f_t(y_1, y_2) = e^{(r+d+\kappa)t} f_0 \left(\begin{array}{c} u_{\text{eq}} + (y_1 - u_{\text{eq}}) e^{(r+d)t} \\ v_{\text{eq}} + (y_2 - v_{\text{eq}}) e^{\kappa t} + \delta(y_1)(e^{\kappa t} - e^{(r+d)t}) \end{array} \right) \quad (y \in \mathcal{R}_t).$$

For example, we might suppose that the initial proportion V_0 of suitable patches follows a Beta(a, b) law on $[0, 1]$ and the initial proportion U_0 of occupied patches follows a Beta(p, q) law on $[0, V_0]$:

$$f_0(u, v) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \frac{\Gamma(p+q)}{\Gamma(p)\Gamma(q)} v^{a-p-q} (1-v)^{b-1} u^{p-1} (v-u)^{q-1} \quad (0 \leq u \leq v \leq 1).$$

To illustrate this, consider the simplest case where V_0 is uniformly distributed on $[0, 1]$ and U_0 is uniformly distributed on $[0, V_0]$, so that $f_0(u, v) = 1/v$ ($0 \leq u \leq v \leq 1$):

$$f_t(y_1, y_2) = \frac{e^{(r+d+\kappa)t}}{v_{\text{eq}} + (y_2 - v_{\text{eq}}) e^{\kappa t} + \delta(y_1)(e^{\kappa t} - e^{(r+d)t})} \quad ((y_1, y_2) \in \mathcal{R}_t).$$

To obtain the diffusion approximation observe that

$$G(x) = G(u, v) = \begin{pmatrix} r + (d-r)u & dv \\ dv & \alpha u + (d+e-\alpha)v \end{pmatrix}.$$

Because $\partial F(u, v) = -A$ is the same for all (u, v) , the evaluation of $\Sigma_t(x_0)$ is simpler:

$$\Sigma_t(x_0) = \int_0^t e^{-A(t-u)} G(x_u(x_0)) e^{-A^\top(t-u)} du.$$

Furthermore,

$$e^{-At} = \begin{pmatrix} e^{-(r+d)t} & 0 \\ \frac{\alpha}{\alpha+e-r} (e^{-(r+d)t} - e^{-\kappa t}) & e^{-\kappa t} \end{pmatrix},$$

and so $\Sigma_t(x_0)$ can in principle be evaluated explicitly. However, since the process moves quickly towards $x_{\text{eq}} = (u_{\text{eq}}, v_{\text{eq}})^\top$, the OU approximation will usually suffice. The unique solution to $B \Sigma_{\text{eq}} + \Sigma_{\text{eq}} B^\top + G(x_{\text{eq}}) = 0$, where $B := \partial F(u_{\text{eq}}, v_{\text{eq}}) = -A$, is

$$\Sigma_{\text{eq}} = \begin{pmatrix} u_{\text{eq}}(1-u_{\text{eq}}) & v_{\text{eq}}(1-u_{\text{eq}}) \\ v_{\text{eq}}(1-u_{\text{eq}}) & v_{\text{eq}}(1-u_{\text{eq}}) \left(1 + \frac{r(e+d)}{d\kappa} \right) \end{pmatrix}.$$

Thus, if t is large and N is not so large that random dynamics can be ignored, $(U_t^{(N)}, V_t^{(N)})$ will have an approximate bivariate normal distribution with mean $(u_{\text{eq}}, v_{\text{eq}})$ and covariance matrix Σ_{eq}/N .

6 Concluding remarks

We have seen that if the population size N is large, the effect of demographic stochasticity becomes negligible, in which case a deterministic model will suffice and we may incorporate random initial conditions by way of (2) (or (3) in the one-dimensional case). If N is not so large that random dynamics can be ignored, a stochastic model should be used. For density dependent models we may exploit diffusion approximation techniques to estimate characteristics of the stochastic model. If N is small we are forced to evaluate the state probabilities, either analytically or numerically, using standard techniques, incorporating random initial conditions as appropriate. Whatever our approach, the effect of uncertainty in initial population size becomes insignificant in the long term ($t \rightarrow \infty$). The following table contains a summary.

N	t	Model and approach
large	small	Deterministic model with random initial conditions
large	large	Deterministic model: identify a stable equilibrium
moderate	small	Stochastic model: full diffusion approximation with random initial conditions
moderate	large	Stochastic model: OU approximation
small	small	Stochastic model: solve forward equations
small	large	Stochastic model: evaluate the stationary distribution or the quasi-stationary distribution

For density dependent models, we have shown that the overall variation is the sum of the variation due to random initial conditions and the variation due to random dynamics, and thus we have quantified the variation not accounted for when random dynamics are ignored (formula (12)).

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Legends

Figure 1. The unexplained variation (a) and the corresponding proportion of total variation not accounted for (b) at times $t \in [0, 15]$ for different population sizes $N \in \{10, 20, 40, 80\}$ in the SI model with transmission rate $\beta = 0.3$ and a $\text{Beta}(8, 1.5)$ distribution for the initial state.

Figure 2. Metapopulation disease spread and HIV prevalence in San Francisco: (a) Nine realisations (red dashed, cross) of the SI model with transmission rate parameter $\beta = 0.5$, a $\text{Beta}(20, 1)$ distribution for the initial proportion of susceptible patches and $N = 50$ patches, along with the mean (blue circles) and two standard error bounds (green dashed – stochastic only; blue dashed – deterministic with random initial conditions; black dashed – stochastic with random initial conditions). (b) Estimates of HIV prevalence from a representative sample of homosexual men in San Francisco 1978–1984 (black, filled circles), seven realisations (red dashed, cross) of the previously fitted SI model with transmission parameter $\beta = 1.18$ and a $\text{Beta}(3.4998, 0.2168)$ distribution for the initial proportion of susceptibles and population size $N = 100,000$ ($[3, 25]$), along with the mean (blue circles) and two standard error bounds (green dashed – stochastic only; blue dashed – deterministic with random initial conditions; black dashed – stochastic with random initial conditions). (c) Five realisations (red dashed, cross) of a modification to the SI model used in (b) to incorporate rational/precautionary behaviour of individuals following the identification of HIV in 1981; $\beta \leftarrow 0.99988\beta$ following each new infection from 1982 onwards, $\beta = 1$ initially, and all realisations commence from the estimated proportion of susceptible individuals in 1978. The data is once again plotted (black, filled circles).

Figure 1 (a)

Figure 1 (b)

Figure 2 (a)

Figure 2 (b)

Figure 2 (c)