Discrete and continuous SIS epidemic models: a unifying approach

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Abstract

We study two different approaches to the Susceptible-Infective-Susceptible (SIS) epidemiological model. The first one consists of a single differential equation, while the second one is given by a discrete time Markov chain (DTMC) model. The large time behaviour of the dynamics of these two models is known to differ whenever the basic reproductible number, R_0, is larger than one. We show, however, that their behaviour is similar for finite time, and that the maximum time (for a given maximum admissible difference between the solution of both models) diverge when the population goes to infinity. We introduce a new model, based on a partial differential equation of drift-diffusion type. The corresponding diffusion is degenerated at one of the boundaries, and we show that this model approximates the evolution of the DTMC in all time scales. We also show that the solution of the SIS ordinary differential equation model gives the most probable state of the DTMC, assuming that the DTMC is not absorbed. In addition, we study the effect of a finite population comparing the DTCM and the PDE model with the classical ODE model. We find that, for initial conditions far from the absorbing state, the ODE is a very good approximation for an exponentially long time, even if the population is not very large. For the initial conditions close to the absorbing state, such as the ones used for the study of the onset of a disease, we find that both the discrete and PDE models differ considerably from the ODE model. In particular, for $R_0 > 1$, we obtain numerically that, with a probability $1/R_0$, the disease extinguishes itself without becoming

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endemic.

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1. Introduction

1.1. Discrete and continuous views of the SIS model

Real populations are always finite. This means that after a sufficiently long time, stochastic effects will prevail. However, the necessary time can be so long that for all practical purposes we are interested in transient states, and not in the final ones. Let us consider, as an example, two different approaches to the most elementary epidemiological model: the SIS (Susceptible-Infectious-Susceptible) model. In this model, each individual in a population can be susceptible (i.e., can be infected) to a certain infectious disease or is in fact infected. Each individuals changes from one group to the other: the SI transition (infection) occurs with probability proportional to the number of infected and to the time of exposition; the IS transition (healing) occurs with constant in time transition probability. This model is summarised in the following diagram:

$$\begin{array}{c} S + I \xrightarrow{\beta} I + I; \\ I \xrightarrow{\alpha} S. \end{array} \tag{1}$$

The constants α and β in (1) can be interpreted as rates (either discrete or continuous) or as probabilities among many other possible choices. We shall focus here on two possible implementations: the first one, based on differential equations (we call it the SIS-ODE model) and one based on discrete time Markov chains (DTMC).

We start by the SIS-ODE, since it is one of the simplest epidemiological models based on the mass action principle—a particular popular interpretation of (1). It is discussed in many classical and more recent references (see, e.g, Rass and Radcliffe (2003); Bailey (1975); Anderson and May (1995); Van Segbroeck et al. (2010)), and it is given by the following system of ODEs:

$$\begin{array}{rcl} \dot{S} & = & -\bar{\alpha}SI + \bar{\beta}I \\ \dot{I} & = & \bar{\alpha}SI - \bar{\beta}I \end{array}.$$

Assuming, without loss of generality, that $S(0) + I(0) = 1$, we find

$$I' = \bar{\alpha} I \left(1 - \frac{\bar{\beta}}{\bar{\alpha}} - I \right). \tag{2}$$

The final value in $t \to \infty$ of the solution for any non trivial initial condition depends on the value $\bar{\mathcal{R}}_0 := \bar{\alpha}/\bar{\beta}$ and is 0 if $\bar{\mathcal{R}}_0 \leq 1$; otherwise it is is a positive constant $I_* = 1 - \bar{\mathcal{R}}_0{}^{-1}$.

Let us discuss the second approach: the DTMC or discrete SIS model. More precisely, what we call the discrete SIS model consists of a population of N individuals, divided in two subgroups: Nx **I**nfected and $N(1-x)$ **S**usceptibles, where $x \in \{0, \frac{1}{N}, \frac{2}{N}, \ldots, 1\}$ is the fraction of infected. At each time step $\Delta t > 0$ one individual is chosen at random and then

- If he or she is of type **I**, then it becomes **S** with probability β;
- If he or she is of type **S**, then it becomes **I** with probability proportional to the number of infected in the population: αx.

Let $P_{(N,\Delta t)}(x,t)$ be the probability to find a fraction x of **I** individuals at time t in a population of size N, evolving in time steps of size Δt. The transition probabilities are given by:

$$\begin{aligned} T^+(x) &= \alpha x(1-x) \ , \\ T^0(x) &= 1 - T^+(x) - T^-(x) \ , \\ T^-(x) &= x\beta \ . \end{aligned}$$

The corresponding master equation is

$$\begin{aligned} P_{(N,\Delta t)}(x, t+\Delta t) = T^+(x-z) P_{(N,\Delta t)}(x-z,t) + T^0(x) P_{(N,\Delta t)}(x,t) + \\ T^-(x+z) P_{(N,\Delta t)}(x+z,t) \ , \end{aligned} \tag{3}$$

where, for notation convenience, we set $z = N^{-1}$. For any choice of $\beta, \alpha > 0$ the only stationary state is given by $P_{(N,\Delta t)}(x,t) = \delta_{x0}$, where δ is the Kronecker delta (see, e.g, Allen (2008)).

Such a master equation can be related with a discrete version of (2) as follows:

Let X_t be the number of infected individuals at time t. Let us define the expected number of infected individuals:

$$n(t) = \mathbb{E}[X_t] = \sum_{x=0}^{1} x P_{(N,\Delta t)}(x,t) \ ,$$

where the summation shall be understood in the set $\{0, N^{-1}, 2N^{-1}, \ldots, 1\}$.

Therefore

$$
\begin{aligned}
n(t+\Delta t) &= \sum_{x=0}^{1} x\alpha(x-z)(1-x+z)P_{(N,\Delta t)}(x-z,t) + \sum_{x=0}^{1} x(1-\alpha x(1-x)-\beta x)P_{(N,\Delta t)}(x,t) \\
&\quad + \sum_{x=0}^{1} x\beta(x+z)P_{(N,\Delta t)}(x+z,t) \\
&= \sum_{x=0}^{1} (x+z)\alpha x(1-x)P_{(N,\Delta t)}(x,t) + \sum_{x=0}^{1} x(1-\alpha x(1-x)-\beta x)P_{(N,\Delta t)}(x,t) \\
&\quad + \sum_{x=0}^{1} (x-z)\beta x P_{(N,\Delta t)}(x,t) \\
&= \sum_{x=0}^{1} x P_{(N,\Delta t)}(x,t) + z(\alpha-\beta)\sum_{x=0}^{1} x P_{(N,\Delta t)}(x,t) - z\alpha \sum_{x=0}^{1} x^2 P(x,t) \\
&= \left[1 + \frac{\alpha}{N}\left(1 - \frac{1}{R_0^*}\right)\right] n(t) - \frac{\alpha}{N}\sum_{x=0}^{1} x^2 P_{(N,\Delta t)}(x,t) \\
&= n(t) + \frac{\alpha}{N} n(t)\left[\left(1 - \frac{1}{R_0^*}\right) - n(t)\right] - \frac{\alpha}{N}\mathbb{V}[X_t],
\end{aligned}
$$

where $\mathbb{V}$ denotes the variance and $R_0^* = \alpha/\beta$. Then, if we let $\alpha/N = \Delta t$, and neglect the variance term, we are left with an Euler discretisation of (2).

See also, Bailey (1963); Allen (1994); Allen and Burgin (2000); Allen (2008); McKane and Newman (2004) and references therein for different interpretations of stochastic modelling in epidemiology.

Despite the fact that, in both cases, the modeling assumptions on the disease dynamics are similar, results obtained differ considerably. In particular, as it was discussed before, for certain choices of parameters, there is a non-trivial stationary solution, which attracts all non-trivial initial conditions of the SIS-ODE model, whereas for the discrete SIS model, the only stationary state is the trivial one.

This apparent contradiction is solved by considering the behaviour of the transient states of the discrete process in the limit of large population. Indeed, the discrete SIS model is a Markov chain with leading eigenvalue $\lambda = 1$; the associated eigenvector denotes the trivial state, the only stationary state of the process and the absorbing state of any initial condition. The

second eigenvalue $\lambda_* \in (0,1)$ is associated to the transient state and the typical time such that the transient state fades out is directly related to the inverse size of the spectral gap $1-\lambda_*$. However, when the population is large $1-\lambda_* \ll 1$, making the transient state a quasi-stationary one. Therefore, in the limit of infinite population (one of the basic assumptions of any modelling by ordinary differential equations) we possibly have a stationary state that is not present in the discrete model.

The solution of this puzzle shows that the ODE-model can be understood as an approximation of the discrete model only for a certain range of time scales. In order to have a continuous model that approximate the discrete model at all time scales, we need to introduce partial differential equations (PDEs). In order to grasp both the deterministic effects (highlighted by the ODE model) and the stochastic effects (the final states of the discrete model), this equation has to be of drift-diffusion type. As the state where all individuals are of S-type (i.e., $x = 0$) is stationary for all populations, we cannot impose boundary conditions at $x = 0$, and the diffusion coefficient will be degenerated at the boundary. The correct solution (in the sense of being an approximation of the discrete process) will be obtained imposing a boundary condition at $x = 1$, and the conservation of probability. For further details, see Chalub and Souza (2009a,b, 2011a).

After introducing the SIS-PDE model, we can solve this equation to obtain information of the solution of the discrete SIS model. Recalling that every population is finite, we have a partial differential equation model that gives information on the final and transient states of the discrete problem. Therefore, it generalises the ODE model to all time scales.

The first goal of this paper is to derive the first order correction for the continuous model for finite size population effects. This can be see as reminiscent of the Kramers-Moyal expansion, but we follow a more analytical route.

In particular, we obtain the PDE:

$$\partial_t p = -\partial_x \left\{ x \left[R_0(1-x) - 1 \right] p \right\} + \frac{1}{2N} \partial_x^2 \left\{ x(R_0(1-x)+1)p \right\}, \qquad (4)$$

supplemented with the boundary equation

$$\frac{1}{2N} \left((1-R_0) r(1,t) + \partial_x r(1,t) \right) + r(1,t) = 0.$$

When N is equal to infinity, we obtain formally the equation:

$$\partial_t p = -\partial_x \left\{ x \left[R_0(1-x) - 1 \right] p \right\} \ , \qquad (5)$$

supplemented by the boundary condition

$$p(1,t) = 0.$$

Equation (5) can be shown to be equivalent to (2). For a similar PDE derivation of the SIR model, see Chalub and Souza (2011b). For a comparison of analogous discrete stochastic SIS models with continuous ones, see Allen (2008). On the other hand, (4) describes an approximation of the probability distribution of the discrete version, while maintaining its main features, in particular that the disease always extinguishes itself in finite time.

The second goal of this work is to probe the difference between the deterministic, the stochastic and the diffusion approximation obtained here. In order to perform such a comparison, we shall, having in mind the difference between the determinstc model and the diffusion approximation, produce numerical simulations of the DTMC model, the diffusion approximation and compare them with the ODE-SIS model. This will show that, in particular, the ODE-SIS model models the interior mode (i.e., the mode of the probability distribution restricted to $x > 0$) of the probability distribution, and not the mean value. Moreover, we shall observe that, when studying the dynamics of model when there is a single infected individual, the deterministic and stochastic models have a significant difference, and that this should be taken into account when deciding about the model to study the onset of a particular disease.

1.2. Outline

The structure of this work is the following. In section 2, we formally derive the SIS-PDE model. The study of the PDE model will be performed in section 3 and in section 5 we will estimate the extinction time for the epidemic in the discrete case using solutions of the PDE model. The agreement between the two approaches is numerically studied in the section 4. We conclude in section 6.

2. Formal Derivation of PDE model

2.1. Asymptotic expansion

We proceed with a second order Taylor expansion and find

$$P_{(N,\Delta t)}(x \pm z, t) = P_{(N,\Delta t)}(x,t) \pm z\partial_x P_{(N,\Delta t)}(x,t) + \frac{z^2}{2}\partial_x^2 P_{(N,\Delta t)}(x,t) + \mathcal{O}\left(z^3\right). \tag{6}$$

Using $P = P_{(N,\Delta t)}(x,t)$, we derive the formal expansion for equation (3):

$$\begin{aligned}
P_{(N,\Delta t)}(x,t+\Delta t) &= \alpha(x-z)(1-x+z)\left(P - z\partial_x P + \frac{z^2}{2}\partial_x^2 P\right) \\
&\quad + (1-\beta x - \alpha x(1-x))\,P + \beta(x+z)\left(P + z\partial_x P + \frac{z^2}{2}\partial_x^2 P\right) \\
&\quad + \mathcal{O}\left(\beta z^3, \alpha z^3\right) \\
&= P + z\left(-\alpha(1-2x)P - \alpha x(1-x)\partial_x P + \beta P + \beta x \partial_x P\right) \\
&\quad z^2\left(-\alpha P + \alpha(1-2x)\partial_x P + \frac{\alpha x(1-x)}{2}\partial_x^2 P + \beta\partial_x P + \frac{\beta x}{2}\partial_x^2 P\right) \\
&\quad + \mathcal{O}\left(\beta z^3, \alpha z^3\right) \\
&= P + z\partial_x\left(\beta x P - \alpha x(1-x)P\right) + \frac{z^2}{2}\partial_x^2\left(\beta x P + \alpha x(1-x)P\right) \\
&\quad + \mathcal{O}\left(\beta z^3, \alpha z^3\right)
\end{aligned}$$

We introduce the following assumptions:

1. $\beta_{(N,\Delta t)} = \beta_0\,(\Delta t)^{\alpha}\,(1+\mathrm{o}(\Delta t))$,
2. $\alpha_{(N,\Delta t)} = \alpha_0\,(\Delta t)^{\alpha}\,(1+\mathrm{o}(\Delta t))$.
3. $N = (\Delta t)^{\alpha-1}$.

with $0 < \alpha \leq 1/2$.

For a more detailed discussion about the role of scaling in obtaining the diffusive limit see Chalub and Souza (2009a, 2011a)

We also introduce the basic reproductive factor

$$R_0\,(1+\mathrm{o}(\Delta t))\ ,$$

with $R_0 = \alpha_0/\beta_0$, and we rewrite the master equation as:

$$\begin{aligned}
\frac{\Delta P}{\Delta t} &= \frac{\beta}{N\Delta t}\partial_x\left[x(1-R_0(1-x))P\right] + \frac{\beta}{2N^2\Delta t}\partial_x^2\left(x(R_0(1-x)+1)P\right) \\
&\quad + \mathcal{O}\left(\Delta t, N^{-2}\right)\ .
\end{aligned}$$

On using the assumptions (and reescaling time $t \to t/\beta_0$), we find

$$\partial_t p = -\partial_x\left\{x\left[R_0(1-x)-1\right]p\right\} + \frac{1}{2N}\partial_x^2\left\{x(R_0(1-x)+1)p\right\} + \mathcal{O}\left(\Delta t\right)\ , \quad (7)$$

The first aproximation of the SIS model, which is size-independent, is given by the hyperbolic equation (5), and it is equivalent to the ODE (2); namely, the characteristics of equation (5) are solutions of (2).

If we consider the first correction due to finite-size effects, we find the parabolic equation (7), setting the $\mathcal{O}(\Delta t)$ term equal to zero.

2.2. Boundary conditions

From now on, we write $\varepsilon = \frac{1}{N}$. Note that we can, in principle, extend equation (3) to values of x larger than 1. The compactness of $P_{(N,\Delta t)}$ is preserved; explicitly, if $P_{(N,\Delta t)}(x,0) = 0$ for any $x \notin [0,1]$ then $P_{(N,\Delta t)}(x,t) = 0$ for any $x \notin [0,1]$, and $t > 0$ (this follows from the fact that $T^-(0) = T^+(1) = 0$). Therefore, in the continuous limit, it is natural to assume that the solution of of the PDE is such that $p(x,t) = 0$ for any $x \notin [0,1]$ and any $t > 0$. From the uniform parabolicity of the PDE in any neighborhood of $x = 1$, we conclude the continuity of the flow of p around $x = 1$. We initially write the PDE (7) (with null $\mathcal{O}(\Delta t)$ term) in divergence form:

$$\partial_t p = \partial_x \left\{ \frac{\varepsilon}{2} \left[(R_0(1-x)+1)p - xR_0 p + x(R_0(1-x)+1)\partial_x p \right] + x\left[R_0(1-x)-1\right]p \right\} .$$

Imposing the continuity of the flow at $x = 1$, we conclude that

$$\begin{aligned} 0 &= \lim_{y\to 0^+} \left[\frac{\varepsilon}{2} \left[(1-R_0)p|_{1+y} + \partial_x p|_{1+y} \right] + p|_{1+y} \right] \\ &= \lim_{y\to 0^+} \left[\frac{\varepsilon}{2} \left[(1-R_0)p|_{1-y} + \partial_x p|_{1-y} \right] + p|_{1-y} \right] = \left[\frac{\varepsilon}{2} \left[(1-R_0)p|_1 + \partial_x p|_1 \right] + p|_1 \right] . \end{aligned}$$

3. Analytical results for the continuous model

We begin from the weak formulation:

$$\begin{aligned} \int_0^\infty \int_0^1 p(x,t)\partial_t \phi(x,t)\,\mathrm{d}x\,\mathrm{d}t + \frac{\varepsilon}{2}\int_0^\infty \int_0^1 p(x,t)x\left(R_0(1-x)+1\right)\partial_x^2\phi(x,t)\,\mathrm{d}x\,\mathrm{d}t \\ \int_0^\infty \int_0^1 p(x,t)x\left(R_0(1-x)-1\right)\partial_x\phi(x,t)\,\mathrm{d}x\,\mathrm{d}t + \int_0^1 p(x,0)\phi(x,0)\,\mathrm{d}x = 0, \end{aligned} \tag{8}$$

where

$$\phi \in C_c^\infty([0,1]\times[0,\infty)).$$

Since we are going to be interested in solution to (8) in a measure sense, we recall the following result proved in Chalub and Souza (2009b):

Lemma 3.1. *Let ν be a Radon measure supported in $[0,1]$. Then we can write $\nu = \nu_0 + \nu_i + \nu_1$, where sing supp$(\nu_0) \subset \{0\}$, sing supp$(\nu_i \in (0,1))$, and sing supp$(\nu_1) \subset \{1\}$.*

In what follows, we shall be interested in positive and bounded Radon measures in [0,1], and we shall denote these by $\mathcal{BM}^+([0,1])$. See Chalub and Souza (2009b) for more details about the choices of spaces.

In view of Lemma 3.1, we shall write for $p_0 \in \mathcal{BM}^+([0,1])$:

$$p_0 = a_0\delta_0 + r_0 + b_0\delta_1.$$

We now proceed to study (8) more thoroughly. We begin by observing that (8) is uniform parabolic on $[\delta, 1]$, for any $0 < \delta < 1$. In particular we have the following

Lemma 3.2. *Let $p \in L^\infty\left([0,\infty); \mathcal{BM}^+([0,1])\right)$ be a solution to (8). Then*

$$p \in C^\infty\left((0,\infty); C^\infty((0,1))\right) \ .$$

Furthermore, $p(x,t) = a(t)\delta_0 + r(x,t)$, where r satisfies:

$$\begin{aligned} &\partial_t r = -\partial_x\left\{x\left[R_0(1-x)-1\right]r\right\} + \frac{\varepsilon}{2}\partial_x^2\left\{x(R_0(1-x)+1)r\right\}, \\ &\frac{\varepsilon}{2}\left((1-R_0)r(1,t) + \partial_x r(1,t)\right) + r(1,t) = 0 \\ &r(x,0) = r_0 + b_0\delta_1 \end{aligned} \tag{9}$$

Moreover,

$$a(t) = \frac{\epsilon(R_0+1)}{2}\int_0^t r(0,s)\ \mathrm{d}s + a_0. \tag{10}$$

Proof. Firstly, in any $(a,b) \subset [0,1]$, (8) is uniformly parabolic, and the local regularity of p follows from standard arguments—see Lieberman (1996).

In view of Lemma 3.1, we write

$$p(t,x) = a(t)\delta_0 + r(x,t) + b(t)\delta. \tag{11}$$

Let $\phi(x,t) = \eta(t)\varphi(x)$, with $\eta \in C_c^\infty((0,\infty))$ and $\varphi \in C_c^\infty((0,1))$. Then ϕ is an appropriate test fuction, and we have recast (8) in terms of r only. Then the regularity of p implies that $r \in C^\infty\left((0,\infty); C^\infty((0,1))\right)$, and that it satisfies the equation (9) in classical sense.

Now, let $\varphi \in C_c^\infty([0,1])$, then on substituting the (11) into (8), and using the regularity of r to integrate by parts we obtain

$$\begin{aligned}
&\int_0^\infty a(t)\eta'(t)\varphi(0)\ \mathrm{d}x\ \mathrm{d}t + \int_0^\infty b(t)\eta'(t)\varphi(1)\ \mathrm{d}x\ \mathrm{d}t + \\
&\quad + \int_0^\infty b(t)\eta(t)\left(\frac{\epsilon}{2}\varphi''(1) - \varphi'(1)\right)\ \mathrm{d}x\ \mathrm{d}t + \\
&\quad + \frac{\epsilon(1+R_0)}{2}\int_0^\infty r(t,0)\varphi(0)\ \mathrm{d}t - \\
&\quad - \int_0^\infty \left(r(1,t) + \frac{\epsilon}{2}\left((1-R_0)r(t,1) + \partial_x r(1,t)\right)\right)\varphi(1)\eta(t)\ \mathrm{d}t + \\
&\quad + \frac{\epsilon}{2}\int_0^\infty r(1,t)\varphi'(1)\eta(t)\ \mathrm{d}t = 0.
\end{aligned}$$

If we choose $\varphi \in C_c^\infty([0,1])$, with $\varphi(0) = \varphi(1) = \varphi'(1) = 0$ and $\varphi''(1) \neq 0$, we find that

$$\frac{\varepsilon}{2}\int_0^\infty b(t)\eta(t)\varphi''(1)\,\mathrm{d}t = 0.$$

Hence $b(t) \equiv 0$ for almost every time.

Now, let us choose φ with $\varphi(0) \neq 0$, and $\varphi(1) = \varphi'(1) = 0$. We then conclude that

$$a(t) = \frac{\epsilon(R_0+1)}{2}\int_0^t r(0,s)\ \mathrm{d}s + a_0,$$

which is (10). Now let $\varphi(x) \equiv 1$. Then we are left with

$$\int_0^\infty \left(r(1,t) + \frac{\epsilon}{2}\left((1-R_0)r(t,1) + \partial_x r(1,t)\right)\right)\eta(t)\ \mathrm{d}t = 0,$$

and hence we obtain again the boundary condition in (9). □

Remark 3.3. *Notice that we are still left with*

$$\frac{\epsilon}{2}\int_0^\infty r(1,t)\varphi'(1)\eta(t)\ \mathrm{d}t = 0.$$

This identity is satisfied if we choose φ with $\varphi'(1) = 0$. However, in general, we need to show that $\partial_x r(1,t)$ is uniformly bounded in ϵ. In this case, the boundary condition in (9) implies that $r(1,t) = \mathcal{O}(\epsilon)$, and hence the above identity is $\mathcal{O}(\epsilon^2)$, which can then be consistently neglected at this truncation order.

Proposition 3.4. *There exists a unique solution to* (9) *with* $r(x,0) = r_0 + b_0\delta_1$. *Furthermore,* $r \in C^\infty\left((0,\infty); C^\infty([0,1])\right) \cap C\left((0,\infty); \mathcal{BM}^+([0,1])\right)$, *and*

$$\lim_{t\to\infty} \|r\|_\infty = 0.$$

Finally, if $r_0, b_0 \geq 0$, *then* $r \geq 0$.

Proof. Let

$$\omega(x) = x\left[R_0(1-x)+1\right], \quad u(x,t) = \omega(x)r(x,t) \quad \text{and} \quad \Pi(x) = \frac{R_0(1-x)-1}{R_0(1-x)+1}.$$

Then equation (9) becomes

$$\begin{aligned} &\partial_t u = \omega\left\{\frac{\varepsilon}{2}\partial_x^2 u - \partial_x\left[\Pi(x)u\right]\right\} \\ &u(t,0) = 0, \quad \frac{\varepsilon}{2}\partial_x u(1,t) + u(1,t) = 0. \end{aligned} \tag{12}$$

Equation (12) is a parabolic equation with smooth coefficients. Moreover, the corresponding Steklov condition yields a well-defined spectral problem, see for instance Auchmuty (2005), and hence all the results follow common spectral arguments—cf. Evans (2010); Taylor (1996). □

The important point about solutions in the sense of (8) is that they satisfy probability conservation as the next result shows

Theorem 3.5. *Let* $p \in L^\infty\left([0,\infty); \mathcal{BM}^+([0,1])\right)$ *be a solution to* (8). *Then*

$$\int_0^1 p(x,t)\ \mathrm{d}x = \int_0^1 p_0(x)\ \mathrm{d}x,$$

for almost everytime.

Proof. Consider $\phi(t,x) = \eta(t)$, with $\eta \in C_c([0,\infty))$, with $\eta(0) = 1$. Substituting in (8) yields

$$\int_0^\infty \int_0^1 p(x,t)\eta'(t)\,\mathrm{d}x\,\mathrm{d}t + \int_0^1 p(x,0)\,\mathrm{d}x = 0$$

and the result follows. □

Theorem 3.6. *Let $p_0 \in \mathcal{BM}^+([0,1])$. Then, equation (8) has a unique solution $p \in L^\infty\left([0,\infty); \mathcal{BM}^+([0,1])\right)$. Moreover, we have*

$$p(x,t) = a(t)\delta_0 + r(x,t), \quad a(t) = \frac{\varepsilon(R_0+1)}{2}\int_0^t r(0,s)\ \mathrm{d}s + a_0, \tag{13}$$

with $r \in C^\infty([0,1]\times[0,\infty))$, and

$$\lim_{t\to\infty} \|r(\cdot,t)\|_\infty = 0$$
$$\lim_{t\to\infty} a(t) = 1.$$

Proof. Let r be the solution to (9). Then all the statements about r follow from Proposition 3.4. Let p be given by (13). Then $p(x,0) = p_0$ and, upon substituting p in (8) and integrating by parts the terms with r, one verifies that p is indeed a solution. The statement about a follows from probability conservation.

Now, let $\tilde{p}$ be another solution to (8). By Lemma 3.2, we can write $\tilde{p}(x,t) = \tilde{a}(t)\delta_0 + \tilde{r}(x,t)$, and $\tilde{r}$ satisfies (9). By virtue of Proposition 3.4, we have that $r = \tilde{r}$. On susbtituting $\tilde{p}$ in (8), we find that $\tilde{a} = a$. Hence $p = \tilde{p}$. □

4. Numerical study of finite population effects

In this section, we study the differences between the ODE approximation that is usually obtained in the infinite population limit and the diffusion approximation that was obtained in Section 2.

From the results in Section 3 and the discussion in the Introduction, it is clear that for very long times, the disease will die out. Nevertheless, when $R_0 > 1$, the meta-stable state should persist for a reasonable long time. Thus, within a time-scale that is relevant for the population in question, the meta-stable state can be considered an effective stationary state. See figures 1 to 5 and explanations in the captions.

5. Extinction time

In what follows, we study the mean extinction time of the disease. First we describe the governing equation, and obtain a representation for the solution in integral form. Such a representation can be used to produce numerical evaluations, and some examples are provided. These examples shows

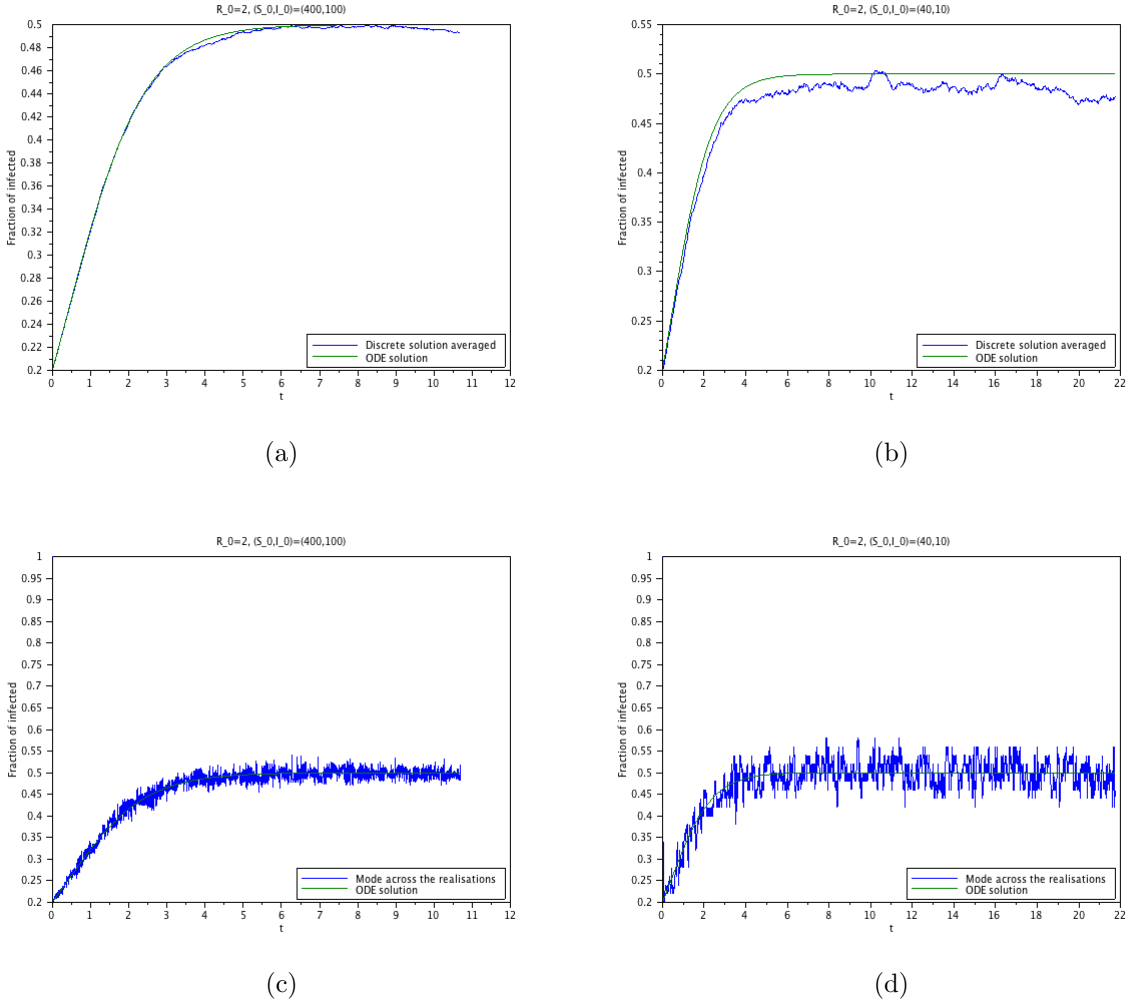
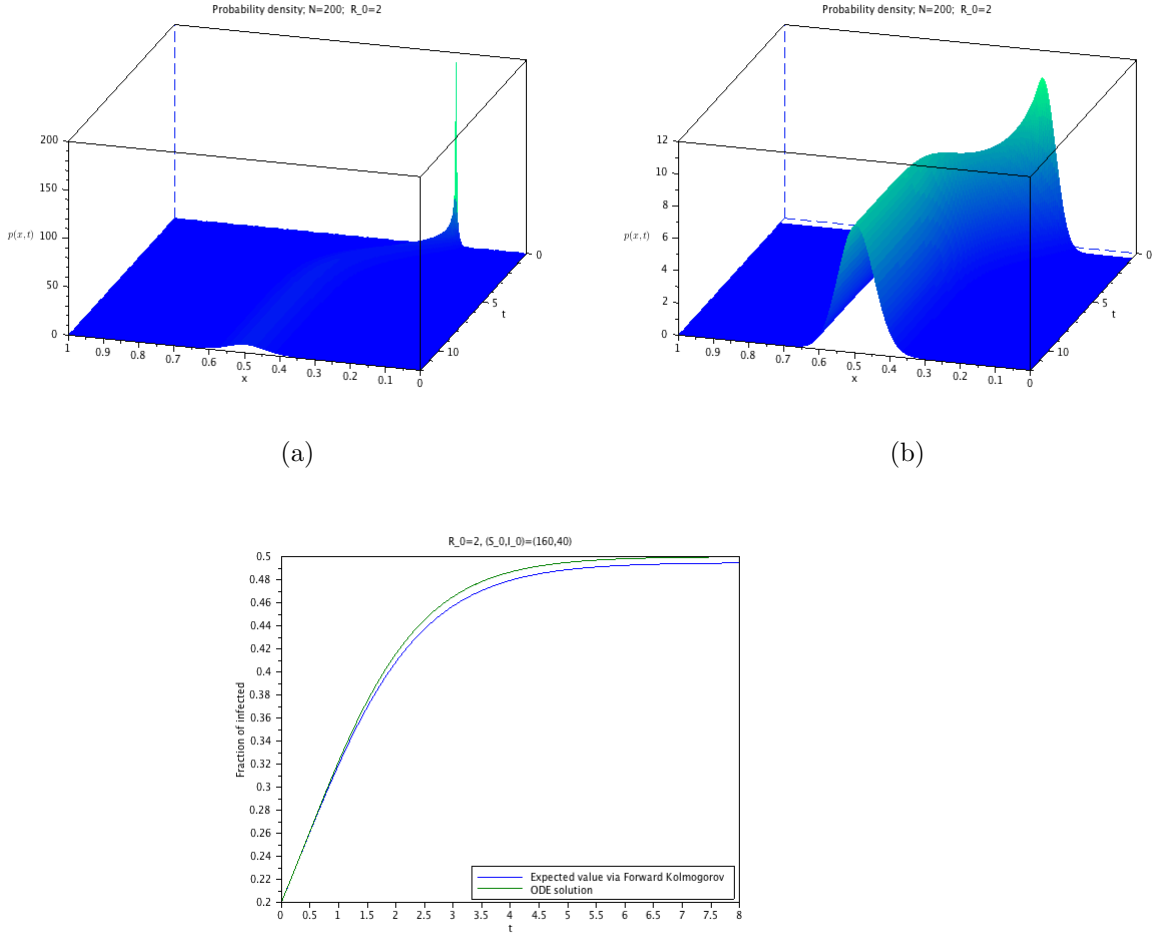


Figure 1: The first set of simulation compares the ODE solutions with the expected values of the simulations obtained using the Gillespie algorithm (see Gillespie (1976)). From the results, it is apparent that even for population that are not extremely large, the ODE approximation works well provided that a fair number of infected individuals already exist in the system. In these figures, we display the ODE solution for the infected fraction compared against the average and mode across realisations obtained from stochastic simulations using the Gillespie algorithm, for populations of sizes $N = 50, 500$. In all cases, the initial condition is $I_0 = 20\%$ of the population. Figures (a) and (c) are for $N = 500$, while figures (b) and (d) were obtained with $N = 50$. In both cases, the the ODE is a good approximation of the expected value, albeit with a larger variance in the case of $N = 50$. The mode across realisations is quite oscillatory, but it also is well approximated by the ODE.



(a) (b)

(c)

Figure 2: This second set depicts the solutions to the forward equation, where the development of a quasi-steady state for large times, and this can be identified with quasi-stationary distribution. The initial condition was a Dirac mass at $0.2N$, with $R_0 = 2$ for $t \geq 0$, (a), and for $t > 0.5$, (b). In (a), one can clearly sees the trajectory that should be done by the mode and also by the expected value. In (b), the regular part is depicted in more detail. Notice that, for this particular initial condition, the Dirac measure at zero did not develop significant mass up to the computed time. In (c), we show the expected value of infected computing using the diffusive approximation, and compare with the ODE solution.

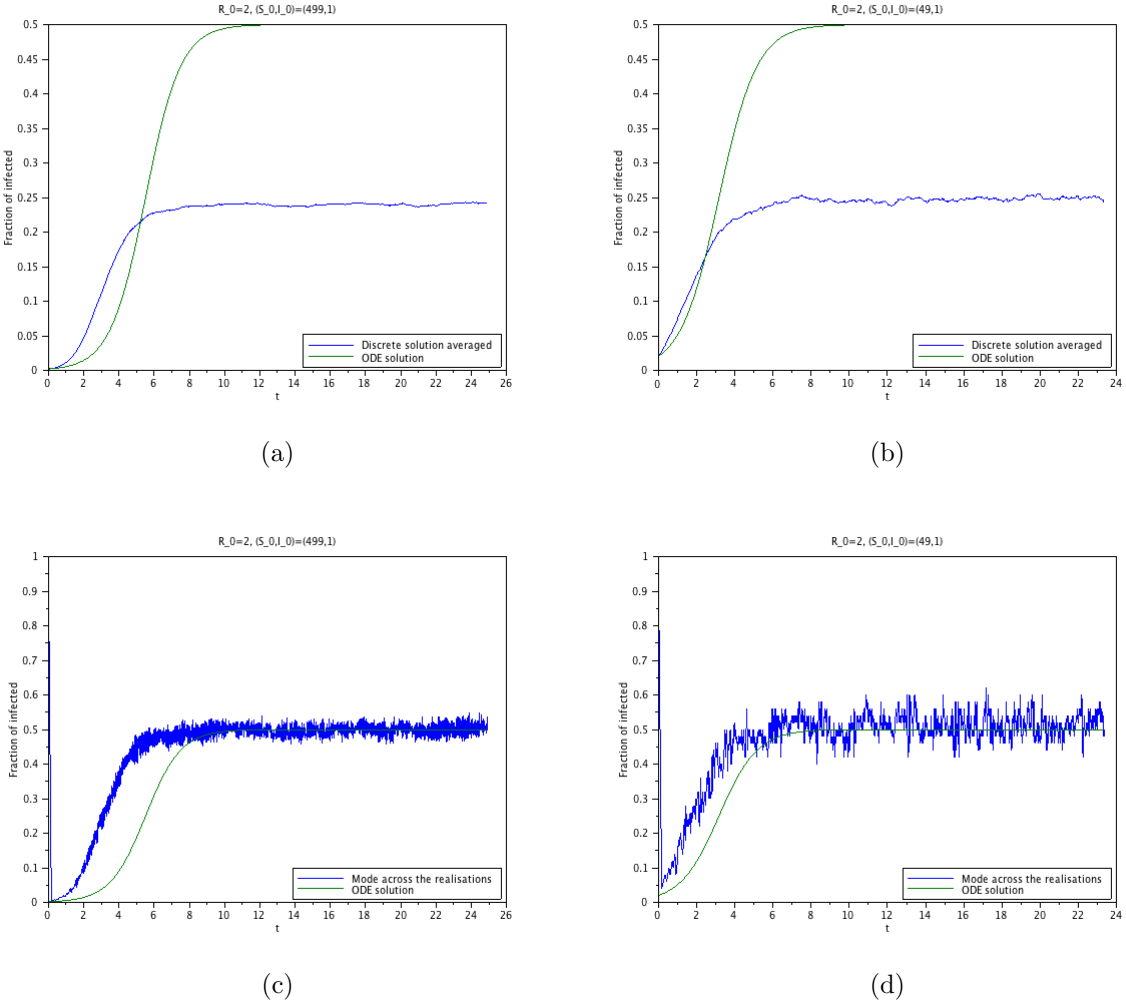


Figure 3: In this set, we look at the performance of both approximations, but when there is only a single infected individual. Now we see, independently of the size of the population, that there is a markedly difference between the ODE approximation, and the expected value of the probability distribuition obtained in the diffusive approximation (see figures (a) and (b)). The difference between the ODE solution and the interior mode of the probability distribution, however, is small (after a certain time) even for populations of $N = 50$ individuals (figures (c) and (d)).

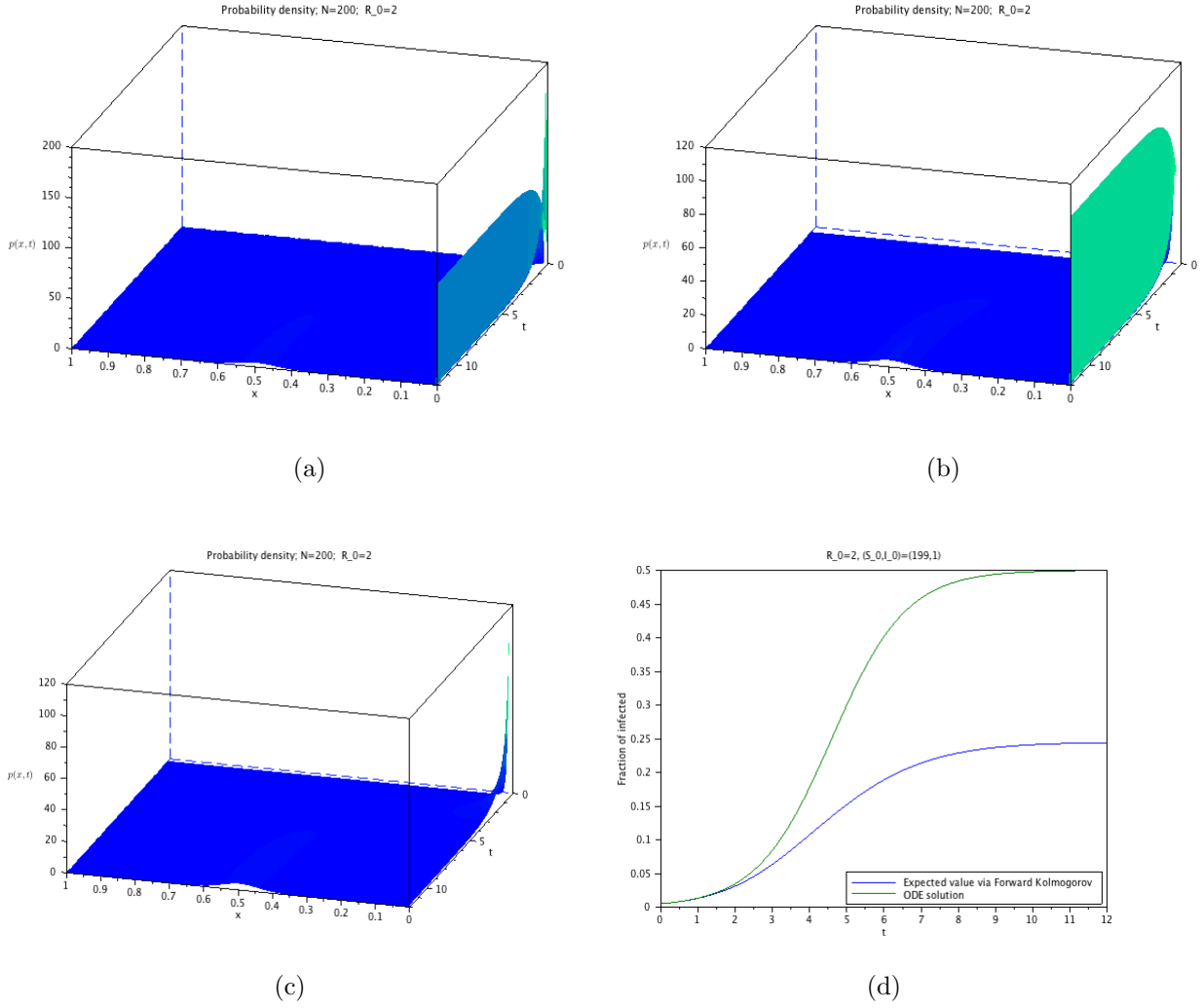


Figure 4: We now study the evolution of the probability density. In this case, we can see that the development of the Dirac mass at $x = 0$ is now significant. Notice also, that the expected value and the ODE differ considerably.

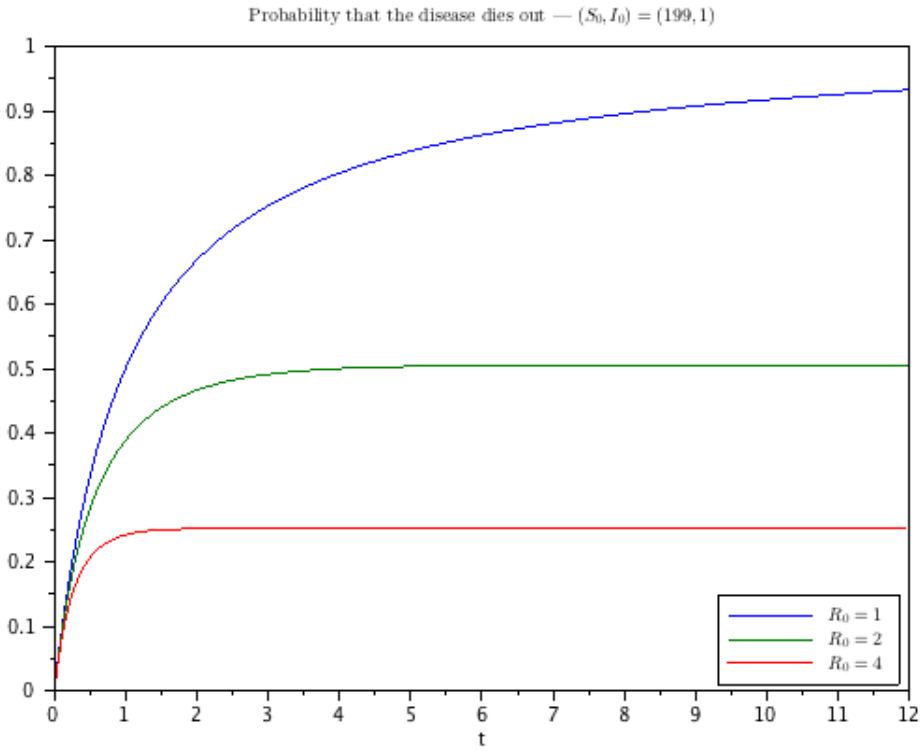


Figure 5: In this final set, we study this behaviour observed for small initial fractions of infected with some more detail. In order to do this, we plot the value of $a(t)$ for various values of R_0. Here we observe an important aspect: when $R_0 > 1$, we see that there is a probability $1/R_0$ that the disease dies out up to a certain time T^*, that goes to zero as R_0 increases.

the boundary-layer nature of the solution when we have $\epsilon \ll 1$, and thus we evaluate asymptotically this solution, for $R_0 > 1$.

5.1. Formulation, integral representation and numerical examples

Let $\tau_\epsilon(x)$ denote the mean extinction time given that there are a fraction of x infected individuals at time zero.

Then, cf. Ewens (2004), we have that

$$\frac{\varepsilon}{2}\tau_\epsilon'' + \Pi(x)\tau_\epsilon' = \frac{-1}{\omega(x)}, \quad \tau_\epsilon(0) = 0, \text{and} \quad \tau_\epsilon'(1) = 0. \tag{14}$$

In (14), we have that

$$\omega(x) = x\left(R_0(1-x)+1\right)$$

and

$$\Pi(x) = 1 - \frac{2}{R_0(1-x)+1}.$$

If we take τ_ϵ' as the dependent variable, then (14) is a first order ODE for τ_ϵ', satisfying $\tau_\epsilon'(1) = 0$.

Its solution is readily seen to be

$$\tau_\epsilon'(x) = \frac{2}{\epsilon}\int_x^1 \frac{\mathrm{e}^{\frac{2}{\epsilon}(s-x)}}{\omega(s)}\left[\frac{R_0(1-s)+1}{R_0(1-x)+1}\right]^{\frac{4}{\varepsilon R_0}} \mathrm{d}s.$$

Hence

$$\tau_\epsilon(x) = \frac{2}{\epsilon}\int_0^x \int_r^1 \frac{\mathrm{e}^{\frac{2}{\epsilon}(s-r)}}{\omega(s)}\left[\frac{R_0(1-s)+1}{R_0(1-r)+1}\right]^{\frac{4}{\varepsilon R_0}} \mathrm{d}s\ \mathrm{d}r. \tag{15}$$

Equation (15) can be rewritten as

$$\tau_\epsilon(x) = \frac{2}{\epsilon(R_0+1)}\int_0^x \int_0^{1-r} \mathrm{e}^{\epsilon^{-1}\phi(z,r)}\left[\frac{1}{z+r} + \frac{1}{\hat{x}-(z+r)}\right] \mathrm{d}z\ \mathrm{d}r, \tag{16}$$

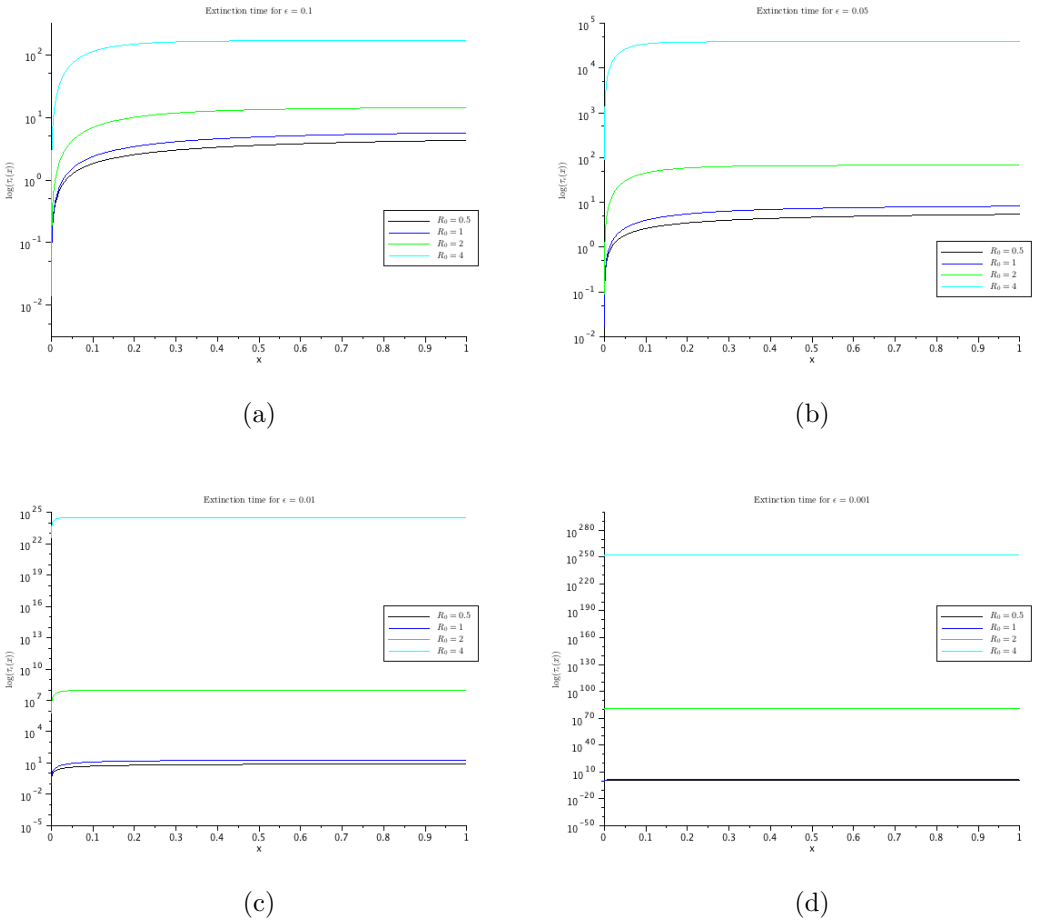
where $s = x + z$,

$$x^* = 1 - \frac{1}{R_0}, \quad \hat{x} = x^* + \frac{2}{R_0},$$

and

$$\phi(z,r) = 4\left[\frac{z}{2} + \frac{1}{R_0}\log\left(1 - \frac{z}{\hat{x}-r}\right)\right].$$

In Figure 6 we see a number of solutions of equation (15)—actually computed using the representation given by (16). See caption for further discussion.



(a) (b)

(c) (d)

Figure 6: Log plot of the mean extinction times as a function of the initial frequency of infected. Graphs display such times for $R_0 = 1/2, 1, 2, 4$ and various values of ϵ. Notice that appart a boundary layer close to $x = 0$ of order ϵ, these times are nearly constant.

5.2. Asymptotic evaluation

In order to evaluate (15) when $\epsilon \ll 1$, we first need to evaluate $\tau'_\epsilon(x)$. From (16), we have that:

$$\tau'_\epsilon(x) = \frac{2}{\epsilon(R_0+1)} \int_0^{1-x} \mathrm{e}^{\varepsilon^{-1}\phi(z,x)} \left[\frac{1}{x+z} - \frac{1}{x+z-\hat{x}} \right] \mathrm{d}z. \tag{17}$$

Before proceeding to evaluate (17) when $\varepsilon \ll 1$, we collect some useful facts about ϕ.

1. $\phi(0,r) = 0$ and, if $R_0 \leq 1$, we have $\phi(z,r) < 0$, for $z > 0$, and $r \geq 0$.
2. For $R_0 > 1$, we have $\partial_z \phi(0,r) > 0$, for $r < x^*$. In this case, $\phi(\cdot, r)$ has a positive maximum at
$$z^* = x^* - r.$$
This maximum will be relevant for the asymptotic evaluation provided that $r < x^*$.

We shall study the case $R_0 > 1$. The case $R_0 \leq 1$ is of less interest and will be discussed elsewhere.

Notice that $z^* > 0$, if $x < x^*$. Additionally, we compute

$$\partial_z^2 \phi(x^* - x, x) = -R_0.$$

Thus, provided that $0 \leq x \leq x^*$—and hence that $1 - x \geq z^* \geq 0$—and using the steepest descent method, we obtain

$$\begin{aligned}
&\tau'_\epsilon(x) \\
&\quad = 2\mathrm{e}^{\epsilon^{-1}\phi(x^*-x,x)} \frac{f(x^*-x)}{x^*} \left(\frac{2\pi}{R_0}\right)^{1/2} \left[N\left((1-x^*) \left(\frac{R_0}{\epsilon}\right)^{1/2} \right) - N\left((x-x^*) \left(\frac{R_0}{\epsilon}\right)^{1/2} \right) \right],
\end{aligned}$$

where N is the cumulative Normal distribution.

For $x > x^*$, we have $\phi(z,x) < 0$ for $z \in [0, 1-x]$, and hence that the integrand is exponentially small, and can be neglected.

Integrating the representation for τ'_ϵ and evaluating using Laplace's method yields

$$\tau_\epsilon(x) = 2\mathrm{e}^{x^*\epsilon^{-1}} \frac{f(x^*)}{|f'(x^*)|x^*} \left(\frac{2\pi}{R_0}\right)^{1/2} \left(1 - \mathrm{e}^{-|f'(x^*)|x/\epsilon}\right). \tag{18}$$

The asymptotic expression given by (18) suggest that, when $R_0 > 1$, we can have a very long persistence of the disease before it is eventually extinct.

Figure 7 displays the behaviour of $\tau_\epsilon(1/N)$ for different values of R_0, with $N = 50$, and confirms this first impression. Nevertheless, this result should be considered together with the results in Section 4; see the discussion in Section 6.

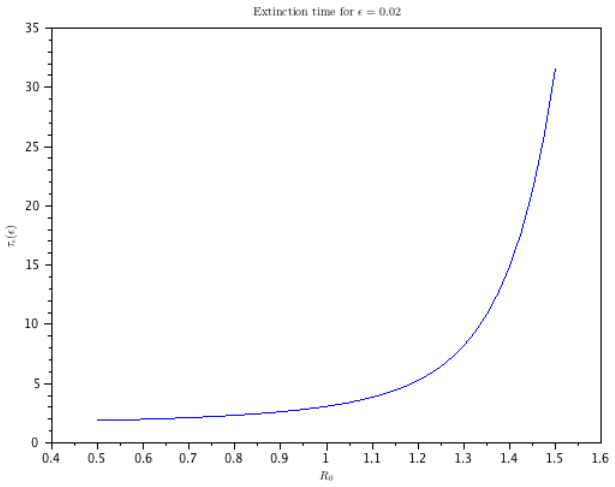


Figure 7: Mean extinction times for the disease when there is a single infected individual initially. Notice that even for such a moderate size population, the mean time of extinction increases exponentially with R_0. Simulations were performed with $N = 50$.

6. Conclusion

We have studied the SIS model in a number of different implementations: we started with the DTMC model, as discussed for instance by Allen (2008) and, using a number of ideas developed by the authors in Chalub and Souza (2009a,b) (and also more recently in Chalub and Souza (2011a) we have obtained a diffusive approximation that is compatible with the discrete model, provided that we use a particular weak formulation for the diffusive equation. In particular, we showed that the large time limit of this process is given is a Dirac mass at $x = 0$, which means that eventually the disease will die out. Such a continuous approximation contains the finite population effects.

We then numerically studied both the DTMC model, the classical ODE model, and the diffusive approximation obtained here. The first observation is that the first and the third models displayed a very good agreement, if the initial condition was far from the absorbing state. This is was the case even for not very large populations. Nevertheless, given the simplicity of the model, such regime is not particularly interesting. We then studied the behaviour for initial conditions with a single infected individual. Such an initial condition is particularly important when trying to study the possible onset of a disease that has just emerged. The results show the diffusive and stochastic model still with good agreement concerning the expected number of cases, but this was not true for the ODE model. However, the ODE did recover the mode of infected cases, after they stabilise.

We then proceed to use the fact that the PDE solution naturally decomposes as a Dirac measure supported at $x = 0$ with a time dependent intensity, and a regular part. The singular measure quantifies the likeliness of extinction of the disease at any given time, while the regular part still approximates the ODE behaviour with respect to the mode. In particular, a comprehensively study was made to understand the behaviour of these different parts. The numerical studies then show that for larger values of R_0 the disease extinction probability increases up to $1/R_0$ at a certain characteristic time T^*, that goes to zero as R_0 increases. The regular part preserves the part of the dynamics that is closer to the ODE approximation. Thus, the disease has a probability of $1/R_0$ to disappear, and if that not occurs in a certain time T^*, we shall have that the number of expected disease cases approaches the one predicted by the ODE.

Also, using the corresponding backward equation, we could obtain the mean extinction time (MET) and this was computed numerically in Section 5. When $R_0 > 1$, such METs can have quite large values. We then derived an asymptotic approximation for the MET in this case, and we also computed its value when there is one single infected. Such METs displayed a very large increase as R_0 increases.

Combining all these findings, we obtain that, when $R_0 > 1$, there is a probability $1/R_0$ that a newly introduced disease will die out. If such extinction does not occur until T^*, it then goes to the inner equilibrium—which is well approximated by the ODE. Such an approximation can be seen as recovering the mode of the cases. Thus, the PDE model accounts correctly for both extreme regimes, and provides and explicit value of the probability of extinction. This might be of interest for public health questions, and we

hope to discuss this more thoroughly elsewhere.

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