Stochastic modelling epidemics with differential equations

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ABSTRACT

Some Mathematical methods of stochastic epidemic models are presented. Models are formulated for continuous time Markov chains and stochastic differential equations. The purpose of modelling is illustrated by studying effects of vaccination and also in terms of inference procedures for important parameters, such as the basic reproduction number and the critical vaccination coverage. Analytical methods for approximating the probability of a disease outbreak are also discussed.

Keywords: *Stochastic epidemic, continuous time Markov chains, stochastic differential equations, Basic reproduction number, critical vaccination coverage, disease outbreak.*

Introduction

Early modelling contributions for infectious disease spread were often for specific diseases. Forexample, Bernoulli (1970) aimed at evaluating the effectiveness a certain technique of variolation against smallpox, and Ross (1911) modelled the transmission of malaria. One of the general studies was made by Kermack and McKendrick (1927). Later important contributions were for example by Bartlett (1949) and Kendall (1956), both also considering stochastic models. We define the deterministic general epidemic model and derive some properties of it, then describe some cases where a deterministic model is insufficient, and end by defining what we called the standard stochastic SIR- epidemic model. Stochastic modelling of epidemics is important when the number of infectious individuals is small or when the variability in transmission, recovery, births, deaths, or the environment impacts the epidemic outcome in[1, 9]. This paper restricted to two types of stochastic settings, continuous-time Markov chains and stochastic differential equations in[2, 10].We study the SIR model with some reasonable assumptions, then include herd immunity and vaccination. Hence both deterministic and stochastic epidemic models have their important roles to play however, the focus in the paper is on stochastic epidemic models.

Stochastic epidemic models: Deterministic epidemic models

The deterministic general epidemic model in [3] can be defined by two differential equations. It is assumed that at any time point an individual is either susceptible (s), infected (i) and recovered (immune) (r). Such individuals are from now one called susceptible, infective and recovered respectively. We shall make some general assumptions which are common to all models: only susceptible individuals can get infected and after having been infectious for some time t, an individual recovers and becomes completely immune for the remainder of the study period. Finally, we assume there are no births, deaths, immigration or emigration during the study period, the community is said to be closed ie, has a fixed size. A consequence of the assumptions is that

individuals can only make two moves, from susceptible to infected and from infected torecovered. For this reason, the model is said to be an SIR epidemic model.

Let s(t), i(t), and r(t), respectively denote the community fractions (ie,$\frac{S(t)}{N} = s(t)$, $\frac{I(t)}{N} = i(t), \frac{R(t)}{N} = r(t)$) and S(t) + I(t) + R(t) = N) of susceptible, infective and recovered. Since these are fractions and the community is closed, we assume that s(t) + i(t) + r(t) = 1 for all t ≥ 0. From the assumptions mentioned above, together with the assumptions of the community being homogeneous and people mixing homogeneously, the deterministic general epidemic model is defined by the following set of differential equations:

$\frac{ds}{dt}$ = - βs(t)i(t),

$\frac{di}{dt}$ = βs(t)i(t) - α i(t), (1)

$\frac{dr}{dt}$=αi(t), where β– transmission rate parameter, α – recovery rate parameter These differential equations, together with the starting configuration s(0) = 1 - ε, i(0) =ε and r(0) = 0, ε > 0 defines the model in [4].

The term βs(t)i(t) in equation (1) comes from the fact that susceptible must have contact with infective in order to get infected, so the assumption about uniform mixing implies that infections occur at a rate proportional to s(t)i(t). This term is non-linear which makes the solution of the system of differential equations non-trivial. By studying the differential equations to show that s(t) is monotonically decreasing down to s(∞) say, and r(t) is monotonically increasing up to r(∞). The differential equation for i(t) can be written as$\frac{di}{dt}$ = i(t) (βs(t) – α).So, ifβs(t) > α, then i(t) initially increases (the disease will spread), and if βs(t) < α, then i(t) decreases (the infection dies out), hence i(∞) tends to zero as t tends to infinity. Here 1/α is an average infectious period, α/β is the removal rate.

Basic Reproduction number:

The inverse of removal rate is defined as basic reproduction number and denoted by

R_o:R_o = β/α (2)

It is defined as the average number of secondary cases arising from an average primary case in an entirely susceptible population ie, the rate at which new infections are produces by an infectious individual in an entirely susceptible population. It measures the maximum reproductive potential for an infectious disease.

When $R_o > 1$ the epidemic takes off and when $R_o < 1$ there is no big epidemic. The differential equations (1) can also be used to obtain a balance equation for the final state $(s(\infty),0,r(\infty))$. By dividing the first equation by the last we get $\frac{ds}{dr} = -R_o s$, which implies that

$s(t) = s(0)e^{-Ror(t)}$. The fact that $i(\infty) = 0$ implies that $s(\infty) = 1 - r(\infty)$, at the end of the epidemic there are no infective, only susceptible and recovered (immune).From this we get a balance equation determining the fraction $u(t) = r(\infty)$ that at the end of the epidemic were infected: $1 - u(t) = (1 - \varepsilon)\, e^{-Rou(t)}$(3)

R_o depends on disease and host population.Example, $R_o = 2.6$ for TB in cattle; 3- 4 for Influenza in humans;3.5- 6 for smallpox in humans; and16–18 for measles in humans [5].

Remark

Is the deterministic epidemic models sufficient? We analysed the deterministic general epidemic model showed that: if $R_o < 1$ there will only be a small outbreak, and if $R_o > 1$ there will be a major outbreak infecting a substantial fraction of the community, and how big fraction is determined by equation (3). The results rely on that the community is homogeneous and that individuals mix uniformly with each other.

Even if the assumption of a homogeneous uniformly mixing community is accepted this model may not be suitable in some cases. For example, if considering a small community like an epidemic outbreak in day care centre or school it seems reasonable to assume some uncertainty / randomness in the final number infected. Also, even if $R_o > 1$ and the community is large but the outbreak is initiated by only one or a few initial infective it should be possible that, the epidemic never takes off in [6].

A standard stochastic SIR epidemic model

We define the standard stochastic SIR epidemic model. Just like for the deterministic general epidemic model we assume a closed homogeneous uniformly mixing community. Let n denote the size of the community; S(t), I(t) and R(t) are the number of susceptible population, infective population, and recovered population at time t. Suppose that the time t = 0 these numbers are given by S(0) = n - m, I(t) = m and R(0) = 0. Infectious individuals have direct contact with other individuals randomly in time t at transmission rate β, and each such contact is with a randomly selected individual, all contacts of different infective being define to be mutually independent.

The disease is transmitted instantaneously when the contact takes place and starts spreading the disease according to the same rules. Infected individuals remain infectious for a random time I(the infectious period), after which they stop being infectious, recover and become immune to the

disease. The infectious periods are defined to be independent and identically distributed having distribution f_i and mean $\mu(i) = 1/\alpha$. The epidemic starts at time t = 0, new individuals get infected and eventually recover, up to the first time T when there are no infective in the community. The final state of the epidemic is described by the number R(T) (recall that I(T) = 0, so S(T) = n – R(T)). It has the mathematical tractability that whether or not an individual makes contact with two separate individuals are independent events with probability $p = 1 - e^{-\beta/n\alpha}$ used in [7].

Model Properties: SIR continuous time Markov chain:

The discrete random variables for the SIR continuous time Markov chain model satisfy S(t), I(t) ∈ {0,1,2....N}, where t ∈ [0,∞). The lower case s and i denote the values of the discrete random variables from the set {0,1,2,.....N}. The transition probabilities associated with the stochastic process are defined for a small period of time Δt > 0;

$$P_{(s,i),(s+k,i+j)}(\Delta t) = P(S(t+\Delta t),I(t+\Delta t)) = \{(s+k,i+j)/(S(t), I(t)) = (s,i)\}$$

The transition probabilities depend on the time between events Δt but not on the specific time t, a time - homogeneous process. In addition, given the current state of the processat time t, the future state of the process at time t + Δt, for any Δt > 0, does not depend in terms prior to t, known as the Markov property. For comparison purposes, the transition probabilities are defined in terms of the rates in the SIR ODE model:

$$P_{(s,i),(s+k,i+j)}(\Delta t) = \{\beta i\frac{S}{N}\Delta t + o(\Delta t), (k,j) = (-1, 1);\ \alpha i\Delta t + o(\Delta t),(k,j) = (0, -1);$$

$$1- (\beta i\frac{S}{N} + \alpha i)\,\Delta t + o(\Delta t), (k,j) = (0, 0);\ o(\Delta t), \text{otherwise.}\}(4)$$

ΔS(t) = S(t + Δt) – S(t) and ΔI(t) = I(t + Δt) – I(t), associated with the two events, infective and recovery. Given S(0) = N – i and I(0) = i > 0, the epidemic ends at time t, when I(t) = 0. The states (S,I), where I = 0 are referred to as absorbing states; the epidemic stops when an absorbing state is reached. The absorbing states are the states (s,i) with i = 0.

Stochastic differential equations

Differential equations for the transition probabilities can be derived from (4), these are often referred to as the forward or the backward Kolmogorov differential equations. The forward equations are used to predict the future dynamics, whereas the backward equations are used to study the end of the epidemic, such as estimating the probability of reaching an absorbing state.

Note that there are (N + 1)(N + 2)/2 ordered pairs of states (s,i); (s,i) ∈ {(N,0), (N – 1, 1), ...(0,0)}, where s+i ≤ N, and u ,v are two ordered pairs from the set of (N + 1)(N + 2)/2. The general form of the forward and the backward Kolmogorov differential equations are

$$\frac{dPu,v(t)}{dt} = \sum_{k\neq u} p_{u,k}(t)\, q_{k,v} - q_{u,u}\, p_{u,v}(t) \quad (5)$$

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Where the values of $q_{k,v}$, $q_{u,u}$ and $q_{u,k}$ are defined from the transition rates in Equation (4)

In the forward equations, the transition rates depend on the future state v = (s,i). If u is any state, for the process to be in state v = (s,i) at time t + Δt, one of the following events occurs (1) the process transitions from u to (s+1,i-1) in time t and an infection occurs with transition probability β(s+1,i-1)Δt/N + o(Δt) or (2) the process transitions from u to (s,i+1) in time t and a recovery occurs with transition probability α(i+1) Δt + o(Δt) or (3) the process transitions from u to (s,i) in time t and no change occurs with transition probability 1- $(\beta i\frac{s}{N} + \alpha i)$ Δt + o(Δt).

That is, $P_{u,(s,i)}(t + \Delta t) = P_{u,(s+1,i-1)}(t)(\beta(s+1,i-1)\Delta t/N) + P_{u,(s,i+1)}(t)\alpha(i+1)\,\Delta t + P_{u,(s,i)}(t)$ [1- $(\beta i\frac{s}{N} + \alpha i)\,\Delta t$] + o(Δt). Subtracting $P_{u,(s,i)}(t)$ from both sides, dividing by Δt, and letting Δt→0, leads to the forward Kolmogorov differential equations,

$$\frac{dPu,(s,i)(t)}{dt} = P_{u,(s+1,i-1)}(t)(\beta(s+1,i-1)/N) + P_{u,(s,i+1)}(t)\alpha(i+1) - P_{u,(s,i)}(t)(\beta i\frac{s}{N} + \alpha i), \quad (7)$$

similar derivation applies to the backward equations,

$$\frac{dP(s,i),v(t)}{dt} = P_{(s+1,i-1),v}(t)(\beta si/N) + P_{(s,i-1),v}(t)\alpha i - P_{(s,i),v}(t)(\beta i\frac{s}{N} + \alpha i). \quad (8)$$

Herd Immunity and Vaccination

One reason for modelling infectious disease spread is to understand how an outbreak can be prevented. Suppose a vaccine is available prior to the arrival of the disease spread, a fraction μ are vaccinated, all vaccinated individuals get completely immune. The number of initially susceptible is reduced from n – m to n(1 - μ) – m. Then the reproduction number R_o, after a fraction has been vaccinated, denoted R_μ satisfies $R_\mu = \beta(1 - \mu)/\alpha = (1 - \mu)R_o$, and the fact that a major outbreak is impossible if $R_\mu \leq 1$.In terms of μ this is equivalent to $\mu \geq 1 - 1/R_o$. The critical vaccination coverage, denoted μ_c and the fraction necessary to vaccinate in order to prevent a major outbreak, hence satisfies $\mu_c = 1 - 1/R_o$. For the numerical example given above, with $R_o = 1.5$ it follows that $\mu_c = 1 - 1/1.5 \approx 0.33$ in[7]. This means that it is enough to vaccinate 33%of the community is hence protected, a state denoted Herd immunity.

Discussion and Conclusions

Mathematical models are very useful as guidance for health professionals when deciding about preventive measures aiming at reducing the spread of a disease. Stochastic epidemic models,

or minor modifications of them, can be used also in other areas. Example: Models for the spread of rumours or knowledge; Computer viruses in[8]. In conclusion, we analyzed and discussed the stochastic SIR epidemic model with various parameters. The model relies on these vital parameters because they play a part in determining epidemic states in population. And the vaccination can be several different ways. When it comes to new emerging severe infections, drastic measures like isolation, closing of schools and travel restrictions are often put in place. All these measures aim at reducing contact rate R_o. The effect of a specific preventive measure depends on the particular disease and also on the community under consideration. The SIR stochastic epidemic model has proven to be a reliable mathematical tool for examining epidemic status in a big community.

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