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Effects of treatment rates in a stochastic Susceptible-Infectious –Removed (SIR) model

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Abstract

In this paper, we formulate a Continuous Time Markov Chain (CTMC) model with two types of treatment rates: (i) Constant treatment rate (ii) simple linear treatment rate. The model has been driven from the standard susceptible-infected-removed (SIR) epidemic model. Numerical simulations are used to assess the effect of variation in the treatment term relative to the constant recruitment rate A. It is shown that with R_{01} or R_{02} less than unity, whether or not the recruitment rate is greater than or equal to the treatment term, the disease sample paths approach a disease free equilibrium, but for the basic reproduction number (R_{01} or R_{02}) greater than unity, the sample paths approach an endemic equilibrium state. While the simple linear treatment rate predicts equal decay rate in all cases, the constant treatment rate shows the deterministic paths have higher disease prevalence at the peak of the outbreak and the stochastic realizations a faster decay rate. Our results further demonstrate the effects of treatment in predicting disease prevalence and decay rate.

Keywords: Basic reproduction number; deterministic; disease equilibrium; Markov chain; Continuous Time Markov Chain.

1.0 Introduction

Epidemics have many a time had a great impact on population sizes and historical events as was seen in the historic bubonic plague [1]hence understanding of the dynamics of its treatment is critical to human survival and happiness. According to Daleh and Gani [2], the modeling of infectious diseases is a tool which has been used to study the mechanism by which diseases spread, to predict future course of an outbreak and to evaluate strategies to curtail or contain the spread. Although the foundation of ecological and epidemiological modeling has been largely deterministic, a major shortcoming of deterministic models is their inability to include an element of uncertainty or noise. Since human disease transmission is inherently stochastic due to random nature of person to person contact [3] and notably too, since human population distribution is subject to a number of disturbances which are also random [4, 5], the need to incorporate stochasticity in disease modeling becomes imperative. In this view a growing body of research suggests that demographic stochastic effects due to the randomness in nature affect this deterministic modeling ideal [6 – 12].

Allen and Burgin [13] presented a comparison of the deterministic and stochastic SIS and SIR models in discrete time and showed that disease extinction and persistence depends on the basic reproduction number in the deterministic model and that ultimate disease extinction was certain in stochastic counterpart regardless of the value of the basic reproduction number R_0.

Allen and Kirupaharan [14] showed that the deterministic and stochastic models differ considerably in predicting coexistence of two pathogens.For more review work on stochastic modeling and models see [15].

Generally SIR disease model deals with an infection where recovered individuals are completely immune [16]. According to Hethcote [17] the SIR model is classified into two: (i) the classic epidemic type – the one without vital dynamicsand (ii) The classic endemic type– one with vital dynamics. The stochastic SIR model is a derivative of the deterministic model. In this paper we use an SIR model of the classic endemic type, formulate the stochastic version of the deterministic model following the method given in Allen [18, 5]and investigate the effects of varied treatment on the stochastic model dynamics.

Treatment programs are common methods used in disease eradication from a given population [19],since treatment is a very important and effective method in preventing and controlling the spread of various infectious diseases. According to Anderson and May [20], in classical epidemic models, the treatment rate of the infectives is assumed to be proportional to the number of the infected individuals. A case of the SARS outbreaks in 2003, the spontaneous increasing of SARS beyond what has ever been seen created a paradigm shift and forced the government of China to create the first and only SARS hospital, Beijing Xiaotangshan Hospital, to treat the large number of SARS patients [21].

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This experience was an eye opener to researchers to the potency of treatment both from the modeling and analyzing point of view. Xu et al [22] formulated a CTMC model for an influenza epidemic with drug resistance and studied the effect of different treatment strategies through numerical simulations. Billings et al. [23] quantified how treatment enhances the extinction of epidemics in a stochastic SIS model. Hussaini and Winter [24] considered a susceptible-infected-removed (SIR) epidemic model with non smooth treatment rates and analysed the travelling wave solutions.

In this paper, we adopt two forms of treatment: simple linear treatment and constant treatment rate using an SIR model as in [24] with a modified treatment function. Following the procedure postulated in [18, 5], we formulate the Stochastic models from the deterministic model. The numerical results from the stochastic model using the CTMC formulation was used to compare the effect of variation in the respective treatment rates relative to the constant recruitment rate. Formulations of the other stochastic models: the SDE and the DTMC were done in the appendix. The deterministic model is used to compute the basic reproduction number under constant and simple linear treatment rates respectively.

The rest of this paper is organized in the following way: In section twowe present the basic deterministic model and the assumptions that will be used in our analysis. In section three we state the basic reproduction numbers for the constant treatment rate and for the simple linear treatment case. In section four, we formulate the stochastic model, the CTMC from the basic deterministic model and carry out numerical simulations in five. In the last section we give a summary of our results.

2.0 Deterministic Model

The deterministic model (1) is a system of ordinary differential equation andrepresents an SIR model in the continuous case with a treatment rates: (i) constant and (ii) simple linear rate as given in (2). This deterministic model forms the basis for the formulation of the CTMC model (and the SDE and the DTMC, in the appendix) which incorporates variability due to death, birth, recovery, infection or transmission process.

$$\frac{ds}{dt} = A - dS - \boldsymbol{\lambda} SI$$
$$\frac{dI}{dt} = \boldsymbol{\lambda} SI - dI - T(I) \quad (1)$$
$$\frac{dR}{dt} = T(I) - dR$$

Where (i) T(I) = r and (ii) T(I) = rI (2)

for the constant treatment rate and simple linear treatment rates respectively.

Let S(t) be the number of susceptible individuals, I(t) the number of infective individuals,and R(t) the number of removed or recovered individuals at time t.The constant A is the recruitment rate of the population,d the natural death rate of the population and $\boldsymbol{\lambda}$the force of infection associated withthe transmission of the disease from susceptibles to infecteds, T(I)is the removal rate of infective individualsdue to the treatment of infectives and takes into account the limited capacity of treatment facilities.

The dynamics of model (1) depends on the basic reproduction number R_0. Since the first two equations of model (1) is independent of the third, it suffices to consider the reduced model (3) in the analysis.

$$\frac{ds}{dt} = A - dS - \boldsymbol{\lambda} SI$$
$$\frac{dI}{dt} = \boldsymbol{\lambda} SI - dI - T(I) \quad (3)$$

3.0 Basic Reproduction number (R_0)

According to Keeling and Rohani[25], R_0 is the mean number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible.The basic reproduction number is very useful in predicting whether or not there will be an outbreak in stochastic models as well, an instance is seen in the simple CTMC SIR epidemic model with I(0) initial infected individuals, where it was shown there is no outbreak with probability $(\frac{1}{R_0})^{I(0)} and$ an outbreak with the probability 1 - $(\frac{1}{R_0})^{I(0)}$[22, 18,15]. The basic reproduction number R_0 of model (1) is computedat the constant and simple linear treatment rates.Now for the simple linear treatment rate, that is for T(I) = rI, following [21].The basic reproduction number is

$$R_{01}=\frac{A}{d}(\frac{\lambda}{d+r}), \quad (4)$$

But for the constant treatment rate, where T(I) = r,the basic reproduction numberis given as:

$$R_{02} = \boldsymbol{\lambda} A/d^2 \quad (5)$$

This thresholdsdetermine whether a disease invades a population or not but the knowledge of which is not sufficient to determine the long term disease dynamics [26, 27]

4.0 Stochastic Models

There are three main stochastic models commonly used in population biology. Discrete-time Markov chain model, continuous-time Markov chain and stochastic differential equation model. These models take into account the random nature of the individual birth and death process, which we call demographic variability [28]. We show the formulations of the stochastic models for the continuous time markov chain model for the model (1). The formulation is done following the method in Allen [18, 5] while incorporating the respective treatment rates: the constant and linear treatment rates.

4.1 Continuous Time Markov Chain (CTMC) Model

The CTMC model is defined on a continuous time scale, $t \in [0, \infty)$ but the state variables are discrete, i.e., S(t) , I(t) , R(t) ∈ { 0,1, 2, …,N). Under the assumption that Δt is sufficiently small and that at most one change occurs during the time interval Δt.The process of formulation is the same with that of DTMC (see Appendix) except that o(Δt) is added to each of the infinitesimal transition probabilities.The o(Δt) symbol represents a negligible remainder term in the sense that if we divide the term by Δt, then the resulting value tends to zero as Δt tends to zero[29].The CTMC model is bivariate and R(t) = N – S (t) – I (t). For this bivariate process a joint probability function is associated with each pair of random variables (S(t), I(t)) , $P_{(s,i)}(t)$ = Prob{S(t), I(t) =(s, i)}. From the deterministic model (1) the infinitesimal transition probabilities associated with the changes in states are given:

$$P_{(s+k,i+j)(s,i)}\,\Delta t = \begin{cases} \lambda SI\Delta t + o(\Delta t) & (k,j) = (-1,1) \\ rI\Delta t + o\Delta t & (k,j) = (0,-1) \\ A\Delta t + o\Delta t & (k,j) = (1,0) \\ dS\Delta t + o\Delta t & (k,j) = (-1,0) \\ dI\Delta t + o\Delta t & (k,j) = (0,-1) \\ 1 - (\lambda SI + rI + dS + A + dI)\Delta t + o\Delta t & (k,j) = (0,0) \\ o\Delta t & otherwise \end{cases} \quad (6)$$

The transition probabilities (6) define completely the CTMC model for the simple linear treatment rate.

$P_{(s+k,i+j)(s,i)}\ \Delta t$ = prob{ $(\Delta S, \Delta I) = (k, j) | S(t), I(t) = (s, i)\}$ satisfies the system of forward Kolmogorov differential equation from the infinitesimal transition probabilities:

$$\frac{dP_{(s,i)}}{dt} = P_{(s+1,i-1)}\lambda(s+1)(i-1) + P_{(s,i+1)}r(i+1) + P_{(s+1,i)}d(s+1) + P_{(s,i+1)}d(i+1) + P_{(s-1,i)}A - P_{(s,i)}[\lambda si + ds + di + ri + A]$$

,s,i ∈{1,2,3,…,N} (7)

In [29], the differential equation forms the limiting value of DTMC (see the appendix) when $\Delta t \to 0$ and can be written in matrix form as

$$dP/dt = Qp, P_{i_0}(0) = 1, \quad (8)$$

the matrix Q is called the infinitesimal generator matrix formulated with respect to the infections class and has the form:

$$Q = \begin{pmatrix} 0 & (dI + rI)(1)\Delta t & 0 & 0 & \dots & 0 \\ 0 & -(\lambda SI(1) + (dI + rI)(1))\Delta t & (dI + rI)(2)\Delta t & 0 & \dots & 0 \\ 0 & \lambda SI(1)\Delta t & -(\lambda SI(2) + (dI + rI)(2))\Delta t & (dI + rI)(3)\Delta t & \dots & 0 \\ 0 & 0 & \lambda SI(2)\Delta t & -(\lambda SI(3) + (dI + rI)(3))\Delta t & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & 0 \\ 0 & 0 & 0 & 0 & \dots & (dI + rI)(N)\Delta t \\ 0 & 0 & 0 & 0 & \dots & -(dI + rI)(N)\Delta t \end{pmatrix} \quad (9)$$

Where the transition matrix P(Δt)of the DTMC model and the generator matrix Q are related as follows: $Q = \lim_{\Delta t \to 0}(P\Delta t - 1)/\Delta t$ [18].

4.2 For constant treatment term: T(I) = r

Following the same process as above the results for the transitional probabilities and the forward Kolmogorov's equation for the CTMC model with a constant treatment termis given in (10) and (11) as:

$$P_{(s+k,i+j)(s,i)}\,\Delta t = \begin{cases} \lambda SI\Delta t + o(\Delta t) & (k,j) = (-1,1) \\ dS\Delta t + o\Delta t & (k,j) = (-1,0) \\ dI\Delta t + o\Delta t & (k,j) = (0,-1) \\ r\Delta t + o\Delta t & (k,j) = (0,-1) \\ A\Delta t + o\Delta t & (k,j) = (1,0) \\ 1 - (\lambda SI + r + dS + dI + A)\Delta t + o\Delta t & (k,j) = (0,0) \\ o\Delta t & otherwise \end{cases} \quad (10)$$

From where we get a system of forward Kolmogorov differential equation which has the form

$$\frac{dP(s,i)}{dt} = P_{(s+1,i-1)}\boldsymbol{\lambda}(s+1)(s-1) + P_{(s,i+1)}r + P_{(s-1,i)}A + P_{(s+1,i)}d(s+1) + P_{(s,i-1)}d(I-1) - P_{(s,i)}[\boldsymbol{\lambda}si + A + ds + di + r](s,i) \in \{1,2,3,\ldots,N\} \quad (11)$$

For another constant treatment case: where T(I) = 0, the formulation gives the result (12) given as:

$$P_{(s+k,i+j)}(s,i)\,\Delta t = \begin{cases} \lambda SI\Delta t + o(\Delta t) & (k,j) = (-1,1) \\ dS\Delta t + o\Delta t & (k,j) = (-1,0) \\ dI\Delta t + o\Delta t & (k,j) = (0,-1) \\ A\Delta t + o\Delta t & (k,j) = (1,0) \\ 1 - (\lambda SI + dS + dI + A)\Delta t + o\Delta t & (k,j) = (0,0) \\ o\Delta t & otherwise \end{cases} \quad (12)$$

From where we get a system of forward Kolmogorov differential equation which has the form

$$\frac{dP_{(s,i)}}{dt} = P_{(s+1,i-1)}\boldsymbol{\lambda}(s+1)(i-1) + P_{(s-1,i)}A + P_{(s+1,i)}d(s+1) + P_{(s,i-1)}d(i-1) - P(s,i)[\boldsymbol{\lambda}si + A + ds + di]$$

with $s, i \in \{1,2,3,\ldots,N\}$ (13)

5.0 Numerical simulations

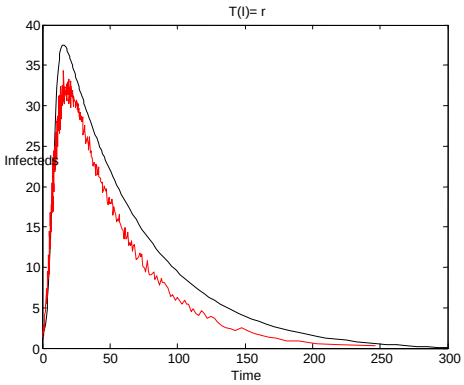
For the numerical simulations, we present examples with treatment rates reflecting: constant treatment (T(I) = r) and simple linear treatment rates (T(I) = rI); with variations in r relative to the recruitment rate A and the basic reproduction numbers at each of the points. Given the recruitment rate A, the values of r chosen reflect the cases for which r >A, r <A and r = A.CasesIIa, IIb and IIcare simple linear treatment correspondents of Cases Ia, Ib and Ic respectively which has a constant treatment rate.A sample path for the stochastic formulation is compared with the deterministic path in all the figures at the respective values of r and A. The initial values were taken for I(0) = 1.Emergence, persistence and extinction behavior of the models were observed with respect to the different treatment terms with their respective reproduction numbers. The basic parameter values for the various cases are given in Table 1.

CASE I: *Constant treatment*

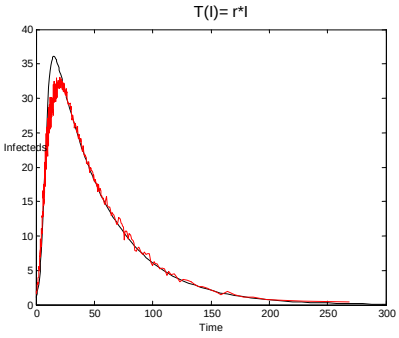
Cases Ia, Ib and Ic show the graphs of the deterministic solution (smooth curve) and a sample path of a stochastic model (non smooth curve) for a constant treatment with parameter values as shown in Table 1 and the population size 50 graphed under 300 days interval. In Fig.1, with r> A and the basic reproduction number less than unity, the sample paths approach a disease free equilibrium and eventual disease extinction. The outbreak is at its peak within 30 days with the deterministic path projecting about 38 infecteds while the stochastic path predicts close to 33 infecteds at the peak. The stochastic path decays faster than the deterministic in all the cases with constant treatment. In Fig.2, with the treatment term less than the recruitment rate and the basic reproduction number more than unity, the sample paths approach endemic equilibrium with the deterministic at 22 infecteds while the stochastic stays at about 5 infecteds in case per population of 50 people. In Fig.3 the treatment rate equals the recruitment rate, and the basic reproduction number is less than unity. The sample realizations tend to a disease free equilibrium.

Table 1; Parameter values used in the simulations for the cases. All other parameters are the same, variations were only done for the recruitment rate A, and r in all the cases.

	$\boldsymbol{\lambda}$	**d**	**A**	**r**	$\mathbf{R_{01}}$	$\mathbf{1/R_{01}}$	$\mathbf{R_{02}}$	$\mathbf{1/R_{02}}$
case Ia	0.0100	0.0167	0.0010	0.0.005			0.0360	27.78
Case Ib	0.0100	0.0167	0.5000	0.1			18	0.0556
Case Ic	0.0100	0.0167	0.0050	0.005			0.18	5.56
CaseIIa	0.0100	0.0167	0.0010	0.005	0.0277	36.111		
CaseIIb	0.0100	0.0167	0.5000	0.1	2.5714	0.3889		
CaseIIc	0.0100	0.0167	0.0050	0.0050	0.1385	7.222		

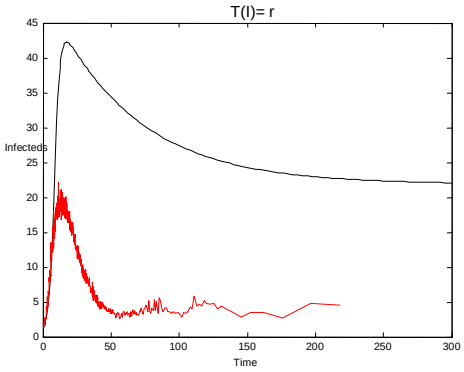


Case Ia: T(I) = r

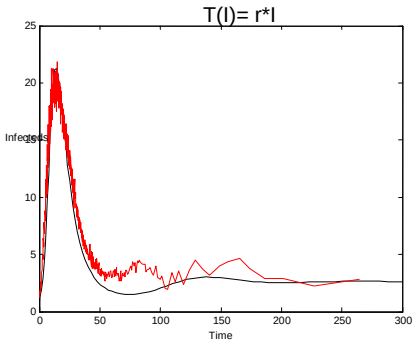


Case IIa: T(I) =rI

Fig. 1A sample path of CTMC model (non smooth curve) with the deterministic path (the smooth curve) with parameter valuesA = 0.001, r = 0.00500, R_{02} = 0.0360, R_{01} = 0.0277 where case 1a represents the constant treatment case and case IIa, the simple linear treatment counterpart, with r > A.



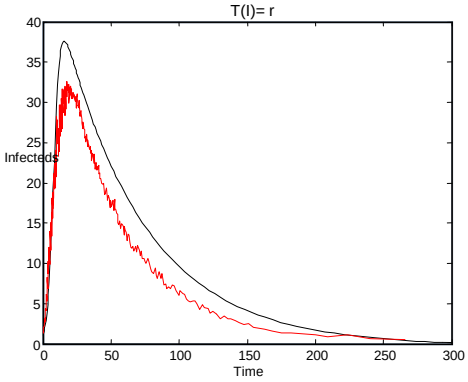
Case Ib: T(I) = r



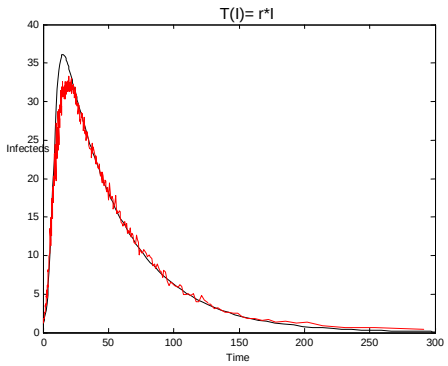
Case IIb

Figure 2. The deterministic solution (smooth curve) and the corresponding stochastic realization (non smooth curve)withr<A and values: r = 0.1, A = 0.5, R_{02}= 18, R_{01}= 2.5714 with other parameter values as shown in Table 1, case 1b is the constant treatment case and IIb is the simple linear treatment counterpart.

Case Ic: T(I) = r



Case Ic: T(I) = r



Case IIc

Figure 3:A graph of the stochastic and deterministic realization for r = A whereA = 0.005, r = 0.005, R_{02} =0.18, R_{01} =0.1385 with other parameter values as shown in Table 1, case Ic is the constant treatment case and IIc is the simple linear treatment counterpart

CASE II: Simple Linear Treatment Rate

A sample path or stochastic realization (non smooth curve) is graphed for the CTMC stochastic model and compared to the solution of the deterministic model for the case of simple linear treatment rate T(I) = rI.CasesIIa, IIb, and IIc are the simple linear treatment rates correspondents of CasesIa, Ib and Ic respectively. Unlike in Case Ia, Case IIa (in Fig. 1) shows an equal decay rate in the stochastic and deterministic realizations though still the paths tend to disease free equilibrium but the incidence is lower than in Case Ia. In Case IIb, in Fig.2 an endemic equilibrium is reached at about 3 persons per population of 50 in contrast to the result of Case Ib which is endemic at a population of 22 and 5 for deterministic and stochastic sample paths respectively showing there is more agreement in the general stochastic results than the deterministic results.CaseIIc the outbreak attain its peak within about 25 days of emergence and tends to disease free equilibrium later. Generally it is observed that with simple linear treatment rate the stochastic and deterministic results coincide, but with the constant treatment rate there is an unequal decay rates in the paths.

6.0 Discussion

We presented in brief, a review of the literature on stochastic modeling and the impact of treatment function on disease control. We formulated a Continuous Time Markov Chain (CTMC) SIR model from the deterministic modelwith respect to constant and linear treatment rates respectively. The basic reproduction number of the model relative to this two treatment types is explored. Since the model under study assumes a constant recruitment rate A,the effect of variation in the treatment term r relative to the constant recruitment rate is investigated numerically. With the basic reproduction number less than unity, whether or not the recruitment rate is greater than the treatment rate, it is observed that the disease sample paths approach a disease free equilibrium position. More so, whenever the basic reproduction number is greater than unity, the sample paths tendto an endemic equilibrium position. In addition, disease prevalence in thestochastic path is observed to be generally lower compared to the deterministic path. Generally stochastic and deterministic results are seen to agree in the simple linear treatment case which is not so for the constant treatment case. Our results further emphasize the importance of understanding treatment in the context of disease modeling and control. These results have far reaching implications for control strategies aiming at total disease eradication from the population. Of course, if an optimal result is sought, which generally is the case, an effective treatment type suitable to the prevailing condition must be adopted. The target for health workers would be on any means to decrease or regulate the recruitment rate into the population so much so as to ensure that the treatment term is raised enough to make the basic reproduction number less than unity for effective disease control.

7.0 Conclusion

These results help to bridge the gap between deterministicand stochastic model analysis for the study of infectious diseases in relation to treatment. There remains much more to be done though, but the above mathematical formulations and insights from computer simulations may serve as a useful basis for further research.

Appendix

A.1. DTMC model

In the DTMC model the population size and time are both discrete valued. If S(t), I(t), and R(t) denote discrete random variables for the number of susceptible, infected and immune or recovered individuals at time t, respectively then S(t), I(t), R(t) and $t \in \{1,2,3,\dots,N\}$.The DTMC model is a bivariate process because the susceptible S(t)and the infectious I(t) class are independent random variables while the recovered class, R(t), is the dependent random variable, given by;R (t) = N - S (t) – I (t).

This bivariate process $\{S(t), I(t)\}_{t=0}^{\infty}$ has a joint probability function given by;

$P_{(s;\, i)}$ (t) = Prob {S(t) = s, I(t) = i} where s, i= 0, 1, 2, . . .,N. According to Allen [30] the bivariate process defined above has the Markov property and is time homogeneous. IfΔt is sufficiently small such that at most one change in state occurs during the time interval Δt, then the transition probabilities:$P_{(s+k,\, i+j),(s,i\,)}(\Delta t)$ = Prob {(ΔS, Δ I) = (k, j) | S(t), I (t) = (s, i)}

whereΔS = S (t+ Δt) - S (t) represents the change in population size of susceptible from time t to time $t + \Delta t$. Hence for the simple linear treatment rate, where T(I) = rI ,the transition probability formulated with respect to the transitions at the various states is given by:

$$P_{(s+k,i+j),(s,i)}(\Delta t) = \begin{cases} \lambda SI\Delta t & (k,j) = (-1,1) \\ rI\Delta t & (k,j) = (0,-1) \\ A\Delta t & (k,j) = (1,0) \\ dS\Delta t & (k,j) = (-1,0) \\ dI\Delta t & (k,j) = (0,-1) \\ 1 - \lambda SI\Delta t - (rI + A + dI + dS)\Delta t & (k,j) = (0,0) \\ 0 & otherwise \end{cases} \quad (14)$$

where Δt is chosen sufficiently small such that each of the transition probabilities lie within the interval [0,1]. Applying the Markov property, the difference equation satisfied by the probability $P_{(s,\,i)}$ (t+ Δt) can be expressed in terms of the transition probabilities as;

$P_{(s,i)}(t+\Delta t) = P_{(s+1,i-1)}(t)\boldsymbol{\lambda}(s+1)(i-1)\Delta t + P_{(s,\,i+1)}(t)\, r(i+1)\Delta t + P_{(s-1,i)}(t)A\Delta t + P_{(s,\,i+1)}(t)\, d(i+1)\Delta t + P_{(s+1,\,i)}(t)\, d(s+1)\Delta t + P(s,i)(1-(\boldsymbol{\lambda} si + di + ds + A + ri)\Delta t)$ for s, i ∈{1,2,3,…,N} (15)

The difference equations project forward in time andcan be expressed in matrix form as

A.1 $P(t+\Delta t) = Qp(t)$, $P_{i_0}(0) = 1$, (16)

where matrix $Q = p_{ij}(\Delta t)$ is the transition matrix . We set p to be the row vector of the $N+1$ probability. In this vector notation, the Kolmogorov forward equation becomes $\frac{dP}{dt} = pQ$,where the matrix Q is

$$\begin{pmatrix} 1 & (dI+rI)(1)\Delta t & 0 & 0 & \dots & 0 \\ 0 & 1-\big(\lambda SI(1)+(dI+rI)(1)\big)\Delta t & (dI+rI)(2)\Delta t & 0 & \dots & 0 \\ 0 & \lambda SI(1)\Delta t & 1-\big(\lambda SI(2)+(dI+rI)(2)\big)\Delta t & (dI+rI)(3)\Delta t & \dots & 0 \\ 0 & 0 & \lambda SI(2)\Delta t & 1-\big(\lambda SI(3)+(dI+rI)(3)\big)\Delta t & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & 0 \\ 0 & 0 & 0 & 0 & \dots & (dI+rI)(N)\Delta t \\ 0 & 0 & 0 & 0 & \dots & 1-(dI+rI)(N)\Delta t \end{pmatrix} \quad (17)$$

To ensure that Q is a stochastic matrix, in the sense that Q is nonnegative and the column elements sum to one, it is assumed thatmax $\{\lambda SI + (dI+rI)\}\Delta t \le 1$.

It is worthy of note to state that the state (N, 0) is an absorbing state; that is a state in which no other state can be reached ($P_{(N,\,0)\,(N,\,0)}(\Delta t)$ =1) and all other states are transient[18, 5, 30]

A.2. SDEmodel

Stochastic differential equations take into account variability in the birth, death, and transmission rates of each of the populations. Here both time and state are continuous variables. Ito's SDEs are derived from model (1) assuming that changes in random variables, over short time steps are normally- distributed and that the random variability is only due to births, deaths, and migrations, i.e. demographic variability without considering environmental variability. We follow here the derivation given in [30].

The stochastic differential equation model also has the markov property with probability $P_{(s+k,\,i+j)\,,\,(s,\,i\,)}(\Delta t)$ = prob{ $\Delta S, \Delta I) = (k, j)|(S(t), I(t) = (s, i))$}

The stochastic process is referred to as a diffusion process since it is a Markov process and the infinitesimal mean and variance exist. An Ito's SDE model can be formulated based on the transition probabilities defined in (10) following the method postulated by Allen [18, 30]. The SDE model is given in terms of the drift vector, diffusion matrix and an independent wiener process. The Ito's SDE is of the form:dX(t) =**f(X(t)**, t)dt + G(X(t), t)dW(t) where f(X(t) is the drift vector, G(X(t), t) is the diffusion matrix and W(t) is an independent wiener process.

To compute the drift vector **f(X(t))**, we apply the transitions (10) and compute the expectations , where

$E(\Delta S(t)) = [A - (\lambda I + d)S]\Delta t + o(\Delta t)$

$= f_1(\mathbf{X(t)}\Delta t + o(\Delta t)$which gives the value of the random variable at time t. Generally

$$E\big(\Delta \boldsymbol{X}(\boldsymbol{t})\big) = E\begin{pmatrix}\Delta S(t)\\ \Delta I(t)\\ \Delta R(t)\end{pmatrix} = \begin{pmatrix} f_1(\mathbf{X(t)}\,\Delta t + o(\Delta t)\\ f_2(\mathbf{X(t)}\,\Delta t + o(\Delta t)\\ f_3(\mathbf{X(t)}\,\Delta t + o(\Delta t)\end{pmatrix} = f\ \mathbf{(X(t)}\Delta t + o(\Delta t) \quad (18)$$

Where in this case the drift vector f **(X(t)** has the same form as the right side of the deterministic model.

Let $X(t) = (\Delta S(t), \Delta I(t))^T$

The covariance matrix of $\Delta X(t)$ is $V(\Delta X(t))$ and is defined :

$E(\Delta \boldsymbol{X}(\boldsymbol{t})[\Delta \boldsymbol{X}(\boldsymbol{t})]^T) - E(\Delta \mathbf{X(t))E(}\Delta \boldsymbol{X}(t))^T \cong E(\Delta X(t)[\,\Delta X(t)]^T + o(\Delta t) = \mathrm{var}(\Delta X(t))$

Hence the diffusion matrix G(X(t), t)is a 3 x3 matrix defined by $\begin{pmatrix}(\Delta S)^2 & \Delta S\Delta I & \Delta S\Delta R\\ \Delta S\Delta I & (\Delta I)^2 & \Delta I\Delta R\\ \Delta S\Delta R & \Delta R\Delta I & (\Delta R)^2\end{pmatrix}$ (19)

Where the non zero entries of $E(\Delta X(t)[\,\Delta X(t)]^T$are gotten from the transitional probabilities in (10) as:

$E((\Delta S)^2) = [A + (\lambda I + d)S]\,\Delta t + o(\Delta t)$

$E(\Delta S\ \ \Delta I) = -\,dS\Delta t + o(\Delta t)$

$E(\Delta S\ \ \Delta I) = -\lambda S\, I\,\Delta t + o(\Delta t)$

$E(\Delta I)^2 = (dI + T(I))\,\Delta t + o(\Delta t)$ (20)

$E(\Delta I \Delta R) = -T(I)\,\Delta t + o(\Delta t)$

$E(\Delta R \Delta I) = -T(I)\,\Delta t + o(\Delta t)$

$E(\Delta R)^2 = dR\ \Delta t + o(\Delta t)$

If we define G(X(t)) as the diffusion matrix, entries in G are defined in terms of the transition changes in a transmission, recovery, recruitment and death in square root i.e. $\sqrt{\lambda SI}, \sqrt{A}, \sqrt{dS}, \sqrt{dI}, \sqrt{rI}$ to denote the changes in the various transitions. Hence the diffusion matrix can be defined as:

$$G(X(t)) = \begin{pmatrix} \sqrt{A} & -\sqrt{\lambda SI} & -\sqrt{dS} & 0 \\ 0 & \sqrt{\lambda SI} & -\sqrt{(d+r)I} & 0 \\ 0 & 0 & \sqrt{rI}\,\sqrt{dR} & \end{pmatrix} \quad (21)$$

Hence Ito's SDE takes the form:

$dX(t) = f(X(t), t)dt + G(X(t), t)dW(t)$

$$dS = -[\lambda SI + dS - A]dt - \sqrt{\lambda SI + dS + A}\,dW_1 \quad (22)$$

$dI = (\lambda SI - dI - rI)dt + \sqrt{\lambda SI + rI + dI}\,dW_2$.

where W_1 and W_2 are two independent Wiener processes.

The terms W_1 and W_2 associated with the Wiener process makes the model a stochastic SDE model; if they are dropped the model becomes an ODE model

A.3. DTMC and SDE for a constant treatment rate

The formulations of theDTMC and SDE models for a constant treatment term follow the same process as we did above for T (I) = rI. Where we have the results for the transitional probabilities and the forward Kolmogorov's equation for the DTMC and the SDE models respectively as:

For the DTMC model the transitional probability will be:

$$P_{(s+k,i+j),(s,i)}\Delta t = \begin{cases} \lambda SI\Delta t & (k,j) = (-1,1) \\ dS\Delta t & (k,j) = (-1,0) \\ r\Delta t & (k,j) = (0,-1) \\ A\Delta t & (k,j) = (1,0) \\ dI\Delta t & (k,j) = (0,-1) \\ 1 - \lambda SI\Delta t - (r + A + dS + dI)\Delta t & (k,j) = (0,0) \\ 0 & otherwise \end{cases} \quad (23)$$

Where the difference equation satisfied by the probability $P_{(s,\ i)}$ (t+ Δt) can be expressed in terms of the transition probabilities:

$P_{(s,i)}(t + \Delta t) = P_{(s+1,i-1)}(t)\boldsymbol{\lambda}(s + 1)(i - 1)\,\Delta t + P_{(s,\,i+1)}(t)\,r\Delta t + P_{(s+1,\,i)}(t)\,ds\Delta t + P(s-1,i)(t)A\,\Delta t + P(s,i)(1 - (\boldsymbol{\lambda}si\Delta t - [A + ds + di + r]\,\Delta t)i,s \in \{1,2,3,\ldots,N\}$ (24)

For the SDE model we will have:

$$dS = -[\lambda SI + dS - A]dt - \sqrt{\lambda SI + dS + A}\,dW_1$$

$$dI = (\lambda SI - dI - r)dt + \sqrt{\lambda SI + r + dI}\,dW_2 \quad (25)$$

where $W_1$and W_2 are independent Wiener process.

Finallyfor case (ii) if T(I) = 0, the formulation follows the same process to give the results below for the DTMC and SDE models respectively.

For the DTMC model the transitional probability will be:

$$P_{(s+k,i+j),(s,i)}\Delta t = \begin{cases} \lambda SI\Delta t & (k,j) = (-1,1) \\ dS\Delta t & (k,j) = (-1,0) \\ A\Delta t & (k,j) = (1,0) \\ dI\Delta t & (k,j) = (0,-1) \\ 1 - \lambda SI\Delta t - (A + dS + dI)\Delta t & (k,j) = (0,0) \\ 0 & otherwise \end{cases} \quad (26)$$

With the difference equation satisfied by the probability $P_{(s,\ i)}$ (t+ Δt) expressed in terms of the transition probabilities as:

$P_{(s,i)}(t + \Delta t) = P_{(s+1,i-1)}(t)\boldsymbol{\lambda}(s + 1)(i - 1)\,\Delta t + P(s-1,i)(t)A\,\Delta t + P(s+1,i)(t)d(s+1)\Delta t + P(s,i+1)(t)d(i+1)\Delta t + P(s,i)(1 - (\boldsymbol{\lambda}si\Delta t + A + ds + di]\,\Delta t), i,s \in \{1,2,3,\ldots,N\}$ (27)

And lastly for the SDE model we have:

$$dS = -[\lambda SI + dS - A]dt - \sqrt{\lambda SI + dS + A}\,dW_1$$

$dI = (\lambda SI - dI)dt + \sqrt{\lambda SI + dI}\,dW_2$ (28)where $W_1$and W_2 are terms associated with an independent Wiener process.

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