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A STOCHASTIC EPIDEMIC MODELFOR DYNAMIC OF INFECTIOUS DISEASES

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Abstract

After a short introduction of the deterministic SIS and SIR models, we present three types of stochastic epidemic models: discrete times Markov chain (DTMC) model, continuous times Markov chain (CTMC) model and stochastic differential equation (SDE) model. We discuss a stochastic epidemic model for dynamic of infectious diseases with variable population size, one which varies according to some population growth laws. Finally, we compare the stochastic differential equation of a SIS epidemic model having a constant population size with a stochastic differential equation having a variable population size.

Keywords**:** *model basic reproduction number, discrete times Markov chain (DTMC) model, continuous times Markov chain (CTMC) model and stochastic differential equation (SDE) model*

INTRODUCTION

The beginnings of mathematical applications in epidemiology relate to the "smallpox" model, by Daniel Bernoulli (1760) and a primary theory was developed between 1900-1935. The research continued and recent progresses recorded in our days, a good example being "The SARS" (Severe Acute Respiratory Syndrome) epidemic (2002-2003). Establishing forecasts on the evolution of infectious disease and the comparison of different control methods maintain at a high level the interest of researchers in mathematical modeling of epidemiology.

MATERIAL AND METHOD

1. The deterministic SIS and SIR Epidemic Models

Most epidemic models are based on the dividing of target population into a small number of compartments, each of them containing members that are identical in terms of their relationship towards a certain disease.

In a SIR model, the population is divided into three groups:

a) **S - susceptible**: individuals who don't have immunity to infectious agents and who have been exposed to the disease contact;
b) **I - infected**: individuals who have been recently infected and who transmit the infection to susceptible individuals who are in contact with them;
c) R- removed: individuals who are immune to the infection and who are not contaminated even if they come in contact with those categories a), b).

An example of SIR Epidemic Model is represented by childhood diseases.

If we denote $S(t), I(t), R(t)$, the number of individuals in each category in relation to time, the total population will be:

$$N(t) = S(t) + I(t) + R(t) \tag{1}$$

We observe that $S(t), I(t), R(t) \in N$ and for a sufficiently large volume of the total population, they are continuous random variables, their variation is characterized by the following system of differential equations:

$$\begin{cases} \dfrac{dS}{dt} = -\dfrac{\beta}{N}\cdot S\cdot I + b\left(I+R\right) \\ \dfrac{dI}{dt} = \dfrac{\beta}{N}\cdot S\cdot I - \left(b+\gamma\right)\cdot I \\ \dfrac{dR}{dt} = \gamma\cdot I - b\cdot R \end{cases} \quad (2)$$

where $\beta > 0$ is the transmission rate, $\gamma > 0$ is the recover rate and $b \geq 0$ is the birth rate.

The initial solution of the system (1) is:

$$S(0) > 0, I(0) > 0, R(0) \geq 0, \quad S(0) + I(0) + R(0) = N \quad (3)$$

where $N(0) = N$ is the population volume at the initial moment, when it downgraded the epidemic.

Observation:

If we note c, the death rate, we assume that in a SIR model, $b = c$ i.e. the birth rate is equal with the death rate, then the population volume is constant with respect to time, and $\dfrac{dN}{dt} = 0$.

Using the **basic reproduction number**, $R_0 = \dfrac{\beta}{b+\gamma}$, which represents the number of secondary infections caused by some infected individuals in the entire susceptible population (the fraction $\dfrac{1}{b+\gamma}$ is the interval of infection relative to deaths and recovery rate) the authorsJ. Mena-Lorca, H.W. Hethcote [6] characterize the system solution (2), in the following theorem:

Theorem 1

If $S(t), I(t), R(t)$ is the system solution (2), then:

a) for $R_0 \leq 1$, $\lim\limits_{t\to\infty} I(t) = 0$ (disease-free equilibrium)

$R_0 > 1$, $\lim\limits_{t\to\infty}(S(t), I(t), R(t)) =$

b) for $\left(\dfrac{N}{R_0}, \dfrac{b\cdot N}{b+\gamma}\left(1-\dfrac{1}{R_0}\right), \dfrac{\gamma\cdot N}{b+\gamma}\left(1-\dfrac{1}{R_0}\right)\right)$ (endemic equilibrium)

c) for $b = 0$ and $R_0 \cdot \dfrac{S(0)}{N} > 1$, there is an initial increase of the number of infected cases $I(t)$ and if $R_0 \cdot \dfrac{S(0)}{N} \leq 1$, then $I(t)$ monotone decreasing.

In a SIS Epidemic Model, a susceptible individual, after contact with an infected person in his turn becomes infected or infectious, but he doesn't develop immunity, i.e., after recovery, he returns in the susceptible category, so in such a model, the population is divided only into two categories: S-susceptible and I-infectious.

An example of a SIS Epidemic Model is represented sexually transmitted diseases (STDs).

With the same notations as in the SIR epidemic model and if we assume that all individuals are born susceptible and we don't find the deaths caused by that epidemic, the dynamics of the SIS epidemic model is described by the following system of differential equations:

$$\begin{cases} \dfrac{dS}{dt} = -\dfrac{\beta}{N}\cdot S\cdot I + \left(b+\gamma\right)\cdot I \\ \dfrac{dI}{dt} = \dfrac{\beta}{N}\cdot S\cdot I - \left(b+\gamma\right)\cdot I \end{cases} \quad (4)$$

In this case, the population size is:

$$N(t) = S(t) + I(t) \quad (5)$$

Observation:

If we assume as in the case of the SIR model $b = c$, then in a SIS epidemic model the population size is constant with respect to time, i.e. $\dfrac{dN}{dt} = 0$. The following theorem [6] characterizes the system dynamics model of differential equations (4) in relation to the variation of the basic reproduction number:

Theorem 2

If $S(t), I(t)$ is the system solution (4), then:

a) for $R_0 \leq 1$, $\lim\limits_{t\to\infty}\left(S(t), I(t)\right) = (N, 0)$ (disease-free equilibrium)

b) for $R_0 > 1$, $\lim\limits_{t\to\infty}(S(t), I(t)) = \left(\dfrac{N}{R_0}, N\cdot\left(1-\dfrac{1}{R_0}\right)\right)$ (endemic equilibrium)

Observation:

The interpretation of the first statements of the theorem is that if the number of secondary infections generated by the infected individuals is less than 1, then, $I(t) \to 0$ si $S(t) \to N$.

2. The Stochastic Epidemic Models

In this section we present three types of stochastic modeling processes: (1) a discrete time Markov chain (DTMC) model, (2) a continuous time

Markov chain (CTMC) model, and (3) a stochastic differential equation (SDE) model. The differences between these processes refer to time and to the set of states. In DTMC model, the time and the state are random discrete variables. In a CTMC model, time is continuous, but the state variable is discrete, finally, the SDE model is based on a diffusion process, where both the time and the state variables are continuous. One of the most important differences between the deterministic and stochastic epidemic models is their asymptotic dynamics. Eventually stochastic solutions (sample paths) converge to the disease-free state even though the corresponding deterministic solution converges to an endemic equilibrium.

2.1. Discrete Time Markov Chain Epidemic Models (DTMC)

Let on consider $S(t), I(t), R(t)$ random variables representing the number of individuals susceptible, infected, respectively immune to the time *t,* in relation to a specific infectious agent.

In a DTMC epidemic model, $t \in T = \{0, \Delta t, 2\Delta t, ...\}$ and the discrete variables $S(t), I(t), R(t) \in \{0,1,...N\}$.

Further, we refer to a SIS Epidemic Model. We consider that $N =$ the population size is constant and $I(t)$ is independent random variable. Then $S(t) = N - I(t)$ and the stochastic process $\{I(t)\}_{t \in T}$ has the probability function

$$p_i(t) = P(I(t) = i), \quad i = \overline{0,N} \; t \in T,$$

$$\sum_{i=1}^{N} p_i(t) = 1 \tag{6}$$

If $p(t) = (p_0(t), p_1(t), ..., p_n(t))^T$ is the probability vector associated of stochastic process $\{I(t)\}_{t \in T}$, then the process has the Markov property:

$$P\left(I(t+\Delta t) \middle| I(0), I(\Delta t), ...I(t)\right) = P\left(I(t+\Delta t) \middle| I(t)\right) \tag{7}$$

i.e. the process state (the number of infected individuals) at the moment $t + \Delta t$, depends only on the process state at the moment *t*.

The probability of transition from the state $I(t) = i$, to the state $I(t+\Delta t) = j$ is given by relationship:

$$p_{ji}(t+\Delta t, t) = P\left(I(t+\Delta t) = j \middle| I(t) = i\right) \tag{8}$$

Observation:

If Δt is a sufficiently small interval, the process $I(t)$ can move from the state $i \to i+1, i \to i-1$ or $i \to i$, i.e. the number of infected people can grow with one, or can be a birth, a death or a cure. In this case, the transition probabilities verify the relationships:

$$p_{ij}(\Delta t) = \begin{cases} \dfrac{\beta i(N-i)}{N} \cdot \Delta t, & j = i+1 \\ (b+\gamma) i \cdot \Delta t, & j = i-1 \\ 1 - \left[\dfrac{\beta i(N-i)}{N} + (b+\gamma) i \right] \cdot \Delta t, & j = i \\ 0, & j \neq i+1, i, i-1 \end{cases} \tag{9}$$

The relations which are above can be interpreted as follows:

- probability of the occurrence of another infected person in an interval Δt, $(i \to i+1)$ is $\dfrac{\beta i(N-i)}{N} \cdot \Delta t$,
- probability of the occurrence of death or recover $(i \to i-1)$ in an interval Δt is $(b+\gamma) i \cdot \Delta t$,
- probability that not occur any change in state $(i \to i)$in an interval Δt is $1 - \left[\dfrac{\beta i(N-i)}{N} + (b+\gamma) i \right] \cdot \Delta t$.

So that the population size remains constant as with the deterministic case, $b = c$ meaning the birth rate must be equal to the death rate.

Observation

If a SIS epidemic model (DTMC) is seen as a process of birth and death, then the system (9) can be written more simple:

$$p_{ij}(\Delta t) = \begin{cases} b(i) \cdot \Delta t, & j = i+1 \\ d(i) \cdot \Delta t, & j = i-1 \\ 1 - [b(i) \cdot \Delta t + d(i) \cdot \Delta t], & j = i \\ 0, & j \neq i+1, i, i-1 \end{cases} \tag{10}$$

with $b(i) \cdot \Delta t$ it noted the probability of new infections and the probability of death or recover $d(i) \cdot \Delta t$. If we apply the previous transition probabilities the Markov property, then $p_i(t+\Delta t)$ can be expressed in terms of probabilities at the time *t* :

$$p_i(t+\Delta t) = p_{i-1}(t)\cdot b(i-1)\cdot\Delta t + p_{i+1}(t)\cdot d(i+1)\cdot\Delta t + p_i(t)\left(1-\left[b(i)\cdot\Delta t + d(i)\cdot\Delta t\right]\right) \quad (11)$$

where

$$i=\overline{1,N},\quad b(i)=\frac{\beta i(N-i)}{N},\quad d(i)=(b+\gamma)i.$$

2.2 Continuous Time Markov Chain Epidemic Models (CTMC)

In a CTMC process, time is a continuous random variable, $t\in[0,\infty)$ and $S(t),I(t),R(t)\in\{0,1,...,N\}$ are discrete random variables.

Further we characterize a CTMC SIS epidemic model. The vector of probability functions associated to stochastic process $\{I(t)\}_{t\in[0,\infty)}$ is

$$p(t)=\left(p_0(t),p_1(t),...,p_n(t)\right)^T \quad (12)$$

with $p_i(t)=P(I(t)=i),\quad i=\overline{0,N}$

The process has the Markov property:

$$P\left(I(t_{n+1})\middle|I(t_0),...I(t_n)\right)=P\left(I(t_{n+1})\middle|I(t_n)\right), \quad (13)$$

$$(\forall)0\le t_0<...<t_n<t_{n+1}$$

The previous relationship indicates that the transition probability at the time t_{n+1} depends only on the state of the process at the time t_n. If in a DTMC, the transition probability refers to a short period of time Δt, in the transition probabilities related CTMC process is included the term $o(\Delta t)$, with the property :

$$\lim_{t\to\infty}\frac{o(\Delta t)}{\Delta t}=0 \quad (14)$$

The infinitesimal transition probabilities are defined as:

$$p_{ji}(\Delta t)=\begin{cases}\dfrac{\beta i(N-i)}{N}\cdot\Delta t+o(\Delta t), & j=i+1\\ (b+\gamma)i\cdot\Delta t+o(\Delta t), & j=i-1\\ 1-\left[\dfrac{\beta i(N-i)}{N}+(b+\gamma)i\right]\Delta t+o(\Delta t), & j=i\\ o(\Delta t), & j\ne i+1,i,i-1\end{cases} \quad (15)$$

As Δt is sufficiently small, there are three possibilities for mood swings: $i\to i+1$, $i\to i-1$ or $i\to i$. With the same notations as in the case of a DTMC process, the formulas (15) become:

$$p_{ji}(\Delta t)=\begin{cases}b(i)\cdot\Delta t+o(\Delta t), & j=i+1\\ d(i)\cdot\Delta t+o(\Delta t), & j=i-1\\ 1-\left[b(i)\cdot\Delta t+d(i)\cdot\Delta t\right]+o(\Delta t), & j=i\\ o(\Delta t), & j\ne i+1,i,i-1\end{cases} \quad (16)$$

If we apply the Markov property to the previous transition probability and given that $P(I(0)=i_0)=1$, then $p_i(t+\Delta t)$ can be expressed in terms of probabilities at the time t :

$$p_i(t+\Delta t)=p_{i-1}(t)\cdot b(i-1)\cdot\Delta t+p_{i+1}(t)\cdot d(i+1)\cdot\Delta t+ +p_i(t)\left(1-\left[b(i)\cdot\Delta t+d(i)\cdot\Delta t\right]\right)+o(\Delta t)$$

2.3. The Stochastic Differential Equations Epidemic Models (SDE)

In a stochastic SDE epidemic model, time is a continuous random variable with $T=[0,\infty)$ and $S(t),I(t),R(t)$ are also continuous random variables, with the state-space interval $[0,N]$. Further we will stop to a SIS stochastic epidemic model. The stochastic process $\{I(t)\}_{t\in[0,\infty)}$ represents the number of individuals affected with respect to time. The random variable $I(t)$ has the probability density $p(x,t)$ and

$$P(a\le I(t)\le b)=\int_a^b p(x,t)\,dx.$$

The process $\{I(t)\}_{t\in[0,\infty)}$ has the Markov property:

$$P\left(I(t_n)\le y\middle|I(t_0),I(t_1),...I(t_{n-1})\right)= P\left(I(t_n)\le y\middle|I(t_{n-1})\right) \quad (17)$$

$(\forall)0\le t_0<...<t_{n-1}<t_n\in T$, and the transition probability density is

$$p(y,t+\Delta t;x,t)\ I(t)=x,\quad I(t+\Delta t)=y \quad (18)$$

In the paper [1], it is shown that a construction of SDE SIS model epidemic, starting from the CTMC SIS epidemic model.

RESULTS AND DISCUSSIONS

We assume that N - population size is not constant, but it varies in relation to the law of population growth. Formulation of an epidemic model requires

that the birth and death rates, which depend on population size.

We suppose that the birth rate is:

$$\lambda(N) = b \cdot N \tag{19}$$

and the death rate:

$$\mu(N) = b \cdot \frac{N^2}{k} \tag{20}$$

where $k > 0$ is the carrying capacity. Then,the number N checks differential equation:

$$\frac{dN}{dt} = \lambda(N) - \mu(N) = bN\left(1 - \frac{N}{k}\right) \tag{21}$$

According to [2] there are many forms of birth rates and death choice, depending on population dynamics that will be modeled. If we assume that the population size checks the differential equation (21), then a deterministic SIS epidemic model can be characterized by the system of differential equations:

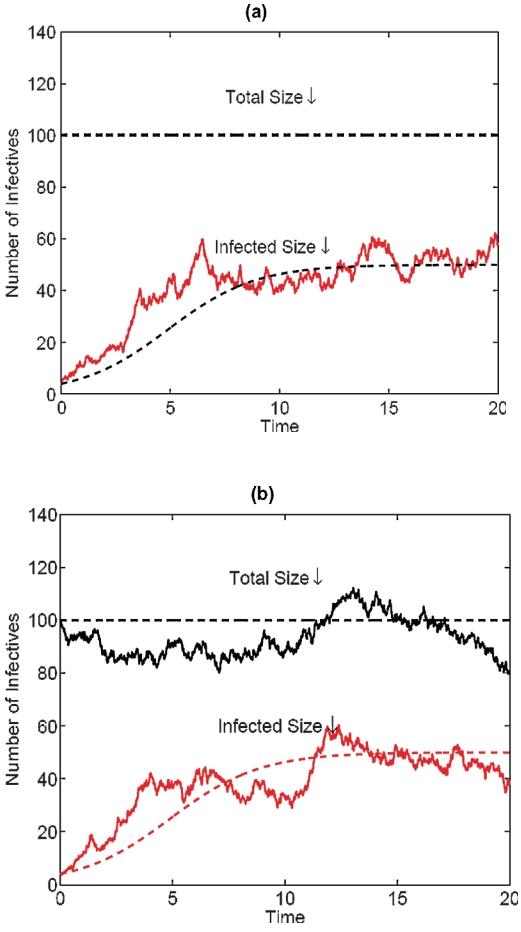
$$\begin{cases} \dfrac{dS}{dt} = \dfrac{S}{N}\left(\lambda(N) - \mu(N)\right) - \dfrac{\beta}{N} S \cdot I + (b+\gamma) I \\ \dfrac{dI}{dt} = -\dfrac{I}{N}\mu(N) + \dfrac{\beta}{N} S \cdot I - \gamma \cdot I \end{cases} \tag{22}$$

with $S(0) > 0$ and $I(0) > 0$.

The previous system solution depends on the basic reproduction number $R_0 = \dfrac{\beta}{b+\gamma}$.

Next, we formulate a stochastic model of type EDS SIS solution and we compare it with the deterministic model [1], [2]. Let us consider $S(t), I(t)$ variables representing the number of individuals susceptible, infected respectively at time t. Obviously $S(t) + I(t) = N(t)$ and $S(t), I(t) \in [0, \infty)$. If we apply the same method as for the model SDE SIS epidemic model, we obtain the system of differential equations

In [4] Brauer, F., Driessche P present a graph of a SDE SIS epidemic model (**a**) with constant population size, N = 100 and (**b**) with variable population size, $N(t)$. The parameter values are β = 1, $\gamma = 0.25 = b$, K = 100, and $R_0 = 2$



CONCLUSIONS

In many cases these three stochastic formulations generate similar results, if the time step Δt is small [2]. There are numerical advantages in applying the discrete time approximations (DTMC model) in that the discrete simulations generally have a shorter computational time than the CTMC model. Mode and Sleeman [7] discuss some computational methods in stochastic processes in epidemiology. The most important consideration in modeling, however, is to choose a model that best represents the demographics and epidemiology of the population being modeled.

In the future we plan to continue studying to application of stochastic modeling in epidemiology to determine the final number of individuals of a population affected by an infectious agent but also for estimating the duration of an epidemic

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