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Letter to the Editor

An epidemic model to evaluate the homogeneous mixing assumption

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ABSTRACT

Many epidemic models are written in terms of ordinary differential equations (ODE). This approach relies on the homogeneous mixing assumption; that is, the topological structure of the contact network established by the individuals of the host population is not relevant to predict the spread of a pathogen in this population. Here, we propose an epidemic model based on ODE to study the propagation of contagious diseases conferring no immunity. The state variables of this model are the percentages of susceptible individuals, infectious individuals and empty space. We show that this dynamical system can experience transcritical and Hopf bifurcations. Then, we employ this model to evaluate the validity of the homogeneous mixing assumption by using real data related to the transmission of gonorrhea, hepatitis C virus, human immunodeficiency virus, and obesity.

1. Introduction

In epidemic models described by ordinary differential equations (ODE), the host population is divided into groups according to their status concerning the disease. Usually, at the instant t, every individual of this population belongs to one of the following groups [2,20]: susceptible (S), exposed (E), infectious (I), recovered (R), and vaccinated (V), with R and V-individuals being either partially or fully immunized. A linear term is commonly used to represent the rate of state transitions that do not depend on the contacts among individuals, such as $E \to I$ (a latently infected individual becomes infectious) and $I \to R$ (natural recovery of an infectious individual). Thus, the rate of such transitions, generically represented by $X \to Y$, is written as $dX(t)/dt = -\alpha X(t)$, in which α is the inverse of the average period spent in the group X, composed of $X(t)$ members at the time t [2,20].

The main difficulty of building an epidemic model is to theoretically express how the susceptible individuals are affected by contacts with infectious ones, which corresponds to the state transition $S \to I$. At this point, models written in terms of ODE rely on the homogeneous mixing assumption, by the which host heterogeneities related to geographic locations and spatial correlations are supposed to be negligible. In this scenario, individuals are randomly mixed, and the probability of two individuals have contact only depends on the concentrations of the groups to which they belong. Thus, the contagion rate is assumed to be a function only of $S(t)$ and $I(t)$, which respectively denote the normalized concentrations of individuals that are susceptible and infectious at the instant t. Usually, contagion is represented by a bilinear rate, given by $aS(t)I(t)$, in

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which a is the infection rate constant [2,20,21]. However, nonlinear infection rates have also been proposed. Some examples are: $aS(t)I(t)^{\gamma}/(1+\delta I(t)^{\gamma})$ [1], $aS(t)I(t)/[1+\delta I(t)]$ [3], $aS(t)I(t)[1-\gamma I(t)/(1+\delta I(t))]$ [23], $aS(t)^{\gamma}I(t)^{\delta}$ [24], $aS(t)I(t)^2$ [26], $aS(t)I(t)^2/(1+\gamma I(t)^2)$ [36], $aS(t)I(t)^{\gamma}$ [43], $aS(t)I(t)[S(t)+I(t)]^{\gamma}$ [49] (γ and δ are constants). These nonlinear rates have been employed to mathematically represent, for instance, effects of multiple exposures to a pathogenic agent, saturation due to crowding of infectious individuals, and behavioral changes of susceptible individuals which can take preventive measures against the disease.

The propagation of contagious diseases conferring no significant immunity is investigated in this work. Thus, after drug treatment or spontaneous recovery, an individual of the host population is not protected against subsequent infections. The lack of specific (acquired) immunity favors the persistence of the corresponding pathogens. These diseases are commonly studied by employing *SIS* models [2,20]. Here, we analyze the following *SISN* model:

$$\frac{dS(t)}{dt} = f_1 = -aS(t)I(t)[1+qI(t)] + bI(t) - eS(t) + g[S(t)+pI(t)]N(t) \tag{1}$$

$$\frac{dI(t)}{dt} = f_2 = aS(t)I(t)[1+qI(t)] - bI(t) - cI(t) \tag{2}$$

$$\frac{dN(t)}{dt} = f_3 = cI(t) + eS(t) - g[S(t)+pI(t)]N(t) \tag{3}$$

in which $N(t)$ is the percentage of non-occupied space. It is important to clarify the meaning of this variable. Agent-based modeling and differential equations are two possible approaches to theoretically study population dynamics. Several authors have shown that these two approaches can give similar results, if the parameter values are suitably chosen [15,40]. In agent-based modeling, an individual is usually represented by a node of a graph and an edge between two nodes stands for a social contact. Thus, in such a model, $N(t)$ would denote the percentage of empty nodes (non-occupied space). The number of nodes corresponding to a particular geographic region would be limited by the availability of resources (such as water and food). Homogenous mixing assumption, in this scenario, would imply that the time evolutions of the percentages of S, I and N-nodes observed in any "large" subgraph should be equivalent to the ones observed in the whole network. This kind of equivalence can be obtained by using regular [28] or irregular [40] neighborhood.

In addition, in our *SISN* model, b is the recovering rate constant, c is the death rate constant related to the disease, e is the death rate constant due to other reasons, and g is the birth rate constant. These four constants are positive numbers. Observe that the state transitions $I \to S$ (recovery of I), $I \to N$ (death of I), and $S \to N$ (death of S) are represented by linear terms. The parameter $p \in [0,1]$ quantifies the fraction of infectious individuals participating in the reproduction process. Susceptible individuals are born only if $N(t) > 0$; that is, if there is available space (available resources) to this process takes place.

The term $1+qI(t)$ in the infection rate expresses a linear deviation from the bilinear choice and here it is used to judge the consistency of the homogeneous mixing assumption; in other words, the forecasting ability of a model based on this assumption. Hence, if the concentrations $S(t)$ and $I(t)$ observed in the real world are found by taking the parameter $q \approx 0$, then this assumption can be considered valid; if these concentrations are obtained by taking $|q| \gg 1$, then such an assumption can not be adequate. Other factors causing heterogeneities are variations in age, gender, genetic constitution, habits, etc. These factors, however, can be taken into account even in models based on ODE. For instance, there are models with age structure and models considering groups with different degrees of sexual activity [2,20].

The nonlinear infection rate $aS(t)I(t)[1+qI(t)]$ was used to explain measles outbreaks by taking a as a time function and $q < 0$ [48], and it was adopted in a *SIRS* model with $q > 0$ [19]. Here, it is employed to evaluate the validity of the homogeneous mixing assumption by using real data concerning the worldwide epidemics of gonorrhea, hepatitis C virus, human immunodeficiency virus, and obesity. We conjecture that the higher the value of $|q|$, the greater the heterogeneity arising from behavioral, spatial, and structural aspects of the host population.

This manuscript about an epidemic model with nonlinear infection and birth rates is organized as follows: in Section 2, the proposed model is analyzed; in Section 3, numerical simulations are presented; in Section 4, the main results are discussed.

2. Analytical results

As $dS(t)/dt + dI(t)/dt + dN(t)/dt = 0$, then $S(t) + I(t) + N(t) =$ constant. This constant represents the maximum number of individuals that can live in the considered region. By imposing that this constant is equal to 1, then the variables $S(t)$, $I(t)$, and $N(t)$ can be considered percentages. Note that the analysis of the model can be performed by taking into account only Eqs. (1) and (2), with $N(t) = 1 - [S(t) + I(t)]$. In fact, this model is of second order.

A steady state is represented by a point (S^*, I^*) in the two-dimensional state space $S \times I$, in which S^* and I^* are constants satisfying $f_1 = 0$ and $f_2 = 0$ for any time t. Two steady states are $(S^*_{ghost}, I^*_{ghost}) = (0,0)$ and $(S^*_{free}, I^*_{free}) = (1-(e/g), 0)$. The first one stands for the situation in which the host population became extinct and the considered spatial region is called *ghost* city; the second one corresponds to a disease-*free* scenario, because $S^* \neq 0$ and $I^* = 0$. *Endemic* steady states (S^*_{end}, I^*_{end}); that is, states with $I^* > 0$, are obtained by solving the polynomial:

$$a_0(I^*_{end})^4 + a_1(I^*_{end})^3 + a_2(I^*_{end})^2 + a_3 I^*_{end} + a_4 = 0 \tag{4}$$