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On a basic model of a two-disease epidemic

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Abstract

This paper considers a basic model for a spread of two diseases in a population. The equilibria of the model are found, and their stability is investigated. In particular, we prove the stability result for a disease-free and a one-disease steady-states. Bifurcation diagrams are used to analyse the stability of possible branches of equilibria, and also they indicate the existence of a co-infected equilibrium with both diseases present. Finally, numerical simulations of the model are performed to study the behaviour of the solutions in different regions of the parameter space.

Keywords: Epidemic model; Co-infection; Stability analysis; Bifurcation diagrams; Numerical simulations

1. Introduction

Since the famous Kermack–McKendrick SIR model for a spread of disease [1], differential equations have been widely used in mathematical epidemiology. Numerous mathematical models were developed to study a disease transmission, to evaluate the spread of epidemics, and more importantly, to understand the mechanisms of epidemics in order to prevent them or minimise the transmission of diseases via quarantine and other measures (see [2–5] and references therein).

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In the last years, statistics on the infected individuals with AIDS, tuberculosis, hepatitis B and C, herpes and other diseases are growing very fast. The understanding of the long-time behaviour of diseases will help to find whether the epidemics will die out or stay in the population and to design strategies of fighting them. Optimal strategies of vaccination developed on the basis of mathematical modelling can help to eradicate some infectious diseases and produce methods for their control [6–9].

There are many mathematical models describing behaviour of diseases, optimisation of treatments, vaccination of the population. Some works consider models with two diseases such as AIDS and tuberculosis [10,11] or describe two strains of one disease present in the population, influenza or tuberculosis, for instance [12–14]. In particular, a realistic situation in which the co-existence of two diseases occurs is the case of sexually transmitted diseases (STD), such as AIDS and gonorrhea [15].

At the same time, it is natural to derive a *basic* model which can allow one to describe general features of a two-disease epidemic and analyse its dynamics in order to gain the understanding of qualitative behaviour in this system. The purpose of this paper is to consider such a two-disease model. These can be two different diseases or two strains of one and the same disease. It is assumed that each individual can be infected with one or both diseases. There is no immunity or cross-immunity which means that an individual recovered from one disease can be infected with another or with the same one again. From a natural background we consider the case when there are deaths from both diseases. Of course, this model can also be used in the case when diseases produce no death, and this will simplify the model. It is assumed that there is a constant recruitment rate with which individuals become susceptibles (Fig. 1).

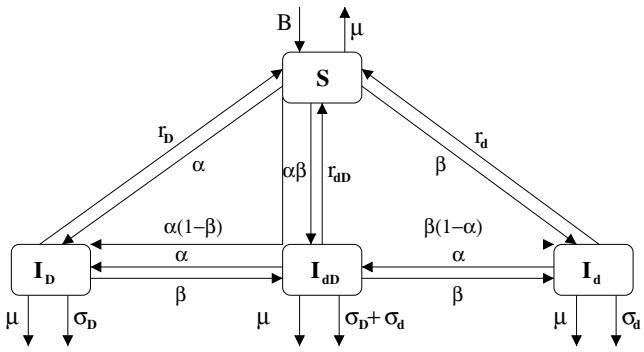

Fig. 1. A diagram for a two-disease epidemic. S stands for susceptibles, I_D, I_d and I_{dD} denote individuals infected with major, minor and both diseases.

The model is represented as a system of four ODEs, and since individuals do not have immunity after disease we reduce this model from SIR to SIS. We give a complete analysis of this system, such as stability of a disease-free and endemic equilibria. Basic reproductive number $\mathscr{R}_0$ is used to analyse the stability of a disease-free equilibrium, and we prove that this state is stable for $\mathscr{R}_0 < 1$ and unstable otherwise. Conditions for the local asymptotic stability are also obtained for one-disease endemic equilibria. We use bifurcation diagrams to detect the branches of equilibria for our model and analyse the regions of parameters where these steady-states change their stability.

The outline of the paper is as follows. In Section 2 we introduce a two-disease model and discuss its main properties. Section 3 deals with the stability analysis for the disease-free equilibrium, while Section 4 treats the case of a one-disease endemic steady-state. In Section 5 we study possible bifurcation scenarios and perform numerical simulations of the model. Section 6 contains the summary of results and discussion.

2. The derivation of the model

The host population is $N = N(t)$, and we divide it into the following classes: susceptibles $S = S(t)$, infected with major $I_{\mathrm{D}}(t)$ and minor $I_{\mathrm{d}}(t)$ diseases, and co-infected (means infected with major and minor diseases simultaneously) $I_{\mathrm{dD}}(t)$ individuals. The total population size is $N = S + I_{\mathrm{D}} + I_{\mathrm{d}} + I_{\mathrm{dD}}$. In our model B denotes the constant recruitment rate, with which individuals become susceptibles; μ is a natural death rate; α and β are the effective transmission rates with which individuals become infected with the major and minor diseases, correspondingly. Also, probabilities to become infected only with major, minor or both diseases after contacting co-infected individual are $\alpha(1-\beta)$, $\beta(1-\alpha)$, and $\alpha\beta$. We note here that the efficiency of a disease transmission is assumed to be the same for both susceptible and infected individuals. This means that the probability for an infected individual to become infected with the second disease is the same as the probability for a susceptible to become infected with that disease. Furthermore, there are death cases from both diseases, therefore, we introduce disease induced mortality rates σ_{D} and σ_{d} for the major and minor diseases, respectively. Hence, for co-infected individuals the disease caused mortality rate becomes $(\sigma_{\mathrm{D}} + \sigma_{\mathrm{d}})$. The recovery rates from the major, minor and both diseases are introduced to be r_{D}, r_{d} and r_{dD}.

Since we consider the model with no immunity, it is assumed that each individual after recovery immediately becomes susceptible again. Therefore, equations for the recovery class can be dropped, and we consider a SIS model instead of an SIR.

After all these assumptions, the model has the following form:

$$\begin{aligned}
\frac{dS}{dt} &= B - \mu S - \alpha(1-\beta) I_{dD}\frac{S}{N} - \alpha I_D \frac{S}{N} - \beta(1-\alpha) I_{dD}\frac{S}{N} - \beta I_d \frac{S}{N} \\
&\quad - \alpha\beta I_{dD}\frac{S}{N} + r_D I_D + r_d I_d + r_{dD} I_{dD}; \\
\frac{dI_D}{dt} &= \alpha(1-\beta) I_{dD}\frac{S}{N} + \alpha I_D \frac{S}{N} - (\sigma_D + \mu + r_D) I_D - \beta(I_d + I_{dD})\frac{I_D}{N}, \\
\frac{dI_d}{dt} &= \beta(1-\alpha) I_{dD}\frac{S}{N} + \beta I_d \frac{S}{N} - (\sigma_d + \mu + r_D) I_d - \alpha(I_D + I_{dD})\frac{I_d}{N}, \\
\frac{dI_{dD}}{dt} &= (\alpha+\beta)\frac{I_D I_d}{N} + (\alpha I_d + \beta I_D)\frac{I_{dD}}{N} - (\sigma_D + \sigma_d + \mu + r_{dD}) I_{dD} + \alpha\beta I_{dD}\frac{S}{N}, \\
N(t) &= S(t) + I_D(t) + I_d(t) + I_{dD}(t).
\end{aligned} \tag{1}$$

Using the *next generation operator approach* described in [4] and subsequently analysed in [16], we obtain basic reproductive numbers associated with the major, minor and both diseases as

$$\mathscr{R}_1 = \frac{\alpha}{\sigma_D + \mu + r_D}, \quad \mathscr{R}_2 = \frac{\beta}{\sigma_d + \mu + r_d}, \quad \mathscr{R}_3 = \frac{\alpha\beta}{\sigma_D + \sigma_d + \mu + r_{dD}}. \tag{2}$$

These numbers give the number of secondary infective cases of the diseases produced by an individual infected with major, minor, and both diseases during his/her effective period when introduced in a population of susceptibles [4] (Table 1).

Consequently, the basic reproductive number associated with the model (1) is

$$\mathscr{R}_0 = \max\{\mathscr{R}_1, \mathscr{R}_2, \mathscr{R}_3\}. \tag{3}$$

The case $\mathscr{R}_0 = 1$ gives a threshold condition. We shall prove that for $\mathscr{R}_0 < 1$ both diseases will die out and for $\mathscr{R}_0 > 1$ at least one disease will be present in the population.

Table 1
Table of parameters

Symbol	Definition
B	Recruitment rate
α, β	Effective transmission rates for the major and minor diseases
μ	Per-capita natural mortality rate
σ_D, σ_d	Per-capita disease induced mortality rates
r_D, r_d, r_{dD}	Per-capita recovery rates

3. Disease-free equilibrium and its stability

The system (1) has several equilibria: when both diseases are absent (uninfected equilibrium), and when a disease (one or both simultaneously) is present. In the latter case an equilibrium is called endemic. In this section the analysis of the disease-free steady-state for the system (1) and its stability is performed. Consideration of stability of a disease-free equilibrium gives certain conditions under which diseases will die out or stay in the population.

Let $E_i = (S, I_D, I_d, I_{dD})$ be the equilibria for the system (1) and $E_0 = (B/\mu, 0, 0, 0)$ be the disease-free steady state. Then the following result holds.

Theorem 1. *The disease-free equilibrium E_0 is locally asymptotically stable if $\mathscr{R}_j < 1$, $j = 1, 2, 3$ and unstable if either of $\mathscr{R}_j > 1$.*

Proof. Linearisation of the system (1) near E_0 gives

$$\begin{pmatrix} -\mu & -\alpha + r_D & -\beta + r_d & -\alpha - \beta + \alpha\beta + r_{dD} \\ 0 & \alpha - \mu - \sigma_D - r_D & 0 & \alpha(1-\beta) \\ 0 & 0 & \beta - \mu - \sigma_d - r_d & \beta(1-\alpha) \\ 0 & 0 & 0 & -\mu - \sigma_d - \sigma_D - r_{dD} + \alpha\beta \end{pmatrix}. \tag{4}$$

If real parts of all the eigenvalues of this matrix are negative, then the disease-free steady-state is locally asymptotically stable. The matrix (4) has four eigenvalues which will have negative real parts if and only if

$$\alpha < \mu + \sigma_D + r_D, \quad \beta < \mu + \sigma_d + r_d, \quad \alpha\beta < \mu + \sigma_d + \sigma_D + r_{dD}.$$

Recalling the expressions for $\mathscr{R}_1, \mathscr{R}_2$ and $\mathscr{R}_3$, we obtain that E_0 is locally asymptotically stable iff $\mathscr{R}_1 < 1$, $\mathscr{R}_2 < 1$ and $\mathscr{R}_3 < 1$. This completes the proof of the theorem. □

4. Endemic equilibria

In this section, we analyse endemic equilibria for the system (1). The non-zero steady-states can be present if there is only major disease, only minor disease or both diseases. Since the system (1) is symmetric with respect to major and minor diseases, therefore, we shall investigate only the case when the major disease is present in the population and the minor disease dies out. In this case there are no co-infected individuals. When the two diseases and the co-infection are present the expression for endemic steady-state cannot be obtained analytically. Thus, in the next section numerical simulations of this steady-state are presented.

Let $E_1 = (\widehat{S}, \hat{I}_D, 0, 0)$, $\widehat{N} = \widehat{S} + \hat{I}_D$ be the endemic equilibrium for (1), where

$$\begin{aligned}
\widehat{N} &= \frac{B\alpha}{-\sigma_D\mu + \alpha\mu + \alpha\sigma_D - \sigma_D^2 - r_D\sigma_D}, \\
\widehat{S} &= \frac{(\mu + \sigma_D + r_D)B}{-\sigma_D\mu + \alpha\mu + \alpha\sigma_D - \sigma_D^2 - r_D\sigma_D}, \\
\hat{I}_D &= \frac{B(\alpha - \mu - \sigma_D - r_D)}{-\sigma_D\mu + \alpha\mu + \alpha\sigma_D - \sigma_D^2 - r_D\sigma_D}.
\end{aligned} \tag{5}$$

From (5) it can be seen that $\hat{N}$, $\hat{S}$ and $\hat{I}_D$ are positive if the following condition holds:

$$\alpha > \mu + \sigma_D + r_D, \tag{6}$$

what can be recast as

$$\mathscr{R}_1 > 1.$$

Linearising system (1) near the equilibrium E_1 and using the Routh–Hurwitz criterion, we obtain the following conditions for local asymptotic stability of this state:

$$f = -\frac{\alpha\beta}{\mathscr{R}_1} + \beta\left(\frac{1}{\mathscr{R}_2} - 1\right) + \alpha\left(1 - \frac{1}{\mathscr{R}_1}\right) + \frac{\alpha\beta}{\mathscr{R}_3} > 0, \tag{7}$$

and

$$\begin{aligned}
g = &-\left(\alpha + \frac{\beta}{\mathscr{R}_2}\right) + \frac{1}{\mathscr{R}_1}\left[\alpha^2 + \alpha\beta\left(1 - \frac{1}{\mathscr{R}_3}\right) + \frac{\beta}{\mathscr{R}_2}(1 - \alpha\beta)\right] \\
&+ \frac{\alpha}{\mathscr{R}_3}\left[\alpha\left(1 - \frac{1}{\mathscr{R}_1}\right) + \frac{\beta}{\mathscr{R}_2}\right] > 0.
\end{aligned} \tag{8}$$

We can summarise these findings in the following theorem

Theorem 2. *The endemic equilibrium E_1 exists if $\mathscr{R}_1 > 1$, and it is locally asymptotically stable if the conditions* (7) *and* (8) *hold.*

Similar results about existence and stability can be obtained for another endemic equilibrium $E_2 = (\tilde{S}, 0, \tilde{I}_d, 0)$ upon the change of variables: $\alpha \to \beta$, $\sigma_D \to \sigma_d$ and $\mathscr{R}_1 \to \mathscr{R}_2$. Both equilibria E_1 and E_2 are exclusive in a sense that only one disease is present in the population, while the second eventually dies out. Therefore, it is reasonable to generalize this situation for a co-infected state when both diseases are present. Unfortunately, analytic expression for this state cannot be found for general values of the parameters, and thus in the next section we use numerics to study the existence and stability of the co-infected state.

5. Bifurcation analysis and numerical simulations

Now we discuss the appearance of different branches of equilibria and analyse their stability as the parameters in the system are varied. In what follows all the parameters will be considered as fixed except for α, which will be used as a control parameter. We take β as fixed but satisfying the condition $\mathscr{R}_2 < 1$, so that for small α only the disease-free equilibrium exists and is stable. When α grows the state E_0 will eventually lose its stability. This will happen when either $\mathscr{R}_1$ or $\mathscr{R}_3$ becomes greater than 1. Using the definitions of $\mathscr{R}_1$ and $\mathscr{R}_3$ from (3) it can be easily seen, that if

$$\beta < \frac{\sigma_D + \sigma_d + \mu + r_{dD}}{\sigma_D + \mu + r_D},$$

than $\mathscr{R}_1 > \mathscr{R}_3$, and it is enough to track the dynamics of $\mathscr{R}_1$ only to obtain the smallest value of α for which E_0 will become unstable.

The endemic state E_1 appears when $\mathscr{R}_1 > 1$. If $\mathscr{R}_1 > \mathscr{R}_3$ then the point when E_1 is born coincides with the point where E_0 becomes unstable. Otherwise, E_0 will be unstable for values of α such that $\mathscr{R}_3 > 1$ but $\mathscr{R}_1 < 1$, and for these values E_1 yet will not exist (this will be illustrated below). Depending on the value of β the line of equilibria E_1 can be stable for all values of α in the range of its existence or only for some of them depending on whether the conditions (7) and (8) are satisfied (Fig. 2).

For illustration purposes, we fix the values of the parameters $\mu = 0.01$, $\sigma_D = 0.04$, $\sigma_d = 0.03$, $r_D = 0.5$, $r_d = 0.8$, and $B = 1$ and start with the case $\beta = 0.3$ as illustrated in Fig. 2. For this value of β the disease-free equilibrium loses its stability at $\alpha = 0.55$, and at this point an endemic state appears. For larger β this endemic state is originally unstable, but it becomes unstable for large α as Fig. 3 shows. For even larger values of β the line of endemic

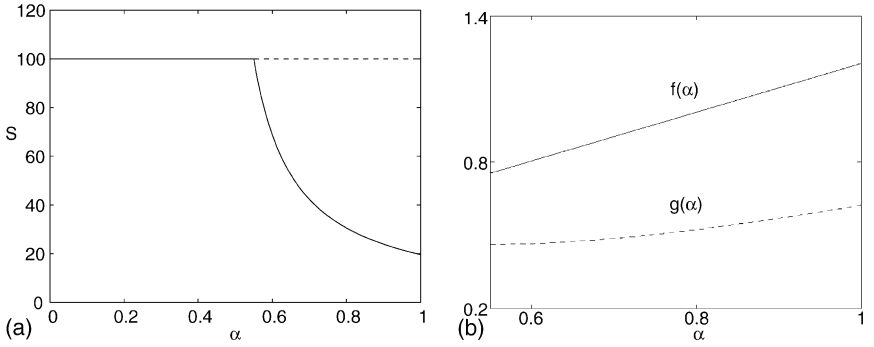

Fig. 2. (a) Bifurcation diagram for system (1) and (b) stability conditions $f(\alpha)$ and $g(\alpha)$. Parameter values are: $\mu = 0.01$, $\sigma_D = 0.04$, $\sigma_d = 0.03$, $r_D = 0.5$, $r_d = 0.8$, $B = 1$ and $\beta = 0.3$.

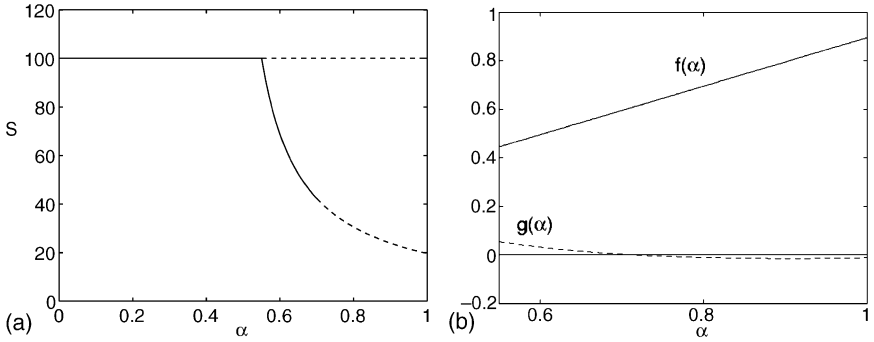

Fig. 3. (a) Bifurcation diagram for system (1). The solid line denotes a stable solution, while the dashed line represents an unstable solution. (b) Stability conditions $f(\alpha)$ and $g(\alpha)$. Parameter values are: $\mu = 0.01$, $\sigma_D = 0.04$, $\sigma_d = 0.03$, $r_D = 0.5$, $r_d = 0.8$, $B = 1$ and $\beta = 0.5$.

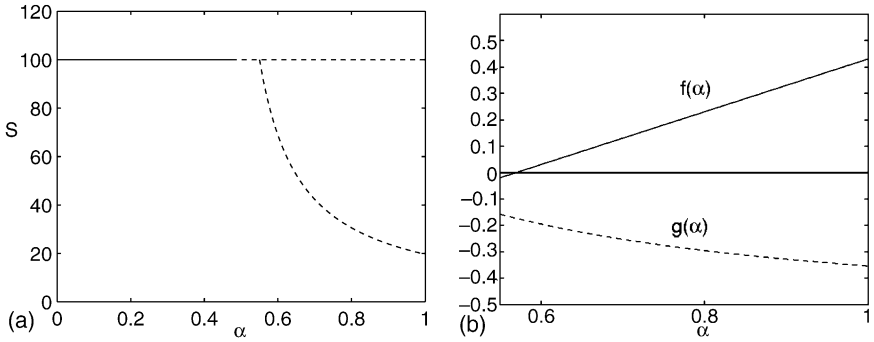

Fig. 4. (a) Bifurcation diagram for system (1). The solid line denotes a stable solution, while the dashed line represents an unstable solution. (b) Stability conditions $f(\alpha)$ and $g(\alpha)$. Parameter values are: $\mu = 0.01$, $\sigma_D = 0.04$, $\sigma_d = 0.03$, $r_D = 0.5$, $r_d = 0.8$, $B = 1$ and $\beta = 0.8$.

equilibria E_1 is unstable for all values of α since the conditions for stability (7) and (8) fail (see Fig. 4).

Besides the steady-states considered above there is an important issue concerning the co-infected equilibrium. For small values of β this state does not exist. If β increases, the co-infected steady-state can be found, and numerical simulations prove its stability. It is noteworthy that in this case the co-infected state can exist and be stable for the same values of α as the equilibrium E_1 does. This is illustrated in Fig. 5(a). For very large β (which are still taken to satisfy the condition $\mathscr{R}_2 < 1$) the disease-free equilibrium loses its stability when $\mathscr{R}_3$ passes through 1, and at this value of α the endemic equilibrium with one disease still does not exist. On the other hand, at this point the co-infected steady-state appears, which is unstable, but it stabilizes for larger α. These transitions are presented in Fig. 5(b).

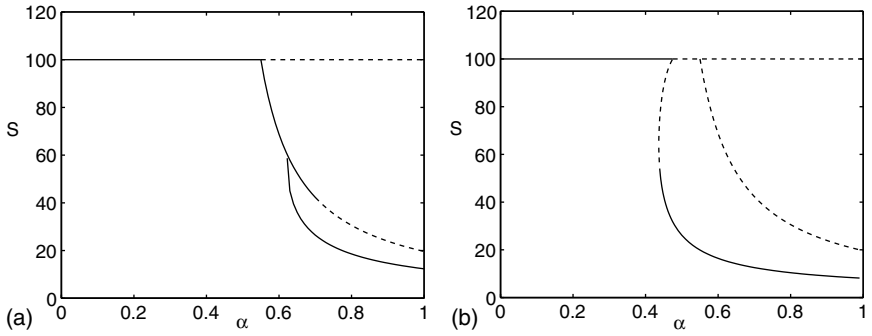

Fig. 5. Parameter values are: $\mu = 0.01$, $\sigma_D = 0.04$, $\sigma_d = 0.03$, $r_D = 0.5$, $r_d = 0.8$, and $B = 1$; (a) bifurcation diagram for system (1) with $\beta = 0.5$ and (b) bifurcation diagram for system (1) with $\beta = 0.8$. The solid line denotes stable solutions, while the dashed line represents unstable solutions.

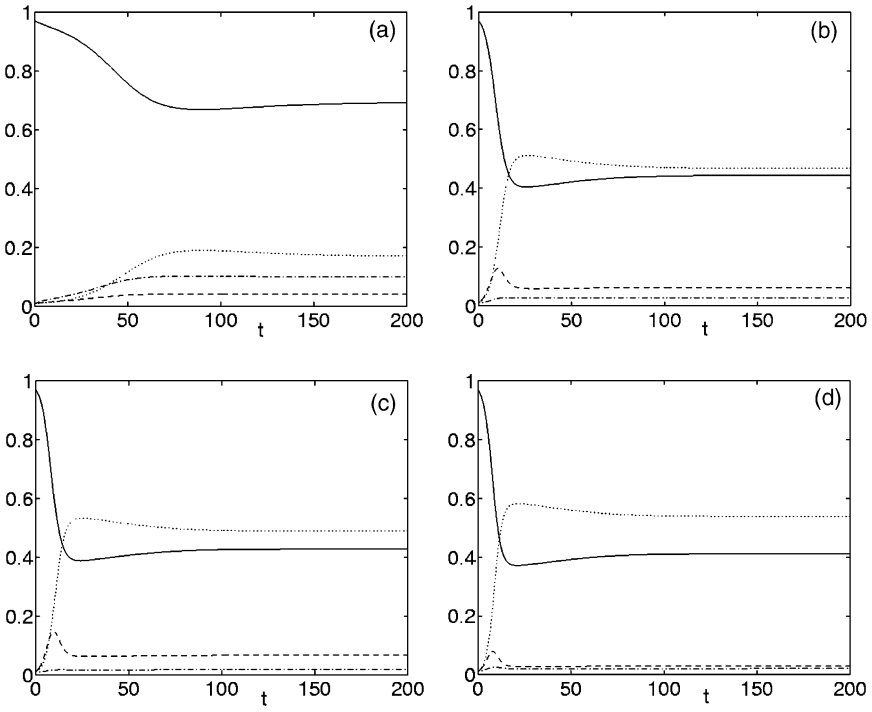

Fig. 6. Population fractions S/N (solid), I_D/N (dashed), I_d/N (dot-dashed), I_{dD}/N (dotted) as functions of time. Parameter values are: $\mu = 0.01$, $\sigma_D = 0.04$, $\sigma_d = 0.03$, $r_D = 0.5$, $r_d = 0.8$ and $B = 1$; (a) $\alpha = 0.52$ and $\beta = 0.75$; (b) $\alpha = 0.6$ and $\beta = 0.4$; (c) $\alpha = 0.8$ and $\beta = 0.8$ and (d) $\alpha = 0.9$ and $\beta = 0.9$.

Next we study the system (1) numerically for some values of α and β to understand the qualitative behaviour of solutions in different stability regions. In Fig. 6(a) we start in the region of parameter space where only the uninfected equilibrium exists and is stable. For larger values of α the uninfected state is unstable, and a stable equilibrium E_1 appears (see Fig. 6(b)), but still there is no co-infected steady-state. Fig. 6(c) corresponds to the case when E_1 is unstable, and the stable co-infected equilibrium exists. Finally, Fig. 6(d) represents the situation when both one-disease equilibria exist, as well as a co-infected steady-state.

6. Conclusions

In this paper, we have derived and analysed a two-disease ODEs model with cross-infectivity. First, we have found the basic reproductive numbers for each disease and for the model in general. The local stability of the disease-free steady-state has been proved for $\mathscr{R}_0 < 1$. A threshold condition is $\mathscr{R}_0 = 1$, and for $\mathscr{R}_0 < 1$ the uninfected steady-state is locally asymptotically stable and unstable otherwise.

There are three types of endemic equilibria for the system (1): when only major, only minor or both diseases are present. Since the system (1) is symmetric with respect to major and minor diseases, we have considered the case when only major disease is present in the population. In this case the endemic equilibrium E_1 has been found analytically. The condition for this steady-state to exist has proved to be $\mathscr{R}_1 > 1$. The stability result for E_1 is formulated in Theorem 2, where it is summarised in two conditions. Similar results can be found for the equilibrium E_2 when only minor disease is present.

For certain values of parameters we have found different branches of steady-states of the system (1), which are illustrated in Figs. 2–5. In the case when two diseases and a co-infection are present, we were unable to obtain an analytical expression for this endemic state for general values of parameters. Numerically, we have found this steady-state and studied its stability in some regions of the parameter space. These results are represented in Fig. 5. We have also studied the system (1) numerically, and results for different values of parameters are illustrated in Fig. 6(a)–(d). The cases considered include the regions when the uninfected equilibrium is stable and when it is unstable but there exist other endemic equilibria including the co-infected state.

As it was noted in Section 1, the model considered in this paper is a basic model, in which we aimed to capture main features in the dynamics of a spread of two diseases in a host population. This model or its generalization can be applied to the study of various two-strain diseases, such as influenza, tuberculosis, etc., or two different co-existing diseases with the same or different transmission route.

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