Research Paper
Computational Methods for Differential Equations
http://cmde.tabrizu.ac.ir
Vol. 10, No. 3, 2022, pp. 656-673
DOI:10.22034/cmde.2021.44619.1881

Backward bifurcation in a two strain model of heroin addiction

Reza Memarbashi[1,*], Atena Ghasemabadi[2], and Zahra Ebadi[1]
[1]Department of Mathematics, Semnan University, P. O. Box 35195-363, Semnan, Iran.
[2]Esfarayen University of Technology, Esfarayen, North Khorasan, Iran.

Abstract

Among the various causes of heroin addiction, the use of prescription opioids is one of the main reasons. In this article, we introduce and analyze a two-strain epidemic model with the superinfection for modeling the effect of prescribed opioids abuse on heroin addiction. Our model contains the impact of relapse of individuals under treatment/rehabilitation to drug abuse in each strain. We extract the basic reproductive ratio, the invasion numbers and study the occurrence of backward bifurcation in strain dominance equilibria, i.e., boundary equilibria. Also, we explore both the local and global stability of DFE and boundary equilibria under suitable conditions. Furthermore, we study the existence of the coexistence equilibrium point. We prove that when $R_0 < 1$, the coexistence equilibrium point can exist, i.e., backward bifurcation occurs in coexistence equilibria. Finally, we use numerical simulation to describe the obtained analytical results.

Keywords. Epidemic model, Multiple strain, Superinfection, Global stability, Backward bifurcation.
2010 Mathematics Subject Classification. 92D30; 34D23; 34C23.

1. Introduction

The issue of opioid drug addiction is one of the complex problems of human societies, which has become a social problem in most countries today. Predicting and analyzing addiction and quantifying the factors involved in it is very useful for decision-makers in societies. So experts in various disciplines, including mathematics and statistics, have been modeled the addiction and studied some of the factors involved in epidemic or control of it. According to [3, 42], "dynamic modeling complements indicators and direct data analysis in drug epidemiology at the macro level. Instead of the usual inductive or empirical method of data collection and interpretation, it can be used to enhance the understanding of drug processes by simulating experiments that are difficult or impossible to perform in real life. Dynamic drug models can help in understanding a phenomenon via scenario analysis, thereby providing a tool to simulate experiments that are not possible in real life due to practical or ethical reasons".

There are three general approaches modeling the dynamics of the spread of drug use. Authors of [14] believe "anyone could be a 'prey' to illicit drugs." They applied the predator-prey paradigm for the modeling of illicit drug consumption, see also [3, 5, 11]. On the other hand, drugs have been considered as an epidemic problem like an infectious disease because most drug initiations start through contact with users, not through contact with drug sellers, see [23]. Also, modeling with the optimal control method has been performed see the monograph [17].

Among illicit drugs, heroin is one of the world's most dangerous opioids, which is highly addictive. In the United States, in the time interval of 2002 to 2014, the number of heroin users increased from about 404,000 to 914,000, and the number of addicted cases increased from about 214,000 to 586,000, see [9].

White and Comiskey assumed that the spread of heroin addiction has a mechanism like the spread of infectious diseases, and introduced the first compartmental model with ordinary differential equations for heroin use in [41].

Received: 17 February 2021 ; Accepted: 30 July 2021.
∗ Corresponding author. Email: r_memarbashi@semnan.ac.ir.

Compartmental models are powerful tools for the study and analysis of infectious diseases. Such models, which are generally expressed by ordinary differential equations, were first introduced by Kermack and McKendrick. These models have been used in modeling many diseases such as AIDS, tuberculosis, and influenza see [1, 12, 24, 28, 38, 43]. The mathematical epidemiology of drugs has been studied by several authors after White and Comiskey's work. Mulone and Straughan revisit their work, [32]. Nyabadza and Hove-Muskava in [36] modified the White and Comiskey model and studied the dynamics of methamphetamine. For the study of the epidemiology of crystal and the effect of rehabilitation and relapse, see [34, 37]. In [29, 30] the authors have studied the effect of information transmission and education on the drug dynamic.

On the other hand, infectious diseases with several strains are of great importance in mathematical epidemiology. Therefore this type of epidemic model, such as influenza, HIV, malaria,..., has been attracted considerable attention see [7, 15, 19, 28].

Several mechanisms can cause stable coexistence of multiple strains, one of them is superinfection. In some cases, individuals who have been previously infected by one strain of a pathogen agent can be infected with another strain of the pathogen at a later time. Such event is called superinfection, see [28]. Superinfection was first introduced in [6]. Studies of heroin addicts have revealed three main pathways to heroin addiction, one of them is prescription opioid abuse, see [22, 33].

Prescribed drugs are commonly used to reduce pain. These substances also cause great peace and feeling in people in a short period of time. This makes them more dependent on these substances, and by increasing their use, people tend to use more effective substances such as heroin. Hydrocodone, oxycodone, oxymorphone, morphine, codeine, and fentanyl are examples of prescribed opioids. Prescription drugs are usually safe if given in a short period of time and with a doctor's prescription. But some people abuse the prescribed drugs, this abuse for example involves the excessive use of these substances or the use of substances prescribed to other people. Easier access to heroin in some places and its greater effectiveness will lead to a tendency for people with prescription drug abuse to be a heroin user. Studies show that about 4 to 6 percent of people who use prescription drugs turn to heroin, and about 80 percent of people who take heroin have a history of prescription drugs, see [20, 33].

We modify in this manuscript the White and Comiskey's model and propose a two-strain epidemic model with superinfection about the impact of prescription opioid abuse on heroin addiction. We consider the effect of relapse of individuals under treatment/rehabilitation infected with each strain. We study the effect of the parameters contained in the model, especially the transition rate of individuals with prescription opioid abuse to heroin-addicted individuals and relapse rate, on the dynamic of the model. This study reveals the impact of changes in these parameters on the drug addiction outbreak.

Naturally, in epidemic models, the infection can be controlled by having $R_0 < 1$ if the initial values of all compartments of the model are in the basin of attraction of the disease-free equilibrium point. Simultaneously, in some epidemic models in the range $R_0 < 1$, the endemic equilibrium points may also exist, which shows that $R_0 < 1$ is not enough for eliminating the disease. In such models, it is said that backward bifurcation occurs, see [28]. We study the occurrence of backward bifurcation in each strain and in general i.e. in the coexistence equilibrium point in our model.

We organize the paper as follows. In section 2, we present the model and study the positivity of the solutions, the basic reproduction number, and the local and global stability of DFE. In section 3, we study the strain dominance equilibria and compute the invasion numbers. We prove that under suitable condition, strain dominance equilibrium points can exist, i.e., backward bifurcation occurs in that strain. Also, we study the local and global stability of them. In section 4, we prove the occurrence of backward bifurcation in strain dominance equilibriums, with the aid of center manifold theory and theorem obtained in [10]. In section 5, we study the existence of coexistence equilibria. We prove that when $R_0 < 1$, the coexistence equilibrium point can exist, i.e., backward bifurcation occurs in the coexistence equilibria. Furthermore, we obtain sufficient conditions for the global asymptotic stability by the geometric method introduced by Li and Muldowney in [26]. Finally, in section 6, we use numerical simulation to describe the obtained analytical results.

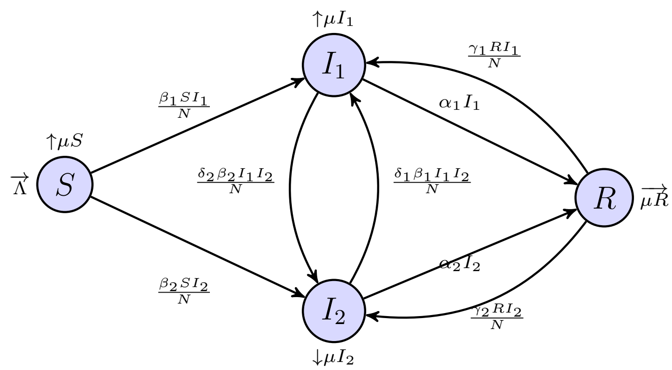

Figure 1. The flowchart of the model

2. Model formulation and basic properties

In our model, the total population of the community is divided into the following groups, susceptible individuals S, individuals infected with strain one, i.e., individuals who abuse prescription opioids I_1, individuals infected with strain two, i.e., individuals addicted to heroin I_2, and individuals under treatment/rehabilitation R. The number of individuals in this compartments is denoted by $S, I_1, I_2, andR$ respectively. The numbers β_1, β_2 show the rate of infection in strains one and two, respectively. Since we consider the superinfection, the infection rate β_2 is enhanced by δ_2, and the transition rate from prescription opioid abuse to heroin addiction becomes $\delta_2\beta_2$. On the other hand, heroin-addicted individuals may tend to misuse prescription opioids. We consider the transition rate from heroin addiction to prescription opioid misuse by $\delta_1\beta_1$. A fraction $\alpha_i, i = 1, 2$, of individuals infected by each strain recover from the infection, i.e., come under rehabilitation/treatment programs and go to the compartment R. Furthermore, individuals under rehabilitation/treatment relapse into the infection in each strain due to contact with infected individuals respectively at rates γ_1, γ_2. In figure 1. the model's flowchart is depicted, and we have the following ODE system,

$$
\begin{cases}
\dot{S} = \Lambda - \beta_1 \dfrac{SI_1}{N} - \beta_2 \dfrac{SI_2}{N} - \mu\, S \\
\dot{I}_1 = \beta_1 \dfrac{SI_1}{N} - \delta_2\, \beta_2 \dfrac{I_1 I_2}{N} + \delta_1\, \beta_1 \dfrac{I_1\, I_2}{N} - (\mu + \alpha_1)\, I_1 + \gamma_1\, \dfrac{R\, I_1}{N}, \\
\dot{I}_2 = \beta_2 \dfrac{SI_2}{N} + \delta_2\, \beta_2 \dfrac{I_1 I_2}{N} - \delta_1\, \beta_1 \dfrac{I_1 I_2}{N} - (\mu + \alpha_2)\, I_2 + \gamma_2\, \dfrac{R\, I_2}{N}, \\
\dot{R} = \alpha_1\, I_1 + \alpha_2\, I_2 - \mu\, R - \gamma_1\, \dfrac{R\, I_1}{N} - \gamma_2\, \dfrac{R\, I_2}{N}.
\end{cases}
\tag{2.1}
$$

At first, we prove that the solutions are nonnegative.

Lemma 2.1. *If the initial conditions are nonnegative, i.e., $S(0) \geq 0, I_1(0) \geq 0, I_2(0) \geq 0$ and $R(0) \geq 0$, then all components of the solution of the system are nonnegative for all $t \geq 0$.*

Proof. All components of the solution $(S(t), I_1(t), I_2(t), R(t))$ of the system are continuously differentiable. Furthermore, if all compartments have nonnegative initial conditions and that if any of the compartments are zero at time $t = t_i \geq 0$, then the derivatives are nonnegative. For example if $S(t_1) = 0$, $I_1(t_1) \geq 0$, $I_2(t_1) \geq 0$ and $R(t_1) \geq 0$, we get

$$
\frac{dS(t_1)}{dt} = \Lambda \geq 0
$$

that implies $S(t_1^+) \geq 0$, and hence, $S(t)$ is nonnegative for all time $t \geq 0$. Next, assume that $I_1(t_2) = 0$, $S(t_2) \geq 0$, $I_2(t_2) \geq 0$, $R(t_2) \geq 0$, we have

$$\frac{dI_1(t_2)}{dt} = 0$$

that implies $I_1(t_2^+) \geq 0$, and hence, $I_1(t)$ is nonnegative for all time $t \geq 0$. Now, assume that $R(t_3) = 0$, $S(t_3) \geq 0$, $I_1(t_3) \geq 0$, $I_2(t_3) \geq 0$, we have

$$\frac{dR(t_3)}{dt} = \alpha_1 I_1(t_3) + \alpha_2 I_2(t_3) \geq 0$$

that implies $R(t_3^+) \geq 0$, and hence, $R(t)$ is nonnegative for all time $t \geq 0$. The same reason is true for I_2, and as mentioned in [35] it can be concluded that all compartments are nonnegative at all time $t \geq 0$. □

Boundedness is one of the basic properties of the solutions that we prove in the following lemma.

Lemma 2.2. *For any set of nonnegative initial values, the total population $N(t) = S(t) + I_1(t) + I_2(t) + R(t)$ is bounded from above.*

Proof. We have $\dot{N} = \Lambda - \mu N$, and integration yields,

$$N(t) = N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}) \leq \max(N(0), \frac{\Lambda}{\mu}) = M.$$

This proves the boundedness of the solutions of the system. □

As in the White-Comiskey model, we consider the total population of the community to be constant, i.e., $N(t) = N_0$. Let

$$s = \frac{S}{N_0},\ i_1 = \frac{I_1}{N_0},\ i_2 = \frac{I_2}{N_0},\ r = \frac{R}{N_0}. \tag{2.2}$$

Therefore (2.1), is converted to:

$$\begin{cases} \dot{i_1} = \beta_1(i_1 - i_1^2 - i_1 i_2 - r i_1) + (\delta_1\,\beta_1 - \delta_2\,\beta_2) i_1\, i_2 - (\mu + \alpha_1) i_1 + \gamma_1\, r\, i_1 \\ \dot{i_2} = \beta_2(i_2 - i_2^2 - i_1 i_2 - r i_2) + (\delta_2\,\beta_2 - \delta_1\,\beta_1) i_1\, i_2 - (\mu + \alpha_2) i_2 + \gamma_2\, r\, i_2 \\ \dot{r} = \alpha_1\, i_1 + \alpha_2\, i_2 - \mu\, r - \gamma_1\, r\, i_1 - \gamma_2\, r\, i_2. \end{cases} \tag{2.3}$$

We study this system in the following region,

$$\Omega = \{(i_1, i_2, r); i_1 \geq 0, i_2 \geq 0, r \geq 0, i_1 + i_2 + r \leq 1\}$$

which is positive invariant with respect to (2.3).
A nonlinear differential equation model with constant coefficients typically has time-independent solutions, that is, solutions that are constant in time. Such solutions are called equilibrium points. Equilibrium points play an important role in the long-term behavior of the solutions. They are easy to find from the differential equation even if we don't know the explicit solution, since their derivative with respect to time is zero. In the mathematical epidemiology literature, the equilibrium in which the disease is not present in the population, and the entire population is susceptible, is referred to as the disease-free equilibrium, see [28]. In (2.3), the disease-free equilibrium point is the point $E_0 = (0, 0, 0)$.
A classical way for computation of the basic reproduction number of a model, which is a key quantity in mathematical epidemiology, is the linearization theorem which uses Jacobian matrix of the system in disease-free equilibrium point, see [28]. The Jacobian matrix of (2.3) has the following form:

$$J = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix}$$

in which

$$\begin{aligned}
a_{11} &= \beta_1(1-2i_1-i_2-r)+(\delta_1\beta_1-\delta_2\beta_2)i_2-(\mu+\alpha_1)+\gamma_1 r,\\
a_{12} &= -\beta_1 i_1+(\delta_1\beta_1-\delta_2\beta_2)i_1, a_{13}=-\beta_1 i_1+\gamma_1 i_1,\\
a_{21} &= -\beta_2 i_2+(\delta_2\beta_2-\delta_1\beta_1)i_2, a_{23}=-\beta_2 i_2+\gamma_2 i_2,\\
a_{22} &= \beta_2(1-i_1-2i_2-r)+(\delta_2\beta_2-\delta_1\beta_1)i_1-(\mu+\alpha_2)+\gamma_2 r,\\
a_{31} &= \alpha_1-\gamma_1 r, a_{32}=\alpha_2-\gamma_2 r, a_{33}=-\mu-\gamma_1 i_1-\gamma_2 i_2.
\end{aligned}$$

And

$$J_0 = J(E_0) = \begin{bmatrix} \beta_1-(\mu+\alpha_1) & 0 & 0 \\ 0 & \beta_2-(\mu+\alpha_2) & 0 \\ \alpha_1 & \alpha_2 & -\mu \end{bmatrix}$$

which has the eigenvalues

$$\beta_1-(\mu+\alpha_1), \quad \beta_2-(\mu+\alpha_2), \quad -\mu. \tag{2.4}$$

We define the basic reproduction of the model by $R_0 = \max\{R_1, R_2\}$ in which, $R_1 = \frac{\beta_1}{\mu+\alpha_1}$, $R_2 = \frac{\beta_2}{\mu+\alpha_2}$. The linearization theorem implies the following result.

Theorem 2.1. *The DFE point E_0 is local asymptotic stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

To determine whether the infection can invade the population, we prove the global asymptotic stability of the DFE point. Backward bifurcation occurs in this model, which is proved in next sections. Hence DFE can not be globally asymptotically stable, across region $R_0 < 1$, unless under certain conditions. In the following proposition we extract sufficient conditions for this problem.

Proposition 2.1. *The DFE point E_0 is global asymptotic stable provided, $R_0 < 1$, $\beta_i < \mu + \frac{m-2}{m-1}\alpha_i$, $\gamma_i < \frac{m}{m-1}\beta_i$, for $i = 1, 2$ and $m \geq 2$.*

Proof. Consider the following function $V : \Omega \to \mathbb{R}^+$.

$$V(i_1, i_2, r) = mi_1 + mi_2 + r.$$

The function V is positive definite with respect to E_0. And the derivative of V on the trajectories of (2.3) with respect to t is,

$$\begin{aligned}
\frac{dV}{dt} &= mi_1' + mi_2' + r' \\
&\leq \beta_1 i_1\left(1-\frac{1}{R_1}\right) + ((m-1)(\beta_1-\mu)-(m-2)\alpha_1)i_1 + ((m-1)\gamma_1 - m\beta_1)ri_1 \\
&+ \beta_2 i_2\left(1-\frac{1}{R_2}\right) + ((m-1)(\beta_2-\mu)-(m-2)\alpha_2)i_2 + ((m-1)\gamma_2 - m\beta_2)ri_2 - \mu r.
\end{aligned}$$

Since $R_1 < 1$, $R_2 < 1$ and $\beta_i < \mu + \frac{m-2}{m-1}\alpha_i$, $\gamma_i < \frac{m}{m-1}\beta_i$, the $\frac{dV}{dt}$ is negative, and Lyapunov theorem implies global stability of E_0. □

3. Boundary equilibrium points and their stabilities

An equilibrium point with the presence of strain one and the absence of strain two is called a strain one dominance equilibrium point, see [28]. Such equilibrium point $E_1 = (\widehat{i}_1, 0, \widehat{r})$ is the solution of the following equations with positive components:

$$\begin{cases} \beta_1(1-\widehat{i}_1-\widehat{r})+\gamma_1\,\widehat{r}=\mu+\alpha_1 \\ \alpha_1\,\widehat{i}_1-\mu\,\widehat{r}-\gamma_1\,\widehat{r}\,\widehat{i}_1=0. \end{cases} \tag{3.1}$$

Therefore $\widehat{i}_1$ is a positive solution of the following equation:

$$F_1(\widehat{i}_1)=A\widehat{i}_1^2+B\widehat{i}_1+C=0 \tag{3.2}$$

in which

$$A=\gamma_1\,\beta_1, C=-\beta_1\mu\left(1-\frac{1}{R_1}\right),$$

$$B=\beta_1(\mu+\alpha_1)-\alpha_1\gamma_1-\gamma_1\beta_1\left(1-\frac{1}{R_1}\right).$$

$F_1(\widehat{i}_1)$ is a convex parabola with a minimum point $\frac{-B}{2A}$ and minimum value $\frac{-\Delta}{2A}$, in which $\Delta=B^2-4AC$. Now by applying the geometric properties of parabolas, we have:

Theorem 3.1. *One of the following cases occur in (2.3):*
Case 1. The system has a unique strain one-dominance equilibrium point $E_1=(\widehat{i}_1,0,\widehat{r})$, provided $C<0$. In this case, $R_1>1$.
Case 2. The system has a unique strain one-dominance equilibrium $E_1=(\widehat{i}_1,0,\widehat{r})$, provided, $B<0$, $C=0$. In this case, $R_1=1$.
Case 3. The system has two strain one-dominance equilibrium, provided $B<0$, $C>0$ and $\Delta>0$. In this case

$$\frac{4\gamma_1\beta_1^2\mu}{4\gamma_1\beta_1^2\mu+B^2}<R_1<1.$$

Case 4. The system has a unique strain one-dominance equilibrium, provided $B<0$, $C>0$, and $\Delta=0$. In this case

$$\frac{4\gamma_1\beta_1^2\mu}{4\gamma_1\beta_1^2\mu+B^2}=R_1<1.$$

In the next theorem, we prove the local stability of E_1.

Theorem 3.2. *Let*

$$\hat{R}_1^2=\frac{\beta_2(1-\widehat{i}_1-\widehat{r})+\delta_2\beta_2\widehat{i}_1+\gamma_2\widehat{r}}{\delta_1\beta_1\widehat{i}_1+(\mu+\alpha_2)}.$$

When, $\hat{R}_1^2<1$ and $\beta_1\widehat{i}_1(\mu+\gamma_1\widehat{i}_1)-\mu(\gamma_1-\beta_1)\widehat{r}>0$, the equilibrium point $E_1=(\widehat{i}_1,0,\widehat{r})$ is local asymptotic stable.

Proof. We compute the Jacobian matrix of the system at E_1 as follows:

$$J_1=J(E_1)=\begin{bmatrix} b_{11} & b_{12} & b_{13} \\ 0 & b_{22} & 0 \\ b_{31} & b_{32} & b_{33} \end{bmatrix}$$

where,

$$b_{11}=\beta_1(1-2\widehat{i}_1-\widehat{r})-(\mu+\alpha_1)+\gamma_1\widehat{r},$$

$$b_{12}=-\beta_1\widehat{i}_1+(\delta_1\beta_1-\delta_2\beta_2)\widehat{i}_1, b_{13}=-\beta_1\widehat{i}_1+\gamma_1\widehat{i}_1,$$

$$b_{22}=\beta_2(1-\widehat{i}_1-\widehat{r})+(\delta_2\,\beta_2-\delta_1\,\beta_1)\widehat{i}_1-(\mu+\alpha_2)+\gamma_2\widehat{r},$$

$$b_{31}=\alpha_1-\gamma_1\widehat{r}, b_{32}=\alpha_2-\gamma_2\widehat{r}, b_{33}=-\mu-\gamma_1\widehat{i}_1.$$

An eigenvalue of the matrix J_1 is

$$\lambda_{11}=\beta_2(1-\widehat{i}_1-\widehat{r})+(\delta_2\,\beta_2-\delta_1\,\beta_1)\widehat{i}_1-(\mu+\alpha_2)+\gamma_2\widehat{r}. \tag{3.3}$$

Furthermore, the eigenvalues of the submatrix:

$$J_{11} = \begin{bmatrix} b_{11} & b_{13} \\ b_{31} & b_{33} \end{bmatrix}$$

have negative real parts if $Tr(J_{11}) < 0$ and $Det(J_{11}) > 0$. By using (3.1) we can easily see that

$$b_{11} = -\beta_1 \widehat{i}_1,\ b_{13} = (\gamma_1 - \beta_1)\widehat{i}_1,\ b_{31} = \mu \frac{\widehat{r}}{\widehat{i}_1},\ b_{33} = -\mu - \gamma_1 \widehat{i}_1$$

and

$$Det(J_{11}) = \beta_1 \widehat{i}_1(\mu + \gamma_1 \widehat{i}_1) - \mu(\gamma_1 - \beta_1)\widehat{r}.$$

Furthermore $Tr(J_{11}) = b_{11} + b_{33} < 0$. Now For the stability of E_1, the sign of eigenvalue λ_{11} must be negative, that is,

$$\hat{R}_1^2 = \frac{\beta_2(1 - \widehat{i}_1 - \widehat{r}) + \delta_2\beta_2\widehat{i}_1 + \gamma_2\widehat{r}}{\delta_1\beta_1\widehat{i}_1 + (\mu + \alpha_2)} < 1.$$

□

Lemma 3.1. *Let $\hat{R}_1^2 < 1$ and $\gamma_1 \leq \beta_1$, then the equilibrium point $E_1 = (\widehat{i}_1, 0, \widehat{r})$ is locally asymptotically stable.*

As it is mentioned in [28], the quantity $\hat{R}_1^2$ is called, the invasion reproduction number or invasion number of strain two at the equilibrium of strain one. Mathematically, the invasion number gives a threshold for the stability of a dominance equilibrium. The strain two cannot grow when strain one is at equilibrium if and only if $\hat{R}_1^2 < 1$. In this case, we say that strain two cannot invade the equilibrium of strain one. Epidemiologically, the invasion number of strain two at the equilibrium of strain one gives the number of secondary infections one individual infected with strain two will produce in a population in which strain one is at equilibrium during its lifetime as infectious.
In theorem 3.1 and section 4 we show the occurrence of backward bifurcation in strain one dominance equilibrium points. In fact, strain one dominance equilibrium points and DFE can exist simultaneously. Therefore, equilibrium point E_1 can be global asymptotic stable only under certain conditions. In the following theorem we extract sufficcient conditions for this problem.

Theorem 3.3. *The equilibrium point $E_1 = (\widehat{i}_1, 0, \widehat{r})$ is global asymptotic stable if,*

$$\beta_1 = \beta_2, \gamma_1 = \gamma_2, \alpha_1 = \alpha_2, \gamma_1 < \beta_1, \hat{R}_1^2 < 1. \tag{3.4}$$

Proof. We use the following function on $\mathbb{R}^3_+$, as a Lyapunov function:

$$V = K_1\left(i_1 - \widehat{i}_1 - \widehat{i}_1 Ln(\frac{i_1}{\widehat{i}_1})\right) + K_2\, i_2 + K_3\,(r - \widehat{r})^2. \tag{3.5}$$

Where K_1, K_2 and K_3 are positive constants to be chosen later. The function V is positive definite with respect to E_1. We compute the derivative of V with respect to t.

$$\begin{aligned}
\frac{dV}{dt} &= K_1\,(i_1 - \widehat{i}_1)\frac{i_1'}{i_1} + K_2\, i_2' + 2K_3\,(r - \widehat{r})\, r' \\
&= -K_1\,\beta_1(i_1 - \widehat{i}_1)^2 - K_2\beta_2 i_2^2 - 2K_3\mu(r - \widehat{r})^2 - 2K_3(\gamma_1 i_1 + \gamma_2 i_2)(r - \widehat{r})^2 \\
&\quad - (K_1\beta_1 + K_2\beta_2)i_2(i_1 - \widehat{i}_1) + [K_1(\gamma_1 - \beta_1) + 2K_3(\alpha_1 - \gamma_1\widehat{r})](i_1 - \widehat{i}_1)(r - \widehat{r}) \\
&\quad + K_2 i_2\left((\beta_2(1 - \widehat{i}_1 - \widehat{r}) + \delta_2\beta_2\widehat{i}_1 + \gamma_2\widehat{r}) - (\mu + \alpha_2 + \delta_1\beta_1\widehat{i}_1)\right) + [K_2(\gamma_2 - \beta_2) + 2K_3(\alpha_2 - \gamma_2\widehat{r})]i_2(r - \widehat{r}).
\end{aligned}$$

Let

$$K_1 = \frac{1}{\beta_1 - \gamma_1}, K_2 = \frac{1}{\beta_2 - \gamma_2}, K_3 = \frac{1}{2(\alpha_1 - \gamma_1\widehat{r})} = \frac{1}{2(\alpha_2 - \gamma_2\widehat{r})}.$$

Since $\gamma_1 < \beta_1$, $\gamma_2 < \beta_2$, and $\gamma_1 \widehat{r} < \alpha_1$, constants K_1, K_2, and K_3 are positive. Since $\gamma_1 = \gamma_2, \beta_1 = \beta_2$ then, $K_1 = K_2$. The following inequality has been obtained from dV/dt and by using the inequalities $a^2 + b^2 \geq 2ab$ and $a^2 + b^2 \geq -2ab$,

$$\frac{dV}{dt} \leq \frac{K_2 i_2}{(\mu + \alpha_2) + \delta_1 \beta_1 \widehat{i}_1} \left(\hat{R}_1^2 - 1 \right) - 2K_3(\gamma_1 i_1 + \gamma_2 i_2)(r - \widehat{r})^2 - 2K_3 \mu (r - \widehat{r})^2.$$

From (3.4) we have $\frac{dV}{dt} < 0$. Therefore, E_1 is globally asymptotic stable. □

The study of the existence of the strain two-dominance equilibrium point, computation of its invasion number, and the proof of local and global asymptotic stability can be done similarly.

4. Backward bifurcation

Naturally, in epidemic models, the infection can be controlled by having $R_0 < 1$ if the initial size of all compartments of the model is in the basin of attraction of the DFE P_0. Simultaneously, in some epidemic models in the range $R_0 < 1$ the endemic equilibrium points may also exists, which shows that $R_0 < 1$ is not enough for eliminating the disease. In such models, it is said that backward bifurcation occurs, see [28]. This phenomenon can also occur in the case of strain one-dominance equilibrium points. We call it the occurrence of backward bifurcation in the strain one. Similarly, one can define the occurrence of backward bifurcation in strain two.
In theorem 3.1, we prove that when $R_i < 1$ under suitable conditions, strain i-dominance equilibrium exists, i.e., the backward bifurcation occurs in strain i. A standard method for studying the occurrence of backward bifurcation is to use the Castillo-Chavez and Song theorem, which was obtained using the center manifold theory. The following results is obtained by directly applying theorem 4.1 of [10]. We consider two cases:

Case 1. $R_1 = 1$ and $R_2 < 1$.
In theorem 4.1 of [10], it is needed that Jacobian of the DFE point has 0 as an eigenvalue of first order, i.e., a simple eigen value. Since $R_1 = 1$, we can compute β_1 as $\beta_1 = \beta_1^* = \mu + \alpha_1$. Now the eigenvalues of $J(E_0, \beta_1^*)$ are 0, $-\mu$, $\beta_2 \left(1 - \frac{1}{R_2}\right)$. Corresponding right and left eigenvalues are $w = \left(1, 0, \frac{\alpha_1}{\mu}\right)$ and $v = (1, 0, 0)$. We consider $x_1 = i_1, x_2 = i_2, x_3 = r$ and compute the quantities a and b in theorem 3.2. of [10], in the following forms,

$$a = \sum_{k,i,j=1}^{3} v_k\, w_i w_j \frac{\partial^2 f_k}{\partial x_i\, \partial x_j} = 2\beta_1^* - \frac{2\alpha_1}{\mu}(\gamma_1 - \beta_1^*) = \frac{2(-\alpha_1\gamma_1 + (\mu + \alpha_1)^2)}{\mu},$$

$$b = \sum_{k,i=1}^{3} v_k w_i \frac{\partial^2 f_k}{\partial x_i\, \partial \varphi}(E_0, \beta_1^*) = \sum_{i=1}^{3} w_i \frac{\partial^2 f_1}{\partial x_i\, \partial \varphi}(0,0) = 1.$$

Therefore $a > 0$ if,

$$\alpha_1 \gamma_1 < (\mu + \alpha_1)^2 \tag{4.1}$$

which shows the occurrence of backward bifurcation in strain one.
Figure 2 shows bifurcation diagram, i.e. the diagram of $\widehat{i_1}$ in term of R_1.

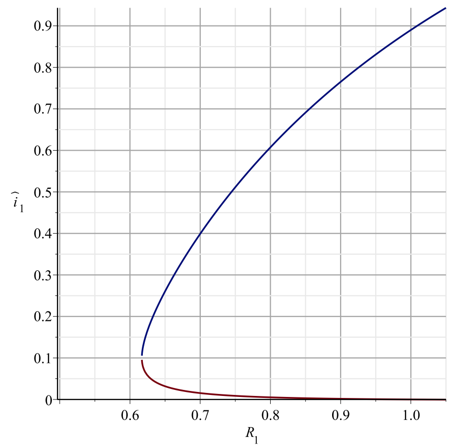

FIGURE 2. The occurrence of backward bifurcation in strain one in a set of parameters including $\mu = 0.1$, $\beta_1 = 0.01$, $\gamma_1 = 0.1$, $\alpha_1 = 0.2$, satisfying (4.1). In this case $R_1 = \frac{1}{30}$.

Case 2. $R_2 = 1$ and $R_1 < 1$.
In theorem 4.1 of [10], it is needed that Jacobian of the DFE point has 0 as an eigenvalue of first order, i.e., a simple eigen value. From $R_2 = 1$, we conclude that $\beta_2 = \beta_2^* = \mu + \alpha_2$, and the Jacobian matrix $J(E_0, \beta_2^*)$, has eigenvalues $0,\ -\mu,\ \beta_1\left(1 - \frac{1}{R_1}\right)$. The right and left eigenvectors of $J(E_0, \beta_2^*)$ associated with $\lambda_1 = 0$ are $w = \left(0, 1, \frac{\alpha_2}{\mu}\right)$ and $v = (0, 1, 0)$. Hence

$$a = \sum_{k,i,j=1}^{3} v_k\, w_i w_j \frac{\partial^2 f_k}{\partial x_i\, \partial x_j} = 2\beta_2^* - \frac{2\alpha_2}{\mu}(\gamma_2 - \beta_2^*) = \frac{2(-\alpha_2\gamma_2 + (\mu + \alpha_2)^2)}{\mu},$$

$$b = \sum_{k,i=1}^{3} v_k w_i \frac{\partial^2 f_1}{\partial x_i\, \partial \varphi}(E_0, \beta_2^*) = \sum_{i=1}^{3} w_i \frac{\partial^2 f_1}{\partial x_i\, \partial \varphi}(0, 0) = 1.$$

Now $a > 0$ if $\alpha_2\gamma_2 < (\mu + \alpha_2)^2$ which shows the occurrence of backward bifurcation in strain two.

5. The coexistence equilibrium point and global stability

An equilibrium point (i_1^*, i_2^*, r^*) in which $i_1^* \neq 0$, $i_2^* \neq 0$, i.e., both strains are present, is called a coexistence equilibrium. In this section, we study the existence and stability of such equilibriums. Such a point is a solution to the following system:

$$\begin{cases} \beta_1(1 - i_1^* - i_2^* - r^*) + (\delta_1\, \beta_1 - \delta_2\, \beta_2)\, i_2^* - (\mu + \alpha_1) + \gamma_1\, r^* = 0 \\ \beta_2(1 - i_2^* - i_1^* - r^*) + (\delta_2\, \beta_2 - \delta_1\, \beta_1) i_1^* - (\mu + \alpha_2) + \gamma_2\, r^* = 0 \\ \alpha_1\, i_1^* + \alpha_2\, i_2^* - \mu\, r^* - \gamma_1\, i_1^*\, r^* - \gamma_2\, i_2^*\, r^* = 0. \end{cases} \tag{5.1}$$

By solving i_1^* and i_2^* in term of r^* and other coefficients, we have,

$$i_1^* = \frac{\beta_1\beta_2(1 - \frac{1}{R_1})}{\delta^2 + \beta_2\delta - \beta_1\delta} + \frac{\beta_2(\delta - \beta_1)(1 - \frac{1}{R_2})}{\delta^2 + \beta_2\delta - \beta_1\delta} + \frac{(\gamma_1 - \beta_1)\beta_2 + (\delta - \beta_1)(\gamma_2 - \beta_2)}{\delta^2 + \beta_2\delta - \beta_1\delta} r^*,$$

and

$$i_2^* = \frac{\beta_1\beta_2(1 - \frac{1}{R_2})}{\delta^2 + \beta_2\delta - \beta_1\delta} - \frac{\beta_1(\delta + \beta_2)(1 - \frac{1}{R_1})}{\delta^2 + \beta_2\delta - \beta_1\delta} + \frac{(\gamma_2 - \beta_2)\beta_1 + (\delta + \beta_2)(\beta_1 - \gamma_1)}{\delta^2 + \beta_2\delta - \beta_1\delta} r^*.$$

Where $\delta = \delta_1\beta_1 - \delta_2\beta_2$. Now we substitute i_1^* and i_2^* in the third equation of the system (5.1) which yields,

$$F(r^*) = A_1\, {r^*}^2 + A_2 r^* + A_3 = 0 \tag{5.2}$$

where

$$\begin{aligned}
A_1 &= \frac{\gamma_1\beta_2(\beta_1-\gamma_1)+\gamma_1(\delta-\beta_1)(\beta_2-\gamma_2)+\gamma_2\beta_1(\beta_2-\gamma_2)+\gamma_2(\delta+\beta_2)(\gamma_1-\beta_1)}{\delta^2+\beta_2\delta-\delta\,\beta_1},\\
A_2 &= \frac{\alpha_1\beta_2(\gamma_1-\beta_1)+\alpha_1(\delta-\beta_1)(\gamma_2-\beta_2)}{\delta^2+\beta_2\delta-\delta\,\beta_1}+\frac{\alpha_2\beta_1(\gamma_2-\beta_2)+\alpha_2(\delta+\beta_2)(\beta_1-\gamma_1)}{\delta^2+\beta_2\delta-\delta\,\beta_1}\\
&+\frac{-\gamma_1\beta_1\beta_2(1-\frac{1}{R_1})-\gamma_1\beta_2(\delta-\beta_1)(1-\frac{1}{R_2})}{\delta^2+\beta_2\delta-\delta\,\beta_1}+\frac{-\gamma_2\beta_1\beta_2(1-\frac{1}{R_2})+\gamma_2\beta_1(\delta+\beta_2)(1-\frac{1}{R_1})}{\delta^2+\beta_2\delta-\delta\,\beta_1},\\
A_3 &= \frac{\alpha_1\beta_1\beta_2(1-\frac{1}{R_1})+\alpha_1\beta_2(\delta-\beta_1)(1-\frac{1}{R_2})}{\delta^2+\beta_2\delta-\delta\,\beta_1}+\frac{\alpha_2\beta_1\beta_2(1-\frac{1}{R_2})-\alpha_2\beta_1(\delta+\beta_2)(1-\frac{1}{R_1})}{\delta^2+\beta_2\delta-\delta\,\beta_1}.
\end{aligned}$$

$F(r^*)$ is a parabola with an extremum point $\frac{-B}{2A}$ and an extremum value $\frac{-\Delta}{2A}$, in which $\Delta = A_2^2 - 4A_1A_3$. Now in the following list, we present the cases in which $F(r^*) = 0$ has positive solutions.
Case 1. When $A_1A_3 < 0$, (5.2) has a positive solution, which is unique.
Case 2. When $A_1 < 0$ and $A_3 < 0$, then if $\Delta > 0$ and $A_2 > 0$, it has two positive real roots. And if $\Delta = 0$ and $A_2 > 0$, (5.2) has a positive solution, which is unique.
Case 3. When $A_1 < 0$, $A_3 = 0$, and $A_2 > 0$, it has a positive solution, which is unique.
Case 4. When $A_1 > 0$, $A_3 > 0$, if $A_2 < 0$ and $\Delta > 0$, it has two positive roots, and when $A_2 < 0$ and $\Delta = 0$, it has a positive solution, which is unique.
Case 5. When $A_1 > 0$, $A_3 = 0$, $A_2 < 0$, and $\Delta = 0$, the equation (5.2) has a unique positive root.
Now we have the following result.

Lemma 5.1. *The coexistence equilibrium point exists if:*
1. $\delta^2 + \beta_2\delta - \delta\,\beta_1 \neq 0$.
2. $F(r^*) = 0$, *has positive real roots.*
3. After substituting the positive r^*, *in* i_1^* *and* i_2^*, *they have positive values.*

Proposition 5.1. *If we choose an* $r^* > 0$ *from the above list and consider the following inequalities:*
1. $\delta < 0$, $-\beta_2 < \delta < \beta_1 - \beta_2$, $\beta_1 < \gamma_1$, $\gamma_2 < \beta_2$, *and* $R_2 < 1$.
2. $\frac{\beta_1}{\beta_1+(\delta-\beta_1)(1-\frac{1}{R_2})} < R_1 < 1$.
3. $\frac{\beta_1(\delta+\beta_2)}{\beta_1(\delta+\beta_2)+\beta_1\beta_1(\frac{1}{R_2}-1)+((\beta_2-\gamma_2)\beta_1+(\delta+\beta_2)(\gamma_1-\beta_1))r^*} < R_1 < 1$.
Then (2.3) *has a coexistence equilibrium point.*

Remark 5.1. *The above proposition shows the occurrence of backward bifurcation in the coexistence equilibria.*

Now we study the global asymptotic stability of the coexistence steady state in the case of the uniqueness of such point by using the geometric method presented in [26].
Let P be the following matrix function as it is needed in the geometric method,

$$P = \begin{bmatrix} e^{3i_1+3i_2} & 0 & 0 \\ 0 & e^{3i_1+3i_2} & 0 \\ 0 & 0 & e^{3i_1+3i_2} \end{bmatrix}.$$

Now we have the matrix,

$$P_f P^{-1} = diag(3i_1' + 3i_2', 3i_1' + 3i_2', 3i_1' + 3i_2'),$$

and,

$$Q = P_f P^{-1} + PJ^{[2]}P^{-1} = \begin{bmatrix} A_{11} & A_{12} & A_{13} \\ A_{21} & A_{22} & A_{23} \\ A_{31} & A_{32} & A_{33} \end{bmatrix},$$

in which,

$$\begin{aligned}
A_{11} &= \beta_1 - \mu + \beta_2 - \mu - \alpha_1 - \alpha_2 + (\beta_1 - \beta_2 - 3(\mu + \alpha_1) - \delta)i_1 \\
&\quad + (-\beta_1 + \beta_2 - 3(\mu + \alpha_2) + \delta)i_2 + (-\beta_1 - \beta_2 + \gamma_1 + \gamma_2)r - 2\beta_1\, i_1^2 \\
&\quad - 2(\beta_1 + \beta_2)i_1\, i_2 + (-2\beta_1 + 2\gamma_1)i_1 r + (-2\beta_2 + 2\gamma_2)i_2 r - 2\beta_2\, i_2^2, \\
A_{12} &= (\beta_2 + \delta)i_1 i_2 + \beta_2 i_2^2 + (\gamma_2 - \beta_2)i_2 + (-\gamma_2 + \beta_2)i_2 r, \\
A_{13} &= -\beta_1 i_1^2 + (-\beta_1 + \delta)i_1 i_2 + (-\gamma_1 + \beta_1)i_1 + (\gamma_1 - \beta_1)i_1 r, \\
A_{21} &= \alpha_2 - \gamma_2 r + \gamma_2 i_2 r + \gamma_1 i_1 r, \\
A_{22} &= (\beta_1 - 2\mu - \alpha_1) - 2\beta_1 i_1^2 - 3\beta_2 i_2^2 + (\beta_1 - 3(\mu + \alpha_1) - \gamma_1)i_1 + (3\gamma_1 - 2\beta_1)i_1 r \\
&\quad + (-\beta_1 - 3(\mu + \alpha_2) - \gamma_2 + 3\beta_2 + \delta)i_2 + (\gamma_1 - \beta_1)r + (4\gamma_2 - 3\beta_2)i_2 r + (-\delta - 2\beta_1 - 3\beta_2)i_1 i_2, \\
A_{23} &= (\delta - \beta_1)i_1 + (\beta_1 - \gamma_1)i_1 r + \beta_1 i_1^2 + (\beta_1 - \delta)i_1 i_2, \\
A_{31} &= -\alpha_1 + \gamma_1 r - \gamma_1 i_1 r - \gamma_2 i_2 r, \\
A_{32} &= (-\delta - \beta_2)i_2 + (\beta_2 - \gamma_2)i_2 r + \beta_2 i_2^2 + (\beta_2 + \delta)i_1 i_2, \\
A_{33} &= (\beta_2 - 2\mu - \alpha_2) - 2\beta_2 i_2^2 - 3\beta_1 i_1^2 + (-\beta_2 - \delta + 3\beta_1 - 3(\mu + \alpha_1) - \gamma_1)i_1 \\
&\quad + (\beta_2 - 3(\mu + \alpha_2) - \gamma_2)i_2 + (4\gamma_1 - 3\beta_1)i_1 r + (\gamma_2 - \beta_2)r + (3\gamma_2 - 2\beta_2)i_2 r + (\delta - 3\beta_1 - 2\beta_2)i_1 i_2.
\end{aligned}$$

We use the following norm for $z = (z_1, z_2, z_1)^T = (i_1, i_2, r)^T$

$$\|z\| = \begin{cases} \max\{|z_1| + |z_3|, |z_2| + |z_3|\} & if \quad z_2\, z_3 \geq 0, \\ \max\{|z_1| + |z_3|, |z_2|\} & if \quad z_2\, z_3 \leq 0. \end{cases} \tag{5.3}$$

Lemma 5.2. *There exists a constant $\tau > 0$ for which $D_+\|z\| \leq -\tau\|z\|$, in which $z \in \mathbb{R}^3$ is a solution of*

$$\frac{dz}{dt} = Q(\phi_t(u))z, \tag{5.4}$$

when

$$2\gamma_1 < \beta_1, 3\gamma_2 < \beta_2, \beta_2 + \beta_1 < \alpha_2, \alpha_2 + \beta_1 < \alpha_1, \gamma_1 + \gamma_2 < \beta_1. \tag{5.5}$$

Proof. We present one case from eight. The other cases are similar. We consider $\delta = \delta_1\beta_1 - \delta_2\beta_2 < 0$. For $\delta > 0$, the proof is similar.

Case 1: $z_1, z_2, z_3 > 0$ and $|z_1| + |z_3| > |z_2| + |z_3|$. In this case, $\|z\| = |z_1| + |z_3|$ and,

$$\begin{aligned}
D_+\|z\| &= D_+(|z_1| + |z_3|) = D_+(z_1 + z_3) = z_1' + z_3' \\
&= (A_{11} + A_{31})z_1 + (A_{12} + A_{32})z_2 + (A_{13} + A_{33})z_3.
\end{aligned}$$

Since $\beta_2 > \gamma_2$ and $\delta < 0$, therefore the coefficient of z_2 is less than $2\beta_2 i_2^2 + 2\beta_2 i_1 i_2 + (2\beta_2 - 2\gamma_2) i_2 r - \delta\, i_2$, and $z_2 < z_1$, hence,

$$\begin{aligned} D_+\|z\| \le\ & [\beta_1 - \mu + \beta_2 - \mu - 2\alpha_1 - \alpha_2 + (\beta_1 - 3(\mu + \alpha_1) - \beta_2 - \delta) i_1 + (-\beta_1 + \beta_2 - 3(\mu + \alpha_2)) i_2 \\ & + (2\gamma_1 - \beta_1 - \beta_2 + \gamma_2) r + (\gamma_1 - 2\beta_1) i_1 r - 2\beta_1 i_1 i_2 - 2\beta_1 i_1^2 - \gamma_2 i_2 r] z_1 \\ & + [-4\beta_1 i_1^2 + (2\delta - 4\beta_1 - 2\beta_2) i_1 i_2 + \beta_2 - 2\mu - \alpha_2 \\ & + (4\beta_1 - \beta_2 - \delta - 3(\mu + \alpha_1) - 2\gamma_1) i_1 (5\gamma_1 - 4\beta_1) i_1 r + (\beta_2 - \gamma_2 - 3(\mu + \alpha_2)) i_2 \\ & + (\gamma_2 - \beta_2) r + (3\gamma_2 - 2\beta_2) i_2 r] z_3 \\ \le\ & \max\{L_{11}, L_{12}\}\, \|z\|, \end{aligned}$$

where

$$\begin{aligned} L_{11} =\ & \beta_1 - \mu + \beta_2 - \mu - 2\alpha_1 - \alpha_2 + (\beta_1 - \mu - \alpha_1 - 2(\mu + \alpha_1) - \beta_2 - \delta) i_1 \\ & + (-\beta_1 + \beta_2 - \mu - \alpha_2 - 2(\mu + \alpha_2)) i_2 + (2\gamma_1 - \beta_1 - \beta_2 + \gamma_2) r + (\gamma_1 - 2\beta_1) i_1 r - 2\beta_1 i_1 i_2 - 2\beta_1 i_1^2, \\ L_{12} =\ & -4\beta_1 i_1^2 + (2\delta - 4\beta_1 - 2\beta_2) i_1 i_2 + \beta_2 - 2\mu - \alpha_2 + (3\beta_1 - 3\mu - \beta_2 - \delta - 3\alpha_1 + \beta_1 - 2\gamma_1) i_1 \\ & - 2\beta_2 i_2^2 (5\gamma_1 - 4\beta_1) i_1 r + (\beta_2 - \gamma_2 - 3(\mu + \alpha_2)) i_2 + (\gamma_2 - \beta_2) r + (3\gamma_2 - 2\beta_2) i_2 r. \end{aligned}$$

From (5.5) we have, $2\beta_1 < \alpha_1, \beta_2 < \alpha_2, 2\gamma_1 < \beta_1, 2\gamma_2 < \beta_2$, which implies the negativity of L_{11} and L_{12}.

□

From Lemma 5.2 we obtain the following theorem.

Theorem 5.1. *Assuming the relations (5.5), positive semi-trajectories of the system converge to a steady-state, i.e., any ω-limit point of the system in Ω°, is a steady-state.*

In the end, we have the following result.

Theorem 5.2. *Assuming the relations (5.5), then:*
(1) If the system has the unique steady state E_0, i.e., DFE, all trajectories converge to E_0;
(2) If the system has a unique endemic steady state E_1, then all trajectories converge to E_1.

6. Numerical simulations

In this section, we will simulate the system using MATLAB software, so that the obtained analytical results can be seen numerically. We present four cases.

6.1. **Case 1.** In this case, we choose a set of parameters which show convergence of trajectories to DFE. Furthermore, we show the sensitivity of infectious individuals in both strains with respect to rates of infection of each strain β_1, β_2. In this case, we have $R_0 < 1$.

6.2. **Case 2.** In this case, we choose a set of parameters for which $R_0 < 1$ and trajectories converge to strain one dominance equilibrium point, i.e., the occurence of backward bifurcation in strain one. Furthermore we show the sensitivity of infectious individuals in both strains with respect to rates of infection of each strain β_1, β_2.

6.3. **Case 3.** In this case, we choose a set of parameters for which $R_0 > 1$ and trajectories converge to strain one dominance equilibrium point. Although i_2 converge to zero, Figures (c) and (d) shows the occurence of an outbreak in strain two and the sensitivity of its peak to β_1, β_2.

6.4. **Case 4.** In this case, we choose a set of parameters for which $R_0 > 1$, and trajectories converge to coexistence equilibrium point. Furthermore, we show the sensitivity of infectious individuals in both strains with respect to rates of infection of each strain β_1, β_2.

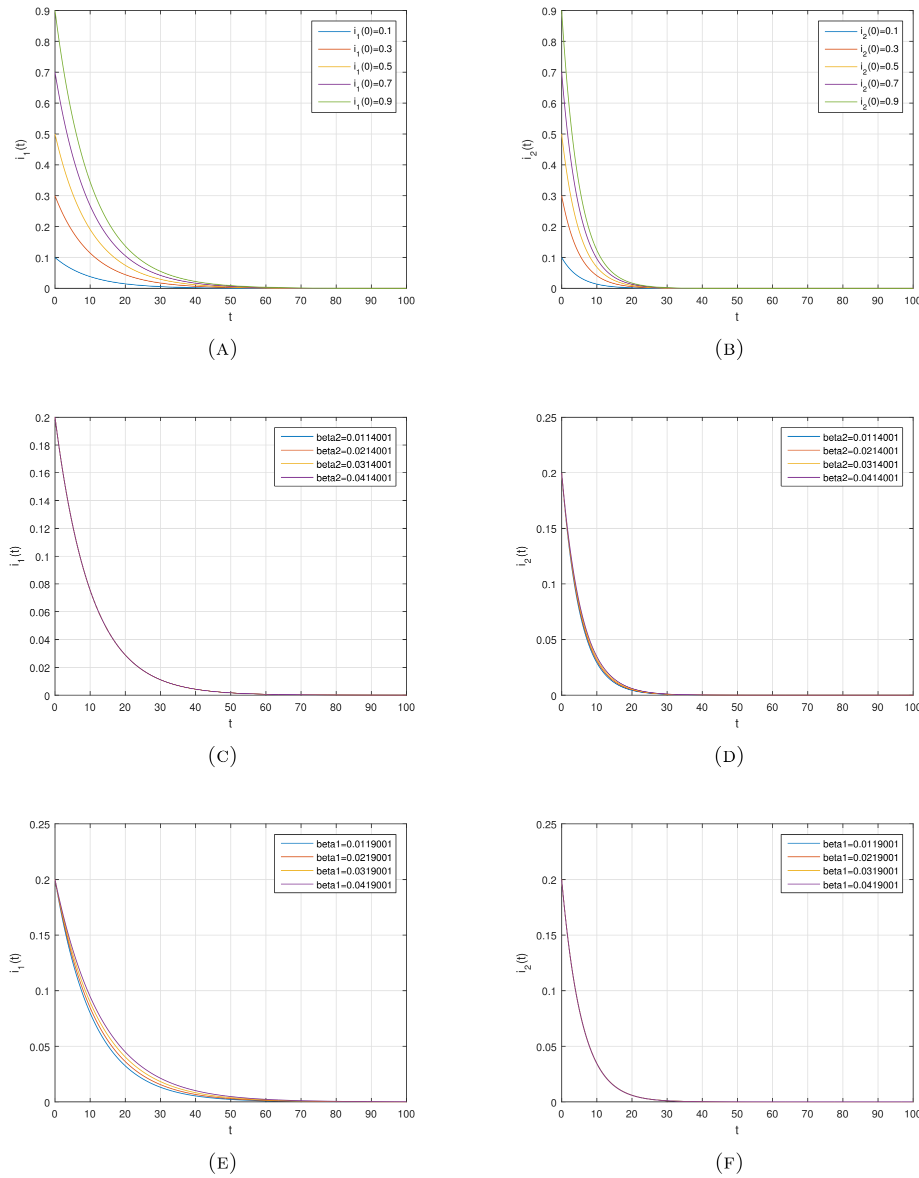

FIGURE 3. Set of parameters in (a) and (b): $\mu = 0.0001$, $\beta_1 = 0.0019001$, $\beta_2 = 0.0014001$, $\delta_1 = 0.01$, $\delta_2 = 0.02$, $\gamma_1 = 0.008001$, $\gamma_2 = 0.003001$, $\alpha_1 = 0.1$ and $\alpha_2 = 0.2$. In this case $R_1 = 0.01898$ and $R_2 = 0.006997001$. (a) and (b) show the convergence of the solutions with various initial conditions. (c), (d), (e) and (f), show the sensitivity of $i_1(t)$ and $i_2(t)$ with respect to β_1, β_2.

7. Conclusion

In this paper, we modified White and Comiskey's, model. We studied the effect of individuals who abuse prescription opioids on individuals addicted to heroin with the aid of a two-strain epidemic model. Our model contains superinfection and the effect of relapse of individuals under rehabilitation/treatment to drug abuse in each strain. We compute the basic reproduction and invasion numbers and study the existence and stability of strain dominance

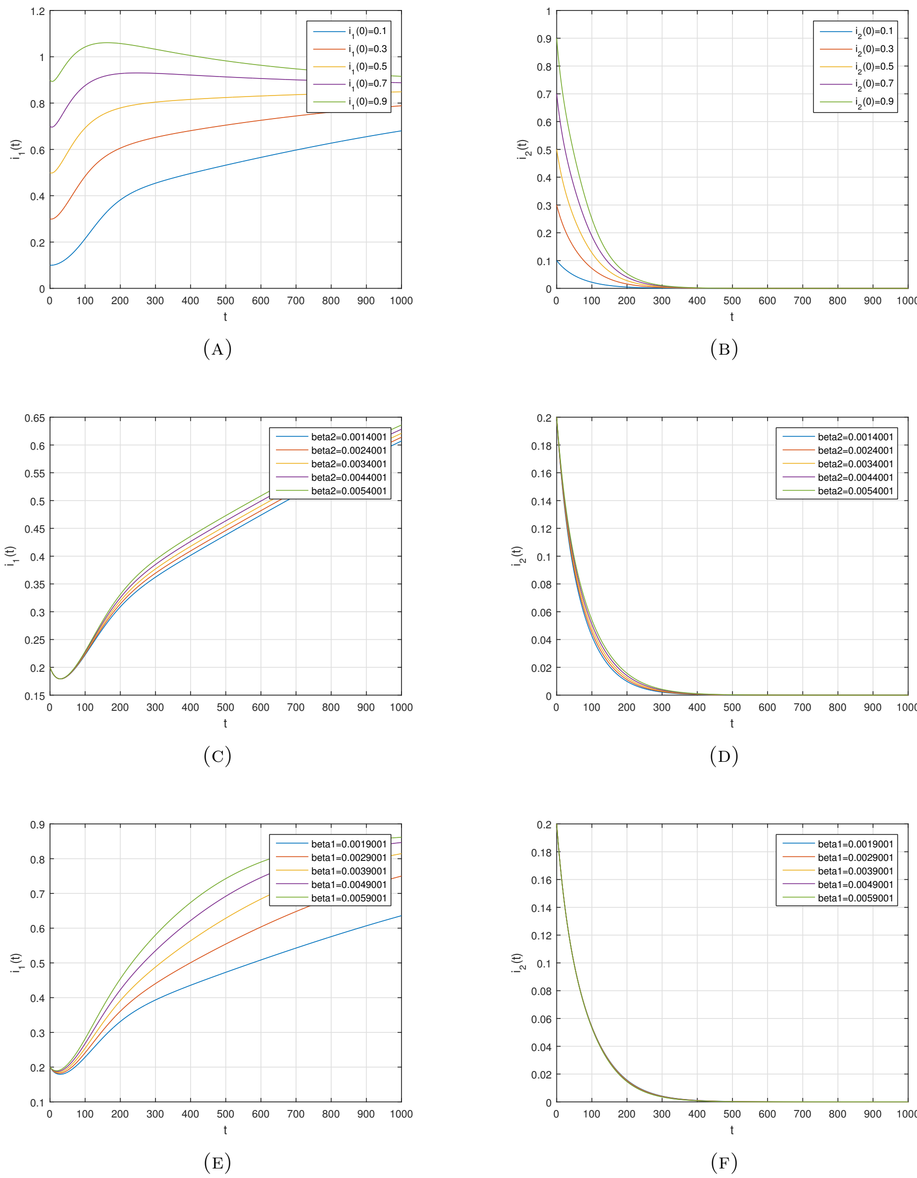

FIGURE 4. Set of parameters in (a): $\mu = 0.00001$, $\beta_1 = 0.0019001$, $\beta_2 = 0.0014001$, $\delta_1 = 0.01$, $\delta_2 = 0.02$, $\gamma_1 = 0.08001$, $\gamma_2 = 0.03001$, $\alpha_1 = 0.01$ and $\alpha_2 = 0.02$. In this case $R_1 = 0.18981$ and $R_2 = 0.06997001$. (a) and (b) show the convergence of the solutions with various initial conditions. (c), (d), (e) and (f) show the sensitivity of $i_1(t)$ and $i_2(t)$ with respect to β_1, β_2.

and coexistence equilibrium points. We proved that backward bifurcation occurs in each strain, i.e., the existence of strain dominance equilibriums if the basic reproduction number of the related strain is less than unity, as a result of the relapse effect. In fact, we showed that if the rate of relapse in strain i is greater than a special value, then the backward bifurcation occurs in the strain, for $i = 1, 2$. Backward bifurcation leads to bistability and makes it more difficult to control the disease, in fact, in order to prevent the outbreak of strain i, the reducing of R_i to $R_i < 1$, is

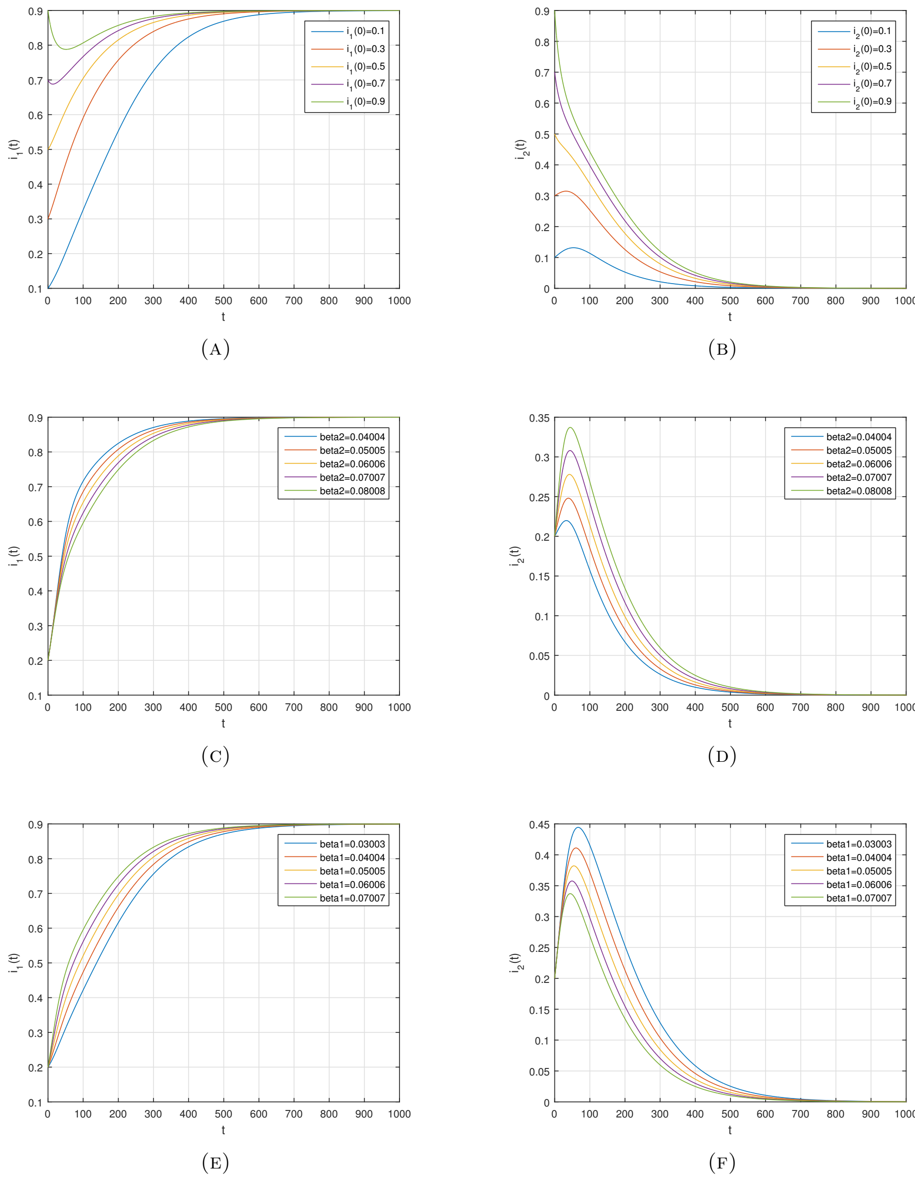

FIGURE 5. Set of parameters in (a): $\mu = 0.00001$, $\beta_1 = 0.03003$, $\beta_2 = 0.04004$, $\delta_1 = 0.01$, $\delta_2 = 0.02$, $\gamma_1 = 0.1001$, $\gamma_2 = 0.1001$, $\alpha_1 = 0.01$ and $\alpha_2 = 0.02$. In this case $R_1 = 3$ and $R_2 = 2.00099$. (a) and (b) show the convergence of the solutions with various initial conditions. (c), (d), (e) and (f) show the sensitivity of $i_1(t)$ and $i_2(t)$ with respect to β_1, β_2.

not enough.
Furthermore, we proved that backward bifurcation might occur in general, i.e., when the reproductive ratio R_0 is less than unity, the coexistence equilibrium point may exist.

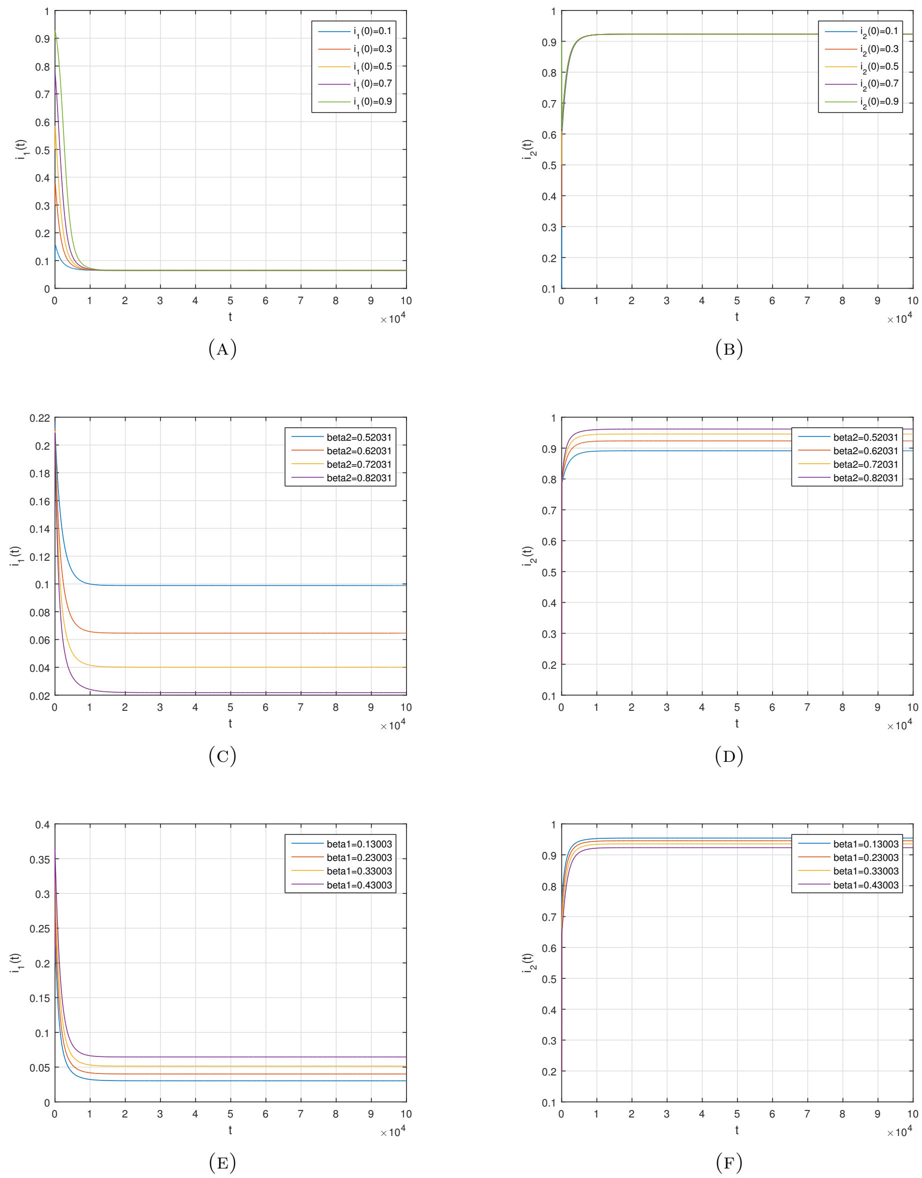

FIGURE 6. Set of parameters in (a): $\mu = 0.0000001$, $\beta_1 = 0.03003$, $\beta_2 = 0.62031$, $\delta_1 = 0.001$, $\delta_2 = 0.002$, $\gamma_1 = 0.1001$, $\gamma_2 = 0.1001$, $\alpha_1 = 0.0001$ and $\alpha_2 = 0.0002$. In this case $R_1 = 300$ and $R_2 = 3100$. (a) and (b) show the convergence of the solutions with various initial conditions. (c), (d), (e) and (f) show the sensitivity of $i_1(t)$ and $i_2(t)$ with respect to β_1, β_2.

Acknowledgment

The authors would like to thank the anonymous referees for their valuable and helpful comments and suggestions.

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