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BACKWARD BIFURCATION AND GLOBAL STABILITY IN A HEROIN EPIDEMIC MODEL

REZA MEMARBASHI*, SOMAYE TAGHAVI

Department of Mathematics, Semnan University, P. O. Box 35195-363, Semnan, Iran

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Abstract. In this paper, we propose and study a heroin epidemic model considering the effect of incarceration of users due to criminal actions. We prove the occurrence of backward bifurcation and compute the threshold quantity R_0^c by a new method. Furthermore the global stability of the equilibrium points of the model is investigated using Lyapunov functions and geometric stability method.

Keywords: backward bifurcation; global stability; drugs; epidemic models.

2010 AMS Subject Classification: 92D30, 34D23, 34C23.

1. INTRODUCTION

As far as usage of illicit drugs damage the physical, mental and social well being of individuals, their families and societies, illicit drugs usage turn into a worldwide, critical public and social health problem. Literature shows expanded researches undertaken to explore the correlation between illicit drugs and criminals, which is critically examined, reliably obtained, and accepted relationships within the criminological and social science research, see [22, 2, 24, 30]. According to, [8], statistics indicate that 60 percent to 80 percent of all crimes is drug-related.

*Corresponding author

E-mail address: r_memarbashi@semnan.ac.ir

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To decrease the accessibility and the level of use of illicit drugs, most governments rely heavily upon incarceration. Incarceration has been shown to have the impact on controlling drug-related crimes. "Research in the US on the correlation between community crime rates and imprisonment rates found that crime tended to fall with mild increases in imprisonment rates. This approach is based on the idea that incarceration will deter potential users and dealers from becoming involved in the illicit drug market", see [3].

Among various drug users, heroin users are at high risk of addiction and criminal actions. As indicated in [16], "the number of heroin users increased from 166,000 in 2002 to 335,000 in 2012, and the death rate of drug-poisoning involving heroin increased from 0.7 to 2.7 per 100,000 persons during 200-2013 in the USA. The heroin addiction was first defined as an epidemic in 1981-1983 in Ireland." White and Comiskey, in [29], have introduced the following epidemic model for the dynamics of heroin users,

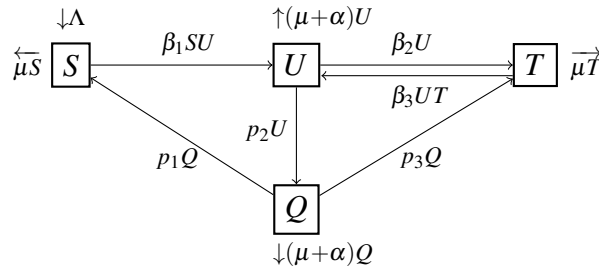
$$(1) \quad \begin{cases} \frac{dS}{dt} = \Lambda - \frac{\beta_1 S U_1}{N} - \mu S \\ \frac{dU_1}{dt} = \frac{\beta_1 S U_1}{N} + \frac{\beta_3 U_1 U_2}{N} - (\mu + \delta_1 + p) U_1 \\ \frac{dU_2}{dt} = p U_1 - \frac{\beta_3 U_1 U_2}{N} - (\mu + \delta_2) U_2 \end{cases}$$

in which $S(t)$, $U_1(t)$ and $U_2(t)$, denotes the number of susceptible individuals, drug users and drug users in treatment, respectively. Their model was revisited by Mulone and Straughan, [17]. After White and Comiskey's work, the epidemiology of drugs has been studied by several authors. For example, Nyabadza and Hove-Muskava, in [20], modified (1.1) to a model of the dynamics of methamphetamine use in a South African province. Njagarah and Nyabadza, in [18], have studied the impact of rehabilitation, amelioration and relapse on drug epidemics. Nyabadza, Njagarah and Smith, in [19], have studied the epidemiology of crystal in South Africa. The reader can see also, [9, 13, 16].

In this paper, we will propose and analyze a modified form of White-Comiskey's model by considering a new compartment, which includes incarcerated drug users due to drug-related crimes. We will investigate dynamical behaviors of the model such as steady states, backward bifurcation and local and global stability.

The paper is organized as follows. In section 2, we present the model and some preliminaries such as, positivity, boundedness and the basic reproduction number of the system. In section 3, we study the existence of endemic equilibrium points and show that backward bifurcation leading to bistability occurs, and we compute the quantity R_0^c by a new method. We prove the occurrence of backward bifurcation, both directly and by using the theorem of Castillo-Chavez and Song. In section 4, we obtain sufficient conditions for the local and global stability of both drug-free and endemic equilibrium points by Lyapunov functions and compound matrices, i.e. geometric stability method. In the application of geometric method, we use a new matrix function P and a hence new proof of its related lemma, lemma 4.5. Finally, we present some numerical simulations for further illustration of our analytical results.

2. MODEL FORMULATION AND BASIC PROPERTIES



Our proposed model is based on dividing the community into four compartments: S susceptible individuals at risk of using drugs, U drug users, T drug users in treatment/rehabilitation and Q drug users incarcerated due to criminal actions and we denote the number of this compartments by $S(t), U(t), T(t)$ and $Q(t)$, respectively. We assume that, new recruits (including travelers, newborns,...) enter the susceptible population at a constant rate Λ , and susceptible individuals become drug users at rate $\beta_1 U$. Drug users under treatment/rehabilitation relapse to the class of untreated drug users at rate $\beta_3 U$. We also assume that infected individuals (users), become under treatment/rehabilitation at rate β_2 , and drug users with criminal actions, imprisoned at rate p_1 . On the other hand incarcerated drug users who have completed their term of imprisonment and become susceptible again have rate p_1 , and incarcerated drug users referred to treatment/rehabilitation centers at rate p_3 . Finally, we assume that there can be drug-related death and define α to be the rate of drug-related death, while μ is the natural death rate.

TABLE 1. Description of parameters used in the model

Symbol	Description
Λ	Recruitment rate into the susceptible population
μ	The natural death rate of the general population
β_1	The probability of becoming a drug user per unit time
β_2	The rate at which drug users recruited into treatment
β_3	Rate of relaps of drug users in treatment to use
p_1	The rate at which offenders complete sentences and back to susceptibles
p_2	The rate at which those in drug-related crimes are sentenced
p_3	The rate at which offenders are referred to treatment
α	The removal rate due to drug use and drug-related crimes

Since the transmission of infection in drug problems is a type of imitation or social learning, drug relevant contact increases with an increase in population size, hence mass action incidence is more suitable than standard incidence.

Based on the flow diagram of the model depicted in the above figure, we have the following system of ordinary differential equations:

$$(2) \quad \left\{ \begin{array}{l} \frac{dS}{dt} = \Lambda - \beta_1 SU - \mu S + p_1 Q \\ \frac{dU}{dt} = \beta_1 SU + \beta_3 UT - (\mu + \alpha + \beta_2 + p_2)U \\ \frac{dT}{dt} = -\beta_3 UT + \beta_2 U + p_3 Q - \mu T \\ \frac{dQ}{dt} = p_2 U - (p_3 + p_1 + \mu + \alpha)Q \end{array} \right.$$

At first we prove the positivity of solutions of (2).

Theorem 2.1. *If initial data $S(0) > 0$, $U(0) > 0$, $T(0) > 0$ and $Q(0) > 0$, then the solution $(S(t), U(t), T(t), Q(t))$ of (2) is positive for all $t \geq 0$.*

Proof: Let $(S(t), U(t), T(t), Q(t))$ be the solution of the system (2) with initial data $S(0) > 0$, $U(0) > 0$, $T(0) > 0$ and $Q(0) > 0$. Suppose that the conclusion is not true, then there is a $t^* > 0$ such that,

$$\min\{S(t^*), U(t^*), T(t^*), Q(t^*)\} = 0$$

and

$$\min\{S(t), U(t), T(t), Q(t)\} > 0$$

for all $t \in [0, t^*)$. If $\min\{S(t^*), U(t^*), T(t^*), Q(t^*)\} = S(t^*)$, then we have, $\frac{dS}{dt} \geq -\beta_1 S U - \mu S$, for all $t \in [0, t^*)$. Hence, $0 = S(t^*) \geq S(0) \exp(-\int_0^{t^*} (\beta_1 U(t) + \mu) dt) > 0$, which leads to a contradiction. Similarly, we can obtain contradictions when, $\min\{S(t^*), U(t^*), T(t^*), Q(t^*)\}$, is equal to other variables of the system. This completes the proof. \square

The total population $N(t) = S(t) + U(t) + T(t) + Q(t)$, satisfies the relation $\frac{dN}{dt} = \Lambda - \mu N(t) - \alpha U(t) - \alpha Q(t) \leq \Lambda - \mu N(t)$, hence $\limsup_{t \rightarrow \infty} N(t) \leq \frac{\Lambda}{\mu}$. This shows that the set,

$$\Omega = \{(S, U, T, Q) \mid S + U + T + Q \leq \frac{\Lambda}{\mu}, S \geq 0, U \geq 0, T \geq 0, Q \geq 0\}$$

is a positively invariant set for (2). Thus the dynamics of the model can be studied only in Ω .

It is easy to see that (2) has a unique drug-free equilibrium (DFE), $P_0 = (\frac{\Lambda}{\mu}, 0, 0, 0)$.

The Jacobian matrix of the system, have the following form:

$$(3) \quad J = \frac{\partial f}{\partial x} = \begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{bmatrix}$$

in which,

$$a_{11} = -\beta_1 U - \mu, a_{12} = -\beta_1 S, a_{13} = 0, a_{14} = p_1, a_{21} = \beta_1 U$$

$$a_{22} = \beta_1 S + \beta_3 T - (\mu + \alpha + \beta_2 + p_2), a_{23} = \beta_3 U, a_{24} = 0$$

$$a_{31} = 0, a_{32} = -\beta_3 T + \beta_2, a_{33} = -\beta_3 U - \mu, a_{34} = p_3$$

$$a_{41} = 0, a_{42} = p_2, a_{43} = 0, a_{44} = -(p_3 + p_1 + \mu + \alpha).$$

and at DFE,

$$(4) \quad J(P_0) = \begin{bmatrix} -\mu & -\beta_1 \frac{\Lambda}{\mu} & 0 & p_1 \\ 0 & \beta_1 \frac{\Lambda}{\mu} - (\mu + \alpha + \beta_2 + p_2) & 0 & 0 \\ 0 & \beta_2 & -\mu & p_3 \\ 0 & p_2 & 0 & -(p_3 + p_1 + \mu + \alpha) \end{bmatrix}$$

Which has the eigen values $-\mu, -(p_3 + p_1 + \mu + \alpha), \beta_1 \frac{\Lambda}{\mu} - (\mu + \alpha + \beta_2 + p_2)$. Now we define the basic reproduction number by,

$$R_0 = \frac{\beta_1 \Lambda}{\mu(\mu + \alpha + \beta_2 + p_2)}.$$

It is clear that $\beta_1 \frac{\Lambda}{\mu} - (\mu + \alpha + \beta_2 + p_2) < 0$ if and only if $R_0 < 1$, and we obtain the following result on the local stability of the drug-free equilibrium.

Theorem 2.2. *The drug-free equilibrium P_0 is asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$.*

3. ENDEMIC EQUILIBRIUM AND BACKWARD BIFURCATION

The endemic equilibrium point $P = (S^*, U^*, T^*, Q^*)$ of 2 is determined by the following equations:

$$\begin{cases} \Lambda - \beta_1 S^* U^* - \mu S^* + p_1 Q^* = 0 \\ \beta_1 S^* U^* + \beta_3 U^* T^* - (\mu + \alpha + \beta_2 + p_2) U^* = 0 \\ -\beta_3 U^* T^* + \beta_2 U^* + p_3 Q^* - \mu T^* = 0 \\ p_2 U^* - (p_3 + p_1 + \mu + \alpha) Q^* = 0 \end{cases}$$

Let $q_1 = \frac{p_2}{p_1 + p_3 + \mu + \alpha}$; the above equations lead to

$$Q^* = q_1 U^*, T^* = (\beta_2 + p_3 q_1) \frac{U^*}{\beta_3 U^* + \mu},$$

and $\beta_1 S^* + \beta_3 T^* - (\mu + \alpha + \beta_2 + p_2) = 0$. By using the sum of four equations, we see that U^* is the positive root of the following quadratic equation:

$$(5) \quad F(U^*) = AU^{*2} + BU^* + C = 0$$

where

$$(6) \quad A = -\beta_3(\mu + \alpha)(1 + q_1)$$

$$(7) \quad B = \beta_3\Lambda\left(1 - \frac{1}{R_0}\right) + \mu(\beta_2 + p_3q_1)\left(\frac{\beta_3}{\beta_1} - 1\right) - \mu(\mu + \alpha)(1 + q_1)$$

$$(8) \quad C = \Lambda\left(1 - \frac{1}{R_0}\right)\mu$$

Since $F''(U^*) = 2A < 0$, The quadratic polynomial $F(U^*)$ is a concave parabola and has a maximum point $U_{\max}^* = -\frac{B}{2A}$ with $F(U_{\max}^*) = \frac{4AC - B^2}{4A}$.

If $R_0 > 1$, since $F(0) = C > 0$, $\Delta = B^2 - 4AC > 0$ and $A < 0$, the equation $F(U^*) = 0$ has exactly one positive solution (an endemic equilibrium).

For the occurrence of backward bifurcation, we must have $U_{\max}^* > 0$ and $F(U_{\max}^*) \geq 0$, which are equivalent to $B > 0$ and $\Delta \geq 0$.

When $R_0 \leq 1$ we consider two cases.

(1): Let $\beta_3 \leq \beta_1$, hence $B \leq 0$, therefore $U_{\max}^* \leq 0$. Now since $F(0) \leq 0$ backward bifurcation can not occur and $U^* = 0$ is the only equilibrium point.

(2): Let $\beta_3 > \beta_1$. We consider the following notations:

$$\begin{aligned} a &= \beta_3\Lambda\left(1 - \frac{1}{R_0}\right) \leq 0, \\ b &= \mu(\beta_2 + p_3q_1)\left(\frac{\beta_3}{\beta_1} - 1\right) > 0, \\ c &= \mu(\mu + \alpha)(1 + q_1) > 0. \end{aligned}$$

In fact $B = a + b - c$.

Now if $b \leq c$ then $B \leq 0$, which is the same as $U_{\max}^* \leq 0$, hence backward bifurcation cannot

occur. Therefore for the occurrence of backward bifurcation, we must have $b > c$ which is equivalent to

$$(9) \quad \frac{\beta_3}{\beta_1} > 1 + \frac{(\mu + \alpha)(1 + q_1)}{\beta_2 + p_3 q_1}.$$

For the occurrence of $B > 0$, we must have

$$(10) \quad \frac{\beta_3 \Lambda}{\beta_3 \Lambda + b - c} < R_0 < 1.$$

Now we determine the values of R_0 for which $\Delta \geq 0$. At first, we rewrite Δ in term of a ,

$$\Delta = \Delta(a) = a(a + 2b + 2c) + (b - c)^2$$

Further more $\Delta'(a) = 2a + 2b + 2c$, $\Delta''(a) = 2 > 0$, hence $\Delta(a)$ has a minimum value $-4bc$ at the point $-b - c$, and $\Delta(0) = (b - c)^2$.

On the other hand $\Delta(a) = 0$ has two solution $a = -b - c - 2\sqrt{bc}$ and $a = -b - c + 2\sqrt{bc}$ and when $a \leq -b - c - 2\sqrt{bc}$ or $a \geq -b - c + 2\sqrt{bc}$, $\Delta = \Delta(a) \geq 0$.

The relation $a \leq -b - c - 2\sqrt{bc}$, implies,

$$R_0 \leq \frac{\beta_3 \Lambda}{\beta_3 \Lambda + b + c + 2\sqrt{bc}} \leq \frac{\beta_3 \Lambda}{\beta_3 \Lambda + b - c}$$

which contradicts 10.

From the relation $a \geq -b - c + 2\sqrt{bc}$, we have,

$$\frac{\beta_3 \Lambda}{\beta_3 \Lambda + b - c} < \frac{\beta_3 \Lambda}{\beta_3 \Lambda + b + c - 2\sqrt{bc}} < R_0 < 1$$

Let $R_0^c = \frac{\beta_3 \Lambda}{\beta_3 \Lambda + b + c - 2\sqrt{bc}}$, in fact; we proved that when $R_0^c < R_0 < 1$ and 9 holds, there exist at least one endemic equilibrium point, i. e. backward bifurcation occurs. The above arguments imply the following theorem.

Theorem 3.1. *System 2, has the drug-free equilibrium P_0 , and:*

(1): *a unique endemic equilibrium point when $R_0 > 1$.*

(2): *there is no endemic equilibrium point if, $R_0 \leq 1$ and $\beta_3 \leq \beta_1$.*

(3): *two endemic equilibrium point when, $R_0^c < R_0 < 1$ and $\frac{\beta_3}{\beta_1} > 1 + \frac{(\mu + \alpha)(1 + q_1)}{\beta_2 + p_3 q_1}$.*

Above theorem demonstrates that in $R_0 = 1$ a bifurcation occurs. In fact, when R_0 cross $R_0 = 1$, the drug-free equilibrium changes its stability.

In the above, we study the bifurcation involving the drug-free equilibrium P_0 for $R_0 = 1$, directly. Now we study backward bifurcation by using the theorem of Castillo-Chavez and Song, which has been proved in [7], by center manifold theory.

We consider a system of ODEs,

$$(11) \quad \frac{dX}{dt} = f(X, \phi); f : \mathbb{R}^n \times \mathbb{R} \rightarrow \mathbb{R}^n, f \in C^2(\mathbb{R}^n \times \mathbb{R})$$

with a parameter ϕ , and assume that 0 is a steady state of this system for all ϕ , i.e. $f(0, \phi) = 0$.

Let $\mathcal{Q} = D_X f(0, 0) = \left(\frac{\partial f_i}{\partial x_j}(0, 0) \right)$ be the Jacobian matrix of $f(X, \phi)$ at $(0, 0)$.

Theorem 3.2. *Assume the following:*

(H1): *0 is a simple eigenvalue of \mathcal{Q} , furthermore the other eigenvalues of \mathcal{Q} have negative real parts.*

(H2): *\mathcal{Q} has a (non-negative) right eigenvector of the form $\mathbf{w} = (w_1, w_2, \dots, w_n)^T$ and a left eigenvector of the form $\mathbf{v} = (v_1, v_2, \dots, v_n)$ corresponding to the zero eigenvalue.*

Suppose $f_k(X, \phi)$ denote the k -th component of $f(X, \phi)$ and

$$\mathbf{a} = \sum_{k,i,j=1}^n v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0, 0), \mathbf{b} = \sum_{k,i=1}^n v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0, 0).$$

Then the quantities \mathbf{a} and \mathbf{b} determine the local dynamics of 11 around $X = 0$ as follows:

(1): *When $\mathbf{a} > 0$ and $\mathbf{b} > 0$, if $\phi < 0$ with $|\phi| \ll 1$, $X = 0$ has asymptotic stability property and also there is a positive and unstable equilibrium point, and if $0 < \phi \ll 1$, $X = 0$ is an unstable equilibrium point and also there is a negative equilibrium point which is asymptotically stable.*

(2): *When $\mathbf{a} < 0$ and $\mathbf{b} < 0$, if $\phi < 0$ with $|\phi| \ll 1$, $X = 0$ is an unstable equilibrium point, and if $0 < \phi \ll 1$, $X = 0$ is asymptotically stable, and there is a positive equilibrium which is unstable.*

(3): *When $\mathbf{a} > 0$ and $\mathbf{b} < 0$, if $\phi < 0$ with $|\phi| \ll 1$, $X = 0$ is an unstable equilibrium point and there is a negative equilibrium which is asymptotically stable. If $0 < \phi \ll 1$, $X = 0$ is asymptotically stable and there is a positive and unstable equilibrium point.*

(4): *When $\mathbf{a} < 0$ and $\mathbf{b} > 0$, if the sign of ϕ varies from negative to positive, then the nature*

of $x = 0$ varies from stability to instability. Furthermore, a negative and unstable steady state becomes a positive steady state which is asymptotically stable.

The requirement that \mathbf{w} is nonnegative is unnecessary, [7].

At first, it is convenient to transform the variables of 2 as follows: $x_1 = S$, $x_2 = U$, $x_3 = T$, $x_4 = Q$, and the system 2, transforms into the following:

$$(12) \quad \begin{cases} \frac{dx_1}{dt} = \Lambda - \beta_1 x_1 x_2 - \mu x_1 + p_1 x_4 = f_1, \\ \frac{dx_2}{dt} = \beta_1 x_1 x_2 + \beta_3 x_2 x_3 - (\mu + \alpha + \beta_2 + p_2) x_2 = f_2, \\ \frac{dx_3}{dt} = -\beta_3 x_2 x_3 + \beta_2 x_2 + p_3 x_4 - \mu x_3 = f_3, \\ \frac{dx_4}{dt} = p_2 x_2 - (p_3 + p_1 + \mu + \alpha) x_4 = f_4. \end{cases}$$

Now we apply theorem 3.2 to show that in 12, backward bifurcation occurs when $R_0 = 1$. The relation $R_0 = 1$ can be interpreted in term of β_1 , as $\beta_1 = \beta_1^* = \frac{\mu(\mu + \alpha + \beta_2 + p_2)}{\Lambda}$.

The eigen values of $J(P_0, \beta_1^*)$, are $0, -\mu, -(p_3 + p_1 + \mu + \alpha)$. Now since 0 is simple and nonzero eigenvalues are nonnegative real numbers, when $\beta_1 = \beta_1^*$ (or $R_0 = 1$) the assumption (1) of Theorem 3.2, is then verified.

Let $w = (w_1, w_2, w_3, w_4)^T$, be the right eigenvector of $J(P_0, \beta_1^*)$ associated with eigenvalue $\lambda_4 = 0$, founded by, $J(P_0, \beta_1^*)\mathbf{w} = 0$. Computation of the solution of this linear system yields:

$$w_1 = p_2 p_1 - (\mu + \alpha + \beta_2 + p_2)(p_3 + p_1 + \mu + \alpha), w_2 = \mu(p_3 + p_1 + \mu + \alpha)$$

$$w_3 = \beta_2(p_3 + p_1 + \mu + \alpha) + p_2 p_3, w_4 = p_2 \mu.$$

On the other hand, $\mathbf{v} = (v_1, v_2, v_3, v_4)$, the left eigenvector associated with zero eigenvalue is founded by, $\mathbf{v}J(P_0, \beta_1^*) = 0$, and turns out to be

$$\mathbf{v} = (0, 1, 0, 0)$$

Now we compute the quantities \mathbf{a} and \mathbf{b} from Theorem 3.2,

$$\begin{aligned} \mathbf{a} &= \sum_{k,i,j=1}^4 v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) = \sum_{i,j=1}^4 w_i w_j \frac{\partial^2 f_2}{\partial x_i \partial x_j}(0,0) = 2w_2(\beta_1 w_1 + \beta_3 w_3) = \\ &= \frac{2p_2 w_2}{q_1} [\beta_1(p_1 q_1 - (\mu + \alpha + \beta_2 + p_2)) + \beta_3(\beta_2 + p_3 q_1)]. \end{aligned}$$

and

$$\mathbf{b} = \sum_{k,i=1}^4 v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(P_0, \beta^*) = \sum_{i=1}^4 w_i \frac{\partial^2 f_2}{\partial x_i \partial \phi}(0,0) = w_2 \frac{\Lambda}{\mu}$$

We observe that \mathbf{b} is positive, so that, it is the sign of \mathbf{a} that determines the dynamics around the drug-free equilibrium for $\beta_1 = \beta_1^*$. Now using

$$(13) \quad \mu + \alpha + p_2 = (\mu + \alpha)(1 + q_1) + p_1 q_1 + p_3 q_1$$

it is clear that $\mathbf{a} > 0$ is equivalent to:

$$\frac{\beta_3}{\beta_1} > 1 + \frac{(\mu + \alpha)(1 + q_1)}{\beta_2 + p_3 q_1}.$$

Which is the same criterion we have obtained directly. Although in most systems the criterions obtained for the occurrence of backward bifurcation, directly and by Castillo-Chavez and Song theorem don't coincide together with. Figure 1 shows bifurcation diagram, i.e. the diagram of U^* in term of R_0 .

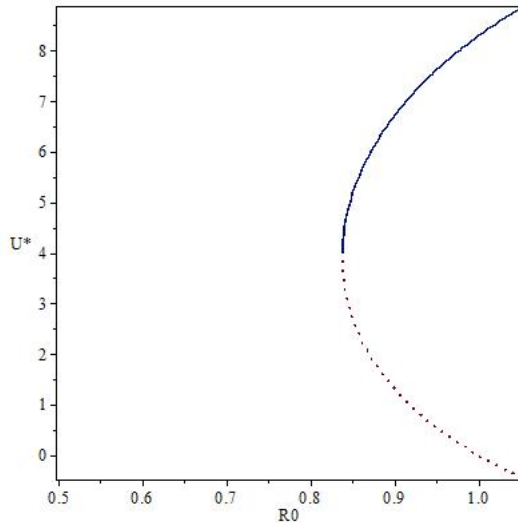


FIGURE 1. The occurrence of backward bifurcation when, $\Lambda = 1$, $\beta_1 = 0.01$, $\beta_2 = 0.3$, $\alpha = 0.2$, $q_1 = 0.4$ and $\mu = \beta_3 = p_3 = 0.1$.

4. GLOBAL STABILITY

In this section, we study the local and global stability of steady states, both drug-free and endemic point in some cases. At first, we consider the drug-free point.

Lemma 4.1. *If $R_0 \leq 1$ and $\beta_3 \leq \beta_1$, then DFE is globally asymptotically stable in Ω .*

Proof. Define $L : \{(S, U, T, Q) \in \Omega : S > 0\} \rightarrow \mathbb{R}$ by

$$V(S, U, T, Q) = U$$

The time derivative of L along the solution curves of (2) is,

$$\dot{L} = \frac{dU}{dt} \leq (\beta_1 S + \beta_1 T - (\mu + \alpha + \beta_2 + p_2))U \leq (R_0 - 1)U,$$

therefore Lasalle invariance principle shows the global asymptotic stability of DFE equilibrium point. □

Proposition 4.1. *If $R_0 < \frac{\beta_1 \Lambda}{\beta_1 \Lambda + \mu(\beta_2 + p_3 q_1)}$, then DFE is globally asymptotically stable in Ω .*

Proof. Define $V : \{(S, U, T, Q) \in \Omega : S > 0\} \rightarrow \mathbb{R}$ by

$$V(S, U, T, Q) = z_1 U + z_2 T + z_3 Q$$

The time derivative of L along the solution curves of (2) is,

$$\begin{aligned} \frac{dV}{dt} &= z_1 \frac{dU}{dt} + z_2 \frac{dT}{dt} + z_3 \frac{dQ}{dt} \\ &= z_1 [\beta_1 S U + \beta_3 U T - (\mu + \alpha + \beta_2 + p_2)] \\ &\quad + z_2 [-\beta_3 U T + \beta_2 U + p_3 Q - \mu T] + z_3 [p_2 U - (p_3 + p_1 + \mu + \alpha) Q] \\ &\leq [z_1 (\frac{\beta_1 \Lambda}{\mu} (1 - \frac{1}{R_0}) + z_2 \beta_2 + z_3 p_2) U + [(z_1 - z_2) \beta_3] U T - z_2 \mu T \\ &\quad + [z_2 p_3 - z_3 (p_3 + p_1 + \mu + \alpha)] Q \end{aligned}$$

Now we take $z_2 p_3 - z_3 (p_3 + p_1 + \mu + \alpha) = -K$ in which $K > 0$. For the negativity of $\frac{dV}{dt}$, we must choose positive coefficients z_1, z_2 such that:

$$(14) \quad z_1 M_1 + z_2 M_2 + M_3 < 0$$

$$(15) \quad z_1 - z_2 < 0$$

In which $M_1 = \frac{\beta_1 \Lambda}{\mu} (1 - \frac{1}{R_0})$, $M_2 = \beta_2 + p_3 q_1$ and $M_3 = q_1 K$. This system of linear inequalities has a positive solution when $M_1 + M_2 < 0$ which is equivalent to $R_0 < \frac{\beta_1 \Lambda}{\beta_1 \Lambda + \mu(\beta_2 + p_3 q_1)}$. Choosing such coefficients, the above relation for $\frac{dV}{dt}$, shows, $\frac{dV}{dt} = 0$ only in drug-free equilibrium (DFE), $(\frac{\Lambda}{\mu}, 0, 0, 0)$. Hence Lasalle invariance principle shows G.A.S. of DFE. \square

In the following, we discuss the local stability of the endemic equilibrium point when $R_0 > 1$. We use the following lemma, from [14].

Lemma 4.2. *Let M be an $n \times n$ matrix with real entries. For M to be stable, it is necessary and sufficient that:*

(1): *The second compound matrix $M^{[2]}$ of M is stable.*

(2): $(-1)^n \det M > 0$.

Theorem 4.1. *When $R_0 > 1$, the endemic equilibrium point P^* , is asymptotically stable.*

Proof. The linearization of 2 at an arbitrary point has form 3. Therefore, $J^{[2]}$, the second compound matrix of $J = \frac{\partial f}{\partial x}$, has the following form:

$$(16) \quad M = J^{[2]} = \begin{bmatrix} M_{11} & M_{12} & 0 & 0 & M_{15} & 0 \\ M_{21} & M_{22} & M_{23} & M_{24} & 0 & M_{26} \\ M_{31} & 0 & M_{33} & 0 & M_{35} & 0 \\ 0 & M_{42} & 0 & M_{44} & M_{45} & 0 \\ 0 & 0 & M_{53} & 0 & M_{55} & M_{56} \\ 0 & 0 & 0 & M_{64} & M_{65} & M_{66} \end{bmatrix}$$

with the following components,

$$M_{11} = -\beta_1 U - \mu + \beta_1 S + \beta_3 T - (\mu + \alpha + \beta_2 + p_2), M_{12} = \beta_3 U, M_{15} = -p_1,$$

$$M_{21} = -\beta_3 T + \beta_2, M_{22} = -(\beta_1 + \beta_3)U - 2\mu, M_{23} = p_3, M_{24} = -\beta_1 S, M_{26} = -p_1,$$

$$M_{31} = p_2, M_{33} = -\beta_1 U - (p_3 + p_1 + \alpha + 2\mu), M_{35} = -\beta_1 S,$$

$$\begin{aligned}
M_{42} &= \beta_1 U, M_{44} = \beta_1 S + \beta_3 T - \beta_3 U - (2\mu + \alpha + \beta_2 + p_2), M_{45} = p_3, \\
M_{53} &= \beta_1 U, M_{55} = \beta_1 S + \beta_3 T - (p_1 + p_2 + p_3 + \beta_2 + 2\mu + 2\alpha), M_{56} = \beta_3 U, \\
M_{64} &= -p_2, M_{65} = -\beta_3 T + \beta_2, M_{66} = -\beta_3 U - (p_1 + p_3 + \alpha + 2\mu).
\end{aligned}$$

By using, Gersgorin's theorem, we see that, the matrix $J^{[2]}(P^*)$ is stable when it is diagonally dominant in rows. In 16, we have:

$$\max\{M_{11}(P^*), M_{22}(P^*), M_{33}(P^*), M_{44}(P^*), M_{55}(P^*), M_{66}(P^*)\} < 0.$$

Hence $J^{[2]}(P^*)$ is stable.

Further more:

$$\begin{aligned}
\det(J(P^*)) &= \frac{p_2}{q_1} U^* [\mu \beta_3 (\beta_3 - \beta_1) T^* + \mu \beta_1 (\beta_1 - \beta_3) S^* - \mu \beta_3 (\beta_2 + p_3 q_1) \\
&\quad + \beta_1 \beta_3 \Lambda - \beta_1 \mu p_1 q_1].
\end{aligned}$$

We show $\det(J(P^*)) > 0$. If $\beta_3 = \beta_1$, then,

$$\det(J(P^*)) = \frac{p_2}{q_1} U^* [\beta_1^2 \Lambda - \mu \beta_1 (\beta_2 + p_3 q_1 + p_1 q_1)]$$

and $R_0 > 1$ and 13, implies $\det(J(P^*)) > 0$.

Now we take $\beta_3 > \beta_1$, in this case,

$$\det(J(P^*)) > \frac{p_2}{q_1} U^* [2\mu \beta_3 (\beta_3 - \beta_1) T^* - \mu \beta_3 (\beta_2 + p_3 q_1) + \beta_1^2 \Lambda - \beta_1 \mu p_1 q_1].$$

We consider two subcases: if $\frac{\beta_3}{\beta_1} < 1 + \frac{(\mu + \alpha)(1 + q_1)}{\beta_2 + p_3 q_1}$, we have the relation $\beta_1^2 \Lambda - \mu \beta_3 (\beta_2 + p_3 q_1) - \beta_1 \mu p_1 q_1 > 0$, therefore in this case $\det(J(P^*)) > 0$. When $\frac{\beta_3}{\beta_1} > 1 + \frac{(\mu + \alpha)(1 + q_1)}{\beta_2 + p_3 q_1}$, the inequality, $2\mu \beta_3 (\beta_3 - \beta_1) - \mu \beta_3 (\beta_2 + p_3 q_1) + \beta_1^2 \Lambda - \beta_1 \mu p_1 q_1 > 0$ holds, hence $\det(J(P^*)) > 0$.

The case $\beta_3 < \beta_1$ is similar to the previous case. □

Now we present the geometric method for the global stability problem, proposed in [14, 15], see [1, 4, 5, 6, 10, 12, 27, 28] for applications of the method. Let us denote unit ball of \mathbb{R}^2 and its boundary and closure by, \mathcal{B} , $\partial\mathcal{B}$, and $\bar{\mathcal{B}}$ respectively. We also denote the collection of all Lipschitzian functions from X to Y , by $Lip(X \rightarrow Y)$. We consider a function

$\phi \in Lip(\bar{\mathcal{B}} \rightarrow \Omega)$ as a simply connected and rectifiable surface in $\Omega \subseteq \mathbb{R}^n$. A closed and rectifiable curve in Ω can be described as a function $\phi \in Lip(\partial\mathcal{B} \rightarrow \Omega)$ and called simple if it is one to one. Suppose $\Sigma(\psi, \Omega) = \{\psi \in Lip(\bar{\mathcal{B}} \rightarrow \Omega) : \phi|_{\partial\mathcal{B}} = \psi\}$. Let Ω be an open domain which is simply connected, then $\Sigma(\psi, \Omega)$ is a nonvoid set, for any simple, closed and rectifiable curve ψ in Ω . Consider a norm $\|\cdot\|$ on $\mathbb{R}^{\binom{n}{2}}$. We define a functional \mathcal{S} on the surfaces in Ω by the following relation:

$$(17) \quad \mathcal{S}\phi = \int_{\bar{\mathcal{B}}} \|P \cdot (\frac{\partial\phi}{\partial u_1} \wedge \frac{\partial\phi}{\partial u_2})\| du.$$

In which the mapping $u \mapsto \phi(u)$ is Lipschitzian on $\bar{\mathcal{B}}$, and $\frac{\partial\phi}{\partial u_1} \wedge \frac{\partial\phi}{\partial u_2}$ is the wedge product in $\mathbb{R}^{\binom{n}{2}}$. Further more the $\binom{n}{2} \times \binom{n}{2}$ matrix function P is invertible and, $\|P^{-1}\|$ is a bounded function on $\phi(\bar{\mathcal{B}})$. The following result is stated in [14].

Lemma 4.3. *For an arbitrary simple, closed and rectifiable curve ψ , in \mathbb{R}^n , there is $\delta > 0$ with $\mathcal{S}\psi \geq \delta$ for all $\phi \in \Sigma(\psi, \Omega)$.*

Consider the vector field $x \mapsto f(x) \in \mathbb{R}^n$, which is a C^1 function on the set $\Omega \subset \mathbb{R}^n$, and the following ODE system,

$$(18) \quad \frac{dx}{dt} = f(x).$$

We consider the function $\phi_t(u) = x(t, \phi(u))$ as the solution of 18, passing through $(0, \phi(u))$, for any ϕ . We define the right-hand derivative of $\mathcal{S}\phi_t$, by the following relation,

$$(19) \quad D_+ \mathcal{S}\phi_t = \int_{\bar{\mathcal{B}}} \lim_{h \rightarrow 0^+} \frac{1}{h} (\|z + hQ(\phi_t(u))z\| - \|z\|) du.$$

In which $Q = P_f P^{-1} + P \frac{\partial f^{[2]}}{\partial x} P^{-1}$, P_f represents the directional derivative of P in the direction of the vector field f , and $\frac{\partial f^{[2]}}{\partial x}$ denotes the second additive compound matrix of $\frac{\partial f}{\partial x}$. Furthermore we consider the following differential equation,

$$(20) \quad \frac{dz}{dt} = Q(\phi_t(u))z$$

For which the solution is of the form $z = P \cdot (\frac{\partial\phi}{\partial u_1} \wedge \frac{\partial\phi}{\partial u_2})$. The formula $D_+ \mathcal{S}\phi_t$ can be expressed as,

$$(21) \quad D_+ \mathcal{S}\phi_t = \int_{\bar{\mathcal{B}}} D_+ \|z\| du.$$

Let P be the following matrix,

$$P = \begin{bmatrix} \frac{1}{U} & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{U} & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{U} & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

Hence we have the matrix $P_f P^{-1} = -diag(\frac{U'}{U}, 0, 0, \frac{U'}{U}, \frac{U'}{U}, 0)$, thus,

$$Q = P_f P^{-1} + P M P^{-1} = \begin{bmatrix} A_{11} & A_{12} & 0 & 0 & A_{15} & 0 \\ A_{21} & A_{22} & A_{23} & 0 & 0 & A_{26} \\ A_{31} & 0 & A_{33} & 0 & A_{35} & 0 \\ 0 & A_{42} & 0 & A_{44} & A_{45} & 0 \\ 0 & 0 & A_{53} & 0 & A_{55} & A_{56} \\ 0 & 0 & 0 & A_{64} & A_{65} & A_{66} \end{bmatrix}$$

in which,

$$A_{11} = -\beta_1 U - \mu, A_{12} = \beta_3, A_{15} = -p_1$$

$$A_{21} = -\beta_3 T U + \beta_2 U, A_{22} = -(\beta_1 + \beta_3) U - 2\mu, A_{23} = p_3, A_{26} = -p_1$$

$$A_{31} = p_2 U, A_{33} = -\beta_1 U - (2\mu + \alpha + p_1 + p_3), A_{35} = -p_1$$

$$A_{42} = \beta_1, A_{44} = -\beta_1 U - \mu, A_{45} = p_3.$$

$$A_{53} = \beta_1, A_{55} = -(\mu + \alpha + p_1 + p_3), A_{56} = \beta_3.$$

$$A_{64} = p_2 U, A_{65} = \beta_3 T U - \beta_2 U, A_{66} = -\beta_1 U - (2\mu + \alpha + p_1 + p_3).$$

Now we use the following norm introduced in [12], for $z = (z_1, z_2, z_3, z_4, z_5, z_6) \in \mathbb{R}^6$, let

$\|z\| = \max\{U_1, U_2\}$, where $U_1(z_1, z_2, z_3)$ has the following form:

$$\left\{ \begin{array}{ll} \max\{|z_1|, |z_2| + |z_3|\} & \text{if } \begin{array}{l} \text{sgn}(z_1) = \text{sgn}(z_2) \\ = \text{sgn}(z_3) \end{array} \\ \max\{|z_2|, |z_1| + |z_3|\} & \text{if } \begin{array}{l} \text{sgn}(z_1) = \text{sgn}(z_2) \\ = -\text{sgn}(z_3) \end{array} \\ \max\{|z_1|, |z_2|, |z_3|\} & \text{if } \begin{array}{l} \text{sgn}(z_1) = -\text{sgn}(z_2) \\ = \text{sgn}(z_3) \end{array} \\ \max\{|z_1| + |z_3|, |z_2| + |z_3|\} & \text{if } \begin{array}{l} -\text{sgn}(z_1) = \text{sgn}(z_2) \\ = \text{sgn}(z_3) \end{array} \end{array} \right.$$

and $U_2(z_4, z_5, z_6)$ has the following form:

$$\left\{ \begin{array}{ll} |z_4| + |z_5| + |z_6| & \text{if } \begin{array}{l} \text{sgn}(z_4) = \text{sgn}(z_5) \\ = \text{sgn}(z_6) \end{array} \\ \max\{|z_4| + |z_5|, |z_4| + |z_6|\} & \text{if } \begin{array}{l} \text{sgn}(z_4) = \text{sgn}(z_5) \\ = -\text{sgn}(z_6) \end{array} \\ \max\{|z_5|, |z_4| + |z_6|\} & \text{if } \begin{array}{l} \text{sgn}(z_4) = -\text{sgn}(z_5) \\ = \text{sgn}(z_6) \end{array} \\ \max\{|z_4| + |z_6|, |z_5| + |z_6|\} & \text{if } \begin{array}{l} -\text{sgn}(z_4) = \text{sgn}(z_5) \\ = \text{sgn}(z_6) \end{array} \end{array} \right.$$

Further more we will use the following relations:

$$|z_2| < U_1, |z_3| < U_1, |z_2 + z_3| < U_1$$

and

$$|z_i|, |z_i + z_j|, |z_4 + z_5 + z_6| \leq U_2(z) \quad i = 4, 5, 6; i \neq j$$

We use this inequalities in the estimation of $D_+\|z\|$. Now we prove the following lemma.

Lemma 4.4. *There is a constant $\tau > 0$, for which $D_+\|z\| \leq -\tau\|z\|$ for all $z \in \mathbb{R}^6$ and all S, U, T, Q , where z is the solution of 20, provided that $\beta_2 < \beta_1 < p_1 + \mu + \alpha, \beta_2 < \beta_3 < p_1 + p_3 + \mu + \alpha$ and $\max(\beta_3 T U - \beta_1 U + p_1 - 2\mu) < 0$.*

Proof. We prove the existence of a $\tau > 0$ for which $D_+\|z\| \leq -\tau\|z\|$, for the solution z of the equation 20. The full calculation to demonstrate this relation contains sixteen separate cases

in term of the different orthants and the definition of the above norm, see [4]. As in [10], we demonstrate five cases with details.

Case 1: $U_1 > U_2, z_2, z_3 > 0 > z_1$, in this case, $\|z\| = \max\{|z_1| + |z_3|, |z_2| + |z_3|\}$.

Subcase 1.1. $|z_1| > |z_2|$, hence $\|z\| = |z_1| + |z_3| = -z_1 + z_3$, and

$$\begin{aligned} D_+ \|z\| &= -z'_1 + z'_3 = -(A_{11}z_1 + A_{12}z_2 + A_{15}z_5) + A_{31}z_1 + A_{33}z_3 + A_{35}z_5 = \\ &= (-\beta_1 U - p_2 U - \mu)|z_1| + (-\beta_3)|z_2| + (-\beta_1 U - (2\mu + \alpha + p_1 + p_3))|z_3| \leq \\ &\leq \max\{-\mu - \beta_3, -(\beta_3 + 2\mu + \alpha + p_1 + p_3)\}|z\| \end{aligned}$$

which is a negative coefficient.

Subcase 1.2. $|z_1| < |z_2|$. In this case, $\|z\| = |z_2| + |z_3|$ and

$$\begin{aligned} D_+ \|z\| &= z'_2 + z'_3 = A_{21}z_1 + A_{22}z_2 + A_{23}z_3 + A_{26}z_6 + A_{31}z_1 + A_{33}z_3 + A_{35}z_5 = \\ &\leq (\beta_3 T U - p_2 U - \beta_2 U)|z_1| + (-\beta_1 + \beta_3)U - 2\mu)|z_2| + \\ &+ (-\beta_1 U - (2\mu + \alpha + p_1))|z_3| + p_1(|z_5| + |z_6|) \leq \\ &\leq (\beta_3 T U - \beta_1 U + p_1 - 2\mu)\|z\| \end{aligned}$$

Case 2: $U_1 < U_2$ and $z_4, z_5, z_6 > 0$. In this case $\|z\| = |z_4| + |z_5| + |z_6|$ and

$$\begin{aligned} D_+ \|z\| &= z'_4 + z'_5 + z'_6 = A_{42}z_2 + A_{44}z_4 + A_{45}z_5 + A_{53}z_3 + A_{55}z_5 + A_{56}z_6 + A_{64}z_4 + \\ &+ A_{65}z_5 + A_{66}z_6 \leq \beta_1 \|z\| + (-\beta_1 U - \mu - p_2 U)|z_4| + \\ &+ (-\beta_3 T U + \beta_2 U - (p_1 + \mu + \alpha))|z_5| + (-\beta_1 U - (p_1 + p_3 + \mu + \alpha) + \beta_3)|z_6| \leq \\ &\leq \max\{\beta_1 - \beta_1 U - \mu - p_2 U, -\beta_3 T U + \beta_2 U - (p_1 + \mu + \alpha) + \beta_1, \\ &- \beta_1 U - (p_1 + p_3 + \mu + \alpha) + \beta_3 + \beta_1\}|z\| \end{aligned}$$

Case 3. If $U_2 > U_1$ and $z_6 < 0 < z_4, z_5$. In this case, $\|z\| = \max\{|z_4| + |z_5|, |z_4| + |z_6|\}$.

Subcase 3.1. $|z_5| > |z_6|$, in this case, $\|z\| = |z_4| + |z_5| = z_4 + z_5$, and:

$$\begin{aligned} D_+\|z\| &= z'_4 + z'_5 = A_{42}z_2 + A_{44}z_4 + A_{45}z_5 + A_{53}z_3 + A_{55}z_5 + A_{56}z_6 \leq \\ &\leq \beta_1(z_2 + z_3) + (-\beta_1U - \mu)|z_4| + (-p_1 - \mu - \alpha)|z_5| + (-\beta_3)|z_6| \leq \\ &\leq \max\{\beta_1 - \beta_1U - \mu, \beta_1 - (p_1 + \mu + \alpha)\}\|z\| \end{aligned}$$

Subcase 3.2. $|z_5| < |z_6|$. In this case $\|z\| = |z_4| + |z_6| = z_4 - z_6$, and:

$$\begin{aligned} D_+\|z\| &= z'_4 - z'_6 = A_{42}z_2 + A_{44}z_4 + A_{45}z_5 - A_{64}z_4 - A_{65}z_5 - A_{66}z_6 \leq \\ &\leq \beta_1\|z\| + (-p_2U - \beta_1U - \mu)|z_4| + (\beta_2U - \beta_1U + \beta_1 - (p_1 + 2\mu + \alpha))|z_6| \leq \\ &\leq \max\{\beta_1 - p_2U - \beta_1U - \mu, (\beta_2 - \beta_1)U + \beta_1 - (p_1 + 2\mu + \alpha)\}\|z\| \end{aligned}$$

Now using the supposed inequalities, in all of the above cases the coefficient of $\|z\|$ is a negative number. □

In [14], the geometric method is applied to investigate the global stability of a unique steady state. In such cases, there exists a compact absorbing set. Hence surfaces remain in Ω for all time. But in models with backward bifurcation, such as model 2, such a set will not exist. Hence as in [1], we prove the existence of the following sequence φ^k of surfaces in the next lemma.

Lemma 4.5. *For an arbitrary simple and closed curve ψ in Ω , there is $\varepsilon > 0$ and surfaces φ^k which minimizes \mathcal{S} with respect to $\Sigma(\psi, \Omega)$, in such a way that, for all $t \in [0, \varepsilon]$ and $k = 2, 3, \dots$, $\varphi_t^k \subseteq \Omega$.*

Proof. Consider the quantity, $\xi = \frac{1}{2} \min\{U : (S, U, T, Q) \in \psi\}$. It is easy to see that $\xi > 0$. Based on the inequality

$$\frac{dU}{dt} \geq -(\mu + \alpha + \beta_2 + p_2)U,$$

which holds in Ω , there exists $\varepsilon > 0$ such that, the solutions with $U(0) \geq \xi$, remains in Ω , for $t \in [0, \varepsilon]$. Hence we must show the existence of a sequence $\{\varphi^k\}$ which minimizes

\mathcal{S} with respect to $\Sigma(\psi, \tilde{\Omega})$, in which $\tilde{\Omega} = \{(S, U, T, Q) \in \Omega : U \geq \xi\}$. Now for $\varphi(u) = (S(u), U(u), T(u), Q(u)) \in \Sigma(\psi, \Omega)$, we define another surface, $\tilde{\varphi}(u) = (\tilde{S}(u), \tilde{U}(u), \tilde{T}(u), \tilde{Q}(u))$ by the following relation,

$$\left\{ \begin{array}{ll} \varphi(u) & \text{if } U(u) \geq \xi \\ (S, \xi, T, Q) & \text{if } \begin{array}{l} U(u) < \xi, \\ S + \xi + T + Q \leq \frac{\Lambda}{\mu} \end{array} \\ \left(\frac{S}{\sqrt{3}(S+T+Q)} \left(\frac{\Lambda}{\mu} - \xi \right), \xi, \frac{T}{\sqrt{3}(S+T+Q)} \left(\frac{\Lambda}{\mu} - \xi \right), \frac{Q}{\sqrt{3}(S+T+Q)} \left(\frac{\Lambda}{\mu} - \xi \right) \right) & \text{if } \begin{array}{l} U(u) < \xi, \\ S + \xi + T + Q > \frac{\Lambda}{\mu} \end{array} \end{array} \right.$$

It is easy to see that $\tilde{\varphi}(u) \in \Sigma(\psi, \tilde{\Omega})$. We will prove $\mathcal{S} \tilde{\varphi} \leq \mathcal{S} \varphi$.

We denote $\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2} = (\tilde{x}_1, \tilde{x}_2, \tilde{x}_3, \tilde{x}_4, \tilde{x}_5, \tilde{x}_6)^T$ and $\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} = (x_1, x_2, x_3, x_4, x_5, x_6)^T$, and prove $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\| \leq \|\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}\|$.

Case 1. If $U(u) \geq \xi$, then $\tilde{\varphi} = \varphi$ and therefore, $|\tilde{x}_i| = |x_i|$

($i = 1, 2, \dots, 6$), hence, $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\| = \|\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}\|$.

Case 2. If $U(u) < \xi$ and $S(u) + \xi + T(u) + Q(u) \leq \frac{\Lambda}{\mu}$, then $\tilde{\varphi}(u) = (S(u), \xi, T(u), Q(u))$.

Therefore,

$$\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2} = \left[\begin{array}{c} \det \left[\begin{array}{cc} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial U}{\partial u_1} & \frac{\partial U}{\partial u_2} \end{array} \right] \\ 0 \\ \det \left[\begin{array}{cc} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial Q}{\partial u_1} & \frac{\partial Q}{\partial u_2} \end{array} \right] \\ 0 \\ \det \left[\begin{array}{cc} \frac{\partial U}{\partial u_1} & \frac{\partial U}{\partial u_2} \\ \frac{\partial Q}{\partial u_1} & \frac{\partial Q}{\partial u_2} \end{array} \right] \\ 0 \end{array} \right]$$

almost everywhere. Hence it follows $\tilde{x}_i = x_i (i = 1, 3, 5)$ and $\tilde{x}_i = 0 (i = 2, 4, 6)$. Thus $|\tilde{x}_i| \leq |x_i|$, which implies $\|\frac{\partial \tilde{\phi}}{\partial u_1} \wedge \frac{\partial \tilde{\phi}}{\partial u_2}\| \leq \|\frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2}\|$.

Case 3. If $U(u) < \xi$ and $S(u) + \xi + T(u) + Q(u) > \frac{\Lambda}{\mu}$, then $\tilde{\phi}(u) = (\frac{S}{\sqrt{3}(S+T+Q)}(\frac{\Lambda}{\mu} - \xi), \xi, \frac{T}{\sqrt{3}(S+T+Q)}(\frac{\Lambda}{\mu} - \xi), \frac{Q}{\sqrt{3}(S+T+Q)}(\frac{\Lambda}{\mu} - \xi))$.

In this case, using $\frac{\partial \tilde{S}}{\partial u_j} + \frac{\partial \tilde{T}}{\partial u_j} + \frac{\partial \tilde{Q}}{\partial u_j} = 0$, we obtain,

$$\frac{\partial \tilde{\phi}}{\partial u_1} = z_1(u_1)f_1 + z_2(u_1)f_2$$

and

$$\frac{\partial \tilde{\phi}}{\partial u_2} = z_1(u_2)f_1 + z_2(u_2)f_2$$

in which,

$$f_1 = \begin{bmatrix} 1 \\ 0 \\ 0 \\ -1 \end{bmatrix}, f_2 = \begin{bmatrix} 0 \\ 0 \\ 1 \\ -1 \end{bmatrix}$$

and

$$z_1(u_j) = \left(\frac{\Lambda}{\mu} - \xi\right) \frac{(T+Q)\frac{\partial S}{\partial u_j} - S\left(\frac{\partial T}{\partial u_j} + \frac{\partial Q}{\partial u_j}\right)}{\sqrt{3}(S+T+Q)^2}$$

$$z_2(u_j) = \left(\frac{\Lambda}{\mu} - \xi\right) \frac{(S+Q)\frac{\partial T}{\partial u_j} - T\left(\frac{\partial S}{\partial u_j} + \frac{\partial Q}{\partial u_j}\right)}{\sqrt{3}(S+T+Q)^2}$$

for $j = 1, 2$. Therefore,

$$\begin{aligned} \frac{\partial \tilde{\phi}}{\partial u_1} \wedge \frac{\partial \tilde{\phi}}{\partial u_2} &= (z_1(u_1)z_2(u_2) - z_2(u_1)z_1(u_2))f_1 \wedge f_2 \\ &= \frac{\left(\frac{\Lambda}{\mu} - \xi\right)^2}{3(S+T+Q)^4} A \begin{bmatrix} 0 \\ 1 \\ -1 \\ 0 \\ 0 \\ 1 \end{bmatrix} \end{aligned}$$

in which,

$$A = Q(S+T+Q)x_2 - T(S+T+Q)x_3 + S(S+T+Q)x_6$$

which yields,

$$\left\| \frac{\partial \tilde{\phi}}{\partial u_1} \wedge \frac{\partial \tilde{\phi}}{\partial u_2} \right\| \leq |x_2| + |x_3| + |x_6| \leq \left\| \frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2} \right\|$$

On the other hand, $\tilde{U}(u) = \max\{U(u), \xi\}$, and thus $\frac{1}{\tilde{U}} \leq \frac{1}{U}$. Therefore,

$$\mathcal{S}\tilde{\phi} = \int_{\tilde{\mathcal{B}}} \|\tilde{P} \cdot \left(\frac{\partial \tilde{\phi}}{\partial u_1} \wedge \frac{\partial \tilde{\phi}}{\partial u_2}\right)\| du \leq \int_{\tilde{\mathcal{B}}} \|P \cdot \left(\frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2}\right)\| du = \mathcal{S}\phi$$

Using lemma, we can choose $\delta = \inf\{\mathcal{S}\phi : \phi \in \Sigma(\psi, \Omega)\}$. Suppose that $\{\phi^k\}$, minimizes \mathcal{S} with respect to $\Sigma(\psi, \Omega)$, then $\lim_{k \rightarrow \infty} \mathcal{S}\phi^k = \delta$. Now consider the sequence $\{\tilde{\phi}^k\} \subset \Sigma(\psi, \tilde{\Omega})$ as in the above definition, from the boundedness of $\{\mathcal{S}\tilde{\phi}^k\}$ and $\mathcal{S}\tilde{\phi}^k \leq \mathcal{S}\phi^k$, we have $\lim_{k \rightarrow \infty} \mathcal{S}\tilde{\phi}^k \leq \delta$. Furthermore $\tilde{\phi}^k \in \Sigma(\psi, \Omega)$, hence $\mathcal{S}\tilde{\phi}^k \geq \delta$, and $\lim_{k \rightarrow \infty} \mathcal{S}\tilde{\phi}^k \geq \delta$, which implies $\lim_{k \rightarrow \infty} \mathcal{S}\tilde{\phi}^k = \delta$. Now

$$\inf\{\mathcal{S}\tilde{\phi} : \tilde{\phi} \in \Sigma(\psi, \tilde{\Omega})\} \leq \inf\{\mathcal{S}\phi : \phi \in \Sigma(\psi, \Omega)\} = \delta.$$

And from $\tilde{\phi} \in \Sigma(\psi, \Omega)$, we have $\inf\{\mathcal{S}\tilde{\phi} : \tilde{\phi} \in \Sigma(\psi, \tilde{\Omega})\} \geq \delta$, which implies $\inf\{\mathcal{S}\tilde{\phi} : \tilde{\phi} \in \Sigma(\psi, \tilde{\Omega})\} = \delta$. At the final we can show that $\lim_{k \rightarrow \infty} \mathcal{S}\tilde{\phi}^k = \delta = \inf\{\mathcal{S}\tilde{\phi} : \tilde{\phi} \in \Sigma(\psi, \tilde{\Omega})\}$, i.e. $\{\tilde{\phi}^k\}$ minimizes \mathcal{S} with respect to $\Sigma(\psi, \tilde{\Omega})$.

Lemmas 4.4, 4.5 and a proof similar to corollary 5.4 in [1], implies the following theorem.

Theorem 4.2. *Positive semi-trajectories of system converges to an equilibrium point, i.e., any ω -limit point of 2 in Ω° , is an equilibrium point.*

Finally, the above theorem implies the following result.

Theorem 4.3. *Suppose the inequalities in Lemma 4.4 holds, then:*

(1) *when the only equilibrium point is the drug-free equilibrium P_0 , then all solutions tend to P_0 ;*

(2) *when $R_0 > 1$, then all solutions of 2 tends to the unique endemic equilibrium point;*

(3) *when there are two endemic equilibrium points, which occurs when $R_0^c < R_0 < 1$, solutions of the system either tend to the drug-free equilibrium P_0 or tend to the upper equilibrium point.*

5. NUMERICAL SIMULATION

Finally, we present numerical examples using Matlab. The aim of this simulations is to illustrate stability results obtained in previous sections. We consider the following three cases.

Case 1. $R_0 \leq 1$ and $\beta_3 \leq \beta_1$.

We choose $\Lambda = 20$, $\mu = 10^{-3}$, $\alpha = 10^{-3}$, $\beta_3 = \beta_1 = 10^{-5}$, $\beta_2 = 10^{-1}$, $p_1 = 10^{-2}$, $p_2 = 10^{-1}$, $p_3 = 2 \times 10^{-2}$, and initial conitions, $(S_0, U_0, T_0, Q_0) = (15000, 1100, 900, 220)$. In this case $R_0 = 0.99$. See figure 2.

Case 2. $R_0 < \frac{\beta_1 \Lambda}{\beta_1 \Lambda + \mu(\beta_2 + p_3 q_1)}$.

We choose $\Lambda = 10$, $\mu = 10^{-3}$, $\alpha = 10^{-3}$, $\beta_1 = 10^{-6}$, $\beta_2 = 10^{-1}$, $p_1 = 10^{-2}$, $p_2 = 10^{-1}$, $p_3 = 10^{-2}$, $\beta_3 = 10^{-2}$ and initial conitions, $(S_0, U_0, T_0, Q_0) = (9800, 1100, 300, 250)$. In this case $R_0 = 0.049 < 0.064 = \frac{\beta_1 \Lambda}{\beta_1 \Lambda + \mu(\beta_2 + p_3 q_1)}$. See figure 3.

Case 3. $R_0 > 1$.

We choose $\Lambda = 100$, $\mu = 10^{-2}$, $\alpha = 10^{-2}$, $\beta_1 = 2 \times 10^{-2}$, $\beta_2 = 2 \times 10^{-6}$, $p_1 = 10^{-2}$, $p_2 = 10^{-2}$, $p_3 = 2 \times 10^{-3}$, $\beta_3 = 2 \times 10^{-6}$ and initial conitions, $(S_0, U_0, T_0, Q_0) = (98000, 1700, 1000, 900)$. In this $R_0 = 6666.2222$. This collection of parameters satisfy the inequalities in Lemma 4.4. See figure 4.

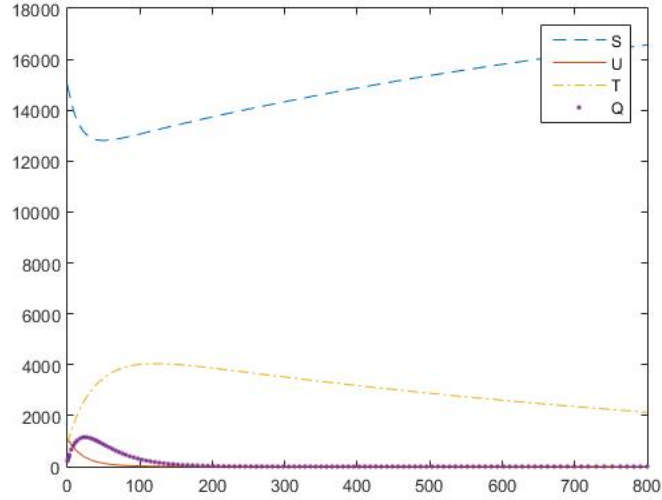


FIGURE 2. The DFE equilibrium point is globally asymptotically stable. In this case $\Lambda = 20$, $\mu = 10^{-3}$, $\alpha = 10^{-3}$, $\beta_3 = \beta_1 = 10^{-5}$, $\beta_2 = 10^{-1}$, $p_1 = 10^{-2}$, $p_2 = 10^{-1}$, $p_3 = 2 \times 10^{-2}$, and $(S_0, U_0, T_0, Q_0) = (15000, 1100, 900, 220)$.

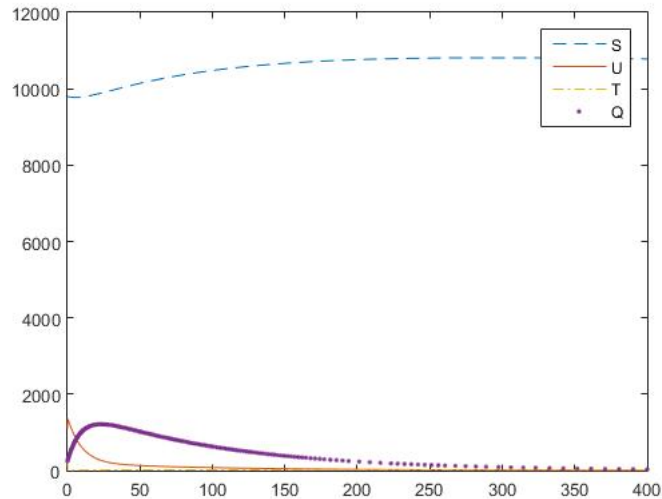


FIGURE 3. The DFE equilibrium point is globally asymptotically stable. In this case $\Lambda = 10$, $\mu = 10^{-3}$, $\alpha = 10^{-3}$, $\beta_1 = 10^{-6}$, $\beta_2 = 10^{-1}$, $p_1 = 10^{-2}$, $p_2 = 10^{-1}$, $p_3 = 10^{-2}$, $\beta_3 = 10^{-2}$ and $(S_0, U_0, T_0, Q_0) = (9800, 1100, 300, 250)$.

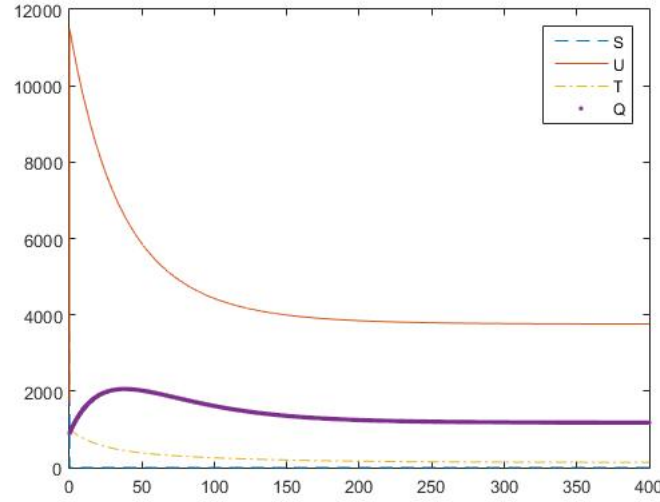


FIGURE 4. The unique endemic equilibrium point is globally asymptotically stable. In this case $\Lambda = 100$, $\mu = 10^{-2}$, $\alpha = 10^{-2}$, $\beta_1 = 2 \times 10^{-2}$, $\beta_2 = 2 \times 10^{-6}$, $p_1 = 10^{-2}$, $p_2 = 10^{-2}$, $p_3 = 2 \times 10^{-3}$, $\beta_3 = 2 \times 10^{-6}$ and $(S_0, U_0, T_0, Q_0) = (98000, 1700, 1000, 900)$.

6. CONCLUSION

The White and Comiskey's model of heroin epidemics is extended in this paper. This extension includes addition of a compartment for the incarcerated drug users due to criminal actions. Complete qualitative study of the model including the existence and local and global stability of the equilibrium points are carried out. The drug free equilibrium P_0 , is shown to be locally and globally stable under suitable conditions. Using compound matrices the sufficient conditions for the local and global stability of the endemic equilibrium points is obtained.

By the analysis of the model, we noted that, the model has a unique and locally asymptotically stable endemic equilibrium when $R_0 > 1$, which shows the persistence of drug users in the community.

The occurrence of backward bifurcation is also proved for the model which shows under some conditions, it is not enough to reduce R_0 to the region $R_0 < 1$, to control the drug epidemic. Infact when $R_0 < 1$, the drug problem may be persistent. Hence we compute another threshold, $R_0^c < 1$, and show that for the control of drug epidemic, R_0 should be reduced to below R_0^c . Through the analysis of the model, we find that the ratio $\frac{\beta_3}{\beta_1}$, is the main factor of the occurrence

of backward bifurcation. Hence for the simpler eradication of the drugs in a community, $\frac{\beta_3}{\beta_1}$, should be reduced below $1 + \frac{(\mu+\alpha)(1+q_1)}{\beta_2+p_3q_1}$.

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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