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BACKWARD BIFURCATION AND GLOBAL STABILITY IN AN EPIDEMIC MODEL WITH TREATMENT AND VACCINATION

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Abstract. In this paper, we consider a class of epidemic models described by five nonlinear ordinary differential equations. The population is divided into susceptible, vaccinated, exposed, infectious, and recovered subclasses. One main feature of this kind of models is that treatment and vaccination are introduced to control and prevent infectious diseases. The existence and local stability of the endemic equilibria are studied. The occurrence of backward bifurcation is established by using center manifold theory. Moveover, global dynamics are studied by applying the geometric approach. We would like to mention that in the case of bistability, global results are difficult to obtain since there is no compact absorbing set. It is the first time that higher (greater than or equal to four) dimensional systems are discussed. We give sufficient conditions in terms of the system parameters by extending the method in Arino et al. [2]. Numerical simulations are also provided to support our theoretical results. By carrying out sensitivity analysis of the basic reproduction number in terms of some parameters, some effective measures to control infectious diseases are analyzed.

1. **Introduction.** Mathematical modeling is an invaluable tool in studying the transmission dynamics of infectious diseases. Various epidemic models have been proposed and analyzed extensively and great progress has been achieved (see Allen and Burgin [1], Brauer [3], Boven et al. [4], Castillon-Charez et al. [6], Hethcote [10, 11], Moghadas [23, 24], Nasell [26, 27]). Many studies based on both deterministic (see Brauer [3], Castillon-Charez et al. [6], Moghadas [23]) and stochastic epidemic models have been carried out (see Allen and Burgin [1], Nasell [26, 27]). The basic reproduction number is a threshold in the sense that the disease is persistent if it is greater than one and dies out if it is less than one. In the last two

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decades, the existence of backward bifurcation has also attracted interest in modeling and studying the transmission dynamics of various infectious diseases (see Arino et al. [2], Hadeler and ven den Driessche [12], Moghadas [24], ven den Driessche and Watmough [31], Wan and Zhu [35]) and it is found that even if the basic reproduction number is less than one, the disease may not be eliminated. In this case, the basic reproduction number does not provide a description of the necessary elimination effort; rather the description of the effort is provided through the value of the critical parameter at the turning point. Thus, it is important to consider backward bifurcation in order to obtain the threshold for controlling diseases.

Treatment is important and effective in controlling infectious diseases. In these articles (see Hu et al. [13], Hu et al. [14], Li et al. [20, 21], Li et al. [22], Tang and Li [29], Wang [32], Wang and Ruan [33], Wang et al. [34], Zhang and Liu [37, 38], Zhou and Fan [39], Zhou and Cui [40],), authors studied SIR, SIS, SEIR epidemic models with different treatment functions. Vaccination is also commonly used for preventing diseases, such as measles, influenza, hepatitis B, encephalitis B. The effect of vaccination on preventing infectious diseases has been modeled and investigated (see Arino et al. [2], Buonomo and Vargas-De-León [5], Gumel and McCluskey [9], Hethcote [10, 11], Hui and Zhu [15], Yang et al. [36]).

Concerning the shortage of medical facilities and the limitation of resources, it is reasonable to use saturated treatment functions in modeling control strategies. Meanwhile, irregularity in the supply of vaccines and waning are major factors in the resurgence and outbreaks of some infectious diseases. It is necessary to take a control strategy that incorporates vaccination and treatment as two complementary programs to prevent disease spreading.

In this paper, we consider the following epidemic model with vaccination and saturated treatment which is described by five nonlinear ordinary differential equations:

$$\begin{aligned}
\frac{dS(t)}{dt} &= (1-\rho)A - \beta S(t)I(t) - \mu S(t) - \phi S(t) + \theta V(t),\\
\frac{dV(t)}{dt} &= \rho A + \phi S(t) - \mu V(t) - \theta V(t),\\
\frac{dE(t)}{dt} &= \beta S(t)I(t) - (\mu+\varepsilon)E(t),\\
\frac{dI(t)}{dt} &= \varepsilon E(t) - (\mu + r + d)I(t) - \frac{cI(t)}{b+I(t)},\\
\frac{dR(t)}{dt} &= rI(t) - \mu R(t) + \frac{cI(t)}{b+I(t)}.
\end{aligned} \tag{1}$$

In (1), the total population is partitioned into five compartments: susceptible (S), vaccinated (V), exposed (E), infectious (I), and recovered (R). Assumed the vaccine is available for both the susceptible individuals and new recruits (including newborns, travelers, etc), the immunity of the vaccinated individuals is temporary, and the recovered individuals do not revert to the susceptible class. It may be readily seen that the first four equations in (1) are independent of the variable R. Thus, the model can be reduced to a four-dimensional system. However, the question of global stability in this type of epidemic models is still a challenging and difficult task (see Buonomo and Vargas-De-León [5]).

For our model, we not only discuss the backward bifurcation by using center manifold theory but also study the global dynamics by applying the geometric method. It is generally known that the geometric method is a powerful tool to prove the global stability of equilibrium states of epidemic models (see Li and Muldowney [17]). However, this method is used mostly for two-dimensional systems (see Hui and Zhu [15]) and three-dimensional systems (see Kar and Jana [16], Li and Muldowney [17], Shu and Wang [28]) and seems to be particularly suitable for low dimensional systems. Applications to four-dimensional systems are not very common in the literature because the procedure becomes particularly involved when $n \geq 4$ (see Buonomo and Varges-De-León [5], Gumel and McCluskey [9]). In particular, in the case of bistability, it is difficult to obtain the global results since there is no compact absorbing set (see Arino et al. [2]). We believe that it is the first time higher dimensional systems are discussed using this method.

This paper is organized as follows. The model is formulated in Section 1. Positivity of solutions, the basic reproduction number and the existence and local stability of the endemic equilibria are obtained in Section 2. The backward bifurcation analysis is performed in Section 3. Section 4 deals with the global dynamics including global stability of the disease-free equilibrium and the endemic equilibrium. In Section 5, numerical simulations are presented to illustrate the results and sensitivity analysis is performed. A brief discussion is presented in Section 6.

2. The basic properties of the model.

In model (1), β is the infection rate, ε is the progression rate at which an infected individual becomes infectious per unite time, r is the removal rate at which an infectious individual recovers per unite time, A is the recruitment rate, ρ $(0 < \rho < 1)$ is the fraction of the vaccinated new recruits, ϕ is the rate at which the susceptible population is vaccinated, θ is the rate coefficient of losing immunity from vaccination, μ is the constant death rate from each compartment, d is the extra disease-related death rate. $h(I) = \frac{cI(t)}{b+I(t)}$ is the treatment function. Here, $c \geq 0$ represents the maximum medical resources supplied per unite of time and $b > 0$ is half-saturation constant, which measures the efficiency of the medical resource supplied. In this paper, we assume that all parameters in model (1) are nonnegative.

The reduced four-dimensional model mentioned above becomes:

$$\begin{aligned}
\frac{dS(t)}{dt} &= (1-\rho)A - \beta S(t)I(t) - \mu S(t) - \phi S(t) + \theta V(t),\\
\frac{dV(t)}{dt} &= \rho A + \phi S(t) - \mu V(t) - \theta V(t),\\
\frac{dE(t)}{dt} &= \beta S(t)I(t) - (\mu+\varepsilon)E(t),\\
\frac{dI(t)}{dt} &= \varepsilon E(t) - (\mu+r+d)I(t) - \frac{cI(t)}{b+I(t)}.
\end{aligned} \tag{2}$$

2.1. Positivity of solutions.

On the positivity of solutions for model (2), we have the following result.

Theorem 2.1. *If initial data $S(0) > 0, V(0) > 0, E(0) > 0$ and $I(0) > 0$, then the solution $(S(t), V(t), E(t), I(t))$ of model (2) is positive for all $t \geq 0$.*

Proof. Let $(S(t), V(t), E(t), I(t))$ be the solution of model (2) with initial data $S(0) > 0, V(0) > 0, E(0) > 0$ and $I(0) > 0$. Suppose that the conclusion is not true, then there is a $t_1 > 0$ such that

$$\min\{S(t_1), V(t_1), E(t_1), I(t_1)\} = 0$$

and

$$\min\{S(t), V(t), E(t), I(t)\} > 0 \quad \text{for all} \quad t \in [0, t_1).$$

If $\min\{S(t_1), V(t_1), E(t_1), I(t_1)\} = S(t_1)$, then from model (1) we have

$$\frac{dS(t)}{dt} \geq -\beta S(t)I(t) - \mu S(t) - \phi S(t) \quad \text{for all} \quad t \in [0, t_1).$$

Hence,

$$0 = S(t_1) \geq S(0)\exp(-\int_0^{t_1}(\beta I(s) + \mu + \phi)ds) > 0,$$

which leads to a contradiction.

Similarly, we can obtain contradictions when $\min\{S(t_1), V(t_1), E(t_1), I(t_1)\} = V(t_1)$, $\min\{S(t_1), V(t_1), E(t_1), I(t_1)\} = E(t_1)$, or $\min\{S(t_1), V(t_1), E(t_1), I(t_1)\} = I(t_1)$. This completes the proof. □

Let $N(t) = S(t) + V(t) + E(t) + I(t)$, then from model (2) and Theorem 2.1 we have

$$N'(t) = A - \mu N(t) - (d + r)I(t) - \frac{cI(t)}{b + I(t)} \leq A - \mu N(t).$$

Hence, $\limsup_{t\to\infty} N(t) \leq \frac{A}{\mu}$. This shows that set

$$\Omega = \{(S, V, E, I) \mid S + V + E + I \leq \frac{A}{\mu}, S > 0, V \geq 0, E \geq 0, I \geq 0\}$$

is a positively invariant set with respect to model (2). Thus, the dynamics of model (2) can be considered only in Ω.

2.2. **The basic reproduction number.** Now, we calculate the basic reproduction number of model (2) by applying the method of the next generation matrix given in van den Driessche and Watmough [30].

It is easy to see that model (2) always has a disease-free equilibrium $P_0 = (S_0, V_0, 0, 0)$, where

$$S_0 = \frac{(\mu + \theta - \mu\rho)A}{(\mu + \phi)(\mu + \theta) - \phi\theta}, \quad V_0 = \frac{\rho A}{\mu + \theta} + \frac{\phi}{\mu + \theta}\frac{(\mu + \theta - \mu\rho)A}{(\mu + \phi)(\mu + \theta) - \phi\theta}.$$

According to Theorem 2 in van den Driessche and Watmough [30], the basic reproduction number of model (2) is calculated as follows

$$\mathcal{R}_v = \rho(\mathrm{FV}^{-1}) = \frac{\beta(\mu + \theta - \mu\rho)A\varepsilon b}{[(\mu + \phi)(\mu + \theta) - \phi\theta](\mu + \varepsilon)(\mu b + rb + db + c)}, \tag{3}$$

where

$$\mathrm{F} = \begin{pmatrix} 0 & \beta S_0 \\ 0 & 0 \end{pmatrix}, \quad \mathrm{V} = \begin{pmatrix} \mu + \varepsilon & 0 \\ -\varepsilon & \mu + r + d + \frac{c}{b} \end{pmatrix},$$

and the following result on the local stability of the disease-free equilibrium P_0 is directly established.

Theorem 2.2. *The disease-free equilibrium P_0 of model (2) is locally asymptotically stable if $\mathcal{R}_v < 1$ and unstable if $\mathcal{R}_v > 1$.*

The basic reproduction number $\mathcal{R}_v$ represents the average number of secondary cases generated by a typical infected individual in a completely susceptible population. From the epidemiological point of view, Theorem 2.2 implies that when $\mathcal{R}_v$ is less than unity, a small influx of infected individual into the community would not generate large outbreaks, and the disease dies out in time.

2.3. **The existence of endemic equilibria.** Firstly, we consider the existence of the endemic equilibrium for model (2). The endemic equilibrium $P = (S, V, E, I)$ of model (2) is determined by the following equations

$$\begin{aligned}
&(1-\rho)A - \beta SI - \mu S - \phi S + \theta V = 0,\\
&\rho A + \phi S - \mu V - \theta V = 0,\\
&\beta SI - (\mu+\varepsilon)E = 0,\\
&\varepsilon E - (\mu + r + d)I - \frac{cI}{b+I} = 0.
\end{aligned} \tag{4}$$

The last two equations in (4) lead to

$$S = \frac{1}{\beta\varepsilon}(\mu+\varepsilon)(\mu + r + d + \frac{c}{b+I}), \quad E = \frac{1}{\varepsilon}[(\mu + r + d)I + \frac{cI}{b+I}]. \tag{5}$$

From the second equation in (4), we have

$$V = \frac{\rho A}{\mu+\theta} + \frac{\phi S}{\mu+\theta}. \tag{6}$$

Substituting (5) and (6) into the first equation in (4), we obtain that I is the positive solution of the following equation

$$a_1 I^2 + a_2 I + a_3 = 0, \tag{7}$$

where

$$\begin{aligned}
a_1 = {} & \beta(\mu+\varepsilon)(\mu + r + d),\\
a_2 = {} & -[(1-\rho) + \frac{\theta\rho}{\mu+\theta}]\beta\varepsilon A + \beta(\mu+\varepsilon)[(\mu + r + d)b + c]\\
& + (\mu + \phi - \frac{\theta\phi}{\mu+\theta})(\mu+\varepsilon)(\mu + r + d),\\
a_3 = {} & (\mu + \phi - \frac{\theta\phi}{\mu+\theta})(\mu b + rb + db + c)(\mu+\varepsilon)(1 - \mathcal{R}_v).
\end{aligned}$$

Let

$$\begin{aligned}
\Delta = {} & a_2^2 - 4a_1a_3\\
= {} & a_2^2 - 4a_1(\mu + \phi - \tfrac{\theta\phi}{\mu+\theta})(\mu b + rb + db + c)(\mu+\varepsilon)(1 - \mathcal{R}_v).
\end{aligned}$$

Solving $\Delta = 0$, we obtain that $\mathcal{R}_v = \mathcal{R}^*$, where

$$\mathcal{R}^* = 1 - \frac{a_2^2}{4a_1(\mu+\varepsilon)(\mu b + rb + db + c)(\mu + \phi - \frac{\mu\phi}{\mu+\theta})},$$

and the following equivalent relations hold,

$$\Delta < 0 \Leftrightarrow \mathcal{R}_v < \mathcal{R}^*; \quad \Delta = 0 \Leftrightarrow \mathcal{R}_v = \mathcal{R}^*; \quad \Delta > 0 \Leftrightarrow \mathcal{R}_v > \mathcal{R}^*.$$

Hence, we have the following conclusions for the existence of equilibria.

Theorem 2.3. *For model (2), there always exists a disease-free equilibrium P_0 and*

(a) if $\mathcal{R}_v < \mathcal{R}^*$ or $\mathcal{R}^* = \mathcal{R}_v$ or $\mathcal{R}^* < \mathcal{R}_v < 1$ and $a_2 > 0$, there is no endemic equilibrium;

(b) if $\mathcal{R}^* < \mathcal{R}_v = 1$ and $a_2 < 0$ or $\mathcal{R}_v > 1$ or $\mathcal{R}^* = \mathcal{R}_v < 1$, there is a unique endemic equilibrium $\bar{P}(\bar{S}, \bar{V}, \bar{E}, \bar{I})$;

(c) if $\mathcal{R}^* < \mathcal{R}_v < 1$ and $a_2 < 0$, there are two distinct endemic equilibria $P_*(S_*, V_*, E_*, I_*)$ and $P^*(S^*, V^*, E^*, I^*)$, where $I_* = \frac{-a_2 - \sqrt{\Delta}}{2a_1}$ and $I^* = \frac{-a_2 + \sqrt{\Delta}}{2a_1}$.

2.4. **The local stability of endemic equilibria.** Jacobian matrix at any equilibrium E of model (2) is

$$J(E)=\begin{pmatrix} -\beta I-(\mu+\phi) & \theta & 0 & -\beta S \\ \phi & -(\mu+\theta) & 0 & 0 \\ \beta I & 0 & -(\mu+\varepsilon) & \beta S \\ 0 & 0 & \varepsilon & -(\mu+r+d)-\frac{bc}{(b+I)^2} \end{pmatrix} \tag{8}$$

and the characteristic equation of $J(E)$ is

$$\Psi(\lambda)=\lambda^4+A_1(I)\lambda^3+A_2(I)\lambda^2+A_3(I)\lambda+A_4(I)=0, \tag{9}$$

where

$$\begin{aligned} A_1(I)= &\ \beta I+4\mu+\phi+\theta+r+d+\varepsilon+\frac{bc}{(b+I)^2}, \\ A_2(I)= &\ \beta I(\mu+\theta)+\mu(\mu+\phi+\theta) \\ &+(2\mu+r+d+\varepsilon+\frac{bc}{(b+I)^2})(\beta I+2\mu+\phi+\theta)-(\mu+\varepsilon)\frac{cI}{(b+I)^2}, \\ A_3(I)= &\ (2\mu+r+d+\varepsilon+\frac{bc}{(b+I)^2})(\beta I(\mu+\theta)+\mu(\mu+\phi+\theta)) \\ &+\beta I(\mu+\varepsilon)(\mu+r+d+\frac{bc}{(b+I)^2})-(2\mu+\phi+\theta)(\mu+\varepsilon)\frac{cI}{(b+I)^2}, \\ A_4(I)= &\ \beta I(\mu+\theta)(\mu+\varepsilon)(\mu+r+d+\frac{bc}{(b+I)^2})-\mu(\mu+\phi+\theta)(\mu+\varepsilon)\frac{cI}{(b+I)^2}. \end{aligned}$$

On the local stability of positive equilibria P_*, P^* and $\bar{P}$, we can obtain the following sufficient conditions.

Theorem 2.4. *If $\mathcal{R}^*<\mathcal{R}_v<1$ and $a_2<0$, then the positive equilibrium P_* is an unstable saddle point.*

Proof. Obviously, $A_1(I)>0$ and

$$A_4(I)=\frac{I}{(b+I)^2}(\mu+\theta)h(I),$$

where

$$\begin{aligned} h(I)= &\ \beta(\mu+r+d)(\mu+\varepsilon)I^2+2b\beta(\mu+r+d)(\mu+\varepsilon)I+b^2\beta(\mu+r+d)(\mu+\varepsilon) \\ &+\beta bc(\mu+\varepsilon)-c\frac{\mu(\mu+\phi+\theta)}{\mu+\theta}(\mu+\varepsilon). \end{aligned}$$

Substituting $I_*=\frac{-a_2-\sqrt{\Delta}}{2a_1}$ into $h(I)$, we have

$$\begin{aligned} h(I_*)= &\ a_1\frac{(-a_2-\sqrt{\Delta})^2}{4a_1^2}+2ba_1\frac{-a_2-\sqrt{\Delta}}{2a_1}+b^2\beta(\mu+r+d)(\mu+\varepsilon) \\ &+\beta bc(\mu+\varepsilon)-c\frac{\mu(\mu+\phi+\theta)}{\mu+\theta}(\mu+\varepsilon) \\ = &\ \frac{-\sqrt{\Delta}(-a_2+\sqrt{\Delta})}{2a_1}+a_3-ba_2-b\sqrt{\Delta}+b^2\beta(\mu+r+d)(\mu+\varepsilon) \\ &+\beta bc(\mu+\varepsilon)-c\frac{\mu(\mu+\phi+\theta)}{\mu+\theta}(\mu+\varepsilon) \\ = &\ -\sqrt{\Delta}(b+\frac{-a_2-\sqrt{\Delta}}{2a_1})<0. \end{aligned}$$

Hence, $A_1(I_*) > 0$ and $A_4(I_*) < 0$.

Let $\lambda_j(I_*)\,(j = 1, 2, 3, 4)$ be the roots of equation (9) with real parts satisfying $Re(\lambda_1(I_*)) \le Re(\lambda_2(I_*)) \le Re(\lambda_3(I_*)) \le Re(\lambda_4(I_*))$. Since

$$\lambda_1(I_*) + \lambda_2(I_*) + \lambda_3(I_*) + \lambda_4(I_*) = -A_1(I_*) < 0$$

and

$$\lambda_1(I_*)\lambda_2(I_*)\lambda_3(I_*)\lambda_4(I_*) = A_4(I_*) < 0,$$

we obtain that $Re(\lambda_1(I_*)) < 0$ and $Re(\lambda_4(I_*)) > 0$. Therefore, P_* is an unstable saddle point when it exists. This completes the proof. $\square$

Theorem 2.5. *Let $\mathcal{R}^* < \mathcal{R}_v < 1$ and $a_2 < 0$. If*
(i) $A_1(I^*)A_2(I^*) - A_3(I^*) > 0$,
(ii) $A_3(I^*)(A_1(I^*)A_2(I^*) - A_3(I^*)) - A_1(I^*)^2A_4(I^*) > 0$,
then the positive equilibrium P^* is locally asymptotically stable.

Proof. By Routh-Hurwitz criterion, we know that all roots of equation (9) have negative real parts if and only if the following conditions hold:

$$A_1(I) > 0,\ A_4(I) > 0, \begin{vmatrix} A_1(I) & 1 \\ A_3(I) & A_2(I) \end{vmatrix} > 0, \begin{vmatrix} A_1(I) & 1 & 0 \\ A_3(I) & A_2(I) & A_1(I) \\ 0 & A_4(I) & A_3(I) \end{vmatrix} > 0.$$

Substituting $I = I^* = \frac{-a_2+\sqrt{\Delta}}{2a_1}$, it is clear that $A_1(I^*) > 0$, $A_4(I^*) = \frac{I^*}{(b+I^*)^2}(\mu + \theta)h(I^*)$ and by a similar calculation as above, we have

$$h(I^*) = \sqrt{\Delta}(b + \frac{-a_2 + \sqrt{\Delta}}{2a_1}) > 0.$$

Therefore, when conditions (i) and (ii) hold, all roots of equation (9) with $I = I^*$ have negative real parts. This completes the proof. $\square$

Similarly, we also have the following result.

Theorem 2.6. *Let $\mathcal{R}_v > 1$. If*
(i) $A_1(\bar{I})A_2(\bar{I}) - A_3(\bar{I}) > 0$,
(ii) $A_3(\bar{I})(A_1(\bar{I})A_2(\bar{I}) - A_3(\bar{I})) - A_1(\bar{I})^2A_4(\bar{I}) > 0$,
then the unique positive equilibrium $\bar{P}$ is locally asymptotically stable.

3. **The backward bifurcation.**

The epidemiological importance of the phenomenon of backward bifurcation is that the classical requirement of $\mathcal{R}_v < 1$ is not enough to eradicate the disease (see Brauer [3], Castillon-Charez and Blower [6], Wang [32], Wang and Ruan [33]). In such a scenario, the initial sizes of the sub-population (state variables) of the model play a critical role in eliminating disease.

In order to study the existence of backward bifurcation of model (2), we need to introduce the following results which are given by Castillo-Chavez and Song [7].

Considering the following general system of ordinary differential equations with a parameter φ:

$$\frac{dx(t)}{dt} = f(x, \varphi), \tag{10}$$

where function $f(x, \varphi) : R^n \times R \to R^n$ with $f \in C^2(R^n \times R)$. Assume that $x = 0$ is an equilibrium of system (10), that is, $f(0, \varphi) \equiv 0$ for all φ. Let $Q = \left(\frac{\partial f_i}{\partial x_j}(0, 0)\right)$ be the Jacobian matrix of $f(x, \varphi)$ at $(0, 0)$.

Lemma 3.1. *Assume that*

(H1) *Zero is a simple eigenvalue of Q and all other eigenvalues of Q have negative real part;*

(H2) *Q has a (non-negative) right eigenvector $\mathbf{w} = (\omega_1, \omega_2, \cdots, \omega_n)^T$ and a left eigenvector $\mathbf{v} = (v_1, v_2, \cdots, v_n)$ corresponding to the zero eigenvalue.*

Let $f_k(x, \varphi)$ denote the k-th component of $f(x, \varphi)$ and

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

Then, the local dynamics of system (10) around $x = 0$ are totally determined by the signs of $\mathbf{a}$ and $\mathbf{b}$.

(1) If $\mathbf{a} > 0$ and $\mathbf{b} > 0$, then when $\varphi < 0$ with $|\varphi| \ll 1$, $x = 0$ is locally asymptotically stable and there exists a positive unstable equilibrium, and when $0 < \varphi \ll 1$, $x = 0$ is unstable and there exists a negative locally asymptotically stable equilibrium;

(2) If $\mathbf{a} < 0$ and $\mathbf{b} > 0$, then when φ changes from negative to positive, $x = 0$ changes its stability from stable to unstable. Correspondingly, a negative unstable equilibrium becomes positive and locally asymptotically stable.

Particularly, if $\mathbf{a} < 0$ and $\mathbf{b} > 0$, then a forward bifurcation occurs at $\varphi = 0$, and if $\mathbf{a} > 0$ and $\mathbf{b} > 0$, a backward bifurcation occurs at $\varphi = 0$.

On the existence of the backward bifurcation for model (2), we have the following results.

Theorem 3.2. *If $c < \bar{c}$, then model (2) exhibits a backward bifurcation when $\mathcal{R}_v = 1$. If $c > \bar{c}$, then model (2) exhibits a forward bifurcation when $\mathcal{R}_v = 1$, where*

$$\bar{c} = \frac{[\beta(\mu + \theta - \mu\rho)A\varepsilon - (\mu + \phi + \theta)\mu(\mu + \varepsilon)(\mu + r + d)]^2}{\varepsilon(\mu + \varepsilon)\beta^2(\mu + \theta - \mu\rho)A(\mu + \theta)}.$$

Proof. Let $S = x_1, V = x_2, E = x_3, I = x_4$, model (2) becomes

$$\begin{aligned}
\frac{dx_1(t)}{dt} &= (1-\rho)A - \beta x_1(t)x_4(t) - \mu x_1(t) - \phi x_1(t) + \theta x_2(t) := f_1, \\
\frac{dx_2(t)}{dt} &= \rho A + \phi x_1(t) - \mu x_2(t) - \theta x_2(t) := f_2, \\
\frac{dx_3(t)}{dt} &= \beta x_1(t)x_4(t) - (\mu + \varepsilon)x_3(t) := f_3, \\
\frac{dx_4(t)}{dt} &= \varepsilon x_3(t) - (\mu + r + d)x_4(t) - \frac{cx_4(t)}{b + x_4(t)} := f_4.
\end{aligned} \tag{11}$$

The Jacobian matrix at the disease free equilibrium P_0 is

$$J(P_0) = \begin{pmatrix} -(\mu+\phi) & \theta & 0 & -\beta\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta} \\ \phi & -(\mu+\theta) & 0 & 0 \\ 0 & 0 & -(\mu+\varepsilon) & \beta\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta} \\ 0 & 0 & \varepsilon & -(\mu+r+d+\frac{c}{b}) \end{pmatrix}.$$

When $\mathcal{R}_v = 1$, the corresponding characteristic equation of $J(P_0)$ is as follows

$$\lambda(\lambda + 2\mu + r + d + \frac{c}{b} + \varepsilon)[\lambda^2 + (2\mu + \phi + \theta)\lambda + (\mu + \phi)(\mu + \theta) - \phi\theta] = 0.$$

Hence, all eigenvalues of $J(P_0)$ are $\lambda_1 = 0, \lambda_2 = -(2\mu + r + d + \frac{c}{b} + \varepsilon), \lambda_3 = -\mu$ and $\lambda_4 = -\mu - \phi - \theta$. Obviously, $\lambda_1 = 0$ is a simple zero eigenvalue and all other eigenvalues of $J(P_0)$ are real and negative. Therefore, we can use the center manifold theory in Guckenheimer and Holmes [8] to discuss the occurrence of bifurcations.

Choosing b as the bifurcation parameter. It follows that $\mathcal{R}_v = 1$ is equivalent to

$$b = b^* = \frac{c[(\mu+\phi)(\mu+\theta) - \phi\theta](\mu+\varepsilon)}{\beta(\mu+\theta-\mu\rho)A\varepsilon - [(\mu+\phi)(\mu+\theta)-\phi\theta](\mu+\varepsilon)(\mu+r+d)}.$$

Hence, when $b = b^*$, the disease-free equilibrium P_0 is a nonhyperbolic equilibrium which satisfies the assumption (H1) of Lemma 3.1.

Now, we denote by $\mathbf{w} = (w_1, w_2, w_3, w_4)^T$ a right eigenvector associated with the zero eigenvalue. It is formulated by

$$\begin{pmatrix} -(\mu+\phi) & \theta & 0 & -\beta\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta} \\ \phi & -(\mu+\theta) & 0 & 0 \\ 0 & 0 & -(\mu+\varepsilon) & \beta\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta} \\ 0 & 0 & \varepsilon & -(\mu+r+d+\frac{c}{b^*}) \end{pmatrix} \begin{pmatrix} w_1 \\ w_2 \\ w_3 \\ w_4 \end{pmatrix} = 0.$$

Hence,

$$\begin{cases} -(\mu+\phi)w_1 + \theta w_2 - \beta\dfrac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta}w_4 = 0, \\ \phi w_1 - (\mu+\theta)w_2 = 0, \\ -(\mu+\varepsilon)w_3 + \beta\dfrac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta}w_4 = 0, \\ \varepsilon w_3 - (\mu+r+d+\dfrac{c}{b^*})w_4 = 0. \end{cases}$$

This implies that

$$\begin{aligned} w_1 &= -w_3\frac{(\mu+\varepsilon)(\mu+\theta)}{(\mu+\phi)(\mu+\theta)-\phi\theta}, \quad & w_2 &= \frac{\phi}{\mu+\theta}w_1, \\ w_3 &= \beta\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta}, & w_4 &= \mu+\varepsilon. \end{aligned}$$

Therefore, the right eigenvector is

$$\mathbf{w} = (w_1, w_2, w_3, w_4)^T \tag{12}$$

with

$$\begin{aligned} w_1 &= -\beta\frac{(\mu+\theta-\mu\rho)A}{[(\mu+\phi)(\mu+\theta)-\phi\theta]^2}(\mu+\varepsilon)(\mu+\theta), \\ w_2 &= -\beta\frac{\phi}{\mu+\theta}\frac{(\mu+\theta-\mu\rho)A}{[(\mu+\phi)(\mu+\theta)-\phi\theta]^2}(\mu+\varepsilon)(\mu+\theta), \\ w_3 &= \beta\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta}, \\ w_4 &= \mu+\varepsilon. \end{aligned}$$

Moreover, the left eigenvector $\mathbf{v} = (v_1, v_2, v_3, v_4)$ associated with the zero eigenvalue satisfying $\mathbf{v} \cdot \mathbf{w} = 1$ is given by

$$\begin{cases} -(\mu+\phi)v_1 + \phi v_2 = 0, \\ \theta v_1 - (\mu+\theta)v_2 = 0, \\ -(\mu+\varepsilon)v_3 + \varepsilon v_4 = 0, \\ -\beta \dfrac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta} v_1 + \beta \dfrac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta} v_3 - (\mu+r+d+\dfrac{c}{b^*})v_4 = 0. \end{cases}$$

Then, the left eigenvector is

$$\mathbf{v} = (0, 0, v_3, v_4) \tag{13}$$

with

$$\begin{aligned} v_3 = &\ \frac{\varepsilon b^*}{(\mu+\varepsilon)(2\mu b^* + rb^* + db^* + \varepsilon b^* + c)}, \\ v_4 = &\ \frac{b^*}{2\mu b^* + rb^* + db^* + \varepsilon b^* + c}. \end{aligned}$$

Calculating the partial derivatives at the disease-free equilibrium P_0, we obtain

$$\frac{\partial^2 f_1}{\partial x_1 x_4} = \frac{\partial^2 f_1}{\partial x_4 x_1} = -\beta, \quad \frac{\partial^2 f_3}{\partial x_1 x_4} = \frac{\partial^2 f_3}{\partial x_4 x_1} = \beta,$$

$$\frac{\partial^2 f_4}{\partial x_4^2} = \frac{2c}{b^2}, \quad \frac{\partial^2 f_4}{\partial x_4 \partial b} = \frac{c}{b^2},$$

all the other second-order partial derivatives are equal to zero.

Furthermore, we can compute the coefficients $\mathbf{a}$ and $\mathbf{b}$ defined in Lemma 3.1, that is,

$$\mathbf{a} = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0), \quad \mathbf{b} = \sum_{k,i,=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial b}(P_0).$$

Taking into account of system (11) and considering in $\mathbf{a}$ and $\mathbf{b}$ only the nonzero derivatives for the terms $\frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0)$ and $\frac{\partial^2 f_k}{\partial x_i \partial b}(P_0)$, it follows that

$$\mathbf{a} = 2v_3 w_1 w_4 \frac{\partial^2 f_3}{\partial x_1 \partial x_4}(P_0) + v_4 w_4^2 \frac{\partial^2 f_4}{\partial x_4^2}(P_0)$$

and

$$\mathbf{b} = v_4 w_4 \frac{\partial^2 f_4}{\partial x_4 \partial b}(P_0).$$

In view of (12) and (13), we obtain

$$\mathbf{a} = \frac{2b^*(\mu+\varepsilon)}{2\mu b^* + rb^* + db^* + \varepsilon b^* + c}\Big(\frac{c(\mu+\varepsilon)}{b^{*2}} - \varepsilon\beta^2 \frac{(\mu+\theta-\mu\rho)A(\mu+\theta)}{[(\mu+\phi)(\mu+\theta)-\phi\theta]^2}\Big)$$

and

$$\mathbf{b} = \frac{\beta(\mu+\varepsilon)^2(\mu+\theta-\mu\rho)A}{\varepsilon(\mu+\theta-\mu\rho)A + (\mu+\varepsilon)^2[(\mu+\phi)(\mu+\theta)-\phi\theta]} \frac{c}{b^{*2}}.$$

Since the coefficient $\mathbf{b}$ is always positive so that, according to Lemma 3.1, model (2) undergoes a backward bifurcation if the coefficient $\mathbf{a}$ is positive (i.e., $c < \bar{c}$). Moreover, model (2) undergoes a forward bifurcation if the coefficient $\mathbf{a}$ is negative (i.e., $c > \bar{c}$). This completes the proof. □

Remark 1. Let

$$\begin{aligned}\bar{\phi} = \quad & \frac{1}{\mu(\mu+\varepsilon)(\mu+r+d)}\Big(- \sqrt{c\varepsilon\beta^2 A(\mu+\theta-\mu\rho)(\mu+\theta)(\mu+\varepsilon)} \\ & +\beta(\mu+\theta-\mu\rho)A\varepsilon\Big) - \mu - \theta,\end{aligned}$$

then from the above expression of $\mathbf{a}$ we easily obtain that when $\phi < \bar{\phi}$ then $\mathbf{a} > 0$ and hence model (2) exhibits a backward bifurcation when $\mathcal{R}_v = 1$, and when $\phi > \bar{\phi}$ then $\mathbf{a} < 0$, and hence model (2) exhibits a forward bifurcation when $\mathcal{R}_v = 1$.

Theorem 3.3. *If $b < \bar{b}$, then model (2) exhibits a backward bifurcation when $\mathcal{R}_v = 1$. If $b > \bar{b}$, then model (2) exhibits a forward bifurcation when $\mathcal{R}_v = 1$, where*

$$\bar{b} = \frac{1}{\mu+r+d}\Big(\sqrt{\frac{c(\mu+\theta-\mu\rho)A\varepsilon}{(\mu+\theta)(\mu+\varepsilon)}} - c\Big).$$

Proof. Choosing β as the bifurcation parameter. Then, $\mathcal{R}_v = 1$ is equivalent to

$$\beta = \beta^* = \frac{[(\mu+\phi)(\mu+\theta)-\phi\theta](\mu+\varepsilon)(\mu b+rb+db+c)}{(\mu+\theta-\mu\rho)A\varepsilon b}.$$

By a similar calculation as in Theorem 3.2, we have that the right eigenvector associated with the zero eigenvalue, denoted by $\mathbf{w} = (w_1, w_2, w_3, w_4)^T$, is given with

$$\begin{aligned} w_1 &= -w_3\frac{(\mu+\varepsilon)(\mu+\theta)}{(\mu+\phi)(\mu+\theta)-\phi\theta}, \quad & w_2 &= \frac{\phi}{\mu+\theta}w_1, \\ w_3 &= \frac{(\mu+\varepsilon)(\mu b+rb+bd+c)}{\varepsilon b}, \quad & w_4 &= \mu+\varepsilon, \end{aligned}$$

and the corresponding left eigenvector is given by $\mathbf{v} = (0, 0, v_3, v_4)$ with

$$v_3 = \frac{\varepsilon b}{(\mu+\varepsilon)(2\mu b+rb+db+\varepsilon b+c)}, \quad v_4 = \frac{b}{2\mu b+rb+db+\varepsilon b+c}.$$

Furthermore, we obtain that

$$\begin{aligned}\mathbf{a} = \quad & 2v_3w_1w_4\beta^* + 2v_4w_4^2\frac{c}{b^2} \\ = \quad & 2v_4w_4\frac{\mu+\varepsilon}{b^2}\Big(c - \frac{(\mu+\theta)(\mu+\varepsilon)(\mu b+rb+bd+c)^2}{(\mu+\theta-\mu\rho)A\varepsilon}\Big)\end{aligned}$$

and

$$\mathbf{b} = v_3w_4S_0 > 0.$$

Note that $\mathbf{a} = 0$ is equivalent to $b = \bar{b}$. This completes the proof. □

Remark 2. Let

$$\bar{\rho} = \frac{\mu+\theta}{\mu} - \frac{(\mu+\theta)(\mu+\varepsilon)(\mu b+rb+bd+c)^2}{c\mu A\varepsilon},$$

then from the above expression of $\mathbf{a}$ we easily obtain that when $\rho < \bar{\rho}$, then $\mathbf{a} > 0$ and hence model (2) exhibits a backward bifurcation when $\mathcal{R}_v = 1$, and when $\rho > \bar{\rho}$ then $\mathbf{a} < 0$, and hence model (2) exhibits a forward bifurcation when $\mathcal{R}_v = 1$.

4. **Global dynamics.** Firstly, we present some preliminaries on the geometric approach to study global dynamics (see Li and Muldowney [17], Shu and Wang [28]). Let B be the Euclidean unit ball in $\mathbb{R}^2$, and let $\overline{B}$ and ∂B be its closure and boundary, respectively. Let $\mathrm{Lip}(X \to Y)$ denote the set of Lipschitzian functions from X to Y. A function $\varphi \in \mathrm{Lip}(\overline{B} \to D)$ is a (simply connected rectifiable) surface in $D \subset \mathbb{R}^n$. A function $\psi \in \mathrm{Lip}(\partial B \to D)$ is a closed rectifiable curve in D and is called simple if it is one-to-one. Let $\Sigma(\psi, D) = \{\varphi \in \mathrm{Lip}(\overline{B} \to D) : \varphi|_{\partial B} = \psi\}$. If D is an open, simply connected set, then $\Sigma(\psi, D)$ is nonempty for each simple closed rectifiable curve ψ in D. Let $\|.\|$ be a norm on $\mathbb{R}^{\binom{n}{2}}$. A function $\mathcal{S}$ on the surface φ in D is defined as follows:

$$\mathcal{S}\varphi = \int_{\overline{B}} \Big\| P \cdot (\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}) \Big\| du, \tag{14}$$

where $u = (u_1, u_2), u \mapsto \varphi(u)$ is Lipschitzian on $\overline{B}$, the wedge product $\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}$ is a vector in $\mathbb{R}^{\binom{n}{2}}$, and P is an $\binom{n}{2} \times \binom{n}{2}$, matrix such that $\|P^{-1}\|$ is bounded on $\varphi(\overline{B})$. The following result follows from the development in Li and Muldowney [18, 19].

Lemma 4.1. *Suppose that ψ is a simple closed rectifiable curve in $\mathbb{R}^n$. Then there exists $\delta > 0$ such that $\mathcal{S}\varphi \geq \delta$ for all $\varphi \in \sum(\psi, \mathbb{R}^n)$.*

Let $x \mapsto f(x) \in \mathbb{R}^n$ be a C^1 function for x in a set $D \subset \mathbb{R}^n$. We consider the autonomous equation in $\mathbb{R}^n$

$$\frac{dx}{dt} = f(x). \tag{15}$$

For any surface φ, the new surface φ_t is defined by $\varphi_t(u) = x(t, \varphi(u))$. If $\varphi_t(u)$ is regarded as a function of u, then $\varphi_t(u)$ is a time t map determined by system (15). When $\varphi_t(u)$ is viewed as a function of t, $\varphi_t(u)$ is the solution of (15) passing through the initial point $(0, \varphi(u))$. The right-hand derivative of $\mathcal{S}\varphi_t$, denoted $D_+\mathcal{S}\varphi_t$, is defined by

$$D_+\mathcal{S}\varphi_t = \int_{\overline{B}} \lim_{h \to 0^+} \frac{1}{h}(\|z + h\mathrm{Q}(\varphi_t(u))z\| - \|z\|)du, \tag{16}$$

where the matrix $\mathrm{Q} = P_f P^{-1} + P \frac{\partial f}{\partial x}^{[2]} P^{-1}$. Here P_f is the directional derivative of P in the direction of the vector field f, $\frac{\partial f}{\partial x}^{[2]}$ is the second additive compound matrix of $\frac{\partial f}{\partial x}$ and $z = P \cdot (\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2})$ is a solution to the differential equation

$$\frac{dz}{dt} = \mathrm{Q}(\varphi_t(u))z. \tag{17}$$

Then, the right-hand derivative $D_+\mathcal{S}\varphi_t$ is expressed as

$$D_+\mathcal{S}\varphi_t = \int_{\overline{B}} D_+\|z\| du.$$

In Arino et al. [2] (see Theorem 4.2), for system (15), the following theorem is proven.

Lemma 4.2. *Suppose that there are a norm $\|.\|$ on $\mathbb{R}^{\binom{n}{2}}$ and a constant $\eta > 0$ such that $D_+\|z\| \leq -\eta\|z\|$ for all $z \in \mathbb{R}^{\binom{n}{2}}$ satisfying (17) and all $x \in D$, where D is simply connected. Further, suppose that for any simple closed curve ψ in D there is a sequence of surfaces $\{\varphi^k\}$ that minimizes S relative to $\Sigma(\psi, D)$ and there is a constant $\varepsilon > 0$ such that $\varphi_t^k \subset D$ for $t \in [0, \varepsilon]$ and $k = 1, 2, \cdots$. Then any omega limit point of system (15) in the interior of D is an equilibrium.*

In order to apply Lemma 4.2 to model (2), if we set $D = \Omega$, it is necessary to find a norm $\|.\|$ and a matrix P such that $D_+\|z\| \le -\eta\|z\|$ (see the following Lemma 4.3) and to show that an appropriate sequence of surfaces exists (see the following Lemma 4.4).

The Jacobian matrix at a general point $P(S, V, E, I)$ is given by

$$\frac{\partial f}{\partial x} = \begin{pmatrix} -\beta I - (\mu + \phi) & \theta & 0 & -\beta S \\ \phi & -(\mu + \theta) & 0 & 0 \\ \beta I & 0 & -(\mu + \varepsilon) & \beta S \\ 0 & 0 & \varepsilon & -(\mu + r + d) - \frac{bc}{(b+I)^2} \end{pmatrix}.$$

The second additive compound of the Jacobian matrix is a 6×6 matrix given by

$$\frac{\partial f}{\partial x}^{[2]} = \begin{pmatrix} j_{11} & 0 & 0 & 0 & \beta S & 0 \\ 0 & j_{22} & \beta S & \theta & 0 & \beta S \\ 0 & \varepsilon & j_{33} & 0 & \theta & 0 \\ -\beta I & \phi & 0 & j_{44} & \beta S & 0 \\ 0 & 0 & \phi & \varepsilon & j_{55} & 0 \\ 0 & 0 & \beta I & 0 & 0 & j_{66} \end{pmatrix},$$

where

$$\begin{aligned} j_{11} &= -\beta I - 2\mu - \phi - \theta, & j_{22} &= -\beta I - 2\mu - \phi - \varepsilon, \\ j_{33} &= -\beta I - 2\mu - \phi - r - d - \frac{bc}{(b+I)^2}, & j_{44} &= -2\mu - \varepsilon - \theta, \\ j_{55} &= -2\mu - \theta - r - d - \frac{bc}{(b+I)^2}, & j_{66} &= -2\mu - \varepsilon - r - d - \frac{bc}{(b+I)^2}. \end{aligned}$$

Let

$$P = \begin{pmatrix} \frac{1}{E} & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{E} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{E} & 0 & 0 \\ 0 & 0 & \frac{1}{I} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{I} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{I} \end{pmatrix}.$$

According to the matrix $\mathrm{Q} = P_f P^{-1} + P \frac{\partial f}{\partial x}^{[2]} P^{-1}$, we obtain

$$\mathrm{Q} = \begin{pmatrix} q_{11} & 0 & 0 & 0 & \beta S \frac{I}{E} & 0 \\ 0 & q_{22} & \theta & \beta S \frac{I}{E} & 0 & \beta S \frac{I}{E} \\ -\beta I & \phi & q_{33} & 0 & \beta S \frac{I}{E} & 0 \\ 0 & \varepsilon \frac{E}{I} & 0 & q_{44} & \theta & 0 \\ 0 & 0 & \varepsilon \frac{E}{I} & \phi & q_{55} & 0 \\ 0 & 0 & 0 & \beta I & 0 & q_{66} \end{pmatrix}, \tag{18}$$

where

$$q_{11} = -\beta S\frac{I}{E} - \beta I - \mu - \phi - \theta + \varepsilon, \quad q_{22} = -\beta S\frac{I}{E} - \beta I - \mu - \phi,$$
$$q_{33} = -\beta S\frac{I}{E} - \mu - \theta, \qquad q_{44} = -\varepsilon\frac{E}{I} - \beta I - \mu - \phi + \frac{cI}{(b+I)^2},$$
$$q_{55} = -\varepsilon\frac{E}{I} - \mu - \theta + \frac{cI}{(b+I)^2}, \qquad q_{66} = -\varepsilon\frac{E}{I} - \mu - \varepsilon + \frac{cI}{(b+I)^2}.$$

The authors in Gumel et al. [9] introduce the following norm on $\mathbb{R}^6$ from one orthant to another

$$\|z\| = \max\{U_1, U_2\},$$

where $z \in \mathbb{R}^6$ with components $z_i (i = 1, 2, 3, 4, 5, 6)$ and

$$U_1(z_1, z_2, z_3) = \begin{cases} \max\{|z_1|, |z_2| + |z_3|\}, & \text{if } \operatorname{sgn}(z_1) = \operatorname{sgn}(z_2) = \operatorname{sgn}(z_3), \\ \max\{|z_2|, |z_1| + |z_3|\}, & \text{if } \operatorname{sgn}(z_1) = \operatorname{sgn}(z_2) = -\operatorname{sgn}(z_3), \\ \max\{|z_1|, |z_2|, |z_3|\}, & \text{if } \operatorname{sgn}(z_1) = -\operatorname{sgn}(z_2) = \operatorname{sgn}(z_3), \\ \max\{|z_1| + |z_3|, |z_2| + |z_3|\}, & \text{if } -\operatorname{sgn}(z_1) = \operatorname{sgn}(z_2) = \operatorname{sgn}(z_3), \end{cases}$$

$$U_2(z_4, z_5, z_6) = \begin{cases} |z_4| + |z_5| + |z_6|, & \text{if } \operatorname{sgn}(z_4) = \operatorname{sgn}(z_5) = \operatorname{sgn}(z_6), \\ \max\{|z_4| + |z_5|, |z_4| + |z_6|\}, & \text{if } \operatorname{sgn}(z_4) = \operatorname{sgn}(z_5) = -\operatorname{sgn}(z_6), \\ \max\{|z_5|, |z_4| + |z_6|\}, & \text{if } \operatorname{sgn}(z_4) = -\operatorname{sgn}(z_5) = \operatorname{sgn}(z_6), \\ \max\{|z_4| + |z_6|, |z_5| + |z_6|\}, & \text{if } -\operatorname{sgn}(z_4) = \operatorname{sgn}(z_5) = \operatorname{sgn}(z_6). \end{cases}$$

Lemma 4.3. *Assume that in model (2) the parameters satisfy the following inequalities:*

$$\varepsilon < \mu + \theta, \quad \frac{c}{4b} < \mu \quad \textit{and} \quad \frac{c}{4b} + \theta < \mu + \varepsilon. \tag{19}$$

Then there exists $\chi > 0$, such that for any $S, V, E, I \geq 0$ and $I \neq 0$, the solution $z(t)$ of $\frac{dz(t)}{dt} = Qz(t)$ satisfies $D_+\|z\| \leq -\chi\|z\|$, where $D_+\|z(t)\|$ is the right-hand derivative of $\|z(t)\|$.

Proof. We only demonstrate the detailed analysis of three cases. Interested readers can try to prove the other five cases similarly.

Case 1. If $U_1(z) > U_2(z)$ and $z_1 < 0 < z_2, z_3$, then $\|z\| = \max\{|z_1|+|z_3|, |z_2|+|z_3|\}$.

Subcase 1.1. $|z_1| > |z_2|$, then $\|z\| = |z_1| + |z_3| = -z_1 + z_3$ and $U_2(z) < |z_1| + |z_3|$. Taking the right-hand derivative of $\|z\|$,

$$\begin{aligned} D_+\|z\| = {} & D_+(|z_1| + |z_3|) \\ = {} & -z_1' + z_3' \\ = {} & (\beta S\tfrac{I}{E} + \beta I + \mu + \phi + \theta - \varepsilon)z_1 - \beta S\tfrac{I}{E}z_5 \\ & +(-\beta I)z_1 + \phi z_2 + (-\beta S\tfrac{I}{E} - \mu - \theta)z_3 + \beta S\tfrac{I}{E}z_5 \\ = {} & (-\beta S\tfrac{I}{E} - \mu - \phi - \theta + \varepsilon)|z_1| + \phi|z_2| + (-\beta S\tfrac{I}{E} - \mu - \theta)|z_3|. \end{aligned}$$

Since $|z_2| < |z_1|$,

$$\begin{aligned} D_+\|z\| < {} & (-\beta S\tfrac{I}{E} - \mu - \theta + \varepsilon)|z_1| + (-\beta S\tfrac{I}{E} - \mu - \theta)|z_3| \\ \leq {} & (-\beta S\tfrac{I}{E} - \mu - \theta + \varepsilon)\|z\| \end{aligned}$$

Thus, in order that $D_+\|z\|$ be bounded away from zero on the negative side for all z, $S>0, I>0$ and $E>0$, we require that

$$\varepsilon < \mu + \theta. \tag{20}$$

Subcase 1.2. $|z_1|<|z_2|$, then $\|z\| = |z_2|+|z_3| = z_2+z_3$ and $U_2(z) < |z_2|+|z_3|$. Taking the right-hand derivative of $\|z\|$, we obtain

$$\begin{aligned} D_+\|z\| = \ & D_+(|z_2|+|z_3|) \\ = \ & z_2' + z_3' \\ = \ & (-\beta S\tfrac{I}{E} - \beta I - \mu - \phi)z_2 + \theta z_3 + \beta S\tfrac{I}{E}z_4 + \beta S\tfrac{I}{E}z_6 \\ & +(-\beta I)z_1 + \phi z_2 + (-\beta S\tfrac{I}{E} - \mu - \theta)z_3 + \beta S\tfrac{I}{E}z_5 \\ = \ & \beta I|z_1| + (-\beta S\tfrac{I}{E} - \beta I - \mu)|z_2| \\ & +(-\beta S\tfrac{I}{E} - \mu)|z_3| + \beta S\tfrac{I}{E}(z_4+z_5+z_6). \end{aligned}$$

Noting that $|z_1|<|z_2|$, and $z_4+z_5+z_6 \le U_2(z) < |z_2|+|z_3|$,

$$D_+\|z\| \le -\mu\|z\|.$$

Thus, in this case, $D_+\|z\|$ is automatically bounded away from zero on the negative side.

Case 2. If $U_2(z) > U_1(z)$ and $z_4, z_5, z_6 > 0$.

In this case, $\|z\| = |z_4|+|z_5|+|z_6|$, then $\|z\| = |z_4|+|z_5|+|z_6| = z_4+z_5+z_6$ and $U_1(z) < |z_4|+|z_5|+|z_6|$. Taking the right-hand derivative of $\|z\|$, we obtain

$$\begin{aligned} D_+\|z\| = \ & z_4'+z_5'+z_6' \\ = \ & \varepsilon\frac{E}{I}z_2 + (-\varepsilon\frac{E}{I} - \beta I - \mu - \phi + \frac{cI}{(b+I)^2})z_4 + \theta z_5 \\ & +\varepsilon\frac{E}{I}z_3 + \phi z_4 + (-\varepsilon\frac{E}{I} - \mu - \theta + \frac{cI}{(b+I)^2})z_5 \\ & +\beta I z_4 + (-\varepsilon\frac{E}{I} - \mu - \varepsilon + \frac{cI}{(b+I)^2})z_6 \\ \le \ & \varepsilon\frac{E}{I}(|z_2+z_3|) + (-\varepsilon\frac{E}{I} - \mu + \frac{c}{4b})|z_4| + (-\varepsilon\frac{E}{I} - \mu + \frac{c}{4b})|z_5| \\ & +(-\varepsilon\frac{E}{I} - \mu - \varepsilon + \frac{c}{4b})|z_6|. \end{aligned}$$

Noting that $|z_2+z_3| \le U_1(z) < |z_4|+|z_5|+|z_6|$,

$$D_+\|z\| \le \ \varepsilon\frac{E}{I}\|z\| + (-\varepsilon\frac{E}{I} - \mu + \frac{c}{4b})\|z\| = (-\mu + \frac{c}{4b})\|z\|.$$

Thus, in order that $D_+\|z\|$ be bounded away from zero on the negative side for all z, we require that

$$\frac{c}{4b} < \mu. \tag{21}$$

Case 3. If $U_2(z) > U_1(z)$ and $z_6 < 0 < z_4, z_5$.

In this case, $\|z\| = \max\{|z_4|+|z_5|, |z_4|+|z_6|\}$. Again we have two subcases.

Subcase 3.1. $|z_5| > |z_6|$, then $\|z\| = |z_4| + |z_5| = z_4 + z_5$ and $U_1(z) < |z_4| + |z_5|$. Taking the right-hand derivative of $\|z\|$, we obtain

$$\begin{aligned} D_+\|z\| = & \ z_4' + z_5' \\ = & \ \varepsilon \frac{E}{I} z_2 + (-\varepsilon \frac{E}{I} - \beta I - \mu - \phi + \frac{cI}{(b+I)^2}) z_4 + \theta z_5 \\ & + \varepsilon \frac{E}{I} z_3 + \phi z_4 + (-\varepsilon \frac{E}{I} - \mu - \theta + \frac{cI}{(b+I)^2}) z_5 \\ \leq & \ \varepsilon \frac{E}{I} (|z_2 + z_3|) + (-\varepsilon \frac{E}{I} - \beta I - \mu + \frac{c}{4b}) |z_4| + (-\varepsilon \frac{E}{I} - \mu + \frac{c}{4b}) |z_5| \\ < & \ (-\mu + \frac{c}{4b}) \|z\|. \end{aligned}$$

Thus, we require that (21) holds.

Subcase 3.2. $|z_5| < |z_6|$, then $\|z\| = |z_4| + |z_6| = z_4 - z_6$ and $U_1(z) < |z_4| + |z_6|$. Taking the right-hand derivative of $\|z\|$,

$$\begin{aligned} D_+\|z\| = & \ z_4' - z_6' \\ = & \ \varepsilon \frac{E}{I} z_2 + (-\varepsilon \frac{E}{I} - \beta I - \mu - \phi + \frac{cI}{(b+I)^2}) z_4 + \theta z_5 \\ & -\beta I z_4 - (-\varepsilon \frac{E}{I} - \mu - \varepsilon + \frac{cI}{(b+I)^2}) z_6 \\ \leq & \ \varepsilon \frac{E}{I} |z_2| + (-\varepsilon \frac{E}{I} - 2\beta I - \mu - \phi + \frac{c}{4b}) |z_4| + \theta |z_5| \\ & (-\varepsilon \frac{E}{I} - \mu - \varepsilon + \frac{c}{4b}) |z_6|. \end{aligned}$$

Since $|z_2| \leq U_1(z) < |z_4| + |z_6|$ and $|z_5| < |z_6|$,

$$D_+\|z\| < \varepsilon \frac{E}{I} \|z\| + \max\big\{ -\varepsilon \frac{E}{I} - 2\beta I - \mu - \phi + \frac{c}{4b}, -\varepsilon \frac{E}{I} - \mu - \varepsilon + \frac{c}{4b} + \theta \big\} \|z\|$$

Thus, in order that $D_+\|z\|$ be bounded away from zero on the negative side for all z and $I > 0$, we require that

$$\frac{c}{4b} + \theta < \mu + \varepsilon \tag{22}$$

and

$$\frac{c}{4b} < \mu + \phi. \tag{23}$$

Note that (21) implies (23). So, in this case, we only require that (22) holds.

Combing the results of the above cases analysis, if the condition (19) hold, then $D_+\|z\| \leq -\chi \|z\|$ for all $z \in \mathbb{R}^6$. This completes the proof. □

Inequalities (19) are not the necessary conditions. Moreover, we can take other form of $\|z\|$, which would lead to sufficient conditions different form (19).

Remark 3. When $\rho = 0, \phi = 0, \theta = 0$ in model (1), it reduces to the model studied in Zhou and Cui [40]. It can be easily founded that the conditions of (20) are simplified in Zhou and Cui [40]. Moreover, the inequalities (19) in our paper is easy to be verified.

For model (2), bistability will possibly occur. In this case, a compact absorbing set will not exist. Hence, we shall consider a sequence of surfaces $\{\varphi^k\}$ in the following lemma.

Lemma 4.4. *Let ψ be a simple close curve in Ω. There exist $\varepsilon > 0$ and a sequence of surfaces $\{\varphi^k\}$ that minimizes $\mathcal{S}$ given by (14) relative to $\sum(\psi, \Omega)$ such that $\varphi_t^k \subset \Omega$ for all $k = 1, 2, 3, \ldots$ and all $t \in [0, \varepsilon]$.*

Proof. Let $\xi = \frac{1}{2}\min\{E, I : (S, V, E, I) \in \psi\}$, it is easy to know that $\xi > 0$. Based on the fact that the inequalities

$$\frac{dE(t)}{dt} \geq -(\mu + \varepsilon)E(t), \quad \frac{dI(t)}{dt} \geq -(\mu + r + d)I(t) - \frac{cI(t)}{b + I(t)}.$$

always hold in Ω, then there is an $\varepsilon > 0$ such that, if a solution satisfies $E(0) \geq \xi, I(0) \geq \xi$, then the solution remains in Ω for $t \in [0, \varepsilon]$.

Therefore, it suffices to show that there exists a sequence of surfaces $\{\varphi^k\}$ that minimizes $\mathcal{S}$ relative to $\sum(\psi, \widetilde{\Omega})$, where $\widetilde{\Omega} = \{(S, V, E, I) \in \Omega : E \geq \xi, I \geq \xi\}$. For $\varphi = (S(u), V(u), E(u), I(u)) \in \sum(\psi, \Omega)$, define a new surface $\widetilde{\varphi}(u) = (\widetilde{S}(u), \widetilde{V}(u), \widetilde{E}(u), \widetilde{I}(u))$ by

$$\begin{cases} \varphi(u), & \text{if } I(u) \geq \xi, E(u) \geq \xi \\ (S, V, \xi, I), & \text{if } I(u) \geq \xi, E(u) < \xi, S + V + \xi + I \leq \frac{A}{\mu}, \\ (\frac{S}{S+V}(\frac{A}{\mu} - 2\xi), \frac{V}{S+V}(\frac{A}{\mu} - 2\xi), \xi, \xi), & \text{if } I(u) \geq \xi, E(u) < \xi, S + V + \xi + I > \frac{A}{\mu}, \\ (S, V, E, \xi), & \text{if } I(u) < \xi, E(u) \geq \xi, S + V + E + \xi \leq \frac{A}{\mu}, \\ (\frac{S}{S+V}(\frac{A}{\mu} - 2\xi), \frac{V}{S+V}(\frac{A}{\mu} - 2\xi), \xi, \xi), & \text{if } I(u) < \xi, E(u) \geq \xi, S + V + E + \xi > \frac{A}{\mu}, \\ (S, V, \xi, \xi), & \text{if } I(u) < \xi, E(u) < \xi, S + V + 2\xi \leq \frac{A}{\mu}, \\ (\frac{S}{S+V}(\frac{A}{\mu} - 2\xi), \frac{V}{S+V}(\frac{A}{\mu} - 2\xi), \xi, \xi), & \text{if } I(u) < \xi, E(u) < \xi, S + V + 2\xi > \frac{A}{\mu}. \end{cases}$$

It is not difficult to know that $\widetilde{\varphi}(u) \in \sum(\psi, \widetilde{\Omega})$. In the following, we will prove that $\mathcal{S}\widetilde{\varphi} \leq \mathcal{S}\varphi$.

According to the definition of wedge product in Mei and Huang [25], we obtain that

$$\frac{\partial\varphi}{\partial u_1} \wedge \frac{\partial\varphi}{\partial u_2} = \begin{bmatrix} \frac{\partial S}{\partial u_1} \\ \frac{\partial V}{\partial u_1} \\ \frac{\partial E}{\partial u_1} \\ \frac{\partial I}{\partial u_1} \end{bmatrix} \wedge \begin{bmatrix} \frac{\partial S}{\partial u_2} \\ \frac{\partial V}{\partial u_2} \\ \frac{\partial E}{\partial u_2} \\ \frac{\partial I}{\partial u_2} \end{bmatrix} = \begin{bmatrix} \det\begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial V}{\partial u_1} & \frac{\partial V}{\partial u_2} \end{pmatrix} \\ \det\begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial E}{\partial u_1} & \frac{\partial E}{\partial u_2} \end{pmatrix} \\ \det\begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \end{pmatrix} \\ \det\begin{pmatrix} \frac{\partial V}{\partial u_1} & \frac{\partial V}{\partial u_2} \\ \frac{\partial E}{\partial u_1} & \frac{\partial E}{\partial u_2} \end{pmatrix} \\ \det\begin{pmatrix} \frac{\partial V}{\partial u_1} & \frac{\partial V}{\partial u_2} \\ \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \end{pmatrix} \\ \det\begin{pmatrix} \frac{\partial E}{\partial u_1} & \frac{\partial E}{\partial u_2} \\ \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \end{pmatrix} \end{bmatrix}$$

is a vector in $\mathbb{R}^6$ for almost every $u \in B$. We note $\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} = (x_1, x_2, x_3, x_4, x_5, x_6)^T$, and $\frac{\partial \widetilde{\varphi}}{\partial u_1} \wedge \frac{\partial \widetilde{\varphi}}{\partial u_2} = (\tilde{x}_1, \tilde{x}_2, \tilde{x}_3, \tilde{x}_4, \tilde{x}_5, \tilde{x}_6)^T$. In the following, we will analyze one case $|\tilde{x}_i| \leq |x_i|$ $(i = 1, 2, \cdots, 6)$.

Case 1. If $I(u) \geq \xi, E(u) \geq \xi$, then $\widetilde{\varphi} = \varphi$ and therefore $|\tilde{x}_i| = |x_i|$ $(i = 1, 2, \cdots, 6)$.

Case 2. If $I(u) \geq \xi, E(u) < \xi$ and $S + V + \xi + I \leq \frac{A}{\mu}$, then $\widetilde{\varphi}(u) = (S(u), V(u), \xi, I(u))$. Therefore

$$\frac{\partial \widetilde{\varphi}}{\partial u_1} \wedge \frac{\partial \widetilde{\varphi}}{\partial u_2} = \begin{bmatrix} \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial V}{\partial u_1} & \frac{\partial V}{\partial u_2} \end{pmatrix} \\ 0 \\ \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \end{pmatrix} \\ 0 \\ \det \begin{pmatrix} \frac{\partial V}{\partial u_1} & \frac{\partial V}{\partial u_2} \\ \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \end{pmatrix} \\ 0 \end{bmatrix}$$

almost everywhere. It follows that $\tilde{x}_i = x_i$ $(i = 1, 3, 5)$ and $\tilde{x}_i = 0$ $(i = 2, 4, 6)$. Thus $|\tilde{x}_i| \leq |x_i|$.

Case 3. If $I(u) \geq \xi, E(u) < \xi$ and $S + V + \xi + I > \frac{A}{\mu}$, then $\widetilde{\varphi}(u) = (\frac{S}{S+V}(\frac{A}{\mu} - 2\xi), \frac{V}{S+V}(\frac{A}{\mu} - 2\xi), \xi, \xi)$. Therefore

$$\frac{\partial \widetilde{\varphi}}{\partial u_j} = (\frac{A}{\mu} - 2\xi) \frac{V \frac{\partial S}{\partial u_j} - S \frac{\partial V}{\partial u_j}}{(S + V)^2} \begin{bmatrix} 1 \\ -1 \\ 0 \\ 0 \end{bmatrix}$$

for $j = 1, 2$. Thus, $\frac{\partial \widetilde{\varphi}}{\partial u_1}$ and $\frac{\partial \widetilde{\varphi}}{\partial u_2}$ are linearly dependent, and so their wedge product is zero. Therefore $\tilde{x}_i = 0$ $(i = 1, 2, 3, 4, 5, 6)$. Obviously $|\tilde{x}_i| \leq |x_i|$ $(i = 1, 2, \cdots, 6)$.

The other four cases can be analyzed similarly.

We also note that $\widetilde{I}(u) = \max\{I(u), \xi\}$ and $\widetilde{E}(u) = \max\{E(u), \xi\}$. Thus $1/\widetilde{I} \leq 1/I$, $1/\widetilde{E} \leq 1/E$. Let

$$\tilde{P} = \begin{pmatrix} \frac{1}{\tilde{E}} & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{\tilde{E}} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{\tilde{E}} & 0 & 0 \\ 0 & 0 & \frac{1}{\tilde{I}} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{\tilde{I}} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{\tilde{I}} \end{pmatrix},$$

by comparing the vector $P \cdot (\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2})$ and the vector $\tilde{P} \cdot (\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2})$, we have $|\frac{1}{\tilde{E}} \tilde{x}_i| \leq |\frac{1}{E} x_i|$ $(i = 1, 2, 4)$ and $|\frac{1}{\tilde{I}} \tilde{x}_i| \leq |\frac{1}{I} x_i|$ $(i = 3, 5, 6)$ for their corresponding component. From (14) and the above norm definition on $\mathbb{R}^6$, it is easy to see that

$$\begin{aligned} \mathcal{S}\tilde{\varphi} = & \int_{\overline{B}} \|\tilde{P} \cdot (\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2})\| \mathrm{d}u \\ \leq & \int_{\overline{B}} \|P \cdot (\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2})\| \mathrm{d}u \\ = & \mathcal{S}\varphi. \end{aligned}$$

According to Lemma 4.1, we can choose $\delta = \inf\{\mathcal{S}\varphi : \varphi \in \sum(\psi, \Omega)\}$. Let $\{\varphi^k\}$ be a sequence of surfaces that minimizes $\mathcal{S}$ relative to $\sum(\psi, \Omega)$, then $\lim_{k\to\infty} \mathcal{S}\varphi^k = \delta$. Let $\{\widetilde{\varphi}^k\}$ be a sequence of surfaces in $\sum(\psi, \widetilde{\Omega})$ defined by the above construction, then $\mathcal{S}\widetilde{\varphi}^k \leq \mathcal{S}\varphi^k$ for each k. Since $\{\mathcal{S}\widetilde{\varphi}^k\}$ is bounded, without loss of generality, we can assume that the sequence $\{\mathcal{S}\widetilde{\varphi}^k\}$ is convergent. From $\mathcal{S}\widetilde{\varphi}^k \leq \mathcal{S}\varphi^k$ for each k, we know $\lim_{k\to\infty} \mathcal{S}\widetilde{\varphi}^k \leq \delta$; on the other hand, we have $\widetilde{\varphi}^k \in \Sigma(\psi, \Omega)$ from $\widetilde{\varphi}^k \in \Sigma(\psi, \widetilde{\Omega})$, then $\mathcal{S}\widetilde{\varphi}^k \geq \delta$ for each k, so $\lim_{k\to\infty} \mathcal{S}\widetilde{\varphi}^k \geq \delta$, it implies that $\lim_{k\to\infty} \mathcal{S}\widetilde{\varphi}^k = \delta$. Because $\mathcal{S}\tilde{\varphi} \leq \mathcal{S}\varphi$, then

$$\inf\{\mathcal{S}\tilde{\varphi} : \tilde{\varphi} \in \sum(\psi, \widetilde{\Omega})\} \leq \inf\{\mathcal{S}\varphi : \varphi \in \sum(\psi, \Omega)\} = \delta.$$

On the other hand, from $\widetilde{\varphi} \in \Sigma(\psi, \Omega)$ we have $\inf\{\mathcal{S}\tilde{\varphi} : \tilde{\varphi} \in \sum(\psi, \widetilde{\Omega})\} \geq \delta$, it implies $\inf\{\mathcal{S}\tilde{\varphi} : \tilde{\varphi} \in \sum(\psi, \widetilde{\Omega})\} = \delta$. Finally, we can obtain that $\lim_{k\to\infty} \mathcal{S}\widetilde{\varphi}^k = \inf\{\mathcal{S}\tilde{\varphi} : \tilde{\varphi} \in \sum(\psi, \widetilde{\Omega})\} = \delta$ holds, i.e., $\{\widetilde{\varphi}^k\}$ minimizes $\mathcal{S}$ relative to $\sum(\psi, \widetilde{\Omega})$. This completes the proof. $\square$

Remark 4. According to Lemma 4.2, we know that if the inequalities (19) hold, any omega limit point of model (2) in the interior of Ω is an equilibrium by the proofs of Lemma 4.3 and Lemma 4.4.

Moreover, we have the following result for model (2).

Theorem 4.5. *If the inequalities (19) hold, then each positive semitrajectory of model (2) in $\overline{\Omega}$ approaches to a single equilibrium.*

Proof. Let Γ be a positive semitrajectory in $\overline{\Omega}$ with omega limit set Θ. There are two cases.
Case 1. Θ intersects the interior of Ω. Since model (2) has a finite number of equilibria, there are only a finite number of points in the interior of Ω which can be in Θ. As $\overline{\Omega}$ is bounded, Θ must be connected. Thus, Θ must consist of a single equilibrium.
Case 2. Θ is contained in the boundary $\partial\Omega$ of Ω. Since omega limit sets are invariant, Ξ must be contained in the largest invariant subset of $\partial\Omega$, and $\{P_0\}$ is the only invariant subset of $\partial\Omega$, so $\Theta = \{P_0\}$. This completes the proof. $\square$

Form Theorem 4.5, we obtain the following results.

Theorem 4.6. *Assume that the inequalities (19) are satisfied*

(1) If there is no endemic equilibrium, then all solutions tend to the disease-free equilibrium P_0.

(2) If $\mathcal{R}_v > 1$, then (S, V, E, I, R) tends to the unique endemic equilibrium $\bar{P}$.

(3) If there are two endemic equilibria, then depending on the initial values, the disease dies out or approaches to the upper endemic equilibrium P^*.

In the following, another sufficient condition involving the basic reproduction number on global stability of the disease-free equilibrium is given.

Theorem 4.7. *If $\mathcal{R}_v < \Lambda < 1$, then the disease-free equilibrium P_0 of model (2) is globally asymptotically stable, where*

$$\Lambda = \frac{(\mu+\theta-\mu\rho)(\mu+r+d+\frac{c}{b+\frac{A}{\mu}})}{(\mu+\phi+\theta)(\mu+r+d+\frac{c}{b})}.$$

Proof. For any $(S,V,E,I)\in\Omega$, we have $0\le I\le \frac{A}{\mu}$ and $0<S\le\frac{A}{\mu}$. Considering the following Lyapunov function:

$$W = \varepsilon E + (\mu+\varepsilon)I,$$

then the derivative of $W(t)$ along the solutions of model (2) satisfies

$$\begin{aligned}\dot{W} =& \ \varepsilon\dot{E} + (\mu+\varepsilon)\dot{I}\\ =& \ \big(\varepsilon\beta S - (\mu+\varepsilon)(\mu+r+d+\frac{c}{b+I})\big)I\\ \le& \ \big(\varepsilon\beta\frac{A}{\mu} - (\mu+\varepsilon)(\mu+r+d+\frac{c}{b+\frac{A}{\mu}})\big)I\\ =& \ (\mathcal{R}_v^*-1)I,\end{aligned}$$

where $\mathcal{R}_v^* = \frac{\beta\varepsilon A}{\mu(\mu+\varepsilon)(\mu+r+d+\frac{c}{b+\frac{A}{\mu}})}$. Let $\mathcal{R}_v^*<1$, thus, $\dot{W}\le 0$ for all $I\ge 0$ and $E\ge 0$. Let $M=\{(S,V,E,I):\dot{W}=0\}$, then $M\subset\{(S,V,E,I):\dot{I}=0\}$.

Let $N\subset M$ be the largest invariant set with respect to model (2) and let $(S(t),V(t),E(t),I(t))$ be any solution in N of model (2), then $(S(t),V(t),E(t),I(t))$ is defined and bounded on $t\in R$.

Since $N\subset\{(S,V,E,I):\dot{I}=0\}$, we have $I(t)\equiv 0$. Moreover, from the fourth equation of model (2), we have $E(t)\equiv 0$. Therefore, we have

$$\begin{aligned}\frac{dS(t)}{dt} =& \ (1-\rho)A - \beta S(t)I(t) - \mu S(t) - \phi S(t) + \theta V(t),\\ \frac{dV(t)}{dt} =& \ \rho A + \phi S(t) - \mu V(t) - \theta V(t).\end{aligned}$$

By adding the two equations, we have

$$S(t)+V(t) = \frac{A}{\mu} + (S(0)+V(0))\exp(-\mu t), \quad t\in R.$$

then $S(0)+V(0)=0$. Otherwise $S(t)+V(t)$ will be unbounded on R. Therefore $S(t)+V(t)\equiv\frac{A}{\mu}$. Substituting $V(t)=\frac{A}{\mu}-S(t)$ and $I(t)\equiv 0$ into the above two equations, similarly, we obtain that

$$S(t)\equiv\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta}, \quad V(t)\equiv\frac{\rho A}{\mu+\theta}+\frac{\phi}{\mu+\theta}\frac{(\mu+\theta-\mu\rho)A}{(\mu+\phi)(\mu+\theta)-\phi\theta}.$$

Finally, we have $(S(t),V(t),E(t),I(t)) = P_0$. This shows that $N\equiv\{P_0\}$. By Lasalle's invariance principle, P_0 is globally attractive. Thus, the disease-free equilibrium P_0 is globally asymptotically stable when $\mathcal{R}_v^*<1$. After some simple calculations, we can easily obtain that $\mathcal{R}_v^*<1$ is equivalent to $\mathcal{R}_v<\Lambda$. This completes the proof. ∎

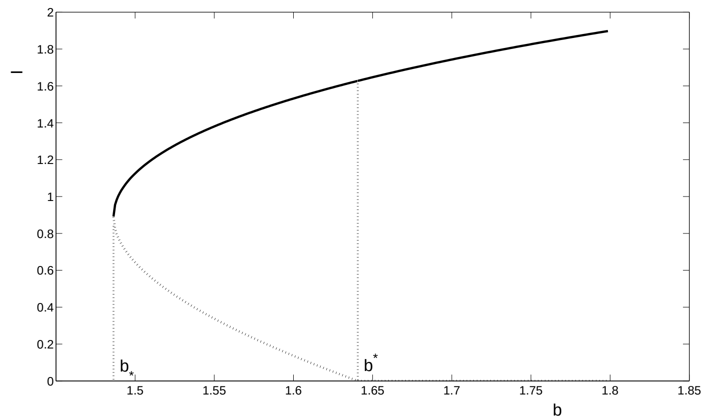
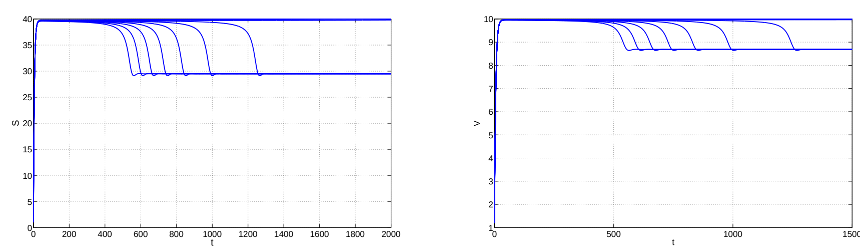


FIGURE 1. Bifurcation diagram of model (2): The infection population at equilibrium versus b shows a backward bifurcation when $b_* < b < b^*$. The lower dashed curve indicates the unstable endemic equilibrium and the upper solid curve represents the locally stable endemic equilibrium. The saddle-node bifurcation occurs at $b = b_*$.

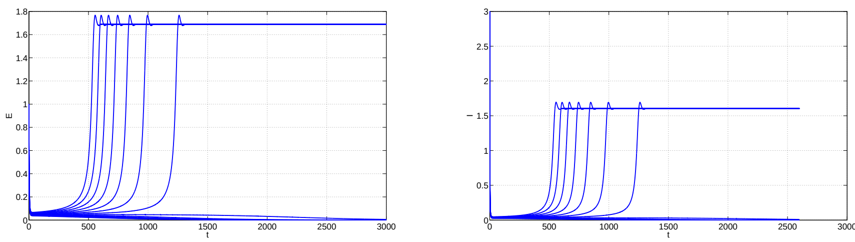


(a) (b)

5. **Numerical simulations.** Now, we give some numerical simulations of model (2) for the conclusions obtained above.

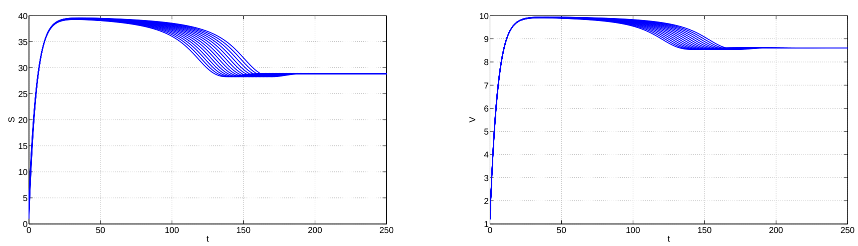
(1) Take the following parameter values: $\rho = 0.2, A = 10, \mu = 0.2, \beta = 0.05, \phi = 0.05, \theta = 0.2, \varepsilon = 1.2, d = 0.2, c = 1.5, r = 0.4$ and $b = 1.63$. By calculating, we have that $\mathcal{R}_v = 0.99653556 < 1$ and $\mathcal{R}^* = 0.94367421$, then $\mathcal{R}^* < \mathcal{R}_v = 0.99653556 < 1$. Hence the conditions of case (c) in Theorem 2.3 may lead to multiple endemic equilibria. $\mathcal{R}_v$ and $\mathcal{R}^* = 0.94367421$ are regarded as the functions of parameter b, while the other parameters are fixed. According to Theorem 3.2, there is a backward bifurcation at $\mathcal{R}_v(b) = 1$, then we could compute the corresponding critical value $b = b^*$. Similarly, we can obtain $b = b_*$ by computing $\mathcal{R}_v(b) = \mathcal{R}^*$. The backward bifurcation diagram on the plan (b, I) is depicted in Figure 1.

(2) For the same parameter values, we note that $\mathcal{R}_v = 0.99653556 < 1$. Figure 2 presents the time series of model (2) when $b = 1.63$ (i.e $\mathcal{R}_v = 0.99653556$). It clearly appears that when $\mathcal{R}_v < 1$, the profiles can converge to either the disease-free equilibrium or an endemic equilibrium point, depending on the initial sizes of the population of the model (owing to the phenomenon of backward bifurcation).

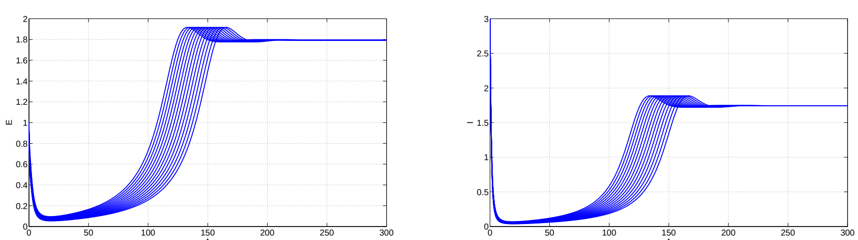


(c) (d)

FIGURE 2. Simulations of model (2). Time series of (a) susceptible individuals, (b) vaccinated individuals, (c) latent individuals, (d) infectious individuals when $b = 1.63$. All other parameters are the same as those in Figure 1.



(a) (b)



(c) (d)

FIGURE 3. Simulations of model (2). Time series of (a) susceptible individuals, (b) vaccinated individuals, (c) latent individuals, (d) infectious individuals when $b = 1.7$ (i.e $\mathcal{R}_v = 1.01898101$).

(3) For the following parameter values: $\rho = 0.2, A = 10, \mu = 0.2, \beta = 0.05, \phi = 0.05, \theta = 0.2, \varepsilon = 1.2, d = 0.2, c = 1.5, r = 0.4$ and $b = 1.7$, we can obtain $\mathcal{R}_v = 1.01898101 > 1$ and $a_2 = -0.0878 < 0$. Hence, model (2) has a disease-free equilibrium P_0 and a unique endemic equilibrium P^*. Figure 3 presents the time series of model (2) when $\mathcal{R}_v > 1$. It clearly appears that the profiles converge to the endemic equilibrium and the disease-free equilibrium P_0 is unstable.

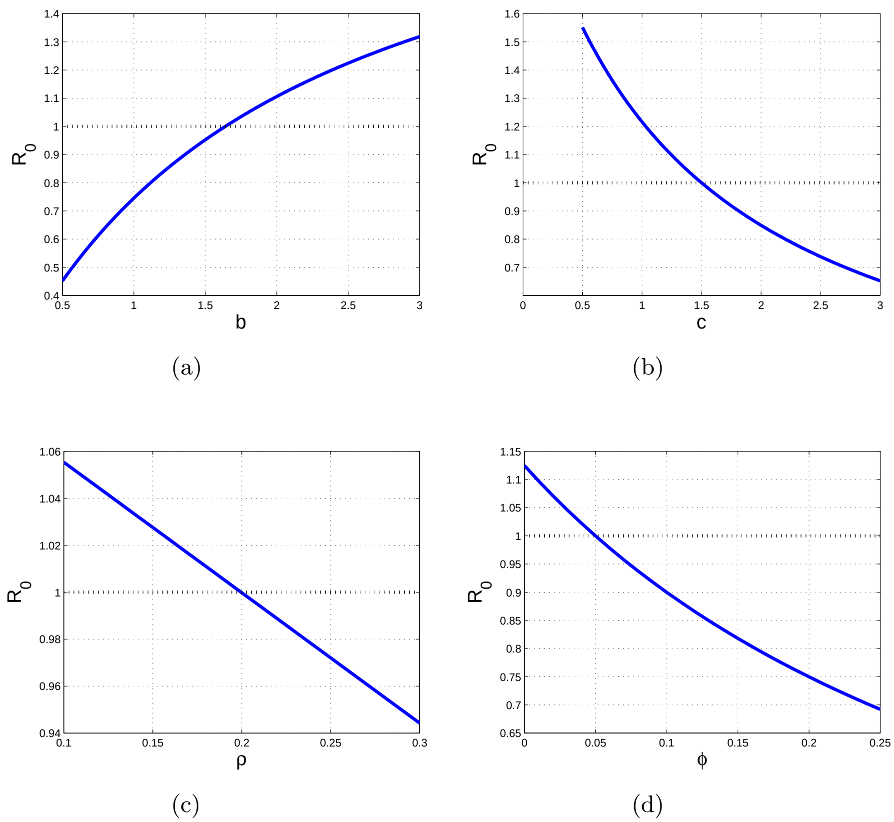
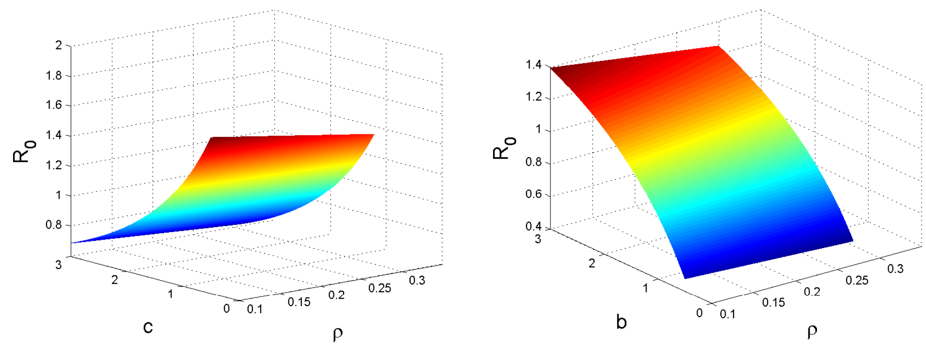


FIGURE 4. $\mathcal{R}_v$ in terms of b, c, ρ and ϕ.

5.1. **Sensitivity analysis.** In this subsection, we carry out some sensitivity analysis on some parameters and all other parameters are the same as those in Figure 1.

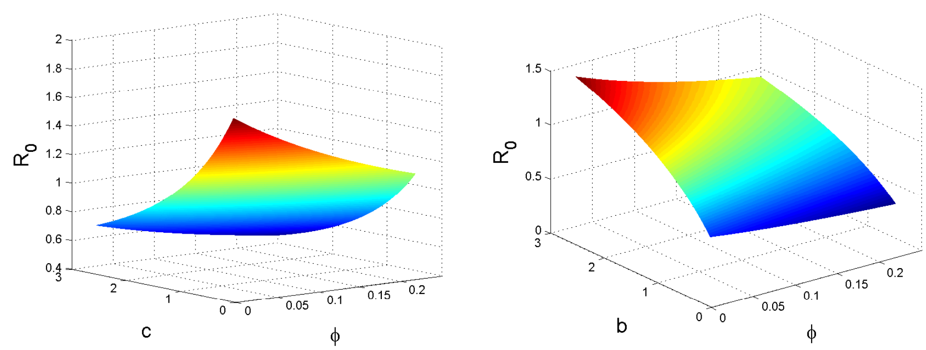
If we fix all parameters except c (the rate at which the maximum medical resources are supplied), b (half-saturation constant), ρ (the fraction of the vaccinated new recruits) and ϕ (the rate at which the susceptible population is vaccination), from Figure 4 we can see that $\mathcal{R}_v$ decreases if b decreases or c increases or ρ increases or ϕ increases. Figure 4(a)-(b) represent the relationship between $\mathcal{R}_v$ and treatment; Figure 4(c)-(d) represent the relationship between $\mathcal{R}_v$ and vaccination. When $\mathcal{R}_v$ is less than unity, $\mathcal{R}_v$ decreases rapidly as the parameters b decreases as shown in Figure 4(a), while the change is slow when the parameters c increases as shown in Figure 4(b). Comparing Figure 4(c) and Figure 4(d), we can see that the influence of parameter ϕ on $\mathcal{R}_v$ is greater than that of the parameters ρ. This indicates that vaccination at susceptible individuals is even more important for controlling infection.

Our theoretical results indicated that the disease free equilibrium point was not always globally stable and model (2) underwent a backward bifurcation and bistability which imply that reducing the basic reproduction below one is not enough to control infectious diseases. Therefore, it is necessary to take different interventions for controlling the disease. In the following Figure 5 and Figure 6, we consider the



(a) (b)

FIGURE 5. $\mathcal{R}_v$ in terms of (ρ, c) and (ρ, b).



(a) (b)

FIGURE 6. $\mathcal{R}_v$ in terms of (ϕ, c) and (ϕ, b).

combined influence of vaccination and treatment on the basic reproduction number $\mathcal{R}_v$.

Comparing Figure 5(a) and Figure 5(b), we can see that the combined influence of b and ρ on $\mathcal{R}_v$ is greater than that of c and ρ. Similarly, the combined influence of b and ϕ on $\mathcal{R}_v$ is greater than that of c and ϕ by comparing Figure 6(a) and Figure 6(b). Moreover, the effect of b and ϕ is greater than b and ρ by Comparing Figure 5(b) and Figure 6(b). In conclusion, increasing the vaccinate rate of new recruits and susceptible individuals, enlarging the medical resources, reducing the half-saturation constant and combining these measures are effective measures to control infectious diseases.

6. **Discussion.** Though vaccination offers a very powerful method of disease control, the vaccines may sometimes be ineffective, and therefore only a proportion of vaccinated individuals are protected. Some vaccines have the disadvantageous side effects. At the same time, in face of outburst epidemic situations, the efficiency of vaccination may prove to be too slow to prevent a large outbreak. Therefore, in many situations, a wide range of control measures (e.g. treatment, vaccination) is

necessary. In our paper, a class of epidemic models with treatment and vaccination is developed. The infection rate is described by a bilinear function and a saturated treatment function is taken. It is generally known that if there is no medical resources (i.e., $c = 0$), model (1) only admits a forward bifurcation and the disease will die out when the basic reproduction number is less than unity. However, our theoretical findings and numerical simulations reveal that if there are medical resources (i.e., $c > 0$), then model (1) has much richer dynamic behaviors such as forward bifurcation and backward bifurcation. The existence of a backward bifurcation is an interesting phenomenon since this means that the disease cannot be eradicated by simply the reduction of the basic reproduction number $\mathcal{R}_v$ below unity. Theorem 2.3 shows that $\mathcal{R}^*$ is a key threshold for eradicating disease. In addition, from the results in Section 3, it is found that the backward bifurcation will not take place if the maximum medical resources c is increasing, or the vaccinate rate is larger than some threshold value. This demonstrates that some corresponding conditions such as hospital capacities, public health infrastructure, budgetary constraints and the number of skilled health workers should be improved. Coupled with vaccination which may be effective at reducing $\mathcal{R}_v$ below 1, the disease may be eradicated.

In order to seek global dynamic properties for the model, it is the first time that higher (greater than or equal to four) dimensional systems are discussed by extending the geometric approach established in Arino et al. [2]. Global stability of the disease-free equilibrium and endemic equilibrium are established under the conditions of (19) in Theorem 4.5. However, we find that the same conclusions may be still reached even if the conditions of (19) do not hold from the numerical simulations. It is an interesting open question that condition (19) may need to be improved further. This deserves our further consideration. Notice that global stability of the disease-free equilibrium is impossible when the basic reproduction number $\mathcal{R}_v$ below 1 under the phenomenon of the backward bifurcation. Theorem 4.7 indicates that the disease will die out when the basic reproduction number $\mathcal{R}_v < \Lambda$ (Λ is strictly less than 1). Compared with Theorem 3.3, another question if Λ is equal to $\mathcal{R}^*$ remains open. It will be discussed in our further work.

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